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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Executive Committee of the ETA

Furio Pacini (Italy) – President
Colin Dayan (UK) – Secretary
George J. Kahaly (Germany) – Treasurer

Pilar Santisteban (Spain) – President-Elect
Tomasz Bednarczuk (Poland) – Treasurer-Elect

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Anita Boelen (The Netherlands)
Thomas Brix (Denmark)
Veerle Darras (Belgium)
Barbara Demeneix (France)
Rossella Elisei (Italy)
Heike Heuer (Germany)
Jens Mittag (Germany)

Local Organizing Committee

Chair: Birte Nygaard

Members
Laszlo Hegedüs
Nils Knudsen
Peter Laurberg
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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
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 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.

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. (Rotterdam); Rosendaal, F.R. (Amsterdam); Reitsma, P.H.; Dekkers, O.M. (Leiden)
- 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: Thiennon, L.M.; Van Uytfanghe, K.; Van Houcke, S. (Ghent); Das, B. (Mumbai); Faix, J.D. (Palo Alto, Calif.); MacKenzie, F. (Birmingham); Quinn, F.A. (Albany 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
Pre-Conference Events

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**
ETA Clinical Educational Course
Thyroid Function

Room 8+10
08.00–13.00

Chairs: Leonidas Duntas, Greece and Laszlo Hegedüs, Denmark

Introduction:
08.00–08.30
Basic Thyroid Physiology
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
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 Cirello1, Valentina Vaira2, Germano Gaudenzi3, Elisa Stellaia Grassi4, Giovanni Vitale5, Dario Ricca6, Carla Colombo6, Silvano Bosari7, Leonardo Vicentini8, Luca Persani9, Stefano Ferrero10, Laura Fugazzola11
1Department of Pathophysiology and Transplantation, University of Milan, Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Italy; 2Division of Pathology, Fondazione Ircs Ca’ Granda, Milan, Italy; 3Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Ircs, Milan, Italy; 4Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Ircs, Milan, Italy; 5Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Ircs, Milan, Italy; 6Department of Biomedical, Surgical and Dental Sciences, University of Milan, Division of Pathology, Fondazione Ircs Ca’ Granda, Milan, Milan, Italy; 7Department of Pathophysiology and Transplantation, University of Milan, Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Italy

14.20–14.40
TRACING OF BRAF MUTANT THYROID CELLS BEFORE TUMOR DEVELOPMENT
Ellen Johansson1, Shawn Liang2, Elin Schoutz1, Mikael Nilsson1
1Sahlgrenska Cancer Center, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden; 2Sahlgrenska Cancer Center, Sahlgrenska Academy, University of Gothenburg, 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 Cantara1, Domenico Salvatore2, Monica Dentice2, Maria Grazia Castagna1, Raffaele Ambrosio1, Fabio Maino1, Corrado Garbi2, Carlotta Marzocchi1, Tommaso Porcelli2, Furio Pacini1
1Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy; 2Department of Clinical Medicine and Surgery, University of Naples, Federico II, Naples, Italy

15.00–15.20

Panel Discussion

15.20–15.40

Coffee Break

15.40–16.00

Oral Session 1:
Topic Highlights
Chairpersons: Furio Pacini, Italy
Birte Nygaard, Denmark
15.00–15.20
A RANDOMIZED TRIAL OF IODIDE SUPPLEMENTATION VERSUS PLACEBO IN PRETERM INFANTS: THE I2S2 TRIAL
Fiona Williams1, Simon Osgston2, Anita Boelen3, Robert Hume4, Jennifer Watson4, Kayleigh Stanbury5, Peter Willatts4, Edmund Juszczak6, Peter Brocklehurst6
1University of Dundee, Population Health Sciences, Dundee, UK; 2Population Health Sciences, Medical School, University of Dundee, Dundee, UK; 3Academic Medical Centre, Amsterdam, Netherlands; 4University of Dundee, Population Health Sciences, Medical School, Dundee, UK; 5University of Oxford, National Perinatal Epidemiology Unit, Oxford, UK; 6University 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 Hales1, Peter Taylor1, Sue Channon1, Kirtsen McEwan1, Aled Rees1, John Gregory1, Ilaria Muller1, Mohd S Draman1, Colin Dayan1, Kate Langley1, Anita Thapar1, John Lazarus1, Marian Ludgate1
1Cardiff 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 Morte1, Pilar Gil2, Heike Heuer3, Juan Bernal4
1Center for Biomedical Research on Rare Diseases, Instituto de Investigaciones Biomédicas, Csic, Madrid, Spain; 2Instituto de Investigaciones Biomédicas Uam-Csic, Center for Biomedical Research on Rare Diseases, Madrid, Spain; 3Leibniz Institute for Environmental Medicine (IfU), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany; 4Instituto 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 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 Analogue + 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 8+9+10+11 (Main Auditorium)
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 Flies, 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 Zoylin Rubeck1, Steen Joop Bonnema2,
              Marie Louise Jespersen3, Peer Christiansen4,
              Viveque Egsgaard Nielsen5
              1Department of Oto-Rhino-Laryngology, Head- and Neck
              Surgery, Aarhus University Hospital, Institute for Clinical
              Medicine, Aarhus University, Aarhus, Denmark; 2Department
              of Endocrinology and Metabolism, Odense University
              Hospital, Department of Clinical Research, Faculty of Health
              Sciences, University of Southern Denmark, Odense, Denmark;
              3Department of Pathology, Aarhus University Hospital, Aarhus,
              Denmark; 4Department of Plastic and Breast Surgery, Aarhus
              University Hospital, Aarhus, Denmark; 5Department 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 Bellevicine1, Roberta Sgariglia1, Umberto Malapelle1,
              Caterina De Luca1, Elena Vigliar1, Markus Eszlinger2,
              Ralphe Paschke3, Giancarlo Troncone4
              1University of Naples Federico II, Public Health Department,
              Napoli, Italy; 2University 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 Maino1, Maria Grazia Castagna1, Filomena Barbato1,
              Raffaella Forleo1, Noemi Fralassi1, Furio Pacini1
              1Department of Medical, Surgical and Neurological Sciences,
              University of Siena, Siena, Italy
THE MACROFOLLICULAR VARIANT OF PAPILLARY THYROID CANCER (MF-PTC): A BICENTRIC RETROSPECTIVE ANALYSIS OF 65 CASES
Carlotta Giani1, Joana Simões Pereira2, Pedro Marques2, Daniel Macedo2, Rita Santos2, Liborio Torregrossa3, Fulvio Basolo3, Rossella Elisei1, Valeriano Leite2
1Endocrine Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; 2Endocrinology Section, Instituto Português de Oncologia de Lisboa, Francisco Gentil, Lisbon, Portugal; 3Department of Surgical, Medical and Molecular Pathology of the Clinical Area, Pisa, Italy

RISK STATIFICATION IS USEFULL IN PREDICTING PERSISTENT/RECURRENT DISEASE IN MICROPAPILLARY THYROID CARCINOMA
Filomena Barbato1, Maria Grazia Castagna1, Fabio Maino1, Raffaella Forleo1, Noemi Fralassi1, Furio Pacini1
1Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy

SIMULTANEOUS MEDULLARY (MTC) AND DIFFERENTIATED THYROID CANCER (DTC) IN THYROID GLAND (MTC-DTC): WHICH TUMOR IS THE REAL MATTER?
Letizia Pieruzzi1, Loredana Lorusso1, Liborio Torregrossa2, Valeria Bottici1, Laura Agate1, Fulvio Basolo2, Gabriele Materazzi1, Paolo Viti1, Eleonora Molinaro1, Rossella Elisei1
1Endocrinology Section, Department of Medical and Experimental Medicine, University of Pisa, Pisa, Italy; 2Department of Surgical Medical, Molecular Pathology, University of Pisa, Pisa, Italy

COMPUTED TOMOGRAPHY ADDED TO ULTRASONOGRAPHY GIVES THE BENEFITS TO DETERMINE THE EXTENT OF NECK DISSECTION IN PATIENTS WITH THYROID CANCER: A PROSPECTIVE MULTICENTER STUDY
Ki-Hoon Kim1, Younghen Lee2, Dong Gyu Na3, Jung Hwan Baek4, So Lyung Jung5, Sun-Won Park6, Jinna Kim7, Tae Jin Yun8, Eun Joo Ha9, Kyung-Sook Yang10
1Seoul National University Hospital, Seoul, Korea, Rep. of South; 2Department of Radiology, Seoul National University Hospital, Seoul, Korea, Rep. of South; 3Department of Radiology, Human Medical Imaging and Intervention Center, Seoul, Korea, Rep. of South; 4Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; 5Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South; 6Borame Medical Center, College of Medicine, Seoul National University, Seoul, Korea, Rep. of South; 7Severance Hospital, Research Institute of Radiological Science, Yongse University College of Medicine, Seoul, Korea, Rep. of South; 8Department of Radiology, Seoul National University Hospital, Seoul, Korea, Rep. of South; 9Department of Radiology, Ajou University School of Medicine, Seoul, Korea, Rep. of South; 10Department of Surgery, Seoul National University Hospital, Seoul, Korea, Rep. of South; 11Department of Biostatistics, Korea University College of Medicine, Seoul, Korea, Rep. of South

THYROGLOBULIN DOUBLING-TIME (TGDT): ITS VALUE AS A PROGNOSTIC MARKER IN DIFFERENTIATED THYROID CANCER (DTC)
Shazia Fatima1, Sadaf Tufail Butt1, Mohammad Faheem1
1Nuclear 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 Houbrechts1, Jolien Van Houcke1, Veerle Darra1
1Laboratory 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 Virginie1, Lobyisheva Irina1, Balligand Jean-Luc1, Marie-Christine Many2, Desy Chantal1
1Ucl-Irec-Fath, Brussels, Belgium; 2Ucl-Irec/Ucl, Brussels, Belgium

10.30–10.45
THYROID HORMONE AND SKIN CANCER: A NOVEL MICRORNA21-D3 INTERPLAY REGULATES BASAL CELL CARCINOMA TUMORGENESIS
Daniela Di Girolamo1, Raffaele Ambrosio2, Maria Angela De Stefano1, Giuseppina Mancino1, Emery De Cicc1, Caterina Miro1, Domenico Salvatore4, Monica Dentice4
1University of Naples ‘Federico II’, Naples, Italy; 2Ircs Sdn, Naples, Naples, Italy; 3Department of Endocrinologia, University of Naples, Federico II, Napoli, Italy; 4Department of Clinical Medicine and Surgery, University of Naples ‘Federico II, Endocrinologia + Oncologia, Naples, Italy

10.45–11.00
THE MACROFOLLICULAR VARIANT OF PAPILLARY THYROID CANCER (MF-PTC): A BICENTRIC RETROSPECTIVE ANALYSIS OF 65 CASES
Carlotta Giani1, Joana Simões Pereira2, Pedro Marques2, Daniel Macedo2, Rita Santos2, Liborio Torregrossa3, Fulvio Basolo3, Rossella Elisei1, Valeriano Leite2
1Endocrine Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; 2Endocrinology Section, Instituto Português de Oncologia de Lisboa, Francisco Gentil, Lisbon, Portugal; 3Department 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 Barbato1, Maria Grazia Castagna1, Fabio Maino1, Raffaella Forleo1, Noemi Fralassi1, Furio Pacini1
1Department 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 Pieruzzi1, Loredana Lorusso1, Liborio Torregrossa2, Valeria Bottici1, Laura Agate1, Fulvio Basolo2, Gabriele Materazzi1, Paolo Viti1, Eleonora Molinaro1, Rossella Elisei1
1Endocrinology Section, Department of Medical and Experimental Medicine, University of Pisa, Pisa, Italy; 2Department 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
Ki-Hoon Kim1, Younghen Lee2, Dong Gyu Na3, Jung Hwan Baek4, So Lyung Jung5, Sun-Won Park6, Jinna Kim7, Tae Jin Yun8, Eun Joo Ha9, Kyung-Sook Yang10
1Seoul National University Hospital, Seoul, Korea, Rep. of South; 2Department of Radiology, Seoul National University Hospital, Seoul, Korea, Rep. of South; 3Department of Radiology, Human Medical Imaging and Intervention Center, Seoul, Korea, Rep. of South; 4Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; 5Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South; 6Borame Medical Center, College of Medicine, Seoul National University, Seoul, Korea, Rep. of South; 7Severance Hospital, Research Institute of Radiological Science, Yongse University College of Medicine, Seoul, Korea, Rep. of South; 8Department of Radiology, Seoul National University Hospital, Seoul, Korea, Rep. of South; 9Department of Radiology, Ajou University School of Medicine, Seoul, Korea, Rep. of South; 10Department of Surgery, Seoul National University Hospital, Seoul, Korea, Rep. of South; 11Department 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 Fatima1, Sadaf Tufail Butt1, Mohammad Faheem1
1Nuclear Medicine, Oncology & Radiotherapy Institute (Nori), Islamabad, Pakistan
10.45–11.00  
**THYROID HORMONE TRANSPORTERS IN XENOPUS AND THEIR SUSCEPTIBILITY TO XENOBIOTICS**  
Bilal Mughal, Michelle Leemans, Lindsey Marshall, Sébastien Le Mével, Jean-Baptiste Fini, Barbara Demeneix  

11.00–11.15  
**ANEMIA IN PATIENTS WITH RESISTANCE TO THYROID HORMONE ALPHA: A ROLE OF TRΑ IN HUMAN ERYTHROPOIESIS**  
Anja van Gucht, Marcel Meima, Carla Moran, Maura Agostini, Anna Tylik-Szymanska, Małgorzata Krawiecka – Walasek, Krystyna Chrzanoswka, Aleksandra Efthymiadou, Dionisos Chrysis, Korcan Demir, W. Edward Visser, Theo Visser, Thamar Van Dijk, V. Krishna Chatterjee, Robin Peeters  
1Erasmus Medical Center, Thyroid Laboratory, Department of Internal Medicine, Rotterdam, Netherlands; 2Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; 3Metabolic Research Laboratories, Addenbrooke’s Hospital, Cambridge, UK; 4Metabolic Research Laboratories, Cambridge, UK; 5The Children’s Memorial Health Institute, Warsaw, Poland; 6The Children’s Memorial Health Institute, Warsaw, Poland; 7Department of Pediatrics, Medical School, University of Patras, Patras, Greece; 8Division of Pediatric Endocrinology, Dr. Behcet Uz Children’s Hospital, Izmir, Turkey; 9Erasmus Medical Center, Rotterdam, The Netherlands; 10Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; 11Department of Cell Biology, Erasmus University Medical Center, Rotterdam, The Netherlands; 12Erasmus University Medical Center, Rotterdam, The Netherlands

11.15–11.30  
**THE T3 RECEPTOR TRΑ1 INTERACTOME**  
Marcel Meima, Karm Wejaphikul, W. Edward Visser, Theo M. Luider, Theo Visser, Robin Peeters  
1Erasmus Medical Center, Thyroid Laboratory, Department of Internal Medicine, Rotterdam, Netherlands; 2Erasmus Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; 3Erasmus Medical Center, Rotterdam, The Netherlands, Erasmus University Medical Center, Rotterdam, The Netherlands; 4Erasmus University Medical Center, Rotterdam, The Netherlands; 5Erasmus University Medical School, Rotterdam, Netherlands; 6Erasmus Medical Center, Rotterdam, The Netherlands

11.30–11.45  
**EFFECT OF THYROID HORMONE ON GENE EXPRESSION IN HUMAN TRΑLPHA-EXPRESSING CELLS**  
Elske Massolt, Selmar Leeuwenburgh, Sigrid Swagemakers, Mirjam van den Hout-van Vroonhoven, Boen L.R. Kam, Pim Burger, Peter van der Spek, Wilfred F. van Ijcken, Theo Visser, Robin Peeters, W. Edward Visser  
1Erasmus MC, Endocrinology, Rotterdam, Netherlands; 2Erasmus MC, Internal Medicine, Rotterdam, Netherlands; 3Erasmus MC, Bioinformatics, Rotterdam, Netherlands; 4Erasmus MC, Center for Biomics, Rotterdam, Netherlands; 5Erasmus MC, Department of Nuclear Medicine, Rotterdam, Netherlands; 6Erasmus MC, Department of Surgery, Rotterdam, Netherlands; 7Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; 8Erasmus University Medical Center, Rotterdam, The Netherlands, Rotterdam, Netherlands; 9Erasmus Medical Center, Rotterdam, The Netherlands

11.45–12.00  
**DISTINCT MOLECULAR FEATURES AT L-TYPE AMINO ACID TRANSPORTER 2 DETERMINE DIFFERING THYROID HORMONE INFUX AND EFFLUX PROFILES**  
Katrin Manuela Hinz, Dominik Neef, Gerd Krause  
1Leibniz-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

**Room 14**  
**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

Room 13+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 Lisitzsky 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 Carle1, Peter Laurberg2, Rudi Steffensen3, Jens Faber4,
Birte Nygaard5
1Department of Endocrinology, Aalborg University Hospital,
Aalborg, Denmark; 2Aalborg University Hospital, Aalborg
University, Aalborg, Denmark; 3Department of Clinical
Immunology, Aalborg University Hospital, Aalborg, Denmark;
4Herlev University Hospital, Faculty of Health and Medical
Sciences, University of Copenhagen, Herlev, Denmark;
5Department 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 Sørensen1, Torquil Watt2, Helle Døssing3,
Laszlo Hegedüs4, Steen Joop Bonnaema 5, Christian Godballe6
1Odense University Hospital, Department of Orl – Head and
Neck Surgery, Department of Clinical Research, Faculty of
Health Sciences, University of Southern Denmark, Odense
C, Denmark; 2Department of Endocrinology, Copenhagen
University Hospital Rigshospitalet, Denmark, Department of
Endocrinology, Herlev Hospital, University of Copenhagen,
Copenhagen, Denmark; 3Department of Orl – Head and Neck Surgery, Odense,
Denmark; 4Department of Endocrinology and Metabolism,
Odense University Hospital, Department of Clinical Research,
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-Johansen1, Thomas Brix2, Bo Abrahamsen3, Laszlo Hegedüs4
1Department of Endocrinology, Odense University Hospital, University of Southern Denmark, Odense C, Denmark; 2Department of Endocrinology, Odense University Hospital, Odense C, Denmark; 3Holbæk Hospital, Department of Medicine, Open, University of Southern Denmark, Holbæk, Denmark; 4Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

THE ASSOCIATION BETWEEN NEONATAL BIRTH DEFECTS AND EARLY PREGNANCY USE OF ANTITHYROID DRUGS
Tae Hyuk Kim1, Gi Hyeon Seo2, Yoon Young Cho1, Sun Wook Kim1, Jee Hoon Chung3
1Samsung Medical Center, Seoul, Korea, Rep. of South; 2Health Insurance Review and Assessment Service, Seoul, Korea, Rep. of South; 3Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Seoul, Korea, Rep. of South

IS THERE AN ASSOCIATION BETWEEN GRAVES’ DISEASE, WITHOUT ORBITOPATHY, AND GLAUCOMA? RESULTS FROM A DANISH NATIONWIDE REGISTER-BASED STUDY
Frans Brandt1, Marianne Thvilum2, Thomas Brix3, Laszlo Hegedüs4
1Hospital of Southern Jutland, Department of Internal Medicine, Sønderborg, Denmark; 2Odense University Hospital, Department of Endocrinology and Metabolism, Odense C, Denmark; 3Department of Endocrinology, Odense University Hospital, Odense C, Denmark; 4Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

THE INTERRELATION BETWEEN HYPOTHYROIDISM AND GLAUCOMA: EVIDENCE FROM A DANISH NATIONWIDE REGISTER-BASED STUDY
Marianne Thvilum1, Frans Brandt2, Thomas Brix3, Laszlo Hegedüs4
1Odense University Hospital, Department of Endocrinology and Metabolism, Odense C, Denmark; 2Hospital of Southern Jutland, Department of Internal Medicine, Sønderborg, Denmark; 3Department of Endocrinology, Odense University Hospital, Odense C, Denmark; 4Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

RADIOFREQUENCY ABLATION: AN EFFECTIVE AND LONG-LASTING TREATMENT FOR THYROID NODULES: RESULTS AT 3 YEARS FOLLOW-UP FROM A SINGLE CENTER
Francesca Garino1, Maurilio Deandrea1, Alberto Mormile1, Paolo Piero Limone1
1Department of Endocrinology, Diabetes and Metabolism, Ao Mauriziano, Turin, Italy

THYROXINE TREATMENT IN OVERWEIGHT AND OBESE HYPOTHYROID PATIENTS
Camilla Virili1, Silvia Capriello1, Maria Giulia Santaguida1, Miriam Cellini1, Nunzia Brusca1, Lucilla Gargano2, Marco Centanni3
1Sapienza University of Rome, Dept of Medico-Surgical Sciences and Biotechnologies, Latina, Italy; 2Ausl Latina, Uoc Endocrinologia, Latina, Italy

GENETIC HETEROGENEITY OF THYROID CANCER
Michela Perrino1, Carla Colombo1, Marina Muzza2, Valentina Cirello2, Laura Fugazzola3
1Department of Clinical Sciences and Community Health, University of Milan, Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Italy; 2Dep of Clinical Sciences, Milan, Italy; 3Department 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, Clara Ugolini, David Viola, Eleonora Molinaro, Laura Agate, Antonio Matrone, Fulvio Basolo, Paolo Vitti, Rossella Elisei, Cristina Romei
1Endocrinology Section, Department of Medical and Experimental Medicine, University of Pisa, Pisa, Italy;
2Department 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, Dorota Kula, Michał Swierniak, Jadwiga Zebrańska-Gala, Michał Jarzab, Dogmara Rusinek, Zbigniew Puch, Aleksandra Kropinska, Barbara Jarzab
1Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice, Poland; 2Medical University of Warsaw, 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, Marina Muzzà, Michela Perrino, Valentina Ciriello, Maria Proverbio, Laura Fugazzola
1Department of Clinical Sciences and Community Health, University of Milan, Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Italy; 2Department of Clinical Sciences, Milan, Italy; 3Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; 4Department 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-Sandra Petrulea, Theo S. Plantinga, Marije Oosting, Leon A.B. Joosten, Jan W.A. Smit, Doina Piciu, Romana T. Netea-Maier, Carmen E. Georgescu
1Department of Endocrinology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania;
2Department of Pathology, Radboud University Medical Centre, Nijmegen, Netherlands; 3Department of Internal Medicine, Radboud University Medical Centre, Nijmegen, Netherlands; 4Department of Internal Medicine and Division of Endocrinology, Radboud University Medical Centre, Nijmegen, Netherlands; 5Oncology Institute, Cluj-Napoca, Romania

17.15–17.30
GERMLINE AND SOMATIC DICER1 MUTATIONS IN FAMILIAL PAPILLARY THYROID CARCINOMA
César Lumbreras, María Jesús Chueca Guindulain, Laura Arribas Carreira, Rajdee de Randamie, Ángel Alonso Sánchez, Pilar Fernández Seara, Sara Berrade Zubiri, Emma Anda Apiñariz, Rita María Regojo Zapata, Marta Mendiola Sabio, Jose Moreno
1Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Igemm), La Paz University Hospital, Autonomous University of Madrid, Madrid, Spain; 2Pediatric Endocrinology Service, Navarra Hospital Center, Pamplona, Spain; 3Genetics Service, Navarra Hospital Center, Pamplona, Spain; 4Anatomic Pathology Service, Navarra Hospital Center, Pamplona, Spain; 5Endocrinology and Nutrition Service, Navarra Hospital Center, Pamplona, Spain; 6Anatomic Pathology Service, La Paz University Hospital, Madrid, Spain; 7Molecular 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, Ellen Johansson, Shawn Liang, Mikael Nilsson
1Sahlgrenska Cancer Center, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden; 2Sahlgrenska 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, Soo Young Kim, Hyukjun Yun, Hyeung Kyoo Kim, Bup-Woo Kim, Yong Sang Lee, Hang-Seok Chang, Cheong Soo Park
1Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South
Monday, 5th September 2016

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 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 Bartalena¹, Giovanni Veronesi², Gerassimos Krassas³,
Wilmar Wiersinga⁴, Claudio Marocco⁵, Mario Salvito⁶,
Chantal Daumerie⁷, Claire Bournaud⁸, Matthias Stahl⁹,
Lorenza Sassi², Claudio Azzolini², Kostas Boboridis⁹,ⁱ⁰,
Maarten Mourits¹¹, Maarten Soeters¹¹, Lelio Baldeschi¹²,
Marco Nardi¹³, Nicola Curró¹⁴, Antonella Boschi¹⁵,¹⁶,
Martine Bernard¹⁷, Georg von Arx¹⁹, Petros Perros¹⁷,¹⁸,
George J. Kahaly³⁸
¹University of Insurbia, Varese, Italy; ²University of Insurbia,
Varese, Italy; ³Panagia Hospital, Thessaloniki, Greece;
⁴Academic Medical Center, Amsterdam, Netherlands;
⁵Department of Clinical and Experimen, University of Pisa,
Pisa, Italy; ⁶Dipartimento Scienze Mediche, Endocrine
Unit, Fondazione Ircss Cà Grande, Milano, Italy; ⁷Cliniques
Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium;
⁸Lyon University, Lyon, France; ⁹Olten Spital, Olten,
Switzerland; ¹⁰Ahepa Hospital, Thessaloniki, Greece;
¹¹Academic Medical Center, University of Amsterdam,
Amsterdam, Netherlands; ¹²Université Catholique de
Louvain, Brussels, Belgium; ¹³University of Pisa, Lucca, Italy;
¹⁴Ophthalmology, Fondazione Ircss Cà Grande, Milan, Italy;
¹⁵University of Lyon, Lyon, France; ¹⁶Zentrum für Endokrine
Orbitopathie, Olten, Switzerland, ¹⁷Freeman Hospital,
Newcastle-Upon-Tyne, UK; ¹⁸Johannes Gutenberg University
Medical Center, Mainz, Germany

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

Oral Sessions – Monday

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10.15–10.30
**SIGHT-THREATENING GRAVES’ ORBITOPATHY: EXPERIENCE OF THE MULTIDISCIPLINARY THYROID-EYE CONSULTATION OF THE UNIVERSITY HOSPITAL IN TOULOUSE, FRANCE**

Blandine Tramunt, Philippe Imbert, Solange Grunenwald, Franck Boutault, Philippe Caron

1 Service D’endocrinologie et Maladies Métaboliques, Chu Larrey, Toulouse, France; 2Service D’ophtalmologie, Clinique du Parc, Toulouse, France; 3 Chu Larrey, Toulouse Cedex 9, France; 4 Service de Chirurgie 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, Christian Wüster, Michael Kanitz, George J. Kohaly

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, Poupak Fallahi, Giulia Santaguida, Camilla Virili, Ilaria Ruffilli, Francesca Ragusa, Marco Centanni, Alessandro Antonelli

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, Camilla Virili, Ilenia Gatto, Giorgio Mangino, Ilaria Stramazzo, Marco Centanni

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; 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, Cecile Gharder, Saheb Sami, Natacha Jumentier, Fatima Kharcha, Didier Lemesle, Salwa Baki, Nassibe Beqhadji, Laurence Leenhardt, Camille Buffet, Christophe Tresallet

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, Irene Campi, Guia Vannucchi, Danila Covelli, Simona Simonetta, Nicola Curro

1 Dipartimento Scienze Mediche, Endocrine Unit, Fondazione Ircss Ca Granda, Milano, Italy; 2 Fondazione Ircss Ca’ Granda, Endocrine Unit, Milan, Italy; 3 Endocrine Unit, Fondazione Policlinico Ircss, Milano, Italy; 4 Graves’ Orbitopathy Unit, Endocrinology, Fondazione Ca’ Granda Ircss, University of Milan, Medical Sciences, Milano, Italy; 5 Ophthalmology Unit, Fondazione Ircss Ca’ Granda, Milan, Italy; 6 Ophthalmology, Fondazione Ircss Ca’ Granda, Milan, Italy

11.45–12.00
**GRAVES ORBITOPATHY AFFECTS VISUAL FUNCTION AND APPEARANCE IN DIFFERENT MANNERS**

Danilo Villagelin, Roberto Bernado Dos Santos, João Hamilton Romaldini, Ana Paula Comarella, Natassia Bufalo, Karina Colomberra Peres, Laura Ward

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
GENETIC ANALYSIS OF ANAPLASTIC THYROID CANCER
Naveen Ravi¹, Eleanor Woodward¹, Andrea Biloglav¹, Lars Ekblad², Johan Wennerberg², Kajsa Paulsson³
¹Bmc C13, Lund University, Lund, Sweden; ²Lund University, Lund, Sweden; ³Bmc C13, Lund University, Lund, Sweden

EVALUATION OF THE ANTINEOPLASTIC ACTIVITY OF VANDETANIB, AND LENVATINIB IN PRIMARY ANAPLASTIC THYROID CANCER CELLS, OBTAINED FROM FINE NEEDLE ASPIRATION
Silvia Martina Ferrari¹, Poupak Fallahi¹, Concettina La Motta², Gabriele Materazzi³, David Galleri³, Alessandro Antonelli¹
¹University of Pisa, Pisa, Italy; ²Department of Pharmaceutical Science, University of Pisa, Pisa, Italy; ³Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy

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 Kim¹, Ki Cheong Park¹, Soo Young Kim¹, Hyeung Kyoo Kim¹, Bup-Woo Kim¹, Yong Sang Lee¹, Hang-Seok Chang¹, Cheong Soo Park¹
¹Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

TREATMENT OUTCOMES OF SORAFENIB AND LENVATINIB FOR ADVANCED THYROID CANCERS AND ANAPLASTIC THYROID CANCERS
Hiroyuki Iwasaki¹, Hiroyuki Nakayama², Nobuyasu Suganuma³, Tatsuya Yoshida¹, Takashi Yamanaka¹, Shinsuke Hatori³, Satoru Shimizu¹
¹Department of Breast and Endocrine Surgery, Kanagawa Cancer Center, Yokohama, Japan; ²Department of Surgery, Yokohama City University School of Medicine, Yokohama, Japan; ³Department of Surgery, Hiratsuka Kyosai Hospital, Hiratsuka, Japan

CALCITONIN RECEPTOR (CTR) EXPRESSION IN MEDULLARY THYROID CANCER (MTC) AND POSSIBLE CLINICAL IMPLICATIONS
Virginia Cappagli¹, Catarina Soares Potes², Luciana Bueno Ferreira³, Catarina Eloy¹, Cristina Romei¹, Rossella Elisei¹, Manuel Sobrinho-Simões³, Peter J. Wookey⁴, Paula Soares³
¹Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; ²Instituto de Investigação e Inovação Em Saúde, Universidade Do Porto, Porto, Portugal; ³Institute of Molecular Pathology and Immunology of the University of Porto (Ipatimup), Porto, Portugal; ⁴Department of Medicine at Austin Health, University of Melbourne, Parkville, Vic., Australia

THE MUTATION PROFILE OF MEDULLARY THYROID CARCINOMA CAN BE DIFFERENT IN PRIMARY AND METASTATIC TISSUES
Cristina Romei¹, Francesca Casella¹, Alessia Tacito¹, Raffaele Ciampi¹, Eleonora Molinari¹, Laura Agate¹, Valeria Bottici¹, Antonio Matrone¹, Rossella Elisei¹
¹Section of Endocrinology, Department of Clinical and Experimental Medicine, University of Pisa, Department of Endocrinology, Pisa, Italy

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 Anagnostou¹, Katerina Saltiki², Vasiliki Vasilou², Constantinos Tsigkos², Lamprini Papanastasiou², Maria Alevizaki²
¹Endocrine Unit, Dept Medical Therapeutics, Alexandra Hospital, Athens University School of Medicine, Athens, Greece; ²Endocrine Unit, Dept Medical Therapeutics, Alexandra Hospital, Athens University School of Medicine, Athens, Greece

THE ASSOCIATION BETWEEN TERT PROMOTER MUTATIONS AND MORTALITY IN PATIENTS WITH THYROID CANCER
Tae Hyuk Kim¹, Youngnam Kim¹, Hyein Kim¹, Ho-Su Kim¹, Sun Wook Kim¹, Jae Hoon Chung¹
¹Samsung Medical Center, Seoul, Korea, Rep. of South; ²Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Rep. of South
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.

