European
Thyroid Journal

39th Annual Meeting of the European Thyroid Association

Programme

Copenhagen, Denmark
September 3–6, 2016

Guest Editors
Furio Pacini, Siena, Italy
Birte Nygaard, Copenhagen, Denmark

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All information in the scientific programme is correct at the time of going to press.

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European
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A Warm Welcome to the ETA Annual Meeting in Wonderful Copenhagen

On behalf of the National Organizing Committee, we would like to give you a warm welcome to Copenhagen and the 39th Annual Meeting of the European Thyroid Association, September 3–6, 2016. It is a great honor and pleasure to host this prestigious scientific convention on the thyroid in Copenhagen.

In the past few months, the Executive Committee has prepared what seems to be an appealing scientific program, including oral and poster sessions, symposia, meet-the-expert sessions, industrial sponsored symposia and award lectures. The number of sessions remained the same as in previous years despite shortening the meeting by one day. To achieve this goal, there will be fewer social events, but we think that shortening the meeting is something that will facilitate the participation of many members without affecting the warm atmosphere that the city of Copenhagen offers. As President of the ETA I am proud of our achievement and I do hope that many, many members will join us for another successful meeting of our association.

Copenhagen is a major regional center of business, media, and science. It is famous for 'Danish design' as well as the 'New Nordic Cuisine'. It has repeatedly been recognized as one of the cities with the best quality of life. It is also considered one of the world's most environmentally friendly cities. The water in the inner harbor is clean enough for swimming, and 36% of all citizens commute to work by bicycle.

Copenhagen has a strategic location and excellent infrastructure with the largest airport in Scandinavia located 14 minutes by train from the city center. The congress center, Hotel Scandic Copenhagen, is located in the very heart of the city within walking distance of the Copenhagen Central Station and brings Copenhagen's attractions to your doorstep. We are sure that you will enjoy our beautiful Copenhagen and we hope to provide the framework for the presentation of excellent and original thyroid research and for interesting and rewarding discussions.

In this city of fairy tales we hope that during the meeting you will follow all aspects of the thyroid – just like the little girl is following the butterfly in the famous fairytale by H.C. Andersen.

Furio Pacini
President of the ETA

Birte Nygaard
Chair of the Local
Organizing Committee

In Memoriam
Prof. Peter Laurberg

Professor Peter Laurberg died on the 20th of June 2016 in a tragic and senseless traffic accident, walking, together with his wife, along a dark street in Tbilisi, Georgia.

Peter Laurberg was not only a leading figure of the Danish endocrine and thyroid community but had the same reputation in Europe and, indeed, worldwide. His efforts to improve iodine status globally will be remembered, as will his impact on clinical and translational science in a number of areas. Peter was a brilliant teacher and speaker, and due to his many talents and active participation in thyroid congresses around the world, he carried out all possible functions at national and international meetings, always actively debating and eager to contribute. Because he was easy to understand, his help as a member of a number of guideline committees was greatly appreciated. During all his four decades in the thyroid and endocrine community he was a leading figure, a significant voice and a key opinion leader. He was the past president of the ETA and, having just turned 71, still at the height of his powers nationally as well as internationally. The Danish Thyroid Association recently acknowledged his immense importance to that society by appointing him Honorary Member.

We, as friends, colleagues, members of the Local Organizing Committee for the upcoming 2016 Copenhagen Annual Meeting of the ETA, and comrades in arms, find this loss incomprehensible. Our thoughts go to his wife Grethe and their large family for whom this sudden loss must be unbearable.

In remembrance of a lost friend

The LOC of the 2016 ETA Annual Meeting

The international journal for basic, translational and clinical thyroidology

European Thyroid Journal

Official Journal of the European Thyroid Association

Official Organ of the

European Thyroid Association
ETA

The *European Thyroid Journal* publishes papers reporting original research in basic, translational and clinical thyroidology. Original contributions cover all aspects of the field, from molecular and cellular biology to immunology and biochemistry, from physiology to pathology, and from pediatric to adult thyroid diseases with a special focus on thyroid cancer. Readers also benefit from reviews by noted experts, which highlight especially active areas of current research. The journal will further publish formal guidelines in the field, produced and endorsed by the European Thyroid Association.

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Selected contributions

- Bioassays for TSH Receptor Antibodies: Quo Vadis?: **Kahaly, G.J.** (Mainz)
- DuOx2 Promoter Regulation by Hormones, Transcriptional Factors and the Coactivator TAZ: **Cardoso-Weide, L.C.** (Niterói); **Cardoso-Penha, R.C.** (Rio de Janeiro); **Costa, M.W.** (Melbourne, Vic.); **Ferreira, A.C.F.; Carvalho, D.P.** (Rio de Janeiro); **Santisteban, P.S.** (Madrid)
- Iodine, Thyroid Autoimmunity and Cancer: **Fiore, E.; Latrofa, F.; Vitti, P.** (Pisa)
- Clinical Consequences of Mutations in Thyroid Hormone Receptor-α1: **van Mullem, A.A.; Visser, T.J.; Peeters, R.P.** (Rotterdam)
- Major Haemorrhage during Vitamin K Antagonist Treatment: The Influence of Thyroid Hormone Levels: **Debeij, J.; Cannegieter, S.C.** (Leiden); **van Zaane, B.; van Zanten, A.P.** (Amsterdam); **Rosendaal, F.R.** (Leiden); **Gerdes, V.E.A.** (Amsterdam); **Reitsma, P.H.; Dekkers, O.M.** (Leiden)
- Basal Serum Thyroglobulin Measured by a Second-Generation Assay Is Equivalent to Stimulated Thyroglobulin in Identifying Metastases in Patients with Differentiated Thyroid Cancer with Low or Intermediate Risk of Recurrence: **Nakabashi, C.C.D.; Kasamatsu, T.S.; Crispim, F.; Yamazaki, C.A.; Camacho, C.P.; Andreoni, D.M.; Padovani, R.P.; Ikejiri, E.S.; Mamone, M.C.O.M.; Aldighieri, F.C.; Wagner, J.; Hidal, J.T.; Vieira, J.G.H.; Biscolla, R.P.M.; Maciel, R.M.B.** (São Paulo)
- 2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children: **Lazarus, J.** (Cardiff); **Brown, R.S.** (Boston, Mass.); **Daumerie, C.** (Brussels); **Hubalewska-Dydejczyk, A.** (Krakow); **Negro, R.** (Lecce); **Vaidya, B.** (Exeter)
- A Progress Report of the IFCC Committee for Standardization of Thyroid Function Tests: **Thienpont, L.M.; Van Uytfanghe, K.; Van Houcke, S.** (Ghent); **Das, B.** (Mumbai); **Faix, J.D.** (Palo Alto, Calif.); **MacKenzie, F.** (Birmingham); **Quinn, F.A.** (Abbott Park, Ill.); **Rottmann, M.** (Penzberg); **Van den Bruel, A.** (Bruges) **for the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT)**
- Structure and Function of Thyroid Hormone Plasma Membrane Transporters: **Schweizer, U.** (Bonn); **Johannes, J.** (Berlin); **Bayer, D.; Braun, D.** (Bonn)

More information at **www.karger.com/etj**

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European
Thyroid Journal

Saturday, 3rd September 2016

Room 8+10
08.00–13.00

ETA Clinical Educational Course

Thyroid Function

Room 9+11
08.30–13.00

ETA Basic Educational Course

Thyroid Hormone Transport and Metabolism in Health and Disease

Room 12
08.00–13.00

ETA Ultrasound Course

Thyroid Ultrasonography and Ultrasound-Assisted Procedures

Room 13
08.00–13.00

ETA-CRN Symposium

Thyroid Cancer in Childhood – Status Quo and Perspectives in Europe

Room 15
08.00–13.00

Iodine Global Network Meeting

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ETA Clinical Educational Course
Thyroid Function

Room 8+10
08.00–13.00

Chairs:	*Leonidas Duntas,* Greece and *Laszlo Hegedüs,* Denmark
Introduction:	**Basic Thyroid Physiology**
08.00–08.30	*Georg Brabant,* Germany
Session I:	**Thyroid Function Testing**
08.30–09.00	Pitfalls in thyroid function testing *Krishna Chatterjee,* UK
09.00–09.30	Syndromes of resistance to thyroid hormone *Luca Persani*, Italy
09.30–10.00	Thyroid function testing in the management of thyroid cancer *Ulla Feldt-Rasmussen,* Denmark
10.00–10.30	Thyroid function testing in pregnancy: which test and why *Marco Medici,* The Netherlands
10.30–11.00	Coffee break
Chairs:	*Leonidas Duntas,* Greece and *Luigi Bartalena,* Italy
Session II:	**Pathways from Subclinical to Manifested Thyroid Disease**
11.00–11.30	From subclinical to overt hypothyroidism *Peter Taylor,* UK
11.30–12.00	From subclinical to overt hyperthyroidism *Luigi Bartalena,* Italy
Session III:	**Mechanisms of Disease**
12.00–12.30	Thyroid function and cancer *Garcilaso Riesco-Eizaguirre,* Spain
12.30–13.00	How are TSH reference values in clinical practice *Henry Völzke*, Germany

ETA Basic Educational Course
Thyroid Hormone Transport and Metabolism in Health and Disease

Room 9+11
08.30–13.00

Chairs: *Pilar Santisteban,* Spain and *Anita Boelen,* The Netherlands

08.30–09.00 **Molecular Aspects of Thyroid Hormone Transporters**
Ulrich Schweizer, Germany

09.00–09.30 **Animal Models of Thyroid Hormone Transporter Deficiencies**
Heike Heuer, Germany

09.30–10.00 **Psychomotor Retardation Caused by MCT8 Mutations**
Edward Visser, The Netherlands

10.30–11.00 Break

11.00–12.30 **Regulation of Tissue Thyroid Hormone Activity by Deiodinases**

1. Brain *Juan Bernal,* Spain
2. Bone *Duncan Bassett,* UK
3. Cancer *Domenico Salvatore,* Italy
4. Illness *Anita Boelen,* The Netherlands

12.30–13.00 **Disorders Associated with Defects in Thyroid Hormone Deiodination**
Krishna Chatterjee, UK

ETA Ultrasound Course
Thyroid Ultrasonography and Ultrasound-Assisted Procedures

Room 12
08.00–13.00

08.00–08.10	**Welcome** *Steen Bonnema*, Denmark
08.10–10.10	**Session 1: 'Focus on Ultrasound'** US in thyroid diseases – the basic part *Paolo Vitti*, Italy (45 min) Risk stratification of the thyroid nodule *Gilles Russ*, France (45 min) Thyroid volume estimation *Steen Bonnema*, Denmark (10 min) Case discussions *Steen Bonnema* and others (20 min)
10.10–10.25	Coffee break
10.25–11.45	**Session 2: 'Thyroid Cancer and Intervention'** Ultrasound in the thyroid cancer patient *Laurence Leenhardt*, France (30 min) Interventional US-guided procedures: an overview *Enrico Papini*, Italy (30 min) Laser ablation for benign thyroid nodules *Teresa Rago*, Italy (20 min)
11.45–12.50	**Session 3: 'Hands on Ultrasound'** An ultrasound experience with instructors on thyroid patients and phantoms
12.50–13.00	**Summary and Distribution of Certificates of Attendance**

ETA-CRN Symposium
Thyroid Cancer in Childhood – Status Quo and Perspectives in Europe

Room 13
08.00–13.00

08.00–08.10 **Welcome Address**
Dagmar Führer, Germany

08.10–10.10 **Epidemiology and Pathology of TC in Childhood**
Markus Luster, Germany and *Cristina Romei,* Italy

Epidemiology and patient paths for DTC in different European countries
Thera Links, The Netherlands, *Kate Newbold,* UK,
Daria Handkiewicz, Poland and *Christian Reiners,* Germany (60 min)
(Molecular) Pathology of childhood DTC
Kurt Werner Schmid, Germany (30 min)
Requirements for surgery in DTC
Henning Dralle, Germany (30 min)

10.10–10.30 Coffee break

10.30–12.30 **Radioiodine Treatment and Thyroid Hormone Therapy**
Thera Links, The Netherlands and *Kate Newbold,* UK

Imaging and radioiodine therapy
Markus Luster, Germany (30 min)
Target(s) of TH replacement
Marek Niedziela, Poland (20 min)
DTC in childhood: unique aspects and challenges in management
Steven G. Waguespack, USA (30 min)
Discussion: requirements for optimized management in Europe (Round Table)
AIM: Consensus statement for ETJ (30 min)

12.30–13.00 **Working Lunch and ETA-CRN General Assembly**

Iodine Global Network
EUthyroid Iodine Meeting

Room 15
08.00–13.00

Harmonisation of Iodine Nutrition in Europe

Chairs: *John Lazarus,* UK and *Peter Smyth,* Ireland

08.00–08.25	Registration and coffee
08.25–08.30	Introduction *John Lazarus* (IGN Regional Coordinator)
08.30–08.50	The EUthyroid Project – progress to date *Matthew Spencer,* Austria
08.50–09.10	How we can cope with bias in iodine and thyroid research *Henry Volzke,* Germany
09.10–09.30	What do we need to evaluate IDD prevention *Ursula Rochau,* Germany
09.30–09.50	What we can learn from birth cohorts *Robin Peeters,* The Netherlands
09.50–10.30	Coffee / tea and posters

Chairs: *John Lazarus,* UK and *Helena Filipsson,* Sweden

10.30–10.50	A model to secure a stable iodine concentration in milk *Lisbeth Dahl,* Norway
10.50–11.10	Dietary iodine and supplements. Is it all in the mix? *Margaret Rayman,* UK
11.10–11.30	How useful is serum Tg as a biomarker for iodine deficiency in non pregnant and pregnant individuals? *Michael Zimmermann,* Switzerland
11.30–11.50	Hungary – the iodine story *Endre Nagy,* Hungary
11.50–12.30	Optimising iodine nutrition – a WHO perspective *Joao Breda,* Denmark
12.30–13.00	Lunch and close

European
Thyroid Journal

Saturday, 3rd September 2016

Room 8+9+10+11 (Main Auditorium)
13.45–14.00

Opening Ceremony

Welcome by
Furio Pacini (ETA President), Italy and
Birte Nygaard (Chair of the Local Organizing Committee), Denmark

Room 8+9+10+11 (Main Auditorium)

14.00–16.00

Oral Session 1: Topic Highlights

Chairpersons: *Furio Pacini*, Italy
Birte Nygaard, Denmark

14.00–14.20
TUMOR AND NORMAL THYROID STEM-LIKE CELLS: FROM TISSUES TO ZEBRAFISH
Valentina Cirello[1], *Valentina Vaira*[2], *Germano Gaudenzi*[3], *Elisa Stellaria Grassi*[4], *Giovanni Vitale*[5], *Dario Ricca*[2], *Carla Colombo*[6], *Silvano Bosari*[7], *Leonardo Vicentini*[8], *Luca Persani*[9], *Stefano Ferrero*[10], *Laura Fugazzola*[11]
[1]Department of Pathophysiology and Transplantation, University of Milan, Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Italy; [2]Division of Pathology, Fondazione Irccs Ca' Granda, Milan, Italy; [3]Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Irccs, Milan, Italy; [4]Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Irccs, Milan, Italy; [5]Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Irccs, Milan, Italy; [6]Department of Clinical Sciences and Community Health, University of Milan, Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Milan, Italy; [7]Department of Pathophysiology and Transplantation, University of Milan, Division of Pathology, Fondazione Irccs Ca' Granda, Milan, Italy; [8]Endocrine Surgery Unit, Fondazione Irccs Ca' Granda, Milan, Italy; [9]Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Irccs, Milan, Italy; [10]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Division of Pathology, Fondazione Irccs Ca' Granda, Milan, Milan, Italy; [11]Department of Pathophysiology and Transplantation, University of Milan, Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Italy

14.20–14.40
TRACING OF BRAF MUTANT THYROID CELLS BEFORE TUMOR DEVELOPMENT
Ellen Johansson[1], *Shawn Liang*[2], *Elin Schoultz*[1], *Mikael Nilsson*[1]
[1]Sahlgrenska Cancer Center, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden; [2]Sahlgrenska Cancer Center, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, Gothenburg, Sweden

14.40–15.00
THE HUMAN SINGLE-NUCLEOTIDE POLYMORPHISM THR92ALA IN TYPE 2 DEIODINASE GENE (DIO2) IMPAIRS ENZYME ACTIVITY AND IS ASSOCIATED WITH REDUCED INTRACELLULAR AND SERUM T3 LEVELS IN ATHYREOTIC PATIENTS
Silvia Cantara[1], *Domenico Salvatore*[2], *Monica Dentice*[2], *Maria Grazia Castagna*[1], *Raffaele Ambrosio*[2], *Fabio Maino*[1], *Corrado Garbi*[2], *Carlotta Marzocchi*[1], *Tommaso Porcelli*[2], *Furio Pacini*[1]
[1]Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy; [2]Department of Clinical Medicine and Surgery, University of Naples, Federico II, Naples, Italy

15.00–15.20
A RANDOMIZED TRIAL OF IODIDE SUPPLEMENTATION VERSUS PLACEBO IN PRETERM INFANTS: THE I2S2 TRIAL
Fiona Williams[1], *Simon Osgston*[2], *Anita Boelen*[3], *Robert Hume*[4], *Jennifer Watson*[4], *Kayleigh Stanbury*[5], *Peter Willatts*[4], *Edmund Juszczak*[5], *Peter Brocklehurst*[6]
[1]University of Dundee, Population Health Sciences, Dundee, UK; [2]Population Health Sciences, Medical School, University of Dundee, Dundee, UK; [3]Academic Medical Centre, Amsterdam, Netherlands; [4]University of Dundee, Population Health Sciences, Medical School, Dundee, UK; [5]University of Oxford, National Perinatal Epidemiology Unit, Oxford, UK; [6]University College London, Institute for Women's Health, London, UK

15.20–15.40
CONTROLLED ANTENATAL THYROID SCREENING (CATS) II; EFFECT OF TREATMENT FOR UNDERACTIVE THYROID FUNCTION DURING PREGNANCY ON CHILDREN'S BEHAVIOUR AT AGE 9
Charlotte Hales[1], *Peter Taylor*[1], *Sue Channon*[1], *Kirtsen McEwan*[1], *Aled Rees*[1], *John Gregory*[1], *Ilaria Muller*[1], *Mohd S Draman*[1], *Colin Dayan*[1], *Kate Langley*[1], *Anita Thapar*[1], *John Lazarus*[1], *Marian Ludgate*[1]
[1]Cardiff University, Cardiff, UK

15.40–16.00
DIFFERENTIAL EFFECTS OF MCT8-DIO2 AND MCT8-OATP1C1 INACTIVATION ON CEREBRAL CORTEX GENE EXPRESSION IN THE MOUSE
Beatriz Morte[1], *Pilar Gil*[2], *Heike Heuer*[3], *Juan Bernal*[4]
[1]Center for Biomedical Research on Rare Diseases, Instituo de Investigaciones Biomedicas, Csic, Madrid, Spain; [2]Intituto de Investigaciones Biomédicas Uam-Csic, Center for Biomedical Research on Rare Diseases, Madrid, Spain; [3]Leibniz Institute for Environmental Medcine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany; [4]Instituto Investigaciones Biomédicas, Center for Biomedical Research on Rare Diseases, Madrid, Spain

16.00–17.00

Poster Discussion P1 and Coffee Break

(for corresponding abstracts see pages 96 to 122)

The poster session will start with a one-minute slide presentation of the poster work, which will be moderated by the session chair. Subsequently, the attendees of the poster session will discuss individually the poster with the presenter.

Room 1
Poster Session P1 – 01 Hyperthyroidism
Chairperson: *Maria Alevizaki*, Greece

Room 2
Poster Session P1 – 02 Iodine
Chairperson: *Roland Gärtner*, Germany

Room 3+4
Poster Session P1 – 03 Clinical Autoimmunity 1
Chairperson: *Endre Nagy*, Hungary

Room 16
Poster Session P1 – 04 Case Reports
Chairperson: *Valentin Fadeyev*, Russia

Room 14
Poster Session P1 – 05 Thyroid Cancer Diagnostic I
Chairperson: *Laurence Leenhardt*, France

Room 12
Poster Session P1 – 06 Thyroid Cancer Pathogenesis
Chairperson: *Christian Selmer*, Denmark

Room 13+15
Poster Session P1 – 07 Thyroid Cancer / Basic
Chairperson: *Raffaele Ciampi*, Italy

East Lounge / 8+9+10+11 (Main Auditorium)
Poster Session P1 – 08 Analogues + Others / Basic
Chairperson: *Duncan Bassett*, UK

Slides will be presented in the Main Auditorium while posters will be discussed in the East Lounge.

Room 8+9+10+11 (Main Auditorium)
17.00–18.00

ETA Industry-Sponsored Satellite Symposium 1

(see p. 179 for details)

Room 8+9+10+11 (Main Auditorium)
18.15–19.00

The European Thyroid Journal Lecture

Chairperson: *Wilmar Wiersinga*, The Netherlands
Editor-in-Chief of the *European Thyroid Journal*

19.30–22.00

Welcome Reception

(see p. 194 for details)

Room 13+15
07.00–08.00

ETA Industry-Sponsored Satellite Symposium 2

(see p. 181 for details)

Room 8+9+10+11 (Main Auditorium)
08.00–09.30

Symposium 1 (Clinical): Should We Care about Benign Thyroid Nodules

Chairpersons: *Paolo Vitti,* Italy
Sophie Leboulleux, France

08.00–08.30 Epidemiology of benign thyroid nodules
Nils Knudsen, Denmark
08.30–09.00 Who should be screened for thyroid nodules
Laurence Leenhardt, France
09.00–09.30 Follow-up of fine needle biopsy
Cosimo Durante, Italy

Room 13+15
08.00–09.30

Symposium 2 (Basic): Thyroid Hormone: Physiological Responses to a Changing Environment

Chairpersons: *Anita Boelen,* The Netherlands
Theo Visser, The Netherlands

08.00–08.30 Response to changing day length
Peter Morgan, UK
08.30–09.00 Response to cold exposure
Eric Fliers, The Netherlands
09.00–09.30 Response to fasting
Csaba Fekete, Hungary

09.30–10.00 **Coffee break**

Room 8+9+10+11 (Main Auditorium)
10.00–12.00

Oral Session 2 (Clinical): Thyroid Cancer Diagnostics

Chairpersons: *Martin Schlumberger,* France
Jens Bentzen, Denmark

10.00–10.15
ELASTICITY INDEX MEASURED BY SHEAR WAVE ELASTOGRAPHY HAS LITTLE CLINICAL VALUE FOR RISK STRATIFICATION OF THYROID NODULES
Kristine Zoylner Rubeck[1], *Steen Joop Bonnema*[2], *Marie Louise Jespersen*[3], *Peer Christiansen*[4], *Viveque Egsgaard Nielsen*[5]
[1]Department of Oto-Rhino-Laryngology, Head- and Neck Surgery, Aarhus University Hospital, Insitute for Clinical Medicine, Aarhus University, Aarhus, Denmark; [2]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; [3]Department of Pathology, Aarhus University Hospital, Aarhus, Denmark; [4]Department of Plastic and Breast Surgery, Aarhus University Hospital, Aarhus, Denmark; [5]Department of Oto-Rhino-Laryngology, Head and Neck Surgery, Aarhus University Hospital, Aarhus C, Denmark

10.15–10.30
NEXT-GENERATION SEQUENCING OF THYROID FNA SAMPLES USING THE ION AMPLISEQ™ CANCER HOTSPOT PANEL V2
Claudio Bellevicine[1], *Roberta Sgariglia*[1], *Umberto Malapelle*[1], *Caterina De Luca*[1], *Elena Vigliar*[1], *Markus Eszlinger*[2], *Ralphe Paschke*[2], *Giancarlo Troncone*[1]
[1]University of Naples Federico II, Public Health Department, Napoli, Italy; [2]University of Calgary, Calgary, Canada

10.30–10.45
PROGNOSTIC VALUE OF MINIMAL EXTRATHYROIDAL INVASION (PT3) IN PATIENTS WITH PAPILLARY THYROID CARCINOMA NOT SUBMITTED TO PROPHYLACTIC LYMPHADENECTOMY
Fabio Maino[1], *Maria Grazia Castagna*[1], *Filomena Barbato*[1], *Raffaella Forleo*[1], *Noemi Fralassi*[1], *Furio Pacini*[1]
[1]Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy

10.45–11.00

THE MACROFOLLICULAR VARIANT OF PAPILLARY THYROID CANCER (MF-PTC): A BICENTRIC RETROSPECTIVE ANALYSIS OF 65 CASES

Carlotta Giani[1], Joana Simões Pereira[2], Pedro Marques[2], Daniel Macedo[2], Rita Santos[2], Liborio Torregrossa[3], Fulvio Basolo[3], Rossella Elisei[1], Valeriano Leite[2]
[1]Endocrine Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]Endocrinology Section, Instituto Português de Oncologia de Lisboa, Francisco Gentil, Lisbon, Portugal; [3]Department of Surgical, Medical and Molecular Pathology of the Clinical Area, Pisa, Italy

11.00–11.15

RISK STATIFICATION IS USEFULL IN PREDICTING PERSISTENT/RECURRENT DISEASE IN MICROPAPILLARY THYROID CARCINOMA

Filomena Barbato[1], Maria Grazia Castagna[1], Fabio Maino[1], Raffaella Forleo[1], Noemi Fralassi[1], Furio Pacini[1]
[1]Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy

11.15–11.30

SIMULTANEOUS MEDULLARY (MTC) AND DIFFERENTIATED THYROID CANCER (DTC) IN THYROID GLAND (MTC-DTC): WHICH TUMOR IS THE REAL MATTER?

Letizia Pieruzzi[1], Loredana Lorusso[1], Liborio Torregrossa[2], Valeria Bottici[1], Laura Agate[1], Fulvio Basolo[2], Gabriele Materazzi[2], Paolo Vitti[1], Eleonora Molinaro[1], Rossella Elisei[1]
[1]Endocrinology Section, Department of Medical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Department of Surgical Medical, Molecular Pathology, University of Pisa, Pisa, Italy

11.30–11.45

COMPUTED TOMOGRAPHY ADDED TO ULTRASONOGRAPHY GIVES THE BENEFITS TO DETERMINE THE EXTENT OF NECK DISSECTION IN PATIENTS WITH THYROID CANCER: A PROSPECTIVE MULTICENTER STUDY

Ji-Hoon Kim[1], Younghen Lee[2], Dong Gyu Na[3], Jung Hwan Baek[4], So Lyung Jung[5], Sun-Won Park[6], Jinna Kim[7], Tae Jin Yun[8], Eun Joo Ha[9], Kyu Eun Lee[10], Kyung-Sook Yang[11]
[1]Seoul National University Hospital, Seoul, Korea, Rep. of South; [2]1department of Radiology, Korea University College of Medicine, Seoul, Korea, Rep. of South; [3]3department of Radiology, Human Medical Imaging and Intervention Center, Seoul, Korea, Rep. of South; [4]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; [5]Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South; [6]Boramae Medical Center, College of Medicine, Seoul National University, Seoul, Korea, Rep. of South; [7]Severance Hospital, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [8]2department of Radiology, Seoul National University Hospital, Seoul, Korea, Rep. of South; [9]8department of Radiology, Ajou University School of Medicine, Seoul, Korea, Rep. of South; [10]Department of Surgery, Seoul National University Hospital, Seoul, Korea, Rep. of South; [11]Department of Biostatistics, Korea University College of Medicine, Seoul, Korea, Rep. of South

11.45–12.00

THYROGLOBULIN DOUBLING-TIME (TGDT): ITS VALUE AS A PROGNOSTIC MARKER IN DIFFERENTIATED THYROID CANCER (DTC)

Shazia Fatima[1], Sadaf Tufail Butt [1], Mohammad Faheem[1]
[1]Nuclear Medicine, Oncology & Radiotherapy Institute (Nori), Islamabad, Pakistan

Room 13+15

10.00–12.00

Oral Session 3 (Basic): Thyroid Hormone Transport, Metabolism and Action

Chairpersons: *Jacques Dumont,* Belgium
Aase Krogh Rasmussen, Denmark

10.00–10.15

KNOCKOUT OF TYPE 2 DEIODINASE SEVERELY DISRUPTS REPRODUCTION IN FEMALE ZEBRAFISH

Anne Houbrechts[1], Jolien Van Houcke[1], Veerle Darras[1]
[1]Laboratory Comparative Endocrinology, Biology Department, Ku Leuven, Leuven, Belgium

10.15–10.30

MICRORNA 199-A3P INHIBITION INDUCES AN INCREASE OF THE EXPRESSION OF DEIODINASE 2 IN AORTIC ENDOTHELIAL CELLS

Joris Virginie[1], Lobysheva Irina[1], Balligand Jean-Luc[1], Marie-Christine Many[2], Dessy Chantal[1]
[1]Ucl-Irec-Fath, Brussels, Belgium; [2]Ss/Mede/Irec/Ucl, Bruxelles, Belgium

10.30–10.45

THYROID HORMONE AND SKIN CANCER: A NOVEL MICRORNA21-D3 INTERPLAY REGULATES BASAL CELL CARCINOMA TUMORIGENESIS

Daniela Di Girolamo[1], Raffaele Ambrosio[2], Maria Angela De Stefano[1], Giuseppina Mancino[1], Emery De Cicco[1], Caterina Miro[1], Domenico Salvatore[3], Monica Dentice[4]
[1]University of Naples 'Federico II', Naples, Italy; [2]Irccs Sdn, Naples, Naples, Italy; [3]Dipartimento di Endocrinologia, University of Naples, Federico II, Napoli, Italy; [4]Department of Clinical Medicine and Surgery, University of Naples 'Federico II, Endocrinologia + Oncologia, Naples, Italy

10.45–11.00

THYROID HORMONE TRANSPORTERS IN XENOPUS AND THEIR SUSCEPTIBILITY TO XENOBIOTICS

Bilal Mughal[1], Michelle Leemans[2], Lindsey Marshall[3], Sébastien Le Mével[4], Jean-Baptiste Fini[4], Barbara Demeneix[5]
[1]Mnhn, Umr7221, Paris, France; [2]Mnhn / Umr7221, Paris, France; [3]Umr Cnrs 7221, Département Régulations, Développement et Diversité Moléculaire, Muséum National D'histoire Naturelle, Evolution des Régulations Endocriniennes, Paris, France; [4]Umr Cnrs 7221, Muséum National D'histoire Naturelle, Paris, France; [5]Umr Cnrs 7221, Département Régulations, Développement et Diversité Moléculaire, Muséum National D'histoire Naturelle, Evolutions des Régulations Endocriniennes, Paris, France

11.00–11.15

ANEMIA IN PATIENTS WITH RESISTANCE TO THYROID HORMONE ALPHA: A ROLE OF TRA IN HUMAN ERYTHROPOIESIS

Anja van Gucht[1], Marcel Meima[2], Carla Moran[3], Maura Agostini[4], Anna Tylki-Szymanska[5], Malgorzata Krajewska – Walasek[6], Krystyna Chrzanowska[5], Alexandra Efthymiadou[7], Dionisios Chrysis [7], Korcan Demir[8], W. Edward Visser[9], Theo Visser[10], Thamar Van Dijk[11], V. Krishna Chatterjee[3], Robin Peeters[12]
[1]Erasmus Medical Center, Thyroid Laboratory, Department of Internal Medicine, Rotterdam, Netherlands; [2]Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; [3]Metabolic Research Laboratories, Addenbrooke's Hospital, Cambridge, UK; [4]Metabolic Research Laboratories, Cambridge, UK; [5]The Children's Memorial Health Institute, Warsaw, Poland; [6]The Children's Memorial Health Institute, Warsaw, Poland; [7]Department of Pediatrics, Medical School, University of Patras, Patras, Greece; [8]Division of Pediatric Endocrinology, Dr. Behcet Uz Children's Hospital, Izmir, Turkey; [9]Erasmus Medical Center, Rotterdam, Netherlands; [10]Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; [11]Department of Cell Biology, Erasmus University Medical Center, Rotterdam, Netherlands; [12]Erasmus University Medical Center, Rotterdam, The Netherlands

11.15–11.30

THE T3 RECEPTOR TRA1 INTERACTOME

Marcel Meima[1], Karn Wejaphikul[1], W. Edward Visser[2], Theo M. Luider[3], Theo Visser[4], Robin Peeters[5]
[1]Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; [2]Erasmus Medical Center, Rotterdam, Netherlands; [3]Erasmus University Medical Center, Department of Neurology, Rotterdam, Netherlands; [4]Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; [5]Erasmus University Medical Center, Rotterdam, The Netherlands

11.30–11.45

EFFECT OF THYROID HORMONE ON GENE EXPRESSION IN HUMAN TRALPHA-EXPRESSING CELLS

Elske Massolt[1], Selmar Leeuwenburgh[2], Sigrid Swagemakers[3], Mirjam van den Hout-van Vroonhoven[4], Boen L.R. Kam[5], Pim Burger[6], Peter van der Spek[3], Wilfred F. van Ijcken[4], Theo Visser[7], Robin Peeters[8], W. Edward Visser[9]
[1]Erasmus MC, Endocrinology, Rotterdam, Netherlands; [2]Erasmus MC, Internal Medicine, Rotterdam, Netherlands; [3]Erasmus MC, Bioinformatics, Rotterdam, Netherlands; [4]Erasmus MC, Center for Biomics, Rotterdam, Netherlands; [5]Erasmus MC, Department of Nuclear Medicine, Rotterdam, Netherlands; [6]Erasmus MC, Department of Surgery, Rotterdam, Netherlands; [7]Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; [8]Erasmus University Medical Center, Rotterdam, The Netherlands, Rotterdam, Netherlands; [9]Erasmus Medical Center, Rotterdam, Netherlands

11.45–12.00

DISTINCT MOLECULAR FEATURES AT L-TYPE AMINO ACID TRANSPORTER 2 DETERMINE DIFFERING THYROID HORMONE INFLUX AND EFFLUX PROFILES

Katrin Manuela Hinz[1], Dominik Neef[1], Gerd Krause[1]
[1]Leibniz-Institut für Molekulare Pharmakologie (Fmp), Berlin, Germany

12.00–13.00

Poster Discussion P2 and Lunch

(for corresponding abstracts see pages 123 to 146)

The poster session will start with a one-minute slide presentation of the poster work, which will be moderated by the session chair. Subsequently, the attendees of the poster session will discuss individually the poster with the presenter.

Room 1
Poster Session P2 – 01 Clinical Autoimmunity 2
Chairperson: *Tanja Diana,* Germany

Room 2
Poster Session P2 – 02 Hypothyroidism 1
Chairperson: *Peter Taylor,* UK

Room 3+4
Poster Session P2 – 03 Goiter 1
Chairperson: *Andrzej Lewinski,* Poland

Room 16
Poster Session P2 – 04 Reproduction
Chairperson: *Chantal Daumerie,* Belgium

Room14
Poster Session P2 – 05 Thyroid Cancer Diagnostic II
Chairperson: *Alicja Hubalewska-Dydejczyk,* Poland

Room 12
Poster Session P2 – 06 Thyroid Cancer Therapeutics
Chairperson: *Thera Links,* The Netherlands

Room13+15
Poster Session P2 – 07 Thyroid Cancer – Clinical I
Chairperson: *Jeppe Lerche La-Cour,* Denmark

East Lounge / 8+9+10+11 (Main Auditorium)
Poster Session P2 – 08 Transporters and Others
Chairperson: *Domenico Salvatore,* Italy

Slides will be presented in the Main Auditorium while posters will be discussed in the East Lounge.

Room 8+9+10+11 (Main Auditorium)
13.00–14.00

ETA Industry-Sponsored Satellite Symposium 3

(see p. 182 for details)

14.00–14.45
Meet the Expert 1–4

Room 8+9+10+11 (Main Auditorium)
14.00–14.45 **MTE 1**
Drug induced thyroid disorders
Colin Dayan, UK

Room 13+15
14.00–14.45 **MTE 2**
Endocrine disruptors – fact or fiction?
Barbara Demeneix, France

Room 12
14.00–14.45 **MTE 3**
TRs and chromatin remodelling
Lars Grøntved, Denmark

Room 14
14.00–14.45 **MTE 4**
Thyroid function and longevity
Dagmar Führer, Germany

Room 8+9+10+11 (Main Auditorium)
14.45–15.00

Posthumous Tribute to Peter Laurberg and Lissitzky Career Award

Chairpersons: *Furio Pacini,* Italy
Colin Dayan, UK

Room 8+9+10+11 (Main Auditorium)
15.00–15.30

Harington-De Visscher Prize

Chairpersons: *Furio Pacini,* Italy
Colin Dayan, UK

15.30–16.00 **Coffee break**

Room 8+9+10+11 (Main Auditorium)

16.00–18.00

Oral Session 4 (Clinical): Clinical Thyroidology

Chairpersons: *Bernadette Biondi,* Italy
Jens Faber, Denmark

16.00–16.15
COMBINATION OF DIO2 AND MCT10 GENE POLYMORPHISMS PREDICTS THE PREFERENCE FOR T4+T3 THERAPY IN HYPOTHYROIDISM – A BLINDED RANDOMIZED CLINICAL STUDY
Allan Carle[1], Peter Laurberg[2], Rudi Steffensen[3], Jens Faber[4], Birte Nygaard[5]
[1]Department of Endocrinology, Aalborg University Hospital, Aalborg, Denmark; [2]Aalborg University Hospital, Aalborg University, Aalborg, Denmark; [3]Department of Clinical Immunology, Aalborg University Hospital, Aalborg, Denmark; [4]Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Herlev, Denmark; [5]Department of Endocrinology, Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

16.15–16.30
THYROIDECTOMY IMPROVES DISEASE RELATED QUALITY OF LIFE IN PATIENTS WITH NON-TOXIC GOITER: A PROSPECTIVE COHORT STUDY
Jesper Roed Sørensen[1], Torquil Watt[2], Helle Døssing[3], Laszlo Hegedüs[4], Steen Joop Bonnema [5], Christian Godballe[6]
[1]Odense University Hospital, Department of Orl – Head and Neck Surgery, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense C, Denmark; [2]Department of Endocrinology, Copenhagen University Hospital Rigshospitalet, Denmark, Department of Endocrinology, Herlev Hospital, University of Copenhagen, Copenhagen, Denmark; [3]Odense University Hospital, Department of Orl – Head and Neck Surgery, Odense, Denmark; [4]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research,

Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; [5]Odense University Hospital, Department of Endocrinology, Odense, Denmark; [6]Dept. of Orl – Head & Neck Surgery, Odense, Denmark

16.30–16.45

EXCESS MORTALITY IN HYPERTHYROIDISM IS DRIVEN BY LACK OF TREATMENT: EVIDENCE FROM A POPULATION-BASED, LARGE-SCALE, LONG-TERM FOLLOW-UP, DANISH REGISTRY-STUDY

Mads Lillevang-Johansen[1], Thomas Brix[2], Bo Abrahamsen[3], Laszlo Hegedüs[4]
[1]Department of Endocrinology, Odense University Hospital, University of Southern Denmark, Odense C, Denmark; [2]Department of Endocirnology, Odense University Hospital, Odense C, Denmark; [3]Holbæk Hospital, Department of Medicine, Open, University of Southern Denmark, Holbæk, Denmark; [4]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

16.45–17.00

THE ASSOCIATION BETWEEN NEONATAL BIRTH DEFECTS AND EARLY PREGNANCY USE OF ANTITHYROID DRUGS

Tae Hyuk Kim[1], Gi Hyeon Seo[2], Yoon Young Cho[1], Sun Wook Kim[1], Jae Hoon Chung[3]
[1]Samsung Medical Center, Seoul, Korea, Rep. of South; [2]Health Insurance Review and Assessment Service, Seoul, Korea, Rep. of South; [3]Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Seoul, Korea, Rep. of South

17.00–17.15

IS THERE AN ASSOCIATION BETWEEN GRAVES' DISEASE, WITHOUT ORBITOPATHY, AND GLAUCOMA? RESULTS FROM A DANISH NATIONWIDE REGISTER-BASED STUDY

Frans Brandt[1], Marianne Thvilum[2], Thomas Brix[3], Laszlo Hegedüs[4]
[1]Hospital of Southern Jutland, Department of Internal Medicine, Sønderborg, Denmark; [2]Odense University Hospital, Department of Endocrinology and Metabolism, Odense C, Denmark; [3]Department of Endocirnology, Odense University Hospital, Odense C, Denmark; [4]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

17.15–17.30

THE INTERRELATION BETWEEN HYPOTHYROIDISM AND GLAUCOMA: EVIDENCE FROM A DANISH NATIONWIDE REGISTER-BASED STUDY

Marianne Thvilum[1], Frans Brandt[2], Thomas Brix[3], Laszlo Hegedüs[4]
[1]Odense University Hospital, Department of Endocrinology and Metabolism, Odense C, Denmark; [2]Hospital of Southern Jutland, Department of Internal Medicine, Sønderborg, Denmark; [3]Department of Endocirnology, Odense University Hospital, Odense C, Denmark; [4]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

17.30–17.45

RADIOFREQUENCY ABLATION: AN EFFECTIVE AND LONG-LASTING TREATMENT FOR THYROID NODULES: RESULTS AT 3 YEARS FOLLOW-UP FROM A SINGLE CENTER

Francesca Garino[1], Maurilio Deandrea[1], Alberto Mormile[1], Paolo Piero Limone[1]
[1]Department of Endocrinology, Diabetes and Metabolism, Ao Mauriziano, Turin, Italy

17.45–18.00

THYROXINE TREATMENT IN OVERWEIGHT AND OBESE HYPOTHYROID PATIENTS

Camilla Virili[1], Silvia Capriello[1], Maria Giulia Santaguida[1], Miriam Cellini[1], Nunzia Brusca[1], Lucilla Gargano[2], Marco Centanni[1]
[1]Sapienza University of Rome, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy; [2]Ausl Latina, Uoc Endocrinologia, Latina, Italy

Room 13+15

16.00–18.00

Oral Session 5 (Basic): Thyroid Cancer Pathogenesis

Chairpersons: *Rossella Elisei,* Italy
Lars Bastholt, Denmark

16.00–16.15

GENETIC HETEROGENEITY OF THYROID CANCER

Michela Perrino[1], Carla Colombo[1], Marina Muzza[2], Valentina Cirello[3], Laura Fugazzola[3]
[1]Department of Clinical Sciences and Community Health, University of Milan, Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Italy; [2]Dep of Clinical Sciences, Milan, Italy; [3]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

16.15–16.30

CORRELATION BETWEEN THE PRESENCE OF MACROPHAGES AND BRAF V600E MUTATION IN DIFFERENT VARIANTS OF WELL DIFFERENTIATED PAPILLARY THYROID CANCER

Luciana Puleo[1], Clara Ugolini[2], David Viola[1], Eleonora Molinaro[1], Laura Agate[1], Antonio Matrone[1], Fulvio Basolo[2], Paolo Vitti[1], Rossella Elisei[1], Cristina Romei[1]

[1]Endocrinology Section, Department of Medical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Department of Surgical Medical, Molecular Pathology, University of Pisa, Pisa, Italy

16.30–16.45

GENETIC PREDISPOSITION TO PAPILLARY THYROID CANCER IN CHILDREN AND ADOLESCENTS

Daria Handkiewicz-Junak[1], Dorota Kula[1], Michal Swierniak[2], Jadwiga Zebracka-Gala[1], Mihcal Jarzab[1], Dagmara Rusinek[1], Zbigniew Puch[1], Aleksandra Kropinska[1], Renata Cyplinska[1], Barbara Jarzab[1]

[1]Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice, Poland; [2]Medical University of Warsaw, University of Warsaw, Warsaw, Poland

16.45–17.00

HABP2 GENE MUTATIONS DO NOT CAUSE FAMILIAL PAPILLARY THYROID CANCER IN A LARGE SERIES OF UNRELATED FAMILIES

Carla Colombo[1], Marina Muzza[2], Michela Perrino[1], Valentina Cirello[3], Maria Proverbio[4], Laura Fugazzola[3]

[1]Department of Clinical Sciences and Community Health, University of Milan, Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Italy; [2]Departement of Clinical Sciences, Milan, Italy; [3]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [4]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

17.00–17.15

GENETIC VARIATION IN NFKB LEADS TO INCREASED IL-1BETA PRODUCTION AND IS ASSOCIATED WITH REDUCED SENSITIVITY TO RADIOACTIVE IODINE IN NON-MEDULLARY THYROID CANCER

Mirela-Sanda Petrulea[1], Theo S. Plantinga[2], Marije Oosting[3], Leo A.B. Joosten[3], Jan W.A. Smit[4], Doina Piciu[5], Romana T. Netea-Maier[4], Carmen E. Georgescu[1]

[1]Department of Endocrinology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; [2]Department of Pathology, Radboud University Medical Centre, Nijmegen, Netherlands; [3]Department of Internal Medicine, Radboud University Medical Centre, Nijmegen, Netherlands; [4]Department of Internal Medicine and Division of Endocrinology, Radboud University Medical Centre, Nijmegen, Netherlands; [5]Oncology Institute, Cluj-Napoca, Romania

17.15–17.30

GERMLINE AND SOMATIC DICER1 MUTATIONS IN FAMILIAL PAPILLARY THYROID CARCINOMA

César Lumbreras[1], María Jesús Chueca Guindulain[2], Laura Arribas Carreira [1], Rajdee de Randamie[1], Ángel Alonso Sánchez[3], Pilar Fernández Seara[4], Sara Berrade Zubiri[2], Emma Anda Apiñariz[5], Rita María Regojo Zapata[6], Marta Mendiola Sabio[7], Jose Moreno[1]

[1]Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Ingemm), La Paz University Hospital, Autonomous University of Madrid, Madrid, Spain; [2]Pediatric Endocrinology Service, Navarra Hospital Center, Pamplona, Spain; [3]Genetics Service, Navarra Hospital Center, Pamplona, Spain; [4]Anatomic Pathology Service, Navarra Hospital Center, Pamplona, Spain; [5]Endocrinology and Nutrition Service, Navarra Hospital Center, Pamplona, Spain; [6]Anatomic Pathology Service, La Paz University Hospital, Madrid, Spain; [7]Molecular Pathology of Cancer and Translational Oncology Laboratory, La Paz University Hospital Research Institute (Idipaz), Madrid, Spain

17.30–17.45

A MOUSE MODEL OF SPORADIC PAPILLARY THYROID CANCER AND TUMOR PROGRESSION

Elin Schoultz[1], Ellen Johansson[1], Shawn Liang[2], Mikael Nilsson[1]

[1]Sahlgrenska Cancer Center, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden; [2]Sahlgrenska Cancer Center, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

17.45–18.00

TREATMENT OUTCOMES IN BRAIN METASTASIS FROM PAPILLARY THYROID CANCER

Seok-Mo Kim[1], Soo Young Kim[1], Hyukjun Yun[1], Hyeung Kyoo Kim[1], Bup-Woo Kim[1], Yong Sang Lee[1], Hang-Seok Chang[1], Cheong Soo Park[1]

[1]Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

Room 8+9+10+11 (Main Auditorium)
18.15–19.45

ETA Industry-Sponsored Satellite Symposium 4

(see p. 183 for details)

Room 8+9+10+11 (Main Auditorium)
07.00–08.00

ETA Industry-Sponsored Satellite Symposium 5

(see p. 185 for details)

Room 8+9+10+11 (Main Auditorium)
08.00–09.30

Symposium 3 (Clinical/Translational): Recent Advances in Graves' Orbitopathy

Chairpersons: *George J. Kahaly,* Germany
Anne Lene Riis, Denmark

08.00–08.30 ETA Guidelines on Graves' Orbitopathy
Luigi Bartalena, Italy
08.30–09.00 Mortality and morbidity in Graves' orbitopathy
Thomas Brix, Denmark
09.00–09.30 Thyrotropin/IGF-1 receptor crosstalk in the pathogenesis of Graves' orbitopathy
Susanne Neumann, USA

Room 13+15
08.00–09.30

Symposium 4 (Basic): Triac Treatment in AHD Syndrome

Chairpersons: *Caterina Di Cosmo,* Italy
Juan Bernal, Spain

08.00–08.30 Triac treatment in the MCT8 KO mouse
Heike Heuer, Germany
08.30–09.00 Triac treatment in the MCT8 zebrafish
Lior Appelbaum, Israel
09.00–09.30 Triac treatment in AHD patients
Stephan Groeneweg, The Netherlands

09.30–10.00 **Coffee break**

Room 8+9+10+11 (Main Auditorium)

10.00–12.00

Oral Session 6 (Clinical): Clinical Aspects of Autoimmunity

Chairpersons: *Nils Knudsen,* Denmark
Thomas Brix, Denmark

10.00–10.15
EVALUATION OF RESPONSE DURING INTRAVENOUS GLUCOCORTICOID (IVGC) TREATMENT FOR MODERATE-TO-SEVERE AND ACTIVE GRAVES' ORBITOPATHY (GO): IS IT A GUIDANCE TO DECIDE WHETHER TREATMENT SHOULD BE CONTINUED OR WITHDRAWN?

Luigi Bartalena[1], *Giovanni Veronesi*[2], *Gerassimos Krassas*[3], *Wilmar Wiersinga*[4], *Claudio Marcocci*[5], *Mario Salvi*[6], *Chantal Daumerie*[7], *Claire Bournaud*[8], *Matthias Stahl*[9], *Lorenza Sassi*[2], *Claudio Azzolini*[2], *Kostas Boboridis*[10], *Maarten Mourits*[11], *Maarten Soeters*[11], *Lelio Baldeschi*[12], *Marco Nardi*[13], *Nicola Currò*[14], *Antonella Boschi*[12], *Martine Bernard*[15], *Georg von Arx*[16], *Petros Perros*[17], *George J. Kahaly*[18]
[1]University of Insubria, Varese, Italy; [2]University of Insubria, Varese, Italy; [3]Panagia Hospital, Thessaloniki, Greece; [4]Academic Medical Center, Amsterdam, Netherlands; [5]Department of Clinical and Experimen, University of Pisa, Pisa, Italy; [6]Dipartimento Scienze Mediche, Endocrine Unit, Fondazione Irccs Cà Granda, Milano, Italy; [7]Cliniques Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium; [8]Lyon University, Lyon, France; [9]Olten Spital, Olten, Switzerland; [10]Ahepa Hospital, Thessaloniki, Greece; [11]Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; [12]Université Catholique de Louvain, Brussels, Belgium; [13]University of Pisa, Lucca, Italy; [14]Ophthalmology, Fondazione Irccs Cà Granda, Milan, Italy; [15]University of Lyon, Lyon, France; [16]Zentrum für Endokrine Orbitopathie, Olten, Switzerland; [17]Freeman Hospital, Newcastle-Upon-Tyne, UK; [18]Johannes Gutenberg University Medical Center, Mainz, Germany

10.15–10.30

SIGHT-THREATENING GRAVES' ORBITOPATHY: EXPERIENCE OF THE MULTIDISCIPLINARY THYROID-EYE CONSULTATION OF THE UNIVERSITY HOSPITAL IN TOULOUSE, FRANCE

Blandine Tramunt[1], Philippe Imbert[2], Solange Grunenwald [3], Franck Boutault[4], Philippe Caron[5]

[1]Service D'endocrinologie et Maladies Métaboliques, Chu Larrey, Toulouse, France; [2]Service D'ophtalmologie, Clinique du Parc, Toulouse, France; [3]Chu Larrey, Toulouse Cedex 9, France; [4]Service de Chirugie Maxillo-Faciale, Chu Pierre-Paul Riquet, Toulouse, France; [5]Chu Larrey, 7eme Etage/Chu Rangueil, Toulouse Cedex 9, France

10.30–10.45

HIGHLY VARIABLE SENSITIVITY AND SPECIFICITY OF FOUR BINDING AND TWO BIO-ASSAYS FOR TSH-RECEPTOR ANTIBODIES

Tanja Diana[1], Christian Wüster[2], Michael Kanitz[1], George J. Kahaly[1]

[1]Johannes Gutenberg University Medical Center, Mainz, Germany; [2]Endocrine Practice, Mainz, Germany

10.45–11.00

HIGH CIRCULATING CXCL10 LEVELS IN NON-SEGMENTAL VITILIGO, IN PRESENCE OR ABSENCE OF AUTOIMMUNE THYROIDITIS

Silvia Martina Ferrari[1], Poupak Fallahi[1], Giulia Santaguida[2], Camilla Virili[2], Ilaria Ruffilli[1], Francesca Ragusa[1], Marco Centanni[2], Alessandro Antonelli[1]

[1]University of Pisa, Pisa, Italy; [2]Sapienza University of Rome, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy

11.00–11.15

BREG IN HASHIMOTO THYROIDITIS ISOLATED OR ASSOCIATED TO FURTHER ORGAN-SPECIFIC AUTOIMMUNE DISEASES

Maria Giulia Santaguida[1], Camilla Virili[2], Ilenia Gatto[3], Giorgio Mangino[4], Ilaria Stramazzo[3], Marco Centanni[5]

[1]'Sapienza' University of Roma, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy; [2]Dept of Experimental Medicine 'Sapienza' University of Rome, Latina, Italy, Dept Medico-Surgical Sciences and Biotechnologies, Rome, Italy; [3]'Sapienza' University of Roma, Latina, Italy; [4]'Sapienza' University of Roma, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy; [5]Sapienza University of Rome, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy

11.15–11.30

HIGH EFFECTIVENESS OF THERAPEUTIC PLASMA EXCHANGE IN REFRACTORY HYPERTHYROIDISM: ABOUT 17 CASES

Clotilde Saie[1], Cecile Ghander[1], Saheb Sami[1], Natacha Jumentier[2], Fatima Kharcha[1], Didier Lemesle[2], Salwa Baki[3], Nassiba Beghdadi[1], Laurence Leenhardt[4], Camille Buffet[1], Christophe Tresallet[5]

[1]Hôpital Pitié Salpêtrière, Paris, France; [2]Hôpital Pitié Salpêtrière, Paris, France; [3]Hôpital Pitié Salpêtrière, Marrakesh, Morocco; [4]La Pitie Salpetriere Hospital, Thyroid and Endocrine Tumors Unit, Paris, France; [5]Hôpital Pitié Salpêtrière, Paris, France

11.30–11.45

QUANTIFICATION OF MOTILITY DYSFUNCTION IN GRAVES' ORBITOPATHY (GO) BY ASSESSING CHANGES IN EYE MUSCLE DUCTIONS

Mario Salvi[1], Irene Campi[2], Guia Vannucchi[3], Danila Covelli[4], Simona Simonetta[5], Nicola Currò[6]

[1]Dipartimento Scienze Mediche, Endocrine Unit, Fondazione Irccs Cà Granda, Milano, Italy; [2]Fondazione Irccs Ca' Granda, Endocrine Unit, Milan, Italy; [3]Endocrine Unit, Fondazione Policlinico Irccs, Milan, Italy; [4]1graves' Orbitopathy Unit, Endocrinology, Fondazione Ca' Granda Irccs, University of Milan, Medical Sciences, Milano, Italy; [5]Ophthalmology Unit, Fondazione Irccs Ca' Granda, Milan, Italy; [6]Ophthalmology, Fondazione Irccs Cà Granda, Milan, Italy

11.45–12.00

GRAVES ORBITOPATHY AFFECTS VISUAL FUNCTION AND APPEARANCE IN DIFFERENT MANNERS

Danilo Villagelin [1], Roberto Bernado Dos Santos[2], João Hamilton Romaldini[2], Ana Paula Comarella[3], Natassia Bufalo[3], Karina Colombera Peres[3], Laura Ward[3]

[1]Pont. Universidade Catolica Campinas, Campinas, Brazil; [2]Pontificia Universidade Catolica Campinas, Campinas, Brazil; [3]Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Brazil

Room 13+15

10.00–12.00

Oral Session 7 (Basic): Medullary and Anaplastic Thyroid Cancer

Chairpersons: *Laura Fugazzola,* Italy
Kristian Winther, Denmark

10.00–10.15

GENETIC ANALYSIS OF ANAPLASTIC THYROID CANCER

Naveen Ravi[1], *Eleanor Woodward*[1], *Andrea Biloglav*[1], *Lars Ekblad*[2], *Johan Wennerberg*[2], *Kajsa Paulsson*[3]
[1]Bmc C13, Lund University, Lund, Sweden; [2]Lund University, Lund, Sweden; [3]Bmc C13, Lund University, Lund, Sweden

10.15–10.30

EVALUATION OF THE ANTINEOPLASTIC ACTIVITY OF VANDETANIB, AND LENVATINIB IN PRIMARY ANAPLASTIC THYROID CANCER CELLS, OBTAINED FROM FINE NEEDLE ASPIRATION

Silvia Martina Ferrari[1], *Poupak Fallahi*[1], *Concettina La Motta*[2], *Gabriele Materazzi*[3], *David Galleri*[3], *Alessandro Antonelli*[1]
[1]University of Pisa, Pisa, Italy; [2]Department of Pharmaceutical Science, University of Pisa, Pisa, Italy; [3]Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy

10.30–10.45

SYNERGISTIC ANTI-CANCER ACTIVITY OF THE HDAC INHIBITOR, N-HYDROXY-7-(2-NAPHTHYLTHIO) HEPTANOMIDE (HNHA) AND SORAFENIB ON ANAPLASTIC THYROID CANCER IN VITRO AND IN VIVO

Seok-Mo Kim[1], *Ki Cheong Park*[1], *Soo Young Kim*[1], *Hyeung Kyoo Kim*[1], *Bup-Woo Kim*[1], *Yong Sang Lee*[1], *Hang-Seok Chang*[1], *Cheong Soo Park*[1]
[1]Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

10.45–11.00

TREATMENT OUTCOMES OF SORAFENIB AND LENVATINIB FOR ADVANCED THYROID CANCERS AND ANAPLASTIC THYROID CANCERS

Hiroyuki Iwasaki[1], *Hiroyaka Nakayama*[2], *Nobuyasu Suganuma*[1], *Tatsuya Yoshida*[1], *Takashi Yamanaka*[1], *Shinsuke Hatori*[3], *Satoru Shimizu*[1]
[1]Department of Breast and Endocrine Surgery, Kanagawa Cancer Center, Yokohama, Japan; [2]Department of Surgery, Yokohama City University School of Medicine, Yokohama, Japan; [3]Department of Surgery, Hiratsuka Kyosai Hospital, Hiratsuka, Japan

11.00–11.15

CALCITONIN RECEPTOR (CTR) EXPRESSION IN MEDULLARY THYROID CANCER (MTC) AND POSSIBLE CLINICAL IMPLICATIONS

Virginia Cappagli[1], *Catarina Soares Potes*[2], *Luciana Bueno Ferreira*[3], *Catarina Eloy*[3], *Cristina Romei*[1], *Rossella Elisei*[1], *Manuel Sobrinho-Simões*[3], *Peter J. Wookey*[4], *Paula Soares*[3]
[1]Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Instituto de Investigação e Inovação Em Saúde, Universidade Do Porto, Porto, Portugal; [3]Institute of Molecular Pathology and Immunology of the University of Porto (Ipatimup), Porto, Portugal; [4]Department of Medicine at Austin Health, University of Melbourne, Parkville, Vic., Australia

11.15–11.30

THE MUTATION PROFILE OF MEDULLARY THYROID CARCINOMA CAN BE DIFFERENT IN PRIMARY AND METASTATIC TISSUES

Cristina Romei[1], *Francesca Casella*[1], *Alessia Tacito*[1], *Raffaele Ciampi*[1], *Eleonora Molinaro*[1], *Laura Agate*[1], *Valeria Bottici*[1], *Antonio Matrone*[1], *Rossella Elisei*[1]
[1]Section of Endocrinology, Department of Clinical and Experimental Medicine, University of Pisa, Department of Endocrinology, Pisa, Italy

11.30–11.45

EXPERIENCE FROM THE ADMINISTRATION OF TYROSINE KINASE INHIBITORS (TKI) IN PATIENTS WITH METASTATIC PROGRESSIVE MEDULLARY THYROID CARCINOMA (MTC) IN A REFERRAL CENTRE IN GREECE

Elli Anagnostou[1], *Katerina Saltiki*[2], *Vasiliki Vasiliou*[2], *Constantinos Tsigkos*[2], *Lamprini Papanastasiou*[2], *Maria Alevizaki*[2]
[1]Endocrine Unit, Dept Medical Therapeutics, Alexandra Hospital, Athens University School of Medicine, Athens, Greece; [2]Endocrine Unit, Dept Medical Therapeutics, Alexandra Hospital, Athens University School of Medicine, Athens, Greece

11.45–12.00

THE ASSOCIATION BETWEEN TERT PROMOTER MUTATIONS AND MORTALITY IN PATIENTS WITH THYROID CANCER

Tae Hyuk Kim[1], *Youngnam Kim*[1], *Hyein Kim*[1], *Ho-Su Kim*[1], *Sun Wook Kim*[1], *Jae Hoon Chung*[2]
[1]Samsung Medical Center, Seoul, Korea, Rep. of South; [2]Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Rep. of South

12.00–13.00

Poster Discussion P3 and Lunch

(for corresponding abstracts see pages 146 to 170)

The poster session will start with a one-minute slide presentation of the poster work, which will be moderated by the session chair. Subsequently, the attendees of the poster session will discuss individually the poster with the presenter.

Room 1
Poster Session P3 – 01 Clinical Thyroidology
Chairperson: *Philippe Caron,* France

Room 2
Poster Session P3 – 02 Hypothyroidism 2, Children + Regulation
Chairperson: *Jose Moreno,* Spain

Room 3+4
Poster Session P3 – 03 Goiter 2 and Environmental
Chairperson: *Leonidas Duntas,* Greece

Room 16
Poster Session P3 – 04 Cardio, Brain and Metabolism
Chairperson: *Frans Brandt,* Denmark

Room 14
Poster Session P3 – 05 Thyroid Cancer Diagnostic III
Chairperson: *Georg Brabant,* Germany

Room 12
Poster Session P3 – 06 Thyroid Cancer – Clinical II
Chairperson: *Tania Pilli,* Italy

Room 13+15
Poster Session P3 – 07 Thyroid Cancer – Clinical III
Chairperson: *Torquil Watt,* Denmark

East Lounge / 8+9+10+11 (Main Auditorium)
Poster Session P3 – 08 Basic Autoimmunity and Thyroidology
Chairperson: *Marie-Christine Many,* Belgium

Slides will be presented in the Main Auditorium while posters will be discussed in the East Lounge.

Room 8+9+10+11 (Main Auditorium)
13.00–14.00

ETA Industry-Sponsored Satellite Symposium 6

(see p. 186 for details)

14.00–14.45

Meet the Expert 5–8

Room 8+9+10+11 (Main Auditorium)
14.00–14.45 **MTE 5**
New guidelines in thyroid nodules and cancer
Furio Pacini, Italy
Martin Schlumberger, France

Room 13+15
14.00–14.45 **MTE 6**
Biomarkers of thyroid hormone action – fact or fiction?
Georg Brabant, Germany

Room 12
14.00–14.45 **MTE 7**
Clustered regularly interspaced short palindromic repeats (CRISPR)/Cas – making bespoke models
Frederic Flamant, France

Room 14
14.00–14.45 **MTE 8**
Abnormal thyroid function in children
Marek Niedziela, Poland

14.45–15.00 **Coffee break**

Room 8+9+10+11 (Main Auditorium)

15.00–17.00

Oral Session 8 (Clinical): Thyroid Cancer Therapeutics

Chairpersons: *Johannes Smit,* The Netherlands
Steen Bonnema, Denmark

15.00–15.15
LONG-TERM HEALTH-RELATED QUALITY OF LIFE, FATIGUE, AND ANXIETY AND DEPRESSION IN ADULT SURVIVORS OF PEDIATRIC DIFFERENTIATED THYROID CARCINOMA
Marloes Nies[1], Mariëlle S. Klein Hesselink[1], Gea A. Huizinga[2], Esther Sulkers[2], Adrienne H. Brouwers[3], Johannes G.M. Burgerhof[4], Eveline W.C.M. van Dam[5], Bas Havekes[6], Marry M. van den Heuvel-Eibrink[7], Eleonora P. M. Corssmit[8], Leontien C.M. Kremer[9], Romana T. Netea-Maier[10], Heleen J.H. van der Pal[11], Robin P. Peeters[12], John T.M. Plukker[13], Cécile M. Ronckers[9], Hanneke M. van Santen[14], Wim J.E. Tissing[15], Thera P. Links[1], Gianni Bocca[16]
[1]University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; [2]University of Groningen, University Medical Center Groningen, Wenckebach Institute, School of

Nursing and Health, Groningen, Netherlands; [3]University of Groningen, University Medical Center Groningen, Department of Nuclear Medicine and Molecular Imaging, Groningen, Netherlands; [4]University of Groningen, University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands; [5]Vu University Medical Center, Department of Internal Medicine, Amsterdam, Netherlands; [6]Maastricht University Medical Center, Department of Internal Medicine, Division of Endocrinology, Maastricht, Netherlands; [7]Erasmus Medical Center, Sophia Children's Hospital, Department of Pediatric Oncology, Rotterdam, Netherlands; [8]Leiden University Medical Center, Department of Internal Medicine, Division of Endocrinology, Leiden, Netherlands; [9]Academic Medical Center, Emma Children's Hospital, Department of Pediatric Oncology, Amsterdam, Netherlands; [10]Radboud University Medical Center, Division of Endocrinology, Nijmegen, Netherlands; [11]Academic Medical Center, Emma Children's Hospital, Department of Medical Oncology, Department of Pediatric Oncology, Amsterdam, Netherlands; [12]Erasmus Medical Center, Department of Internal Medicine, Rotterdam Thyroid Center, Rotterdam, Netherlands; [13]University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; [14]University Medical Center Utrecht, Wilhelmina Children's Hospital, Department of Pediatrics, Utrecht, Netherlands; [15]University of Groningen, Beatrix Children's Hospital, Department of Pediatric Oncology, Groningen, Netherlands; [16]University of Groningen, Beatrix Children's Hospital, Department of Pediatric Endocrinology, Groningen, Netherlands

15.15–15.30

REAL-LIFE PRACTICES IN THE INITIAL TREATMENT OF DTCS IN ITALY: AN ANALYSIS OF PROSPECTIVE DATA COLLECTED BY THE ITALIAN THYROID CANCER OBSERVATORY

Livia Lamartina[1], Giorgio Grani[1], Alfredo Pontecorvi[2], Celestino Pio Lombardi[2], Rocco Bellantone[2], Emanuela Arvat[3], Efisio Puxeddu[4], Maria Chiara Zatelli[5], Massimo Torlontano[6], Teresa Montesano[7], Gianluca Aimaretti[8], Fabio Monzani[9], Fabio Orlandi[10], Cecilia Francese[11], Paolo Limone[12], Giovanna Spiazzi[13], Laura Fugazzola[14], Ezio Ghigo[15], Marco Attard[16], Alessandro Antonelli[17], Giuseppe Lucisano[18], Antonio Nicolucci[18], Cosimo Durante[1], Sebastiano Filetti[1]

[1]Department of Internal Medicine and Medical Specialties, University of Rome Sapienza, Rome, Italy; [2]Division of Endocrinology, 'Agostino Gemelli' School of Medicine, Catholic University of the Sacred Heart, Rome, Italy; [3]School of Medicine, University of Turin, Turin, Italy; [4]Department of Medicine, University of Perugia, Perugia, Italy; [5]Section of Endocrinology and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy; [6]Department of Medical Science, Ospedale Casa Sollievo Della Sofferenza-Irccs, San Giovanni Rotondo (Foggia), Italy; [7]Department of Nuclear Medicine, University of Rome Sapienza, Rome, Italy; [8]Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale 'A. Avogadro', Novara, Italy; [9]Geriatrics Unit, Department of Clinical & Experimental Medicine, University of Pisa, Pisa, Italy; [10]Division of Internal Medicine, Department of Medical Sciences, Gradenigo Hospital, University of Turin, Turin, Italy; [11]Endocrinology Division, Salerno, Italy; [12]Division of Endocrinology, Diabetology and Metabolism, Mauriziano Umberto I Hospital, Turin, Italy; [13]Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Verona, Verona, Italy; [14]University of Milan, Milan, Italy; [15]Division of Endocrinology, Diabetology and Metabolism, Department of Medical Sciences, Molinette Hospital, A.O.U. Città Della Salute e Della Scienza di Torino, University of Turin, Turin, Italy; [16]Division of Endocrinology, Cervello Hospital, Palermo, Italy; [17]Department of Clinical and Experimental Medicine, University of Pisa, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [18]Center for Outcomes Research and Clinical Epidemiology, Pescara, Italy

15.30–15.45

DIASTOLIC DYSFUNCTION IS COMMON IN LONG-TERM SURVIVORS OF PEDIATRIC DIFFERENTIATED THYROID CARCINOMA

Marielle Klein Hesselink[1], Gianni Bocca[2], Yoran Hummel[3], Adrienne Brouwers[4], Johannes Burgerhof[5], Eveline van Dam[6], Jourik Gietema[7], Bas Havekes[8], Marry van den Heuvel-Eibrink[9], Eleonora Corssmit[10], Leontien Kremer[11], Romana Netea-Maier[12], Heleen van der Pal[13], Robin Peeters[14], John Plukker[15], Cecile Ronckers[16], Hanneke van Santen[17], Peter van der Meer[3], Thera Links[1], Wim Tissing[18]

[1]Department of Endocrinology, University Medical Center Groningen, Groningen, Netherlands; [2]Department of Pediatric Endocrinology, Beatrix Children's Hospital, University Medical Center Groningen, Groningen, Netherlands; [3]Department of Cardiology, University Medical Center Groningen, Groningen, Netherlands; [4]Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, Netherlands; [5]Department of Epidemiology, University Medical Center Groningen, Groningen, Netherlands; [6]Department of Internal Medicine, Vu University Medical Center, Amsterdam, Netherlands; [7]Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands; [8]Department of Internal Medicine, Division of Endocrinology, Maastricht University Medical Center, Maastricht, Netherlands; [9]Department of Pediatric Oncology, Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, Netherlands; [10]Department of Internal Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, Netherlands; [11]Department of Pediatric Oncology, Emma Children's Hospital, Academic Medical Center, Amsterdam, Netherlands; [12]Department of Internal Medicine, Division of Endocrinology, Radboud University Medical Center, Nijmegen, Netherlands; [13]Department of Pediatric Oncology, Emma Children's Hospital, Academic Medical Center, Department of Medical Oncology, Academic Medical Center, Amsterdam, Netherlands; [14]Department of Internal Medicine, Erasmus

Medical Center, Rotterdam Thyroid Center, Erasmus Medical Center, Rotterdam, Netherlands; [15]Department of Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; [16]Department of Pediatric Oncology, Emma Children's Hospital, Amsterdam, Netherlands; [17]Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, Netherlands; [18]Department of Pediatric Oncology, Beatrix Children's Hospital, University Medical Center Groningen, Groningen, Netherlands

15.45–16.00

PREDICTORS OF VANDETANIB RESPONSE IN THE LOCALLY ADVANCED OR METASTATIC MEDULLARY THYROID CANCER: A SINGLE CENTER EXPERIENCE

Laura Valerio[1], Valeria Bottici[2], Antonio Matrone[2], Alessia Tacito[2], Francesca Casella[2], Cristina Romei[2], Paolo Vitti[2], Rossella Elisei[2]
[1]Endocrine Unit, University of Pisa, Pisa, Italy; [2]Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

16.00–16.15

LONG-TERM SURGICAL RESULTS OF PATIENTS WITH LOCALLY ADVANCED PAPILLARY THYROID CANCER ONLY TO HAVE RECURRENT INFERIOR LARYNGEAL NERVE INVASION

Yuna Ogimi[1], Takashi Uruno[1], Kenichi Matsuzu[1], Tetsuyo Maeda[1], Chie Masaki[1], Tadatoshi Osaku[1], Junko Akaishi[1], Kiyomi Y. Hames[1], Chisato Tomoda[1], Akifumi Suzuki[1], Keiko Ohkuwa[1], Hiroshi Shibuya[1], Wataru Kitagawa[1], Mitsuji Nagahama[1], Kiminori Sugino[1], Koichi Ito[1]
[1]Ito Hospital, Tokyo, Japan

16.15–16.30

INHIBITION OF ERK DIMERIZATION BLOCKS THYROID TUMOR PROGRESSION

Miguel Zaballos[1], Adrián Acuña-Ruiz[1], Garcilaso Riesco-Eizaguirre[2], Piero Crespo[3], Pilar Santisteban[1]
[1]Instituto de Investigaciones Biomédicas 'Alberto Sols', Madrid, Spain; [2]Hospital Universitario de Móstoles, Madrid, Spain; [3]Instituto de Biomedicina Y Biotecnología de Cantabria, Santander, Spain

16.30–16.45

MULTIKINASE INHIBITOR SP EFFECTS ON ALTERED PROLIFERATIVE PATHWAYS IN THYROID CANCER STEM-LIKE CELLS

Elisa Stellaria Grassi[1], Valentina Cirello[2], Carla Colombo[3], Valeria Vezzoli[1], Leonardo Vicentini[4], Luca Persani[5], Laura Fugazzola[6]
[1]Laboratory of Endocrine and Metabolic Research, Irccs Istituto Auxologico Italiano, Milan, Italy; [2]Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [3]Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Department of Clinical Sciences and Community Health, University of Milan, Italy; [4]Endocrine Surgery Unit, Fondazione Irccs Ca' Granda, Milan, Milan, Italy; [5]Dept. of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases and Laboratory of Endocrine and Metabolic Research, Irccs Istituto Auxologico Italiano, Milan, Italy; [6]Endocrine Unit, Fondazione Irccs Ca' Granda, Milan, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

16.45–17.00

GLUCOSE-COATED SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES PREPARED BY METAL VAPOUR SYNTHESIS ARE ELECTIVELY INTERNALIZED IN THYROID TUMORS LINES EXPRESSING GLUT1 TRANSPORTER

Daniele Barbaro[1], Lorenzo Di Bari[2], Valentina Gandin[3], Claudio Evangelisti[4], Giovanni Vitulli[5], Elenora Schiavi[5], Cristina Marzano[6], Anna M. Ferretti[7], Piero Salvadori[5]
[1]Spedali Riuniti di Livorno, Endocrinology, Livorno, Italy; [2]Department of Chemistry University of Pisa, Pisa, Italy; [3]Department of Pharmaceutical Science University of Padova, Padova, Italy; [4]Institute of Molecular Science and Technology National Research Council, Milano, Italy; [5]Erre Due Spa, Livorno, Italy; [6]Department of Pharmaceutical Pharmacological Science University of Padova, Padova, Italy; [7]Institute of Molecular Science and Technology National Research Council, Milano, Italy

Room 13+15

15.00–17.00

Oral Session 9 (Basic): T3 Signalling in Brain and Periphery

Chairpersons: *Lutz Schomburg,* Germany
Hans Perrild, Denmark

15.00–15.15

IMPAIRED MATERNAL THYROID HORMONE RECEPTOR A1 SIGNALING PROGRAMS OFFSPRING METABOLISM

Rebecca Oelkrug[1], Milica Vujovic[2], Lisbeth Harder[3], Beate Herrmann[4], Sogol Gachkar[1], Jens Mittag[5]
[1]Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany; [2]Department of Cell & Molecular Biology, Karolinska Institutet, Stockholm, Sweden; [3]Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany; [4]University of Lübeck, Center of Brain, Behavior and Metabolism, Lübeck, Germany; [5]Universität zu Lübeck, Center of Brain, Behavior and Metabolism, Lübeck, Germany

15.15–15.30

MIXTURES OF XENOBIOTICS FOUND IN HUMAN AMNIOTIC FLUID MODIFY EMBRYONIC THYROID HORMONE SIGNALLING AND BRAIN DEVELOPMENT

Jean-Baptiste Fini[1], Bilal Mughal[1], Sébastien Le Mével[1], Michelle Leemans[1], Mélodie Lettmann[1], Petra Spirhanzlova[1], Pierre Affaticati[2], Jean-Stéphane Joly[2], Barbara Demeneix[3]
[1]Umr Cnrs 7221, Muséum National D'histoire Naturelle, Paris, France; [2]Cnrs/Tefor, Gif Sur Yvette, France; [3]Umr Cnrs 7221, Département Régulations, Développement et Diversité Moléculaire, Muséum National D'histoire Naturelle, Evolutions des Régulations Endocriniennes, Paris, France

15.30–15.45

EPITHELIAL BMP-SMAD1/5 SIGNALING AND ENDOTHELIAL CELLS ARE REQUIRED FOR THYROID FOLLICLE DEVELOPMENT

Mylah Villacorte[1], Anne-Sophie Delmarcelle[1], Manon Lernoux[1], Mahé Bouquet[1], Pascale Lemoine[1], Jennifer Bolsee[1], Lieve Umans[2], Susana Chuva de Sousa Lopez[3], Patrick Van Der Smissen[1], Takako Sasaki[4], Guido Bommer[1], Patrick Henriet[1], Samuel Refetoff[5], Frédéric Lemaigre[1], An Zwijsen[2], Pierre Courtoy[1], Christophe Pierreux[6]
[1]De Duve Institute, Brussels, Belgium; [2]Vib-Kul, Leuven, Belgium; [3]Lumc, Leiden, Netherlands; [4]Oita University, Oita, Japan; [5]Chicago University, Chicago, Ill., USA; [6]De Duve Institute, Université Catholique de Louvain, Bruxelles, Belgium

15.45–16.00

CENTRAL HYPOTHYROIDISM AND BIALLELIC DEFECT NEAR THE D/ERY MOTIF OF THE TRHR GENE

Marta Garcia[1], Jesús González de Buitrago[2], Leonardo Pardo[3], Patricia M. Hinkle[4], Jose Moreno[5]
[1]Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Ingemm), La Paz University Hospital, Autonomous University of Madrid, Madrid, Spain; [2]Department of Pediatrics, San Pedro de Alcántara Hospital, Cáceres, Spain; [3]Computational Medicine Laboratory, Biostatistics Unit, Faculty of Medicine, Autonomous University of Barcelona, Barcelona, Spain; [4]Department of Pharmacology and Physiology, University of Rochester Medical Center, Rochester, Minn., USA; [5]Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Ingemm), La Paz University Hospital, Autonomous University of Madrid, Madrid, Spain

16.00–16.15

CENTRAL ROLE FOR THYROID HORMONE SIGNALING IN PERIPHERAL METABOLIC PLASTICITY

Stephanie Decherf[1], Isabelle Seugnet[2], Jeremy Terrien[3], Emmely De Vries[4], Anita Boelen[5], Fekete Csaba[6], Balazs Gereben[7], Ducos Bertrand[8], Serge Luquet[9], Marie-Stéphanie Clerget-Froidevaux[10], Barbara Demeneix[11]
[1]Muséum National D'histoire Naturelle, Umr Cnrs 7221, Paris, France; [2]Umr 7221 'Evolution of Endocrine Regulations', National Museum of Natural History, Paris, France; [3]Team Bioadapt Umr Cnrs/Mnhn 7179, Brunoy, France; [4]Department of Clinical Chemistry, Laboratory of Endocrinology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; [5]Academic Medical Centre, Amsterdam, Netherlands; [6]Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary; [7]Institute of Experimental Medicine, Lab Molecular Cell Metabolism, Budapest, Hungary; [8]Genomic Paris Centre, Institut de Biologie de L'ecole Normale Supérieure (Ibens), Paris, France; [9]Umr 8251 Team Coffee – Université Paris Diderot – Paris 7, U.F.R. Sciences du Vivant Bâtiment Buffon, Paris Cedex 13, France; [10]Mnhn/Cnrs Umr7221, Paris, France; [11]Umr Cnrs 7221, Département Régulations, Développement et Diversité Moléculaire, Muséum National D'histoire Naturelle, Evolutions des Régulations Endocriniennes, Paris, France

16.15–16.30

THYROID HORMONE T3 MAY PROTECT FROM FASTING INDUCED SKELETAL MUSCLE ATROPHY

Cecilia Verga Falzacappa[1], Claudia Mangialardo[2], Camilla Virili[3], Maria Giulia Santaguida[4], Viviana Moresi[5], Marco Centanni[6]
[1]Medical Surgical Sciences and Biotechnologies Department,Sapienza, University of Rome, Pasteur Institute, Italy, Rome, Italy; [2]Pasteur Institute, Italy, Medical Surgical Sciences and Biotechnologies, Sapienza, Rome, Italy; [3]Dept of Experimental Medicine 'Sapienza' University of Rome, Latina, Italy, Dept Medico-Surgical Sciences and Biotechnologies, Rome, Italy; [4]Medico-Surgical Sciences and Biotechnologies Department, Medico-Surgical Sciences and Biotechnologies, Latina, Italy; [5]Saimlal Department, Sapienza, Rome, Italy; [6]Sapienza University of Rome, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy

16.30–16.45

THE GENOMIC RESPONSE OF THE MOUSE THYROID TO IODINE OVERLOAD, AND THE ROLE OF THE NRF2 ANTIOXIDANT SYSTEM

Panos Ziros[1], Dionysios Chartoumpekis[2], Ioannis Habeos[3], Adam Smith[4], Ana Claudia Marques[4], Gerasimos Sykiotis[1]
[1]Lausanne University Hospital, Lausanne, Switzerland; [2]University of Pittsburgh Medical Center, Pittsburgh, Pa., USA; [3]University of Patras Medical School, Patras, Greece; [4]University of Lausanne, Lausanne, Switzerland

16.45–17.00

3-IODOTHYRONAMINE AND TRACE AMINE-ASSOCIATED RECEPTOR 1 ARE INVOLVED IN THE EXPRESSION OF LONG-TERM POTENTIATION IN MOUSE ENTORHINAL CORTEX

Alice Accorroni[1], Chiara Criscuolo[2], Martina Sabatini[3], Riccardo Donzelli[4], Alessandro Saba[5], Nicola Origlia[2], Riccardo Zucchi[5]
[1]Scuola Superiore Sant'Anna, Pisa, Italy; [2]Cnr Neuroscience Institute, Pisa, Italy; [3]Dept. of Pathology, University of Pisa, Pisa, Italy; [4]University of Pisa, Department of Pathology, Pisa, Italy; [5]University of Pisa, Pisa, Italy

Room 8+9+10+11 (Main Auditorium)
17.10–17.50

ETA Pinchera Prize Lecture

Chairpersons: *Furio Pacini,* Italy
Colin Dayan, UK

Room 8+9+10+11 (Main Auditorium)
18.00–19.15

General Assembly

20.00

ETA – Network Dinner

(see p. 194 for details)

Room 8+9+10+11 (Main Auditorium)

07.30–08.30

Short-Call Abstracts

Chairperson: *Colin Dayan,* UK

Room 8+9+10+11 (Main Auditorium)

08.30–10.30

Oral Session 10: Young Investigators Session / Clinical + Translational

Chairpersons: *Luigi Bartalena,* Italy
Tomasz Bednarczuk, Poland

08.30–08.45

5 YEARS FOLLOW UP OF THYROGLOBULIN (TG), THYROGLOBULIN ANTIBODIES (TGAB) AND NECK ULTRASOUND (NUS) IN PATIENTS WITH PAPILLARY THYROID MICROCARCINOMA (MPTC) TREATED WITH TOTAL THYROIDECTOMY BUT NOT ABLATED WITH 131I

Antonio Matrone[1], *Alessio Faranda*[2], *Eleonora Molinaro*[3], *Laura Agate*[3], *David Viola*[3], *Laura Valerio*[3], *Carlotta Giani*[3], *Liborio Torregrossa*[4], *Paolo Piaggi*[5], *Paolo Vitti*[3], *Rossella Elisei*[3]
[1]University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy, Department of Endocrinology, Pisa, Italy; [2]University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy; [3]University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy; [4]Department of Surgical Pathology, Medical, Molecular and Critical Area – Unit of Pathological Anatomy, Pisa, Italy; [5]Phoenix Epidemiology and Clinical Research Branch National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health, Phoenix, Ariz., USA

08.45–09.00

COMPARISION OF HEMITHYROIDECTOMY AND TOTAL THYROIDECTOMY FOR PATIENTS WITH PAPILLARY THYROID MICROCARCINOMA: A RETROSPECTIVE MATCHED COHORT STUDY

Hyemi Kwon[1], *Min Ji Jeon*[1], *Won Gu Kim*[1], *Mijin Kim*[1], *Suyeon Park*[1], *Dong Eun Song*[1], *Tae-Yon Sung*[1], *Jong Ho Yoon*[1], *Suck Joon Hong*[1], *Tae Yong Kim*[1], *Young Kee Shong*[1], *Won Bae Kim*[1]
[1]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South

09.00–09.15

STIMULATORY TSH-RECEPTOR ANTIBODIES INDUCE OXIDATIVE STRESS IN THYROCYTES AND PERIPHERAL BLOOD

Tanja Diana[1], *Andreas Daiber*[2], *Matthias Oelze*[2], *Paul Stamm*[2], *Michael Kanitz*[1], *Susanne Neumann*[3], *George J. Kahaly*[1]
[1]Johannes Gutenberg University Medical Center, Mainz, Germany; [2]Molecular Cardiology, Johannes Gutenberg University Medical Center, Mainz, Germany; [3]NIH, NIDDK, USA

09.15–09.30

MUTATIONS IN TBL1X AS A NOVEL CAUSE OF FAMILIAL CENTRAL HYPOTHYROIDISM

Charlotte Heinen[1], *Monique Losekoot*[2], *Yu Sun*[2], *Peter Watson*[3], *Louise Fairall*[3], *Sjoerd Joustra*[2], *Nitash Zwaveling-Soonawala*[1], *Wilma Oostdijk*[2], *Erica van den Akker*[4], *Mariëlle Alders*[1], *Gijs Santen*[2], *Rick van Rijn*[1], *Wouter Dreschler*[1], *Olga Surovtseva*[1], *Nienke Biermasz*[2], *Raoul Hennekam*[1], *Jan Maarten Wit*[2], *John Schwabe*[3], *Anita Boelen*[1], *Paul van Trotsenburg*[1], *Eric Fliers*[5]
[1]Academic Medical Centre, Amsterdam, Netherlands; [2]Leiden University Medical Center, Leiden, Netherlands; [3]Henry Wellcome Laboratories of Structural Biology, University of Leicester, Leicester, UK; [4]Erasmus MC, Rotterdam, Netherlands; [5]Amc, University of Amsterdam, Amsterdam, Netherlands

09.30–09.45

THYROID FUNCTION TESTING IN BIOBANK SERA FROM 9,768 DANISH PREGNANT WOMEN SHOWS UNIDENTIFIED THYROID DYSFUNCTION IN UP TO 50% – BOTH IN WOMEN WITH KNOWN THYROID DISEASE AND IN WOMEN DIAGNOSED WITH THYROID DISEASE AFTER THE PREGNANCY

Stine Linding Andersen[1], *Jørn Olsen*[2], *Peter Laurberg*[3]
[1]Aalborg University Hospital, Aalborg, Denmark; [2]Aarhus University Hospital, Aarhus University, Aarhus, Denmark; [3]Aalborg University Hospital, Aalborg University, Aalborg, Denmark

09.45–10.00

TPO-ANTIBODY POSITIVE WOMEN HAVE AN IMPAIRED RESPONSE TO HCG WHICH UNDERLIES THEIR HIGHER RISK OF PREMATURE DELIVERY

Tim Korevaar[1], Victor Pop[2], Layal Chaker[3], Yolanda de Rijke[4], Maarten Broeren[5], Vincent Jaddoe[4], Marco Medici[6], Eric Steegers[7], Theo Visser[8], Henning Tiemeier[4], Robin Peeters[4]

[1]Erasmus MC, Rotterdam, The Netherlands, Endocrinology, Rotterdam, Netherlands; [2]University of Tilburg, Tilburg, Netherlands; [3]Erasmus Medical Center, Rotterdam, Netherlands; [4]Erasmus University Medical Center, Rotterdam, Netherlands; [5]Máxima Medisch Centrum, Veldhoven, Netherlands; [6]Erasmus Medical Center, Endocrinology, Rotterdam, Netherlands; [7]Erasmus University MC, Rotterdam, Netherlands; [8]Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands

10.00–10.15

IODINE FORTIFICATION HAS REDUCED OVERT THYROTOXICOSIS INCIDENCE IN DENMARK WITH 40 %: A 16-YEAR PROSPECTIVE POPULATION STUDY

Mads Petersen[1], Inge Bülow Pedersen[1], Allan Carlé[1], Nils Knudsen[2], Stine Linding Andersen[3], Lars Ovesen[4], Lone Banke Rasmussen[2], Torben Jørgensen[5], Betina Heinsbæk Thuesen[5], Hans Perrild[2], Peter Laurberg[1]

[1]Department of Endocrinology, Aalborg University Hospital, Aalborg, Denmark; [2]Department of Endocrinology, Bispebjerg Hospital, Copenhagen, Denmark; [3]Department of Endocrinology & Department of Clinical Chemistry, Aalborg University Hospital, Aalborg, Denmark; [4]Department of Gastroenterology, Slagelse Hospital, Aalborg, Denmark; [5]Reasearch Centre for Prevention and Health, Glostrup Hospital, Copenhagen, Denmark

10.15–10.30

THE EXCESS MORTALITY IN GRAVES' ORBITOPATHY, COMPARED TO THE BACKGROUND POPULATION, IS PRIMARILY DUE TO HIGHER MORTALITY IN MALES THAN IN FEMALES

Charlotte Andersson[1], Thomas Brix[2], Laszlo Hegedüs[1]

[1]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; [2]Department of Endocirnology, Odense University Hospital, Odense C, Denmark

Room 13+15

08.30–10.30

Oral Session 11: Young Investigators Session / Basic

Chairpersons: *Luca Persani,* Italy
Pilar Santisteban, Spain

08.30–08.45

ELUCIDATING THE THERAPEUTIC POTENTIAL OF THYROID HORMONE ANALOGS IN MCT8 DEFICIENCY

Jiesi Chen[1], Eva Salveridou[2], Heike Heuer[3]

[1]Leibniz Institute for Environmental Medicine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany; [2]Düsseldorf, Germany; [3]Leibniz Institute for Environmental Medcine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany

08.45–09.00

A FUNCTIONAL ROLE FOR THE DEIODINASE ENZYMES IN NEUTROPHILS AND MACROPHAGES

Anne van der Spek[1], Aldona Karaczyn[2], Elena Martinez[2], Olga Surovtseva[3], Bernadine Snell[1], Eric Fliers[4], Arturo Hernandez[2], Anita Boelen[3]

[1]Academic Medical Center, Amsterdam, Netherlands; [2]Maine Medical Research Center, Scarborough, Maine, USA; [3]Academic Medical Centre, Amsterdam, Netherlands; [4]Amc, University of Amsterdam, Amsterdam, Netherlands

09.00–09.15

ROLE OF CAR AND MTOR IN THE REGULATION OF TYPE 3 DEIODINASE DURING FASTING

Emmely de Vries[1], Marte Molenaars[1], Olga Surovtseva[2], Evita Belegri[1], Albert Van Wijk[3], Marinus Maas[3], Eric Fliers[1], Anita Boelen[1]

[1]Academic Medical Center, Departement of Endocrinology and Metabolism, Amsterdam, Netherlands; [2]Academic Medical Centre, Amsterdam, Netherlands; [3]Academic Medical Center, Departement of Experimental Surgery, Amsterdam, Netherlands

09.15–09.30

A SONIC HEDGEHOG-GLIS3 PATHWAY IS INVOLVED IN THE SPECIFICATION OF THE THYROID GLAND IN ZEBRAFISH

Federica Marelli[1], Giuditta Rurale[2], Federica Buna[3], Franco Cotelli[4], Luca Persani[5]

[1]Irccs Istituto Auxologico Italiano, Endocrinology and Metabolic Disorder, Milan, Italy; [2]Università Degli Studi di Milano, Dipartimento di Biotecnologie Mediche e Medicina Translazionale, Milan, Italy; [3]Irccs Istituto Auxologico Italiano, Milan, Italy; [4]Università degli Studi di Milano, Dipartimento di Bioscienze, Milan, Italy; [5]University of Milan, Ospedale San Luca, Irccs Istituto Auxologico Italiano, Milan, Italy

09.30–09.45

IDENTIFICATION OF A PI3K REGULATED FEEDBACK WITH A DOUBLE-NEGATIVE LOOP BETWEEN MIR30A AND LIN28B CONTROLLING THYROID CANCER PROGRESSION

León Wert-Lamas[1], Garcilaso Riesco-Eizaguirre[2], Richard Gregory[3], Pilar Santisteban[4]

[1]Iib Alberto Sols, Madrid, Spain; [2]Móstoles Universitary Hospital, Móstoles, Spain; [3]Boston Children's Hospital, Dept of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, USA; [4]Biomedical Research Institute, Biomedical Research Institute, Madrid, Spain

09.45–10.00

INCREASED GLOBAL DNA HYPOMETHYLATION IN METASTATIC AND DEDIFFERENTIATED THYROID CANCER

Esther Klein Hesselink[1], Carles Zafón[2], Nuria Villalmanzo[3], Carmela Iglesias[4], Bettien van Hemel[5], Mariëlle Klein Hesselink[1], Dídac Mauricio[6], Manel Puig-Domingo[7], Jordi Reverter[6], Garcilaso Riesco-Eizaguirre[8], Mercedes Robledo[9], Thera Links[1], Mireia Jordà[10]

[1]University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; [2]Vall D'hebron University Hospital, Department of Endocrinology, Barcelona, Spain; [3]Germans Trias I Pujol Health Sciences Research Institute (Igtp), Badalona, Barcelona, Spain; [4]Vall D'hebron Universtiy Hospital, Department of Pathology, Barcelona, Spain; [5]University of Groningen, University Medical Center Groningen, Department of Pathology, Groningen, Netherlands; [6]Germans Trias I Pujol University Hospital, Department of Endocrinology and Nutrition, Badalona, Barcelona, Spain; [7]Germans Trias I Pujol University Hospital, Department of Endocrinology and Nutrition, Badalona, Barcelona, Spain; [8]University Hospital of Móstoles, Endocrinology and Nutrition Service, Madrid, Spain; [9]Hereditary Endocrine Cancer Group, Spanish National Cancer Research Centre (Cnio), Madrid, Spain; [10]Germans Trias I Pujol Health Sciences Research Institute (Igtp), and Institute of Predictive and Personalized Medicine of Cancer (Imppc), Badalona, Barcelona, Spain

10.00–10.15

VARIABLY DEFECTIVE TRANSCRIPTIONAL ACTIVITY OF T3 RECEPTOR TRA1 MUTANTS ON DIFFERENT THYROID RESPONSE ELEMENTS

Karn Wejaphikul[1], Anja van Gucht[2], W. Edward Visser[3], V. Krishna Chatterjee[4], Theo Visser[5], Robin Peeters[6], Marcel Meima[1]

[1]Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; [2]Erasmus Medical Center, Thyroid Laboratory, Department of Internal Medicine, Rotterdam, Netherlands; [3]Erasmus Medical Center, Rotterdam, Netherlands; [4]Metabolic Research Laboratories, Addenbrooke's Hospital, Cambridge, UK; [5]Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; [6]Erasmus University Medical Center, Rotterdam, Netherlands

10.15–10.30

AUTOPHAGY ACTIVATING COMPOUNDS FACILITATE REDIFFERENTIATION AND CELL CYCLE ARREST OF NON-MEDULLARY THYROID CANCER THROUGH INTRACELLULAR CA2+, FOS AND P21 DEPENDENT PATHWAYS

Marika Tesselaar[1], Thomas Crezee[1], Danny Gerrits[2], Otto Boerman[2], Henk Stunnenberg[3], Mihai Gheorghe Netea[4], Johannes Smit[5], Romana Teodora Netea-Maier[6], Theo Plantinga[1]

[1]Radboud University Medical Center, Department of Pathology, Nijmegen, Netherlands; [2]Radboud University Medical Center, Department of Nuclear Medicine, Nijmegen, Netherlands; [3]Radboud University Medical Center, Department of Molecular Biology, Nijmegen, Netherlands; [4]Radboud University Medical Center, Department of Internal Medicine and Radboud Center for Infectious Diseases, Nijmegen, Netherlands; [5]Radboud University Nijmegen Medical Centre, 463 Internal Medicine, Nijmegen, Netherlands; [6]Radboud University Medical Centre, Dept. of Endocrinology, Nijmegen, Netherlands

10.30–11.00 **Coffee break and lunch box**

Room 8+9+10+11 (Main Auditorium)

11.00–13.00

Oral Session 12 (Clinical): Clinical Aspects of Pregnancy, Childhood and Brain

Chairpersons: *Kris Poppe,* Belgium
Stine Linding Andersen, Denmark

11.00–11.15

TSH REFERENCE LIMITS ARE HIGHLY DEPENDENT ON THE WEEK OF GESTATION IN THE FIRST TRIMESTER OF PREGNANCY: A STUDY OF 6,671 HEALTHY PARTICIPANTS IN THE DANISH NATIONAL BIRTH COHORT

Peter Laurberg[†, 1], Stine Linding Andersen[2], Peter Hindersson[3], Ellen Nohr[4], Jørn Olsen[5]

[1]Aalborg University Hospital, Aalborg University, Aalborg, Denmark; [2]Departments of Clinical Biochemistry and Endocrinology, Aalborg University Hospital, Aalborg, Denmark; [3]Department of Clinical Biochemistry, North Jutland Regional Hospital, Hjørring, Denmark; [4]Research Unit for Gynecology and Obstetrics, University of Southern Denmark, Odense, Denmark; [5]Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

11.15–11.30

THYROID FUNCTION AND BRAIN IMAGING

Layal Chaker[1], Lotte Cremers[2], Albert Hofman[3], Mohammad Arfan Ikram[4], Meike Vernooij[2], Robin Peeters[5]

[1]Erasmus Medical Center, Rotterdam, Netherlands; [2]Erasmus University Medical Center, Rotterdam, Netherlands; [3]Erasmus University Medical Center, Rotterdam, The Netherlands, Harvard T.H. Chan School of Public Health, Boston, Mass., USA; [4]Erasmus MC, Rotterdam, Netherlands; [5]Erasmus University Medical Center, Rotterdam, The Netherlands,

11.30–11.45

EFFECT OF THYROID HORMONES ON COGNITION AND BRAIN

Anna Göbel[1], Marcus Heldmann[2], Martin Göttlich[2], Georg Brabant[3], Anna-Luise Dirk[3], Relana Nieberding[3], Rene Goerges[3], Thomas Münte[4]

[1]UKSH Lübeck, Lübeck, Germany; [2]UKSH Lübeck, Cbbm, Lübeck, Germany; [3]UKSH Lübeck, Medizinische Klinik 1, Lübeck, Germany; [4]UKSH Lübeck, Klinik für Neurologie, Lübeck, Germany

11.45–12.00

MATERNAL HYPOTHYROIDISM CONTRIBUTES TO ATYPICAL HIPPOCAMPAL FUNCTION IN HUMAN OFFSPRING

Joanne Rovet[1], Victoria McLelland[2]

[1]The Hospital for Sick Children, University of Toronto, Toronto, Ont., Canada; [2]The Hospital for Sick Children, Toronto, Ont., Canada

12.00–12.15

IODINE STATUS AND EFFECTS OF SUPPLEMENTATION WITH 150 MG/DAY IODINE DURING PREGNANCY IN SWEDEN: A RANDOMIZED PLACEBO-CONTROLLED TRIAL

Sofia Manousou[1], Robert Eggertsen[2], Lena Hulthen[3], Helena Filipsson Nyström[4]

[1]Department of Medicine at Kungälv Hospital, Institute of Medicine Sahlgrenska Academy, Gothenburg, Sweden; [2]Mölnlycke Health Care Center, Mölnlycke, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Gothenburg, Sweden; [3]Department of Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [4]Department of Endocrinology, University of Gothenburg, Göteborg, Sweden

12.15–12.30

BARIATRIC SURGERY REDUCES URINARY IODINE LEVELS DESPITE NORMAL IODINE INTAKE – A PROSPECTIVE 10-YEAR REPORT FROM THE SWEDISH OBESITY SUBJECT (SOS) STUDY

Sofia Manousou[1], Lena Carlsson[2], Robert Eggertsen[3], Lena Hulthén[4], Peter Jakobsson[2], Lars Sjöström[2], Per-Arne Svensson[2], Helena Filipsson Nyström[5]

[1]Department of Medicine at Kungälv Hospital, Institute of Medicine Sahlgrenska Academy, Gothenburg, Sweden; [2]Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [3]Mölnlycke Health Care Center, Mölnlycke, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [4]Department of Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [5]Department of Endocrinology, Sahlgrenska University Hospital, Göteborg, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Borås, Sweden

12.30–12.45

RETINAL PHOTORECEPTOR FUNCTIONS ARE COMPROMISED IN PATIENTS WITH RESISTANCE TO THYROID HORMONE SYNDROME (RTHB)

Irene Campi[1], Gabriella Cammarata[2], Stefania Bianchi Marzoli[3], Diletta Santarsiero[2], Davide Dazzi[4], Alessandra Bottari De Castello[5], Elena Giuliana Taroni[5], Francesco Viola[6], Luca Persani[7], Paolo Beck-Peccoz[8]

[1]Fondazione Irccs Ca' Granda, Endocrine Unit, Milan, Italy; [2]Neuro-Ophthalmology Service and Electrophysiology Lab, Irccs Istituto Auxologico Italiano, Milan, Italy; [3]Chief, Neuro-Ophthalmology Service and Electrophysiology Lab, Irccs Istituto Auxologico Italiano, Milan, Italy; [4]Ospedale Vaio Fidenza, Division of Internal Medicine, Fidenza, Italy; [5]Fondazione Irccs Ca' Granda, Ophtalmology Unit, Milan, Italy; [6]University of Milan and Fondazione Irccs Ca' Granda, Ophtalmology Unit, Milan, Italy; [7]University of Milan, Ospedale San Luca, Irccs Istituto Auxologico Italiano, Milan, Italy; [8]Department of Medical Sciences, Fondazione Irccs Cà Granda Policlinico, Milan, Italy

12.45–13.00

THYROID STIMULATING HORMONE IS ASSOCIATED WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN GERMAN CHILDREN

Diana Albrecht[1], Till Ittermann[2], Michael Thamm[3], Henry Völzke[4]

[1]University Medicine Greifswald, Institute for Community Medicine, Greifswald, Germany; [2]University Medicine Greifswald, Greifswald, Germany; [3]Robert Koch-Institut, Berlin, Germany; [4]Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany

Room 13+15

11.00–13.00

Oral Session 13 (Basic): Basic Mechanisms in Graves' Disease

Chairpersons: *Stefano Mariotti,* Italy
Laszlo Hegedüs, Denmark

11.00–11.15
OXIDATIVE STRESS IN SKIN ADIPOCYTES FROM GRAVES' PATIENTS
Marie-Christine Many[1], Virginie Joris[2], Marique Lancelot[1], Elliott Van Regemorter[3], Christine de Ville de Goyet[1], Marc de Bournonville[1], Antonella Boschi[4], Michel Mourad[5], Chantal Daumerie[5], Julie Craps[1]
[1]Ss/Mede/Irec/Ucl, Bruxelles, Belgium; [2]Ucl-Irec-Fath, Brussels, Belgium; [3]Ucl, Brussels, Belgium; [4]Cliniques Universitaires Saint-Luc, Ophtalmologie, Bruxelles, Belgium; [5]Cliniques Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium

11.15–11.30
INCREASE OF NOX-4, VEGF AND GLUT-1 IN GRAVES' DISEASE
Julie Craps[1], Virginie Joris[2], Michael Hepp[1], Lida Papasokrati[1], Alexis Werion[1], Christine de Ville de Goyet[1], Marc de Bournonville[1], Chantal Daumerie[3], Michel Mourad[3], Marie-Christine Many[1]
[1]Ss/Mede/Irec/Ucl, Bruxelles, Belgium; [2]Ucl-Irec-Fath, Brussels, Belgium; [3]Cliniques Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium

11.30–11.45
CHARACTERISTICS OF HYALURONAN AND PAI-1 EXPRESSION IN CULTURES OF ORBITAL FIBROBLASTS
Erika Galgoczi[1], Florence Jeney[1], Annamaria Gazdag[1], Annamaria Erdei[1], Mónika Katkó[1], Domonkos M. Nagy[1], Bernadett Ujhelyi[2], Zita Steiber[2], Ferenc Gyory[3], Eszter Berta[1], Endre Nagy V.[1]
[1]Division of Endocrinology, Department of Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary; [2]Department of Ophthalmology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary; [3]Department of Surgery, Faculty of Medicine, University of Debrecen, Debrecen, Hungary

11.45–12.00
IDENTIFICATION OF A NEW HIGHLY TSH-RECEPTOR-SELECTIVE SMALL MOLECULE INHIBITOR
Inna Hoyer[1], Patrick Marcinkowski[1], Edgar Specker[1], Jens Furkert[1], Marc Nazaré[1], Jens-Peter von Kries[1], Claudia Rutz[1], Ralf Schülein[1], Gerd Krause[1]
[1]Leibniz-Institut für Molekulare Pharmakologie Berlin, Berlin, Germany

12.00–12.15
THE EXPRESSION OF NEONATAL FC RECEPTOR IN THYROCYTES OF HASHIMOTO'S THYROIDITIS
Yang Zhang[1], Chenxu Zhao[2], Ying Gao[2], Lanlan Zhao[3], Suxia Wang[2], Hong Zhang[2], Guizhi Lu[4], Yanming Gao[2], Xiaohui Guo[4]
[1]Peking University First Hospital, Peking, China; [2]Peking University First Hospital, Beijing, China; [3]Civil Aviation General Hospital, Beijing, China; [4]Perking University First Hospital, Beijing, China

12.15–12.30
EFFECTS OF OXIDATIVE STRESS ON SIRT-1, HIF-1A AND GLUT-1 IN HASHIMOTO'S THYROIDITIS
Michael Hepp[1], Virginie Joris[2], Alexis Werion[1], Christine de Ville de Goyet[1], Chantal Daumerie[3], Michel Mourad[3], Marie-Christine Many[1], Julie Craps[1]
[1]Ss/Mede/Irec/Ucl, Bruxelles, Belgium; [2]Ucl-Irec-Fath, Brussels, Belgium; [3]Cliniques Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium

12.30–12.45
HYPOXIA-DEPENDENT HIF-1 ACTIVATION IMPACTS ON TISSUE REMODELING IN GRAVES' ORBITOPATHY
Gina-Eva Görtz[1], Mareike Horstmann[1], Buena Delos Reyes[1], Joachim Fandrey[2], Anja Eckstein[3], Utta Berchner-Pfannschmidt[1]
[1]University Hospital Essen, Essen, Germany; [2]University Hospital Essen, Essen, Germany; [3]Universität Essen, Essen, Germany

12.45–13.00
ORBITAL FIBROBLASTS FROM A MURINE MODEL OF GRAVES' ORBITOPATHY SHOW A UNIQUE PHENOTYPE PROMOTING ADIPOGENESIS AND HYALURONAN SECRETION
Gina-Eva Görtz[1], Moshkelgosha Sajad[1], Christoph Jesenek[1], Mareike Horstmann[1], Banga Paul[1], Anja Eckstein[2], Utta Berchner-Pfannschmidt[1]
[1]University Hospital Essen, Essen, Germany; [2]Universität Essen, Essen, Germany

Room 8+9+10+11 (Main Auditorium)

13.10–14.40

Symposium 5 (Translational): Genomic Landscape of Papillary Thyroid Cancer

Chairpersons: *Ralf Paschke,* Canada
Ulla Feldt-Rasmussen, Denmark

13.10–13.40 Molecular fingerprints in thyroid pathology
Barbara Jarzab, Poland

13.40–14.10 Linking the genomic atlas to pathology
Manuel Sobrinho Simões, Portugal

14.10–14.40 Potential clinical Implications of genomic insights TH and sensory development
Rossella Elisei, Italy

Room 13+15

13.10–14.40

Symposium 6 (Basic): Thyroid Hormones (TH) and Development

Chairpersons: *Veerle Darras,* Belgium
Jens Mittag, Germany

13.10–13.40	TH and bone development *John Logan*, UK
13.40–14.10	TH and brain development *Pieter Vancamp*, Belgium
14.10–14.40	TH and sensory development *Douglas Forrest*, USA

Room 8+9+10+11 (Main Auditorium)

14.40–15.00

Prize Ceremony and Closure

Chairpersons: *Pilar Santisteban,* Spain
Colin Dayan, UK

European
Thyroid Journal

Saturday, 3rd September 2016

Room 1

16.00–17.00

Poster Session P1

01 Hyperthyroidism

Chairperson: *Maria Alevizaki,* Greece

P1–01–01 **EFFECT OF SELENIUM ON HYPERTHYROIDISM IN PATIENTS WITH GRAVES' DISEASE TREATED WITH METHIMAZOLE: RESULTS OF A RANDOMIZED CLINICAL TRIAL**

Ilaria Ionni[1], *Marenza Leo*[1], *Paola Premoli*[2], *Giovanna Rotondo Dottore*[1], *Marialuisa Di Cera*[2], *Lorenza Sassi*[2], *Paolo Vitti*[1], *Luigi Bartalena*[2], *Claudio Marcocci*[1], *Michele Marinò*[1]
[1]Department of Clinical And Experimental Medicine, Endocrinology, University of Pisa, Pisa, Italy; [2]Department of Clinical and Experimental Medicine, Endocrinology, University of Insubria, Varese, Italy

P1–01–02 **DIO2 POLYMORPHISMS ROLE IN GRAVES' DISEASE AND GRAVES' OPHTHALMOPATHY**

Ana Paula Comarella[1], *Danilo Villagelin*[2], *Natassia Bufalo*[1], *Jessica Euflauzino*[3], *Raquel Pereira Rios*[3], *Vitoria Arbulu Pitol*[3], *Roberto Bernardo dos Santos*[3], *João Hamilton Romaldini*[3], *Laura Ward*[1]
[1]Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Brazil; [2]Pont. Universidade Catolica Campinas, Campinas, Brazil; [3]Pontifícia Universidade Católica Campinas, Campinas, Brazil

P1–01–03 **DIAGNOSTIC UTILITY OF ACOUSTIC STRUCTURE QUANTIFICATION FOR EVALUATION OF RADIATION SIALADENITIS AFTER RADIOACTIVE IODINE THERAPY**

Sun Hye Jeong[1], *Hyun Sook Hong*[1]
[1]Soonchunhyang University Bucheon Hospital, Bucheon-Si, Korea, Rep. of South

P1–01–04 **FALSELY ELEVATED FT4 OR FT3 DUE TO INFERENCE SUBSTANCES IN THYROID HORMONE ASSAYS**

Grigoris Effraimidis[1], *Pia Bükman Larsen*[2], *Mads Nybo*[3], *Lise Bathum*[4], *Lennart Friis-Hansen*[2]
[1]Internal Medicine Department, Endocrinology and Diabetes Section, Nykøbing F Hospital, Nykøbing F, Denmark; [2]Department of Clinical Biochemistry, Næstved Hospital, Næstved, Denmark; [3]Department of Clinical Biochemistry, Odense University Hospital, Odense, Denmark; [4]Department of Clinical Biochemistry, Hvidovre Hospital, Hvidovre, Denmark

P1–01–05 **WITHDRAWN**

P1–01–06 **MONITORING THE PREVALENCE OF THYROID DISORDERS IN THE ADULT POPULATION OF NORTHEAST GERMANY**

Rehman Khattak[1], *Till Ittermann*[2], *Matthias Nauck*[3], *Below Harald*[4], *Henry Völzke*[5]
[1]Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany; [2]University Medicine Greifswald, Greifswald, Germany; [3]Universitätsklinikum Greifswald, Greifswald, Germany; [4]Institute of Hygiene and Environmental Medicine, Ernst Moritz Arndt University Greifswald, Germany, Greifswald, Germany; [5]Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany

P1–01–07 **FEATURES OF NEWLY DIAGNOSED GRAVES' DISEASE IN A LARGE LONGITUDINAL COHORT STUDY**

Elvira Masiello[1], *Eleonora Bianconi*[2], *Flavia Magri*[3], *Giovanni Veronesi*[2], *Francesca Zerbini*[3], *Margherita Gaiti*[3], *Emanuele Spreafico*[2], *Daniela Gallo*[4], *Paola Premoli*[2], *Eliana Piantanida*[5], *Maria Laura Tanda*[2], *Marco Ferrario*[2], *Luca Chiovato*[6], *Luigi Bartalena*[4]
[1]Dept. Clinical & Exp. Medicine, Varese, Italy; [2]University of Insubria, Varese, Italy; [3]University of Pavia, Pavia, Italy; [4]University of Insubria, Varese, Italy; [5]University of Insubria, Varese, Italy; [6]Fondazione S. Maugeri, University of Pavia, Pavia, Italy

P1–01–08 **THE CLINICAL VALUE OF REGULAR THYROID FUNCTION TESTS DURING AMIODARONE TREATMENT**

Stan Benjamens[1], *W.J. Sluiter*[1], *M. Rienstra*[2], *I.C. Van Gelder*[2], *Thera Links*[1]
[1]University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; [2]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands

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P1–01–09 **IS CHROMOGRANIN A BIOMARKER FOR THYROID DYSFUNCTION?**
Janna Zimmermann[1], Tanja Diana[1], Niklas Lohmann[1], Lukas Reuter[1], Michael Kanitz[1], George J. Kahaly[1]
[1]Johannes Gutenberg University Medical Center, Mainz, Germany

P1–01–10 **SERUM 25-HYDROXYVITAMIN D IS ASSOCIATED WITH RECURRENCE OF GRAVES' DISEASE**
Hwa Young Ahn[1], Yun Jae Chung[1]
[1]Chung-Ang University College of Medicine, Seoul, Korea, Rep. of South

P1–01–11 **HOW HIGH CAN BE A TSH VALUE IN A THYROTROPINOMA? ITS CONSEQUENCES AND BEYOND**
Kristina Dyacenko[1], Andra Caragheorgheopol[1], Sergiu Stoica[2], Corin Badiu[1]
[1]National Institute of Endocrinology, Bucharest, Romania; [2]Brain Institute, Bucharest, Romania

Room 2

02 Iodine

Chairperson: *Roland Gärtner,* Germany

P1–02–01 **DEVELOPMENT OF AN 'IODINE EXCHANGE SCORE' IN PREGNANCY AND ITS RELATIONSHIP TO THYROGLOBULIN CONCENTRATION**
Sarah Bath[1], Margaret Rayman[2]
[1]University of Surrey, Guildford, UK; [2]Universary of Surrey, Guildford, UK

P1–02–02 **THE RELATIONSHIP BETWEEN IODINE STATUS, THYROID FUNCTION, AND THYROGLOBULIN IN A COHORT STUDY OF UK PREGNANT WOMEN**
Margaret Rayman[1], Sarah Bath[2], Victor Pop[3], Victoria Furmidge-Owen[2], Maarten Broeren[4]
[1]Universary of Surrey, Guildford, UK; [2]University of Surrey, Guildford, UK; [3]University of Tilburg, Tilburg, Netherlands; [4]Máxima Medisch Centrum, Veldhoven, Netherlands

P1–02–03 **RELATIONSHIP BETWEEN MATERNAL IODINE STATUS WITH MATERNAL AND FETAL THYROID FUNCTION IN EUTHYROID GRAVIDAE CARRYING SINGLETON PREGNANCIES**
Terence Lao[1], Russell Ng[1]
[1]Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

P1–02–04 **POPULATION-BASED TSH INTERVALS IN ANTIBODY-POSITIVE AND ANTIBODY-NEGATIVE SUBJECTS, DETERMINED BY TWO DIFFERENT MEASUREMENT METHODS**
Alexander Shinkov[1], Anna-Maria Borissova[1], Roussanka Kovatcheva[1], Jordan Vlahov[1], Lilia Dakovska[1], Iliana Atanassova[1]
[1]Medical University of Sofia, University Hospital of Endocrinology, Sofia, Bulgaria

P1–02–05 **THE VALIDATION OF THYROID VOLUME REFERENCE VALUES AS THE MARKER OF IODINE DEFICIENCY IN SCHOOLCHILDREN**
Malgorzata Trofimiuk-Muldner[1], Zbigniew Szybinski[2], Grzegorz Sokołowski[3], Monika Buziak-Bereza[4], Filip Gołkowski[4], Andrzej Lewiński[5], Arkadiusz Zygmunt[6], Marek Ruchała[7], Elżbieta Bandurska-Stankiewicz[8], Krzysztof Sworczak[9], Alicja Hubalewska-Dydejczyk[4]
[1]Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]Polish Council for Control of Iodine Deficiency Disorders, Kraków, Poland; [3]Department of Endocrinology, University Hospital in Krakow, Kraków, Poland; [4]Chair and Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; [5]Department of Endocrinology and Metabolic Diseases, the Polish Mother's Memorial Hospital – Research Institute, Łódź, Poland; [6]Department of Endocrinology and Metabolic Diseases, the Polish Mother's Memorial Hospital – Research Institute, Łódź, Poland; [7]Chair and Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poznań, Poland; [8]Clinic of Endocrinology, Diabetology and Internal Medicine, Department of Internal Medicine, Faculty of Medical Sciences, University of Warmia and Mazury, Olsztyn, Poland; [9]Chair and Department of Endocrinology and Internal Diseases, Medical University of Gdansk, Gdańsk, Poland

P1–02–06 **IODINE STATUS OF PREGNANT WOMEN RESIDING IN NORTHERN CYPRUS**
Hasan Sav[1], Umut Mousa[2], Osman Koseoglulari[1], Murat Faik Erdogan[3]
[1]B Nalbantoglu Hospital, Department of Endocrinology and Metabolism, Lefkosa, Cyprus; [2]B Nalbantoglu Hospital, Department of Endocrinology and Metabolism, Lefkosa, Cyprus; [3]Ankara University Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey