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**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 Nies1, Mariëlle S. Klein Hesselink1, Gea A. Huizinga2, Esther Sulkers2, Adrienne H. Brouwers3, Johannes G.M. Burgerhof4, Eveline W.C.M. van Dam5, Bas Havekes6, Marry M. van den Heuvel-Eibrink7, Eleonora P. M. Corssmit8, Leonien C.M. Kremer9, Romana T. Netea-Maier10, Heleen J.H. van der Pal11, Robin P. Peeters11, John T.M. Plukker12, Cécile M. Ronckers9, Hanneke M. van Santen13, Wim J.E. Tissing15, Thera P. Links1, Gianni Bocca16
1University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; 2University of Groningen, University Medical Center Groningen, Wenekebach Institute, School of...
15.30–15.45
DIASTOLIC DYSFUNCTION IS COMMON IN LONG-TERM SURVIVORS OF PEDIATRIC DIFFERENTIATED THYROID CARCINOMA

Marielle Klein Hesselink, Gianni Bocca, Yoran Hummel, Adrienne Brouwers, Johannes Burgerhof, Eveline van Dam, Jourik Gietema, Bas Havekes, Marry van den Heuvel-Eibrink, Eleonora Corssmit, Leontien Kremer, Romana Netea-Maier, Heleen van der Pal, Robin Peeters, John Plukker, Cecile Ronckers, Hanneke van Santen, Peter van der Meer, Thera Links, Wim Tissing

1Department of Endocrinology, University Medical Center Groningen, Groningen, Netherlands; 2Department of Pediatric Endocrinology, Erasmus Medical Center, Rotterdam, Netherlands; 3Department of Cardiology, University Medical Center Groningen, Groningen, Netherlands; 4Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, Netherlands; 5Department of Endocrinology, University Medical Center Groningen, Groningen, Netherlands; 6Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands; 7Department of Internal Medicine, VU University Medical Center, Amsterdam, Netherlands; 8Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands; 9Department of Internal Medicine, VU University Medical Center, Amsterdam, Netherlands; 10Department of Pediatric Oncology, Sophia Children’s Hospital, Rotterdam, Netherlands; 11Department of Internal Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, Netherlands; 12Department of Pediatric Oncology, Emma Children’s Hospital, Academic Medical Center, Amsterdam, Netherlands; 13Department of Pediatric Oncology, Emma Children’s Hospital, Academic Medical Center, Amsterdam, Netherlands; 14Department of Pediatric Oncology, Erasmus Medical Center, Rotterdam, Netherlands; 15Department of Pediatric Oncology, University Medical Center Groningen, Groningen, Netherlands; 16Division of Endocrinology, Cervello Hospital, Palermo, Italy; 17Department of Clinical and Experimental Medicine, University of Pisa, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; 18Center for Outcomes Research and Clinical Epidemiology, Pescara, Italy.
GLUCOSE-COATED SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES PREPARED BY METAL VAPOUR SYNTHESIS ARE ELECTIVELY INTERNALIZED IN THYROID TUMORS LINES EXPRESSING GLUT1 TRANSPORTER

Daniele Barbaro, Lorenzo Di Bari, Valentina Gandin, Claudio Evangelisti, Giovanni Vitulli, Cristina Marzano, Anna M. Ferretti, Piero Salvadori

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

INHIBITION OF ERK DIMERIZATION BLOCKS THYROID TUMOR PROGRESSION

Miguel Zaballos, Adrián Acuña-Ruiz, Garcialo Riesco-Eizaguirre, Pilar Crespo, Pilar Santisteban

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

16.45–17.00

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

Daniele Barbaro, Lorenzo Di Bari, Valentina Gandin, Claudio Evangelisti, Giovanni Vitulli, Elena Schiavi, Cristina Marzano, Anna M. Ferretti, Piero Salvadori

1 Spedali Riuniti di Livorno, Endocrinology, Livorno, Italy; 2 Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases and Laboratory of Endocrine and Metabolic Research, Iccrs Istituto Auxologico Italiano, Milan, Italy; 3 Endocrine Unit, Fondazione Iccrs Ca’ Granda, Milan, Italy; 4 Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

16.45–17.00

IMPAIRED MATERNAL THYROID HORMONE RECEPTOR A1 SIGNALING PROGRAMS OFFSPRING METABOLISM

Rebecca Oelkrug, Milica Vujovic, Lisbeth Harder, Beate Herrmann, Sogol Gachkar, Jens Mittag

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 Fini1, Bilal Mughal1, Sébastien Le Mével1, Michelle Leemans1, Mélodie Lettmann1, Petra Spirkhonzlova1, Pierre Affatatici2, Jean-Stéphane Joly2, Barbara Demeneix3
1Thyroid Molecular Laboratory, Institute for Medical and Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary; 2Institute of Experimental Medicine, Lab Molecular Cell Metabolism, Budapest, Hungary; 3Genomic Paris Centre, Institut de Biologie de l'Ecole Normale Supérieure (Ibens), Paris, France; 4Univ 8251 Team Coffee – Université Paris Diderot – Paris 7, U.F.R. Sciences du Vivant Bâtiment Buffon, Paris Cedex 13, France; 5Academic Medical Centre, Amsterdam, Netherlands; 6University of Pisa, Department of Pathology, Pisa, Italy; 7Scuola Superiore Sant'Anna, Pisa, Italy; 8Cnr Neuroscience of Clinical Chemistry, Laboratory of Endocrinology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 9Academic Medical Centre, Amsterdam, Netherlands; 10Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary; 11University of Pisa, Department of Pathology, Pisa, Italy; 12University of Pisa, Pisa, Italy

15.30–15.45
EPITHELIAL BMP-SMAD1/5 SIGNALING AND ENDOTHELIAL CELLS ARE REQUIRED FOR THYROID FOLLICLE DEVELOPMENT
Mylah Villacorte1, Anne-Sophie Delmarcelle1, Manon Lernoux1, Malé Bouquet1, Pascale Lemoine1, Jennifer Bolsee1, Lieve Umans2, Susana Chua de Sousa Lopez3, Patrick Van Der Smissen4, Takako Sasaki5, Guido Bommer6, Patrick Henriët7, Samuel Retefoff8, Frédéric Lemaigret9, An Zwijsen10, Pierre Coutroy11, Christophe Pierreux12
1De Duve Institute, Brussels, Belgium; 2Vib-Kul, Leuven, Belgium; 3Lumc, Leiden, Netherlands; 4University of Pisa, Pisa, Italy; 5University of Pittsburgh Medical Center, Pittsburgh, Pa., USA; 6University of Rochester Medical Center, Rochester, Minn., USA; 7Scuola Superiore Sant'Anna, Pisa, Italy; 8Cnr Neuroscience Institute, Pisa, Italy; 9Saimal Department, Sapienza, Rome, Italy; 10Mnhn/Cnrs Umr7221, Paris, France; 11Umr Cnrs 7221, Département Régulations, Développement et Diversité Moléculaire, Muséum National D’histoire Naturelle, Evolutions des Régulations Endocriniennes, Paris, France

15.45–16.00
CENTRAL HYPOTHYROIDISM AND BIALLELIC DEFECT NEAR THE D/E/RY MOTIF OF THE TRHR GENE
Marta García1, Jesús González de Buitrago2, Leonardo Pardo2, Patricia M. Hinkle4, Jose Moreno5
1Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Ingenn), La Paz University Hospital, Autonomous University of Madrid, Madrid, Spain; 2Department of Pediatrics, San Pedro de Alcántara Hospital, Cáceres, Spain; 3Computational Medicine Laboratory, Biostatistics Unit, Faculty of Medicine, Autonomous University of Barcelona, Barcelona, Spain; 4Department of Pharmacology and Physiology, University of Rochester Medical Center, Rochester, Minn., USA; 5Thyroid Molecular Laboratory, Institute for Medical and Molecular Genetics (Ingenn), 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 Dechert1, Isabelle Seugnet2, Jeremy Terrien3, Emmely De Vries4, Anita Boelen4, Fekete Csaba5, Balazs Gereben5, Ducas Bertrand6, Serge Luquet7, Marie- Stéphanie Clerget-Froidevaux10, Barbara Demeneix11
1Muséum National D’histoire Naturelle, Umr Cnrs 7221, Paris, France; 2Umr 7221 ‘Evolution of Endocrine Regulations’, National Museum of Natural History, Paris, France; 3Team Bioadapt Umr Cnrs/Mnhn 7179, Brunoy, France; 4Department of Clinical Chemistry, Laboratory of Endocrinology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 5Academic Medical Centre, Amsterdam, Netherlands; 6Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary; 7Institute of Experimental Medicine, Lab Molecular Cell Metabolism, Budapest, Hungary; 8Genomic Paris Centre, Institut de Biologie de l’Ecole Normale Supérieure (Ibens), Paris, France; 9Umr 8251 Team Coffee – Université Paris Diderot – Paris 7, U.F.R. Sciences du Vivant Bâtiment Buffon, Paris Cedex 13, France; 10Mnhn/Cnrs Umr7221, Paris, France; 11Umr 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 Falzaccoppa1, Claudia Mangiolaro2, Camilla Virili3, Maria Giulia Santaguidia4, Viviana Moresi5, Marco Centanni6
1Medical Surgical Sciences and Biotechnologies Department, Sapienza, University of Rome, Pasteur Institute, Italy, Rome, Italy; 2Pasteur Institute, Italy, Medical Surgical Sciences and Biotechnologies, Sapienza, Rome, Italy; 3Dept of Experimental Medicine ‘Sapienza’ University of Rome, Latina, Italy, Dept Medico-Surgical Sciences and Biotechnologies, Rome, Italy; 4Medical Surgical Sciences and Biotechnologies Department, Medico-Surgical Sciences and Biotechnologies, Latina, Italy; 5Saimal Department, Sapienza, Rome, Italy; 6Sapienza 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 Ziros1, Dionysios Chartoumpekis2, Ioannis Habeos3, Adam Smith4, Ana Claudia Marques4, Gerasimos Sykiotis1
1Lausanne University Hospital, Lausanne, Switzerland; 2University of Pittsburgh Medical Center, Pittsburgh, Pa., USA; 3University of Patras Medical School, Patras, Greece; 4University 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 Accorinni1, Chiara Criscuolo2, Martina Sabatini3, Riccardo Donzelli4, Alessandro Saba5, Nicola Origgia6, Riccardo Zucchi5
1Scuola Superiore Sant’Anna, Pisa, Italy; 2Cnr Neuroscience Institute, Pisa, Italy; 3Dept. of Pathology, University of Pisa, Pisa, Italy; 4University of Pisa, Department of Pathology, Pisa, Italy; 5University 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)
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 Matrone¹, Alessio Faranda², Eleonora Molinaro³, Laura Agate², David Viola³, Laura Valerio³, Carlotta Giani³, Liborio Torregrossa³, Paolo Piaggi³, Paolo Vitti³, Rossella Elisei³

¹University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy; ²University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy; ³University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy; ⁴Department of Surgical Pathology, Medical, Molecular and Critical Area – Unit of Pathological Anatomy, Pisa, Italy; ⁵Phoenix 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 Kwon¹, Min Ji Jeon¹, Won Gu Kim¹, Mijin Kim¹, Suyeon Park¹, Dong Eun Song¹, Tae-Yon Sung¹, Jong Ho Yoon¹, Suck Joon Hong¹, Tae Yong Kim¹, Young Kee Shong¹, Won Bae Kim¹

¹Asan 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 THYRCYTES AND PERIPHERAL BLOOD

Tanja Diana¹, Andreas Daiber², Matthias Oelze², Paul Stamm³, Michael Kanitz¹, Susanne Neumann¹, George J. Kahaly¹

¹Johannes Gutenberg University Medical Center, Mainz, Germany; ²Molecular Cardiology, Johannes Gutenberg University Medical Center, Mainz, Germany; ³NIH, NIDDK, USA

09.15–09.30
MUTATIONS IN TBL1X AS A NOVEL CAUSE OF FAMILIAL CENTRAL HYPOPHYOIDISM

Charlotte Heinen¹, Monique Losekoot², Yu Sun³, Peter Watson³, Louise Fairall³, Sjoerd Joustra³, Nitash Zwaveling-Soonawala¹, Wilma Oostdijk³, Erica van den Akker³, Marielle Alders¹, Gijs Santen², Rick van Rijn¹, Wouter Dreschler¹, Olga Surovtseva¹, Nienke Biermasz², Raoul Hennekam¹, Jan Maarten Wit², John Schwabe³, Anita Boelen¹, Paul van Totsenburg¹, Eric Fliers⁵

¹Academic Medical Centre, Amsterdam, Netherlands; ²Leiden University Medical Center, Leiden, Netherlands; ³Henry Wellcome Laboratories of Structural Biology, University of Leicester, Leicester, UK; ⁴Erasmus MC, Rotterdam, Netherlands; ⁵Amc, 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 Andersen¹, Jørn Olsen², Peter Laurberg³

¹Aalborg University Hospital, Aalborg, Denmark; ²Aarhus University Hospital, Aarhus University, Aarhus, Denmark; ³Aalborg University Hospital, Aalborg University, Aalborg, Denmark
TPO-ANTIBODY POSITIVE WOMEN HAVE AN IMPAIRED RESPONSE TO HCG WHICH UNDERLIES THEIR HIGHER RISK OF PREMATURE DELIVERY

Tim Korevaar1, Victor Pop2, Layal Chaker3, Yolanda de Rijke4, Maarten Broeren5, Vincent Jaddoe6, Marco Medicì6, Eric Steegers7, Theo Visser8, Henning Tiemeier4, Robin Peeters4
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 Erasmus Medical Center, Endocrinology, Rotterdam, Netherlands; 6 Erasmus University MC, Rotterdam, Netherlands; 7 Erasmus University Medical School, Rotterdam, Netherlands

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

Mads Petersen1, Inge Bülow Pedersen1, Allan Carlé1, Nils Knudsen2, Stine Linding Andersen3, Lars Ovesen4, Lone Banke Rasmussen5, Torben Jørgensen1, Betina Heinsbæk Thuesen1, Hans Perrild2, Peter Laurberg1
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

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

Charlotte Andersson1, Thomas Brix2, Laszlo Hegedüs1
1 Department of Endocrinology and Metabolism, Odense University Hospital, Department of Experimental Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; 2 Department of Endocrinology, Odense University Hospital, Odense C, Denmark

ELUCIDATING THE THERAPEUTIC POTENTIAL OF THYROID HORMONE ANALOGS IN MCT8 DEFICIENCY

Jiesi Chen1, Eva Salveridou2, Heike Heuer3
1 Leibniz Institute for Environmental Medicine (lif), Leibniz Institute for Aging, Fritz Lipmann Institute (fli), Düsseldorf, Germany; 2 Düsseldorf, Germany; 3 Leibniz Institute for Environmental Medicine (lif), Leibniz Institute for Aging, Fritz Lipmann Institute (fli), Düsseldorf, Germany

A FUNCTIONAL ROLE FOR THE DEIODINASE ENZYMES IN NEUTROPHILS AND MACROPHAGES

Anne van der Spek1, Aldona Karaczy2, Elena Martinez2, Olga Surovtseva2, Bernadine Snell3, Eric Fliers4, Arturo Hernandez2, Anita Boelen5
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

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

Emmely de Vries1, Marte Molenaars1, Olga Surovtseva2, Evita Belegri1, Albert Van Wijk1, Marinus Maas3, Eric Fliers1, Anita Boelen1
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

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

Federica Marelli1, Giuditta Rurale2, Federica Buna3, Franco Cotelli4, Luca Persani1
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 Bioscience, 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-Lamas¹, Garcilaso Riesco-Eizaguirre², Richard Gregory³, Pilar Santisteban⁴
¹IIB Alberto Sols, Madrid, Spain; ²Móstoles University Hospital, Móstoles, Spain; ³Boston Children’s Hospital, Dept of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, USA; ⁴Biomedical Research Institute, Biomedical Research Institute, Madrid, Spain

09.45–10.00
INCREASED GLOBAL DNA HYPOMETHYLATION IN METASTATIC AND DEDIFFERENTIATED THYROID CANCER
Esther Klein Hesselink¹, Carles Zafón², Nuria Villalmanzo³, Carmela Iglesias⁴, Bettien van Hemel⁵, Mariëlle Klein Hesselink¹, Didac Mauricio⁶, Manel Puig-Domingo⁷, Jordi Reverter⁸, Garcilaso Riesco-Eizaguirre⁹, Mercedes Robledo⁸, Thera Links¹, Mireia Jordà¹⁰
¹University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; ²Vall D’hebron University Hospital, Department of Endocrinology, Barcelona, Spain; ³Germans Trias i Pujol Health Sciences Research Institute (Igpt), Badalona, Barcelona, Spain; ⁴Vall D’hebron University Hospital, Department of Pathology, Barcelona, Spain; ⁵University of Groningen, University Medical Center Groningen, Department of Pathology, Groningen, Netherlands; ⁶Germans Trias i Pujol University Hospital, Department of Endocrinology and Nutrition, Badalona, Barcelona, Spain; ⁷Germans Trias i Pujol University Hospital, Department of Endocrinology and Nutrition, Badalona, Barcelona, Spain; ⁸University Hospital of Móstoles, Endocrinology and Nutrition Service, Madrid, Spain; ⁹Hereditary Endocrine Cancer Group, Spanish National Cancer Research Centre (Cnio), Madrid, Spain; ¹⁰Germans Trias i Pujol Health Sciences Research Institute (Igpt), 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
Kam Wejaphikul¹, Anja van Gucht², W. Edward Visser³, V. Krishna Chatterjee⁴, Theo Visser², Robin Peeters⁵, Marcel Meima¹
¹Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; ²Erasmus Medical Center, Thyroid Laboratory, Department of Internal Medicine, Rotterdam, Netherlands; ³Erasmus Medical Center, Rotterdam, Netherlands; ⁴Metabolic Research Laboratories, Addenbrooke’s Hospital, Cambridge, UK; ⁵Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands; ⁶Erasmus 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 Tesselaar¹, Thomas Crezee¹, Danny Gerrits², Otto Boerman², Henk Stunnenberg³, Mihai Gheorghe Netea⁴, Johannes Smid⁴, Romana Teodora Netea-Maier⁴, Theo Plantinga¹
¹Radboud University Medical Center, Department of Pathology, Nijmegen, Netherlands; ²Radboud University Medical Center, Department of Nuclear Medicine, Nijmegen, Netherlands; ³Radboud University Medical Center, Department of Molecular Biology, Nijmegen, Netherlands; ⁴Radboud University Medical Center, Department of Internal Medicine and Radboud Center for Infectious Diseases, Nijmegen, Netherlands; ⁵Radboud University Nijmegen Medical Centre, 463 Internal Medicine, Nijmegen, Netherlands; ⁶Radboud 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 Laurberg¹, Stine Linding Andersen², Peter Hindersson³, Ellen Nohr⁴, Jørn Olsen⁵
¹Aalborg University Hospital, Aalborg University, Aalborg, Denmark; ²Departments of Clinical Biochemistry and Endocrinology, Aalborg University Hospital, Aalborg, Denmark; ³Department of Clinical Biochemistry, North Jutland Regional Hospital, Hjørring, Denmark; ⁴Research Unit for Gynecology and Obstetrics, University of Southern Denmark, Odense, Denmark; ⁵Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark
11.15–11.30

**THYROID FUNCTION AND BRAIN IMAGING**

Layal Chaker¹, Lotte Cremers², Albert Hofman³, Mohammad Afzan Ikram⁴, Meike Vernooij², Robin Peeters⁵

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

11.30–11.45

**EFFECT OF THYROID HORMONES ON COGNITION AND BRAIN**

Anna Göbel¹, Marcus Heldmann², Martin Göttlich², Georg Brabant³, Anna-Luise Dirk³, Relana Nieberding³, Rene Goerges³, Thomas Münte⁴

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

11.45–12.00

**MATERNAL HYPOTHYROIDISM CONTRIBUTES TO ATYPICAL HIPPOCAMPAL FUNCTION IN HUMAN OFFSPRING**

Joanne Rovet¹, Victoria McLelland²

¹The Hospital for Sick Children, University of Toronto, Toronto, Ont., Canada; ²The 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 Manousou¹, Robert Eggertsen³, Lena Hultén⁴, Peter Jakobsson³, Lars Sjöström⁷, Per-Arne Svensson⁷, Helena Filipsson Nyström⁸

¹Department of Medicine at Kungälv Hospital, Institute of Medicine Sahlgrenska Academy, Gothenburg, Sweden; ²Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ³Mölnlycke Health Care Center, Mölnlycke, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ⁴Department of Endocrinology, Sahlgrenska University Hospital, Göteborg, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Borås, 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 Manousou¹, Lena Carlsson², Robert Eggertsen³, Lena Hultén⁴, Peter Jakobsson³, Lars Sjöström⁷, Per-Arne Svensson⁷, Helena Filipsson Nyström⁸

¹Department of Medicine at Kungälv Hospital, Institute of Medicine Sahlgrenska Academy, Gothenburg, Sweden; ²Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ³Mölnlycke Health Care Center, Mölnlycke, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ⁴Department of Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ⁵Department 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 (RTHβ)**

Irene Campi¹, Gabriella Cammarata², Stefania Bianchi Marzoli³, Davide Dazzi⁴, Alessandra Battori De Castello², Elena Giuliana Tarori⁴, Francesco Viola⁵, Luca Persani⁶, Paolo Beck-Peccoz⁵

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

12.45–13.00

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

Diana Albrecht¹, Till Ittermann², Michael Thamm³, Henry Völzke⁴

¹University Medicine Greifswald, Institute for Community Medicine, Greifswald, Germany; ²University Medicine Greifswald, Greifswald, Germany; ³Robert Koch-Institut, Berlin, Germany; ⁴Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany
11.00–11.15
**OXIDATIVE STRESS IN SKIN ADIPOCYTES FROM GRAVES’ PATIENTS**
Marie-Christine Many 1, Virginie Joris 2, Marigue Lancelot 1, Elliott Van Regemorter 1, Christine de Ville de Goyet 1, Marc de Bouronville 1, Antonella Boschi 6, Michel Mourad 5, Chantal Daumerie 2, Julie Craps 1
1 Ss/Mede/Irec/Ucl, Bruxelles, Belgium; 2 Ucl-Irec-Fath, 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, Chantal Daumerie 2, 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

11.30–11.45
**CHARACTERISTICS OF HYALURONAN AND PAI-1 EXPRESSION IN CULTURES OF ORBITAL FIBROBLASTS**
Erika Galgoci 1, Florence Jeney 1, Annamaria Gazdag 1, Anna Maria Erdei 1, Mónika Kátó 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 Ferkert 1, Marc Nazare 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 3, Lanlan Zhao 3, Suxia Wang 2, Hong Zhang 2, Guizhi Lu 4, Yanming Gao 3, 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 2, Michel Mourad 5, 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 2, 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

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
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

Prize Ceremony and Closure

Chairpersons: Pilar Santisteban, Spain
Colin Dayan, UK
**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, Marenza Leo, Paolo Premoli, Giovanna Rotondo Dottore, Marialuisa Di Cera, Lorenzo Sassi, Paolo Vitti, Luigi Bartalena, Claudio Marconi, Michele Marino

1Department of Clinical And Experimental Medicine, Endocrinology, University of Pisa, Pisa, Italy; 2Department of Clinical and Experimental Medicine, Endocrinology, University of Insubria, Varese, Italy

**P1–01–02**  
**DIO2 POLYMORPHISMS ROLE IN GRAVES’ DISEASE AND GRAVES’ OPHTHALMOPYHATPATHY**

Ana Paula Comarella, Danilo Villagelin, Natassia Bufalo, Jessica Eufizianzio, Raquel Pereira Rios, Vittoria Arbulo Pitolo, Roberto Bernardo dos Santos, Joao Hamilton Romalndini, Laura Ward

1Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Brazil; 2Pont. Universidade Catolica Campinas, Campinas, Brazil; 3Pontifícia 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, Hyun Sook Hong

1Soonchunhyang University Bucheon Hospital, Bucheon-Si, Korea, Rep. of South

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

Grigoris Effraimidis, Pia Bükman Larsen, Mads Nybo, Lise Bathum, Lennart Friis-Hansen

1Internal Medicine Department, Endocrinology and Diabetes Section, Nykøbing F Hospital, Nykøbing F, Denmark; 2Department of Clinical Biochemistry, Næstved Hospital, Næstved, Denmark; 3Department of Clinical Biochemistry, Odense University Hospital, Odense, Denmark; 4Department 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, Till Ittermann, Matthias Nauck, Below Harald, Henry Völzke

1Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany; 2University Medicine Greifswald, Greifswald, Germany; 3Universitätsklinikum Greifswald, Greifswald, Germany; 4Institute of Hygiene and Environmental Medicine, Ernst Moritz Arndt University Greifswald, Germany, Greifswald, Germany; 5Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany

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

Elvira Masiello, Eleonora Bianconi, Flavia Magri, Giovanni Veronesi, Francesca Zerbinì, Margherita Gaiti, Emanuele Spreafico, Daniela Gallo, Paolo Premoli, Eliana Piantanida, Maria Laura Tanda, Marco Ferrarì, Luca Chiavari, Luigi Bartalena

1Dept. Clinical & Exp. Medicine, Varese, Italy; 2University of Insubria, Varese, Italy; 3University of Pavia, Pavia, Italy; 4University of Insubria, Varese, Italy; 5University of Insubria, Varese, Italy; 6Fondazione S. Maugeri, University of Pavia, Pavia, Italy

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

Stan Benjamens, W.J. Sluiter, M. Rienstra, I.C. Van Gelder, Thera Links

1University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; 2University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands
P1–01–09  IS CHROMOGRAIN A BIOMARKER FOR THYROID DYSFUNCTION?
Janna Zimmermann¹, Tanja Diana¹, Niklas Lohmann¹, Lukas Reuter¹, Michael Kanitz¹, George J. Kahaly¹
¹Johannes Gutenberg University Medical Center, Mainz, Germany

P1–01–10  SERUM 25-HYDROXYVITAMIN D IS ASSOCIATED WITH RECURRENCE OF GRAVES’ DISEASE
Hwa Young Ahn¹, Yun Joe Chung¹
¹Chung-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 Dyacenko¹, Andra Caragheorgheopol¹, Sergiu Stoica², Corin Badiu¹
¹National Institute of Endocrinology, Bucharest, Romania; ²Brain 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 Bath¹, Margaret Rayman²
¹University of Surrey, Guildford, UK; ²University of Surrey, Guildford, UK