P1–02–07 **PRELIMINARY RESULTS OF A MULTICENTRIC STUDY OF URINARY IODINE CONCENTRATION IN PREGNANT WOMEN FROM ROMANIA**

Horea Ursu[1], Monica Livia Gheorghiu[2], Irina Dumitrescu[3], Mihaela Stanciu[4], Dragos Popescu[5], Corina Elena Delia[6], Geanina Mirela Toma[6], Ramona Aldea[7], Corina Raducanu Lichiardopol[8], Stefania Tudorache[8], Mihaela Vasile[8], Claudia Podia-Igna[9], Carmen Elena Georgescu[10], Mariana Purice[11]

[1]'C.I. Parhon' National Institute of Endocrinology, 'C. Davila' University of Medicine and Pharmacy, Bucharest, Romania; [2]'C.I.Parhon' National Institute of Endocrinology, Bucharest, Romania; [3]'Gr. T. Popa' University of Medicine and Pharmacy, Iasi, Romania; [4]'L Blaga University', Faculty of Medicine, Sibiu, Romania; [5]'L Blaga' University, Faculty of Medicine, Sibiu, Romania; [6]'Alessandrescu Rusescu' National Institute for Mother and Child Care, Bucharest, Romania; [7]Campulung Hospital, Campulung, Romania; [8]Craiova University of Medicine and Pharmacy, Craiova, Romania; [9]Astra Clinic, Sibiu, Romania; [10]'I Hatieganu' University of Medicine and Pharmacy, Cluj-Napoca, Romania; [11]'C.I. Parhon' National Institute of Endocrinology, Bucharest, Romania

P1–02–08 **ASSESSING THE PROBLEM OF IODINE DEFICIENCY DISORDERS IN THE RUSSIAN FEDERATION**

Nuriya Platonova[1]

[1]Endocrinology Research Centre, Moscow, Russian Federation

P1–02–09 **IODINE NUTRITION STATUS AND AWARENESS OF IODINE DEFICIENCY IN ADULT POPULATIONS INCLUDING PREGNANT WOMEN IN TUGUEGARAO, PHILIPPINES**

Dohyeong Lee[1], Bu Kyung Kim[2], ShinJun Lee[3], So Young Ock[3], Jee-Yeong Jeong[3], Young Sik Choi[3]

[1]Kosin University College of Medicien, Busan, Korea, Rep. of South; [2]Kosin University College of Medicine, Busan, Korea, Rep. of South; [3]Kosin University College of Medicine, Busan, Korea, Rep. of South

P1–02–10 **PRACTICAL MANAGEMENT OF IODINE PROPHYLAXIS IN CASE OF PREGNANCY WITH PRIOR THYROID PATHOLOGY IN MILD IODINE DEFICIENCY AREA OF GEORGIA**

David Metreveli[1]

[1]Tbilisi State Medical University, David Metreveli Medical Centre Ltd, Tbilisi, Georgia

Room 3+4

03 Clinical Autoimmunity 1

Chairperson: *Endre Nagy,* Hungary

P1–03–01 **CORRELATION BETWEEN AUTOIMMUNE THYROID DISEASES AND OTHER ORGAN SPECIFIC/SYSTEMIC AUTOIMMUNE DISORDERS**

Poupak Fallahi[1], Silvia Martina Ferrari[1], Ilaria Ruffilli[1], Giusy Elia[1], Marco Biricotti[2], Roberto Vita[3], Salvatore Benvenga[3], Alessandro Antonelli[1]

[1]University of Pisa, Pisa, Italy; [2]Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy; [3]Endocrinology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

P1–03–02 **SERUM THYROID HORMONE AUTOANTIBODIES (THAB) IN PATIENTS WITH CHRONIC HEPATITIS C (CHC) WITH ASSOCIATED NEITHER AUTOIMMUNE THYROID DISEASE (AITD) NOR AUTOIMMUNE NONTHYROID DISEASES (NAITD), AND IN PATIENTS WITH GRAVES' DISEASES (GD) OR HASHIMOTO'S THYROIDITIS (HT)**

Alessandro Antonelli[1], Poupak Fallahi[1], Silvia Martina Ferrari[1], Marina Galletti[2], Mattia Grazia Mandolfino[2], Grazia Giorgianni[3], Flavia Di Bari[2], Roberto Vita[2], Salvatore Benvenga[2]

[1]University of Pisa, Pisa, Italy; [2]Endocrinology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [3]Unit of Immunometry and Diagnostic Laboratory Service, University Hospital Policlinio G. Martino, Messina, Italy

P1–03–03 **HASHIMOTO'S THYROIDITIS AND VITAMIN D INSUFFICIENCY: RELATIONSHIP WITH SERUM THYROID HORMONES, INTERLEUKINS AND THYROID VOLUME**

Ilka Botelho[1], Arnaldo Moura Neto[1], Marcos Antonio Tambascia[1], Conceição Silva[1], Sarah Monte Alegre[1], Denise Engelbrecht Zantut Wittmann[2]

[1]Unicamp, Campinas, Brazil; [2]Endocrinology Division, Department of Clinical Medicine, Faculty of Medical Sciences, University of Campinas-Unicamp, Campinas, Brazil

P1–03–04 **THYROID IMAGING REPORTING AND DATA SYSTEM SCORE: EVALUATION OF RISK STRATIFICATION IN THYROID NODULES WITH HASHIMOTO'S THYROIDITIS AND THYROID NODULES WITHOUT HASHIMOTO'S THYROIDITIS UNDERWENT FINE-NEEDLE ASPIRATION CYTOLOGY: RESULTS FROM A PROSPECTIVE STUDY**

Fabiana Pani[1], Francesco Boi[1], Chiara Satta[1], Chiara Serafini[1], Stefania Casula[1], Nicolò Arisci[1], Ivan Maurelli[1], Maria Letizia Lai[2], Stefano Mariotti[3]

[1]Endocrine Unit, Department of Medical Sciences M. Aresu, University of Cagliari, Cagliari, Italy; [2]Department of Citomorphology, University of Cagliari, Cagliari, Italy; [3]Department of Medical Scieces, M. Aresu, University of Cagliari, Cagliari, Italy

P1–03–05 **PREVALENCE OF ELEVATED LEVELS OF TSH-RECEPTOR ANTIBODIES (TRAB) IN PATIENTS WITH AUTOIMMUNE THYROIDITIS**

Ralitsa Mekova[1], Mihail Boyanov[1], Deniz Bakalov[2], Adelina Tsakova[3]

[1]Medical University Sofia, University Hospital Alexandrovska, Clinic of Endocrinology and Metabolism, Department of Internal Medicine, Sofia, Bulgaria; [2]University Hospital Alexandrovska, Endocrinology Clinic, Medical University Sofia, Sofia, Bulgaria; [3]Medical University Sofia, University Hospital Alexandrovska, Department of Clinical Laboratory and Clinical Immunology, Sofia, Bulgaria

P1–03–06 **THE ROLE OF MAGNETIC RESONANCE IMAGING IN DIAGNOSING OF DYSTHYROID OPTIC NEUROPATHY**

Tomasz Bednarczuk[1], Beata Rutkowska-Hinc[1], Edyta Maj[2], Anna Jabłońska[3], Piotr Miśkiewicz[1]

[1]Warsaw University of Medicine, Department of Endocrinology, Warsaw, Poland; [2]Warsaw University of Medicine, 2nd Department of Clinical Radiology, Warsaw, Poland; [3]Warsaw University of Medicine, Department of Ophthalmology, Warsaw, Poland

P1–03–07 **INCREASED INCIDENCE OF AUTOIMMUNE THYROID DISORDERS IN PATIENTS WITH PSORIATIC ARTHRITIS**

Poupak Fallahi[1], Silvia Martina Ferrari[1], Ilaria Ruffilli[1], Giusy Elia[1], Andrea Delle Sedie[1], Lucrezia Riente[1], Alessandro Antonelli[1]

[1]University of Pisa, Pisa, Italy

P1–03–08 **MISDIAGNOSIS OF GRAVES' HYPERTHYROIDISM DUE TO INTERFERENCE IN FT4, FT3 AND TRAB ASSAYS: A CASE REPORT**

Grigoris Effraimidis[1], Pia Bükmann Larsen [2], Mads Nybo[3], Lise Bathum[4], Lennart Friis-Hansen[2]

[1]Internal Medicine Department, Endocrinology and Diabetes Section, Nykøbing F Hospital, Nykøbing F, Denmark; [2]Department of Clinical Biochemistry, Næstved Hospital, Næstved, Denmark; [3]Department of Clinical Biochemistry, Odense University Hospital, Odense, Denmark; [4]Department of Clinical Biochemistry, Hvidovre Hospital, Hvidovre, Denmark

P1–03–09 **THE IMPORTANT ROLE OF DOPPLER ULTRASOUND IN THE DIFFERENTIAL DIAGNOSIS BETWEEN HASHITOXICOSIS AND GRAVES' DISEASE**

Enalda Demaj[1], Marjeta Kermaj[2], Thanas Fureraj[3], Laurant Kollcaku[3], Ylli Agron[4]

[1]Hospital of Berat, Internal, Berat, Albania; [2]University Hospital Center 'Mother Tereza', Tirana, Albania; [3]Mother Theresa Hospital Center, Tirana, Albania; [4]Endocrinology and Nuclear Medicine, Tirana, Albania

P1–03–10 **THE ROLE OF D3 VITAMIN DEFICIENCY IN AUTOIMMUNE THYROIDITIS**

Armine Khroyan[1], Maria Badalyan[1], Edvard Toromanyan[1], Meline Tovmasyan[1]

[1]Yerevan State Medical University, Yerevan, Armenia

P1–03–11 **USE OF INTRAVENOUS GLUCOCORTICOIDS FOR TREATMENT OF GRAVES' ORBITOPATHY**

Mariami Asatiani[1], Zurab Robitashvili[2]

[1]V.Ierieli Endocrinology, Metabology, Dietology Center 'enmedic', Tbilisi, Georgia; [2]V. Iverieti Endocrinology, Matabology, Dietology Center Enmedic, Tbilisi, Georgia

Room 16

04 Case Reports

Chairperson: *Valentin Fadeyev,* Russia

P1–04–01 **INCREASED REQUIREMENT OF LEVOTHYROXINE IN TWO GYNECOMASTIC PATIENTS WITH EXCESS OF THYROXINE-BINDING GLOBULIN (TBG): IN ONE BECAUSE OF EXPOSURE TO EXOGENOUS ESTROGENS IN MEAT, IN THE OTHER BECAUSE OF LIVER CIRRHOSIS-RELATED HYPERESTROGENEMIA**

Salvatore Benvenga[1], Flavia Di Bari[2]

[1]Sezione di Endocrinologia, Policlinico Universitario, Messina, Italy; [2]Sezione di Endocrinologia, Policlinico Universitario di Messina, Messina, Italy

P1–04–02 **DESTRUCTIVE THYROIDITIS CAUSING THYROTOXICOSIS LONG AFTER AMIODARONE WITHDRAWAL – A DIAGNOSTIC AND THERAPEUTIC CHALLENGE**

Minodora Andreea Betivoiu[1], Sorina Martin[2], Alexandra Nila[3], Simona Fica[2]

[1]Elias Hospital, Endocrinology, Bucharest, Romania; [2]Elias Hospital, Endocrinology Department, Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Bucharest, Romania; [3]Elias Hospital, Endocrinology Department, Bucharest, Romania

P1–04–03 **THYROID STORM FOLLOWING TOTAL THYROIDECTOMY FOR THYROID CANCER, DUE TO THYROTROPIN RECEPTOR ANTIBODIES STIMULATING THE METASTATIC THYROID TISSUE**

Lars Folkestad[1], Frans Brandt Kristensen[2], Thomas Brix[3], Marianne Vogsen[4], Lars Bastholm[4], Peter Grupe[5], Jeanette Krogh Petersen[6], Laszlo Hegedüs[7]

[1]Department of Endocrinology and Metabolism, Odense Universityhospital, Odense, Denmark; [2]Department of Endocinology and Metabolism, Odense Universityhospital, Odense, Denmark; [3]Department of Endocrinology and Metabolism, Odense Universityhospital, Odense, Denmark; [4]Department of Oncology, Odense Universityhospital, Odense, Denmark; [5]Department of Nuclear Medicine, Odense

University Hospital, Odense, Denmark; [6]Department of Clinical Pathology, Odense Universityhospital, Odense, Denmark; [7]Department of Endocrinology and Metabolism, Odense Universityhospital, Odense, Denmark

P1–04–04 **SPONTANEOUS TRANSFORMATION OF PRIMARY AUTOIMMUNE HYPOTHYROIDISM TO GRAVES' DISEASE IN A CLINICAL CASE OF AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 2**

Narine Martirosian[1], Nina Petunina[1], Liubov Trukhina[1]
[1]Sechenov First Moscow State Medical University, Moscow, Russian Federation

P1–04–05 **AUTOIMMUNE THYROID DISEASE AND CHRONIC URTICARIA – A CASE STUDY**

Fadila Gadallah[1]
[1]Ain Shams University, Abbasiya Square, Cairo, Egypt

P1–04–06 **PRIMARY HYPERTHYROIDISM IN A PATIENT WITH HYPOTHYROIDISM SECONDARY TO PITUITARY SURGERY – A RARE ASSOCIATION**

Rita Silva[1], Daniela Magalhães[1], Sandra Belo[1], Josué Pereira[2], Olinda Faria[3], Joana Queirós[1], Paula Freitas[1], David Carvalho[1]
[1]Department of Endocrinology, Diabetes and Metabolism, Centro Hospitalar São João, E.P.E., Porto, Portugal; [2]Department of Neurosurgery, Centro Hospitalar São João, E.P.E., Porto, Portugal; [3]Department of Ophthalmology, Centro Hospitalar São João, E.P.E., Porto, Portugal

P1–04–07 **A CASE REPORT OF TYPE 2 AMIODARONE INDUCED THYROTOXICOSIS, WHICH UNDERWENT TOTAL THYROIDECTOMY**

Edvina Gregoric[1], Gregor Vercek[2], Olga Blatnik[3]
[1]Dept of Nuclear Medicine, Nuclear Medicine, Izola, Slovenia; [2]Medical Faculty, University of Ljubljana, Ljubljana, Slovenia; [3]Institute of Oncology, Department of Pathology, Ljubljana, Slovenia

P1–04–08 **EFFECT OF GLUCOCORTICOSTEROIDS ON THE THYROID SUPPLEMENTATION THERAPY IN A PATIENT WITH AUTOIMMUNE HYPOTHYROIDISM: A CASE REPORT**

Bojan Lozanov[1], Desislava Gorcheva[2], Vesselina Koleva[3], Lachezar Lozanov[3]
[1]Tokuda Hospital, Dept. Endocrinology, Sofia, Bulgaria; [2]Tokuda Hospital Sofia, Sofia, Bulgaria; [3]Tokuda Hospital Sofia, Sofia, Bulgaria

P1–04–09 **A RARE CAUSE OF PAIN AND SWELLING IN NECK: THYROID ABSCESS**

Samet Yaman[1], Sevgul Faki[2], Murat Basaran[3], Didem Ozdemir[4], Reyhan Ersoy[2], Bekir Cakir[2]
[1]Ankara Yildirim Beyazit University, Faculty of Medicine, Ataturk Education and Research Hospital, Department of Internal Medicine, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, Faculty of Medicine, Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Yildirim Beyazit University, Faculty of Medicine, Ataturk Education and Research Hospital, Department of Gastroenterology, Ankara, Turkey; [4]Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey

P1–04–10 **WITHDRAWN**

P1–04–11 **MARINE-LENHART SYNDROME – A RARE CAUSE OF THYROTOXICOSIS**

Mirjana Stojkovic[1], Savica Savic[1], Jasmina Ciric[1], Biljana Beleslin[1], Tanja Nisic[1], Milos Stojanovic[1], Tijana Lalic[1], Milos Zarkovic[1]
[1]Clinic of Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia, Thyroidology Department, Belgrade, Serbia

Room 14

05 Thyroid Cancer Diagnostic I

Chairperson: *Laurence Leenhardt,* France

P1–05–01 **INDETERMINATE THYROID LESIONS: POTENTIAL DISCRIMINATORY OF THE NUCLEAR MORPHOMETRIC COMPUTERIZED ANALYSIS**

Flávia Oliveira Valentim[1], Bárbara Parente Coelho[2], Hélio Amante Miot[2], Mariangela Marques[2], Jose Vicente Tagliarini[2], Gláucia Mazeto[2]
[1]Botucatu Medical School, Botucatu, Brazil; [2]Botucatu Medical School, Sao Paulo State University, Unesp, Botucatu, Brazil

P1–05–02 **ADEQUACY OF PATHOLOGY REPORTS OF PATIENTS WITH DIFFERENTIATED THYROID CANCER OPERATED IN A HIGH VOLUME TERTIARY ENDOCRINE CENTER**

Sefika Burcak Polat[1], Berna Evranos Ogmen[2], Muhammet Cüneyt Bilginer[3], Sevgül Fakı[1], Reyhan Ersoy[4], Bekir Cakir[4]
[1]Yildirim Beyazit University, Ataturk Education and Research Hospital, Endocrinology Department, Ankara, Turkey; [2]Ankara Ataturk Research and Training Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Yildirim Beyazit University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [4]Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

P1–05–03 **THYROID CORE NEEDLE BIOPSY: PATIENTS' PAIN AND SATISFACTION COMPARED TO FINE NEEDLE ASPIRATION**

Jaesun Ji[1], Yeo Koon Kim[2], Sang Il Choi[3], Ji-Hoon Kim[4], Yunho Song[5], Joohyun Kim[6], Eun Hee Seo[6], Gwan Hong Min[6]

[1]Seoul National University Bundang Hospital, Gyeong-Gi, Korea, Rep. of South; [2]Seoul National University, Seongnam-Si, Korea, Rep. of South; [3]Seoul National University Bundang Hospital, Seongnam-Si, Korea, Rep. of South; [4]Seoul National University Hospital, Seoul, Korea, Rep. of South; [5]Seoul National University Bundang Hospital, Bundang, Korea, Rep. of South; [6]Seoul National Universiy Bundang Hospital, Bundang, Korea, Rep. of South

P1–05–04 **ATYPIA OF UNDETERMINED SIGNIFICANCE ON THYROID FINE NEEDLE ASPIRATION – RISK FACTORS FOR MALIGNANCY**

Eunji Lee[1], Jong Chul Hong[1], Ji-Won Seo[1], Dong-Kun Lee[2], Heon-Soo Park[1]

[1]Department of Otolaryngology-Head and Neck Surgery, Dong-A University College of Medicine, Busan, Korea, Rep. of South; [2]Department of Otolaryngology-Head and Neck Surgery, Inje University College of Medicine, Busan, Korea, Rep. of South

P1–05–05 **THE RELATIONSHIP BETWEEN THE BRAFV600E MUTATION IN PAPILLARY THYROID MICROCARCINOMA AND CLINICOPATHOLOGIC FACTORS**

Jong Chul Hong[1], Ji-Won Seo[1], Eunji Lee[1], Dong-Kun Lee[2], Heon-Soo Park[1]

[1]Department of Otolaryngology-Head and Neck Surgery, Dong-A University College of Medicine, Busan, Korea, Rep. of South; [2]Department of Otolaryngology-Head and Neck Surgery, Inje University College of Medicine, Busan, Korea, Rep. of South

P1–05–06 **PRIMARY THYROID LYMPHOMA: A 10-YEAR EXPERIENCE AT A TERTIARY CARE CENTRE IN THAILAND**

Jaruwan Kongkit[1], Natnicha Houngngam[2], Thiti Snabboon[3]

[1]Chulalongkorn University, Bangkok, Thailand; [2]King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand; [3]Chulalongkorn University, Medicine, Bangkok, Thailand

P1–05–07 **IMPACT OF F18-FDG PET/CT ON THE CLINICAL OUTCOME AND MANAGEMENT OF DIFFERENTIATED THYROID CANCER PATIENTS WITH POSITIVE I-131 WHOLE BODY SCAN AND ELEVATED THYROGLOBULIN**

Yen-Hsiang Chang[1]

[1]Nuclear Medicine Department, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan

P1–05–08 **COEXISTENCE OF DIFFERENTIATED AND UNDIFFERENTIATED THYROID CARCINOMA WITH CHRONIC LYMPHOCYTIC LEUKEMIA**

Dilek Yazici[1], Serdar Tezelman[2], Onur Demirkol[3], Omer Faruk Unal[4], Sukru Dilege[5], Ozlem Aydin[6], Yersu Kapran[7], Bulent Colakoglu[8], Tarik Terzioglu[9], Burhan Ferhanoglu[10], Faruk Alagol[1]

[1]Koc University Medical School, Section of Endocrinology and Metabolism, Istanbul, Turkey; [2]Koc University Medical School, Department of General Surgery, Istanbul, Turkey; [3]Koc University Medical School, Department of Nuclear Medicine, Istanbul, Turkey; [4]Koc University Medical School, Department of Otorhinolaryngology, Istanbul, Turkey; [5]Koc University Medical School, Department of Thoracic Surgery, Istanbul, Turkey; [6]American Hospital, Department of Pathology, Istanbul, Turkey; [7]Koc University Medical School, Department of Pathology, Istanbul, Turkey; [8]American Hospital, Department of Radiology, Istanbul, Turkey; [9]American Hospital, Department of General Surgery, Istanbul, Turkey; [10]Koc University Medical School, Section of Hematology, Istanbul, Turkey

P1–05–09 **A CASE OF BLACK THYROID ACCOMPANIED BY PAPILLARY CARCINOMA**

Songl Yang[1], KwangKuk Park[2], Jeong Hoon Kim[3]

[1]Kosin University College of Medicine, Department of Surgery, Seo-Gu, Busan, Korea, Rep. of South; [2]Hub-Hu Hospital, Department of Surgery, Sahagu, Busan, Korea, Rep. of South; [3]Kosin University College of Medicine, Department of Surgery, Seogu, Busan, Korea, Rep. of South

Room 12

06 Thyroid Cancer Pathogenesis

Chairperson: *Christian Selmer,* Denmark

P1–06–01 **PROGNOSTIC FACTORS OF DISEASE IN PATIENTS WITH REFRACTORY TO RADIO-IODINE (RAI) TREATMENT DIFFERENTIATED THYROID CANCER (DTC)**

Katerina Saltiki[1], Elli Anagnostou[1], Mihalis Apostolakis[1], Evangelia Zapanti[1], Eleni Anastasiou[1], Maria Alevizaki[1]

[1]Endocrine Unit, Dept Medical Therapeutics, Alexandra Hospital, Athens University School of Medicine, Athens, Greece

P1–06–02 **USEFULNESS OF INTRAOPERATIVE PTH MEASUREMENTS FOR PREDICTING PERMANENT HYPOPARATHYROIDISM AFTER TOTAL THYROIDECTOMY**

Takashi Uruno[1], Yuna Ogimi[1], Chie Masaki[1], Junko Akaishi[1], Kiyomi Y. Hames[1], Chisato Tomoda[1], Akifumi Suzuki[1], Kenichi Matsuzu[1], Keiko Ohkuwa[1], Hiroshi Shibuya[1], Wataru Kitagawa[1], Mitsuji Nagahama[1], Kiminori Sugino[1], Koichi Ito[1]

[1]Ito Hospital, Tokyo, Japan

P1–06–03 **THE 2015 AMERICAN THYROID ASSOCIATION RISK STRATIFICATION SYSTEM: A TOOL FOR PREDICTING THE TUMOR BURDEN OF PERSISTENT/RECURRENT DISEASE IN PATIENTS WITH DIFFERENTIATED THYROID CANCER**

Renaud Ciappuccini[1], Natacha Heutte[2], David Blanchard[3], Dominique de Raucourt[3], Dominique Vaur[4], Emmanuel Babin[5], Stephane Bardet[1]

[1]Centre Francois Baclesse, Nuclear Medicine and Thyroid Unit, Caen, France; [2]Centre Francois Baclesse, Inserm U1086, Caen, France; [3]Centre Francois Baclesse, Head and Neck Surgery, Caen, France; [4]Centre Francois Baclesse, Biology, Caen, France; [5]Centre Hospitalo-Universitaire, Head and Neck Surgery, Caen, France

P1–06–04 **A NEW PROPOSAL FOR A DIFFERENTIAL MANAGEMENT OF INDETERMINATE THYROID NODULES: CONTRIBUTION OF ULTRASONOGRAPHY, REPEATED FINE NEEDLE ASPIRATION BIOPSY AND BRAF ANALYSIS**

Martina Rossi[1], Sabrina Lupo[1], Roberta Rossi[1], Paola Franceschetti[1], Giorgio Trasforini[1], Stefania Bruni[1], Federico Tagliati[1], Mattia Buratto[1], Giovanni Lanza[1], Luca Damiani[1], Ettore Degli Uberti[1], Maria Chiara Zatelli[2]

[1]Section of Endocrinology and Internal Medicine, University of Ferrara, Ferrara, Italy; [2]University of Ferrara, Section of Endocrinology, Section of Endocrinology, Ferrara, Italy

P1–06–05 **THE ASSOCIATION BETWEEN LYMPH NODE METASTASIS AND MOLECULAR MARKERS IN DIFFERENTIATED THYROID CANCER**

Berna İmge Aydoğan[1], Cevriye Cansız Ersöz[2], Serpil Dizbay Sak[2], Sevim Gullu[1]

[1]Ankara University School of Medicine, Department of Endocrinology and Metabolic Diseases, Ankara, Turkey; [2]Ankara University School of Medicine, Department of Pathology, Ankara, Turkey

P1–06–06 **ASSOCIATION BETWEEN BODY MASS INDEX AND CLINICOPATHOLOGICAL FEATURES OF THYROID CANCER**

Songl Yang[1], Jeong Hoon Kim[1], KwangKuk Park[2]

[1]Kosin University College of Medicine, Department of Surgery, Seo-Gu, Busan, Korea, Rep. of South; [2]Hub-Hu Hospital, Department of Surgery, Sahagu, Busan, Korea, Rep. of South

P1–06–07 **BRAF AND RAS MUTATION STATUS IN TURKISH PATIENTS WITH PAPILLARY THYROID CARCINOMA AND CORRELATION WITH CLINICOPATHOLOGICAL FEATURES OF THE PRIMARY TUMOUR**

Seda Sancak[1], Ahmet Aslan[2], Funda Eren[3], Duygu Altınok[4], Hasan Aydın[5], Dilek Dereli Yazici[6], Nefise Sema Akalin[7], Eileen Böesenberg[8], Paschke Ralf[9], Markus Eszlinger[10]

[1]1fatih Sultan Mehmet Training and Research Hospital, 2department of Endocrinology and Metabolism, Medical School of Marmara University, Istanbul, Turkey; [2]Department of Radiology, Umraniye Training and Research Hospital, Department of Radiology, Medical School of Marmara University, Istanbul, Turkey; [3]Department of Pathology of Marmara Medical School, Istanbul, Turkey; [4]Van Training and Educational Hospital, Section of General Surgery, Department of Surgery, Medical School of Marmara University, Van, Turkey; [5]Yeditepe University Medical Faculty, Department of Endocrinology and Metabolism, Istanbul, Turkey, Department of Endocrinology and Metabolism, Medical School of Marmara University, Istanbul, Turkey; [6]Marmara University Medical School, Section of Endocrinology and Metabolism, Koç University, Altunizade Istambul, Turkey; [7]Department of Endocrinology and Metabolism, Marmara Medical School, Koç University, Section of Endocrinology and Metabolism, Istanbul, Turkey; [8]Division of Endocrinology and Nephrology, University of Leipzig, Leipzig, Germany; [9]Department of Oncology and Arnie Charbonneau Cancer Institute, Cumming School of Medicine, University of Calgary, Division of Endocrinology and Nephrology, University of Leipzig, Calgary, Canada; [10]Department of Oncology and Arnie Charbonneau Cancer Institute, Cumming School of Medicine, Division of Endocrinology and Nephrology, University of Leipzig, Calgary, Canada

P1–06–08 **IS THYROTOXICOSIS ASSOCIATED WITH MORE AGGRESSIVE VARIANTS OF PAPILLARY THYROID CANCER? A SINGLE CENTER STUDY**

Sefika Burcak Polat[1], Berna Evranos Ogmen[2], Gurkan Dumlu[3], Nuran Sungu[4], Reyhan Ersoy[5], Bekir Cakir[5]

[1]Yildirim Beyazit University, Ataturk Education and Research Hospital, Endocrinology Department, Ankara, Turkey; [2]Ankara Ataturk Research and Training Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Yildirim Beyazit University, Ataturk Education and Research Hospital, General Surgery Department, Ankara, Turkey; [4]Yildirim Beyazit University, Ataturk Education and Research Hospital, Pathology Department, Ankara, Turkey; [5]Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

P1–06–09 **POSTOPERATIVE STIMULATED THYROGLOBULIN LEVELS AS A PREDICTIVE FACTOR FOR INCOMPLETE RESPONSE IN LOW TO INTERMEDIATE RISK PAPILLARY THYROID CARCINOMAS**

Catarina Machado[1], Patrícia Tavares[1], Lilite Barbosa[1], Antónia Póvoa[1], Carlos Soares[1], José Manuel Oliveira[2], Sara Monteiro[1], Maria João Oliveira[1]

[1]Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal; [2]Hpp-MM-Lanitudes, Porto, Portugal

P1–06–10 **CASE OF THYROID CARCINOMA OCCASIONALLY FOUND IN YOUNG PATIENT AND THE IMPORTANCE OF IMMEDIATE RADICAL THERAPY**

Natia Katamadze[1]

[1]Tbilisi, Georgia

Room 13+15

07 Thyroid Cancer / Translational

Chairperson: *Raffaele Ciampi,* Italy

P1–07–01 **THE EXPRESSION OF E-CADHERIN, YAP1, STAT3 OF MULTICELLULAR TUMOR SPHEROIDS OF THYROID**

Woo Young Kim[1], Sang Uk Woo[1], Jae Bok Lee[1]
[1]Korea University Guro Hospital, Department of Surgery, Seoul, Korea, Rep. of South

P1–07–02 **USING NEXT GENERATION SEQUENCING IN THE DETECTION OF GENETIC CHANGES IN THE BRAF AND IDH1 GENES IN PAPILLARY THYROID CARCINOMA**

Sarka Dvorakova[1], Vlasta Sykorova[2], Eliska Vaclavikova[2], Rami Katra[3], Pavla Sykorova[4], Petr Vlcek[4], Daniela Kodetova[5], Petr Lastuvka[6], Jan Betka[6], Josef Vcelak[2], Bela Bendlova[2]
[1]Institute of Endocrinology, Prague 1, Czech Republic; [2]Institute of Endocrinology, Dept. of Molecular Endocrinology, Prague 1, Czech Republic; [3]Department of Ent, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [4]Department of Nuclear Medicine and Endocrinology, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [5]Departments of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [6]Department of Otorhinolaryngology and Head and Neck Surgery, 1st Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic

P1–07–03 **TGFB1 GENE POLYMORPHIMS CLINICAL UTILITY IN THYROID BENIGN AND MALIGNANT NODULES**

Karina Colombera Peres[1], Natassia Bufalo[2], Laís Helena Pereira Amaral[2], Jacqueline Almeida[2], Larissa Teodoro[2], Ana Paula Comarella[2], Laura Ward[2]
[1]Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, São Paulo, Brazil; [2]Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Brazil

P1–07–04 **CONTINUOUS INTRAOPERATIVE NEUROMONITORING IN TRANSAXILLARY ROBOTIC THYROIDECTOMY: IS IT POSSIBLE? A PROSPECTIVE RANDOMIZED STUDY**

Seul Gi Lee[1], Cho Rok Lee[2], Eun Jeong Ban[3], Min Jhi Kim[2], Tae Hyung Kim[2], Jungbum Choi[1], Sang-Wook Kang[2], Jandee Lee[2], Jong Ju Jeong[4], Kee-Hyun Nam[4], Woungyoun Chung[5]
[1]Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [2]Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [3]Yonsei Univsersity College of Medicine, Seoul, Korea, Rep. of South; [4]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [5]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South

P1–07–05 **STUDY OF NOVEL GALECTIN-1 TARGETED PEPTIDES IN THE CONTEXT OF A NEW AND NON-INVASIVE PAPILLARY THYROID CANCER DIAGNOSIS AND EVALUATION OF THEIR POTENTIAL INHIBITOR EFFECT**

Deborah Fanfone[1], Nadège Despretz[2], Dimitri Stanicki[2], Sophie Laurent[2], Robert Muller[2], Sandrine Rorive[3], Luce Vander Elst[2], Sven Saussez[4], Carmen Burtea[2]
[1]Department of General, Organic, Mons, Belgium; [2]University of Mons, Department of General, Organic and Biomedical Chemistry, Mons, Belgium; [3]Center for Microscopy and Molecular Imaging, Diapath, Charleroi, Belgium; [4]University of Mons, Laboratory of Anatomy and Cell Biology, Mons, Belgium

P1–07–06 **CD56 EXPRESSION IS HIGHLY DEPENDENT ON THE HISTOLOGIC SUBTYPE OF PAPILLARY THYROID CARCINOMA: A STUDY OF QUANTITATIVE DIGITAL IMAGE ANALYSIS OF CD56 IMMUNOHISTOCHEMISTRY**

Chan Kwon Jung[1], Yourha Kim[2], Sora Jeon[3], Sohee Lee[4], Ja Seong Bae[4]
[1]College of Medicine, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Korea, Rep. of South; [2]Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Kore, Seoul, Korea, Rep. of South; [3]Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South; [4]Department of Surgery, Catholic University of Korea College of Medicine, Seoul St. Mary's Hospital Seoul, Republic of Korea, Seoul, Korea, Rep. of South

P1–07–07 **RESVERATROL INDUCES CELL APOPTOSIS IN ANAPLASTIC THYROID CARCINOMA CELLS BY ACTIVATION OF THE ERK AND JNK SIGNALING PATHWAYS**

Se Eun Han[1], Se Eun Han[2], Il Sung Nam-Goong[2], Young Il Kim[2], Eun Sook Kim[2]
[1]College of Korean Medicine, Donggok University, Kyung Ju, Korea, Rep. of South; [2]Internal Medicine, Ulsan University Hospital, College of Medicine University of Ulsan, Ulsan, Korea, Rep. of South

P1–07–08 **THE GENETIC SCREENING OF RET PROTO-ONCOGENE IN POLISH POPULATION AND COMPARISON OF THE RET MUTATIONS PREVALENCE WITH RESULTS OF EUROPEAN STUDIES**

Malgorzata Oczko-Wojciechowska[1], Maria Sromek[2], Agnieszka Pawlaczek[1], Malgorzata Czetwertynska[3], Dorota Kula[1], Jadwiga Zebracka-Gala[1], Dagmara Rusinek[1], Monika Kowal[1], Elzbieta Gubala[1], Tomasz Gawlik[1], Sylwia Szpak-Ulczok[1], Renata Zub[3], Tomasz Tyszkiewicz[1], Kornelia Hasse-Lazar[1], Zbigniew Wygoda[1], Jolanta Krajewska[1], Malgorzata Wiench[4], Marek Dedecjus[3], Barbara Jarzab[1]
[1]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland; [2]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [3]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw, Warsaw, Poland; [4]College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

P1–07–09 **STRUCTURAL AND FUNCTIONAL STATE OF THE THYROID GLAND DURING PAPILLARY CANCER**

Tamar Dundua[1], Lali Javashvili[1], Ana Mamasakhlisi[1], Maia Kobulia[1], Meri Rekvava[1], Tamar Kaloiani[2], Medea Papava[3]
[1]Clinic Cortex, Tbilisi, Georgia; [2]National Centre of Oncology, Tbilisi, Georgia; [3]Research Institute of Clinical Medicine, Tbilisi, Georgia

P1–07–10 **FOLLOWING LONG TERM FOLLOW-UP, SAFE EXCISION OF METASTATIC FOCUS AFTER ARTERIAL EMBOLISATION IN A PATIENT WITH BONE METASTASES OF PAPILLARY THYROID CARCINOMA: CASE REPORT**

Sevgül Faki[1], Oya Topaloglu[2], Samet Yaman[3], Mahmut Nedim Aytekin[4], Oktay Algın[5], Reyhan Ersoy[6], Bekir Cakir[6]
[1]Yildirim Beyazit University, Ataturk Education and Research Hospital, Endocrinology Department, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Yildirim Beyazit University, Ataturk Education and Research Hospital, Department of Internal Medicine, Ankara, Turkey; [4]Ankara Yildirim Beyazit University, School of Medicine, Department of Orthopedic Surgery, Ankara, Turkey; [5]Ankara Yildirim Beyazit University, School of Medicine, Department of Interventional Radiology, Ankara, Turkey; [6]Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

East Lounge / 8+9+10+11 (Main Auditorium)

08 Analogues + Others / Basic

Chairperson: *Duncan Bassett,* UK

P1–08–01 **THERMOREGULATORY EFFECTS OF 3-IODOTHYRONAMINE IN MICE**

Sogol Gachkar[1], Rebecca Oelkrug[2], Amy Warner[3], Jens Mittag[4]
[1]University of Lübeck, Molecular Endocrinology, 23538 Luebeck, Germany; [2]Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany; Karolinska Institutet, Cell and Molecular Biology, Stockholm, Sweden; [4]Universität Lübeck, Cbbm, Lübeck, Germany

P1–08–02 **SYSTEMICALLY ADMINISTERED 3-IODOTHYRONAMINE (T1AM) AND THYRONAMINE-LIKE ANALOG SG-2 ENHANCE MEMORY AND THERMAL NOCICEPTION IN MICE**

Lorenza Bellusci[1], Annunziatina Laurino[2], Martina Sabatini[1], Giulia Nesi[3], Simona Rapposelli[3], Riccardo Zucchi[1], Laura Raimondi[4], Grazia Chiellini[1]
[1]Dept. of Pathology, University of Pisa, Pisa, Italy; [2]Department Ofneurofarba; Pharmacology, University of Florence, Florence, Italy; [3]Dept. of Pharmacy, University of Pisa, Pisa, Italy; [4]Department Ofneurofarba, Pharmacology, University of Florence, Florence, Italy

P1–08–03 **3-IODOTHYRONAMINE (T1AM) AND SYNTHETIC THYRONAMINE-LIKE ANALOGS SG-1 AND SG-2 INDUCE AUTOPHAGY IN HUMAN GLIOBLASTOMA CELLS (U-87MG)**

Martina Sabatini[1], Lorenza Bellusci[1], Gloria Lazzeri[2], Paola Lenzi[2], Alessandra Salvetti[3], Giulia Nesi[4], Simona Rapposelli[4], Francesco Fornai[2], Riccardo Zucchi[1], Grazia Chiellini[1]
[1]Dept. of Pathology, University of Pisa, Pisa, Italy; [2]Dept. of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy; [3]Dept. of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [4]Dept. of Pharmacy, University of Pisa, Pisa, Italy

P1–08–04 **THE FLAME RETARDANT DE-71 INHIBITS CULTURED HUMAN THYROID CELLS**

Ulla Feldt-Rasmussen[1], Thit Mynster Kronborg[1], Juliana Frohnert Hansen[1], Jacob Hofman-Bang[1], Åse Krogh Rasmussen[1], Marie Frederiksen[2], Katrin Vorkamp[3], Christoffer Holst Hahn[4], Louise Ramhøj[5], Claus Henrik Nielsen[6], Klaus Bendtzen[6]
[1]Copenhagen University Hospital, Dept of Endocrinology, Pe 2132, Copenhagen, Denmark; [2]Aalborg University, Dept of Construction and Health, Copenhagen, Denmark; [3]Aarhus University, Dept of Environmental Science, Roskilde, Denmark; [4]Rigshospitalet, Dept of Ear Nose Throat Head and Neck Surgery, Copenhagen, Denmark; [5]Technical University of Denmark, National Food Institute, Søborg, Denmark; [6]University of Copenhagen, Institute of Inflammation, Copenhagen, Denmark

P1–08–05 **EFFECTS OF THYROID HORMONES AND 3-IODOTHYRONAMINE ON SIRTUIN EXPRESSION IN HEPATOCYTES**

Ginevra Sacripanti[1], Leonardo Lorenzini[1], Riccardo Zucchi[1], Sandra Ghelardoni[2]
[1]University of Pisa, Pisa, Italy; [2]Dpt of Pathology, Pisa, Italy

P1–08–06 **DIFFERENTIAL GENE EXPRESSION IN PREGNANCY AS A TOOL FOR PRIMARY HYPOTHYROIDISM DIAGNOSIS**

Lucas dos Santos Bacigalupo[1], Robson José de Almeida[1], Valdelena Alessandra da Silva[1], Patrícia Varella Lima Teixeira[2], Leonardo Martins da Silva[2], Juliana de Almeida Pires[1], Mariana Fabbris Pereira[1], João Bosco Pesquero[2], Cleber Pinto Camacho[3]
[1]Universidade Nove de Julho (Uninove), São Paulo, Brazil; [2]Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil; [3]Laboratory of Molecular Medicine Technology, Universidade Nove de Julho (Uninove), São Paulo, Brazil

P1–08–07 **DETECTING 3-IODOTHYRONAMINE IN THE PRESENCE OF FETAL BOVINE SERUM: ISOTOPE KINETIC EFFECT AND OTHER PITFALLS**

Leonardo Lorenzini[1], Sandra Ghelardoni[2], Alessandro Saba[1], Riccardo Zucchi[1]
[1]University of Pisa, Pisa, Italy; [2]Dpt of Pathology, Pisa, Italy

P1–08–08 **CENTRAL AND PERIPHERAL INFLAMMATORY RESPONSES ARE IMPLICATED IN DIET-INDUCED OBESITY RESISTANCE IN WSB/EIJ MICE**

Isabelle Seugnet[1], Maria J. Herrero[2], Terrien Jeremy[3], Bolaji Seffou[1], Stephanie Decherf[4], James Bowers[1], Chakib Djediat[5], Bertrand Ducos[6], Barbara Demeneix[7], Marie-Stéphanie Clerget-Froidevaux[7]

[1]Mnhn/Cnrs Umr 7221, Paris, France; [2]Mnhn/Cnrs Umr 7221, Paris, France; [3]Team Bioadapt Umr Cnrs/Mnhn 7179, Brunoy, France; [4]Muséum National D'histoire Naturelle, Umr Cnrs 7221, Paris, France; [5]Mnhn, Paris, France; [6]Genomic Paris Centre, Institut de Biologie de L'ecole Normale Supérieure (Ibens), Paris, France; [7]Mnhn/Cnrs Umr7221, Paris, France

P1–08–09 **CHOLECALCIFEROL (VIT. D3) AFFECTS THYROID HYSTOLOGY AND FUNCTION IN ORCHIDECTOMIZED MIDDLE-AGED MALE RATS**

Branka Sosic-Jurjevic[1], Branko Filipović[1], Jasmina Živanović[1], Gordana Uśćebrka[2], Svetlana Trifunović[1], Vladimir Ajdžanović[1], Nataša Ristić[1], Verica Milošević[1]

[1]Institute for Biological Research, University of Belgrade, Belgrade, Serbia; [2]Faculty of Agriculture, University of Novi Sad, Novi Sad, Serbia

P1–08–10 **MOLECULAR ECONOMY OF IODINE: A PHYSIOLOGICAL STRATEGY IN IODINE-DEFICIENT VERTEBRATES**

Atul Kathait[1], Anjana Faraswan[2], Patrick Shyaka[1], Asha Chandola-Saklani[1]

[1]Centre for Biosciences and Clinical Research, School of Biosciences, Apeejay Stya University, Gurgaon, India; [2]Government Degree College, Agastya Muni, Uttarakhand, India

Room 1
12.00–13.00
Poster Session P2

01 Clinical Autoimmunity 2
Chairperson: *Tanja Diana,* Germany

P2–01–01 **OUTCOME OF ACUTE ORBITAL EDEMA FOLLOWING A MINUTE DOSE OF RITUXIMAB FOR GRAVES' ORBITOPATHY (GO)**
Guia Vannucchi[1], Irene Campi[2], Nicola Currò[3], Mario Salvi[4]
[1]Endocrine Unit, Fondazione Policlinico Irccs, Milan, Italy; [2]Ospedale Maggiore Policlinico, Endocrine Unit, Fondazione Irccs Cà Granda, Milan, Italy; [3]Ophthalmology, Fondazione Irccs Cà Granda, Milan, Italy; [4]Dipartimento Scienze Mediche, Endocrine Unit, Fondazione Irccs Cà Granda, Milan, Italy

P2–01–02 **PREVALENCE OF ORGAN-SPECIFIC AUTOANTIBODIES IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE**
Tania Pilli[1], Valeria Cenci[1], Giulia Massari[1], Giulia Busonero[1], Brunetta Porcelli[2], Antonella Tabucchi[2], Alessandro Pini[2], Adriano Spreafico[2], Vittorio Fossombroni[2], Carlo Scapellato[2], Furio Pacini[1]
[1]Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy; [2]Department of Emergency and Diagnostic Services, University of Siena, Siena, Italy

P2–01–03 **CLINICAL SIGNIFICANCE OF TSH-RECEPTOR ANTIBODIES (TRAB) IN PATIENTS WITH AUTOIMMUNE THYROIDITIS**
Mihail Boyanov[1], Ralitsa Mekova[1], Deniz Bakalov[2], Adelina Tsakova[3]
[1]Medical University Sofia, University Hospital Alexandrovska, Clinic of Endocrinology and Metabolism, Department of Internal Medicine, Sofia, Bulgaria; [2]University Hospital Alexandrovska, Endocrinology Clinic, Medical University Sofia, Sofia, Bulgaria; [3]Medical University Sofia, University Hospital Alexandrovska, Department of Clinical Laboratory and Clinical Immunology, Sofia, Bulgaria

P2–01–04 **THE CLINICAL ROLE OF PROAPOPTOTIC CYTOKINES TNF-A AND SFASL IN DIAGNOSIS OF AUTOIMMUNE THYROID DISEASE IN CHILDREN**
Hanna Mikos[1], Marcin Mikos[2], Marek Niedziela[3]
[1]Department of Pediatric Endocrinology and Rheumatology, Poznan University of Medical Sciences, Poznan, Poland; [2]Department of Pneumology, Allergology and Clinical Immunology, Poznan University of Medical Sciences, Poznan, Poland; [3]Poznan University Med Sci, Dept Pediatr Endocrinol and Rheumatol, Poznan, Poland

P2–01–05 **AUTOIMMUNE CO-MORBIDITIES AND AGE AT DIAGNOSIS IN HASHIMOTO'S THYROIDITIS (HT)**
Rosaria Ruggeri[1], Francesco Trimarchi[1], Giuseppe Giuffrida[1], Rosaria Certo[1], Angela Alibrandi[2], Filippo de Luca[3], Malgorzata Wasniewska[3]
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P2–01–06 **THYROIDITIS AND VITAMIN D**
Miskic Blazenka[1], Sidbela Zukanovic[2], Vesna Ćosić[3], Marijana Knežević Praveček[4], Matica Jandric Balen[5], Karla Miškić[6], Natasa Moser[5]
[1]Gh Dr Josip Bencevic Sl.Brod, University Jj Strosmayer Osijek Medical Faculty Osijek, Slav. Brod, Croatia; [2]University Jj Strossmayer Osijek, Medical Faculty Osijek, Osijek, 1.Endocrinology Gh 'Dr J Benčević' Sl.Brod Croatia, Osijek, Croatia; [3]University Jj Strossmayer Osijek, Medical Faculty Osijek, Osijek, Hystori of Medicine, Gynecology, Polyclinic Cosic, Slavonski Brod, Croatia, Osijek, Croatia; [4]University Jj Strossmayer Osijek, Medical Faculty Osijek, Kardiolology Gh 'Dr J Benčević' Sl.Brod Croatia, Osijek, Croatia; [5]University Jj Strossmayer Osijek, Medical Faculty Osijek, Osijek, Endocrinology Gh 'Dr J Benčević' Sl.Brod Croatia, Osijek, Croatia; [6]Medical Faculty Rijeka, Study of Dental Medicine, Rijeka, Croatia

P2–01–07 **CLINICAL AND HISTOLOGICAL DIFFERENCES OF THYROID PAPILLARY CARCINOMA IN PATIENTS WITH CHRONIC LYMPHOCYTIC THYROIDITIS**
Ana Margarida Monteiro[1], Vera Fernandes[1], Selma Souto[1], Olinda Marques[1], Marta Alves[1]
[1]Serviço de Endocrinologia, Hospital de Braga, Braga, Portugal

P2–01–08 **AUTOIMMUNE THYROID DISORDERS IN TYPE 1 DIABETES – 15 YEARS RETROSPECTIVE STUDY**

Claudia Matta-Coelho[1], Ana Margarida Monteiro[1], Fernando Mota-Garcia[2]
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P2–01–09 **THE INFLUENCE OF METHIMAZOLE TREATMENT ON THYROID VASCULARITY IN PATIENTS WITH GRAVES' DISEASE**

Katja Zaletel[1], Ana Kisovar[2], Polona Klavžar[2], Simona Gaberšček[3]
[1]University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia; [2]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia; [3]University Medical Centre Ljubljana, Department of Nuclear Medicine, University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

P2–01–10 **ORBITAL TUMOR MASSES DIAGNOSIS – GRAVES DISEASE WITH ORBITAL LYMPHOMA**

Kristina Dyacenko[1], Daniel Mihai[1], Daniela Alexandrescu[1], Corin Badiu[1]
[1]National Institute of Endocrinology, Bucharest, Romania

P2–01–11 **THE CORRELATION OF THYROID AUTO-IMMUNITY AND TYPE 1 DIABETES MELLITUS**

Miranda Miminoshvili[1], Lali Nikoleishvili[1], Ramaz Kurashvili[1], Tamar Maghradze[1]
[1]LTD 'Diacor', Tbilisi, Georgia

Room 2

02 Hypothyroidism 1

Chairperson: *Peter Taylor,* UK

P2–02–01 **SELENIUM SUPPLEMENTATION SIGNIFICANTLY REDUCES SERUM THYROID PEROXIDASE AUTOANTIBODIES IN PATIENTS WITH CHRONIC AUTOIMMUNE THYROIDITIS: A META-ANALYSIS**

Johanna Wichman[1], Kristian Winther[2], Steen Joop Bonnema[1], Laszlo Hegedüs[1]
[1]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; [2]Odense University Hospital, University of Southern Denmark, Odense, Denmark

P2–02–02 **PHYSICAL PERFORMANCE IN OVERT AND SUBCLINICAL HYPOTHYROIDISM: A PILOT STUDY**

Daniela Gallo[1], Eliana Piantanida[2], Giovanni Veronesi[2], Maria Laura Tanda[2], Adriana Lai[2], Lorenza Sassi[2], Valentina Lombardi[2], Elvira Masiello[3], Paola Premoli[2], Eleonora Bianconi[2], Marco Ferrario[2], Luigi Bartalena[1]
[1]University of Insubria, Varese, Varese, Italy; [2]University of Insubria, Varese, Italy; [3]Dept. Clinical & Exp. Medicine, Varese, Italy

P2–02–03 **QUALITY OF COMPENSATION AND WELL-BEING OF PATIENTS WITH PRIMARY HYPOTHYROIDISM AND OBESITY**

Valentin Fadeyev[1], Tatyana Morgunova[1], Yulia Manuylova[2]
[1]I.M. Sechenov First Moscow Medical University, Moscow, Russian Federation; [2]I.M. Sechenov First Moscow State Medical University, Department of Endocrinology, Moscow, Russian Federation

P2–02–04 **EFFECTS OF SELENIUM SUPPLEMENTATION ON CLINICALLY RELEVANT OUTCOMES IN CHRONIC AUTOIMMUNE THYROIDITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

Kristian Winther[1], Johanna Wichman[2], Laszlo Hegedüs[2], Steen Joop Bonnema[2]
[1]Odense University Hospital, University of Southern Denmark, Odense, Denmark; [2]Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

P2–02–05 **L-T4 IN SOFT GEL CAPSULE AND IN ORAL LIQUID FORM IS BETTER ABSORBED COMPARED TO TABLET IN A PATIENT WITH BILIOPANCREATIC DIVERSION**

Damiano Gullo[1], Federica Vinciguerra[1], Maria Luisa Arpi[1], Giuseppina Parrinello[1], Patrizia Tita[1], Roberto Baratta[1], Sebastiano Squatrito[1]
[1]Endocrine Unit, Garibaldi-Nesima Hospital, University of Catania Medical School, Catania, Italy

P2–02–06 **IMPROVED QUALITY OF LIFE DURING L-T4/L-T3 COMBINATION THERAPY OF HYPOTHYROIDISM WAS NOT RELATED TO CHANGE IN WEIGHT**

Michaelsson Luba Freja[1], Jeppe Lerche la Cour[2], Bjarke Borregaard Medici[3], Torquil Watt[4], BIrte Nygaard[5], Jens Faber[6]
[1]Department of Endocrinology, Herlev University Hospital, Copenhagen, Denmark; [2]Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [3]Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Gentofte University Hospital, Copenhagen, Denmark; [4]Department of Endocrinology, Copenhagen University Hospital Rigshospitalet, Denmark, Department of Endocrinology, Herlev Hospital, University of Copenhagen, Copenhagen, Denmark; [5]Department of Endocrinology, Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; [6]Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Herlev, Denmark

P2–02–07 **HYPOTHYROIDISM TODAY IN AN OFFICE BASED PRACTICE**

Esa Soppi[1]
[1]Eira Hospital, Outpatient Clinic, Internal Medicine, Helsinki, Finland

P2–02–08 **'SUBCLINICAL HYPOTHYROIDISM IN PREGNANCY' OR 'GESTATIONAL HYPOTHYROIDISM'?**
David Metreveli[1]
[1]Tbilisi State Medical University, David Metreveli Medical Centre Ltd, Tbilisi, Georgia

P2–02–09 **THYROGLOBULIN AND OTHER THYROID LABORATORY PARAMETERS IN TREATING HYPOTHYROIDISM IN CHILDREN**
Radovan Bílek[1], *Marcela Dvorakova*[2]
[1]Institute of Endocrinology, Dept of Steroids and Proteofactors, Prague 1, Czech Republic; [2]Institute of Endocrinology, Prague, Czech Republic

Room 3+4

03 Goiter 1

Chairperson: *Andrzej Lewinski,* Poland

P2–03–01 **RADIOFREQUENCY ABLATION FOR BENIGN THYROID NODULES IN 375 PATIENTS: 2 YEARS SINGLE CENTER EXPERIENCE**
Vyacheslav Solovov[1], *Michael Vozdvizhenskiy*[1], *Alexander Makhonin* [1], *Andrew Orlov*[1]
[1]Samara Oncology Center, Samara, Russian Federation

P2–03–02 **ASSOCIATION OF SERUM CALCITONIN LEVELS WITH MULTINODULAR THYROID DISEASE: 10-YEAR SINGLE CENTER EXPERIENCE**
George Simeakis[1], *Ioanna Patinioti*[2], *Marina Mitropoulou*[2], *Elli Anagnostou*[2], *Spiros Sapounas*[2], *Evangelia Zapanti*[2], *Vasiliki Vasileiou*[2], *Antonis Polymeris*[2], *Katerina Saltiki*[3], *Eleni Anastasiou*[2], *Maria Alevizaki*[3]
[1]Athens University School of Medicine, Athens, Greece; [2]Endocrinology Dept, Alexandra Hospital, Athens, Greece; [3]Endocrinology Unit, Clinic of Therapeutics, Medical School, University of Athens, Athens, Greece

P2–03–03 **FUNCTIONAL AND SERUM THYROGLOBULIN CHANGES AFTER US-GUIDED HIFU ABLATION OF BENIGN SOLID THYROID NODULES IN EUTHYROID PATIENTS**
Roussanka Kovatcheva[1], *Jordan Vlahov*[1], *Katja Zaletel*[2], *Alexander Shinkov*[1], *Julian Stoinov*[1], *Radina Ivanova-Boyanova*[3], *Georgi Kirilov*[1]
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P2–03–04 **ROBOT ASSISTED TRANSAXILLARY THYROIDECTOMY FOR BENIGN THYROID DISEASES: THE OPERATIVE OUTCOMES OF 177 CONSECUTIVE PATIENTS**
Min Jhi Kim[1], *Jungbum Choi*[2], *Tae Hyung Kim*[1], *Seul Gi Lee*[2], *Eun Jeong Ban*[3], *Cho Rok Lee*[1], *Sang-Wook Kang*[1], *Jandee Lee*[1], *Jong Ju Jeong*[4], *Kee-Hyun Nam*[4], *Woungyoun Chung*[5]
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P2–03–05 **THE EFFECT OF J-131 THERAPY IN PATIENTS WITH AUTONOMOUSLY FUNCTIONING THYROID NODULES AND NORMAL TSH LEVEL**
Miodrag Lacic[1]
[1]Polyclinic Lacic, Thyroid Department, Zagreb, Croatia

P2–03–06 **ADIPOSE TISSUE ACCUMULATION AND SEDENTARY LIFESTYLE ARE PREDICTIVE OF SPECIFIC THYROID NODULE ULTRASOUND FEATURES**
Grigorios Panagiotou[1], *Despina Komninou*[1], *George Linardos*[1], *Eleni Karoglou*[1], *Maria Somali*[2], *Konstantinos Tziomalos*[1], *Marina Kita*[3], *Kalliopi Pazaitou-Panayiotou*[4]
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P2–03–07 **THE IMPACT OF ULTRASOUND SCREENING ON THE EVALUATION OF THYROID PATIENT: A COMPARATIVE STUDY OF 1,000 PATIENTS INVESTIGATED IN 2005 AND 2015**
Tamas Solymosi[1]
[1]Bugat Hospital, Dept. of Thyroidology, Gyöngyös, Hungary

P2–03–08 **COMPARISON BETWEEN THREE THERMOABLATION TECHNICS FOR BENIGN THYROID NODULES TREATMENT: EXPERIENCE IN A SINGLE CENTER**
Herve Monpeyssen[1], *Christine Terestchenko*[1], *Alain Dana*[1], *Patrick Aidan*[1]
[1]American Hospital of Paris, Neuilly Sur Seine, France

P2–03–09 **THYROID NODULES AND CYSTS IN TYPE 1 DIABETIC CHILDREN AND ADOLESCENTS**
Lusine Navasardyan[1], *Yelena Aghajanova*[1], *Renata Markosyan*[1], *Marianna Gevorgyan*[1]
[1]Yerevan State Medical University, Yerevan, Armenia

P2–03–10 **SERUM THYROGLOBULIN LEVEL AS A PREDICTIVE FACTOR OF NODULE SIZE AND MALIGNANCY IN PATIENTS WITH THYROID NODULES**

Simona Gaberscek[1], Sara Kukman[2], Ajda Biček[3], Adrijana Oblak[3], Edvard Pirnat[3], Katja Zaletel[3]

[1]University Medical Centre Ljubljana, Ljubljana, Slovenia; [2]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia; [3]University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia

Room 16

04 Reproduction

Chairperson: *Chantal Daumerie,* Belgium

P2–04–01 **CLINICAL AND MOLECULAR CHARACTERISTIC OF PATIENTS WITH THYROID DYSGENESIS AND PAX8 MUTATION**

Malgorzata Kumorowicz-Czoch[1], Anna Madetko-Talowska[2], Pia Hermanns[3], Joachim Pohlenz[3]

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P2–04–02 **CONTROLLED ANTENATAL THYROID SCREENING (CATS) STUDY: OBSTETRIC OUTCOMES**

Peter Taylor[1], Arron Lacey[2], Daniel Thayer[2], Mohd Shazli Draman[3], Arshiya Tabasum[4], Ilaria Muller[5], Luke Marsh[1], Arwel Poacher[1], Marian Ludgate[5], Alexandra Rees[4], Kristien Boelaert[6], Aled Rees[5], Shiao Chan[7], Scott Nelson[8], John Lazarus[9], Colin Dayan[5], Bijay Vaidya[10], Onyebuchi Okosieme[1]

[1]Cardiff University, Cardiff, UK; [2]Swansea University, Swansea, UK; [3]Imem, Cardiff University, Cardiff, UK; [4]University Hospital of Wales, Cardiff, UK; [5]Institute of Molecular & Experimental Medicine, Cardiff University, Cardiff, UK; [6]University of Birmingham, Birmingham, UK; [7]National University of Singapore, Singapore, Singapore; [8]University of Glasgow, Glasgow, UK; [9]Cardiff University, Cardiff School of Medicine, Cardiff, UK; [10]Department of Endocrinology, Endocrinology, Exeter, UK

P2–04–03 **THE ROLE OF ANTITHYROGLOBULIN AUTOANTIBODIES IN COMPARISON WITH THYROID PEROXIDASE AUTOANTIBODIES IN PREGNANT DANISH WOMEN**

Sofie Bliddal[1], Malene Boas[2], Linda Hilsted[3], Lennart Friis-Hansen[4], Ann Tabor[5], Ulla Feldt-Rasmussen[6]

[1]Rigshospitalet (Copenhagen University Hospital), Department of Medical Endocrinology, Copenhagen, Denmark; [2]Department of Growth and Reproduction, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [3]Department of Clinical Biochemistry, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [4]Department of Clinical Biochemistry, Slagelse-Naestved Hospital, Copenhagen, Denmark; [5]Center of Fetal Medicine, Department of Obstetrics, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [6]Department of Medical Endocrinology, Rigshospitalet, University of Copenhagen. Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

P2–04–04 **PREVALENCE OF THYROID AUTOIMMUNITY AND DYSFUNCTION IN WOMEN WITH IRON DEFICIENCY DURING EARLY PREGNANCY: IS IT ALTERED?**

Veltri Flora[1], Sarah Decaillet[2], Pierre Kleynen[2], Lidia Grabczan[2], Julie Belhomme[2], Serge Rozenberg[1], Thierry Pepersack[1], Kris Poppe[3]

[1]Centre Hosptilalier Universitaire Saint Pierre, Université Libre de Bruxelles (Ulb), Brussels, Belgium; [2]Centre Hosptilalier Universitaire Saint Pierre, Brussels, Belgium; [3]Dr. Poppe Bvba Yl Brucha, Overijse, Belgium

P2–04–05 **CLINICAL RELATIONSHIP BETWEEN HASHIMOTO'S THYROIDITIS AND BRAFV600E MUTATION STATUS IN PAPILLARY THYROID CARCINOMA PATIENTS**

Sang Yull Kang[1], Hyun Jo Youn[2], Sung Hoo Jung[1]

[1]Chonbuk National University Hospital, Jeonju, Korea, Rep. of South; [2]Chonbuk National University Hospital, Jeonju, Korea, Rep. of South

P2–04–06 **CHANGES IN THYROID HORMONE AND INSULIN RESISTANCE PARAMETERS IN HEALTHY AND YOUNG WOMEN DURING THE FIRST YEAR OF USE OF THE CONTRACEPTIVE DEPOT MEDROXYPROGESTERONE ACETATE**

Alessandra Quintino Moro[1], Priscila Nazaré Santos[1], Aglécio Souza[2], Denise Engelbrecht Zantut Wittmann[3], Arlete Maria Fernandes[1]

[1]Human Reproduction Unit, Department of Obstetrics and Gynecology, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil; [2]Metabolic Unity, Department of Clinical Medicine, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil; [3]Endocrinology Division, Department of Clinical Medicine, Faculty of Medical Sciences, University of Campinas-Unicamp, Campinas, Brazil

P2–04–07 **ASSOCIATION OF HLA-B*46 POLYMORPHISM AND GRAVES' DISEASE IN THAI POPULATIONS**
Natnicha Houngngam[1], Jaruwan Kongkit[1], Lilly Pathomyok[1], Thiti Snabboon[2]
[1]Chulalongkorn University, Bangkok, Thailand; [2]Chulalongkorn University, Medicine, Bangkok, Thailand

P2–04–08 **THYROID HOMEOSTASIS IN IODINE-DEFICIENT AND IODINE-SUFFICIENT HEALTHY INDIAN PREGNANT WOMEN**
Nikku Yadav[1], Atul Kathait[2], Vineet Sharma[2], Asha Chandola-Saklani[3]
[1]Centre for Biosciences and Clinical Research, School of Biosciences, Apeejay Stya University, School of Biosciences, Gurgaon, India; [2]Centre for Biosciences and Clinical Research, School of Biosciences, Apeejay Stya University, Gurgaon, India; [3]Dept Biosciences & Clinical Research, Sohna- Gurgaon, India

P2–04–09 **PRESCRIBE THYROXIN OR NOT**
Hermine Ayvazyan[1]
[1]Rmc Armenia, Erevan, Armenia

P2–04–10 **HYPOTHYROIDISM AS A CAUSE OF INFERTILITY**
Armine Khroyan[1]
[1]Yerevan State Medical University, Endocrinology, Yerevan, Armenia

Room 14

05 Thyroid Cancer Diagnostic II

Chairperson: *Alicja Hubalewska-Dydejczyk,* Poland

P2–05–01 **COMPARISON OF THYROID FINE NEEDLE ASPIRATION BIOPSY RESULTS BEFORE AND AFTER IMPLEMENTATION OF BETHESDA CLASSIFICATION**
Didem Ozdemir[1], Nagihan Bestepe[1], Sevgul Faki[1], Aydan Kilicarslan[2], Omer Parlak[3], Reyhan Ersoy[1], Bekir Cakir[1]
[1]Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, School of Medicine, Department of Pathology, Ankara, Turkey; [3]Ankara Yildirim Beyazit University, School of Medicine, Department of General Surgery, Ankara, Turkey

P2–05–02 **THYROID MALIGNANCY RISK IN DIFFERENT CLINICAL THYROID DISEASES**
Ahmet Dirikoc[1], Sevgul Faki[1], Husniye Baser[1], Didem Ozdemir[1], Cevdet Aydin[1], Reyhan Ersoy[1], Mehmet Kilic[2], Aydan Kilicarslan[3], Bekir Cakir[1]
[1]Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, School of Medicine, Department of General Surgery, Ankara, Turkey; [3]Ankara Yildirim Beyazit University, School of Medicine, Department of Pathology, Ankara, Turkey

P2–05–03 **CLINICAL IDENTIFICATIONS OF REMNANT RADIOIODINE DISTRIBUTIONS ON DIAGNOSTIC I-131 SPECT/CT IN PATIENTS WITH DIFFERENTIATED THYROID CANCER AFTER THYROID REMNANT ABLATION**
Joji Kawabe[1], Shigeaki Higashiyama[1], Atsushi Yoshida[1], Kohei Kotani[1], Susumu Shiomi[1]
[1]Department of Nuclear Medicine, Graduate School of Medicine, Osaka City University, Osaka City, Japan

P2–05–04 **THE ROLE OF FDG-PET/CT IN DIFFERENTIATED THYROID CANCER**
Barbara Vidergar Kralj[1], Ivana Žagar[1], Andreja Antonija Schwarzbartl Pevec[1], Nikola Besic[2]
[1]Institute of Oncology Ljubljana, Ljubljana, Slovenia; [2]Institute of Oncology, Ljubljana, Slovenia

P2–05–05 **THE ROLE OF THE NODULE VOLUME IN EVALUATING THE RISK OF MALIGNANCY IN THYROID NODULES**
Nagihan Bestepe[1], Didem Ozdemir[2], Husniye Baser[1], Berna Evranos[1], Nuran Sungu[3], Mehmet Kilic[4], Reyhan Ersoy[1], Bekir Cakir[1]
[1]Ankara Yildirim Beyazit University School of Medicine Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Yildirim Beyazit University School of Medicine Department of Pathology, Ankara, Turkey; [4]Ankara Yildirim Beyazit University School of Medicine Department of General Surgery, Ankara, Turkey

P2–05–06 **CORRELATION OF THYROID CYTOLOGY REPORT WITH SURGICAL PATHOLOGY IN THYROID NODULE**
Tada Kunavisarut[1], Intira Masayavanich[2]
[1]Faculty of Medicine, Bangkok, Bangkok, Thailand; [2]Siriraj Hospital, Mahidol University, Bangkok, Thailand

P2–05–07 **THYROID CANCER INCIDENCE FOLLOWING THYROIDECTOMY: A TERTIARY CENTRE EXPERIENCE IN ROMANIA**
Sorina Martin[1], Oana Budianu[2], Oana Ion[2], Andreea Grigore[2], Anca Sirbu[1], Alice Albu[1], Carmen Barbu[1], Cosmin Giulea[3], Adrian Miron[3], Florin Andrei[4], Simona Fica[1]
[1]Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Elias Hospital, Endocrinology Department, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [3]Elias Hospital, Surgery Department, Carol Davila University of Medicine and Pharmacy, Surgery Department, Bucharest, Romania; [4]Elias Hospital, Pathology Department, Bucharest, Romania

P2–05–08 **A RARE CAUSE OF POSTPARTUM RAPIDLY ENLARGING GOITER**

Berna Evranos Ogmen[1], Muhammet Cüneyt Bilginer[2], Cevdet Aydin[3], Yetkin Ağaçkıran[4], Hakan Korkmaz[5], Reyhan Ersoy[2], Bekir Cakir[6]

[1]Ankara Ataturk Research and Training Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Yildirim Beyazit University School of Medicine Department of Endocrinology and Metabolism, Ankara, Turkey; [4]Ankara Ataturk Research and Training Hospital Department of Pathology, Ankara, Turkey; [5]Ankara Yildirim Beyazit University School of Medicine Department of Ear, Nose and Throat, Ankara, Turkey; [6]Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

Room 12

06 Thyroid Cancer Therapeutics

Chairperson: *Thera Links,* The Netherlands

P2–06–01 **CENTRAL LYMPH NODE DISSECTION USING FLUORESCENCE IMAGING IN THE ROBOTIC THYROID SURGERY**

Wan Wook Kim[1], Jin Hyang Jung[1], Jin Ho Jung[1], Taek Ju Kwon[1], Jeeyeon Lee[1], Seung Ook Hwang[1], Ho Yong Park[1]

[1]Kyungpook National University, School of Medicine, Daegu, Korea, Rep. of South

P2–06–02 **MINIMALLY INVASIVE OPEN THYRODIECTOMY: SURGICAL COMPLETENESS OF CONSECUTIVE 108 PATIENTS**

Tae Hyung Kim[1], Min Jhi Kim[1], Jungbum Choi[2], Seul Gi Lee[2], Eun Jeong Ban[3], Cho Rok Lee[1], Sang-Wook Kang[1], Jandee Lee[1], Jong Ju Jeong[4], Kee-Hyun Nam[4], Woungyoun Chung[5], Cheong Soo Park[5]

[1]Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [2]Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [3]Yonsei Univsersity College of Medicine, Seoul, Korea, Rep. of South; [4]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [5]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South

P2–06–03 **IS IT SUFFICIENT TO DO LOBECTOMY ALONE FOR PAPILLARY THYROID CARCINOMA MEASURING 4CM OR LESS WITHOUT EXTRA-THYROIDAL EXTENSION AND CLINICAL LYMPH NODE METASTASIS?**

Jin-Woo Park[1], Dong Ju Kim[2], Ok-Jun Lee[3]

[1]Department of Surgery, College of Medicine Chungbuk National University, Department of Surgery, Chungbuk National University Hospital, Cheongju, Korea, Rep. of South; [2]Department of Surgery, Chungbuk National University Hospital, Cheongju, Korea, Rep. of South; [3]Department of Pathology, College of Medicine Chungbuk National University, Cheongju, Korea, Rep. of South

P2–06–04 **CAN T1A MULTIFOCAL PAPILLARY THYROID MICROCARCINOMAS WITH A TOTAL TUMOR DIAMETER OF 1–2 CM BE RECLASSIFIED AS T1B?**

Abbas Ali Tam[1], Didem Özdemir[1], Berna Evranos Öğmen[1], Sevgül Fakı[1], Ersin Gürkan Dumlu[2], Hayriye Tatlı Doğan[3], Reyhan Ersoy[1], Bekir Çakır[1]

[1]Yıldırım Beyazıt University Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Yıldırım Beyazıt University Faculty of Medicine, Department of General Surgery, Ankara, Turkey; [3]Ataturk Training and Research Hospital, Department of Pathology, Ankara, Turkey

P2–06–05 **DYNAMIC RISK STRATIFICATION IN MEDULLARY THYROID CANCER OF SINGLE CENTER'S RESULT**

Jong Ju Jeong[1], Jungbum Choi[2], Seul Gi Lee[2], Min Jhi Kim[3], Tae Hyung Kim[3], Eun Jeong Ban[4], Cho Rok Lee[3], Jandee Lee[3], Sang-Wook Kang[3], Kee-Hyun Nam[1], Woungyoun Chung[5], Cheong Soo Park[3]

[1]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [2]Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [3]Yonsei University College of Medicine, Seoul, Korea, Rep. of South; [4]Yonsei Univsersity College of Medicine, Seoul, Korea, Rep. of South; [5]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South

P2–06–06 **CLINICOPATHOLOGICAL FACTORS ASSOCIATED WITH POOR RESPONSE TO 131I IN LOW TO INTERMEDIATE RISK PAPILLARY THYROID CANCER**

Patrícia Tavares[1], Catarina Machado[1], Lilite Barbosa[1], Antónia Póvoa[1], Carlos Soares[1], José Manuel Oliveira[2], Gustavo Rocha[1], Maria João Oliveira[1]

[1]Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal; [2]Hpp-MM, Vila Nova de Gaia, Portugal

P2–06–07 **SKIP METASTASIS TO LATERAL NECK LYMPH NODES IN PAPILLARY THYROID CANCER**

Young Jae Ryu[1], Jin Seong Cho[1], Dong Hoon Cho[1], Jung Han Yoon[1], Min Ho Park[1]

[1]Chonnam National University Hwasun Hospital and Medical School, Hwasun, Korea, Rep. of South

P2–06–08 **RISK GROUP STRATIFICATION FOR DISTANT METASTASIS IN PATIENTS WITH MINIMALLY INVASIVE FOLLICULAR THYROID CARCINOMA**

Yi Ho Lee[1], Yu-mi Lee[1], Tae-Yon Sung[1], Jong Ho Yoon[1], Ki-Wook Chung[1], Suck Joon Hong[1]

[1]Asan Medical Center, Seoul, Korea, Rep. of South

P2–06–09 **USEFULNESS OF DETERMINATION FOR CENTRAL LYMPH NODE METASTASIS BY SURGEON USING THE PALPATION IN PAPILLARY THYROID CANCER**

Wan Wook Kim[1], Jin Hyang Jung[1], Seung Ook Hwang[1], Jeeyeon Lee[1], Taek Ju Kwon[1], Jin Ho Jung[1], Ho Yong Park[1]

[1]Kyungpook National University, School of Medicine, Daegu, Korea, Rep. of South

P2–06–10 **MYOCARDIAL INFARCT AFTER LONG TERM TREATMENT WITH A TYROSINE KINASE INHIBITOR (TKI) WITH ANTI-VEGF RECEPTOR ACTIVITY**

Luisa Paschke[1], Lincke Thomas[2], Mühlberg Katja[1], Lindner Tom[1], Paschke Ralf[3]

[1]University of Leipzig, Leipzig, Germany; [2]University of Leipzig, Leipzig, Germany; [3]University of Calgary, Calgary, Alta., Canada

Room 13+15

07 Thyroid Cancer – Clinical I

Chairperson: *Jeppe Lerche La-Cour,* Denmark

P2–07–01 **EVALUATION OF ULTRASOUND SCORING AND THYROID IMAGING REPORTING AND DATA SYSTEM (TIRADS) IN PREDICTION OF MALIGNANCY IN PATIENTS WITH BETHESDA CATEGORY III (AUS/FLUS)**

Husniye Baser[1], Bekir Cakir[2], Oya Topaloglu[2], Afra Alkan[3], Burcak Polat[2], Hayriye Tatli Dogan[4], Mustafa Omer Yazicioglu [5], Cevdet Aydin[2], Reyhan Ersoy[2]

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P2–07–02 **HIGH RESISTIVE BLOOD FLOW IN PAPILLARY THYROID CANCERS: AN IMAGING STUDY FOR CLINICAL USE**

Ahmet Aslan[1], Seda Sancak[2], Ercan Ayaz[3], İbrahim İnan[3], Mine Aslan[4], Orhan Alimoğlu[5], Murat Acar[3]

[1]Department of Radiology, Umraniye Training and Research Hospital, Department of Radiology, Medical School of Marmara University, Istanbul, Turkey; [2]1fatih Sultan Mehmet Training and Research Hospital, 2department of Endocrinology and Metabolism, Medical School of Marmara University, Istanbul, Turkey; [3]Department of Radiology, Göztepe Training and Research Hospital, Medical School of Istanbul Medeniyet University, Istanbul, Turkey; [4]Department of Radiology, Umraniye Training and Research Hospital, Istanbul, Turkey; [5]Department of General Surgery, Göztepe Training and Research Hospital, Medical School of Istanbul Medeniyet University, Istanbul, Turkey

P2–07–03 **AGE AT DIAGNOSIS IS NOT A VARIABLE THAT AFFECTS THE FREQUENCY OF STRUCTURAL INCOMPLETE RESPONSE IN ANY OF THE RISKS OF RECURRENCE FROM PATIENTS WITH DIFFERENTIATED THYROID CANCER**

Fabian Pitoia[1], Fernando Jerkovich[1], Fernanda Bueno[1], Anabella Smulever[1], Graciela Cross[1]

[1]Hospital de Clínicas – University of Buenos Aires, Buenos Aires, Argentina

P2–07–04 **CLINICOPATHOLOGICAL FEATURES OF THYROID CARCINOMAS IN GERIATRIC PATIENTS**

Fatma Dilek Dellal[1], Didem Ozdemir[2], Abbas Ali Tam[2], Husniye Baser[3], Hayriye Tatlı Doğan[4], Omer Parlak[5], Reyhan Ersoy[6], Bekir Cakir[6]

[1]Ankara Training and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [4]Atatürk Education and Research Hospital, Department of Pathology, Ankara, Turkey; [5]Ankara Yildirim Beyazit University, School of Medicine, Department of General Surgery, Ankara, Turkey; [6]Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

P2–07–05 **IS THERE ANY DIFFERENCE BETWEEN FEMALE AND MALE GENDER IN TERMS OF TUMOR HISTOPATHOLOGY AND TNM STAGES IN PATIENTS WITH THYROID CANCER?**

Husniye Baser[1], Berna Evranos[1], Oya Topaloglu[2], Cevdet Aydin[2], Aydan Kilicarslan[3], Ersin Gurkan Dumlu[4], Reyhan Ersoy[2], Bekir Cakir[2]

[1]Ankara Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Yildirim Beyazit University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Yildirim Beyazit University School of Medicine, Department of Pathology, Ankara, Turkey; [4]Yildirim Beyazit University School of Medicine, Department of General Surgery, Ankara, Turkey

P2–07–06 **THE RELATIONSHIP BETWEEN THE BRAFV600E MUTATION IN PAPILLARY THYROID MICROCARCINOMA AND CLINICOPATHOLOGIC FACTORS**

Jong-Chul Hong[1], Ji-won Seo[2], Eunji Lee[2], Dong-Kun Lee[3], Heon-Soo park[1]

[1]Department of Otolaryngology, Head and Neck Surgery, College of Medicine, Dong-A University, Busan, Korea, Rep. of South; [2]Department of Otolaryngology-Head and Neck Surgery, Dong-A University College of Medicine, Busan, Korea, Rep. of South; [3]Department of Otolaryngology, Head and Neck Surgery, College of Medicine, Inje University, Busan, Korea, Rep. of South

P2–07–07 **PROGNOSIS OF PAPILLARY THYROID CANCER WITH EXTRATHYROIDAL EXTENSION ACCORDING TO THE LOCATION OF PRIMARY TUMOR**

Seok-Mo Kim[1], Soo Young Kim[1], Chi Young Lim[1], Bup-Woo Kim[1], Yong Sang Lee[1], Hang-Seok Chang[1], Cheong Soo Park[1]

[1]Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

P2–07–08 **THYROID CANCER HISTOLOGICAL TYPES AND CHARACTERISTICS OF THE FUNCTIONAL CONDITION IN THE REPUBLIC OF ARMENIA**

Sergey Hakobyan[1]
[1]Yerevan State Medical University, Echmiadzin, Armenia

P2–07–09 **PATIENT WITH HIGH-MALIGNANT B-CELL LYMPHOMA AND INFILTRATION INTO THE THYROID**

Carsten Koerber[1], *Nicole Körber-Hafner*[2]
[1]Gemeinschaftspraxis, Nuklearmed. Praxis, Fulda, Germany; [2]Gemeinschaftspraxis, Fulda, Germany

East Lounge / 8+9+10+11 (Main Auditorium)

08 Transporters and Others

Chairperson: *Domenico Salvatore,* Italy

P2–08–01 **A NEW ROLE FOR MONOCARBOXYLATE TRANSPORTER 8: REGULATION OF THYROID HORMONE AVAILABILITY DURING RETINAL DEVELOPMENT**

Pieter Vancamp[1], *Veerle Darras*[1]
[1]Laboratory Comparative Endocrinology, Biology Department, Ku Leuven, Leuven, Belgium

P2–08–02 **DIFFERENTIAL EFFECTS OF THYROID HORMONE ON CORTICAL AND HYPOTHALAMIC PARVALBUMIN NEURONS IN MICE**

Lisbeth Harder[1], *Susi Dudazy-Gralla*[2], *Heike Heuer*[3], *Jens Mittag*[4]
[1]Center of Brain, Behavior and Metabolism, University of Lübeck, Luebeck, Germany; [2]Karolinska Institutet, Department of Cell and Molecular Biology, Stockholm, Sweden; [3]Leibniz Institute for Environmental Medcine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany; [4]Universität Lübeck, Cbbm, Lübeck, Germany

P2–08–03 **ROLE OF THE MURINE THYROID HORMONE TRANSPORTERS MCT8 AND OATP1C1 IN THE CARDIOVASCULAR AND THERMOREGULATORY SYSTEMS**

Beate Herrmann[1], *Lisbeth Harder*[2], *Jiesi Chen*[3], *Rebecca Oelkrug*[4], *Heike Heuer*[5], *Jens Mittag*[6]
[1]University of Lübeck, Center of Brain, Behavior and Metabolism, Lübeck, Germany; [2]Center of Brain, Behavior and Metabolism, University of Lübeck, Luebeck, Germany; [3]Leibniz Institute for Environmental Medicine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany; [4]Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany; [5]Leibniz Institute for Environmental Medcine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany; [6]Universität Lübeck, Cbbm, Lübeck, Germany

P2–08–04 **CHEMICAL CHAPERONES CAN ALSO RESCUE PATHOGENIC MCT8 MUTATIONS THAT LEAD TO THE SEVERE FORM OF AHDS**

Doreen Braun[1], *Ulrich Schweizer*[2]
[1]Institut für Biochemie und Molekularbiologie, Universität Bonn, Bonn, Germany; [2]Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany

P2–08–05 **TRANSMEMBRANE MCT8-MEDIATED T3 TRANSPORT IS INHIBITED BY SOME COMMONLY USED DRUGS AND BY L-CARNITINE**

Caterina Di Cosmo[1], *Giuseppina De Marco*[1], *Patrizia Agretti*[1], *Eleonora Ferrarini*[1], *Antonio Dimida*[1], *Salvatore Benvenga*[2], *Paolo Vitti*[1], *Massimo Tonacchera*[1]
[1]Department of Clinical and Experimental Medicine, Endocrinology Unit, University of Pisa, Pisa, Italy; [2]Department of Clinical and Experimental Medicine, Section of Endocrinology, University of Messina, Messina, Italy

P2–08–06 **MCT8 MUTANTS F287V AND S313A SEVERELY IMPACT THYROID HORMONE TRANSPORT**

Dorothea Bayer-Kusch[1], *Doreen Braun*[1], *Ulrich Schweizer*[1]
[1]Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany

P2–08–07 **THYROID FUNCTION IN PSEUDOHYPOPARATHYROIDISM TYPE 1A**

Slavica Savic[1], *Tijana Lalić*[2], *Marija Barać*[2], *Mirjana Stojković*[2], *Tanja Nišić*[2], *Biljana Nedeljković-Beleslin*[3], *Miloš Stojanović*[2], *Jasmina Ćirić*[3], *Miloš Žarković*[3]
[1]Belgrade, Serbia; [2]Clinic of Endocrinology, Belgrade, Serbia; [3]Clinic of Endocrinology, School of Medicine, University of Belgrade, Belgrade, Serbia

P2–08–08 **THYROTROPIN-SECRETING ADENOMA: CASE REPORT**

Ani Karapetyan[1], *Ekaterina Gormolysova*[2], *Boris Pinkhasov*[3]
[1]Fsbi Federal Neurosurgical Center of Ministry of Public Health, Research Institute of Experimental and Clinical Medicine, Novosibirsk, Russian Federation; [2]Fsbi Federal Neurosurgical Center of Ministry of Public Health, Novosibirsk, Russian Federation; [3]Research Institute of Experimental and Clinical Medicine., Novosibirsk, Russian Federation

Room 1
12.00–13.00
Poster Session P3

01 Clinical Thyroidology
Chairperson: *Philippe Caron,* France

P3–01–01 **A COMPARISON OF LEVELS OF T4 AND TSH FROM SERUM AND WHOLE BLOOD ON FILTER PAPER**
Simon Osgston[1], Fiona Williams[2], Anita Boelen[3]
[1]Population Health Sciences, Medical School, University of Dundee, Dundee, UK; [2]University of Dundee, Population Health Sciences, Dundee, UK; [3]Academic Medical Centre, Amsterdam, Netherlands

P3–01–02 **CIRCULATING FREE TRIIODOTHYRONINE CONCENTRATIONS ARE ASSOCIATED WITH PHYSICAL FUNCTION IN EUTHYROID ELDERLY SUBJECTS**
Michela Marina[1], Fulvio Lauretani[2], Marcello Giuseppe Maggio[1], Stefania Bandinelli[3], Gian Paolo Ceda[1], Luigi Ferrucci[4], Graziano Ceresini[1]
[1]Department of Clinical and Experimental Medicine, University of Parma, Parma, Italy; [2]University Hospital of Parma, Parma, Italy; [3]Azienda Sanitaria DI Firenze, Toscana, Firenze, Italy; [4]National Institute on Aging, Baltimore, Md., USA

P3–01–03 **THYROID DYSFUNCTION IN CHRONIC KIDNEY DISEASE PATIENTS**
Olga Vasilkova[1], Tatjana V. Mokhort[2], Irina Vasiukhina[3], Margarita Zmailik[3]
[1]Gomel State Medical University, Gomel, Belarus; [2]Belarusian State Medical University, Minsk, Belarus; [3]The Republican Research Center for Radiation Medicine and Human Ecology, Gomel, Belarus

P3–01–04 **EVALUATION OF VAGAL NERVE SIZE IN STANDARDIZED MONITORED THYROIDECTOMY**
Alberto Mangano[1], Andrea Leotta[1], Matteo Lavazza[1], Vincenzo Pappalardo[1], Davide Inversini[1], Cesare Carlo Ferrari[1], Francesco Frattini[1], Stefano Rausei[1], Wen Tian [2], Hoon Yub Kim[3], Che-Wei Wu [4], Gianlorenzo Dionigi[1]
[1]1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy; [2]Department of General Surgery, The Chinese People's Liberation Army General Hospital, Beijing, China; [3]Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; [4]Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

P3–01–05 **STAGE-THYROIDECTOMY: SINGLE INSTITUTION PERSPECTIVE**
Alberto Mangano[1], Vincenzo Pappalardo[1], Matteo Lavazza[1], Cesare Carlo Ferrari[1], Davide Inversini[1], Andrea Leotta[1], Francesco Frattini[1], Stefano Rausei[1], Wen Tian[2], Hoon Yub Kim[3], Che-Wei Wu[4], Gianlorenzo Dionigi[1]
[1]1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Via Guicciardini 9, 21100 Varese, Italy, Varese, Italy; [2]Department of General Surgery, The Chinese People's Liberation Army General Hospital, Beijing, China; [3]Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; [4]Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

P3–01–06 **RECURRENT LARYNGEAL NERVE (RLN) INJURY IN THYROID SURGERY: CLINICAL PATHWAYS AND RESOURCES CONSUMPTION**
Cesare Carlo Ferrari[1], Vincenzo Pappalardo[1], Andrea Leotta[1], Matteo Lavazza[1], Davide Inversini[1], Alberto Mangano[1], Francesco Frattini[1], Stefano Rausei[1], Wen Tian[2], Hoon Yub Kim [3], Che-Wei Wu[4], Gianlorenzo Dionigi[1]
[1]1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy; [2]Department of General Surgery, The Chinese People's Liberation Army General Hospital, Beijing, China; [3]Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; [4]Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan,

P3–01–07 **CAPACITY BUILDING OF PRIMARY CARE PHYSICIANS IN MANAGEMENT OF THYROID DISORDERS: IMPLEMENTATION EXPERIENCES FROM A PAN INDIA CERTIFICATE COURSE**
Tanu Soni[1], Sandeep Bhalla[2], Deepak Monga[2], Anirudh Gaurang[2], Variyata Bagre[2], Arshit Koundal[2], A.G. Unnikrishnan[3], Shailesh R. Deshpande[3], Anjali Bhatt[3], D. Prabhakaran[2]
[1]Gurgaon, India; [2]Public Health Foundation of India, Gurgaon, India; [3]Chellaram Diabetes Institute, Pune, India

P3–01–08 **ACUTE SUPPURATIVE THYROIDITIS – FORGOTTEN BUT UNFORGETTABLE CAUSE OF CERVICAL PAIN**
Ana Ferreira[1], Tiago Silva[1], Henrique Luiz[1], Maria Carlos Cordeiro[1], Isabel Manita[1], Ana Catarina Matos[1], Jorge Portugal[1]
[1]Hospital Garcia de Orta, Almada, Portugal

P3–01–09 **A REVIEW AND CLINICAL ANALYSIS OF 12 CASES OF PRIMARY THYROID LYMPHOMA**
Yang Zhang[1], Ying Gao[2], Zhenfang Yuan[1], Yan Ming Gao[1], Xiaohui Guo[1]
[1]Peking University First Hospital, Peking, China; [2]Peking University First Hospital, Beijing, China

P3–01–10 **GASTRIC ACID SECRETION AND GASTRIN RELEASE MONITORING DURING CONTINUOS INTRAOPERATIVE NEUROMONITORING (CIONM) THYROID SURGERY**
Cesare Carlo Ferrari[1], Vincenzo Pappalardo[1], Alberto Mangano[1], Davide Inversini[1], Andrea Leotta[1], Matteo Lavazza[1], Francesco Frattini[1], Stefano Rausei[1], Wen Tian[2], Hoon Yub Kim[3], Che-Wei Wu[4], Gianlorenzo Dionigi[1]
[1]1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy; [2]Department of General Surgery, The Chinese People's Liberation Army General Hospital, Beijing, China; [3]Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; [4]Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

P3–01–11 **PREDICTORS OF FAILURE OF PLANNED TOTAL THYROIDECTOMY: THE ROLE OF IONM**
Davide Inversini[1], Andrea Leotta[1], Matteo Lavazza[1], Cesare Carlo Ferrari[1], Vincenzo Pappalardo[1], Alberto Mangano[1], Francesco Frattini[1], Stefano Rausei[1], Wen Tian[2], Hoon Yub Kim [3], Che-Wei Wu[4], Gianlorenzo Dionigi[1]
[1]1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy; [2]Department of General Surgery, The Chinese People's Liberation Army General Hospital, Beijing, China; [3]3. Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; [4]Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

Room 2

02 Hypothyroidism 2, Children + Regulation

Chairperson: *Jose Moreno,* Spain

P3–02–01 **SEASONAL VARIATIONS OF TSH LEVELS IN ATHYREOTIC PATIENTS UNDER L-T4 REPLACEMENT THERAPY**
Damiano Gullo[1], Adele Latina[2], Francesco Frasca[1], Sebastiano Squatrito[1], Antonino Belfiore[3], Riccardo Vigneri[1]
[1]Endocrine Unit, Garibaldi-Nesima Hospital, University of Catania Medical School, Catania, Italy; [2]Endocrine Unit, S. Croce e Carle Hospital, Cuneo, Italy; [3]Clinical and Experimental Medicine, Endocrine Unit, University Magna Graecia, Catanzaro, Italy

P3–02–02 **CONGENITAL SUBCLINICAL HYPOTHYROIDISM IN CHILDREN – TO TREAT OR NOT TO TREAT?**
Kiiaev Aleksei[1], Osipovskaya Maria[1], Makretskaya Nina[2], Vasilyev Evgeny[2]
[1]Ural State Medical University, Yekaterinburg, Russian Federation; [2]Endocrinology Research Centre, Moscow, Russian Federation

P3–02–03 **DOES BASELINE OR CHANGES IN SERUM T3 DURING L-T4/L-T3 COMBINATION THERAPY PREDICT A POSITIVE RESPONSE TO THIS TREATMENT MODALITY IN HYPOTHYROID PATIENTS WITH PERSISTENT SYMPTOMS?**
Bjarke Borregaard Medici[1], Jeppe Lerche la Cour[2], Michaelsson Luba Freja[3], Jens Faber[4], BIrte Nygaard[5]
[1]Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Gentofte University Hospital, Copenhagen, Denmark; [2]Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [3]Department of Endocrinology, Herlev University Hospital, Copenhagen, Denmark; [4]Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Herlev, Denmark; [5]Department of Endocrinology, Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

P3–02–04 **GENE EXPRESSION PANEL TO MARK THERAPEUTIC EFFICACY ON LEVOTHYROXINE-TREATED PATIENTS WITH PRIMARY HYPOTHYROIDISM**
Valdelena Alessandra da Silva[1], Robson José de Almeida[1], Patrícia Varella Lima Teixeira[2], Leonardo Martins da Silva[2], João Bosco Pesquero [2], Cleber Pinto Camacho[3]
[1]Universidade Nove de Julho (Uninove), São Paulo, Brazil; [2]Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil; [3]Laboratory of Molecular Medicine Technology, Universidade Nove de Julho (Uninove), São Paulo, Brazil

P3–02–05 **PSYCHOEMOTIONAL STATUS, QUALITY OF LIFE AND LIPID PROFILE IN PATIENTS WITH DIFFERENT SERUM TRIIODOTHYRONINE LEVELS ON THE REPLACEMENT THERAPY WITH LEVOTHYROXINE**

Tatyana Morgunova[1], Valentin Fadeyev[1], Meruert Madiyarova[1]
[1]I.M. Sechenov First Moscow Medical University, Moscow, Russian Federation

P3–02–06 **BIOEQUIVALENCE AND DOSE PROPORTIONALITY OF A NEW LEVOTHYROXINE FORMULATION THAT MEETS THE 95–105% SPECIFICATION OVER THE WHOLE SHELF-LIFE: EVIDENCE FROM TWO RANDOMIZED PHARMACOKINETIC TRIALS**

Bogumila Urgatz[1], Ulrike Hostalek[1], Wolfgang Uhl[1], George J. Kahaly[2]
[1]Merck Kgaa, Darmstadt, Germany; [2]Johannes Gutenberg University Medical Center, Mainz, Germany

P3–02–07 **DIFFERENTIAL EXPRESSION PANEL AS BIOMARKER IN HYPOTHYROIDISM: AN RNA-SEQ TRANSCRIPTOME IN INDIVIDUALS WITH PRIMARY HYPOTHYROIDISM**

Robson José de Almeida[1], Valdelena Alessandra da Silva[1], Patrícia Varella Lima Teixeira[2], Leonardo Martins da Silva[2], João Bosco Pesquero[2], Cleber Pinto Camacho[3]
[1]Universidade Nove de Julho (Uninove), São Paulo, Brazil; [2]Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil; [3]Laboratory of Molecular Medicine Technology, Universidade Nove de Julho (Uninove), São Paulo, Brazil

P3–02–08 **THE THYROID REGISTRY: CLINICAL AND HORMONAL CHARACTERISTICS OF ADULT INDIAN PATIENTS WITH HYPOTHYROIDISM**

Bipin Sethi[1], Dr Deepak Khandewal[2], Dr Jagdish Gotur[3], Dr M.S. Raghvendra[4], Dr Sumitav Barua[5], Dr Upal Vyas[6]
[1]Care Hospital, Telangana, India; [2]Dr Khandelwal's Endocrinology Clinic, Delhi, India; [3]Dr Bhagat's Polyclinic, Ambedkar and Bhagvati Muncipal Hospital, Mumbai, India; [4]Dot Speciality Clinic, Bangalore, India; [5]Down Town Hospitla, Guwahati, India; [6]Abbott India Limited, Mumbai, India

P3–02–09 **ON INTERACTION OF AUTOIMMUNE THYROIDITIS AT THE STAGE OF SUBCLINICAL HYPOTHYROIDISM AND GASTROENTEROLOGICAL PATHOLOGY**

Elina Gasparyan[1], Mikhail Solovev[2], Alexander Gordienko[3]
[1]Medical Centre, Medical Academy of Postgraduate Studies, St. Petersburg, Russian Federation; [2]Military Medical Academy N.A. S.M.Kirov, 'Professor' Medical Center, Saint-Petersburg, Russian Federation; [3]S.M.Kirov Military Medical Academy, Saints Petersburg, Russian Federation

Room 3+4

03 Goiter 2 and Environmental

Chairperson: *Leonidas Duntas,* Greece

P3–03–01 **A US-CYTOLOGIC SCORE ALLOWS SIMPLE AND ACCURATE DEFINITION OF THE RISK OF MALIGNANCY IN CYTOLOGICALLY INDETERMINATE THYROID NODULES**

Gilles Russ[1], Royer Benedict[2], Claude Bigorgne[3], Marie Bienvenu[2], Agnes Rouxel[4], Laurence Leenhardt[5]
[1]Centre de Pathologie et D'imagerie, Pierre and Marie Curie University, Paris, France; [2]Centre de Pathologie et D'imagerie, Cochin Hospital, Paris, France; [3]Centre DE Pathologie et D'imagerie, La Pitie-Salpetriere Hospital, Paris, France; [4]Centre de Pathologie et D'imagerie, La Pitie Salpetriere Hospital, Paris, France; [5]La Pitie Salpetriere Hospital, Thyroid and Endocrine Tumors Unit, Paris, France

P3–03–02 **THYROID DYSFUNCTION AND ULTRASONOGRAPHY FEATURES IN PATIENTS WITH METASTATIC COLORECTAL CANCER TREATED WITH REGORAFENIB: RESULTS FROM A SINGLE CENTRE PROSPECTIVE COHORT STUDY**

Fabiana Pani[1], Laura Orgiano[2], Elena Massa[2], Francesco Boi[1], Giorgio Astara[2], Valeria Pusceddu[2], Mario Scartozzi[2], Stefano Mariotti[3]
[1]Endocrine Unit, Department of Medical Sciences M.Aresu, University of Cagliari, Cagliari, Italy; [2]Medical Oncology, Department of Medical Sciences M.Aresu, University of Cagliari, Cagliari, Italy; [3]Department of Medical Scieces, M.Aresu, University of Cagliari, Cagliari, Italy

P3–03–03 **SHORT-TERM AMIODARONE TREATMENT FOR ATRIAL FIBRILLATION AFTER CATHETER ABLATION INDUCES A TRANSIENT THYROID DYSFUNCTION: RESULTS FROM THE PLACEBO-CONTROLLED, RANDOMIZED AMIO-CAT TRIAL**

Søren Zöga Diederichsen[1], Stine Darkner[1], Xu Chen[1], Arne Johannessen[2], Steen Pehrson[1], Jim Hansen[2], Ulla Feldt-Rasmussen[3], Jesper Hastrup Svendsen[1]
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P3–03–04 **THE 'WHITE THYROID' ON UNENHANCED CT IN AMIODARONE INDUCED THYROTOXICOSIS TYPE 2 (AIT2)**

Annick Van den Bruel[1], Joost Delanote[1], Carine De Vroe[1], Lotte Pyfferoen[1], Johan Ghekiere[1], Mathias Duytschaever[1], Rene Tavernier[1]
[1]General Hospital Sint Jan Brugge Oostende, Brugge, Belgium

P3–03–05 **ESTABLISHING AND COMPARING THE DISTRIBUTION OF TIRADS SCORES IN RECENTLY DISCOVERED THYROID NODULAR DISEASE: A PROSPECTIVE MULTI-CENTER STUDY**

Gilles Russ[1], Jean Tramalloni[2]
[1]Centre de Pathologie et D'imagerie, Pierre and Marie Curie University, Paris, France; [2]Radiologie Paris Ouest, Neuilly Sur Seine, France

P3–03–06 **THE SANTORINI STUDY: ON THE INCIDENCE OF THYROID AUTOIMMUNITY AND THYROID CANCER ON A VOLCANIC ISLAND**

Leonidas Duntas[1], Eleni Loukari[2], Brigitte Grab-Duntas[3], Anastasios Boutsiadis[2], Charalambos Kelidis[4]
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P3–03–07 **HOW AND AT WHICH SIZE ARE THYROID NODULES DISCOVERED AND CONSEQUENCES ON THE RISK OF MALIGNANCY**

Gilles Russ[1], Agnes Rouxel[2], Marie Bienvenu[3], Claude Bigorgne[4], Royer Benedict[3], Laurence Leenhardt[5]
[1]Centre de Pathologie et D'imagerie, Pierre and Marie Curie University, Paris, France; [2]Centre de Pathologie et D'imagerie, La Pitie Salpetriere Hospital, Paris, France; [3]Centre de Pathologie et D'imagerie, Cochin Hospital, Paris, France; [4]Centre de Pathologie et D'imagerie, La Pitie-Salpetriere Hospital, Paris, France; [5]La Pitie Salpetriere Hospital, Thyroid and Endocrine Tumors Unit, Paris, France

P3–03–08 **VEGETARIAN DIETARY PATTERN AND OXIDATIVE STRESS MARKERS**

Rosaria Ruggeri[1], Mariateresa Cristani[2], Teresa Manuela Vicchio[1], Rosaria Certo[1], Giuseppe Giuffrida[1], Salvatore Giovinazzo[1], Antonina Saija[2], Angela Alibrandi[3], Francesco Trimarchi[1]
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P3–03–09 **VESSEL SEALING SYSTEM (VSS) SAFETY AROUND THE RECURRENT LARYNGEAL NERVE (RLN)**

Alberto Mangano[1], Andrea Leotta[1], Matteo Lavazza[1], Cesare Carlo Ferrari[1], Davide Inversini[1], Vincenzo Pappalardo[1], Francesco Frattini[1], Stefano Rausei[1], Wen Tian[2], Hoon Yub Kim[3], Che-Wei Wu[4], Gianlorenzo Dionigi[1]
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Room 16

04 Cardio, Brain and Metabolism

Chairperson: *Frans Brandt,* Denmark

P3–04–01 **SERUM LEVELS OF FREE TRIIODOTHYRONINE AND FREE THYROXINE ARE ASSOCIATED WITH PREVALENT TYPE II DIABETES MELLITUS IN A POPULATION-BASED SAMPLE FROM NORTHEAST GERMANY**

Till Ittermann[1], Markus Marcello Ricardo Paulista[1], Sabine Schipf[2], Henry Völzke[3]
[1]University Medicine Greifswald, Greifswald, Germany; [2]Universitaetsmedizin Greifswald, Greifswald, Germany; [3]Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany

P3–04–02 **LOW NORMAL FREE THYROXINE LEVELS ARE INVERSELY ASSOCIATED WITH METABOLIC SYNDROME IN EUTHYROID SUBJECTS**

Eun Sook Kim[1], Sung Dae Moon[1], Je Ho Han[1]
[1]The Catholic University of Korea College of Medicine, Incheon, Korea, Rep. of South

P3–04–03 **COGNITIVE FUNCTIONING IN WOMEN WITH GRAVES' DISEASE AND ITS ASSOCIATION WITH MEDIAL TEMPORAL PATHOLOGY**

Mats Holmberg[1], Helena Filipsson Nyström[2], Helge Malmgren[2], Erik Olsson[3], Birgitta Johansson[3], Simon Skau[3], Niklas Klasson[3], Rolf Heckemann[3], Peter Berglund[4], Göran Starck[5]
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P3–04–04 **THYROID DISEASE IN OLDER PATIENTS HOSPITALIZED FOR ACUTE ILLNESS: PREVALENCE AND THERAPEUTIC APPROPRIATENESS**

Giuseppe Pasqualetti[1], Umberto Dell'Agnello[1], Sara Bernardini[1], Antonio Polini[1], Sara Tognini[2], Valeria Calsolaro[1], Fabio Monzani[1]
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P3–04–05 **SUBTLE CHANGES IN THYROID FUNCTION ARE ASSOCIATED WITH DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES**

Eun Sook Kim[1], Sung Dae Moon[1], Je-Ho Han[1]
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P3–04–06 **ADIPOCYTOKINES, INSULIN RESISTENCE AND CHRONIC INFLAMMATION STATUS IN HYPOTHYROID PATIENTS**

Lachezar Lozanov[1], Desislava Gorcheva[2], Boyka Kostova[3], Radoslav Borisov[1], Mariana Nedeva[1], Bojan Lozanov[4], Veselina Koleva[1], Radka Argirova[5], Mircho Vukov[3]
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P3–04–07 **CIRCULATING THYROXINE SERUM LEVELS ARE ASSOCIATED WITH SYSTOLIC PULMONARY ARTERIAL PRESSURE (SPAP) IN SYSTEMIC SCLEROSIS (SSC)**

Rosaria Ruggeri[1], Gianluca Bagnato[2], Rosaria Certo[1], Alessia Fiorenza[2], Scipione Carerj[3], Antonio Bracco[3], Maurizio Cusma'[3], William Neal Roberts[4], Gianfilippo Bagnato[2], Francesco Trimarchi[1]
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P3–04–08 **IMPACT OF AUTOIMMUNE THYROIDITIS AND SUBCLINICAL HYPOTHYROIDISM IN CARDIOVASCULAR RISK**

Celestino Neves[1], João Sérgio Neves[1], Sofia Castro Oliveira[1], Ana Oliveira[1], Camila Dias[2], Oksana Sokhatska[3], José Luís Medina[4], Luís Delgado[5], Davide Carvalho[6]
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P3–04–09 **GENETIC RISK FACTORS FOR THE THYROTOXIC ATRIAL FIBRILLATION AND ITS' OUTCOMES**

Alina Babenko[1], Daria Savitskaya[2], Elena Grineva[3]
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P3–04–10 **RISK FACTORS OF VENOUS THROMBOEMBOLISM IN PATIENTS TREATED FOR DIFFERENTIATED THYROID CARCINOMA**

Trynke van der Boom[1], Esther N. Klein Hesselink[1], Hilde Kooistra[2], Karina Meijer[2], Anouk N. A. van der Horst-Schrivers[3], Joop D. Lefrandt[4], Thera P. Links[3]
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Room 14

05 Thyroid Cancer Diagnostic III

Chairperson: *Georg Brabant*, Germany

P3–05–01 **COMPARISON OF ULTRASOUND-GUIDED FINE NEEDLE NON-ASPIRATION AND ASPIRATION TECHNIQUE IN EVALUATION OF PATIENTS WITH NECK LYMPH NODES IN TERMS OF CYTOLOGICAL DIAGNOSITICITY**

Cevdet Aydin[1], Fatma Dilek Dellal[2], Abbas Ali Tam[1], Berna Evranos Ogmen[3], Aydan Kilicarslan[4], Oya Topaloglu[1], Reyhan Ersoy[5], Bekir Cakir[5]
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P3–05–02 **THE COMPARISON OF HYDRO-ALCOHOLIC EXTRACT HULL LESS SEED PUMPKIN AND PACLITAXEL ON TREATMENT OF HUMAN PAPILLARY THYROID CANCER CELLS**

Mohammad Hadi Bahadori[1], Zoleykha Azari[1], Arash Zaminy[1]
[1]Cellular and Molecular Research Center, Faculty of Medicine, Guilan University of Medical Sciences, Rasht, Iran

P3–05–03 **LONG-TERM OUTCOME OF PERCUTANEOUS ETHANOL ABLATION OF SELECTED RECURRENT CERVICAL NODAL METASTASES IN THYROID CANCER**

Soo Young Kim[1], Seok-Mo Kim[1], Chi Young Lim[1], Bup-Woo Kim[1], Yong Sang Lee[1], Hang-Seok Chang[1], Cheong Soo Park[1]
[1]Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

P3–05–04 **DISCORDANCE IN TUMOR DIAMETER DETERMINED BY PREOPERATIVE ULTRASONOGRAPHY AND POSTOPERATIVE HISTOPATHOLOGY IN DIFFERENTIATED THYROID CANCER**

Muhammet Cuneyt Bilginer[1], Didem Ozdemir[1], Husniye Baser[2], Hayriye Tatlı Doğan[3], Abdussamed Yalçın[4], Reyhan Ersoy[1], Bekir Cakir[1]
[1]Yildirim Beyazit University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [3]Atatürk Education and Research Hospital, Department of Pathology, Ankara, Turkey; [4]Ankara Yildirim Beyazit University School of Medicine, Department of General Surgery, Ankara, Turkey

P3–05–05 **DIFFERENTIAL DIAGNOSIS OF THYROID NODULES USING STRAIN ULTRASOUND ELASTOGRAPHY**

Mira Valentinova Siderova[1], Kiril Hristozov[2], Ivan Krasnaliev[3]
[1]Univesity Hospital 'St. Marina', Department of Endocrinology and Metabolism, Varna, Bulgaria; [2]Medical University – Varna, Department of Endocrinology and Metabolism, Varna, Bulgaria; [3]Univesity Hospital 'St. Marina', Department of Pathology, Varna, Bulgaria

P3–05–06 **EFFECTS OF BODY MASS INDEX ON THYROID CANCER AGGRESSIVENESS AND RECURRENCE**

Eun Sook Kim[1]
[1]The Catholic University of Korea College of Medicine, Incheon, Korea, Rep. of South

P3–05–07 **CAN NODULAR HYPERPLASIA OF THE THYROID GLAND BE DIFFERENTIATED FROM FOLLICULAR ADENOMA AND FOLLICULAR CARCINOMA BY ULTRASONOGRAPHY?**

Sun Hye Jeong[1], Hyun Sook Hong[1], Eun Hye Lee[1]
[1]Soonchunhyang University Bucheon Hospital, Bucheon-Si, Korea, Rep. of South

P3–05–08 **MEN2A IN A PATIENT WHO IS IN THE THIRD GENERATION OF A FAMILY WITH FAMILIAL MEDULLARY THYROID CANCER**

Dilek Yazici[1], Serdar Tezelman[2], Tarik Terzioglu[3], Nurdan Gul[4], Ayse Kubat Uzum[4], Ferihan Aral[4], Refik Tanakol[4], Yersu Kapran[5], Bulent Colakoglu[6], Havva Sezer[1], Faruk Alagol[1]
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P3–05–09 **HEMI-THYROIDECTOMY FOR FOLLICULAR THYROID CARCINOMA – 'HEMI-THYROID' AS AN OBSTACLE FOR FURTHER MANAGEMENT AFTER 8 YEARS FOLLOWING SURGERY**

Nino Khabeishvili[1]
[1]V. Iverieli Endocrinology, Metabology, Dietology Center 'Enmedic', Endocrinology, Tbilisi, Georgia

P3–05–10 **HYALINIZING TRABECULAR TUMOR: CASE REPORT**

Nazibrola Chiradze[1], Lali Nikoleishvili[2], Ramaz Kurashvili[2], Miranda Miminoshvili[2]
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Room 12

06 Thyroid Cancer – Clinical II

Chairperson: *Tania Pilli,* Italy

P3–06–01 **TWO YEAR PROSPECTIVE MOLECULAR TESTING OF ROUTINE AIR-DRIED FINE NEEDLE ASPIRATION (FNA) SMEARS USING A 7-GENE-PANEL IN A ROUTINE DIAGNOSTIC SETTING IN GERMANY**

Markus Eszlinger[1], Katharina Böhme[2], Maha Ullmann[2], Anna Neumann[3], Ilka Ruschenburg[4], Ralf Paschke[5]
[1]Department of Oncology and Arnie Charbonneau Cancer Institute, Cumming School of Medicine, Division of Endocrinology and Nephrology, University of Leipzig, Calgary, Canada; [2]Division of Endocrinology and Nephrology, University of Leipzig, Leipzig, Germany; [3]Amedes Mvz Wagnerstibbe für Laboratoriumsmedizin, Hämostaseologie, Humangenetik und Mikrobiologie Hannover, Hannover, Germany; [4]Mvz Wagnerstibbe für Gynäkologie, Reproduktionsmedizin, Zytologie, Pathologie und Innere Medizin GmbH, Einbeck, Germany; [5]University of Calgary, Cumming School of Medicine, Dept of Endocrinology and Oncology, Calgary, Canada

P3–06–02 **CERVICAL LYMPH NODE METASTASES AFTER THYROIDECTOMY FOR PAPILLARY THYROID CARCINOMA USUALLY REMAIN STABLE OVER YEARS**

Chisato Tomoda[1], Kiminori Sugino[1], Yuna Ogimi[1], Chie Masaki[1], Junko Akaishi[1], Kiyomi Y. Hames[1], Akifumi Suzuki[1], Kenichi Matsuzu[1], Takashi Uruno[1], Keiko Ohkuwa[1], Hiroshi Shibuya[1], Wataru Kitagawa[1], Mitsuji Nagahama[1], Koichi Ito[1]
[1]Ito Hospital, Tokyo, Japan

P3–06–03 **DISEASE STATUS AT PRESENTATION AND DISEASE RELATED MORTALITY FROM DIFFERENTIATED THYROID CANCER**

Eyal Robenshtok[1], Yuval Nachalon[2], Carlos Benbassat[3], Dania Hirsch[1], Aharon Popovtzer[4]

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P3–06–04 **IMPACT OF PREOPERATIVE DETECTION OF SODIUM-IODIDE SYMPORTER EXPRESSION LEVEL ON DIFFERENTIATED THYROID CANCER (DTC) PROGNOSIS**

Marina Boriskova[1], Dmitriy Semenov[1], Uliana Farafonova[1], Ludmila Koloskova[2]

[1]Pavlov First Saint Petersburg State Medical University, General Surgery Department, Sainkt-Petersburg, Russian Federation; [2]Medlab, Sainkt-Petersburg, Russian Federation

P3–06–05 **NATURAL HISTORY OF CONTRALATERAL NODULES AFTER LOBECTOMY IN PATIENTS WITH PAPILLARY THYROID CARCINOMA**

Amit Ritter[1], Gideon Bachar[2], Orna Katz[2], Nadav Kochen[2], Dania Hirsch[3], Carlos Benbassat[4], Eyal Robenshtok[3]

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P3–06–06 **CLINICAL CHARACTERISTICS AND LONG TERM OUTCOME OF PATIENTS WITH DIFFERENTIATED CARCINOMA THYROID WITH BONE METASTASES – A RETROSPECTIVE STUDY**

Sadaf Butt[1], Shazia Fatima[2], Kahkashan Mir[3], Ayesha Ammar[2], Faheem Mohammad[2]

[1]Nori, Islamabad, Islamabad, Pakistan; [2]Nori, Islamabad, Pakistan; [3]Nori, Nori, Pakistan

P3–06–07 **BASELINE PATIENT CHARACTERISTICS FROM RIFTOS: A GLOBAL NONINTERVENTIONAL STUDY EVALUATING THE USE OF MULTIKINASE INHIBITORS FOR TREATMENT OF ASYMPTOMATIC DIFFERENTIATED THYROID CANCER REFRACTORY TO RADIOACTIVE IODINE (RIFTOS MKI)**

Johannes Smit[1], Marcia Brose[2], Chia-Chi Lin[3], Marc Fellous[4], Fabian Pitoia[5], Iwao Sugitani[6], Martin Schlumberger[7]

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P3–06–08 **OUTCOME OF THYROID CARCINOMA ASSOCIATED TO CLINICALLY MANIFEST AUTOIMMUNE THYROID DISEASE**

Camila Moma[1], Ligia Vera Montali Assumpção[2], Patrícia Sabino de Matos[3], Denise Engelbrecht Zantut Wittmann[4]

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P3–06–09 **ANALYSIS OF FACTORS PREDICTING BILATERAL LATERAL NECK METASTASES IN PATIENTS WITH UNILATERAL PAPILLARY THYROID CARCINOMA**

Ho Jin Chang[1], Soo Young Kim[1], Hyukjun Yun[1], Seok-Mo Kim[1], Bup-Woo Kim[1], Yong Sang Lee[1], Hang-Seok Chang[1], Cheong Soo Park[1]

[1]Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

P3–06–10 **THE LOW IODINE DIET: TIME FOR IMPROVEMENT**

Rixte J. Jagersma[1], Anneke M. Muller Kobold[1], Linda G. Swart[1], Bernadette L. Dekker[1], Thera Links[2], Anouk van der Horst – Schrivers[2]

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Room 13+15

07 Thyroid Cancer – Clinical III

Chairperson: *Torquil Watt,* Denmark

P3–07–01 **OPTIMAL CUTOFF VALUE OF AGE PREDICTING CANCER SPECIFIC SURVIVAL FOR PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA**

Mijin Kim[1], Tae Yong Kim[1], Suyeon Park[1], Hyemi Kwon[1], Min Ji Jeon[1], Won Gu Kim[1], Dong Eun Song[1], Jong Ho Yoon[2], Suck Joon Hong[3], YoungKee Shong[4], Won Bae Kim[5]

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P3–07–02 **LIMITS OF FROZEN SECTION IN INDETERMINATE THYROID NODULES: A RETROSPECTIVE ANALYSIS OF 75 HISTOLOGICALLY PROVEN THYROID NODULES**

Pascaline Huynh[1]
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P3–07–03 **US ELASTOGRAPHY USING CAROTID ARTERY PULSATION: EFFICACY AND REPRODUCIBILITY ANALYSIS IN DIFFERENTIAL DIAGNOSIS OF THYROID NODULES**

Eun Ju Ha[1], *Miran Han*[2]
[1]Ajou University School of Medicine, Department of Radiology, Suwon, Korea, Rep. of South; [2]Ajou University School of Medicine, Suwon, Korea, Rep. of South

P3–07–04 **A MULTICENTER, PROSPECTIVE VALIDATION STUDY FOR THE KOREAN THYROID IMAGING REPORTING AND DATA SYSTEM IN PATIENTS WITH THYROID NODULES (K-TIRADS)**

Eun Ju Ha[1], *Won-Jin Moon*[2], *Donggyu Na*[3], *Young Hen Lee*[4], *Nami Choi*[2], *Jae Kyun Kim*[5]
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[1]Seoul National University, Seongnam-Si, Korea, Rep. of South; [2]Seoul National University Hospital, Seoul, Korea, Rep. of South; [3]Seoul National University Bundang Hospital, Seongnam-Si, Korea, Rep. of South

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[1]Sismanoglio General Hospital, Amalia Fleming Department, Athens, Greece; [2]Sismanoglio General Hospital, Department OF Amalia Fleming, N. Erithrea, Athens, Greece

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[1]Lund University, Dpt. Clinical Sciences Malmö, Diabetes & Endocrinology, Malmö, Sweden; [2]Lund University, Dpt. Clinical Sciences Malmö, Diabetes & Endocrinology, Skåne University Hospital, Malmö, Sweden; [3]Lund University, Dpt. Clinical Sciences Malmö Opthalmology, Skåne University Hospital Dpt. of Opthalmology, Malmö, Sweden; [4]Department of Endocrinology, Skåne University Hospital, Malmö, Sweden

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[1]Peking University First Hospital, Beijing, China

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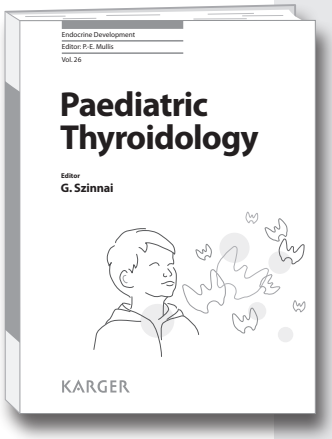
Margaret Rayman[1], Shiqian Hu[2]
[1]Universary of Surrey, Guildford, UK; [2]University of Surrey, Guildford, UK

State of the art of diagnosis and treatment of paediatric thyroid diseases



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This book presents a comprehensive overview of paediatric thyroid diseases and thus provides a useful tool for clinical problem solving. Opinion leaders in the field present reviews on all relevant diseases of the hypothalamic-pituitary-thyroid axis. Sixteen chapters cover topics ranging from foetal thyroidology, congenital hypothyroidism, central hypothyroidism, inherited defects of thyroid hormone action, cell transport and metabolism to iodine deficiency, autoimmune thyroid disease and thyroid tumours.
Written by clinicians, the chapters provide in-depth information and current guidelines for clinical problems encountered in paediatric thyroidology. As a unique feature, a case seminar collection for each chapter presents typical patient histories providing key learning points and key references for clinical problem solving in family medicine, paediatric endocrinology and medical genetics.
Providing a succinct update on clinical paediatric thyroidology, this book is an essential tool for paediatric and adult endocrinologists, as well as for general practitioners, paediatricians and medical geneticists.