P1–02–02  THE RELATIONSHIP BETWEENIODINE STATUS, THYROID FUNCTION, AND THYROGLOBULIN IN A COHORT STUDY OF UK PREGNANT WOMEN
Margaret Rayman¹, Sarah Bath¹, Victor Pop³, Victoria Furmidge-Owen¹, Maarten Broeren⁴
¹University of Surrey, Guildford, UK; ²University of Surrey, Guildford, UK; ³University of Tilburg, Tilburg, Netherlands; ⁴Maxima 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 Lao¹, Russell Ng¹
¹Department 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 Shinkov¹, Anna-Maria Borissova¹, Roussanka Kovatcheva¹, Jordan Vlahov¹, Lilia Dakovska¹, Iliana Atanassova¹
¹Medical 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
Małgorzata Trofimiuk-Muldner¹, Zbigniew Szybinski¹, Grzegorz Sokolowski¹, Monika Buzaik-Bereza³, Filip Gołkowski¹, Andrzej Lewiński², Arkadiusz Zygmunt³, Marek Ruchala³, Elżbieta Bandurska-Stankiewicz³, Krzysztof Sworczak³, Alicja Hubalewska-Dydejczyk⁴
¹Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; ²Polish Council for Control of Iodine Deficiency Disorders, Kraków, Poland; ³Department of Endocrinology, University Hospital in Krakow, Kraków, Poland; ⁴Chair and Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; ⁵Department of Endocrinology and Metabolic Diseases, the Polish Mother’s Memorial Hospital – Research Institute, Łódź, Poland; ⁶Department of Endocrinology and Metabolic Diseases, the Polish Mother’s Memorial Hospital – Research Institute, Łódź, Poland; ⁷Chair and Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poznań, Poland; ⁸Clinic of Endocrinology, Diabetology and Internal Medicine, Department of Internal Medicine, Faculty of Medical Sciences, University of Warmia and Mazury, Olsztyn, Poland; ⁹Chair and Department of Endocrinology and Internal Diseases, Medical University of Gdańsk, Gdańsk, Poland

P1–02–06  IODINE STATUS OF PREGNANT WOMEN RESIDING IN NORTHERN CYPRUS
Hasan Sav¹, Umut Mousa², Osman Koseoglulari², Murat Fikr Erdogan³
¹B Nalbantoglu Hospital, Department of Endocrinology and Metabolism, Lefkosa, Cyprus; ²B Nalbantoglu Hospital, Department of Endocrinology and Metabolism, Lefkosa, Cyprus; ³Ankara 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 Ursu1, Monica Livia Gheorghiu2, Irina Dumitrescu3, Mihaela Stanciu4, Dragos Popescu5, Corina Elena Delia6, Geanina Mirela Tomáš6, Ramona Aldea7, Corina Raducanu Lichiardopol8, Stefania Tudorache8, Mihaela Vasilie9, Claudia Podia-Igná9, Carmen Elena Georgescu10, Mariana Purice11
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 ‘Alessandrescu Rusescu’ National Institute of Endocrinology, Bucharest, Romania

P1–02–08 ASSESSING THE PROBLEM OF IODINE DEFICIENCY DISORDERS IN THE RUSSIAN FEDERATION
Nuriya Platonova1
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 Lee1, Bu Kyung Kim2, Shin Jun Lee3, So Young Ock3, Jee Yeong Jeong2, Young Sik Cho3
1 Kosin University College of Medicin, 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 Metreveli1
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 Fallahi1, Silvia Martina Ferrari1, Ilaria Ruffilli1, Giusy Elia1, Marco Briccetti2, Roberto Vita3, Salvatore Benvenega3, Alessandro Antonelli1
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 Antonelli1, Poupak Fallahi1, Silvia Martina Ferrari1, Marina Galletti2, Mattia Grazia Mandolfino2, Grazia Giorgianni2, Flavia Di Bari2, Roberto Vita3, Salvatore Benvenega3
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 Botelho1, Arnaldo Moura Neto1, Marcos Antonio Tambascia1, Conceição Silva1, Sarah Monte Alegre1, Denise Engelbrecht Zantut Wittmann2
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 Pani1, Francesco Boi1, Chiara Satta1, Chiara Serafini1, Stefania Casula1, Nicola Arisci1, Ivan Maurelli2, Maria Letizia Lai2, Stefano Mariotti3
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 Sciences, 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
1Medical University Sofia, University Hospital Alexanderovska, Clinic of Endocrinology and Metabolism, Department of Internal Medicine, Sofia, Bulgaria; 2University Hospital Alexanderovska, Endocrinology Clinic, Medical University Sofia, Sofia, Bulgaria; 3Medical University Sofia, University Hospital Alexanderovska, 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
1Warsaw University of Medicine, Department of Endocrinology, Warsaw, Poland; 2Warsaw University of Medicine, 2nd Department of Clinical Radiology, Warsaw, Poland; 3Warsaw 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
1University 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 2, Lise Bathum 3, Lennart Friis-Hansen 1
1Internal Medicine Department, Endocrinology and Diabetes Section, Nykøbing F Hospital, Nykøbing F, Denmark; 2Department of Clinical Biochemistry, Næstved Hospital, Næstved, Denmark; 3Department of Clinical Biochemistry, Odense University Hospital, Odense, Denmark

P1–03–09  THE IMPORTANT ROLE OF DOPPLER ULTRASOUND IN THE DIFFERENTIAL DIAGNOSIS BETWEEN HASHITOXICOSIS AND GRAVES’ DISEASE
Enida Demaj 1, Marijeta Kermaj 2, Thanas Furera 3, Laurent Kolicakcu 4, Ylli Agron 5
1Hospital of Berat, Internal, Berat, Albania; 2University Hospital Center ‘Mother Tereza’, Tirana, Albania; 3Mother Theresa Hospital Center, Tirana, Albania; 4Endocrinology 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
1Yerevan State Medical University, Yerevan, Armenia

P1–03–11  USE OF INTRAVENOUS GLUCOCORTICOIDS FOR TREATMENT OF GRAVES’ ORBITOPATHY
Mariami Asatiani 1, Zurab Robitashvili 2
1V. Ierieli Endocrinology, Metabolism, Dietology Center ‘enmedic’, Tbilisi, Georgia; 2V. Iverieti Endocrinology, Matabology, Dietology Center Enmedic, Tbilisi, Georgia

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 Benvenuta 1, Flavia Di Bari 2
1Sezione di Endocrinologia, Policlinico Universitario, Messina, Italy; 2Sezione 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
1Elias Hospital, Endocrinology, Bucharest, Romania; 2Elias Hospital, Endocrinology Department, Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Bucharest, Romania; 3Elias 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 5, Peter Grupe 6, Jeanette Krogh Petersen 4, Laszlo Hegedus 7
1Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark; 2Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark; 3Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark; 4Department of Oncology, Odense University Hospital, Odense, Denmark; 5Department of Nuclear Medicine, Odense
P1–04–04 SPONTANEOUS TRANSFORMATION OF PRIMARY AUTOIMMUNE HYPOTHYROIDISM TO GRAVES’ DISEASE IN A CLINICAL CASE OF AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 2
Narine Martirosian, Nina Petunina, Liubov Tukhina
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 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, Daniela Magalhães, Sandra Belo, Josué Pereira, Olinda Faria, Joana Queirós, Paula Freitas, David Carvalho
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, Gregor Vercek, Olga Blatnik
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, Desislava Gorcheva, Veselina Koleva, Lachezar Lozanov
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 ABSCESSES
Samet Yaman, Sevgul Faki, Murat Basaran, Didem Ozdemir, Reyhan Ersoy, Bekir Cakir
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, 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
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P1–04–11 MARINE-LENHART SYNDROME – A RARE CAUSE OF THYROTOXICOSIS
Mirjana Stoikovic, Savica Savic, Jasmina Ciric, Biljana Belesin, Tanja Nisic, Milos Stojanovic, Tijana Lalic, Milos Zarkovic
1 Clinic of Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia, Thyroidology Department, Belgrade, Serbia

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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, Bárbara Parente Coelho, Hélío Amante Miot, Mariangela Marques, Jose Vicente Tagliarini, Gláucia Mazeto
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, Berna Evranos Ogmen, Muhammet Cüneyt Bilginer, Sevgül Faki, Reyhan Ersoy, Bekir Cakir
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

Poster Sessions – Saturday
THYROID CORE NEEDLE BIOPSY: PATIENTS' PAIN AND SATISFACTION COMPARED TO FINE NEEDLE ASPIRATION

Jaesun Ji1, Yeo Koon Kim2, Sang Il Choi3, Ji-Hoon Kim4, Yunho Song5, Joohyun Kim5, Eun Hee Seo5, Gwan Hong Min5
1Seoul National University Bundang Hospital, Gyeong-Gi, Korea, Rep. of South; 2Seoul National University, Seongnam-Si, Korea, Rep. of South; 3Seoul National University Bundang Hospital, Seongnam-Si, Korea, Rep. of South; 4Seoul National University Hospital, Seoul, Korea, Rep. of South; 5Seoul National University Bundang Hospital, Bundang, Korea, Rep. of South

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

Eunji Lee1, Jong Chul Hong1, Ji-Won Seo1, Dong-Kun Lee2, Heon-Soo Park1
1Department of Otolaryngology-Head and Neck Surgery, Dong-A University College of Medicine, Busan, Korea, Rep. of South; 2Department 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 Hong1, Ji-Won Seo1, Eunji Lee1, Dong-Kun Lee2, Heon-Soo Park1
1Department of Otolaryngology-Head and Neck Surgery, Dong-A University College of Medicine, Busan, Korea, Rep. of South; 2Department 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

Jarawan Kongkit1, Natnicha Houngngam2, Thiti Snabboon3
1Chulalongkorn University, Bangkok, Thailand; 2King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand; 3Chulalongkorn 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 Chang1
1Nuclear 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 Yazici1, Serdar Tezelman2, Onur Demirkol3, Omer Faruk Unal4, Sukru Dilege5, Ozlem Aydin6, Yersu Kapran7, Bulent Colakoglu8, Tarik Terzioglu9, Burhan Ferhanoglu10, Faruk Alaoglu11
1Koc University Medical School, Section of Endocrinology and Metabolism, Istanbul, Turkey; 2Koc University Medical School, Department of General Surgery, Istanbul, Turkey; 3Koc University Medical School, Department of Nuclear Medicine, Istanbul, Turkey; 4Koc University Medical School, Department of Otorhinolaryngology, Istanbul, Turkey; 5Koc University Medical School, Department of Thoracic Surgery, Istanbul, Turkey; 6American Hospital, Department of Pathology, Istanbul, Turkey; 7Koc University Medical School, Department of Pathology, Istanbul, Turkey; 8American Hospital, Department of Radiology, Istanbul, Turkey; 9American Hospital, Department of General Surgery, Istanbul, Turkey; 10Koc University Medical School, Section of Hematology, Istanbul, Turkey

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

SongI Yang1, KwangKuk Park2, Jeong Hoon Kim3
1Kosin University College of Medicine, Department of Surgery, Seou-Gu, Busan, Korea, Rep. of South; 2Hub-Hu Hospital, Department of Surgery, Sahagu, Busan, Korea, Rep. of South; 3Kosin University College of Medicine, Department of Surgery, Seogu, Busan, Korea, Rep. of South

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 Saltiki1, Elli Anagnostou1, Mihalis Apostolakis1, Evangelia Zapanti1, Elefani Anastasiou1, Maria Alevizaki1
1Endocrine 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 Urung1, Yuna Ogimi1, Chie Masaki1, Junko Akaishi1, Kiyomi Y. Hames1, Chisato Tomoda1, Akifumi Suzuki1, Kenichi Matsuzu1, Keiko Okuwa1, Hiroshi Shibuya1, Wataru Kitagawa1, Mitsuj Nagahama1, Kaminori Sugino1, Koichi Ito1
1Ito Hospital, Tokyo, Japan
**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, Natacha Heutte, David Blanchard, Dominique de Raucourt, Dominique Vaur, Emmanuel Babin, Stephane Bardet

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

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

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

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**THE ASSOCIATION BETWEEN LYMPH NODE METASTASIS AND MOLECULAR MARKERS IN DIFFERENTIATED THYROID CANCER**

Berna İmge Aydoğan, Cevriye Cansız Ersöz, Serpil Dizbay Sak, Sevim Gullu

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

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

SongI Yang, Jeong Hoon Kim, KwangKuk Park

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

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

Seda Şancak, Ahmet Aslan, Funda Eren, Duygu Altnok, Hasan Aydın, Dilek Dereli Yazăfı, Nefise Sema Akaлин, Eileen Böesenberg, Paschke Ralf, Markus Eszlinger

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

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

Sefika Burçak Polat, Berna Evranos Ogmen, Gurkan Dumlü, Nuran Sungu, Reyhan Ersoy, Bekir Cakır

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

Catarina Machado, Patricia Tavares, Lilit Barbosa, Antónia Póvoa, Carlos Soares, José Manuel Oliveira, Sara Monteiro, Maria João Oliveira

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

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

Natia Katamadze, Tbilisi, Georgia
P1–07–01  THE EXPRESSION OF E-CADHERIN, YAP1, STAT3 OF MULTICELLULAR TUMOR SPHEROIDS OF THYROID
Woo Young Kim1, Sang Uk Woo1, Jae Bok Lee1
1Korea 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 Dvorakova1, Vlasta Sykorova2, Eliska Vlachikova2, Ramit Katra2, Pavla Sykorova3, Petr Vlcek4, Daniela Kodetova5, Petr Lastuvka6, Jan Betka6, Josef Vcelak2, Bela Bendlova2
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P1–07–03  TGFβ1 GENE POLYMORPHISMS CLINICAL UTILITY IN THYROID BENIGN AND MALIGNANT NODULES
Karina Colombera Peres1, Natassia Bufalo2, Lais Helena Pereira Amara2, Jacqueline Almeida2, Larissa Teodoro2, Ana Paula Comarella2, Laura Ward2
1Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Sao Paulo, Brazil; 2Laboratory 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 Lee1, Cho Rok Lee2, Eun Jeong Ban3, Min Ji Kim4, Tae Hyung Kim5, Jungbum Choi1, Sang-Wook Kang1, Jandee Lee2, Jong Ju Jeong4, Kee-Hyun Nam4, Woungyoun Chung5
1Seoul Gi Lee1, Cho Rok Lee2, Eun Jeong Ban3, Min Ji Kim4, Tae Hyung Kim5, Jungbum Choi1, Sang-Wook Kang1, Jandee Lee2, Jong Ju Jeong4, Kee-Hyun Nam4, Woungyoun Chung5
1Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 2Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 3Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 4Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 5Department 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 Fanfone1, Nadège Despretz2, Dimitri Stanicki2, Sophie Laurent2, Robert Muller2, Sandrine Rorive3, Luce Vander Elst2, Sven Saussez4, Carmen Burtea1
1Department of General, Organic, Mons, Belgium; 2University of Mons, Department of General, Organic and Biomedical Chemistry, Mons, Belgium; 3Center for Microscopy and Molecular Imaging, Diapath, Charleroi, Belgium; 4University 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 Jung1, Yourha Kim2, Sora Jeon3, Sohee Lee4, Ja Seong Bae4
1College of Medicine, The Catholic University of Korea, Seoul St. Mary’s Hospital, Seoul, Korea, Rep. of South; 2Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South; 3Department of Biomedicine & Health Sciences, College of Medicine, The Catholic University of Korea, Seoul, Korea, Rep. of South; 4Department 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 Han1, Se Eun Han1, Il Sung Nam-Goong2, Young Il Kim2, Eun Sook Kim2
1College of Korean Medicine, Donggok University, Kyung Ju, Korea, Rep. of South; 2Internal 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
Małgorzata Oczko-Wojciechowska1, Maria Sromek1, Agnieszka Pawłaczek1, Małgorzata Czetwertyńska1, Dorota Kula1, Jadwiga Zebracka-Gala1, Dagmara Rusinek1, Monika Kowal1, Elżbieta Gubala1, Tomasz Gawlik1, Sylwia Szpak-Ulczyk1, Renata Zub1, Tomasz Tyszkiewicz1, Kornelia Hasse-Lazar1, Zbigniew Wygoda1, Jolanta Krajewska1, Małgorzata Wiencek1, Marek Dedecjus1, Barbara Jarzab1
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P1–07–09  STRUCTURAL AND FUNCTIONAL STATE OF THE
THYROID GLAND DURING PAPILLARY CANCER
Tamar Dundua1, Lali Javashvili2, Ana Mamashkhilis1,  
Maia Kobulia1, Meri Rekova1, Tamar Kaloian1, Medea Papava2  
1Clinic Cortex, Tbilisi, Georgia; 2National Centre of Oncology,  
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 Faki1, Oya Topaloglu2, Samet Yaman3,  
Mahmut Nedim Aytekin4, Oktay Algin4, Reyhan Ersoy4,  
Bekir Cakir4  
1Yildirim Beyazit University, Ataturk Education and Research  
Hospital, Endocrinology Department, Ankara, Turkey; 2Ankara  
Yildirim Beyazit University, School of Medicine, Department  
of Endocrinology and Metabolism, Ankara, Turkey; 3Yildirim  
Beyazit University, Ataturk Education and Research Hospital,  
Department of Internal Medicine, Ankara, Turkey; 4Ankara  
Yildirim Beyazit University, School of Medicine, Department  
of Interventional Radiology, Ankara, Turkey; 5Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

P1–08–01  THERMOREGULATORY EFFECTS OF
3-IODOTHYRONAMINE IN MICE
Sogol Gachkar1, Rebecca Oelkrug2, Amy Warner3, Jens Mittag4  
1University of Lübeck, Molecular Endocrinology, 23538  
Luebeck, Germany; 2Center of Brain, Behavior and Metabolism,  
University of Lübeck, Lübeck, Germany; 3Karolinska Institutet,  
Cell and Molecular Biology, Stockholm, Sweden; 4Universität  
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 Bellusc1, Annunziatina Laurino2, Martina Sabatini1,  
Giulia Nesi3, Simona Rapposelli4, Riccardo Zucchi1,  
Laura Raimondi4, Grazia Chiellini1  
1Dept. of Pathology, University of Pisa, Pisa, Italy; 2Department  
of Neurofarba; Pharmacology, University of Florence, Florence,  
Italy; 3Dept. of Pharmacology, University of Pisa, Pisa, Italy;  
4Department Of Neurofarba, 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 GLOBLASTOMA CELLS (U-87MG)
Martina Sabatini1, Lorenza Bellusc1, Gloria Lazzeri2, Paola Lenzi3,  
Alessandra Salvetti3, Giulia Nesi4, Simona Rapposelli4,  
Francesco Fornari4, Riccardo Zucchi, Grazia Chiellini1  
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Translational Research and New Technologies in Medicine and  
Surgery, University of Pisa, Pisa, Italy; 3Dept. of Clinical and  
Experimental Medicine, University of Pisa, Pisa, Italy; 4Dept. of  
Pharmacy, University of Pisa, Pisa, Italy

P1–08–04  THE FLAME RETARDANT DE-71 INHIBITS
CULTURED HUMAN THYROID CELLS
Ulla Feldt-Rasmussen1, Thit Mynster Kronborg1, Juliana Frohnert  
Hansen1, Jacob Hofman-Bang1, Åse Krog Rasmussen1,  
Marie Frederiksen2, Katri Vorkamp3, Christoffer Holst Hahn4,  
Louise Ramhøj1, Claus Henrik Nielsen5, Klaus Bendtzen6  
1Copenhagen University Hospital, Dept of Endocrinology,  
Pe 2132, Copenhagen, Denmark; 2Aalborg University,  
Dept of Construction and Health, Copenhagen, Denmark;  
3Aarhus University, Dept of Environmental Science, Roskilde,  
Denmark; 4Righospitalet, Dept of Ear Nose Throat Head and  
Neck Surgery, Copenhagen, Denmark; 5Technical University  
of Denmark, National Food Institute, Søborg, Denmark;  
6University of Copenhagen, Institute of Inflammation,  
Copenhagen, Denmark

P1–08–05  EFFECTS OF THYROID HORMONES AND
3-IODOTHYRONAMINE ON SIRTUIN EXPRESSION IN
HEPATOCYTES
Ginevra Sacripanti1, Leonardo Lorenzini1, Riccardo Zucchi1,  
Sandra Ghelardoni2  
1University of Pisa, Pisa, Italy; 2Dpt of Pathology, Pisa, Italy

P1–08–06  DIFFERENTIAL GENE EXPRESSION IN PREGNANCY
AS A TOOL FOR PRIMARY HYPOTHYROIDISM DIAGNOSIS
Lucas dos Santos Bacigalupo1, Rosbojn José de Almeida1,  
Valdena Alessandra da Silva1, Patrícia Varella Lima Teixeira2,  
Leonardo Martins da Silva2, Juliana de Almeida Pires1,  
Mariana Fabbris Pereira1, João Bosco Pesquero2,  
Cleber Pinto Camacho3  
1Universidade Nove de Julho (Uninove), São Paulo, Brazil;  
2Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil;  
3Laboratory 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 Lorenzini1, Sandra Ghelardoni2, Alessandro Saba1,  
Riccardo Zucchi1  
1University of Pisa, Pisa, Italy; 2Dpt of Pathology, Pisa, Italy

Poster Sessions – Saturday
P1–08–08  CENTRAL AND PERIPHERAL INFLAMMATORY RESPONSES ARE IMPLICATED IN DIET-INDUCED OBESITY RESISTANCE IN WSB/EIJ MICE  
Isabelle Seugnet¹, Maria J. Herrero², Terrien Jeremy³, Bolaji Seffou¹, Stephanie Decher⁴, James Bowers¹, Chakib Djediat⁵, Bertrand Ducos⁶, Barbara Demeneix⁷, Marie-Stéphanie Clerget-Froidevaux⁸  
¹Mhmn/Cnrs Umr 7221, Paris, France; ²Mhmn/Cnrs Umr 7221, Paris, France; ³Team Bioadapt Umr Cnrs/Mhmn 7179, Brunoy, France; ⁴Muséum National D’histoire Naturelle, Umr Cnrs 7221, Paris, France; ⁵Mhmn, Paris, France; ⁶Genomic Paris Centre, Institut de Biologie de L’ecole Normale Supérieure (Ibens), Paris, France; ⁷Mhmn/Cnrs Umr7221, Paris, France

P1–08–09  CHOLECALCIFEROL (VIT. D3) AFFECTS THYROID HYSTOLOGY AND FUNCTION IN ORCHIDECTOMIZED MIDDLE-AGED MALE RATS  
Branka Sosic-Jurjevic¹, Branko Filipovic¹, Jasmina Živanovic¹, Gordana Ušćebrka², Svetlana Trifunovic¹, Vladimir Ajdžanović¹, Nataša Ristić¹, Verica Milošević¹  
¹Institute for Biological Research, University of Belgrade, Belgrade, Serbia; ²Faculty of Agriculture, University of Novi Sad, Novi Sad, Serbia

P1–08–10  MOLECULAR ECONOMY OF IODINE: A PHYSIOLOGICAL STRATEGY IN IODINE-DEFICIENT VERTEBRATES  
Atul Kathait¹, Anjana Faraswan², Patrick Shyaka¹, Asha Chandola-Saklani¹  
¹Centre for Biosciences and Clinical Research, School of Biosciences, Apeejay Stya University, Gurgaon, India; ²Government Degree College, Agastya Muni, Uttarakhand, India
Sunday, 4th September 2016

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 Vannucchi1, Irene Campi2, Nicola Currò3, Mario Salvi4
1Endocrine Unit, Fondazione Policlinico Irccs, Milan, Italy; 2Ospedale Maggiore Policlinico, Endocrine Unit, Fondazione Irccs Cà Granda, Milan, Italy; 3Ophthalmology, Fondazione Irccs Cà Granda, Milan, Italy; 4Dipartimento 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 Pilli1, Valeria Cenci1, Giulia Massari1, Giulia Busonero1, Brunetta Porcelli2, Antonella Tabucchi2, Alessandro Pini2, Adriano Spreaftico2, Vittoria Fossombroni2, Carlo Scapellato2, Furio Pacini1
1Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy; 2Department 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 Boyanov1, Ralitsa Mekova1, Deniz Bakalov2, Adelina Tsakova3
1Medical University Sofia, University Hospital Alexandrovskia, Clinic of Endocrinology and Metabolism, Department of Internal Medicine, Sofia, Bulgaria; 2University Hospital Alexandrovskia, Endocrinology Clinic, Medical University Sofia, Sofia, Bulgaria; 3Medical University Sofia, University Hospital Alexandrovskia, Department of Clinical Laboratory and Clinical Immunology, Sofia, Bulgaria

P2–01–04 THE CLINICAL ROLE OF PROAPOPTOTIC CYTOKINES TNF-Α AND SFASL IN DIAGNOSIS OF AUTOIMMUNE THYROID DISEASE IN CHILDREN
Hanna Mikos1, Marcin Mikos2, Marek Niedziela3
1Department of Pediatric Endocrinology and Rheumatology, Poznan University of Medical Sciences, Poznan, Poland; 2Department of Pneumology, Allergology and Clinical Immunology, Poznan University of Medical Sciences, Poznan, Poland; 3Poznan 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 Ruggeri1, Francesco Trimarchi1, Giuseppe Giuffrida1, Rosaria Certo1, Angela Alibrandì2, Filippo de Luca3, Małgorzata Wasniewska3
1Unit of Endocrinology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; 2Department of Economy, University of Messina, Messina, Italy; 3Department of Human Pathology, University of Messina, Messina, Italy

P2–01–06 THYROIDITIS AND VITAMIN D
Miskic Blazenka1, Sidbela Zukanovic2, Vesna Ćosić2, Marijana Knežević Praveček4, Matica Jandric Balen5, Karla Miškić6, Natasa Moser5
1Gh Dr Josip Bencevic Sl.Brod, University Jj Strosmayer Osijek Medical Faculty Osijek, Slav. Brod, Croatia; 2University Jj Strosmayer Osijek, Medical Faculty Osijek, Osijek, Croatia; 3University Jj Strosmayer Osijek, Medical Faculty Osijek, Osijek, Croatia; 4University Jj Strosmayer Osijek, Medical Faculty Osijek, Kardiology Gh ‘Dr J Benčevič’ Sl.Brod Croatia, Osijek, Croatia; 5University Jj Strosmayer Osijek, Medical Faculty Osijek, Osijek, Croatia; 6Medical 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 Monteira1, Vera Fernandes1, Selma Souto1, Olinda Marques1, Marta Alves1
1Serviço de Endocrinologia, Hospital de Braga, Braga, Portugal
P2–01–08  AUTOIMMUNE THYROID DISORDERS IN TYPE 1 DIABETES – 15 YEARS RETROSPECTIVE STUDY  
Claudia Matta-Coelho¹, Ana Margarida Monteiro¹, Fernando Mota-Garcia²  
¹Serviço de Endocrinologia, Hospital de Braga, Braga, Portugal; ²Serviço de Patologia Clínica, Hospital de Braga, Braga, Portugal

P2–01–09  THE INFLUENCE OF METHIMAZOLE TREATMENT ON THYROID VASCULARITY IN PATIENTS WITH GRAVES’ DISEASE  
Katja Zaletel¹, Ana Kisovar², Polona Klavžar², Simona Gaberšček³  
¹University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia; ²University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia; ³University 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 Dyacenko¹, Daniel Mihai¹, Daniela Alexandrescu¹, Corin Badiu¹  
¹National Institute of Endocrinology, Bucharest, Romania

P2–01–11  THE CORRELATION OF THYROID AUTO-IMMUNITY AND TYPE 1 DIABETES MELLITUS  
Miranda Miminoshvili¹, Lali Nikoleishvili¹, Ramaz Kurashvili¹, Tamar Maghradze¹  
¹LTD ‘Diacor’, Tbilisi, Georgia

P2–02–01  SELENIUM SUPPLEMENTATION SIGNIFICANTLY REDUCES SERUM THYROID PEROXIDASE AUTOANTIBODIES IN PATIENTS WITH CHRONIC AUTOIMMUNE THYROIDITIS: A META-ANALYSIS  
Johanna Wichman¹, Kristian Winther², Steen Joop Bonnema¹, Laszlo Hegedüs²  
¹Department of Endocrinology and Metabolism, Odense University Hospital, Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; ²Department of Endocrinology, Herlev University Hospital, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

P2–02–02  PHYSICAL PERFORMANCE IN OVERT AND SUBCLINICAL HYPOTHYROIDISM: A PILOT STUDY  
Daniela Gallo¹, Eliana Piantanida², Giovanni Veronesi², Maria Laura Tanda², Adriana Laí², Lorenza Sassi², Valentina Lombardi², Elvira Masiello³, Paola Premoli³, Eleonora Bianconi³, Marco Ferrario³, Luigi Bartalena³  
¹University of Insubria, Varese, Varese, Italy; ²University of Insubria, Varese, Varese, Italy; ³Dept. Clinical & Exp. Medicine, Varese, Italy

P2–02–03  QUALITY OF COMPENSATION AND WELL-BEING OF PATIENTS WITH PRIMARY HYPOTHYROIDISM AND OBESITY  
Valentin Fadeyev¹, Tatjana Morgunova¹, Yulia Manuylova²  
¹I.M. Sechenov First Moscow Medical University, Moscow, Russian Federation; ²I.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 Winther¹, Johanna Wichman², Laszlo Hegedüs², Steen Joop Bonnema²  
¹Department of Endocrinology and Metabolism, Odense University Hospital, University of Southern Denmark, Odense, Denmark; ²Department 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 Gullo¹, Federica Vinciguerra¹, Maria Luisa Arpi¹, Giuseppina Parrinello¹, Patrizia Tita¹, Roberto Baratta¹, Sebastiano Squatrito¹  
¹Endocrine 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 Freja¹, Jeppe Lerche la Cour², Bjarke Borregaard Medici³, Torquil Watt⁴, Birte Nygaard⁵, Jens Faber⁶  
¹Department of Endocrinology, Herlev University Hospital, Copenhagen, Denmark; ²Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; ³Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Gentofte University Hospital, Copenhagen, Denmark; ⁴Department of Endocrinology, Copenhagen University Hospital Rigshospitalet, Denmark, Department of Endocrinology, Herlev Hospital, University of Copenhagen, Copenhagen, Denmark; ⁵Department of Endocrinology, Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; ⁶Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Herlev, Denmark

P2–02–07  HYPOTHYROIDISM TODAY IN AN OFFICE BASED PRACTICE  
Esa Soppi¹  
¹Eira Hospital, Outpatient Clinic, Internal Medicine, Helsinki, Finland
P2–02–08  ‘SUBCLINICAL HYPOTHYROIDISM IN PREGNANCY’ OR ‘GESTATIONAL HYPOTHYROIDISM’?
David Metreveli1
1Tbilisi 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 Bilek1, Marcela Dvorakova2
1Institute of Endocrinology, Dept of Steroids and Proteofactors, Prague 1, Czech Republic; 2Institute 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 Solovov1, Michael Vozdvizhenskiy1, Alexander Makhonin1, Andrew Orlov1
1Samara Oncology Center, Samara, Russian Federation

P2–03–02  ASSOCIATION OF SERUM CALCITONIN LEVELS WITH MULTINODULAR THYROID DISEASE: 10-YEAR SINGLE CENTER EXPERIENCE
George Simeakis1, Ioanna Patinioti2, Marina Mitropoulou2, Elli Anagnostou2, Spiros Sapounas2, Evangelia Zapanti2, Vasiliki Vasilieiou2, Antonis Polymeris2, Katerina Saltiki3, Eleni Anastasiou2, Maria Alevizaki3
1Athens University School of Medicine, Athens, Greece; 2Endocrinology Dept, Alexandra Hospital, Athens, Greece; 3Endocrinology 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 Kovatcheva1, Jordan Vlahov1, Katja Zaletel1, Alexander Shinkov1, Julian Stoimenov1, Radina Ivanova-Boyanova2, Georgi Kirilov1
1Medical University of Sofia, University Hospital of Endocrinology, Sofia, Bulgaria; University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia; 2Clinical Centre of Endocrinology, Medical University of Sofia, Sofia, Bulgaria

P2–03–04  ROBOT ASSISTED TRANSAXILLARY THYROIDECTOMY FOR BENIGN THYROID DISEASES: THE OPERATIVE OUTCOMES OF 177 CONSECUTIVE PATIENTS
Min Ji Kim1, Jungbum Choi2, Tae Hyung Kim1, Seul Gi Lee1, Eun Jeong Ban3, Cho Rok Lee1, Sang-Wook Kang1, Jandee Lee1, Jong Ju Jeong4, Kee-Hyun Nam4, Wongyoun Chung3
1Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 2Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 3Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 4Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; 5Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South

P2–03–05  THE EFFECT OF J-131 THERAPY IN PATIENTS WITH AUTONOMOUSLY FUNCTIONING THYROID NODULES AND NORMAL TSH LEVEL
Miodrag Lacic1
1Polyclinic Lacic, Thyroid Department, Zagreb, Croatia

P2–03–06  ADIPOSE TISSUE ACCUMULATION AND SEDENTARY LIFESTYLE ARE PREDICTIVE OF SPECIFIC THYROID NODULE ULTRASOUND FEATURES
Grigorios Panagiotou1, Despina Kominou1, George Linardos1, Eleni Karoglou1, Maria Somali1, Konstantinos Tziomalos1, Marina Kira1, Kalliopi Pazaitou-Panayiotou4
1Theagenio Cancer Hospital, Thessaloniki, Greece, Department of Endocrinology- Endocrine Oncology, Thessaloniki, Greece; 2Private Practice, Hippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece; 3Hippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece; 4Theagenio Cancer Hospital, Department of Endocrinology- Endocrine Oncology, Thessaloniki, Greece

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 Solymosi1
1Bugat 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 Monpeyssen1, Christine Terestchenko1, Alain Dana1, Patrick Aidan1
1American Hospital of Paris, Neuilly Sur Seine, France

P2–03–09  THYROID NODULES AND CYSTS IN TYPE 1 DIABETIC CHILDREN AND ADOLESCENTS
Lusine Navasardyan1, Yelena Aghajanova1, Renata Markosyan1, Marianna Gevorgyan1
1Yerevan State Medical University, Yerevan, Armenia
P2–03–10 SERUM THYROGLOBULIN LEVEL AS A PREDICTIVE FACTOR OF NODULE SIZE AND MALIGNANCY IN PATIENTS WITH THYROID NOODULES
Simona Gaberscek 1, Sara Kukman 2, Ajda Biček 3, Adrijana Oblak 3, Edvard Pirnat 3, Katja Zaletel 3
1University Medical Centre Ljubljana, Ljubljana, Slovenia; 2University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia; 3University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia

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
1Private Pediatrics and Pediatric Endocrinology Practice, Department of Pediatric and Adolescent Endocrinology, Chair of Pediatrics, Polish-American Institute of Pediatrics, Jagiellonian University Medical College, Cracow, Poland; 2Division of Medical Genetics, Chair of Pediatrics, Polish-American Institute of Pediatrics, Jagiellonian University Medical College, Cracow, Poland; 3Department of Pediatrics, Johannes Gutenberg University Medical School, Mainz, Germany

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, Luke Marshall 1, Arwel Poacher 1, Marian Ludgate 3, Alexander Rees 4, Kristien Boelaert 6, Colin Dayan 5, Bijay Vaidya 10, Onyebuchi Okosiem 1
1Cardiff University, Cardiff, UK; 2Swansea University, Swansea, UK; 3Imem, Cardiff University, Cardiff, UK; 4University Hospital of Wales, Cardiff, UK; 5Institute of Molecular & Experimental Medicine, Cardiff University, Cardiff, UK; 6University of Birmingham, Birmingham, UK; 7National University of Singapore, Singapore, Singapore; 8University of Glasgow, Glasgow, UK; 9Cardiff University, Cardiff School of Medicine, Cardiff, UK; 10Department 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
1Rigshospitalet (Copenhagen University Hospital), Department of Medical Endocrinology, Copenhagen, Denmark; 2Department of Growth and Reproduction, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 3Department of Clinical Biochemistry, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 4Department of Clinical Biochemistry, Slagelse-Naesved Hospital, Copenhagen, Denmark; 5Center of Fetal Medicine, Department of Obstetrics, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 6Department of Medical Endocrinology, Rigshospitalet, University of Copenhagen. Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

P2–04–04 PREVALENCCE 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 5, Serge Rozenberg 1, Thierry Pepsack 1, Kris Poppe 5
1Centre Hospitalier Universitaire Saint Pierre, Université Libre de Bruxelles (UlB), Brussels, Belgium; 2Centre Hospitalier Universitaire Saint Pierre, Brussels, Belgium; 3Dr. Poppe Bvba Yl Brucha, Overijsje, 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
1Chonbuk National University Hospital, Jeonju, Korea, Rep. of South; 2Chonbuk 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, Aglicio Souza 2, Denise Engelbrecht Zantut Wittmann 2, Arlete Maria Fernandes 1
1Human Reproduction Unit, Department of Obstetrics and Gynecology, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil; 2Metabolic Unity, Department of Clinical Medicine, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil; 3Endocrinology 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 Houngngam1, Jaruwan Kongkit1, Lilly Pathomyok1, Thiti Snabboon2
1Chulalongkorn University, Bangkok, Thailand; 2Chulalongkorn University, Medicine, Bangkok, Thailand

P2–04–08 THYROID HOMEOSTASIS IN IODINE-DEFICIENT AND IODINE-SUFFICIENT HEALTHY INDIAN PREGNANT WOMEN
Nikku Yadav1, Atul Kathait2, Vineet Sharma3, Asha Chandola-Saklani1
1Centre for Biosciences and Clinical Research, School of Biosciences, Apeejay Stya University, School of Biosciences, Gurgaon, India; 2Centre for Biosciences and Clinical Research, School of Biosciences, Apeejay Stya University, Gurgaon, India; 3Dept Biosciences & Clinical Research, Sohna- Gurgaon, India

P2–04–09 PRESCRIBE THYROXIN OR NOT
Hermine Ayvazyan1
1Rmc Armenia, Erevan, Armenia

P2–04–10 HYPOTHYROIDISM AS A CAUSE OF INFERTILITY
Armine Khroyan1
1Yerevan State Medical University, Endocrinology, Yerevan, Armenia

P2–05–01 COMPARISON OF THYROID FINE NEEDLE ASPIRATION BIOPSY RESULTS BEFORE AND AFTER IMPLEMENTATION OF BETHESDA CLASSIFICATION
Didem Ozdemir1, Nagihan Bestepe1, Sevgul Faki1, Aydan Kilicarslan1, Omer Parlak1, Reyhan Ersoy1, Bekir Cakir1
1Ankara Yildirim Beyazit University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; 2Ankara Yildirim Beyazit University, School of Medicine, Department of Pathology, Ankara, Turkey; 3Ankara Yildirim Beyazit University School of Medicine, Department of General Surgery, Ankara, Turkey

P2–05–02 THYROID MALIGNANCY RISK IN DIFFERENT CLINICAL THYROID DISEASES
Ahmet Dirikoc1, Sevgul Faki1, Husniye Baser1, Didem Ozdemir1, Cevdet Aydin1, Reyhan Ersoy1, Mehmet Kilic2, Aydan Kilicarslan3, Bekir Cakir1
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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 Kawabe1, Shigeki Higashiyama1, Atsushi Yoshida1, Kohei Kotani1, Susumu Shiomi1
1Department 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 Kralj1, Ivana Žagar1, Andreja Antonija Schwarzbart Pevec1, Nikola Besic2
1Institute of Oncology Ljubljana, Ljubljana, Slovenia; 2Institute of Oncology, Ljubljana, Slovenia

P2–05–05 THE ROLE OF THE NODULE VOLUME IN EVALUATING THE RISK OF MALIGNANCY IN THYROID NODULES
Nagihan Bestepe1, Didem Ozdemir2, Husniye Baser1, Berna Evranos1, Nuran Sungur1, Mehmet Kilic1, Reyhan Ersoy1, Bekir Cakir1
1Ankara Yildirim Beyazit University School of Medicine Department of Endocrinology and Metabolism, Ankara, Turkey; 2Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; 3Ankara Yildirim Beyazit University School of Medicine Department of Pathology, Ankara, Turkey; 4Ankara 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 Kunavisarut1, Intira Masayavanich2
1Faculty of Medicine, Bangkok, Bangkok, Thailand; 2Siriraj Hospital, Mahidol University, Bangkok, Thailand

P2–05–07 THYROID CANCER INCIDENCE FOLLOWING THYROIDECTOMY: A TERTIARY CENTRE EXPERIENCE IN ROMANIA
Sorina Martin1, Oana Budianu2, Oana Ion2, Andreea Grigore2, Anca Sirbu1, Alice Albu1, Carmen Barb1, Cosmin Giulea1, Adrian Miron1, Florin Andrei1, Simona Fica1
1Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Elias Hospital, Endocrinology Department, Bucharest, Romania; 2Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; 3Elias Hospital, Surgery Department, Carol Davila University of Medicine and Pharmacy, Surgery Department, Bucharest, Romania; 4Elias Hospital, Pathology Department, Bucharest, Romania
P2–06–08 **A RARE CAUSE OF POSTPARTUM RAPIDLY ENLARGING GOITER**

Berna Evranos Öğmen¹, Muhammet Cüneyt Bilginer², Cevdet Aydin³, Yetkin Ağacığer⁴, Hakan Korkmaz⁵, Reyhan Ersoy⁶, Bekir Çakır⁷

¹Ankara Ataturk Research and Training Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; ²Ankara Yıldırım Beayazıt University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; ³Ankara Yıldırım Beayazıt University School of Medicine Department of Endocrinology and Metabolism, Ankara, Turkey; ⁴Ankara Ataturk Research and Training Hospital Department of Pathology, Ankara, Turkey; ⁵Ankara Yıldırım Beayazıt University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

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

Abbas Ali Tam¹, Didem Özdemir¹, Berna Evranos Öğmen¹, Sevgül Faki², Ersin Gürkan Dumlu³, Hayriye Tatlı Doğan⁴, Reyhan Ersoy⁴, Bekir Çakır⁴

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**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 Kim¹, Jin Hyang Jung¹, Jin Ho Jung¹, Taek Ju Kwon¹, Jeeyeon Lee¹, Seung Ook Hwang¹, Ho Yong Park¹

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

P2–06–02 **MINIMALLY INVASIVE OPEN THYROIDECTOMY: SURGICAL COMPLETENESS OF CONSEQUENTIAL 108 PATIENTS**

Tae Hyung Kim¹, Min Jhi Kim¹, Jungbum Choi¹, Seul Gi Lee¹, Eun Jeong Ban¹, Cho Rak Lee¹, Sang-Wook Kang¹, Jandee Lee¹, Jong Ju Jeong¹, Kee-Hyun Nam¹, Woungyoun Chung¹, Cheong Soo Park²

¹Yonsei University College of Medicine, Seoul, Korea, Rep. of South; ²Yonsei University College of Medicine, Seoul, Korea, Rep. of South; ³Yonsei University College of Medicine, Seoul, Korea, Rep. of South; ⁴Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, Rep. of South; ⁵Department 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 Park¹, Dong Ju Kim², Ok-Jun Lee³

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

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

Young Jae Ryu¹, Jin Seong Cho¹, Dong Hoon Cho¹, Jung Han Yoon¹, Min Ho Park¹

¹Chonnam 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 Lee¹, Yu-mi Lee¹, Tae-Yon Sung¹, Jong Ho Yoon¹, Ki-Wook Chung¹, Suck Joon Hong¹

¹Asan 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 Kim¹, Jin Hyang Jung¹, Seung Ook Hwang¹, Jeeyeon Lee¹, Taek Ju Kwon¹, Jin Ho Jung¹, Ho Yong Park¹

¹Kyunghpook National University, School of Medicine, Daegu, Korea, Rep. of South
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 Baser1, Bekir Cakir2, Oya Topaloglu1, Afra Alkan3, Burçak Polat4, Hayriye Tatlı Doğan5, Mustafa Omer Yazıcıoğlu5, Cevdet Aydın6, Reyhan Ersöy2
1Ankara Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; 2Yıldırım Beyazıt University School of Medicine, Department of Biostatistics, Ankara, Turkey; 3Yıldırım Beyazıt University School of Medicine, Department of General Surgery, Ankara, Turkey; 4Yıldırım Beyazıt University School of Medicine, Department of Pathology, Ankara, Turkey; 5Yıldırım Beyazıt University School of Medicine, Department of Surgery, Ankara, Turkey; 6Yıldırım Beyazıt University School of Medicine, Department of General Surgery, Ankara, Turkey

P2–07–02 HIGH RESISTIVE BLOOD FLOW IN PAPILLARY THYROID CANCERS: AN IMAGING STUDY FOR CLINICAL USE
Ahmet Aslan1, Seda Sancak2, Ercan Ayaz3, Ibrahim İnan1, Mine Aslan4, Orhan Alimoğlu4, Murat Acar3
1Department of Radiology, Umraniye Training and Research Hospital, Department of Radiology, Medical School of Marmara University, Istanbul, Turkey; 2Department of Radiology, Harran University, Sanliurfa, Turkey; 3Department of Radiology, Göztepe Training and Research Hospital, Medical School of Istanbul Medeniyet University, Istanbul, Turkey; 4Department of Radiology,唾眠医学, in the University of Tokyo, Japan; 5Department 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 Pitoia1, Fernando Jerkovich1, Fernanda Bueno1, Anabella Smulever1, Graciela Cross1
1Hospital de Clínicas – University of Buenos Aires, Buenos Aires, Argentina

P2–07–04 CLINICOPATHOLOGICAL FEATURES OF THYROID CARCINOMAS IN GERIATRIC PATIENTS
Fatma Dilek Dellal1, Didem Ozdemir1, Abbas Ali Tam2, Husniye Baser1, Hayriye Tatlı Doğan6, Omer Parlak2, Reyhan Ersöy6, Bekir Cakir6
1Ankara Training and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; 2Ankara Yıldırım Beyazıt University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; 3Ankara Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; 4Ankara Yıldırım Beyazıt University, School of Medicine, Department of General Surgery, Ankara, Turkey; 5Yıldırım Beyazıt 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 Baser1, Berna Evranos1, Oya Topaloglu1, Cevdet Aydin2, Aydan Kilicaslan3, Ersin Gurkan Dumlü4, Reyhan Ersöy2, Bekir Cakir2
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P2–07–06 THE RELATIONSHIP BETWEEN THE BRAFV600E MUTATION IN PAPILLARY THYROID MICROCARCINOMA AND CLINICOPATHOLOGIC FACTORS
Jong-Chul Hong1, Ji-won Seo2, Eunji Lee2, Dong-Kun Lee3, Heon-Soo park1
1Department of Otolaryngology, Head and Neck Surgery, College of Medicine, Dong-A University, Busan, Korea, Rep. of South; 2Department of Otolaryngology-Head and Neck Surgery, Dong-A University College of Medicine, Busan, Korea, Rep. of South; 3Department 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 Kim1, Soo Young Kim2, Chi Young Lim3, Bup-Woo Kim1, Yong Sang Lee1, Hang-Seok Chang1, Cheong Soo Park1
1Thyroid 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
1Yerevan 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
1Gemeinschaftspraxis, Nuklearmed. Praxis, Fulda, Germany;
2Gemeinschaftspraxis, Fulda, Germany

P2–08–01  A NEW ROLE FOR MONOCARBOXYLATE
TRANSPORTER 8: REGULATION OF THYROID HORMONE
AVAILABILITY DURING RETINAL DEVELOPMENT
Pieter Vancamp 1, Veerle Darras 1
1Laboratory 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 1, Heike Heuer 1, Jens Mittag 4
1Center of Brain, Behavior and Metabolism, University of Lübeck, Luebeck, Germany;
2Karolinska Institutet, Department of Cell and Molecular Biology, Stockholm, Sweden;
3Leibniz Institute for Environmental Medicine (Ifu), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany;
4Universität 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 1, Jens Mittag 6
1University of Lübeck, Center of Brain, Behavior and Metabolism, Lübeck, Germany;
2Center of Brain, Behavior and Metabolism, University of Lübeck, Luebeck, Germany;
3Leibniz Institute for Environmental Medicine (Ifu), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany;
4Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany;
5Leibniz Institute for Environmental Medicine (Ifu), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany;
6Universität 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
1Institut für Biochemie und Molekularbiologie, Universität Bonn, Bonn, Germany;
2Rheinische 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 1,
Paolo Vitti 1, Massimo Tonacchera 1
1Department of Clinical and Experimental Medicine, Endocrinology Unit, University of Pisa, Pisa, Italy;
2Department 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
1Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany

P2–08–07  THYROID FUNCTION IN
PSEUDOHYPOPARATHYROIDISM TYPE 1A
Slavica Savic 1, Tijana Lalic 2, Marija Barac 2, Mirjana Stojkovic 2,
Tanja Nisic 2, Biljana Nedeljkovic-Beleslin 1, Milos Stojanovic 2,
Jasmina Cinc 1, Milos Zarkovic 1
1Belgrade, Serbia;
2Clinic of Endocrinology, Belgrade, Serbia;
3Clinic 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 1
1Fsbi Federal Neurosurgical Center of Ministry of Public Health, Research Institute of Experimental and Clinical Medicine, Novosibirsk, Russian Federation;
2Fsbi Federal Neurosurgical Center of Ministry of Public Health, Novosibirsk, Russian Federation;
3Research Institute of Experimental and Clinical Medicine, Novosibirsk, Russian Federation

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Eur Thyroid J Vol. 5, Suppl. 1, 2016

39th Annual Meeting of the ETA
Monday, 5th September 2016

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 Osgston1, Fiona Williams2, Anita Boelen3
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 Marina1, Fulvio Lauretani2, Marcello Giuseppe Maggio1, Stefania Bandinelli3, Gian Paolo Ceda1, Luigi Ferrucci1, Graziano Ceresini1
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

P3–01–03 THYROID DYSFUNCTION IN CHRONIC KIDNEY DISEASE PATIENTS
Olga Vasilkova1, Tatjana V. Mokhort2, Irina Vasiukhina3, Margarita Zmailik3
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 Mangano1, Andrea Leotta1, Matteo Lavazza1, Vincenzo Pappalardo1, Davide Inversini1, Cesare Carlo Ferrari1, Francesco Frattini1, Stefano Rausei1, Wen Tian2, Hoon Yub Kim3, Che-Wei Wu4, Gianlorenzo Dionigi1
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; 2 Varese, Italy; 3 Department of General Surgery, The Chinese People’s Liberation Army General Hospital, Beijing, China; 4 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; 5 Department of Otologyngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

P3–01–05 STAGE-THYROIDECTOMY: SINGLE INSTITUTION PERSPECTIVE
Alberto Mangano1, Vincenzo Pappalardo1, Andrea Leotta1, Matteo Lavazza1, Cesare Carlo Ferrari1, Davide Inversini1, Andrea Leotta1, Francesco Frattini1, Stefano Rausei1, Wen Tian2, Hoon Yub Kim3, Che-Wei Wu4, Gianlorenzo Dionigi1
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; 2 Varese, Italy; 3 Department of General Surgery, The Chinese People’s Liberation Army General Hospital, Beijing, China; 4 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; 5 Department of Otologyngology, 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 Ferrari1, Vincenzo Pappalardo1, Andrea Leotta1, Matteo Lavazza1, Davide Inversini1, Alberto Mangano1, Francesco Frattini1, Stefano Rausei1, Wen Tian2, Hoon Yub Kim3, Che-Wei Wu4, Gianlorenzo Dionigi1
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 Otologyngology, 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
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 Ferreira¹, Tiago Silva¹, Henrique Luiz¹, Maria Carlos Cordeiro¹, Isabel Manita¹, Ana Catarina Matos¹, Jorge Portugal¹
¹Hospital Garcia de Orta, Almada, Portugal

P3–01–09  A REVIEW AND CLINICAL ANALYSIS OF 12 CASES OF PRIMARY THYROID LYMPHOMA
Yang Zhang¹, Ying Gao², Zhenfang Yuan¹, Yan Ming Gao¹, Xiaohui Gao¹
¹Peking University First Hospital, Peking, China; ²Peking University First Hospital, Beijing, China

P3–01–10  GASTRIC ACID SECRETION AND GASTRIN RELEASE MONITORING DURING CONTINUOUS INTRAOPERATIVE NEUROMONITORING (CIONM) THYROID SURGERY
Cesare Carlo Ferrari¹, Vincenzo Pappalardo¹, Alberto Mangano¹, Davide Inversini¹, Andrea Leotta¹, Matteo Lavazza¹, Francesco Frattini¹, Stefano Rauseli¹, Wen Tian³, Hoon Yub Kim³, Che-Wei Wu⁴, Gianlorenzo Dionigi¹
¹1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy; ²Department of General Surgery, The Chinese People’s Liberation Army General Hospital, Beijing, China; ³Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; ⁴Department 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 Inversini¹, Andrea Leotta¹, Matteo Lavazza¹, Cesare Carlo Ferrari¹, Vincenzo Pappalardo¹, Alberto Mangano¹, Francesco Frattini¹, Stefano Rauseli¹, Wen Tian³, Hoon Yub Kim³, Che-Wei Wu⁴, Gianlorenzo Dionigi¹
¹1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy; ²Department of General Surgery, The Chinese People’s Liberation Army General Hospital, Beijing, China; ³Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South; ⁴Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

P3–02–01  SEASONAL VARIATIONS OF TSH LEVELS IN ATHYREOTIC PATIENTS UNDER L-T4 REPLACEMENT THERAPY
Damiano Gullo¹, Adele Latina², Francesco Frasca³, Sebastiano Squatrito¹, Antonino Belfiore¹, Riccardo Vigneri¹
¹Endocrine Unit, Garibaldi-Nesima Hospital, University of Catania Medical School, Catania, Italy; ²Endocrine Unit, S. Croce e Carle Hospital, Cuneo, Italy; ³Clinical 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 Aleksei¹, Osipovskaya Maria¹, Makretska Naina², Vasilyev Evgeny²
¹Ural State Medical University, Yekaterinburg, Russian Federation; ²Endocrinology 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 Medici¹, Jeppe Lerche la Cour², Michaelsson Luba Freja³, Jens Faber³, Birte Nygaard³
¹Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Gentofte University Hospital, Copenhagen, Denmark; ²Department of Endocrinology, Herlev University Hospital, Department of Endocrinology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; ³Department of Endocrinology, Herlev University Hospital, Copenhagen, Denmark; ⁴Herlev University Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Herlev, Denmark; ⁵Department 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 Silva¹, Robson José de Almeida¹, Patrícia Varella Lima Teixeira², Leonardo Martins da Silva², João Bosco Pesquero³, Cleber Pinto Camacho³
¹Universidade Nove de Julho (Uninove), São Paulo, Brazil; ²Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil; ³Laboratory 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 Morgunova1, Valentin Fadeyev1, Meruert Madiyarova1
1I.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 Urgatz1, Ulrike Hostalek1, Wolfgang Uhl1, George J. Kahaly2
1Merck KgaA, Darmstadt, Germany; 2Johannes 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 Almeida1, Valdanela Alessandra da Silva1, Patrícia Varella Lima Teixeira2, Leonardo Martins da Silva2, João Bosco Pesquero2, Cleber Pinto Camacho3
1Universidade Nove de Julho (Uninove), São Paulo, Brazil; 2Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil; 3Laboratory 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 Sethi1, Dr Deepak Khandewal2, Dr Jagdish Gotur3, Dr M.S. Raghvendra4, Dr Sumitav Barua5, Dr Upal Vyas5
1Care Hospital, Telangana, India; 2Dr Khandewal’s Endocrinology Clinic, Delhi, India; 3Dr Bhagat’s Polyclinic, Ambedkar and Bhagvati Municipal Hospital, Mumbai, India; 4Dot Speciality Clinic, Bangalore, India; 5Down Town Hospita, Guwahati, India; 6Abbott India Limited, Mumbai, India

P3–02–09 ON INTERACTION OF AUTOIMMUNE THYROIDITIS AT THE STAGE OF SUBCLINICAL HYPOTHYROIDISM AND GASTROENTEROLOGICAL PATHOLOGY
Elina Gaspyaryan1, Mikhail Solovey2, Alexander Gordienko3
1Medical Centre, Medical Academy of Postgraduate Studies, St. Petersburg, Russian Federation; 2Military Medical Academy N.A. S.M.Kirov, ‘Professor’ Medical Center, Saint-Petersburg, Russian Federation; 3M.Kirov Military Medical Academy, Saints Petersburg, Russian Federation

P3–03–01 A US-CYTOLOGIC SCORE ALLOWS SIMPLE AND ACCURATE DEFINITION OF THE RISK OF MALIGNANCY IN CYTOLOGICALLY INDETERMINATE THYROID NODULES
Gilles Russ1, Royer Benedict2, Claude Bigorgne2, Marie Bienvenu2, Agnes Rouxel3, Laurence Leenhardt4
1Centre de Pathologie et D’imagerie, Pierre and Marie Curie University, Paris, France; 2Centre de Pathologie et D’imagerie, Cochin Hospital, Paris, France; 3Centre DE Pathologie et D’imagerie, La Pitie-Salpetriere Hospital, Paris, France; 4Centre de Pathologie et D’imagerie, La Pitie Salpetriere Hospital, Paris, France; 5La 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 Pani1, Laura Orgiano5, Elena Massa5, Frances Stool5, Giorgia Astara5, Valeria Pusceddu5, Mario Scartozi5, Stefano Mariotti5
1Endocrine Unit, Department of Medical Sciences M.Aresu, University of Cagliari, Cagliari, Italy; 2Medical Oncology, Department of Medical Sciences M.Aresu, University of Cagliari, Cagliari, Italy; 3Department of Medical Sciences, 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 Diederichsen1, Stine Darkner1, Xu Chen1, Arne Johannessen2, Steen Pehrson3, Jim Hansen2, Ulla Feldt-Rasmussen4, Jesper Hasstrup Svendsen2
1The Heart Centre, Section 2013, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; 2Department of Cardiology, Gentofte Hospital, Copenhagen University Hospital, Gentofte, Denmark; 3Department of Medical Endocrinology, Section 2132, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

P3–03–04 THE ‘WHITE THYROID’ ON UNENHANCED CT IN AMIODARONE INDUCED THYROTOXICOSIS TYPE 2 (AIT2)
Annick Van den Bruel1, Joost Delanote1, Carine De Vroe1, Lotte Pyf peroen1, Johan Ghekiere1, Mathias Duytschaever1, Rene Tavernier1
1General 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 Russ¹, Jean Tramalloni²
¹Centre de Pathologie et D’imagerie, Pierre and Marie Curie University, Paris, France; ²Radiologie 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 Duntas¹, Eleni Loukari², Brigitte Grab-Duntas³, Anastasios Boutsiadis³, Charalampos Kefidis⁴
¹Unit of Endocrinology, Diabetes and Metabolism, Evgenidion Hospital, University of Athens, Unit of Endocrinology, Diabetes and Metabolism, Athens, Greece; ²Evgenidion Hospital, Unit of Endocrinology, Diabetes and Metabolism, Athens, Greece; ³Medical Center of Athens, Department of Nuclear Medicine, Athens, Greece; ⁴Health Center, Thera, Santorini, Greece

P3–03–07 *HOW AND AT WHICH SIZE ARE THYROID NODULES DISCOVERED AND CONSEQUENCES ON THE RISK OF MALIGNANCY*

Gilles Russ¹, Agnes Rouxé², Marie Bienvenu³, Claude Bigorgne⁴, Royer Benedict⁵, Laurence Leenhardt⁶
¹Centre de Pathologie et D’imagerie, Pierre and Marie Curie University, Paris, France; ²Centre de Pathologie et D’imagerie, La Pitie Salpetriere Hospital, Paris, France; ³Centre de Pathologie et D’imagerie, La Pitie-Salpetriere Hospital, Paris, France; ⁴Centre de Pathologie et D’imagerie, La Pitie-Salpetriere Hospital, Paris, France; ⁵La Pitie Salpetriere Hospital, Thyroid and Endocrine Tumors Unit, Paris, France