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Oral Session 1: Topic Highlights

14.00–14.20

TUMOR AND NORMAL THYROID STEM-LIKE CELLS: FROM TISSUES TO ZEBRAFISH

Valentina Cirello[1], *Valentina Vaira*[2], *Germano Gaudenzi*[3], *Elisa Stellaria Grassi*[4], *Giovanni Vitale*[3], *Dario Ricca*[2], *Carla Colombo*[5], *Silvano Bosari*[6], *Leonardo Vicentini*[7], *Luca Persani*[3], *Stefano Ferrero*[8], *Laura Fugazzola*[1]

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Introduction: Cells with stem-like properties have been reported in benign and malignant thyroid diseases, and can be propagated by culturing them as non-adherent spheres.

Design: Aim of the present study was to widely characterize the stem-like cells in tumor and normal thyroid tissues and in the corresponding *in vitro*-cultured thyrospheres, and to investigate *in vivo* the proangiogenic potential of patient-derived thyrospheres xenograft (PDX).

Result: Among the stemness markers tested, POU5F1/OCT4 has the highest expression in both tumor tissues and thyrospheres. POU5F1/OCT4 is expressed in the core of tumor thyrospheres, whereas TG and TTF1 differentiation markers are expressed at the periphery, indicating a progressive differentiative process from the center to the border of the spheres. Endothelial markers (CD34 and CD31) are co-expressed in both tumor and normal spheres, mimicking the formation of vascular structures, consistent with the pluripotency of the spheres cells which are able to directly contribute to their own vasculature. Interestingly, normal and tumor tissues have a detectable p53 expression, whereas the derived thyrospheres are mainly constituted by cells that express p53 at a lower level and in a fluctuating manner, consistent with their stemness properties. Finally, we show that PDXs derived from tumor or normal thyrospheres stimulate the migration and growth of sprouting vessels toward the implant into the zebrafish embryos.

Conclusion: We widely characterized stem-like cells in thyroid tissues and in the corresponding thyrospheres, and established xenografts in zebrafish. These *in vitro* and *in vivo* models are expected to become a valuable platform to test the effects of novel compounds on stem-like cells.

14.20–14.40

TRACING OF BRAF MUTANT THYROID CELLS BEFORE TUMOR DEVELOPMENT

Ellen Johansson[1], *Shawn Liang*[2], *Elin Schoultz*[1], *Mikael Nilsson*[1]

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It is suggested that primary somatic mutations of oncogenes leading to sporadic thyroid cancer in adulthood occurs in early life. Mechanisms that delay onset of tumor development and restrain tumor growth until inactivating mutations of tumor suppressors convey a more malignant phenotype are largely unknown. Current genetic mouse models recapitulating PTC by targeted expression of $Braf^{v600e}$ under e.g. the thyroglobulin (Tg) promoter are afflicted by the fact that *Cre* is globally activated, implicating that the MAPK pathway is constitutively activated (CA) simultaneously in most if not all thyroid cells. As a consequence $TgCre;Braf^{CA/+}$ mice develop hypothyroidism leading to supraphysiological TSH levels and TSH-dependent thyroid hyperplasia, which will confound any early analysis of Braf mutant cells and the initial events of clonal tumorigenesis.

We investigated whether spontaneous Cre activation occurring stochastically at low rate in the absence of tamoxifen in mice with inducible $TgCre;Braf^{CA/+}$ might allow detection and fate determination of thyroid cells early on after expression of oncogenic $Braf^{V600e}$. These mice were crossed with the *mTmG* reporter. In the absence of Cre all thyroid cells showed red fluorescence (mT+), when Cre was globally activated by tamoxifen all cells turned green (mG+). Tamoxifen-independent sporadic Cre activation was evident postnatally by the occurrence of few mG+ follicular cells that increased slowly in number with time. Occasional clustered mG+ cells suggested multiplication. However, as long as after 3 months most mG+ cells stayed within the follicular epithelial lining and only rarely formed solid presumably precancerous microtumors. Of interest, mG+ cells were encountered in follicle lumina at a higher incidence than expected by the limited numbers of mG+ cells.

These observations pinpoint for the first time *in vivo* the earliest stages of Braf mutant thyroid follicular cells before overt tumors develop. Oncogene-induced senescence may explain why most cre-activated cells did not proliferate.

14.40–15.00

THE HUMAN SINGLE-NUCLEOTIDE POLYMORPHISM THR92ALA IN TYPE 2 DEIODINASE GENE (DIO2) IMPAIRS ENZYME ACTIVITY AND IS ASSOCIATED WITH REDUCED INTRACELLULAR AND SERUM T3 LEVELS IN ATHYREOTIC PATIENTS

Silvia Cantara[1], *Domenico Salvatore*[2], *Monica Dentice*[2], *Maria Grazia Castagna*[1], *Raffaele Ambrosio*[2], *Fabio Maino*[1], *Corrado Garbi*[2], *Carlotta Marzocchi*[1], *Tommaso Porcelli*[2], *Furio Pacini*[1]

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Levothyroxine (LT4) replacement is considered the standard of care for hypothyroidism. However, a significant proportion of athyreotic LT4-treated patients experiences hypothyroid-like symptoms. During LT4 replacement, circulating and tissue levels of triiodothyronine (T3) strictly depend on type-2-deiodinase (D2)-mediated activation of exogenous LT4. The single-nucleotide polymorphism Thr92Ala in the *Dio2* gene has been implicated in impairing D2 function. To investigate the clinical significance of Thr92Ala,

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we compared the post-surgical hormonal status of 140 thyroidectomized LT4-treated patients to their pre-surgery status, and identified a subset of individuals [48/140 patients (34.3%)] with low FT3 levels despite normal TSH. *Dio2* genotyping revealed a close association between low FT3 values and Thr92Ala. In particular, the percentage of patients with reduced post-surgical FT3 levels significantly correlates with the severity of the polymorphism being 18.9% in wild-type patients (Thr/Thr), 36.4% in heterozygous (Thr/Ala) and 58.3% in mutant homozygous (Ala/Ala) (p = 0.04). By using a generated 3xFlag-D2 mouse and muscle stem cells (MuSCs), in which D2 is physiologically implicated in the control of cell differentiation as cellular model, we disclosed the intracellular localization of protein D2. We found that endogenous wild-type D2 mainly localized in the endoplasmic reticulum during cell proliferation and shuttle to the perinuclear region during cell differentiation. Thr92Ala share the same subcellular localization of the wild-type D2 but differ in protein stability. Importantly, Thr92Ala reduced D2 enzymatic activity and T4 to T3 conversion in primary proliferating muscle stem cells and pituitary thyrotrophs. In conclusion, thyroidectomized patients carrying Thr92Ala have reduced intra-cellular and serum T3 levels not adequately compensated for by LT4 replacement therapy despite normal TSH levels. This study might support the advocated use of T4+T3 therapy in selected patients with the Thr92Ala polymorphism.

15.00–15.20

A RANDOMIZED TRIAL OF IODIDE SUPPLEMENTATION VERSUS PLACEBO IN PRETERM INFANTS: THE I2S2 TRIAL

Fiona Williams[1], *Simon Osgston*[2], *Anita Boelen*[3], *Robert Hume*[4], *Jennifer Watson*[4], *Kayleigh Stanbury*[5], *Peter Willatts*[4], *Edmund Juszczak*[5], *Peter Brocklehurst*[6]
[1]University of Dundee, Population Health Sciences, Dundee, UK, [2]Population Health Sciences, Medical School, University of Dundee, Dundee, UK, [3]Academic Medical Centre, Amsterdam, Netherlands, [4]University of Dundee, Population Health Sciences, Medical School, Dundee, UK, [5]University of Oxford, National Perinatal Epidemiology Unit, Oxford, UK, [6]University College London, Institute for Women's Health, London, UK

Context: Observational studies in preterm infants show an association between transient hypothyroxinaemia and compromised neurodevelopmental outcome. The aetiology of transient hypothyroxinaemia is multi-factorial and has a contribution from iodide deficiency. Balance studies in healthy preterm infants show that they require 30–40 mcg iodide/kg/day. Many preterm infants are fed parenterally, which provides only 1–3 mcg iodide/kg/day.

Objective: Does nutritional iodide supplementation improve neurodevelopmental status?

Methods: A randomised controlled trial of daily iodide supplementation (sodium iodide 30 mcg/kg/day) versus placebo in infants born <31 weeks' gestation from within 42 hours of birth to the equivalent of 34 week's gestation. Whole blood levels of T4, TSH and TBG were measured on postnatal days 7, 14 and 28 and the equivalent of 34 week's gestation. The primary outcome was neurodevelopment, which was assessed using the Bayley-III scales, at 2 years' age corrected for prematurity.

Results: 1275 infants were recruited from 21 neonatal units in the UK. Bayley assessments were completed on 499 placebo and 498 supplemented infants; 131 infants died. Overall, there were no significant differences in any of the main or sub-set domains of the Bayley-III between the placebo and intervention arms of the trial.

Sub-group analysis, by thyroxinaemic status, showed no evidence in the iodide arm of a difference in Bayley-III scores between infants classified as hypothyroxinaemic and euthyroid; but, in the placebo arm, the hypothyroxinaemic group performed significantly worse on the main domains of the Bayley-III and the language sub-sets, than the euthyroid group. A test of interaction showed evidence of an interaction between iodide supplementation and hypothyroxinaemic status in the language composite score and its sub-sets.

Conclusion: Overall, iodide supplementation provided no benefit to neurodevelopment in infants born less than 31 weeks' gestation; there was limited evidence of benefit in infants classified as hypothyroxinaemic. Daily iodide supplementation, at 30 mcg/kg/day, caused no adverse events and supplementation of all preterm infants could provide the pragmatic solution to correcting this condition.

'Funded by MRC and managed by NIHR on behalf of the MRC-NIHR partnership.'

Table 1. (for abstract time 15.00–15.20)

Primary outcomes intention-to-treat population	Mean difference (iodide – placebo)	95% CI (P value)
Bayley-III cognitive score	–0.34	–2.57 to 1.89 (0.77)
Bayley-III motor composite score	0.21	–2.23 to 2.65 (0.87)
Bayley-III language composite score	–0.05	–2.48 to 2.39 (0.97)

15.20–15.40

CONTROLLED ANTENATAL THYROID SCREENING (CATS) II; EFFECT OF TREATMENT FOR UNDERACTIVE THYROID FUNCTION DURING PREGNANCY ON CHILDREN'S BEHAVIOUR AT AGE 9

Charlotte Hales[1], *Peter Taylor*[1], *Sue Channon*[1], *Kirtsen McEwan*[1], *Aled Rees*[1], *John Gregory*[1], *Ilaria Muller*[1], *Mohd S. Draman*[1], *Colin Dayan*[1], *Kate Langley*[1], *Anita Thapar*[1], *John Lazarus*[1], *Marian Ludgate*[1]
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Objectives: The Controlled Antenatal Thyroid Screening (CATS) study was the first randomised controlled trial to explore the effect of treatment for suboptimal gestational thyroid function (SGTF, i.e. TSH in the highest 2.5% and/or fT4 in the lowest 2.5%); many studies have investigated the effect on childhood cognition, but little is known about childhood behaviour.

Methods: A total of 452 were recruited into CATS II (treated SGTF = 118, untreated SGTF = 101, and those with normal GTF = 233). Mothers completed questionnaires about their children at age 9; The Strengths and Difficulties Questionnaire (SDQ), Child ADHD Questionnaire, and the Social Communication Questionnaire (SCQ); higher scores indicated less favourable behaviour. Primary analysis used a MANCOVA, firstly with SGTF groups merged, and secondly by individual group. Secondary analysis explored fT4 during pregnancy and offspring behaviour; all analyses were Bonferroni corrected.

Results: The merged SGTF group had fewer peer problems (SDQ) (p = 0.008, mean difference = 0.416 (95% CI 0.111–0.720)), but more ADHD overactivity problems (p = 0.020, mean difference = 0.545 (0.085–1.005)) than the normal GTF group. The analysis of the three groups revealed that treated SGTF scored higher than normal GTF (for ADHD overactivity, p = 0.024, mean difference = 0.751 (0.072–1.430)), and the untreated SGTF (for SCQ, p = 0.047, mean difference = 1.212 (0.013–2.411)). ADHD overactivity was positively correlated to maternal fT4 at six weeks post initiation of therapy. Children of over-treated mothers (T4 >17.7 pmol/l) had higher scores for ADHD overactivity compared to the rest of the study group (p = 0.008, mean difference = 1.212 (0.322–2.103)). At 30 weeks gestation, ADHD overactivity was also positively correlated to fT4, with sustained higher scores compared to the rest of the study group (p = 0.004, mean difference = 1.644 (0.542, 2.746)).

Conclusion: Treatment of SGTF may exacerbate ADHD overactivity difficulties e.g. 11% of treated had scores >2 SDs above the mean compared with 4% in normal and untreated. The analysis supports recent literature that SGTF over-treatment may have a negative effect and requires close monitoring throughout pregnancy.

15.40–16.00

DIFFERENTIAL EFFECTS OF MCT8-DIO2 AND MCT8-OATP1C1 INACTIVATION ON CEREBRAL CORTEX GENE EXPRESSION IN THE MOUSE

Beatriz Morte[1], *Pilar Gil*[2], *Heike Heuer*[3], *Juan Bernal*[4]
[1]Center for Biomedical Research on Rare Diseases, Instituo de Investigaciones Biomedicas, Csic, Madrid, Spain, [2]Intituto de Investigaciones Biomédicas Uam-Csic, Center for Biomedical Research on Rare Diseases, Madrid, Spain, [3]Leibniz Institute for Environmental Medcine (Iuf), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany, [4]Instituto Investigaciones Biomédicas, Center for Biomedical Research on Rare Diseases, Madrid, Spain

Objectives: Thyroid hormone (TH) action in the brain requires specific transporters for the passage of T4 and T3 through the blood-brain barrier (BBB), mainly MCT8 for T4 and T3, and OATP1C1 for T4. T4 is delivered directly to the astrocytes after crossing the BBB through OATP1C1. DIO2 is expressed in astrocytes, and generates T3 from T4. The T3 formed is available for regulation of gene expression in practically all neural cells. On the other hand, both T4 and T3 are delivered to the interstitial space through MCT8. The goal of this work was to analyze how the combined inactivation of MCT8-DIO2 and of MCT8-OATP1C1 differentially affects gene expression in the mouse cerebral cortex.

Methods: Cerebral cortices from P21 hypothyroid mice and from MCT8-DIO2 and MCT8-OATP1C1 KO P21 mice were used to perform differential gene expression analysis using RNA-Seq. The databases generated in each condition were compared to each other and to databases of genes enriched more than 5-fold in neural cells.

Results: From the set of genes differentially expressed in hypothyroidism, inactivation of MCT8-DIO2 and of MCT8-OATP1C1 affects gene expression in astrocytes, neurons, and oligodendrocytes but in different proportions. In MCT8-OATP1C1 KO about 90% of TH-dependent, cell type-enriched genes are from astrocytes and only 7% from neurons, whereas in the combined inactivation of MCT8-DIO2, 34% of cell type-enriched genes were astrocytic and 28% neuronal.

Conclusion: The effects of MCT8-DIO2 and MCT8-OATP1C1 inactivation on gene expression are not equivalent, even if the final outcome is a strong decrease of T3 availability. The main difference is that in the MCT8-DIO2 KO the transfer of T4 to the astrocytes is preserved. This appears to protect a fraction of astrocyte-enriched genes from hypothyroidism even in the absence of T4 to T3 conversion.

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Oral Session 2 (Clinical): Thyroid Cancer Diagnostics

10.00–10.15

ELASTICITY INDEX MEASURED BY SHEAR WAVE ELASTOGRAPHY HAS LITTLE CLINICAL VALUE FOR RISK STRATIFICATION OF THYROID NODULES

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Objectives: To assess the diagnostic accuracy of shear wave elastography (SWE) in identifying malignant thyroid nodules.

Methods: SWE was performed preoperatively in unselected patients with thyroid nodular disease. Elasticity Index (EI) was registered in three regions of interest (ROI) of varying size around the stiffest area of the nodule. The diagnosis was determined histologically in all patients.

Results: 329 patients (mean age: 55 ± 13 years) with 413 thyroid nodules were enrolled. 88 nodules were malignant, of which nine microcarcinomas – embedded in an otherwise benign nodule – were excluded from the comparative analyses.

There was no significant difference in EI between malignant and benign nodules for any of the outcomes investigated (table 1). Furthermore, there were no associations between any of the EI parameters and the diagnosis by receiver operating characteristics (ROC) analyses, reflected by the area under the curve (AUC) being close to 0.50. Consequently, defining a cut-off value of EI for the prediction of malignancy is not clinically meaningful.

Conclusion: Since EI, measured by SWE, showed huge overlap between malignant and benign nodules, the diagnostic validity is low in the prediction of malignancy. Further, taken the rather large variability of SWE into account, we strongly question if SWE has any role in the routine diagnostic set-up in patients with thyroid nodules.

Table 1. (for abstract time 10.00–10.15)

EI-outcome	Malignant, EI* kPa	Benign, EI* kPa	p-value	ROC AUC mean, 95% CI
ROI-mean[1]	27 (3–100)	28 (4–182)	0.78	0.51 (0.42–0.59)
ROI-max[1]	40 (11–148)	39 (6–242)	0.50	0.53 (0.44–0.61)
ROI-nn[1]	2.4 (1.0–15.1)	2.4 (1.1–27.6)	0.13	0.55 (0.48–0.62)
Stiff-mean[2]	33 (4–116)	32 (4–192)	0.96	0.52 (0.44–0.60)
Stiff-max[2]	39 (11–148)	38 (6–242)	0.52	0.52 (0.44–0.61)
Center-mean[3]	17 (4–51)	16 (4–88)	0.61	0.52 (0.44–0.61)
Center-sd[3]	8.1 (1.5–31.6)	7.1 (1.3–56.5)	0.16	0.56 (0.48–0.64)

* Median (range); nn: ratio comparing stiff and soft areas of the nodule.
[1] 3 mm; [2] 1–3 mm; [3] 10 mm.

10.15–10.30

NEXT-GENERATION SEQUENCING OF THYROID FNA SAMPLES USING THE ION AMPLISEQ™ CANCER HOTSPOT PANEL V2

Claudio Bellevicine[1], *Roberta Sgariglia*[1], *Umberto Malapelle*[1], *Caterina De Luca*[1], *Elena Vigliar*[1], *Markus Eszlinger*[2], *Ralf Paschke*[2], *Giancarlo Troncone*[1]

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Background: Fine needle aspiration (FNA) cytology is accurate and cost-effective in the evaluation of thyroid nodules. However, molecular techniques may contribute to risk-stratification in indeterminate cases. Although next generation sequencing (NGS) is a promising technique for the molecular testing of thyroid FNAs, thyroid-specific cancer gene panels are not commercially available. Conversely, the Ion AmpliSeq™ Cancer Hotspot Panel v2 (CHPv2), which includes the genes most frequently mutated in thyroid cancer, is commercially available and may represent an alternative to thyroid-specific panels. To date, CHPv2 has performed well only on 'ideal' cytological samples featuring >10 ng DNA input and satisfactory post-sequencing metrics. The aim of this study was to extend NGS to less than ideal samples, which represent a large portion of routine clinical specimens.

Methods: To this end, we retrospectively analyzed 37 thyroid smears using CHPv2, regardless of any pre-analytical and post-sequencing metrics thresholds. Specifically, we evaluated the performance of CHPv2 on the *BRAF*, *NRAS*, *HRAS*, *KRAS* and *RET* genes. Results were verified by pyrosequencing.

Results: Thirty-four of the 37 (91.8%) thyroid FNAs were successfully processed. *BRAF*, *NRAS* and *RET* somatic variants were detected in 22/34 (64.7%) samples. Post-sequencing metrics are reported in Table 1. Next-generation sequencing had a high sensitivity (94.4%), specificity (85.7%) and accuracy (88.4%).

Conclusion: CHPv2 is a valid option for the molecular evaluation of thyroid FNAs by NGS. Notably, this approach is accurate and effective even when applied to routine cytology samples that usually do not have optimal pre-analytical and post-sequencing requirements.

Table 1. Mean and ranges of post-sequencing metrics in cytology samples successfully processed by NGS (for abstract time 10.15–10.30)

	Mean	Max	Min
Mapped reads	160,120.26	732,933	963
On-target reads (%)	76.05	99.15	3.06
Average base coverage	967.91	3,740	4.13
Uniformity (%)	78.93	99.99	40.23

10.30–10.45

PROGNOSTIC VALUE OF MINIMAL EXTRATHYROIDAL INVASION (PT3) IN PATIENTS WITH PAPILLARY THYROID CARCINOMA NOT SUBMITTED TO PROPHYLACTIC LYMPHADENECTOMY

Fabio Maino[1], *Maria Grazia Castagna*[1], *Filomena Barbato*[1], *Raffaella Forleo*[1], *Noemi Fralassi*[1], *Furio Pacini*[1]

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According to the most recent guidelines, in the presence of minimal extrathyroid invasion (ETI), all papillary thyroid cancer (PTC) are classified at 'intermediate risk' of persistence/recurrence disease. We hypothesized that the clinical impact of ETI may be related to the size of the tumor rather than ETI and that therefore the risk of small tumors with ETI may be up-scored.

Objective of the study was to evaluate the prognostic significance of ETI in patients with PTC not submitted to prophylactic lymphadenectomy according to tumor size.

We retrospectively evaluated 504 patients (pT1-T3NX): 118/504 (23.4%) had a ETI and 386/504 (76.6%) had intrathyroidal tumor. At a median follow-up of 8.3 years, a poor outcome (persistence/recurrence/death; PRD) was observed in 21/118 (17.8%) patients with ETI and 33/386 (7.8%) patients with intrathyroidal tumor (p = 0.006); the risk of PRD increased two-fold in patients with ETI at diagnosis [OR: 2.0 (1.254–3.455, p = 0.004)]. When we compared the clinical outcome of PTC patients with (n = 118) and without ETI (n = 386) according to tumor diameter, no significantly differences was found both in patients with PTC ≤1 cm (PRD: 5.4% in tumor with ETI and 3.4 in tumor without ETI, p = 0.63) and in patients with PTC >1.0-≤2.0 cm (PRD: 15% in tumor with ETI and 9.2% in tumor without ETI, p = 0.31). Conversely, an higher rate of PRD was found in patients with PTC >2 cm and ETI when compared with patients with PTC >2 cm without ETI (PRD: 46.6% and 17.3% respectively, p = 0.007).

In conclusion, the ETI is an unfavorable prognostic factor in larger tumors than 2 cm but not in small tumors suggesting that, in the absence of other unfavorable characteristics, small tumors with ETI could be classified and managed as 'low risk' tumors.

10.45–11.00

THE MACROFOLLICULAR VARIANT OF PAPILLARY THYROID CANCER (MF-PTC): A BICENTRIC RETROSPECTIVE ANALYSIS OF 65 CASES

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Objectives: MF-PTC is a rare well-differentiated histological variant of PTC characterized by macrofollicles (>50% of a cross-sectional area) lined by follicular cells with nuclear features of PTC. The prognosis is excellent even though some reported cases have an aggressive course. Aim of this study was to analyze the clinical and pathological data of a double cohort of patients (pts) with MF-PTC selected from 2 centres: Endocrinology Unit of the Oncologic Institute of Lisbon (IPO-pts) and Endocrinology Unit of Pisa (PISA-pts).

Methods: The medical records of 65 pts with MF-PTC, followed between 1992–2015, were retrospectively reviewed.

Results: No statistical difference in epidemiological data between the 2 groups. 97% of pts underwent total thyroidectomy; among these 7/63 (11%) pts underwent also central compartment dissection; 2/65 (3%) pts underwent lobectomy. The mean tumour diameter was statistical different between the 2 groups: 40 ± 14 mm (range 20–70) in IPO-pts vs 22 ± 15 mm (range 5–65) in Pisa-pts. At the diagnosis there were no statistical differences between the 2-groups for the tumoral stage (64%, 18%, 11%, 7% belonged to I, II, III, IV stage, respectively) and the ATA risk classes (86%, 12% and 2% had low, intermediate and high recurrence risk, respectively). According to the pathology features IPO-pts and PISA-pts were statistically different for the multifocality (50% vs 80%) and bilaterality (17% vs 40%). 88% of pts after surgical treatment performed ^{131}I-ablation. The whole body scan post-^{131}I-therapy showed cervical uptake in all pts; 1IPO-pt and 2 PISA-pts showed as well lung and bone metastases with an excellent answer (one of this reached the clinical remission). After 9 years of follow-up 91% had no evidence disease, 7% had biochemical evidence disease and 2% had a structural evidence disease without difference between the 2 groups. The tumor dimension and the presence of lymph node metastases correlated with the outcome.

Conclusion: 1) This is the first study on MF-PTC with such a large series and with a medium to long-term follow-up. 2) We confirm that MF-PTC has an excellent prognosis also in the metastatic cases, responding exceptionally to ^{131}I-therapy. 3) In the future the molecular analysis could explain the reasons of this exceptional respond.

11.00–11.15

RISK STATIFICATION IS USEFULL IN PREDICTING PERSISTENT/RECURRENT DISEASE IN MICROPAPILLARY THYROID CARCINOMA

Filomena Barbato[1], *Maria Grazia Castagna*[1], *Fabio Maino*[1], *Raffaella Forleo*[1], *Noemi Fralassi*[1], *Furio Pacini*[1]
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Papillary thyroid microcarcinomas (PMC) defined as tumors ≤10 mm in diameter, has good prognosis although persistence/recurrence are possible. Clinicians are interested in using a scoring system to accurately predict persistence/recurrence and manage patients accordingly.

We aimed to identify prognostic factors for persistence/recurrence in 304 patients with PMC and to develop a scoring system. The second objective was to compare the clinical outcome among PMC and papillary thyroid carcinoma (>1 cm, PTC) in the presence of minimal extrathyroidal invasion (ETI) and lymph node metastases at diagnosis (N1).

At 7.3 years median follow-up, unfavourable prognostic factors were N1 ($p < 0.0001$), male gender ($p = 0.01$), age ≤45 years ($p = 0.001$) and ETI ($p < 0.0001$). Based on these results PMC patients were divided into 3 groups: 'very low risk' (intrathyroidal PMC; 64.8%), 'low risk' (patients with ETI; 14.8%,) and 'Intermediate risk' (N1 with/without ETI; 20.4%). Clinical outcome was similar among 'low risk' and 'very low risk' patients [clinical remission (CR): 95.6% versus 96.4%, $p = 0.67$] whereas the rate of CR was significantly lower in 'intermediate risk' when compared with 'low risk' patients (CR: 72.6% versus 95.6%, $p < 0.0001$). Risk of persistent/recurrent disease increased eight-fold in N1 patients at diagnosis [OR: 8.2 (1645–54255, $p = 0.002$]. Four hundred forty-five PTC patients were divided into the same three groups and compared with the PMC. The clinical outcome was better in the PMC both in the group of 'very low risk' (CR 96.4% versus 87.7%, $p = 0.004$) and of 'low risk' patients (CR 95.6% versus 79.6% in PTC, $p = 0.02$). Conversely, no difference was observed among PMC and PTC patients in 'intermediate risk' group patients (CR 72.6% versus 62.9%, $p = 0.24$).

In conclusion the results of this study demonstrate that risk stratification allows to better define individual risk and to better modulate the subsequent follow-up in PMC.

11.15–11.30

SIMULTANEOUS MEDULLARY (MTC) AND DIFFERENTIATED THYROID CANCER (DTC) IN THYROID GLAND (MTC-DTC): WHICH TUMOR IS THE REAL MATTER?

Letizia Pieruzzi[1], *Loredana Lorusso*[1], *Liborio Torregrossa*[2], *Valeria Bottici*[1], *Laura Agate*[1], *Fulvio Basolo*[2], *Gabriele Materazzi*[2], *Paolo Vitti*[1], *Eleonora Molinaro*[1], *Rossella Elisei*[1]
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Introduction: The simultaneous presence of MTC and DTC is a rare event, but more frequent than expected. The cellular origin, the clinical-pathological and prognostic characteristics of these tumors are completely different and, as consequence, their clinical management.

Object to evaluate the clinical and pathological features and the outcome of the simultaneous MTC-DTC patients followed at Endocrinology Department of Pisa.

Materials and Methods: We selected 101 cases of simultaneous MTC-DTC thyroid tumors from the Anatomy-Pathology Unit database, diagnosed between 2000 and 2015.

Results: 101 patients were evaluated, 58 females (57%) and 43 males (43%) with a mean age of 54 years. 58/101 (57%) cases underwent surgery for MTC, 8/101 (8%) cases for DTC, 1/101 (1%) for simultaneous MTC-DTC. In the remaining 34/101 (34%) cases, patients underwent thyroidectomy for goiter or other benign conditions. In 97/101 (97%) cases the hystotype of DTC was represented by papillary carcinoma (PTC); in one case by follicular carcinoma (FTC) and in two cases by double tumor histology (PTC/FTC). In one case a mixed thyroid tumor (i.e. tumoral cells positive for both calcitonin and thyroglobulin) was observed. MTC was larger than the simultaneous DTC (0.88 cm ± 1.16 vs 0.46 cm ± 0.86; p:0.0004) and showed a more advanced stage [MTC Stage 1–2: 60/89 (67.4%); Stage 3–4: 29/89 (32.6%) vs DTC Stage 1–2: 83/90 (92.2%), Stage 3–4: 7/90 (7.8%) ($p < 0.001$)]. After a mean follow-up of 3.8 years, no patients showed structural evidences of DTC disease, while 14/89 (15.7%) had evidences of metastases and/or local persistence related to MTC, in particular 4/14 (29%) patients died for MTC progression. The only patient with mixed type of thyroid tumor died for progression of metastatic disease.

Conclusion: 1) In the presence of simultaneous MTC-DTC, PTC is the almost exclusive (97%) DTC hystotype; 2) Among the 2 tumors, MTC is the hystotype with a more advanced stage at diagnosis and affecting tumor prognosis; 3) Although rare, the mixed hystotype also showed an aggressive phenotype.

11.30–11.45

COMPUTED TOMOGRAPHY ADDED TO ULTRASONOGRAPHY GIVES THE BENEFITS TO DETERMINE THE EXTENT OF NECK DISSECTION IN PATIENTS WITH THYROID CANCER: A PROSPECTIVE MULTICENTER STUDY

Ji-Hoon Kim[1], *Younghen Lee*[2], *Dong Gyu Na*[3], *Jung Hwan Baek*[4], *So Lyung Jung*[5], *Sun-Won Park*[6], *Jinna Kim*[7], *Tae Jin Yun*[8], *Eun Joo Ha*[9], *Kyu Eun Lee*[10], *Kyung-Sook Yang*[11]
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Objective: To determine the diagnostic role of computed tomography (CT) added to ultrasonography (US) for the diagnosis of lymph node metastasis (LNM) in patients with thyroid cancers.

Background: The benefit of CT for the diagnosis of LNM is still unclear.

Methods: A prospective multicenter study at 7 hospitals was performed for the 351 patients with thyroid cancers who underwent both US and CT prior to surgery. We compared diagnostic accuracy of combination of US and CT (US/CT) with that of US for the evaluation of LNM and calculated patient-based benefits of CT added to US to determine the extent of neck dissection.

Results: Out of 801 neck levels, US/CT showed higher sensitivities [32.4% (71/219) vs. 17.8% (39/219) and 88.1% (140/159) vs. 73.6% (117/159), $p < 0.0001$, respectively] in both central and lateral compartments, while accuracy was improved only in lateral compartment [85.9% (226/263) vs. 80.2% (211/263), $p = 0.010$] compared with US.

When US showed negative results, the sensitivity and accuracy of CT were higher in lateral compartment than central compartment [54.8% (23/42) and 80.1% (109/136) vs. 17.8% (32/180) and 59.8% (291/487), respectively, $p < 0.0001$].

Patient-based overall benefits were 11.1% (39/351) and 13.1% (46/351) for therapeutic neck dissections preferring modified radical lateral neck dissection and selective lateral neck dissection, respectively, and were larger in patients with cancer >1 cm than cancer ≤1 cm ($p = 0.0003$ and $p = 0.0001$, respectively).

Conclusion: In patients with thyroid cancer, CT added to US gives the benefits to determine the extent of neck dissection, especially for lateral compartment and patients with cancer >1 cm.

11.45–12.00

THYROGLOBULIN DOUBLING-TIME (TGDT): ITS VALUE AS A PROGNOSTIC MARKER IN DIFFERENTIATED THYROID CANCER (DTC)

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Introduction: Serum thyroglobulin (Tg) is most important disease predictor in post thyroidectomy differentiated thyroid cancer (DTC) patients. Raised Thyroglobulin indicates unsuccessful surgery or disease recurrence in post treatment patients. Objective of this study was to evaluate the prognostic value of the serum Thyroglobulin doubling-time in differentiated thyroid cancer patients.

Methods: We retrospectively analyzed total of 679 patients with DTC presenting to department of Nuclear Medicine between January 2008 to December 2013. Patent having raised anti-Tg antibody were excluded from the study. Total 398 patients' data with 3 or more serum Tg measurements was finally submitted for analysis. The Tg doubling-time was computed using Tg values measured during routine follow-up. Patients were followed for a mean of 26.9 months and a median of 27.2 months.

Results: Of the 398 patients, 129 patients had 4 or more measurements that revealed detectable serum Tg. The Tg doubling-time (Tg-DT), calculated using all available data, varied widely, and were grouped into those that were <1 year (12 patients), those that were 1–3 years (18 patients), and those that were ≥3 years (27 patients), as well as those with a negative value due to decrease in serum Tg (72 patients). There were also 83 patients who had three or fewer serum Tg measurements that showed detectable but stable Tg levels, as well as 186 patients in whom serum Tg measurements were below the lower limit of detection. In the group of patients with a Tg-DT of <1 year the cause specific survival at 5 years was 50%, and in the group with a Tg-DT of 1–3 years it was 95%. In all other groups it was 100%. Many classical prognostic factors (age, gender, tumor type, tumor size and stage) as well as the Tg-DT were significant indicators of survival by univariate analysis, but Tg-DT remained the only independent predictor by multivariate analysis. Tg-DT was also the only independent predictor of distant metastases and locoregional recurrence on multivariate analysis.

Conclusion: Tg-DT is a very strong prognostic predictor superior to the classical prognostic factors in patients with DTC.

Oral Session 3 (Basic): Thyroid Hormone Transport, Metabolism and Action

10.00–10.15

KNOCKOUT OF TYPE 2 DEIODINASE SEVERELY DISRUPTS REPRODUCTION IN FEMALE ZEBRAFISH

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Objectives: Reproduction is a thyroid hormone (TH)-dependent process and vertebrate gonads express TH transporters and deiodinases to regulate local 3,5,3'-triiodothyronine (T_3) availability. Type 2 deiodinase (Dio2) is the major TH activator in fish and it is abundantly expressed in both ovary and testis. Therefore zebrafish is an attractive model to study the impact of Dio2 deficiency on reproduction.

Methods: Adult mutant dio2$^{-/-}$ fish and wild types (WT) from the same stock population were used in spawning experiments to assess fertility. Female gonads were sampled to compare oocyte production and maturation, TH content and expression of TH-regulatory genes.

Results: The onset of egg laying was on average 1 month delayed in mutant fish and continued for only 2–3 months vs approximately 18 months in WT. For 3 separate batches, the total number of eggs laid by the mutants over a 2-month period was on average only 14% that of WT fish. Fertilisation percentages varied from 60–84% for WT and from 10–51% for mutants. At the onset of sexual maturity, ovaries of mutant fish (4-month-old) were 35% larger than in WT (3-month-old). Counting of primary and mature oocytes on ovary sections showed a clear predominance of mature oocytes in WT fish. In mutants, relative number of primary oocytes was strongly increased while relative mature oocyte number was decreased, resulting in a strong predominance of immature oocytes. In 1-year-old mutants, no longer active in reproduction, ovaries were doubled in size compared to WT of the same age. Ovarian T_3 levels were strongly decreased in mutant vs WT fish. This was accompanied by an increased expression of *dio1* and *thraa* while *dio3a*, *dio3b* and *thrb* expression remained unaffected.

Conclusion: Dio2 deficiency severely disrupts reproduction in zebrafish. The resulting decrease in ovarian T_3 content seems to affect both oocyte maturation, deposition and fertilisation.

10.15–10.30

MICRORNA 199-A3P INHIBITION INDUCES AN INCREASE OF THE EXPRESSION OF DEIODINASE 2 IN AORTIC ENDOTHELIAL CELLS

Joris Virginie[1], *Lobysheva Irina*[1], *Balligand Jean-Luc*[1], *Marie-Christine Many*[2], *Dessy Chantal*[1]
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Objectives: The cardiovascular system is a known target of thyroid hormones (THs), altered thyroid function being often associated with increased risks of cardiovascular events. It has been observed that endothelial cells express both TH receptors and deiodinases suggesting that the endothelium might also modulate TH availability. Interestingly, rats treated with THs present an increased NO-dependent relaxation. Furthermore, THs, activated by deiodinase 2 (D2), initiate rapid non-genomic effects on endothelial cells through PI3K/Akt signaling. Recently, miR-199a-3p, mostly known for its implication in several cancers including thyroid carcinoma, has been implicated in the control of vascular functions. We focused on roles of microRNA-199a-3p in the modulation of endothelial function by THs.

Methods: Bovine Aortic Endothelial Cells were transfected with a specific miR199a-3p inhibitor or a scramble sequence (Lock-Nucleic Acid (LNA)). After 48 h, cells were harvested and eNOS activation was evaluated by analyzing its phosphorylation on serine1177 on Western Blot. The expression of D2 and activation of Akt, a known modulator of eNOS activity were also measured by Western Blotting.

Results: Endothelial cells treated with LNA showed a rise of NO production associated with an increase of the phosphorylation on serine1177 of eNOS without any change of the total protein expression. Interestingly, an increase of D2 expression was also observed in treated cells, associated with an increase of Akt phosphorylation on threonine308 highlighting an activation of the PI3K/Akt pathway. Cells treated with LY294002, an inhibitor of PI3K pathway, still present an increase of D2 expression when co-treated with LNA against miR199a-3p.

Conclusion: These results show an implication of miR-199a-3p in the modulation of NO-dependent relaxation. The increase of D2 expression suggests that miR199a-3p inhibition could improve endothelial function by modulating T3 availability in endothelial cells. Furthermore, results with LY suggest that D2 could be ahead of the PI3K/Akt pathway.

10.30–10.45

THYROID HORMONE AND SKIN CANCER: A NOVEL MICRORNA21-D3 INTERPLAY REGULATES BASAL CELL CARCINOMA TUMORIGENESIS

Daniela Di Girolamo[1], *Raffaele Ambrosio*[2], *Maria Angela De Stefano*[1], *Giuseppina Mancino*[1], *Emery De Cicco*[1], *Caterina Miro*[1], *Domenico Salvatore*[3], *Monica Dentice*[4]
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Type 3 iodothyronine deiodinase (D3), the thyroid hormone (TH)-inactivating enzyme, is an oncofetal protein rarely expressed in adult life, but re-activated in proliferating and neoplastic contexts. By terminating TH action within the tumor microenvironment, D3 enhances cancer cell proliferation. However, the pathological role of D3 and the significance of TH metabolism in cancer have yet to be fully explored. We have previously shown that D3 is highly expressed in basal cell carcinoma (BCC) under the regulation of the Sonic Hedgehog (Shh) pathway. D3 depletion from BCC cells drastically attenuates their proliferative and tumorigenic potential. Here we describe a reciprocal regulation between TH action and the cancer-associated microRNA-21 (miR21) in basal cell carcinoma (BCC) skin tumors. We found that, besides being negatively regulated by TH at transcriptional level, miR21 attenuates the TH signal by increasing D3 levels. We found that the ability of miR21 to positively regulate D3 was mediated by *GRHL3*, a tumor suppressor gene and a D3 transcriptional inhibitor. Finally, we found that keratinocyte-specific D3-depletion significantly reduced tumor growth in a BCC mouse model, which establishes the functional relevance of this network in vivo. These novel findings identify TH action as a critical hub of multiple oncogenic pathways and provide functional and mechanistic evidence of the involvement of TH metabolism in BCC tumorigenesis. TH-mediated miR21 suppression illustrates a previously unrecognized regulation of miR21 by a hormonal endocrine signal and offers a potential therapeutic approach to BCC.

10.45–11.00

THYROID HORMONE TRANSPORTERS IN XENOPUS AND THEIR SUSCEPTIBILITY TO XENOBIOTICS

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Disruption of Thyroid Hormone (TH) action, either due to genetic and/or environmental factors, has been implicated in neurological defects such as autism, attention deficit hyperactivity disorders (ADHD) and IQ loss. Genetic disruption is evident in the Allan-Herndon-Dudley (AHD) syndrome where, in humans, the mutation of the brain specific TH transporter (THT), monocarboxylate transporter 8 (MCT8), leads to severe intellectual disability. Various xenobiotics have also been shown to disrupt the TH signaling pathway at various levels (receptor, blood transporter or deiodinases), however, little is known about the effect of xenobiotics on the TH transporter MCT8, especially in the Xenopus model where we observe a dynamic in vivo tissue specific expression of the THT. Using the radiolabeled cell uptake in vitro assay, we demonstrate that Xenopus mct8 actively transports both T3 and T4 bi-directionally. Effects of various environmental xenobiotics on in vitro MCT8 function are currently being tested. Furthermore, in order to pin point, the exact pathophysiological mechanism of TH deficiency in the in vivo developing brain, we have created a model of thyroid deficient brain, by knocking out the mct8 expression in Xenopus using the CRISPR-Cas9 system. We show that the CRISPR-Cas9 can generate highly efficient deletions using a multiple guide-RNA strategy in Xenopus in order to create a F0 disease model. We are currently phenotyping F0 animals using existing transgenic neuronal marker-lines for injections, and conducting an in-depth transcriptomic analysis on various pertinent areas of brain.

11.00–11.15

ANEMIA IN PATIENTS WITH RESISTANCE TO THYROID HORMONE ALPHA: A ROLE OF TRA IN HUMAN ERYTHROPOIESIS

Anja van Gucht[1], *Marcel Meima*[2], *Carla Moran*[3], *Maura Agostini*[4], *Anna Tylki-Szymanska*[5], *Malgorzata Krajewska-Walasek*[5], *Krystyna Chrzanowska*[5], *Alexandra Efthymiadou*[6], *Dionisios Chrysis*[6], *Korcan Demir*[7], *W. Edward Visser*[8], *Theo Visser*[9], *Thamar Van Dijk*[10], *V. Krishna Chatterjee*[3], *Robin Peeters*[8]
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Introduction: Patients with Resistance to Thyroid Hormone (RTHα), due to heterozygous mutations in TRα, are characterized by growth retardation, macrocephaly and abnormal thyroid function tests. In addition, almost all RTHα patients have mild anemia, the pathogenesis of which is unknown. Since animal studies suggest an important role for TH and TRα in the latter stages of erythroid development, we hypothesized that erythropoiesis in RTHα patients is impaired.

Objective: Our objective was to elucidate the pathogenesis of anemia in RTHα patients and delineate the role of TH and TRα in human erythropoiesis.

Methods: Cultures of primary human erythroid progenitors (HEPs), from peripheral blood of RTHα patients harboring different inactivating mutations in TRα (F397fs406X, A382fs388X, C392X) were established and compared to healthy controls. During terminal differentiation, erythroid cells become smaller, accumulate hemoglobin, and exhibit an altered pattern of cell surface marker expression. We therefore assessed cell number, cell size distribution, and used immunofluorescence staining and FACS analysis to monitor erythroid maturation of the HEP cultures at different time points.

Results: After ~14 days of *ex vivo* expansion, control HEP cells started to differentiate spontaneously. In contrast, the majority of HEPs from all RTHα patients continued to proliferate and showed less differentiated morphology. Throughout the differentiation phase, HEPs from RTHα patients were larger in size and more positive for c-Kit (an early proliferation marker) and CD44 (an early differentiation marker), whereas control cells were more positive for GPA (a late differentiation marker). Interestingly, addition of T3 (10 nM) accelerated differentiation of both control and RTHα patient-derived HEPs.

Conclusion: Inactivating mutations in TRα affect the balance between proliferation and differentiation of progenitor cells in human erythropoiesis, which likely explains the occurrence of mild anemia in most RTHα patients.

11.15–11.30

THE T3 RECEPTOR TRα1 INTERACTOME

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Introduction: Unliganded T3 receptors (TRs) are associated with a complex of co-repressors that are exchanged for co-activators upon binding of T3 to the TR. Mutations in TRs cause resistance to TH (RTH) in tissues that express the affected isoform. The phenotypical consequences of mutations likely depend on the consequences for co-factor release and recruitment. To determine the isoform-specificity of co-factor association and the effects of mutations, we developed a tandem-affinity purification

protocol and present here the interactome for wild-type TRα1 in HepG2 human hepatocytes.

Objective: To purify and identify an interactome for wild-type TRα1.

Methods: TRα1 and TRβ1 were N-terminally tagged with a FLAG- and HA-epitope and stably expressed in HepG2 cells using lentiviral transduction. Expression was confirmed by western blotting and activity using a luciferase-based reporter assay. HepG2/FH-TRα1 or control cells were incubated for 4 hrs with either vehicle or 100 nM T3. Nuclear extracts were subjected to sequential purifications on anti-FLAG and anti-HA resins, and isolated proteins were identified by LC/MS-MS. For co-immunoprecipitations, FLAG-tagged TRs transiently expressed in HepG2 cells were precipitated using anti-FLAG resin and immuno-complexes blotted with available antibodies.

Results: Over seventy proteins co-purified specifically with FH-TRα1. The presence of known interactors, such as retinoid X receptors regardless of T3, the NCoR1/Ski/HDAC3 repressor complex in the absence of T3, and SRCs and Mediator in the presence of T3 validated our approach. In addition, several novel putative interacting proteins were identified, including the transcription factor prospero homeobox protein 1 (PROX1). The association of PROX1 was T3-dependent, as confirmed by co-immunoprecipitation with FLAG-tagged TRα1 transiently expressed in HepG2 cells.

Conclusion: We successfully purified the interactomes for unliganded and T3-bound TRα1 from HepG2 cells, which was validated by the presence of known interacting proteins. In addition, we identified potential novel binding partners and confirmed the T3-dependent recruitment of PROX1.

11.30–11.45

EFFECT OF THYROID HORMONE ON GENE EXPRESSION IN HUMAN TRALPHA-EXPRESSING CELLS

Elske Massolt[1], *Selmar Leeuwenburgh*[2], *Sigrid Swagemakers*[3], *Mirjam van den Hout-van Vroonhoven*[4], *Boen L.R. Kam*[5], *Pim Burger*[6], *Peter van der Spek*[3], *Wilfred F. van Ijcken*[4], *Theo Visser*[7], *Robin Peeters*[8], *W. Edward Visser*[8]

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Context: Normal serum TSH concentrations reflect only pituitary euthyroidism and therefore, novel markers representing tissue thyroid state are needed. Genomic actions of thyroid hormone (TH) are mediated by binding to nuclear T3 receptors (TRalpha and TRbeta isoforms), which regulate transcription of target genes. It is currently unknown which genes are regulated by TH in human tissues.

Objective: To study the effect of TH on human gene expression profiles in whole blood, mainly consisting of TRalpha expressing leucocytes.

Methods: We studied whole blood samples (collected in PAXgene RNA tubes) from 8 thyroidectomized patients (4 females) with differentiated thyroid cancer on and after 4 weeks off levothyroxine replacement. We performed next-generation RNA sequencing after removal of ribosomal RNA and globin mRNA. A paired differential expression analysis was performed using DESeq2.

Results: Mean age was 46.8 years, median TSH level was 78.0 mU/l off and 0.07 mU/l on levothyroxine treatment. We detected 1227 differentially expressed (DE) genes (multiple testing corrected P-value <0.05), of which 67.7% were positively and 32.3% were negatively regulated. Of the DE genes, 486 had a fold-change above 1.5. Gene ontology enrichment analysis revealed that 34 biological processes were significantly overrepresented of which the process translational elongation showed the highest fold enrichment (7.3 fold, FDR adjusted $P = 1.8 \times 10^{-6}$) followed by the process coagulation (5.5 fold, $P = 0.006$). Of the 486 DE-genes (fold-change >1.5), 26 genes overlapped with DE-genes in muscle samples on and off levothyroxine treatment previously reported (3.1 fold enrichment; $P = 5.8 \times 10^{-9}$).

Conclusion: Physiological levels of TH regulate numerous genes in human whole blood, presumably TRalpha expressing leucocytes. Easily accessible whole blood samples potentially can be used as a proxy for other tissues in humans. The identification of newly identified TH-responsive genes may provide the molecular explanation of clinical effects in subjects with different TH status.

11.45–12.00

DISTINCT MOLECULAR FEATURES AT L-TYPE AMINO ACID TRANSPORTER 2 DETERMINE DIFFERING THYROID HORMONE INFLUX AND EFFLUX PROFILES

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Thyroid hormones (TH) are traversed via transporters across the cell membrane. The L-type amino acid transporter 2 (Lat2) imports apart amino acids also certain TH, 3,3'-T2 and T3, but not rT3 and T4. Recently we localized 3,3'-T2-uptake sensitive residues of Lat2 and reported specific substrate properties by varying TH-like derivatives. However, the molecular determinants for substrate transport by Lat2 especially for efflux of TH and amino acids are still unclear. Thus we utilized Lat2 mutations (Y3.36A, N3.39S, F6.46W) that increased 3,3'-T2 uptake differently and focus here on the influx and efflux capacity of amino acids, T4, T3, BCH and derivatives thereof to investigate molecular features for influx and efflux.

Cell surface expression of the Lat2 variants are verified by two conventional techniques. Transport studies and competitive inhibition import analysis by radiolabeled TH and amino acids were studied in *Xenopus laevis* oocytes.

Influx is enabled for T4 and increased for T3 by one channel widening mutation Y3.36A only. The import of amino acids remains unaffected for all mutants. Mutant F6.46W showed increased 3,3'-T2 import but decreased import and export rates for other TH derivatives. Apart from bulky size of iodine, its ð-system interactions may influence the TH import positively along aromatic residues. No efflux was detected for all TH by Lat2-WT. Mutation Y3.36A and N3.39S enabled the efflux of 3,3'-T2 only, while N3.39S increased also amino acids export.

Distinct molecular features determine bidirectional amino acid transport but only a unidirectional import of T2/T3 by Lat2. According to the molecular model N3.39 is closer located to the central recognition pattern for amino acid moiety than Y3.36, which obstructs T4 and hampers T3 uptake. Both Y3.36 and N3.39 prevent the efflux of any TH. Revealing molecular and structural determinants for traversing TH and amino acids provide insights into transport mechanisms of Lat2.

Oral Session 4 (Clinical): Clinical Thyroidology

16.00–16.15

COMBINATION OF DIO2 AND MCT10 GENE POLYMORPHISMS PREDICTS THE PREFERENCE FOR T4+T3 THERAPY IN HYPOTHYROIDISM – A BLINDED RANDOMIZED CLINICAL STUDY

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Objectives: The intracerebral availability of thyroid hormones is partly regulated by the local type II deiodinase (DIO2) and the cellular membrane transport-facilitating monocarboxylate transporter (MCT10). In several studies, hypothyroid patients have preferred combined therapy with T4-T3 over T4 monotherapy. Based on a previous prospective randomized study of hypo-

Table 1. (for abstract time 16.00–16.15)

	rs225014 and rs17606253 gene polymorphisms			All patients
	wild type in both genes (no SNP)	one SNP	SNP in both genes	
T3 preference	8 (42.1%)	12 (63.2%)	7 (100%)	27 (60%)
No T3 preference	11	7	0	18

thyroid patients (1), in which 49% of patients preferred T4-T3 combination therapy against T4, we now studied DIO2 and MCT10 gene polymorphisms in relation to T4+T3 preference.

Methods: 44 previously hypothyroid patients now with long-time stable (≥6 months) euthyroidism on T4 therapy participated in a prospective double blind cross-over study. Half of the patients were randomized into continuous three months T4 therapy followed by 3 months T4-T3-combination therapy, the rest into combination therapy followed by T4-therapy. In both periods, 50 µg of T4 was blindly replaced by either identical 50 µg T4 or by 20 µg T3. We investigate four single-nucleotide polymorphisms (SNPs) with predesigned TaqMan assay (Applied Biosystems, Foster City, CA) in two genes: DIO2 (rs225014, rs12885300, rs502215) and MCT10 (rs17606253). We further asked in which of the two treatment periods patients felt better (which treatment was preferred).

Results: 27 out of 45 patients (60%) preferred the combination therapy. Patients with a gene polymorphism in rs225014 (DIO2, Thr92Ala) and/or rs17606253 (MCT10) (n = 26) preferred the combined treatment more often than patients who had no such polymorphisms (19/26 vs. 8/19, p = 0.036). As indicated in the table, a high T4+T3 preference was especially observed in those patients with polymorphisms in both genes (linear-by-linear association, p = 0.009). Thus, the rs225014 and rs17606253 polymorphisms associated with T3 preference in our hypothyroid patients.

Conclusion: The present study indicated that the combination of polymorphisms in DIO2 (rs225014) and MCT10 (rs17606253) enhances hypothyroid patients' preference for T4+T3 replacement therapy. However, confirmative studies with a higher number of patients are needed.

Reference

1 Nygaard et al: PMID 19666698.

16.15–16.30

THYROIDECTOMY IMPROVES DISEASE RELATED QUALITY OF LIFE IN PATIENTS WITH NON-TOXIC GOITER. A PROSPECTIVE COHORT STUDY

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Objectives: Investigate changes in quality of life (QoL) after surgical treatment for non-toxic goiter using the recently developed and validated thyroid-specific ThyPRO questionnaire.

Methods: Thyroid-specific QoL was examined before and three and six months after surgery for benign non-toxic goiter. A paired t-test with a Bonferroni adjusted level of significance was used for the comparison. The effect size (ES) was estimated as mean change by standard deviation at baseline with ES of 0.2–0.5 defined as small, values of 0.5–0.8 as moderate, and scores >0.8 as large.

Results: 115 patients, mean age 53.1 years (range 20–77); females: n = 95/males: n = 20, referred for surgical treatment of non-toxic nodular goiter (lobectomy: 85, total thyroidectomy: 26, isthmectomy: 4), were consecutively enrolled from November 2014 through February 2016.

Prior to surgery the 'Tiredness scale', 'Goiter symptom scale', and the 'Overall QoL scale' had the highest, i.e. worst, scores. The 'Goiter symptom scale' showed large improvements (ES = 1.24) three months after surgery (p < 0.001). The 'Overall QoL scale' (ES = 0.57), 'Anxiety scale' (ES = 0.45) and 'Hyperthyroid symptoms scale' (ES = 0.44) had moderate size improvements at three months (p < 0.001). Six months following surgery significant improvements were seen in all the mentioned scales, but also the 'Cosmetics symptoms scale' (ES = 0.47), 'Emotional susceptibility scale' (ES = 0.046) and the 'Tiredness scale' improved (ES = 0.61) (p < 0.001).

Increasing goiter size correlated to a decrease in overall QoL (p = 0.02), cosmetic concerns (p = 0.01), and hyperthyroid symptoms (p = 0.046) at baseline. Increasing age was associated with less improvement in goiter symptoms (p = 0.01) at three months after surgery, but the difference disappeared six months after surgery. Neither thyroid morphology nor extent of surgery impacted the results.

Conclusion: We for the first time document the patient-perceived benefits of thyroid surgery in benign non-toxic goiter. Next, this methodology could be used for head-to-head comparisons of surgery with non-surgical alternatives, such as radioactive iodine, laser or radiofrequency ablation.

16.30–16.45

EXCESS MORTALITY IN HYPERTHYROIDISM IS DRIVEN BY LACK OF TREATMENT. EVIDENCE FROM A POPULATION-BASED, LARGE-SCALE, LONG-TERM FOLLOW-UP, DANISH REGISTRY-STUDY

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Objectives: Cumulative time dependent excess mortality in hyperthyroid individuals has been suggested. However, the effect of treatment of thyroid dysfunction on mortality remains unclarified. We aimed at investigating the association between biochemically verified hyperthyroidism and mortality in both treated and untreated hyperthyroid patients.

Methods: Population- and registry-based follow-up (median 7.3 years) study of 232447 individuals who in the period 1995–2011 had at least one serum TSH-measurement from hospitals or general practice. Mortality rates for hyperthyroid subjects compared to euthyroid individuals were calculated using multivariate Cox-regression, adjusted for age, sex and comorbidity, using the Charlson Comorbidity Index. Individuals with increased TSH (>4.0 mIU/l) were excluded.

Results: In untreated individuals with decreased TSH (<0.3 mIU/l) (n = 3734), HR for mortality was 1.35 (95% confidence interval (CI) 1.29–1.41, p < 0.0001). In individuals who at any point after their first TSH measurement had received anti-thyroid medication (n = 5200) HR was 1.00 (0.94–1.06). Subdividing according to disease severity, HR for mortality in untreated overt hyperthyroid individuals (decreased TSH and elevated thyroid hormones)(n = 2139) was 1.19 (1.09–1.29; p < 0.0001), while no excess mortality was found in overt hyperthyroid patients who had received treatment (HR 1.00; 0.92–1.08) (n = 2533). In untreated individuals with subclinical hyperthyroidism (decreased TSH and normal thyroid hormones) (n = 1999), HR for mortality was 1.30 (1.21–1.40; p < 0.0001), while no excess mortality was demonstrated in treated individuals (HR 0.96; 0.82–1.12) (n = 435).

Conclusion: This study suggests that the excess mortality, also in mild/subclinical hyperthyroidism, is driven by refraining from therapy. If therapeutic intervention is mainly offered those with the most pronounced disease manifestations, our data most probably underestimate hyperthyroidism related

mortality and the effect of normalizing thyroid function. More aggressive therapy seems warranted, and we question the appropriateness of performing randomized studies with one arm left without active treatment.

16.45–17.00

THE ASSOCIATION BETWEEN NEONATAL BIRTH DEFECTS AND EARLY PREGNANCY USE OF ANTITHYROID DRUGS

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Background: In pursuit of safe management of pregnant women with Graves' disease, we investigated the association of antithyroid drug (ATD) therapy during early pregnancy with an increased prevalence of neonatal birth defects in national cohort.

Methods: Using the National Health Insurance database in Korea, we included pregnant women aged 20–39 years between January 2008 and December 2014 and analyzed linked neonatal records of women with delivered pregnancies. We compared the prevalence of neonatal birth defects by ATD exposure status.

Results: We identified 12 667 neonates who were born from mothers with early pregnancy ATD use and the overall rate of birth defects was 4.24%, compared with 3.65% of non-exposed cohort (n = 2 779 361) (P < 0.001). The ORs for propylthiouracil (PTU) only, methimazole (MMI)/carbimazole (CMZ) only, and both PTU and MMI/CMZ exposed groups were 1.10 (95% CI 0.99–1.22), 1.27 (95% CI 0.96–1.67), and 1.44 (95% CI 1.18–1.76).

Conclusion: Neonates who were born from mothers with early pregnancy ATD use are at increased risk of birth defects. Exposure to both MMI/CMZ and PTU during this critical period seems to increase the risk.

17.00–17.15

IS THERE AN ASSOCIATION BETWEEN GRAVES' DISEASE, WITHOUT ORBITOPATHY, AND GLAUCOMA? RESULTS FROM A DANISH NATIONWIDE REGISTER-BASED STUDY

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Background: Graves' disease is complicated by orbitopathy (GO) in a significant proportion. However, whether Graves' disease without eye disease (GD), *per se*, could lead to increased intraocular pressure and glaucoma has not been investigated in detail. Our objective was to investigate, at a nationwide level, whether there is an association between GD and glaucoma.

Subjects and Methods: Observational cohort study using record-linkage data from nationwide Danish health registers. After excluding individuals with GO, 28,461 individuals diagnosed with a first episode of GD were included. Cases were matched with 4 non-hyperthyroid controls, according to age and sex, and followed over a mean period of 8.0 years (range 0–17.5 years). Data on the prevalence of glaucoma was obtained by person-to-person record linkage with the National Danish Patient Register and/or the Danish National Prescription Registry. Logistic and Cox regression models were used to assess the risk of glaucoma before and after the diagnosis of GD, respectively. All Cox regression analyses were adjusted for the degree of co-morbidity preceding the diagnosis of GD, using the Charlson score.

Results: Mean age at diagnosis of GD was 55 years. Overall, we found glaucoma significantly more prevalent in GD individuals (4.58%) than in controls (4.21%; p = 0.006). Prior to the diagnosis of thyroid disease, the odds ratio (OR) was not significantly increased for glaucoma in GD (1.09; 95% CI: 1.00–1.18). The hazard ratio (HR) for glaucoma following GD was increased (1.19; 95% CI 1.09–1.30) but vanished after adjusting for pre-existing co-morbidity (1.08; 95% CI 0.98–1.18).

Conclusion: GD is associated with glaucoma. Stratification in the period before and after the diagnosis of GD showed only an increased risk of glaucoma following the thyroid diagnosis. However, this seems to be explained by pre-existing co-morbidity indicating no causal association between GD and glaucoma.

17.15–17.30

THE INTERRELATION BETWEEN HYPOTHYROIDISM AND GLAUCOMA. EVIDENCE FROM A DANISH NATIONWIDE REGISTER-BASED STUDY

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Background: A number of small studies, in selected individuals, have evaluated the association of hypothyroidism and glaucoma. An association could, theoretically, be explained by an autoimmune component of the diseases, but the data do not justify a clear conclusion. Our objective was to investigate, at a nationwide and population-based level, whether there is such an association, and, if so, whether hypothyroidism precedes glaucoma or *vice versa*.

Subjects and Methods: In this observational cohort study we used record-linkage data from nationwide Danish health registers and identified 121,799 individuals diagnosed with a first episode of hypothyroidism. These were matched with 4 non-hypothyroid controls according to age and sex. Prevalence of glaucoma was recorded and cases and controls were followed over a mean of 7.1 years (range 0–17). Logistic and Cox regression models were used to assess the risk of glaucoma before and after the diagnosis of hypothyroidism, respectively.

Results: Overall, we found a higher prevalence of glaucoma in subjects with hypothyroidism as compared to controls (4.6% vs. 4.3%, p < 0.001). Prior to the diagnosis of hypothyroidism, the odds ratio (OR) was significantly increased for glaucoma [1.09; 95% confidence interval (CI): 1.04–1.13, p-value <0.001]. The hazard ratio (HR) for glaucoma after the diagnosis of hypothyroidism was also significantly increased, (1.05; 95% CI: 1.00–1.10, p = 0.03) but vanished after adjusting for pre-existing co-morbidity (HR 0.88; 95% CI: 0.84–0.93).

Conclusion: Hypothyroidism is associated with glaucoma. Before the diagnosis of hypothyroidism, there is an increased risk of glaucoma, indicating that glaucoma could be a risk factor for subsequently being diagnosed with hypothyroidism. Following the diagnosis of hypothyroidism, there is a slightly increased risk for developing glaucoma. However, this seems to be explained by pre-existing co-morbidity. The role of hypothyroidism type and treatment effects should be explored.

17.30–17.45

RADIOFREQUENCY ABLATION: AN EFFECTIVE AND LONG-LASTING TREATMENT FOR THYROID NODULES. RESULTS AT 3 YEARS FOLLOW-UP FROM A SINGLE CENTER

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Objectives: Percutaneous radiofrequency thermal ablation (RFA) was reported as an effective tool for the management of thyroid nodules (TNs) but long term follow-up on standardized populations are lacking at present time. The aim of this study was to prospectively evaluate the volume reduction of

benign medium sized thyroid nodules after a single session of RFA with a 'moving-shot technique'.

Methods: 49 patients with medium sized (median 20.5 ml, IQR 15.5–33.5) citologically benign thyroid nodules were enrolled; all patients underwent a single RFA session and were clinically, biochemically, and morphologically evaluated at baseline and after 1 and 6 months and them annually until the third year.

Results: Volume reduction of the nodules was significant starting at the first month of follow-up (median volume 12.1 ml, median reduction 39%, $p < 0.0001$ vs baseline), with a further reduction over time (median volume at 6 months 10 ml, at 1 year 8.7 ml). After a 2 years follow-up the shrinkage was significant vs 1 month (median volume 6.9 ml, with a 45% reduction vs 1 month, p 0.01 and an overall shrinkage of 66%). After 3 years nodules appeared stable (median 7.7 ml, p 0.73 vs 2 years). Both symptoms and cosmetic scores significantly improved after 6 months, and at the end of observation were resolved in all but 4 patients (1 patient still presenting compressive and cosmetic complaint, 3 with not normalized cosmetic score). RFA was safe and well tolerated in all patients without any significant side effect.

Conclusion: This trial shows good efficacy of RFA on benign solid thyroid nodules in term of volume reduction and symptoms improvement, with progressive shrinkage until 2 years from treatment; volume reduction is stable after 3 years follow-up. Further studies with more patients are needed to confirm this observation.

17.45–18.00

THYROXINE TREATMENT IN OVERWEIGHT AND OBESE HYPOTHYROID PATIENTS

Camilla Virili[1], *Silvia Capriello*[1], *Maria Giulia Santaguida*[1], *Miriam Cellini*[1], *Nunzia Brusca*[1], *Lucilla Gargano*[2], *Marco Centanni*[1]
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Objective: Levothyroxine (LT4) is used by almost 13 million patients in USA and in the same country it has been estimated that 35% of subjects are obese. Oral thyroxine has a narrow therapeutic index and the dose must be tailored on the patient to avoid the over- or under-treatment and the related side effects. Studies on this subject were mostly carried out in thyroidectomized patients and/or in non standardized treatment schedule. Our study was aimed at investigating LT4 daily requirement in overweight or obese patients taking T4 in a tightly controlled fashion.

Methods: Upon the exclusion of patients non-compliant and/or using drugs and/or with diagnosed gastrointestinal disorders, 60 overweight/obese hypothyroid patients with Hashimoto's thyroiditis (55 F/5 M; median age = 44 ys) represented the study group. They were subdivided in: 26 overweight (O), 17 class I obese (C-I), 10 class II obese (C-II), 7 class III obese (C-III). Thirtyfive (34 F/1 M; median age = 40 ys) age-matched patients with normal BMI (<25 kg/m^2), treated in the very same way, represented the reference group (RG). All those patients were treated with oral T4 under fasting conditions and abstaining from eating or drinking for at least one hour after treatment. Once stably attained the desired serum TSH (median TSH: RG = 1.16 mU/l; O = 1.24 mU/l; C I-III = 1.46 mU/l; p = ns), daily T4 requirement was compared in each subgroup.

Results: Normal and overweight patients showed an identical LT4 requirement (1.27 µg/Kg/day) to attain similar median TSH value. In contrast, a significantly reduced need for T4 (–17%; $p < 0.0001$) was observed in obese as compared to both normal- and over-weight patients. T4 requirement inversely correlated with BMI ranging from 1.12 µg/Kg/day (BMI < 35 kg/m^2; n = 17) to 1.00 µg/Kg/day; (BMI >35 kg/m^2; n = 17) (–12%; p = 0.023).

Conclusion: Daily T4 requirement is similar in normal and overweight patients while all classes of obese patients show a progressively reduced need for T4 requirement.

Oral Session 5 (Basic): Thyroid Cancer Pathogenesis

16.00–16.15

GENETIC HETEROGENEITY OF THYROID CANCER

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There are growing evidences suggesting the existence of intra-tumor heterogeneity within the same patient, leading to a different genetic pattern between primary tumour and metastases. We report a paradigmatic example of genetic heterogeneity in thyroid cancer (TC). A 42 years old female patient was submitted, for a follicular TC, to total thyroidectomy and lymphadenectomy followed by radioiodine residue ablation in late 1999. In 2000 and 2001 diagnostic total body scans (TBS) were negative, thyroglobulin (Tg) and anti-thyroglobulin antibodies (TgAb) under TSH stimulation were negative, and patient was considered cured until April 2005 when Tg levels began to progressively increase. Between July 2006 and February 2008 the patient was submitted to four additional radioiodine treatments for lung metastases (total dose 27750 MBq), with Tg levels ranging 30–40 ng/ml and negative TgAb neg. Since then, Tg and TgAb levels continued to increase and in November 2014 the patient was submitted to the surgical removal of a vertebral metastasis. At the molecular analysis, this bone metastasis was shown to harbour a C228T TERT mutation, while both the primary tumor and the lymph-node metastases were negative for the mutation. Possible explanation to this interesting finding are: a) TERT mutation could have been acquired as a secondary event and transmitted to a subset of tumor cells at the primary site (sub-clonal distribution), b) TERT mutation could have been acquired at the metastatic site, c) the primary tumor could have been polyclonal. The present case clearly demonstrate that thyroid cancer can be genetically heterogeneous. This finding is highly relevant because clinicians must consider that the genetic pattern found in the primary tumor, that in some cases have oriented the clinical and therapeutic decisions, may evolve during tumor progression, in particular in the regional or distant metastases, also due to the selection pressure of treatment.

16.15–16.30

CORRELATION BETWEEN THE PRESENCE OF MACROPHAGES AND BRAF V600E MUTATION IN DIFFERENT VARIANTS OF WELL DIFFERENTIATED PAPILLARY THYROID CANCER

Luciana Puleo[1], *Clara Ugolini*[2], *David Viola*[1], *Eleonora Molinaro*[1], *Laura Agate*[1], *Antonio Matrone*[1], *Fulvio Basolo*[2], *Paolo Vitti*[1], *Rossella Elisei*[1], *Cristina Romei*[1]
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Background: The presence of macrophages (TAM), is a common feature in many human tumors; in thyroid tumors, the presence of TAM has been reported in both PTC and anaplastic thyroid carcinoma.

Objectives: To evaluate the presence of TAM in variants of PTC and to verify the correlation with tumor aggressiveness and BRAF mutation.

Patients and Methods: We examined data of 207 patients with PTC. The presence of TAM was evaluated by immunohistochemistry using a monoclonal antibody directed against the CD68. In all cases we evaluated the presence of intra- and peritumoral TAM. In 171 cases we studied the presence of BRAFV600E mutation.

Results: Ninety out of 207 PTC patients had a follicular variant (FV), 61 had a classical variant (CV), 30 had a classical variant with more aggressive areas (CVA) and 26 had a tall cell variant (TCV). Of all samples, 187/207 were

CD68 positive (CD68+) in the intratumoral tissue and 86 were CD68+ in the peritumoral tissue. In particular in the peritumoral tissue TAMs were present in 88% (n = 23/26) of the PTC with TCV, in 53% (n = 16/30) of the PTC with the CVA, in 44% of the CV (n = 27/61) and in 22% (n = 20/90) with FV. We also evaluated the intensity of positivity for CD68 and we observed that an increased staining intensity was in the intratumoral tissue of the TCV ($p < 0.0001$). The BRAFV600E mutation was found in 78/171 (45.6%) samples. The presence of the BRAF mutation correlated with the presence of TAM in the peritumoral tissue ($p < 0.0001$) and with the staining intensity in the intratumoral tissue ($p = 0.0025$).

Conclusion: Our study confirmed the presence of TAM in PTC and demonstrated that the presence of TAM is significantly associated with more aggressive variants of PTC (TCV) and with the presence of the BRAFV600 mutation.

16.30–16.45

GENETIC PREDISPOSITION TO PAPILLARY THYROID CANCER IN CHILDREN AND ADOLESCENTS

Daria Handkiewicz-Junak[1], *Dorota Kula*[1], *Michal Swierniak*[2], *Jadwiga Zebracka-Gala*[1], *Mihcal Jarzab*[1], *Dagmara Rusinek*[1], *Zbigniew Puch*[1], *Aleksandra Kropinska*[1], *Renata Cyplinska*[1], *Barbara Jarzab*[1]

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Background: Familial predisposition to papillary thyroid cancer (PTC) is well known, although its molecular background is still not discovered but is expected to be multigenetic with low- to moderate-penetrance genes. A genome wide association study (GWAS) of PTC in adult population pointed to single nucleotide polymorphism (SNP) near FOXE1 gene. However, there are no data concerning children/adolescents with PTC.

Aim: The purpose of this study was to identify children-specific differentiated thyroid cancer (DTC) risk variants based on GWAS.

Material and Methods: DNA was isolated from *peripheral* lymphocytes (Genomic Maxi AX, A&A BIOTECHNOLOGY). In the GWAS performed with SNP HumanOmni ExpressExome v 1.0 DNA Analysis BeadChip (Illumina Netherlands B.V.) 104 patients were included with histological conformed PTC diagnosed ≤18 years of age. The data from GWAS were compared to 375 controls derived from 1000 Genomes Project. Validation study with allelic discrimination technique was performed on independent sample set of 162 children/adolescents with DTC and 190 healthy controls in whom thyroid cancer was excluded by anamnesis and thyroid ultrasound.

Results: GWAS showed different genotype distribution ($p < 10^6$) for 172 SNPs. Next, 14 of these SNPs, located in the genes, were validated with allelic discrimination technique in the independent sample sets. Among 14 validated SNPs, rs2069987 located in SERPINA5 gene was significantly associated with DTC in children/adolescents diagnosed ≤21 years of age ($p = 0.025$, OR = 1.73).

Conclusion: These study showed, that rs2069987 located in SERPINA5 gene could be involved in childhood/adolescents PTC etiology.

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16.45–17.00

HABP2 GENE MUTATIONS DO NOT CAUSE FAMILIAL PAPILLARY THYROID CANCER IN A LARGE SERIES OF UNRELATED FAMILIES

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Background: Familial non-medullary thyroid cancer (NMTC) can occur either as an isolated hereditary tumor or as part of known hereditary syndromes. Recently, a c.1601G>A, p.G534E mutation in the HABP2 gene was reported to be the underlying genetic defect in a large kindred with familial papillary thyroid cancer (PTC). However this variant has also been reported to occur in about 4.7% of cases of the Thyroid Cancer Genome Atlas (TCGA) database and more recent studies do not confirm the important role of this genetic variant in some series of familial and sporadic PTCs.

Objectives: To investigate HABP2 as a potential susceptibility gene in 51 members of 22 unrelated families affected with familial PTC.

Methods: We screened for the G534E variant of HABP2 a total of 51 members of 22 families with NMTC using DNA isolated from peripheral blood, PCR and direct sequencing. Moreover, we studied HABP2 RNA expression in formalin fixed paraffin embedded tissues obtained from 1 case harboring the mutation, from 1 wild-type case and from some normal thyroid tissues.

Results: Three of the 22 NMTC families (13.6%) carried HABP2 mutation, for a total of 8 members. The genotyping of these three families showed that the variant does not segregate with PTC. Indeed, in each of the three families, at least one affected individual not carrying the HABP2 variant was identified. Moreover, the expression analyses showed that HABP2 can be detected in both wild type and HABP2 mutated cases, as well as in normal thyroid tissues.

Conclusion: In a large series of familial PTCs, a 13.6% prevalence for the G534E variant of HABP2 was found. The genotypic analysis performed in 3 mutated families indicated that this variant does not play a role in the predisposition to familial PTC.

17.00–17.15

GENETIC VARIATION IN NFKB LEADS TO INCREASED IL-1BETA PRODUCTION AND IS ASSOCIATED WITH REDUCED SENSITIVITY TO RADIOACTIVE IODINE IN NON-MEDULLARY THYROID CANCER

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Background: Proinflammatory cytokines *e.g.* TNFα, IL-1β and IL-6 have inhibitory effects on the sodium iodide symporter (NIS) expression. Advanced nonmedullary thyroid carcinomas (TC) often lose NIS expression and become resistant to radioactive iodine (RAI). We hypothesize that inflammation is critically involved in this process.

Aim: To assess the role of genetic variation in gene encoding for one of the main transcription factors that induce proinflammatory cytokines, *NFKB*, in TC susceptibility and outcome.

Objectives and Methods: A Romanian discovery cohort (159 TC patients, 259 controls) and a Dutch validation cohort (154 TC patients, 188 controls) were genotyped for two single nucleotide polymorphisms in the *NFKB* (*NFKB1* (rs4648068) and *NFKB1A* (rs2233406)). We assessed the influence of the genetical variants on production of proinflammatory cytokines. We correlated genetic and functional data with clinical characteristics including outcome and response to therapy including RAI.

Results: There was no statistically significant association between the genetic variants *NFKB1* rs4648068 and *NFKB1A* rs2233406 and the susceptibility to develop TC. Heterozygotes for *NFKB1A* rs2233406 variant showed significantly higher IL-1β production upon stimulation with LPS than either GG or AA homozygotes ($p < 0.001$ and $p = 0.02$ respectively). This genetic variant was associated in both cohorts with a significantly higher cumulative dose of RAI received (OR (95% CI) 3.03 (1.84–4.99), $p < 0.001$ in the Romanian cohort and OR (95% CI) 1.27 (1.05–1.98), $p = 0.03$) in the Dutch cohort) and with a higher number of RAI treatments in the Romanian cohort (OR (95% CI) 3.18 (1.85–5.45), $p < 0.001$). No associations with other clinical parameters such as TNM stageing and clinical remission rates were observed. The *NFKB1* rs4648068 genetic variant was not associated with clinical outcome.

Conclusion: Genetic variations in *NFKB* that lead to increased IL-1β production are associated with reduced sensitivity to RAI in TC. These results suggest that inflammatory tumor microenvironment could contribute to resistance to RAI therapy.

17.15–17.30

GERMLINE AND SOMATIC DICER1 MUTATIONS IN FAMILIAL PAPILLARY THYROID CARCINOMA

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The inheritable component of familial Papillary Thyroid Cancer (fPTC) was recently attributed to monogenic defects in a reduced number of genes including *DICER1*. *DICER1* codes for a ribonuclease of the RNaseIII family essential for the biogenesis of microRNAs.

Objective: To identify germline and/or somatic mutations of *DICER1* in familial pedigrees with PTC.

Patients and Methods: Four index patients with fPTC were investigated and segregation analyses performed in the rest of family members. Germline *DICER1* mutations were screened for in lymphocyte DNA of affected and non-affected individuals. Somatic *DICER1* mutations were studied from all available paraffin-embedded tissues when germline changes were identified, using PCR of mutational 'hot-spots', T-A cloning and Sanger sequencing. *BRAF* and *H/K/N-RAS* 'hot-spots' were also studied.

Results: A novel germline heterozygous *DICER1* 2-bp deletion (c.1440_1441delTG) was identified in the index patient of 1/4 families, her mother, and maternal aunt and grandfather. The mutation prematurely truncates the functional RNase IIIa and IIIb domains of the protein (p.Gly481Thrfs*25). The patient, an 11-year-old girl, was diagnosed with cystic nephroblastoma (CN) as an infant, multinodular goiter (MNG) at age 8 and follicular variant PTC at age 10 (fvPTC1); her mother presented MNG at 9 years of age and fvPTC at 11 (fvPTC2). The aunt was thyroidectomized for compressive MNG (MNG1) at age 30. The patient's father and maternal grandparents were healthy. Tissue samples showed three different heterozygous mutations in the RNase IIIb domain of *DICER1*: c.5438A>G (p.E1813G) in fvPTC1, c.5113G>A (p.E1705K) in fvPTC2 and CN, and c.5432T>A (p.I1811N) in MNG1. *BRAF* and *RAS* mutations were absent.

Conclusion: A novel monoallelic germline mutation in *DICER1* increases the susceptibility to papillary thyroid carcinoma. Familial segregation analyses suggest that additional tissue-specific mutations in the RNase IIIb domain, unreported to date in PTC, are necessary for the efficient neoplastic or hyperplastic transformation of the thyroid tissue.

17.30–17.45

A MOUSE MODEL OF SPORADIC PAPILLARY THYROID CANCER AND TUMOR PROGRESSION

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Mutant BRAF is oncogenic driver in the majority of sporadic papillary thyroid cancers (PTC). Most tumors show an indolent course presenting as microcarcinomas, although *BRAFV600E* also conveys progression to poorly differentiated and anaplastic phenotypes associated with inactivation of tumor suppressor genes, most notably *TRP53*. The time course of tumor development is probably very long, considering recent epidemiologic data suggesting that the primary oncogenic mutation occurs early in life.

Genetic mouse models recapitulating PTC may be instrumental to identify key steps of tumor progression and novel means of treatment. A confounding problem with current models, using thyroglobulin (Tg) or thyroid peroxidase as Cre drivers, is that $Braf^{V600E}$ is constitutively activated ($Braf^{CA/+}$) in nearly all thyroid cells. This causes hypothyroidism and supraphysiological TSH levels that co-stimulate cell proliferation, making it impossible to discern tumorigenic clones within a globally hyperplastic gland.

We investigated whether Cre activation occurring spontaneously in the absence of tamoxifen in mice with inducible $iTgCre;Braf^{CA/+}$ might be a suitable model of sporadic PTC. Theoretically Cre can be activated from onset of Tg expression in the embryonic thyroid. By recombining $TgCre;Braf^{CA/+}$ with *mTmG* reporter mice occasional Cre activation was evident in a minority of thyroid follicular cells postnatally. Small tumors surrounded by normal thyroid tissue developed after 3–6 months. Concurrent targeted inactivation of p53 ($trp53^{-/-}$) conferred metastatic disease but animals survived up to 18 months with the tumor phenotype still classic PTC, although with anaplastic foci. Notably, anaplastic conversion was also observed in sporadic tumors of $iTgCre;Braf^{CA/+};trp53^{+/-}$ mice.

In conclusion, stochastic Cre-mediated activation of $Braf^{V600E}$ and inactivation of p53 in few cells of the young mouse thyroid induce microtumors and delayed onset of tumor progression, thus recapitulating the developing process of sporadic PTC in humans.

17.45–18.00

TREATMENT OUTCOMES IN BRAIN METASTASIS FROM PAPILLARY THYROID CANCER

Seok-Mo Kim[1], *Soo Young Kim*[1], *Hyukjun Yun*[1], *Hyeung Kyoo Kim*[1], *Bup-Woo Kim*[1], *Yong Sang Lee*[1], *Hang-Seok Chang*[1], *Cheong Soo Park*[1]

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Background: Brain metastasis (BM) is a rare form of distant metastasis with papillary thyroid cancer (PTC). Patients with BM of PTC carry a poor prognosis. The aim of this study was to contribute to the understanding of this disease by analyzing patients with BM of PTC.

Methods: Between March 2003 and December 2013, the patient database at the Thyroid Cancer Center, Gangnam Severance Hospital of Korea was conducted to identify thyroid cancer patients treated. The medical records of 14 patients with BM were retrospectively reviewed, focusing on the following: patient characteristics, synchronous or previous distant metastasis, treatments including whole brain radiotherapy (WBRT), stereotactic radiosurgery (SRS) and surgery, and characteristics on radiologic findings, time interval between first diagnosis of primary thyroid cancer and BM and survival after BM.

Results: The mean age at initial diagnosis (ID) and BM were 50.9 ± 15.8 years and 61.3 ± 12.7 years. The mean duration between ID and BM was 124.7 ± 95.5 months. Patients were treated with varied combinations of surgery, SRS and WBRT except 4 patients who had refused treatment. The median overall survival (OS) time after BM diagnosis was 10 months (range 1–19). Patients receiving treatment (WBRT and/or surgery, SRS) had a significant longer median OS of 16.5 months in comparison to 3.5 months for those treated without treatment statistically ($p = 0.005$).

Conclusion: Patients who received aggressive treatment had a longer OS than those with only supportive care. Aggressive treatment such as surgery, SRS and WBRT should be considered in patients with BM.

Oral Session 6 (Clinical): Clinical Aspects of Autoimmunity

10.00–10.15

EVALUATION OF RESPONSE DURING INTRAVENOUS GLUCOCORTICOID (IVGC) TREATMENT FOR MODERATE-TO-SEVERE AND ACTIVE GRAVES' ORBITOPATHY (GO): IS IT A GUIDANCE TO DECIDE WHETHER TREATMENT SHOULD BE CONTINUED OR WITHDRAWN?

Luigi Bartalena[1], Giovanni Veronesi[1], Gerassimos Krassas[2], Wilmar Wiersinga[3], Claudio Marcocci[4], Mario Salvi[5], Chantal Daumerie[6], Claire Bournaud[7], Matthias Stahl[8], Lorenza Sassi[1], Claudio Azzolini[1], Kostas Boboridis[9], Maarten Mourits[10], Maarten Soeters[10], Baldeschi Lelio[11], Marco Nardi[12], Nicola Currò[13], Antonella Boschi[11], Martine Bernard[7], Georg von Arx[14], Petros Perros[15], George J. Kahaly[16]

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To evaluate response trend during 12-week ivGC treatment, we analyzed 159 patients of the EUGOGO randomized trial of different ivGC doses (2.25, 4.98, 7.47 g), comparing outcome at 6 weeks with outcomes at 12 (end of intervention) and 24 weeks, as overall ophthalmic assessment (Composite Index, CI), Clinical Activity Score (CAS) and quality of life (QoL).

None of 8 worsened-CI patients at 6 weeks improved later. Among 100 unchanged-CI patients at 6 weeks, 28% and 35% improved, while 7% and 13% worsened at 12 and 24 weeks, respectively. Of 51 improved-CI patients at 6 weeks, 65% and 53% remained in this class, while 2% and 12% worsened at 12 and 24 weeks, respectively. The probability ratio (PR) for worse/unchanged-CI patients at 6 weeks to improve later was 0.44 (95% confidence interval:0.26; 0.76; $p < 0.002$), indicating a 56% lower chance to improve than improved patients have to remain improved, with no treatment-dose differences. Among 69 unchanged-CAS patients at 6 weeks, 58% and 53% improved at 12 and 24 weeks, respectively. PR was 0.70 (0.47; 1.03; $p = 0.07$), i.e., a 30% lower chance to improve than improved patients have to remain improved; this chance was significantly lower with the lowest dose. Among unchanged-QoL patients at 6 weeks, 40% improved and 20% worsened at 12 weeks. Figures were similar at 24 weeks. The probability ratio was 0.39 (0.25; 0.61; $p < 0.0001$), increasing with cumulative dose.

Conclusion: Patients worsened at 6 weeks have no chance to improve as CI, although CAS can further improve. They can either be shifted to a second-line treatment to try and ameliorate CI, or continue ivGCs to inactivate GO and allow earlier rehabilitative surgery. Unchanged patients have a relevant chance to improve, although deterioration may occur. Under these circumstances, shared decision-making with patients concerning harms and benefits of continuing treatment is advised.

10.15–10.30

SIGHT-THREATENING GRAVES' ORBITOPATHY: EXPERIENCE OF THE MULTIDISCIPLINARY THYROID-EYE CONSULTATION OF THE UNIVERSITY HOSPITAL IN TOULOUSE, FRANCE

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Context: Sight-threatening Graves' orbitopathy occurs in 3 to 5% of patients with Graves' orbitopathy.

Objectives: Describe diagnosis and treatment modalities of patients with sight-threatening Graves' orbitopathy seen in a multidisciplinary thyroid-eye consultation dedicated to Graves' orbitopathy (GO) patients.

Patients and Methods: We include all patients with sight-threatening GO (dysthyroid optic neuropathy and corneal breakdown as defined in EUGOGO statement) seen in a multidisciplinary thyroid-eye consultation.

Results: Between 1995 and 2015, 726 patients were seen in the multidisciplinary thyroid-eye consultation in Toulouse. Among them, 31 (4%) patients (24 women, 7 men), aged 51 (46–58) years with Graves' disease (n = 29) or Hashimoto thyroiditis (n = 2), active smokers 18/31 (58%) presented 47 cases of sight-threatening GO (case = eye). Dysthyroid optic neuropathy (DON) occurred in 40 eyes, corneal breakdown in 15 eyes and both in 8 cases. At presentation, clinical features of DON were: reduced visual acuity (85%), visual fields defects (85%), optic disc swelling (42%), and reduced color vision (100%). At one-year, surgical orbital decompression (OD) was performed in 83% of DON cases. Only 7 eyes with DON were treated with pulses of intravenous glucocorticoids. For 10 patients, several therapeutic strategies (OD, punctal plug, amniotic membrane graft, tarsorrhaphy, botulinum toxin injection) were used to treat corneal breakdown.

Conclusion: We report 47 cases of sight-threatening Graves' orbitopathy in 31 patients. Orbital decompression was performed in the majority of patients with dysthyroid optic neuropathy, and several therapeutic strategies were necessary to treat corneal breakdown. The ophthalmic results are satisfactory in those sight-threatening GO patients seen in a multidisciplinary thyroid-eye consultation.

10.30–10.45

HIGHLY VARIABLE SENSITIVITY AND SPECIFICITY OF FOUR BINDING AND TWO BIO-ASSAYS FOR TSH-RECEPTOR ANTIBODIES

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Objective: TSH-receptor (TSHR) antibodies can be measured either with binding or cell-based bioassays. Sensitivity and specificity of four binding and two bio-assays were compared.

Methods: TSHR blocking (TBAb) -and stimulating (TSAb) antibodies (Ab) were measured with bioassays that utilize CHO cells expressing a chimeric TSHR and a cAMP response element-dependent luciferase on two luminometers (Tecan and Promega). Blocking activity was defined as percent inhibition of luciferase expression relative to induction with bTSH alone (cut-off <40% inhibition). TSAb activity was reported as percentage of specimen-to-reference ratio (SRR% <140). Thyroid-binding inhibitory immunoglobulins (TBII) were measured with Dynex (Teco Medical, <2 U/l), Kryptor (ThermoFisher, <1.8 IU/l), Cobas (Roche <1.75 IU/l) and Immulite 2000 XPi (Siemens, <0.55 IU/l).

Results: Sixty patients with Graves' disease (GD), 20 patients with Hashimoto's thyroiditis (HT) and 20 healthy controls (C) were included. C tested negative in all assays (specificity 100%) while all 60 hyperthyroid GD patients tested positive in the TSAb bioassay (sensitivity 100%). Among these 60 GD patients, 20 had low TSAb positivity (SRR 140–279), but were TBII-positive in only 18 (90%), 11 (55%), 9 (45%), and 7 (35%) using the Immulite, Cobas, Kryptor, and Dynex, respectively. In 20 moderate TSAb-positive (SRR 280–420) GD patients, TBII tested positive in 19 (95%), 16 (80%), 13 (65%),

and 14 (70%), respectively. The high (SRR >420) TSAb positive patients were all TBII positive. All 20 hypothyroid HT patients tested TBAb positive (sensitivity 100%) in the bioassay while they tested TBII-positive in 20 (100%), 18 (90%), 18, and 18 using the Kryptor, Immulite, Cobas and Dynex, respectively. There was a significant correlation of results obtained with the two luminometers for TSAb-positive ($r = 0.99$, $p < 0.001$), TBAb-positive ($r = 0.88$, $p < 0.001$), and C ($r = 0.86$, $p < 0.001$). None of the binding assays differentiated between TSAb and TBAb.

Conclusion: Sensitivity is highly variable between binding and bio-assays for TSHR-Abs.

10.45–11.00

HIGH CIRCULATING CXCL10 LEVELS IN NON-SEGMENTAL VITILIGO, IN PRESENCE OR ABSENCE OF AUTOIMMUNE THYROIDITIS

Silvia Martina Ferrari[1], *Poupak Fallahi*[1], *Giulia Santaguida*[2], *Camilla Virili*[2], *Ilaria Ruffilli*[1], *Francesca Ragusa*[1], *Marco Centanni*[2], *Alessandro Antonelli*[1]

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Objective: The important role of CXCL10 in the pathogenesis of non-segmental vitiligo (NSV) and autoimmune thyroid disorders (AITD) has been lately shown. Until now there are no data about CXCL10 (Th1 prototype) and CCL2 (Th2 prototype) circulating levels in NSV patients with/without thyroiditis (AT).

Methods: We measured serum CXCL10 and CCL2 concentrations respectively in: 50 consecutive NSV patients; 40 consecutive patients with NSV and AT (NSV+AT); 50 sex- and age-matched healthy controls without AT (control 1); 40 sex- and age-matched patients with AT without NSV (control 2).

Results: Significantly high serum CXCL10 levels were found in control 2 with respect to control 1 ($P = 0.001$; ANOVA). NSV patients have serum CXCL10 levels significantly higher than control 1, or control 2 ($P = 0.001$). NSV+AT patients have serum CXCL10 levels higher than control 1, or 2 ($P < 0.001$), and than NSV ($P = 0.01$).

Conclusion: We first demonstrate high serum CXCL10 in NSV patients especially in presence of AT and hypothyroidism. These findings suggest the importance of a common Th1 immune response in their immune-pathogenesis. Further studies are still needed to evaluate if serum CXCL10 might be used as a clinical marker of NSV and/or AT.

11.00–11.15

BREG IN HASHIMOTO THYROIDITIS ISOLATED OR ASSOCIATED TO FURTHER ORGAN-SPECIFIC AUTOIMMUNE DISEASES

Maria Giulia Santaguida[1], *Camilla Virili*[2], *Ilenia Gatto*[3], *Giorgio Mangino*[1], *Ilaria Stramazzo*[3], *Marco Centanni*[1]

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Objectives: Hashimoto thyroiditis (HT) is the most frequent autoimmune disorder, is characterized by a prevalent CD4+Th1 and -Th17 polarization and often occurs with concurrent autoimmune disorders. Recently, the role of B regulatory cells (Breg) gained attention in that they may contribute to the pathogenesis of autoimmune disorders by IL-10 production. The aim of our study was to measure Breg cells in HT isolated or associated with other non endocrine autoimmune disorders (NEAD).

Patients and Methods: Freshly PBMCs were assessed by FACS to characterize $CD4^{+}Th17$ and Breg lymphocytes specific phenotypes ($CD24^{hi}CD38^{hi}$) in 45 patients (40F/5M), 19 of whom with isolated HT and 26 with HT+NEAD; eighteen age- and sex-matched healthy donors (HD) represented the control group. PBMCs stimulation with CpG oligonucleotide as a functional assay of B cells was also performed in a total of 35 subjects.

Results: As expected, Th17 lymphocytes were higher in HT patients than in HD (2.6 ± 1.6 vs $1.6 \pm 0.9\%$; $p = 0.0337$), while in HT+NEAD patients were similar to that in HD and in isolated HT (p = ns). The mean percentage of unstimulated Breg lymphocytes in isolated HT and in HD were similar (2.4 ± 0.9 and vs. $2.0 \pm 0.7\%$; p = ns), while patients with HT+NEAD showed higher percentages ($3.9\% \pm 1.2$) than those with HT ($p = 0.0003$) and HD ($p < 0.0001$). Following CpG stimulation, we found higher percentage of Breg $IL\text{-}10^{+}$ cells in patients with isolated HT than in HD (3.9 ± 1.8 vs $2.4 \pm 1.1\%$; $p = 0.0303$). Surprisingly, Breg $IL10^{+}$cells percentage ($2.9\% \pm 1.8$) in patients with HT+NEAD was similar to patients with isolated HT and even to that in HD.

Conclusion: Patients with isolated HT showed a similar percentage of total Breg cells, while, after CpG stimulation, the fraction of functional Breg $IL10^{+}$cells was higher in HT patients than in healthy donors. In patients with HT+ NEAD, despite the increased percentage of Breg, the fraction of IL-10-producing regulatory B cells appeared to be reduced.

11.15–11.30

HIGH EFFECTIVENESS OF THERAPEUTIC PLASMA EXCHANGE IN REFRACTORY HYPERTHYROIDISM: ABOUT 17 CASES

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Introduction: Hyperthyroid patients who are unresponsive to anti-thyroid agents or those with severe adverse events during anti-thyroid therapy remain a challenging clinical problem. The goal of our study was to evaluate the clinical and biological efficiency of therapeutic plasma exchange (TPE) in hyperthyroid patients and to describe surgical and treatment-related complications.

Methods: We retrospectively reviewed 17 patients with refractory thyrotoxicosis: 10 patients with Graves' disease (GD), 6 patients with iodine-induced hyperthyroidism and 1 pregnant patient with familial non-autoimmune thyrotoxicosis.

Results: Before treatment, all patients had severe hyperthyroidism. For all patients anti-thyroid drugs were contraindicated or inefficient. Median T4 was 70 pmol/l and median T3 23.5 pmol/l. After one TPE, T4 decreased by 32.5% and T3 by 32%; after all TPEs, T4 decreased significantly by 48% ($p = 0.008$) and T3 by 52% ($p = 0.0003$). The majority of patient needed 3 TPE. 6 patients required more than 4 TPE (3 Grave's disease (GD), 1 iodine-induce thyrotoxicosis and 1 familial non auto-immune thyrotoxicosis). For patients with GD, median TRAK was 23.7 U/l, and median thyroid's volume 63 g. In iodine-induce thyrotoxicosis, the median thyroid's volume was 22 g. 10 of the 15 patients underwent total thyroidectomy without major complications. The anaesthetic conditions were safe. One patient was treated by radioactive iodine without side effects. For the 6 patients with amiodarone induced hyperthyroidism, biological and clinical improvement was obtained after iterative TPE, and one patient continue amiodarone, despite major thyrotoxicosis.

Conclusion: We described one of the largest series of therapeutic plasma exchange in refractory thyrotoxicosis patients. TPE is an effective, safe and rapid option in cases with severe hyperthyroidism and could be considered as a first line treatment in refractory hyperthyroid patients regardless of the cause of thyrotoxicosis, when anti-thyroid drug are contraindicated or inefficient.

11.30–11.45

QUANTIFICATION OF MOTILITY DYSFUNCTION IN GRAVES' ORBITOPATHY (GO) BY ASSESSING CHANGES IN EYE MUSCLE DUCTIONS

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Purpose: We calculated a total motility score (TMS) as a numerical index to quantitate the overall function of extraocular muscles (EOM) in patients with Graves' Orbitopathy (GO) and compared TMS with the motility changes assessed by the Gorman Score.

Patients: A group of 100 GO patients (Group 1) was compared with a control group of 100 age- and sex-matched volunteers (Group 2) to define the normal values of TMS. We then studied a group of 30 GO patients treated with intravenous methylprednisolone (ivMP) (Group 3) and calculate TMS as the outcome.

Methods: TMS was measured as the sum of the degrees of ductions in the four main gaze directions, assessed by a Foerster-Goldman arc. In Group 3 TMS was measured at baseline, 12 and 24 weeks after ivMP. We measured mean patients' TMN in relation to the classes of motility according with the Gorman Score.

Results: Mean TMS was greater in Group 2 than in Group 1 ($P < 0.0001$), suggesting EOM restriction in GO. Interestingly, in Group 1 we found a progressive reduction of the TMS in relation with the worsening of the Gorman score ($P < 0.0001$).

In the Group 3, mean TMS increased at 12 weeks compared to baseline and was stable at 24 weeks. TMS did not significantly improved in the 7/30 patients who required subsequent squint surgery.

Conclusion: The TMS correlates well with the Gorman Score for diplopia in the assessment of the eye motility in patients with GO. This score allows quantification of the severity of EOM dysfunction in GO and can be used to detect changes in eye motility in response to therapy.

11.45–12.00

GRAVES ORBITOPATHY AFFECTS VISUAL FUNCTION AND APPEARANCE IN DIFFERENT MANNERS

Danilo Villagelin[1], Roberto Bernado Dos Santos[1], João Hamilton Romaldini[1], Ana Paula Comarella[2], Natassia Bufalo[2], Karina Colombera Peres[2], Laura Ward[2]
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Introduction: Graves' ophthalmopathy (GO) is an inflammatory disease of the orbit. The orbit injury may vary from minor changes to visible deformities on the face, compromising the visual capacity and the aesthetics of the patient. These consequences affect both biological and emotional aspects of the patients' quality of life. We aimed to investigate how the use of current routine questionnaires can improve the quality of care and, mainly, identify patients who are in need of psychological support.

Methods: 140 consecutive patients with GD were investigated and compared according to the severity of their ophthalmopathy using the Clinical Activity Score, No SPECS and EUGOGO classifications, in addition to a quality of life questionnaire in Graves' ophthalmopathy (GO-QoL).

Results: The mean age was 48 years (range: 13 to 82 years); 115 were women (82%) and the time of diagnosis was 70 ± 68 months GO-QoL correlated with the values of CAS ($p < 0.0001$), NOSPECS ($p < 0.0001$) and EUGOGO ($p < 0.0001$). The mean QoL index was 91.4 ± 16.5 for visual function and 88.4 ± 20.5 for appearance. The index appearance showed an inverse correlation with asymmetry between the eyes ($p = 0.003$) and age ($p \leq 0.02$), while visual function scale was associated with the time of GO ($p \leq 0\ 02$). The visual function scale was associated with reading ($p < 0.0001$) and watching TV ($p < 0.0001$). Factors associated with decreased QoL were: find that people react unpleasantly to ophthalmopathy ($p < 0.0001$); looking to the patient due to ophthalmopathy ($p < 0.0001$).

Conclusion: GO significantly affects the quality of life and the use of questionnaires is important to identify these patients. The choice of Graves' disease treatment in these patients must take into consideration this evaluation.

Oral Session 7 (Basic): Medullary and Anaplastic Thyroid Cancer

10.00–10.15

GENETIC ANALYSIS OF ANAPLASTIC THYROID CANCER

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Background: Anaplastic thyroid cancer (ATC) is one of the most malignant tumor types and is associated with a very poor prognosis. No effective treatment is available. The genetic events leading to this aggressive tumor type is unclear. The aim of the present study was to investigate genetic aberrations in ATC.

Methods: 10 ATC and 3 PTC early-passage cell lines were investigated by SNP array analysis, RNA sequencing (RNA-seq) and whole exome sequencing (WES).

Results: ATC cell lines harbored large variations in copy number and multiple breakpoints with a median of 62 (range 12–165) per case. Frequent breaks in centromeric regions and loss of heterozygosity (LOH) involving whole chromosomes were common. Genes deleted in at least three cell lines comprised *NEGR1*, *PTPRD*, *AUTS2, MACROD2, CDKN2A,* and *FHIT.* Twenty-four fusion genes were identified and validated in 6 ATC and 2 PTC by RNA-seq; none of which was recurrent. 6 of these fusions were in-frame in ATC and 2 in PTC. Using supervised hierarchical clustering, 49 genes were differentially expressed between ATC and PTC. The most significantly enriched pathways in ATC were *KRAS* signaling, MAPK signaling and regulation of transcription. Recurrent point mutations in *BRAF, TP53, NRAS* and *PIK3CA* were identified by WES.

Conclusion: SNP array, RNA-seq and WES on ATC revealed the complexity of genetic aberrations harbored in ATC. Recurrent interstitial deletions and LOH was prominent. ATC harbored multiple out of frame fusions genes and recurrent point mutations in *BRAF, TP53, NRAS* and *PIK3CA.* Our findings provide a better understanding of the complex genetic events in ATC.

10.15–10.30

EVALUATION OF THE ANTINEOPLASTIC ACTIVITY OF VANDETANIB, AND LENVATINIB IN PRIMARY ANAPLASTIC THYROID CANCER CELLS, OBTAINED FROM FINE NEEDLE ASPIRATION

Silvia Martina Ferrari[1], Poupak Fallahi[1], Concettina La Motta[2], Gabriele Materazzi[3], David Galleri[3], Alessandro Antonelli[1]
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Objective: The possibility to test the sensitivity of 'primary anaplastic thyroid cancer (ATC) cell' (pATC) cultures from each subject to different drugs could permit an increase in the effectiveness of the treatment, avoiding the administration of inactive therapeutics. Here, we study the antineoplastic effect of vandetanib, and lenvatinib in primary cells from anaplastic thyroid cancer obtained both from biopsy (biop-pATC), such as from fine needle aspiration (FNA-pATC).

Methods: The antiproliferative effect was tested in ATC-cells obtained both from biopsy (biop-pATC), such as from fine needle aspiration (FNA-

pATC), in 5 patients. The concentrations of vandetanib, and lenvatinib used in the in vitro experiments were 1 nM, 30 nM, 100 nM, 300 nM, 1000 nM.

Results: The results of WST-1 assay in FNA-pATC, or biop-pATC, cells showed a significant reduction of proliferation with respect to the control with lenvatinib, and a slight level with vandetanib. Both compounds increased the percentage of apoptotic cells in FNA-pATCs, or biop-pATC, dose-dependently. There were no significant differences in sensitivity to vandetanib, and lenvatinib between the tested ATC cells from FNA, or biopsy.

Conclusion: In conclusion 1) primary cells obtained by FNA-ANA have a sensitivity to TKIs agents quite similar to that observed in primary cells from biopsy; 2) vandetanib, and lenvatinib are effective in reducing cell growth, increasing apoptosis in ATC; 3) the possibility to test sensitivity to different TKIs in each patient is able to increase the efficacy of treatments, avoiding the administration of ineffective drugs.

10.30–10.45

SYNERGISTIC ANTI-CANCER ACTIVITY OF THE HDAC INHIBITOR, N-HYDROXY-7-(2-NAPHTHYLTHIO) HEPTANOMIDE (HNHA) AND SORAFENIB ON ANAPLASTIC THYROID CANCER IN VITRO AND IN VIVO

Seok-Mo Kim[1], *Ki Cheong Park*[1], *Soo Young Kim*[1], *Hyeung Kyoo Kim*[1], *Bup-Woo Kim*[1], *Yong Sang Lee*[1], *Hang-Seok Chang*[1], *Cheong Soo Park*[1]
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Background: Anaplastic thyroid carcinoma (ATC) although rare is the most deadly form of thyroid cancer. The fatality rate for ATC is high-pitched, the survival rate at 1 year after diagnosis is <20%. Control of ATC is severely hard and widespread with unpredictability. We Previous proved that histone gene reviser and epigenetic changes role significant parts in papillary and anaplastic thyroid cancer tumorigenesis. Herein, the goal of this study was to investigate the anti-tumor activities of a histone deacetylase (HDAC) inhibitor, N-hydroxy-7-(2-naphthylthio) hepatonomide (HNHA) alone and in combination with sorafenib in anaplastic thyroid cancer cells *in vitro* and *in vivo* and to explore its effects on apoptotic cell death pathways.

Methods: Two ATC cell lines were exposed to sorafenib in the presence or absence of HNHA, and cell viability was determined by MTT assay. Effects of combined treatment on cell cycle and intracellular signaling pathways were assessed by flow cytometry and western blot analysis. The ATC cell lines xenograft model was used to examine the antitumor activity *in vivo*.

Results: Our data showed that HNHA and sorafenib synergistically decreased cell viability in ATC cells, and also significantly increased apoptotic cell death in these cells, as proved by the cleavage of caspase-3 and DNA fragmentation. MPT0E028 altered the global modifications of histone and nonhistone proteins regardless of the presence of sorafenib. HNHA induced histone H3 acetylation and reduced anti apoptotic factor in ATC. Thus, sorafenib well-know that was a multikinase inhibitor that targeted the vascular endothelial growth factor receptor family (VEGFR-2 and -3) and platelet-derived growth factor receptor family (PDGFR-beta and Kit), which play key roles in tumor progression and angiogenesis. Combination therapy with HNHA and sorafenib significantly decreased vessel density, and most significantly reduced tumor volume and increased survival in ATC xenografts.

Conclusion: These results propose that HNHA in combination with sorafenib has significant anti-cancer activity in preclinical models, potentially suggesting a new clinical approach for patients of advanced thyroid cancer type.

10.45–11.00

TREATMENT OUTCOMES OF SORAFENIB AND LENVATINIB FOR ADVANCED THYROID CANCERS AND ANAPLASTIC THYROID CANCERS

Hiroyuki Iwasaki[1], *Hiroyaka Nakayama*[2], *Nobuyasu Suganuma*[1], *Tatsuya Yoshida*[1], *Takashi Yamanaka*[1], *Shinsuke Hatori*[3], *Satoru Shimizu*[1]
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Introductions: The availability of Tyrosin-kinase inhibitor (TKI) that can stabilize progressive metastatic disease has changed the standard approach to treating patients with thyroid cancer. In Japan, sorafenib and lenvatinib were approved indication for radioiodine resistant metastatic thyroid cancer and lenvatinib was done for anaplastic thyroid cancer also.

Methods: Twentyfive patients (fourteen women, eleven men) met indication criteria, with a median age of 67.6 yr (range, 53–80 yr). Nineteen patients had papillary, two had follicular, and four had anaplastic thyroid carcinoma. All patients had evidence of progressive disease (PD) before start of therapy. They were treated with sorafenib or lenvatinib, and had both baseline and at least one follow-up scan for restaging purposes. All imaging data were collected, as well as the serum thyroglobulin (Tg) levels.

Results: We report that the response in target lesions was partial response (PR) in nine (36%), stable disease (SD) in one (4%) in 10 patients who were successfully continuing taking TKI drug. On the other hand, the progress of 15 patients who suffered from over Grade 3 adverse event was change the other TKI in four (16%), not evaluable (NE) in three (12%), and progressive disease (PD) in eight (32%). In detail of those PDs, two patients died from massive bleeding, one died from perforated digestive organ, and the other five died from progressive disease.

Discussions: All patients who stopped taking TKI drug and could not resume it turned out to be PD and died. To continue taking TKI drug is the most important for improving outcomes even in anaplastic cancers. Although judicious use for aged patients with progressive disease involved large vessel is necessary, it is not too late to start TKI drug in any stage of progressive thyroid cancer.

Table 1. Treatment summary of TKI drugs for thyroid cancer (for abstract time 10.45–11.00)

TKI drugs	Patients number	Ongoing patients		Cessation because of adverse event		
		PR	SD	second-line	NE	PD to death
Sorafenib	10	2	0	4	1	3
Lenvatinib	15	7	1	0	2	5

11.00–11.15

CALCITONIN RECEPTOR (CTR) EXPRESSION IN MEDULLARY THYROID CANCER (MTC) AND POSSIBLE CLINICAL IMPLICATIONS

Virginia Cappagli[1], *Catarina Soares Potes*[2], *Luciana Bueno Ferreira*[3], *Catarina Eloy*[3], *Cristina Romei*[1], *Rossella Elisei*[1], *Manuel Sobrinho-Simões*[3], *Peter J. Wookey*[4], *Paula Soares*[3]
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Objective: CTR expression has been described in several primary tumours and tumoral cell lines. The aim of this work was to study CTR expression in MTC and to correlate it with clinical-pathological and molecular features of the tumor.

Methods: We analyzed by immunoistochemestry 75 MTC samples. To recognize CTR, we used a monoclonal antibody (31/01-1H10); the expression was evaluate taking into account the extension and the intensity of the staining and semi-quantified with a score used for the correlation. Calcitonin (CT) expression was semiquantified in the same samples and correlated with CTR expression. Using real-time PCR (RT-PCR), CTR mRNA expression was quantified in 4 samples (both in normal and tumoral tissue) and in two MTC derived cell-lines (TT e MZ-CRC-1).

Results: CTR expression was found in 62/75 (82.7%) of the MTC, while 13/75 (17.3%) were completely negative. The staining pattern was cytoplasmatic in all the positive samples. The correlation between CTR and wild-type status for RET or RAS mutations was statistical significant ($p = 0.04$) as well as the absence of tumoral stroma ($p = 0.04$), the cytoplasmatic expression of PTEN ($p = 0.03$) and OPN expression ($p = 0.009$). We observed a positive association with female gender and smaller tumoral size although not attaining the statistical significance. With RT-PCR we observed a higher CTR expression in tumoral tissue compared to surrounding normal tissue and in both cell lines compared to tumoral tissue. CT expression showed a positive and significant association with CTR expression ($p = 0.001$).

Conclusion: The association of CTR expression with less aggressive tumoral features could suggest its role as a marker of good prognosis; moreover the association of CTR and OPN, marker of differentiation of parafollicular C-cells, suggests a role of CTR in normal thyroid C-cells. Further studies are necessary to evaluate CTR functions in normal and tumoral thyroid tissues.

11.15–11.30

THE MUTATION PROFILE OF MEDULLARY THYROID CARCINOMA CAN BE DIFFERENT IN PRIMARY AND METASTATIC TISSUES

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In this study, aimed to investigate genetic heterogeneity in MTC, we analyzed RET mutation profile in primary tumors (pMTC) and in the corresponding metastases (mets).

We looked for RET somatic mutations in exons 10, 11, 13–16 in pMTC and mets of 23 MTC sporadic cases.

Eighty-seven percent of patients showed the presence of a RET somatic mutation. Eighteen cases (78.3%) had a corresponding mutation profile in different types of tissue. In 5 cases (21.7%) a different RET mutation profile was observed in the primary tumor and in the metastases. In particular in one case a M918T was found in the pMTC but only in 3/5 mets; in another case, a 3 bp in frame deletion in exon 15 was found in 8 lymphnode mets but not in the primary tumor and in 4 additional lymphnode mets. Interestingly we found one patient with a double RET mutation in the pMTC (S891A+M918T) who showed the only presence of the M918T in a kidney metastases. A complex genetic heterogeneity was demonstrated in one MTC patient with a very severe disease. The primary tumor displayed a heterozygous 6 bp in frame deletion in exon 11 that was found also in 4/5 lymphnode metastases and in 1/2 liver metastatisis. In 1/5 lymphnode and in 1/2 liver metastasis the deletion was homozygous. The analysis of RET SNPs demonstrated that 1 RET allele was missing.

In conclusion our study shows that a) the prevalence of RET somatic alterations is elevated in metastatic MTC; b) about 22% of cases have a different RET mutation profile in the primary tumor and in the metastases.

This information should be taken into consideration in the planning of personalized target therapies and raise the question of whether RET mutations play a real driving role in the development of MTC.

11.30–11.45

EXPERIENCE FROM THE ADMINISTRATION OF TYROSINE KINASE INHIBITORS (TKI) IN PATIENTS WITH METASTATIC PROGRESSIVE MEDULLARY THYROID CARCINOMA (MTC) IN A REFERRAL CENTRE IN GREECE

Elli Anagnostou[1], *Katerina Saltiki*[1], *Vasiliki Vasiliou*[1], *Constantinos Tsigkos*[1], *Lamprini Papanastasiou*[1], *Maria Alevizaki*[1]

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Objective: Most MTC patients with persistent post-surgical hypercalcitoninemia usually have slow disease progression. Few patients present metastatic or rapidly progressive disease early at follow-up. Additional therapeutic interventions such as TKI administration may then be required.

Methods: Of 225 MTC patients followed-up in our department, 18 (8%) presented rapidly progressive metastatic disease (in ≤1 year, confirmed by imaging). We analyzed clinical, biochemical and therapeutic data before and after TKI treatment in these patients.