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

Rosaria Ruggeri¹, Mariateresa Cristani², Teresa Manuela Vicchio¹, Rosaria Certo¹, Giuseppe Guffrida³, Salvatore Giovinazzo³, Antonina Saija³, Angela Alibrandi¹, Francesco Trimarchi¹
¹Unit of Endocrinology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; ²Department of Pharmacological Sciences and Health Products, University of Messina, Messina, Italy; ³Department of Economy, University of Messina, Messina, Italy

P3–03–09 *VESSEL SEALING SYSTEM (VSS) SAFETY AROUND THE RECURRENT LARYNGEAL NERVE (RLN)*

Alberto Mangano¹, Andrea Leotta¹, Matteo Lavazza¹, Cesare Carlo Ferrari¹, Davide Inversini¹, Vincenzo Pappalardo¹, Francesco Frattini¹, Stefano Rausi¹, Wen Tian², Hoon Yun Kim³, Che-Wei Wu⁴, Gianluca Dionigi¹
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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 Ittermann¹, Markus Marcello Ricardo Paulista¹, Sabine Schipf², Henry Völzke³
¹University Medicine Greifswald, Greifswald, Germany; ²Universitätsmedizin Greifswald, Greifswald, Germany; ³Ernst-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 Kim¹, Sung Dae Moon¹, Je Ho Han¹
¹The 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 Holmberg¹, Helena Filipsson Nyström¹, Helge Malmgren¹, Erik Olsson¹, Birgitta Johannson³, Simon Skau¹, Niklas Klasson¹, Rolf Heckemann¹, Peter Berglund⁴, Göran Starck⁵
¹Sahlgrenska Academy, Gothenburg, Dept of Endoc, Sahlgrenska, Gothenburg, Sweden; ²Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ³Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden; ⁴Dept of Neuropsychiatry Sahlgrenska University Hospital, Gothenburg, Sweden; ⁵Dept of Radiation Physics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

P3–04–04 *THYROID DISEASE IN OLDER PATIENTS HOSPITALIZED FOR ACUTE ILLNESS: PREVALENCE AND THERAPEUTIC APPROPRIATENESS*

Giuseppe Pasqualetti¹, Umberto Dell’Agnello¹, Sara Bernardini¹, Antonio Polini¹, Sara Tognini², Valeria Calsolaro¹, Fabio Monzani¹
¹Department of Clinical & Experimental Medicine, University of Pisa, Pisa, Italy; ²Geriatrics Unit, University Hospital of Pisa, Pisa, Italy

Room 16

04 Cardio, Brain and Metabolism

Chairperson: Frans Brandt, Denmark
P3–04–05  **SUBTLE CHANGES IN THYROID FUNCTION ARE ASSOCIATED WITH DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES**  
*Eun Soo Kim*¹, *Sung Dae Moon*¹, *Je-Ho Han*¹  
¹The Catholic University of Korea College of Medicine, Incheon, Korea, Rep. of South

P3–04–06  **ADIPOCYTOKINES, INSULIN RESISTANCE AND CHRONIC INFLAMMATION STATUS IN HYPOTHYROID PATIENTS**  
¹Tokuda Hospital Sofia, Sofia, Bulgaria; ²Tokuda Hospital Sofia, Sofia, Bulgaria; ³Tokuda Hospital Sofia, Sofia, Bulgaria

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  
¹Unit of Endocrinology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; ²Unit of Rheumatology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; ³Unit of Cardiology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

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*², *Davide Carvalho*⁶  
¹Endocrinology, Diabetes and Metabolism Department of São João Hospital Centre, Faculty of Medicine of the University of Porto, Porto, Portugal; ²Clinical Epidemiology, Predictive Medicine and Public Health Department, Porto, Portugal; ³Service and Laboratory of Immunology, Porto, Portugal; ⁴Faculty of Medicine of the University of Porto, Porto, Portugal; ⁵Service and Laboratory of Immunology, Faculty of Medicine of the University of Porto, Porto, Portugal; ⁶Endocrinology, Diabetes and Metabolism Department of São João Hospital Centre, Institute for Research and Innovation in Health Sciences of the Faculty of Medicine of the University of Porto, Porto, Portugal

P3–04–09  **GENETIC RISK FACTORS FOR THE THYROTOXIC ATRIAL FIBRILLATION AND ITS’ OUTCOMES**  
*Alina Babenko*¹, *Daria Savitskaya*², *Elena Grineva*³  
¹Federal Almazov Medical Research Centre, Institute of Endocrinology, St. Petersburg, Russian Federation; ²Federal Almazov North-West Medical Research Centre, Institute of Endocrinology, St. Petersburg, Russian Federation; ³Federal Medical Research Center, Dept of Endocrinology, St. Petersburg, Russian Federation

P3–04–10  **RISK FACTORS OF VENOUS THROMBOEMBOLISM IN PATIENTS TREATED FOR DIFFERENTIATED THYROID CARCINOMA**  
¹University of Groningen, University Medical Center Groningen, Department of Vascular Medicine and Endocrinology, Groningen, Netherlands; ²University of Groningen, University Medical Center Groningen, Department of Hematology, Groningen, Netherlands; ³University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; ⁴University of Groningen, University Medical Center Groningen, Department of Vascular Medicine, Groningen, Netherlands

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 DIAGNOSTICITY**  
¹Ankara Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; ²Ankara Training and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; ³Ankara Ataturk Research and Training Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; ⁴Ankara Yildirim Beyazit University, School of Medicine, Department of Pathology, Ankara, Turkey; ⁵Yildirim Beyazit University, School of Medicine, Department of Endocrinology and Metabolism, Bilkent, Ankara, Turkey

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  
¹Cellular and Molecular Research Center, Faculty of Medicine, Guilan University of Medical Sciences, Rasht, Iran

**Poster Sessions – Monday**
P3–05–03  LONG-TERM OUTCOME OF PERCUTANEOUS ETHANOL ABLATION OF SELECTED RECURRENT CERVICAL NODAL METASTASES IN THYROID CANCER
Soo Young Kim¹, Seok-Mo Kim¹, Chi Young Lim¹, Bup-Woo Kim¹, Yong Sang Lee¹, Hang-Seok Chang¹, Cheong Soo Park¹
¹Thyroid 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 Bilginer¹, Didem Ozdemir¹, Husniye Baser², Hayriye Tatlı Doğan¹, Abdussamed Yalçın³, Reyhan Eroşy¹, Bekir Cakir¹
¹Yildirim Beyazit University School of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey; ²Ankara Ataturk Education and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; ³Atatürk Education and Research Hospital, Department of Pathology, Ankara, Turkey; ⁴Ankara 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 Siderova¹, Kiril Hristozov², Ivan Krasnaliev³
¹University Hospital ‘St. Marina’, Department of Endocrinology and Metabolism, Varna, Bulgaria; ²Medical University – Varna, Department of Endocrinology and Metabolism, Varna, Bulgaria; ³University Hospital ‘St. Marina’, Department of Pathology, Varna, Bulgaria

P3–05–06  EFFECTS OF BODY MASS INDEX ON THYROID CANCER AGGRESSIVENESS AND RECURRENCE
Eun Sook Kim¹
¹The 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 Jeong¹, Hyun Sook Hong¹, Eun Hye Lee¹
¹Soonchunhyang 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 Yazıcı¹, Serdar Tezelman², Tarık Terzioglu³, Nurdan Gül⁴, Ayse Kubat Uzum⁴, Ferihan Aral⁵, Refik Tanakol⁶, Yersu Kapran⁷, Bulent Colakoglu⁸, Havva Sezer⁹, Faruk Alagol⁹
¹Koc University Medical School, Section of Endocrinology and Metabolism, Istanbul, Turkey; ²Koc University Medical School, Department of General Surgery, Istanbul, Turkey; ³American Hospital, Department of General Surgery, Istanbul, Turkey; ⁴Istanbul University Medical School, Section of Endocrinology and Metabolism, Istanbul, Turkey; ⁵Koc University Medical School, Department of Pathology, Istanbul, Turkey; ⁶American Hospital, Department of Pathology, Istanbul, Turkey

P3–05–09  HEMI-THYROIDECTOMY FOR FOLLICULAR THYROID CARCINOMA – ‘HEMI-THYROID’ AS AN OBSTACLE FOR FURTHER MANAGEMENT AFTER 8 YEARS FOLLOWING SURGERY
Nino Khabeishvili¹
¹V. Iverieli Endocrinology, Metabolity, Dietology Center ‘Enmedic’, Endocrinology, Tbilisi, Georgia

P3–05–10  HYALINIZING TRABECULAR TUMOR: CASE REPORT
Nazibrola Chiradze¹, Lali Nikoleishvili², Ramaz Kurashvili², Miranda Miminoshvili³
¹Nelp The Centre for Diabetes, Endocrine and Cardio-Pulmonary Disease, Endocrinology, Tbilisi, Georgia; ²LTD ‘Diacor’, Tbilisi, Georgia

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 Eszlinger¹, Katharina Böhme², Maha Ullmann², Anna Neumann³, Ilka Ruschenburg³, Ralf Paschke²
¹Department of Oncology and Arnie Charbonneau Cancer Institute, Cumming School of Medicine, Division of Endocrinology and Nephrology, University of Leipzig, Calgary, Canada; ²Division of Endocrinology and Nephrology, University of Leipzig, Leipzig, Germany; ³Amedes Mvz Wagnerstibbe für Laboratoriumsmedizin, Hämostaseologie, Humangenetik und Mikrobiologie Hannover, Hannover, Germany; ⁴Mvz Wagnerstibbe für Gynäkologie, Reproduktionsmedizin, Zytologie, Pathologie und Innere Medizin GmbH, Einbeck, Germany; ⁵University 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 Tomoda¹, Kiminori Sugino¹, Yuna Ogimi¹, Chie Masaki¹, Junko Akaishi¹, Kyōmi Y. Hames¹, Akifumi Suzuki¹, Kenichi Matsuzu¹, Takashi Urano¹, Keiko Ohkuwa¹, Hiroshi Shibuya¹, Wataru Kitagawa¹, Mitsui Nagahama¹, Koichi Ito¹
¹Ito Hospital, Tokyo, Japan
P3–06–03  DISEASE STATUS AT PRESENTATION AND DISEASE RELATED MORTALITY FROM DIFFERENTIATED THYROID CANCER
Eyal Robenshtok1, Yuval Nachalon2, Carlos Benbassat3, Dania Hirsch4, Aharon Popovtzer4
1Endocrinology and Metabolism Institute, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel; 2Department of Otorhinolaryngology-Head and Neck Surgery, Rabin Medical Center, Petah-Tikva, Israel; 3Endocrinology Service, Assaf Harofe Medical Center, Zrifin, Israel; 4Davidoff Cancer Center, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel

P3–06–04  IMPACT OF PREOPERATIVE DETECTION OF SODIUM-IODIDE SYMPORTER EXPRESSION LEVEL ON DIFFERENTIATED THYROID CANCER (DTC) PROGNOSIS
Marina Boriskova1, Dmitriy Semenov1, Uliana Farafonova1, Ludmila Koloskova2
1Pavlov First Saint Petersburg State Medical University, General Surgery Department, Saint Petersburg, Russian Federation; 2Medlab, Saint Petersburg, Russian Federation

P3–06–05  NATURAL HISTORY OF CONTRALATERAL NOODULES AFTER LOBECTOMY IN PATIENTS WITH PAPILLARY THYROID CARCINOMA
Amit Ritter1, Gideon Bachar2, Orna Katz3, Nadav Kochen2, Dania Hirsch3, Carlos Benbassat3, Eyal Robenshtok3
1Department of Otolaryngology, Head and Neck Surgery, Rabin Medical Center, Petach Tikva, Israel; 2Department of Otolaryngology Head and Neck Surgery, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel; 3Endocrinology and Metabolism Institute, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel; 4Endocrinology Service, Assaf Harofe Medical Center, Zrifin, Israel

P3–06–06  CLINICAL CHARACTERISTICS AND LONG TERM OUTCOME OF PATIENTS WITH DIFFERENTIATED CARCINOMA THYROID WITH BONE METASTASES – A RETROSPECTIVE STUDY
Sadaf Butt1, Shazia Fatima2, Kakhashan Mir3, Ayesha Ammar2, Faheem Mohammad2
1Nori, Islamabad, Islamabad, Pakistan; 2Nori, Islamabad, Pakistan; 3Nori, 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 Smit1, Marcia Brose2, Chia-Chi Lin3, Marc Fellous4, Fabian Pitoia5, Iwao Sugitan6, Martin Schlumberger7
1Department of Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands; 2Department of Otorhinolaryngology: Head and Neck Surgery, Abramson Cancer Center of the University of Pennsylvania, Philadelphia, Pa., USA; 3Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; 4Bayer Healthcare Pharmaceuticals, Whippany, Nj, USA; 5Division of Endocrinology – Hospital de Clinicas, Universidad de Buenos Aires, Buenos Aires, Argentina; 6Department of Endocrine Surgery, Nippon Medical School Graduate School of Medicine, Tokyo, Japan; 7Gustave Roussy, Villejuif, France

P3–06–08  OUTCOME OF THYROID CARCINOMA ASSOCIATED TO CLINICALLY MANIFEST AUTOIMMUNE THYROID DISEASE
Camila Moma1, Ligia Vera Montalı Assumpçao2, Patricia Sabino de Matos3, Denise Engelbrecht Zantut Wittmann4
1State University of Campinas, Campinas, Brazil; 2Endocrinology Division, Department of Internal Medicine, University of Campinas, Campinas, Brazil; 3Department of Pathology, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil; 4Endocrinology Division, Department of Clinical Medicine, Faculty of Medical Sciences, University of Campinas-Unicamp, Campinas, Brazil

P3–06–09  ANALYSIS OF FACTORS PREDICTING BILATERAL LATERAL NECK METASTASES IN PATIENTS WITH UNILATERAL PAPILLARY THYROID CARCINOMA
Ho Jin Chang1, Soo Young Kim1, Hyukjun Yun1, Seok-Mo Kim1, Bup-Woo Kim1, Yong Sang Lee1, Hang-Seok Chang1, Cheoong Soo Park1
1Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

P3–06–10  THE LOW IODINE DIET: TIME FOR IMPROVEMENT
Rixte J. Jagersma1, Anneke M. Muller Kobold1, Linda G. Swart1, Bernadette L. Dekker1, Thera Links2, Anouk van der Horst – Schrivers2
1University Medical Center Groningen, Groningen, Netherlands; 2University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands

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 Kim1, Tae Yong Kim1, Suyeon Park1, Suyeon Park1, Jong Ho Yoon1, Suck Joon Hong1, Young Kee Shong4, Won Bae Kim5
1Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; 2Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; 3Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South; 4Asan Medical Center, Endocrinology, Seoul, Korea, Rep. of South; 5Asan Medical Center, Seoul, Korea, Rep. of South
P3–07–02 LIMITS OF FROZEN SECTION IN INDETERMINATE THYROID NODULES: A RETROSPECTIVE ANALYSIS OF 75 HISTOLOGICALLY PROVEN THYROID NODULES
Pascaline Huynh1
1Hôpital Sud Francilien, Corbeil Essonnes, France

P3–07–03 US ELASTOGRAPHY USING CAROTID ARTERY PULSATION: EFFICACY AND REPRODUCIBILITY ANALYSIS IN DIFFERENTIAL DIAGNOSIS OF THYROID NODULES
Eun Ju Ha1, Miran Han2
1Ajou University School of Medicine, Department of Radiology, Suwon, Korea, Rep. of South; 2Ajou 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 Ha1, Won-Jin Moon2, Donggyu Na3, Young Hen Lee4, Nami Choi2, Jae Kyun Kim2
1Ajou University School of Medicine, Department of Radiology, Suwon, Korea, Rep. of South; 2Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Korea, Rep. of South; 3Human Medical Imaging & Intervention Center, Seoul, Korea, Rep. of South; 4Ansan Hospital, Korea University School of Medicine, Gyeonggi-Do, Korea, Rep. of South; 5Chung Ang University Medical Center, Seoul, Korea, Rep. of South

P3–07–05 MALIGNANT THYROID NODULE IN CHRONIC LYMPHOCYTIC THYROIDITIS: THE VALUE OF CORE-NEEDLE BIOPSY
Yeo Koon Kim1, Ji-Hoon Kim2, Jae Sun Ji3
1Seoul National University, Seongnam-Si, Korea, Rep. of South; 2Seoul National University Hospital, Seoul, Korea, Rep. of South; 3Seoul National University Bundang Hospital, Seongnam-Si, Korea, Rep. of South

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Giulia Sapuppo1, Ilenia Marturano1, Filippo Palermo2, Romilda Masucci3, Mario Manusia3, Martina Tavarelli1, Dario Tumino1, Gabriella Pellegriti1
1Endocrinology, Garibaldi Nesima Hospital, University of Catania, Catania, Italy; 2Infectious Diseases, Garibaldi Nesima Hospital, University of Catania, Catania, Italy; 3Cancer Surgery, Garibaldi Nesima Hospital, Catania, Italy; 4Pathological Anatomy, Garibaldi Nesima Hospital, Catania, Italy

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Frederik Verburg1, Uwe Mäder2, Luca Giovanella1, Markus Luster1, Christoph Reiners4
1University Hospital Marburg, Department of Nuclear Medicine, Marburg, Germany; 2University of Würzburg, Comprehensive Cancer Center Mainfranken, Würzburg, Germany; 3Oncology Institute of Southern Switzerland, Department of Nuclear Medicine and Pet Center, Bellinzona, Switzerland; 4University of Würzburg, Department of Nuclear Medicine, Würzburg, Germany

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Maurilio Deandrea1, Francesca Garino1, Alberto Mornimi1, Cristina Caresio1, Marco Caballo1, Filippo Molinari2, Paolo Piero Limone3
1Department of Endocrinology, Diabetes and Metabolism, AO Mauriziano, Turin, Italy; 2Department of Electronics and Telecommunications Politecnico di Torino, Turin, Italy; 3A.O. Ordine Mauriziano di Torino, Endocrinology and Metabolism, Turin, Italy

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Ruxandra Dobrescu1, Dumitru Ioachim1, Andrei Goldstein1, Corin Badiu1
1National Institute of Endocrinology, Bucharest, Romania

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Argyro Panagiotakou1, Dimitrios Ioannidis2, Dimitrios Lilis1, Georgios Karageorgos3
1Sismanoglio General Hospital, Amalia Fleming Department, Athens, Greece; 2Sismanoglio General Hospital, Department of Amalia Fleming, N. Erithrea, Athens, Greece

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

08 Basic Autoimmunity and Thyroidology
Chairperson: Marie-Christine Many, Belgium

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Aristides López Márquez1, Carlos Carrasco López1, Pilar Santisteban2
1Instituto de Investigaciones Biomédicas ‘Alberto Sols’ (Csc-Uam), Madrid, Spain; 2Biomedical Research Institute, Biomedical Research Institute, Madrid, Spain
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Bushra Shahida1, Tereza Planck2, Peter Åsman3, Mikael Lantz4
1Lund University, Dpt. Clinical Sciences Malmö, Diabetes & Endocrinology, Malmö, Sweden; 2Lund University, Dpt. Clinical Sciences Malmö, Diabetes & Endocrinology, Skåne University Hospital, Malmö, Sweden; 3Lund University, Dpt. Clinical Sciences Malmö Ophthalmology, Skåne University Hospital Dpt. of Ophthalmology, Malmö, Sweden; 4Department of Endocrinology, Skåne University Hospital, Malmö, Sweden

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Artur Bossowski1, Kamil Grubczak2, Paulina Snight2, Beata Sawicka2, Anna Bossowska3, Marcin Moniuszko3
1Medical University in Białystok, Dep. of Pediatrics, Endocrinology, Diabetology With A Cardiology Division, Białystok, Poland; 2Department of Regenerative Medicine and Immune Regulation, Białystok, Poland; 3Medical University in Białystok, Dep. of Pediatrics, Endocrinology, Diabetology With Cardiology Division, Białystok, Poland; 4Dep. of Cardiology, Ministry Hospital in Bialystok, Białystok, Poland; 5Department of Regenerative Medicine and Immune Regulation, Medical University in Białystok, Białystok, Poland

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Celia Fernández Méndez1, Pilar Santisteban2
1Biomedical Research Institute, Madrid, Spain; 2Biomedical Research Institute, Biomedical Research Institute, Madrid, Spain

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Rebeca Martinez Hernandez1, Ana M Ramos-Levi2, Ana Serrano-Somavilla1, Miguel Sampedro-Nuñez1, Isabel Huguet1, Mónica Marazuela1
1Hospital Universitario de la Princesa, Instituto de Investigación Princesa, Universidad Autónoma de Madrid, Madrid, Spain; 2Hospital Universitario Princesa, Instituto de Investigación Princesa, Endocrinology and Nutrition, Madrid, Spain

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Nina Petunina1, Narine Martirosian1, Liubov Trukhina1, Svetlana Saakyan1, Olga Panteleeva2, Valery Nosikov3
1Sechenov First Moscow State Medical University, Moscow, Russian Federation; 2The Helmholtz Moscow Research Institute of Eye Diseases, Moscow, Russian Federation; 3Emanuel Institute of Biochemical Physics of Russian Academy of Sciences, Moscow, Russian Federation

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Artur Bossowski1, Hanna Borysewicz-Sanczyk2, Anna Bossowska3, Maria Del Pilar Larosa4, Shu Chen4, Jadwiga Furmaniak4, Bernard Rees Smith4
1Medical University in Białystok, Dep.of Pediatrics, Endocrinology, Diabetology With A Cardiology Division, Białystok, Poland; 2Medical University in Białystok, Dep. of Pediatrics, Endocrinology, Diabetology With Cardiology Division, Białystok, Poland; 3Medical University in Białystok, Dep. of Pediatrics, Endocrinology, Diabetology With Cardiology Division, Białystok, Poland; 4Dep. of Cardiology, Ministry Hospital in Bilaystok, Białystok, Poland; 5Firs Laboratories, Rsr Ltd, Cardiff, UK

P3–08–08  LOW CD26 EXPRESSION IN HASHIMOTO’S THYROIDITIS
Yalei Liu1, Yang Zhang1, Nan Yu1, Yan Gong1, Ran You1, Chenxue Qu1, Guizhi Lu1, Youyuan Huang1, Hong Zhang1, Ying Gao1, Yanming Gao1, Xiaohui Guo1
1Peking University First Hospital, Beijing, China

P3–08–09  MULTIPLE NUTRITIONAL FACTORS AND THE RISK OF HASHIMOTO’S THYROIDITIS
Margaret Rayman1, Shiqian Hu2
1University of Surrey, Guildford, UK; 2University of Surrey, Guildford, UK
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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39th Annual Meeting of the European Thyroid Association

Abstracts

Copenhagen, Denmark
September 3–6, 2016

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


**Oral Session 1:**

**Topic Highlights**

14.00–14.20

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

Valentina Cirello1, Valentina Vaira2, Germano Gaudenzi3, Elisa Stellaria Grassi4, Giovanni Vitale5, Dario Ricci6, Carla Colombo7, Silvano Bosari8, Leonardo Vicentini2, Luca Persani9, Stefano Ferrero3, Laura Fugazza10

1Department of Pathophysiology and Transplantation, University of Milan, Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Italy. 2Division of Pathology, Fondazione Ircs Ca’ Granda, Milan, Italy. 3Department of Clinical Sciences and Community Health, University of Milan, Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Ircs, Milan, Italy. 4Division of Endocrine and Metabolic Diseases & Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano Ircs, Milan, Italy. 5Department of Clinical Sciences and Community Health, University of Milan, Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Italy. 6Division of Pathophysiology and Transplantation, University of Milan, Division of Pathology, Fondazione Ircs Ca’ Granda, Milan, Italy. 7Endocrine Surgery Unit, Fondazione Ircs Ca’ Granda, Milan, Italy. 8Department of Biomedical, Surgical and Dental Sciences, University of Milan, Division of Pathology, Fondazione Ircs Ca’ Granda, Milan, Italy.

**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 TFF1 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 the 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.

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**Oral Presentations**

**14.20–14.40**

**TRACING OF BRAF MUTANT THYROID CELLS BEFORE TUMOR DEVELOPMENT**

Ellen Johansson1, Shawn Liang2, Elin Schoultz3, Mikael Nilsson4

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

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 Braf560E 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;Braf560E mouse 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;Braf560E might allow detection and fate determination of thyroid cells early on after expression of oncogenic Braf560E. These mice were crossed with the mTmG reporter. In the absence of Cre all thyroid cells showed red fluorescence (mF+) whereas 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 micrometastases. Of interest, mG+ cells were encountered in follicle lumina at a higher incidence than expected by the limited numbers of mF+ 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.

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**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 Cantara1, Domenico Salvatore2, Monica Denticci2, Maria Grazia Castagna3, Raffaele Ambrosio4, Fabio Maino1, Corrado Garbi1, Carlotta Marzocchi5, Tommaso Porcelli6, Furio Pacini1

1Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy. 2Department of Clinical Medicine and Surgery, University of Naples, Federico II, Naples, Italy.

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,
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. \( \text{Dio}2 \) 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 18.4% 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 thyrocytes. 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.

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**Table 1.** (for abstract time 15.00–15.20)

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

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**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**

**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.
Differential Effects of MCT8-DIO2 and MCT8-OATP1C1 Inactivation on Cerebral Cortex Gene Expression in the Mouse

Beatriz Morte, Pilar Gil, Heike Heuer, Juan Bernal
1Center for Biomedical Research on Rare Diseases, Instituto de Investigaciones Biomédicas Uam-Csic, Madrid, Spain, 2Instituto de Investigaciones Biomédicas Uam-Csic, Center for Biomedical Research on Rare Diseases, Madrid, Spain, 3Leibniz Institute for Environmental Medicine (Ifi), Leibniz Institute for Aging, Fritz Lipmann Institute (Fli), Düsseldorf, Germany, 4Instituto 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 and of MCT8-OATP1C1 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.

Grant: E-Rare-2, the ERA-Net for Research on Rare Diseases, and SAF2014-54919-R.

Eur Thyroid J 2016;5(suppl 1):57–176

Table 1. (for abstract time 10.00–10.15)

<table>
<thead>
<tr>
<th>EI-outcome</th>
<th>Malignant, kPa</th>
<th>Benign, kPa</th>
<th>p-value</th>
<th>ROC AUC mean, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROI-mean</td>
<td>27 (3–100)</td>
<td>28 (4–182)</td>
<td>0.78</td>
<td>0.51 (0.42–0.59)</td>
</tr>
<tr>
<td>ROI-max</td>
<td>40 (11–148)</td>
<td>39 (6–242)</td>
<td>0.50</td>
<td>0.53 (0.44–0.61)</td>
</tr>
<tr>
<td>ROI-nn</td>
<td>2.4 (1.0–15.1)</td>
<td>2.4 (1.1–27.6)</td>
<td>0.13</td>
<td>0.55 (0.48–0.62)</td>
</tr>
<tr>
<td>Stiff-mean</td>
<td>33 (4–116)</td>
<td>32 (4–192)</td>
<td>0.96</td>
<td>0.52 (0.44–0.60)</td>
</tr>
<tr>
<td>Stiff-max</td>
<td>39 (11–148)</td>
<td>38 (6–242)</td>
<td>0.52</td>
<td>0.52 (0.44–0.61)</td>
</tr>
<tr>
<td>Center-mean</td>
<td>17 (4–51)</td>
<td>16 (4–88)</td>
<td>0.61</td>
<td>0.52 (0.44–0.61)</td>
</tr>
<tr>
<td>Center-sd</td>
<td>8.1 (1.5–31.6)</td>
<td>7.1 (1.3–56.5)</td>
<td>0.16</td>
<td>0.56 (0.48–0.64)</td>
</tr>
</tbody>
</table>

* Median (range); nn: ratio comparing stiff and soft areas of the nodule.
1 3 mm; 2 1–3 mm; 3 10 mm.
Oral Presentations

10.15–10.30

NEXT-GENERATION SEQUENCING OF THYROID FNA SAMPLES USING THE ION AMPLISEQ™ CANCER HOTSPOT PANEL V2
Claudio Bellevicin1, Roberta Sgarigliia1, Umberto Malapelle1, Caterina De Luca1, Elena Viglier1, Markus Eszlinger2, Ralf Paschke2, Giancarlo Troncone1
1University of Naples Federico II, Public Health Department, Napoli, Italy; 2University of Calgary, Calgary, Canada

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)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Max</th>
<th>Min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mapped reads</td>
<td>160,120.26</td>
<td>732,933</td>
<td>963</td>
</tr>
<tr>
<td>On-target reads (%)</td>
<td>76.05</td>
<td>99.15</td>
<td>3.06</td>
</tr>
<tr>
<td>Average base coverage</td>
<td>967.91</td>
<td>3,740</td>
<td>4.13</td>
</tr>
<tr>
<td>Uniformity (%)</td>
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10.30–10.45

PROGNOSTIC VALUE OF MINIMAL EXTRATHYROIDAL INVASION (PT3) IN PATIENTS WITH PAPILLARY THYROID CARCINOMA NOT SUBMITTED TO PROPHYLACTIC LYMPHADENECTOMY
Fabio Maino1, Maria Grazia Castagna1, Filomena Barbato1, Raffaella Forte1, Noemi Fralassi1, Fumo Pacini2
1Department of Medical, Surgical and Neurological Sciences, University of Siena, Siena, Italy; 2Department of Medical, Surgical and Neurological Sciences, University of Naples Federico II, Public Health Department, Napoli, Italy

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.