Results: We studied 13 men and 5 women (median age at diagnosis: 48 yrs, range 5–76, familial MTC 6/18). The age at TKI administration was 8–79 years. The stage at diagnosis was III in 4 patients and IV in 14. Fourteen patients underwent 2–6 surgeries. At diagnosis, tumor size was 0.3–7 cm, 16 patients had lymph node, capsule and/or soft tissue invasion and 2/16 (with MEN2) had distant metastases. During follow-up, new metastatic sites were detected in mediastinum (n = 13 patients), lungs (n = 8), liver (n = 13), bones (n = 10). 3 patients presented unusual metastatic sites. Disease progression (estimated by RECIST) occurred in 0.5–20 years from diagnosis (median 3 years). Calcitonin doubling time was 3–36 months (median 8). Additional therapeutic interventions were performed in 11 and different TKI treatments were administered in 7 patients. Sixteen patients received Vandetanib (full dose for their age). During Vandetanib treatment 7/16 presented stable disease (monitoring-interval 0.9–3 yrs), 5/16 partial response (monitoring-interval 0.5–3 years) 3/16 disease progression (in 0.2–2 years, one died) and one MEN2B patient with partial response for 2 years, died after rapid disease progression. Adverse events (AE) manifested mostly in the first 9 months of treatment (leading to dose reduction in three, interruption in one patient).

Conclusion: TKIs and especially Vandetanib are an effective treatment for disease stabilization in progressive metastatic MTC. AE are mild, occur at the initiation of treatment and are well tolerated.

11.45–12.00

THE ASSOCIATION BETWEEN TERT PROMOTER MUTATIONS AND MORTALITY IN PATIENTS WITH THYROID CANCER

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Objectives: To investigate the prognostic value of TERT promoter mutations for the outcome of mortality in patients with thyroid cancer.

Background: The clinical significance of recently identified TERT promoter mutations for the long-term prognosis of patients with thyroid cancer has not been established.

Methods: This was a retrospective study of 409 patients (339 female and 70 male) with a median age of 44 years (range, 16 to 81 years) and median follow-up time of 13 years (interquartile range, 11 to 16 years). Analyses of associations between mutational status and various clinicopathologic variables were performed.

Results: TERT promoter mutations were identified in 12.2% (50/409) of all thyroid cancer and 9.8% (32/327) of papillary thyroid cancer (PTC) patients. The presence of TERT promoter mutations was associated with factors such as increased age ($P < 0.001$), extrathyroidal invasion ($P = 0.01$), increased stage at diagnosis ($P < 0.001$), and dedifferentiated histologic type ($P = 0.001$). TERT promoter mutation was independently associated with poorer overall survival in all patients included (10-year survival rate, 56.0% vs 96.1% for wild-type; adjusted hazard ratio, 4.06; 95% CI, 2.02–8.15) and in patients with

PTC (71.9% vs 99.0%; 17.63; 3.82–81.45). In addition, presence of the BRAF T1799A mutation was not associated with differences of PTC patient survival.

Conclusion: Presence of TERT promoter mutations is independently associated with increased mortality in patients with thyroid cancer. The results suggest that inclusion of TERT promoter mutation analysis with conventional clinicopathologic evaluation can lead to better prognostication and management for individual patients.

Oral Session 8 (Clinical): Thyroid Cancer Therapeutics

15.00–15.15

LONG-TERM HEALTH-RELATED QUALITY OF LIFE, FATIGUE, AND ANXIETY AND DEPRESSION IN ADULT SURVIVORS OF PEDIATRIC DIFFERENTIATED THYROID CARCINOMA

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Introduction: Pediatric differentiated thyroid carcinoma (DTC) is an uncommon malignancy with an excellent survival. Little is known about long-term quality of life (QoL) of survivors. The aim of this study was to evaluate self-reported levels of health-related quality of life (HRQoL), fatigue, anxiety and depression in adult survivors of pediatric DTC, compared with controls.

Methods: Adult survivors of pediatric DTC, diagnosed between 1970 and 2013 at age ≤18 years and treated in The Netherlands were included. Exclusion criteria were a follow-up ≤5 years, diagnosis of a secondary malignancy or lack of command of the Dutch language. Controls were matched by age, gender and socio-economic status. All survivors and controls were asked to complete 3 questionnaires (SF-36 (HRQoL), MFI-20 (fatigue) and HADS (anxiety/depression)).

Results: Sixty-seven survivors and 56 controls were included. Median age of survivors at evaluation was 34.0 years (range 19–60). Most survivors (all Dutch) were female (86.6%), were married/in a relationship (64.2%), and were employed/active students (91.0%). Median follow-up after diagnosis was 17.6 years (range 5–45). On most subscales of the three QoL questionnaires, scores of survivors and controls did not differ significantly. Survivors suffered more than controls from physical problems ($P = 0.031$), role limitations due to physical problems ($P = 0.021$), and mental fatigue ($P = 0.016$). For 13/16 subscales, scores were more dispersed towards worse well being in survivors. Longer follow-up was correlated with higher vitality ($P = 0.044$). Other tumor-, treatment-, and follow-up characteristics were not associated with well being in survivors.

Discussion and Conclusion: This is the first study to evaluate long-term QoL in adult survivors of pediatric DTC. Overall, survivors of pediatric DTC do well with regard to HRQoL, fatigue, and anxiety and depression. However, a small subset of the survivors is more prone to develop worse QoL. Longer follow-up after diagnosis is associated with better QoL.

15.15–15.30

REAL-LIFE PRACTICES IN THE INITIAL TREATMENT OF DTCS IN ITALY: AN ANALYSIS OF PROSPECTIVE DATA COLLECTED BY THE ITALIAN THYROID CANCER OBSERVATORY

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Objectives: The American Thyroid Association (ATA) Guidelines published in January 2016 recommend more conservative, individualized strategies for the initial treatment of differentiated thyroid cancer (DTC). We characterized current practices in Italy when these guidelines were published.

Methods: The Italian Thyroid Cancer Observatory (ITCO) was established in 2013 to collect prospectively data on thyroid cancers consecutively diagnosed in member centers (currently 28, uniformly distributed across the nation). We analyzed data on the initial treatment of all pathologically confirmed DTC cases present in the database on 4 March 2016.

Results: 1913 patients (75% females; median age 38 years [10–96]) were enrolled in the study. Initial treatments included total thyroidectomy (97% of patients) and lobectomy (3%)**.** Forty percent of patients had central neck dis-

section; 10% also underwent lateral compartment dissection. Largest tumor diameters ranged from 1–93 mm (median 8.5 mm). Histological evaluation revealed papillary forms (n = 1816, 95%, including 98 poorly differentiated/aggressive variants), follicular forms (n = 64, 3%, 11 of which were invasive variants); Hürthle-cell and other rare variants (n = 43, 2%). Postoperative disease staging (TNM AJCC/UICC, 7th edition) revealed 1418 (74%) stage I tumors, 87 (4.5%) that were stage II, 314 (16%) stage III and 94 (5%) stage IV tumors. Radioiodine remnant ablation was performed in 885 (46%) cases: 321 (30%) of the 1086 classified by 2009 ATA guidelines as low-risk patients, 460 (65%) of the 706 intermediate-risk patients and 104 (86%) of the 121 who were high-risk.

Conclusion: Extensive surgical treatment is still widely used for DTC in Italy, regardless of disease stage and risk status. Use of radioiodine remnant ablation appeared to be more consistent with the 2009 ATA risk stratification. These data provide a useful baseline for future analyses of ITCO data aimed at assessing the impact of international guidelines on real-life clinical management of DTCs in Italy.

15.30–15.45

DIASTOLIC DYSFUNCTION IS COMMON IN LONG-TERM SURVIVORS OF PEDIATRIC DIFFERENTIATED THYROID CARCINOMA

Marielle Klein Hesselink[1], *Gianni Bocca*[2], *Yoran Hummel*[3], *Adrienne Brouwers*[4], *Johannes Burgerhof*[5], *Eveline van Dam*[6], *Jourik Gietema*[7], *Bas Havekes*[8], *Marry van den Heuvel-Eibrink*[9], *Eleonora Corssmit*[10], *Leontien Kremer*[11], *Romana Netea-Maier*[12], *Heleen van der Pal*[13], *Robin Peeters*[14], *John Plukker*[15], *Cecile Ronckers*[16], *Hanneke van Santen*[17], *Peter van der Meer*[3], *Thera Links*[1], *Wim Tissing*[18]

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Introduction: Long-term exogenous subclinical hyperthyroidism has been associated with diastolic dysfunction in survivors of adult-onset differentiated thyroid carcinoma (DTC). The presence of cardiac abnormalities in survivors of pediatric DTC is unknown. Our objectives were to study the prevalence of systolic and diastolic dysfunction in survivors of pediatric DTC in relation to the level of TSH suppression during follow-up, and to assess the association between diastolic dysfunction and plasma biomarkers.

Patients and Methods: In this prospective multicenter study, cardiac assessments were performed in 66 more than 5-year survivors of pediatric DTC (age at diagnosis ≤18 years) treated in the Netherlands between 1970 and 2009. Evaluation included echocardiography with measurements of systolic and diastolic functions, and assessment of plasma biomarkers (N-Terminal-pro brain natriuretic peptide, high-sensitive Troponin-T, galectin-3). Echocardiographic measurements were compared with retrospective data of 66 sex- and age matched unaffected Dutch controls. Multivariate linear regression analysis was performed to explore the association between diastolic function and TSH level.

Results: The survivors (86.4% women) had a median age at diagnosis of 15.9 (7.9–18.9) years. Median follow-up time was 16.7 (range 4.8 to 42.9) years. Left ventricular ejection fraction <50% was found in 1 survivor, and median longitudinal strain was –19.6% (range –24.2 to –17.6%). However, diastolic dysfunction was present in 14 asymptomatic survivors (21.2%). Overall, diastolic function of survivors was decreased compared to controls (e' mean 14.8 versus 16.0 cm/s, p = 0.013). TSH level during follow-up was not associated with diastolic function in survivors. Biomarkers were not associated with diastolic dysfunction.

Conclusion: While systolic function is unaffected, diastolic dysfunction is frequently observed in asymptomatic long-term survivors of pediatric DTC compared to unaffected age- and sex matched controls. TSH levels during follow-up are not associated with diastolic function. More research is needed to reveal the cause and clinical implications of our findings.

15.45–16.00

PREDICTORS OF VANDETANIB RESPONSE IN THE LOCALLY ADVANCED OR METASTATIC MEDULLARY THYROID CANCER: A SINGLE CENTER EXPERIENCE

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Objectives: Vandetanib (V) is a new option in the metastatic medullary thyroid cancer (MTC) treatment. In this study it was evaluated the presence of epidemiological, clinical and genetic predictors of V response in locally advanced or metastatic MTC patients (pts) treated for at least 12 months.

Methods: Forty-five locally advanced or metastatic MTC pts with progression or symptomatic disease, referred to our Center and already treated surgically and with other systemic therapies, were treated with V. During follow-up it was performed clinical examination, biochemical and morphological evaluation. All pts have taken V for at least 12 months.

Results: The genetic screening showed that 7/45 (15.6%) pts were inherited forms and 38/45 (84.4%) were sporadic cases. The evaluation of somatic mutations were performed in 36/38 (94.7%) pts and it was observed that 34/36 (94.4%) were carriers of a hereditary or somatic genetic mutation. However, the presence of RET mutations, it wasn't a predictor of response to treatment. All three pts with V804M RET mutation, that was demonstrated to confer resistance to V in 'in vitro' studies, responded to treatment. In our study group, the metastases site wasn't correlated with the outcome. In 36/45 (80%) pts it was observed the presence of adverse events (AE) with a correlation between AE, particularly cutaneous rash, and V response (p = 0.01). A long-term outcome showed a morphologic and biochemical response in 39/45 (86.7%) pts. The Progression Free-Survival was 85% after six months.

Conclusion: It was observed that the presence of AE was the only predictor of response to V treatment. Moreover, RET somatic mutations were very frequent in the metastatic MTC patients and also patients with 'resistant mutations' responded to treatment.

16.00–16.15

LONG-TERM SURGICAL RESULTS OF PATIENTS WITH LOCALLY ADVANCED PAPILLARY THYROID CANCER ONLY TO HAVE RECURRENT INFERIOR LARYNGEAL NERVE INVASION

Yuna Ogimi[1], *Takashi Uruno*[1], *Kenichi Matsuzu*[1], *Tetsuyo Maeda*[1], *Chie Masaki*[1], *Tadatoshi Osaku*[1], *Junko Akaishi*[1], *Kiyomi Y. Hames*[1], *Chisato Tomoda*[1], *Akifumi Suzuki*[1], *Keiko Ohkuwa*[1], *Hiroshi Shibuya*[1], *Wataru Kitagawa*[1], *Mitsuji Nagahama*[1], *Kiminori Sugino*[1], *Koichi Ito*[1]
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Objective: Most patients with differentiated papillary thyroid cancer (PTC) have excellent treatment outcomes. However, some patients have extrathyroidal invasion to adjacent tissues such as the trachea, larynx, and esophagus, which results in a poor prognosis. In contrast, patients with PTC with only invasion to a recurrent inferior laryngeal nerve (RN) may have a better prognosis than the above patients. In the present study, long-term outcomes of PTC patients with RN invasion alone were evaluated.

Methods: Between 1986 and 1995, 1820 patients with PTC underwent curative surgery, excluding patients who had distant metastases preoperatively and those who underwent extensive surgery of the trachea, larynx, and esophagus. These patients were classified into two groups: group A (n = 86), who underwent RN resection due to cancer invasion; and group B (n = 1734), with limited disease within the thyroid or minimal extrathyroidal extension. Cause-specific survival (CSS), local recurrence-free survival (LFS), and distant metastasis-free survival (DFS) were calculated.

Results: Median follow-up periods of group A and B were 209 and 219 months, respectively. In patients ≥45 years old, group A patients (n = 69) had significantly poorer CSS ($p < 0.0001$), LFS ($p < 0.0001$) and DFS ($p < 0.0001$) than group B (n = 954). In patients <45 years old, there were no significant differences in CSS, LFS and DFS between groups A (n = 17) and B (n = 780). On multivariate analysis, tumor size >40 mm ($p = 0.001$), palpable lymph node metastases ($p = 0.026$), and RN invasion ($p < 0.0001$) were correlated to poor CSS in patients ≥45 years old, while no significant prognostic factor was found in patients age <45 years old.

Conclusion: Younger (<45 years) patients with PTC with RN invasion alone had a favorable prognosis, while older patients had a poor prognosis, even with curative surgery.

Table 1. Risk factor analysis for cause specific death (multivariate) (for abstract time 16.00–16.15)

Age <45 years old	Odds ratio	95% Cl	P value
Tumor size >40 mm	<0.0001	0.027–2.423	0.1558
Preoperative LN metastasis(+)	13.76	0.544–347.8	0.0972
RN invasion(+)	<0.0001	0.685–101.9	0.7858
Age ≥45 years older	**Odds ratio**	**95% Cl**	**P value**
Tumor size >40 mm	3.64	1.736–7.067	0.0011
Preoperative LN metastasis(+)	2.53	1.124–5.23	0.0264
RN invasion(+)	7.03	3.447–13.76	<0.0001

16.15–16.30

INHIBITION OF ERK DIMERIZATION BLOCKS THYROID TUMOR PROGRESSION

Miguel Zaballos[1], *Adrián Acuña-Ruiz*[1], *Garcilaso Riesco-Eizaguirre*[2], *Piero Crespo*[3], *Pilar Santisteban*[1]
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In the last years most studies addressing thyroid tumorigenesis have focused their efforts in the inhibition of key kinases of the most frequently mutated signaling pathways, with special attention to the MAPK (Mitogen-activated protein kinase) pathway. Despite initial good results complete inhibition of those essential signaling cascades has been largely ineffective, mainly due to the generation of drug-resistance in the tumors and to a high toxicity in the whole organism. In this work we propose a new way of approaching to the thyroid tumorigenesis therapy by partially inhibiting ERK (Extracellular signal-regulated kinase) signaling. To this end we studied the effects of an inhibitor of ERK dimerization (DEL22379), a drug that specifically impairs ERK signals arising from the cytoplasm, in a panel of thyroid cell lines derived from tumors of different origin and mutational status. Furthermore we analyzed the effect of impairing ERK dimerization *in vivo* in an orthotopic mouse model of thyroid cancer. We found that DEL22379 effectively inhibits ERK dimerization without altering its phosphorylation, preventing the activation of ERK cytoplasmic effectors. DEL22379 decreases cell viability, migration and expression of EMT (Epithelial-mesenchymal transition) markers in a cell type and dose-dependent manner and reduces growth rate of a human thyroid tumor-derived cell line in an orthotopic mouse model. Together these results show that impairing local signals emerging from ERK rather than the complete ablation of the pathway may represent a valid option to hamper thyroid tumorigenesis.

16.30–16.45

MULTIKINASE INHIBITOR SP EFFECTS ON ALTERED PROLIFERATIVE PATHWAYS IN THYROID CANCER STEM-LIKE CELLS

Elisa Stellaria Grassi[1], *Valentina Cirello*[2], *Carla Colombo*[3], *Valeria Vezzoli*[1], *Leonardo Vicentini*[4], *Luca Persani*[5], *Laura Fugazzola*[6]
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The crucial role of cancer stem-like cells (CSCs) in relapse and metastatization has recently emerged. In thyroid tumors, CSCs are involved in the treatment resistance of aggressive and fatal cases of undifferentiated thyroid cancer. CSCs are able to form three-dimensional thyrospheres in vitro, and allows to test the response of CSCs to novel therapeutic compounds. In this study, we tested the effects of a multikinase inhibitor that we recently characterized, SP, on the spheres derived from differentiated and undifferentiated thyroid tumors (TS) and from paired normal tissues (NS) obtained after surgery. Both TS and NS were treated for 96 hours with SP and effects on growth, morphology and signaling pathways were analyzed by different methods. Our results showed that SP has significant growth inhibitory effects only on TS. After SP treatment, TS are smaller and tend to disaggregate, indicating the loss of CSCs characteristics. Moreover, TS showed significant alterations in two main regulators of cell proliferation and stem-like phenotype, b-catenin and p53. SP treatment was able to significantly reduce the levels of b-catenin and had slight but consistent effects on p53. In addition, our findings revealed for the first time that there is a significant increase in ROCK activity in TS with respect to either NS or tumor and normal tissues. The treatment with SP is able to restore the normal levels of ROCK activity. These data are in agreement with our previous findings in thyroid cancer tissues. Moreover the enrichment in CSCs revealed that SP is effective also against differentiated thyroid cancers, especially on that subset of cells responsible for metastasization and therapy resistance. Taken together these data show that SP has the potential to revert the alterations present in stem-like cells that are responsible for thyroid cancer aggressiveness.

16.45–17.00

GLUCOSE-COATED SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES PREPARED BY METAL VAPOUR SYNTHESIS ARE ELECTIVELY INTERNALIZED IN THYROID TUMORS LINES EXPRESSING GLUT1 TRANSPORTER

Daniele Barbaro[1], *Lorenzo Di Bari*[2], *Valentina Gandin*[3], *Claudio Evangelisti*[4], *Giovanni Vitulli*[5], *Elenora Schiavi*[5], *Cristina Marzano*[6], *Anna M. Ferretti*[4], *Piero Salvadori*[5]
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Background and Objectives: Iron oxide nanoparticles (IONP) can have a variety of biomedical applications due to their properties of visualization by Magnetic Resonance Imaging and heating with radio frequency alternating magnetic field. To take advantage of the high avidity of tumor cells for glucose, we report the development of very small glucose-coated IONP (glc-IONP) by employing an innovative technique, named Metal Vapor Synthesis (MVS). Moreover, we tested the internalization of our glc-IONP on two thyroid tumor lines.

Methods: Glc-IONP were prepared with MVS, which is a high temperature co-condensation of iron and acetone in a static reactor, then the solution of iron/acetone is added to an acqueuos solution of D-glucose kept a 0 degree, the dispersion is warmed up at room temperature. Glc-IONP were tested on lines B-CPAP and 8505C. On both lines we investigated the internalization of glc-IONP at the concentration of 0.1 mg/ml of glc-IONP at different times (1, 3, 6, 24 h.). The expression of GLUT1 transporter was evaluated by Western Blot technique. To evaluate the role of GLUT-1 transporter, we also investigated the effect of the addition of a polyclonal anti-GLUT1 antibody. The iron value was assessed by atomic absorption spectrometer, reported in mcg/l, and expressed for mg of protein.

Results: Our IONP prepared with MVS were very small and homogeneously distributed in a narrow range (1.75–3.75 nm) and were superparamagnetic. Glc-IONP were internalized by both lines with a time-dependent kinetic of saturation. After pretreatment with anti-GLUT1, a reduction cellular accumulation of glc-IONP was observed (47% in BCPAP and 32% in 8505C).

Conclusion: MVS allowed us to prepare small, homogeneous, superparamagnetic glc-IONP which are electively internalized by thyroid tumor lines and the internalization appear to be, at least in part, GLUT1 transporter dependent. Our glc-IONP appear to have many requisites for in vivo use.

Oral Session 9 (Basic): T3 Signalling in Brain and Periphery

15.00–15.15

IMPAIRED MATERNAL THYROID HORMONE RECEPTOR A1 SIGNALING PROGRAMS OFFSPRING METABOLISM

Rebecca Oelkrug[1], *Milica Vujovic*[2], *Lisbeth Harder*[1], *Beate Herrmann*[1], *Sogol Gachkar*[1], *Jens Mittag*[1]
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Maternal-fetal programming occurs during pregnancy and lactation and leads to epigenetic changes in the physical structure of DNA with life-long effects on the offspring. Thereby, maternal factors, such as nutrients and hormones, have considerable impact on the development of embryos and can, already in the prenatal stage, increase the risk for the development of metabolic and cardiovascular disorders.

We here show that impaired maternal thyroid hormone receptor α1 signaling induces changes in the fetal programming of the offspring metabolic set point. Using female mice harboring a mutation in thyroid hormone receptor α1 (TRα1+m mice) as dams, we observed that their male offspring displayed a normal early postnatal development but showed a reduction in body weight later during adulthood. Furthermore, animals showed a faster glucose clearance and improved insulin sensitivity. To test whether the cause of this beneficial metabolic phenotype could be maternal hypermetabolism due to overactivated brown adipose tissue of TRα1+m mice, we pharmacologically mimicked a situation of elevated maternal thermogenesis and hypermetabolism. Therefore, we treated female wild type mice with prazosin (50 µg/ml oral), a α-adrenergic antagonist that is commonly used for the treatment of hypertension, during pregnancy and lactation. Prazosin treatment enforced heat loss over the tail surface by decreasing the sensitivity of tail arteries to contractile stimuli, thereby stimulating facultative thermogenesis and metabolism. Interestingly, male offspring of prazosin-treated dams showed a similar reduction in body weight as male offspring of TRα1+m dams. However, their glucose clearance was remarkably reduced as animals were suffering from an insulin resistance.

Taken together, although the underlying mechanism of fetal programming by maternal thyroid hormone signaling needs further investigation, our results clearly demonstrate the complexity and particular importance of thyroid hormone for fetal programming of metabolic diseases.

15.15–15.30

MIXTURES OF XENOBIOTICS FOUND IN HUMAN AMNIOTIC FLUID MODIFY EMBRYONIC THYROID HORMONE SIGNALLING AND BRAIN DEVELOPMENT

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Humans are currently exposed to myriads of chemicals, from early gestation onwards. Whilst data exists for such individual chemicals, few if any studies have focused on effects of a mixture of these compounds. Here, we studied the potential thyroid disrupting effect of 15 chemicals commonly found in pregnant women in the USA. Using a previously validated *in vivo Xenopus* assay for identifying potential Thyroid hormone (TH) disrupters, we confirmed that the 9 out of the 15 individual chemicals exerted an inhibiting or activating effect on the Thyroid hormone, T_3, signalling pathway.

Application of the mixture of the 15 chemicals together, at concentrations reported in amniotic fluid, we observed a significant and dose-dependent potentialisation of T_3 dependent transcription. RT-qPCR analysis on the dissected brain tissue from the mixture-exposed *Xenopus* embryos revealed modifications of TH related genes including *thrb*, *klf9* and especially the deiodinases (*dio1, 2, 3*). Using a locomotor tracking system we observed that tadpoles exposed to increasing concentrations displayed severely and significantly reduced mobility. In order to study the mixture impact on neurogenesis we further subjected the amniotic mixture exposed embryonic brains to immuno-histochemistry. We observed increased proliferation within the developing brain and modification of cell fate (neurons, neuroblasts) when exposed to the mixture. Taken together these results show that a mixture of chemicals found in human at legal levels affect T_3 signalling at a critical moment for a proper brain development.

15.30–15.45

EPITHELIAL BMP-SMAD1/5 SIGNALING AND ENDOTHELIAL CELLS ARE REQUIRED FOR THYROID FOLLICLE DEVELOPMENT

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Objectives: Thyroid follicles, the functional units of the thyroid gland, are delineated by a monolayer of thyrocytes resting on a continuous basement membrane. Here, we wish to decipher the developmental mechanisms whereby thyroid progenitors organize in tridimensional follicles.

Methods: We inactivated Smad1 and Smad5 in developing mouse thyroid using the Pax8-Cre deleter strain and characterized thyroid development. To manipulate thyroid development, we used thyroid explants in culture.

Results: Thyroid-specific double Smad1 and Smad5 knockout mice ($Smad1/5^{dKO}$) displayed growth retardation, hypothyroidism and defective follicular architecture. In $Smad1/5^{dKO}$ embryonic thyroids, epithelial cells remained associated in large clusters and formed small follicles. Although similar follicular defects are found in $Vegfa^{KO}$ thyroids, that display reduced angiogenesis, $Smad1/5^{dKO}$ thyroids had normal endothelial cell density yet impaired endothelial differentiation. Interestingly, both $Vegfa^{KO}$ and $Smad1/5^{dKO}$ thyroids displayed impaired basement membrane assembly. Furthemore, conditioned medium (CM) from embryonic endothelial progenitor cells (eEPC) rescued the folliculogenic defects of both $Smad1/5^{dKO}$ and $Vegfa^{KO}$ thyroids. Laminin $\alpha1\beta1\gamma1$, abundantly released by eEPC into CM, was critically required for folliculogenesis.

Conclusion: Our work thus reveal that assembly of the epithelial basement membrane is critical for folliculogenesis and is controlled by endothelial cell invasion and by BMP-Smad signaling in thyrocytes.

15.45–16.00

CENTRAL HYPOTHYROIDISM AND BIALLELIC DEFECT NEAR THE D/ERY MOTIF OF THE TRHR GENE

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The TRH receptor (TRHR) is a G-protein coupled receptor activated by hypothalamic TRH. In thyrotropes, TRH-TRHR signalling controls synthesis, secretion and bioactivity of TSH. Human *TRHR* defects are extremely rare, and only three cases are known with central hypothyroidism and short stature as variable presenting feature.

Objective: Phenotypical characterization of a family with suspected central hypothyroidism and investigation of the molecular mechanism underlying the disorder.

Patients and Methods: Mutation screening of the *TRH*, *TRHR* and *TSHB* genes in seven individuals of a consanguineous pedigree. Determination of membrane expression, ligand affinity and transactivation properties of a TRHR mutant using ELISA, ligand ($[^3H]$MeTRH) binding and luciferase reporter assays, respectively.

Results: A homozygous missense mutation in *TRHR* was identified (c.392T>C; p.I131T) in an 8 year old boy with mild central hypothyroidism (FT4: 0.74 ng/dl, TSH: 2.61 mIU/ml) and overweight, but normal stature. TRH test showed borderline-low TSH response, indicating pituitary hypothyroidism. The parents, three siblings and grandmother of the index patient were heterozygotes for the mutation, and showed isolated TSH elevation (4.6–8 mIU/l). The mutation localises in the 2nd intracellular loop of the TRHR, adjacent to the D/ERY motif involved in G protein activation. The I131T mutant does not interfere with the receptor trafficking to the membrane, but decreases its affinity to the TRH ligand (wild type = 9.1 ± 0.4 nM *vs.* mutant = 3.1 ± 0.3 nM) and impairs transactivation of an AP1-containing promoter by TRH (wild type EC_{50} = 2.8 ± 0.9 nM *vs.* mutant EC_{50} = 20.4 ± 0.8 nM).

Conclusion: A novel defect in *TRHR* causes central hypothyroidism in the homozygous state but leads to hyperthyrotropinemia in heterozygotes, suggesting compensatory elevation of TSH with reduced biopotency. The mutation impairs TRH-TRHR signalling by decreasing the affinity of receptor for TRH and suggests incomplete activation of G-proteins by dysfunction of the D/ERY motif.

16.00–16.15

CENTRAL ROLE FOR THYROID HORMONE SIGNALING IN PERIPHERAL METABOLIC PLASTICITY

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The hypothalamus is a key central integrator of homeostasis and the upstream regulator of the pituitary-thyroid axis. Sympathetic nervous system (SNS) afferents from the hypothalamus innervate brown adipose tissue (BAT). Thyroid hormones (TH) modulate total energy balance both centrally, at the hypothalamic level, and peripherally through the BAT, stimulating thermogenesis. In both cases, local availability of T3 is determined by deiodinase 2 (D2).

We questioned the role of D2 in central regulation of BAT thermogenesis by comparing two mouse strains: C57BL/6J (BL6) and WSB/EiJ (WSB). These strains differ by their longevity, resistance to high fat diet (HFD) and circulating T4 levels. BL6 mice display average T4 levels and are sensitive to HFD, whereas the longer lived WSB have lower circulating T4 and a lean phenotype even when fed HFD.

By measuring BAT temperature and carrying out calorimetric recordings, we found that WSB mice burn more energy despite their lower circulating TH levels. We analysed whether this was related to D2 in the hypothalamus. ISH showed that WSB mice have higher levels of D2 mRNA in the mediobasal-hypothalamus. We next tested the hypothesis that a privileged link exists between hypothalamic D2 and BAT thermogenesis in WSB. To this end we induced central blockade of D2 activity using intra-cerebro-ventricular (icv) injections of rT3. Measurement of BAT temperature showed that rT3 injections significantly decrease BAT thermogenic activity specifically in WSB mice, thereby promoting negative energy balance in this strain.

Our results show central D2 to be a major player in controlling peripheral metabolism, directly implicated in maintaining the lean phenotype of WSB mice through increased thermogenesis, despite low circulating TH levels. This strain could prove useful for identifying new thyroid-related targets to promote healthy metabolic homeostasis.

16.15–16.30

THYROID HORMONE T3 MAY PROTECT FROM FASTING INDUCED SKELETAL MUSCLE ATROPHY

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Skeletal muscle atrophy may ensue from several pathological conditions including prolonged muscle disuse, cancer cachexia, anorexia etc. All atrophic conditions feature an imbalance between protein synthesys and degradation. Skeletal muscle represents a major target for thyroid hormones (THs) action. Hence, adequate intracellular T3 concentrations warrant healthy muscle homeostasis, since both hyper- and hypothyroidism lead to muscle weakness, hypotrophy and atrophy. However, whether T3 may play a role to protect muscle from progressive wasting is, as yet, unknown.

Based on our previous unpublished observations on the positive action of T3 against starvation induced myotubes atrophy, aim of the study was to analyze the effects of T3 treatment on muscle atrophy in vivo and to investigate the T3-related intracellular signaling involved.

To this end adult male BALB/c mice were used as an in vivo model. Muscle atrophy was induced by food-deprivation for 48 hours in half of mice (starved). At the same time, starved and fed mice were treated with daily, intraperitoneal injections of T3 [50 and 100 mcg/kg BW] or vehicle [NaCl 0.95%] as a control. Free T3 serum levels were measured to exclude a iatrogenic hyperthyroidism. Starvation led to a 20% drop of body weight, independently from T3 treatment. Similarly, when muscle mass was measured at the level of Tibialis anterior (TA), it has been observed a significant weight reduction of TA (15%) in untreated starved mice as compared to untreated fed mice. However, in mice treated with 100 mcg/kg BW T3 no such a significant muscle mass weight reduction was observed (8%). Morphometric analyses confirmed that the higher T3 dose counteracts the fasting induced reduction in myofibers size. A Real Time analysis of Deiodinase 2 revealed a strong reduction (50%) of its expression in the fasted animals, regardless the hormone treatment.

In summary, our data indicate that while fasting induced a reduction of total weight, muscle mass and myofiber size in untreated mice, in T3-treated mice muscle mass and myofibers size were comparable to fed controls. So far, in this model, the overall effect of T3 treatment is a protective one on fasting-induced muscle atrophy.

16.30–16.45

THE GENOMIC RESPONSE OF THE MOUSE THYROID TO IODINE OVERLOAD, AND THE ROLE OF THE NRF2 ANTIOXIDANT SYSTEM

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Objectives: Despite mice being workhorses of mammalian genetics, the tiny size of their thyroid has precluded generalized use in studies of iodine effects on the thyroid, which have been traditionally performed in rats. There is also paucity of in vivo gene expression analyses of the thyroid's response to iodine using next-generation sequencing technologies. Employing a custom extraction protocol optimized for miniscule samples, we characterized the genomic response of the mouse thyroid gland to an iodine challenge in wild-type (WT) mice. In parallel, by testing mice lacking the transcription factor Nrf2, we investigated the role of this major antioxidant response system in thyroidal gene expression and in response to iodine.

Methods: Male 3 months-old male C57Bl6J WT or Nrf2 knockout (KO) mice were exposed to 0.05% sodium iodide in their water for 7 days. Thyroid gland was excised and used for RNA preparation. RNA-seq was performed by Exiqon. The fold-change cutoff was set to 1.5. Pathway analysis of the differentially expressed genes (DEG) was performed using the Ingenuity Pathway Analysis (IPA) software.

Results: Nearly 1700 genes were differentially expressed in response to iodine; most were up-regulated. Highly enriched pathways include those related to fibrosis; integrin signaling; leukocyte extravasation; inflammation (IL-1, IL-6, IL-8) and the acute phase response; production of reactive oxygen species and nitric oxide; and the Nrf2-mediated antioxidant stress response.

Nearly 500 genes were differentially expressed between WT and Nrf2-KO mice. Highly enriched pathways were related to glutathione-mediated detoxification, xenobiotic metabolism, and the Nrf2 antioxidant response; all were down-regulated in the KO. Nfr2 also impacted the expression of thyroid-specific genes including the sodium-iodide symporter and thyroglobuline.

Conclusion: These data provide a rich foundation for understanding the adaptation mechanisms to iodine challenge such as the escape from the Wolff-Chaikoff effect, as well as the role of oxidative stress in thyroid physiology.

16.45–17.00

3-IODOTHYRONAMINE AND TRACE AMINE-ASSOCIATED RECEPTOR 1 ARE INVOLVED IN THE EXPRESSION OF LONG-TERM POTENTIATION IN MOUSE ENTORHINAL CORTEX

Alice Accorroni[1], *Chiara Criscuolo*[2], *Martina Sabatini*[3], *Riccardo Donzelli*[3], *Alessandro Saba*[4], *Nicola Origlia*[2], *Riccardo Zucchi*[4]
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3-iodothyronamine (T1AM), a derivative of thyroid hormones, has been considered as a memory enhancer as it improves learning and memory in mice. We investigated the effects of T1AM and its putative receptor trace amine-associated receptor 1 (TAAR1) on long-term potentiation (LTP), one of the electrophysiological correlates of memory. LTP is inhibited by beta-Amyloid oligomers (Aβ), and in the early stage of AD in the entorhinal cortex (EC). In this study, we employed EC slices taken from wild type (WT) mice exposed to Aβ, from a transgenic model of AD (hAPP-J20 mouse) and from TAAR1 KO mice.

Field potentials were evoked in EC layer II after stimulation of the same layer and LTP was elicited by high frequency stimulation (HFS), consisting of three trains of 100 pulses at 100 Hz. T1AM (5 μM) and/or Aβ (200 nM) and/or EPPTB (5 and 10 nM), a selective antagonist of TAAR1, were administered for 10 minutes, starting 5 minutes before HFS.

In WT EC, T1AM did not affect either basal synaptic transmission or LTP. Exposure to Aβ inhibited LTP, but T1AM perfusion restored it (98 ± 6% vs 123 ± 10%, $P < 0.05$). In EC from hAPP-J20 mice, LTP could not be elicited, but it was rescued by T1AM (90 ± 7% vs 120 ± 9%, $P < 0.05$). In WT EC slices, EPPTB inhibited LTP, and abolished the protective effect of T1AM vs Aβ toxicity. TAAR1 KO EC slices showed an altered response to HFS, with inhibited LTP when compared to control slices.

Our results suggest that T1AM and TAAR1 are involved in the expression of LTP in the EC. Indeed, TAAR1 affects basal LTP expression, while T1AM plays a neuroprotective effect, rescuing Aβ-induced neuronal dysfunction, possibly through the interaction with TAAR1. Further insight into the role of T1AM and TAAR1 might open new perspectives in the understanding of LTP in physiological and pathological conditions.

Oral Session 10: Young Investigators Session / Clinical + Translational

08.30–08.45

5 YEARS FOLLOW UP OF THYROGLOBULIN (TG), THYROGLOBULIN ANTIBODIES (TGAB) AND NECK ULTRASOUND (NUS) IN PATIENTS WITH PAPILLARY THYROID MICROCARCINOMA (MPTC) TREATED WITH TOTAL THYROIDECTOMY BUT NOT ABLATED WITH 131I

Antonio Matrone[1], *Alessio Faranda*[2], *Eleonora Molinaro*[2], *Laura Agate*[2], *David Viola*[2], *Laura Valerio*[2], *Carlotta Giani*[2], *Liborio Torregrossa*[3], *Paolo Piaggi*[4], *Paolo Vitti*[2], *Rossella Elisei*[2]
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Background: Serum thyroglobulin (Tg) and Thyroglobulin Antibodies (TgAb) assays are considered as the cornerstone for the post-operative management of patients with differentiated thyroid cancer (DTC) after the initial treatment. Less is known about the significance of this parameters in pts who do not perform radioiodine ablation (RRA) as in case of mPTC.

Materials and Methods: We retrospectively evaluated epidemiological, clinical and pathological data of 293 consecutive patients with mPTC, surgically treated at our Department (2005–2012). We included [T1a] pts that had at least three determinations of serum Tg, TgAb and nUS. The aim of our study was to clarify the significance of the Tg and TgAb trends during the follow-up.

Results: We divided our pts in group A (238 pts) (TgAb <20 mU/l) and group B (55 pts) (TgAb >20 mU/l) and we analyzed the Tg and TgAb course during the follow-up (mean 5.1-median 5 yrs). In Group A, 159/238 (66.8%) pts [A1] had Tg <0.5 ng/ml at the first control, 42/238 (17.65%) pts [A2] had a Tg between 0.5–1 ng/ml and 37/238 (15.55%) pts [A3] had Tg >1 ng/ml; at the end of follow up only in 35/238 (14.7%) pts, Tg was >1 ng/ml. In all pts neck US was negative for lymphnode metastases. In all pts of group B there was a decrease >20% of TgAb levels and nUS was negative. Basal TSH (bTSH) in [A1] (mean 0.93 ± 1.95 μU/ml) was significantly lower of final TSH (fTSH) (mean 1.36 ± 6.05 μU/ml) ($p < 0.05$), as far as in [A3], bTSH (mean 3.73 ± 9.74 μU/ml), was significantly higher that fTSH (mean 0.78 ± 0.77 μU/ml) ($p < 0.01$).

Conclusion: 1) Almost 70% of our mPTC pts were 'surgically ablated' since their Tg was <0.5 ng/ml, three months after surgery; 2) After 5 years follow-up about 15% of pts had Tg >1 ng/ml without any evidence of structural disease in the neck; 3) All cases with positive TgAb showed a decrease of TgAb titer; 4) The 5 yrs follow-up of mPTC not submitted to RRA showed a very good outcome and the absence of recurrence: these pts can be monitored at longer intervals.

08.45–09.00

COMPARISION OF HEMITHYROIDECTOMY AND TOTAL THYROIDECTOMY FOR PATIENTS WITH PAPILLARY THYROID MICROCARCINOMA: A RETROSPECTIVE MATCHED COHORT STUDY

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Objectives: Papillary thyroid microcarcinoma (PTMC) has contributed to most of the increase in thyroid cancer in recent decades. There is a debate about the initial surgery extent for patients with PTMC because the presence of lateral cervical lymph node (LN) metastases or distant metastases in some patients. This study aimed to compare hemithyroidectomy and total thyroidectomy for patients with PTMC.

Methods: In this retrospective matched cohort study, 2,031 patients with PTMC were initially included. Patients who underwent hemithyroidectomy or total thyroidectomy were one-to-one matched according to the individual risk factors including age, sex, primary tumor size, extrathyroidal invasion, multifocality, and cervical LN metastasis. We compared clinical outcomes of 1,376 patients with PTMC according to surgical extent.

Results: The mean age was 47.4 ± 9.6 years, and 120 patients (8.7%) were male. The mean maximum tumor size was 0.6 ± 0.2 cm. Extrathyroidal invasion and multifocal tumors were present in 522 patients (37.9%) and 138 patients (10.0%), respectively. Cervical LN metastases were present in 178 patients (25.9%). Twenty-six patients (3.8%) in hemithyroidectomy group and 11 patients (1.6%) in total thyroidectomy group had recurrences during median 8.5 years of follow-up. The recurrences in total thyroidectomy group were significantly less than hemithyroidectomy group (hazard ratio [HR] 0.41; 95% confidence interval [CI] 0.21–0.81; $P = 0.01$). Most recurrences (84.6%, 22 of 26 patients) in hemithyroiectomy group were occurred at the contralateral lobe. All of these patients were remained disease-free after completion thyroidectomy during median 5.7 years (interquartile range [IQR] 3.7–7.8) of follow-up.

Conclusion: Total thyroidectomy for patients with PTMC could improve recurrence-free survival. When hemi-thyroidectomy is applied for patients with PTMC, pre- and post-operative imaging studies are very important because of recurrences in the contralateral lobe.

09.00–09.15

STIMULATORY TSH-RECEPTOR ANTIBODIES INDUCE OXIDATIVE STRESS IN THYROCYTES AND PERIPHERAL BLOOD

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Objective: The impact of thyroid-stimulating antibodies (TSAb) in Graves' hyperthyroidism (GH) on oxidative stress in cultured thyrocytes and peripheral blood was investigated.

Methods: Superoxide was investigated by dihydroethidium (DHE, 50 μM) oxidation in HEK cells ($1.1x10^5$ cells/well) overexpressing the human TSH-receptor incubated with 20% untreated GH serum over 6, 24 and 48 h using high performance liquid chromatography (HPLC). The lipid peroxidation marker, 4-hydroxy-2-nonenal (4-HNE) was determined by immuno-dot-blot analysis in human primary thyrocytes ($5x10^5$ cells/well) stimulated as described for HEK cells. Oxidative burst under basal conditions or upon stimulation with phorbol 12, 13-dibutyrate, (PDBu, 10 μM) or zymosan A (50 μg/ml) as a read-out for the activation of the phagocytic NADPH oxidase in whole blood was detected by L-012 (100 μM) enhanced chemiluminescence.

Results: Twelve patients with untreated GH and 12 matched controls (C) were included. HPLC-based analysis revealed increased levels of the superoxide-specific 2-hydroxyethidium product ($p < 0.05$) in HEK cells stimulated with serum from patients with untreated GH (after 48 h) vs. all C groups (6, 24, 48 h) and vs. the 6 h patient group. 4-HNE was significantly higher in C

6 h vs. C 24 h (p = 0.00314), C 6 h vs C 48 h (p = 0.0156), GH 6 h vs. GH 48 h (p = 0.0104) and GH 12 h vs. GH 48 h (p = 0.0170), respectively. The white blood cell count (number of cells x 10^3/µl) from patients with GH and C were (mean±SEM) 6.08 ± 0.39 vs. 6.15 ± 0.35, respectively. The kinetics of the respiratory burst of leucocytes in whole blood from patients with untreated GH and C showed that the maximum stimulation peaks were 1.5-fold increased after stimulation with both zymosan A and with PDBu. Zymosan was significantly different in C vs. GH ($p < 0.05$).

Conclusion: TSAb significantly augment the generation of superoxide and induce lipid peroxidation in untreated patients with GH.

09.15–09.30

MUTATIONS IN TBL1X AS A NOVEL CAUSE OF FAMILIAL CENTRAL HYPOTHYROIDISM

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Background: Congenital central hypothyroidism (CeH) may occur isolated, or in combination with other pituitary hormone deficiencies. Although a third causative gene for CeH was recently reported (*IGSF1*), the aetiology of isolated CeH has remained unexplained in most cases.

Methods: We studied a family with three relatives with isolated CeH, in whom mutations in all known causative genes for CeH were excluded. Using X-exome sequencing in these three patients, we identified a missense mutation in the Transducin β-like protein 1, X-linked (*TBL1X*) gene. The TBL1X protein is part of the thyroid hormone receptor corepressor complex. Sanger sequencing of this gene in unrelated cases of unexplained isolated CeH revealed five additional missense mutations. We performed clinical and biochemical characterization of the probands and relatives with a mutation identified by family screening. We investigated the functional consequences of the mutations *in vitro*, and used qPCR and immunostaining to study TBL1X expression in post-mortem human hypothalamus and pituitary tissue.

Results: All probands (n = 8, 6 males) had CeH with plasma free thyroxine (FT4) concentrations below the reference interval accompanied by thyrotropin concentrations within the reference interval. Family screening identified mutations in 9 females and 2 males, all with FT4 concentrations in the lower half of the reference interval. Eleven out of 15 evaluated individuals with a mutation had hearing loss. The *TBL1X* mutations were located in the highly conserved WD40-repeat domain of the protein and influenced its expression and thermal stability. *TBL1X* mRNA and protein were expressed in the human hypothalamus and pituitary.

Conclusion: Mutations in *TBL1X* are associated with a novel syndrome of familial isolated CeH and hearing loss, presumably resulting from impaired function of the nuclear NCoR/SMRT corepressor complex.

Funding: Wellcome Trust, Biological Sciences Research Council Project Grant; AMC Foundation Grant.

09.30–09.45

THYROID FUNCTION TESTING IN BIOBANK SERA FROM 9,768 DANISH PREGNANT WOMEN SHOWS UNIDENTIFIED THYROID DYSFUNCTION IN UP TO 50% – BOTH IN WOMEN WITH KNOWN THYROID DISEASE AND IN WOMEN DIAGNOSED WITH THYROID DISEASE AFTER THE PREGNANCY

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Objectives: Thyroid dysfunction may severely complicate a pregnancy. A high frequency of abnormal thyroid test results in pregnant women with known thyroid disease has been reported, but the frequency of unidentified thyroid dysfunction in women first time diagnosed with thyroid disease *after* a pregnancy is unknown.

Methods: Pregnant women from the Danish National Birth Cohort (1997–2003) who had a blood sample drawn in early pregnancy and terminated with singleton live-birth (n = 77,571). We identified all women who had a registration of thyroid disease before and up to 5 years after the pregnancy in nationwide registers and in addition we selected a 12% random sample. TSH and fT4 were measured in sera stored in the Danish National Biobank using Siemens Dimension-Vista immunoassays. Pregnancy-week-specific references ranges were used for classification of thyroid dysfunction.

Results: Table shows results for 7,323 women in the random sample and for 2,445 women with thyroid disease diagnosed before or after blood sampling. Women with known thyroid disease had a high frequency of thyroid dysfunction in early pregnancy (55.1% among women who received current treatment for thyroid disease (n = 350)). One third of women diagnosed with thyroid disease *after* blood sampling had unidentified thyroid dysfunction in the pregnancy (unidentified hypothyroidism in women with a later diagnosis of hypothyroidism (n = 452) was most frequent (50.9%)).

Conclusion: The frequency of thyroid dysfunction in Danish pregnant women was high. More than 50% of women who received current treatment for thyroid disease had TSH and/or fT4 outside the week-specific reference ranges, and up to 50% of women with thyroid disease diagnosed *after* the pregnancy had unidentified thyroid dysfunction in the early pregnancy.

Table 1. (for abstract time 09.30–09.45)

	No diagnosis of thyroid disease n = 7,323		Thyroid disease diagnosed before blood sampling n = 1,241		Thyroid disease diagnosed after blood sampling n = 1,204	
	n	%	n	%	n	%
Early pregnancy thyroid dysfunction	824	11.3	433	34.9	436	36.2
Overt hyperthyroidism	98	1.3	76	6.1	70	5.8
Subclinical hyperthyroidism	139	1.9	64	5.2	45	3.7
Overt hypothyroidism	40	0.6	41	3.3	117	9.7
Subclinical hypothyroidism	234	3.2	169	13.6	151	12.6
Isolated low fT4, normal TSH	162	2.2	35	2.8	32	2.7
Isolated high fT4, normal TSH	151	2.1	48	3.9	21	1.7

09.45–10.00

TPO-ANTIBODY POSITIVE WOMEN HAVE AN IMPAIRED RESPONSE TO HCG WHICH UNDERLIES THEIR HIGHER RISK OF PREMATURE DELIVERY

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Context: Thyroperoxidase antibody (TPOAb) positivity may decrease the thyroid functional capacity. This may become apparent during a state of increased demand, as effectuated by high human chorionic gonadotropin (hCG) during early pregnancy. Meta-analyses show that TPOAb positive women have a higher risk of premature delivery, but the underlying mechanism is unknown.

Objective: To study whether TPOAb-positivity interferes with thyroid stimulation by hCG and if variation in hCG response changes the risk of premature delivery.

Methods: TSH, FT4, TPOAbs and hCG concentrations were measured in early and late pregnancy of 7587 pregnant women from two prospective cohorts. We used multivariable linear regression models to investigate if TPOAb-positivity changes the response of FT4 and TSH to hCG. Subsequently, we investigated if the risk of premature delivery in TPOAb positive women differed according to hCG response (inappropriate response defined as high hCG with low FT4).

Results: In TPOAb negative women, higher hCG was associated with higher FT4 and lower TSH (in both cohorts $P < 0.0001$). In TPOAb positive women, hCG was not associated with FT4 or TSH (in both cohorts $P > 0.40$).

In all women, TPOAb-positivity was associated with a 1.7-fold higher risk of premature delivery. However, TPOAb positive women with an appropriate FT4 response based on hCG had a similar risk of premature delivery as TPOAb negative women.

In contrast, TPOAb positive women with an inappropriate FT4 response based on hCG had a 2.3 to 2.8-fold higher risk of premature delivery ($P = 0.012$). These results were similar in women with a spontaneous delivery only (2.0 to 2.9-fold higher) and were amplified in nulliparous women (a risk factor TPOAb positivity; 2.9 to 6.1-fold higher).

Conclusion: This study shows that TPOAb-positivity impairs the thyroidal response to hCG, which may explain the higher risk of premature delivery in TPOAb positive women that has consistently been reported.

10.00–10.15

IODINE FORTIFICATION HAS REDUCED OVERT THYROTOXICOSIS INCIDENCE IN DENMARK WITH 40%. A 16 YEAR PROSPECTIVE POPULATION STUDY

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Objective: Iodine fortification is widespread, but the long-term consequences for thyrotoxicosis incidence are unknown. We performed the first population based prospective monitoring of the incidence rate of overt thyrotoxicosis starting before iodine fortification (IF), in an area with moderate iodine deficiency.

Methods: In an open cohort (n = 309,434) in and around Aalborg city (moderate iodine deficiency prior to IF), overt cases of thyrotoxicosis were prospectively identified from 1997 to 2012 by applying a diagnostic algorithm to all thyroid function testing. Incident cases were verified by contacting the requesting physician. Mandatory IF was initiated in the year 2000 with the iodization of household salt and salt used for production of bread leading to a ~50 µg/day increase in iodine intake. Population composition was followed using data from the Danish Bank of Statistics.

Results: The incidence rate standardized to the Danish population (SIR) of thyrotoxicosis was 128.5/100.000/year at baseline (1997–1998). SIR increased significantly during the first years of IF with a peak in 2001–2002 (RR to baseline: 1.39; 95% CI: 1.25–1.54) after which a gradual decrease occurred leading to 2011–2012 values being 40% lower than baseline (RR to baseline 0.60; 95% CI: 0.53–0.69). The decline was caused by a marked decrease in incidence rate among elderly subjects (60+ years; RR 0.42 (0.35–52)), and a moderate decrease among middle-aged subjects, whereas the incidence rate in younger subjects (<40 yrs) was still significantly higher compared to baseline at study end. Variations were equal among men and women.

Conclusion: The very cautious IF program led to a 40% reduction in thyrotoxicosis incidence after 11–12 years of IF. The IF effect was very positive in elderly subjects, but not in the young. Overall, IF had a major positive effect, but it should be careful to avoid overdosing young people with iodine.

10.15–10.30

THE EXCESS MORTALITY IN GRAVES' ORBITOPATHY, COMPARED TO THE BACKGROUND POPULATION, IS PRIMARILY DUE TO HIGHER MORTALITY IN MALES THAN IN FEMALES

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Objective: To investigate the mortality risk in Graves' disease with (GO) or without (GD) orbitopathy compared to the background population.

Methods: An observational cohort study covering all adult Danes diagnosed with GO or GD during 1995–2012. Median follow-up time 7.9 years (range 0–17.5). Utilizing the Danish National Patient Registry (in- and outpatients), 28,461 subjects with GD and 3,965 with GO were identified. GO and GD cases were matched for age and gender with four euthyroid individuals from the background population. Using the Charlson score, we adjusted for pre-existing comorbidity. Through the Danish Register of Causes of Death we obtained date of death. Hazard ratios (HR) for mortality were calculated using Cox regression analyses.

Results: Mortality in Graves' disease overall (GD + GO), was significantly increased compared to the background population [HR = 1.53 (95% confidence interval: 1.49–1.57)], also after adjusting for pre-existing comorbidity [HR 1.18 (1.15–1.21)]. The adjusted mortality risk in GO and GD separately was also significantly higher than in their respective control populations [HR 1.23 (1.12–1.35) and HR 1.19 (1.16–1.22), respectively]. However the mortality risk in GO compared to GD was decreased [HR 0.64 (0.59–0.69)], although this attenuated after adjustment for pre-existing comorbidity, age and gender.

Among GO patients, males had a significantly higher mortality than females [HR 1.98 (1.69–2.32)]. This persisted after adjusting for pre-existing comorbidity and age [HR 1.96 (1.63–2.36)]. The same gender related pattern with respect to mortality was seen in GD individuals.

Conclusion: Mortality in Graves' disease, overall, is higher than in the background population. The excess mortality in GO and GD persists after correction for pre-existing comorbidity and is predominantly driven by higher mortality in males. Unexpected, and unexplained, in Graves' disease patients, a GO diagnosis seems to be associated with decreased mortality.

Oral Session 11: Young Investigators Session / Basic

08.30–08.45

ELUCIDATING THE THERAPEUTIC POTENTIAL OF THYROID HORMONE ANALOGS IN MCT8 DEFICIENCY

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Patients with inactivating mutations in the thyroid hormone transporter MCT8 suffer from a severe form of psychomotor retardation and abnormal serum TH levels (Allan-Herndon-Dudley Syndrome). The neurological symptoms are most likely due to an impaired transport of TH into the CNS and, consequently, due to a disturbed differentiation and maturation of brain cells. Treatment of patients with TH analogs that can activate TH receptors thereby replacing T3 in the brain but are not dependent on MCT8 for cellular entry have been suggested to be a promising therapeutic approach.

Here, we tested the TH analogs DITPA (3,5-Diiodothyropropionic Acid) and Triac (3,5,3′-Triiodothyroacetic Acid) in Mct8/Oatp1c1 double knockout (dko) mice, an animal model for human MCT8 deficiency. Treatment of these mice with Triac (TA3) during the first three postnatal weeks resulted in robust effects on brain parameters and restored normal neural differentiation while a treatment of Mct8/Oatp1c1 dko mice with DITPA was less effective. In particular, only TA3-treated Mct8/Oatp1c1 dko mice displayed a normal cerebellar Purkinje cell development, cortical myelination and development of Parvalbumin expressing cortical interneurons. Most interestingly, behavioral studies of these TA3-treated Mct8/Oatp1c1 dko mice at the age of 10 weeks revealed normal locomotor functions in Rotarod, hanging wire and beam walk tests indicating that already a transient application of TA3 during the early postnatal period is sufficient to prevent locomotor deficits in Mct8/Oatp1c1 dko animals. In order to determine the critical time window during which TA3 improves brain maturation and function, Mct8/Oatp1c1 dko mice of different postnatal age (P12, P22) are treated with Triac for three consecutive weeks. Ongoing studies will reveal to which extent such a treatment initiated later in life leads to an improvement in brain parameters as well as in locomotor performance.

08.45–09.00

A FUNCTIONAL ROLE FOR THE DEIODINASE ENZYMES IN NEUTROPHILS AND MACROPHAGES

Anne van der Spek[1], *Aldona Karaczyn*[2], *Elena Martinez*[2], *Olga Surovtseva*[1], *Bernadine Snell*[1], *Eric Fliers*[3], *Arturo Hernandez*[2], *Anita Boelen*[1]
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Recent evidence suggests that the deiodinase enzymes play an important role in the function of innate immune cells. The thyroid hormone inactivating type 3 deiodinase (D3) is expressed in infiltrating neutrophils and is thought to be important for bacterial killing capacity. The thyroid hormone activating type 2 deiodinase (D2) plays a crucial role in macrophage phagocytosis and response to lipopolysaccharide (LPS) stimulation in an *in vitro* model. The underlying mechanisms behind the effect of D3 and D2 on the inflammatory response of these cells are currently unknown. To further elucidate this, we performed functional analyses in neutrophils from D3 knockout (KO) mice and macrophages from D2KO mice.

We assessed neutrophil function in cells derived from D3KO mice and wildtype (WT) littermates including phagocytosis of fluorescent particles, spontaneous apoptosis and hydrogen peroxide production upon treatment with the protein kinase C activator PMA, which strongly induces the neutrophil immune response. In bone marrow-derived macrophages from D2KO and WT mice we evaluated phagocytosis of fluorescent particles and response to LPS stimulation.

D3KO neutrophils exhibited impaired hydrogen peroxidase production upon activation compared to WT counterparts indicating decreased NADPH-oxidase activity, an important component of bacterial killing. Phagocytosis and spontaneous apoptosis in neutrophils were not affected by D3 deficiency. D2KO macrophages exhibit impaired phagocytosis compared to macrophages from WT mice. The LPS-induced transcriptional upregulation of proinflammatory cytokines GM-CSF, IL-1β and TNF-α was similar in D2KO and WT macrophages.

Our study provides novel insights into the mechanisms underlying the crucial role of the deiodinase enzymes in the inflammatory response of neutrophils and macrophages. The observed impaired NADPH-oxidase activity in D3KO neutrophils potentially explains the bacterial killing deficits previously seen in D3KO mice. A lack of D2 impairs phagocytosis in primary macrophages. This is in accordance with previous studies in an *in vitro* knockdown model.

09.00–09.15

ROLE OF CAR AND MTOR IN THE REGULATION OF TYPE 3 DEIODINASE DURING FASTING

Emmely de Vries[1], *Marte Molenaars*[1], *Olga Surovtseva*[2], *Evita Belegri*[1], *Albert Van Wijk*[3], *Marinus Maas*[3], *Eric Fliers*[1], *Anita Boelen*[1]
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Fasting induces pronounced changes in systemic thyroid hormone (TH) concentrations and local tissue deiodination, e.g., i liver type 3 deiodinase (D3), the main T_3 inactivating enzyme, increases while liver type 1 deiodinase (D1) decreases. As deiodinases are regulated in a tissue specific manner, we aimed to study the effects of fasting on D3 expression and activity in other T_3 responsive tissues like white adipose tissue (WAT) and hypothalamus. Furthermore, we studied the underlying mechanism involved focusing on the energy sensing constitutive androstane receptor (CAR) and mTOR pathways. Previous work by others had shown that fasting induces the expression of CAR in the liver while fasting associated signals inhibit mTOR.

We measured D3 expression and activity in WAT from 48 h fasted mice, and in liver and hypothalamus of 24 and 36 hour fasted rats. CAR knock out and WT mice were fasted for 24 hours and liver D3 expression and activity was measured. In relevant cell models (rat primary hepatocytes, a murine adipose cell line (3T3L1) and the SK-N-AS neuroblastoma cell line), we mimicked a fasting state by stimulating the cells with a CAR activator or the mTOR inhibitors Torin (mTORC1) and Rapamycin (mTOR1/2) respectively.

Fasting induced D3 expression and activity in liver, D3 expression in WAT, but did not affect hypothalamic D3 expression and activity. The fasting-induced liver D3 increase was absent in CAR knock out mice. CAR activation in primary hepatocytes directly upregulated D3 expression and activity. Inhibition of mTOR induced D3 expression in 3T3L1 adipocytes and both D3 expression and activity in primary hepatocytes. In SK-N-AS cells, torin increased D3 expression, while rapamycin decreased D3 expression.

In conclusion, we showed that fasting differentially affects D3 expression and activity in WAT, liver and hypothalamus. In addition, energy sensing pathways such as CAR and mTOR are involved in the regulation of D3 during fasting.

09.15–09.30

A SONIC HEDGEHOG-GLIS3 PATHWAY IS INVOLVED IN THE SPECIFICATION OF THE THYROID GLAND IN ZEBRAFISH

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In the last few years, *GLIS3* (GLI-Similar protein 3) has emerged as a new candidate gene for congenital hypothyroidism (CH), since homozygous and heterozygous mutations have been identified in patients with syndromic and isolated CH, respectively. *GLIS3* is a member of the five Kruppel-like zinc-finger transcription factors that can act as activator or repressor of gene expression. The aim of this study is to gain insight on GLIS3 activity during the early steps of thyroid specification in zebrafish.

In situ hybridization (ISH) in zebrafish embryos revealed that *glis3* is expressed in the pharyngeal endoderm at 1 day post-fertilization (dpf) but is absent in the differentiated thyrocytes. Moreover, transient knockdown obtained by morpholino microinjection in zebrafish embryos (called *glis3*_MOs) resulted in a reduced expression of *nkx2.4* and *pax2a* at 1 dpf, thyroid hypoplasia with low T4 production and high TSH at 5 dpf, demonstrating that *glis3* is involved in thyroid development. The Sonic hedgehog (Shh) pathway is a critical regulator of embryonic development, which sets off a chain of events in target cells, regulating gene expression by transcription factors of the Gli-family. Recently, it has been reported that GLIS3 physically interacts with the Shh-suppressor Sufu in mice, although the link between Shh and GLIS3 is presently unknown. By ISH, we observed that the expression of the Shh-genes (*shha*, *shhb, ptch1* and *smo*) was significantly reduced in the pharyngeal endoderm of *glis3*_MOs. The injection of a morpholino against *shh* transcripts abolished the expression of *glis3* in the endodermal layer at 1 dpf, confirming their association during the endocrine cells specification. Furthermore, the treatment with cyclopamine (Shh-antagonist) resulted in a reduced or absent expression of *glis3*, *shha*, *shhb*, *ptch1*, *smo*, and *gli1* whereas Shh agonists induced the expression of *glis3* and *smo* in the pharyngeal endoderm of zebrafish embryos.

In conclusion, this is the first instance of Shh-Glis3 interactions in the early specification of thyroid primordium. These data provide novel insights into the molecular mechanisms involved in CH pathogenesis.

09.30–09.45

IDENTIFICATION OF A PI3K REGULATED FEEDBACK WITH A DOUBLE-NEGATIVE LOOP BETWEEN MIR30A AND LIN28B CONTROLLING THYROID CANCER PROGRESSION

León Wert-Lamas[1], *Garcilaso Riesco-Eizaguirre*[2], *Richard Gregory*[3], *Pilar Santisteban*[4]

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Our recent results showed that tumor supressor miR30a is firmly down-regulated in Thyroid carcinomas. On the other hand, recent studies showed RNA- and DNA-binding proteins LIN28B and HMGA2 induce EMT, thus playing an important role in dedifferentiation and cancer malignification. Finally, latterly several authors agreed on the importance of a robust activation of PI3K for thyroid cancer emergency and progression.

The aim of this work was to study the link between the emergency of LIN28B and HMGA2, miR30a silencing and PI3K hyperactivation, and to determine their effect on thyroid cancer progression.

MiRNA targets computational predictions were performed with MiRanda algorythm. LIN28B and miR-30a expression vectors were transfected in ATC derived and normal thyroid cell lines; mRNA and protein levels were determined by qPCR, Luciferase and Western Blot. Invasion, proliferation and cell cycle assays were performed in Transwell, cell counter, and FACScan respectively.

MiRanda algorythm identified multiple miR30a recognition elements in all LIN28B, HMGA2 and PI3K effectors. Lin28B expression correlated with PI3K activating mutations in ATC derived cell lines. Overexpression of miR30a resulted in LIN28B, HMGA2, and several PI3K effectors silencing, and in an increase in p27(Kip) protein levels. Inversely, LIN28B overexpressing cells showed a decrease in miR30a levels and an increased expression of HMGA2 and PI3K effectors.

The general outcome was a significant decrease in invasion and proliferation in miR30a overexpressing cells and, conversely, an increase in these parameters by LIN28B.

These data suggest the existence of a PI3K regulated feedback with a double-negative loop between miR30a and LIN28B. Here, PI3K activation acts to switch the steady states. Initially, high miR30 levels repress LIN28B expression. After PI3K is activated, LIN28B is produced and miR30a is repressed. This state reinforces PI3K hyperactivation. Thus, the feedback implements a tumoral gene expression shift, contributing to thyroid cancer progression.

09.45–10.00

INCREASED GLOBAL DNA HYPOMETHYLATION IN METASTATIC AND DEDIFFERENTIATED THYROID CANCER

Esther Klein Hesselink[1], *Carles Zafón*[2], *Nuria Villalmanzo*[3], *Carmela Iglesias*[4], *Bettien van Hemel*[5], *Mariëlle Klein Hesselink*[1], *Dídac Mauricio*[6], *Manel Puig-Domingo*[6], *Jordi Reverter*[6], *Garcilaso Riesco-Eizaguirre*[7], *Mercedes Robledo*[8], *Thera Links*[1], *Mireia Jordà*[9]

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Introduction: Genetic and epigenetic alterations are crucial for the development and progression of cancer. One of these events is global DNA hypomethylation, of which the significance in thyroid cancer remains unclear. Therefore, we aimed to investigate whether global DNA hypomethylation plays a role in thyroid cancer progression and can act as a prognostic marker.

Methods: DNA was extracted from formalin-fixed paraffin-embedded tissues, as well as from fresh frozen tumors. Global hypomethylation of Alu elements (the most abundant repetitive elements of the human genome) was used as a surrogate marker for DNA global hypomethylation, and was assessed using the Quantification of Unmethylated Alu (QUAlu) technique.

Results: Primary tumors of 90 thyroid cancer patients were included (n = 28 low-risk differentiated thyroid cancer (DTC), n = 13 pediatric DTC, n = 33 distant metastatic DTC, n = 7 poorly differentiated (PDTC) and n = 9 anaplastic thyroid cancer (ATC)), as well as tissues from 20 distant metastases, and 20 normal thyroid tissues. An increasing hypomethylation was found for distant metastatic DTC (median 4.0, IQR 3.1–6.2) and PDTC/ATC tumors (median 9.3, IQR 7.0–12.1) as compared to normal thyroid tissue (median 2.75, IQR 2.30–3.15), $p < 0.001$ for both, whereas low-risk and pediatric DTC tumors were not affected by hypomethylation. Global Alu hypomethylation was similar between distant metastatic tissues and matched primary tumors. Kaplan-Meier and unadjusted and age-adjusted Cox regression analyses showed that thyroid cancer-related and all-cause mortality were related to tumor hypomethylation, but this association was lost after further adjustment for thyroid cancer risk category.

Conclusion: Metastatic DTC, PDTC and ATC tumors were increasingly affected by global Alu hypomethylation, which suggests that this epigenetic entity may be involved in thyroid cancer progression and dedifferentiation.

10.00–10.15

VARIABLY DEFECTIVE TRANSCRIPTIONAL ACTIVITY OF T3 RECEPTOR TRα1 MUTANTS ON DIFFERENT THYROID RESPONSE ELEMENTS

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Introduction: Mutations in the ligand binding domain of TRα1 cause resistance to TH alpha (RTHα). TRs initiate gene transcription by binding to thyroid response elements (TREs), which usually consist of two half site, hexanucleotide sequences arranged in either direct (DR) or inverted (IR) or everted (ER) repeat configurations. Studies of TRβ mutants in RTHβ indicate that the orientation of TREs can influence the functional properties of mutant receptors. Because of the high degree of homology between TRα1 and TRβ1, we hypothesized that the transcriptional activity of TRα1 mutants could also vary depending on TRE configuration. This may, in part, contribute to phenotypic variability in both patients and murine models for RTHα.

Objective: To determine the transcriptional activity of WT and mutants TRα1 on reporter genes containing different configurations of TRE.

Methods: JEG3 cells were transfected with 20 ng of FLAG-tagged wild-type TRα1 (WTα1) or mutant TRα1 expression vectors, 120 ng of luciferase reporter construct containing either DR (MAL), IR (PAL) or ER (F2) TRE, and 60 ng of pMaxGFP control reporter. After 24 hours, cells were incubated for 24 hours with 0–10,000 nM T3. Luciferase and GFP activities were measured, and half maximal effective T3 concentration (EC50) and maximum responses were determined. Cellular receptor expression was verified by immunoblotting of nuclear extracts with FLAG antibodies.

Results: WT and mutant receptors were expressed at similar levels. The EC50s of WTα1 for DR and ER (0.15 and 0.17 nM respectively) were comparable and lower than for IR (0.88 nM). All mutants showed a clear increase in EC50, which varied between TREs. Overall, the fold increase in EC50 was highest on ER (~80 fold), intermediate on DR (~20 fold) and lowest on IR (~10 fold). The EC50s of L287Vα1 and D211Gα1 were significantly higher compared with WT on all TREs. In contrast, P398Hα1 showed a significantly increased EC50 only on DR and ER, and A263Sα1 only on ER. The maximum response was modestly decreased for most mutants, but reached significance only for T223Aα1 (~60%WT) and P398Hα1 (~40%WT) on all TREs, except for P398Hα1 on ER.

Conclusion: The degree of defective transcriptional function of TRα1 mutants does vary depending on configuration of TRE. This likely contributes to the variable tissue resistance and phenotypes seen in RTHα patients with different TRα mutations.

10.15–10.30

AUTOPHAGY ACTIVATING COMPOUNDS FACILITATE REDIFFERENTIATION AND CELL CYCLE ARREST OF NON-MEDULLARY THYROID CANCER THROUGH INTRACELLULAR CA2+, FOS AND P21 DEPENDENT PATHWAYS

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Objectives: About 20–30% of non-medullary thyroid cancer (TC) patients have persistent/recurrent disease requiring subsequent therapy caused by decreased radioactive iodide (RAI) avidity through loss of human sodium-iodide symporter (hNIS) expression. Restoration of RAI sensitivity by tumor redifferentiation is considered a promising strategy to overcome RAI resistance. Autophagy has emerged as an important and clinically relevant player in cancer initiation, progression and dedifferentiation because of its potent inhibitory effects on oncogenic pathways driving these processes. We aimed to investigate the therapeutic potential and underlying mechanisms of autophagy activation for induction of redifferentiation in thyroid cancer cell lines.

Methods: Dedifferentiated TC cell lines TPC-1, BC-PAP and FTC-133 were treated with autophagy activating compounds, previously identified by high-throughput screening, and were assessed for hNIS expression and ^{125}I RAI uptake capacity. Responsible molecular pathways were investigated by transcriptome profiling and functional validation studies. Furthermore, intracellular calcium transients and degree of cell proliferation was measured.

Results: Of 15 autophagy activating compounds tested, five were demonstrated to restore hNIS expression and iodide uptake in at least one of the cell lines tested, all well characterized drugs known as cardiac glycosides, including digoxin, that increase intracellular Ca^{2+} by inhibition of Na^+/K^+ ATPases. Subsequent molecular studies identified crucial roles for Ca^{2+} and the transcription factor FOS driving hNIS upregulation. In addition, these compounds strongly inhibited cell proliferation by downregulating Akt1 and by induction of autophagy- and p21-dependent cell cycle arrest.

Conclusion: Clinically approved cardiac glycosides induce TC redifferentiation by modulation of intracellular Ca^{2+}-dependent pathways, thereby partially overlapping TSH receptor signaling. Importantly however, concomitant activation of autophagy leads to inhibition of proliferative effects of these pathways on TC cells. All together, cardiac glycosides could represent a promising treatment modality to be further investigated in patients with dedifferentiated TC for their capacity to restore RAI sensitivity and to reduce proliferation.

Oral Session 12 (Clinical): Clinical Aspects of Pregnancy, Childhood and Brain

11.00–11.15

TSH REFERENCE LIMITS ARE HIGHLY DEPENDENT ON THE WEEK OF GESTATION IN THE FIRST TRIMESTER OF PREGNANCY. A STUDY OF 6,671 HEALTHY PARTICIPANTS IN THE DANISH NATIONAL BIRTH COHORT

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Thyroid hormones are important developmental factors and levels should be adequate both in the pregnant woman and in the fetus. However, the newly formed uteroplacental unit strongly influences thyroid physiology in early pregnancy. Maternal thyroid test reference limits in first trimester of pregnancy are debated, but guidelines suggest a uniform upper TSH limit of 2.5 mU/l.

Objectives: We estimated week-to-week changes in TSH and fT4 reference limits in early pregnancy using pregnancy week 5–19 sera from randomly selected healthy participants (n = 6,671) of the Danish National Birth Cohort that enrolled 101,032 pregnant women in 1996–2002.

Methods: Individual participant characteristics were evaluated using interview data and data from Danish nationwide health registers, and healthy participants were identified. Sera stored at –80°C were retrieved from the Danish National Biobank. TSH and fT4 were measured using Dimension Vista immunoassays (Siemens) and 2.5 and 97.5 percentiles with 95% confidence intervals for TSH and fT4 in each first trimester pregnancy week were estimated using non-parametric statistics.

Results: TSH reference limits were very variable (Table). Up to and including week 6, non-pregnancy reference limits could be used. From this level to the lower week 9–12 level, the 2.5 percentile for TSH decreased with 84% and the 97.5 percentile with 8.5%. An upper TSH reference limit of 2.5 mU/l was not observed in any week, and would lead to diagnosis of hypothyroidism in 10% (19% in weeks 5–6). fT4 varied opposite to TSH, but changes were small with ~4% higher reference limits during the weeks 9–12.

Conclusion: Week specific TSH reference limits differ widely in the first trimester of pregnancy. The use of a uniform set of reference limits is a simplification that may lead to frequent misclassification and possibly to incorrect choice of therapy.

11.15–11.30

THYROID FUNCTION AND BRAIN IMAGING

Layal Chaker[1], *Lotte Cremers*[1], *Albert Hofman*[2], *Mohammad Arfan Ikram*[1], *Meike Vernooij*[1], *Robin Peeters*[1]
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Background: Thyroid hormone plays a key role in most organs, including the brain, and differences in thyroid function levels have been associated with dementia. There is no information on the association of thyroid function with brain volumes and microstructural integrity of brain white matter.

Aim: To investigate the association of thyroid function measurements, thyroid-stimulating hormone (TSH) and free thyroxine (FT4), with structural brain volumes and diffuse tensor imaging (DTI) outcomes on MRI in a general population based cohort study.

Methods: We investigated the association of thyroid function with total intracranial volume (as a measurement of development), total brain, white matter and grey matter volume on MRI. We analyzed the association of thyroid function with fractional anisotropy, mean diffusivity, axial diffusivity and radial diffusivity. Linear regression adjusting for among others sex, age, and cardiovascular risk factors, was used.

Results: We included 4683 participants (mean age 60.2 years), free of dementia and stroke. FT4 levels were associated with a larger total intracranial volume in the overall population with a beta of 8.03 (95% confidence interval 4.11, 11.94). There was no association in TSH or grey matter volume analyses. FT4 was also associated with a larger total brain and white matter volume in younger individuals. However, in elderly FT4 was associated with smaller total brain and white matter volume (p for interaction 0.002). There was also an interaction by age for the association of FT4 with mean diffusivity (p for interaction 0.026) and axial diffusivity (p for interaction 0.017) on DTI.

Conclusion: Our results show that FT4 is associated with larger brain volumes and better microstructural white matter integrity in younger individuals and with smaller brain volumes and worse microstructural white matter integrity in older individuals. These results can contribute to a better understanding of the association of thyroid function with dementia.

11.30–11.45

EFFECT OF THYROID HORMONES ON COGNITION AND BRAIN

Anna Göbel[1], *Marcus Heldmann*[2], *Martin Göttlich*[2], *Georg Brabant*[3], *Anna-Luise Dirk*[3], *Relana Nieberding*[3], *Rene Goerges*[3], *Thomas Münte*[4]
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Objective: Disturbed levels of thyroid hormones can be associated with cognitive impairments. Our aim was to evaluate effects mild induced thyrotoxicosis as well as induced hypothyroidism on brain structure and function as well as working memory.

Methods: Twentynine healthy men were subjected to a comprehensive neuropsychological and MRI assessment prior to and after 8 weeks of 250 µg L-thyroxin per day, a dosage designed to lead to subclinical thyrotoxicosis. In addition, for 15 athyroid patients neuropsychological and MRI analysis was performed during euthyroid state and after reduction of thyroid hormone

Table 1. Early pregnancy TSH (mU/l) median and reference limits (95% confidence intervals) (for abstract time 11.00–11.15)

Pregnancy week	5–6	7	8	9	10	11	12	13–19
n	639	884	1,193	1,287	1,006	690	448	524
Median	1.62	1.45	1.21	1.10	1.03	0.99	0.98	1.24
2.5 percentile	0.60	0.32	0.20	0.13	0.061	0.066	0.093	0.14
(95% CI)	0.53–0.69	0.25–0.40	0.13–0.25	0.10–0.16	0.049–0.11	0.048–0.11	0.044–0.14	0.096–0.22
97.5 percentile	3.55	3.68	3.46	3.41	3.27	3.09	3.37	3.29
(95% CI)	3.35–3.79	3.36–3.83	3.27–3.70	3.07–3.62	2.99–3.49	2.91–3.31	2.96–3.78	3.08–3.73

intake leading to an induced hypothyroid state. Thyroid hormone levels were analyzed confirming hypo/hyperthyroid state as well as euthyroid state. Functional MRI (fMRI) was acquired during a working memory task. Voxel based morphometry (VBM) was performed for evaluating structural changes in brain grey matter. Arterial spin labeling (ASL) was conducted for evaluation of brain perfusion. Each method was performed comparing hypo/hyperthyroid state with euthyroid state.

Results: In the hyperthyroid condition subjects showed slower reaction times, but higher accuracy in working memory tests, whereas in the hypothyroid condition a slower reaction time and a decreased accuracy in working memory tests was obtained. Significant functional and structural changes could be seen especially in the posterior cerebellum in both hyperthyroidism and hypothyroidism. Literature shows that the posterior cerebellum is involved in memory processes. Many rodent studies have shown that especially the cerebellum is involved in thyroid hormone production and thyroid hormone receptor expression.

Conclusion: Our study provides further evidence for functional and structural brain effects of thyroid hormones. The cerebellum appears to be a site of particular thyroid hormone sensitivity.

11.45–12.00

MATERNAL HYPOTHYROIDISM CONTRIBUTES TO ATYPICAL HIPPOCAMPAL FUNCTION IN HUMAN OFFSPRING

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The hippocampus (H), which is critical for learning and memory, requires thyroid hormone (TH) in development including prior to onset of fetal thyroid function. Early in gestation, maternal TH is the sole source of hormone and later, serves a supplementary role. However, if the mother experiences hypothyroidism during pregnancy, this supply will be inadequate. We previously found children born to women with clinical hypothyroidism had selective volume reductions in left and right H, as well as specific memory deficits and difficulties with everyday memory. To assess if their H functioning is also abnormal, we gave 12 young adolescents born to hypothyroid women (HYPO) and 15 controls born to normothyroid women (C) a functional MRI (fMRI) memory paradigm shown to activate H in healthy adults and function atypically in youth with congenital hypothyroidism. This task required learning associations between novel object pairs in different spatial locations and inside the scanner, perform two recall tasks, both involving a larger series of paired stimuli. One task asked if object pairs were the same as originally learned (Objects Task) and the other, if objects were in same locations as before (Places Task). Results showed HYPO manifested a different activation profile than C. On Objects, C like healthy young adults demonstrated left H activation, whereas HYPO showed increased right posterior H activation. On Places, HYPO performed significantly below C for novel locations and failed to activate H, whereas C showed significantly increased right posterior hippocampal activation. Importantly in HYPO, higher maternal TSH in the second half of pregnancy was correlated with reduced MRI signal in right posterior H when identifying places. Overall, these findings suggest that HYPO tends to use right posterior H for functions normally carried out by left H (i.e., object associations) and as a consequence, right H in HYPO may be no longer specialized for usual functions (viz., spatial memory). Overall, these findings signify maternal hypothyroidism disrupts functioning of the offspring's H and likely accounts for their observed memory deficits.

12.00–12.15

IODINE STATUS AND EFFECTS OF SUPPLEMENTATION WITH 150 µg/DAY IODINE DURING PREGNANCY IN SWEDEN: A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Objectives: Iodine is part of thyroid hormones. As the iodine need is doubled during pregnancy, iodine deficiency (ID) may occur, although the general population has adequate iodine intake. As thyroid hormones are important for fetal brain development, ID may have undesired consequences. The effects of severe/moderate ID on the brain are non-questionable. Observational studies indicate that even mild ID during pregnancy may affect cognitive outcome in the offspring, but solid evidence is still lacking. The aims of this study were: 1) to evaluate the iodine levels during pregnancy in Sweden, a country with adequate iodine intake in the general population 2) to examine the effect on urinary iodine concentration (UIC) from 150 µg iodine supplementation during pregnancy.

Methods: This was a randomized, double-blinded placebo-controlled trial of 200 pregnant women, who were randomized to 150 µg iodine/day or placebo in pregnancy week 7–12. Spot UIC, thyroid stimulating hormone (TSH), free thyroxin (FT4) and thyroglobulin (Tg) were collected longitudinally. UIC was also collected in mothers and newborns directly after delivery.

Results: UIC (µg/l), FT4 (pmol/l), TSH (mIU/l), Tg (µg/l) are analyzed cross-sectionally with Mann-Whitney test.

Conclusion: This study confirmed ID among pregnant women in Sweden. Thyroglobulin was higher in the placebo group, but thyroid hormones were not affected, which confirmed mild ID. The study needs to be expanded for enough power for a children follow-up to decide if extra iodine shall be given in pregnancy to secure brain development.

Table 1. (for abstract time 12.00–12.15)

	1st trimester	p	2nd trimester	p	3rd trimester	p	Mother postpartum	p	Baby	p
UIC-iodine	111		140		136		41		93	
UIC-placebo	110	0.528	90	<0.001	65	<0.001	23	0.001	47	0.002
FT4-iodine	15		13		12					
FT4-placebo	15	0.434	12	0.557	12	0.065				
TSH-iodine	1.20		1.65		1.90					
TSH-placebo	1.20	0.566	1.60	0.940	2.05	0.524				
Tg-iodine	21				22					
Tg-placebo	18	0.280			30	0.002				

12.15–12.30

BARIATRIC SURGERY REDUCES URINARY IODINE LEVELS DESPITE NORMAL IODINE INTAKE – A PROSPECTIVE 10-YEAR-REPORT FROM THE SWEDISH OBESITY SUBJECT (SOS) STUDY

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Objectives: Bariatric surgery (BS) reduces urinary iodine excretion (UIE) that remains within the normal, 100–200 µg/day. The objectives were to examine if the UIE reduction depends on reduced dietary iodine intake and if BS patients without iodine supplements have subnormal UIE.

Methods: From the Swedish Obesity Subject study, a non-randomized prospective study in 1987–2000, gastric by-pass (GBP) patients were retrieved and matched to ventricle banding gastroplasty (VBG) and obese non-surgery (OB) patients. 24 h-UIE, intake data on dietary iodine and multivitamins were collected at baseline and after 2 and/or 10 years.

Results: Median 24 h-UIE from baseline (B-UIE), 2 (2-UIE) and 10 (10-UIE) years, median dietary iodine and multivitamin intake at 10 years, 10-UIE for the subgroups with or without iodine containing multivitamins (10-UIE-iodine and 10-UIE-non-iodine, respectively) are presented table 1.

Conclusion: The reduction in 24-UIE, 10 years after BS, is not explained by lower dietary iodine intake. Opposing recommendations, a minority of BS patients take multivitamins. BS patients not taking iodine supplements have normal UIE, whereas those taking iodine supplements have high UIE, in risk for excessive levels. BS patients may not be recommended iodine supplements in iodine sufficient countries.

12.30–12.45

RETINAL PHOTORECEPTOR FUNCTIONS ARE COMPROMISED IN PATIENTS WITH RESISTANCE TO THYROID HORMONE SYNDROME (RTHβ)

Irene Campi[1], Gabriella Cammarata[2], Stefania Bianchi Marzoli[3], Diletta Santarsiero[2], Davide Dazzi[4], Alessandra Bottari De Castello[5], Elena Giuliana Taroni[5], Francesco Viola[6], Luca Persani[7], Paolo Beck-Peccoz[8]

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Background: Resistance to thyroid hormones syndrome (RTHβ) is a rare condition caused by dominant-negative mutations in the TR gene. In animal models, the TRβ regulates the commitment of the cones toward the long/medium wavelength (L/M)-phenotype, by inhibiting the short wavelength-(S-) cone development but no data on the colour vision are available in patients.

Patients: 17 RTHβ patients and 27 unaffacted controls were examined. Six patients inherited the disorder from the mother, 3 from the father, 5 carried de-novo mutations while the inheritance was unknown in the remaining 3.

Methods: We assessed thyroid function status, and a complete ophthalmic exam, including color-vision tests (HRR and Farnsworth 100-Hue), optical coherence tomography (OCT, Spectralis) and ISCEV standard full-field electroretinogram (ERGs) and S-cone ERGs at high flash strength.

Results: Farnsworth Total Score Error (√TES) was higher in RTHβ compared to controls ($p < 0.0004$). The mean OCT macular thickness was not different between the two study groups ($p = 0.54$). The mean dark-adapted DA0.01 and 10 ERG responses were reduced in RTH compared to controls, ($p = 0.02$ and 0.018, respectively). No significant differences were found in the light-adapted responses, although mean LA3.0 ERG was lower in RTHβ compared to controls (mean ± SD 134.4 ± 35.93 and 151.8 ± 44.17, respectively).

The L/M component amplitude was lower in RTHβ than controls ($p = 0.018$), while no differences were found in the S-cone component.

In RTH, no correlations were found between serum TH levels and the √TES or the electrophysiological results. Furthermore, no significant differences were found between patients with maternal, paternal or de-novo inheritance.

Conclusion: This is the first evidence that RTHβ patients display qualitative and quantitative functional defects of the retinal photoreceptors. Interestingly, these functional defects occur independently of endogenous levels of serum thyroid hormone or the prenatal exposure to high or normal levels of maternal thyroid hormone.

Table 1. (for abstract time 12.15–12.30)

	GBP	VBG	OB	p-value		
				GBP vs. VBG	GBP vs. OB	VBG vs. OB
B-UIE (µg/day) [n]	215 [187]	201 [187]	203 [186]	ns	ns	ns
2-UIE (µg/day) [n]	191 [181]	187 [177]	202 [179]	ns	ns	ns
10-UIE (µg/day) [n]	161 [126]	149 [144]	189 [126]	ns	0.009	0.002
Dietary iodine intake (µg/week) [n]	660 [138]	900 [147]	700 [137]	<0.001	ns	0.002
Use of multivitamins (%) [n]	39.1 [54]	24.2 [37]	28.4 [38]			
Proportion of multivitamins containing iodine (%) [n]	16.7 [9]	18.9 [7]	5.3 [2]			
10-UIE-iodine (µg/day) [n]	209 [12]	285 [14]	234 [5]	ns	ns	ns
10-UIE-non-iodine (µg/day) [n]	156 [111]	168 [126]	186 [117]	ns	0.007	0.001

12.45–13.00

THYROID STIMULATING HORMONE IS ASSOCIATED WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER IN GERMAN CHILDREN

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Objective: Maternal thyroid hormone insufficiency is associated with attention deficit/hyperactivity disorder (ADHD) in children. The behavioral outcomes of children afflicted with thyroid hormone insufficiency are incompletely understood. The objective of this study was to investigate how serum thyroid stimulating hormone (TSH), free triiodothyronine (fT3), and free thyroxine (fT4) are related to suspected and confirmed cases of ADHD in German children.

Methods: Data of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS, collected between 2003 and 2006) was used for analysis. After distinguishing children from adolescents by maturity age (Tanner scale), a total of 8,688 children were included. Exclusion criteria were age <3 years, thyroid medication and missing data. ADHD symptoms were assessed with the Strength and Difficulties Questionnaire (SDQ). Hyperactivity subscale scores ≥ indicated ADHD symptoms. Clinically confirmed ADHD cases were reported in self-administered parent questionnaires. Serum TSH, fT3 and fT4 concentration were determined enzymatically and associated with suspected as well as confirmed cases of ADHD using logistic regression models adjusted for sex and age.

Results: ADHD was suspected in 486 children (5.6%) and confirmed in 420 (4.8%). Higher TSH concentration was related to lower odds in confirmed [OR 0.901; 95% CI (0.812; 0.999); $p < 0.05$] but not in suspected ADHD cases. A strong inverse trend for the relation between ft4 and confirmed cases of ADHD was also found [OR 0.952; 95% CI (0.904; 1.004); $p = 0.07$]. No associations were observed with fT3.

Conclusion: In children low TSH and ft4 is related with an increased risk of ADHD. This is the first large investigation to suggest that not only insufficient intrauterine exposure to thyroid hormones but also low TSH and ft4 levels in young offspring increase the risk for ADHD. Future studies need to explore how thyroid hormones influence child behavior.

Oral Session 13 (Basic): Basic Mechanisms in Graves' Disease

11.00–11.15

OXIDATIVE STRESS IN SKIN ADIPOCYTES FROM GRAVES' PATIENTS

Marie-Christine Many[1], *Joris Virginie*[2], *Marique Lancelot*[1], *Van Regemorter Elliott*[3], *de Ville de Goyet Christine*[1], *de Bournonville Marc*[1], *Antonella Boschi*[4], *Mourad Michel*[5], *Chantal Daumerie*[5], *Julie Craps*[1]
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Background: Graves' orbitopathy (GO) and pretibial myxedema are associated with Graves' hyperthyroidism. The link between these 3 manifestations may be explained by the immune reaction against the TSH-receptor which has been localized on fibroblasts of pretibial dermis. Pretibial skin is the commonest region of edema but other sites (face, arms, shoulders…) are also affected. The aims of our study were to analyze the morphology of neck skins in Graves' patients, to evaluate the oxidative stress (OS) in adipocytes from the hypodermis region, and to determine the roles of caveolin-1 (Cav-1) and NADPH oxidase (Nox)-2 in OS. Indeed, Cav-1 is involved in glucose transport inside the adipocytes via regulation of Glut 4 translocation, and the reduction of glucose supply is associated to expression of Nox-2 generating superoxide anions into cytoplasm.

Materials and Methods: Neck skin samples were obtained from patients operated for multinodular goiters (controls, n = 10) or for Graves' disease (n = 10). They were processed for a morphological analysis on toluidine blue stained sections and for immunodetection of HNE (lipid peroxidation and OS), catalase (detoxification of H2O2), Cav-1, and Nox-2.

Results: The staining with toluidine blue demonstrates that mast cells were very numerous all over the dermis and hypodermis in Graves' patients. Mast cells are involved in the production of glycosaminoglycans dissociating collagen fibers which showed a fragmented aspect.

HNE and catalase immunolabelling was increased in Graves' adipocytes, as compared to controls, indicating OS. Cav-1 expression was reduced in Graves' adipocytes whereas Nox-2 expression was increased.

Conclusion: Mast cells infiltration in several tissues is a hallmark of Graves' disease as well as the oxidative stress of adipocytes in the orbit and in the skin. This could be due to a downregulation of Cav-1 and a reduced supply of glucose associated to Nox-2 overexpression.

11.15–11.30

INCREASE OF NOX-4, VEGF AND GLUT-1 IN GRAVES' DISEASE

Julie Craps[1], *Joris Virginie*[2], *Hepp Michael*[1], *Papasokrati Lida*[1], *Werion Alexis*[1], *de Ville de Goyet Christine*[1], *de Bournonville Marc*[1], *Chantal Daumerie*[3], *Mourad Michel*[3], *Marie-Christine Many*[1]
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Introduction: Graves' disease (GD) is an autoimmune disease associated to hyperthyroidism. Oxidative stress due to an unbalance between ROS production and antioxidant defenses is considered as a pathogenic mechanism of GD, although the source of ROS has not been elucidated.

In this study, we analyzed firstly the expression of NADPH oxidases, Nox-2 and Nox-4, in GD as compared to controls, Nox-2 being a source of superoxide anions and Nox-4 generating H2O2 inside the cytoplasm. Secondly, we correlated the Nox-derived ROS production with the expression of VEGF and Glut-1.

Material and Methods: Thyroid samples were obtained from patients operated for multinodular goiters (controls, n = 6) or for GD (n = 6). They were processed for immunodetection of T4, HNE (oxidative stress), catalase (H202 detoxification) caspase-3 (apoptosis), Nox-2, Nox-4, VEGF and Glut-1, or for Western Blots (Glut-1 and Nox-4).

Results: In GD, the follicles were hyperactive and T4 was detected in all the follicular lumina. The thyrocytes were columnar and surrounded by large capillaries. HNE expression was increased as compared to controls indicating lipid peroxidation and ROS production.

Nox-2 was not modified as compared to controls, whereas, Nox-4 immunolabelling was strongly increased all over the cytoplasm. However, the proportion of caspase-3 labeled nuclei remained low, suggesting that the intracytoplasmic H2O2 production was tightly controlled by antioxidant defenses, as demonstrated by the strong expression of catalase.

The expression of VEGF and of Glut-1 was also highly increased in GD thyroids, the increase of Glut-1 being statistically significant at the protein level on western blots.

Conclusion: Nox-4 derived ROS could induce the overexpression of two hypoxic markers: VEGF and Glut-1, as already shown in cancers but not in Graves' disease. Increased VEGF expression could be related with the high vascularization in GD.

11.30–11.45

CHARACTERISTICS OF HYALURONAN AND PAI-1 EXPRESSION IN CULTURES OF ORBITAL FIBROBLASTS

Erika Galgoczi[1], *Florence Jeney*[1], *Annamaria Gazdag*[1], *Annamaria Erdei*[1], *Mónika Katkó*[1], *Domonkos M. Nagy*[1], *Bernadett Ujhelyi*[2], *Zita Steiber*[2], *Ferenc Gyory*[3], *Eszter Berta*[1], *Endre V. Nagy*[1]

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Increased proliferation rate and hyaluronan (HA) overproduction of orbital fibroblasts (OFs) are important factors during the course of Graves' orbitopathy (GO). The plasminogen activator inhibitor type 1 (PAI-1) has a role in maintaining a supporting scaffold for proliferating cells, and elevated expression of PAI-1 results in accumulation of extracellular matrix components. It is unclear whether alterations in PAI-1 synthesis could contribute to the pathomechanism of GO.

OFs established from orbital connective tissue samples of GO (n = 5) and non-GO patients (n = 5) were plated at different cell densities to obtain cultures with different proliferation rates. PAI-1 protein and mRNA expression, HA production, mRNA expression of HA synthases (HAS1, 2, and 3) and hyaluronidases (HYAL1 and 2) were measured. The effect of transforming growth factor β (TGF-β), a potent inducer of PAI-1 production was tested in this model.

The proliferation rate of OFs declined with increasing cell densities, and correlated positively with PAI-1 production ($r = 0.70$, $p < 0.0001$), but not with HA synthesis per cell. HAS2 was found predominant among synthases in OFs. 24-hour treatment with TGF-β stimulated PAI-1 protein level in a proliferation rate dependent manner ($p < 0.00001$), achieving five fold increase at postconfluent cultures, where elevated HA synthesis was also observed. The same pattern was observed in PAI-1 and HAS1 mRNA expression up to 12 and 500 fold increase, respectively. No differences were detected between OFs derived from GO and non-GO orbital connective tissues.

TGF-β induced HA secretion diminishes contact inhibition and, together with increased PAI-1 expression, may promote proliferation and leukocyte infiltration. Since OFs responded in the same manner to TGF-β regardless of their origin, no inherent difference was assumed between GO and non-GO OFs in this respect.

11.45–12.00

IDENTIFICATION OF A NEW HIGHLY TSH-RECEPTOR-SELECTIVE SMALL MOLECULE INHIBITOR

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Graves' Disease (GD) and Graves' Ophthalmopathy (GO) are triggered by thyroid stimulating antibodies, which pathologically activate the TSHR in the thyroid and in retroorbital fibroblasts respectively. Drugs acting directly at TSHR are not available in clinics. Neumann et al. (Endocrinology 2014) have previously reported a small molecule inverse agonist (ANTAG3) identified by modifying a TSHR agonist.

We here conducted a high-throughput screen for TSHR inhibitors of the FMP ChemBioNet library. In a 384-well format 16544 compounds were screened using a commercial enzyme fragment complementation technique in CHO cells stably expressing TSHR (z-factor 0.62–0.9). Inhibition of cAMP accumulation at 50 µM compound induced by 9.8 mIU/ml bTSH was determined. In a secondary screen hits and derivatives were verified by radioimmunoassay in stable HEK293-TSHR cells. Alamar blue and BrdU toxicity tests were performed in several cell lines.

The primary screen including concentration-dependent studies and excluding TSHR-independent inhibition in TSHR-free CHO cells stimulated by forskolin yielded 12 TSHR-related inhibitors. Three showed over 50% inhibition also in the secondary screen. Similar compounds with several chiral centers were purchased. Structure-function studies and subsequent own stereoselective synthesis and separation of enantiomers led to the inhibitor S37 with an IC_{50} in comparable low micromolar range as ANTAG3. In contrast to other hits, S37 was highly selective for TSHR and did not at all affect the closely homologous LH- and FSH-receptors. Additionally S37 inhibits the human thyroid stimulating GD derived antibody M22 with similar potency comparable to bTSH inhibition. No toxicity of S37 was observed at up to 100 µM in HEK293 cells as well as in hepatocellular carcinoma cell lines.

We have identified by screening and relative stereochemistry a new small molecule as a TSHR inhibitor with enhanced selectivity over closely related receptors, with potential to be further developed as therapeutic agent for GO. (Supported by DFG-KR1273/4-1).

12.00–12.15

THE EXPRESSION OF NEONATAL FC RECEPTOR IN THYROCYTES OF HASHIMOTO'S THYROIDITIS

Yang Zhang[1], *Chenxu Zhao*[1], *Ying Gao*[1], *Lanlan Zhao*[2], *Suxia Wang*[1], *Hong Zhang*[1], *Guizhi Lu*[1], *Yanming Gao*[1], *Xiaohui Guo*[1]

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Background: Thyroglobulin (Tg) antibody (TgAb) and thyroid peroxidase (TPO) antibody (TPOAb), mainly immunoglublin (Ig) G class, can mediate antibody-dependent cell-mediated cytotoxicity (ADCC) *in vitro*. However, it's unclear whether there are any molecules that can facilitate the transport of TgAb and TPOAb from basolateral to thyroid follicular lumen and apical membranes of thyrocytes where Tg and TPO reside *in vivo*. The neonatal Fc receptor (FcRn), an IgG and albumin transport receptor, is a candidate molecule to mediate these processes.

Objective: To evaluate the expression of FcRn on normal and Hashimoto thyroiditis' thyrocytes.

Methods: We detected the expression of FcRn in eight primary thyrocytes cultures, which were divided into two groups: normal (n = 4) and Hashimoto' s thyroiditis (HT) (n = 4) groups. The expression of FcRn on mRNA and protein levels was determined by polymerase chain reaction (PCR) and western blot respectively. Localization of FcRn in thyrocytes was demonstrated by immunoelectron microscopy. Laser confocal double immunofluorescence staining method was used to detect FcRn and the internalized human IgG in thyrocytes. Stimulation experiments on the regulation of FcRn expression were performed with T helper cell (Th) 1 (IFN-γ, TNF-α) and Th2 cytokines (IL-10, IL-4).

Results: FcRn was expressed in normal thyrocytes and in smaller amounts in HT thyrocytes. The localization of FcRn in thyrocytes was mainly in cytoplasm, membranes, mitochondrions and transport vesicles. The internalized human IgG was colocalized with FcRn in thyrocytes. FcRn in normal and HT thyrocytes were downregulted in response to Th1 and Th2 cytokines.

Conclusion: FcRn might be involved in IgG transport and metabolism in thyrocytes. These results indirectly support a pivotal role for FcRn in the pathogenesis of the HT.

12.15–12.30

EFFECTS OF OXIDATIVE STRESS ON SIRT-1, HIF-1α AND GLUT-1 IN HASHIMOTO'S THYROIDITIS

Hepp Michael[1], *Joris Virginie*[2], *Werion Alexis*[1], *de Ville de Goyet Christine*[1], *Chantal Daumerie*[3], *Mourad Michel*[3], *Marie-Christine Many*[1], *Julie Craps*[1]

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Introduction: Oxidative stress (OS) present in Hashimoto's thyroiditis (HT) is driven by a Th1 cytokines response interfering with the normal function of thyrocytes. It has already been demonstrated that NADPH oxidase (Nox)-2 is upregulated in Th1 cytokines treated thyrocytes and in HT thyroids leading to an increase of intracellular reactive oxygen species (ROS). It is also known in other cell types that ROS inhibit Sirtuin (Sirt)-1 which is able to prevent hypoxia-inducible-factor (HIF)-1α stabilization upregulating Glut-1

expression. The aim of this study was to determine if Sirt1 and HIF-1α are modulated in HT thyroids and could regulate the glycolytic state of the thyrocytes via the Glucose transporter (Glut)-1 expression.

Methods: The expression of Sirt-1, HIF-1α and Glut-1 were analyzed by western blot in human primary cultures of thyrocytes incubated with Th1 cytokines (Interleukin-1α and Interferonγ) to mimic HT. In thyroid samples from HT patients those proteins were analyzed by immunohistochemistry and western blot and compared to paranodular tissue from multinodular goiter patients (controls). In addition, Nox-2 labelling was performed in HT thyroids.

Results: A significant decrease of Sirt1 protein expression was observed in human thyrocytes incubated with Th1 cytokines. Moreover HIF-1α and Glut-1 proteins expression was highly increased. In sections of HT thyroids, a main heterogeneity of follicles was perceived. In normal type 1 follicles, no changes were observed. In hyperactive type 2 follicles we detected high Nox-2, Glut-1 and HIF-1α expressions and inactive type 3 follicles (unable to form T4) did not express those proteins.

Conclusion: The OS mediated by an increase of Nox-2 leads to a reduction of Sirt1 and upregulates HIF-1α and Glut-1. This suggests a link between OS and glucose uptake via Sirt-1 in Hashimoto's thyroids, as in cancer.

12.30–12.45

HYPOXIA-DEPENDENT HIF-1 ACTIVATION IMPACTS ON TISSUE REMODELING IN GRAVES' ORBITOPATHY

Gina-Eva Görtz[1], *Mareike Horstmann*[1], *Buena Delos Reyes*[1], *Joachim Fandrey*[1], *Anja Eckstein*[2], *Utta Berchner-Pfannschmidt*[1]
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Graves' orbitopathy (GO) is an inflammatory autoimmune condition characterized by inflammation, enlargement and remodeling of the orbital tissues. However, inflammation with tissue expansion in a closed compartment like the bony orbit can cause tissue hypoxia and consequently induce hypoxia-inducible factor-1 (HIF-1) pathways. In this study we investigated whether HIF-1 action impacts on tissue remodeling in GO with the aim to identify possible new targets for therapeutic intervention. Orbital tissues from GO patients and healthy control persons (Ctrl) were collected and orbital fibroblasts (OF) were culture. To investigate the impact on tissue remodeling we analyzed HIF-1 dependent vascular endothelial growth factor (VEGF) release and adipogenic differentiation in response to hypoxia by using HIF-1α siRNA and HIF-1 activation inhibitor BAY 87-2243. Higher HIF-1α levels in OF were correlated with clinical activity score of GO patients. In response to hypoxia HIF-1 dependent VEGF secretion was enhanced in GO-derived OF compared to Ctrl-OF and as an *in vivo* consequence, we found a higher vessel density in GO-tissue than in Ctrl-tissue. Hypoxia strongly stimulated HIF-1 dependent adipogenesis and adiponectin release of GO-derived OF and enhanced thyroid-stimulating hormone receptor (TSHR) mediated adipogenesis. Hypoxia impacts on tissue remodeling in GO by stimulating angiogenesis and adipogenesis through activation of HIF-1 dependent pathways in OF. Our results offer an explanation why in some patients anti-inflammatory/immunosuppressive therapeutic strategy is ineffective but decompression can improve the outcome. Drug targeted inhibition of HIF-1/VEGF may provide a therapeutic strategy to control tissue expansion in GO.

12.45–13.00

ORBITAL FIBROBLASTS FROM A MURINE MODEL OF GRAVES' ORBITOPATHY SHOW A UNIQUE PHENOTYPE PROMOTING ADIPOGENESIS AND HYALURONAN SECRETION

Gina-Eva Görtz[1], *Moshkelgosha Sajad*[1], *Christoph Jesenek*[1], *Mareike Horstmann*[1], *Banga Paul*[1], *Anja Eckstein*[2], *Utta Berchner-Pfannschmidt*[1]
[1]University Hospital Essen, Essen, Germany, [2]Universität Essen, Essen, Germany

A mouse model of Graves' orbitopathy (GO) induced by genetic immunization of human thyrotropin hormone receptor A-subunit encoding plasmid has recently been established. The orbital pathology was characterized by adipogenesis, myopathy and fibrosis. Human orbital fibroblasts (OF) express TSHR and insulin-like growth factor 1 receptor (IGF-R) and are considered to be the pathogenic in GO. We established conditions for growing *ex vivo* cultures of mouse OF (mOF) from eye bulbar tissue of immune animals undergoing experimental GO and controls. Early passage mOF from GO animals and controls showed characteristic fibroblast morphology and expressed mesenchymal stem cell markers including a strong expression of CD90.2 and CD40, whilst display of all other leucocyte markers was uniformly absent. Importantly, mOF derived from GO animals expressed elevated levels of TSH and IGF-1 receptors and adipogensis compared to controls. Activation of TSHR and/or IGF-1R in mOF cultures established from GO animals with TSH, monoclonal thyroid stimulating antibody M22 or IGF-1 induced hyaluronan secretion to significantly elevated levels from controls. In conclusion, mOF established from GO model recapitulate the pathogenicity of human OF from GO patients by their increased propensity for adipogenesis and hyaluronan production leading to disease activity. To our knowledge, this is the first report to show the OF from the preclinical mouse GO model have intrinsic pathogenic properties and will prove useful in understanding the molecular and genetic changes during different stages of adipogenesis and hyaluronan deposition to provide future novel targets for treatment of GO.

European
Thyroid Journal

Poster Plan

Saturday, 3rd September, 16.00–17.00

Topic	Posters	Room
P1 – 01 Hyperthyroidism	P1-01-01 – P1-01-11	1
P1 – 02 Iodine	P1-02-01 – P1-02-10	2
P1 – 03 Clinical Autoimmunity 1	P1-03-01 – P1-03-11	3+4
P1 – 04 Case Reports	P1-04-01 – P1-04-11	16
P1 – 05 Thyroid Cancer Diagnostic I	P1-05-01 – P1-05-09	14
P1 – 06 Thyroid Cancer Pathogenesis	P1-06-01 – P1-06-10	12
P1 – 07 Thyroid Cancer / Basic	P1-07-01 – P1-07-10	13+15
P1 – 08 Analogues + Others / Basic	P1-08-01 – P1-08-10	East Lounge / 8+9+10+11 (Main Auditorium)

Sunday, 4th September, 12.00–13.00

Topic	Posters	Room
P2 – 01 Clinical Autoimmunity 2	P2-01-01 – P2-01-11	1
P2 – 02 Hypothyroidism 1	P2-02-01 – P2-02-09	2
P2 – 03 Goiter 1	P2-03-01 – P2-03-10	3+4
P2 – 04 Reproduction	P2-04-01 – P2-04-10	16
P2 – 05 Thyroid Cancer Diagnostic II	P2-05-01 – P2-05-08	14
P2 – 06 Thyroid Cancer Therapeutics	P2-06-01 – P2-06-10	12
P2 – 07 Thyroid Cancer – Clinical I	P2-07-01 – P2-07-09	13+15
P2 – 08 Transporters and Others	P2-08-01 – P2-08-08	East Lounge / 8+9+10+11 (Main Auditorium)

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Monday, 5th September, 12.00–13.00

Topic	Posters	Room
P3 – 01 Clinical Thyroidology	P3-01-01 – P3-01-11	1
P3 – 02 Hypothyroidism 2, Children + Regulation	P3-02-01 – P3-02-09	2
P3 – 03 Goiter 2 and Environmental	P3-03-01 – P3-03-09	3+4
P3 – 04 Cardio, Brain and Metabolism	P3-04-01 – P3-04-10	16
P3 – 05 Thyroid Cancer Diagnostic III	P3-05-01 – P3-05-10	14
P3 – 06 Thyroid Cancer – Clinical II	P3-06-01 – P3-06-10	12
P3 – 07 Thyroid Cancer – Clinical III	P3-07-01 – P3-07-10	13+15
P3 – 08 Basic Autoimmunity and Thyroidology	P3-08-01 – P3-08-09	East Lounge / 8+9+10+11 (Main Auditorium)

European Thyroid Journal

Presenting authors are underlined

P1-01 Hyperthyroidism

P1-01-01

EFFECT OF SELENIUM ON HYPERTHYROIDISM IN PATIENTS WITH GRAVES' DISEASE TREATED WITH METHIMAZOLE: RESULTS OF A RANDOMIZED CLINICAL TRIAL

Ilaria Ionni[1], *Marenza Leo*[1], *Paola Premoli*[2], *Giovanna Rotondo Dottore*[1], *Marialuisa Di Cera*[2], *Lorenza Sassi*[2], *Paolo Vitti*[1], *Luigi Bartalena*[2], *Claudio Marcocci*[1], *Michele Marinò*[1]
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Objectives: Selenoproteins play an important antioxidant role in thyroid homeostasis. In conditions of selenium deficiency, protection from free-radicals is inadequate, which in Graves' disease (GD) may contribute thyroid and peripheral tissue damage, thereby favouring antigen presentation and the same time worsening signs and symptoms of hyperthyroidism. In this regard, selenium may be beneficial for GD. The aim of the present randomized clinical trial was to evaluate the effects of selenium in patients with Graves' hyperthyroidism treated with methimazole (MMI), both on short-term biochemical control and on peripheral manifestations of hyperthyroidism.

Methods: 30 patients with newly diagnosed and untreated GD hyperthyroidism were randomized into two groups: MMI (15 patients) and MMI-selenium (15 patients). Patients in both groups were given MMI, and patients in the MMI-selenium group received also selenium 167 mcg/day. Patients were evaluated at baseline, and then after 45 and 90 days.

Results: At baseline the two groups were similar for age, gender, serum selenium levels, thyroid volume, duration of hyperthyroidism, body weight, BMI, heart rate, FT4, FT3, anti-TSH receptor autoantibodies, SHBG, total cholesterol and symptoms of hyperthyroidism (assessed by questionnaire). The administration of selenium was associated with a significant increase in serum selenium ($P = 0.0006$) in the MMI-selenium group. There were no significant differences between the two groups, both at 45 or at 90 days, in terms of control of hyperthyroidism (FT4 and FT3 levels). Similarly, peripheral markers of thyroid hormone action (body weight, BMI, heart rate, SHBG, total cholesterol) and the symptoms of hyperthyroidism did not differ between the two groups.

Conclusion: Selenium does not affect the short-term control of Graves' hyperthyroidism by MMI. However, it is still possible that selenium may have a positive long-term action, to investigate which further studies are needed.

P1-01-02

DIO2 POLYMORPHISMS ROLE IN GRAVES' DISEASE AND GRAVES' OPHTHALMOPATHY

Ana Paula Comarella[1], *Danilo Villagelin*[2], *Natassia Bufalo*[1], *Jessica Euflauzino*[3], *Raquel Pereira Rios*[3], *Vitoria Arbulu Pitol*[3], *Roberto Bernardo dos Santos*[3], *João Hamilton Romaldini*[3], *Laura Ward*[1]
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The type 2 deiodinase is expressed both in the thyroid gland and the intra orbital adipose tissue in Graves' disease (GD). In order to investigate its role in GD, we studied 171 GD patients (28 men and 143 women-40.08 ± 10.59 years old) treated with antithyroidal drugs (ATD). Seventeen evolved with euthyroidism after 12 months upon treatment completion and 154 relapsed and were further treated with radiodine (100), low dose of methimazole (MMI) (48) or submitted to thyroidectomy (06). Ninety patients presented Graves' Ophthalmopathy (GO), 35 in the low-MMI dose and 49 in the radiodine group. We employed TaqMan SNP Genotyping to analyze the polymorphisms of *DIO2* rs 225010, rs225014, rs225015 and rs 12885300 using DNA extracted from peripheral blood of all patients.

The inheritance of TT genotype (rs12885300) was correlated with higher goiter volume by ultrasound (mean 28.89 ± 8.57) when compared with CT genotype (mean 24.36 ± 19.44), $p = 0.0491$ and was more frequent in patients with new-onset of GO (25%) following radiodine and CC genotype with its absence (60.61%-$p = 0.0320$). The CT genotype of rs225014 was more frequent in patients with positive anti Tg antibodies (TgAb-59.32%-$p = 0.0035$) when compared with negative TgAb patients and CC genotype was associated with more body weight variation at first year of treatment with radiodine (mean 7.17 ± 5.33) when compared with CT (mean 1.98 ± 4.5) and TT (mean 5.23 ± 5.55) genotype, $p = 0.00105$. There was no relationship of the investigated polymorphisms with relapse or remission of GD patients treated with ATD; GO presence/absence and severity of the eye disease measured with the Clinical Activity Score (CAS); serum levels of free T4, TRAb and TPOAb; impaired glycose metabolism, type 2 diabetes and arterial hypertension.

The polymorphisms of *DIO2* rs 225014 and rs12885300 are associated with clinical features of GD and new-onset of GO following Radiodine, respectively.

P1-01-03

DIAGNOSTIC UTILITY OF ACOUSTIC STRUCTURE QUANTIFICATION FOR EVALUATION OF RADIATION SIALADENITIS AFTER RADIOACTIVE IODINE THERAPY

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Background: Acoustic structure quantification (ASQ) software is used to analyze statistical information on acquired echo signals. To date, no study has quantified the echogenicity of the salivary gland using this tool.

Objective: To determine the ability of ASQ to distinguish the normal salivary gland from a gland with radiation sialadenitis (RS) after radioactive iodine (RAI) therapy. To compare between the asymptomatic patients with RAI treatment and RS group.

Methods: A total of 192 salivary glands in 96 consecutive patients (mean age, 47.6 years) were divided into three groups: control, asymptomatic patients who had undergone RAI therapy, and those with chronic RS. The ASQ results are presented as Cm^2 (modified chi-squared distribution) histograms showing the mode, average, ratio, blue-mode, and blue-average. The resulting ASQ values were compared by multinomial logistic regression analysis. Receiver Operating Characteristic (ROC) curves were constructed to determine the diagnostic performance.

Results: The mean ASQ values of patients with chronic RS, or asymptomatic patients who had undergone RAI therapy, were significantly greater than those of patients with normal salivary glands ($p < 0.001$). Multinomial logistic regression analysis showed that the ASQ data were significant in terms of mode, average, ratio, blue-mode, and blue-average ($p < 0.001$). When normal control data served as the reference, the ratio was associated with the highest odds ratio in patients with RS. ROC analysis showed moderate diagnostic performance.

Conclusion: ASQ can objectively differentiate RS from normal salivary tissue, and is thus valuable for clinically diagnosing RS after RAI therapy.

P1-01-04

FALSELY ELEVATED FT4 OR FT3 DUE TO INFERENCE SUBSTANCES IN THYROID HORMONE ASSAYS

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Background: When discordance between the clinical status and the thyroid function tests (TFT) status exists, assay interference must be considered.

Patients: Six cases with elevated fT4 and/or fT3 in the presence of normal or high TSH were tested for assay interference in Region Zealand, Denmark in Q3-Q4 2015.

Methods: The routine platform for TFT analysis is a two-step immunoassay using antibodies of mouse (fT4) and sheep (fT3) origin (Siemens Dimension Vista). TSH, fT4 or TT4, fT3 or TT3 measurements were repeated after dilution and were assessed on two different platforms (Roche Cobas 6000 and Abbott Diagnostics Architect) both two-step immunoassays using antibodies of sheep and mouse origin respectively. One sample was incubated with heterophilic blocking agent (HBA – Scandibodies Laboratory Inc.).

Results: All samples (Table) returned normal fT4/TT4 and fT3/TT3 levels when measured in the alternatives platforms while TSH returned comparable with the routine platform results. Test results from the dilutions were non-linear, supporting interference. Test for heterophilic antibodies with the HBA in the one sample was negative.

Discussion: The discordant results in fT4 and/or fT3 levels from the same sample in the alternatives assays and the abnormal dilutions suggest the presence of a factor causing assay interference. The three common substances that interfere with TFT immunoassays are heterophile antibodies, rheumatoid factors and autoantibodies. The negative HBA test indicates another interfering source than heterophilic antibodies. The major difference between the Architect and Cobas versus the Siemens assays is that there is no washing step between the two steps in the Siemens assay.

Conclusion: Assay interference should be considered when incongruity between the clinical status and the TFT is present. Incorrect laboratory results may lead to unnecessary examinations and inappropriate treatment. Assays including a washing step between the two steps seem better protected against interfering antibodies.

P1-01-05

WITHDRAWN

P1-01-06

MONITORING THE PREVALENCE OF THYROID DISORDERS IN THE ADULT POPULATION OF NORTHEAST GERMANY

Rehman Khattak[1], *Till Ittermann*[2], *Matthias Nauck*[3], *Harald Below*[4], *Henry Völzke*[5]

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Background: Only few studies like ours have investigated the effect of long-term stable iodine supply on thyroid disorders in a historically iodine deficient population, but not with a long follow up time between 2000 and 2010 in Northeast Germany.

Methods: Data derived from two independent population-based cohorts of the Study of Health in Pomerania (SHIP-0 [1997–2001] and SHIP-TREND [2008–2012]) comprising 4308 and 4420 subjects, respectively. Diagnosed thyroid disorders were assessed. Thyroid gland dimensions were examined by ultrasound. Serum thyrotropin (TSH) and autoantibodies to thyroperoxidase (anti-TPO Abs) levels were measured from blood samples.

Results: Median urinary iodine excretion levels decreased from 123.0 µg/l to 112.0 µg/l ($p \leq 0.001$) between 2000 and 2010. The prevalence of known thyroid disorders increased from 7.6% [CI 6.9–8.5] to 18.9% [CI 17.6–20.1] and of thyroid medication from 6.2% to 11.1%. The prevalence of goiter decreased from 35.1% to 29.4% ($p \leq 0.001$), while the prevalence of positive anti-TPO Abs decreased from 3.9% to 2.9% ($p = 0.022$). Median serum TSH levels increased from 0.69 mIU/l to 1.19 mIU/l ($p \leq 0.001$). Consequently, prevalence of high TSH (mIU/l) increased from 2.6% to 2.9% ($p = 0.452$), and low TSH (mIU/l) decreased from 6.6% to 6.4% ($p = 0.737$).

Conclusion: The decreased prevalence of iodine-deficient disorders and a stable prevalence of markers of autoimmune thyroid disorders argue for an improved iodine supply of the adult population in Northeast Germany. In contrast, the prevalence of diagnosed thyroid disorders and the intake of thyroid medication increased, which, however, might be related to inappropriate therapeutical decisions.

Table 1. (for abstract P1-01-04)

	1	2	3	4	5	6
Age (years)	71	64	42	41	42	60
TSH (IU/l)*	6.10	1.12	2.12	2.72	0.31	0.68
Assay interfered	fT4	fT4/fT3	fT3	fT4	fT4/fT3	fT3
Dimension Vista (pmol/l)*	fT4 41.9	fT4 67.07/fT316.4	fT3 29.2	fT4 39.7	fT4 30.3/ T3 23.0	fT3 13.0
Cobas 6000 (pmol/l)**	fT4 14.7	fT4 14.4/fT3 6.1	fT3 4.6	fT4 15.9	fT4 14.6/fT3 4.1	fT3 4.4
Architect (nmol/l)***	TT4 78.0	TT4 69.6/TT3 1.34	TT3 1.52	fT4 15.3	TT4 95/TT3 N/A¶	TT3 1.5

Reference Interval: * TSH 0.3–4.0 IU/l, fT4 10.0–26.0 pmol/l, fT3 3.3–6.1 pmol/l; ** fT4: 14–23 pmol/l, fT3: 4.1–6.9 pmol/l; *** TT4 67–134 nmol/l, TT3 1.35–2.33 nmol/l; ¶ no available.

P1-01-07

FEATURES OF NEWLY DIAGNOSED GRAVES' DISEASE IN A LARGE LONGITUDINAL COHORT STUDY

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Aim of this study was to assess whether the Merseburg triad (hyperthyroidism, goiter, orbitopathy) still characterizes newly diagnosed Graves' disease (GD). To this purpose, a longitudinal study was carried out on a cohort of 283 consecutive, untreated GD patients (211 women, 72 men; median age 47.4 years; duration of disease <6 months) during the years 2010–2014. Goiter, assessed ultrasonographically, was absent in 127 patients (45%), small (<1.5-fold above upper normal limit) in 85 patients (30%), moderate (1.5–2.5-fold above upper normal limit) in 51 patients (18%), large (>2.5-fold above upper normal limit) in 20 patients (7%). Hyperthyroidism was subclinical (normal FT4, ≤18 pg/ml) in 49 patients (17.4%), mild (FT4 ≤1.5-fold above upper normal limit, range 18.1–27 pg/ml) in 83 patients (29.3%), moderate (FT4 >1.5–2.5-fold above upper normal limit, range 27.1–44 pg/ml) in 113 patients (39.9%), severe (FT4 >2.5-fold above upper normal limit, >44 pg/ml) in 38 patients (13.4%). GO was present in 57 patients (20.2%), but was moderate-to-severe and active (CAS >3) in only 7 patients (2.5%). We designed a GD severity score: for each of the 3 components of the Merseburg triad, a score of 1 was given for normal findings, 2 for mild, 4 for moderate, 8 for severe findings. The resulting severity score could range from 3 to 24. The severity score was mild (3–5) in 38.6%, moderate (6–8) in 33.3%, severe (>9) in 28.1% of patients. In multivariate analysis, moderate and severe scores were associated with an increased risk of persistent hyperthyroidism at 6 months (RR 1.5 and 2.5, respectively) and at 12 months (RR 1.4 and 1.7, respectively) during antithyroid drug treatment.

In conclusion, the majority of patients with newly diagnosed GD (and short duration of disease) have no or small goiter, normal or slightly elevated FT4, no or mild GO, and an overall mild-to-moderate disease.

P1-01-08

THE CLINICAL VALUE OF REGULAR THYROID FUNCTION TESTS DURING AMIODARONE TREATMENT

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Background: Amiodarone is used for the maintenance of sinus rhythm in patients with arrhythmias, but is regularly associated with thyroid dysfunction (amiodarone-induced thyrotoxicosis (AIT) or -hypothyroidism (AIH)). As the onset of AIT/AIH may often be sudden, the value of regularly monitoring amiodarone treated patients for thyroid dysfunction is unclear. We, therefore, have observed the frequency in which overt thyroid dysfunction was preceded by subclinical thyroid dysfunction.

Method: To analyze the yield of regular thyroid function tests during amiodarone treatment, we retrospectively studied 303 patients treated with amiodarone in a single university hospital setting. AIT was defined as TSH level below the reference range (0.25 mU/l) in combination with an elevated free thyroxine (FT4). AIH was defined as a TSH level above the normal-range (10.0 mU/l) in combination with normal/elevated FT4. Subclinical thyroid dysfunction was defined as TSH within the subclinical range (sAIT: 0.25–0.5 mU/l; sAIH 4.0–10.0 mU/l) and elevated/normal FT4.

Results: 200 (66%) male and 103 (34%) female were evaluated, 260 atrial/43 ventricular arrhythmias, mean age was 62 ± 12.0 years. During a mean follow-up of 4.6 ± 4.2 years, 77 (25%) patients developed overt thyroid dysfunction (44 AIT/33 AIH). A significantly higher incidence of subclinical events (65 sAIT/62 sAIH) was observed in comparison to overt events for both AIT ($p = 0.015$) and AIH ($p < 0.001$). In 35 of 77 (45%) patients AIT/AIH was preceded by a sAIT/sAIH (16/44 for AIT and 19/33 for AIH). Conversely, of 127 sAIT/sAIH cases, 35 (28%) were followed by overt AIT/AIH.

Conclusion: For the majority of patients who developed AIT/AIH, earlier thyroid function tests showed no subclinical AIT/AIH. Only a minority of subclinical events was followed by AIT/AIH. Our data suggests limited value of regular testing of thyroid function to predict overt thyroid dysfunction in patients on amiodarone treatment.

P1-01-09

IS CHROMOGRANIN A BIOMARKER FOR THYROID DYSFUNCTION?

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Objective: Chromogranin A (CgA) is stored and secreted by the thyroid gland. A recent report suggested pathological serum values in patients with thyroid dysfunction. This novel, prospective and longitudinal study evaluates the clinical relevance of CgA in hyperthyroidism.

Methods: CgA and TSH receptor antibodies (Abs) were measured with an automated, time-resolved amplified cryptate emission method (Brahms TRAK and CgA II Kryptor, Thermo Scientific, Henningsdorf, Germany). Thyroid-related hormones (TSH, FT4, and FT3) and Abs (thyroperoxidase and thyroglobulin) were measured with commercially available assays (Architect, Abbot, Wiesbaden, Germany).

Results: Sixty four well-characterized, untreated and hyperthyroid patients (median age 47 years, 52 female (76.5%) with Graves' disease (GD) and 47 healthy controls (40 years, 33 female (67.3%) were included. CgA tested negative in all controls (cut-off <102 ng/ml) but positive in eight of 64 (12.5%) patients ($p < 0.05$). The GD patients were put on methimazole (starting dose 20 mg/day) and sequentially followed for six months. In GD, CgA positively correlated with thyroglobulin Abs ($r = 0.913$, $p = 0.002$), body weight ($r = 0.883$, $p = 0.004$), age of all patients and age at diagnosis of GD (both $r = 0.4$, $p < 0.001$), while no correlations were registered with presence of Graves' orbitopathy, methimazole dose, serum levels of TSH, TSH receptor and thyroperoxidase Abs. Serum thyroid-related hormone levels normalized during antithyroid drug treatment and TSH receptor Ab levels decreased. At baseline, CgA was increased in 4/64 (6.25%, 2 female, 2 male) GD patients (median CgA 22.6 ng/ml, range 13.6–1178 ng/ml) while CgA values markedly decreased in three of four at 24 weeks (range 0–719 ng/ml). Furthermore, CgA pathologically increased in additional four female patients during methimazole treatment.

Conclusion: Serum baseline levels of CgA can be increased in hyperthyroid patients with GD while variable responses are noted during antithyroid drug treatment.

P1-01-10

SERUM 25-HYDROXYVITAMIN D IS ASSOCIATED WITH RECURRENCE OF GRAVES' DISEASE

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Objective: Graves' disease is a most common cause of thyrotoxicosis. Although medical treatment with anti-thyroid drug is commonly selected as first choice of treatment, the remission rate is low. Undetectable serum TSH receptor antibody during anti-thyroid drug therapy was considered to affect the remission of Graves' disease.

In this study, we evaluate the correlation between serum 25-hydroxyvitamin D and TSH receptor antibody and the effect of 25-hydroxyvitamin D to recurrence of Graves' disease.

Methods: Total 131 subjects diagnosed with Graves' disease and treated with anti-thyroid drug were included in our study. All of these subjects were followed-up more than 1 year after discontinuation of anti-thyroid drug. Serum 25-hydroxyvitamin D, TSH receptor antibody (both TBII and TSI) and thyroid function test were examined at the time of discontinuation of anti-thyroid drug. Recurrence was evaluated every 3 months during follow-up period. Recurrence was defined when overt thyrotoxicosis was occurred during follow-up period.

Results: Median latency period of recurrence was 185 days (range 28 to 1219 days). Recurrence was occurred in 88 subjects (67.2%). Serum 25-hydroxyvitamin D at the time of discontinuation of anti-thyroid drug was not correlated with both TBII and TSI. In cox proportional hazard regression, 25-hydroxyvitamin D level was associated with lower recurrence rate (HR 0.938, 95% CI 0.882 to 0.998, $P = 0.044$) and TBII was associated with higher recurrence rate (HR 1.232, 95% CI 0.975 to 1.557, $P = 0.080$) after adjustment of age, sex, treatment duration and seasonal variation.

Conclusion: Higher serum 25-hydroxyvitamin D level was associated with lower recurrence rate of Graves' disease. Therefore, together with TSH receptor antibody, serum 25-hydroxyvitamin D might be helpful when we predict the recurrence or remission of Graves' disease after discontinuation of anti-thyroid drugs.

P1-01-11

HOW HIGH CAN BE A TSH VALUE IN A THYROTROPINOMA? ITS CONSEQUENCES AND BEYOND

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Objective: Thyrotropinoma are a rare cause of hyperthyroidism, while in children this is even rarer. Higher values of TSH could be involved in cross-stimulation of gonadotrophin receptors.

Case Report: An 11 years girl was admitted first at 7 years with severe thyrotoxicosis, diffuse goiter and a giant pituitary adenoma. TSH, fT4, T3, were evaluated basal, during TRH and Octreotide tests. GH was measured during OGTT and IGF1, while PRL, E2, FSH and LH as basal sampling. TSH started from 3488 mU/l and at various moments, during this long evolution, ranged between 4370 mU/l and 48 mU/l. Pituitary tumor was serially evaluated by 1.5 T MRI scan, octreoscan and DOPA PET scan. She was submitted to SMSa, then to transphenoidal neurosurgery (5 times) and gamma knife surgery on the pituitary remnant. Antithyroid drugs and beta blockers were used to ensure peripheral euthyrodism, but multinodular goiter was eventually submitted to surgery, which further revealed PTC.

Results: TSH was as high as 3450 mU/l, not stimulated *iv* TRH test but suppressed by SMS analogue (octreotide) to 2450 mU/l. GH co-secretion was documented directly and by increased IGF1, despite lack of clinical signs. After three months with SMSa, she was submitted to trans-sphenoidal neurosurgery. A functional tumor remnant was at 30 mm on postero-lateral extension and TSH decreased at 950 mU/l while GH was increased at an average of 60 ng/ml, not suppressible during OGTT. Pathology confirmed the highly invasive pituitary adenoma with Ki67 at 20%, intense TSH and GH immunoreactivity. Genetic analysis-negative for AIP. Thyrotoxicosis was managed by methimazole. After γknife radiosurgery, she developed precocious puberty with telarche and big ovarian cysts, and height at + 3 SD. After a new series of SMS analogues, cyproterone and tamoxifen, E2 normalized, as well as the ovaries.

Conclusion: Thyrotropinoma in children are very aggressive tumors, impact upon height progress and pubertal development, requiring a multiple approach. The high TSH levels are involved into pathogenesis of ovarian cysts and thyroid cancer.

P1-02 Iodine

P1-02-01

DEVELOPMENT OF AN 'IODINE EXCHANGE SCORE' IN PREGNANCY AND ITS RELATIONSHIP TO THYROGLOBULIN CONCENTRATION

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Objectives: We aimed to develop an IODine EXchange score (IODEX) as a simple system of estimating iodine intake in pregnancy. To test the usefulness of the score, it was compared to serum thyroglobulin concentration, a biomarker of iodine status that relates to thyroid volume.

Methods: We used data from a study of 230 pregnant women from Oxford, UK, a region of mild-to-moderate iodine deficiency. At 12 weeks of gestation, women completed a Food Frequency Questionnaire (FFQ) and provided a serum sample that was used for thyroglobulin (Tg) measurement. Women with thyroid disease and those positive for thyroid antibodies were excluded. The iodine concentration of iodine-rich foods (milk, white fish, fish fingers/cakes, oily fish, and shellfish) was estimated from UK food tables and converted to a score on the basis that one exchange was equivalent to approximately 10 μg/iodine. For example, a portion of white fish was estimated to have 297 μg, or an exchange score of 30. The number of portions of the food consumed daily (from FFQ data) was multiplied by the exchange score for that food group and summed to give a daily IODEX score.

Results: Data were available for 174 women. The IODEX score was negatively correlated with Tg concentration ($r = –0.17$, $p = 0.03$). After controlling for age and smoking status (ex/non-smoker), women with a low IODEX score (bottom tertile, equivalent to 8 points/80 μg iodine) had significantly higher Tg (Table) and greater odds (OR 3.12 95% CI 1.34, 7.26, $p = 0.008$) of high Tg (i.e. >40 μg/l).

Conclusion: The IODEX score was predictive of serum Tg concentration in this population and suggests that a low intake of iodine-rich foods is linked to poorer iodine status and increased thyroid volume. The IODEX score needs to be tested in other studies with more comprehensive FFQ data.

Table 1. (for abstract P1-02-01)

Daily IODEX (iodine exchange) score	N	Estimated marginal mean Tg (μg/l)	p value[a]
<8	51	27	0.03
≥8	123	19	

[a] From general linear model, controlling for maternal age and smoking status.

P1-02-02

THE RELATIONSHIP BETWEEN IODINE STATUS, THYROID FUNCTION, AND THYROGLOBULIN IN A COHORT STUDY OF UK PREGNANT WOMEN

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Objectives: The thyroid-specific protein, thyroglobulin (Tg), reflects thyroid size and has potential as a functional biomarker of iodine status that is more sensitive than thyroid stimulating hormone (TSH). We aimed to explore the usefulness of this biomarker in a cohort of mildly-to-moderately iodine-deficient UK pregnant women.

Methods: We used samples and data from the 230 women recruited to the Selenium in PRegnancy INTervention (SPRINT) study. Repeated measures of urinary iodine-to-creatinine ratio, serum (TSH), and Tg were available at 12, 20, and 35 weeks of gestation. Women were dichotomised according to their iodine-to-creatinine ratio (<150 or ≥150 μg/g). Linear mixed models were used to evaluate the relationship between iodine status and TSH and Tg concentrations, controlling for confounders. Women with thyroid antibodies were excluded from the analysis.

Results: Median Tg concentration was 21, 19, and 23 μg/l in the 1st, 2nd and 3rd trimesters respectively. Serum Tg was higher in the <150 μg/g than in the ≥150 μg/g group at each time point of gestation, the difference increasing with gestational age, and was significantly higher at the mean gestational week (estimated marginal mean 18 *vs.* 16 μg/l; $p < 0{\cdot}001$). By contrast, there was no difference in TSH between groups (estimated marginal mean 1·49 *vs.* 1·55 mUI/L; $p = 0{\cdot}27$). Gestational week was an effect modifier on the effect of iodine on both TSH ($p = 0{\cdot}01$) and Tg ($p = 0{\cdot}012$); there was no increase with gestational week in Tg in the ≥150 μg/g group but there was in the <150 μg/g, and TSH increased more in the <150 μg/g than in the ≥150 μg/g group.

Conclusion: Low iodine status in pregnancy is associated with higher serum Tg, suggesting that iodine deficiency increases thyroid volume. Tg appears to be a more sensitive biomarker of iodine status in pregnancy than does TSH.

P1-02-03

RELATIONSHIP BETWEEN MATERNAL IODINE STATUS WITH MATERNAL AND FETAL THYROID FUNCTION IN EUTHYROID GRAVIDAE CARRYING SINGLETON PREGNANCIES

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Objectives: To examine the prevalence of iodine deficiency in the obstetric population using the new World Health Organization (WHO) median urinary iodine concentration (UIC) cutoff of 1.18 μmol/l, and to compare maternal and fetal thyroid function and iodine intake between the deficient and sufficient groups.

Methods: 109 healthy clinically euthyroid gravidae with singleton uncomplicated pregnancy in the third trimester were recruited to study maternal and fetal (cord blood) thyroid stimulating hormone (TSH), free thyroxine (fT4), and thyroglobulin (Tg), maternal urinary iodine concentration (UIC) and iodine/creatinine ratio (I/Cr) in a spot urine sample, and iodine intake in the past 30 days using a food frequency questionnaire that included medications and multivitamin supplement. The results were compared between those with UIC below or at/above the WHO cutoff value.

Results: There were 82 gravidae (75.2%) with iodine deficiency. There was no difference in the mean maternal age (32.8 ± 4.1 versus 32.5 ± 4.5 years), gestation at delivery (39.0 ± 1.4 versus 38.9 ± 1.6 weeks), or infant birth weight (3073 ± 379 versus 3095 ± 310 g), but UIC, I/Cr, and cord fT4 were significantly lower, while maternal Tg was significantly higher, in the deficient group (Table). However, no difference in the daily iodine intake or cord Tg could be found.

Conclusion: Although the new WHO definition of iodine deficiency was associated with higher maternal Tg and lower fetal fT4, no difference in the other thyroid hormone parameters or dietary intake were found, and the appropriateness of this definition should be re-examined.

P1-02-04

POPULATION-BASED TSH INTERVALS IN ANTIBODY-POSITIVE AND ANTIBODY-NEGATIVE SUBJECTS, DETERMINED BY TWO DIFFERENT MEASUREMENT METHODS

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Objectives: Current guidelines recommend an upper limit of normal of TSH about 4 mIU/l for the general population. Some authors have proposed that in the elderly the limit should be shifted to the right. The aim of the study was to determine the age and gender differences in population TSH levels measured by two different methods.

Material and Methods: Data from two population-based studies of endocrine disorder prevalence (2006 and 2012) were used for this post hoc analysis – 2402 subjects participated in the first and 2032 – in the second one. TSH and Anti-TPO had been measured and thyroid ultrasound had been done in all participants. In the 2006 cohort TSH was determined by a microparticulate immunoenzyme analysis (MEIA) (reference range 0.39–4.2 mIU/l), and in the 2012 one – by a two-site immunoenzyme ''sandwich'' assay (reference range 0.34–5.6 mIU/l). After exclusion of subjects with known thyroid disorders and using antithyroid drugs or levothyroxine and/or operated for a thyroid disorder, 2265 and 1871 subjects were analyzed. Those with positive Anti-TPO antibodies were further excluded from certain analyses as were the subjects with nodules on the thyroid ultrasound.

Results: Antibody positivity was found in 13% in 2006 and in 16% in 2012. Nodules were resent in 23.1% in 2006 and in 23.7% in 2012. In both studies median TSH was slightly higher in the females (2006: 1.34 mIU/l vs. 1.22 mIU/l, $p < 0.001$ and 2012: 1.93 mIU/l vs. 1.71 mIU/l, $p < 0.001$) in both irrespective of the measurement method. The 3-th percentile and the median of TSH did not increase with age in either group. The 97-th percentile increased

Table 1. (for abstract P1-02-03)

	Iodine deficient (n = 82)	Iodine sufficient (n = 27)	P value
UIC (μmol/L, median, 25–75th %)	0.63 (0.41–0.82)	1.50 (1.30–2.40)	<0.001*
I/Cr (median, 25–75th %)	0.11 (0.08–0.16)	0.21 (0.15–0.28)	<0.001*
Iodine intake (ug/day, median, 25–75th %)	213.8 (124.3–896.4)	210.9 (138.2–1028.4)	NS*
Maternal TSH (mIU/l, median, 25–75th %)	1.7 (1.0–2.4)	1.3 (0.9–1.9)	NS*
fT4 (pmol/l)	12.2±1.4	12.6±1.6	NS
Tg (μg/l, median, 25–75th %)	13.9 (6.9–26.6)	8.4 (4.8–13.7)	0.020*
Cord TSH (mIU/l, median, 25–75th %)	6.8 (4.6–10.0)	6.7 (5.0–9.7)	NS*
fT4 (pmol/l)	15.9±1.8	16.8±1.9	0.031
Tg (μg/l, median, 25–75th %)	59.8 (35.3–89.4)	62.8 (40.5–93.8)	NS*

Comparison with the t test or * Mann Whitney U test.

with age in both genders except the males in 2012 if Anti-TPO positive subjects were included (2006: females from 4.04 to 18.83 mIU/l; males from 2.83 to 9.36; 2012: females from 5.8 to 49.45 mIU/l) When Antibody-positive subjects were excluded, the age-dependent increase in the 97-th percentile was less pronounced. The TSH distribution fell within the manufacturer-determined reference range in the younger TPO-negative subjects, but tended to move to the right of the upper limit in the elderly. In TPO-positive subjects it reached beyond the upper limit of 'normal' in almost all age/gender groups.

Conclusion: With age the population TSH range doesn't shift, but widens to the right, even in TPO-negative subjects.

P1-02-05

THE VALIDATION OF THYROID VOLUME REFERENCE VALUES AS THE MARKER OF IODINE DEFICIENCY IN SCHOOLCHILDREN

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The reference values for thyroid volume (TV) in children have been extensively discussed during past decades. Reference established by Delange et al. in 1997 has been criticized and replaced by the one proposed by Zimmermann et al. in 2004.

Aim: To assess 1997 and 2004 TV references as the markers of iodine deficiency in schoolchildren.

Material and Methods: The study, conducted between 1999 and 2011, included 9264 Polish schoolchildren (48.7% of boys) aged 6–12 years. In each child TV was assessed by ultrasound and iodine urinary concentration (UIC) was measured using Sandell-Kolthoff method. In 9002 children body surface area (BSA) was calculated.

Results: A very weak correlation between UIC and TV adjusted to age and sex was found ($r = –0.04$; $p < 0.1$). Median UIC in the whole group was 96.03 ug/ml. Goiter was found in 5.4% and 55.57% of children, respectively, when 1997 and 2004 TV references for age were applied. When 1997 and 2004 TV references for BSA were used, goiter frequency was 4.93% and 56.4%, respectively. Statistically significant differences in UIC between the children with and without goiter were found only if 2004 TV references for age ($p = 0.44$) and BSA ($p < 0.001$) were applied). Anova analysis showed a statistically significant difference ($p < 0.001$) in UIC between three subgroups of children: without goiter according to both BSA-related references, with goiter according only to 2004 reference, and with goiter according to both references (no such trend was seen for age-related references) – particularly between two first subgroups ($p < 0.001$).

Conclusion: The 2004 reference values better mirror the iodine nutrition status in children and should be preferred as the epidemiologic tool for assessment of iodine deficiency in children. However, considering the particularly large proportion of goitrous children in the area of borderline iodine sufficiency, they cannot be recommended as reference for clinical decisions.

P1-02-06

IODINE STATUS OF PREGNANT WOMEN RESIDING IN NORTHERN CYPRUS

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Introduction: Data of iodine intake is limited in the northern region of Cyprus. We have no data for pregnant women. Before the introduction of iodized salt in 1999 we performed a study in children and established that the median urinary iodine excretion (UIE) was 120 µg/l. The aim of this study was to analyze the UIE in a cohort of pregnant women residing in the northern region of Cyprus.

Subjects and Methods: We included 258 pregnant female subjects in all trimesters of pregnancy. We excluded subjects with urinary infection; those who were not residing in the same region in the last 1 month; those using multivitamins containing iodine; those using iodine supplements; those who have had a radiological analysis with iodine containing contrast media; having a hysterosalphingography in the previous 6 months; those having a history of thyroid disorder prior to pregnancy; using thyroid hormones or anti-thyroid drugs.

Results: We analyzed the UIE of 258 pregnant women being referred to the Endocrinology outpatient unit of our hospital between June 2014 and January 2016. The median age was 28 and the mean age was 28.62 ± 5.8 years (17–46). 185 (71.7%) subjects were using iodized salt, 12 (4.7%) were using salt without iodine and 61 (23.6%) subjects had no knowledge of the nature of salt intake. 34 (13.2%) subjects were in the first trimester; 134 (51.9%) were in the second trimester; 90 (34.9%) were in the third trimester of pregnancy. The median UIE was 110 µg/l. The proportion of subjects with UIE <150 µg/l was 157 (60.8%); under 100 µg/l: 119 (46.1%) and under 50 µg/l: 41 (15.8%).

Conclusion: From our results we determined that more than half of pregnant subjects have insufficient iodine intake in the northern area of Cyprus. We advise iodized salt and also need to argue the routine use of iodine supplements in this region.

P1-02-07

PRELIMINARY RESULTS OF A MULTICENTRIC STUDY OF URINARY IODINE CONCENTRATION IN PREGNANT WOMEN FROM ROMANIA

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Objective: To assess iodine status (median urinary iodine concentration) in pregnant women from multiple endemic or non-endemic areas, a decade after implementation of the Universal Salt Iodization in Romania.

Subjects and Methods: The study group included 247 pregnant women in the third trimester from 5 geographical regions in Romania (age range: 16–46 years, mean age: 28.4 years). Median urinary iodine concentration in the morning urine (UIC) was evaluated by spectrophotometry in a single laboratory. Data regarding education level, iodized salt intake, bread intake, iodine supplements, smoking and iron deficiency anemia were assessed. The study was approved by the Local Ethics Committee.

Results: Median UIC in the study group was 161.7 mcg/l, reflecting iodine sufficiency during pregnancy. However, 46.1% of women had values below 150 mcg/l. There is a trend to lower urinary iodine in women not receiving iodine supplements during pregnancy ($p = 0.056$). Statistically significant difference between pregnant women with and without iodine supplements was

recorded in women from rural areas (173.1 versus 129.9 mcg/l, p = 0.025), as well as in pregnant women with a daily intake of less than 5 slices of bread (usually containing iodized salt), 173.8 versus 109.1 mcg/l, p = 0.01. Iron deficiency anemia was found in 28.45% and 19.02% were current smokers during pregnancy. Lower median UIC were recorded in the endemic regions of Transilvania (95 mcg/l), Moldova (127.9 mcg/l) and Muntenia (149.4 mcg/l) as compared to Bucharest area (206 mcg/l) and non-endemic regions (206.6 mcg/l). In Transilvania region there is a discrepancy between schoolchildren (normal median UIC) and pregnant women (low median UIC).

Conclusion: In 46% of pregnant women from iodine deficiency regions median UIC are still subnormal and lower than in non-endemic regions from Romania, despite iodine supplementation during pregnancy. Iodine supplements seem to be beneficial especially in women from rural area and in those with a low consumption of bread.

P1-02-08

ASSESSING THE PROBLEM OF IODINE DEFICIENCY DISORDERS IN THE RUSSIAN FEDERATION

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In Russian Federation with population of 142,467,651 people mild iodine deficiency with median UIC 78 µg/l (ICCIDD.org) were estimated from 1990s.

Since 2000, according to the decision of the Government of the Russian Federation 'On Measures for the prevention of diseases caused by iodine deficiency (dated October 5, 1999 No. 1119) and regional programs and the decisions of heads of administrations of areas and regions in all child care institutions only iodized salt should be used. But there is still no legislation for salt iodization for all country.

Aim: For evaluation of the main epidemiological indicators of iodine deficiency in children and adults were retrospectively studied the special statistical form of Ministry of Health of Russian Federation 'Information on diseases related to micronutrient deficiency' between 2003 and 2014.

In children the median prevalence of diffuse goiter amounted to 835.4 cases and ranged from 1199.0 to 583.5 per 100. 000 child population. The incidence rate of of diffuse goiter over the same period averaged 902.1 cases per 100 000 child population. Minimum incidence was recorded in 2014 (209.3 cases per 100 000 child population), the maximum – in 2003 (1157.4 cases per 100 000 child population). All investigators observed a decrease in the incidence of diffuse goiter in young population, while the data in the elderly are controversial. It should be noted that, despite the identification of trends, goiter prevalence has not reached its sporadic level. In addition, it notes that there are differences in the dynamics of these. For example, the 'gaps' in 2007–2009, and then the rise of the incidence of diffuse goiter and suddenly a sharp fall in 2014, which requires further study. There is no reasonable explanation and a drop in the incidence of hyperthyroidism and hypothyroidism in adults, whereas the incidence of hypothyroidism in children has increased.

Thus, according to the results of research it was concluded that «voluntary» model of IDD control was not effective enough.

In addition, to fully evaluate the effectiveness of IDD control programs in Russia is necessary to obtain reliable statistical information on the prevalence and incidence of each region separately.

P1-02-09

IODINE NUTRITION STATUS AND AWARENESS OF IODINE DEFICIENCY IN ADULT POPULATIONS INCLUDING PREGNANT WOMEN IN TUGUEGARAO, PHILIPPINES

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Objective: Iodine deficiency causes multiple health problems including endemic goiter, cretinism, intellectual impairments, growth retardation, neonatal hypothyroidism, increased pregnancy loss and infant mortality. Previously we reported that 96% of high school students of Tuguegarao, Philippines had adequate iodine levels. However, iodine deficiency associated problems still remain in adult populations in this country. Therefore, we now evaluated iodine nutrition status and goiter prevalence of adults including pregnant women in Tuguegarao, Philippines.

Methods: A total of 245 adults including 31 pregnant women provided samples for urinary iodine analysis, all pregnant women completed questionnaire for iodine deficiency.

Results: The median urinary iodine level was 164.0 ± 138.4 µg/l and 38.4% of the subjects were in the range of iodine deficiency status according to the ICCIDD criteria. No severe iodine deficiency was noted though. Among 31 pregnant women, 24 (77.5%) fell into iodine deficiency status defined by a stricter WHO guideline, in which iodine deficiency is set when urinary iodine level is below 150 µg/l. Almost half (42%) of pregnant women didn't know about the harmful effects of iodine deficiency on the human body and their fetus.

Conclusion: Although iodine nutrition status of Philippines has been improved, iodine deficiency still existed in adults, especially in pregnant women. Therefore, our study strongly suggests that a better strategy should be established to monitor iodine nutrition status in adults continually, and to focus on populations susceptible for iodine deficiency, including pregnant women and women at reproductive age to achieve the total elimination of iodine deficiency.

P1-02-10

PRACTICAL MANAGEMENT OF IODINE PROPHYLAXIS IN CASE OF PREGNANCY WITH PRIOR THYROID PATHOLOGY IN MILD IODINE DEFICIENCY AREA OF GEORGIA

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According to the current guidelines, as intra-thyroidal iodine stores should be maximised before conception to facilitate the increased thyroid hormone produc-tion during pregnancy, women who are planning to become pregnant should start iodine supplementation before conception and continue it during pregnancy and lactation in iodine deficiency regions.

However, there are no clear recommendations on the timing of the beginning of iodine prophylaxis for women with prior thyroid pathology living in iodine deficiency regions.

In case of overt or subclinical hypothyroidism patient need adequate replace-ment therapy with levothyroxine to keep TSH level less than 2.5 mU/l before and during the first trimester of pregnancy. In such cases we don't start iodine supple-mentation before or during the first trimester of pregnancy. We use 200 mcg/d iodine supplementation after 12–14 weeks of pregnancy, once the fetus thyroid starts to uptake iodine.

In case of hyperthyroidism in pregnancy, we manage it according to the modern guidelines and iodine supplementation (200 mcg/d) use only after the cessation of hyperthyroidism.

P1-03 Clinical Autoimmunity 1

P1-03-01

CORRELATION BETWEEN AUTOIMMUNE THYROID DISEASES AND OTHER ORGAN SPECIFIC/SYSTEMIC AUTOIMMUNE DISORDERS

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Objectives: There is a correlation between autoimmune thyroid diseases (AITD) and other organ specific/systemic autoimmune disorders. However, the small sample sizes and the use of control populations not matched for age, or gender, or geographic location, might have hampered the results of several studies.

Methods: Three thousand and sixty-nine patients, with diagnosed chronic autoimmune thyroiditis (AT), were investigated in oupatient clinic to evaluate the prevalence of other autoimmune disorders with respect to two age- and sex-matched control groups: a first control group of 1023 subjects, collected from a random sample of the general population without thyroid disorders; a second group of 1023 patients with non-toxic multinodular goiter, collected from the same random sample of the general population, who had similar iodine intake.

Results: A significant increase of the prevalence of autoimmune disorders, such as chronic autoimmune gastritis (CAG), vitiligo (Vit), rheumatoid arthritis, polymialgia rheumatica (Polym), celiac disease, diabetes, sjogren disease, multiple sclerosis, systemic lupus erythematosus, sarcoidosis, alopecia, psoriathic arthritis, systemic sclerosis, HCV-related cryoglobulinemia, was demonstrated in AT patients (with respect to both controls). The association of three autoimmune disorders was observed in AT patients; expecially, the most frequent associations were AT+CAG+Vit and AT+CAG+Polym.

Conclusion: This study in patients with AT (who continue to be sick, or with new not specific symptoms) suggests the screening for other autoimmune disorders, to avoid the delay in the diagnosis of these disorders.

P1-03-02

SERUM THYROID HORMONE AUTOANTIBODIES (THAB) IN PATIENTS WITH CHRONIC HEPATITIS C (CHC) WITH ASSOCIATED NEITHER AUTOIMMUNE THYROID DISEASE (AITD) NOR AUTOIMMUNE NONTHYROID DISEASES (NAITD), AND IN PATIENTS WITH GRAVES' DISEASES (GD) OR HASHIMOTO'S THYROIDITIS (HT)

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Background/Objective: HC virus (HCV) infection triggers AITD and NAITD. THAb prevalence in NAITD (rheumatoid artitritis [RA], primary Sjogren syndrome [pSS]), GD and HT has increased over time (NAITD>AITD). In the late 90's, IgG-THAb prevalence was reported as 32% (GD), 20% (HT), 26% (RA) and 50% (pSS). IgM-THAb were not investigated systematically previously. THAb are directed against iodinated epitopes of Tg (some T3-hormonogenic, some T4-hormonogenic and others T3- and T4-hormonogenic), and they are the first circulating thyroid Ab appearing in experimental AIT. THAb were never studied in cHC.

Methods: We measured serum THAb (T3IgM, T3IgG, T4IgM, T4IgG) by radioimmunoprecipitation in 40 untreated cHC patients (17.5% TgAb+, 22.5% TPOAb+) without NAITD and AITD, and in 102 patients with AITD (GD = 61, HT = 41) without coexistent NAITD.

Results: Prevalence of positivity for at least one THAb was 65% (cHC), 56% (GD), 44% (HT), and for any IgG-THAb was 57%, 39% or 52%. THAb were mostly single (31.1%, 36.6% or 27.5%), with T4IgG prevailing in cHC (15%) or HT (19%). Detected only in cHC were T4IgM+T3IgG (2.5%) and T3IgM+T3IgG+T4IgM+T4IgG (7.5%). Present only in GD or HT were T3IgM+T4IgM, T3IgM+T4IgG, T3IgM+T3IgG+T4IgG and T3IgM+T4IgM+T4IgG (1.6 to 4.9%). These six THAb were reported to be absent in RA and pSS. Of the 15 possible THAb combinations, there were 10, 11 or 6 detected in cHC, GD or HT, while 4 or 5 combinations were reported for RA or pSS.

Conclusion: In cHC, prevalence of THAb (65%) exceeds TgAb or TPOAb prevalence (0–31% or 5–30% in the literature). Our data suggest a frequent and precocious thyroid damage by HCV, and may explain the relatively high (i) rate of TgAb positivity compared to TPOAb positivity in cHC, (ii) risk of developing AITD spontaneously or after interferon treatment. A close follow-up of THAb-positive cHC patients is warranted.

P1-03-03

HASHIMOTO'S THYROIDITIS AND VITAMIN D INSUFFICIENCY: RELATIONSHIP WITH SERUM THYROID HORMONES, INTERLEUKINS AND THYROID VOLUME

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Objectives: To study the association of vitamin D insufficiency in HT and serum interleukins, thyroid hormones, thyroid volume and anti-thyroid autoantibodies.

Material and Methods: Blood samples were collected from 88 patients with HT and 71 healthy individuals, aged 18 to 65 years. We measured serum interleukins (TNF-alfa, IFN-gama, IL-2, IL-4, IL-5, IL-17), 25-OHVitD, TSH, free T4, calcium, phosphorus, PTH, anti-thyroid antibodies. Thyroid volume was estimated by ultrasound. Patients and control group were matched by sex, age. The significance level for statistical analysis was 5%.

Results: Vitamin D insufficiency was present in 39 (59.1%) controls and 61 (71.8%) patients ($p = 0.1024$). Serum IL-2 were higher in HT group ($p < 0.0001$). Vitamin D showed a positive correlation with FT4, TNF-α, IL-5 and IL-17 in HT. In HT, we found higher concentrations of IL-2 in individuals with higher thyroid volumes, IFN-γ was positively correlated with TPOAb, while interleukins IL-5 and IL-17 were negatively related with TRAb. Free T4 ($p = 0.0286$) was predictor factor of vitamin D insufficiency in HT. In the control group, age ($p = 0.0182$) and IL-4 concentrations ($p = 0.0415$) were predictors of vitamin D insufficiency.

Conclusion: Patients had no significantly lower levels of vitamin D that controls. In agreement with recent studies, we have demonstrated a relation between HT, Th1 interleukins as IL-2 and higher volume of thyroid. The positive correlation between IFN-γ and TPOAb indicates relationship between autoimmune inflammatory activity and thyroid lymphocytic infiltration. Higher concentrations of FT4 were associated with higher levels of vitamin D and FT4 was an independent risk factor for vitamin D insufficiency, suggesting that adequate levothyroxine replacement in HT would be an important element in maintaining sufficient vitamin D concentrations.

P1-03-04

THYROID IMAGING REPORTING AND DATA SYSTEM SCORE: EVALUATION OF RISK STRATIFICATION IN THYROID NODULES WITH HASHIMOTO'S THYROIDITIS AND THYROID NODULES WITHOUT HASHIMOTO'S THYROIDITIS UNDERWENT FINE-NEEDLE ASPIRATION CYTOLOGY: RESULTS FROM A PROSPECTIVE STUDY

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Background: Thyroid imaging reporting and data system (TI-RADS) was designed to better select thyroid nodules (TN) to fine needle aspiration cytology (FNAC) with high sensitivity and accuracy. However, the comparison of TI-RADS scores in TN with Hashimoto's thyroiditis (HT) (HTN+) versus TN without HT (HTN-) has not been examined so far. The aim of this study was to compare the diagnostic performance of TI-RADS score in TN associated or not associated to HT.

Methods: 308 unselected TN consecutively submitted to FNAC from June 2014 to March 2015 were included to compare the diagnostic performance of TI-RADS score in HTN+ and in HTN–; individual TI-RADS score was correlated to FNAC categories in all cases. All suspicious ultrasound features (hypoechogenicity, microcalcifications, irregular margins, taller-than-wide shape, central vascularization) of TN were classified according French TI-RADS categories using a risk score of malignancy.

Results: HTN+ had higher prevalence of suspicious/malignant cytology (Tir 4-5) (HTN+ 48/121 = 40%) compared to HTN– (40/163 = 29%, $p < 0.05$). The distribution of all TI-RADS categories (from 2 to 5) in HTN+ was not significantly different from that found in HTN– (Table).

At difference with TI-RADS, the individual features of hypoechogenicity and irregular margins had higher prevalence in HTN+ (77/121 64%) than in HTN– (58/157 37%, $p < 0.001$), and were more present in suspicious/malignant cytology (TIR 4-5) (69/88 78%) than in benign (Tir 2) cytology (25/196 13%, $p < 0.0001$).

Conclusion: This study confirms our previous observation of higher prevalence of malignant FNAC in nodules associated to HT. TI-RADS score appears not significantly influenced by presence of HT, in spite of the higher prevalence in HTN+ of individual suspicious ultrasound features such as hypoechogenicity and irregular margins and may be proposed as an useful diagnostic tool to select nodules for FNA independently from associated HT.

P1-03-05

PREVALENCE OF ELEVATED LEVELS OF TSH-RECEPTOR ANTIBODIES (TRAB) IN PATIENTS WITH AUTOIMMUNE THYROIDITIS

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Data on the prevalence of elevated TSH-receptor antibodies (TRAb) in patients with autoimmune thyroiditis (AIT) with different thyroid function are controversial. Most of the studies in the past used first and second generation immunoassays, and included mainly hypothyroid patients.

Objectives: To measure TRAb levels in patients with AIT and to evaluate their relationship with the thyroid function.

Patients and Methods: 207 patients with AIT participated (170 women, 37 men). Levels of TRAb, antithyroglobulin and antiTPO antibodies and thyroid hormones (TSH, FT4, FT3) were measured using third generation ECLIA assays (Roche Diagnostics). Thyroid ultrasound and physical examination were performed.

Results: 100 patients were newly diagnosed with AIT; the remaining 107 had an average duration of 66.0 months. 56 of the patients (27.1%) were euthyroid, 63 (30.3%) were hypothyroid, and 88 (42.5%) were hyperthyroid. The mean TRAb value was 1.03 IU/l ± 2.0 (median – 0.55) and did not differ significantly in eu-, hypo- and hyperthyroid patients. TRAb levels were above the upper limit (>1.5 UI/l) in 39 patients (18.8%). The prevalence of elevated TRAb levels was 14.3% (8/56) in the euthyroid group, 19.0% (12/63) – in the hypothyroid group and 21.6% (19/88) – in the hyperthyroid group. Eight of the patients with elevated TRAb were euthyroid (20.5%), 12 were hypothyroid (30.8%) and 19 were hyperthyroid (48.7%). The prevalence of eu-, hypo- and hyperthyroidism did not differ significantly in the groups with and without elevated TRAb levels.

Conclusion: The prevalence of elevated TRAb in patients with AIT is 18.8% but their levels do not correlate with the thyroid function.

P1-03-06

THE ROLE OF MAGNETIC RESONANCE IMAGING IN DIAGNOSING OF DYSTHYROID OPTIC NEUROPATHY

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Objectives: Distinguishing dysthyroid optic neuropathy (DON) from less severe forms of Graves' orbitopathy (GO) is still a challenging task. The aim of our analysis was to test the ability of magnetic resonance imaging (MRI) in differentiating patients with DON from patients with moderate to severe GO.

Methods: MRI scans of 14 consecutive patients (23 eyes) with diagnosis of DON and 23 patients (46 eyes) with diagnosis of active, moderate to severe GO were reassessed by a single radiologist. The presence of following features was noted: apical crowding, optic nerve stretching, lack of the cerebrospinal fluid in optic nerve sheath and value of muscle index. Diagnosis of DON was

Table 1. (for abstract P1-03-04)

	TI-RADS 2	TI-RADS 3	TI-RADS 4	TI-RADS 5
HTN+ (n = 35+29+37+20)	35 (49.3%)	29 (33.3%)	37 (45.7%)	20 (51.3%)
HTN– (n = 36+58+44+19)	36 (50.7%)	58 (66.7%)	44 (54.3%)	19 (48.7%)

$p = 0.125$ (NS).

based on at least two signs from such as: deterioration of visual acuity, loss of colour vision, optic disc swelling and/or visual field defect, relative afferent pupillary defect and typical feature in MRI. Comparisons of clinical evaluation, laboratory and MRI results between eyes with moderate to severe GO and eyes with DON were performed.

Results: At least one of the radiological features of DON was found in 22 (96%) and 23 (50 %) of eyes with DON and moderate to severe GO respectively. Each of them occurred statistically more often in patients with DON. They were no ophthalmological signs of DON observed before therapy, during treatment and follow-up that lasted 57 weeks (from 15 to 194) in group with moderate to severe GO.

Conclusion: MRI is a very useful tool in evaluating features typical DON, however they are found in up to 50% of eyes of patients with active, moderate to severe GO. Ophthalmological evaluation seems to be the most important part in DON recognition.

P1-03-07

INCREASED INCIDENCE OF AUTOIMMUNE THYROID DISORDERS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Objective: Till nowadays, incidence of new cases of thyroid autoimmunity (AT) and dysfunction (TD) in patients with psoriatic arthritis (PsA) was not longitudinally evaluated. For this reason, our purpose was to study the incidence of new cases of clinical and subclinical TD in a wide group of patients with PsA, versus an age- and gender-matched control from the same geographic area.

Methods: We have excluded from the study PsA patients with TD at the initial evaluation, whereas we have evaluated the appearance of new cases of thyroid disorders in 97 PsA patients and 97 matched controls, with similar iodine intake (median follow-up 74 months in PsA versus 92 in controls).

Results: PsA patients, especially female gender, compared to controls, showed a high incidence of new cases of hypothyroidism, TD, positive *anti-thyroid peroxidase* (AbTPO) antibodies, and appearance of a small thyroid and a hypoechoic thyroid pattern. Thyroid-stimulating hormone (TSH) value at a border line high level (although in the normal range), the presence of AbTPO positivity, and a small thyroid volume are risk factors in female gender for the development of TD.

Conclusion: Female patients at high risk [a border line high (although in the normal range) TSH, positive AbTPO, hypoechoic and small thyroid] should periodically follow a thyroid function follow-up and appropriate treatments.

P1-03-08

MISDIAGNOSIS OF GRAVES' HYPERTHYROIDISM DUE TO INTERFERENCE IN FT4, FT3 AND TRAB ASSAYS. A CASE REPORT

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Various substances can interfere with immunoassays and many cases of interference in thyroid function tests (TFT) assays have been reported. In contrast, to the best of our knowledge, interference in TSH receptor antibodies (TRAb) assays has rarely been described.

A 39 year old man presented with palpitations. Cardiology evaluation did not show abnormalities. He didn't report other symptoms and had no clinical features of hyperthyroidism. The thyroid gland was not enlarged. There was no personal or family history of thyroid disorders.

The TFT requested by his GP showed normal TSH and elevated fT4 and fT3 (Table). TPO antibodies were negative but the TRAb were elevated to 5.3 U/l. Based on these tests, he was diagnosed with Graves' hyperthyroidism and methimazole (MMI) was initiated. Further investigations with thyroid scintigraphy and ultrasound revealed normal. Pituitary MRI requested in order to exclude a TSH secreting adenoma but the examination was canceled due to claustrophobia. Over the next 1.5 year, MMI treatment was adjusted according to the TFT results. Under MMI fT3 was persistently high, fT4 normal/high, TSH normal/high and TRAb positive (Table). The patient was referred to us for a second opinion.

Due to the discrepancy between clinical features and laboratory results, assay interference was considered. TFT and TRAb were assessed by immunoassay of different origin and the analysis returned normal TSH, fT4, TT4, fT3 and undetectable TRAb. The discordant results in the alternatives assays suggests assay interference.

Our case suggests that interference not only in TFT assays but also in TRAb assays should be strongly considered when incongruity between the clinical features and the laboratory results is present. Pitfalls in these tests may lead to unnecessary examinations and unappropriated treatment.

Table 1. (for abstract P1-03-08)

	TSH (0.30–4.0 mU/l)*	fT4 (10.0–26.0 pmol/l)*	fT3 (3.3–6.1 pmol/l)*	TRAb (<1.2 U/l)*	MMI
04/2014	0.41	44.1	31.4	–	–
06/2014	0.45	36.4	–	5.3	?
11/2014	3.9	26.4	27.6	–	20 mg
12/2014	5.3	27.5	28.3	–	20 mg
05/2015	6.1	25.6	23.3	3.8	30 mg
09/2015	2.3	27.5	22.2	4.3	10 mg
11/2015	1.1	29.7	23.0	4.1	10 mg
Alternative assay¶	1.4	14.6	4.1	–	10 mg
02/2016	0.31	37.2	22.7	4.0	–
Alternative assay¤	0.41	TT4¤¤ 95 nmol/l	–	<0.7	–

* Reference interval; ¶ reference interval: TSH: 0.35–4.00 mU/l, fT4: 14–23 pmol/l, fT3: 4.1–6.9 pmol/l; ¤ reference interval: TSH: 0.30–4.0 mU/l, TT4 67–134 nmol/l, TRAb <1.0 U/l; ¤¤ Total T4.

P1-03-09

THE IMPORTANT ROLE OF DOPPLER ULTRASOUND IN THE DIFFERENTIAL DIAGNOSIS BETWEEN HASHITOXICOSIS AND GRAVES' DISEASE

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Introduction: The diagnosis of Hashitoxicosis may be complicated, as presenting features sometimes exhibit a significant overlap with Graves' disease. The autoantibody titres are not always helpful. Doppler ultrasonography is a useful tool in the differential diagnosis between Hashitoxicosis and Graves' disease, based on the grade of vascularisation.

Case Report: A14 yo girl complaining from a persistent headache, was referred from the neuropediatrician for evaluation of suspected hyperthyroidism. She had a history of significant headache and anxiety for the last 6 months. Her family history for thyroid disorders was negative. Physical examination revealed hypertension, mild tachycardia and diffuse goiter. Her TSH level was 0.014 mIU/ml, and free T3 level was 15.8 pmol/l (2.3–6.3). The autoantibody profile was Anti-thyroid peroxidase (anti-TPO) 234 mIU/ml (<84), TSH-receptor antibodies (TSI)TRAb 2.03 U/ml (<1). The ultrasonography demonstrated an enlarged non-homogeneous hypoechoic thyroid gland. Methimazole and propranolol were prescribed. Thyroid hormone levels were still high after 4 weeks and TSH suppressed. No clinical improvement. Then a Doppler ultrasonography was performed, which demonstrated a slightly increased vascularisation of the thyroid gland; confirming autoimmune thyroiditis. Treatment with methimazole was stopped. The patient was followed for 5 months. Correction of the hyperthyroid state was achieved after 5 months of therapy, without headache or hypertension.

Conclusion: Our patient represents a further example of the variability of the clinical and biochemical manifestations of autoimmune thyroid disease in children:who was thought to have GD based on the initial findings and was treated with an anti-thyroid drug. Although the the major thyroid autoantibodies provided estimates the prevalence of thyroid disease, in Hashitoxicosis it is necessary to distinguish this picture from Graves' disease. Whereas Graves' disease is characterised by highly increased vascularisation in colour Doppler 'vascular inferno', In Hashitoxicosis shows a normal or only slightly increased vascularisation.

P1-03-10

THE ROLE OF D3 VITAMIN DEFICIENCY IN AUTOIMMUNE THYROIDITIS

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Objectives: The objective of our investigation is to find out the role of D3 vitamin deficiency in patients with autoimmune thyroiditis and calcified nodules.

Methods: The research has been carried out at 'Muratsan' University Hospital and 'Armenia' Medical Center, in 2013–2015. 80 patients (ages ± 40, of which 68 women and 12 men) with autoimmune thyroiditis and calcified nodules have taken part in the clinical research. They have been tested on TSH, FT4, anti – TPO, Vit D3, $Ca^{2+,}$ PTH, as well as undergone a thyroid ultrasound.

Results:

TSH – 58%↑, 42% N
FT4–60% ↓, 40%N
Anti-TPO – 100%↑
Vit D3–84%↓, 16%N
Ca^{2+} – 94%N, 6%↓
PTH – 89% ↑, 11%N

Thyroid ultrasound – Calcificates proved to be present in 76% of nodules, which have been formed on the background of autoimmune thyroidits. The increased level of PTH hormone and lower Vit D3 should be taken into consideration, since this can result from secondary hyperparathyroidism and cause formation of calcificates.

Conclusion: Vit D3 shout be tested in the first place during the treatment of any kind of calcified nodular goiter, since calcificates can be caused not only by oncologic processes, but also secondary hyperparathyroidism.

P1-03-11

USE OF INTRAVENOUS GLUCOCORTICOIDS FOR TREATMENT OF GRAVES' ORBITOPATHY

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Introduction: Graves' ophthalmopathy (GO) also known as thyroid-associated orbitopathy (TAO), is an autoimmune disorder of the retrobulbar tissue, closely linked to autoimmune thyroid disease. Less than 5–10% patients with Graves' disease will develop clinically relevant, active and progressive orbital complications. Treatment of this disease is difficult and often unsatisfactory. Glucocorticoids have been used for treatment of GO because of their anti-inflammatory and immunosuppressive actions during the active phase of GO.

Case Report: In June 2013, 57 years old female patient referred to our clinic with complains of: heat intolerance, weight loss, fatigue, tachycardia, and high blood pressure – classical picture of thyrotoxicosis. In 2006 subtotal resection of thyroid gland for Grave's disease was performed.

Laboratory studies revealed: TSH-**0.01** (N = 0.4–4.0 μIU/ml); FT4–**2.68** (N = 0.89–1.76 ng/dl); Hematology-leukocytes **4.7** (N = 5.2–12.4 μL); ESR-14 (N = 2–15);

Thyroid ultrasound showed two nodules in the left lobe: 7X8X11 mm, 8X8X8 mm.

Thyroid scintigraphy with TC-^{99m} excluded hot and cold nodules.

Anti-THS-Rec.-**2.45** (N ≤ 2.0 LU/l).

The patient was given thiamazole 30 mg/day, propranolol 10 mg/day, prednisolone 15 mg/day.

After six weeks of treatment the patient's general condition was significantly improved: FT4-0.96; The dose of thiamazole was decreased till 10 mg/day, propranolol 5 mg/day, prednisolone withheld.

After 4 months the patient attended our clinic with complains of: lacrimation and duality, pain and exophthalmoses of left eye. Thyroid function was within normal range. In order to exclude tumor, MRI of the head was performed- the tumor was excluded. Graves' ophthalmopathy was diagnosed. Pulse therapy was begun with Intravenous Methylprednisolone infusion according the following scheme: 1st week 1000 mg once a day during 3 days, then 500 mg weekly for 3 weeks and 250 mg weekly for 3 weeks. After that the same infusion once in ten days – (total 4 infusions). Methylprednisolone 4 mg 4 tab. 3 times a day and panangin 2 tab. two times a day was given peros. Glucose levels were monitored, it was always normal.

After 14 weeks of pulse therapy optimized visual acuity and improvement of soft-tissue inflammatory signs and symptoms were evident.

Conclusion: High-dose of i/v steroid therapy provides efficient and stable improvement in Graves' ophthalmopathy.

P1-04 Case Reports

P1-04-01

INCREASED REQUIREMENT OF LEVOTHYROXINE IN TWO GYNECOMASTIC PATIENTS WITH EXCESS OF THYROXINE-BINDING GLOBULIN (TBG): IN ONE BECAUSE OF EXPOSURE TO EXOGENOUS ESTROGENS IN MEAT, IN THE OTHER BECAUSE OF LIVER CIRRHOSIS-RELATED HYPERESTROGENEMIA

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TBG is the liver-synthesized major plasma carrier of thyroid hormones. Pregnancy, a physiologic state of estrogen-driven elevation of serum TBG, raises the requirement of L-T4 dose in hypothyroid women, especially if thyroidectomized. In contrast, androgen therapy in L-T4 treated hypothyroid women decreases TBG and L-T4 requirement. Liver disease (LD) is known to cause relative hyperestrogenemia, gynecomastia and TBG excess, but LD is rarely mentioned to cause increased L-T4 requirement. We are unaware of reports of TBG excess-associated increase of L-T4 requirement in hypothyroid male patients.

Table 1 summarizes our patients. In patient #1 history was relevant for dietary changes (increased consumption of veal meat from a local farm that illicitly used estrogens in animal feeds). FT4 and FT3 were normal (not shown). Acquired TBG excess was suspected and verified (Table). Upon stopping the veal meat consumption, gynecomastia disappeared, and biochemical indices normalized (data in Table are at one year post-observation). Patient #2 had liver cirrhosis-associated gynecomastia. He was lost at follow-up. However, four years later, we learned of his liver transplant, and disappearance of gynecomastia.

The increased L-T4 requirement in LD may stem from (i) hepatocellular cholestasis and subsequent diminished arrival in the duodenum of bile, which is important for T4 absorption; (ii) TBG increase TBG at gestational levels due to liver damage and relative hyperestrogenemia.

P1-04-02

DESTRUCTIVE THYROIDITIS CAUSING THYROTOXICOSIS LONG AFTER AMIODARONE WITHDRAWAL – A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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Introduction: Amiodarone-induced thyrotoxicosis (AIT) develops in 15% of patients, occurring either early or long after initiation of amiodarone or even months after drug withdrawal. The main forms are type 1 AIT (iodine-induced hyperthyroidism in patients with underlying thyroid abnormalities) and type 2 AIT (destructive thyroiditis due to cytotoxic effects of amiodarone).

Case Report: We report the case of a 71-year-old female who presented to our Department in October 2015 with complaints of insomnia, fatigue, palpitations. From her medical history we notice atrial fibrillation treated with amiodarone for two years (2011–2013). She denied having any kind of imaging with contrast, cervical discomfort or fever lately. Laboratory tests: VSH = 44 mm/h, TSH = 0.004 mcIU/ml, TT3=298 ng/dl, FT4=4.03 ng/dl, negative TPOAb, ATA, TSHRAb. Thyroid ultrasound revealed slightly hypoecogenic, inhomogeneous gland with decreased vascularity. Treatment with methimazole 30 mg/day was started. Evaluation after two months: TSH = 0.022 mcIU/ml, TT3=213 ng/dl, FT4=4.13 ng/dl, VSH = 69 mm/h, positive CRP. A thyroid uptake and scan revealed low uniform uptake 3% at 2 h, 1.5% at 24 h. We excluded subacute thyroiditis (no history of respiratory tract infection or neck tenderness), silent thyroiditis (negative thyroid autoantibodies), choriocarcinoma (normal betaHCG). The presumed diagnosis was type 2 AIT occurring two years after the withdrawal of this drug. The patient was treated with methimazole 20 mg/day and medrol 32 mg/day, gradually decreasing doses. Evolution was slowly favorable (TT3=54.4 ng/dl, FT4=2.60 ng/dl, VSH = 28 mm/h). In March 2015 the patient became hypothyroid (TSH = 10.7 mcIU/ml, TT3=74.3 ng/dl, FT4=0.75 ng/dl). We decided to stop methimazole and reevaluate the thyroid function after 2 weeks.

Conclusion: Our case draws attention to the risk of developing AIT even after a long time since amiodarone withdrawal, because of tissue storage of the drug and its metabolites and their slow release into circulation. Recent studies suggest that thyroid function should be monitored for at least 2 years after amiodarone discontinuation, particularly in patients without apparent thyroid abnormalities.

P1-04-03

THYROID STORM FOLLOWING TOTAL THYROIDECTOMY FOR THYROID CANCER, DUE TO THYROTROPIN RECEPTOR ANTIBODIES STIMULATING THE METASTATIC THYROID TISSUE

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Background: Graves' disease (GD) is an autoimmune condition characterized by the presence of antibodies against the thyrotropin receptor (TRAB), which stimulate the thyroid gland to produce excess thyroid hormone. Theoretically, TRAB could stimulate highly differentiated thyroid cancer tissue and/or metastases to produce thyroid hormone. Whether GD affects the prognosis of thyroid cancer (TC) is unclarified.

The Patient: A 68-year old male contacted his primary care physician because of weight loss and palpitations. He was diagnosed with hyperthyroidism and started on Methimazole. An MRI, revealing multiple bone-metastases, was performed due to complaints of shoulder pain for 18 months. Bone biopsy from metastatic tissue was diagnostic for follicular variant of papillary thyroid carcinoma and total thyroidectomy was performed. Methimazole was stopped; the patient was started on Liothyronine (40 micrograms daily), and referred to the department of oncology. One week post-thyroidectomy

Table 1. (for abstract P1-04-01)

Patient	TSH (mU/l)	T4 (mcg/dl)	TBG (mcg/ml)	Notes
1 (before gynecomastia)	1.2–2.8 nv 0.35–5.5	8.7–9.5 nv 5.4–11	Not done nv 15–36	On 100 mcg/d L-T4 after thyroidectomy
1 (gynecomastia)	5.7; 4.4	12.5	55	L-T4 increased (125 mcg/d)
1 (disappearance of gynecomastia)	3.0	10.2	28	L-T4 decreased (100 mcg/d)
2 (before cirrhosis)	always ≤3.4 nv 0.27–4.2	ND	ND	Hashimoto's thyroiditis. On 100 mcg/d L-T4
2 (cirrhosis)	6.6–9.3	ND	60 nv 15–36	L-T4 increased (150 mcg/d)
2 (after transplant)	2.4	ND	ND	On 100 mcg/d L-T4

the patient was admitted through the emergency department due to nausea, vomiting, and thyrotoxic symptoms. According to the Thyroid Storm Scale the patient scored 50 points (raised core temperature, delirium and a precipitating event), which strongly indicates thyroid storm. This was confirmed biochemically. Liothyronine was stopped and the patient started on glucocorticoids, propranolol, and high-dose propylthiouracil. Elevated TRAB level (> 40 IU/ml; reference range <0.7 IU/ml) was demonstrated. Initial anti-thyroid drug-treatment (ATD) was followed by high dose radioiodine (RAI) and local radiotherapy covering the right shoulder. Despite thyroidectomy and three RAI doses (cumulative dose: 11,1GBq), the patient remained euthyroid (medio December 2015).

Summary and Conclusion: We present a rare patient, initially diagnosed with hyperthyroidism and subsequently metastastic follicular variant of papillary thyroid cancer. It is suggested that TRAB stimulated not only the thyroid but also the extrathyroidal metastatic thyroid tissue, causing the highly differentiated tumor tissue to produce excessive amounts of thyroid hormone, delayed diagnosis, and potential aggravation of the course of TC.

P1-04-04

SPONTANEOUS TRANSFORMATION OF PRIMARY AUTOIMMUNE HYPOTHYROIDISM TO GRAVES' DISEASE IN A CLINICAL CASE OF AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 2

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Introduction: Autoimmune polyglandular syndrome type 2 is characterized by occurrence of adrenal failure with either autoimmune thyroid disease (AITD) and/or type 1 diabetes. Hashimoto thyroiditis (HT) and Graves' diseases represent the main two types of AITD. About 15–20% patients with GD may have spontaneous hypothyroidsm after treatment discontinuation. The transformation to Graves' disease following autoimmune hypothyroidism is very rare. It can be explained by changes of relative levels of TSH receptor stimulating antibodies (TSAb) and blocking antibodies (TBAb).

Case Report: A 35 years old woman was presented with nausea, vomiting, fatigue, weight loss and palpitation. She has 2 years history of primary adrenal insufficiency and primary hypothyroidism due to HT and treatment with hydrocortisone 10 mg, fludrocortisone 0.05 mg and levothyroxine 67.5 mkg. One month before admission was determined suppressed TSH and levothyroxine was withdrawal. Examination revealed: TSH – 0.011 ME/ml, FT4–44.41 pmol/l (7.86–14.41), TRAb – 6.82 U/l. She has low glucose, sodium and high potassium levels. The diagnosis of Graves Disease was confirmed based on positive TRAb levels, thyroid ultrasonography and family history. She was treated with iv hydrocortisone, fludrocortisone and methimazole.

Conclusion: This case demonstrate a rare change of the thyroid functional activity from hypothyroidism to hyperthyroidism, which led to adrenal insufficiency decompensation. We suggest close monitoring of thyroid function in patients with AITD and autoimmune polyglandular syndrome and think of the possibility of switching in thyroid function.

P1-04-05

AUTOIMMUNE THYROID DISEASE AND CHRONIC URTICARIA – A CASE STUDY

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Introduction: Chronic urticaria is defined as at the occurrence of wheals and itches for at least 6 weeks. The association of autoimmune thyroid disease and chronic urticaria was first described by Leznoff in1983. The thyroid antibodies might reflect susceptibility to autoimmunity. No data to date proved that thyroid antibodies are pathogenic in terms of chronic urticaria and both conditions could be associated as parallel outcome events.

Case Report: A 26 year old female presents for recurrence of thyrotoxicosis, 6 months after radioiodine therapy for presumably Grave's disease. She reported that skin hives developed for one year with the onset of thyrotoxic manifestations and increased after the start of medical treatment. After radioiodine therapy, the skin condition aggravated with breathlessness necessitating parenteral corticosteroids and admission to the emergency room. She was diagnosed as chronic urticaria and angioaedema.

She received L-Thyroxine, antihistaminics and a Triple therapy Course for eradication of H. pylori. Chronic urticaria persisted necessitating addition of anti-IgE monoclonal antibodies.

Investigations:
– TSH: 0.01 IU/ml;
– Free T4:1.6 ng/dl;
– Free T3: 4.7 pg/ml;
– Thyroid peroxidase antibodies: 508 IU/ml;
– Neck U/S: diffuse goiter.

Conclusion: The onset of chronic urticaria coincided with the onset of autoimmune thyroid disease suggesting a predisposition in the patient to develop autoimmune disease. The treatment of autoimmune thyroid disease would be an important therapeutic target. However, L-thyroxine was not beneficial to chronic urticaria. Further studies are needed to clarify the association between autoimmune thyroid disease and chronic urticaria as well as the role of treating thyroid disease and H. pylori on the clinical course of chronic urticaria.

P1-04-06

PRIMARY HYPERTHYROIDISM IN A PATIENT WITH HYPOTHYROIDISM SECONDARY TO PITUITARY SURGERY – A RARE ASSOCIATION

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Background: Secondary hypothyroidism is rare and may result from surgical resection of a pituitary lesion. Secondary hypothyroidism and primary hyperthyroidism can coexist in the same patient.

Case Report: Nineteen year-old female, without relevant medical history or medication, presented with galactorrhea, primary amenorrhea and left hemianopia. Complementary study detected hyperprolactinemia >200 ng/ml (ref.1.2–29.9 ng/ml) and pituitary adenoma with cavernous sinus invasion and suprasellar growth. She was treated with cabergoline and bromocriptine in the maximum doses, without clinical or analytical improvement. Partial resection of pituitary lesion was performed and invasion of nasal mucosa was detected, consistent with diagnosis of prolactin-producing pituitary carcinoma. She underwent radiation therapy for residual disease and persistent symptoms. Post-operatively, she developed hypogonadotropic hypogonadism, diabetes insipidus and secondary hypothyroidism with thyroid-stimulating hormone (TSH) 0.006 µUI/ml (ref.0.35–5.0) and free thyroxine (FT4) 0.76 ng/dl (ref.0.88–1.58). Levothyroxine was initiated up to 75 mcg/day. Six years later, the patient presented nausea, asthenia, tachycardia, tremor and weight loss (15 kg in 2 months). Weeks before admission, she self-withdrew levothyroxine. Physical examination highlighted a thyroid bruit. Plasma sampling revealed TSH 0.001 µUI/ml (ref.0.35–4.94), FT4 2.42 ng/dl (ref.0.70–1.48), free triiodothyronine (FT3) 16.74 pg/ml (ref.1.71–3.71), thyroglobulin antibody (TgAb) 67.2 IU/ml (ref.<4.11), peroxidase antibody 0.5 IU/ml (ref.<5.61) and TSH-receptor antibody (TRAb) 1.8 U/l (ref.0–1.8). Methimazole 20 mg/day and β-blocker were initiated with symptomatic improvement. Thyroid ultrasound revealed increased vascularity and no nodular lesions. Thyroid scintigraphy revealed an iodine-131 uptake of 70.2% at 24 h (normal 10–30%). As methimazole was stopped to perform thyroid scintigraphy, FT4 and FT3 increased. The patient was discharged with methymazole 10 mg/day and oriented to outpatient clinic.

Conclusion: The association between primary hyperthyroidism and secondary hypothyroidism is extremely rare. Despite TRAb levels at upper normal range, TgAb positivity suggests that hyperthyroidism had an autoimmune aetiology. The thyroid bruit, increased vascularity and high iodine uptake excluded silent or subacute thyroiditis. The most probable diagnosis was Graves' disease.

P1-04-07

A CASE REPORT OF TYPE 2 AMIODARONE INDUCED THYROTOXICOSIS, WHICH UNDERWENT TOTAL THYROIDECTOMY

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Introduction: Amiodarone is a class 3 antiarrhythmic drug, commonly used in the treatment of ventricular and supraventricular arrhythmias. It can cause many side effects, including thyroid disfunction, which can lead to either hypo- or hyperthyroidism. There are two types amiodarone induced thyrotoxicosis (AIT). Type 1 AIT affects patients with preexisting thyroid pathology and is the consequence of iodine overload. Type 2 is not related to preexisting thyroid pathology and is characterised by the presence of destructive thyroid inflammation.

Case Report: 55-year old patient presented to our hospital because of chest pain. He was diagnosed with atrial fibrillation and three vessel corronary artery disease, serum TSH concentration was normal. The patient later underwent CABG surgery and was subsequently prescribed amiodarone as an antiarrhythmic. Two years later he became hyperthyrotic, thyroid ultrasonography was consistent with an autoimmune disease, however antithyroid antibodies were negative. Amiodarone was discontinued and thyrostatic treatment was introduced, leading to remission of hyperthyroidism. One month after the discontinuation of the thyrostatic the patient had a primary cardiac arrest, there were signs of diffuse ischemic cerebral injury. Due to unsustained ventricular tachicardias an ICD was inserted, the patient was again prescribed amiodarone, and after three years of continuous amiodarone treatment there has been a relapse of hyperthyroidism. As amiodarone discontinuation in conjunction with thyrostatic and high-dose steroid treatment did not result in remission, a total thyroidectomy was safely performed. A pathohistologic examination of the thyroid revealed AIT type 2. On the 17th postoperative day levothyroxine substitution therapy was introduced.

Conclusion: Peroral steroid therapy is the first line treatment of type 2 AIT. However, in a selected group of patients, where medication therapy is unsuccessful, total thyroidectomy is an effective and safe modality, despite high-dose steroid treatment and other possible comorbidities. Furthermore, thyroidectomy may be the only viable option, when continuous amiodarone therapy is necessary. It is important to keep in mind that high serum concentrations of free T3 and T4 may persist for several days after total thyroidectomy.

P1-04-08

EFFECT OF GLUCOCORTICOSTEROIDS ON THE THYROID SUPPLEMENTATION THERAPY IN A PATIENT WITH AUTOIMMUNE HYPOTHYROIDISM: A CASE REPORT

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Introduction: A variety of compounds and hormones interact with the thyroid gland or alter the effect of thyroid hormones. This communication addresses glucocorticoids (GC) which might interfere with thyroxin (T4) at the different levels influencing T4-replacement in some hypothyroid patients.

Case Report: We observed a 42 year old woman with Hashimoto's thyroiditis who underwent a subtotal thyroidectomy, resulting in postoperative hypothyroidism 4 years earlier. She was admitted to the hospital under combined therapy by levothyroxine (L-T4) 150 mg and liothyronine (L-T3) 37.5 mg. Laboratory results were as followed: TSH 23.8 mU/l, baseline FT4-6.18 pmol/l and 8.94 pmol/l 180 min after administration of 150 mcg L-T4, FT3-4.79 pmol/l, TG-6.0 ng/ml, TG-ab –818 IU/ml, TPO-ab-696 IU/ml and positive T4 antibodies 3% of serum T4 bound to IgG (ref. range <2%) On the same doses of T4/T3 therapy we administered pulses of Methyl-prednisolon (MPS) 500 mg i.v. for 3 consecutive days resulting in following effect on the 4-th day: TSH-0.18 (ref. range 0.35–4.94 mU/l), FT4-14.5 pmol/l, TG-ab-450 IU/ml, TPO-ab-114 IU/ml, T4-ab – 2%. Replacement with L-T4 150 mg/d was continued but L-T3 was stopped. Serum hormone levels remained in the normal range for up the 90-day when these returned to the previous values (TSH-98.8 mU/l, FT4-8.72 pmol/l, T4-ab-2.6%) and decreased significantly after repeated 2 pulses of MPS.

Discussion: It was known that GC potentiate the metabolic effect of T3. There are experimental data of increased transcriptional effects of GC on the nuclear T3-receptor β1 promoter and synergistic interaction of T3 and GC. We suggested a second effect in this case mediated by the immunosuppressive effects of GC which decreased the T4 antibodies level resulting in the release of FT4 from circulating immune complexes.

P1-04-09

A RARE CAUSE OF PAIN AND SWELLING IN NECK: THYROID ABSCESS

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Introduction: We report thyroid abscess in an immunocompetent patient presenting with pain, swelling, erythema and induration in neck.

Case Report: A 35 years old woman applied to our clinic with sore throat accompanied by fever, difficulty in swallowing and swelling in right neck. She used amoxicillin clavulanate 2x1000 mg for 1 week. She did not have any systemic disease or history of trauma to neck. She had fever 38.2°C and there was a 4x4 cm tender, warm and erythematous lesion in right part of the neck. Sedimentation rate was 83 mm, C-reactive protein (CRP) 93.7 mg/l (0–5), thyrotrophin 0.38 mUI/ml (0.27–4.2), fT3 3.12 pg/ml (1.8–4.6) and fT4 1.83 ng/dl (0.9–1.7). Ultrasonographically, a hypoechoic area of 13.4x16.5x17.5 mm in right thyroid lobe and a 26.5x42.3x46.7 mm heterogenous isohypoechoic lesion with irregular margins and septas in right neck were detected. There was a communication between these two lesions. Neck computerized tomography revealed 4x2 cm abscess in soft tissue of right anterior neck extending to the thyroid gland. Only 2 ml material was obtained by aspiration, gram positive cocci and bacil were observed in smears, however culture was negative probably because the patient was on antibiotic therapy. Intravenous sulbactam ampicillin 4x2 gr was started. Examinations for viral diseases, infective endocarditis and tuberculosis were negative. Thyroid functions became normal at first and third weeks. Sedimentation rate was 26 mm, CRP was <3.2 mg/dl and a prominent decrease in size was observed at the 21th day of treatment. She received intravenous antibiotic treatment for 6 weeks and oral antibiotic for an additional 2 weeks.

Conclusion: Although pain and swelling in thyroid region might be suggestive for subacute thyroiditis at first glance, thyroid abscess which has a mortality of 20–25% when left untreated should always be kept in mind.

P1-04-10

WITHDRAWN

P1-04-11

MARINE-LENHART SYNDROME – A RARE CAUSE OF THYROTOXICOSIS

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Marine-Lenhart syndrome, a rare cause of thyrotoxicosis, is the coincidence of Graves' disease with autonomously functioning nodules. The syndrome was initially described in 1911. by Marine and Lenhart and is considered a distinct sub-entity of Graves' disease.

A 51-year old woman was admitted to our hospital because of hyperthyroidism in spite of high doses of antithyroid drugs. Signs and symptoms of hypermetabolism started in September 2011, medical treatment in February 2012, without reaching eumetabolism in next two years on high doses of antithyroid drugs (propylthiouracil 600 mg/day, thiamazole 60 mg/day). She had a history of mycrocitic, sideropenic anemia, and few month prior to admission vitiligo appeared. On admission, thyroid functions tests were as follows: TSH ≤0.01 uIU/ml (range 0.4–4.20); fT4 60 pmol/l (range 9–19.1;); fT3 20.5 pmol/l (range 2.6–5.7;), TRAb 3.4 IU/l, TPOAb <28.0 IU/ml, TgAb <15.0 IU/ml. On physical examination, she was hypermetabolic with smooth, velvety skin, palmar tremor and tachycardia, 104/min. She had enlarged thyroid gland, with palpable 4 cm large node in left lobe. On ultrasound, the thyroid gland was asymmetrically enlarged with a heteroechogenic nodule, 51x32x56 mm, in the left lobe and enhanced blood flow on color Doppler in the node, as well as in the rest of the gland. Because of her hypermetabolism on high doses of antithyroid drugs, we performed thyroid scintigraphy without pause in her medical treatment. Tc-99m pertechnetate thyroid scan showed increased uptake in the left lobe, corresponding to the palpable an ultrasonographically detected nodule, with persisting diffuse homogeneously uptake of the pertechnetate throughout the rest of the gland.

We concluded that thyrotoxicosis in our patient was due to coexistence of Graves' disease and toxic nodule and we recommended surgical treatment since radioactive therapy requires higher doses in these cases, and may not be enough due to high activity of toxic nodule.

P1-05 Thyroid Cancer Diagnostic I

P1-05-01

INDETERMINATE THYROID LESIONS: POTENTIAL DISCRIMINATORY OF THE NUCLEAR MORPHOMETRIC COMPUTERIZED ANALYSIS

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Introduction: In the cytological analysis, both benign lesions such as follicular adenomas (FA), and malignant such as follicular carcinomas (FC) and follicular variants of papillary carcinomas (FVPC) can be categorized as class III and IV of Bethesda, diagnoses that carry risk of malignancy quite variable. The computerized image analysis has shown as an objective and reproducible tool in the evaluation of different tissues, representing a promising diagnostic possibility also for thyroid lesions.

Objectives: To evaluate the diagnostic discriminatory efficiency of the computerized image analysis of cell nuclei in histological material obtained from FA, FC, and FVPC.

Methods: We selected paraffin-embedded material from 32 AF, 26 FVPC, 20 CF, and 39 normal thyroid tissues. We assembled slides, which were stained with hematoxylin-eosin, examined and photographed. The cell nuclei were analyzed using the computer program ImageJ, being studied morphometric and nuclear textural aspects. The samples were classified as AF, FC, FVPC, or normal, according to these features, through the CRT regression model (Classification and Regression Trees), through Twoing algorithm.

Results: The tumor diameter was greater (p = 0.014) in CF (3.6 ± 1.4 cm) than in FVPC (2.18 ± 1.32 cm); without correlation between this dimension and the different nuclear parameters evaluated. Starting from the RA (roughness) nuclear parameter and progressing up to the CV-AR (coefficient of variation-Aspect Ratio), we got a global correct classification of the histological diagnosis in 87.2% of the tumors. Individually, it was possible to correctly classify 87.5%, 84.6%, 80.0%, and 92.3% of AF, FVPC, CF and normal tissues, respectively. We observed high rates of sensitivity and specificity (84.6% and 96.7% for FVPC, 80% and 100% for the CF, and 87.5 and 89.4% for AF, respectively).

Conclusion: Computerized image analysis of the nuclear characteristics proved a useful tool in histological differentiation between the AF, FVPC, and CF, with high sensitivity and specificity. Acknowledgements: PIBIC/PROPE-Unesp (ID:33347), and FAPESP (2014/10028-2).

P1-05-02

ADEQUACY OF PATHOLOGY REPORTS OF PATIENTS WITH DIFFERENTIATED THYROID CANCER OPERATED IN A HIGH VOLUME TERTIARY ENDOCRINE CENTER

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Introduction: Differentiated thyroid carcinoma is the most common endocrine malignancy. It usually has an excellent prognosis with low rates of recurrence and metastasis. Risk scoring and initial treatment plan depends on the histopathology of the tumor. This study aimed to investigate the adequacy of the pathology reports of patients operated in our institution and diagnosed with differentiated thyroid carcinoma (DTC).

Method: This is a cross sectional study of DTC patients operated between January 2007 and December 2014. We performed the retrospective analysis of the pathology reports. Data collected from the pathology reports of patients with DTC were: (1) histological type and subtype, (2) maximum diameter of the tumor, (3) whether the tumor was uni-or multifocal, (4) information regarding lymphovascular invasion, (5) extrathyroid extension of the tumor, (6) completeness of excision, and (7) site, size and number of lymph nodes involved, if they were excised. In the case of FTCs, data regarding invasiveness [minimal invasion (either capsular and/or vascular) or wide invasion] were also recorded.

Result: 960 pathology reports of DTC patients were analyzed. Size of the tumor was reported in 100% of the patients. Extrathyroidal invasion, vascular invasion, completeness of the surgery were missing in 2% of the patients. Variant of PTC was reported in 85% of the patients and the missing cases were mostly microcarcinomas. The most missing items were the information about the capsule invasion of the involved lymph node, the size of the metastasis within the lymph node and number of invaded vessels in follicular cancers.

Conclusion: The pathology reports of DTC specimens frequently miss some of the information considered necessary to provide a comprehensive patient care.

P1-05-03

THYROID CORE NEEDLE BIOPSY: PATIENTS' PAIN AND SATISFACTION COMPARED TO FINE NEEDLE ASPIRATION

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Purpose: The core needle biopsy (CNB) has been proposed as a complementary tool for thyroid nodules with inconclusive cytology by fine-needle aspiration (FNA). The purpose of this study was to compare the patients' pain and satisfaction between the two procedures.

Material and Methods: The patients who had underwent thyroid FNA (n = 90, 13 males, age 52.9 ± 13.4) or CNB (n = 80, 18 males, age 51.4 ± 11.2) were consecutively included. The degree of pain was surveyed using 0 to 10 scales in both groups at three time points (during procedure, after procedure, and 20 minutes after procedure). The telephone surveys were made after 2 weeks after procedures for the remaining pain and overall satisfaction. The rate of inconclusive diagnosis (insufficient specimen[IS] and atypia of undetermined significance[AUS]) in cytopathology were recorded. Student's t test was used for the comparative analysis.

Results: The pain scores were not significantly different between the two groups (mean scores±standard deviation, FNA vs. CNB; during procedure, 2.88 ± 1.46 vs. 2.54 ± 1.79, after procedure, 1.41 ± 1.54 vs. 1.49 ± 1.79, 20 minutes after procedure, 0.74 ± 0.82 vs. 0.90 ± 1.13, all $p > 0.05$). There was no case of acute complication in both groups. After 2 weeks after procedure, the remaing pain was reported in 6 patients (score 3 and 4) in FNA group, and 4 patients (score 3 and 4) in CNB group. Overall satisfaction scores after 2 weeks were also not different between the two groups (FNA 8.00 ± 1.92, CNB 8.25 ± 1.69, $p = 0.41$). The rate of inconclusive diagnosis were 36.6% in FNA group (15 IS and 18 AUS) and 1.2% in CNB group (no IS, 1 AUS) ($p < 0.001$).

Conclusion: CNB showed comparable patients' pain and overall satisfaction to FNA, and significantly lower rates of inconclusive pathologic diagnosis. This finding suggests that CNB may replace the role of FNA as first approach to obtain pathologic diagnosis of thyroid nodules.

P1-05-04

ATYPIA OF UNDETERMINED SIGNIFICANCE ON THYROID FINE NEEDLE ASPIRATION – RISK FACTORS FOR MALIGNANCY

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Purpose: The Bethesda System for reporting thyroid cytopathology introduced the atypia of undetermined significance (AUS) category, but did not provide adequate guidance for the appropriate use of this diagnosis. This study is designed to determine the cilinical predictors of malignancy in the AUS category.

Methods: A retrospective analysis was done on sixty-two patients who underwent thyroid surgery from January 2010 to December 2013, following a diagnosis of AUS from preoperative thyroid FNA. We investigated the age, gender, maximum size and site of the nodules, ultrasonographic findings, cytological features, BRAF gene mutation, surgical method, number of AUS on repeated FNA, and final pathologic results.

Results: Fourty-one out of sixty-two patients underwent total thyroidectomy and the rest had lobectomy. The final pathologic results were fourty-one malignancies and twenty-one benign diseases. Nodules less then 1.5 cm, ultrasonographic findings suggestive of malignancy were risk factors for malignancy on univariated analysis. Multivariated analysis showed that nodules less than 1.5 cm, ultrasonographic findings suggestive of malignancy and more than 2 results of atypia from prepeated FNAs were significant risk factors for malignancy.

Conclusion: From the results of our study, we recommend surgery or close observation with follow-up examination such as ultrasound-guided needle biopsy for thyroid AUS patients who has high risk factors for malignancy.

P1-05-05

THE RELATIONSHIP BETWEEN THE BRAFV600E MUTATION IN PAPILLARY THYROID MICROCARCINOMA AND CLINICOPATHOLOGIC FACTORS

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Objectives: The BRAFV600E mutation which account for about 60–80% papillary thyroid carcinoma (PTC) has risen as a prognostic marker for risk stratification of PTC patients. The BRAFV600E mutation as a prognostic marker in papillary thyroid microcarcinoma (PTMC) is unclear.

Materials and Methods: We performed a retrospective review of 101 patients who underwent surgery for PTMC. We studied the prevalence of the BRAFV600E mutation. The associations between the BRAFV600E mutation and clinicopathologic characteristics were analyzed.

Results: The BRAFV600E mutation was observed in 72 patients (71.3%). There was no statistically significant correlation in age, gender, multifocality, extrathyroidal extension, presence of Hashimoto thyroiditis and lymph node metastasis between the BRAFV600E mutant group and wild group.

Conclusion: The BRAFV600E mutation is not significantly associated with prognostic factors in PTMC.

P1-05-06

PRIMARY THYROID LYMPHOMA: A 10-YEAR EXPERIENCE AT A TERTIARY CARE CENTRE IN THAILAND

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Background: Primary thyroid lymphoma (PTL) is a rare tumor, comprising about 1–5% of thyroid malignancies. With a limited number of large-scale studies, the management of PTL is still determined by the expert opinion. The aim of this study was to review our experience with PTL and to discuss the diagnostic and therapeutic considerations.

Methods: We retrospectively analyzed the medical records of the patients with pathological proven PTL between 2006 and 2015 at King Chulalongkorn Memorial Hospital to determine the clinicopathological features and treatment outcomes.

Results: This study included 3 men and 8 women with a median age of 63 years (range, 31–82 years). All patients showed symptoms of a rapidly enlarging neck mass at initial presentation and three of them also developed compressive symptoms. All of them had underlying Hashimoto's thyroiditis and about 80% of the patients had abnormal thyroid function test. Fine-needle aspiration cytology yielded an accurate diagnosis of lymphoma in only 40% of the patients, whereas the remaining patients required a subsequent incisional biopsy/thyroidectomy for definitive diagnosis. The pathological diagnosis revealed that all of the patients were in an early stage (stage I/II) of non-Hodgkin lymphoma with diffuse large B cell lymphoma (DLBCL) in 7 cases (63.6%), mucosa-associated lymphoid tissue (MALT) lymphoma in 3 cases (27.3%) and follicular lymphoma in one case (9.1%). A case of co-existing tumor of DLBCL and papillary thyroid carcinoma was also identified. All but one responded well to the treatments regarding to their pathological findings. Nine patients are currently alive and in complete remission; one patient died from sepsis during the treatment and the other one died from a cause unrelated to the disease.

Conclusion: Clinicians should be aware of PTL in patients with Hashimoto's thyroiditis presenting with an enlarging thyroid mass or compressive symptoms. PTL has an excellent prognosis with early diagnosis and management by single or combined treatment modalities.

P1-05-07

IMPACT OF F18-FDG PET/CT ON THE CLINICAL OUTCOME AND MANAGEMENT OF DIFFERENTIATED THYROID CANCER PATIENTS WITH POSITIVE I-131 WHOLE BODY SCAN AND ELEVATED THYROGLOBULIN

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Background: ^{18}F-fluoro-deoxyglucose positron emission tomography and computed tomography (^{18}F-FDG PET/CT) has a role in the surveillance of patients with differentiated thyroid cancer (DTC), especially those with thyroglobulin (Tg)-positive and a negative radioiodine whole body scan (^{131}I WBS). Its usefulness in DTC patients with positive ^{131}I WBS had seldom been discussed. The aim of this study was to evaluate the impact of ^{18}F-FDG PET/CT on the management and clinical outcome of DTC patients with positive ^{131}I WBS and detectable Tg.

Methods: From 2005 to 2013, we retrospectively evaluated a total of 27 DTC patients with positive ^{131}I WBS and concurrent detectable stimulated-Tg who underwent an ^{18}F-FDG PET/CT study within one year. All of the patients had undergone total or near-total thyroidectomy followed by radioiodine ablation. Patients with any other form of malignancy were not included in this study. The ^{18}F-FDG PET/CT findings were analyzed, with disease progression as a primary endpoint.

Results: Among the 27 patients, 20 patients (74%) had positive ^{18}F-FDG PET/CT findings. The sensitivity, specificity, and diagnostic accuracy of ^{18}F-FDG PET/CT for detecting recurrent/residual lesions were 86.3%, 80%, and 85%, respectively. In 12 patients (44%), ^{18}F-FDG PET/CT provided additional information than ^{131}I WBS and conventional imaging; 8 (30%) of them resulted in a change of clinical management.

Twelve patients (44%) experienced disease progression after ^{18}F-FDG PET/CT during follow-up. The maximal standard uptake value (SUVmax) of the lesion with strongest ^{18}F-FDG uptake was significantly higher in patients with progression than those without progression. Patients with lesion SUVmax over 4.5 were suggestive for disease progression with sensitivity of 90% and specificity of 87.5%. Of the 7 patients (26%) with negative ^{18}F-FDG PET/CT result, 6 patients achieved undetectable Tg at the end of follow-up and none of them experienced disease progression.

Conclusion: In DTC patients with positive ^{131}I WBS and detectable Tg, ^{18}F-FDG PET/CT plays a complementary role to conventional follow-up methods. Lesion SUVmax provides prognostic information in identifying DTC patients with disease progression, while a negative ^{18}F-FDG PET/CT result suggests a favorable prognosis.

P1-05-08

COEXISTENCE OF DIFFERENTIATED AND UNDIFFERENTIATED THYROID CARCINOMA WITH CHRONIC LYMPHOCYTIC LEUKEMIA

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Introduction: Chronic lymphocytic leukemia (CLL) has been shown to be coexisting with several malignities, especially hematologic ones. There have been several cases of its coexistence with thyroid carcinoma. There have also been rare reports of differentiated and undifferentiated forms of thyroid cancer existing in the same patient. These are generally cases of malign transformation of the lung or retroperitoneal metastases of the original cancers. Moreover there are a few cases of tumor thrombus due to thyroid cancer.

Case Report: Our case is a 58 year old man who had been following with the diagnosis of CLL for 6 years. He has had chemotherapy for CLL one year ago. He has been in remission afterwards when two 2 cm-lymph nodes appeared at level II on the left side. These were taken out en bloc and the pathology was consistent with foci of both CLL and papillary thyroid cancer in the same nodes. Thyroid ultrasonography revealed a 1 cm nodule on the left tyroid lobe. Total thyroidectomy and central and left lateral neck dissecton were performed. It was noticed intraoperatively that left vena cava was filled with thrombus. The surgical team did not touch the vena cava. Radioiodine therapy with 150 mCi was given to patient 6 weeks after surgery. Then the patient had worsening neck and ear pain and was reoperated where the vena cava with the thrombus was taken out. The pathology of the new specimen was concordant with poorly differentiated thyroid carcinoma infiltration, along with foci of undifferentiated component. The patient then was started on radiotherapy and chemotherapy simultaneously.

Conclusion: Our case is a very rare case where we observed the presence of classical thyroid carcinoma of the thyroid, the coexistence of CLL and papillary carcinoma in metastatic lymph nodes and simultaneous undifferentiated thyroid carcinoma in the tumor thrombus.

P1-05-09

A CASE OF BLACK THYROID ACCOMPANIED BY PAPILLARY CARCINOMA

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We report a rare case of black thyroid accompanied by papillary carcinoma in a patient. A 28-year-old man was referred to our outpatient clinic with swelling in his neck. Neck ultrasonography and computed tomography demonstrated a 0.53 x 0.67 cm nodule in the left thyroid lobe, 1.4 x 2.2 cm sized lymph node with cystic change at level 3 of the left cervical chain, another variable sized variable natured lymph nodes at the left cervical chain. Fine-needle aspiration cytology identified it as a papillary carcinoma. The patient underwent a total thyroidectomy and Lt. mRND. During the procedure, a distinct black discoloration of the thyroid parenchyma was observed. Histopathology confirmed both the black thyroid and the papillary carcinoma.

P1-06 Thyroid Cancer Pathogenesis

P1-06-01

PROGNOSTIC FACTORS OF DISEASE IN PATIENTS WITH REFRACTORY TO RADIO-IODINE (RAI) TREATMENT DIFFERENTIATED THYROID CANCER (DTC)

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Introduction: Patients diagnosed with DTC have excellent prognosis. A small percentage of patients with disease persistence do not respond to treatment with therapeutic RAI (RAI-refractory DTC) and have low median survival (3.5 years). We investigated the prognostic factors and the disease course in patients with RAI-refractory DTC.

Methods: Of all DTC patients (n = 1160) followed-up in our department recently, 800 received RAI treatment and were classified in 2 groups: RAI-refractory DTC (5.8%) and DTC with response to RAI (94.3%). Clinical and histological characteristics between the 2 groups were compared.

Results: The incidence of RAI-refractory DTC was increased in patients >45 yrs and particularly in those >65 yrs (17.4% vs 7.4%, p = 0.001). Men presented more frequently RAI-refractory DTC than women (p = 0.02). RAI-refractory DTC patients presented higher incidence of capsular, lymph node and extra-thyroid invasion (p < 0.004), larger size (p < 0.001), worse histological type (follicular/high risk papillary: 34.9% vs 12% and features of poor differentiation: 14% vs 0.6%, p < 0.001, respectively). No RAI-refractory DTC patient had history of thyroid autoimmunity compared with 50% of non-RAI-refractory patients who presented autoimmunity. The 10-year probability of lack of progression of disease was 27.9%vs98.8% (x2=297, p < 0.001). In cox proportional hazard analysis, the only predictor for disease progression was resistance to RAI (HR 0.032, 95% CI 0.007–0.146, p < 0.001). Within the RAI-refractory DTC subgroup, when age at diagnosis, gender, tumor size, histological type, lymph node, capsular and tissue invasion were taken into account, the only predictor for disease progression and occurrence of distant metastases was tumor size (p = 0.008 and p = 0.015 respectively).

Conclusion: Patients with RAI-refractory DTC present disease progression at high percentage (72%). In these patients, tumor size is the most important unfavorable factor predicting disease progression and occurrence of distant metastases. These data are useful in designing treatment strategy.

P1-06-02

USEFULNESS OF INTRAOPERATIVE PTH MEASUREMENTS FOR PREDICTING PERMANENT HYPOPARATHYROIDISM AFTER TOTAL THYROIDECTOMY

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Objective: Hypoparathyroidism is a complication of total thyroidectomy. Postoperative parathyroid function depends on hormone secreted from in situ-preserved parathyroid glands and autotransplanted parathyroid tissue. Because the half-life in blood of intact PTH (i-PTH) is only 5 min, and because autotransplanted parathyroid tissue starts to function a few days after operation, intraoperative i-PTH measurement (PTT-PTH: post-total thyroidectomy i–PTH) is useful to estimate the function of only the in situ parathyroid glands. In the present study, the PTT-PTH and the number of autotransplanted parathyroid glands required to prevent permanent hypoparathyroidism was evaluated.

Methods: Between October 2012 and September 2014, 612 patients who underwent total thyroidectomy had their PTT-PTH measured 5 min after thyroid resection. The number of in situ-preserved and autotransplanted parathyroid glands and the occurrence of symptoms of hypocalcemia were prospectively evaluated. One year postoperatively, patients who needed vitamin D or calcium to maintain serum Ca ≥8.0 mg/dl were diagnosed with permanent hypoparathyroidism.

Results: Of 612 patients, 411 with papillary thyroid cancer (PTC) underwent central node dissection (CND), and 75 with nodular goiter and 126 with Graves' disease underwent simple total thyroidectomy. There were no significant differences between patients with PTT-PTH ≥15 pg/ml and <15 pg/ml (lower limit of normal) in the incidence of numbness and tetany. Permanent hypoparathyroidism developed in 9 (3.2%) of 278 patients with PTT-PTH ≥15 pg/ml and 43 (12.9%) of 334 patients with PTT-PTH <15 pg/ml (p < 0.0001). In patients who underwent CND, permanent hypothyroidism was seen in 33.3% (2 of 6) and 13.0% (34/262), respectively, of patients with PTT-PTH <15 pg/ml with or without autotransplantation (≥1 gland). Permanent hypothyroidism was seen in 14.3% (1/7) and 5.1% (7/136) of patients with PTT-PTH ≥15 pg/ml with or without autotransplantation, respectively.

Conclusion: PTT-PTH ≥15 pg/ml or autotransplantation of ≥1 gland resulted in a 93.8% (558/595) success rate in the prevention of permanent hypoparathyroidism after total thyroidectomy.

Table 1. Table Success rates in the prevention of permanent hypoparathyroidism in patients who underwent total thyroidectomy with CND (n = 411) (for abstract P1-06-02)

		PTT-PTH		Total
		<15 (pg/ml)	≥15 (pg/ml)	
Autotransplantation (AT)	No	66.7% (4/6)	85.7% (6/7)	76.9% (10/13)
	Yes (≥1gland)	87.0% (228/262)	94.9% (129/136)	89.7% (357/398)
Total		86.6% (232/268)	94.4% (135/143)	89.3% (367/411)
ARR (Absolute Risk Reduction) by AT		20.3%	9.2%	12.8%
RRR (Relative Risk Reduction) by AT		61.0%	64.3%	55.4%

P1-06-03

THE 2015 AMERICAN THYROID ASSOCIATION RISK STRATIFICATION SYSTEM: A TOOL FOR PREDICTING THE TUMOR BURDEN OF PERSISTENT/RECURRENT DISEASE IN PATIENTS WITH DIFFERENTIATED THYROID CANCER

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Objectives: In patients with differentiated thyroid cancer (DTC), the goal of risk-stratification systems is to predict the likelihood of persistent/recurrent disease (PRD) after surgery, and in particular to select patients for radioiodine (RAI) ablation. In a perspective of individualized risk assessment and personalized therapy, it would also be interesting to predict the tumor burden of PRD. We aimed to assess whether such tumor burden could be predicted by the new 2015 American Thyroid Association (ATA) risk-stratification system.

Methods: This retrospective cohort study included 460 consecutive and unselected DTC patients referred for RAI ablation. Patients were risk-stratified using the revised 2015 ATA guidelines according to data available after surgery and before RAI ablation. Tumor burden of PRD was assessed using post-RAI whole-body scintigraphy with SPECT/CT, 18F-FDG-PET/CT in case of RAI-refractory lesions and conventional radiology (ultrasound, CT scan or MRI). We distinguished small-volume and large-volume PRD. Small-volume disease was defined by the presence of abnormal scintigraphic foci, in or outside the neck, without any abnormality on conventional radiology. Conversely, large-volume disease was defined by locoregional or distant lesions clearly evidenced on conventional radiology, whatever the presence of scintigraphic abnormalities.

Results: Among 460 patients, there were 67%, 30% and 3% of low, intermediate and high-risk patients, respectively. During a mean follow-up of 49 months, PRD was found in 75 patients (16%). PRD was evidenced in 5%, 33% and 92% of patients at low, intermediate and high-risk, respectively. The proportion of large-volume PRD significantly increased from low, intermediate to high-risk patients (29%, 64% and 100% respectively, P = 0.02).

Conclusion: This study shows that the 2015 ATA risk-stratification system also enables to predict tumor burden in patients with PRD.

P1-06-04

A NEW PROPOSAL FOR A DIFFERENTIAL MANAGEMENT OF INDETERMINATE THYROID NODULES: CONTRIBUTION OF ULTRASONOGRAPHY, REPEATED FINE NEEDLE ASPIRATION BIOPSY AND BRAF ANALYSIS

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Indeterminate thyroid nodules consist of a highly heterogeneous group of lesions, characterized by varying malignancy risk (MR) and should be managed differently. We aimed at assessing the contribution of ultrasound (US), repeated fine needle aspiration biopsy (RFNAB) and BRAFV600E molecular analysis in the therapeutic decision to indicate surgery or conservative follow-up in the management of Bethesda System for Reporting Thyroid Cytopathology (BSRTC) III and IV thyroid nodules. To this aim, we assessed 460 patients, each with a single nodule consisting with BSRTC III (269) or BSRTC IV (191) class. Among these, 344 patients were operated on (surgical group SG) and 116 followed-up conservatively (follow up group, FG). In order to better manage BSRTC III nodules, we divided this class in 4 subcategories (III-1, III-2, III-3, III-4) on the basis of cytomorphological features. We found that each class and related subcategories are associated to a different MR, that was higher in BSRTC III (34.4%) vs. BSRTC IV (26.2%; $p < 0.01$). BRAF analysis displayed high accuracy (87%) and was positive almost exclusively in BSRTC III-1. Nearly 40% of nodules were identified as benign after RFNAB. Nearly 70% of FG patients displayed a stationary nodule; growing nodules belonged to BSRTC III-2 and BSRTC IV, but were not associated with an increased MR. Histological, cytological, and US data contributed to define clinical risk (CR), that was higher in BSRTC III-1, III-4 and IV classes. We therefore propose to diversify the management of indeterminate nodules according to CR: BSRTC III-1, III-4 and IV may be addressed to surgery, while III-2 may undergo RFNAB and III-3 may be managed by a conservative US follow up.

P1-06-05

THE ASSOCIATION BETWEEN LYMPH NODE METASTASIS AND MOLECULAR MARKERS IN DIFFERENTIATED THYROID CANCER

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Objective: Differentiated thyroid cancer accounts for 90% of all thyroid malignancies. There is no consensus regarding routine usage and benefits of molecular markers for prediction of prognosis and assessment of risk groups.

Aim: In our study, we aimed to investigate NIS, Galectin-3, PTEN, P53 and Ki67 expressions in tumor tissue and metastatic lymph nodes in DTC and their association with lymph node metastasis and prognosis.

Material and Method: Ninety two papillary thyroid cancer patients who underwent total thyroidectomy and central lymph node dissection were included in this study. NIS, Galectin-3, PTEN, P53 and Ki67 immunohistochemical stainings were performed for all surgical tumor tissues. Metastatic lymph nodes of the 38 patients were also analyzed immunohistochemically. Age, gender, tumor size, multifocality, capsular invasion, extrathyroidal extansion and lymphocytic thyroiditis were assessed retrospectively.

Results: Seventy three female (%79.3) and nineteen male (%20.7) patients were included in this study. Mean age at the diagnosis was 39.6 ± 13.8 years. Mean tumor diameter was 15.3 ± 11 mm. Lymph node metastasis risk was higher in tumors with capsular invasion and extrathyroidal extension ($p = 0.03$ and $p < 0.001$). NIS, PTEN and Galectin-3 protein expressions in tumor tissue were not associated with gender, tumor size, multifocality, extrathyroidal extension, capsular invasion and lymph node metastasis. Mean Ki 67 proliferation index was 2.08 ± 0.95%. Ki 67 proliferation index was associated with tumor size ($p = 0.012$). Distribution and intensity of NIS and PTEN expression in tumor tissue were concordant with distribution and intensity in metastatic lymph nodes ($p < 0.001$). Ki 67 proliferation index in tumor was concordant with lymph node metastasis ($p = 0.02$).

Conclusion: NIS, PTEN, Galectin-3, Ki67 and P53 expressions were not associated with the risk of lymph node metastasis in PTC patients. Routine analysis of these markers does not seem to be favorable. Further studies with new markers are necessary for determination of prognostic predictors.

P1-06-06

ASSOCIATION BETWEEN BODY MASS INDEX AND CLINICOPATHOLOGICAL FEATURES OF THYROID CANCER

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Purpose: Obesity is associated with aggressive pathological features and poor clinical outcomes in breast and prostate can\-cers. However, the associations between excess weight and prognostic factors for thyroid cancer are uncertain. This study aimed to evaluate the associ\-ations between body mass index (BMI) and the clinical outcomes of patients with PTC.

Methods: Retrospective analysis of 5025 patients with PTC was performed. Patients were grouped according to BMI (underweight, normal weight, overweight and obesity)-based World Health Organization standard-

ized categories. Clinicopathological factors were analyzed and compared between normal and other groups.

Results: According to the results, 4525 patients were women (90.0%) and mean age was 47.5 years. There were no significant associations between BMI quartiles and Multifocality, cervical lymph node metastasis, or distant metastasis. Increased BMI was strongly associated with extrathyroidal invasion ($P < 0.001$) and advanced TNM stage ($P = 0.005$). There were no differences in recurrence-free survivals according to BMI quartiles ($P = 0.26$).

Conclusion: Increased BMI might elevate the risks of aggressive clinicopathological features, such as extrathyroi\-dal invasion and advanced TNM stage. To confirm this result, further studies with long-term follow-up and more patients are required.

P1-06-07

BRAF AND RAS MUTATION STATUS IN TURKISH PATIENTS WITH PAPILLARY THYROID CARCINOMA AND CORRELATION WITH CLINICOPATHOLOGICAL FEATURES OF THE PRIMARY TUMOUR

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Background: Papillary thyroid cancer (PTC) is a common endocrine malignancy that frequently harbors *BRAF* and *RAS* mutation. As novel prognostic molecular markers, these mutations have received considerable attention in recent years for its potential utility in the risk stratification and management of PTC. In PTC, *BRAF* and *RAS* mutations are closely associated with extrathyroidal extension, lymph node metastasis, advanced tumor stages, disease recurrence, and even patient mortality. The aim of this study was to determine the frequency of *BRAF* and *RAS* mutations and correlation with clinicopathological features in a population with PTC.

Subjects and Methods: We analyzed 38 patients who underwent surgery for PTC between 2003–2010. *BRAF* and *RAS* mutations were analyzed in tissue samples by pyrosequencing. The results were correlated with clinicopathological factors.

Results: The prevalence of *BRAF* and *NRAS* mutations was 21% and 14%, respectively. *BRAF*(+) patients tend to be older and have a smaller tumor size but there was no statiscally significant difference between *BRAF*(+) and *BRAF*(–) patients. While there was no significant difference regarding the occurence of *BRAF* mutations and the histologic subtypes of PTC, there was a significant difference between *BRAF* (+) and *BRAF* (–) patients with regard to tumor angioinvasion, node metastases and distant metastases ($p < 0.0001$). Furthermore, there was a trend towards younger age and larger tumor size in *NRAS*(+) patients but there was no significant difference between *NRAS*(+) and *NRAS*(–) patients. A significant difference was observed between NRAS(–) and NRAS (+) patients with regard to tumor angioinvasion, node metastases, distant metastasis and extracapsular growth ($p < 0.0001$).

Conclusion: In this small group of patients *BRAF* and *RAS* did not show prognostic significance. Larger studies are required for conclusions regarding the role of these mutations in risk stratification of patients with PTC.

P1-06-08

IS THYROTOXICOSIS ASSOCIATED WITH MORE AGGRESSIVE VARIANTS OF PAPILLARY THYROID CANCER? A SINGLE CENTER STUDY

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Introduction: There are studies suggested that TSH can stimulate the development of thyroid malignancy, and that elevated serum TSH levels are also associated with a higher incidence of thyroid cancer and advanced tumor stage. In contrast, some have suggested that clinical hyperthyroidism might be associated with aggressiveness of tumors, because thyroid hormone can act as a tumor growth factor mediated by integrin $\alpha v\beta 3$ in solid tumors, including thyroid cancer. There is scarce data in the literature searching whether the incidence of PTC variants differ between patients with normal or suppressed TSH.

Methods: Between January 2007 and December 2004, 2910 thyroid surgeries were performed at our institution. Of these, 960 patients with histologically confirmed PTC were involved in the study. Patients were divided in two groups as 'euthyroid' or 'toxic' according to their thyroid function tests performed preoperatively at the time of first admission to the endocrinology clinics. Euthyroid status was defined as normal levels of serum TSH, free T4, and T3, and thyrotoxicosis was defined as a decrease in serum TSH level below the reference range, with normal or elevated serum free T4 and T3 concentrations. Those two groups were compared according to the frequency of different variants of PTC.

Result: There were no statistical differences between the 2 groups with respect to age, gender, primary tumor size and lymph node metastasis at the time of initial diagnosis. Follicular variant PTC was significantly more prevalent in patients with thyrotoxicosis (15.9% vs 4.8%, $p < 0.001$).

Conclusion: In our study, patients with subclinical hyperthyroidism had greater proportion of FVPTC compared with patients with the euthyroid state. If we consider that FVPTC is more akin to minimally invasive follicular thyroid cancer, a lesion that is known to be of low risk than to classical PTC, we can conclude that thyrotoxicosis is not associated with worse prognostic subtypes of PTC.

P1-06-09

POSTOPERATIVE STIMULATED THYROGLOBULIN LEVELS AS A PREDICTIVE FACTOR FOR INCOMPLETE RESPONSE IN LOW TO INTERMEDIATE RISK PAPILLARY THYROID CARCINOMAS

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Background: Total thyroidectomy followed by radioiodine ablation is a treatment strategy for most patients with papillary thyroid carcinoma (PTC). According to ATA, postoperative stimulated thyroglobulin (sTg) levels can help classify patients regarding their risk of tumor recurrence.

Objectives: The aim of this study was to investigate the clinical role of postoperative sTg levels on predicting primary treatment response in patients with low to intermediate risk PTC.

Methods: Retrospective review of patients diagnosed with PTC with low to intermediate risk of recurrence since 2010. Evaluation of sTg and antithyroglobulin antibodies after surgery and 12 months after radioablation. Patients were classified into groups according to the value of postoperative sTg (group 1: <2 ng/ml; group 2: ≥2 ng/ml and <10 ng/ml; group 3: ≥10 ng/ml).

Results: 84 patients were included in this study, 72 (85.7%) were female, mean age 49.9 (±14.4 years).

After total thyroidectomy, patients were classified according to pTNM classification system: 37 (44%) were T1b; 13 (15.5%) were T2; 2 (2.4%) were T3 (>4 cm) and 32 (38.1%) were T3 with minimal extrathyroidal extension (ETE). The majority had classic PTC (63.1%).

Median postoperative sTg level was 5.30 ng/ml to T1b patients; 9.25 ng/ml to T2 patients; 42.9 ng/ml to T3 (>4 cm) patients and 6.24 ng/ml to patients with T3 with minimal ETE. There was no statistical difference between the groups.

At 12 month follow up, 37 (44.4%) patients had incomplete response (biochemical, structural or indeterminate). There was a statistically significant association between postoperative sTg levels and incomplete response, as therapeutic failure significantly increased as the sTg levels increased (23.5%, 28.1% and 68.0% for groups 1, 2 and 3 respectively; $p < 0.05$), regardless of their pTNM staging.

Conclusion: A high level of postoperative sTg can help assess the response of primary therapy and risk of recurrence in low to intermediate risk PTC.

P1-06-10

CASE OF THYROID CARCINOMA OCCASIONALLY FOUND IN YOUNG PATIENT AND THE IMPORTANCE OF IMMEDIATE RADICAL THERAPY

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Introduction: The number of thyroid cancer is progressively increasing and the majority of those diagnosis are papillary thyroid cancer – the most common type of thyroid cancer. Females are more likely to have thyroid cancer. Thyroid cancer can occur in any age group, although it is most common after age 30, and its aggressiveness increases significantly in older patients. Thyroid cancer does not always cause symptoms. Often the first sign of thyroid cancer is a thyroid nodule.

Case Report: 27 years old woman attended our clinic with the complains of fatigue, tachycardia especially at night time. She had no other complains. The patient was sent from cardiologist to check thyroid function. 1 year ago, during pregnancy her thyroid function and thyroid ultrasonography was normal.

We performed laboratory studies: TSH 1.57 (0.4–4.0) FT4 1.14 (0.89–1.76) anti TPO 126.23 (0–60) anti TG 126.23 (0–60.0); Thyroid ultrasonography was performed: in the right lobe hypoechogenic solid nodule 5x5x6 mm was found. As the nodule had fibrotic areas Fine Needle Aspiration (FNA) was performed. The conclusion was TIR3A: low–risk indeterminate lesion (we use classification provided by Italian society of anatomic pathology and diagnostic cytology). We suggested chirurgical intervention, but she was against.

We aimed to recheck her hormonal status and ultrasonography after 3 months. So she attended our clinic once again after 3 months, hormonal status was within normal range, the size of nodule was 5x5x8 mm and enlarged lymph nodes were found. Once again FNA was performed and the conclusion was TIR5-Papillary carcinoma. So she was immediately sent to radical treatment. Total thyroidectomy, lymph dissection was performed.

Conclusion: With this case we want to say that when TIR3 is diagnosed it is necessary to perform immediately thyroidectomy in order to prevent metastatic lesion and the progression of disease.

P1-07 Thyroid Cancer / Translational

P1-07-01

THE EXPRESSION OF E-CADHERIN, YAP1, STAT3 OF MULTICELLULAR TUMOR SPHEROIDS OF THYROID

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Introduction: To date, numerous 3D models have been specifically developed in cancer research to take into account these tumor architectural features in biological processes to as great an extent possible. We were able to culture multicellular tumor spheroid of thyroid, which is the one of spherical cancer models, and identify the expression of E-cadherin, YAP1, STAT3 in thyroid spheroids.

Methods: The human papillary thyroid carcinoma cell line SNU790 was provided by Korean cell line bank. Cells were cultured in the 'spheroid medium' in 60 mm polystyrene Petri culture dishes (BD Falcon, Becton Dickinson (BD), Franklin Lakes, NJ, USA). This 'spheroid medium' consisted of a 1:1 mixture of Dulbecco's Modified Eagle's Medium (DMEM) (high glucose content; Gibco) and F12 nutrient (1:1 (v/v), Sigma Chemical C), Western blots were developed with Immun-Star WesternC chemiluminescence kit (BIO-RAD) and visualized by using ChemiDoc MP Imaging System (BIO-RAD). The results were analysed with Image Lab software version 5.2.1 (BIO-RAD). Antibodies and dilutions used were: E-cadherin (1:500), YAP1 (1:500), STAT3 (1:300), beta-actin (1:1000). All antibodies were purchased from Santa Cruz Biotechnology.

Results: Spheroids were discovered as they were formed at the third day on the 60 mm dish. The number of spheroids was about 4.0×10^3/60 mm dish. We could observe spheroids at the 5th and 10th day. Blots revealed that two cell lines expressed E-cadherin, YAP1, STAT3 and beta-actin, but SNU790 spheroid expressed less E-cadherin and STAT3 than SNU790 cell line. It was suggested that SNU790 spheroid has more characteristics of cancer stem cell than SNU790 original cell line.

Conclusion: This was the preliminary study for thyroid organoid and its response to several anticancer drugs. We succeeded the thyroid spheroid culture from original thyroid cancer cell line. It was suggested that thyroid spheroids had more cancer stem cell characteristics than original cell line because they were cultured as spheroid and expressed less E-cadherin and STAT3 than original cell line. However, we will make sure for it to have cancer stem cell characteristics through the expression of specific proteins and responses to several anticancer drugs through the next studies.

P1-07-02

USING NEXT GENERATION SEQUENCING IN THE DETECTION OF GENETIC CHANGES IN THE BRAF AND IDH1 GENES IN PAPILLARY THYROID CARCINOMA

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Objectives: Several genetic mutations are recognized to cause papillary thyroid carcinoma (PTC). The most common genetic change found in PTC is a V600E mutation in the *BRAF* gene. Some rare mutations in the *BRAF*

gene were published, too. Recently, the *IDH1* gene was reported as one of the causal genes in the development of PTC. This gene is involved in Krebs cycle, but only little is known about its function in PTC.

Methods: Exon 15 of the *BRAF* gene and exons 4 and 6 of the *IDH1* gene were analyzed by next generation sequencing (NGS) using Nextera XT kit on Miseq platform in 385 PTC tissues. Subsequently, all unusual genetic variants were confirmed and tested in blood samples.