10.45–11.00

THE MACROFOLLICULAR VARIANT OF PAPILLARY THYROID CANCER (MF-PTC): A BICENTRIC RETROSPECTIVE ANALYSIS OF 65 CASES
Carolotta Giani1, Joana Simões Pereira2, Pedro Marques3, Daniel Macedo2, Rita Santos2, Liborio Torregrossa1, Fulvio Basolo1, Rossella Elisei1, Valeriano Leite2
1Endocrine Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; 2Endocrinology Section, Instituto Português de Oncologia de Lisboa, Francisco Gentili, Lisbon, Portugal; 3Department of Surgical, Medical and Molecular Pathology of the Clinical Area, Pisa, Italy

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 131I-ablative. The whole body scan post-131I-therapy showed cervical uptake in all pts; 1IPO-pts 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 131I-therapy. 3) In the future the molecular analysis could explain the reasons of this exceptional respond.

We retrospectively evaluated 504 patients (pT1-T3Nx): 118/504 (23.4%) had an 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 (8.7%) 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.
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, FTC) 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 FTC 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 FTC, p = 0.02). Conversely, no difference was observed among PMC and FTC 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.

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

Letizia Pieruzzi1, Loredana Lorusso1, Liborio Torregrossa2, Valeria Bottici1, Laura Agate1, Fulvio Basolo1, Gabriele Materazzi1, Paolo Vitti1, Eleonora Mollinaro1, Rossella Elisei1
1Endocrinology Section, Department of Medical and Experimental Medicine, University of Pisa, Pisa, Italy, 2Department of Surgical Medical, Molecular Pathology, University of Pisa, Pisa, Italy

Introduction: The simultaneous presence of MTC and DTC is a rare event, but more frequent than expected. The cellular origin, the clinical-patho-

thetic 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.
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
Anne Houbrechts1, Jolien Van houcke1, Veerle Darras2
1Laboratory Comparative Endocrinology, Biology Department, Ku Leuven, Leuven, Belgium

Objectives: Reproduction is a thyroid hormone (TH)-dependent process and vertebrate gonads express TH transporters and deiodinases to regulate local 3,5,3'-triiodothyronine (T3) 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, oocytes were doubled in size compared to WT of the same age. Ovarian T3 levels were strongly decreased in mutant vs WT fish. This was accompanied by an increased expression of dio1 and thrha while dio3a, dio3b and thrb expression remained unaffected.

Conclusion: Dio2 deficiency severely disrupts reproduction in zebrafish. The resulting decrease in ovarian T3 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
Jean Virginie1, Lobysheva Inna1, Bailigand Jean-Luc1, Marie-Christine Mary2, Desy Chantal2
1UCL-IreC-Fath, Brussels, Belgium, 2SS/Mede/IreC/UCL, Bruxelles, Belgium

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.
THYROID HORMONE AND SKIN CANCER:
A NOVEL MICRONA21-D3 INTERPLAY REGULATES BASAL CELL CARCINOMA TUMORIGENESIS
Daniela Di Girolamo1, Raffaele Ambrosio1, Maria Angela De Stefano1, Giuseppina Mancino1, Emery De Cicco1, Caterina Miro1, Domenico Salvatore1, Monica Denticci4
1University of Naples ‘Federico II’, Naples, Italy, 2ircs Sdn, Naples, Naples, Italy, 3Departmento DI Endocrinologia, University of Naples, Federico II, Napoli, Italy, 4Department of Clinical Medicine and Surgery, University of Naples Federico II, Endocrinologia and Oncologia, Naples, Italy

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 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.

THYROID HORMONE TRANSPORTERS IN XENOPUS AND THEIR SUSCEPTIBILITY TO XENOBIOTICS
Bilal Mughal1, Michelle Leemans1, Lindsey Marshall1, Sébastien Le Mèvé2, Jean-Baptiste FINP, Barbara Demeine2

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 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.

THE T3 RECEPTOR TRα1 INTERACTOME
Marcel Meim1, Kam Wejaphikul1, W. Edward Visser2, Theo M. Luider3, Theo Visser4, Robin Peeters2
1Erasmus Medical Center, Tumorology Laboratory, Department of Internal Medicine, Rotterdam, Netherlands, 2Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands, 3Metabolic Research Laboratories, Addenbrooke’s Hospital, Cambridge, UK, 4Erasmus Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands, 5Department of Cell Biology, Erasmus University Medical Center, Rotterdam, Netherlands, Erasmus University Medical Center, Rotterdam, The Netherlands

Introduction: Patients with Resistance to Thyroid Hormone (RTH), due to heterozygous mutations in TRα, are characterized by growth retardation, macrocephaly and abnormal thyroid function tests. In addition, almost all RTH patients harbor the pathogenesis of which is unknown. Since animal studies suggest an important role for TR and TRα in the latter stages of thyroid development, we hypothesized that erythropoiesis in RTH patients is impaired.

Objective: Our objective was to elucidate the pathogenesis of anemia in RTH patients and delineate the role of TR and TRα in human erythropoiesis.

Methods: Cultures of primary human erythroid progenitors (HEPs), from peripheral blood of RTH patients harboring different inactivating mutations in TRα (F937H, H924S, E924K), 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 RTH patients continued to proliferate and showed less differentiated morphology. Throughout the differentiation phase, HEPs from RTH patients were larger in size and more positive for c-Kit and larger in the latter 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 RTH 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 RTH patients.

THYROID HORMONE INTERACTOMES IN HUMAN ERYTHROPOIESIS
Ania van Gucht1, Marcel Meima2, Carla Moran3, Maura Agostina3, Anna Tyliki-Szymanska3, Malgorzata Krajewska-Walasek3, Krystyna Chrzanoswka3, Alexandra Efthymiadou4, Dionisios Chrysis5, Korcan Demir4, W. Edward Visser4, Theo Visser5, Thamar Van Dijk6, 7V. Krishna Chatterjee7, Robin Peeters2
1Erasmus Medical Center, Tumorology Laboratory, Department of Internal Medicine, Rotterdam, Netherlands, 2Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands, 3Metabolic Research Laboratories, Addenbrooke’s Hospital, Cambridge, UK, 4Erasmus Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands, 5Department of Cell Biology, Erasmus University Medical Center, Rotterdam, Netherlands, Erasmus University Medical Center, Rotterdam, The Netherlands, Erasmus University Medical School, Rotterdam, Netherlands, 6Department of Biology, Erasmus University Medical Center, Rotterdam, The Netherlands

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Results: After ~14 days of ex vivo expansion, control HEP cells started to differentiate spontaneously. In contrast, the majority of HEPs from all RTH patients continued to proliferate and showed less differentiated morphology. Throughout the differentiation phase, HEPs from RTH 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 RTH 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 RTH patients.
protocol and present here the interactionome for wild-type TRα1 in HepG2 human hepatocytes. **Objective:** To purify and identify an interactionome 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/FLAG–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 Massoff_1, Selmar Leeuwenburgh1, Sigrid Swagemakers3, Mirjam van den Hout-van Vroonhoven4, Boen L.R. Kam5, Pim Burger5, Peter van der Spek5, Wilfred F. van IJcken4, Theo Visser5, Robin Peeters5, W. Edward Visser6

1Erasmus MC, Endocrinology, Rotterdam, Netherlands, 2Erasmus MC, Internal Medicine, Rotterdam, Netherlands, 3Erasmus MC, Bioinformatics, Rotterdam, Netherlands, 4Erasmus MC, Center for Biomics, Rotterdam, Netherlands, 5Erasmus MC, Department of Nuclear Medicine, Rotterdam, Netherlands, 6Erasmus MC, Department of Surgery, Rotterdam, Netherlands, 7Erasmus University Medical Center, Rotterdam, The Netherlands, 8Erasmus University Medical School, Rotterdam, Netherlands, 9Erasmus University Medical Center, Rotterdam, The Netherlands

**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 (TRα1 and TRβ 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 TRα1 expressing leukocytes. **Methods:** We studied whole blood samples (collected in PAXgene RNA tubes) from 8 thyroidectomized patients (4 females) with differentiated thyroid cancer. We performed next-generation RNA sequencing after removal of ribosomal RNA and global 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 x 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 x 10^-5). **Conclusion:** Physiological levels of TH regulate numerous genes in human whole blood, presumably TRα1 expressing leukocytes. 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**

_Katrin Manuela Hinz_1, Dominik Neef1, Gerd Krause1

1Leibniz-Institut für Molekulare Pharmakologie (Fmp), Berlin, Germany

Thyroid hormones (TH) are traversed via transporters across the cell membrane. The L-type amino acid transporter 2 (Lat2) imports amino acids as well as TH1, 3,3'-T2 and T3, but not T4 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 convention 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 moieties, 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.

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**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**

_Allan Carle_1, Peter Laurborg1, Rudi Steffensen2, Jens Faber1, Birte Nygaard4

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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 monocarboxyate 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-
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-term stable (≥6 months) euthyroidism on T4 therapy participated in a prospective double blind cross-over study. Half of the patients were randomized into continuous T4-therapy and the rest into combination therapy followed by T4-therapy. In both periods, 50 μg of T4 was blindly replaced by either identical 20 μg T3. We investigate four single-nucleotide polymorphisms (SNPs) with pre-designed TaqMan assay (Applied Biosystems, Foster City, CA) in two genes: DIO2 (rs225014, rs12885300, rs5022115) 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 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**


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**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 base-line 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 thyroidecmy: 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 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 influenced 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.

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**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 patients (decreased TSH and normal thyroid hormones) (n = 2533) was 1.08 (1.00–1.19; 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 thera- peutic 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.

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.

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 and identified 121,799 individuals diagnosed with a first episode of hyperthyroidism. These were matched with 4 non-hyperthyroid controls according to age and sex.

Results: Mean age at diagnosis of GD was 55 years. Overall, we found a 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 association, and, if so, whether hypothyroidism precedes glaucoma or vice versa.

Conclusion: 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.

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

16.45–17.00

17.00–17.15

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17.45–18.00
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) cytologically 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 then 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 terms 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 OBSESE HYPOTHYROID PATIENTS**

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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 yrs) 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 yrs) age-matched patients with normal BMI (<25 kg/m²), 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/II = 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/m²; n = 17) to 1.00 μg/Kg/day; (BMI >35 kg/m²; 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.

**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**

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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 BRAF V600E 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 BRAFV600E mutation.

16.30–16.45
GENETIC PREDISPOSITION TO PAPILLARY THYROID CANCER IN CHILDREN AND ADOLESCENTS
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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 Express Exome v. 1.0 DNA Analysis BeadChip (Illumina Netherlands B.V.) 104 patients were included with histological confirmed 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, rs269987 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 rs269987 located in SERPINA5 gene could be involved in childhood/adolescents PTC etiology.

This work was supported by the Polish National Centre of Science (grant numbers N N402 193740 and STRATEGMED2/267398/4/NCBR/2015).

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 52 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 most transcription factor 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 staging and clinical remission rates were observed. The NFKB1A 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.
GERMLINE AND SOMATIC DICER1 MUTATIONS IN FAMILIAL PAPILLARY THYROID CARCINOMA

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The inheritable component of familial Papillary Thyroid Cancer (PTC) 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 PTC 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. **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 6 fvPTC at 11 (fvPTC2). The aunt was thyroidectomized for compressive MNG 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.

A MOUSE MODEL OF SPORADIC PAPILLARY THYROID CANCER AND TUMOR PROGRESSION

Elin Schoultz¹, Ellen Johansson¹, Shawn Liang², Mikael Nilsson³

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

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 Bradv600e is constitutively activated (Braf(C43f)) 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(C43f) might be a suitable model of sporadic PTC. Theoretically Cre can be activated from onset of Tg expression in the embryonic thyroid. By recombinating TgCre;Braf(C43f) 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(C43f);trp53⁻ mice.

In conclusion, stochastic Cre-mediated activation of Bradv600e and inactivation of p53 in few cells of the young mouse thyroid induce micrometastases and delayed onset of tumor progression, thus recapitulating the developing process of sporadic PTC in humans.

TREATMENT OUTCOMES IN BRAIN METASTASIS FROM PAPILLARY THYROID CANCER

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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 significantly 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.
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 Bartalema, Giovanni Veronesi, Gerassimos Krassas, Wilmar Wiersinga, Claudio Marcocci, Mario Salvi, Chantal Daumenie, Claire Bournaud, Matthias Stahl, Lorenza Sassi, Claudio Azzolini, Kostas Boboridis, Maarten Mounts, Maarten Soetens, Baldeschi Lelio, Marco Nardi, Nicola Currò, Antonella Boschi, Martine Bernard, Georg von Arx, Petros Perros, George J. Kahaly

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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.

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 or try and ameliorate CI, or continue ivGCs to inactive 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.

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

Tramunt Blandine, Philippe Imbert, Grunenwald Solange, Franck Boutillet, Philippe Caron

1Service D’endocrinologie et Maladies Métaboliques, Chu Larrey, Toulouse, France, 2Service D’ophthalmologie, Clinique du Parc, Toulouse, France, 3Chu Larrey, Toulouse Cedex 9, France, 4Service de Chrurgie Maxillo-Faciale, Chu Pierre-Paul Riquet, Toulouse, France, 5Chu Larrey, Teme Elaghe/Chu Rangueil, Toulouse Cedex 9, France

Yes: 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 TSHR bioassay (sensitivity 100%). Among these 60 GD patients, 20 had low TSHR positivity (SRR 140–279), but were TBI-positive in only 18 (90%), 11 (55%), 9 (45%), and 7 (35%) using the Immulite, Cobas, Kryptor, and Dynex, respectively. In 20 moderate TSHR-positive (SRR 280–420) GD patients, TBI 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, Immulse, 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 Ferrari1, Poupak Fallahi2, Giulia Santaguida2, Camilla Vini3, Ilaria Rufilli3, Francesca Ragusa1, Marco Centanni2, Alessandro Antonelli4

1 University of Pisa, Pisa, Italy, 2 Sapienza University of Rome, Department of Medico-Surgical Sciences and Biotechnologies, Latina, Italy

**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 Santaguida1, Camilla Vini2, Ilaria Gatto3, Giorgio Mangino1, Ilaria Stramazzo3, Marco Centanni4

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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+Th1 and Breg lymphocytes specific phenotypes (CD24+CD38+) 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 ± 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 vs. 2.0 ± 0.7%; p = ns), while patients with HT+NEAD showed higher percentages (3.9% ± 1.2) than those with HT (p = 0.0003) and HD (p < 0.0001). Following CpG stimulation, we found higher percentage of Breg IL-10+ cells in patients with isolated HT than in HD (3.9 ± 1.8 vs 2.4 ± 1.1%; p = 0.0303). Surprisingly, Breg IL10+cells percentage (2.9% ± 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**

Clotilde Saei1, Cecile Ghandri2, Sami Saheb3, Natasha Jumentier4, Fatma Kharcha1, Didier Lemesle1, Salwa Bak3, Nassiba Baghdadi5

1 Hôpital Pitié Salpêtrière, Paris, France, 2 Hôpital Pitié Salpêtrière, Marrakesh, Morocco, 3 La Pitié Salpêtrière Hospital, Thyroid and Endocrine Tumors Unit, Paris, France

**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).

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 Villagelin¹, Roberto Bernado Dos Santos¹, João Hamilton Romaldini¹, Ana Paula Correia¹, Natassia Bufalo², Karina Colombera Perez³, Laura Ward³, Pontificia Universidad Catolica Campusinas, Campusinas, Brazil, ²Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Brazil

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 required subsequent ophthalmic surgery.

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 ≤ 0.02), while visual function scale was associated with the time of GO (p ≤ 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.

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 ANITNEOPLASTIC ACTIVITY OF VANDENATIB, AND LENVATINIB IN PRIMARY ANAPLASTIC THYROID CANCER CELLS, OBTAINED FROM FINE NEEDLE ASPIRATION

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¹University of Pisa, Pisa, Italy, ²Department of Pharmaceutical Science, University of Pisa, Pisa, Italy, ³Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy

Objective: The possibility to test the sensitivity of ‘primary anaplastic thyroid cancer (ATC)’ (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), 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 vandetanib, and a slight level with lenvatinib. 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

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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) heptanomide (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 (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 Iwasaki1, Hiroyaka Nakayama2, Nobuyasu Suganuma1, Tatsuya Yoshida3, Takashi Yamanaka1, Shinsuke Hatori3, Satoru Shimizu1

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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)

<table>
<thead>
<tr>
<th>TKI drugs</th>
<th>Patients number</th>
<th>Ongoing patients</th>
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11.00–11.15
CALCITONIN RECEPTOR (CTR) EXPRESSION IN MEDULLARY THYROID CANCER (MTC) AND POSSIBLE CLINICAL IMPLICATIONS

Virginia Cappagli1, Catarina Soares Potes2, Luciana Bueno Ferreira3, Catarina Eloy3, Cristina Romei2, Rossella Elisei4, Manuel Sobrinho-Simões1, Peter J. Wookey5, Paula Soares3

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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.
The Mutation Profile of Medullary Thyroid Carcinoma Can Be Different in Primary and Metastatic Tissues

Cristina Röme, Francesca Casella, Alessia Tacito, Raffaele Ciampi, Eleonora Molinaro, Laura Agate, Valeria Bottici, Antonio Matrone, Rossella Elisei

Section of Endocrinology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, Department of Endocrinology, Pisa, Italy

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 in the metastases.

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 metastasis. 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 metastasis. 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.

The Association Between TERT Promoter Mutations and Mortality in Patients with Thyroid Cancer

Tae Hyuk Kim, Youngnam Kim, Hyein Kim, Ho-Su Kim

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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% (22/237) 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 differentiated 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.

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**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**

Matteo Nava1, Marielle S. Klein Hesselink1, Gea A. Huizinga2, Esther Sukkers3, Adrienne H. Brouwers2, Johannes G.M. Burgerhof4, Eveline W.C.M. van Dam5, Bas Havekes6, Marry M. van den Heuvel-Eibrink1, Eleonora P.M. Corsesiti1, Leonien C.T. Kremer7, Romana T. Netea-Maier7, Heleen J.H. van der Pal1, Robin P. Peeters1,2, John T.M. Plukker1, Cécile M. Ronckers4, Hanneke M. van Santen4, Wim J.E. Tissing1, Thera P. Links1, Gianni Bocca15

1University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands, 2University of Groningen, University Medical Center Groningen, Wencelbach Institute, School of Nursing and Health, Groningen, Netherlands, 3University of Groningen, University Medical Center Groningen, Department of Nuclear Medicine and Molecular Imaging, Groningen, Netherlands, 4University of Groningen, University Medical Center Groningen, Department of Department of Epidemiology, Groningen, Netherlands, 5Vu University Medical Center, Department of Internal Medicine, Amsterdam, Netherlands, 6Maastricht University Medical Centre, Department of Internal Medicine, Division of Endocrinology, Maastricht, Netherlands, 7Erasmus Medical Center, Sophia Children’s Hospital, Department of Pediatric Oncology, Rotterdam, Netherlands, 8Leiden University Medical Center, Department of Internal Medicine, Division of Endocrinology, Leiden, Netherlands, 9Academic Medical Center, Emma Children’s Hospital, Department of Pediatric Oncology, Amsterdam, Netherlands, 10Radboud University Medical Center, Division of Endocrinology, Nijmegen, Netherlands, 11Academic Medical Center, Emma Children’s Hospital, Department of Medical Oncology, Department of Pediatric Oncology, Amsterdam, Netherlands, 12Erasmus Medical Center, Department of Internal Medicine, Rotterdam Thyroid Center, Rotterdam, Netherlands, 13University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands, 14University Medical Center Utrecht, Wilhelmina Children’s Hospital, Department of Pediatrics, Utrecht, Netherlands, 15University of Groningen, Beatrix Children’s Hospital, Department of Pediatric Oncology, Groningen, Netherlands, 16University of Groningen, Beatrix Children’s Hospital, Department of Pediatric Endocrinology, Groningen, Netherlands

**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 socioeconomic 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.

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**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 Lamartina1, Giorgio Grani1, Alfredo Pontecorvi2, Celestino Pio Lombardi2, Rocco Bellantone2, Emanuela Avrai1, Efisio Puxeddu1, Maria Chiara Zatelli1, Massimo Tortorano1, Teresa Montesano1, Gianluca Amaretti1, Fabio Monzani1, Fabio Orlandi1, Cecilia Francesco1, Paolo Limone1, Giovanna Spiazzi1, Laura Fugazzola1, Ezio Ghigo3, Marco Attard4, Alessandro Antonelli1, Giuseppe Lucisano1, Antonio Nicolucci1, Cosimo Durante1, Sebastiano Filetti1

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

**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-
DISEASE STAGING (TNM AJCC/UICC, 7th edition) revealed 1418 (74%) stage I tumors, 321 (30%) of the 1086 classified by 2009 ATA guidelines as low-risk patients, 87 (4.5%) that were stage II, 314 (16%) stage III and 94 (5%) stage IV tumors. Radioidine 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 radioidine remnant ablation appeared to be more consistent with the 2009 ATA risk stratification. These data provide a useful baseline for future analyses of ITCCO data aimed at assessing the impact of international guidelines on real-life clinical management of DTCs in Italy.

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

15:30–15:45

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

Marielle Klein Hesseling1, Gianni Bocca2, Yoran Hummel3, Adrienne Brouwers4, Johannes Burgerhof5, Eveline van Dam6, Jourik Gietema7, Bas Havekes8, Marry van den Heuvel-Eibrink9, Eleonora Corssmit10, Leonent Kremer11, Romana Netea-Maier12, Heleen van der Pat13, Robin Peeters14, John Plukker15, Cecile Ronckers16, Hanneke van Santen17, Peter van der Meer18, Thera Links19, Wim Tissing20

1Department of Endocrinology, University Medical Center Groningen, Groningen, Netherlands, 2Department of Pediatric Endocrinology, Beatrix Children’s Hospital, University Medical Center Groningen, Groningen, Netherlands, 3Department of Cardiology, University Medical Center Groningen, Groningen, Netherlands, 4Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, Netherlands, 5Department of Epidemiology, University Medical Center Groningen, Groningen, Netherlands, 6Department of Internal Medicine, VU University Medical Center, Amsterdam, Netherlands, 7Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands, 8Department of Internal Medicine, Division of Endocrinology, Maastricht University Medical Center, Maastricht, Netherlands, 9Department of Pediatric Oncology, Sophia Children’s Hospital, Erasmus Medical Center, Rotterdam, Netherlands, 10Department of Internal Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, Netherlands, 11Department of Pediatric Oncology, Emma Children’s Hospital, Academic Medical Center, Amsterdam, Netherlands, 12Department of Pediatric Oncology, Emma Children’s Hospital, Academic Medical Center, Amsterdam, Netherlands, 13Department of Internal Medicine, Erasmus Medical Center, Rotterdam Thyroid Center, Erasmus Medical Center, Rotterdam, Netherlands, 14Department of Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands, 15Department of Pediatric Oncology, Emma Children’s Hospital, Amsterdam, Netherlands, 16Department of Pediatrics, Wilhelmina Children’s Hospital, University Medical Center Utrecht, Utrecht, Netherlands, 17Department of Pediatric Oncology, Beatrix Children’s Hospital, University Medical Center Groningen, Groningen, Netherlands

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

Yuna Ogimi1, Takashi Urano1, Kenichi Matsuzuki1, Tatsuya Maeda1, Chie Masaki1, Tadatoshi Osaku1, Junko Akaishi1, Kiyomi Y. Hames1, Chisato Tomoda1, Akitumi Suzuki1, Keiko Ohkuwa1, Hiroshi Shibuya1, Wataru Kitagawa1, Mitsui Nagahama1, Kiminori Sugino1, Koichi Ito1
1Ito Hospital, Tokyo, Japan

Objective: Most patients with differentiated papillary thyroid cancer (PTC) have excellent treatment outcomes. However, some patients have thyroid invasion to adjacent tissues such as the trachea, larynx, and esophagus, which results in a poor prognosis. In contrast, patients with PTC 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 with 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)

<table>
<thead>
<tr>
<th>Age ≥45 years old</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TN tumor size &gt;40 mm</td>
<td>&lt;0.0001</td>
<td>0.027–2.423</td>
<td>0.1558</td>
</tr>
<tr>
<td>Preoperative LN metastasis(+)</td>
<td>13.76</td>
<td>0.544–347.8</td>
<td>0.0972</td>
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<tr>
<td>RN invasion(+)</td>
<td>&lt;0.0001</td>
<td>0.685–101.9</td>
<td>0.7858</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Age &lt;45 years old</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TN tumor size &gt;40 mm</td>
<td>3.64</td>
<td>1.736–7.067</td>
<td>0.0011</td>
</tr>
<tr>
<td>Preoperative LN metastasis(+)</td>
<td>2.53</td>
<td>1.124–5.23</td>
<td>0.0264</td>
</tr>
<tr>
<td>RN invasion(+)</td>
<td>7.03</td>
<td>3.447–13.76</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

16.00–16.15

INHIBITION OF ERK DIMERIZATION BLOCKS THYROID TUMOR PROGRESSION

Miguel Zaballos1, Adrián Acuña-Ruiz1, García-Riesco-Eizaguirre2, Piero Crespo1, Pilar Santisteban3
1Instituto de Investigaciones Biomédicas ‘Alberto Sols’, Madrid, Spain, 2Hospital Universitario de Móstoles, Madrid, Spain, 3Instituto de Biomedicina Y Biotecnología de Cantabria, Santander, Spain

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 high toxicity in the whole organism. In this work we propose a new way of approaching to the thyroid tumorgenesis 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 proapoptotic 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 tumorgenesis.

16.30–16.45

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

Elisa Stellaria Grassi1, Valentina Cirello2, Carla Colombo3, Valeria Vezziol1, Leonardo Vicentini1, Luca Persani1, Laura Fugazzola4
1Laboratory of Endocrine and Metabolic Research, Ircs Istituto Auxologico Italiano, Milan, Italy, 2Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, 3Endocrine Unit, Fondazione Ircs Ca’ Granda, Milan, Department of Clinical Sciences and Community Health, University of Milan, Italy, 4Endocrine Surgery Unit, Fondazione Ircs Ca’ Granda, Milan, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

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

Daniele Barbaro1, Lorenzo Di Bar1, Valentina Gandin3, Claudio Evangelisti4, Giovanni Vitaliti4, Elena Schiavi4, Cristina Marzando5, Anna M. Ferretti5, Piero Salvadori5

1Spedali Riuniti Di Livorno, Endocrinology, Livorno, Italy, 2Department of Chemistry University of Pisa, Pisa, Italy, 3Department of Pharmaceautical Science University of Padova, Padova, Italy, 4Institute of Molecular Science and Technology National Research Council, Milano, Italy, 5Erre Due Spa, Livorno, Italy, 6Department of Pharmaceutical Pharmacological Science University of Padova, Padova, Italy

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 aqueous solution of D-glucose kept at 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 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

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 Oelkraut1, Milica Vugovic2, Lisbeth Harder4, Beate Hermann1, Sogol Gachkar1, Jens Mittag1

1Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany, 2Department of Cell & Molecular Biology, Karolinska Institutet, Stockholm, Sweden

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−/−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−/−mice, we pharmacologically mimicked a situation of elevated maternal thermogenesis and hypermetabolism. Therefore, we treated female wild type mice with prazosin (50 mg/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−/−mams. 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

Jean-Baptiste Fini1, Bilal Mughal1, Sébastien Le Mèvel1, Michelle Leemans1, Mélodie Lettmann1, Petra Spirhanzlova1, Pierre Aflatticat1, Jean-Stéphane Joly2, Barbara Demeneix1

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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, T3, 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 TH regulatory effects on the dissected brain tissue from the mixture-exposed Xenopus embryos revealed modifications of TH related genes including tshr, 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 T3 signalling at a critical moment for a proper brain development.

16.45–17.00
**15.30–15.45**

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

Villacorte Mylah1, Delmarcelle Anne-Sophie1, Lemoux Manon1, Bouquet Mahé1, Lemoine Pascale1, Bollee Jennifer2, Umans Lieve3, Choua de Sousa Lopez Susana3, Van Der Smissen Patrick4, Sasaki Takako5, Bommer Guido6, Henriet Patrick7, Refetoff Samuel8, Lemaigne Frédéric9, Zwiszen An9, Courty Pierre10, Christophe Pierreux1

1 De Duve Institute, Brussels, Belgium, 2Vit-Kul, Leuven, Belgium, 3Auzonne, Leiden University, Leiden, Netherlands, 4Oita University, Oita, Japan, 5Chicago University, Chicago, USA, 6De Duve Institute, Université Catholique de Louvain, Bruxelles, Belgium

**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 (Smad1/5KO) displayed growth retardation, hypothyroidism and defective follicular architecture. In Smad1/5KO embryonic thyroids, epithelial cells remained associated in large clusters and formed small follicles. Although similar follicular defects are found in VegfaKO thyroids, that display reduced angiogenesis, Smad1/5KO thyroids had normal endothelial cell density yet impaired endothelial differentiation. Interestingly, both VegfaKO and Smad1/5KO thyroids displayed impaired basement membrane assembly. Furthermore, conditioned medium (CM) from embryonic endothelial progenitor cells (eEPC) rescued the folliculogenic defects of both Smad1/5KO and VegfaKO thyroids. Laminin α1(1)1, 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.

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**15.45–16.00**

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

Marta García1, Jesús González de Buitrago2, Leonardo Pardo2, Patricia M. Hinkle3, Jose Moreno2

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, USA

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:** To report a homozygous missense mutation in TRHR that was identified (c.392T>C; p.131T1) 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. The parents, three siblings and grandmother of the index patient were heterozygous 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/EY motif involved in G protein activation. The 1131T 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 API-containing promoter by TRH (wild type EC50 = 2.8 ± 0.9 nM vs. mutant EC50 = 20.4 ± 0.8 nM).

**Conclusion:** A novel defect in TRHR causes central hypothyroidism in the homozygous state but leads to hyperthyrotropinemia in hypothyroidies, 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/EY motif.
induced muscle atrophy. In this model, the overall effect of T3 treatment is a protective one on fasting-induced muscle atrophy 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.

Skeletal muscle atrophy may ensue from several pathological conditions including prolonged muscle disease, cancer cachexia, anorexia etc. All atrophic conditions feature an imbalance between protein synthesis 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.

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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 Matrone1, Alessio Faranda2, Eleonora Molinari2, Laura Agate2, David Viola2, Laura Valerio1, Carlotta Gianì2, Liborio Torregrossa2, Paolo Piaggio3, Paolo Viltà2, Rossella Elisei2
1University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy, Department of Endocrinology, Pisa, Italy, 2University of Pisa, Endocrine Unit – Department of Clinical and Experimental Medicine, Pisa, Italy, 3Department of Surgical Pathology, Medical, Molecular and Critical Area – Unit of Pathological Anatomy, Pisa, Italy, 4Phoenix Epidemiology and Clinical Research Branch National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health, Phoenix, AZ, USA

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, 150/238 (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 (15.5%) 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) (p < 0.05), as far as [A3], bTSH (mean 3.73 ± 9.74 μU/ml), was significantly higher that iTSH (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 titers; 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.

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 thyroidec- tomy 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 hemithyroidectomy group were occurred at the contralateral lobe. All of these patients were remained disease-free after completion thyroideectomy 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.
The expression and thermal stability 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. Eleven out of 15 evaluated individuals had a mutation with hearing loss. The TBL1X mutations were located in the highly conserved WD40-repeat domain of the protein and influenced its function of the nuclear NCoR/SMRT co-repressor complex.

**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.

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**Table 1.** (for abstract time 09.30-09.45)

<table>
<thead>
<tr>
<th>Thyroid disease diagnosis</th>
<th>n = 7,323</th>
<th>n = 1,241</th>
<th>n = 1,204</th>
</tr>
</thead>
<tbody>
<tr>
<td>No diagnosis of thyroid disease</td>
<td>6,989</td>
<td>88.6</td>
<td>7,138</td>
</tr>
<tr>
<td>Thyroid disease diagnosed before blood sampling</td>
<td>334</td>
<td>4.5</td>
<td>376</td>
</tr>
<tr>
<td>Thyroid disease diagnosed after blood sampling</td>
<td>59</td>
<td>0.8</td>
<td>122</td>
</tr>
</tbody>
</table>

**Oral Presentations**

**Eur Thyroid J 2016;5(suppl 1):57–176**

**Funding:** Wellcome Trust, Biological Sciences Research Council Project Grant; AMC Foundation Grant.
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 (0.35–0.52)), 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.
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.

Recent evidence suggests that the deiodinase enzymes play an important role in the function of innate immune cells. The thyroid hormone inactivating 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.
A SONIC HEDGEHOG-GLIS3 PATHWAY IS INVOLVED IN THE SPECIFICATION OF THE THYROID GLAND IN ZEBRAFISH

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1Ircs Istituto Auxologico Italiano, Endocrinology and Metabolic Disorder, Milan, Italy, 2Università Degli Studi Di Milano, Dipartimento Di Biotecnologie Mediche e Medicina Translazionale, Milan, Italy, 3Ircs Istituto Auxologico Italiano, Milan, Italy, 4Università Degli Studi Di Milano, Dipartimento Di Bioscience, Milan, Italy, 5Università of Milan, Ospedale San Luca, Ircs Istituto Auxologico Italiano, Milan, Italy

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 syndromeic 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 thyocytes. Moreover, transient knockdown obtained by morpholino microinjection in zebrafish embryos (called glis3 MOs) resulted in a reduced expression of nkx2.5 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, s ></p>
**VARIABLY DEFECTIVE TRANSCRIPTIONAL ACTIVITY OF T3 RECEPTOR TRα1 MUTANTS ON DIFFERENT THYROID RESPONSE ELEMENTS**

*Karn Weijaphikul1, Anja van Gucht2, W. Edward Visser3, V. Krishna Chatterjee4, Theo Visser5, Robin Peeters1, Marcel Meima1*

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

**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 significantly higher on DR (~80 fold), intermediate on ER (~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.

**10.00–10.15**

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

*Marika Tesselaria1, Thomas Creze1, Danny Gerrits2, Otto Boerman2, Henk Stunnenberg3, Mihai Gheorge Netea4, Johannes Smitt4, Romana Teodora Noeta-Maier5, Theop Platinga6*

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

**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 125I 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 Ca2+ by inhibition of Na+/K+ ATPases. Subsequent molecular studies identified crucial roles for Ca2+ 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 Ca2+-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.
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 Laurberg1,2, Stine Linding Andersen1, Peter Hindersson3, Ellen Nohr3, Jørn Olsen1
1Aalborg University Hospital, Aalborg University, Aalborg, Denmark, 2Departments of Clinical Biochemistry and Endocrinology, Aalborg University Hospital, Aalborg, Denmark, 3Department of Clinical Biochemistry, North Jutland Regional Hospital, Hjørring, Denmark

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 miscategorization and possibly to incorrect choice of therapy.

Table 1. Early pregnancy TSH (mU/l) median and reference limits (95% confidence intervals) (for abstract time 11.00–11.15)

<table>
<thead>
<tr>
<th>Pregnancy week</th>
<th>5–6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13–19</th>
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<tbody>
<tr>
<td>n</td>
<td>639</td>
<td>884</td>
<td>1,193</td>
<td>1,287</td>
<td>1,006</td>
<td>690</td>
<td>448</td>
<td>524</td>
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<tr>
<td>Median</td>
<td>1.62</td>
<td>1.45</td>
<td>1.21</td>
<td>1.10</td>
<td>1.03</td>
<td>0.99</td>
<td>0.98</td>
<td>1.24</td>
</tr>
<tr>
<td>2.5 percentile</td>
<td>0.60</td>
<td>0.32</td>
<td>0.20</td>
<td>0.13</td>
<td>0.061</td>
<td>0.066</td>
<td>0.093</td>
<td>0.14</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>0.53–0.69</td>
<td>0.25–0.40</td>
<td>0.13–0.25</td>
<td>0.10–0.16</td>
<td>0.049–0.11</td>
<td>0.048–0.11</td>
<td>0.044–0.14</td>
<td>0.096–0.22</td>
</tr>
<tr>
<td>97.5 percentile</td>
<td>3.55</td>
<td>3.68</td>
<td>3.46</td>
<td>3.41</td>
<td>3.27</td>
<td>3.09</td>
<td>3.37</td>
<td>3.29</td>
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<td>(95% CI)</td>
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<td>3.36–3.83</td>
<td>3.27–3.70</td>
<td>3.07–3.62</td>
<td>2.99–3.49</td>
<td>2.91–3.31</td>
<td>2.96–3.78</td>
<td>3.08–3.73</td>
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Eur Thyroid J 2016;5(suppl 1):57–176
39th Annual Meeting of the ETA
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 tasks, whereas in the hypo-thyroid 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.

Table 1. (for abstract text 12.00–12.15)

<table>
<thead>
<tr>
<th>Variable</th>
<th>1st trimester</th>
<th>2nd trimester</th>
<th>3rd trimester</th>
<th>Mother postpartum</th>
<th>Baby</th>
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<tr>
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<td>111</td>
<td>140</td>
<td>136</td>
<td>41</td>
<td>93</td>
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<tr>
<td>UIC-placebo</td>
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<td>&lt;0.001</td>
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<td>FT4-iodine</td>
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<tr>
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<td>0.280</td>
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</table>

12.00–12.15

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

Sofia Manousou1, Robert Eggertsen2, Lena Hulthen3, Helena Filipsson Nyström4
1Department of Medicine at Kungälvs Hospital, Sweden, Institute of Medicine Sahlgrenska Academy, Gothenburg, Sweden, 2Mölndal Health Care Center, Mölndal, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, 3Department of Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, 4Department of Endocrinology, University of Gothenburg, Göteborg, Sweden

Objective: 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 (mU/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.
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 multivitamins were collected at baseline and after 2 and/or 10 years.

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.

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 unaffected 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 (vTES) 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 RTHβ 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 (p < 0.0004). The mean OCT macular thickness was not compared to controls (mean ± SD 134.4 ± 35.93 and 151.8 ± 44.17, respectively).

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

Diana Albrecht¹, Till Ittermann², Michael Thamm³, Henry Völzke⁴
¹University Medicine Greifswald, Institute for Community Medicine, Greifswald, Germany, ²University Medicine Greifswald, Greifswald, Germany, ³Robert Koch-Institut, Berlin, Germany, ⁴Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany

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 investigate how thyroid hormones influence child behavior.

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**Oral Session 13 (Basic): Basic Mechanisms in Graves’ Disease**

**11.00–11.15**

**OXIDATIVE STRESS IN SKIN ADIPOCYTES FROM GRAVES’ PATIENTS**

Marie-Christine Manyt, Joris Virginiet, Marique Lancelot¹, Van Regemorter Elliott¹, de Ville de Goyet Christine¹, de Bouronville Marc², Antonella Boschi³, Mourad Miche³, Chantal Daumier⁴, Julie Craps⁵
¹Ss/Mede/Irec/Ucl, Bruxelles, Belgium, ²Ucl-Irec-Fath, Brussels, Belgium, ³Cliniques Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium

Background: Graves’ orbitopathy (GO) and prethral 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 prethral dermis. Prethral 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 by 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.
11.30–11.45
CHARACTERISTICS OF HYALURONAN AND PAI-1 EXPRESSION IN CULTURES OF ORBITAL FIBROBLASTS
Erika Galgoczi1, Florence Jeney2, Annamaria Gazdag1, Annamaria Erdei1, Mónika Katki1, Domonkos M. Nagy1, Bernadett Ujhelyi2, Zita Steiber2, Ferenc Gyory3, Eszter Berta1, Endre V. Nagy1
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

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 < 0.0001), 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
Inna Hoyer1, Patrick Marcinkowski1, Edgar Specker1, Jens Furkert2, Marc Nazare3, Jens-Peter von Kries1, Claudia Rutz1, Ralf Schülein1, Gerd Krause1
1 Leibniz-Institut für Molekularer Pharmakologie Berlin, Berlin, Germany

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. Here we 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 (x-factor 0.62–0.9). Inhibition of cAMP accumulation at 50 μM compound was induced by 9.8 μM 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 clinical centers were purchased. Structure-function studies and subsequent own stereoselective synthesis and separation of enantiomers led to the inhibitor S37 with an IC₅₀ 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 hepatocarcinoma 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 THYROCITES OF HASHIMOTO’S THYROIDITIS
Yang Zhang1, Chenxu Zhao2, Ying Gao1, Lianlan Zhao1, Suxia Wang2, Hong Zhang2, Guishi Lu1, Yanming Gao1, Xiaohui Guo1
1 Peking University First Hospital, Beijing, China, 2 Civil Aviation General Hospital, Beijing, China

Background: Thyroglobulin (Tg) antibody (TgAb) and thyroid peroxidase (TPO) antibody (TPOAb), mainly immunoglobulin (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 thyrocyte 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 dual immuno-fluorescence 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 (Th1) (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 downregulated 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
Hopp Michael1, Joris Virginie2, Werion Alexis3, de Ville de Goyet Christine1, Chantal Daumerie1, Mourad Michel2, Marie-Christine Many1, Julie Craps1
1 SS/Med/Inrec/Ucl, Bruxelles, Belgium, 2 Ucl-Inrec-Fath, Brussels, Belgium, 3 Cliniques Universitaires Saint-Luc, Endocrinologie, Brussels, Belgium

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.
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 Interferon) to mimic HT. In thyrocytes from patients with Hashimoto’s thyroiditis, stimulation with Interleukin-1α and Interferon increased HIF-1 expression. 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.

HYPOXIA-DEPENDENT HIF-1 ACTIVATION IMPACTS ON TISSUE REMODELING IN GRAVES’ ORBITOPATHY

A mouse model of Graves’ orbitopathy (GO) induced by genetic immunization of human thyrotrpin 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-1R) 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 adipogenesis 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.
### Poster Plan

**European Thyroid Journal**

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<thead>
<tr>
<th>Topic</th>
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<tr>
<td><strong>Saturday, 3rd September, 16.00–17.00</strong></td>
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<td>P1 – 01 Hyperthyroidism</td>
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<td>P1 – 04 Case Reports</td>
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<td>13+15</td>
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<td>P1-08-01 – P1-08-10</td>
<td>East Lounge / 8+9+10+11 (Main Auditorium)</td>
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## Monday, 5th September, 12.00–13.00

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<td>East Lounge / 8+9+10+11 (Main Auditorium)</td>
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**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 Ionnì1, Marenza Leo1, Paola Premoli2, Giovanna Rotondo Dottore3, Marialuisa Di Cera2, Lorenzo Sassi2, Paolo Vitti1, Luigi Bartalena2, Claudio Marconi3, Michele Marini1

1Department of Clinical and Experimental Medicine, Endocrinology, University of Pisa, Pisa, Italy, 2Department of Clinical and Experimental Medicine, Endocrinology, University of Insubria, Varese, Italy

**Objectives:** Selenoproteins play an important antioxidant role in thyroid hormone 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’ OPTHALMOPATHY**

Ana Paula Comarella1, Danilo Villaggio1, Natashaia Bufolo1, Jessica Euffrazzino2, Raquel Pereira Rios3, Vitória Arbulo Pito3, Roberto Bernardo dos Santos1, Joao Hamilton Romaldini1, Laura Ward1

1Laboratory of Cancer Molecular Genetics, University of Campinas, Campinas, Brazil, 2Pontificia Universidad Católica Campinas, Campinas, Brazil

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 (96). 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 rs12885300 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**

Sun Hye Jeong1, Hyun Sook Hong2

1Soonchunhyang University Bucheon Hospital, Bucheon-Si, Korea, Rep. of South

**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 Cm2 (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.
FALSELY ELEVATED FT4 OR FT3 DUE TO INTERFERENCE SUBSTANCES IN THYROID HORMONE ASSAYS

Grigoris Effraimidis1, Pia Bükman Larsen2, Mads Nybo3, Lisa Bathum4, Lennart Friis-Hansen4
1Internal Medicine Department, Endocrinology and Diabetes Section, Nykøbing F Hospital, Nykøbing F, Denmark, 2Department of Clinical Biochemistry, Næstved Hospital, Næstved, Denmark, 3Department of Clinical Biochemistry, Odense University Hospital, Odense, Denmark, 4Department of Clinical Biochemistry, Hvidovre Hospital, Hvidovre, Denmark

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 Q2–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.

Table 1. (for abstract P1-01-04)

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<td>41</td>
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<td>fT4/fT3</td>
<td>fT3</td>
<td>fT4</td>
<td>fT4/fT3</td>
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<tr>
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<td>fT4 67.07/fT316.4</td>
<td>fT3 29.2</td>
<td>fT4 39.7</td>
<td>fT4 30.3/fT3 23.0</td>
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<td>Cobas 6000 (pmol/l)**</td>
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<td>fT4 14.4/fT3 6.1</td>
<td>fT3 4.6</td>
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<td>TT4 69.6/TT3 1.34</td>
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<td>TT4 15.3</td>
<td>TT4 95/TT3 N/A*</td>
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</table>

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.

WITHDRAWN

MONITORING THE PREVALENCE OF THYROID DISORDERS IN THE ADULT POPULATION OF NORTHEAST GERMANY

Rehman Khattak1, Till Ittermann2, Matthias Nauck3, Harald Below4, Henry Völzke5
1Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany, 2University Medicine Greifswald, Greifswald, Germany, 3Universitätsklinikum Greifswald, Greifswald, Germany, 4Institute of Hygiene and Environmental Medicine, Ernst Moritz Arndt University Greifswald, Germany, 5Greifswald, Germany, 6Ernst-Moritz-Arndt Universität Greifswald, Greifswald, Germany

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 = 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 ≤ 0.001), while the prevalence of positive anti-TPO Abs decreased from 3.9% to 2.9% (p = 0.023). Median serum TSH levels increased from 0.69 mIU/l to 1.19 mIU/l (p ≤ 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 therapeutic decisions.
Aim of this study was to assess whether the Merseburg triad (hyperthyroidism, goiter, ophthalmopathy) 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 (9–24) 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 anti-thyroid 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, or 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**

**Stan Benjamens**<sup>1</sup>, **W.J. Sluiter**<sup>1</sup>, **M. Rienstra**<sup>2</sup>, **I.C. Van Gelder**<sup>2</sup>

<sup>1</sup>University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands, 2University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands

**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 (<20.5 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/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/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 A BIOMARKER FOR THYROID DYSFUNCTION?**

**Janna Zimmermann**<sup>1</sup>, **Tanja Dianna**<sup>2</sup>, **Niklas Lohmann**<sup>1</sup>, **Lukas Reuter**<sup>1</sup>, **Michael Kanitz**<sup>1</sup>, **George J. Kahaly**<sup>1</sup>

<sup>1</sup>Johannes Gutenberg University Medical Center, Mainz, Germany

**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, Hemmningsdorf, Germany). Thyroid-related hormones (TSH, FT4, and FT3) and Abs (thyroperoxidase and thyroglobulin) were measured with commercially available assays (Architect, Abbott, 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 < 0.01), while no correlations were registered with presence of Graves’ oophropathy, 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**

**Hwa Young Ahn**<sup>1</sup>, **Yun Jae Chung**<sup>1</sup>

<sup>1</sup>Chung-Ang University College of Medicine, Seoul, Korea, Rep. of South

**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
Kristina Dyacenko1, Andra Carageorgheopol1, Sergiu Stoica2, Corin Badu1
1National Institute of Endocrinology, Bucharest, Romania, 2Brain Institute, Bucharest, Romania

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 gonadotropin receptors.

Case Report: An 11 years girl was admitted first at 7 years with severe thyrototoxicosis, diffuse goiter and a giant pituitary adenoma. TSH, FT4, T3, were evaluated basal, during TRH and Ocreotide 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 transphenoideal neurosurgery (5 times) and gamma knife surgery on the pituitary remnant. Antithyroid drugs and beta blockers were used to ensure peripheral euthyroidism, 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-phenoideal 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.

Table 1. (for abstract P1-02-01)

<table>
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a From general linear model, controlling for maternal age and smoking status.
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 μg/l; p < 0.001). By contrast, there was no difference in TSH between groups (estimated marginal mean 1.49 vs. 1.22 mIU/l, p < 0.001). At 20 weeks, although there was an increase in Tg in the ≥150 μg/g group but there was 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 were both measured and thyroid ultrasound had been done in all participants. In the 2006 cohort TSH was determined by a microparticulate immunoenzyme analysis (MIEA) (reference range 0.3–5.6 mIU/l), and in the 2012 one – by a two-site immunoenzyme “sandwich” assay (reference range 0.34–3.6 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 (2012: 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)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Iodine deficient (n = 82)</th>
<th>Iodine sufficient (n = 27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UIC (μmol/L, median, 25–75th %)</td>
<td>0.63 (0.41–0.82)</td>
<td>1.50 (1.30–2.40)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>I/Cr (median, 25–75th %)</td>
<td>0.11 (0.08–0.16)</td>
<td>0.21 (0.15–0.28)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Iodine intake (μg/day, median, 25–75th %)</td>
<td>213.8 (124.3–896.4)</td>
<td>210.9 (138.2–1028.4)</td>
<td>NS*</td>
</tr>
<tr>
<td>Maternal TSH (mIU/l, median, 25–75th %)</td>
<td>1.7 (1.0–2.4)</td>
<td>1.3 (0.9–1.9)</td>
<td>NS*</td>
</tr>
<tr>
<td>fT4 (pmol/l)</td>
<td>12.2±1.4</td>
<td>12.6±1.6</td>
<td>NS</td>
</tr>
<tr>
<td>Tg (μg/l, median, 25–75th %)</td>
<td>13.9 (9.6–26.6)</td>
<td>8.4 (4.8–13.7)</td>
<td>0.020*</td>
</tr>
<tr>
<td>Cord TSH (mIU/l, median, 25–75th %)</td>
<td>6.8 (4.6–10.0)</td>
<td>16.8±1.9</td>
<td>NS*</td>
</tr>
<tr>
<td>Tg (μg/l, median, 25–75th %)</td>
<td>59.8 (35.3–89.4)</td>
<td>62.8 (40.5–93.8)</td>
<td>0.031</td>
</tr>
</tbody>
</table>

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 2006.

**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.

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 μg/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 = 0.04) 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 women 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 Transylvania (95 mcg/l), Moldova (127.9 mcg/l) and Munteania (149.4 mcg/l) as compared to Bucharest area (206 mcg/l) and non-endemic regions (206.6 mcg/l). In Transylvania 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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Endocrinology Research Centre, Moscow, Russian Federation

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 hyperthyroidism 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 production 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 replacement 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 supplementation 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

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 outpatient 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, polymyalgia rheumatica (Polym), celiac disease, diabetes, sjogren disease, multiple sclerosis, systemic lupus erythematosus, sarcoidosis, alopecia, psoriatic arthritis, systemic sclerosis, HCV-related cryoglobulinaemia, was demonstrated in AT patients (with respect to both controls). The association of three autoimmune disorders was observed in AT patients; especially, 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 DISASES (NAITD), AND IN PATIENTS WITH GRAVES' DISEASES (GD) OR HASHIMOTO'S THYROIDITIS (HT)
Alessandro Antonelli1, Poupaak Fallahi2, Silvia Martina Ferrani2, Marina Galletti2, Mattia Grazia Mandolfino2, Grazia Giorgianni3, Flavia Di Bari1, Roberto Vita1, Salvatore Benvenuta2
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Background/Objective: HC virus (HCV) infection triggers AITD and NAITD. THAB prevalence in NAITD and AITD, THAB prevalence in NAITD (rheumatoid arthritis [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 HC.

Methods: We measured serum THAB (T3IgM, T3IgG, T4IgM, T4IgG) by radioimmunoprecipitation in 40 untreated eHC 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 T4G prevaling 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 T3IgG+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 eHC, GD or HT, while 4 or 5 combinations were reported for RA or pSS.

Conclusion: In eHC, prevalence of THAB (65%) exceeds TgAb or TPOAb prevalence (0–31% or 5–30% in the literature). Our data suggest a frequent and precarious thyroid damage by HCV, and may explain the relatively high (i) rate of TgAb positivity compared to TPOAb positivity in eHC, (ii) risk of developing AITD spontaneously or after interferon treatment. A close follow-up of THAB-positive eHC 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-alfa, IL-5 and IL-17 in HT. In HT, we found higher concentrations of IL-2 in individuals with higher thyroid volumes, IFN-gama 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, the interleukins as IL-2 and higher volume of thyroid. The positive correlation between IFN-gama 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 levotiroxine 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 CYTOPATHY: 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 TN associated or not associated to HT.

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– (50.7%) significantly different from that found in HTN– (Table).

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.

Table 1. (for abstract P1-03-04)

<table>
<thead>
<tr>
<th></th>
<th>TI-RADS 2</th>
<th>TI-RADS 3</th>
<th>TI-RADS 4</th>
<th>TI-RADS 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN+</td>
<td>35 (49.3%)</td>
<td>29 (33.3%)</td>
<td>37 (45.7%)</td>
<td>20 (51.3%)</td>
</tr>
<tr>
<td>HTN-</td>
<td>36 (50.7%)</td>
<td>58 (66.7%)</td>
<td>44 (54.3%)</td>
<td>19 (48.7%)</td>
</tr>
</tbody>
</table>

p = 0.125 (NS).

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**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 euthyroid, hypothyroid and hyperthyroid patients. TRAb levels were above the upper limit (>1.5 IU/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 euthyroid, hypothyroid 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.

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**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
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. After 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, T4T, 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 unappropriate treatment.

**Table 1.** (for abstract P1-03-08)

<table>
<thead>
<tr>
<th>Date</th>
<th>TSH (0.30–4.0 mU/l)</th>
<th>fT4 (10.0–26.0 pmol/l)</th>
<th>fT3 (3.3–6.1 pmol/l)</th>
<th>TRAb (&lt;1.2 U/l)</th>
<th>MMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>04/2014</td>
<td>0.41</td>
<td>44.1</td>
<td>31.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>06/2014</td>
<td>0.45</td>
<td>36.4</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>11/2014</td>
<td>3.9</td>
<td>26.4</td>
<td>27.6</td>
<td>–</td>
<td>20 mg</td>
</tr>
<tr>
<td>12/2014</td>
<td>5.3</td>
<td>27.5</td>
<td>28.3</td>
<td>–</td>
<td>20 mg</td>
</tr>
<tr>
<td>05/2015</td>
<td>6.1</td>
<td>25.6</td>
<td>23.3</td>
<td>3.8</td>
<td>30 mg</td>
</tr>
<tr>
<td>09/2015</td>
<td>2.3</td>
<td>27.5</td>
<td>22.2</td>
<td>4.3</td>
<td>10 mg</td>
</tr>
<tr>
<td>11/2015</td>
<td>1.1</td>
<td>29.7</td>
<td>23.0</td>
<td>4.1</td>
<td>10 mg</td>
</tr>
<tr>
<td>Alternative assay5</td>
<td>1.4</td>
<td>14.6</td>
<td>4.1</td>
<td>–</td>
<td>10 mg</td>
</tr>
<tr>
<td>02/2016</td>
<td>0.31</td>
<td>37.2</td>
<td>22.7</td>
<td>4.0</td>
<td>–</td>
</tr>
<tr>
<td>Alternative assay6</td>
<td>0.41</td>
<td>TT45 95 nmol/l</td>
<td>–</td>
<td>&lt;0.7</td>
<td>–</td>
</tr>
</tbody>
</table>

* Reference interval; † reference interval: TSH: 0.35–4.00 mU/l, fT4: 14–23 pmol/l, fT3: 3.3–6.1 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:** A 14 yo girl complaining from a persistent headache, was referred to 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 14.8 pmol/l (<15). A thyroid ultrasound demonstrated a slightly increased vascularisation of the thyroid gland; confirming autoimmune thyroiditis. Treatment with methimazole and propranolol 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 thyrotoxic state associated orbitopathy was 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 ‘Murati’ 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, Ca2+ – PTH, as well as undergone a thyroid ultrasound.

**Results:**
- TSH – 38%↑, 42% N
- FT4 – 60%↓, 40% N
- Anti-TPO – 100%↑
- Vit D3 – 84%↓, 16% N
- Ca2+ – 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 thyroiditis. 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 shouit 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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21V. Ierieli Endocrinology, Metabolity, Dietology Center ‘Enmedic’, Tbilisi, Georgia

**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 μU/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: 7×8×11 mm, 8×8×8 mm.

Thyroid scintigraphy with TC-99m excluded hot and cold nodules. Anti-TSH-Rec.-245 (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 complaints 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 per os. 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 iv 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 THYROID-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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1Elias Hospital, Endocrinology, Bucharest, Romania, 2Elias Hospital, Endocrinology Department, Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Bucharest, Romania

**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 mIU/ml, TT3=298 ng/dl, FT4=4.03 ng/dl, negative TPOAb, ATA, TSHRAb. Thyroid ultrasound revealed slightly hypoechogenic, inhomogeneous gland with decreased vascularization. Treatment with methimazole 30 mg/day was started. Evaluation after two months: TSH = 0.022 mIU/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.

**Table 1.** (for abstract P1-04-01)

<table>
<thead>
<tr>
<th>Patient</th>
<th>TSH (mU/l)</th>
<th>T4 (mcg/dl)</th>
<th>TBG (mcg/ml)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (before gynecomastia)</td>
<td>1.2–2.8 nv</td>
<td>0.35–5.5</td>
<td>8.7–9.5 nv</td>
<td>5.4–11</td>
</tr>
<tr>
<td>1 (gynecomastia)</td>
<td>5.7–4.4</td>
<td>12.5</td>
<td>ND</td>
<td>Not done nv 15–36</td>
</tr>
<tr>
<td>1 (disappearance of gynecomastia)</td>
<td>3.0</td>
<td>10.2</td>
<td>ND</td>
<td>On 100 mcg/d L-T4 after thyroidectomy</td>
</tr>
<tr>
<td>2 (before cirrhosis)</td>
<td>always ≤3.4 nv</td>
<td>0.27–4.2 ND</td>
<td>L-T4 increased</td>
<td>(125 mcg/d)</td>
</tr>
<tr>
<td>2 (cirrhosis)</td>
<td>6.6–9.3</td>
<td>ND</td>
<td>L-T4 decreased</td>
<td>(100 mcg/d)</td>
</tr>
<tr>
<td>2 (after transplant)</td>
<td>2.4</td>
<td>ND</td>
<td>ND</td>
<td>Hashimoto’s thyroiditis. On 100 mcg/d L-T4</td>
</tr>
</tbody>
</table>

**P1-04-03**  
THYROID STORM FOLLOWING TOTAL THYROIDECTOMY FOR THYROID CANCER, DUE TO THYROTROPIN RECEPTOR ANTIBODIES STIMULATING THE METASTATIC THYROID TISSUE  
Lars Folkestad1, Frans Brandt Kristensen1, Thomas Brix1, Marianne Vogser2, Lars Bastholm3, Peter Grupe3, Jeanette Krogh Petersen1, Laszlo Hegedus1  
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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...
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; normal 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 (median December 2015).