Results: The mutation V600E was detected in 37% of PTCs. In 14 cases NGS revealed this *BRAF* mutation in very low percentage (under 5%) in cancer tissue that had not been previously detected by capillary Sanger sequencing. Only in 4 cases there were detected another rare mutations in the *BRAF* gene – deletion VK600-1E, mutation K601E, double mutations V600E+Q609E and V600E+K601G. In the *IDH1* gene two genetic variants V178I and G105G were detected in 13 patients and one rare genetic variant Y183C was detected in 3 patients with PTC. These all *IDH1* variants were found in germline status. Interestingly, 9 *IDH1* positive patients are carrying *BRAF* V600E mutation in tumor.

Conclusion: Beside the most common V600E we have detected rare *BRAF* mutations in 4 cases. NGS helped to increase the detection rate of *BRAF*-positive samples in comparison with capillary sequencing. The role of rare genetic variants in the *IDH1* gene has not been clear yet. It is possible that these variants influence the cell metabolism and contribute to cancer development in connection with *BRAF* mutation. Supported by AZV16-32665A, 1RVO-EU/2016 grants.

P1-07-03

TGFB1 GENE POLYMORPHIMS CLINICAL UTILITY IN THYROID BENIGN AND MALIGNANT NODULES

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TGF-β1 is a cytokine involved in cell proliferation, migration, cellular differentiation and apoptosis in different cell types. In addition, TGF-β1 has been described as an important regulator of immune system, mediating intracellular activations of pro inflammatory cytokines. Immune cells are frequent in malignant tissues, and frequently found in differentiated thyroid cancer (DTC), suggesting an immune response against tumor cells; because of this role, they may also influence patients' outcome. In order to investigate the clinical utility of *TGFB1* genotypic inheritance as diagnostic and prognostic marker and better delineate its function in thyroid cancer, we studied 2 gene polymorphisms (rs1800469 and rs1800472) involved in *TGFB1* expression using Taqman SNP Genotyping technique. There were 50 patients with thyroid nodules: 22 follicular adenomas (FA), and 4 goiters (G), 15 classic papillary thyroid carcinomas (CPTC) and 9 follicular variants of PTC (FVPTC). All patients were treated and followed-up according to a standard protocol for 112.62 ± 39 months. There was no difference in rs1800469 polymorphism between malignant and benign nodules; likewise, there was no difference between FA versus FVPTC ($p = 0.4564$), goiter versus CPTC ($p = 1.000$); and CPTC versus FVPTC ($p = 0.4003$). We were also unable to find differences in rs1800472 polymorphism distribution in malignant versus benign nodules ($p = 1.000$), or between FA versus FVPTC ($p = 0.6610$), goiter versus CPTC ($p = 1.000$) and CPTC versus FVPTC ($p = 1.000$). None of these polymorphisms was associated with any characteristic of aggressiveness. Although an increase in the number of cases investigated is essential to confirm these data, besides the analysis of TGFB1 expression, these data suggest no important role for *TGFB1* gene polymorphisms in thyroid cancer.

P1-07-04

CONTINUOUS INTRAOPERATIVE NEUROMONITORING IN TRANSAXILLARY ROBOTIC THYROIDECTOMY: IS IT POSSIBLE? A PROSPECTIVE RANDOMIZED STUDY

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Introduction: Continuous intraoperative neuromonitoring (CIONM) by vagal nerve stimulation seems to be a technological improvement. Although CIONM is a promising technology at the cutting edge of research in thyroid surgery, it still remains unclear whether IONM adds any value to the clinical outcome of transaxillary robotic thyroidectomy (RT). To the best of our knowledge, the study of standardized CIONM technique during transaxillary RT has not yet been demonstrated. The aim of this study was to assess the risk of recurrent larynageal nerve injury in transaxillary RT performed with or without CIONM.

Methods: This study was performed from May 2015 to November 2015. We prospectively evaluated 50 patients with thyroid cancer who had transaxillary RT with or without nerve monitoring. Of those patients 21 were in monitored group and 29 were in unmonitored group. Laryngoscopy and voice function test were assessed before surgery and at 2 weeks, 3 months, and 6 months after the surgery.

Results: All procedures of CIONM during transaxillary RT were performed safely and effectively. Moreover, CIONM application was also performed safely on contralateral side even for total thyroidectomy. At first postoperative laryngoscopy, two patients (10%) in monitored group showed vocal cord palsy and 4 patients (13.9%) in unmonitored group. There was 1 loss of signal with corresponding unilateral transient vocal cord palsy. The voice function was not significantly different between the two groups. All patients with vocal cord palsy recovered completely at 3 months after surgery.

Conclusion: CIONM in transaxillary RT is safe and feasible to test the functional integrity of the RLN. CIONM can help to give surgeons more confidence during surgery and might be helpful for advanced training in RT.

P1-07-05

STUDY OF NOVEL GALECTIN-1 TARGETED PEPTIDES IN THE CONTEXT OF A NEW AND NON-INVASIVE PAPILLARY THYROID CANCER DIAGNOSIS AND EVALUATION OF THEIR POTENTIAL INHIBITOR EFFECT

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Currently, the worldwide incidence of thyroid cancer, the most common endocrine malignancy, is still increasing. 90% of surgeries performed on nodules reveal a benign phenotype, suggesting a challenging diagnosis of patients who really need a surgery. Current diagnosis approaches imply painful and useless thyroid surgeries. Thereby, we propose to develop a new and non-invasive diagnosis approach by molecular MRI of papillary carcinoma (~80% of malignant tumours of the thyroid) by targeting galectin-1 (gal-1) with peptide functionalized imaging probes. Gal-1, a small protein involved in cellular adhesion, aggregation, migration and cell cycle regulation phenomena, has been found overexpressed in several cancers such as in thyroid cancer. Actually, gal-1 is implied in tumour progression and in metastasis development.

Thanks to phage display technique, phage clones expressing gal-1-targeted peptides were identified. Based on their affinity, three of them were selected and their corresponding peptides synthesized: P1, P7 and P8. Their

binding to gal-1 expressed by well-differentiated thyroid cancer sections has been validated by immunohistochemistry, P1 and P7 showing a better specific affinity. Immunofluorescence assays revealed colocalisation between the peptides and gal-1 in TPC-1 cells (derived from papillary thyroid cancer). P1 and P7 showed no toxicity on hepatocytes, allowing subsequent *in vivo* experiments. Each one of them was conjugated to ultra-small particles of iron oxide (USPIO-P1/P7) in order to obtain imaging probes able to diagnose non-invasively papillary thyroid carcinoma. The binding of vectorized nanoparticles to TPC-1 cells and their absence of toxicity have been validated. The two contrast agents will be assessed on murine models of papillary thyroid cancer, after evaluation of biodistribution and pharmacokinetic parameters.

The therapeutic context of papillary thyroid cancer was also investigated. The potential of these two peptides to inhibit TPC-1 cell adhesion to gal-1 has been confirmed, suggesting thus an anti-metastatic effect.

P1-07-06

CD56 EXPRESSION IS HIGHLY DEPENDENT ON THE HISTOLOGIC SUBTYPE OF PAPILLARY THYROID CARCINOMA: A STUDY OF QUANTITATIVE DIGITAL IMAGE ANALYSIS OF CD56 IMMUNOHISTOCHEMISTRY

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Introduction: CD56 is normally expressed at a high level in the thyroid tissue and its expression is reduced or lost in papillary thyroid carcinoma (PTC). However, little is known about the expression pattern and role of CD56 in various histologic subtypes of PTCs.

Methods: We performed immunohistochemistry for CD56 on 201 PTCs (60 classic variants, 30 classic variants with tall cell features, 30 encapsulated follicular variants, 30 infiltrative follicular variants, 30 tall cell variants, 15 Warthin-like variants, and 6 other variants). The expression of CD56 was measured by digital image analysis using GenASIs HiPath image capture and analysis platform. The histochemical score (H-score) of 0–300 was assessed for CD56 membranous staining of tumor cells, based on the intensity and percentage of immunostained cells. H-score >10 was considered positive.

Results: The mean and median (range) for the H-scores in total PTCs were 30.9 and 0 (0–288). The positive rates of CD56 were significantly lower in classic PTCs (10%) and infiltrative follicular variant (13%) than in classic type with tall cell features (53%), encapsulated follicular variant (93%), tall cell variant (43%), Warthin-like variants (100%), and other variant (50%) ($P < 0.001$). In the PTC subgroup with a follicular growth pattern, loss of CD56 expression was correlated with extrathyroidal extension ($P < 0.001$) and lymph node metastasis ($P < 0.001$), whereas in the PTCs with a papillary morphology, CD56 expression had no significant relationship with any clinicopathologic factors.

Conclusion: CD56 expression is predominantly lost in classic and infiltrative follicular PTCs and increased in other histologic subtypes. Threshold for the expression of CD56 immunostaining should be adjusted with histologic findings to improve its role as a diagnostic marker of PTC.

P1-07-07

RESVERATROL INDUCES CELL APOPTOSIS IN ANAPLASTIC THYROID CARCINOMA CELLS BY ACTIVATION OF THE ERK AND JNK SIGNALING PATHWAYS

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Anaplastic thyroid cancer (ATC) is an extremely aggressive malignancy with undifferentiated feature. Although several conventional medications including radioactive iodine ablation, have been applied for the treatment of anaplastic thyroid cancer, but current therapies still rather limited and novel therapeutic strategies are required. Resveratrol is a polyphenol phytoalexin contained naturally in grapes, berries and several medicinal plants, and is known various biological properties such as antiinflammation, antioxidation, antiallergy, anticancer, antiaging, and neuroprotection. However, little is known about the antitumor effect of resveratrol on ATC cells. In this present study, we aimed to investigate the potential effects of resveratrol on FRO anaplastic thyroid cancer cells.

Resveratrol suppressed the cell viability in a dose-dependent manner in FRO cells. Resveratrol increased expression of the apoptosis-inducing proteins such as Bax, caspase-3, PARP, and cytochrome c and also induced phosphorylation of the ERK, and JNK MAP kinases in a dose-dependent manner.

These results indicate that resveratrol can induce apoptosis in APC by inhibition of the ERK and JNK signaling pathways.

P1-07-08

THE GENETIC SCREENING OF RET PROTO-ONCOGENE IN POLISH POPULATION AND COMPARISON OF THE RET MUTATIONS PREVALENCE WITH RESULTS OF EUROPEAN STUDIES

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Introduction: Gain of function mutations of *RET* protooncogene are associated with hereditary medullary thyroid cancer. There are mainly specific hotspot *RET* gene mutations however they may differ between population.

Aim of the Study: In this study we report the prevalence of *RET* mutations in Polish population based on 20 years of experience of referral polish centers.

Material and Methods: *RET* genetic screening was performed in 2405 patients of Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology (1975 from Gliwice Branch and 430 patients from Warsaw). There were 1394 probands and 1011 family members.

Results: We have found 271 RET positive families (19.4% of all probands) and 273 *RET* gene carriers. Codon 634 (c.1901G>A/C/F) was the most frequent *RET* alteration among all *RET* mutations (34% of families) in MEN2A/FMTC patients and only codon 918 (c.2753T>C) (100% families) was observed in MEN2B patients. Those results are similar to the other European countries (average rate of codon 634 was 39% of all *RET* mutation). Characteristic for Polish population is relatively high frequency (48/296; 25%) of aminoacid substitution in codon 791 (c.2372A>T) and mutation in codon 649 (c.1946 C>T) (12/296; 6.1%) which is very rarely observed in other European populations. Routinely we did not analyze mutation in codon 533 (c.1597G>A/T) of *RET* gene which is characteristic for Greek population,

however we performed such screening in 104 MTC patients who were negative in standard hot-spot analysis. We did not find any mutation in codon 533. **Conclusion:** The most frequent alteration of *RET* gene in Polish population is mutation in codon 634 (c.1901G>A/C/F) of *RET* protooncogene which is characteristic for all European populations. However variation related to different ethnic origin is also reflected in Polish population and is related to two *RET* gene SNP changes: codon 649 and codon 791.

P1-07-09

STRUCTURAL AND FUNCTIONAL STATE OF THE THYROID GLAND DURING PAPILLARY CANCER

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Objectives: The goal of our study was to investigate structural and functional state of the thyroid gland in the patients diagnosed with thyroid papillary carcinoma.

Materials and Methods: We have investigated 47 patients with papillary cancer (39 female, 8 male). Age range 17–68 yy. 11 patients were receiving levothyroxine (25–75 μg). Papillary cancer was diagnosed in these patients with fine-needle aspiration cytology (FNAC), (The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) diagnostic categories VI – malignant). The diagnosis was later confirmed by post-operational histo-morphologic study.

To evaluate thyroid function, we measured the serum levels of thyroid-stimulating hormone (TSH), free thyroxine (FT_4) and also antibodies against thyroid peroxidase and thyroglobulin.

Thyroid gland was evaluated by ultrasound: location, sizes, volume, echogenicity, structure, vascularization, presence of nodules – their location, quantity, sizes, structure and the condition of the regional lymph nodes.

Results: Serum TSH levels were normal (0.4–4.0 mU/l) in 78.72% (8 patients were receiving levothyroxine), elevated in 21.28% (3 patients on levothyroxine). FT_4 levels normal (0.7–1.8 ng/dl) in 82.98% (9 patients on levothyroxine), elevated in 2.12%, decreased in 14.89% (2 patients on levothyroxine). Anti-TPO was elevated in 12.77%, anti-TG in 17.02%.

Thyroid volume was in normal range (female <18 ml, male <25 ml) in 68.09%, elevated 31.91%. Thyroid structure diffusely non-homogenous in 29.79%. Single nodule was present in 51.06%, two or more nodules in 48.94%. Nodule diameter less than 1 cm in 46.81%, 1 cm-4 cm in 53.19%. Complex nodules in 21.28%, hypoechoic in 40.43%, isoechoic in 34.04%, hyperechoic in 4.26%. Intranodular vascularization was present in 55.32%. Unchanged regional lymph nodes were found in 29.79%, lymph nodes with structural changes in 10.64%.

Conclusion: In the majority of cases strong correlation between the presence of papillary cancer and changes in thyroid structural and functional status were not detected.

P1-07-10

FOLLOWING LONG TERM FOLLOW-UP, SAFE EXCISION OF METASTATIC FOCUS AFTER ARTERIAL EMBOLISATION IN A PATIENT WITH BONE METASTASES OF PAPILLARY THYROID CARCINOMA: CASE REPORT

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Background: Differentiated thyroid cancer is a slowly progressive malignancy and have a low metastatic potential. The most common sites of distant metastases are lungs and bones. Sternum, ribs and spine are being the most frequent sites of osseous metastases. Here, we presented a female patient with uncommon metastasis to pelvis during 3 years associated with papillary thyroid carcinoma.

Case: A 52-year-old female patient was examined in our department 3 years after she had undergone total thyroidectomy of papillary thyroid carcinoma (PTC). She presented with severe pain in her left buttock radiating to her lower leg. After total thyroidectomy, radioactive iodine whole-body scan revealed iodine uptake in left sacroiliac region. A positron emission tomography scan revealed hypermetabolic mass in left iliac fossa (SUVmax:10.7). Magnetic resonance imaging scan of the patient revealed a 12×11 cm lesion in the posterior region of left sacroiliac joint. Fine-needle aspiration cytology showed follicular variant of PTC. Patient was referred to the oncology center for palliative radiotherapy and completed 13 cycles. Patient received a total dose of 750 mCi radioiodine-131. Post-therapy scan demonstrated no change of uptake in mass and high serum thyroglobulin titer was sustained. The sciatic nerve could not be identified throughout its trajectory due to the close proximity of the mass to the sciatic nerve. In addition this hypervascular mass had particular challenge for the surgeon and it represented a significant danger of massive blood loss during surgery. The patient had undergone preoperative transcatheter arterial embolization. After reduction of vascularity, mass excision was performed safely in 3rd day of embolization. The patient's postoperative course was symptom free.

Conclusion: Bone metastases may cause severe complications that need multidisciplinary approach. Preoperative transcather arterial embolization for hypervascular bone metastasis is widely accepted as a safe procedure for reducing intraoperative blood loss and surgical morbidity.

P1-08 Analogues + Others / Basic

P1-08-01

THERMOREGULATORY EFFECTS OF 3-IODOTHYRONAMINE IN MICE

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T3, a thyroid hormone (TH), regulates the basal metabolic rate, hence also influencing body temperature. Individuals with hyperthyroidism show hypersensitivity to heat, while cold sensitivity is observed in hypothyroid patients.

Recent studies in mice have shown that THs are also involved in additional mechanisms of body temperature regulation, for instance by affecting vaso-

contractility of peripheral arteries, or by central actions in the hypothalamus regulating brown fat thermogenesis. Moreover, thyroid hormone derivatives such as 3-iodothyronamine (T1AM) also display thermoregulatory properties: a single i.p. injection of this metabolite was shown to reduce body temperature by several degrees. However, it remains unknown whether this effect is tissue autonomous or centrally mediated.

To test the hypothesis that T1AM could facilitate heat loss over peripheral surfaces, we tested whether mouse aorta and tail artery possess the molecular repertoire to respond to T1AM using RT-PCR. Besides the expected expression of TH Receptor-alpha in both vessels, our results showed expression of adrenergic receptor alpha2a in aortas and TAAR1 receptor in tail arteries, both of which are known to mediate T1AM signaling. We then addressed the question if T1AM can directly change the vasocontractility of the aorta and the tail artery by stimulating isolated vessels ex vivo with T1AM using a wire myograph. While we observed a partial vasodilation after T3 stimulation as expected, no effect on vasocontractility of the vessels with a T1AM stimulus was observed.

Our results demonstrate that although aorta and tail artery in mice express the molecular machinery to respond to T1AM stimulation, the drastic effect of this metabolite on body temperature are likely not mediated by direct effects on tail heat loss. Consequently, further studies on possible central actions of T1AM are required.

P1-08-02

SYSTEMICALLY ADMINISTERED 3-IODOTHYRONAMINE (T1AM) AND THYRONAMINE-LIKE ANALOG SG-2 ENHANCE MEMORY AND THERMAL NOCICEPTION IN MICE

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Introduction: 3-iodothyronamine (T1AM) is known to stimulate learning and induce hyperalgesia when administered i.c.v. to mice. Noticeably, these effects appear to involve the histaminergic system. The new synthetic thyronamine-like analog SG-2, was found to produce a good mimic of the behavioral and metabolic effects exerted *in vivo* by T1AM. In the present study, we investigated whether i) T1AM and SG-2 elicit memory enhancement and hyperalgesia when administered i.p. to mice, ii) SG-2 shares the ability to activate the histaminergic system.

Methods: CD-1 male mice were injected i.p. with vehicle or test compounds (i.e. T1AM or SG-2) at the dosages of 4 or 11 μg/kg (n = 20) and memory acquisition-retention (passive avoidance paradigm with a light-dark box) was evaluated. In other sets of experiments mice were injected i.p. with vehicle or T1AM, SG-2 and its oxidative metabolite SG-6, at the dosages of 1.32, 4, or 11 μg/kg (n = 20) with or without pretreatment with clorgyline (2.5 mg/Kg) or pyrilamine (10 mg/kg) and pain threshold to thermal stimulus (hot plate test) was evaluated.

Results: The passive avoidance test showed that when administered i.p. at 11 μg/kg either T1AM or SG-2 induced significant memory enhancement. T1AM also significantly increased retention when administered at a lower dosage (4 μg/kg). At doses that proved to be effective in the passive avoidance test, either T1AM or SG-2 significantly reduced the threshold of pain perception to hot insults. For both compounds the effect was lost after pretreatment with the MAO inhibitor clorgyline or with the H1 antagonist pyrilamine. Noticeably, SG-6, showed hyperalgesic effects at doses of 4 and 11 μg/kg, which were completely abolished by pretreatment with pyrilamine.

Conclusion: T1AM and SG-2 given i.p. to mice improve learning capacity and decrease pain threshold to hot stimuli. SG-6 might contribute to SG-2 nociceptive effects, which seem to involve the histaminergic system.

P1-08-03

3-IODOTHYRONAMINE (T1AM) AND SYNTHETIC THYRONAMINE-LIKE ANALOGS SG-1 AND SG-2 INDUCE AUTOPHAGY IN HUMAN GLIOBLASTOMA CELLS (U-87MG)

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Introduction: Autophagy is one of the most important mechanisms of neuroprotection. Inducing autophagy may represent a new approach to the treatment of neurodegenerative diseases, since hyperactivity of the PI3K/AKT/mTOR pathway, leading to autophagy disruption, has been reported in neurodegenerative disease. T1AM and recently developed TAAR1 agonists (SG1, SG2) have emerged as efficient neuronal modulators, therefore, we investigated their ability to induce autophagy in human glioblastoma cells (U-87MG).

Methods: Cultured U-87MG cells were treated with 1 μM T1AM, SG-1, SG-2 or vehicle (DMSO) for 30 min, 4, 8 and 24 h. Autophagy was monitored morphologically by using transmission electron microscopy (TEM) and immunofluorescence (IF) microscopy to detect autophagic vacuoles and LC3 aggregation. Western blot analysis was used to determine the expression of autophagy protein marker LC3-II, and the level of Akt activation.

Results: Ultrastructural analysis of U-87MG cells exposed to 1 μM T1AM or SG-1 showed a time dependent increase of autophagy-like vacuoles density and LC3 puncta formation (>10 dots/cell) as compared to vehicle treated cells, whereas treatment with 1 M SG-2 appeared less effective. Along with extensive cytoplasmic vacuolization after treatment for 24 h with T1AM ($P < 0.05$, vs. control) and SG-1 ($P < 0.05$, vs. control), we also observed LC3-II up regulation. The increase of LC3-II was ~3.5-fold after 24 h treatment with 1 μM T1AM and ~5.5-fold after 24 h treatment with 1 μM SG-1. No significant changes were observed after treatment with SG-2. Decreased Akt phosphorylation was also observed following T1AM or SG-1 treatment.

Conclusion: T1AM and SG-1 were found to be potent autophagy inducers, whereas SG-2 showed lower activity. Notably, the efficacy to promote autophagy observed for the tested compounds doesn't correlate with their potency to activate TAAR1.

P1-08-04

THE FLAME RETARDANT DE-71 INHIBITS CULTURED HUMAN THYROID CELLS

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Background: Endocrine disrupting chemicals (EDCs), including flame retardants (PBDEs), are suspected to affect thyroid function, which is essential for general growth and metabolism. The production of flame retardants is banned, but there is a continuous release from previously produced upholstery and electronic equipment. The aim of this study was therefore to investigate a possible direct effect of the flame retardant mixture DE-71 on human thyroid cell function *in vitro*.

Material and Methods: Primary human thyroid cells (paraadenomatous tissue from thyroidectomies) were cultured in monolayer. Cells were starved for TSH for 3 days before addition of DE-71 (from 10 to 50,000 μg/l) for 72 h

in presence of TSH. Cell supernatants were harvested and centrifuged before analysis of cyclic adenosine monophosphate (cAMP) (competitive protein binding assay) and thyroglobulin (Tg) (ELISA). Cellular gene expression was measured by qPCR of Tg, thyroid peroxidase (TPO), sodium iodine symporter (NIS), thyroid stimulating hormone receptor (TSHr) and interleukin (IL-) 6.

Results: Inhibitory dose-responses of DE-71 were found on TSH stimulated thyrocytes (n = 13 cell cultures). Maximal inhibition was seen in cells exposed to 50,000 µg/l where the Tg level was reduced (7 cultures) by 71.9% (range: 8.5–98.7%), and cAMP (6 cultures) was reduced by 95.1% (91.5–98.8%) compared to controls (Tg-range: 16.7–2399.3 ng/ml, cAMP-range: 32–1786 pmol/ml). Similar reductions were seen in mRNA of the differentiated thyroid genes, but not of IL-6. There was no evidence of cytotoxicity, and the added DE-71 could be measured in the culture medium by mass spectrometry.

Conclusion: DE-71 inhibited thyroid cells at the level of a signal molecule (cAMP), a protein (Tg) and several thyroid specific genes. This is relevant in elucidating a specific effect of flame retardants. However, further experiments are needed to confirm a more precise causative influence of DE-71 on thyrocytes as well as translation into in vivo situations.

P1-08-05

EFFECTS OF THYROID HORMONES AND 3-IODOTHYRONAMINE ON SIRTUIN EXPRESSION IN HEPATOCYTES

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Background: 3-iodothyronamine (T1AM) is an endogenous messenger chemically related to thyroid hormone. Among its functional effects a shift from carbohydrates to lipids as principal energy resource has been observed. Recent results indicate significant transcriptional effects of chronic T1AM administration involving genes of the sirtuin family. Sirtuins regulate important metabolic pathways involved in apoptosis, stress resistance, energy metabolism. Therefore the aim of this work was to compare the effect of T1AM and T3 chronic treatment on mammalian sirtuin expression in hepatoma cells (HepG2) and isolated hepatocytes.

Methods: Isolated hepatocytes were obtained by liver in-situ collagenase perfusion. Sirtuin expression was evaluated by Western Blot analysis in cells treated for 24 h with 1–20 µM T1AM or T3. In addition, cell viability was evaluated by MTT test upon 24 h treatment with 0.5 nM to 20 µM T1AM or T3.

Results: Protein expression: In HepG2, T1AM significantly reduced SIRT1 and SIRT4 expression at 20 µM while T3 strongly decreased the expression of SIRT1 (20 µM), and SIRT2 (any concentration tested). In primary rat hepatocytes T1AM decreased SIRT4 expression (10–20 µM) whether T3 decreased SIRT2 at 10 µM. Cell viability: T1AM caused a moderate but significant reduction in the number of viable cells particularly in HepG2 cells in which the effect occurred at concentration starting from 5 nM that did not caused any change in sirtuin expression. T3 did not affect cell viability in both HepG2 and isolated hepatocytes.

Conclusion: T1AM and T3 differently affect sirtuin expression in hepatocytes. Since SIRT1 and SIRT4 are important regulator of lipid and glucose metabolism, whereas SIRT2 has a key role in regulating cell cycle and genomic integrity, our observations are consistent with the shift from carbohydrates to lipids induced by T1AM. T1AM has also a moderate effect on cell viability in HepG2 cells which seems however independent from sirtuin modulation.

P1-08-06

DIFFERENTIAL GENE EXPRESSION IN PREGNANCY AS A TOOL FOR PRIMARY HYPOTHYROIDISM DIAGNOSIS

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Background: Thyroid hormone evaluation during pregnancy is a complex situation. Pregnancy modifies the normal physiology and difficult the use of thyroid hormones for diagnostic purposes. The aim of this work was to analyse the differential gene expression to find a transcript or a panel of transcripts with diagnostic utility during pregnancy.

Methods: We selected eight pregnant women (four euthyroid and four with hypothyroidism) for transcriptome analysis. The peripheral blood was collected in RNA preservation tubes (PAXgene blood RNA). The extraction was performed by PAXgene Blood RNA kit (Qiagen). NGS platform Ion Proton System was used for transcriptome analysis following the Ion AmpliSeq transcriptome Human Gene Kit protocols (Thermo Fisher Scientific Manufacturer). We analyzed the library data in rstudio 0.99.491 software, Package Edger 3.12.0 of Bioconductor (Robinson MD, DJ McCarthy and Smyth GK, 2010).

Results: We sequenced 22,786 transcripts in the eight pregnant women. The differential expression analysis revealed 27 genes (twenty-one under expressed and six overexpressed genes). The panel was constructed with 24 mRNA and 3 non-coding genes.

Conclusion: These genes may become an alternative diagnostic tool in pregnancy where free T4, total T4 or TSH are less useful.

P1-08-07

DETECTING 3-IODOTHYRONAMINE IN THE PRESENCE OF FETAL BOVINE SERUM: ISOTOPE KINETIC EFFECT AND OTHER PITFALLS

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Background: Difficulties have been reported in quantitating 3-iodothyronamine (T1AM) in blood or serum, and most in vitro studies have been performed in the absence of serum proteins. The aim of this study was to develop a method to measure T1AM in a standard cell culture medium, namely DMEM supplemented with fetal bovine serum (FBS), and to investigate potential complications caused by serum components.

Methods: FBS and DMEM+10–50% FBS samples were spiked with T1AM and/or deuterated T1AM (T1AM-d4) at the concentration of 10 ng/ml and incubated between 0 and 2 hours. Samples were then extracted using a liquid/liquid method and analyzed using liquid chromatography coupled to mass spectrometry (LC-MS/MS). The catabolites thyronamine, 3-iodothyroacetic acid (TA1) and thyroacetic acid were also measured.

Results: Within 1 hour incubation, T1AM signal decreased to 0.1–14% (depending on FBS content), with an half-life of 5–18 min, while T1AM-d4 signal decreased to 41–76% of the initial peak area. TA1 was detected and accounted about 10% of the missing T1AM, while other catabolites were not present. T1AM decrease was prevented by preincubating samples with 8 M urea or 0.3 mg/ml proteinase K, and reduced over 50% by 0.1 mM semicarbazide, while monoamine oxidase inhibitors were ineffective. Moreover, significant TA1 production was observed by providing NG108-15 cells with DMEM+FBS that had been preincubated for 2 hours, in which T1AM was no longer detectable.

Conclusion: T1AM signal decreases exponentially in FBS-supplemented media, and the decay is much slower with T1AM-d4, suggesting a remarkable isotope kinetic effect. This phenomenon depends on serum proteins, and semicarbazide-sensitive proteins, possibly semicarbazide-sensitive amine oxidases, appear to play the major role. These issues should be taken in account to develop an effective method to assay T1AM in blood and in the usual cell culture media.

P1-08-08

CENTRAL AND PERIPHERAL INFLAMMATORY RESPONSES ARE IMPLICATED IN DIET-INDUCED OBESITY RESISTANCE IN WSB/EIJ MICE

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Thyroid hormones (TH) are intimately linked to both inflammation and metabolism, with TH modulating inflammatory responses and energy expenditure. Metabolism and inflammation also interact: high-fat diet (HFD) induces central and peripheral inflammatory responses in the short and the long term. Moreover, accumulation of circulating and stored lipids, combined with altered metabolic responses, leads to obesity and metabolic syndrome. When compared to the more commonly studied C57BL/6 mouse strain, the wild-derived WSB/EiJ strain shows both lower circulating TH levels and a striking resistance to diet-induced obesity (DIO).

To identify factors underlying obesity resistance, we characterized metabolic and inflammatory responses in both strains exposed to three days (3 d) or eight weeks (8 w) HFD.

After 3 d and 8 w HFD, C57BL/6 mice displayed significantly increased body weight, paralleled by increased circulating levels of leptin, cholesterol, HDL and LDL. In contrast, WSB/EiJ mice showed no or only modest changes in these parameters, except for increased hydroxybutyrate levels indicating an enhanced β-oxidation. In control conditions, WSB/EiJ mice displayed much lower levels of most of the circulating inflammatory-markers analysed than the C57Bl6 mice, thus demonstrating a global lower inflammatory status in the WSB/EiJ strain. Within the hypothalamus, C57Bl/6 mice consistently displayed higher numbers of inflammatory microglial cells and astrocytes in both arcuate (ARC) and paraventricular (PVN) nuclei, with lipid droplets accumulation in the region lining the third ventricle. Despite a total absence of lipid droplets in the hypothalamus, WSB mice displayed a transient response to 3d HFD in the PVN in terms of increased microglial cell number and mitochondrial activity.

Taken together, these findings show that WSB/EiJ mice acutely detect HFD and rapidly adjust thereby preventing deleterious inflammatory peripheral responses. Centrally, this adjustment involves PVN-specific changes in microglia density associated with enhanced peripheral lipid catabolism, the net outcome curbing obesity onset.

P1-08-09

CHOLECALCIFEROL (VIT. D3) AFFECTS THYROID HYSTOLOGY AND FUNCTION IN ORCHIDECTOMIZED MIDDLE-AGED MALE RATS

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Elevated blood level of vitamin D is associated with multiple health benefits. However, vitamin D deficiency is common among the elderly population. Despite multiple cellular targets in both adjacent thyroid C cells and chief parathyroid cells, little is known about how vitamin D affects thyroid follicles and their function in thyroid hormone production. In this study we administered 50 mg of vitamin D3 (that corresponds to 2000 IU/daily), during three weeks, to orchidectomized middle-aged male rats, which we used as a model of andropause with osteoporosis. After animals' decapitation, thyroid tissues were histologically analyzed and serum concentrations of total T4 and TSH were determined by the corresponding rat ELISAs. In comparison with the controls, which received the same amount of the sterile olive oil, thyroids of Vit.D3-treated rats were characterized by interstitial C cell hyperplasia, while the follicular tissue remained preserved. However, depletion of follicular colloid was clearly evident within the follicles. Serum concentration of total T4 was decreased more than 90% ($p < 0.01$), while TSH remained unaltered. In conclusion, treatment with vitamin D3 induced mild changes in thyroid histology, namely by decreasing amount of luminal colloid in the follicles and inducing interstitial C cell hyperplasia. However, serum total T4 was markedly decreased without affecting serum TSH level.

P1-08-10

MOLECULAR ECONOMY OF IODINE: A PHYSIOLOGICAL STRATEGY IN IODINE-DEFICIENT VERTEBRATES

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Background: Wild birds are known to be iodine deficient showing typically hypothyroidic features e.g. high thyroidal 131I uptake, prolonged retention of iodine in thyroid gland, low-normal T4 and high-normal T3. And yet, they survive successfully in iodine-deficient mountainous areas, to the extent of becoming pests. Our earlier published studies on seasonal hormonal profiles, comparative effects of equimolar doses and suppression of peripheral conversion of T4→T3 indicated intrinsic hormonal activity of T4 challenging the existing concept that T4 is a pro-hormone.

Objective: To examine relative roles of T4 and T3 in the process of molt .

Method: Spotted munia, a finch, was maintained in laboratory conditions.

Seven groups of 10–12 birds each were established. GroupI, II, III received 0.37, 0.74 and 1.48 nM of L-T4 per day (sodium salt, Sigma) respectively, and IV, V, VI received the same equimolar doses of T3 in 0.1 ml 0.9% (w/v) alkaline saline over14 days. Control GroupVII received vehicle. The head and right breast of birds was examined every third day and proportion of feather loss/regeneration assessed. A thin wire ring of known diameter divided into six equal sections was used. The ring was placed along the centre of the feather tract and the areas within the six sections examined for feather loss/regeneration. Licence was obtained for wild birds.

Result: T3 lead to significant feather loss from head region with almost no effect on regeneration. T4 had no effect on feather loss but significantly stimulated regeneration in head and body.

Conclusion: Results indicate independent roles for T4 and T3 in the process of molt. A direct independent effect of T4 on cellular processes, along with an indirect one through mono-deiodination to T3 may be a physiological strategy to economise on iodine to cope with iodine deficiency.

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Table 1. (for abstract P1-08-10)

Treatment		Head feathers (mean ± SE)		Body feathers (mean ± SE)	
		loss day 9	regeneration day 9	loss day 9	regeneration day 9
T3	0.37 nM	2.5±0.17	0.6±0.22	0.00	0.00
	0.74 nM	2.8±0.13	0.00	0.00	0.00
	1.48 nM	3.8±0.13	0.00	0.00	0.00
T4	0.37 nM	0.00	4.00±0.10	0.00	4.40±0.22
	0.74 nM	0.00	4.10±0.10	0.00	5.00±0.10
	1.48 nM	0.00	4.00±0.10	0.00	5.00±0.10

P2-01 Clinical Autoimmunity 2

P2-01-01

OUTCOME OF ACUTE ORBITAL EDEMA FOLLOWING A MINUTE DOSE OF RITUXIMAB FOR GRAVES' ORBITOPATHY (GO)

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A 67-year old woman with Graves' disease presented with active GO in OS treated successfully elsewhere with methylprednisolone up a to cumulative dose of 2.5 gr, then discontinued because of concurrent pyelonefritis which led to nephrectomy. In December 2015 the patient was seen for the first time in our centre because of active moderate-severe GO in OD that had developed over the past six months. A complete ophthalmological assessment was carried out and showed active GO in OD (clinical activity score, CAS 4/8) and inactive GO in OS, whereas NOSPECS score was 2b3c4b5060. Due to the previous untoward effects of steroid therapy, we proposed to the patient treatment with a single dose of Rituximab (RTX), administered after premedication with paracetamol, clorphenamine and 100 mg hydrocortisone. RTX is generally infused with progressively increasing concentrations starting from 25 mg in the first 30 minutes, then 50 mg in the following 30 minutes up to 100 mg/hr up until the total administered dose (500 mg). After the infusion of 25 mg RTX (after 30 minutes) the patient presented with an acute orbital edema accompanied by pain and transient decrease of vision in OD. RTX was withdrawn and 100 mg hydrocortisone was administered to control the orbital edema. The orbital pain improved over the next 15 minutes and visual acuity completely recovered in one hour. An orbital CT scan was performed and showed no optic nerve compression. A week later the patient was re-examined and GO was inactive (CAS 3/10) and vision was 10/10. In conclusion, acute orbital edema induced by the rapid cytokine release after very low dose RTX, previously observed in unilateral GO, is not associated with compression of the optic nerve and, at variance with dysthyroid optic neuropathy, may be caused by transient reduced venous outflow from the orbit.

P2-01-02

PREVALENCE OF ORGAN-SPECIFIC AUTOANTIBODIES IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE

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Introduction: Autoimmune diseases tend to aggregate in the same individual or in families. Four types of Multiple Autoimmune Syndromes (MAS) have been described: MAS type 1 (at least 2 among chronic candidiasis, chronic hypoparathyroidism, disease Addison); MAS type 2 [Addison's disease plus autoimmune thyroid disease (AT) and/or diabetes mellitus type 1]; MAS type 3 (AT plus other autoimmune diseases) and MAS Type 4 (association of diseases that do not fit in type 1, 2 and 3). The natural history of autoimmune diseases are characterized by three different phases: a) potential (presence of circulating autoantibodies) b) subclinical (presence of subclinical alteration of the target organ function) and c) clinical (appearance of symptoms and signs of the disease).

Purpose: The aims of the study are: 1) to determine the prevalence of organ-specific autoantibodies [anti adrenal Ab (ACA), anti ovary Ab (StCA), anti pituitary Ab (APA), anti parietal gastric cells Ab (PCA), anti transglutaminase Ab (tTGAb), anti glutamic acid decarboxylase Ab (GADA), anti muscle nicotinic acetylcholine receptor Ab (Arab)] in patients with AT; 2) to define the stage of disease (potential, subclinical or clinical) in patients with one or more autoimmune disease 3) to characterize HLA class II aplotype in a subgroup of subjects.

Patients and Methods: To date 455, out of the planned 2000 patients, [397 F / 58 M; 52.2 ± 15 (mean ± SD) years] with chronic autoimmune thyroiditis (416/455) or Graves disease (39/455), have been enrolled prospectively. ACA, StCA, APA and PCA were measured by indirect immunofluorescence assay, tTGAb and GADA by an enzyme immunoassay and Arab by a radioimmunoassay.

Results: ACA were positive in 3/349 patients (0.86%), StCA in 1/108 (1.85%) APA in 1/295 (0.34%), PCA in 32/293 (10.9%), GADA in 22/391 (5.6%), tTGAb in 7/293 (2.4%) and Arab in 4/321 (1.25%). The prevalence of different types of MAS were: 1.7% for type 2, 4.2% for type 3A, 10.8% for type 3B, 3.8% for type 3C, 2.4% for 3D type and 5.9% for type 4; no case of MAS type 1 was documented. HLA DR4 and DR4, as expected, were the most common haplotypes.

Conclusion: The most frequent MAS is type 3B in particular the association between AT and chronic atrophic gastritis. The potential forms are the most common allowing to plan an appropriate follow-up for early detection and timely treatment of the autoimmune disease.

P2-01-03

CLINICAL SIGNIFICANCE OF TSH-RECEPTOR ANTIBODIES (TRAB) IN PATIENTS WITH AUTOIMMUNE THYROIDITIS

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Objectives: To examine the relationship between TRAb levels and thyroid status and thyroid-associated ophthalmopathy (TAO) in patients with AIT.

Methods: 207 patients (170 women, 37 men) with AIT participated. Levels of TRAb, antithyroglobulin and antiTPO antibodies and thyroid hormones (TSH, FT4, FT3) were measured with third generation ECLIA assays. Thyroid ultrasound and physical examination were performed. Patients were evaluated for presence ot TAO, its severity (according to NOSPECS) and activity (according to CAS). Past medical history, smoking status, presence of other autoimmune diseases and family history for thyroid disease were reviewed.

Results: The median TRAb value was 0.55 IU/l and did not differ significantly in eu-, hypo- and hyperthyroid patients. Linear regression analysis showed correlation between FT3 and TRAb levels ($r2 = 0.128$, $B = 0.357$). 39 patients (18.8%) had TRAb levels above the upper limit (>1.5 UI/l) (TRAb+), while the remaining 168 patients had TRAb levels in the reference range (TRAb-). In TRAb+ thyroid volume was significantly lower than in TRAb– (13.4 ml vs. 16.3 ml, $p = 0.044$). Higher TRAb levels were associated with presence of nodular and pseudonodular changes on thyroid ultrasound ($p = 0.041$). 19 patiens had TAO and they had significantly higher TRAb levels – 1.35 vs. 0.99 IU/l in patients without TAO ($p = 0.002$). In TRAb+ 19.4% had TAO, while in TRAb – only 7.4% ($p = 0.027$). TAO severity negatively correlated with TRAb levels ($p = 0.016$) and was lower in TRAb+ ($p = 0.015$).

Conclusion: In patients with AIT TRAb levels are risk factor for development of TAO and are positively correlated with FT3, and negatively – with TAO severity and thyroid volume.

P2-01-04

THE CLINICAL ROLE OF PROAPOPTOTIC CYTOKINES TNF-α AND SFASL IN DIAGNOSIS OF AUTOIMMUNE THYROID DISEASE IN CHILDREN

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Objectives: The effect of binding death ligands TNF-α and FasL with their surface receptors TNF-R1 and Fas is the induction of apoptosis and subsequently lysis of thyroid cells. The apoptosis pathway is up-regulated in chronic autoimmune thyroiditis (cAIT) and destruction of the thyroid leads to hypothyroidism (hypoT). This phenomenon is also present in Graves' disease (GD) manifested with hyperthyroidism (hyperT). The aim of the study was to determine the relationship between concentration of cytokines TNF-α and sFasL with anthropometric, hormonal and immune thyroid factors in serum of children with autoimmune thyroid disease (AITD).

Methods: The group comprised 45 newly diagnosed children with Hashimoto thyroiditis and Graves' disease vs. euthyroid control group: 11 hypoT (10 girls, 1 boy), 19 hyperT (15 girls, 4 boys), 15 healthy subjects (7 girls, 8 boys). Thyroid function, autoimmune and anthropometric parameters were evaluated.

Results: No significant difference was observed between TNF-α serum concentrations in cAIT ([median] 15.08 pg/ml) and GD (13.63 pg/ml) vs. control group (0.96 pg/ml) ($p = 0.067$). Significantly higher sFasL level ([median] 0.26 ng/ml) was identified in children with hypothyroidism (0.06 ng/ml, $p < 0.001$) and hyperthyroidism (0.14 ng/ml, $p < 0.05$) compared to the controls. The following significant positive correlations were identified between studied cytokines: TNF-α and sFasL ($r = 0.54$; $p < 0.5$) and sFasL and BMI SDS ($r = 0.48$; $p < 0.05$) in GD, as well as TNF-α and TPOAb ($r = 0.54$; $p < 0.01$) in cAIT. ROC analysis indicates that sFasL effectively discriminated hypothyroid and healthy children (AUC = 0.897; $p < 0.001$); sensitivity: 100%, specificity: 73.3%, as well as both clinically opposing states: hyperthyroidism and hypothyroidism among themselves (AUC = 0.833; $p = 0.003$); sensitivity: 94.7%, specificity: 72.7%. TNF-α exhibits efficacy to discriminate healthy children and cAIT children (AUC = 0.691, $p = 0.034$) with low sensitivity 54.5% but high specificity 85%.

Conclusion: Our work shows that TNF-α and sFasL may be useful markers in the assessment of thyroid dysfunction in children with autoimmune thyroid disease.

P2-01-05

AUTOIMMUNE CO-MORBIDITIES AND AGE AT DIAGNOSIS IN HASHIMOTO'S THYROIDITIS (HT)

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Objective: HT, the most common autoimmune thyroid disease at any age, is often associated with other autoimmune diseases. Aim of our study was to assess whether age at presentation may affect autoimmune comorbidity in HT patients and to describe the type and frequency of the non-thyroidal autoimmune diseases (NTAD) that are associated with HT in different ages.

Materials and Methods: The study included 1053 consecutive HT patients: 500 adults (467 F, 33 M, mean age at HT presentation 40.2 ± 13.7 yr) and 553 children (449 F, 104 M, mean age at HT presentation 11.1 ± 2.9 yr). All HT patients were evaluated for common NTAD by means of careful recording of pertinent medical history, physical examination and assessment of selected autoantibodies profiles, when appropriate.

Results: The prevalence of associated NTAD was significantly higher in adults than in pediatric patients: 29.4 *vs.* 18.8% of patients ($p < 0.0001$). Moreover, the number of adults who suffered from two or more associated NTAD was significantly higher than that of children (27.2% *vs.* 6.7%; $p < 0.0001$). A female prevalence was predominant in both cohorts, but was more evident in the adults ($p < 0.0001$). The epidemiological distribution of NTAD was strongly different in the two cohorts. In adults, the most frequent associated diseases were artropathies (psoriasic and rheumatoid arthritis), and connective tissue diseases (Sjögren syndrome and the undifferentiated connectivitis). In the pediatric cohort these disorders were absent or rarely found, and the most prevalent ones were coeliac disease and type 1 diabetes mellitus. Skin diseases showed similar prevalence in both cohorts, and vitiligo was the most common.

Conclusion: HT patients are at significantly increased risk of additional autoimmune diseases. Age at HT presentation may determine a different clustering of autoimmune disorders, favoring the association of some specific NTADs, such as coeliac disease and type 1 diabetes in childhood and rheumatic diseases in adults. Moreover, the aggregation of TH with NTADs occur most frequently in adults. Female subjects are more frequently affected by additional autoimmune comorbidities with increasing age.

P2-01-06

THYROIDITIS AND VITAMIN D

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Introduction: A low level of vitamin D accelerates the lack of immune tolerance on thyroid cells. High level of interleukins and chemotaxic factors contributed to inflamatory state. It's presented with high level of antibody. We wanted to estimated level of vitamin D, level of Thyroid stimulate hormon (TSH) thyroid perioxidase antibody (TPOAb) and thyreoglobulin antibody (TGAb) in our patients with thyroid disturbances. (TD).

Materials and Methods: We measured serum levels of vitamin D3 and calcium, TSH; TGAb, TPOAb with 284 patients: Man (M) N = 79 (27.8%), woman (W) N = 203 (72.2%) with thyroid disease (TD) which included Hypothyroid (Hypo). Hyperthyroid (Hyper) and euthyroid state (Eu) and 349 healthy controls M; N = 109 (31.2%), W; N = 240 (68.8%) during the last three years. All who used vitamin D3 or thyroid hormons either thyroid suppresive drugs were excluded from the analysis.

We used T-test, analysis of variance, Pearson's coefficient per Ellis guidelines (2010).

Results: The patients with TD had significantly lower values of Vitamin D3 26.18 ± 5.32 nmol/l compared to the control: 60.00 ± 16.58 nmol/l. ($P < 0.001$). We had 61.3% Hypothyreosis, 23% euthyreosis and 11.6% Hyperthyreosis. We got a very high level od antibodies: TGAb 158 ± 38.7, IU/ml; TPOAb 896.5 ± 87.4 IU/ml.

Conclusion: We found a significantly lower levels of vitamin D3 in patients with all variance of TD than control. We got statistically significant negative correlation between level of vitamin D and level of ATAb (Pearson correlation coeficient (r) was 0.11 ($p = 0.005$).

All types of thyroid disease showed a low level of vitamin D and a high level thyroid antibodies. We can assume that the normal levels of vitamin D3 could possibly prevent the incidence of inflammatory diseases of the thyroid or better control.

P2-01-07

CLINICAL AND HISTOLOGICAL DIFFERENCES OF THYROID PAPILLARY CARCINOMA IN PATIENTS WITH CHRONIC LYMPHOCYTIC THYROIDITIS

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Introduction: The relationship between chronic lymphocytic thyroiditis (CLT) and papillary thyroid carcinoma (PTC) is controversial since its first description, continuing to be an area of ongoing research.

Objectives: Determination of prevalence of CLT in patients with PTC and evaluation of the clinicopathological differences of PTC in patients with and without CLT.

Methods: Retrospective study of consecutive patients admitted to our hospital for the total thyroidectomy for PTC, between Jan/2009 and Jun/2014. Patients with other histopathological types of tumor and with missing data were excluded. CLT was diagnosed based on histology of the surgical piece. Statistical analysis: IBM SPSS (v.20) – $\chi 2$, Fisher exact test, Student's t and Mann-Whitney. Statistical significance: $p < 0.05$.

Results: Of the 119 patients with PTC, 33.6% (n = 40) showed CLT coexistence. There were no differences on age and sex between patients with and without CLT. Patients with CLT coexistence had a statistical tendency to smaller tumors (11.0 vs. 14.0 mm; $p = 0.055$) and to lower prevalence of lateral neck lymph node involvement (5.0 vs. 16.5%; $p = 0.075$). At diagnosis, there were no statistically significant differences in extrathyroidal extension, lymphatic and venous invasion, multifocality, central neck lymph node involvement and distance metastasis.

Conclusion: In this study, there were no statistically significant differences between groups in the different clinicopathologic characteristics that influence the prognosis of PTC. However, there was a statistical trend for smaller tumor size in patients with CLT as well as a lower lateral cervical lymph node involvement, as suggested by some studies in the literature.

P2-01-08

AUTOIMMUNE THYROID DISORDERS IN TYPE 1 DIABETES – 15 YEARS RETROSPECTIVE STUDY

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Introduction: Although with significant geographic differences, the prevalence of autoimmune thyroid disorders (AIDT) is higher in type 1 diabetic (T1DM) patients. Female sex, age and diabetes duration have been associated with higher risk of AITD. We aim to determine, in our population, the prevalence of thyroid autoimmunity in T1DM and determination of eventual differences between age and sex.

Methods: Retrospective study of the laboratory results with clinical information of T1DM in the last 15 years in our hospital. Thyroid autoimmunity (TA) was defined if patients had positive peroxidase antibodies (anti-TPO) and/or thyroglobulin antibodies (anti-Tg). Statistical analysis: IBM SPSS™ v. 20.

Results: We analyzed data from 554 T1DM patients with median age of 32.0 years (AIQ 27.0).

The majority of patients were females (53.4%) and adults (73.5%). Almost half of the patients had at least one determination of anti-TPO and anti-Tg, 46.9% and 34.3%, respectively. There were no differences between assays request and sex ($p = 0.121$) but younger patients had higher prevalence of anti-TPO and anti-Tg determinations ($p < 0.001$). TA were present in 23.8% of the patients and there were no differences between prevalence of TA and the sex ($p = 0.276$) of the patients. There was a tendency to statistical significance on the prevalence of TA in older patients (25.5 vs 21.0; $p = 0.061$).

Conclusion: TA was present in almost one quarter of T1DM patients, which is consistent with other similar studies. Despite previous studies reported higher prevalence of TA in females, our study failed to demonstrate that female bias.

P2-01-09

THE INFLUENCE OF METHIMAZOLE TREATMENT ON THYROID VASCULARITY IN PATIENTS WITH GRAVES' DISEASE

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Objectives: In untreated Graves' disease (GD), significantly increased thyroid vascularity most likely reflects the action of thyroid stimulating autoantibodies (TSAb). Since less data is available on thyroid vascularity during the treatment of hyperthyroidism, our aim was to evaluate the effect of methimazole on thyroid blood flow in GD patients.

Methods: In our prospective clinical study, which was performed between November 2014 and November 2015, we enrolled 23 consecutive newly diagnosed hyperthyroid patients with GD (19 females and 4 males), aged between 26 and 78 years (mean, 50.7 ± 13.9 years). All patients were prescribed with initial dose of methimazole between 20–40 mg per day, which was reduced to 10 mg per day during the follow-up. Before as well as 7 weeks, 4 months and 7 months after initiation of treatment we determined thyroid function and TSAb. We measured thyroid volume and the peak systolic velocity (PSV) at the level of intrathyroid arteries. We compared the measurements during the treatment and determined correlations.

Results: Before treatment, patients had TSH 0.008 ± 0.0004 mU/l, fT_4 48.68 ± 18.73 pmol/l, fT_3 21.68 ± 8.08 pmol/l and TSAb 7.58 pmol/l (range, 2–60 pmol/l). Thyroid volume was 20.52 ± 9.43 ml and PSV was 18.77 ± 4.84 cm/s. During treatment with methimazole, initial PSV significantly decreased to 13.38 ± 2.01 cm/s at 7-week follow-up ($p < 0.001$), to 12.00 ± 1.94 cm/s at 4-month follow-up ($p < 0.001$), reaching 10.43 ± 0.77 cm/s by the 7-month follow-up ($p < 0.001$). Before treatment, a significant correlation between PSV and TSAb was confirmed ($R = 0.608$, $p = 0.002$), whereas no correlation with thyroid hormones was found. During the follow-up, no correlation with TSH, thyroid hormones or TSAb was found until the final evaluation when the laboratory tests showed TSH 2.49 ± 3.30 mU/l, fT_4 14.36 ± 3.35 pmol/l, fT_3 5.56 ± 2.68 pmol/l and TSAb 2.50 pmol/l (range, 0.0–45.19 pmol/l).

Conclusion: Our findings indicate that treatment of GD patients with methimazole significantly decreases thyroid vascularity.

P2-01-10

ORBITAL TUMOR MASSES DIAGNOSIS – GRAVES DISEASE WITH ORBITAL LYMPHOMA

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Orbital tumor is a rare presentation of lymphoma and it can mimic other common orbital diseases and often make the diagnosis difficult.

A 64-year-old woman with a 19-years history of Graves disease with asymmetrical ophthalmopathy for which she received treatment with antithyroid drugs and corticosteroids, presented with worsening right eye symptoms simultaneously with the development of a right preauricular tumor. Approximately 9 years before, a diagnosis of right orbital tumor had been made by an orbital MRI with a follow-up CT scan after 2 years showing no progression. Physical examination reveals right eye exophthalmia, swelling of periorbital tissues, chemosis, redness and limitation of eye movements. Other findings on physical examination suggested Cushing's syndrome, with supraclavicular and dorsocervical fat and facial rounding with minimal facial hirsutism. The thyroid function was normal. Further investigations performed revealed impaired normal circadian rhythm and lack of suppression of serum cortisol levels after oral administration of dexamethasone with suppressed ACTH levels. The abdominal CT scan showed a left adrenal mass, 27/29 mm in diameter and the head MRI showed right orbital infiltrative lesion involving the lacrimal gland and optic nerve with intracranial extension and multiple parotid lymph nodes. Excisional biopsy of the preauricular nodule demonstrate lymphomatous infiltration, while bone marrow biopsy reveald involvement of this. Treatment will includ surgical removal of the left adrenal gland

followed by corticosteroid replacement therapy and then radiotherapy and chemotherapy for the hematologic disease.

This case illustrates the difficulty in differentiating between inflammatory lesion and orbital tumor in patients with unilateral proptosis in the course of Graves' ophthalmopathy and the importance of a detailed evaluation of patients with suspected hypercortisolism even they do not have many of the typical signs associated with Cushing's syndrome.

P2-01-11

THE CORRELATION OF THYROID AUTO-IMMUNITY AND TYPE 1 DIABETES MELLITUS

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Background: Type 1 diabetes mellitus is an auto-immune disease. Frequently it is associated with other auto-immune endocrine disorders. Auto-immune thyroid disease is one of the most frequent auto-immune diseases associated with T1DM. Diabetes and thyroid disorders have been shown to mutually influence each other and associations between both conditions have long been reported. On one hand, thyroid hormones contribute to the regulation of carbohydrate metabolism and pancreatic function, and on the other hand, diabetes affects thyroid function tests to variable extents. Hypothyroidism may increase susceptibility to hypoglycemia thus complicating diabetes management. Furthermore, it seems that unidentified thyroid dysfunction could negatively impact diabetes and its complications. A higher frequency of retinopathy and nephropathy was observed in diabetic patients with hypothyroidism.

Aim: This study attempts to review the correlation of auto-immune thyroid disease and T1DM.

Methods and Materials: 140 type 1 diabetes mellitus patients were selected from clinic LTD 'Diacor' database, between 2010–2016 years. The patients' age was 22–46 years. After detailed anamnesis, physical examination, investigation of Free-T4, TSH and anti-TPO levels, as well as thyroid ultrasound were performed. The prevalence of thyroid disease in T1DM was 42.9% (60 patients from 140). The prevalence of auto-immune thyroid disease in T1DM was 43.5% (26 patients); 29.9% (18 patients) having subclinical hypothyroidism; 23.3% (14 patients) having primary hypothyroidism; 3.3% (2 patients) having subclinical hyperthyroidism.

Conclusion: Thus, we in our study suggest high prevalence of thyroid disorders in patients with T1DM, especially auto -immune thyroiditis. However, no definitive guidelines exist regarding screening for thyroid dysfunction in T1DM patients. In our opinion, all patients with T1DM are recommended monitoring thyroid status.

P2-02 Hypothyroidism 1

P2-02-01

SELENIUM SUPPLEMENTATION SIGNIFICANTLY REDUCES SERUM THYROID PEROXIDASE AUTOANTIBODIES IN PATIENTS WITH CHRONIC AUTOIMMUNE THYROIDITIS: A META-ANALYSIS

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Objectives: By a systematic review and a meta-analysis to investigate the effect of selenium supplementation on serum thyroid peroxidase autoantibody (TPO-Ab) levels.

Methods: A literature search identified 3366 records. Controlled trials in adults (≥ 18 years) with chronic autoimmune thyroiditis (AIT), comparing selenium with or without levothyroxine (LT4), versus placebo and/or LT4, were eligible for inclusion. After screening and full-text assessment, sixteen controlled trials were included in the systematic review. Using STATA 13.1, random effects meta-analyses in weighted mean difference (WMD) were performed for 3, 6 and 12 months in two different populations: one receiving LT4-therapy and one newly diagnosed and untreated. Heterogeneity was tested by I^2 and quality of evidence was assessed per outcome, using GRADE.

Results: In the LT4-treated population, the selenium group demonstrated significantly lower TPO-Ab concentrations after 3 months (7 studies, WMD: –271, 95% CI: –366 to –175, $p < 0.0001$, $I^2 = 45.4\%$), 6 months (3 studies, WMD: –469, 95% CI: –617 to –322, $p < 0.0001$, $I^2 = 52.4\%$) and 12 months (one study, WMD –423, 95% CI: –450 to –396, $p < 0.0001$). In the untreated population, the selenium group demonstrated significantly lower TPO-Ab concentrations after 3 months (3 studies, WMD: –512, 95% CI: –626 to –398, $p < 0.0001$, $I^2 = 0.0\%$), but not after 6 or 12 months. Quality of evidence was assessed as moderate at all time points in the LT4-treated population as well as at 3 months in the untreated population, being downgraded for indirectness because TPO-Ab is a surrogate marker, and as very low at 6 and 12 months in the untreated population.

Conclusion: Selenium supplementation significantly reduced serum TPO-Ab concentrations after 3, 6 and 12 months in an LT4-treated population and after 3 months in an untreated population. However, TPO-Ab is merely a surrogate marker, and clinically relevant effects remain to be demonstrated.

P2-02-02

PHYSICAL PERFORMANCE IN OVERT AND SUBCLINICAL HYPOTHYROIDISM: A PILOT STUDY

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Hypothyroid patients often complain of neuromuscular symptoms (myalgias, slowness of movements, tiredness) and signs (easy fatigability, cramps) impairing general health and quality of life. Our study aimed at evaluating muscle dysfunction in hypothyroidism by disease-questionnaire, biochemical measures, and physical performance tests, at diagnosis and after restoration of euthyroidism. The cohort study consisted of 57 consecutive patients with newly diagnosed hypothyroidism, 27 with subclinical (S-Hypo; 24 women, 3 men; mean age 45 ± 13 years) and 30 with overt hypothyroidism (O-Hypo; 24 women, 6 men; mean age 49 ± 10 years). Hypothyroidism was due to chronic autoimmune thyroiditis in all cases but one. Thirty euthyroid subjects, matched for gender and age, served as controls. At diagnosis, O-Hypo patients had at least one neuromuscular symptom in 60%, two symptoms in 4%, three symptoms in 36%; prevalence of easy fatigability ($p < 0.002$), muscle weakness, cramps and myalgias ($p < 0.05$), as well as serum CPK levels ($p < 0.0001$) were significantly higher than in controls. S-Hypo patients had slightly, but not significantly higher CPK levels and prevalence of neuromuscular symptoms than controls. Both S-Hypo and O-Hypo performed worse than controls in 6-minute walking test (median walked distance: S-Hypo 444 meters, 95% CI 415–473; O-Hypo 445 meters, 95% CI 419–471; Controls: 501 meters, 95% CI 476–526; $p < 0.0002$). Differences between patients and controls in hand-grip-strength test and sit-to-stand test failed to reach statistical significance (although there was a skight trend) likely due to small sample size, but there was an inverse correlation between CPK levels and hand-grip-strength test in O-Hypo ($p < 0.001$). Restoration of euthyroidism resulted in normalization of questionnaire responses and 6-minute walking test, as well as of CPK levels. In conclusion, these preliminary results indicate that hypothyroidism is associated with reversible abnormalities of physical performance, and 6-minute walking test is the most valuable test to assess them also in S-Hypo.

P2-02-03

QUALITY OF COMPENSATION AND WELL-BEING OF PATIENTS WITH PRIMARY HYPOTHYROIDISM AND OBESITY

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Aim: The aim of the study was to compare quality of hypothyroidism compensation and well-being of patients with hypothyroidism with normal weight, overweight and obesity.

Methods: 306 patients (12 men, 294 women) with hypothyroidism on replacement therapy with L-T4 were included. Later a group of 150 patients with compensated hypothyroidism was selected. All patients were divided into groups depending on their body mass index: with normal body weight (18–24.9 kg/m^2), overweight (25–29.9), obesity I (30–34.9) and obesity II – III degree. We calculated the ideal body weight (IdBW) by Devine formula: for men IdBW = 50+2.3*(0.394*height-60); for women IdBW = 45.5+2.3*(0.394*height-60). Evaluation at baseline included: height, weight, BMI, quality of life (SF-36), TSQ, TSH, freeT3 (fT3), freeT4 (fT4) levels.

Results: There were no difference in the quality of compensation between groups of normal-weight, overweight and obese patients ($p > 0.05$). L-T4 dose in patients with obesity and overweight was significantly higher compared to normal-weight patients ($p < 0.05$). The L-T4 dose per 1 kg of actual body weight was significantly higher ($p < 0.001$) in the normal-weight (1.47 [1.22, 1.68]) and overweight euthyroid patients (1.37 [1 14; 1.64]) compared to patients with obesity (1.25 [1.09; 1.49] 1.04 [0.93; 1.24]). In contrast, L-T4 dose per 1 kg of ideal body weight was significantly higher (*$p < 0.001$*) in overweight (1.78 [1.52, 2.06]) and obese patients (1 9 [1.71, 2.4] 1.99 [1.72, 2.4]), as compared with normal-weight patients (1.49 [1.27, 1.78]). There were no correlation between the fT3, fT4 levels and weight, and also between the L-T4 dose and weight. QOL and TSQ levels were the same in the groups of normal-weight, overweight and obese patients (*$p > 0.05$*).

Conclusion: The compensation of hypothyroidism in patients with overweight/obesity is not worse than that of normal-weight patients. The achievement of euthyroidism requires less L-T4 dose per 1 kg of the actual weight and significantly higher dose for 1 kg of ideal weight in obesity/overweight patients. In patients with hypothyroidism and overweight/obesity the quality of life and severity of hypothyroidism symptoms are not worse than in patients with normal body weight.

P2-02-04

EFFECTS OF SELENIUM SUPPLEMENTATION ON CLINICALLY RELEVANT OUTCOMES IN CHRONIC AUTOIMMUNE THYROIDITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives: By a systematic review and meta-analysis to investigate clinically relevant effects of selenium supplementation in patients with chronic autoimmune thyroiditis (AIT).

Methods: Controlled trials in adults (≥ 18 years) with AIT, comparing selenium with or without LT4, versus placebo and/or LT4, were eligible for inclusion. Identified outcomes were serum thyrotropin (TSH) levels and health-related quality of life (HRQL). After screening and full-text assessment, sixteen controlled trials were included in the systematic review. A random effects model meta-analysis, grouped by intervention duration, was performed in weighted mean difference (WMD) for TSH. Change in HRQL could not be pooled in a meta-analysis. Quality of evidence was assessed per outcome, using GRADE.

Results: No change in TSH was detected between patients assigned to selenium supplementation and placebo after three months (three trials, WMD: –0.11, 95% CI: –0.34 to 0.11, p = 0.322), six months (four trials, WMD: –0.02 95% CI: –0.30 to 0.25, p = 0.862), and twelve months (two trials, WMD 0.62, 95% CI –0.27 to 1.62, p = 0.164). Of the five trials assessing HRQL, two used the SF-36 questionnaire and found no effect following six or twelve months of selenium supplementation. Two other studies used the SF-12 questionnaire, one found no effect, and the other an improvement in well-being after three months. The fifth study, not stating the questionnaire used, reported improvements in tiredness and mood after six months. The quality of evidence was very low for TSH, at all time points, and low for HRQL.

Conclusion: While selenium supplementation effectively reduces thyroid autoantibody concentrations in AIT, previous trials showed no effect on TSH, yielded inconsistent results for HRQL and sparsely evaluated other clinically relevant outcomes. There is need for future well-powered RCTs evaluating e.g. disease progression, morbidity, or HRQL to support or refute efficacy. At present, selenium supplementation in AIT is not warranted.

P2-02-05

L-T4 IN SOFT GEL CAPSULE AND IN ORAL LIQUID FORM IS BETTER ABSORBED COMPARED TO TABLET IN A PATIENT WITH BILIOPANCREATIC DIVERSION

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Objective: Bariatric surgery is a treatment for obesity that along with substantial weight loss causes malabsorption of vitamins, minerals and drugs. In biliopancreatic diversion (BPD) two third of the stomach is removed. The remaining portion is re-connected to the ileum significantly shortening the distance between the stomach and the colon. Reduced drug absorption, especiallly L-thyroxine (LT4), cyclosporine, phenytoin and rifampin may occur post-bariatric surgery. Individual dose-adjustment and therapeutic monitoring may be required.

Methods: In a 34-year-old male with subclinical hypothyroidism who underwent BPD 10 years before, we assessed absorption of LT4 using different formulations of the hormone: soft gel capsule (A), liquid solution (B) and tablet (C), manufactured by IBSA, Lugano, Switzerland. Baseline samples were collected and 150 µg of LT4 were administered. Blood samples were collected at 1, 2, 4, 8 and 24 hr. The pharmacokinetics parameters were assessed measuring the time to peak FT4 concentration (Tmax), the increase FT4 (ΔFT4) calculated subtracting from the baseline value and the area under the curve (AUC).

Results: All L-T4 preparations reached Tmax at 2 hrs. However, maximum ΔFT4 was much higher for A and B compared with C (2.4, 1.8 and 0.25 pmol, respectively). AUC of FT4 were also higher for A and B compared to C, although to a lesser extent (AUC = 305.1, 301.7 and 275.8, respectively).

Conclusion: In a patient treated with BPD the pharmacokinetic parameters of LT4 absorption are improved using soft gel capsule and liquid preparation compared to tablet. The stomach, duodenum and the upper part of the jejunum are not sites for LT4 absorption and, as a consequence, the use of tablets of L-T4 may result in a delay in the absorption in BPD patients. Soft gel capsule and liquid formulations show better and faster absorption of L-T4 and should be considered for treatment of hypothyroid subjects undergoing BPD. However, the clinical significance of this finding must be assessed in larger studies.

P2-02-06

IMPROVED QUALITY OF LIFE DURING L-T4/L-T3 COMBINATION THERAPY OF HYPOTHYROIDISM WAS NOT RELATED TO CHANGE IN WEIGHT

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Objectives: The purpose of this uncontrolled cohort pilot-study was to describe Quality of Life (QoL) during combination therapy, including associations between change in QoL and changes in body weight, as suggested by previous studies.

Methods: Candidates for L-T_4/L-T_3 combination therapy were identified and treated (at dose ratio 17/1) according to guidelines from the European Thyroid Association. We measured weight, body composition (DEXA), thyroid hormones, resting energy expenditure (REE) and QoL (ThyPRO questionnaire) at baseline and after three month of treatment. A change in the Composite ThyPRO 0-100 Impaired QoL-score (higher score worse) >8 was considered clinically significant. Change was evaluated by paired t-test or related-samples Wilcoxon signed-rank test and associations between QoL and clinical variables were evaluated by Spearman correlation.

Results: Twenty-two patients participated (91% women, median age 48, 73% with autoimmune thyroiditis). QoL improved in all participants (median change 31 (5–72)). Ten participants lost weight and 12 participants gained weight: median change –0.30 kg (–5.0 to +2.7 kg). No significant change in weight, REE or S-TSH was observed.

There was no significant correlation between change in QoL and change in: weight, REE, S-TSH or total or free T_3 levels. Baseline QoL-score was positively correlated to free T3 (r_s = 0.587; p = 0.004), i.e. high T3 level correlated with poorer QoL. However, this was no longer present at 3 months.

Conclusion: There was an improvement of QoL for all participants in this study. However, since this study is uncontrolled, we cannot distinguish the true effect of treatment from placebo-effect. Nevertheless, it is noteworthy that this improvement could not be explained by changes in weight, REE or thyroid hormone levels.

Table 1. (for abstract P2-02-06)

	Baseline (n = 22)	3 month (n = 22)
Median ThyPRO QoL (0–100)	54 (27–91)	15 (1–63) (p < 0.0001)
Mean weight (kg)	80.7	80.2 (ns)
Median REE (Kcal/dag)	1,383.0	1,392.0 (ns)
Median S-TSH (mU/l)	0.96	0.59 (ns)

Table 1. Patient data (for abstract P2-02-07)

Group (TSH, mU/l)	Age (mean, yrs)	M/F ratio	Females (N)	Hypo- or hyperthyroidism in close relatives (%)	N
A (<5)	49	1/6.1	73	49	85
B (5–9.9)	43	1/6.5	130	52	150
C (≥10)	43	1/3.9	51	42	64

P2-02-07

HYPOTHYROIDISM TODAY IN AN OFFICE BASED PRACTICE

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During the last 15 years the threshold to treat patients with suspected hypothyroidism has lowered (Taylor et al 2014). I have examined the characteristics of outpatients for whom levothyroxine treatment is currently initiated.

Patients: 299 consecutive patients who after careful differential diagnostics were started on levothyroxine in 2010–2014 were studied. They were divided into three groups based on their TSH value before therapy: A) TSH <5 mU/l, B) TSH 5–9.9 mU/l and C) TSH ≥10 mU/l (overt hypothyroidism) (Table). The treatment goal was a TSH value of about 1 mU/l.

Results: Only 21.4% of the patients had overt hypothyroidism and about half of the patients had close relatives with thyroid disease.

When the TSH was below 20 mU/l, less than 20% of the patients had a free T4 concentration below 10 pmol/l. The presence of TPO antibodies increased as the TSH value increased (TSH <5 mU/l, 41% positive; TSH ≥10, 83% positive). About 65% of patients became symptomless in the subclinical hypothyroidism groups; in the overt hypothyroidism group the rate was 85%. Additionally, some 10–15% of patients had a major response.

Conclusion: In subclinical hypothyroidism, the free T4 is rarely below the reference range. Furthermore, hypo- or hyperthyroidism in close relatives and the presence of TPO antibodies occur only in half of the patients. For patients with subclinical hypothyroidism, test treatment with levothyroxine long enough is often the only means to establish the diagnosis.

P2-02-08

'SUBCLINICAL HYPOTHYROIDISM IN PREGNANCY' OR 'GESTATIONAL HYPOTHYROIDISM'?

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Recently published '2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children' emphasizes the need to maintain the mother's serum thyroid-stimulating hormone (TSH) at a safe level for conception and the development of the embryo and fetus. It is suggested the following reference range for TSH in pregnancy: first trimester, 0.1 to 2.5 mU/l; second trimester, 0.2 to 3.0 mU/l; third trimester, 0.3 to 3.0–3.5 mU/l. According to above mentioned European guideline, subclinical hypothyroidism in pregnancy is defined as a serum TSH concentration higher than the upper limit of the pregnancy related reference range associated with a normal serum thyroxine[T_4; either total (TT_4) or free (FT_4)] and triiodothyronine (T_3) concentrations.

The well-known definition of subclinical hypothyroidism in non-pregnant individuals is significantly different from the one that offers to determine subclinical hypothyroidism in pregnancy. To avoid terminological misunderstandings, we propose to use the new term 'Gestational hypothyroidism' to refer to such degree of thyroid hypofunction, when TSH concentration is higher than the upper limit of the pregnancy related reference range but not more than the upper limit of the TSH reference range for non-pregnant persons, associated with a normal level of thyroid hormones concentration. Such changes of thyroid hormonal concentrations may be dangerous for conception or for embryonal and fetus development but not for non pregnant persons.

We propose to distinguish three degrees of severity of hypothyroidism in pregnancy: 1) 'Gestational hypothyroidism'; 2) 'Subclinical hypothyroidism' and 3) 'Overt hypothyroidism'.

Terms 'Subclinical hypothyroidism' and 'Overt hypothyroidism' during pregnancy should be used in the classical notion.

Our point of view has precedent. According to this principle, the new definition of 'gestational diabetes' has been recently introduced in clinical diabetology.

P2-02-09

THYROGLOBULIN AND OTHER THYROID LABORATORY PARAMETERS IN TREATING HYPOTHYROIDISM IN CHILDREN

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Objectives: This work discusses thyroglobulin and other thyroid laboratory parameters as an appropriate indicators of physiological and pathophysiological processes taking place in the thyroids of six child patients with thyroid hypofunction.

Methods: 6 patients (4 girls and 2 boys aged 9–14 years, 2 patients with a chronic auto-immune thyroiditis and with auto-antibodies against the TSH receptor detected in the initial phase, 2 patients with a chronic form of auto-immune thyroiditis without auto-antibodies against the TSH receptor, 2 patients with a chronic form of non-autoimmune thyroiditis) were, at the beginning of their treatment and over the course of approximately 3–5 month intervals, monitored from both a clinical examination perspective as well as that of complete laboratory diagnosis of the thyroid's function (in total, 6 complete sets of TSH, FT4, FT3, T4, T3, rT3, Tg, TBG, anti-Tg, anti-TPO, anti-TSHr, and urinary iodine). After the diagnosis was determined, the patients were administered L-thyroxine in a daily dose of 0.73 to 2.13 µg L-T4/kg per day.

Results: It can be confirmed that the Tg level drops during the successful treatment of hypothyroidism. The decrease in Tg is thus an indicator of the thyroid's improving state.

Conclusion: The dynamics of change of the circulating Tg can contribute to an improvement of the laboratory diagnosis of the thyroid and the significance of determining the Tg is much broader than its common use as an indicator of the state of the patient with differentiated carcinoma of the thyroid.

P2-03 Goiter 1

P2-03-01

RADIOFREQUENCY ABLATION FOR BENIGN THYROID NODULES IN 375 PATIENTS: 2 YEARS SINGLE CENTER EXPERIENCE

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Purpose: This study aimed at estimating RFA efficacy and safety of treatment of benign thyroid nodules.

Material and Methods: The prospective analysis included the results of RFA of 397 patients with benign tumors of the thyroid gland, received in the Samara Oncology Center from June 2014 till Feb 2016. 94 (23.7%) patients had autonomously functioning thyroid nodules and 303 (76.3%) had symptomatic ones. The nodules size were 3.8 (2.5–8) cm. To exclude malignant tumors all patients underwent ultrasound evaluation at the TIRADS system, double-biopsy with the assessment of biopsy material by BETHESTA system. After RFA all patients were determined the levels of thyroid hormone and had ultrasound control after 1, 6 and 12 months.

Results: After RFA the volume of the thyroid nodules decreased from baseline by 54%, 62%, 76% after 1, 6, 12 months respectively. Therapeutic effect was achieved in one session at 377 (94.9%) patients, 20 (5.1%) patients underwent repeated RFA due to insufficient reduction of nodules. In patients with autonomously functioning thyroid nodules thyroid function normalized completely after 1–2 weeks after RFA. All patients noted a decrease or complete disappearance of symptoms withing a month after RFA. No serious complications such as thyroiditis, voice change, and hematomas were observed.

Conclusion: RFA was effective and safe for treating benign thyroid nodules. RFA might be recommended for treating benign thyroid nodules as the first-line treatment.

P2-03-02

ASSOCIATION OF SERUM CALCITONIN LEVELS WITH MULTINODULAR THYROID DISEASE: 10-YEAR SINGLE CENTER EXPERIENCE

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Objectives: During the decade 2005–2015 routine calcitonin (CT) screening was performed in our department in all patients presenting multinodular goiter (MNG). The objective of this study was to investigate possible association between unstimulated serum CT levels and the presence of either thyroid autoimmunity (AITD) or thyroid neoplasia.

Methods: This is a retrospective study of 648 patients (559 female [F] 86.3%, 89 male [M] 13.7%, median age 58 years, range 18–89 years). CT ≤4.6 pg/ml [F] and ≤11.5 pg/ml [M] was defined as normal. Patients were stratified into 4 groups according to CT. Group1: CT <0.05 (undetectable), Group2: CT [F&M] within normal range, Group3: CT:4.7–10 [F] & 11.6–20 [M], Group4: CT >10 [F] & >20 [M]. Furthermore patients were subcategorized in those with Autoimmune Thyroid Disease (AITD) and those without (non-AITD).

Results: The distribution of patients was: Group 1: n = 184 (28.4%), Group 2: n = 419 (65.3%), Group 3: n = 30 (4.7%), Group 4: n = 9 (1.4%). Of patients with AITD history 23.6% belonged to Group 1, 69.2% to Group 2, 6.0% to Group 3 and 1.2% to Group 4 (x^2, p = 0.037). Forty six patients (7.1%) underwent total thyroidectomy. Histopathological examination revealed: Medullary Thyroid Carcinoma (MTC) n = 3 (3/3 Group 4), C-Cell Hyperplasia (CCH) n = 4 (3/4 Group 3, 1/4 Group 4), Papillary Thyroid Carcinoma (PTC) n = 17 (7/17 Group 1, 10/17 Group 2), MNG n = 22 (9/22 Group 1, 10/22 Group2, 1/22 Group 3, 2/22 Group 4). 2/4 patients with CCH had PTC. 1/17 PTC patient had mixed PTC-MTC. Patients with MTC had remarkably higher CT levels (253–1222 pg/ml) compared to those with CCH (5.8–16.1 pg/ml).

Conclusion: This study reaffirms the positive correlation between CT levels and the presence of MTC or CCH, clearly and conspicuously distinguished by the range of CT levels, although in a small number of patients with these diagnoses. Patients with AITD have more frequently detectable or slightly increased CT levels.

P2-03-03

FUNCTIONAL AND SERUM THYROGLOBULIN CHANGES AFTER US-GUIDED HIFU ABLATION OF BENIGN SOLID THYROID NODULES IN EUTHYROID PATIENTS

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Objectives: High-intensity focused ultrasound (HIFU) ablation induces coagulative necrosis inside the treated target. Our purpose was to assess the changes in thyroid function and serum thyroglobulin (Tg) immediately and 3 months after HIFU treatment of benign thyroid nodules.

Material and Methods: Fifteen euthyroid patients, mean age 45.6 years, with solitary or dominant benign solid nodule, were treated once with US-guided moving-beam HIFU (EchoPulse BEAMOTION, Theraclion), under conscious sedation. Serum TSH, FT4, FT3, and Tg were assessed before and 1 day, 1 week and 3 months after HIFU. Thyroid ultrasound was performed at baseline and at 3-month follow-up. Written informed consent was acquired from all patients.

Results: The mean basal volume was 2.98 ± 1.59 ml, the total applied energy was 5.05 ± 2.38 kJ with mean procedure duration of 23.11 ± 13.41 minutes. One day and 1 week after ablation, the mean serum Tg increased significantly (19.2 ng/ml [range, 0.9–183 ng/ml] vs. 383 ng/ml [range, 34–500 ng/ml] and 38.4 ng/ml [range, 5.9–500 ng/ml], respectively, p = 0.0007) and

returned to baseline at 3-month follow-up. Mean TSH decreased significantly 1 day after HIFU ($p = 0.004$), but no significant differences were found at 1-week and 1-month follow-up, as well as for FT4 and FT3. The mean nodule volume decreased significantly at 3 months (2.03 ± 0.93, $p = 0.005$), with mean volume reduction of $27.7 \pm 17.3\%$. We found significant positive correlation between the total applied energy and FT4 ($r = 0.618$, $p = 0.014$), FT3 ($r = 0.580$, $p = 0.023$) and Tg ($r = 0.750$, $p = 0.001$) at 1 week, as well as between the volume reduction and FT4 ($r = 0.707$, $p = 0.003$) and FT3 ($r = 0.573$, $p = 0.025$) at 1 week. There was also a significant negative correlation between the Tg and the volume reduction at 3 months ($r = –0.530$, $p = 0.042$).

Conclusion: US-guided beam-motion HIFU ablation reduces effectively thyroid nodule volume and has only transient influence on thyroid function and Tg. The dynamic of hormonal and Tg changes could serve as an effect-predictor of HIFU treatment.

P2-03-04

ROBOT ASSISTED TRANSAXILLARY THYROIDECTOMY FOR BENIGN THYROID DISEASES : THE OPERATIVE OUTCOMES OF 177 CONSECUTIVE PATIENTS

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Purpose: Recently Robot-assisted transaxillary surgery for benign thyroid diseases is accepted because of mainly cosmetic considerations and overcoming the technical limitations of endoscopic procedures. The present study was designed to report on our experiences with robotic transaxillary thyroidectomy for the management of benign thyroid diseases.

Method: From Octorber 2007 to September 2015, total 1094 patients underwent thyroidectomy for a benign thyroid disease and 177 patients (16.2%) underwent transaxillary robotic thyroidectomy in Yonsei University Health System. Clinicopathologic features and perioperative results were analyzed by retrospective medical chart review.

Result: All surgical procedures required no conversion to open procedure and were performed without any major incidents. A total of 177 patients, 161 was female, who was 10 times more than male. Mean age (year) and postoperative hospital stay (day) was 36.76 ± 10.71 and 3.03 ± 0.57 respectively. Mean tumor size was 2.12 ± 1.48 cm. A total of 122 patients (68.9%) underwent less than total thyroidectomies and 25 patients (31.1%) total thyroidectomies. The most common pathology was adenomatous hyperplasia (54.8%) followed by follicular and Hurthle cell adenoma (27.6%) and 22 patients (12.4%) were Graves' disease. The perioperative result in terms of mean operating time with robotic procedure was 132.07 ± 41.23 minutes and the average console time was 52.20 ± 23.64 minutes.

Conclusion: We report the largest series to date of our experiences with robotic transaxillary thyroidectomy for benign thyroid procedure. Although expected total operating time is long, robotic transaxillary thyroidectomy is favorable procedure for benign thyroid diseases and cosmetic effect with no scar on anterior neck is a major advantage.

P2-03-05

THE EFFECT OF J-131 THERAPY IN PATIENTS WITH AUTONOMOUSLY FUNCTIONING THYROID NODULES AND NORMAL TSH LEVEL

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The effect of J-131 therapy in patients (pts) with autonomously functioning thyroid nodules (AFTNs) and a normal thyroid stimulating hormone (TSH) value has been evaluated. Up to our knowledge, this is the first study which has scintigraphically evaluated the effect of J-131 therapy in patients with AFTNs and normal TSH level.

50 cytological benign AFTNs in 46 pts (41 female and 5 male) with normal TSH level have been treated with a fixed J-131 doses (370 MBq). Clinical exam, ultrasonography with color Doppler (US), fine needle aspiration biopsy (FNAB), TSH, FT4, FT3, anti-TPO, anti-Tg and thyroid scan (scintigraphy) have been performed in all pts before and after J-131 therapy. A 6 month post J-131 therapy a thyroid scan has been performed in 33 pts with 37 AFTNs.

The median age of the pts was 57 (range 37–83) years. AFTNs were located more frequently in the right thyroid lobe (28 nodules) than in the left lobe (22 nodules). In 10 pts a solitary AFTN has been found on ultrasonography and the other 36 patients had AFTNs in multinodular goiter. Four pts had two AFTN. On post J-131 therapy thyroid scan in 31 AFTNs complete therapy effect has been observed, but in 6 AFTNs a scintigraphycally partial effect has been noted. Statistical analysis showed a significant reduction in the thyroid ($p = 5.74E-14$) and AFTNs ($p = 5.59386E-07$) volume after J-131 therapy. TSH value significantly increased ($p < 0.001$) and FT4 value significantly decreased ($p < 0.001$) after J-131 therapy. FT3 ($p = 0.91054$), anti-TPO ($p = 0.80461$) and anti-Tg ($p = 0.39097$) values did not change significantly.

J-131 therapy in pts with AFTN and normal TSH level is a simple and very effective modality. The effect of the J-131 therapy on AFTNs can be exactly evaluated only with a post J-131 therapy thyroid scan.

P2-03-06

ADIPOSE TISSUE ACCUMULATION AND SEDENTARY LIFESTYLE ARE PREDICTIVE OF SPECIFIC THYROID NODULE ULTRASOUND FEATURES

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Objective: Thyroid nodule existence has been associated with obesity, but data regarding associations of body composition parameters with specific ultrasound features are currently missing. In this study, we aimed to investigate possible associations between obesity-related parameters and thyroid nodule ultrasound characteristics.

Subjects and Methods: We offered free ultrasound screening to general population for the diagnosis of thyroid nodules. In every subject we recorded ultrasound findings as well as medical history, demographic and anthropometric characteristics. Body composition parameters were evaluated using Bioelectrical Impedance.

Results: 306 subjects [215 females (70.3%)], aged 50.3 ± 14.5 years, were included in the study. Of those, 168 (54.9%) were harbouring one or more nodules; these individuals had higher age ($p < 0.001$), percentage of total body fat (% TBF) ($p < 0.001$), waist circumference ($p = 0.045$), and a trend towards higher visceral fat rating ($p = 0.056$), waist-to-hip ratio (WHR) ($p = 0.048$) and body mass index (BMI) ($p = 0.097$), compared with individuals without nodules. Age (OR = 1.04; 95% CI= [1.02–1.05]; $p < 0.001$) and female gender (OR = 1.98; 95% CI= [1.18–3.51]; $p = 0.01$) were the only independent predictors of thyroid nodule existence. However, in bivariate correlation analysis, % TBF was associated with nodule size ($r = 0.167$, $p = 0.031$) and was also an independent predictor of presence of a hypoechoic thyroid nodule (OR = 118.4; 95% CI= [5.29–2650.36]; $p = 0.003$) and peripheral vascularity (OR = 89.12; 95% CI= [2.66–2982.50]; $p = 0.012$), while lack of exercise was associated with internal vascularity (OR = 5.19; 95% CI=[1.49–18.12]; $p = 0.01$).

Conclusion: Age, as well as total body fat accumulation and self-reported lack of exercise, used as surrogate markers of sedentary lifestyle herein, may increase the risk of specific thyroid nodule ultrasound patterns. Therefore, routine ultrasound screening of obese patients and active lifestyle and/or weight-loss strategies to prevent thyroid nodule appearance and possible progression to cancer might be warranted.

P2-03-07

THE IMPACT OF ULTRASOUND SCREENING ON THE EVALUATION OF THYROID PATIENT. A COMPARATIVE STUDY OF 1,000 PATIENTS INVESTIGATED IN 2005 AND 2015

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Objective and Methods: Thyroid ultrasound screening (TUS) has a well-known adverse effect as regards overdiagnosis and overtreatment of thyroid nodules (TN). We investigated the impact of the TUS on the diagnosis and on the evaluation system in a moderately iodine deficient region by comparing the data of patients admitted consecutively to thyroid investigation with the diagnosis of TN, 500 patients in 2005 and 500 in 2015.

Results: 739 patients were sent because of complaints or palpable TN (Gr1) while 261 was referred on the result of screening (Gr2). 97 patients had palpable nodule in Gr2. Lesions larger than 1 cm in maximal diameter (80.4% vs. 47.9%), the number of carcinomas (26 vs. 9), the number of thyroid carcinomas other than papillary microcarcinoma (17 vs. 2), the proportion of patients requiring surgery (16.5% vs. 6.9%) were significantly higher in Gr1 vs. in Gr2. In 14.6% of Gr2 patients the discrete lesions were in fact not nodules but focal presentations of autoimmune process. The proportion of Gr2 patients has almost doubled over a decade, 18.4% and 33.8%, 2005 and 2015, respectively.

Conclusion: In addition to overdiagnosis and overtreatment of TN, one of the most important but only rarely mentioned drawback of TUS is the continuously decreasing capacity of a thyroid team managing patients indeed requiring evaluation. The negative consequences of screening are hardly compensated by the recognition of a few potentially significant non-palpable nodules or by that of autoimmune thyroiditis.

P2-03-08

COMPARAISON BETWEEN THREE THERMOABLATION TECHNICS FOR BENIGN THYROID NODULES TREATMENT: EXPERIENCE IN A SINGLE CENTER

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The very important progresses of the association Thyroid Ultrasound – Fine needle aspiration cytology give us the possibility to avoid surgery in a lot of cases of thyroid nodules. But some benign nodules require efficient treatment because of their volume, their evolution, of their location. Thermoablation procedures make it possible to reduce the volume of the nodules without surgery, without conventional hospitalization, and without necessity of LT4 substitution. The three commonly used technics are laser ablation, radiofrequency and Echopulse (HIFU). There are a very few number of institutions to have available these three devices. We used laser since 2014 and the two other technics since 2015. The number of procedures are: Laser: 20 Radiofrequency: 37 HIFU: 6. The sex-ratio is M9/F54. The volume of the nodules are Laser 12.6 ml (1.1/31) Radiofrequency 18.5 ml (2.8/100) HIFU 3.8 (1.1/7.5). The results are good with a main early reduction of volume of 50% and later around 70%. We have not observed serious side effect (one hematoma). One nodule increased after an early good result and the patient referred to surgeon (Benign histology). Two patients were lost to follow up. This triple experience is able to draw precise indications for each technic.

P2-03-09

THYROID NODULES AND CYSTS IN TYPE 1 DIABETIC CHILDREN AND ADOLESCENTS

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Background: Thyroid nodules and cysts are rare disorders of thyroid gland in pediatric population. It needs to be investigated and compared with the control group of healthy population. The impact of thyroid autoimmunity on the nodule formation processes is unclear yet.

Objective: The aim of this study is to reveal thyroid nodules and cysts of thyroid gland in non-diabetic and type 1 diabetic patients, to evaluate their connection with thyroid autoimmunity and hypothyroidism comparing with.

Methods: 372 children and adolescents with type 1 diabetes mellitus as well as 372 non-diabetic patients (control group) under 18 year of age were included in the investigation (male/female ratio was 1.2:1). Statistical analyses were performed to determine the significance of findings. In all cases null hypothesis was rejected if $p < 0.05$.

Results: 9 diabetic patients (2.42%) found to have nodules versus to 2 (0.54%) non-diabetic patients, and 5 cases of cysts versus to 1 respectively. Autoimmune thyroiditis was diagnosed by thyroid ultrasound, clinical and laboratory examination in 60 (16.1%) patients in diabetic group, and 7 cases of nodules were revealed in association with autoimmunity in thyroid gland, versus to 0 in the control group ($p < 0.05$). In 4.8% of diabetic patients goiter have been found but without significant correlation with nodules and cysts ($p < 0.05$).

Conclusion: This data shows an increase rate of thyroid nodules and cysts development in type 1 diabetic children and adolescents comparing with those without diabetes. Further investigations should be done to evaluate the prevalence and mechanisms of thyroid nodule development in type 1 diabetic children and adolescents.

P2-03-10

SERUM THYROGLOBULIN LEVEL AS A PREDICTIVE FACTOR OF NODULE SIZE AND MALIGNANCY IN PATIENTS WITH THYROID NODULES

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Objectives: According to latest guidelines, measurement of serum thyroglobulin (Tg) level in the diagnostics of thyroid nodules is not recommended. In some studies, serum Tg level was associated with the nodule size. In follicular and Hürthle-cell neoplasms, preoperative serum Tg level was reported either as a poor or as a useful predictor of thyroid malignancy. Therefore, our aim was to establish the role of Tg measurement in our patients with thyroid nodules.

Methods: We reviewed medical records of all patients who were first diagnosed with thyroid nodules between May 2014 and December 2015 at our thyroid department. In all patients, a volume of thyroid nodules was measured by ultrasound (US), and a serum concentration of Tg was measured. In some patients, US-guided fine-needle aspiration biopsy (FNAB) was performed. The cytology report was categorized as suspicious or unsuspicious. Patients with cytology report suspicious for papillary thyroid cancer were not included in the study.

Results: Out of 801 consecutive patients with thyroid nodules (603 women and 198 men), 107 patients with Tg level above 100 ng/ml had significantly higher volume of thyroid nodules than 694 patients with Tg level below 100 ng/ml (median (range), 11.1 (0.02−95.5) and 1.1 (0.003−84.7) ml, respectively, $p = 0.006$). We found a significantly positive correlation between the serum Tg level and the volume of thyroid nodules ($R = 0.469$, $p < 0.001$). Out of 413 patients with cytology reports, 41 patients with thyroid nodules suspicious for follicular and Hürthle cell neoplasm had significantly higher Tg level than 372 patients with unsuspicious thyroid nodules (median (range), 65.0 (7.0−34,650.0) and 23.5 (0.0−6,248) ng/ml, respectively, $p = 0.001$).

Conclusion: In our patients with thyroid nodules, serum level of Tg turned out to be a useful predictive factor of nodule size and malignancy.

P2-04 Reproduction

P2-04-01

CLINICAL AND MOLECULAR CHARACTERISTIC OF PATIENTS WITH THYROID DYSGENESIS AND PAX8 MUTATION

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Context: Thyroid dysgenesis (TD) is the most common cause of congenital hypothyroidism (CH). The *PAX8* gene mutations have been described in patients with both familial and sporadic form of dysgenesis and variable thyroid phenotype.

Objective: The aim of the study was to correlate clinical and biochemical phenotype of children with CH and TD with *PAX8* mutation.

Material and Methods: The study included children from south-eastern Poland selected via already established neonatal screening for primary CH. Molecular investigations (Sanger sequencing method and MLPA analysis) were performed in 45 patients with sporadic CH due to TD. *PAX8* gene variants were reveled in seven inmates (4 girls, 3 boys), finally enrolled into the study.

Results: See table 1.

Conclusion: There was no exact correlation between clinical phenotypes and *PAX8* genotypes.

We observed an individual variability of the phenotype in patients with *PAX8* genetic variants.

Thyroid ectopy (P6) was associated with heterozygous deletion in exon 7 of *PAX8*, a finding that has not been reported previously.

Various clinical presentations of CH indicate necessity of genetic studies regardless of type of TD.

Table 1. Clinical and biochemical data in patients with CH and detected genetic variants (for abstract P2-04-01)

Patient/ gender	Etiology	TSH [mIU/l]/ fT4 [pmol/l]	PAX8 variants
P1/Male	*Thyroid dysgenesis	49.5/no data	p.E234K
P2/Male	*Thyroid dysgenesis	no data	p.P409S
P3/Male	*Thyroid dysgenesis	>100/2.34	–456C>T promoter variant
P4/Female	*Thyroid dysgenesis	88/11.4	–456C>T promoter variant
P5/Female	Thyroid ectopy	270/9.31	–456C>T promoter variant
P6/Female	Thyroid ectopy	>80/7.49	Heterozygous del in exon 7
P7/Female	Thyroid agenesis	96/6.99	Heterozygous del in exon 7

* Lack of thyroid scintiscan restrics defining an exact type of abnormality.

P2-04-02

CONTROLLED ANTENATAL THYROID SCREENING (CATS) STUDY: OBSTETRIC OUTCOMES

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Context: Suboptimal thyroid function in pregnancy is associated with adverse obstetric outcomes but it is unclear whether levothyroxine treatment, initiated during pregnancy is beneficial.

Design: Retrospective analysis of the CATS study with obstetric outcomes obtained through data-linkage in the Secure Anonymised Information Linkage (SAIL) databank.

Participants: 13,224 pregnant women; 12,608 women had normal thyroid function, 340 had subclinical hypothyroidism (SCH), 305 had isolated hypothyroxinemia (IH). 518 women with abnormal thyroid function were randomized to receive levothyroxine (N = 263) or no treatment (N = 255) at the end of the first trimester.

Outcome Measures: Primary Composite of stillbirth, neonatal death, early preterm delivery (<34 weeks), APGAR score at 5 minutes <7, length of hospital stay >5 days. Secondary: preterm delivery (<37 weeks), preterm caesarean section (<37 weeks).

Results: In individuals with abnormal thyroid function randomized to treatment or control, treated individuals had lower odds of having one of the composite outcomes although this was not statistically significant OR = 0.75 95% CI (0.40, 1.40) p = 0.39.

Untreated women with SCH had increased odds of stillbirth compared to women with normal thyroid function OR = 4.37 (95% CI 1.04, 18.3) p = 0.03. No stillbirths occurred in women on levothyroxine. Untreated women with IH had increased odds of a preterm delivery than women with normal thyroid function OR = 1.58 (95% CI 1.04, 2.50) p = 0.03. Women with IH randomized to levothyroxine treatment had reduced odds of preterm delivery (<37 weeks) OR = 0.37 (95% CI 0.14, 0.99) p = 0.04 and preterm caesarean section (0% vs 4%) p = 0.04 than untreated women.

Conclusion: Both SCH and IH were associated with key adverse obstetric outcomes. Potential benefits of levothyroxine therapy were observed, however, our sample was under-powered to properly assess this effect in our composite outcome. Larger studies are required to confirm benefits of screening and treatment.

P2-04-03

THE ROLE OF ANTITHYROGLOBULIN AUTOANTIBODIES IN COMPARISON WITH THYROID PEROXIDASE AUTOANTIBODIES IN PREGNANT DANISH WOMEN

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Introduction: Thyroid autoimmunity in pregnant women has been associated with adverse obstetric outcomes. However, distinction between thyroid peroxidase autoantibodies (TPOAbs) and thyroglobulin autoantibodies (TgAbs) is seldom applied, and most studies focus on TPOAbs. Our aim was to investigate possible differences between the two types of thyroid antibodies and pregnant women's thyroid function and obstetric outcome.

Methods: Cohort study of 923 randomly selected pregnant Danish women attending the national Down's syndrome screening at Copenhagen University Hospital in 2008. fT4 and TSH levels were measured by radioimmunoassay (Roche Diagnostics GmbH, Mannheim, Germany). TPOAb- and TgAb-levels were measured by automated Kryptor immunoflourescent assays (BRAHMS, Hennigsdorf, Germany; functional assay sensitivity 50 kU/l). Antibody-positivity: >60 kU/l (clinical cut-off). Primary obstetric outcome: preterm birth (gestational week <37). Tests for trends: $\chi 2$-tests, independent samples t-tests. Adjusted regression analyses included covariates: gestational week at blood sampling, maternal age, BMI, smoking status, and conception method (preterm birth only).

Results: Among 923 pregnant women, 149 (16.2%) were antibody-positive: 86 (9.3%) TgAb-positive, 111 (12.0%) TPOAb-positive, hereof 48 (32%) were positive for both autoantibodies. Sligthly lower fT4-levels were found in TgAb-positive women ($p = 0.03$), but not in TPOAb-positive women ($p = 0.14$). This remained in adjusted regression analysis of (log)fT4-levels (TgAb-positive: $p = 0.02$, Exp(B) = –0.02, 95% CI (–0.03–(–0.003)), TPOAb-positive: $p = 0.52$, Exp(B): –0.004, 95% CI (–0.02–(–0.01)). Both antibodies were associated with slightly higher TSH-levels ($p < 0.05$). Antibody-positivity was not significantly associated with preterm birth, however, TgAb-positivity showed a trend towards an association (aOR = 2.3, 95% CI (0.78–6.86), $p = 0.13$) and TgAb-positive women gave birth at an earlier gestational week ($p = 0.02$, Exp(B): –0.49, 95% CI (–0.92–(–0.07)).

Conclusion: In our cohort of pregnant Danish women with no prior thyroid disease, nearly as many women were TgAb-positive as TPOAb-positive with limited overlap. While presence of either antibody was associated with higher TSH-levels, only TgAb-positivity was associated with lower fT4-levels. TgAb-positive women tended to give birth slightly earlier in gestation. Reconsideration should be given to the role of TgAbs in pregnant women.

P2-04-04

PREVALENCE OF THYROID AUTOIMMUNITY AND DYSFUNCTION IN WOMEN WITH IRON DEFICIENCY DURING EARLY PREGNANCY: IS IT ALTERED?

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Objective: Thyroid disorders and iron deficiency (ID) are associated with obstetrical and fetal complications. Iron is essential for the normal functioning of thyroid peroxidase (TPO-abs) and ID is frequent during pregnancy. The aim of the study was to compare the prevalence of thyroid autoimmunity (TAI) and dysfunction during the first trimester of pregnancy in women with and without ID.

Design: Cross-sectional data analysis of 1900 pregnant women nested within an ongoing prospective collection of pregnant women's data. Method: The study was performed in a single, tertiary referral center. During the first antenatal visit, Ferritin, TPO-abs, TSH and FT4 were measured and age, BMI were recorded. ID was defined as Ferritin <15 ug/L, TAI when TPO-abs >60 kIU/l and subclinical hypothyroidism (SCH) when TSH >2.5 mIU/l.

Results: ID was present in 36% of women. Age and BMI were comparable between both groups. In the ID group, the prevalence of TAI and SCH was significantly higher, compared to that in the non-ID group (10% vs. 6% and 20% vs. 16%; $p = 0.011$ and 0.049 respectively). Ferritin was inverse correlated with serum TSH ($r = –0.076$; $p = 0.001$) and positive with FT4 levels ($r = 0.112$; $p < 0.001$). In the logistic regression model, ID remained associated with TAI after correction for confounding factors ($p = 0.014$). The association with SCH was absent after correction for the confounders in the logistic regression model, but remained present in the linear regression model ($p = 0.035$).

Conclusion: ID is frequent during the first trimester of pregnancy and associated with a higher prevalence of TAI, higher TSH and lower FT4 levels.

P2-04-05

CLINICAL RELATIONSHIP BETWEEN HASHIMOTO'S THYROIDITIS AND BRAFV600E MUTATION STATUS IN PAPILLARY THYROID CARCINOMA PAIENTS

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Purpose: Concomitant papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis (HT) is a frequent occurrence. Whether these two conditions are linked and whether PTC with concurrent HT has distinct clinicopathological characteristics are still debated issues. Lymphocytic infiltration is abundant in HT and might be relevant in the pathogenesis and progression of PTC. $BRAF^{V600E}$ mutation is associated with a more advanced PTC at diagnosis; however, its role in the clinicopathological characteristics of PTC with concurrent HT is unknown. The purpose of this study was to evaluate the potential relationship between Hashimoto's thyroiditis and $BRAF^{V600E}$ mutation status in patients with PTC.

Methods: A total of 198 patients who underwent surgery for PTC between January 2013 and June 2013 were enrolled in this study. $BRAF^{V600E}$ mutation analysis was performed using polymerase chain reaction (PCR)-based amplification of DNA extracted from paraffin-embedded tumor specimens.

Results: $BRAF^{V600E}$ mutation and HT were detected in the numbers of 149 (70.2%) patients and 73 patients (36.9%), respectively. BRAFV600E mutation was not correlated with HT ($P = 0.749$). Lymph node metastasis was more frequent in $BRAF^{V600E}$ mutation patients (OR = 2.04, $P = 0.039$). However, age, tumor size, extrathyroidal extention, and mutifocality were not significantly associatied with the $BRAF^{V600E}$.

Conclusion: The results of our study suggest that $BRAF^{V600E}$ mutation were associated with aggressive PTC. However, there was no clinicopathological association between $BRAF^{V600E}$ mutation and HT.

P2-04-06

CHANGES IN THYROID HORMONE AND INSULIN RESISTANCE PARAMETERS IN HEALTHY AND YOUNG WOMEN DURING THE FIRST YEAR OF USE OF THE CONTRACEPTIVE DEPOT MEDROXYPROGESTERONE ACETATE

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Objective: To evaluate the behavior of thyroid hormones in new depot medroxyprogesterone acetate (DMPA) users during the first year of using the method.

Methods: Nonrandomized clinical trial, conducted at the Human Reproduction Unit, Department of Obstetrics and Gynecology from February 2011 to February 2012. We interviewed 290 women, 72 women met the inclusion criteria. Twenty eight women matched by age (± 1) and BMI (± 1) with 24 women users of cooper intrauterine device (IUD Cu380A) completed the study. Inclusion criteria were age 18–40 years, body mass index (BMI, kg/m^2) <30, fasting glucose <100 mg/dL and <140 mg/dL after glucose load (75 g). The variables studied were sociodemographic, BMI, body composition (dual energy absorptiometry, DXA), TSH (thyrotropin), FT3 (free triiodothyronine), FT4 (free thyroxine), glucose and lipids parameters, HOMA-IR, adiponectin and leptin. All measurements were performed at baseline (T0) and after 12 months of use of the method (T12).

Results: The mean age of women was 29.6 and 28.6 years and BMI of 23.8 and 24.7 kg/m^2 in the DMPA group and IUDs, respectively. It was observed elevated mean LDL cholesterol (p = 0.04), total mass (p = 0.02) and total body fat (p = 0.002) in the DMPA group compared to the IUD group. FT4, T4/T3 ratio, insulin, HOMA-IR, BMI, total mass and total body fat increased significantly after one year the use of DMPA. We verified a positive correlation between the variation T12-T0 in levels of FT3 (p = 0.02, r = 0.4246), FT4 (p = 0.04, r = 0.3890) and triglyceride levels only in DMPA users.

Conclusion: After one year of DMPA use was found increase in thyroid hormones concentration and insulin resistance parameters. The positive correlation between elevated levels of FT4 and FT3 with the elevation of triglycerides under the use of DMPA indicates influence of HT on changes of lipid metabolism in these users.

P2-04-07

ASSOCIATION OF HLA-B*46 POLYMORPHISM AND GRAVES' DISEASE IN THAI POPULATIONS

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Background: Graves' disease is an autoimmune disease with complex pathogenesis involving genetics and environmental factors. Similar to other autoimmune disorders, the human leukocyte antigen (HLA) system has shown an intriguing candidate gene predisposing to Graves' disease; however, the evidence remains inconsistent and inconclusive. The aim of this study was to determine whether the HLA-B*46 is linked to Graves' disease in Thai populations.

Methods: A case-control study was performed in patients with Graves' disease and gender-matched control subjects. HLA genotyping was analyzed by PCR amplification with sequence-specific primers (PCR-SSP). Allele and genotype frequencies were compared between the study groups using the chi-square test. Other clinical parameters including onset and severity of the disease, size of thyroid goiter, the presence of Graves' ophthalmopathy and thyroid periodic paralysis, and the presence of family history of autoimmune thyroid disease were also analyzed.

Results: Fifty-four Graves' disease (GD) patients and 61 control subjects were recruited into this study. The prevalence of HLA-B*46 was 20.3% (11 in 54) among the GD group and 8.1% (5 in 61) in the control group nonetheless there was no significant difference between the two groups (P = 0.060). In the GD groups, there were also no differences in the clinical parameters between the GD patients with the HLA-B*46 polymorphism and the negative group.

Conclusion: We found a slight increasing frequencies of HLA-B*46 in Thai patients with Graves' disease. Thus, future studies with a larger sample size should attempt to confirm our results.

P2-04-08

THYROID HOMEOSTASIS IN IODINE-DEFICIENT and IODINE-SUFFICIENT HEALTHY INDIAN PREGNANT WOMEN

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Background: Pregnancy is a physiological state characterized by increased metabolic demand resulting in alterations in thyroid hormones. However, our understanding of thyroid homeostasis is very much limited because of paucity of longitudinal studies in iodine-sufficient and iodine-deficient populations.

Objective: To understand homeostatic adjustments of thyroid hormones during pregnancy with special reference to Iodine deficient population.

Method: Epidemiological observational survey included pregnant women (19–28 year) from rural region of Haryana (2013–2015) through Government Primary Health Centers. Total 307 healthy pregnant women fulfilling inclusion criteria were enrolled. On the basis of UIE 279 subjects were identified as iodine-deficient (IDS) and the remaining iodine-sufficient (ISS). Finger prick blood samples were taken on 10, 20, 30 week of pregnancy. TSH & FT4 were measured in Dry blood spots using ELISA. IEC approval & informed consent were also taken.

Results: Trimester specific range of TSH and FT4 are summarized in Table 1.

Examining the patterns of hormones it is evident that in 2/3rd of subjects (n = 192) TSH shows a steep rise of 28–37% over the trimesters as against the 1/3rd individuals (n = 87) in which TSH rises with a slow steady trend (by 7–15%), the difference being significant (p < 0.001). In the Iodine-sufficient group 29% of subjects with steep rise in TSH and 71% with steady rise were observed.

In pregnant subjects TSHvsFT4 correlation was observed in both Iodine-deficient and iodine-sufficient, noticeable in Iodine-sufficient only in 3rd trimester.

Conclusion: TSH values increased in IDS from 1st-3rd trimester with a concomitant decline in FT4. But the levels of TSH in 70% subjects and FT4 levels in 81% subjects remained in normal range suggesting that equilibrium was achieved despite iodine deficiency. Furthermore, a steep TSH increase is more representative of iodine deficient status, an attempt to restore equilibrium, is understandable.

Financial assistance from Apeejay Education Society is gratefully acknowledged.

Table 1. Trimester specific range of TSH and FT4 in Iodine-deficient & Iodine-sufficient subjects (for abstract P2-04-08)

Hormone range 2.5–97.5 percentile	Iodine deficient group (n=279)			Iodine sufficient group (n=28)		
	trimester I	trimester II	trimester III	trimester I	trimester II	trimester III
TSH (mIU/l)	1.02–3.70	1.49–4.87	2.20–5.78	1.02–3.60	2.21–3.95	2.78–4.50
FT4 (pmol/l)	10.38–18.63	9.00–17.60	8.20–16.16	12.00–18.60	11.20–17.40	10.36–14.45

P2-04-09

PRESCRAIBE THYROXIN OR NOT

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The aim of the study was to find relationships between organic changes of thyroid gland and menstrual disorders and to try to correct it by thyroxine therapy.

Materials and Methods: 12 women were involved in the study since 2012 till 2015.

All investigated women were in reproductive age (22 ± 2.5 y.). BMI = 22 ± 2.2 kg/m^2 with secondary amenorreha treated with estrogen-gestagen pills(Diane-35) by gynecologists.

There were no other endocrine disorders which can be reason for menstrual disorder. Among investigated women LH/FSH was 2 ± 0.5, DHEA-S, $_{Free}$Testosterone, 17-OH progesterone, proinsulin, prolactin levels were in normal range.

All women were euthyroid TSH- 2.5 ± 0.4 (0.3–4.5 mkU/ml), FT4- 10 ± 3 (8.0–20.0 ng/l); 33.3% were anti TPO positive; 100% had diffuse changes of thyroid parenchyma on ultrasound (US).

All the women were given euthyrox 25 mkg daily.

Results: After 2–3 months of the treatment the menstrual cycle recovered in all the patients, one of them has become pregnant.

Conclusion: In case of secondary amenorrhea of unknown cause combined with diffuse changes of thyroid gland on US, we may consider TSH 2.5 mkU/ml as supraphysiological and try to make correction with thyroxine in small doses.

P2-04-10

HYPOTHYROIDISM AS A CAUSE OF INFERTILITY

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Introduction: Although thyroid hormones are in normal range, but the patient had clinical signs of hypothyroidism and problems with fertility.

Case Report: The patient is 32 years old, married for 6 years and has never had pregnancy, despite the fact that never took contraceptives. Twice she underwent ECO, but without any positive results. No problems in the reproductive system of the patient have been detected. On 15.09.15 the patient visited endocrinologist with the following complaints: general weakness, dry skin, headache, dizziness, low blood pressure, tendency towards constipation. The patient has undergone tests for TSH-1.12, FT4- 1.0, anti-T PO-15.0. But taking into account the complaints, 25 mcg Levothyroxine has been prescribed. A month later the patient has been tested on TSH-1.3, FT4-1.1 and 50 mcg Levothiroxine has been prescribed, however the TSH, FT4, remained unchanged, the Levothiroxine dosage has been increased to 75 mcg, then 100 mcg. After TSH reached 0.7 and FT4-1.4, pregnancy has been registered.

Conclusion: One should not always rely on hormones. In this case, considering the clinical process, Levothyroxine has been prescribed and pregnancy has been registered. Supposedly, the patient has receptor resistance towards thyroxine.

P2-05 Thyroid Cancer Diagnostic II

P2-05-01

COMPARISON OF THYROID FINE NEEDLE ASPIRATION BIOPSY RESULTS BEFORE AND AFTER IMPLEMENTATION OF BETHESDA CLASSIFICATION

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Objectives: Bethesda classification was introduced in 2008 to overcome variations in the evaluation of fine needle aspiration biopsy (FNAB) and provide standardization for this method. We aimed to compare diagnostic value of pre-Bethesda and Bethesda classification systems to differentiate benign and malignant thyroid nodules.

Methods: Data of 3037 patients operated between June 2007-June 2014 were reviewed retrospectively. Nodules evaluated with FNAB before and after March 2010 (the time Bethesda classification was implemented) were grouped as pre-Bethesda and Bethesda, respectively. Pre-Bethesda classification was categorized as nondiagnostic, benign, indeterminate, suspicious for malignancy and malignant. According to Bethesda, nodules were classified as nondiagnostic, benign, atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasia (FN), suspicious for malignancy and malignant.

Results: There were 1810 (26.1%) nodules in pre-Bethesda and 5115 (73.9%) in Bethesda groups. Cytologically, nondiagnostic rate was lower, and benign and suspicious for malignancy rates were higher in pre-Bethesda group ($p < 0.001$ for each). Frequency of malignant cytologies were similar. In pre-Bethesda 10.7% of nodules were indeterminate and in Bethesda 12.8% of nodules were AUS/FLUS and 1.3% were FN. When benign cytology was considered negative and suspicious for malignancy/malignant cytologies were considered positive, sensitivity, specifity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of pre-Bethesda were 71.8%, 98.0%, 79.5%, 97.0% and 95.4%, respectively. For Bethesda, these parameters were 77.0%, 98.7%, 84.6%, 97.8% and 96.8%, respectively. When indeterminate cytology in pre-Bethesda and FN in Bethesda were also included as positive, PPV was 42.8% and NPV was 97.0% in pre-Bethesda, PPV was 72.6% and NPV was 97.8% in Bethesda. Accuracies of pre-Bethesda and Bethesda were 85.7% and 95.3%, respectively.

Conclusion:, A majority of nodules interpreted as indeterminate previously has switched to AUS/FLUS category with the implementation of Bethesda classification. When suspicious for malignancy and malignant cytologies were considered positive, although sensitivity of Bethesda was higher, most of diagnostic performance criteria including accuracy did not change.

P2-05-02

THYROID MALIGNANCY RISK IN DIFFERENT CLINICAL THYROID DISEASES

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Objectives: We aimed to evaluate malignancy risk and compare tumoral features in different clinical thyroid diseases classified according to functional and nodular status.

Methods: Patients who underwent thyroidectomy between June 2007 and June 2014 were classified as euthyroid nodular goiter (ENG), euthyroid multinodular goiter (EMNG), hypothyroidism with single nodule, hypothyroidism

with multiple nodules, toxic nodular goiter (TNG), toxic multinodular goiter (TMNG), Graves', Graves' with solitary nodule and Graves' with multiple nodules according to preoperative functional status, etiology of hyperthyroidism and presence of solitary/multiple nodules. Postoperative malignancy rates and tumoral characteristics were compared.

Results: There were 2203 (76.8%) female and 667 (23.2%) male patients. 1719 (59.9%) were euthyroid, 962 (33.5%) were hyperthyroid and 189 (6.6%) were hypothyroid (Table 1). Overall malignancy was detected in 980 (34.1%) patients and 47.9% was incidental. Malignancy rates were 42.1%, 42.9% and 18.3%% in euthyroid, hypothyroid and hyperthyroid patients, respectively ($p < 0.001$). 41.4% of ENG and 46.3% of EMNG patients had malignant histopathology ($p = 0.169$). Mean tumor size, capsular invasion and vascular invasion were lower in EMNG than ENG ($p < 0.001$, $p = 0.003$ and $p = 0.015$, respectively). Among hypothyroid patients, 45.7% of patients with solitary and 42.2% of patients with multiple nodules were malignant ($p = 0.705$). Sex distribution, mean age and tumoral characteristics were similar. Malignancy rates were similar in all subgroups of hyperthyroidism, exceptionally Graves' had lower malignancy rate compared to others ($p \leq 0.01$ for each). When TMNG and TNG were analysed together, malignancy rate was 24.7% (104/421), and when Graves' with nodule/nodules were considered, it was 19.7% (59/299).

Conclusion: In hypothyroid or euthyroid patients who underwent thyroidectomy for various reasons**,** malignancy rate was higher than 40%. Although prevalence of malignancy was lower in hyperthyroid patients, it does not confer protection against thyroid cancer. Patients with multiple nodules carry a similar risk of malignancy as patients with solitary nodule independent of the functional status.

P2-05-03

CLINICAL IDENTIFICATIONS OF REMNANT RADIOIODINE DISTRIBUTIONS ON DIAGNOSTIC I-131 SPECT/CT IN PATIENTS WITH DIFFERENTIATED THYROID CANCER AFTER THYROID REMNANT ABLATION

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Objectives: To retrospectively identify anatomical regions of remnant radioiodine distributions on planar images of diagnostic I-131 scintigraphy by single-photon emission computed tomography (SPECT/CT).

Methods: Twenty-two patients (7 men and 15 women, age range 31–76 years, average, 52.7 years) with remnant neck I-131 distributions on diagnostic scintigraphy planar images 3 months after thyroid remnant ablation (RRA) were enrolled. We compared remnant neck I-131 distributions on SPECT/CT images 3 months after RRA with thyroid bed I-131 uptake on SPECT/CT just after RRA.

Results: I-131 distribution was determined with SPECT/CT in a region of the pyramidal lobe in 16 patients, tracheoesophageal region in 3 patients, esophagus in 2 patients, and isthmus in 1 patient.

In 5 of these 22 patients, regions of I-131 distribution 3 months after RRA did not match regions of thyroid bed uptake just after RRA. There was a mismatch between the esophagus and superior pole in patient 1, between the superior pole and tracheoesophageal region in patient 2, between the pyramidal lobe and superior pole in patient 3, between the pyramidal lobe and tracheoesophageal region in patient 4 and between the pyramidal lobe and Berry's ligament region in patient 5, respectively.

Conclusion: In 5 patients, both comparative SPECT/CT images suggested that thyropid bed I-131 uptake had disappeared. SPECT/CT is useful for identification of anatomical regions of remnant radioiodine distributions of on diagnostic I-131 scintigraphy planar images, and can prevent false -positive diagnoses.

P2-05-04

THE ROLE OF FDG-PET/CT IN DIFFERENTIATED THYROID CANCER

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Objectives: Treatment of recurrent or advanced thyroid cancer depends on various factors such as extent of disease, number and location of metastases, progression rate, radioiodine avidity. The aim of our study was to assess the role of FDG-PET/CT in management of recurrent or advanced differentiated thyroid cancer.

Methods: Altogether 138 FDG-PET/CT studies (1–5 per patient) were performed in 82 patients with differentiated thyroid cancer in our institute from 2008–2015. Indications for FDG-PET/CT were: elevated thyroglobulin (Tg) or Tg antibodies and negative radioiodine scan in 72 studies, follow-up of metastatic disease with rising Tg in 51 studies, evaluation of extent of disease in 9 studies, and follow-up after treatment of recurrent disease in 6 studies. FDG-PET/CT findings were retrospectively evaluated.

Results: Recurrent or metastatic disease was correctly detected in 90 studies, sensitivity was 73%. Locoregional recurrence was detected in 38 cases, mediastinal lymph-node metastases in 27 cases, lung metastases in 53 cases, bone metastases in 28 cases, lymph-node metastases in upper abdomen in 8 cases, liver metastases in 5 cases and other metastases in 4 cases. There were 33/138 (24%) false negative studies: in 3 cases metastases were radioiodine avid, in 6 cases locoregional recurrence, lung metastases and bone metastases were detected by other imaging modalities, while in 24 cases with elevated Tg level (unstimulated, 0.7–114.2 ng/ml, median 10.4 ng/ml) cause remained unrevealed. FDG-PET/CT findings changed disease management in 38 cases (27%); treatment modalities after PET/CT studies were: surgery in 19 cases, therapy with kinase inhibitors in 7 cases, cytostatic therapy in 2 cases, irradiation in 20 cases. Based on FDG-PET/CT findings, in 47 cases only surveillance was used due to small, asymptomatic and/or slowly progressive distant metastases.

Conclusion: FDG-PET/CT has the role in detecting noniodine avid disease and management of advanced differentiated thyroid cancer.

P2-05-05

THE ROLE OF THE NODULE VOLUME IN EVALUATING THE RISK OF MALIGNANCY IN THYROID NODULES

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Background: In evaluating thyroid nodules by ultrasonography (US), the nodule diameter is routinely measured. However, the relationship between the nodule size and malignancy is not certain. In this study, we aimed to determine the role of the nodule volume in evaluating the risk of malignancy in thyroid nodules.

Methods: The medical records of patients who underwent total thyroidectomy or lobectomy between January 2007 and December 2014 in our institution were reviewed. Demographic and clinical data as well as preoperative ultrasonography (US) findings were analyzed. The nodules in these patients were grouped as ≥4.0 cm, 1.0–3.9 cm and <1 cm according to US measurements. For these groups, the histopathological findings were compared.

Results: Data from 5,561 nodules in 2,463 patients were analyzed. There were 1,008 nodules ≥4.0 cm, 4,013 nodules 1.0–3.9 cm, and 540 nodules <1.0 cm. Based on histopathological findings, 8.5%, 10.2%, and 25.6% of nodules ≥4.0 cm, 1.0–3.9 cm, and <1.0 cm were malignant, respectively ($p < 0.001$). There was no significant difference between benign and malign nodules <1 cm and 1.0–3.9 cm in terms of mean nodule volume ($p = 0.20$ and $p = 0.11$, respectively). However, significant difference between benign and malign nodules in terms of mean nodules volumes was observed for the nodules ≥4.0 cm ($p = 0.012$).

Conclusion: In evaluating the risk of malignancy in the thyroid nodules ≥4.0 cm, considering the volume of nodule instead of maximum diameter of the nodule may be more significant and predictive.

P2-05-06

CORRELATION OF THYROID CYTOLOGY REPORT WITH SURGICAL PATHOLOGY IN THYROID NODULE

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Background: Fine-needle aspiration (FNA) has become the diagnostic tool of choice for the initial evaluation of solitary thyroid nodule because of its accuracy, safety, and cost effectiveness. The use of FNA has reduced the rate of unnecessary surgery. The Bethesda System for Reporting Thyroid Cytopathology was used to categorized thyroid nodule into 6 groups: 1) Non-diagnostic (ND), 2) Benign, 3) Atypia of Undetermined significance (AUS)/ Follicular of undetermined significance (FLUS), 4) Follicular neoplasm (FN)/ Suspicious follicular neoplasm (SFN), 5) Suspicious of malignancy (SOM), 6) Malignancy. ND, AUS/FLUS, FN/SFN, SOM had malignancy risk 1–4%, 5–15%, 15–30% and 60–75% respectively. The aim of this study was evaluated malignancy risk of 4 indeterminate cytology in Siriraj hospital.

Methods: This study was retrospective chart review. One-hundred and ninety patients at Siriraj hospital with indeterminate cytology (ND, AUS/FLUS, FN/SFN, SOM) and underwent thyroid surgery were studied.

Results: From 190 cytology reports, fifty six samples (29.5%) were ND, 64 samples (33.7%) were AUS/FLUS, 25 samples (13.2%) were FN/SFN and 45 samples (23.7%) were SOM. The malignancy risk was 51.6% in indeterminate cytology. The malignancy risk was 39.3% in ND, 42.2% in AUS/FLUS, 52% in FN/SFN and 80% in SOM.

Conclusion: Opportunity to be malignant was high in indeterminate cytology in our institute. Surgery may be appropriate in this group of patients because approximately 50% chance to be malignant.

P2-05-07

THYROID CANCER INCIDENCE FOLLOWING THYROIDECTOMY. A TERTIARY CENTRE EXPERIENCE IN ROMANIA

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Objectives: In the last decades, thyroid cancer incidence has increased all over the world, being the 18th most common cancer in Europe. This increased incidence may be due to increased detection of small cancers in the preclinical stage or to environmental carcinogens in the industrialized lifestyle (radiations, iodine intake, chronic autoimmune thyroiditis). The aim of our study was to present the prevalence and histological subtypes of primary thyroid carcinoma in patients undergoing thyroidectomy.

Methods and Results: We retrospectively analysed the files of 493 patients who underwent thyroidectomy in our surgery department between 01.01.2012–30.09.2015. Anthropometric, biologic and imagistic data, indications of thyroid surgery, surgical procedures and pathology results were recorded.

Results: 94 (19.06%) patients presented primary thyroid carcinoma. 86 (91.48%) suffered from differentiated thyroid carcinoma [81 (86.17%) papillary, 5 (5.31%) follicular], 4 (4.25%) from medullary thyroid carcinoma, 2 (2.12%) from poorly differentiated and 2 (2.12%) from anaplastic thyroid carcinoma. Multifocality was present in 29 (30.85%) patients. Pathological tumor stage was: T1 in 32 (34.04%), T2 in 13 (13.82%), T3 in 42 (44.68%) and T4 in 7 (7.44%) patients. 20 (21.27%) patients associated histopathologic chronic autoimmune thyroiditis. The primary indications for thyroid surgery included: Graves' disease and nodular goiter 3 (3.19%), multinodular goiter 68 (72.34%), uninodular goiter 14 (14.89%) and thyroid cancer 9 (9.57%). The surgical procedure was lobectomy in 2 and total thyroidectomy in the remaining 92 patients. The mean age was 54.41 ± 14.22, range 25–83 years; 23 (24.46%) were diagnosed before the age of 45 years. The female to male ratio was 75:19 = 3.94.

Conclusion: There is a high malignancy rate in nodular goiters. Differentiated thyroid carcinoma is the most common primary malignancy of the thyroid gland. Papillary thyroid carcinomas constitute the vast majority of these neoplasms, which is usually associated with an iodide-sufficient area.

P2-05-08

A RARE CAUSE OF POSTPARTUM RAPIDLY ENLARGING GOITER

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Introduction: Diffuse sclerosing variant of papillary thyroid carcinoma (DSV-PTC) is an uncommon variant of PTC. The prevalence of DSV-PTC varies from 0.7–6.6% of all papillary thyroid carcinomas. This subtype was first described in 1985 by Vickery et al., and is characterized histologically by diffuse involvement of one or both thyroid lobes with dense sclerosis, patchy to dense lymphocytic infiltrates, abundant psammoma bodies and extensive squamous metaplasia. Compared with classic PTC, DSV-PTC has unique clinical features, including a higher prevalence of underlying Hashimoto's thyroiditis, higher female to male ratio and younger age. Ultrasonographic (US) findings of DSV-PTC are also distinctive. The characteristic US features of DSV-PTC are diffuse enlargement of the thyroid gland with heterogeneous hypoechogenicity, diffuse scattered microcalcifications with or without a mass (a 'snowstorm' appearance) and the presence of extensive cervical lymph node metastasis. Echographically it looks similar to Hashimoto thyroiditis and sometimes could be easily overlooked. The most common initial manifestations were neck swelling (85%) and general fatigue (10%).

Case Report: A 20 years old woman admitted to our policlinic with dispne, disphagia and throat swelling. She gave birth to her first child two months ago and her complaints started one month after the birth. She had a firm, grade III non-tender goiter. Thyroid stimulating hormone, thyroxine, triiodothyronine, thyroglobin antibody and antithyroid peroxidase antibody were; 6 uIU/ml (0.27–4.2), 0.8 ng/dl (0.9–1.7), 3 pg/ml (1.8–4.6), >4000 IU/ml, 13.7 IU/ml (0–34) respectively. Levothyroxin therapy was started. Diffuse enlargement of the thyroid gland (thyroid volume:76 $cm^{3)}$ with heterogeneous hypoechogenicity, diffuse scattered microcalcifications and bilateral extensive cervical lymph node metastases were detected on cervical ultrasonography. Thyroid fine needle aspiration biopsy (FNAB) was performed on the calcified areas of the bilateral thyroid lobes and cervical lymph nodes. FNAB was compatible with suspicious for malignancy according to the Bethesda System. Bilateral cervical lympadenopathy, and chronic thyroiditis on ultrasonography caused suspicion for thyroid lymphoma. So trucut thyroid biopsy was done and *immunohistochemical studies* was performed and lymphoma diagnosis was excluded. Patient underwent bilateral total thyroidectomy, bilateral and santral neck dissection. DSV-PTC was diagnosed on histopathology.

Conclusion: Iodine deficiency related goiter on postpartum period is frequently encountered in our country. On ultrasonography, DSV-PTC looks similar to Hashimato thyroiditis. Rapidly enlarging goiter of young women and detecting diffuse microcalcifications on ultrasonography must remind malign causes of goiter. These patients also need cervical ultrasonography instead of lone thyroid ultrasonography because of tendency to metastasize.

P2-06 Thyroid Cancer Therapeutics

P2-06-01

CENTRAL LYMPH NODE DISSECTION USING FLUORESCENCE IMAGING IN THE ROBOTIC THYROID SURGERY

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Purpose: The purpose of this study is to evaluate the feasibility of complete central lymph node dissection (CLND) using fluorescence imaging (FireFly technology) in the robotic thyroid surgery using bilateral axillo-breast approaches (BABA).

Methods: Forty patients diagnosed with papillary thyroid cancer (PTC) who underwent robotic thyroidectomy and CND from December 2015 to March 2016 were analyzed. A total of 21 patients underwent a robotic surgery using fluorescence imagine (FI group), and the other 19 patients underwent surgery without it (control group). FI group was injected with 0.1 ml of indocyanine green (ICG) dye into ipsilateral thyroid tissue to improve the identification of lymph node.

Results: Lymph node green-stained by ICG could be detected easily under near-infrared camera. The number of harvested lymph nodes was 7.7 in FI and 5.4 control group ($p = 0.04$). The rates of post-operative transient hypocalcemia were low in FI (23.8%) and control group (21.1%) without significant differences. The number of unintentionally dissected parathyroid were one and two in groups respectively.

Conclusion: Fluorescence imaging for robotic thyroid surgery facilitated identification of lymph node and guided complete CLND in PTC patients.

P2-06-02

MINIMALLY INVASIVE OPEN THYRODIECTOMY: SURGICAL COMPLETENESS OF CONSECUTIVE 108 PATIENTS

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Background: The cosmetic consideration motivated the development of various minimally invasive thyroidectomies even in the thyroid cancer patients. We had performed a minimally invasive open open thyroidectomy (MT, using mini-incision, 2.5 cm sized).

This study describes the technique of its method and analyzes the surgical outcomes.

Methods: Between Jan.2005 and Dec.2014, 4257 patients with thyroid cancer (papillary thyroid cancer) underwent ipsilateral thyroidectomy with prophylactic central compartment neck dissection (preoperative evaluation: T1 or T2, N0, M0).

Of these patients, 108 patients have been performed Minimally invasive open thyroidectomy (MIT), and 2805 underwent the conventional open thyroidectomy (OG).

The clinicopathologic characteristics, surgical outcomes and follow-up data between two groups were retrospectively compared.

Results: There were no significant difference tumor size, multifocality, extrathyroidal invasion, central lymph node metastasis, and TNM stage between MIT and other groups. The operation time and postoperative hospital day were significantly shorter in the MIT than OG ($p < 0.001$). The retrieved LN number in MIT was significantly smaller than open group ($p < 0.001$). And there were no recurrence case in MIT during that period. Only one complication case was reported, It was transient hoarseness. Mean follow up duration of MIT was 40.33 months, OG was 29.22 months ($p < 0.001$).

Conclusion: Minimally invasive thyroid surgery can be performed with an equivalent surgical completeness to conventional hemi-thyroidectomy using a standard cervicotomy with excellent cosmesis and same medical costs. Although MIT have shown benefits, a long-term follow up data with more patients and function study (patient satisfaction and evaluation of postoperative voice quality) are needed to assess of surgical completeness of MT. MT can be safely performed for the selected patients with low-risk thyroid cancer such as less than total thyroidectomy.

P2-06-03

IS IT SUFFICIENT TO DO LOBECTOMY ALONE FOR PAPILLARY THYROID CARCINOMA MEASURING 4 CM OR LESS WITHOUT EXTRA-THYROIDAL EXTENSION AND CLINICAL LYMPH NODE METASTASIS?

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Background: Traditionally, a bilateral procedure had been recommended for papillary thyroid carcinoma (PTC) >1 cm. However, 2015 ATA guidelines strongly recommended that the initial surgical procedure for PTC, 1~4 cm without extra-thyroidal extension (ETE) and clinical lymph node metastasis (cLNM) can be either a bilateral or a unilateral procedure.

Purpose: Aim of this study was to evaluate the appropriateness of new 2015 ATA recommendation for these specific tumors.

Methods: From Jan. 1st 2007 to Dec. 30th 2013, medical records for patients who underwent surgery for PTCs <4 cm, were reviewed. Prophylactic central neck dissections were performed routinely. Patients who had PTC with gross ETE and/or cLNM were excluded. A control group of PTCs <1 cm without ETE (n = 381) were compared with study groups: group I, PTCs, 1~4 cm without ETE (n = 150); group II, PTCs, <1 cm with minimal ETE (n = 186); group III, PTCs, 1~4 cm with minimal ETE (n = 121). Mean follow-up period was 48.5 ± 21.9 months. Statistical analyses were performed using SPSS 19.0KO for windows with a $p < 0.05$ as a significant difference.

Results: The larger tumors were, the more frequent multiplicity and bilaterality were. Total thyroidectomies were performed more often for PTC >1 cm. Although there were a substantial number of microscopic LNM, locoregional recurrences were relatively infrequent: none, 3, 7, and 6 patients in control, group I, II, and III, respectivelyI ($p = 0.001$). Five year disease free survival (5YDFS) was 100%, 95.8%, 84.1%, 75.0% in in control, group I, II, and III, respectively ($p < 0.001$).

Conclusion: PTC, 1~4 cm without ETE and cLNM showed a higher recurrence rate and a lower 5YDFS than PTC <1 cm without ETE and cLNM, for which lobectomy is strongly recommended. Although the differences are statistically significant, they are small and most of patients who have this kind of tumor may benefit from lobectomy. Therefore lobectomy might be sufficient initial treatment for PTCs which size under 4 cm without ETE and clinical LNM. However, PTCs with minimal ETE need more aggressive management.

P2-06-04

CAN T1A MULTIFOCAL PAPILLARY THYROID MICROCARCINOMAS WITH A TOTAL TUMOR DIAMETER OF 1–2 CM BE RECLASSIFIED AS T1B?

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Objective: Intrathyroidal differentiated thyroid carcinomas (DTC) ≤2 cm are subgrouped as T1a when ≤1 cm and T1b when 1–2 cm in the last TNM classification. Using the largest tumor diameter and ignoring the other foci while determining T stage in multifocal papillary thyroid microcarcinomas (PTMC) might cause underestimation of tumoral stage. In this study, we aimed to investigate the effect of total tumor diameter (TTD) on TNM classification of T1a multifocal PTMCs.

Methods: Medical records of 783 patients with papillary thyroid carcinoma (PTC) ≤2 cm were reviewed retrospectively and 724 patients with intrathyroidal tumor were included. T1 tumors were grouped as T1a and T1b according to 7th TNM edition. TTD was calculated as the sum of the maximal diameter of each tumor. T1a multifocal PTMCs were further subgrouped as TTD ≤1 cm and TTD 1–2 cm.

Results: There were 527 (72.8%) patients in T1a and 197 (27.2%) in T1b groups. Lymph node metastasis (LNM), capsular invasion and lymphovascular invasion were significantly higher in T1b compared to T1a tumors ($p < 0.001$, $p < 0.001$ and $p = 0.015$, respectively). All patients with recurrence were in T1b group and persistence was similar in two groups ($p = 0.002$). Number of tumor foci, LNM and capsular invasion were significantly higher in T1a patients with TTD 1–2 cm compared to with TTD ≤1 cm, while lymphovascular invasion was similar in two subgroups. ($p < 0.001$, $p = 0.032$, $p = 0.014$ and $p = 0.164$, respectively). There was no significant difference in terms of clinicopathological features between T1a patients with TTD of 1–2 cm and T1b patients, except higher mean age in T1a patients with TTD of 1–2 cm ($p = 0.006$).

Conclusion: Clinical behaviour of T1a multifocal tumors with a TTD of 1–2 cm seems to be more aggressive than T1a multifocal tumors with a TTD of ≤1 cm.

P2-06-05

DYNAMIC RISK STRATIFICATION IN MEDULLARY THYROID CANCER OF SINGLE CENTER'S RESULT

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Introduction: Recently dynamic risk stratification has been approved to be more valuable than static anatomic staging system in non-medullary thyroid cancer and this notion has been also accepted in medullary thyroid cancer (MTC). The present study was designed to compare the clinical usefulness of response to initial therapy stratification with a traditional anatomic staging system.

Method: From August 1982 to December 2012, a total of 125 MTC patients underwent thyroidectomy in Yonsei University Hospital. Among them, 117 (93.6%) patients with complete clinical data and sustained follow-up were enrolled in this study. Clinicopathologic features and surgical outcomes were analyzed by retrospective medical chart review. Mean follow up duration was 85.78 ± 62.51 months.

Result: In this study, 16 (13.6%) patients had hereditary MTC, 101 (86.4%) patients had sporadic MTC. Stage I patients had highest probability of excellent response to initial therapy (92.1%). Stage IV patients had highest probability of biochemical and structural incomplete response to initial therapy (57.5% and 30.3%) and lowest probability of excellent response to initial therapy (12.1%). Response to initial therapy stratification and TNM staging system were significantly difference in statistically ($p = 0.000$). The TNM staging system provided risk stratification regarding to disease free survival (DFS), disease specific survival (DSS) and the probability of having no evidence of disease at final outcome, but did not provide risk stratification regarding to the probability of having biochemical persistent/recurrence disease at final outcome. However response to initial therapy stratification provided risk stratification regarding to not only DFS, DSS and the probability of having no evidence of disease at final outcome but also the probability of having biochemical persistent/recurrence disease at final outcome.

Conclusion: In this study, we demonstrated that dynamic risk stratification with adjusted response to initial therapy system can offer more useful prognostic information than anatomic staging system in MTC.

P2-06-06

CLINICOPATHOLOGICAL FACTORS ASSOCIATED WITH POOR RESPONSE TO ^{131}I IN LOW TO INTERMEDIATE RISK PAPILLARY THYROID CANCER

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According to ATA risk stratification, patients with differentiated thyroid cancer T1b, T2, T3 (>4 cm), T3 (minimal extrathyroid extension – ETE) N0 have low to intermediate risk and postsurgical ^{131}I is not universally indicated. In our department all these patients used to have ^{131}I therapy.

Objectives: The objective is to evaluate the response to initial therapy and to find any prognostic factors of poor therapy response.

Methods: Retrospective analysis of clinicopathological data of patients with pT1b, T2, T3 (>4 cm), T3 (minimal ETE) N0 papillary thyroid cancer (PTC) treated in the last 5 years. Thyroglobulin was evaluated after surgery, and after one year primary treatment response was classified as excellent, biochemical or structural incomplete response or indeterminate (ATA guidelines 2015).

Results: The study included 84 patients, 72 female (85.7%) with an average age of 49.9 years (±14.4).

37 patients (44%) were T1b; 13 patients (15.5%) were T2; 2 patients (2.4%) were T3 (>4 cm) and 32 patients (38.1%) were T3 (minimal ETE). All patients underwent total thyroidectomy and ablative ^{131}I therapy.

At one year follow-up 47 patients (56%) were classified as excellent response, 14 (16.7%) with structural incomplete response, 4 (4.8%) with biochemical incomplete response and 19 patients (22.6%) as indeterminate response.

On univariate analysis the factors associated with excellent response vs incomplete response were the T stage (incomplete response <T3 13.9% vs. T3 44.8%), post-surgical stimulated thyroglobulin (8.3 vs. 26.2 ng/ml) and one year stimulated thyroglobulin (0.3 vs. 18.4 ng/ml).

On multivariate analysis the same factors maintained statistical significance. Male gender and multifocality showed a tendency for incomplete response.

Conclusion: T3 stage and higher post-surgical thyroglobulin are associated with incomplete response after total thyroidectomy and ^{131}I therapy. PTC patients with these risk factors should have ablative ^{131}I therapy. In patients of male gender and with multifocal tumors it should be strongly considered.

P2-06-07

SKIP METASTASIS TO LATERAL NECK LYMPH NODES IN PAPILLARY THYROID CANCER

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Background: Skip metastases, leaping metastasis to lateral neck lymph node (LN) without central LN metastasis, are uncommonly observed in papillary thyroid cancer (PTC). There is still rare evidence of effect between skip metastasis and disease-free survival (DFS). We conducted this study to evaluate the clinicopathological features and DFS according to skip metastases in PTC.

Methods: We retrospectively reviewed the records of 154 patients who underwent total thyroidectomy, central lymph node dissection, and modified radical neck dissection between June 2006 and December 2010.

Results: Skip metastases were found in 35 patients (22.8%). Patients who were more than 45 years old tended to have skip metastases. The lateral lymph node metastases ratio was lower (0.29 ± 0.18 vs. 0.19 ± 0.19, p = 0.003) and the frequency of single lateral neck level involvement was higher (32.8% vs. 60.0%, p = 0.007) in the patients with skip metastases. In univariate and multivariate logistic regression analyses, there are significance of age ≥45 years (odds ratio 3.48, p = 0.004; odds ratio 3.60, p = 0.005) and tumor size >1 cm (odds ratio 0.46, p = 0.048; odds ratio 0.40, p = 0.03) respectively. There was no significance between skip metastasis and DFS.

Conclusion: Skip metastases can occur frequently in PTC patients. Nevertheless, there were no difference of recurrence according to skip metastasis.

P2-06-08

RISK GROUP STRATIFICATION FOR DISTANT METASTASIS IN PATIENTS WITH MINIMALLY INVASIVE FOLLICULAR THYROID CARCINOMA

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Objectives: This study evaluated risk factors for distant metastasis and compared outcome between the subgroups which were divided by the number of risk factors.

Methods: A review of patient records identified 195 patients who underwent initial surgery at Asan Medical Center from 1996 to 2010 and were subsequently diagnosed with MIFTC. After evaluating risk factors for distant metastasis, patients were subdivided into four groups based on the number of risk factors; group 0 with no risk factor, group 1 with any one risk factor, group 2 with any two risk factors, and group 3 with all risk factors.

Results: The median follow-up period was 99.5 months (range, 13–244). 15 patients (7.7%) had distant metastases. Age >45 years (Hazard ratio, HR [95% Confidence interval, CI] = 3.79 [1.79–11.13], p = 0.025), tumor size >4 cm (HR [95% CI] = 2.27 [1.5–8.07], p = 0.041), and vascular invasion (HR [95% CI] = 4.32 [1.46–15.02], p = 0.01) were shown to be independent risk factors in multivariate analysis. Group 2 and group 3 patients showed significantly lower distant metastasis-free survival (DMFS) rates as compared with those of group 0 patients (p = 0.005 and <0.001, respectively). Group 1 patients tended to have poor outcome compared to that of group 0 patients, but there was no significant difference (p = 0.069).

Conclusion: MIFTC patients with 2 or more risk factors for distant metastasis showed significantly worse DMFS rates rather than those having no or only one risk factor, while DMFS rates between patients with no and only one risk factor did not show significant difference. MIFTC patients with no or only one distant metastasis-related risk factor may become candidates for close observation without additional treatments after hemithyroidectomy.

P2-06-09

USEFULNESS OF DETERMINATION FOR CENTRAL LYMPH NODE METASTASIS BY SURGEON USING THE PALPATION IN PAPILLARY THYROID CANCER

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Purpose: The purpose of this study was to evaluate the accuracy of judgment for central lymph node (LN) metastasis in papillary thyroid cancer (PTC) by the single surgeon using inspection and palpation.

Methods: From October 2014 to February 2015, 127 patients who had thyroidectomy and central lymph node dissection (CND) excluding modified radical neck dissection were enrolled in this study. The criterion of suspicious LN was hardness rather than enlargement. Surgeon was numbering each of any suspicious LN and sent to pathologist for frozen section biopsy.

Results: Central LN metastases were found in 50.4% (64/127) and micro-metastases were 36 patients (57.8%) among them. Suspicious LN according to determination by surgeon were in 20.5% (28/127) and 26 of them (92.8%) were diagnosed with metastasis on final pathology. The metastatic LNs were found in 38 patients (38.3%) among 99 patients with no suspicious LN, 29 patients of them (76.3%) had micro-metastases. The sensitivity, specificity, positive and negative predictive values of determination of LN metastasis by surgeon were 96.8%, 40.6%, 60.3% and 92.8% respectively.

Conclusion: The determination of central LN metastasis by the surgeon had relatively reliability due to high sensitivity and negative predictive value.

P2-06-10

MYOCARDIAL INFARCT AFTER LONG TERM TREATMENT WITH A TYROSINE KINASE INHIBITOR (TKI) WITH ANTI-VEGF RECEPTOR ACTIVITY

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Introduction: TKIs including anti-VEGF receptor activity have been approved for the treatment of patients with radioiodine resistant thyroid carcinomas. For lenvatinib arterial thromboembotic events are listed as adverse events of special interest with lenvatinib. In the phase III study, arterial thromboembolic events were reported in 3% of lenvatinib-treated patients and 1% in the placebo group. Most of the patients had predisposing factors. Only one myocardial infarct was reported in the lenvatinib phase III study.

Material and Patient: We report a 73 year old female patient with metastatic thyroid papillary carcinoma who was treated with total thyroidectomy in 12/2004, followed by four radioiodine therapies, last in 2010 with lung metastasis without radioiodine uptake. Progression of lung metastasis according to RECIST criteria occurred in 2011. Treatment with lenvatinib was begun 10/2012 resulting in prolonged partial response with disappearance of a hepatic metastasis.

Results: During further treatment with lenvatinib with dose reduction from initially 24 to 10 mg (since 3/14) a myocardial infarct occurred 11/2015 resulting in implantation of 3 stents and a two chamber pacemaker. Treatment with lenvatinib was discontinued 11/2015. Except for well controlled hypertension there were neither predisposing diseases like diabetes nor symptoms of cardiac ischemia on exertion, quarterly repeated echocardiography at rest showed normal results. However, the family history for cardiovascular diseases was positive with cardiac infarcts reported for both parents and one brother.

Conclusion: Whereas only one myocardial infarct was reported in the lenvatinib phase III study with 392 patients this case suggests that long term treatment with lenvatinib may be associated with an increased risk for myocardial infarct also in asymptomatic patients (with positive family history for cardiovascular diseases) and no predisposing diseases except well controlled hypertension. Therefore, family history for cardiovascular diseases and cardiac stress testing to identify those at increased risk for cardiac events should be

performed before starting and at annual intervals during prolonged lenvatinib therapy. Further data on adverse events during long term treatment should be systematically collected.

P2-07 Thyroid Cancer – Clinical I

P2-07-01

EVALUATION OF ULTRASOUND SCORING AND THYROID IMAGING REPORTING AND DATA SYSTEM (TIRADS) IN PREDICTION OF MALIGNANCY IN PATIENTS WITH BETHESDA CATEGORY III (AUS/FLUS)

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Objectives: Thyroid Imaging Reporting and Data System (TIRADS) is a simple and reliable reporting system which uses the number of suspicious ultrasound (US) features and US risk scores in estimation of malignancy risk. In this study, we aimed to determine the role of TIRADS in prediction of malignancy in nodules with atypia of undetermined significance (AUS) and follicular lesion of undetermined significance (FLUS).

Methods: 318 nodules with AUS and 121 with FLUS cytology were included. US features and postoperative histopathology (benign/malignant) results were documented. Thyroid nodules without any suspicious US features were classified as TIRADS category 3. Nodules representing one, two, three or four, or five suspicious US features were determined as category 4a, 4b, 4c, and 5, respectively. Every suspicious US feature was scored according to presence or not as 1 and 0, respectively.

Results: In AUS group, TIRADS categories of histopathologically benign nodules were significantly different compared to malignant nodules ($p = 0.028$). Malignant group had more frequent TIRADS 4c category nodules than benign ones ($p = 0.027$). The rates of microcalcification and hypoechogenicity were higher in malignant group ($p = 0.015$ and $p = 0.007$) and there was no difference in solid nodule texture and marginal irregularity between groups ($p > 0.05$). Malignant group had higher nodule anteroposterior diameter/transverse diameter ratio ($p = 0.009$). In FLUS group, there was no difference between malignant and benign groups with respect to TIRADS categories and US features ($p > 0.05$, all). In AUS nodules, the cut-off value of US score at maximum sensitivity and specificity were calculated as ≥3 (AUC: 0.596).

Conclusion: Preoperative prediction of malignancy is very important for appropriate treatment and prevention of unnecessary surgeries in patients with AUS/FLUS cytologies. Combinations of suspicious US features seems to be helpful in prediction of malignancy in these nodules.

P2-07-02

HIGH RESISTIVE BLOOD FLOW IN PAPILLARY THYROID CANCERS; AN IMAGING STUDY FOR CLINICAL USE

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Objectives: It is thought that papillary thyroid cancers (PTC) have high fibrotic content. Therefore, stenosis or occlusions of vascular structures in the cancer can take place, which can be shown by spectral duplex Doppler ultrasonography (DDUS). In this study, we aimed to introduce the vascularization parameters of PTC and benign thyroid nodules and find optimal cut-off values for differentiating PTCs from benign thyroid nodules.

Methods: Ultrasonography (US) and DDUS were performed on patients scheduled for thyroidectomy by one of the observers who was blind to the clinical findings of the patients. The maximum velocity (cm/sec) (Vmax), minimum velocity (cm/sec) (Vmin), systolic to diastolic ratio (S/D), pulsatility index (PI), and resistivity index (RI) were noted for all thyroid nodules detected on US. For the statistical analysis, thyroid nodules were classified according to histopathological findings as PTC or benign thyroid nodules and the mean values of each were compared as well. Statistically significant parameters were further evaluated by receiver operating characteristic curve analysis and an optimal cut-off value for predicting PTC was selected by Youden index. Statistical significance was accepted as $p < 0.05$.

Results: 140 nodules from 86 patients (69 (80.2%) women and 17 (19.8%) men) (mean age 44.72 ± 12.8 (range 9–70) years) were included in the study. Thirty nodules were diagnosed as PTC, and 110 nodules diagnosed as benign thyroid nodules (15 follicular adenomas and 95 non-neoplastic nodules) histopathologically. Vmin, S/D, PI, and RI differences were statistically significant (<0.001, <0.001, <0.001, and 0.001, respectively). The cut off value, sensitivity, specificity, positive and negative predictive values and accuracy are given in the table.

Conclusion: DDUS can easily show high resistant blood flow in PTC and this can be used to differentiate PTCs from benign nodules in clinical practice.

Table 1. Optimal cut off values for Vmin, S/D, PI and RI (for abstract P2-07-02)

	Vmin	S/D	PI	RI
AUC	0.719	0.732	0.724	0.738
P value	<0.0001	<0.0001	0.0001	<0.0001
Criterion	≤13.3	>3.11	>0.92	>0.68
Sensitivity	85.19 (66.3–95.8)*	59.26 (38.8–77.6)*	81.48 (61.9–93.7)*	55.56 (35.3–74.5)*
Specificity	55.45 (45.7–64.9)*	82.73 (74.3–89.3)*	55.45 (45.7–64.9)*	82.73 (74.3–89.3)*
PPV	65.66 (56.75–73.62)*	77.43 (66.89–85.35)*	64.65 (55.98–72.45)*	76.28 (65.35–84.58)*
NPV	78.92 (67.23–87.39)*	67.00 (58.30–74.67)*	74.96 (64.02–83.43)*	65.05 (56.43–72.79)*
Accuracy (%)	70.32	70.995	68.465	69.145

* 95% CI.

Vmin = Minimal flow velocity; S/D = systolic to diastolic flow ratio; PI = pulsatility index; RI = resistivity index; AUC = area under curve, PPV = positivite predictive value, NPV = negative predictive value, CI = confidence interval.

P2-07-03

AGE AT DIAGNOSIS IS NOT A VARIABLE THAT AFFECTS THE FREQUENCY OF STRUCTURAL INCOMPLETE RESPONSE IN ANY OF THE RISKS OF RECURRENCE FROM PATIENTS WITH DIFFERENTIATED THYROID CANCER

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Objective: To evaluate the influence of age on the frequency of structural incomplete response (SIR) according to the modified risk of recurrence (RR) staging system from the ATA 2016.

Methods: Retrospective analysis of 268 patients with DTC followed-up for at least 3 years after initial treatment (total thyroidectomy and remnant ablation). The median follow-up was 6.2 years (range 3–26.5 years) and the median age at diagnosis was 45.9 years (range 18–87 years). Association between age at diagnosis and the initial and final response to treatment was assessed by using the analysis of variance (ANOVA). Patients were also divided into three groups (older and younger than that limit) by using different cut-offs and compared with the chi-square test.

Results: Age at diagnosis was not associated with neither different initial nor final response to treatment (p = 0.14 and p = 0.58, respectively, ANOVA). Also, there was no significant difference between the percentage of SIR neither at initial ***(data not shown)*** nor at final outcome ***(table 1)***, between older and younger groups using different age cut-offs.

Conclusion: Age at diagnosis seems no to be involved in the risk of having a SIR neither at initial nor at final response to treatment.

Table 1. Comparison of percentages of structural incomplete response at final outcome between DTC patients by using different age cut-offs according to the initial risk of recurrence (for abstract P2-07-03)

	Age cut-off (years old)	Final outcome		
		% SIR < age cutoff	% SIR ≥ age cutoff	p
Low RR	40	2.0	1.1	0.74
n = 146	50	2.4	1.6	0.59
	60	1.7	3.6	0.47
Intermediate RR	40	9.1	22.6	0.18
n = 64	50	13.9	19.0	0.72
	60	14.8	20.0	0.65
High RR	40	44.0	66.7	0.14
n = 58	50	57.1	56.5	0.82
	60	56.5	58.3	0.83

RR = Risk of recurrence; SIR = structural incomplete response.

P2-07-04

CLINICOPATHOLOGICAL FEATURES OF THYROID CARSINOMAS IN GERIATRIC PATIENTS

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Objective: Biological aggressivity, and recurrence and mortality rates of thyroid cancer are known to be higher in geriatric patients. We aimed to determine clinicopathological features of thyroid cancer in patients ≥65 years old.

Methods: Data of 933 patients diagnosed with thyroid cancer histopathologically between January 2009-December 2014 in our clinic were retrospectively reviewed. Malignant nodules in patients ≥65 and <65 years old were taken as Group 1 and Group 2, respectively. Thyroid functions, ultrasonography (US) features and cytological and histopathological findings were compared.

Results: There were 109 (11.7%) patients ≥65 and 824 (88.3%) <65 years old. Thyroid functions, thyroid autoantibody positivity and thyroidectomy indications were similar. There were 153 (11.4%) and 1185 (88.6%) malignant foci in Group 1 and 2, respectively. Among nodules with available preoperative US features, mean nodule diameter was significantly higher in Group 1 (p = 0.008). Echogenity, texture, micro and macrocalcifications, margin irregularity and vascularization pattern were similar in two groups. Hypoechoic halo was observed in 16.4% and 28.6% of nodules in Group 1 and 2, respectively (p = 0.034). Cytological results were distributed similarly in two groups (p = 0.433). Histopathologically, tumor diameter, rates of microcarcinomas and incidentality were similar (p = 0.605, p = 0.759 and p = 0.605, respectively). Of all cancer types, 88.8% in Group 1 and 93.9% in Group 2 were papillary thyroid cancer (p = 0.028). Hurthle cell cancer constituted 3.9% of Group 1 and 1.1% of Group 2 carcinomas (p = 0.015). 2.0% and 0.2% of tumors in Group 1 and 2 were anaplastic, respectively (p = 0.012). There was not any significant difference in capsular and vascular invasion and extracapsular extension between groups.

Conclusion: Rates of Hurthle cell cancer which is known to have worser prognosis among other DTCs and anaplastic cancer are increased in geriatric ages. Cytological evaluation of thyroid nodules should strongly be considered due to increased tendency for agressive tumor types in these patients.

P2-07-05

IS THERE ANY DIFFERENCE BETWEEN FEMALE AND MALE GENDER IN TERMS OF TUMOR HISTOPATHOLOGY AND TNM STAGES IN PATIENTS WITH THYROID CANCER?

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Objectives: Previous studies have reported that patients with differentiated thyroid cancer (DTC) are most frequently females whereas incidences of aggressive type thyroid cancer, anaplastic thyroid cancer (ATC), and medullary thyroid cancer (MTC) are not different in both sexes. In this study, we aimed to evaluate the distribution of gender in patients with thyroid cancer, and also to compare the histopathologic features and tumor stages of patients according to gender.

Methods: In this retrospective study, we evaluated 1009 thyroid cancer patients who were followed-up in our clinic. The demographics, postoperative histopathologic features, and tumor stages (TNM) were reviewed.

Results: There were 224 (22.2%) male and 785 (53.5%) female patients. Mean ages of male and female patients were 51.18 ± 12.88 and 8.96 ± 12.51 years, respectively ($p = 0.020$). Among the 1425 carcinoma foci, 304 (21.3%) were detected in males and 1121 (78.6%) were in females (F/M = 3.7). The rate of incidental carcinoma was similar in two sexes ($p = 0.730$). The most frequent cancer type was papillary thyroid carcinoma (PTC) (n = 1331, 93.4%), followed by the follicular thyroid carcinoma (FTC) (n = 31, 2.2%), thyroid tumor of uncertain malignant potential (TT-UMP) (n = 24, 1.7%), hurthle cell cancer (HCC) (n = 21, 1.5%), ATC (n = 5, 0.4%), and MTC (n = 13, 0.9%). PTC was seen more frequently in females ($p = 0.010$), while the rate of FTC, TT-UMP, HCC, and MTC were similar in two groups ($p > 0.05$, all parameters). ATC was more prevalent in males (1.0% vs 0.2%, $p = 0.034$). The incidence of PTC variants was similar in both sexes ($p = 0.424$). There was no difference in both groups according to TNM stages ($p = 0.392$).

Conclusion: In our study, we found that ATC was more frequent in males. However, there was no difference between the two groups according to other aggressive type cancers and PTC variants with probable aggressive course. Furthermore, male and female patients had similar TNM stages.

P2-07-06

THE RELATIONSHIP BETWEEN THE BRAFV600E MUTATION IN PAPILLARY THYROID MICROCARCINOMA AND CLINICOPATHOLOGIC FACTORS

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Objectives: The BRAFV600E mutation which account for about 60–80% papillary thyroid carcinoma (PTC) has risen as a prognostic marker for risk stratification of PTC patients. The BRAFV600E mutation as a prognostic marker in papillary thyroid microcarcinoma (PTMC) is unclear.

Materials and Methods: We performed a retrospective review of 101 patients who underwent surgery for PTMC. We studied the prevalence of the BRAFV600E mutation. The associations between the BRAFV600E mutation and clinicopathologic characteristics were analyzed.

Results: The BRAFV600E mutation was observed in 72 patients (71.3%). There was no statistically significant correlation in age, gender, multifocality, extrathyroidal extension, presence of Hashimoto thyroiditis and lymph node metastasis between the BRAFV600E mutant group and wild group.

Conclusion: The BRAFV600E mutation is not significantly associated with prognostic factors in PTMC.

P2-07-07

PROGNOSIS OF PAPILLARY THYROID CANCER WITH EXTRATHYROIDAL EXTENSION ACCORDING TO THE LOCATION OF PRIMARY TUMOR

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Background: Extrathyroid extension (ETE) has been recognized as a prognostic factor in papillary thyroid carcinoma (PTC). Even though there were posterior extensions to larynx, trachea, esophagus, or recurrent laryngeal nerve, complete resection with no microscopic residual tumor (R0 resection) could be performed. In this study, we investigated the prognostic significance of location of primary tumor in PTC with ETE.

Methods: Between January 2007 and December 2009 at Gangnam Severance Hospital (Seoul, Korea), we identified 1,078 patients who had PTC with ETE and 1,199 patients with no or microscopic ETE. In 1,078 patients, we compared patients with anterior and posterior ETE.

Results: The mean follow-up period was 6.4 years. Although patients with ETE showed a significantly worse disease free survival (DFS) rate than those with no or microscopic extension ($P < 0.001$), there was no difference in the DFS rate between patients with anterior extension and those with posterior extension in case of R0 resection.

Conclusion: Extrathyroidal extension of primary tumor appears to be an important prognostic factor for PTC, however the location of primary tumor could have little or no prognostic significance in case of R0 resection.

P2-07-08

THYROID CANCER HISTOLOGICAL TYPES AND CHARACTERISTICS OF THE FUNCTIONAL CONDITION IN THE REPUBLIC OF ARMENIA

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Objectives: Evaluate the prevalence of thyroid cancer and thyroid functional condition of these patients in the Republic if Armenia.

Methods and Results: Biopsy examination was carried out in 340 patients (age 33–78) with a nodular goiter. During the examination in 31.76% thyroid cancer was revealed. In the group who had cancer woman:man relationship was 3:1. The histological characteristics of cancer were the following: 57.41% papilyar cancer, 31.48% follicular cancer, 4.63% anaplastic cancer, 3.7% medullary cancer, 0.93% medullary-papilyar cancer, 1.85% flat-cellular cancer. In all the patients who had cancer, thyroid functional condition was presented. Thus, in 43.55% of the patients who had papilyar cancer was in thyreosis condition, in 45.16% was found hypothyreosis and in 11.29% thyreotoxicosis. In 32.35% of the patients who had follicular cancer was in euthyreosis condition, in 58.82% was in hypothyreosis and 8.82% in thyreotoxicosis phase. In 50% of the patients had medullary cancer with thyreotoxicosis, in 50% euthyreosis). All the patients who had medullary-papilyar, flat-cellular and anaplastic cancer were in hypothyreosis phase. RET gene mutation was detected in the patients, considering that medullary cancer is typical syndromal forms. In the result of the examination 2 patients were diagnosed MEN 2a (2 patients were in thyreotoxicosis phase) and 2 patients were diagnosed a sporadic form of the disease. It should be paid attention that patients who had a follicular cancer, the genetic examination was made to detect Carney complex. A follicular cancer could be a complex component in 5.88%.

Conclusion: Thyroid cancer is a frequent pathology in the Republic of Armenia. Biopsy examination plays the major role in early and proper diagnosis of thyroid cancer and remember possible syndromal types of cancer.

P2-07-09

PATIENT WITH HIGH-MALIGNANT B-CELL LYMPHOMA AND INFILTRATION INTO THE THYROID

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The patient presented due to pain in the neck since 3 weeks. The last investigation was 6 years back, showing a thyroid of a normal volume and slightly dense characteristics in the ultrasound pictures.

The left thyroid lobe showed signs of low echogenicity and a lymph node 1.3 cm of diameter. Under the estimated diagnosis of a Thyreoiditis de Quervain because of a pain in the left lobe a corticiod therapy was given and a control examination was appointed in 3 weeks. Then the lymph node was revealed with a doubled volume, the clinical symptoms with pain over the thyroid gland prolonged. In the ultrasound the hypoechogenic parts of the thyroid were shown in the isthmic part of the thyroid.

So under the estimated of a lymphoid infiltration into the thyroid operation was intended and performed.

The histologic differentiation showed an infiltration of a high-malignant B cell-lymphoma into the thyroid. In a PET CT scan only a lymph node involvement could be shown in the left beck side.

P2-08 Transporters and Others

P2-08-01

A NEW ROLE FOR MONOCARBOXYLATE TRANSPORTER 8: REGULATION OF THYROID HORMONE AVAILABILITY DURING RETINAL DEVELOPMENT

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Objective: The importance of monocarboxylate transporter 8 (MCT8) for brain development has been studied extensively over the past decade. However, its function during retinal development has not been addressed yet, although this layered photosensitive structure is also part of the central nervous system. Therefore, we examined how MCT8 contributes to retinal development in chicken.

Method: Chicken embryonic development only takes 20 days and most retinal cell types are formed between embryonic day 4 (E4) and E8, concomitant with strong *MCT8* expression in all primitive retinal layers. Therefore, we electroporated an RNAi construct or the empty vector into the central retina to knock down *MCT8* expression starting at E4.

Results: Successful electroporation was monitored by co-expression of red fluorescent protein in transfected cells and knockdown of *MCT8* expression was confirmed using *in situ* hybridisation. We performed a 1 h EdU-labelling on E5 and on E6, the period of maximal progenitor cell proliferation. Knockdown of MCT8 decreased cell proliferation at both stages, resulting in a 3-fold reduction compared to the control condition at E6. Furthermore, radial migration of early photoreceptor cells from the inner to the outer neuroblastic layer (ONBL) was delayed as detected by the specific marker visinin at E6. This can account for the 25% reduction in number of photoreceptors present in the ONBL at this stage. Using NeuN as a neuronal cell marker, we found a 2-fold reduction in retinal ganglion cells at E6, indicating also impaired neuronal differentiation.

Conclusion: MCT8 is indeed necessary for both proliferation and differentiation in the developing retina, making this neural structure an interesting model to uncover new insights in MCT8-dependent regulation of thyroid hormone availability during neurogenesis.

P2-08-02

DIFFERENTIAL EFFECTS OF THYROID HORMONE ON CORTICAL AND HYPOTHALAMIC PARVALBUMIN NEURONS IN MICE

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Thyroid hormones (THs) are essential for brain development and maintenance. In humans the importance of TH is best illustrated in congenital hypothyroidism, a disorder characterized by reduced TH signaling in newborns. If not treated immediately, it can lead to severe and irreversible mental retardation. On the anatomical level, a specific subtype of inhibitory interneurons that express the calcium binding protein parvalbumin have been identified as primary targets of TH action during development. While parvalbumin neurons in the cerebral cortex have been associated with motoric functions, parvalbumin neurons in the hypothalamus are implicated in heart rate and blood pressure. Interestingly, both cell populations are strongly decreased in TRa1 mutant mice; however, the molecular mechanisms by which reduced TH signaling affects the development of parvalbumin expressing neurons in the cortex and hypothalamus remain elusive.

Our studies in Pax8 knock out mice, an animal model for congenital hypothyroidism, surprisingly revealed that the number of parvalbumin neurons was reduced in the cerebral cortex, whereas no differences were detected in the hypothalamic population. We also included Mct8/Oatp1c1 double knockout mice in our study that due to an impaired transport of TH across the blood brain barrier exhibit a strongly reduced TH brain content. Again, these animals showed a strongly reduced parvalbumin immunoreactivity in the cerebral cortex, while the number of parvalbumin neurons in hypothalamus was unchanged. Our current analyses using different in vivo tracing techniques point to further distinct neuroanatomical differences between these two types of parvalbumin neurons. Taken together, our findings suggest that although both populations are strongly dependent on TH signaling during development, the timing and mechanism of TH action differs substantially. Given the importance of parvalbumin neurons in motor and cardiovascular functions, our studies will contribute to provide valuable insight for the development and treatment of associated disorders.

P2-08-03

ROLE OF THE MURINE THYROID HORMONE TRANSPORTERS MCT8 AND OATP1C1 IN THE CARDIOVASCULAR AND THERMOREGULATORY SYSTEMS

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Thyroid hormone (TH) is well known to regulate the autonomic nervous system by central actions. One of the most specific TH transporters is the monocarboxylate transporter 8 (MCT8). In humans, inactivating mutations in MCT8 lead to the Allan-Herndon-Dudley Syndrome (AHDS), characterized by psychomotor retardation, severe developmental delay, neurological damage, as well as abnormal thyroid hormone serum levels. Mct8 knockout (ko) mice replicate the endocrine abnormalities of the patients but develop without any neurological defects. Previous studies revealed that the organic anion transporting polypeptide 1c1 transporter (Oatp1c1), which accepts preferentially T4 and reverse T3 as substrates, compensates for the absence of Mct8 in the mouse brain. Consequently, only the Mct8/Oatp1c1-double knockout (dko) mice exhibit pronounced TH deficiency in the brain despite high circulating T3 levels. As these animals fully recapitulate the phenotype of the patients, they constitute an excellent model to study the thermoregulatory and cardiovascular system and their autonomic regulation in AHDS.

Our preliminary studies already revealed that the thermoregulatory mechanisms in Mct8-ko, Oatp1c1-ko, and Mct8/Oatp1c1-dko mice are severely altered. In contrast to Mct8-ko animals, Oatp1c1-ko mice were unable to defend their body temperature at cold ambient temperatures pointing towards a mild cold sensitivity of these animals. Interestingly, this effect was reversed in the Mct8/Oatp1c1-dko mice. On the molecular level, we determined the expression pattern of Mct8 and Oatp1c1 in the different tissues as well as of genes involved in body temperature and cardiovascular regulation, and observed several alterations in TH-regulated genes that might explain the observed differences in thermosensitivity. However, further investigations of the central and peripheral regulators of thermogenesis are needed to fully elucidate the autonomic alterations in AHDS.

P2-08-04

CHEMICAL CHAPERONES CAN ALSO RESCUE PATHOGENIC MCT8 MUTATIONS THAT LEAD TO THE SEVERE FORM OF AHDS

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Introduction: Mutations in monocarboxylate transporter 8 (MCT8, *SLC16A2*) lead to severe psychomotor retardation in male patients, the Allan-Herndon-Dudley syndrome (AHDS). Mutations in MCT8 can either affect T_3 binding and transport or impair the translocation of the protein to the cell surface and its stability. The latter two effects may lead to functional, but reduced numbers of MCT8 molecules at the cell surface. This partial inactivation

is probably responsible for a milder phenotype of AHDS. We have already reported that exogenous chaperones like sodium phenylbutyrate and genistein increase the protein stability and function of these partially inactivated MCT8 variants (e.g. delF501, L434W) *in vitro*. We were now able to identify two other pathogenic mutations which responded to chaperones albeit are known to lead to a severe AHDS phenotype.

Methods: Several mutations were introduced into human MCT8 by site directed mutagenesis and stably transfected into MDCK1 (Madin-Darby canine kidney) cells. The cells were treated with increasing concentrations of chaperones for two days. Western blotting and radioactive thyroid hormone-uptake experiments were performed to analyze chaperone effects.

Results: Here we show two mutants previously regarded severe, G495A and G282C, which are responsive to sodium phenylbutyrate and genistein. The chemical chaperones increase protein expression AND function of the mutant proteins *in vitro*.

Conclusion: Chemical and pharmacological chaperones which can be safely used in Humans (i.e. sodium phenylbutyrate and genistein) can functionally rescue the pathogenic $MCT8^{G495A}$ and $MCT8^{G282C}$ mutants. The administration of these compounds might point to a new direction for the therapy of MCT8.

P2-08-05

TRANSMEMBRANE MCT8-MEDIATED T3 TRANSPORT IS INHIBITED BY SOME COMMONLY USED DRUGS AND BY L-CARNITINE

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MCT8 is the most specific thyroid hormone (TH) cell membrane transporter identified to date that has been linked to human disease. Mutations in the *MCT8* gene are associated with severe psychomotor retardation and thyroid function tests (TFTs) abnormalities. Besides genetic alterations other factors can impair MCT8 activity.

The aim of this study was to investigate whether some commonly used drugs having a structural similarity with TH and/or whose treatment is associated with TFTs abnormalities and L-carnitine, a peripheral antagonist of TH action, are able to inhibit MCT8-mediated TH transport.

COS-7 cells were transiently transfected with hMCT8 or pcDNA3 and then incubated with [125I] T3. Transfected cells were exposed to increasing concentrations of hydrocortisone, dexamethasone, prednisone, prednisolone, amiodarone, desethylamiodarone, dronedarone, buspirone, carbamazepine, valproic acid and L-carnitine and [125I] T3 uptake and efflux were measured. The mode of inhibition was also determined.

Exposure to each glucocorticoids gave different results. hydrocortisone dose-dependently inhibited T3 uptake, which was significantly reduced at the highest concentration (77% of inhibition at 1000 μM); dexamethasone significantly inhibited T3 uptake even at the lowest concentration and showed at the highest (100 μM) a 67% of inhibition; conversely, prednisone and prednisolone were entirely devoid of inhibitory potential. Among the antiarrhythmic agents, amiodarone caused a significant reduction of MCT8-mediated T3 uptake only at the highest concentration (40% at 100 μM), this effect was weaker than that produced by desethylamiodarone and dronedarone at the same concentrations; at 100 μM they showed a 52% and 87% of inhibition, respectively; buspirone resulted a potent inhibitor, significantly reducing the uptake of T3 even at low concentrations (inhibition from 40 to 87%). Carbamazepine and valproic acid had no effect. L-carnitine significantly inhibited T3 uptake only a 1 M. All drugs inhibiting T3 uptake did not affect T3 release from cells. Kinetic experiments revealed a noncompetitive mode of inhibition for all compound except amiodarone.

Conclusion: This study shows a novel effect of some commonly used drugs and of L-carnitine, that is inhibition of T3 transport into cells mediated by MCT8. Specifically, hydrocortisone, amiodarone and L-carnitine modestly inhibit T3 uptake whereas dexamethasone, desethylamiodarone, dronedarone behave as potent inhibitors. Treatment with these substances may interfere with T3 delivery and action in the tissues where MCT8 represents the main mediator of transmembrane passage of TH.

P2-08-06

MCT8 MUTANTS F287V AND S313A SEVERELY IMPACT THYROID HORMONE TRANSPORT

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Introduction: Thyroid hormones (TH) are important regulators of development and metabolism. TH set the basal metabolic rate. Lack of TH causes severe retardation of brain development and impairs brain function. One of the most important plasma membrane TH-transporter proteins is the monocarboxylate transporter 8 (MCT8). Its gene is localized on the X-chromosome and mutations (resulting in dysfunctional transporters) lead to severe psychomotor retardation, known as the Allan-Herndon-Dudley Syndrome (AHDS). Affected patients cannot walk, stand, or speak, and suffer from abnormal TH levels. For gaining better understanding of MCT8's transport properties several residues were chosen for evaluation upon their involvement in TH transport.

Methods: By site-directed mutagenesis amino acid residues F287, S313, S314 and E423 were tested for their influence on TH transport in stably transfected Madin-Darby canine kidney (MDCK1) cells. The resulting clones were examined by radioactive ^{125}I labelled thyroid hormone uptake- and efflux experiments. Furthermore, K_M-values of the mutants were determined.

Results: Exchange of the aromatic residue phenylalanine at position F287 to valine (F287V) severely impairs TH transport of MCT8, while F287W was functional at reduced efficiency. Exchange of hydrophilic S313 and S314 to alanine also reduced T3-uptake activity. In contrast, exchange of the negatively charged glutamic acid at position E423 by asparagine or aspartic acid does not impair MCT8 TH-transport.

Conclusion: The results presented here support the hypothesis that residues at positions S313, S314 and F287 play an important role in MCT8 mediated TH transport across plasma membranes.

P2-08-07

THYROID FUNCTION IN PSEUDOHYPOPARATHYROIDISM TYPE 1A

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Resistance to thyrotropin (TSH) is condition of impaired thyroid cell sensitivity to TSH action, and usually occurs as a result of TSH receptor alterations. In rare cases this condition develops as part of multihormonal resistance syndrome – pseudohypoparathyroidism type 1a (PHP 1a) due to germline loss-of-function mutations in the GNAS gene, encoding α-subunit of the Gs protein. Consequently, resistance to hormones which activate signal pathways via Gs protein (PTH, TSH, gonadotropins and GHRH) develops in target organs. The most relevant caracteristics of TSH resistance are high serum TSH, normal/low serum thyroid hormones, and normal/hypoplastic thyroid gland, in absence of thyroid autoimmunity.

We present 6 patients (4 men, 2 women) diagnosed with PHP 1a at the age of 4–32 years, based on presence of Albright's hereditary osteodistrophy features with PTH resistance (hypocalcemia and hyperphosphatemia with elevated PTH). At the time of investigation patients were aged 19–32 years, with no clinical evidence of hypothyroidism and no levothyroxine supplementation

Table 1. (for abstract P2-08-07)

Patient	Sex	Current age	PTH (pg/ml)	FT4 (pmol/l)	TSH (mIU/l)	Calcitonin (ng/l)
1	M	22	332.5	7.6	11.85	103.6
2	M	19	322.9	10.69	6.55	12.0
3	M	21	120.9	7.9	12.1	28.1
4	M	21	359.0	10.2	6.46	22.0
5	F	32	430.0	8.40	5.98	9.2
6	F	28	183.0	13.0	10.61	36.1

therapy. TSH concentration (normal range 0.4–4.9 mIU/l) was elevated in all subjects, but high (>10 mIU/l) only in three. Free thyroxine (FT4) concentration was normal in three patients (normal range 9–19 pmol/l), and slightly low in other three (50%). Out of six patients, one had antithyroid antibodies in significant titers, with ultrasonographic parenchymal heterogeneity, while others had unremarkable findings on thyroid ultrasonography.

Serum calcitonin was mildly to markedly elevated in all patients (normal range 0–6 ng/L). This finding is explained by the resistance to calcitonin (G family receptor) and/or low 1,25 dihidroxycholecalciferol which blocks synthesis of calcitonin in thyroid C-cells.

Our results are in compliance with previous studies, showing that all subjects with PHP1a have mild to moderate TSH resistance. However, there are remarkable differences regarding age at the time of disease recognition, diagnosis of thyroid dysfunction and initiation of therapy.

P2-08-08

THYROTROPIN-SECRETING ADENOMA. CASE REPORT

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Introduction: Prevalence of thyrotropin-secreting adenomas (TSHomas) is about one case per million. They comprise 1 to 2.8% of all pituitary adenomas, characterized by hyperthyroidism, misdiagnosed as the Graves' disease and leads to radioiodine therapy or thyroidectomy, without remission. This late diagnosis can explain the fact that TSHomas are typically invasive neoplasms, and surgical resection, which remains the basis for definitive treatment of TSHomas, has such complications as postoperative hypopituitarism, damage to the cavernous sinus and the internal carotid artery.

Case Report: 66 year old woman previously misdiagnosed as having primary hyperthyroidism and treated with antithyroid drugs, presented to us with overt hyperthyroidism, high levels of thyroid hormones and elevated thyroid-stimulating hormone (TSH). Magnetic resonance imaging (MRI) revealed a pituitary adenoma extending suprasellarly. Transsphenoidal surgical resection of the adenoma was held after initial treatment with somatostatin analogs for 1 month to achieve euthiriosis. There was no any complications in the postoperative period. Laboratory and clinical remission was retained. 6 day after operation the patient was discharged at home, without receiving any antithyroid or another drug therapy. 3–6.9 months follow up shows remission (clinical and laboratory euthiriosis, MRI evidence).

Conclusion: Diagnostic advances, which led to frequent and earlier detection of pituitary adenomas can prevent the dramatic consequences, such as invasive growth and related surgical complications, as well as vain removal of the thyroid gland in patients with central hyperthyroidism.

P3-01 Clinical Thyroidology

P3-01-01

A COMPARISON OF LEVELS OF T4 AND TSH FROM SERUM AND WHOLE BLOOD ON FILTER PAPER

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Context: The circulating blood volume of a preterm neonate is 80 ml/kg. Blood loss due to phlebotomy is a primary cause of anaemia in preterm infants. To measure a panel of thyroid hormones in serum requires a venous sample of roughly 1.3 ml; the volume required to measure the same hormones in blood spotted on filter paper (dried blood spot, DBS) is 0.2 ml. DBS is used primarily for neonatal screening and research studies; the relation between thyroid hormones measured in venous blood and in DBS is unknown.

Objective: To describe the relation between paired levels of T4 and TSH measured in DBS and serum.

Methods: A cross-sectional sample was recruited that included adults and preterm infants. Leftover blood, which was taken by venepuncture for clinical reasons, was collected and stored as matched samples of sera and DBS. Sera were sent to Rotterdam* for analysis by radio-immune assay (T4) and immuno-assay (TSH), and DBS cards were sent to Amsterdam (AB) for analysis by immune-assay in the newborn screening laboratory.

Results: 122 participants were recruited: 30 adults and 92 infants. The correlations between DBS and serum were: T4 +0.882 and TSH +0.950.

Serum levels can be estimated from DBS levels using a correction factor, specific for T4 and TSH, derived from linear regression modelling i.e.

T4/TSH serum correction factor = [constant + (gradient of line* T4/TSH in DBS)] ± residual standard deviation.

Conclusion: T4 and TSH serum samples correlates highly with those measured in DBS. Compared to venepuncture for serum samples, DBS samples have several advantages (they require less blood per sample, are more likely to be successful on the first attempt and are logistically easier to transport). Whenever appropriate, DBS samples should take precedence over serum samples for clinical research.

*The lab of Prof TJ Visser (Erasmus University Medical Center) whose help we gratefully acknowledge.

Table 1. Linear regression of T4 and TSH in DBS on T4 and TSH in serum (for abstract P3-01-01)

Model	Unstandardised coefficients		Standardised coefficients		p level
	B	std error	beta	t	
Constant	41.286	6.971		5.923	<0.0001
T4 DBS	1.841	0.097	0.882	19.080	<0.0001
$R = 0.882$, $R^2 = 0.778$, Adjusted $R^2 = 0.776$, residual standard deviation = 24.979					
Constant	1.810	0.427		4.238	<0.0001
TSH DBS	1.602	0.053	0.950	30.424	<0.0001
$R = 0.950$, $R^2 = 0.902$, Adjusted $R^2 = 0.902$, residual standard deviation = 3.912					

P3-01-02

CIRCULATING FREE TRIIODOTHYRONINE CONCENTRATIONS ARE ASSOCIATED WITH PHYSICAL FUNCTION IN EUTHYROID ELDERLY SUBJECTS

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Objectives: To determine the association between plasma thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) levels and physical function (PF) in both young (<65 yrs) and old (≥65 yrs) euthyroid individuals.

Methods: PF was evaluated by the Short Physical Performance Battery (SPPB) score and correlated with TSH, FT4 and FT3 in 245 young (age: 44.5 ± 13 yrs [M ± SD], M 113, F 132) and 815 old (age: 75.0 ± 7.3 yrs, M 359, F 456) community-dwelling euthyroid subjects, participating in the InCHIANTI Study. Euthyroidism was defined by plasma TSH concentrations within the reference normal range. Subjects with low-T3 syndrome or non-thyroidal illness were excluded from analyses. SPPB score it's a well documented instrument that includes three simple tests: a measure of standing balance, the 4-meter walking speed, and the ability to rise from a chair, the final score ranging from 0 to 12 with higher scores representing better performance.

Results: At the age- and sex-adjusted univariate analysis no significant relationship was demonstrated between TSH, FT4, FT3 and SPPB score in young individuals. On the contrary, a $p < 0.0001$ significant association was found between FT3, but not TSH or FT4, and SPPB score in elderly subjects. After adjusting for multiple confounders, such as age, sex, instrumental activity of daily living, physical activity, circulating levels of Interleukine-6, body mass index, history of stroke, history of cancer, chronic kidney disease, smoke, cognitive function, SPPB score was significantly associated (beta = 0.36 ± 0.16; $p = 0.03$) with FT3 in these subjects.

Conclusion: These data demonstrate an association between circulating FT3 within the normal reference range and physical function in euthyroid elderly subjects. These results could represent a useful information to further evaluate the role played by FT3 in the clinical outcome of euthyroid individuals.

P3-01-03

THYROID DYSFUNCTION IN CHRONIC KIDNEY DISEASE PATIENTS

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Objectives: Chronic kidney disease (CKD) is a serious health problem. Progression of CKD is associated with having a number of complications, including thyroid dysfunction, dyslipidemia and cardiovascular diseases. This study was aimed to investigate association of thyroid dysfunction with renal dysfunction.

Methods: 220 patients both sexes with Stage 3 to 5 CKD aged 54.56 ± 11.07 years were studied. The renal function of the diabetic patients was evaluated using the albumin-creatinine ratio (ACR) and Kidney Disease Outcome Quality Initiative-Kidney Disease Improving Global Outcomes (K/DOQI-KDIGO) classification. Multivariate logistic regression was used to find the association between eGFR and hypothyroidism (defined as serum TSH >4.95 mIU/l)

Results: Of the 220 study patients, 171 (77.9%) had stage 3 CKD; 43 (19.6%) had stage 4 CKD; and 6 (2.5%) had stage 5 CKD. There was positive relationship between eGFR and TSH in male, female and total subjects ($p < 0.05$). In multiple regression analysis, eGFR was positively related with TSH (standardized coefficient 0.134, $R^2 = 0.045$, $P < 0.001$), independent of age. For every 10 ml/min/1.73 m^2 lower eGFR, there was a 15% higher risk of hypothyroidism: adjusted odds ratio 1.15 [95% confidence interval (CI) 1.14–1.19, $P < 0.001$].

Conclusion: Our data suggest an inverse association between eGFR and risk of hypothyroidism.

P3-01-04

EVALUATION OF VAGAL NERVE SIZE IN STANDARDIZED MONITORED THYROIDECTOMY

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Objectives: Vagal nerve (VN) stimulation is mandatory in standardized intraoperative nerve monitoring (IONM) in thyroid surgery. This study prospectively evaluates the diameter of the VN during surgery.

Methods: 100 consecutive patients underwent thyroidectomy, providing 191 intraoperative VN measurements. The tips of a caliper were adjusted to laterally fit the VN to be measured. 70 VN underwent electrode placement for continuous IONM (CIONM). VN measurement was performed before (V1) and after thyroid resection (V2) to document size changes.

Results: 36% VN measured less than 2 mm diameter, 64% more than 2 mm. Correlation tests did not demonstrate significant relationships between VN diameter and gender, age, weight, side, thyroid pathology, VN distribution within the carotid sheath, recurrent laryngeal nerve (RLN) anatomy and neurophysiologic data. Increase in VN diameter between V1 and V2 has been observed. Temporary RLN palsy rate was 4.7%.

Conclusion: The study describes precise VN measurements. The information is useful for appropriate CIONM electrode selection to overcome electrode VN compression. VN size increased between V1 and V2 is probably due to edema. Therefore, an important feature of a CIONM electrode design is adaptability over the time during the surgical procedure.

P3-01-05

STAGE-THYROIDECTOMY: SINGLE INSTITUTION PERSPECTIVE

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Objectives: Neuromonitoring (NM) in thyroid surgery improves the intraoperative assessment of RLN function. We describe our patient management after loss of EMG signal at the end of the first lobectomy.

Methods: Standard NM technique was applied with both vagal and RLN stimulation (V1, R1, R2, V2). Patients underwent pre- and postoperative laryngoscopy. Patients were preoperatively informed about the possibility of stage thyroidectomy.

Results: In 23 patients over 803 consecutive thyroidectomy procedure (2.8%), V2 signal was missing after first lobe exeresis (loss of signal LOS <150 mcV). In 20/23 cases we stopped the surgical procedure (stage-thyroidectomy). In the 3 cases with malignancy and severe co-morbidities (ASA3-4 score) total thyroidectomy was performed at once. In these cases, such strategy was preoperatively discussed with patients, in none of these cases occurred bilateral RLN (only monolateral transient). Postoperative laringoscopy confirmed RLN palsy in 21/23 cases. All true positive patients were supported by speech therapy. False positive (N.2), malignant (N.8) and symptomatic goiters (N.7) underwent completion thyroidectomy within 6 months. One case underwent RAI for hyperthyroidism. Two patients underwent only follow-up.

Conclusion: NM changes surgical decision-making process in a multidisciplinary manner. A reduced EMG signal at the first side, may induce the surgeon not to complete total thyroidectomy avoiding in this way a bilateral RLN injury risk. We stress the importance of a dedicated informed consent with emphasis on shared decision making with patient, anesthesiologist and endocrinologist.

P3-01-06

RECURRENT LARYNGEAL NERVE (RLN) INJURY IN THYROID SURGERY: CLINICAL PATHWAYS AND RESOURCES CONSUMPTION

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Objectives: To assess resources consumption in RLN injury versus non-injured patient management. Patient, National Healthcare System (NHS) and society perspectives were investigated.

Methods: Direct/indirect RLN injury costs were estimated. The analysis was based on hospitalization costs, medications, diagnostic tests, outpatient visits, rehabilitation and general practitioner visits. Five clinical pathways were identified after RLN injury with vocal fold paralysis: vocal folds function recovery within one, three and six months (1^{st} -2^{nd} -3^{rd} clinical pathways) and vocal fold permanent paralysis after six months until one year without and with phono-surgery (4^{th}-5^{th} clinical pathway). Based on the specific exemption code, direct costs were valued from the NHS and patient perspectives. From the societal perspective, indirect costs were valued in terms of productivity losses (Human Capital Approach).

Results: Significant cost increase depending on damage duration/severity. Direct medical costs supported by NHS range from €80,58 (vocal fold recovery within one month) to €3.261,95 (permanent paralysis with phono-surgery). Direct medical costs increase, supported by the patient, from €3,60 (first clinical pathway) to €506,75 (fifth clinical pathway). Productivity losses were accounted in €156 per-day-per-patient. The no-RLN injury clinical pathway was the baseline. Minimum/maximum costs supported by NHS/by the patient were considered. From NHS perspective, the percentage increased ranging from 43.25% (first-clinical pathway versus no-RLN injury clinical pathway) to 98.15% (fifth-clinical pathway versus no-RLN injury clinical pathway). From patient perspective, the percentage increase ranging from 51.56% to 80.88%.

Conclusion: Significant economic impact of RLN injury management, which is variable depending on damage duration/severity with considerable additional costs supported by NHS/by the patient. Incidence reduction strategies of the RLN damage would lead to improved clinical outcomes/reduced resource consumption.

P3-01-07

CAPACITY BUILDING OF PRIMARY CARE PHYSICIANS IN MANAGEMENT OF THYROID DISORDERS: IMPLEMENTATION EXPERIENCES FROM A PAN INDIA CERTIFICATE COURSE

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Introduction: Thyroid diseases are the commonest endocrine diseases affecting 750 million people worldwide and over 42 million people in India. More than one-third of patients with hyperthyroidism remain undiagnosed due to lack of awareness. Strengthening of primary health care through capacity building of Primary Care Physicians (PCPs) is an effective short term intervention for improving the management of thyroid disorders. 'Certificate Course in Management of Thyroid Disorders' (CCMTD) was conceptualized as a nationwide programme with an objective of improving skills and core competencies of the PCPs in the management of thyroid disorders across India.

Objective: To illustrate the model adopted and to document implementation experiences from the capacity building initiative for PCPs in management of thyroid disorders.

Method: This joint collaboration is implemented by Public Health Foundation of India; the curriculum was developed by Chellaram Diabetes Institute which was reviewed by 15 national experts (endocrinologists) and later vetted by 38 specialists who trained the PCPs. The course comprises of didactic lectures, case studies, learning activities and instructional videos. A monitoring mechanism comprising of onsite random visits was developed to ensure standardised delivery of the course.

Result: A total of 746 doctors were trained in Cycle I and over 1000 participants have enrolled in Cycle II. The mean age of the participants is 41 years with an average clinical experience of 14 years. One-third of participants are from the public sector and 45% are post-graduates. End line evaluation score of the course from participants was rated 'excellent' (9.1/10). The initiative is being delivered across 30 cities (18 states & 1 UT) with participants from 320 out of 676 districts in India**.** CCMTD is accredited by South Asian Federation of Endocrine Societies-SAFES (2016–2017) and endorsed by Asia Oceania Thyroid Associations – AOTA (2016–2025).

Conclusion: This unique educational model has met an excellent response from physicians, in terms of enrolment rate over two cycles which probably reflects the felt need of physician community in India for skill improvement in thyroid disease management.

P3-01-08

ACUTE SUPPURATIVE THYROIDITIS – FORGOTTEN BUT UNFORGETTABLE CAUSE OF CERVICAL PAIN

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Introduction: Acute suppurative thyroiditis is a very rare condition, accounting for 0.1–0.7% of all thyroid disease.

Objectives: Review all cases diagnosed and treated at our Endocrinology and Diabetes Department.

Methods: Retrospective analysis of clinical files since 2006 to 2016.

Results: Four cases were identified, three women, one man, aged 35, 41, 87 and 45 years, respectively. They were all bacterial: two caused by *Streptococcus millieri*, one by *Hemophilus influenzae* and one by *Mycobacterium tuberculosis*. We found predisposing factors in two patients: previous fine needle aspiration of a thyroid nodule and advanced age. Clinical presentation was similar, mainly with anterior cervical pain and sudden cervical enlargement; fever and dysphagia were also common. The one with tuberculosis presented with characteristic systemic features of the disease (weight loss, night sweats, fever, cough and hemoptysis). All patients were euthyroid, except for one case of subclinical hyperthyroidism that later became permanent hypothyroidism. Thyroidal antibodies were negative, with exception of one patient that had positive anti-thyroglobulin antibodies. Elevated inflammatory markers were seen in all of them. Imaging studies showed thyroi-

dal abscesses in those caused by *S. millieri.* In one case, they were multiple and extended into the mediastinum; in the other one, they were associated with laryngeal infiltration and tracheal deviation and relapsed after antibiotic treatment, needing subsequent percutaneous drainage and even total thyroidectomy to solve. Apart from that, all patients were treated successfully with antibiotics, requiring long courses of treatment.

Conclusion: Despite being a rare disease, acute suppurative thyroiditis is a serious condition that requires immediate diagnosis and treatment with antibiotics and supportive measures. The treatment can be prolonged and even so not enough, requiring surgical resolution in some cases.

P3-01-09

A REVIEW AND CLINICAL ANALYSIS OF 12 CASES OF PRIMARY THYROID LYMPHOMA

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Objective: To discuss the diagnostic and therapeutic considerations of primary thyroid lymphoma (PTL).

Method: Cases of PTL diagnosed and treated in our hospital between January 1995 and September 2015 were collected and retrospective reviewed.

Result: Four males and eight females PTL patients were collected, with an average age of 63 years old at diagnosis. The average time to clarify diagnosis was seven months. 11 patients visited surgical department because of rapidly enlarging neck mass, except one patients only complained of coughing and suffocated. Seven patients were hypothyroid, four were euthyroid at the time of diagnosis. Ten patients were concomitant with Hashimoto's thyroiditis (HT). In sonography of 11 cases, nine showed bilateral nodules. To confirm the diagnosis, four underwent partial thyroidectomy, eight had core needle biopsy (CNB), two of them underwent fine-needle aspiration cytology (FNAC) first but were confirmed PTL by further CNB. Pathologic diagnosis of non-Hodgkin's lymphoma was confirmed in all cases, the pathological subtypes were diffuse large B cell lymphoma in nine patients, mucosa-associated lymphoid tissue lymphoma (MALToma) in two, and small B cell lymphoma in only one patient. 11 patients received chemotherapy. Only one patient did not have any additional treatment (following surgery) due to an inertia type of tumor. The median overall survival time was 24 months, three patients died. Among survival patients, seven patients completed chemotherapy without disease progression, one MALToma case did not receive chemotherapy after thyroidectomy but still alive with PTL, and one patient just finished his second period of chemotherapy.

Conclusion: Diagnosis of PTL should be considered when dealing with rapidly growing goiters in elder HT patients. The role of FNAC in diagnosing PTL is limited without immunohistochemically. Elder, long period of diagnose and combined with B group symptoms indicated bad prognosis.

P3-01-10

GASTRIC ACID SECRETION AND GASTRIN RELEASE MONITORING DURING CONTINUOS INTRAOPERATIVE NEUROMONITORING (CIONM) THYROID SURGERY

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Objectives: The vagus nerve (VN) plays a central role in the regulation of gastric acid secretion and gastrin release. CIONM is a promising technique to prevent imminent RLN injury in thyroid and parathyroid surgery. We present an analysis of gastric acid secretion and gastrin release during CIONM.

Methods: Exclusion criteria were: smokers patients, acid suppression medications, drugs affecting gastric motility, previous history/symptoms for GERD, peptic ulcer disease, helicobacter pylori infection, chronic kidney disease. 24 hrs before surgery alcohol/caffeine intake was stopped. Patients were nil-by-mouth since 6 hours before surgery. We prospectively evaluated serial measurements of gastric pH and gastrin hormone during CIONM via APS electrode. Monitoring intragastric pH was performed with a standard dual sensor pH monitoring. We compared 5 separate ph and gastrin blood determinations: (I) before skin incision; (II) after CIONM probe baseline calibration; (III) +20 min from baseline; (IV) before probe removal; (V) extubation.

Results: 39 females (mean age 38.5 years, range 18–68) and 19 males (mean age 47.7 years, range 18–71) underwent total thyroidectomy. Mean gastric pH values were: (I) 2.2 ± 0.2, (II) 2.0 ± 0.8, (III) 2.5 ± 0.5, (IV) 2.9 ± 0.9, (V) 2.6 ± 1.0 ($P = 0.50$, $P = 0.62$, $P = 0.24$, $P = 0.52$, $P = 0.60$ respectively). We obtained differences not statistically significant in the pH monitoring parameters analyzed: age, gender, left vs. right side, first vs. second side, duration of CIONM, type of APS utilized (2 mm vs. 3 mm). Gastrin values were within the normal range in sequential determinations (<100 pg/ml) and no significant differences were noted for either the time periods.

Conclusion: CIONM for total thyroidectomy in healthy patients has been validated in terms of pH and gastrin monitoring as a safe technique

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P3-01-11

PREDICTORS OF FAILURE OF PLANNED TOTAL THYROIDECTOMY. THE ROLE OF IONM

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Background: To determine the rate and predictors of failure of planned total thyroidectomy (TT).

Methods: Retrospective analysis, prospective collection of 988 patients with benign bilateral thyroid disease admitted for surgery between 1999–2012. Main outcome: failure of total thyroidectomy (f-TT).

Results: TT was planned for 988 patient, the treatment failed in 71 patients (7.2%). Multivariate analysis identified as pre-operative independent predictors of f-TT: age >75 years. Intra-operative predictors of f-TT: non identification of recurrent laryngeal nerve, no use of neuromonitoring. Post-operative predictors: gland volume >85 ml. The likelihood of f-TT was 10% if no predictor was present, 32% if 1 was present, and 56% if >2 were present. The percentage\distribution curve of f-TT is correlated with time period. Overall morbidity of f-TT patients was almost 6-fold higher than those with successful TT (s-TT)(8.7% vs 4.7%; P<.05). During the study period, 18% of patients (13/71) required completion thyroidectomy.

Conclusion: 7% of patients underwent less than total thyroidectomy. We identify pre-, intra- and post-operative factors predicting the failure of TT. This data must be taken into account when generalizations are made about the overall high success rates of TT.

P3-02 Hypothyroidism 2, Children + Regulation

P3-02-01

SEASONAL VARIATIONS OF TSH LEVELS IN ATHYREOTIC PATIENTS UNDER L-T4 REPLACEMENT THERAPY

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Objective: The pattern of TSH and free Thyroid Hormone (TH) in the different months of the year was analyzed in a large population of L-T4 treated athyreotic patients and euthyroid controls.

Methods: The study was a 10 *years (2004–2014) retrospective cross sectional* analysis of TSH and free TH in 3,934 L-T4 treated athyreotic patients *and* 11,806 euthyroid controls *performed in* Sicily, an island characterized by a typical temperate mediterranean climate with long hot summers and short mild winters. Correlations were calculated between TSH, TH levels and the local climatic parameters.

Results: Euthyroid controls did not show significant yearly TSH levels fluctuations (mean of medians = 1.41 mU/l). In contrast, monthly median TSH values in L-T4-treated patients varied from 0.87 mU/l in January to 0.30 mU/l between August to October (Kruskal Wallis test; $p < 0.001$). Median L-T4 dose (μg/Kg/d) in the different months of the year was very similar. In athyreotic patients both FT4 and FT3 were lower in the coldest months of the year and higher in the summer months. No correlation was found between the climatic factors and TSH and free TH in the euthyroid controls. In contrast, in L-T4-treated patients median TSH levels in the different months showed a significant inverse correlation ($p < 0.01$) with environmental temperature whereas other climatic factors, such as photoperiod duration or solar radiation were not correlated with either serum TSH or with TH levels.

Conclusion: Seasonal TSH pattern differed markedly between L-T4 treated athyreotic patients and euthyroid subjects in our studied area. L-T4 treated athyreotic patients showed TSH serum values significantly higher during the cold season when TH levels are significantly lower; temperature changes rather than the photoperiod or other climatic variables were correlated with the TH and TSH seasonal changes. This finding should be considered in the treatment of hypothyroidism to evaluate the risk of undesired hyperthyroidism in summer and of mood deterioration related to TH decrease in winter.

P3-02-02

CONGENITAL SUBCLINICAL HYPOTHYROIDISM IN CHILDREN – TO TREAT OR NOT TO TREAT?

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Objective: To determine the cause and assess natural history of congenital subclinical hypothyroidism (SH) in children.

Materials and Methods: 2 female dizygotic twins diagnosed by neonatal screening, congenital SH was for 5 years treated by iodine only. Molecular genetic analysis was performed by targeted NGS (Ion Torrent).

Results: During 5 year follow-up in sister 1 TSH levels ranged from 37.6 to 11.9 mIU/l by the end of observation remained elevated (25.5), while fT4 levels was normal (16.5 pmol/l). In sister 2: TSH levels ranged from 25.1 to 14.0 mIU/l by the end of observation and remained elevated (19.5), while level of fT4 also remained normal (17.2 pmol/l). Compared to background observations indicators of thyroid hormone (fT4 and periodically controlled fT3) remained within the reference range, there were no complains from the parents, school performance and neuropsychological developmental were appropriate, and the results of general clinical and biochemical analyses were normal. Molecular analysis in both sisters showed identical homozygous p.R450H mutation in TSHR gene.

Conclusion: In case of detection of subclinical hypothyroidism in neonatal screening, or in young children congenital causes should be considered. The 5 year follow-up of children with moderate resistance to TSH did not show clinical and laboratory signs of progression of thyroid dysfunction without treatment with levothyroxine. Indications for hormone replacement therapy in the SH should be discussed individually, taking into account the views of parents.

P3-02-03

DOES BASELINE OR CHANGES IN SERUM T3 DURING L-T4/L-T3 COMBINATION THERAPY PREDICT A POSITIVE RESPONSE TO THIS TREATMENT MODALITY IN HYPOTHYROID PATIENTS WITH PERSISTENT SYMPTOMS?

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Background: Despite being biochemically euthyroid, some L-T4 treated hypothyroid patients report persisting symptoms and are tentatively treated with a combination of L-T4 and L-T3. Combination therapy and appropriate choice of blood tests to monitor treatment are debated among specialists and patients.

Aim: To evaluate whether measuring of S-T3 at baseline or during combination therapy can be used as an indicator of effect of L-T4/L-T3 combination therapy.

Materials and methods: Observational retrospective study of patients (n = 42) with persisting symptoms of hypothyroidism despite L-T4 therapy, who had normal and stabile S-TSH levels and no co-morbidity that could explain their symptoms. All were treated with L-T4/L-T3 combination therapy at a dose ratio 1/17 according to ETA guidelines. Based on patient reported outcome they were divided into responders and non-responders.

Results: Five patients were lost to follow-up and thus excluded. At 3 months follow-up 11 were classified as non-responders and 26 as responders. At 12 months these figures had changed to 13 (35%) and 24 (65%), respectively.

Conclusion: Among hypothyroid patients with persisting symptoms on L-T4 therapy, 65% responded to L-T4/L-T3 combination therapy after 12 months of treatment. We found no difference in S-T3 explaining the difference between responders and non-responders. This indicates that measurement S-T3 is not a valid indicator for indication or effect of L-T4/LT3 combination therapy in clinical practise.

Table 1. (for abstract P3-02-03)

Baseline (n = 37)	Responders (n = 24)	Non-responders (n = 13)	p-value
TSH (mU/l)	0.78 (0.08–4.20)	0.92 (0.1–3.06)	0.1
T3 (nmol/l)	1.2 (0.7–1.9)	1.2 (0.8–2.00)	0.94
Free-T3 index	1.16 (0.55–1.82)	1.08 (0.76–2.10)	0.63
Evaluation (n = 35)	**Responders (n = 24)**	**Non-responders (n = 11)**	**p-value**
TSH (mU/l)	0.57 (0.01–4.02)	0.33 (0.02–2.42)	0.37
T3 (nmol/l)	1.5 (0.8–2.4)	1.3 (0.9–2.30)	0.5
Free-T3 index	1.41 (0.73–2.54)	1.33 (0.86–2.02)	0.56

P3-02-04

GENE EXPRESSION PANEL TO MARK THERAPEUTIC EFFICACY ON LEVOTHYROXINE-TREATED PATIENTS WITH PRIMARY HYPOTHYROIDISM

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Background: The primary hypothyroidism is characterized by the dysfunction of the thyroid gland. The available therapy is the treatment with levothyroxine, which has synthetic conformation of the hormone thyroxine. The aim of the study is to create a gene panel to mark the response to the levothyroxine use.

Methods: We evaluated 320 individuals and selected 8 patients with levothyroxine therapy to RNA-Seq Transcriptome analysis. They are divided into two groups. The first group has 4 hypothyroid patients with Thyroid Stimulant Hormone (TSH) between 0.5 mU/l and 2.0 mU/l and 4 patients with TSH between 4.0 mU/l and 20.0 mU/l. Venous blood samples were collected (5 L) and stored in PAXgene RNA tubes. The RNA extraction was realized with PAXgene RNA extraction kit (Qiagen). The transcriptome library was created in an NGS platform, Ion Proton System, following the kit protocols of Ion AmpliSeq Gene human transcriptome (Thermo Fisher Scientific Manufacturer). The computational analysis of data was performed in 0.99.491 rstudio software, Package Edger 3.12.0 of Bioconductor (Robinson MD, DJ McCarthy and Smyth GK, 2010).

Results: We sequenced 22,786 transcripts in the eight individuals. Differential analysis revealed 353 genes (a hundred and seventy-nine genes understated and one hundred and seventy-four genes overexpressed) were explored. The panel was constructed with 289 mRNA and 64 non-coding genes.

Conclusion: We constructed a panel to characterize the response to levothyroxine treatment in Hypothyroid patients. The panel may be useful in future studies as a tool to correctly measure the levothyroxine response.

P3-02-05

PSYCHOEMOTIONAL STATUS, QUALITY OF LIFE AND LIPID PROFILE IN PATIENTS WITH DIFFERENT SERUM TRIIODOTHYRONINE LEVELS ON THE REPLACEMENT THERAPY WITH LEVOTHYROXINE

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Aim: The aim of the study was to compare the psychoemotional status, quality of life and lipid profile in patients with different serum triiodothyronine levels on the replacement therapy with levothyroxine (L-T4).

Methods: 140 women with primary hypothyroidism receiving adequate replacement therapy with L-T4 were included. We evaluated the TSH, free T3 (fT3), free T4 (fT4), total cholesterol (TC), low (high) density lipoprotein (LDL/HDL), triglyceride (TG) levels; anxiety and depression, symptoms of hypothyroidism, quality of life, cognitive functions. Patients were divided into 3 groups according to fT3 level: Group I ≤3.7 pmol/l; Group II >3.7 and ≤4.7 pmol/l; Group III >4.7 pmol/l.

Results: There were no difference in TC, HDL, TG levels between groups with different fT3 levels ($p > 0.05$). The LDL level was significantly lower in the Group with high fT3 (Group III) compared to Groups I and II ($p < 0.05$). There were no correlation between the levels of fT3, TSH and lipid parameters ($p > 0.05$). There was only weak positive correlation between the levels of fT4 and HDL, VLDL, TG. Indicators of cognitive functions, anxiety and depression, quality of life did not differ between the groups. In Group III severity of the symptoms was significantly higher than in Groups I, II ($p < 0.05$).

Conclusion: In most cases the replacement therapy with L-T4 lead to normalization of fT3 level. But in some cases the fT3 level remains low. According to our results, high-normal fT3 level is associated with lower LDL level than middle- or low-normal fT3. Differences in fT3 levels were not accompanied by changes in indicators of cognitive, psychoemotional status and quality of life.

P3-02-06

BIOEQUIVALENCE AND DOSE PROPORTIONALITY OF A NEW LEVOTHYROXINE FORMULATION THAT MEETS THE 95–105% SPECIFICATION OVER THE WHOLE SHELF-LIFE: EVIDENCE FROM TWO RANDOMIZED PHARMACOKINETIC TRIALS

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Objective: Small changes in levothyroxine dose can lead to significant clinical effects. Thus, increasingly authorities are adopting stricter potency specifications for levothyroxine, 95–105% of the label claim over the whole shelf-life. Levothyroxine Sodium (Euthyrox, Eutirox and Lévothyrox) has been reformulated, and two studies performed to ensure bioequivalence and dose form proportionality of the new formulation to the existing product.

Methods: Two pharmacokinetic were conducted. The bioequivalence study was single-dose, two-period, two-sequence crossover comparing the highest dosage strength of 200 µg at a total dose of 600 µg. The dose form proportionality study was three period, six-sequence crossover, with subjects receiving three tablet strengths (50 µg, 100 µg and 200 µg) at a total dose of 600 µg. Blood samples were taken at pre-defined time intervals for analysis T4 in plasma. Primary outcomes were AUC and C_{max} of T4 in plasma.

Results: In the bioequivalence study, comparing the T4 profiles for the new (Test) and current formulation (Reference) of levothyroxine, the geometric LS mean ratio of the $AUC_{0-72,adj}$ was 99.3% (90% CI: 95.6–103.2) and the $C_{max,adj}$ was 101.7% (90% CI: 98.8–104.6). Bioequivalence can therefore be established as the CI for lie within the predefined 0.9–1.11 limits. In the dose form proportionality study, pairwise comparisons ranged from 99.3–104.8% and all 95% CI were within the pre-defined CI range (0.8–1.25). Therefore the three dose strengths were found to be dose proportional.

Conclusion: The new formulation of levothyroxine that meets the most stringent potency specification guidelines has been demonstrated to be bioequivalent to the old formulation and to show dose form proportionality. The new formulation will enable patients to receive a more exact dose according to their medical needs, improving control of thyroid hormone levels, and contributing to improved safety in the use of levothyroxine.

P3-02-07

DIFFERENTIAL EXPRESSION PANEL AS BIOMARKER IN HYPOTHYROIDISM. AN RNA-SEQ TRANSCRIPTOME IN INDIVIDUALS WITH PRIMARY HYPOTHYROIDISM

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Objectives: The thyroid hormone modulates the primary physiological processes in the development and maintenance of the human body. Hypothyroidism is defined as the inability of the thyroid gland to produce enough thyroid hormone to meet the metabolic needs of the body. However, the diagnostic accuracy for detection of primary hypothyroidism with TSH still has limitations. The aim of this work was to create a differential gene expression panel to function as a biomarker in primary hypothyroidism.

Methods: The eight individuals (four euthyroid and four with clinical hypothyroidism with TSH above 10 mU/l) were selected for transcriptome analysis from a total population of 320 volunteers. The collection and extraction of total RNA in peripheral blood were made in RNA preservation tubes PAXgene blood RNA and their respective extraction kit (PAXgene Blood

RNA kit) (Qiagen). The transcriptome was performed on the NGS platform Ion Proton System, following the Ion AmpliSeq transcriptome Human Gene Kit protocols (Thermo Fisher Scientific Manufacturer). Computational analysis of the data was performed in rstudio 0.99.491 software, Package Edger 3.12.0 of Bioconductor (Robinson MD, DJ McCarthy and Smyth GK, 2010). **Results:** We sequenced 22,879 transcripts in the eight individuals. Differential expression analysis revealed 20 genes (thirteen under expressed and seven overexpressed genes). The panel was constructed with 13 mRNA and 7 non-coding genes. **Conclusion:** These are the first study to develop a genetic panel to diagnose the hypothyroidism independently of the TSH.

P3-02-08

THE THYROID REGISTRY: CLINICAL AND HORMONAL CHARACTERISTICS OF ADULT INDIAN PATIENTS WITH HYPOTHYROIDISM

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Objectives: Hypothyroidism is common, has multiple manifestations and appropriate treatment requires an accurate diagnosis. This registry aimed to study the disease profile and treatment paradigm in hypothyroid patients in India.

Methods: We registered 1500 newly diagnosed, treatment-naïve, adult hypothyroid males and non-pregnant females across 33 centres with follow-ups as per routine clinical practice. Data on demography, clinical signs and symptoms, diagnosis, thyroid hormone profile, co-morbidities and treatment were recorded. This interim analysis focuses only on baseline data.

Results: Mean age of study population was 41.1 ± 14 years with female to male ratio of 7:3. The most frequently reported symptom was fatigue (60.2%), followed by weight gain with poor appetite (36.2%), hair loss (30.9%), poor memory and concentration (19.8%), constipation (18.2%), swelling of limbs (18.1%) and dry coarse skin (17%). Menstrual abnormalities (irregular cycle, menorrhagia or inter-menstrual bleeding) were reported in all women (n = 730) who had not attained menopause. Grade 1 and 2 goiter (per WHO) was observed in 15.4% and 3.3% patients, respectively. Co-morbidities were reported in 545 patients (36.6%): type 2 diabetes mellitus (13.5%), hypertension (11.3%), hypovitaminosis (5.9%) and dyslipidemia (4.3%). In majority of patients (n = 1203) treatment with levothyroxine was based on serum thyroid stimulating hormone (TSH) levels alone. Before starting treatment with levothyroxine, total serum thyroxine (T4) and TSH levels were assessed in 291 patients only. The dose of levothyroxine ranged from 12.5 to 375 mcg. The most frequently prescribed doses were 50 (31.5%), 100 (24.2%), 25 (23.2%), and 75 mcg (10.1%).

Conclusion: Guidelines suggest a diagnosis of hypothyroidism based on TSH and T4 levels. However most of the patients from this registry study were advised treatment with Levothyroxine based on TSH levels alone, thus highlighting the need for awareness and scientific education amongst clinicians in India. Levothyroxine replacement is the standard of treatment for hypothyroidism and is tailored.

P3-02-09

ON INTERACTION OF AUTOIMMUNE THYROIDITIS AT THE STAGE OF SUBCLINICAL HYPOTHYROIDISM AND GASTROENTEROLOGICAL PATHOLOGY

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Goal: To define peculiarities of nosologic structure of GIT upper parts diseases in patients with AIT at the stage of subclinical hypothyroidism (SH) in order to prescribe adequate pathogenetic therapy.

Materials and Methods: We have observed 24 ambulant patients (19 females and 5 males) aged 48–69 who consulted a gastroenterologist about possible GIT disturbances. Earlier all the patients were diagnosed with AIT at SH stage. Average AIT duration was 4.2 ± 0.3 years. All the patients underwent complex investigation of GIT upper parts, including laboratory tests, ultrasound tests of abdominal and dynamic cholecystography, as well as esophagogastroduodenoscopy.

Results: All observed patients showed different combinations of functional and organic GIT pathology. Chronic nonatrophic gastritis has been found in 21 patients, of them 19 showed helicobacter-associated gastritis. Sphincter of Oddy dysfunction of biliary type was diagnosed in 15 patients, non-alcoholic fatty liver disease – in 17 persons, gallbladder dysfunction of hypomotoric type – in 13 persons, and cholelithiasis – in 9 cases. There have been rare cases of GORD, chronic acalculous cholecystitis, chronic pancreatitis, chronic calculous cholecystitis, chronic atrophic gastritis, gastric and duodenal ulcer. Pathogenic connection of prevailing pathology, namely, chronic nonatrophic gastritis with AIT requires further clarification and can be mediated by combined influence of the thyroid hormone deficit and the products of systemic immune inflammation on stomach secretory activity and its motor function.

Conclusion:

• Different combinations of functional and organic GIT pathology has been found in all observed patients with AIT at SH stage.

• Chronic nonatrophic gastritis, functional disorders of the biliary tract and non-alcoholic fatty liver disease dominate in patients with AIT at SH stage.

• Obtained data should be considered both at administration of pathogenetic therapy of GIT upper parts diseases, and thyroid pathology.

P3-03 Goiter 2 and Environmental

P3-03-01

A US-CYTOLOGIC SCORE ALLOWS SIMPLE AND ACCURATE DEFINITION OF THE RISK OF MALIGNANCY IN CYTOLOGICALLY INDETERMINATE THYROID NODULES

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Goal: To help the clinician defining simply the risk of malignancy of a thyroid nodule cytologically indeterminate using a table crossing TIRADS and Bethesda results.

Patients and Methods: 750 thyroid nodules were prospectively scored with the TIRADS system. They then underwent a fine-needle aspiration and the results were expressed according to the Bethesda system. All patients were operated on. Among them, 515 had an indeterminate cytological result (44 atypia of undetermined significance, 305 follicular neoplasms and 166 suspi-

Table 1. (for abstract P3-03-01)

	Bethesda III	Bethesda IV	Bethesda V
TIRADS 2	0%	0%	0%
TIRADS 3	2.8%	2.0%	9.6%
TIRADS 4A	5.9%	2.5%	28.1%
TIRADS 4B	13.8%	4.8%	43.2%
TIRADS 5	NA	NA	100.0%

% Indicate directly the risk of malignancy of a thyroid nodule by crossing the TIRADS score and Bethesda result.
NA = Not applicable.

cious for malignancy). For those, a quantitative risk of malignancy was calculated for each couple of TIRADS and Bethesda scores, based on the final histological reports. Results were expressed as a table.

Results: In a population with a prevalence of malignancy of 10%, the risk of malignancy for scores TIRADS 3, 4A and 4B was 3%, 6% and 14% in Bethesda III nodules, respectively, 2%, 3% and 5% in Bethesda IV nodules and 10%, 28% et 43% in Bethesda V nodules. For scores TIRADS 2 and 5, the risk was 0% and 100% respectively in all cases.

Conclusion: TI-RADS score allows stratifying precisely the malignancy risk of cytologically indeterminate nodules, and thus to tailor the management of patients individually. The cytological risk is markedly dependent on the ultrasound pattern. Finally, follicular neoplasms have a lower risk of malignancy than nodules with atypia of undetermined significance. An easy to use table is provided to define the risk of a particular nodule.

P3-03-02

THYROID DYSFUNCTION AND ULTRASONOGRAPHY FEATURES IN PATIENTS WITH METASTATIC COLORECTAL CANCER TREATED WITH REGORAFENIB. RESULTS FROM A SINGLE CENTRE PROSPECTIVE COHORT STUDY

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Introduction: Regorafenib (Reg) a Tyrosine kinase inhibitor (TKI) recently approved for the treatment of metastatic colorectal cancer patients could be responsible, like others TKIs of potential endocrine side effects, but scanty data are presently available on this specific drug.

Methods: Prospective evaluation of thyroid function, autoimmunity and morphology during treatment with Regorafenib. From November 2015, 17 consecutive patients (7 males and 10 females; mean age 64.2 ± 7.8) with metastatic colorectal cancer with comparable tumor staging, normal thyroid function and no evidence of associated thyroid autoimmunity, were studied before and at monthly intervals after beginning Regorafenib at scheduled dose of 160 mg oral daily according to standard protocols. In all cases FT3, FT4, TSH and thyroid antibodies (TgAb and TPOAb) were measured together with clinical assessment and thyroid ultrasonography up to five months.

Results: 8/17 patients (66%) became hypothyroid (TSH 7.9 ± 4.9 mIU/l, range 7.0–18.5) within 30 days of therapy. Interestingly, in 4 of those who developed higher degree of hypothyroidism, we observed highest score of fatigue (G3), the most common general serious adverse event during Reg administration. TPOAb became detectable in 2 (12%) patients 1 month after therapy.

Thyroid volume significantly decreased in 9 (52%) patients (from 8.6 ± 2.2 ml before to 4.8 ± 1.6 ml 5 months after Reg, $p < 0.01$ by paired Student t test), together with the appearance of mild hypoechogenicity and a significant reduction of parenchymal thyroid vascularity ($p < 0.05$).

Conclusion: These data indicate that Reg, similarly to other TKIs inhibitors, may rapidly cause hypothyroidism in about one half of patients, and probably trigger thyroid autoimmunity. An early diagnosis and management of hypothyroidism is therefore mandatory for an effective clinical control of fatigue in most of the cases, in order to prevent unnecessary Reg dose reductions and modifications. Further studies are needed to characterize longer-term effects on thyroid function/autoimmunity and to assess whether hypothyroidism may have a prognostic value as a potential biomarker of clinical response.

P3-03-03

SHORT-TERM AMIODARONE TREATMENT FOR ATRIAL FIBRILLATION AFTER CATHETER ABLATION INDUCES A TRANSIENT THYROID DYSFUNCTION: RESULTS FROM THE PLACEBO-CONTROLLED, RANDOMIZED AMIO-CAT TRIAL

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Background: Amiodarone is known to affect the thyroid, but little is known about thyroid recovery after short-term amiodarone treatment.

Objectives: We aimed to evaluate the impact of 8 weeks of amiodarone treatment on thyroid function in patients with atrial fibrillation (AF) undergoing catheter ablation in a randomised, double-blind clinical trial.

Methods: 212 patients referred for AF ablation at two centres were randomized to 8 weeks of oral amiodarone or placebo. Thyroid function tests (TSH, thyroid stimulating hormone; T4, thyroxine; T3, triiodothyronine; fT4, free T4; fT3, free T3) were performed at baseline and 1, 3 and 6 months.

Results: Study drug was discontinued due to mild thyroid dysfunction in 1 patient in the placebo vs. 3 in the amiodarone group ($p = 0.6$). In linear mixed models there were significant effects of amiodarone on thyroid function tests, modified by follow-up visit ($p < 10^{-9}$ for both TSH, T4, T3, fT4 and fT3). The amiodarone group had higher TSH, fT4 and T4 after 1 and 3 months compared to placebo, whereas T3 and fT3 were lower. In all cases, the amiodarone-induced thyroid dysfunction was largest at 1 month, declining at 3 months, and with no differences at 6 months, compared to baseline.

Conclusion: We found amiodarone to have a significant impact on thyroid function after only 1 month, but with a fast recovery of thyroid function after amiodarone discontinuation. Our study indicates that short-term amiodarone can be considered safe in patients without prior thyroid dysfunction.

P3-03-04

THE 'WHITE THYROID' ON UNENHANCED CT IN AMIODARONE INDUCED THYROTOXICOSIS TYPE 2 (AIT2)

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Objectives: After an incidental observation of a 'white thyroid' on unenhanced chest CT in an AIT2 patient we investigated thyroid density (in Hounsfield Units (HU)) in amiodarone treated patients, in cases of AIT2 and in euthyroid patients (AEuth).

Methods: Prospectively enrollment of AIT2 (amiodarone >3 months (3 m), thyrotoxicosis, normal thyroid sonography and pattern 0 ColourFlowDoppler) and AEuth patients (amiodarone >3 m, normal TSH/thyroid palpation, CT for clinical reasons). Exclusion criteria for both groups: history of thyroid disease, significantly elevated TSI or antiTPO, use of iodine containing medication/contrast in the preceding 3 m. Procedure: unenhanced CT (3 slices of the thyroid with a 64 slice MDCT). The mean value of two measurements of thyroid density was calculated. Institutional approval B049201316794.

Table 1. (for abstract P3-03-04)

	AEuth	AIT2	P
N	34	20	
Amiodarone intake (months)	23 [13–64]	35 [27–44]	NS
Age (years)	75 [62–82]	63 [55–73]	<0.05
Male/Female	20/14	18/2	<0.05
FT4 (11.6–21.9 pmol/l)	19.0 [16.5–21.9]	70.8 [50.2–99.1]	<0.0001
FT3 (3.1–6.8 pmol/l)	3.7 [2.3–4.5]	8.8 [6.2–13.9]	<0.0001
TSH (0.27–4.20 mU/l)	1.6 [0.6–3.5]	<0.03 in all	<0.0001
Density (HU) nl: 95 [77–104]	101 [94–120]	133 [122–162]	<0.0001

Results: The treatment duration was similar in both groups. We found a significantly elevated thyroid density in AIT2 as compared to AEuth (table, results given as median and [IQR]). In within patient groups there was no significant correlation of density and treatment duration neither was there a correlation between density and age.

Conclusion: We confirmed our hypothesis of a higher thyroid density in AIT2 as compared to AEuth. Thyroid density has been shown to correlate with intra-thyroidal iodine concentration and the white thyroid in AIT2 may be related to enhanced amiodarone deposition in lysosomes, disordered processing of heavily iodinated thyroglobulin and enlarged follicles as described in AIT2. Our observation raises the hypothesis of a limited rise of thyroid density in AEuth but a rise above threshold in patients with AIT2. This novel finding warrants a prospective trial for evaluation of the 'white thyroid' as a possible herald of AIT2.

P3-03-05

ESTABLISHING AND COMPARING THE DISTRIBUTION OF TIRADS SCORES IN RECENTLY DISCOVERED THYROID NODULAR DISEASE: A PROSPECTIVE MULTI-CENTER STUDY

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Objectives: To establish the distribution of TIRADS scores in recently discovered thyroid nodular disease and to compare it between two expert centers.

Patients and Methods: 1304 nodules in 431 patients whose thyroid nodular disease had been detected for less than a year were scored prospectively according to the TIRADS system by two experienced observers. Nodules scored 3 and 4A were subdivided according to their size. Sex ratio, mean age and number of nodules measuring at least 5 mm per patient, distribution of each TIRADS scores were calculated for the two observers and globally. The results between the two observers were compared using Student's, Khi2's and Fisher's tests. The reasons of the discrepancies were studied qualitatively.

Results: Sex ratio (0.3 et 0.38) and mean age of the two populations were identical. A slight difference in the mean number of nodules per patient (2.5 vs. 3.2) was found. Global distribution of TIRADS scores were 5%, 62%, 27%, 4% and 1% for TIRADS scores 2, 3, 4A, 4B and 5, respectively. Distribution of nodules scored 2, 4B and 5 and of supracentimetric nodules scored 3 and 4A showed no significant differences between the two observers. A significant difference was noted in subcentimetric nodules scored 3 and 4A and was explained qualitatively as a different appreciation of echogenicity in these small nodules.

Conclusion: A good inter-observer agreement of the distribution of TIRADS scores was found, confirming the robustness of the system, which can be used as a tool for selecting which nodule should undergo FNA. Nodules scored 2 and 3 represented two thirds of all nodules, allowing for simple follow-up and avoiding FNA in 75% of all cases.

P3-03-06

THE SANTORINI STUDY: ON THE INCIDENCE OF THYROID AUTOIMMUNITY AND THYROID CANCER ON A VOLCANIC ISLAND

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Santorini in the southern Aegean Sea is a volcanic island.

Aim: This study was designed to investigate a representative part of the population for thyroid diseases, particularly autoimmune thyroiditis (AIT) and cancer (TC), and to correlate disease incidence with the environmental factors.

Methods: It was a two-cohort study conducted in the towns of Thera (Th) and Emporio/Akrotiri (EA). In Th 420 persons (from a population of approximately 10,000) and in EA 118 out of about 1,200 inhabitants were clinically examined and via ultrasound, while in 148/420 subjects in Th and 60/140 in EA, blood samples were collected for measurements of TSH, TPOAb, TgAB and selenium (Se); iodine was measured in spontaneous urine. Selenium was also measured in seawater and in aquiferous samples.

Results: A high incidence of AIT was found in Th (16%) as compared to EA (19%). TSH was not different between the two groups. UIE was 134 ± 17 μg/l in Th and with 104 ± 13 borderline in EA, while Se was 74 ± 14 μg/l (Th) and 66 17.8 μg/l (EA), i.e. slightly low, while very high Se content was measured in seawater from the caldera as compared to the low Se content from the local water supply samples. Thyroid cancer (4 cases PTC) with an incidence of 103/100.00 was higher than that in mainland Greece. Three out of four TC patients were from EA. Interestingly, the US analysis showed a more diffuse, inhomogeneous image in Th than the more nodular aspect in EA.

Conclusion: Despite a degree of bias, our results demonstrate an increasing incidence rate of AIT and TC in Santorini. Low levels of Se, together with other geophysical and genetic factors, may be involved.

P3-03-07

HOW AND AT WHICH SIZE ARE THYROID NODULES DISCOVERED AND CONSEQUENCES ON THE RISK OF MALIGNANCY

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Objectives: To determine the detection mode detection of thyroid nodules, their size and risk of malignancy.

Methods: Prospective study of 962 thyroid nodules discovered in less than a year. The mode of detection was recorded as well as the size and TIRADS score. 839 of these nodules were submitted to FNA and the results expressed according to the Bethesda system. The average size, the % of supracentimetric nodules and the risk of malignancy were compared according to the mode detection of the nodule.

Results: The nodules were discovered in 16% of the cases by the patients, their benignity was asserted cytologically in 66% of the cases and the average size was 30 mm. In the 84% other cases, they corresponded to a radiological or clinical incidentaloma with an average size of 21 mm, 84% of supracentimetric cases and 71% cytologically benign results. The most frequent 3 modes of detection were respectively imaging procedures (33%), systematic palpation by a doctor (24%) and exploration of a thyroid dysfunction (14%).

Conclusion: The majority of the recently detected thyroid nodules are incidentalomas, for the greater part above 10 mm and benign. Nevertheless, in 29% of the cases the cytological result are malignant or indeterminate and management is necessary.

P3-03-08

VEGETARIAN DIETARY PATTERN AND OXIDATIVE STRESS MARKERS

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Background: Oxidative stress occurs as a result of an imbalance between free radical production and antioxidant defense mechanisms, and has been implicated in the pathogenesis of several inflammatory and immune-mediated disorders. Aim of our study was to investigate the relationship between vegetarian dietary habit and redox homeostasis, in order to better define the impact of diet on health outcomes.

Methods: In this pilot study, we investigated the changes in oxidative balance in 20 healthy subjects on vegetarian diet, by means of specific serum tests, such as derived Reactive Oxygen Metabolites (d-ROMs) and Biological Antioxidant Potential (BAP) test. Advanced Glycation End Products (AGEs), compounds formed by the transformation of proteins, were also evaluated as markers of oxidative stress. Moreover, we included 63 age and sex-matched healthy controls, who had been already evaluated for the same parameters. None of them was under any pharmacological treatment.

Results: Compared to non-vegetarians, vegetarians had significantly lower levels of d-ROMs (mean value 141.27 *vs* 271.87 U CARR; $P < 0.0001$), and tendentially higher levels of BAP (mean value: 3854.79 *vs* 3380.31 µmol/l; $P = 0.052$), indicating a reduced oxidative stress. As a result, total oxidant/antioxidant ratio, expressed as Oxidative Stress Index (OSI), was significantly lower in vegetarians compared to non-vegetarians (3.80 *vs* 7.18; $P < 0.001$), and significantly correlated to d-ROMs levels ($r = 0.0921$; $P < 0.0001$).

Conclusion: Oxidative stress markers, both total (dROMs and OSI) and specific (AGEs) ones, are significantly lower in vegetarian subjects than in non-vegetarians, and also BAP is higher in vegetarians, with a slightly significant trend; thus, the oxidative/anti-oxidative balance is shifted towards the anti-oxidative side. This suggests a positive influence of vegetarian diet on the redox balance, and a potential protective effect of such dietary habit towards oxidative stress-related disorders. These findings motivate further evaluation of vegetarian diets and their special characteristics.

P3-03-09

VESSEL SEALING SYSTEM (VSS) SAFETY AROUND THE RECURRENT LARYNGEAL NERVE (RLN)

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Objectives: VSS safety around RLN is still not fully understood. **(1)** What is the safe distance and duration of VSS use close to RLN? **(2)** Is it safe to dissect RLN immediately after using VSS?

Method: The protocol was approved by Animal-Care-Kaohsiung-University (Taiwan). 14 Duroc–Landrace-piglets were intubated with EMG endotracheal tube. To investigate EMG changes we used continuous neuromonitoring. Safety was evaluated in different conditions: **(1)** VSS ($N = 4$, power 2) distance to nerve: 2 and 5 mm; duration: 1st 5 sec (f/u 3 min), if no EMG change 2nd 10 sec (f/u 3 min); if no EMG change 3rd 15 sec; if EMG change, f/u 20 min to observe the recovery. **(2)** How long before use VSS to dissect the nerve? ($N = 2$) test VSS on muscle, then touch RLN immediately. Duration: 1st 5 sec (f/u 3 min), if no EMG change 2nd 10 sec (f/u 3 min), if no EMG change 3rd 15 sec if EMG change, f/u 20 min to observe the recovery.

Results: Do not directly touch the RLN with VSS immediately after the latter has been used. Safe margin and duration is 2 mm for less than 5 sec.

Conclusion: We propose a standardized use of VSS near the RLN.

P3-04 Cardio, Brain and Metabolism

P3-04-01

SERUM LEVELS OF FREE TRIIODOTHYRONINE AND FREE THYROXINE ARE ASSOCIATED WITH PREVALENT TYPE II DIABETES MELLITUS IN A POPULATION-BASED SAMPLE FROM NORTHEAST GERMANY

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Objective: Our aim was to investigate the association of thyroid function defined by serum levels of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), and free thyroxine (fT4) with prevalent type II diabetes mellitus in a large population-based study from Northeast Germany.

Methods: Analyses are based on data from the Study of Health in Pomerania (SHIP), a population-based study with 4308 individuals. Type II diabetes mellitus was defined by self-report or intake of anti-diabetic medication. Serum levels of TSH, fT3, and fT4 were measured by immunochemiluminescent procedures. Multivariable logistic regression models adjusted for age, sex, body mass index and hepatic steatosis were used to investigate the association between thyroid hormones and type II diabetes mellitus.

Results: There was no significant association between TSH levels and prevalent type II diabetes mellitus (odds ratio [OR] = 0.99; 95%-confidence interval [CI] = 0.93–1.06; $p = 0.829$), but fT3 levels were significantly inversely (OR = 0.81; 95%-CI = 0.68–0.98; $p = 0.025$) and fT4 levels significantly positively (OR = 1.06; 95%-CI = 1.01–1.10; $p = 0.038$) associated with prevalent type II diabetes mellitus. Interactional analyses revealed sex as effect modifier for the association of fT3 ($p = 0.001$) and fT4 ($p = 0.053$) with prevalent type II diabetes. The inverse association between fT3 levels and prevalent type II diabetes mellitus was mainly seen in males, whereas the positive association between fT4 levels and prevalent type II diabetes mellitus was predominantly seen in females.

Conclusion: We demonstrated sex-specific effects of thyroid hormones on type II diabetes mellitus with the highest risk for type II diabetes mellitus in males with low fT3 and in females with high fT4.

P3-04-02

LOW NORMAL FREE THYROXINE LEVELS ARE INVERSELY ASSOCIATED WITH METABOLIC SYNDROME IN EUTHYROID SUBJECTS

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Objectives: Thyroid hormone has a significant role in regulating metabolic homeostasis. We conducted this study to investigate whether free thyroxine (FT4) levels are associated with metabolic alteration and metabolic syndrome in euthyroid healthy subjects.

Methods: We recruited a total of 11802 healthy subjects with euthroid function who visited our hospital for a health checkup. Metabolic syndrome was defined by anthropometric and biochemical measurements whereas thyroid function was determined by serum thyrotropin and FT4 concentrations.

Results: Amongst components of metabolic syndrome, quintiles of FT4 had inverse association with obesity ($P < 0.001$), hyperlipidemia including hypertriglyceridemia ($P < 0.001$), decreased HDL-C ($P = 0.001$) but no asso-

ciation with hypertension or hyperglycemia after adjusting for age in men. Women had also significant association between FT4 with obesity ($P < 0.001$), hypertrigleceridemia ($P < 0.001$), and low HDL-C ($P = 0.019$). The risk for metabolic syndrome was decreased from reference including the lowest three quintiles to fourth [odds ratio (OR) = 0.78, 95% confidence interval (CI) = 0.69–0.90] and fifth quintiles (OR = 0.77, 95% CI = 0.67–0.88) after adjustment for age and sex. This association remained significant further adjustment for other metabolic variables and even TSH concentration and also in subgroups divided by sex, age or obesity.

Conclusion: FT4 levels were inversely associated with metabolic syndrome in euthyroid subjects independently of metabolic risk factors. Careful assessment and timely management of combined metabolic risk factors might be beneficial on the CVD reduction even in euthyroid subjects with low normal FT4 might be beneficial on the CVD reduction.

P3-04-03

COGNITIVE FUNCTIONING IN WOMEN WITH GRAVES' DISEASE AND ITS ASSOCIATION WITH MEDIAL TEMPORAL PATHOLOGY

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Objectives: Patients with Graves' Disease (GD) may unpredictably develop persistent cognitive impairment with poor quality of life (QoL). Mechanisms are unknown, but similar cognitive impairment in Cushing's disease and chronic corticosteroid therapy are accompanied with reduced volume of brain medial temporal lobe (MTL) structures like hippocampus and amygdala – structures known to play an important role in forming and retrieving new memories. These structures also have high density of thyroid hormone receptors (TR) and data from TR knock-out mice indicates that the TR is involved in hippocampal structure and function. This project therefore hypothesizes that: 1) MTL structures are smaller in hyper- than in euthyroidism 2) small MTL predicts cognitive deterioration and 3) the MTL volume reduction is prolonged in those with persistent cognitive impairment. We are now presenting data from the baseline evaluation.

Methods: This is a case-control 15-month study recruiting 50 consecutive premenopausal women with newly diagnosed GD. Investigations include cognitive testing, QoL, free tetraiodothyronine (FT4), TSH receptor antibodies (TRab) and MTL volumetry with magnetic resonance imaging. An important instrument for cognitive testing is a self-evaluation questionnaire, the Mental Fatigue Scale (MFS), originally developed for traumatic brain injuries, where higher scores indicate more severe fatigability.

Results: The MFS score correlates positively with FT4 and TRab levels. A preliminary analysis indicates that MFS score and TRab level correlate negatively with left amygdala volume measured by manual volumetry.

Conclusion: These preliminary data support the hypotheses that MTL structures like amygdala are involved in the cognitive dysfunction experienced by patients with GD. The correlation with TRab levels needs further evaluation. The MFS and MTL volume measurements may be important tools to capture the cognitive impairment in GD patients and may target individualized treatment. The future 15-monthdata and the comparisons to controls will spread further lights on the brain involvement in GD.

P3-04-04

THYROID DISEASE IN OLDER PATIENTS HOSPITALIZED FOR ACUTE ILLNESS: PREVALENCE AND THERAPEUTIC APPROPRIATENESS

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Rationale: Thyroid diseases are common in the general population with an estimated prevalence of about 3–5%, affecting mostly women and increasing with ageing. Few data exist about the actual prevalence of thyroid disease and therapeutic appropriateness in older patients hospitalized for acute illness.

Patients and Methods: Older patients consecutively admitted to the Geriatrics Unit of the University Hospital of Pisa for acute illnesses from 1 October 2013 to 30 June 2015 were enrolled. A detailed medical and pharmacological history was collected and, thyroid hormone profile and circulating autoantibody titer were measured in patients with positive history for thyroid disease. Patients were classified as euthyroid (TSH 0.4–4.0 mIU/l), hyperthyroid (TSH <0.4 mIU/l) or hypothyroid (TSH >4.0 or >7.0 mIU/l).

Results: 2058 patients [55.7% women, aged 83.5 ± 7.9 years (mean±SD)] admitted for medical acute disease were enrolled: 275 (14%, 66.9% women) suffered from thyroid disease. Of them, 139 (50.5%) were affected by chronic autoimmune thyroiditis (HT), 73 (26.5%) by non-toxic nodular goitre (NG), 45 (16.4%) by toxic nodular goitre (TNG), 14 (5.1%) by differentiated thyroid cancer while, 4 (1.5%) had amiodarone-induced thyrotoxicosis. Thirty-eight out of 118 (32.2%) patients with NG or TNG had undergone lobectomy or total thyroidectomy; 9/14 (64.3%) with thyroid cancer had been submitted to total thyroidectomy and radioiodine remnant ablation, 4/14 (28.5%) to lobectomy and 1/14 (7.2%) had not received any therapy. At baseline, 157/275 hypothyroid patients (57.1%) received L-T4 while 15 (5.4%) hyperthyroid patients methimazole therapy. Among the 157 patients receiving L-T4, 41 (39%) were still hypothyroid [19 (46.3%) with serum TSH value >7 mIU/l)] while, 16 (15.2%) had iatrogenic hyperthyroidism. Among the 15 patients receiving methimazole, 8 (66.6%) were still hyperthyroid.

Conclusion: The prevalence of known thyroid disease in very old patients hospitalized for acute illness is very high, with a slight higher prevalence in women. More than half hypothyroid patients and two third of those with hyperthyroidism received inappropriate treatments (either excessive or ineffective). Taking together, these results emphasize the need of careful monitoring of thyroid hormone profile in acute ill older patients with known thyroid disease, also considering the negative impact of thyroid dysfunction on clinical outcome. Moreover, giving the possible over-diagnosis of hypothyroidism due to the shift with ageing of serum TSH value toward the upper reference range, the actual need of L-T4 replacement therapy should be carefully assessed.

P3-04-05

SUBTLE CHANGES IN THYROID FUNCTION ARE ASSOCIATED WITH DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES

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Background: Thyroid deficiency is known to be associated with reduced renal plasma flow, unfavorable metabolic profiles and increased cardiovascular risk. This study was conducted to investigate the association of subclinical hypothyroidism (SCH) with kidney disease by measuring estimated glomerular filtration rate (eGFR) and albuminuria in type 2 diabetic patients.

Research Design and Methods: A cross-sectional analysis was conducted among subjects with type 2 diabetes and subclinical hypothyroidism was diagnosed based on serum free T4 and TSH levels. GFR was estimated (eGFR) by the Modification of Diet in Renal Disease formula whereas albuminuric status was determined by urinary albumin/creatinine ratio.

Results: Among the 520 subjects, 18 (3.5%) had subclinical hypothyroidism. Compared with euthyroid subjects, those with subclinical hypothyroidism had higher prevalence eGFR <60 ml/min/1.73 m^2 (16.7% vs. 7.8%) and macroalbuminuria (27.8% vs. 8.8%). After an adjustment for age, sex, duration of diabetes, HbA1c, BMI, hypertension, lipid profiles and smoking, SCH

was associated with greater prevalence of macroalbuminuria (odds ratio = 5.4, 95% confidence interval = 1.4–20.1; $P = 0.013$) but not associated with reduced eGFR.

Conclusion: Type 2 diabetic patients with SCH are associated with an increased risk of macroalbuminruia rather than decline of the eGFR. Our study suggests that subclinical hypothyroidism might be a risk factor for progression of diabetic nephropathy.

P3-04-06

ADIPOCYTOKINES, INSULIN RESISTENCE AND CHRONIC INFLAMMATION STATUS IN HYPOTHYROID PATIENTS

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Background: The thyroid dysfunction may influences the production of many adipocytokines and chronic inflammation factors resulting in a variety of metabolic disturbances, insulin resistance, dyslipidemia and arterial hypertension.

Objective: Of the study was to investigate the relations of adiponectin, leptin, indices of tissue inflammation and metabolic disturbances in patients with hypothyroidism as compared to euthyroid controls with obesity and normal body weight.

Material and Methods: A total of 118 studied patients (85 female, 33 male, aging 43 ± 11 years) were divided into 4 groups: gr.A–obese hypothyroid patients (BMI-36 kg/m^2), gr.B–obese euthyroid (BMI-38 kg/m^2), gr.C – hypothyroid (BMI <25 kg/m^2), gr.K (control) – euthyroid (BMI 22.3 kg/m^2). Adiponectin, leptin (ELISA), interleucin-6 (ECLIA), Lp(a) and ApoB (ITDM), CRP, cholesterol, HDL, OGTT and HOMA-Index were determined. Diabetes type 2 (DM-2) and arterial hypertension (AH) were registered in each group.

Results: Significant differences of adiponectin mean values were found between hypothyroid patients with high or normal BMI (gr.A, gr.C), euthyroid obese patients of gr. B ($p < 0.05$) and controls ($p < 0.0001$); the median of adiponectin was 12.2, 6.9 and 5 mcg/ml respectively. The obese patients (gr.A, gr.B) showed the much higher leptin, CRP and IL-6 mean values compared to those of gr.C and controls ($p < 0.001$) corresponding to frequency of DM-2 and AH (55.0% vs 12.2%, $p < 0.0001$). It was obtained negative nonparametric correlations between BMI, visceral fat%, cholesterol, ApoB, insulin, HOMA-I and TSH.

Conclusion: The data of the study demonstrated that hypothyroidism might be accompanied by increased adiponectin which was independent of the body weight. Leptin, chronic inflammation and insulin resistance correlated with BMI, TSH, dyslipidemia, diabetes-2 and arterial hypertension. Adiponectin might be considered as a protective factor.

P3-04-07

CIRCULATING THYROXINE SERUM LEVELS ARE ASSOCIATED WITH SYSTOLIC PULMONARY ARTERIAL PRESSURE (SPAP) IN SYSTEMIC SCLEROSIS (SSC)

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Objective: Pulmonary arterial hypertension (PAH) is one of the most frequent vascular complications and the most important cause of death in SSc. Thyroid disorders are associated with both PAH and SSc independently. Aim of this study was to evaluate the relationship, if any, between serum thyroid hormones and systolic pulmonary arterial pressure (sPAP) in SSc patients, compared to Hashimoto's thyroidits (HT) patients as controls.

Methods: In this cross-sectional study, we included 73 euthyroid women: 41 affected by SSc (mean age 59 ± 10 yr) and 32 age-matched HT as controls. None of them was under thyroxine therapy. In each subject, we measured serum TSH, free thyroxine (FT4), and free tri-iodothyronine (FT3) concentrations. sPAP was determined by echocardiography. Based on recent evidences of the literature concerning sPAP values and related mortality [Hachulla et al. Rheumatology 2015;54:1262–9], an estimated sPAP ≥36 mm Hg at baseline was chosen as cut-off value in our cohort.

Results: Among SSc patients, 20/41 (48%) had sPAP values ≥36 mm Hg. In these patients, serum FT4 was 12.3 ± 2.3 pm/L, thus significantly higher than in those with sPAP values <36 mm Hg (10.7 ± 1.3 pm/L; P = 0.014). Moreover, serum FT4 directly correlated with sPAP in the whole group of SSc (P = 0.011), as well as in HT patients (P = 0.004). After excluding SSc patients with sPAP values <36 mm Hg, the correlation remained highly significant (P = 0.004). Moreover, SSc patients with serum FT4 higher than 12.3 pmol/l (i.e. the average value of our SSC patients with sPAP ≥36 mm Hg) tend to have a two-fold risk of developing high sPAP values.

Conclusion: Serum FT4 levels are higher in SSc patients with higher sPAP values, and the two parameters are significantly correlated. Thus, higher FT4 levels, even within normal ranges, seem to be associated to PAH in SSc patients. Thyroxine could represent a central modulator of vascular function and integrity in SSc-PAH.

P3-04-08

IMPACT OF AUTOIMMUNE THYROIDITIS AND SUBCLINICAL HYPOTHYROIDISM IN CARDIOVASCULAR RISK

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Background: Thyroid dysfunction is associated with increased cardiovascular risk which appears be dependent on lipid profile, insulin resistance, thyroid function and thyroid autoimmunity.

Aim: To evaluate the association between thyroid function, antithyroid antibody levels, insulin resistance, and lipid profile in patients with autoimmune thyroiditis.

Methods: In 253 subjects with autoimmune thyroiditis, we evaluated levels and variations from 2012 to 2015 of thyroid function, anti-Tg, anti-TPO, high sensitivity C-reactive protein (hs-CRP), insulin resistance markers comprising the HOMA, QUICKI, HISI, WBISI and IGI; folic acid and vitamin B12 levels. Two groups were defined: euthyroid group (n = 185, TSH 0.35–2.50 μUI/ml), and subclinical hypothyroid (SH) group (n = 66, TSH 2.50–10.00 μUI/ml with normal FT4 and FT3). Statistical analysis was performed with Spearman correlation coefficients, Wilcoxon test, and logistic regression.

Results: Patients in the SH group were younger than euthyroid (42.77 ± 17.10 vs 48.61 ± 15.94 years, p = 0.018). There were no significant differences in gender (92.9% vs 95.5% females, p = NS) and BMI (27.23 ± 5.12 vs 26.04 ± 5.29 Kg/m^2, p = NS) between euthyroid and SH groups. In the total group, T3 variations were negatively correlated with HOMA-IR (r = –0.222, p = 0.003), IGI (r = –0.184, p = 0.012) and positively correlated with QUICKI (r = 0.210, p = 0.004), HISI (r = 0.222, p = 0.003), and WBISI (r = 0.226, p = 0.002). Regarding the lipid profile, we found a positive correlation between variations of TSH and LDL (r = 0.189, p = 0.004), as well as between variation of T3 and HDL (r = 0.131, p = 0.042). In the euthyroid group, HDL levels presented a direct correlation with T3 (r = 0.165, p = 0.025). In the SH group, T4 levels were positively correlated with HOMA-β (r = 0.310, p = 0.043) and negatively with anti-TPO (r = –0.242, p = 0.05). In SH group, the variation of serum TSH variation levels were positively correlated with anti-Tg (r = 0.383, p = 0.003) as well as anti-TPO (r = 0.368, p = 0.003) variations. A negative

correlation between vitamin B12 and T3 variations was observed in SH group (r = –0.360, p = 0.023).

Conclusion: This study highlights the association between thyroid function, antithyroid antibodies levels, lipid profile, insulin resistance, and vitamin B12, which may underlie the increased cardiovascular risk in patients with autoimmune thyroiditis.

P3-04-09

GENETIC RISK FACTORS FOR THE THYROTOXIC ATRIAL FIBRILLATION AND ITS' OUTCOMES

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Objectives: The first aim was to estimate a impact of single nucleotide polymorphisms (SNPs) Gly389Arg and Ser49Gly in $ß_1$-adrenoreceptors gene and Ser38Gly in KCNE1 gene on cardiovascular complications development in thyrotoxic patients. Another intent was to investigate a course of thyrotoxic atrial fibrillation (AF) and its' outcomes after euthyroid state is attained.

Methods: 165 patients with Graves' disease and thyrotoxicosis (TT) were enrolled to evaluate the influence of enumerated SNPs on thyrotoxic AF. Genotyping was performed by real time polymerase chain reaction. We also have analyzed 58 cases of thyrotoxic AF and conducted survey to investigate patient reported outcomes of AF.

Results: We've found no relationship between the genotypes of studied SNPs and thyrotoxic AF. The study of the group with AF (n = 58) indicated that men have persistent AF more frequently than women: 85.8% vs 37.8%, p = 0.003. Severe heart failure was also more common in men: 79% vs 42.9%, p = 0.01. After euthyroid state was attained, 24.1% (n = 14) of AF reverted to sinus rhythm (SR) spontaneously or had no AF paroxysms during follow-up period (6–60 months) in case of paroxysmal AF. We didn't reveal statistically significant difference in spontaneous restoration to SR depending on sex or AF duration, but there was association with some echocardiographic parameters: left atrial diameter (LAD) (p = 0.22), volume index (LAVI), left ventricular end diastolic volume (LVED), LV mass index (LVMMI) and ejection fraction (LVEF).

Conclusion: Our study didn't prove a crucial role of investigated genetic polymorphisms in development thyrotoxic AF. Thyrotoxic AF outcomes evaluation revealed that risk of adverse outcome in men higher, because persistent AF and severe heart failure developed more often. The probability of spontaneous restoration to SR depends on some echocardiographic parameters: LAD, LAVI, LVED, LVMMI and LVEF.

P3-04-10

RISK FACTORS OF VENOUS THROMBOEMBOLISM IN PATIENTS TREATED FOR DIFFERENTIATED THYROID CARCINOMA

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Context: Although in general cancer is a strong risk factor for developing venous thromboembolism (VTE), in patients with differentiated thyroid carcinoma (DTC) the risk factors for venous thromboembolic events have never been assessed. This is remarkable, as several parts of the treatment comprise a hypercoagulable state and limited data suggest an increased risk for VTE in subgroups of DTC patients.

Objective: The aim of this study was to assess the risk factors for developing VTE in patients with DTC.

Patients and Methods: We performed a case-control study, in which cases were DTC patients treated from 1980 to 2014 with confirmed VTE after the diagnosis of DTC. Controls were defined as DTC patients without VTE. In all subjects, we collected information about thyroid cancer characteristics, treatment modalities, traditional risk factors for VTE, and additional clinical data, and performed univariate and multivariate regression analyses.

Results: We included 27 cases and 54 controls matched according to age and gender. In the univariate regression analysis, histology, recent surgery, and the presence of distant metastases were associated with VTE. Patients with follicular thyroid carcinoma or recent surgery had an 5.0 and 8.7-fold increased risk of developing VTE, in multivariate analysis, respectively. The presence of distant metastases was not independently associated with VTE.

Conclusion: Recent surgery and follicular thyroid carcinoma are independent risk factors for developing VTE. Therefore, patients with (a combination of) these risk factors should be monitored carefully for the development of VTE.

P3-05 Thyroid Cancer Diagnostic III

P3-05-01

COMPARISON OF ULTRASOUND-GUIDED FINE NEEDLE NON-ASPIRATION AND ASPIRATION TECHNIQUE IN EVALUATION OF PATIENTS WITH NECK LYMPH NODES IN TERMS OF CYTOLOGICAL DIAGNOSITICITY

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Objective: Recent studies concerning fine needle cytology of lymph node (FNCLN) have shown that non-aspiration (NAS) technique is superior to aspiration (AS) in terms of obtaining easily interpretable material without significant difference between two methods. We aimed to compare NAS and AS technique in evaluation of FNCLN in point of cytological diagnositicity.

Method: Of 134 patients, 123 LNs in 75 patients who underwent NAS- and AS-FNCLN in the same visit were evaluated in this retrospective study. Ultrasonographic and cytopathologic features of all LNs were noted. Cytopathologic results were categorized in 5 groups as insufficient, benign, atypia of undetermined significance (AUS), suspicious for malignancy, and malign. However, all of results except insufficient cytology were accepted as diagnostic, the insufficient results were categorized as non-diagnostic.

Results: The numbers of LNs located in Level (L) 1, L2, L3, L4, L5, L6, and L7 were 2, 28, 29, 26, 6, 30, and 2, respectively. Median LN volume was 0.41 (0.07–20.08) ml. Ultrasonographic features of LNs were heterogen echogenicity in 82.8%, solid texture in 82.9%, presence of micro/macrocalcification in 29.3%, spheric shape in 11.5%, coalescence feature in 6.5%, absence of hilum in 74.8%, and presence of irregular hilum in 5.7%. The rates of malignancy were 13.8% in AS vs 16.3% in NAS technique, whereas benign cytology was detected in 32.5% and 43.1%, respectively. The diagnositicity rates were 56.9% in AS and 74.8% in NAS technique (p < 0.001) (Table 1).

Conclusion: Diagnositicity rate in NAS-FNCLN was significantly higher than AS-FNCLN. Lesser degree of cellular trauma and degeneration, and better maintained architecture because of the lack of vacuum pressure may be the reasons of increase in the rate. To reduce non-diagnostic cytology results, we suggest NAS-FNCLN technique which is easier to perform and causes less worry in the patient.

P3-05-02

THE COMPARISON OF HYDRO-ALCOHOLIC EXTRACT HULL LESS SEED PUMPKIN AND PACLITAXEL ON TREATMENT OF HUMAN PAPILLARY THYROID CANCER CELLS

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Objectives: Cancer is the most common cause of death in the world. Thyroid cancer is the most common endocrine malignant tumor, with an increasing incidence. Papillary thyroid carcinoma (PTC) is the most communal form of thyroid malignancy. Paclitaxel is a well-known anticancer drug that is used for treatment of many kinds of cancers. Previous pharmacological tests have shown that hull less seed pumpkin involves antibacterial, antiviral, anti-inflammatory, anti-mutagenic and anti-cancer effects. The purpose of this study was assessment of cytotoxic effects of hydro-alcoholic extract hull less seed pumpkin on papillary thyroid cancer cells (PTC), in comparison with Paclitaxel.

Methods: Papillary thyroid cancer cells were treated by different concentrations of hydro-alcoholic extract hull less seed pumpkin and Paclitaxel for 24, 48, and 72 hrs. Cytotoxicity was examined through MTT and colonogenic assay. Ethidium bromide/acridine orange (EB/AO) staining and Tunel were used for apoptotic cell detection. The observations were tabulated and analyzed statistically.

Results: Results of this study showed that IC50 of hydro-alcoholic extract hull less seed pumpkin on PTCs were 1312, 1379 and 1782 µg/ml in 24, 48 and 72 hrs respectively. Also results showed that IC50 of Paclitaxel was 11.60, 6.831 and 0.670 µg/ml in 24, 48 and 72 hrs respectively. The EB/AO staining showed an increase in the apoptotic cell number with increasing of extract and Paclitaxel dose. The clonogenic assay showed a decrease in colonies with dose increasing. Comparing the groups treated by Paclitaxel or extract with the control group showed significant differences ($P < 0.05$).

Conclusion: Extract had cytotoxic effect on human papillary thyroid cancer cells. It can be considered as a beneficiall agent that may use for thyroid cancer treatment.

P3-05-03

LONG-TERM OUTCOME OF PERCUTANEOUS ETHANOL ABLATION OF SELECTED RECURRENT CERVICAL NODAL METASTASES IN THYROID CANCER

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Background: Surgery is recommended for recurrence in the central or lateral compartments after thyroidectomy. Repeated operations can cause severe complications and in old age patients with underlying medical disease surgery may not be able. Alternatively to surgery percutaneous ethanol injection can be used. This study is conducted to evaluate the long-term outcomes of percutaneous ethanol injection in patients with limited cervical nodal metastases from thyroid carcinoma.

Methods: During October 2002 and August 2009, 34 patients with 46 lesions of recurrent cervical nodal metastases of differentiated papillary thyroid cancer were enrolled. As primary surgery, all patient underwent total thyroidectomy and central compartment node dissection. Ethanol injection with 99.9% ethanol under ultrasonic guidance were performed. Minimum follow up period was 60 months.

Results: Increase in size was observed in 7 (17.1%), no change in size in 10 (24.4%) lesions. In 24 (58.5%) of the lesions, decrease in size was observed. Mean recurrent lesion size prior to the injection was 11.8 ± 5.9 mm, with 17 (41.5%) lesions measuring more than 10 mm. Mean lesions size after the last ethanol injection treatment was 8.9 6.5 mm. When patients with increased lymph nodes were compared to patients with no change or decrease in size, there were statistically significant difference in age (65.3 ± 14.4 vs 48.2 ± 16.3; $p = 0.02$) and mass size (9.3 1.0 vs 12.3 ± 6.4; $p = 0.012$). No significant difference was shown in gender, follow up months and injection site.

Conclusion: Local progression was detected after ablation in 7 lesions of 41 lesions. There are no significant differences in sex, injection site, follow up months. Nevertheless surgery is the best treatment for recurrence, in patients with old age and high risk for surgery, ethanol injection therapy may be an option.

P3-05-04

DISCORDANCE IN TUMOR DIAMETER DETERMINED BY PREOPERATIVE ULTRASONOGRAPHY AND POSTOPERATIVE HISTOPATHOLOGY IN DIFFERENTIATED THYROID CANCER

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Aim: Ultrasonographically determined nodule diameter plays an important role in the differential diagnosis of thyroid nodules and decision of the surgical approach. Whether this diameter represents postoperative tumor diameter is not clear. We aimed to compare ultrasonographical and histopathological diameters in differentiated thyroid cancer (DTC) and also tried to find out possible ultrasonography (US) features that can predict the discordance between two diameters.

Materials and Methods: Data of patients with histopathologically confirmed DTC between june 2007 and june 2014 were reviewed retrospectively. Nodules evaluated by preoperative US were matched with histopathologically examined nodules according to localization and size. Incidental tumors, medulalry and anaplastic thyroid cancer, and nodules that can not be matched by US and histopathology reports were excluded. Preoperative US and postoperative histopathological diameters were compared and difference between two diameters which was defined as (Δ) was determined for each lesion.

Results: There were 562 patients (110 male and 452 female) with a mean age of 48.0 ± 12.8. Among 607 tumor foci, 542 (89.3%) were papillary thyroid cancer, 42 (6.9%) were follicular thyroid cancer, 23 (3.8%) were thyroid tumor of unknown malignant potential. Overall, mean US diameter was significantly higher than histopathological diameter (21.0 ± 15.6 mm vs 17.3 ± 13.6, $p < 0.001$). US diameter was higher than tumor diameter in 444 (73.1%), equal in 15 (2.5%) and lower in 148 (24.4%) nodules. In nodules with US diameter>tumor diameter, higher nodule diameter (≥3 cm), regular margins, mixed texture, isoechoic appearence, presence of halo and microcalcification were related with higher (Δ) values. In nodules with US diameter<tumor diameter, there was not any US feature that can be predictive for increased (Δ) values.

Conclusion: Ultrasonographically determined diameter is higher than histopathologically determined size in a considerable ratio of DTCs. It might be helpful to consider this discordance while deciding extent of surgery in these patients.

P3-05-05

DIFFERENTIAL DIAGNOSIS OF THYROID NODULES USING STRAIN ULTRASOUND ELASTOGRAPHY

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Objectives: The aim of the study was to determine different types of thyroid nodules according to their elasticity and to evaluate the diagnostic accuracy of strain elastography in detection of thyroid cancer. 114 thyroid nodules in 84 patients were examined prospectively with B-mode US, color Doppler, strain elastography (SE) and fine needle aspiration biopsy

(FNAB). 72 nodules in 50 patients were submitted to surgery and histologically assessed. For final diagnosis we accepted histology in operated cases and cytology for the rest.

Results: After performing SE, the image was matched to a modified 5 scale scoring system, based on that of Ueno and Ito. 32.9% of benign and 0% of malignant nodules presented with highly elastic structure – score 1 ($p < 0.0001$). Elasticity in a large area of the nodule (score 2) was present in 34.2% of benign and 5.3% of malignant nodules ($p = 0.0005$). Indeterminate elasticity (score 3) had 26.3% of benign and 18.4% of malignant lesions ($p = 0.4839$). No elasticity (score 4) was determined in 6.6% of benign and in 55.3% of malignant nodules ($p < 0.0001$). Stiffness in nodule and surrounding tissue (score 5) was registered in 21.1% of malignant and none of benign lesions ($p < 0.0001$). Sensitivity, specificity, PPV, NPV and accuracy were 76.3%; 93.4%; 85.3%; 88.8%; 87.7% for SE; 89.5%; 86.2; 79.1%; 94.4%; 89% for combining B-mode and SE; and 92.1%; 93.4%, 87.5%; 95.9%; 93% for combining B-mode, SE and FNAB, respectively.

Conclusion: The high specificity and NPP of SE alone or as an adjunct to conventional US suggests that high elasticity is a promising criterion for excluding malignancy and that this non-invasive technique may limit the indications for FNAB. Combination of three methods (B-mode, SE and FNAB) has the highest diagnostic accuracy in differentiating malignant from benign nodules and permits the clinician exact selection of patients who would benefit from surgery.

P3-05-06

EFFECTS OF BODY MASS INDEX ON THYROID CANCER AGGRESSIVENESS AND RECURRENCE

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Backgroud: While the overall thyroid cancer incidence has increased rapidly, the relationship between obesity and thyroid cancer is uncertain. We aimed this study to investigate whether preoperative measured body size is more associated with more advanced stage of thyroid cancer and may predict increased risk of tumor recurrence.

Methods: A total of 970 patients with papillary thyroid cancer (PTC) over 20 year of age who underwent total or near-total thyroidectomy were included. Central lymph node dissection was routinely performed in 883 patients regardless of clinical suspicion of metastatic lymph node. The evaluated histopathologic parameters included primary tumor size, multifocality, extrathyrodial extension and lymph node metastasis. Patients received suppressive dose of L-T4 and were evaluated for cancer recurrence/persistence by physical examination, serum thyroglobulin, anti-thryoglobulin antibody levels every 3–6 months and neck ultrasonogrpahy, computed tomography or I^{131} whole body scan every year.

Results: When we analyzed the relationship between body weights and aggressive of thyroid cancer, there was no increased risk for larger tumor size, extrathyroidal extension or node involvement according to body weight group after adjustment for age and sex. Thereafter, we evaluated body weight affect tumor recurrence. In univariate model, the hazard ratio for recurrence was 1.07 (95% CI 0.59–1.93) in overweight group and 1.43 (0.84–2.41) in obese group. In multivariate model, initial age, lymph node involvements were significant predictor for recurrence but no significant association was observed among body weight groups.

Conclusion: Body size was not associated with aggressiveness and recurrence of thyroid cancer in Korean men and women.

P3-05-07

CAN NODULAR HYPERPLASIA OF THE THYROID GLAND BE DIFFERENTIATED FROM FOLLICULAR ADENOMA AND FOLLICULAR CARCINOMA BY ULTRASONOGRAPHY?

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Objectives: To evaluate the ultrasonographic features for differentiation of follicular thyroid lesions.

Methods: Ultrasonographic features of surgically confirmed 56 follicular adenoma (FA) and 22 follicular carcinoma (FC) and 100 nodular hyperplasia (NH) were evaluated using univariable and multivariable multinomial logistic regression analyses, receiver operating characteristics analyses and the areas under the curve (AUC).

Results: Tumor diameter, margin, echotexture, cystic changes, calcification, hypoechoic rim, and vascularity were significant on univariable analysis. On multivariable logistic regression analyses, tumor diameter (FA: $p = 0.002$, odds ratio (OR) = 1.75; FC: $p = 0.001$, OR = 2.02), absence of cystic changes (FA: $p = 0.127$, OR = 2.21; FC: $p \leq 0.001$, OR = 17.74), absence of spongiform appearance (FA: $p = 0.234$, OR = 0.31; FC: $p < 0.001$, OR = 1673.46), and peripheral vascularity (FA: $p = 0.004$, OR = 26.64; FC: $p < 0.001$, OR = 145060.38) differed significantly among the three follicular lesions, with NH as a reference. The AUCs for NH, FA, and FC were 0.844, 0.858, and 0.705 and diagnostic accuracy was 72.6%.

Conclusion: Tumor diameter, cystic changes, spongiform appearance, and peripheral vascularity differed significantly among follicular lesions. The diagnostic capability was moderate.

P3-05-08

MEN2A IN A PATIENT WHO IS IN THE THIRD GENERATION OF A FAMILY WITH FAMILIAL MEDULLARY THYROID CANCER

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Introduction: Approximately 25% medullary thyroid carcinoma (MTC) is familial. We present a family with medullary thyroid cancer, with a patient having MEN2A in third generation.

Case Report: A 78 year old woman (index case) was diagnosed with MTC 23 years ago. She was found to have RET C618S mutation. Her father also had thyroid carcinoma. The patient's brother has multinodular goitre with a 31x32 mm and is found to be heterozygous for RET C618S. The index patient has 3 sons and a daughter. The daughter had thyroidectomy for MTC and RET mutation was C618R. One of the sons had three foci of medullary thyroid cancer (left lobe 0.9 cm ve 0.5 cm) and (right lobe 0.8 cm). The other son had MTC, with RET C618R mutation. This son had 3 sons. The first son had foci of C cell hyperplasia (right lobe) and 0.7 cm MTC (left lobe). Another son had multinodular goitre, with RET C618R ve G619S mutations, heterozygous L769L ve heterozygous S904S polymorphisms.

The patient's daughter's son had 12 mm nodule in right lobe with elevated calcitonin (353.8 pg/ml). His cathecholamine metabolites were elevated and there was 30x26x30 mm mass in the left adrenal gland. He also had hyperparathyroidism. Parathyroid scintigraphy revealed a lesion on the left upper adrenal. The patient first had left adrenalectomy and the pathology was consistent with pheochromocytoma. Then he had total thyroidectomy and central lymph node dissection and left upper and lower parathyroidectomies. He is followed up subsequently with calcium and calcitriol replacement.

Conclusion: The last case, being in the third generation within the family, has components of MEN2A with medullary thyroid carcinoma, pheochromocytoma and hyperparathyroidism. It is evident that familial medullary thyroid carcinoma is a variant of MEN2A. Thus all the members of such families should be screened for other components of MEN2A.

P3-05-09

HEMI-THYROIDECTOMY FOR FOLLICULAR THYROID CARCINOMA – 'HEMI-THYROID' AS AN OBSTACLE FOR FURTHER MANAGEMENT AFTER 8 YEARS FOLLOWING SURGERY

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Introduction: Follicular thyroid carcinoma (FTC) is a well-differentiated tumor and is the second most common cancer of the thyroid, after papillary carcinoma. Despite its well-differentiated characteristics, follicular carcinoma may be overtly or minimally invasive. Patients with FTC are more likely to develop lung or bone metastases than patients with papillary thyroid cancer.

Herein, we present a case of a young female patient, who underwent a hemi-thyroidectomy 8 years ago. Final histologic assessment revealed follicular thyroid carcinoma. No repeatedly total thyroidectomy was performed. Despite lack of information about tumor aggressiveness patient was managed without considering her cancer issues.

Case Report: A 30-year-old female attended our clinic (17.07.14) with complaints on yellowness of nails, slightly expressed tiredness and tachycardia, with past medical history of hemi-thyroidectomy 8 years ago (2006). Postoperative morphology showed well-differentiated follicular carcinoma; with no information about tumor size or capsular invasion. As patient noted after operation she was under surveillance of endocrinologist, was on levothyroxine therapy with no TSH suppression. Two years later (2008) levothyroxine was stopped. On consultation in 2014, thyroid function tests showed primary hypothyroidism with TSH of 4.78 μIU/ml (normal range – 0.4–4.0) and FT4 of 0.86 ng/dl (normal range – 0.89–1.76). Thyroid ultrasound showed hypoechogenic solid nodule with size 5×5×5 mm, total volume was 8.16 sm3.

For further management of such patient it was important to take in consideration that there was insufficient information about cancer size or its aggressiveness. The whole body scan for detection of metastatic lesion was also unavailable. In our minds, the clearest and safest solution would be a total thyroidectomy, than a whole body scan to ensure about the absence of metastatic lesion. On the other hand, 8 years after hemi-thyroidectomy how probable would it be to have metastasis in bones or lungs without any specific complaints.

Eventually, an ultrasound guided FNA biopsy of thyroid nodule was performed; pathology revealed colloid nodule. Levothyroxine therapy was initiated.

Conclusion: Despite hard work on thyroid nodule guidelines still there are unanswered questions, Clinical cases where all responsibility should be assumed by physician. Sometimes it is quite challenging to find an ideal gap between over and under-diagnosis or management.

P3-05-10

HYALINIZING TRABECULAR TUMOR – CASE REPORT

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Hyalinizing trabecular tumor (HTT) of the thyroid gland is a rare neoplasm first described by Carney et al in 1987 as hyalinizing trabecular adenoma, also known as paraganglioma-like adenoma. HTT usually occurs in middle-aged patients, mostly in females. Grossly, HTTs are adenomas. They are usually well-circumscribed, yellow tan, solid, and encapsulated with a thin fibrous capsule. This tumor has follicular derivation with peculiar nuclear, architectural, histochemical, and immunohistochemical features. We report a case of HTT in a 75-year-old woman with a multinodular goiter. Patient suffered from breathlessness, heartbeat acceleration during rest, anxiety. She has T2DM with multiple complications, Myocardial Infarction, Heart Failure, Dyslipidemia.

Ultrasound revealed multinodular goitre with calcified nodules. Hormonal status and antibodies' level were normal. Fine needle aspiration biopsy (FNAB) of the right lobe-dominant node was performed with cytologic diagnosis: category THY-3, Follicular Neoplasm, hypothetically Hyalinizing Trabecular Tumor. Patient underwent total thyroidectomy, with a histologic diagnosis of HTT. We discuss pathologic features of HTT with special reference to the possible differential diagnosis. Adequate treatment of HTT Total – or hemithyroidectomy is enough in most cases. However, very rare cases of malignancy of HTT are documented. Radioiodine ablation is not necessary mostly. HTT should be considered as non-malignant benign neoplasm or a neoplasm of extremely low malignant potential. When diagnosis of HTT is established, clinical management should be conservative, which include follow-ups in order to exclude the very rare possibility of recurrence. As a result patient is now on stable dose of Levotiroxin and has no complaints after surgery.

HTT is a puzzling entity due to uncertainty of its nature, the diagnostic challenges, and the mimicry of other types of thyroid tumors. In order to avoid overtreatment, endocrinologists and thyroid surgeons should know originality of HTT, and suspicious cases should be assessed by experienced cytopathologists.

P3-06 Thyroid Cancer – Clinical II

P3-06-01

TWO YEAR PROSPECTIVE MOLECULAR TESTING OF ROUTINE AIR-DRIED FINE NEEDLE ASPIRATION (FNA) SMEARS USING A 7-GENE-PANEL IN A ROUTINE DIAGNOSTIC SETTING IN GERMANY

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Recently we described the feasibility of molecular testing using routine air-dried FNA smears. Subsequent retrospective studies showed variable impact of molecular testing especially with regard to the mutation rates in follicular carcinoma and the risk of malignancy (ROM) for *RAS* positive samples. Now we prospectively analyzed the impact of molecular testing in a routine diagnostic setting in Germany over a period of two years.

Molecular testing was done for all atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) and follicular neoplasms/suspicious for a follicular neoplasm (FN/SFN) samples. RNA and DNA was extracted from 564 FNAs. For 322 of these histology and for further 74 follow-up of up to one year was available. *PAX8/PP*ARG and *RET/PTC* rearrangements were detected by qPCR, while *BRAF* and *RAS* mutations were detected by pyrosequencing.

0.4% and 10.1% of samples were non-satisfactory for the DNA and RNA based analysis, respectively. The presence of a *BRAF* and *RET/PTC* mutation was associated with cancer in 98% and 100% of samples respectively, whereas the presence of a *RAS* mutation was associated with cancer in 35% of samples. 58% of cancers were identified by molecular testing in the AUS/FLUS group, 27% of cancers were identified in the FN/SFN group. While FNAs with an AUS/FLUS diagnosis alone had a 21% ROM, it increased to 44% for mutation-positive test outcomes and decreased to 13% for mutation-negative test outcomes. In the FN/SFN group, with an 18% ROM, the detection of a mutation resulted in a 40% ROM, mutation-negative test outcomes had a 15% ROM.

Our data show that *BRAF* and *RET/PTC* mutations are highly specific for cancer. In contrast, the impact of *RAS* mutation detection is limited. In summary, the current mutation panel strongly needs an improvement by the addition of further cancer specific mutations and further markers for *RAS* positive cases.

P3-06-02

CERVICAL LYMPH NODE METASTASES AFTER THYROIDECTOMY FOR PAPILLARY THYROID CARCINOMA USUALLY REMAIN STABLE OVER YEARS

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Objectives: Lymph node (LN) recurrence detected by ultrasound (US) is a very common problem after initial treatment for papillary thyroid carcinoma (PTC). Most patients with PTC have an excellent disease-specific survival even with LN recurrence. Recently, watchful waiting would be considered a reasonable approach to management of LN recurrence in selected patients. On the other hand, some patients with LN recurrence have demonstrated clinically significant disease progression during follow-up. The objective was to document the changes of cervical LN metastases after initial treatment and identify useful information for making decision how best to manage individual patients with LN recurrence.

Methods: This retrospective review identified 83 PTC patients with at least one LN on the postoperative US diagnosed with fine needle aspiration biopsy or the thyroglobulin titer in the wash-out of the needle.

Results: The subjects were 15 men and 68 women, with a median age at initial surgery of 50.6 years (range, 18–80 years). The median LN size at the start of the observation period was 1.3 cm (range, 0.5–2.4 cm) in largest diameter. After a median follow-up of 7.2 years, the median growth rate of the nodes showing structural progression was 1.4 mm per year (range, 0–12.0 mm/year). Seventeen of 83 patients (20.5%) demonstrated an increase in LN size of at least 3 mm, only 8.4% (7 of 83) had an increase of at least 5 mm. 10-year and 15-year disease-specific survival rate after diagnosis of LN recurrence were 84.7% and 72.6%, respectively. Older age and recurrent LN growth of more than 3 mm/year were recognized as independent predictors for short survival on both univariate and multivariate analyses ($p < 0.05$).

Conclusion: Most lymph node recurrences may remain stable for a long time. However, recurrence LN growth of more than 3 mm per year could be related to mortality.

P3-06-03

DISEASE STATUS AT PRESENTATION AND DISEASE RELATED MORTALITY FROM DIFFERENTIATED THYROID CANCER

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Background: The current trend is non-aggressive treatment in low risk thyroid cancer patients. This approach is partially based on the fact that disease related mortality (DRM) from differentiated thyroid cancer is rare, affecting 1–2% of patients. However, this permissive approach is questioned due to studies reporting up to 11.6% DRM in low risk patients with long term follow-up (Verburg 2014).

Goal: To characterize the initial presentation of patients who will eventually die from disease.

Methods: Patients with documented DRM were included. The Rabin thyroid cancer registry and the Davidoff Head & Neck cancer clinic databases were reviewed for eligible patients.

Results: Fifty three patients with DRM were included, representing database of over 2,000 DTC patients. The median age at diagnosis was 62 years (range 22–83, 83% older than 45), with median survival of 9 years (range 1–36). Histology was PTC in 66%, poorly differentiated in 21%, follicular carcinoma in 11%, and follicular adenoma in 2%. Patients were initially categorized as high risk for recurrence in 92% of cases (in 5 cases due to high Tg levels), intermediate risk in 6% (three older patients with N1b disease), benign in one case (2%), and none was low risk. Most patients had upfront advanced disease stage (stage IV-88%, III-2%, II-2%, I-8%). All patients with stage I disease were <45 years, with aggressive features (1 poorly differentiated, 3 gross extra-thyroidal extension). One patient with stage II disease was <45 year with distant metastases. Detection of distant metastases was within the first year in 25 patients, and during follow-up in 25 patients. Overall, apart from one patient who was misdiagnosed as benign follicular adenoma at presentation, all patients had aggressive disease features at presentation.

Conclusion: None of the patients with DRM had low risk features at presentation, supporting the current paradigm of less aggressive approach in this group.

P3-06-04

IMPACT OF PREOPERATIVE DETECTION OF SODIUM-IODIDE SYMPORTER EXPRESSION LEVEL ON DIFFERENTIATED THYROID CANCER (DTC) PROGNOSIS

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Nowadays it is of utmost importance to forecast a cancer progression, in particular, thyroid cancer in order to make a decision about the optimal treatment tactics.

Aim: To evaluate the possibility of preoperative detection of membrane located NIS expression level in fine needle aspiration biopsy (FNAB) material as a markers of unfavorable prognosis of DTC.

Materials and Methods: The research was of prospective character. 91 patients with DTC who underwent medical treatment in general surgery department of St. Petersburg Pavlov State Medical University in the period 2009–2012 were enrolled in the study. Level of NIS expression in FNAB material analyzed preoperatively. Expression was accessed quantitavely by FC method.

Results: According to the results of routine histology examination: 58 patients needed radioiodine ablation (RIA). During 48 months of observation recurrences were detected in 24 cases. All recurrences were of local character. Not a single patient from the group without RIA had recurrence. When studying the level of membrane located NIS expression in DTC it was found that the mean level in the group without RIA and disease recurrence is 6.5% with maximum up to 11.6%. The lowest mean level of NIS expression was in patients group with recurrence of DTC after RIA ($p = 0.00083$). We proved that crucial for recurrence of DTC after RIA were decreased level of membrane located NIS expression less than 1%. That means that when NIS level is less than 1% a patient should considered to a high-risk group and more aggressive surgical tactics must be used to decrease the risk of recurrence.

Conclusion: If it is detected NIS level is lower than 1%, these patients belong to high-risk group and for this group thyroidectomy and central compartment lymph node dissection are recommended.

P3-06-05

NATURAL HISTORY OF CONTRALATERAL NODULES AFTER LOBECTOMY IN PATIENTS WITH PAPILLARY THYROID CARCINOMA

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Background: Bilateral thyroid nodularity in papillary thyroid carcinoma (PTC) patients is considered to be an indication for total thyroidectomy. However, there are no data on the natural history of small benign appearing nodules in the contralateral lobe.

Objective: To investigate the natural history of contralateral nodules after lobectomy for patients with PTC.

Methods: Patients after lobectomy for PTC, with one or more nodules (size ≥3 mm) in the contralateral lobe prior to surgery were included. Growth was defined as change of ≥3 mm.

Results: Ninety-four patients were operated between January 2002 and December 2013. The median age was 57 years (range 25–84). The median size of the primary tumor in the lobectomy specimen was 8 mm (range 0.5–20 mm). The median size of contralateral remaining nodules prior to surgery was 7.5 mm. Twenty-eight nodules (30%) were assessed by FNA prior to surgery, none of which was suspicious for malignancy. Over a median follow-up of 6.5 years, 24 nodules (26%) increased in size, with a median growth of 6 mm (range 4–19 mm). Twenty patients (21%) developed new nodules in the remaining lobe. Twelve patients (13%) underwent completion thyroidectomy due to significant growth of contralateral nodules (3 patients), suspected malignancy on FNA (7 patients with Bethesda groups III-V), or malignancy (1 patient with group VI). Overall, 6 patients (6%) were diagnosed with contralateral PTC (5 microPTC, one 20 mm). There were no surgical difficulties or local complications (nerve palsy or local invasion) related to completion surgery.

Conclusion: Lobectomy in patients with bilateral small nodularity is safe, but requires regular ultrasound follow-up as growth is seen in 26% of patients. Our results provide data to guide therapy in patients with low risk PTC and bilateral nodularity.

P3-06-06

CLINICAL CHARACTERISTICS AND LONG TERM OUTCOME OF PATIENTS WITH DIFFERENTIATED CARCINOMA THYROID WITH BONE METASTASES – A RETROSPECTIVE STUDY

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Background: Bone is the second most frequent target of distant metastases in patients with differentiated thyroid cancer. Long term outcome of these patients is controversial.

Objective: To define the clinical characteristics and assess the long term outcome and evaluate the prognosis of patients with bone metastases.

Materials and Methods: We reviewed the medical records of 360 patients of Differentiated Thyroid Cancer followed at our institute from 2000 to 2005. 57 patients were found having bone metastases. We analyzed those patients with regard to basic demographic data, clinical characteristics, treatment and clinical outcomes.

Results: The incidence of bone metastases from thyroid carcinoma was 15.8%. The mean age at the diagnosis of bone metastases was 47 ± 18 years (range 16 to 80 years); 46% patients were below 40 yrs of age and 53.8% patients were above 40 yrs. 15.3% were males and 84.6% were females. Histopathologic subtypes included papillary (38%), and follicular (45.6%). Multiple sites of bones were involved in 50% patient. 29% of the patients had single bone site involved and 20.8% of the patients had metastasis to other organs in addition to bone.

All patients underwent near total thyroidectomy followed by aggressive radioiodine therapy. Number of ^{131}I doses received ranged from 3 to 12 with a mean of 6.6. Mean dose of I131 per patient was 48914 MBq ± 20424 (Range: 18130–76960). Base line Thyroglobulin (TG) level ranged from 380 ng/ml to 17300 ng/ml with a mean value of 2250 ng/ml ± 5644. 60% of patients showed declining trend in TG over time, while 23% of total patients showed rising trend, 6.2% of the patients had normal TG/ATG (antithyroglobulin) values throughout the course of disease. 10.4% patient had static TG levels. 64% of the patients with bone metastases showed 5 yr survival.

Conclusion: Multiple bone metastases represent a frequent complication of DTC especially of follicular thyroid cancer. In our population it is more common in females and in patients above 40 years of age. Overall survival rate is very good in the patients with bone metastasis if they are managed aggressively with total thyroidectomy and repeated radioactive iodine.

P3-06-07

BASELINE PATIENT CHARACTERISTICS FROM RIFTOS: A GLOBAL NONINTERVENTIONAL STUDY EVALUATING THE USE OF MULTIKINASE INHIBITORS FOR TREATMENT OF ASYMPTOMATIC DIFFERENTIATED THYROID CANCER REFRACTORY TO RADIOACTIVE IODINE (RIFTOS MKI)

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Objectives: The primary objective of this study is to compare time to symptomatic progression between pts who were initiated with MKIs at study entry and those who were not. Here we report the patient characteristics and prior treatment for the first 100 patients.

Methods: RIFTOS MKI is an international, non-interventional study of asymptomatic, MKI-naive pts with documented RAI-refractory and progressive DTC. Pts may receive any therapy including sorafenib or other MKI. Seven hundred pts are planned to be enrolled from >20 countries. Final analysis will be conducted once the last enrolled pt has been followed for 24 months.

Results: Out the 100 first pts, 26, 44 and 30 are from US, Japan and rest of the world respectively; 57% are female and the median age is 70 years old. More than 90% are ECOG PS 0 or 1. The most frequent histology was papillary (76%). Time from initial diagnosis of DTC to study entry was 8.5 years. RAI refractoriness was mainly due to lack of RAI uptake (69%). Most patients had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment and median cumulative dose of RAI were lower in Japanese pts (1.11 Gbq for both) compared to other regions (see table). The time from RAI refractoriness to initial visit was also shorter (1.3 mo).

Conclusion: There are regional differences in baseline patient characteristics and treatment history from RIFTOS. The study is ongoing and will further gather information on the real-life practice across several countries.

Table 1. (for abstract P3-06-07)

	USA (n = 26)	Japan (n = 44)	ROW* (n = 30)	Total (n = 100)
Median cumulative dose of RAI, Gbq (mCi)	12.63 (341.35)	1.11 (29.73)	15.71 (424.59)	7.40 (200)
Average dose of RAI, Gbq (mCi)	5.83 (157.57)	1.11 (29.73)	5.43 (146.76)	3.80 (102.70)
Median time from RAI-refractory classification to initial visit (mo)	23.60	1.30	11.15	8.40

P3-06-08

OUTCOME OF THYROID CARCINOMA ASSOCIATED TO CLINICALLY MANIFEST AUTOIMMUNE THYROID DISEASE

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Objective: To estimate the clinical, histopathological and prognostic characteristics of the thyroid carcinoma associated to clinically manifest autoimmune thyroid disease.

Methods: A retrospective study was designed, including 328 patients with thyroid cancer, divided in four groups: 1) Grave's Disease (n = 32), 2) Hashimoto's Thyroiditis (n = 34), 3) Euthyroid patients with thyroid lymphocytic infiltration (EP+LI) (n = 99) and 4) Euthyroid patients with no lymphocytic infiltration (EP-LI) (n = 163). To compare the groups, Kruskal-Wallis and Chi-square tests were adopted. To identify the risk factors associated to free disease time, COX regression was applied.

Results: A smaller tumoral size was found in Grave's Disease and Hashimoto's Thyroiditis groups ($p < 0.0001$). EP-LI had enhanced tumoral aggressiveness, presented as a larger number of cervical metastasis ($p = 0.0127$), neck dissections ($p < 0.0001$) and detectable thyroglobulin levels during follow up ($p = 0.0156$). The Euthyroid patients (with or without lymphocytic infiltration) showed more vascular invasion ($p = 0.0485$). The risk factors associated to longer free disease time were vascular invasion absent (HR 1.622 [95% CI 1.145–2.299]), no-IV TNM stage (HR 2.664 [95% CI 1.513–4.690]) and extrathyroidal extension absent (HR 1.800 [95% CI 1.239–2.614]). In multivariate analysis, both Grave's Disease and Hashimoto's Thyroiditis groups revealed as protective factor when compared to EP-LI (respectively, HR 1.642 [95% CI 1.009–2.672] and HR 2.260 [95% CI 1.412–3.618]). EP+LI presented as protective factor, however, it had no statistical significance.

Conclusion: The clinically manifest autoimmune thyroid disease appears to be related to decrease tumoral aggressiveness. Besides that, the lower risk of tumoral aggressiveness was present when associated to clinically manifest autoimmune disease, intermediate in the presence of isolated lymphocytic thyroiditis without thyroid dysfunction, and major risk in absence of lymphocytic thyroiditis.

P3-06-09

ANALYSIS OF FACTORS PREDICTING BILATERAL LATERAL NECK METASTASES IN PATIENTS WITH UNILATERAL PAPILLARY THYROID CARCINOMA

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Background: Papillary thyroid carcinoma (PTC) frequently involves lymph nodes in the lateral compartment, but PTC located in one lobe rarely metastasizes to bilateral lateral nodes. This study was designed to evaluate the clinicopathological features of patients with PTC limited to one lobe but with bilateral lateral neck metastasis (LNM).

Materials and Methods: Between January 2009 and December 2013, 698 patients with unilateral PTC with LNM were analyzed. Of these patients, 651 had unilateral LNM (ULNM) and 47 had bilateral LNM (BLNM). The clinicopathological characteristics of the two groups were analyzed.

Results: There were no significant between group differences in age, extrathyroidal extension, multifocality in one lobe, thyroiditis, or psammomatous calcification. Male sex (51.1% vs. 29.8%; $p = 0.002$), central compartment metastasis (91.5% vs. 78.6%, $p = 0.035$), aggressive subtype of PTC (23.4% vs. 8.8%, $p = 0.001$), and Delphian node metastasis (36.2% vs. 18.1% vs. 36.2%, $p = 0.002$) were significantly more frequent, and mean primary tumor size (1.79 ± 1.12 cm vs. 1.34 ± 0.83 cm, $p = 0.010$) significantly larger in the BLNM than in the ULNM group.

Conclusion: Although few patients with PTC located in one lobe have BLNM, the contralateral lateral compartment should be carefully evaluated for BLNM in males and in patients with a primary tumor size >2 cm, aggressive subtype of PTC, central node metastasis, and Delphian node metastasis.

P3-06-10

THE LOW IODINE DIET: TIME FOR IMPROVEMENT

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Introduction: Patients with differentiated thyroid cancer (DTC) are instructed to follow a low iodine diet (LID) before radioactive iodine therapy (RAIT). There is no consensus on the definition of adequate preparation, an urinary iodine excretion (UIE) <100 µg/l, is commonly used.

To improve compliance, guidance seems important, but the optimal way, has not been studied. We studied whether structured individualized dietary counselling should be standard care for DTC patients who have to follow an LID.

Methods: In this single-centre prospective, non-randomized study, individualized counselling was offered to patients, who prepared for RAIT after thyroid hormone withdrawal. Patients in the counselling group were compared with patients, who received standard written instructions (control group). UIE was measured, on day 7 of the LID, in 24 hour urine collection. Primary endpoint was the success rate defined as an UIE <100 µg/l, the secondary was more strict; a success rate defined as an UIE <50 ugr/L.

Results: 27 patients were included; 12 counselling group (41.7% male, age 53 (±15) years) and 15 control group (46.7% male, age 49 (±18) years). Sixteen patients followed the LID for the first time, 7 in the counselling and 9 in the control group.

The success rate (UIE <100 µg/l) was 100% in the counselling and 93.3% in the control group ($P = 1.00$). An UIE of <50 µg/l, was reached in 8/12 patients (66.7%) in the counselling and 13/15 patients (86.7%) in the control group ($P = 0.36$).

89% of patients in the counselling group rated the individualized counselling with a 7 or higher (scale of 1 to 10) and 77.8% told they received new information.

Conclusion: Individualized counselling did not improve the success rate, but in our opinion should be offered to DTC patients. An universal definition of appropriate preparation should be defined.

P3-07 Thyroid Cancer – Clinical III

P3-07-01

OPTIMAL CUTOFF VALUE OF AGE PREDICTING CANCER SPECIFIC SURVIVAL FOR PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

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Background: Age greater than 45 years old has been included as a staging variable in differentiated thyroid cancer (DTC) in the American Joint Cancer Committee/Union for International Cancer Control (AJCC/UICC) staging sys-

tem. Recently, there is mounting evidence that age cutoff of 45 years leads to overstaging. This study aimed at evaluating optimal cutoff value of age to predict cancer specific survival (CSS) for patients with DTC.

Methods: We enrolled 3,152 DTC patients and evaluated CSS according to cutoff values of age between 45 and 65 years using Kaplan-Meier method. The proportion of variation in survival time explained (PVE) in Cox-proportional hazard model was calculated to compare the relative validation of each groups.

Results: Using age 45 years as a cutoff, 10-year CSS rates of stage I–IV were 98.8%, 98.8%, 95.1%, and 78.6%, respectively (PVE = 4.14%). When we applied age cutoff as 55 years, 10-year CSS rates of stage I–IV were 98.5%, 95.4%, 91.8%, and 67.5%, respectively (PVE = 5.35%). Using age 65 years as a cutoff, 10-year CSS rates of stage I–IV were 97.9%, 82.1%, 78.7%, and 50.9%, respectively (PVE = 4.50%). The 12%, 22%, 30%, and 36% of patients were down-staged when we increased the cutoff value by 5 year between 50 and 65 years, compared with the AJCC/UICC staging system using 45 years as the cutoff. The optimal age cutoff point for predicting survival was 56 years by ROC curve analysis (AUC = 0.783, $p < 0.001$).

Conclusion: The cutoff age of 55 years seems to be more appropriate than 45 years for AJCC/UICC staging system to achieve better survival predictability and to avoid over-staging for patients with DTC.

P3-07-02

LIMITS OF FROZEN SECTION IN INDETERMINATE THYROID NODULES: A RETROSPECTIVE ANALYSIS OF 75 HISTOLOGICALLY PROVEN THYROID NODULES

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Objectives: To determine the usefulness of intra operative frozen section (FS) in indeterminate thyroid nodules according to the Bethesda classification and its influence on surgical decision at a single tertiary referral center.

Methods: Retrospective analysis of 224 indeterminate thyroid nodules. 75 patients underwent surgery with intra operative FS (9 atypia of undetermined significance/follicular lesion of indetermined significance (AUS/FLUS) – 31 follicular neoplasm/suspicious for follicular neoplasm (FN/SFN) – 35 suspicious for malignancy (SM)).

Results: In the AUS/FLUS category, FS were conclusive in 5 of 9 cases (56%), inconclusive in 4 of 9 cases (44%), all nodules were benign. No change in surgical procedure was performed. In the FN/SFN category, FS were conclusive in 6 of 31 cases (19%), and inconclusive in 25 of 31 (81%). FS changed the initial surgical procedure in 3 cases (total thyroidectomy associated with lymph node dissection (LND) instead of loboisthmectomy or thyroidectomy alone). One patient with inconclusive FS result underwent reoperation to complete total thyroidectomy with LND. In the SM category, the rate of conclusive and inconclusive FS results were 29% (10 of 35 cases) and 71% (25 of 35 cases) respectively. Surgical decision changed in 18 cases, included 9 of them guided by the FS results (lateral LND instead of central LND only). Of the 29 thyroid carcinomas, 11 had lymph node metastasis.

Conclusion: All indeterminate categories combined, FS was inconclusive in 53 of 75 nodules (71% – IC 95% = 0.59–0.79) and changed the surgical procedure in only 12 of 75 cases (16%), of which 9 were in the SM category of Bethesda (leading to a lateral LND). It seems that FS is useful only in the SM category of Bethesda. The cost-effectivness and time spent for FS is discussed.

P3-07-03

US ELASTOGRAPHY USING CAROTID ARTERY PULSATION: EFFICACY AND REPRODUCIBILITY ANALYSIS IN DIFFERENTIAL DIAGNOSIS OF THYROID NODULES

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Objective: To prospectively evaluate the diagnostic performance of ultrasound elastography (USE) using carotid arterial pulsation in the differential diagnosis of thyroid nodules, and to determine interobserver agreement and intraobserver reproducibility of USE.

Methods: This study was approved by the ethics committee of the institution, and all patients provided written informed consent. US examination and USE using carotid artery pulsation were performed in 151 patients with 176 nodules in a prospective design. The US features and elasticity contrast index (ECI) were assessed by observer 1 and the ECI was reassessed by observer 2. ROC curve analysis was performed to evaluate the diagnostic performance of ECI. Pearson correlation coefficient was used to evaluate the interobserver and intraobserver agreement in the measured ECI values.

Results: Among a total of 176 nodules, 96 nodules were malignant and 80 nodules were benign. The mean ECI was significantly higher in malignant nodules (3.01 ± 1.51) than in benign nodules (1.84 ± 1.03) ($p < 0.001$). Sensitivity, specificity, positive predictive value, and negative predictive value for predicting malignancy were 95.6%, 63.8%, 68.5%, and 60.7%, respectively, with ECI cut-of value of 2.14. The Az value for the ECI was 0.745 (95 CI: 0.673–0.816). Pearson correlation coefficients between two observers were 0.94 ($p < 0.001$), and Pearson correlation coefficients for intraobserver agreement were 0.97 ($p < 0.001$) and 0.99 ($p < 0.001$) for observer 1 and 2, respectively. Significant interobserver and intraobserver agreement was found in thyroid USE.

Conclusion: Excellent interobserver and intraobserver agreement exists in USE using carotid artery pulsation. USE using carotid artery pulsation may be helpful in differential diagnosis of thyroid nodules with reproducible results.

P3-07-04

A MULTICENTER, PROSPECTIVE VALIDATION STUDY FOR THE KOREAN THYROID IMAGING REPORTING AND DATA SYSTEM IN PATIENTS WITH THYROID NODULES (K-TIRADS)

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Objective: We sought to validate a new risk stratification system for thyroid nodules, the Korean Thyroid Imaging Reporting and Data System (K-TIRADS), using a prospective design.

Methods: From June 2013 to May 2015, in total, consecutive 902 thyroid nodules were enrolled from four institutions. We analyzed the type and predictive value of ultrasonography (US) predictors according to the combination of the solidity and echogenicity of nodules, calculated the malignant risk and diagnostic performance for each category of K-TIRADS, and compared the efficacy of fine-needle aspiration (FNA) with a three-tier risk categorization system published in 2011.

Results: The malignant risk of thyroid nodules was significantly higher in solid hypoechoic nodules than partially cystic or isohyperechoic nodules (each $p < 0.001$). The presence of any suspicious US features had a significantly higher malignancy risk (73.4%) in solid hypoechoic nodules than in partially cystic or isohyperechoic nodules (4.3–38.5%; $p < 0.001$). The calculated malignancy risk in K-TIRADS categories 5, 4, 3, and 2 nodules were 73.4%, 19.0%, 3.5%, and 0.0%, respectively, and the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for malignancy were 95.5%, 58.6%, 44.5%, 96.9%, and 69.5%, respectively, in K TIRADS categories 4 and 5. The efficacy of FNA for detecting malignancy based on K TIRADS was significantly increased, from 18.6% (101/544) to 22.5% (101/449), compared with the three-tier risk categorization system ($p < 0.001$).

Conclusion: The proposed new risk stratification system based on solidity and echogenicity was useful with respect to risk stratification of thyroid nodules and the decision for FNA. The malignancy risk of K-TIRADS was reproducible in this prospective multicenter study.

P3-07-05

MALIGNANT THYROID NODULE IN CHRONIC LYMPHOCYTIC THYROIDITIS: THE VALUE OF CORE-NEEDLE BIOPSY

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Objective: The detection and diagnosis of thyroid cancer can be more difficult in patients with chronic lymphocytic thyroiditis (CLT). The aim of this study is to compare the diagnostic accuracy of fine-needle aspiration biopsy (FNAB) and core-needle biopsy (CNB) for malignant thyroid nodule in CLT patients.

Methods: Institutional review board approved and waived informed consent for this retrospective study. From January 2010 to April 2014, 1815 CLT patients (183 men, 1632 women; mean age, 53.6 years; age range, 11–87 years) who underwent ultrasound-guided FNAB (FNAB group, 993 nodules in 970 patients; 90 men, 880 women; mean age, 55.5 years; age range, 18–87 years) or CNB (CNB group, 912 nodules in 845 patients; 93 men, 752 women; mean age, 52.1 years; age range, 11–86 years) for thyroid nodule were included. Final diagnosis with surgical resection was obtained for 353 nodules.

Chi-square test was used to compare the inconclusive results from both groups. Diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value for the diagnosis of thyroid cancer were calculated on the basis of binomial probabilities.

Results: In FNAB group, the nondiagnostic specimens were obtained in 160 (16.1%) nodules, and 146 (14.7%) nodules were categorized to atypia/follicular atypia of unknown significance (AUS/FLUS). In CNB group, 6 (0.6%) cases were nondiagnostic specimens and 27 (2.9%) nodules were AUS/FLUS. The rate of inconclusive results (nondiagnostic or AUS/FLUS) were significantly lower in CNB group (FNAB group, n = 306 (30.8%); CNB group, n = 33 (3.6%); $p < 0.001$).

With correlation to final surgical pathology, the sensitivity and negative predictive value (NPV) of cytologic results by FNAB were lower than histologic results by CNB (FNAB sensitivity 49.5%, NPV 18.9% vs. CNB sensitivity 83.5%, NPV 63.6%).

Conclusion: Inconclusive pathologic results were significantly lower with use of CNB. CNB showed better diagnostic accuracy for thyroid cancer in patients with CLT.

P3-07-06

LYMPH NODE METASTASES IN PAPILLARY THYROID CANCER: CLINICAL RELEVANCE AND PROGNOSTIC ROLE

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Context: Papillary thyroid carcinoma (PTC), the most common thyroid cancer histotype, has a good prognosis even when spread to the neck lymph nodes. Therefore, the prophylactic [central compartment] lymph node dissection is controversial.

Objective: To evaluate the clinical relevance and the prognostic role of lymph node metastases at diagnosis.

Setting: Referral Thyroid Clinic at an academic hospital.

Design and Patients: We retrospectively reviewed a consecutive series of 1,653 patients undergone thyroidectomy with lymph node dissection for PTC (mean follow-up 5.9 years). According to the lymph node status patients were subdivided into 569 N0 (34.4%), 644 N1a (39.0%) and 440 N1b (26.6%).

Main Outcome Measures: Clinical outcome in terms of disease free survival (DFS) and occurrence of distant metastases.

Results: Average age at diagnosis was significantly lower in N1b (41.7 ± 15.2) and N1a (41.3 ± 13.6) vs N0 (45.7 ± 13.3 yrs). The male gender was more prevalent in N1b patients vs N1a and N0 (F/M = 1.9/1, 4.0/1 and 5.5/1, respectively). Persistent/recurrent disease at last control was significantly more frequent in N1b (29.8%) vs N1a (14.3%) and N1a vs N0 (4.2%) and when more than 5 lymph node were involved.

Also distant metastases were significantly more frequent in N1b (14.1%) than in N1a (4.3%) and N0 (1.6%).

Conclusion: Lymph node metastases at diagnosis are more frequent in PTC patients that are young and male. Persistent/recurrent disease and distant metastasis are significantly more frequent in patients with local advanced disease, particularly in the N1b category.

Table 1. FNAB and CNB results correlated with final diagnosis (for abstract P3-07-05)

Category	FNAB (n = 993)	Surgical diagnosis (n = 133)		CNB (n = 912)	Surgical diagnosis (n = 219)	
		benign (n = 14)	malignant (n = 119)		benign (n = 49)	malignant (n = 170)
Nondiagnostic	160 (16.1)	3	18	6 (0.6)	0	1
Benign	609 (61.3)	4	5	609 (66.6)	16	4
AUS/FLUS	146 (14.7)	7	37	25 (2.7)	2	9
FN/SFN	0 (0)	0	0	92 (10.0)	31	14
Suspicious for malignancy	24 (2.4)	0	18	9 (0.8)	0	6
Malignancy	54 (5.4)	0	41	171 (18.7)	0	136*

Data are number of nodules, with percentages in parenthesis.

Table 1. Final outcome in 1653 PTC patients according to N status (for abstract P3-07-06)

	All patients	N0	N1a	N1b
n	1,653	569	644	440
Disease at last visit	247 (14.9%)	24 (4.2%)	92 (14.3%)	131 (29.8%)
Biochemical	77 (31.2%)	11 (45.8%)	36 (39.1%)	30 (22.9%)
Structured	170 (68.8%)	13 (54.2%)	56 (60.9%)	101 (77.1%)
Distant metastases	99 (6%)	9 (1.6%)	28 (4.3%)	62 (14.1%)

P3-07-07

LOW OR UNDETECTABLE BASAL THYROGLOBULIN LEVELS OBVIATE THE NEED FOR NECK ULTRASOUND IN DIFFERENTIATED THYROID CANCER PATIENTS AFTER TOTAL THYROIDECTOMY AND I-131 ABLATION

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Aim: To determine whether there is a clinical benefit from routine neck ultrasound (CUS) in differentiated thyroid cancer (DTC) patients regardless of non-TSH-stimulated thyroglobulin (Tg) levels, as measured with sensitive Tg assays with a functional sensitivity (FS) below 1 ng/ml, after total thyroidectomy and I-131 ablation.

Patients and Methods: A retrospective database study of 3176 cervical ultrasound exams performed in 773 patients between June 15, 1996 and July 1, 2012. Correctness of ultrasound results was assessed based on further examinations and follow-up registered in the database.

Results: 2199 CUS exams were classified as true negative, 216 as true positive, 692 as false positive in 339 (43.9%) individual patients, 170 of whom were low risk, and 69 as false negative. Thus overall sensitivity, specificity, PPV, NPV and accuracy (95% confidence interval) were 75.8 (70.1–81.5)%, 76.1 (74.3–77.8)%, 23.8 (18.1–29.5)%, 97.0 (96.2–97.7)% and 76.0 (74.3–77.7)%, respectively. No significant differences between low and high risk patients were found. There were no significant differences between patients with an undetectable and a low detectable (<1 ng/ml) Tg level; these two groups however both showed significantly lower PPV and higher NPV than patients with a Tg ≥1 ng/ml. From January 2007 onwards true positive and false negative neck ultrasounds no longer occur in patients with Tg <1 ng/ml.

Conclusion: After total thyroidectomy and I-131 ablation, the indication for neck ultrasound should be determined by Tg level, as patients with a Tg <1 ng/ml will no longer show true positive CUS results but will have a considerable number of false positive ones.

P3-07-08

QUANTITATIVE ANALYSIS AND OPTIMIZED RENDERING OF 3-D CANCER VASCULAR PATTERNS

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Objectives: Tumor vascularization is a relevant and prognostic factor correlated with the malignancy grade of different cancer types. 3-D medical imaging techniques have been applied in order to evaluate vascular patterns. We developed a technology for a rapid automatic reconstruction and quantification of vascular architecture.

Methods: The algorithm is composed of the following steps: i) novel and simple Vessel Enhancement Filter for noise suppression and contrast improvement; ii) 3-D iterative thinning process to obtain the morphological skeleton of tumor vascular network; iii) mathematical-based centerline extraction for the subsequent quantitative analysis. Six features, tortuosity measurements as Distance Metric (DM), Inflection Count Metric (ICM) and Sum Of Angles Metric (SOAM), number of branches (NB), vascular volume density (VVD), spatial vascularity pattern (SPV) are calculated from the centerlines results. As an example, the system was tested on 19 three-dimensional power Doppler Ultrasound (PDUS) scans of thyroid tumors, including 9 benign and 10 malignant lesions.

Results: The averaged values of features of malignant nodules are significantly higher than those of benign lesions (Benign: DM = 9.18 ± 7.33, ICM = 29.25 ± 19.50, SOAM = 2.86 ± 1.92, NB = 11.11 ± 6.41, VVD = 29.44% ± 16.81%. Malignant: DM = 30.90 ± 15.01, ICM = 193.09 ± 152.68, SOAM = 10.00 ± 6.00; NB = 27.80 ± 14.38; VVD = 40.00% ± 13.09%). Regarding to SPV feature, six out of eight benign lesions are classified as perilesional, while all cancers as intranodular.

Conclusion: This method automatically analyzes tumor vascularity in terms of 3-D rendering and numerical analysis, and enables a cancer characterization, extracting vascular features which can predict the differential diagnosis between benign and malignant lesions, being safe, non-invasive and user-independent. The results demonstrate a correlation between the morphology of blood vessels and malignancy, allowing an accurate differential diagnosis of thyroid nodules.

P3-07-09

MOLECULAR MARKERS OF THYROID CANCER IN CHILDREN IN A TERTIARY CENTER IN ROMANIA

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Introduction: Differentiated thyroid carcinoma (DTC) is the most common endocrine malignancy and represents ~1% of all types of human cancer. Despite a general good outcome, with cure in most cases after surgery and radioiodine ablation, in children DTC is more aggressive and requires specific management.

Objective: To assess the cases of thyroid cancer in children across the last 15 years, in terms of diagnosis, pathology spectrum and response to therapy.

Patients and Methods: Between 2001–2015, a number of 5204 cases of thyroid cancer were recorded, while 59 cases were operated before 18 years. The goal was to find molecular markers that could improve be useful in children with DTC. BRAF V600E mutation occurs in 83% of PTC in children, being associated with increased tumour aggressiveness. RET rearrangements are often involved in PTC occurrence. Matched tumour and normal thyroid tissue samples were obtained from children who were enrolled for surgery after informed consent.

Results: DTC in children was considered medium or high risk. Previous neck irradiation, family history, progressive tumour and lymph nodes are the most important risk factors. Thyroid surgery with radical neck dissection is mandatory, followed by several consecutive radioiodine doses, with a good outcome and excellent survival. Thyroxine substitution/suppressive therapy is required in DTC. One case developed multifocal PTC after 3 years of TSH stimulation due to a huge thyrotropinoma. Another, with cribriform-morular type of PTC was harbouring a double genetic event: BRAF V600E and RET/PTC1 rearrangement.

Conclusion: Thyroid cancer in children is more aggressive and a multidisciplinary approach is mandatory, including paediatric endocrinologist, surgeon, nuclear medicine and genetics. Gene expression is altered in papillary thyroid carcinoma in children. Beside BRAF status analysis, RET/PTC rearrangements identification is a complementary method aiming to individualize the therapy in aggressive forms of PTC.

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P3-07-10

ATYPICAL NON-SECRETORY MEDULLARY THYROID CARCINOMA: CASE REPORT

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Introduction: Medullary thyroid carcinoma (MTC) is a rare malignancy of the thyroid. MTC is quite aggressive with mortality rate that ranges between 13, 4–38%. Preoperative diagnosis of MTC is crucial in order to plan extend of surgery. In the majority of cases the diagnosis is secured based on the level of serum calcitonin.

Case Report: The patient was a 71 year old female with a history of autoimmune 'Hashimoto' thyroiditis. The patient's thyroid ultrasound showed on the upper left lobe 0.83 X 0.86 cm long with partially calcified capsule, irregular borders and vascularization. The patient had an FNA of the suspicious nodule and the result was inconclusive. Her serum calcitonin was 0.94 ng/ml. She was advised for follow up and a new FNA of the suspicious nodule

in six months. The patient however decided to have thyroidectomy. The histology report revealed a 7 mm MTC with diffuse staining for Chromogranin A, TTF1 and weak focal staining for Calcitonin. The tumor was completely negative for thyroglobulin, CK7, CK19, CK20 and CEAm. The patient had a RET oncogene analysis which reveal a double mutation in exon 11 (G691S) and in exon 15 (S904S). In regards to her follow up, the first year she will every three months have a cervical ultra sound, an x-Ray of the thorax, measurement of serum calcitonin, CEA, PTH and 24-hour urinary collection for evaluation of catecholamines and metanephrines. After the first year her follow up will be every six months and after five years, once per year.

Discussion: Atypical non-secretory MTC have been reported in the past. To this date only 25 such cases have been described. Is this a new subgroup of MTC? Only one is certain the diagnosis and follow up of such patients is challenging.

P3-08 Basic Autoimmunity and Thyroidology

P3-08-01

SOX9 IS INVOLVED IN THE THYROID DIFFERENTIATION PROGRAM

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Transcription factors Nkx2.1, Pax8, Foxe1 (TTFs) are required to define the thyroid differentiated phenotype. The knowledge about their function has increased lately, but transcription factors upstream of those genes controlling their expression are still unknown. We analyzed *in silico* the promoter of the TTFs genes founding that they contain consensus sequences for transcription factors involved in endoderm differentiation. Among them, we focus in the transcription factor Sox9, a HMG box DNA binding protein essential for development of endoderm-derived-organs. The aim of this work was to study the regulation of Sox9 expression in thyroid cells differentiation.

To achieve our goals inmunohistochemistry analysis and determination of mRNA and protein levels by RT-qPCR and Western-blot were performed. Co-transfections assays with promoter constructs and expression vectors were performed in Hela cells. The binding capacity of Sox9 to its consensus sequence promoter was analyzed by Electrophoretic Mobility Shift Assays (EMSA). Sox9 was silenced in PCCl3 cells using specific siRNA.

The results showed that Sox9 is expressed in the nucleus of thyroid adult mice and in PCCl3 cells. Interestingly its expression is increased by TSH while TGFβ repressed this induction in a transcriptional fashion as has been shown by promoter transfection experiments. The TSH effect was mediated by cAMP/PKA and the TGFβ by Smads proteins. Furthermore, CREB and Pax8 activated Sox9 promoter activity while FoxE1 inhibited it. Sox9 binds to its target sequence in the FoxE1 promoter activating it, which demonstrate the existence a circuit of regulation among these two factors.

These results confirm that Sox9 plays an important role in the transcriptional regulation that controls the differentiation of thyroid follicular cell, something hitherto unknown. Future experiments will provide more knowledge regarding their role in development and pathology of the thyroid.

P3-08-02

TYPE 2 DEIODINASE (DIO2) SNP RS225011 IS ASSOCIATED WITH GRAVES' DISEASE IN A SWEDISH POPULATION

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Objective: We have previously shown downregulation of DIO2 in orbital tissue from patients with opthalmopathy. Polymorphisms in the type 2 deiodinase **(**DIO2) were previously associated with thyroid hormone levels. The objective was to examine whether genetic variation in DIO2 is associated with Graves' disease (GD) or Graves' ophthalmopathy (GO).

Methods: The study consisted of 712 patients with GD with (n = 311) or without (n = 399) GO and 1183 sex-matched controls from Malmö, in southern Sweden (Table 1). Seven SNPs rs225014, rs12885300, rs2267872, rs225011, rs224995, rs225015, and rs2267873 in DIO2 were genotyped using Sequenom and TaqMan. Logistic regression with age, smoking, and ethnicity as covariates was used for estimating SNP associations.

Results: Rs225011 was associated with GD (OR 1.18, CI 1.01–1.37, p = 0.036). None of the SNPs were associated with GO.

Conclusion: Rs225011 in DIO2 was associated with GD in a Swedish population. Further studies are needed to show whether this finding is of importance for the development, clinical course, or treatment response in GD.

P3-08-03

LOWER PROPORTIONS OF CD19+CD24HICD27+IL-10+ AND CD19+IL-10+, BUT NOT CD1D+CD5+CD19+CD24+CD27+IL-10+ B CELL LEVELS IN CHILDREN WITH AUTOIMMUNE THYROID DISEASES

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Autoimmune thyroid disease (AITD) is the most common organ-specific autoimmune disorder. Genetic background, environmental and endogenous factors are play important roles in determining the activation of immune cells or the efficacy of the immunoregulatory pathways. Recently emphasizes the immunosuppressive role of B regulatory cells (phenotype $CD19^{+}CD24^{hi}CD27^{+}IL\text{-}10^{+}$, $CD19{+}IL\text{-}10^{+}$) in regulation of immune response.

Table 1. Final outcome in 1653 PTC patients according to N status (for abstract P3-08-02)

		Cases	%	Controls	%
N		712		1183	
Age at diagnosis/inclusion		49+14		57+6	
Sex	Male/Female (%)	127/585	17.8/82.2	211/972	17.8/82.2
Ethnicity	Swedish (%)	531	74.6	833	70.4
	European (%)	117	16.4	177	15.0
	Other (%)	61	8.6	83	7.0
	Missing (%)	3	0.4	90	7.6
Smoking	Yes/No/Missing (%)	288/395/29	40.4/55.5/4.1	343/801/39	29.0/67.7/3.3
Ophthalmopathy	Yes/No/Missing (%)	311/399/2	43.7/56.0/0.3	0/1183/0	0.0/100.0/0

The aim of the study was to estimate the expression of $CD19^{+}CD24^{hi}CD27^{+}IL\text{-}10^{+}$ and $CD19{+}IL\text{-}10^{+}$(B10) B cells in patients with Graves' disease (GD) (n = 24, mean age 14.9 years old), in patients with Hashimoto's thyroiditis (HT) (n = 22, mean age 15.2 years old) in comparison with sex- and age-matched healthy control subjects (n = 30, mean age 15.4 years old). The expression of the immune cells populations were analyzed by the four-color flow cytometry using a FACSCanto II cytometer (BD Biosciences).

In untreated patients with Graves' disease and HT we observed a significant decrease of $CD19^{+}CD24^{hi}CD27^{+}IL\text{-}10^{+}$ ($p < 0.033$ for GB and $p > 0.05$ for HT) and $CD19{+}IL\text{-}10^{+}$ ($p < 0.0431$ for GD and $p < 0.033$ for HT) B lymphocytes in comparison to the healthy controls. The analysis of CD1d+CD5+CD19+CD24+CD27+IL-10+ B cells in the peripheral blood revealed comparable percentages of these cells in patients with thyroid autoimmune diseases to the healthy controls.

We conclude that the reduction number of Breg cells with expression of $CD19^{+}CD24^{hi}CD27^{+}IL\text{-}10^{+}$ and $CD19{+}IL\text{-}10^{+}$ (B10) could be responsible for loses immune tolerance and development of autoimmune process in thyroid disorders.

P3-08-04

ROLE OF TAZ/WWTR1 IN THE TGFβ REPRESSION OF NIS

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TAZ/WWTR1 (transcriptional coactivator with PDZ-binding domain) is a transcriptional regulator involved in the Hippo signaling pathway and it takes part in the control of cell proliferation, apoptosis, cell-cell contact inhibition, stem cell self-renewal and tissue regeneration. TAZ has been reported to regulate those processes through the transactivation of transcription factors in the nucleus. For instance, it is described to co-activate Nkx2-1 and Pax8, the main thyroid transcription factors, over the thyroglobulin promoter. As both transcription factors control the activity of sodium iodide symporter (NIS) promoter, we decided to study the involvement of TAZ in the expression of NIS, an essential protein for thyroid hormones synthesis and for radioiodide treatment in thyroid cancer. Strikingly, we detected that TAZ negatively regulates the transcriptional activity of Pax8 over the NIS promoter. Besides, we provided evidence that TAZ could play an important role in the downregulation of NIS expression by TGFβ; we observed TAZ protein is mainly located in the nucleus under treatment with this cytokine and its silencing induces a partial recovering of NIS protein and mRNA levels. Additionally, our results demonstrated an increased expression of TAZ in thyroid carcinoma cell lines, in which NIS levels are typically decreased. Specifically, TAZ nuclear translocation is augmented in those thyroid carcinoma cells mutated in BRAFV600E. Since we have described that this mutation increases the secretion of TGFβ, this could be connected with the decreased levels of NIS in these cells. Altogether, this study has shed light on the important role of the Hippo pathway in the regulation of NIS expression in thyroid cells. Given the fact that this protein has been characterized as overexpressed in the thyroid carcinoma future research of TAZ in the thyroid will enable the development of new strategies to treat thyroid cancer.

P3-08-05

MICRORNAS IN THYROID TISSUE AND SERUM IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE

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Background: Autoimmune thyroid diseases (AITD), including Graves' disease (GD) and Hashimoto's thyroiditis (HT), are autoimmune, organ-specific diseases. MicroRNAs (miRNAs) are small, non-coding RNAs, which regulate gene expression. Their differential expression in tissue and serum is not fully characterized, and their potential role in the development of autoimmunity, or as biomarkers of disease, is not yet fully understood.

Methods: We determined miRNA expression through sequencing of miRNA (HiSeq) in 20 thyroid tissues: 10 from patients with GD, 5 from patients with HT and 5 from healthy controls. We then selected five top-ranked miRNAs and validated them by qRT-PCR in thyroid tissue samples from 26 patients with AITD (17 with GD, 9 with HT and 10 controls). miRNA expression in serum was analyzed in 36 patients with AITD (22 GD, 14 HT) and 22 controls.

Results: Expression of hsa-miR-21-5p, hsa-miR-96-5p, hsa-miR-142-3p, hsa-miR-146a-5p, and hsa-miR-155-5p was significantly increased in thyroid tissue from patients with AITD. Validation of miR-21-5p and miR-96-5p in tissue samples revealed that it was only upregulated in patients with GD, but validation in serum revealed its increased expression in all patients with AITD. miR-142-3p and miR-146a-5p were upregulated in both tissue and serum samples in all AITD. A trend for an increased expression of miR-155-5p was observed in its validation in all AITD thyroids, although no significant upregulation was observed in serum.

Conclusion: miR-142-3p and miR-146a-5p exhibit a similar behavior in both tissue and serum, suggesting their potential role in the development of AITD. In contrast, miR-21-5p and miR-96-5p exhibit an increased expression in tissue samples from patients with GD, but an increased serum expression in all types of AITD, denoting their circulating levels could play a potential role in autoimmunity. The absence of an increased expression of miR-155-5p in serum suggests its potential specific influence in thyroid tissue exclusively.

P3-08-06

ASSOCIATIONS OF IL10 AND IL16 GENE POLYMORPHISMS WITH THE SUSCEPTIBILITY OF GRAVES OPHTHALMOPATHY IN A RUSSIAN POPULATION WITH GRAVES DISEASE

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Objectives: Graves' ophthalmopathy (GO) is an autoimmune inflammatory disorder affecting the retroorbital tissues. In 90% of patients GO associated with Graves' disease (GD) however only 30–50% of GD patients have GO. The occurrence of GO has been demonstrated as a consequence of cumulative effects of both genetic and environmental factors. In the current study, we have performed the association study of several SNPs located within *IL10* and *IL16* genes in Russian patients with GO.

Methods: In case-control study 248 patients with GD were recruited, 141 patients with GD with GO and 107 patients with GD without GO. We studied an association of two SNPs: rs4778641 of *IL16* and rs1800896 of *IL10* genes. Statistical analysis has been performed using Fisher's exact test. The results were corrected for multiple comparisons.

Results: There were no significant difference in the allele and genotype frequencies of the *IL16* gene polymorphous marker between patients with GO and patients with GD without GO. In case of polymorphous marker rs1800896 of *IL10* gene we have shown that the carriers of *A* allele and *AA* genotype had higher risk of GO development (*OR* = 4.45, 95% CI = 2.93–6.75, <0.001; *OR* = 6.34, 95% CI = 3.63–11.08, <0.001, respectively). Carriers of *G* allele and *GG* genotype had lower risk of GO development (*OR* = 0.22, 95% CI = 0.15–0.34, <0.001; *OR* = 0.09, 95% CI = 0.03–0.33, <0.001 respectively).

Conclusion: The results of our study shows strong association of *IL10* gene polymorphism with GO in Russian patients with GD.

P3-08-07

ANALYSIS OF ZINC TRANSPORTER ZNT8 AUTOANTIBODIES IN CHILDREN AND ADOLESCENTS WITH AUTOIMMUNE THYROID DISEASES

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Recent studies have revealed the presence of zinc and the expression of zinc transporter (ZnT) family members in most endocrine cell types and plays an important role in the synthesis and secretion of many hormones. We studied the prevalence of ZnT8 Ab in patients with autoimmune thyroid diseases (AITD) to assess the association of AITD and T1DM at the serological level.

The study was performed in the group consisting of 20 Graves' disease (GD) patients (mean age, 17.8 years ± 14 years), 44 Hashimoto's thyroiditis (HT) patients (mean age, 13.8 years ± 3.5 years) and 57 healthy controls (mean age, 13.1 years ± 3.5 years). Patients were recruited from few Polish endocrine centers. GAD, IA-2, IAA, ZnT8, 21-OH and acetylcholine receptor (AChR) antibody concentrations were evaluated in the sera using RSR kits.

In our study, ZnT8Ab were found in 4 patients (20%) with GD while 3 patients (15%) were positive for GADAb, one patient (5%) was positive for IAA and one patient (5%) was positive for IA-2Ab. Of these, one GD patient was positive for all four diabetes associated antibodies. In the case of HT patients, 4 (9%) were positive for ZnT8Ab, while 3 patients (7%) were positive for GADAb, 2 (4.5%) were positive for IA-2Ab and 1 (2.3%) was positive for IAAAb. Of these, one HT patient had 3 diabetes associated antibodies (ZnT8, GAD and IA-2Abs) and one had 2 diabetes associated antibodies (GADAb and IAA). Out of 57 healthy controls studied, 2 (3.5%) controls were positive for ZnT8 Ab, one (1.8%) was positive for GADAb and none of them was positive for IA-2Ab or IAA. Furthermore, one GD patient (5%) and 2 HT patients (4.5%) were positive for 21-OHAb only. None of the patients with AITD and healthy controls studied was positive for AChRAb.

In conclusion, these results suggest that the presence of ZnT8Ab can be associated with other autoimmune diseases other than T1DM in particular Graves' disease and Hashimoto's thyroiditis.

P3-08-08

LOW CD26 EXPRESSION IN HASHIMOTO'S THYROIDITIS

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Hashimoto's thyroiditis (HT) is an organ-specific autoimmune disease characterized by lymphocytic infiltration. CD26, also known as dipeptidyl peptidase 4 (DPP-4), is a multifunctional molecule involved in autoimmune diseases' pathophysiology. The aim of our study was to investigate the plasma levels of sCD26, sCD26 enzymatic activity and CD26 surface expression on lymphocytes in HT patients.

Blood samples from 31 newly diagnosed HT patients and 20 healthy control subjects were collected. The plasma concentration of sCD26 was analyzed using ELISA. sCD26 enzymatic activity was measured using a luciferase-based assay. CD26 surface expression was analyzed by flow cytometry.

Plasma concentration of sCD26 was lower in HT patients compared with healthy controls, though not reaching statistical significance ($P = 0.070$). sCD26 enzymatic activity was similar between HT patients and healthy controls. The expression levels of CD26 on monocytes, B cells and CD4+ T cells were comparable between HT patients and healthy controls, while the frequency of CD26 on CD8+ T cells was lower in HT patients than that in healthy controls ($P < 0.05$). The mean fluorescence intensity (MFI) levels of CD26 on CD8+ T cells and Tc2, Tc17 subsets were decreased in HT patients. In HT patients, TgAb titers was negatively correlated with sCD26 enzymatic activity ($r = –0.467$, $P = 0.016$). TSH levels and the MFI of CD26 on Tc1 cells were negatively correlated ($r = –0.425$, $P = 0.017$).

Our data indicate that decreased plasma levels of sCD26 and CD26 on CD8+ T cells might be important for the pathogenesis of HT.

P3-08-09

MULTIPLE NUTRITIONAL FACTORS AND THE RISK OF HASHIMTO'S THYROIDITIS

Margaret Rayman[1], *Shiqian Hu*[1]
[1]Universary of Surrey, Guildford, UK

Objectives: To elucidate the role of nutritional factors in the risk, pathogenesis and treatment of Hashimoto's Thyroiditis (HT).

Methods: PubMed and the Cochrane Library were searched for publications on iodine, iron, selenium and vitamin D and risk/treatment of HT.

Results:

Iodine: Chronic exposure to excess iodine intake induces autoimmune thyroiditis, partly because highly-iodinated thyroglobulin is more immunogenic. Recent introduction of universal salt iodization can have a similar, though transient, effect.

Iron: Iron deficiency impairs thyroid metabolism. Thyroid peroxidase (TPO), the enzyme responsible for the production of thyroid hormones is a haem (iron-containing) enzyme; it becomes active at the apical surface of thyrocytes only after binding haem. HT patients are frequently iron-deficient owing to the association between HT and autoimmune gastritis which impairs iron absorption. Treatment of anaemic women with impaired thyroid function with iron improved thyroid-hormone concentrations while thyroxine and iron together were more effective in improving iron status.

Selenium: Selenoproteins are essential to thyroid action. In particular, the glutathione peroxidases protect the thyroid by removing excessive hydrogen peroxide produced there for thyroglobulin iodination. Genetic data implicate the anti-inflammatory selenoprotein S in HT risk. There is evidence from observational studies and RCTs that selenium/selenoproteins can reduce TPO-antibody titre, hypothyroidism and post-partum thyroiditis.

Vitamin D: Lower vitamin D status has been found in HT patients than in controls and inverse relationships of serum vitamin D with TPO/thyroglobulin antibodies have been seen. However, other data plus the lack of trial evidence suggest that low vitamin-D status is more likely the result of autoimmune disease processes that include vitamin D-receptor dysfunction.

Conclusion: Clinicians should check patients' iron- (particularly in menstruating women) and vitamin-D status to correct any deficiency. Adequate selenium intake is vital in areas of iodine-deficiency/excess so in regions of low selenium status, a supplement of 100 µg/d selenium may be appropriate.

European Thyroid Journal

Author Index for Abstracts

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European
Thyroid Journal

39th Annual Meeting of the European Thyroid Association

Industry-Sponsored Satellite Symposia

Copenhagen, Denmark
September 3–6, 2016

Guest Editors
Furio Pacini, Siena, Italy
Birte Nygaard, Copenhagen, Denmark

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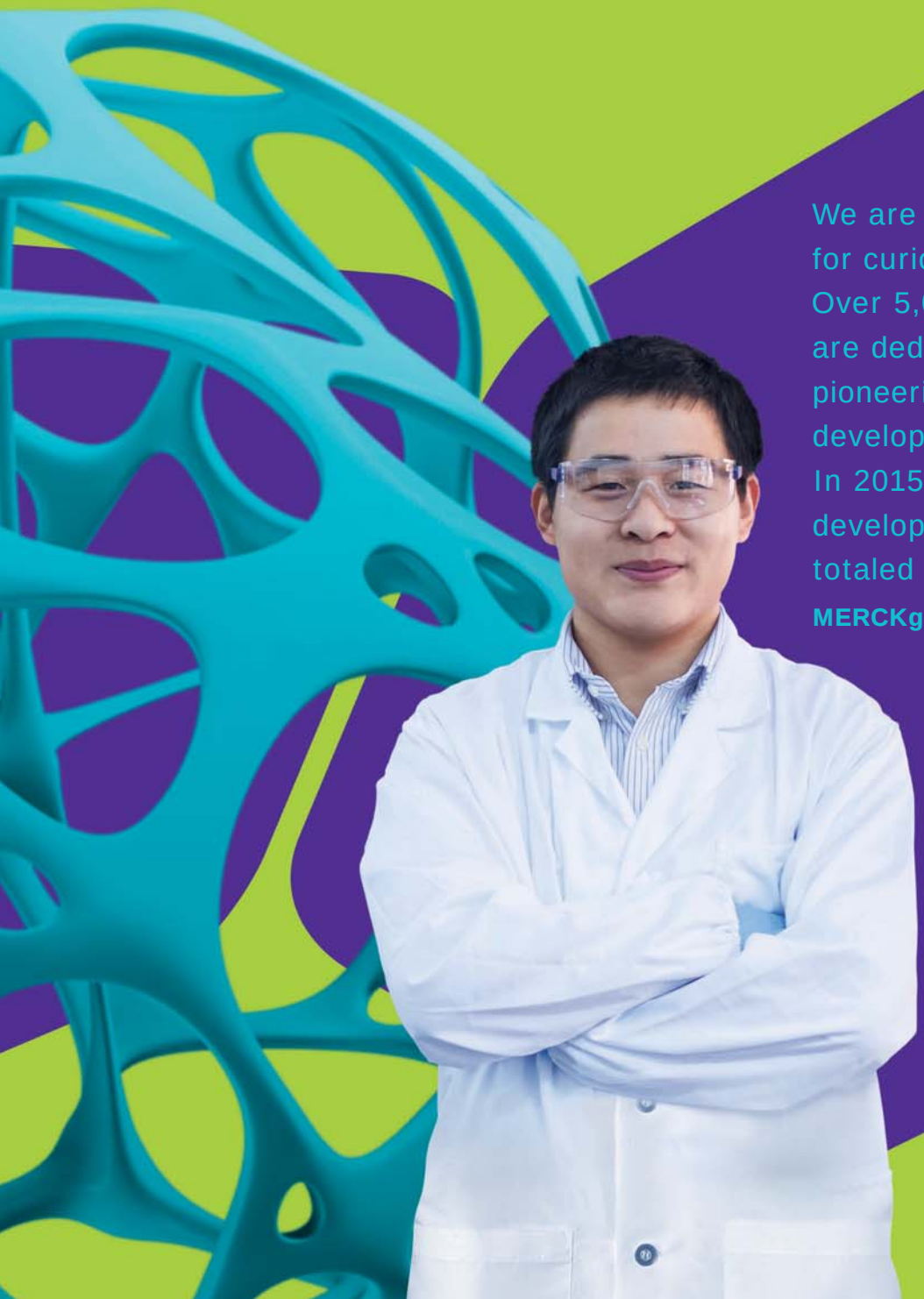
DISCOVERING TOMORROW



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European
Thyroid Journal

Saturday, 3rd September 2016

Room 8+9+10+11 (Main Auditorium)
17.00–18.00

MERCK

ETA Industry-Sponsored Satellite Symposium 1

Update in Hyperthyroidism

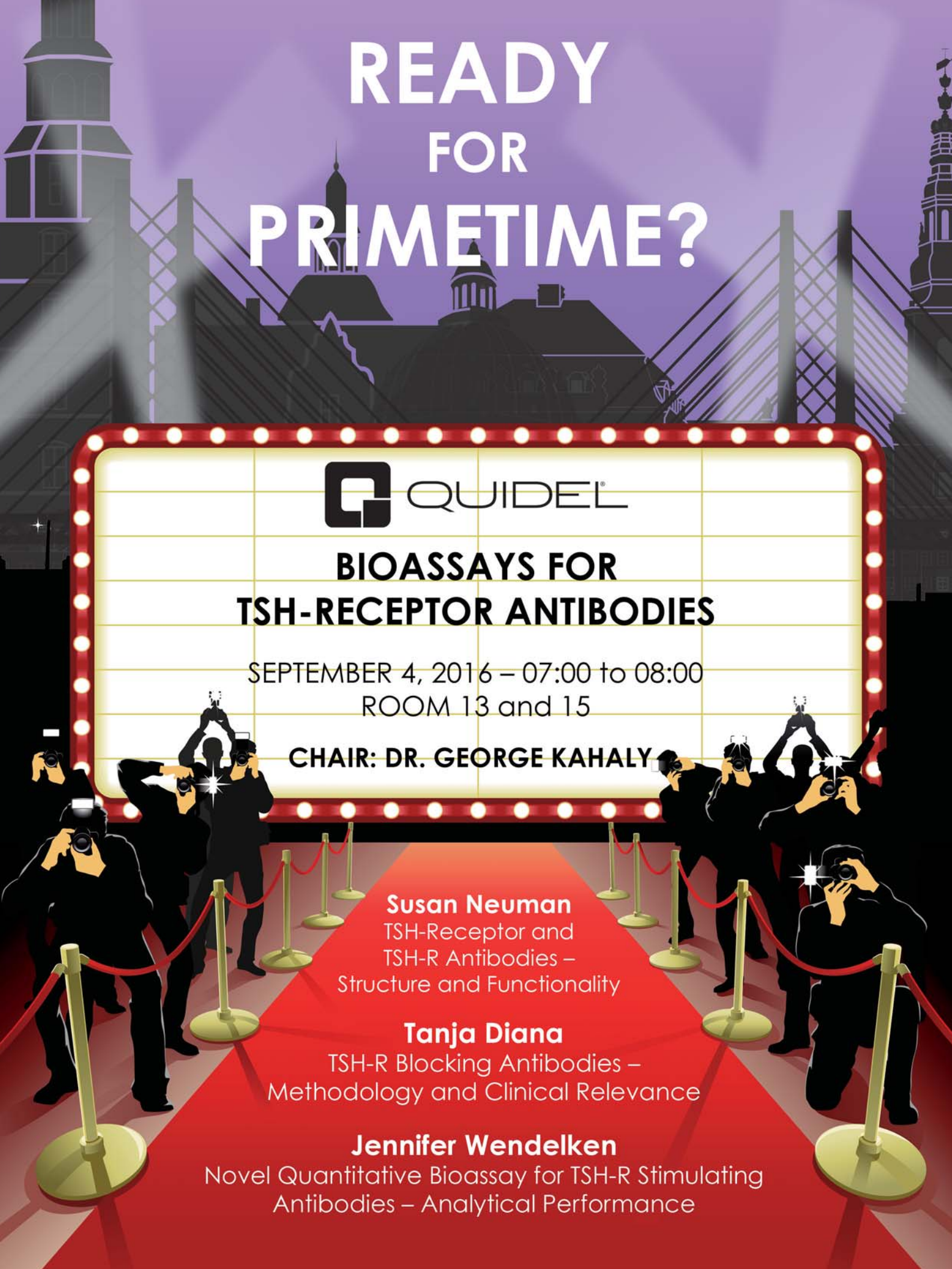
Chair: *George J. Kahaly*

Welcome and Introduction
George J. Kahaly, Mainz, Germany

ETA Guidelines on Subclinical Hyperthyroidism: Strengths and Weaknesses
Laszlo Hegedüs, Odense, Denmark

A Current State of the Art on the Antithyroid Drug Treatment during Pregnancy
Stine Linding Andersen, Aalborg, Denmark

Novel Treatment Modalities with Small Non-Peptide Molecules
Marvin Gershengorn, NIH, Bethesda, USA


READY
FOR
PRIMETIME?
QUIDEL
BIOASSAYS FOR
TSH-RECEPTOR ANTIBODIES
SEPTEMBER 4, 2016 – 07:00 to 08:00
ROOM 13 and 15
CHAIR: DR. GEORGE KAHALY
Susan Neuman
TSH-Receptor and
TSH-R Antibodies –
Structure and Functionality
Tanja Diana
TSH-R Blocking Antibodies –
Methodology and Clinical Relevance
Jennifer Wendelken
Novel Quantitative Bioassay for TSH-R Stimulating
Antibodies – Analytical Performance

Sunday, 4th September 2016

Room 13+15
07.00–08.00

ETA Industry-Sponsored Satellite Symposium 2

Bioassays for TSH-Receptor Antibodies: Ready for Primetime?

Chair: *George J. Kahaly,* Mainz, Germany

TSH-Receptor and TSH-R Antibodies – Structure and Functionality
Susanne Neumann, Bethesda, USA

TSH-R Blocking Antibodies – Methodology and Clinical Relevance
Tanja Diana, Mainz, Germany

Novel Quantitative Bioassay for TSH-R Stimulating Antibodies – Analytical Performance
Jennifer Wendelken, Athens, USA

Room 8+9+10+11 (Main Auditorium)
13.00–14.00

ETA Industry-Sponsored Satellite Symposium 3

Burning Questions on Differentiated Thyroid Cancer Management

Chair: *Furio Pacini*, Siena, Italy

When Is Ablative Treatment Necessary?
Miguel Melo, Coimbra, Portugal

How to Define Free-of-Disease Status?
Robin Peeters, Rotterdam, The Netherlands

Sunday, 4th September 2016

Room 8+9+10+11 (Main Auditorium)
18.15–19.45

IBSA
Evidence of Life

ETA Industry-Sponsored Satellite Symposium 4

Pregnancy and Hypothyroidism

Chairpersons: *George J. Kahaly*
Elizabeth N. Pearce

18.15–18.20	Welcome and Introduction *George J. Kahaly*, Mainz, Germany
18.20–18.45	Hypothyroidism and Infertility *Kris Poppe,* Brussels, Belgium
18.45–19.10	Diagnosis and Treatment of Hypothyroidism during Pregnancy *Elizabeth N. Pearce,* Boston, USA
19.10–19.35	Fetal and Neonatal Consequences of Maternal Hypothyroidism and Hypothyroxinemia *Robin P. Peeters,* Rotterdam, The Netherlands
19.35–19.45	Discussion and Conclusions *Elizabeth N. Pearce*

Bayer-sponsored satellite symposium

Steps to success: taking treatment further for your patients with RAI-R DTC

Monday 5 September 2016 | 07:00–08:00 am | Room 8+9+10+11

PROGRAMME

Chair: Martin Schlumberger

07:00 **Step 1: Addressing the challenge of RAI-refractory disease**
Martin Schlumberger

07:10 **Step 2: Choosing the right patient for systemic treatment**
Rossella Elisei

07:25 **Step 3: Maximizing treatment in practice**
Johannes Smit

07:45 **Step 4: Sharing experience**
Martin Schlumberger

PLEASE JOIN US

L.DK.MKT.06.2016.1522

Room 8+9+10+11 (Main Auditorium)
07.00–08.00

ETA Industry-Sponsored Satellite Symposium 5

Steps to Success: Taking Treatment Further for your Patients with RAI-R DTC

Chair: *Martin Schlumberger*
Faculty: *Rossella Elisei, Johannes Smit*

07.00 Step 1: Addressing the Challenge of RAI-Refractory Disease
Martin Schlumberger, Villejuif, France

07.10 Step 2: Choosing the Right Patient for Systemic Treatment
Rossella Elisei, Pisa, Italy

07.25 Step 3: Maximizing Treatment in Practice
Johannes Smit, Nijmegen, The Netherlands

07.45 Step 4: Sharing Experience
Martin Schlumberger, Villejuif, France

Room 8+9+10+11 (Main Auditorium)
13.00–14.00

SANOFI GENZYME

ETA Industry-Sponsored Satellite Symposium 6

Burning Questions on Advanced Medullary Thyroid Cancer Management

Chair: *Martin Schlumberger,* Villejuif, France

When to Start TKI Treatment?
Lars Bastholt, Odense, Denmark

How to Manage TKI Treatment Side Effects?
Enrique Grande, Madrid, Spain

Is RET Status Important?
Rossella Elisei, Pisa, Italy

Industrial Exhibition – Sponsors

The Executive Committee of the ETA and the Danish Local Organising Committee would like to thank the following companies for their generous support of the 39th ETA Annual Meeting.

Transparency Declaration

The Executive Committee and the Standing Office of the ETA are most grateful to the following ETA Corporate members and all other sponsors for their generous logistical support of the ETA 2016 Annual Meeting.

Bayer HealthCare Pharmaceuticals Inc.	15,000 € for a satellite symposium 1,500 € for a one-page advert
Eisai Europe Ltd	2,500 € for a coffee break
Esaote S.p.A. Italy	Provision of 4 ultrasound machines
IBSA Institut Biochimique SA	30,000 € for a satellite symposium 6,000 € for an exhibition booth
Merck	30,000 € for a satellite symposium 6,000 € for an exhibition booth 8,000 € for a hospitality corner ETA Pinchera Prize: the sponsorship comprises the value of 3,000 € for the prize plus reimbursement of the travel expenses (economy class flights), hotel accommodation and congress registration fee 1,500 € for a one-page advert
QUIDEL	15,000 € for a satellite symposium and an exhibition booth 1,500 € for a one-page advert
RF Medical Co. Ltd., Korea	3,000 € for an exhibition booth
Sanofi Genzyme	60,000 € for two satellite symposia 6,000 € for an exhibition booth
Sobi	6,000€ for an exhibition booth
STARmed Co., Ltd.	3,000 € for an exhibition booth Provision of lanyards
Theraclion SA	3,000 € for an exhibition booth
Thermo Fisher Scientific	6,000 € for an exhibition booth 1,500 € for the Young Investigator Prize
Veracyte	4,000 € for an exhibition booth

Registration Information

Main Conference Registration Fees

Member Category	before 30th June	1st July – 25th August	on site
ETA Ordinary and ETA Senior	150 €	175 €	200 €
ETA Junior <35 yrs	60 €	80 €	100 €
ETA Corresponding	250 €	300 €	350 €
Non-Member	500 €	550 €	600 €
ATA, LATS, AOTA, JTA Members	250 €	300 €	350 €
Students/Res. Fellows <30 yrs	125 €	160 €	200 €

Pre-Conference Events Fees

ETA Ultrasound Course	150 €
ETA-CRN Symposium	50 €
Iodine Global Network Meeting	40 €
ETA Basic Educational Course	free
ETA Clinical Educational Course	free

Available Day Tickets

Ordinary Members	100 € per day
Junior Members	50 € per day
Members of the Danish Endocrine Society	50 € per day
Non-Members	250 € per day

Main Conference Registration Entitlements

Delegate registration includes:
– Access to all congress sessions and commercial exhibition
– All congress materials and a name badge
– Scientific Programme/Abstract Book
– Lunch boxes
– Refreshment breaks during the congress
– Welcome Reception

Registration does not include:
– Accommodation, tickets to the social events (unless stated)

Pre-Conference Events Registration Entitlements

Admission to the Scientific Sessions, congress materials, lunch and coffee breaks

Social Events (separate registration)

Welcome Reception at the 'Carlsberg Brewery' on Saturday, 3rd September	free for registered participants
Network Dinner at the Teaterkælderen Det Ny Teater on Monday, 5th September	80 €

On-Site Registration / Secretariat Desk / Membership Information

The Congress Registration Desk will be located in the entrance area of the Congress Venue and will operate the following hours:

Friday, 2nd September	16.00–20.00
Saturday, 3rd September	07.00–19.00
Sunday, 4th September	06.30–19.00
Monday, 5th September	06.30–19.15
Tuesday, 6th September	07.00–15.00

During these hours, staff at the Registration Desk can be contacted at this number: +45 33 75 71 18.

ETA Commercial Exhibition Opening Hours

The commercial exhibition will commence on Saturday, 3rd September and finish on Tuesday, 6th September.

Saturday, 3rd September	09.00–18.00
Sunday, 4th September	09.00–18.00
Monday, 5th September	09.00–18.00
Tuesday, 6th September	09.00–13.30

General Information

Congress Venue

Scandic Hotel Copenhagen
Vester Søgade 6, 1601 Copenhagen, Denmark
copenhagen@scandichotels.com

Directions from Copenhagen Airport to the Scandic Hotel

Take the train to Copenhagen Central Station 'København Hovedbanegård'. The journey takes about 15 minutes. At the Central Station, use the exit to 'Vesterbrogade'. Follow the streets 'Trommesalen' and then 'Gammel Kongevej'. After a 5-minute walk, you arrive at the Scandic Hotel at 'Vester Søgade'.

Official Language in Denmark

Danish and English as second language.

Currency

The currency in Denmark is Danish Kroner (DKK). 100 DKK is equivalent to approx. 13.4 EUR or 16.7 USD.

Emergency Contacts

Emergency: 112
Police emergency: 114
Copenhagen Police: +45 33 14 88 88
Doctor: 118

Safety in Copenhagen

Copenhagen is a safe city with a very low crime rate. Nevertheless, good urban and cautious behavior is always recommended.

Transportation in Copenhagen

The public transport infrastructure of Copenhagen is among the most efficient and reliable in the world, and it is still being developed and improved. Public transport will get you anywhere you wish to go in the capital region.
The meeting venue is situated within walking distance of Vesterport and the Central Station (Københavns Hovedbanegård).
Information about tickets and prices can be found at www.visitcopenhagen.com/transport/how-to-get-around/tickets.and-prices.
Taxi: all taxis run on meter and they all take credit cards.

Weather in Copenhagen in September

The temperature during the daytime in September is about 15–20°C.

Congress Information:

Accreditation

The 39th Annual Meeting of the European Thyroid Association has been granted 23 European CME credits (ECMEC) by the European Accreditation Council for Continuing Medical Education (EACCME) in Brussels. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity. The EACCME credit system is based on 1 ECMEC per hour with a maximum of 3 ECMECs for half a day and 6 ECMECs for a full-day event. Through an agreement between the European Union of Medical Specialists and the American Medical Association, physicians may convert EACCME credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME credit to AMA credit can be found at www.ama-assn.org/go/internationalcme.

Coffee Breaks and Congress Lunches

Coffee breaks and lunch boxes will be provided in the exhibition area.

Congress Material

The Congress participants who have pre-registered will receive the congress material, together with their name badge from the registration desk of the Congress Secretariat.

Insurance

The registration fee does not include the insurance of participants against personal accidents, illness, cancellations by any party, loss or damage to personal possessions, theft. All participants are strongly advised to make adequate personal insurance arrangements to cover travel, accommodation, cancellation and personal effects prior to travel.

Internet

WIFI will be provided at the conference venue.

Language

The official congress language is English.

Media Check

The congress venue is equipped with state-of-the art, multi-functional installations. Powerpoint is the preferred format for presentations. Please note that the format for presentations needs to be 16:9!
All lecture halls are connected to the Media Check Room, where speakers can hand over their presentations and also check their presentation at several working stations.

Opening times of media check:

Saturday:	07.00–18.15
Sunday:	06.30–18.15
Monday:	06.30–18.00
Tuesday:	07.00–13.00

All presenters are requested to hand in their lecture at least 1 hour before the scheduled talk, or the day before if your talk is early the next morning.
NO personal laptops are allowed!!!

Name Badges

Entrance to the Congress area will be limited to badge holders only. If the badge is lost, please contact the Congress registration desk.

Photography Policy

The ETA has adopted a 'No photography' policy. Kindly appreciate that taking photos of posters and presentations during the whole meeting is not permitted.

Poster Displays

Important guidelines:
Posters must be prepared in portrait format, 120 cm x 90 cm, in English. Mounting material will be available on site. All poster boards will be numbered. Staff will assist you in locating your poster wall and setting up your poster.
Additionally, poster authors are requested to prepare one PowerPoint slide with a short summary of the poster. The slide format required is 16:9.
Authors must be present at their poster session. The poster session will start with a one-minute slide presentation of the poster work, which will be moderated by the session chair. Subsequently, the attendees of the poster session will discuss the poster individually with the presenter.

Poster discussion sessions will take place at the following times:
Saturday: 16.00–17.00 (Poster Session 1)
Sunday: 12.00–13.00 (Poster Session 2)
Monday: 12.00–13.00 (Poster Session 3)

Mounting time guide:
Poster Session 1 – Saturday
Poster authors presenting their poster during Poster Session 1 HAVE TO mount the posters on Saturday from 13.45 to 16.00.
All posters have to be taken down by 18.00 at the latest.

Poster Session 2 – Sunday
Poster authors presenting their poster during Poster Session 2 HAVE TO mount the posters on Sunday from 07.00 to 10.00.
EXCEPTION: Posters for Topic P2–07 Thyroid Cancer – Clinical I in Room 13+15 can only be mounted during the coffee break from 09.30 to 10.00.
All posters have to be taken down by 18.00.

Poster Session 3 – Monday
Poster authors presenting their poster during Poster Session 3 HAVE TO mount the posters on Monday from 07.00 to 10.00.
EXCEPTION: Posters for Topic P3–07 Thyroid Cancer – Clinical III in Room 13+15 can only be mounted during the coffee break from 09.30 to 10.00.
All posters have to be taken down by 18.00.

Thank you for your understanding that posters not removed by the above-mentioned times cannot be stored.

Programme Changes

The organisers do not assume liability for any changes in the programme due to external or unforeseen circumstances.

Smoking Policy

For the general comfort and health of all participants, smoking is not permitted at any of the official functions during the Congress. This includes all scientific sessions, business and other meetings, evening functions and registration area and foyers.

Young Thyroidologists Networking Event

2nd September

Sponsored by The Danish Thyroid Association

A new initiative for the young thyroidologists: a get-together for up to 80 individuals, who would like to share an informal evening before the congress starts. It will be a great opportunity to get to know fellow young thyroidologists from other countries or research groups, prior to the congress. Hopefully, the event will serve as an icebreaker and catalyze contact and interactions with new colleagues during the rest of the congress and onwards.

Venue:	Salon K, Rådhusstræde 13, 1466 København K
Dress Code:	Casual
Time:	19.00–00.00 – you can join at any time convenient for you

Free, but **registration is necessary**

Welcome Reception

3rd September

Venue:	Carlsberg Brewery, Vesterfælledvej 6, 1750 København V
Dress Code:	Business casual
Time:	19.30–22.00
Bus Shuttle:	19.00 from the Scandic Hotel and back to the hotel around 22.00
Meeting Point:	Scandic Hotel, main entrance

Free for registered participants and exhibitors

ETA – Network Dinner

5th September

Venue:	Teaterkælderen – Det Ny Teater, Gammel Kongevej, 1610 København V Within walking distance from the congress center
Dress Code:	Lounge suit / formal
Time:	19.00–22.00
Price:	80 €