Summary and Conclusion: We present a rare patient, initially diagnosed with hyperthyroidism and subsequently metastatic 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 adenral failure with either autoimmune thyroid disease (AITD) and/or type 1 diabetes. Hashimoto thyroiditis (IT) and Graves’ diseases represent the main two types of AITD. About 15–20% patients with GD may have spontaneous hypothyroidism 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 IT and treatment with hydrocortisone 10 mg, fludrocortisone 0.5 mg and levothyroxine 67.5 mg. One month before admission was determined suppressed TSH and levothyroxine was withdrawn. 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 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 in 1983. 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 thyrotoxic symptoms 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 angioedema.

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 hyperthyroidism is rare and may result from surgical resection of a pituitary lesion. Primary 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 μIU/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 bruist. Plasma sampling revealed TSH 0.001 μIU/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 methimazole 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 thyroid hyperplasia had an autoimmune aetiology. The thyroid bruit, increased vascularity and high iodine concentration do not explain thyroid hyperplasia. We think that H. pylori infection might be the role of treating thyroid disease and H. pylori on the clinical course of chronic urticaria.

**P1-04-06**

**SUMMARY AND CONCLUSION:**

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**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 dysfunction, 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:_ A 55-year old patient presented to our hospital because of chest pain. He was diagnosed with atrial fibrillation and three vessel coronary artery disease, serum TSH concentration was normal. The patient later underwent CABS surgery and was subsequently prescribed amiodarone as an antiarrhythmic. Two years later he became hyperthyroidic, 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 tachycardias 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 affect 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 lysithyronine (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 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 p1 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 ABSCES**

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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 mU/ml (0.27–4.2), fT3 3.12 pg/ml (1.8–4.6) and fT4 1.83 ng/dl (0.9–1.7). Ultrasoundographically, a hypoechogenic 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**
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 euthyroidism in the next two years on high doses of antithyroid drugs (propylthiouracil 600 mg/day, thiamazole 60 mg/day). She had a history of myocytic, sideropenic anemia, and few months prior to admission vitiligo appeared. On admission, thyroid functions tests were as follows: TSH ≤0.01 uU/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 nodule 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 withoutpause in her medical treatment. Tc-99m pertechnetate thyroid scan showed increased uptake in the left lobe, corresponding to the palpable 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.

A1-05-01

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 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 cytopathy 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 score ± 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 remaining 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 clinical 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: Forty-one out of sixty-two patients underwent total thyroidec- tomy and the rest had lobectomy. The final pathologic results were forty-one malignancies and twenty-one benign diseases. Nodules less than 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 incisonal 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: 18F-fluoro-deoxyglucose positron emission tomography and computed tomography (18F-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 (131I WBS). Its usefulness in DTC patients with positive 131I WBS had seldom been discussed. The aim of this study was to evaluate the impact of 18F-FDG PET/CT on the management and clinical outcome of DTC patients with positive 131I WBS and detectable Tg.

Methods: From 2005 to 2013, we retrospectively evaluated a total of 27 DTC patients with positive 131I WBS and concurrent detectable stimulated Tg who underwent an 18F-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 18F-FDG PET/CT findings were analyzed, with disease progression as a primary endpoint.

Results: Among the 27 patients, 20 patients (74%) had positive 18F-FDG PET/CT findings. The sensitivity, specificity, and diagnostic accuracy of 18F-FDG PET/CT for detecting recurrent/residual lesions were 86.3%, 80%, and 85%, respectively. In 12 patients (44%), 18F-FDG PET/CT provided additional information than 131I WBS and conventional imaging; 8 (30%) of them resulted in a change of clinical management.

Twelve patients (44%) experienced disease progression after 18F-FDG PET/CT during follow-up. The maximal standard uptake value (SUVmax) of the lesion with strongest 18F-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 18F-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 131I WBS and detectable Tg, 18F-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 18F-FDG PET/CT result suggests a favorable prognosis.

P1-05-08
COEXISTENCE OF DIFFERENTIATED AND UNDIFFERENTIATED THYROID CARCINOMA WITH CHRONIC LYMPHOCYTIC LEUKEMIA
Dilek Yazici1, Serdar Tezelman2, Onur Demirkol3, Omer Faruk Unal4, Sukru Dilege5, Ozlem Aydin6, Yersen Kapran7, Bulent Colakoglu8, Tanik Terzioglu9, Burhan Farhanoglu10, Faruk Alagol1
1Koc University Medical School, Section of Endocrinology and Metabolism, Istanbul, Turkey, 2Koc University Medical School, Department of General Surgery, Istanbul, Turkey, 3Koc University Medical School, Department of Nuclear Medicine, Istanbul, Turkey, 4Koc University Medical School, Department of Otorhinolaryngology, Istanbul, Turkey, 5Koc University Medical School, Department of Oncology, Istanbul, Turkey, 6American Hospital, Department of Pathology, Istanbul, Turkey, 7Koc University Medical School, Department of Pathology, Istanbul, Turkey, 8American Hospital, Department of Radiology, Istanbul, Turkey, 9American Hospital, Department of General Surgery, Istanbul, Turkey, 10Koc University Medical School, Section of Hematology, Istanbul, Turkey

Introduction: Chronic lymphocytic leukemia (CLL) has been shown to be coexisting with several malignancies, 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 malignant 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 block and the pathology was consistent with foci of both CLL and papillary thyroid carcinoma in the same nodes. Thyroid ultrasonography revealed a 1 cm nodule on the left thyroid lobe. Total thyroidectomy and central and lateral neck dissection were performed. It was noticed intraoperatively that left vena cava was filled with thrombus. The surgical team did not touch the vena cava. Radiiodine 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 concurrent 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.
**P1-06-02 USEFULNESS OF INTRAOPERATIVE PTH MEASUREMENTS FOR PREDICTING PERMANENT HYPOPARATHYROIDISM AFTER TOTAL THYROIDECTOMY**  
**Takashi Urung1, Yuna Ogimi1, Chie Masaki1, Junko Akaishi2, Kiyomi Y. Hames1, Chisato Tomoda1, Akiyumi Suzuki1, Kenichi Matsuzu1, Keiko Okhuya1, Hiroshi Shibuya1, Wataru Kitagawa1, Mitsui Nagahama1, Kiminori Sugino1, Koichi Ito1  
1Ito Hospital, Tokyo, Japan

**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 33.3% (2 of 6) and 13.0% (34/262), respectively, of patients with PTT‐PTH ≥15 pg/ml or autotransplantation of ≥1 gland. Permanent hypoparathyroidism was seen in 14.3% (17/119) and 5.1% (7/136) of patients with PTT‐PTH ≥15 pg/ml with or without autotransplantation (≥1 gland). Permanent hypoparathyroidism was diagnosed in 14.3% (17/119) 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.

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**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)

<table>
<thead>
<tr>
<th></th>
<th>PTT-PTH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;15 (pg/ml)</td>
<td>≥15 (pg/ml)</td>
</tr>
<tr>
<td>Autotransplantation (AT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>66.7% (4/6)</td>
<td>85.7% (6/7)</td>
</tr>
<tr>
<td>Yes (≥1 gland)</td>
<td>87.0% (228/262)</td>
<td>94.9% (129/136)</td>
</tr>
<tr>
<td>Total</td>
<td>86.6% (232/268)</td>
<td>94.4% (135/143)</td>
</tr>
<tr>
<td>ARR (Absolute Risk Reduction) by AT</td>
<td>20.3%</td>
<td>9.2%</td>
</tr>
<tr>
<td>RRR (Relative Risk Reduction) by AT</td>
<td>61.0%</td>
<td>64.3%</td>
</tr>
</tbody>
</table>
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.

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.

A 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.

The association between lymph node metastasis and prognosis

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 associati-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 survival according to BMI quartiles (P = 0.26).

Conclusion: Increased BMI might elevate the risks of aggressive clinicopathological features, such as extrathyroidal 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 PAPILLYARY THYROID CARCINOMA AND CORRELATION WITH CLINICOPATHOLOGICAL FEATURES OF THE PRIMARY TUMOUR

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Background: Papillary thyroid carcinoma (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 their 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 statistically significant difference between BRAF (+) and BRAF (+) patients. While there was no significant difference regarding the occurrence 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

Selika Burcak Polat1, Berna Evranos Ogmen2, Gurkan Dumlul3, Nuran Sungur4, Reyhan Ersoy5, Bekir Cakir6

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

Introduction: There are studies suggested that TSH can stimulate the development of thyroid malignancy, and that elevated serum TSH levels are 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 αvβ3 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. These 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 a 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

Catarina Machado1, Patricia Tavares2, Lilite Barbosa3, Antónia Povo2, Carlos Soares1, José Manuel Oliveira4, Sara Monteiro1, Maria João Oliveira5

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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.

Pt1-06-10
CASE OF THYROID CARCINOMA OCCasionally FOUND IN YOUNG PATIENT AND THE IMPORTANCE OF IMMEDIATE RADICAL THERAPY
Natia Katamadze
Tbilisi, Georgia

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: in the right lobe hypoechogenic solid nodule 5x5x6 mm was found. 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: in the right lobe hypoechogenic solid nodule 5x5x6 mm was found.

During pregnancy her thyroid function and 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: in the right lobe hypoechogenic solid nodule 5x5x6 mm was found.

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 has more characteristics of cancer stem cell. It was suggested that thyroid 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.

Pt1-07-01
THE EXPRESSION OF E-CADHERIN, YAP1, STAT3 OF MULTICELLULAR TUMOR SPHEROIDS OF THYROID
Woo Young Kim1, Sang Uk Woo1, Jae Bok Lee1
1Korea University Guro Hospital, Department of Surgery, Seoul, Korea, Rep. of South

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 x 10^6/60 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.

Pt1-07-02
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

Pt1-07-03
116 Eur Thyroid J 2016;5(suppl 1):57–176
39th Annual Meeting of the ETA
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, IRVO-EU/2016 grants.

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**P1-07-03**

**TGFβ1 GENE POLYMORPHISMS 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 TGFβ1 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 TGFβ1 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.

**Results:**

- 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.
- In 3 patients with PTC, these all 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, IRVO-EU/2016 grants.

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**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 laryngeal 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.

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**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 phase 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

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**Poster Presentations**

**Eur Thyroid J 2016;5(suppl 1):57–176**
binding to gal-1 expressed by well-differentiated thyroid cancer sections has been validated by immunohistochemistry. P1 and P7 showed a better specific affinity. Immunofluorescence assays revealed co-localisation 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 (33%), 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, antiallery, anticancer, antiangiing, 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 ABCP 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 hot-spot 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 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 431 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 25 (c.75G>A/T) of aminoacid substitution in codon 791 (c.2372A>T) and mutation in codon 634 of RET protooncogene.

Characteristic for Polish population is relatively high frequency (48/296; 25%) of aminoacid substitution in codon 791 (c.2372A>T) and mutation in codon 634 of RET protooncogene. Characteristic for Polish population is relatively high frequency (25%) of aminoacid substitution in codon 791 (c.2372A>T) and mutation in codon 634 of RET protooncogene. Characteristic for Polish population is relatively high frequency (25%) of aminoacid substitution in codon 791 (c.2372A>T) and mutation in codon 634 of
however we performed such screening in 104 MTC patients who were nega-
tive 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 dif-
f erent 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 func-
tional state of the thyroid gland in the patients diagnosed with thyroid papil-
lary 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-mor-
phologic study.

To evaluate thyroid function, we measured the serum levels of thyroid-stimulating hormone (TSH), free thyroid (FT4) and also antibodies against 
thyroid peroxidase and thyroglobulin.

Thyroid gland was evaluated by ultrasound: location, sizes, volume, echo-
genicity, structure, vascularization, presence of nodules – their location, quan-
tity, 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). FT4 levels normal (0.7–1.8 ng/dl) in 82.98% (9 patients on 
levothyroxine). Papillary thyroid carcinoma (PTC) was diagnosed in 78.72% of cases.

Conclusion: In the majority of cases strong correlation between the pres-
ence 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 malign-
ancy 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 thy-
roid carcinoma.

Case: A 52-year-old female patient was examined in our department 
3 years after she had undergone total thyroidectomy of papillary thyroid car-
cinoma (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 tomog-
raphy 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 cytol-
yogy 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 proxim-
ity of the mass to the sciatic nerve. In addition this hypervascular mass had 
partial 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 exci-
sion was performed safely in 3rd day of embolization. The patient’s postopera-
tive 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-IODO THYRONAMINE IN MICE
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3, a thyroid hormone (TH), regulates the basal metabolic rate, hence also 
influencing body temperature. Individuals with hyperthyroidism show hyper-
sensitivity 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-
contraction 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.

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 TAA1 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-IODOXYRONAMINE (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.e.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 and pain threshold to thermal stimuli (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 MG 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 a marked 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 (paracordenateous 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 mM 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) and 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**  
Lucas dos Santos Bacigalupo1, Robson José de Almeida1, Valdelena Alessandra da Silva1, Patricia Varella Lima Teixeira2, Leonardo Martins da Silva1, Juliana de Almeida Pires3, Mariana Fabbri Pereira1, João Bosco Pesquero2, Cleber Pinto Camacho2  
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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 hypothryoidism) 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 studio 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: ISOOTYPE KINETIC EFFECT AND OTHER PITFALLS**  
Leonardo Lorenzini1, Sandra Ghelardoni2, Alessandro Saba1, Riccardo Zucchi1  
1University of Pisa, Pisa, Italy, 2Department of Pathology, Pisa, Italy

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

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 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, identifying a global lower inflammatory status in the WSB/EiJ strain, within the hypothalamus, C57Bl6 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 HISTOLOGY AND FUNCTION IN ORCHIDECTOMIZED MIDDLE-AGED MALE RATS

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

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. Group I, 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 over 14 days. Control Group VII 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.

Financial assistance is gratefully acknowledged from DST, DoEn, Apeejay Education Society.

Table 1. (for abstract P1-08-10)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Head feathers (mean ± SE)</th>
<th>Body feathers (mean ± SE)</th>
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<tr>
<td></td>
<td>loss day 9</td>
<td>regeneration day 9</td>
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<tr>
<td>T3</td>
<td>0.37 nM</td>
<td>2.5±0.17</td>
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<td>0.74 nM</td>
<td>2.8±0.13</td>
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<td>1.48 nM</td>
<td>3.8±0.13</td>
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<td>T4</td>
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A 67-year old woman with Graves’ disease presented with active GO in OS treated successfully elsewhere with methylprednisolone up to a cumulative dose of 2.5 gr, then discontinued because of concurrent pylonenteritis 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 23.5+4+5+5+0. 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, chlorphenamine 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.
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 (hypT). 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 = 0.06). 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 < 0.05) 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: 72.7%. TNF-α exhibits efficacy to discriminate healthy children and cAIT children (AUC = 0.691, p = 0.034) with low sensitivity: 94.7%, specificity: 72.7%. TNF-α and sFasL with anthropometric, hormonal and immune thyroid factors in serum of children with autoimmune thyroid disease (AITD).

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.
**P2-01-07**

**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 history of the surgical piece. Statistical analysis: IBM SPSS™ v.20 – χ², 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 (IQR 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 25 consecutively 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 the thyroid arteries. We compared the measurements during the treatment and determined correlations.

Results: Before treatment, patients had TSH 0.008 ± 0.004 mIU/l, fT₄ 48.68 ± 18.73 pmol/l, fT₃ 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 thyroid hormones or TSAb was found until the final evaluation when the laboratory tests showed TSH 2.49 ± 3.30 mIU/l, fT₄ 14.36 ± 3.35 pmol/l, fT₃ 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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¹National Institute of Endocrinology, Bucharest, Romania

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 anti-thyroid 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 examination 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 demonstrated lymphomatous infiltration, while bone marrow biopsy revealed involvement of this. Treatment will include 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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¹LTD ‘Diacor’, Tbilisi, Georgia

**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 43.5% (26 patients); 29.9% (18 patients) having subclinical hyperthyroidism; 23.3% (14 patients) having primary hypothyroidism; 3.3% (2 patients) having subclinical hyperthyroidism; 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 data show to mutually influence each other and associations between both conditions in T1DM patients. In our opinion, all patients with T1DM are recommended monitoring thyroid status.

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**P2-02 Hypothyroidism 1**

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**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), compar-

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**P2-02-02**

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

Daniela Gallo¹, Eliana Piantanida¹, Giovanni Veronesi¹, Maria Laura Tanda¹, Adriana Lai¹, Lorena Sassì¹, Valentina Lombardi¹, Elvira Maseliello¹, Paola Premoli¹, Eleonora Bianconi¹, Marco Ferrario¹, Luigi Bartalena¹
¹University of Insubria, Varese, Varese, Italy, ²Department Clinical & Exp. Medicine, Varese, Italy

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 CKP 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 slight trend) likely due to small sample size, but there was an inverse correlation between CKP 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.

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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 hypothryoidism compensation and well-being of patients with hypothryoidism with normal weight, overweight and obesity.

Methods: 306 patients (12 men, 294 women) with hypothryoidism on replacement therapy with L-T4 were included. Later a group of 150 patients with compensated hypothryoidism was selected. All patients were divided into groups depending on their body mass index: with normal body weight (18–24.9 kg/m2), overweight (25–29.9) and 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), TSH, T4, 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] 1.94 [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]) 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 TSH levels were the same in the groups of normal-weight, overweight and obese patients (p > 0.05).

Conclusion: The compensation of hypothryoidism 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 actual weight and significantly higher dose for 1 kg of ideal weight in obesity/overweight patients. In patients with hypothryoidism and overweight/obesity the quality of life and severity of hypothryoidism 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 we 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 BIOPANCREATIC 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 thirds 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, especially L-T4-oxine (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 hypothryoidism 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.
Table 1. (for abstract P2-02-06)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 22)</th>
<th>3 month (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median ThyPRO QoL (0–100)</td>
<td>54 (27–91)</td>
<td>15 (1–63) (p &lt; 0.0001)</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>80.7</td>
<td>80.2 (ns)</td>
</tr>
<tr>
<td>Median REE (Kcal/dag)</td>
<td>1,383.0</td>
<td>1,392.0 (ns)</td>
</tr>
<tr>
<td>Median S-TSH (mU/l)</td>
<td>0.96</td>
<td>0.59 (ns)</td>
</tr>
</tbody>
</table>

Table 1. Patient data (for abstract P2-02-07)

<table>
<thead>
<tr>
<th>Group (TSH, mU/l)</th>
<th>Age (mean, yrs)</th>
<th>M/F ratio</th>
<th>Females (N)</th>
<th>Hypo- or hyperthyroidism in close relatives (%)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (&lt;5)</td>
<td>49</td>
<td>1/6.1</td>
<td>73</td>
<td>49</td>
<td>85</td>
</tr>
<tr>
<td>B (5–9.9)</td>
<td>43</td>
<td>1/6.5</td>
<td>130</td>
<td>52</td>
<td>150</td>
</tr>
<tr>
<td>C (≥10)</td>
<td>43</td>
<td>1/3.9</td>
<td>51</td>
<td>42</td>
<td>64</td>
</tr>
</tbody>
</table>
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, 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, a-Tg, a-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 usual use as an indicator of the state of the patient with differentiated carcinoma of the thyroid.

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: Group 1: CT <0.05 (undetectable), Group 2: CT [F&M] within normal range, Group 3: CT>4.7–10 [F] & 11.6–20 [M], Group 4: 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 (x2, 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 Group 2, 2/22 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.
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 ± 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 = 0.025) 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 October 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 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 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 scintigraphically 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 = 0.30997) 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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1Theaghenion Cancer Hospital, Department of Endocrinology-Endocrine Oncology, Thessaloniki, Greece, 2Private Practice, Hippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece, 3Hippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece

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 thyroid 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.
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 (30.4% 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.

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, or 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.

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.
### P2-04-01

**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 revealed 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)**

<table>
<thead>
<tr>
<th>Patient/gender</th>
<th>Etiology</th>
<th>TSH [mIU/l]</th>
<th>fT4 [pmol/l]</th>
<th>PAX8 variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1/Male</td>
<td><em>Thyroid dysgenesis</em> 49.5/no data</td>
<td>p.E234K</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2/Male</td>
<td><em>Thyroid dysgenesis</em> no data</td>
<td>p.P409S</td>
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<tr>
<td>P3/Male</td>
<td><em>Thyroid dysgenesis</em> &gt;100/2.34</td>
<td>-456C&gt;T promoter variant</td>
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<tr>
<td>P4/Female</td>
<td><em>Thyroid dysgenesis</em> 88/11.4</td>
<td>-456C&gt;T promoter variant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P5/Female</td>
<td>Thyroid ectopy 270/9.31</td>
<td>-456C&gt;T promoter variant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P6/Female</td>
<td>Thyroid ectopy &gt;80/7.49</td>
<td>Heterozygous del in exon 7</td>
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<tr>
<td>P7/Female</td>
<td>Thyroid agenesis 96/6.99</td>
<td>Heterozygous del in exon 7</td>
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</tr>
</tbody>
</table>

* Lack of thyroid scintiscan restricts defining an exact type of abnormality.
**P2-04-03**
THE ROLE OF ANTITHYROID 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).


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. Slightly 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 BMI were recorded. ID was defined as Ferritin <15 µg/L, TAI when TPO-abs >60 kU/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. BRAFV600E 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 BRAFV600E 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. BRAFV600E mutation analysis was performed using polymerase chain reaction (PCR)-based amplification of DNA extracted from paraffin-embedded tumor specimens.

Results: BRAFV600E 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 BRAFV600E mutation patients (OR = 2.04, P = 0.039). However, age, tumor size, extrathyroidal extension, and multifocality were not significantly associated with the BRAFV600E.

Conclusion: The results of our study suggest that BRAFV600E mutation were associated with aggressive PTC. However, there was no clinicopathological association between BRAFV600E 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 users of cooper intrauterine device (IUD Cu380A) completed the study. Inclusion criteria were age 18–40 years, body mass index (BMI, kg/m²) <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/m² 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 T1-T2 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.

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**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.

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**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 2/3<sup>rd</sup> of subjects (n = 192) TSH shows a steep rise of 28–37% over the trimesters as against the 1/3<sup>rd</sup> 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-deficient group 29% of subjects with steep rise in TSH and 71% with steady rise were observed. In pregnant subjects TSHs-FT4 correlation was observed in both iodine-deficient and iodine-sufficient, noticeable in iodine-sufficient only in 3<sup>rd</sup> trimester.

**Conclusion:** TSH values increased in IDS from 1<sup>st</sup>-3<sup>rd</sup> 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.

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**Table 1.** Trimester specific range of TSH and FT4 in iodine-deficient & iodine-sufficient subjects (for abstract P2-04-08)

<table>
<thead>
<tr>
<th>Hormone range</th>
<th>Iodine deficient group (n=279)</th>
<th>Iodine sufficient group (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5–97.5 percentile</td>
<td>trimester I</td>
<td>trimester II</td>
</tr>
<tr>
<td>TSH (mIU/l)</td>
<td>1.02–3.70</td>
<td>1.49–4.87</td>
</tr>
<tr>
<td>FT4 (pmol/l)</td>
<td>10.38–18.63</td>
<td>9.00–17.60</td>
</tr>
</tbody>
</table>

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**Eur Thyroid J 2016;5(suppl 1):57–176**

39th Annual Meeting of the ETA
P2-04-09
PREScribes THYRoxine 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/m² with secondary amenorrhea 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, 

Testosterone, 17-OH progesterone, proinsulin, prolactin levels were in normal range.

All women were euthyroid TSH- 2.5 ± 0.4 (0.3–4.5 mU/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 mU/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 Levothyroxine 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 to 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, atypia of undetermined significance, 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, specificity, 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 have 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, hyperthyroid and hypothyroid patients, respectively (p < 0.001). 41.4% of ENG and 46.3% of EMNG patients had malignant histopathology (p = 0.169). Mean tumor size, capular 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 ≤ 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 radiiodine 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 thyroid bed I-131 uptake had disappeared. SPECT/CT is useful for identification of anatomical regions of remnant radiiodine distributions 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 malignant 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 malignant nodules in terms of mean nodule 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%), uninodeular 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 hypoechochogenicity, 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, dispahgia 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, thyroglobulin 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 (0.0–6.6) respectively. A thyroid nodule was detected. Diffuse enlargement of the thyroid gland (thyroid volume:76 cm3) with heterogeneous hypoechochogenicity, 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 lymphadenopathy 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 sanract 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 Hashimoto 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 image (FI group), and the other 19 patients underwent surgery without it (control group). FL 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 THYROIDECTOMY: SURGICAL COMPLETENESS OF CONSECUTIVE 108 PATIENTS

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Purpose: To evaluate the completeness of surgical procedures for thyroid mass in consecutive 108 patients and to compare the results with previous studies.

Methods: This retrospective study included 108 patients who underwent open thyroidectomy from January 2007 to December 2013. The completeness of surgical procedures was assessed using the ATA classification system.

Results: The completeness of surgical procedures was assessed in 108 patients. The mean follow-up period was 48.5 ± 21.9 months. The rate of post-operative complications was low, with no significant differences between groups.

Conclusion: Minimally invasive open thyroidectomy is a safe and effective surgical procedure for thyroid masses.

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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Purpose: To determine whether lobectomy alone is sufficient for papillary thyroid carcinoma (PTC) measuring 4 cm or less without extrathyroidal extension (ETE) and clinical lymph node metastasis (cLNM).

Methods: A retrospective review of 902 patients diagnosed with PTC measuring 4 cm or less was conducted. The surgical outcomes were compared between lobectomy alone and total thyroidectomy.

Results: There were no significant differences in terms of disease-free survival and recurrence rates between the two groups. However, lobectomy alone was associated with a lower rate of complications and shorter hospital stay.

Conclusion: Lobectomy alone is a suitable surgical option for patients with PTC measuring 4 cm or less without ETE and cLNM.

References:


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: Intra-thyroidal 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 in.Brandthyroidal 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 different 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 it 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 131I 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 131I is not universally indicated. In our department all these patients used to have 131I 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 131I therapy.

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 131I therapy. PTC patients with these risk factors should have ablative 131I therapy. In patients of male gender and with multifocals 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 metastasis. The lateral neck lymph node metastasis 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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Objective: 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 hardeness rather than enlargement. Surgeon was numbering any of 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% (25/127) 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 carcinoma. For lenvatinib arterial thromboembolic 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 during further treatment with lenvatinib with dose reduction from initially 24 to 10 mg (since 3/14) a myocardial infarct occurred 11/2015. Whereas only one myocardial infarct was reported in the lenvatinib phase III study. 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
Poster Presentations

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).

Conclusions: 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.

Table 1. Optimal cut off values for Vmin, S/D, PI and RI (for abstract P2-07-02)

<table>
<thead>
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<th></th>
<th>Vmin</th>
<th>S/D</th>
<th>PI</th>
<th>RI</th>
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<tbody>
<tr>
<td>AUC</td>
<td>0.719</td>
<td>0.732</td>
<td>0.724</td>
<td>0.738</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Criterion</td>
<td>≤3.3</td>
<td>&gt;3.11</td>
<td>&gt;0.92</td>
<td>&gt;0.68</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>85.19 (66.3–95.8)*</td>
<td>59.26 (38.8–77.6)*</td>
<td>81.48 (61.9–93.7)*</td>
<td>55.56 (35.3–74.5)*</td>
</tr>
<tr>
<td>Specificity</td>
<td>55.45 (45.7–64.9)*</td>
<td>82.73 (74.3–89.3)*</td>
<td>55.45 (45.7–64.9)*</td>
<td>82.73 (74.3–89.3)*</td>
</tr>
<tr>
<td>PPV</td>
<td>65.66 (56.75–73.62)*</td>
<td>77.43 (66.89–85.35)*</td>
<td>64.65 (55.98–72.45)*</td>
<td>76.28 (65.35–84.58)*</td>
</tr>
<tr>
<td>NPV</td>
<td>78.92 (67.23–87.39)*</td>
<td>67.00 (58.30–74.67)*</td>
<td>74.96 (64.02–83.43)*</td>
<td>65.05 (56.43–72.79)*</td>
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<td>Accuracy (%)</td>
<td>70.32</td>
<td>70.995</td>
<td>68.465</td>
<td>69.145</td>
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</table>

* 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.

Eur Thyroid J 2016;5(suppl 1):57–176
**P2-07-03**  
**AGE AT DIAGNOSIS IS NOT A VARIABLE THAT AFFECTS THE FREQUENCY OF STRUCTURAL INCOMPLETE RESPONSE IN ANY OF THE RISKS OF RECURRENT 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>
<thead>
<tr>
<th>Age cut-off (years old)</th>
<th>Final outcome</th>
<th>% SIR &lt; age cutoff</th>
<th>% SIR ≥ age cutoff</th>
<th>p</th>
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<tbody>
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<tr>
<td>n = 146</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>60</td>
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<tr>
<td>Intermediate RR</td>
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</tr>
<tr>
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<tr>
<td>High RR</td>
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</tr>
<tr>
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</tbody>
</table>

RR = Risk of recurrence; SIR = structural incomplete response.

**P2-07-04**  
**CLINICOPATHOLOGICAL FEATURES OF THYROID CARCINOMAS 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 thyroideody 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). Echogenicity, texture, micro and macrocalcifications, margin irregularity and vascularization pattern were similar in two groups. Hypoechoic halo was observed in 16.4% and 28.5% 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 aggressive 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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**Objective:** 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 cancer of uncertain malignant potential (TT-UMP) (n = 24, 1.7%), hurtle cell cancer (HCC) (n = 21, 1.5%), ATC (n = 5, 0.4%), and MTC (n = 13, 0.9%). FTC 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.

P2-07-07
THE RELATIONSHIP BETWEEN THE BRAFV600E MUTATION IN PAPILLARY THYROID MICROCARCINOMA AND CLINICOPATHOLOGIC FACTORS
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4Department of Otolaryngology, Head and Neck Surgery, College of Medicine, Inje University, Busan, Korea, Rep. of South

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.

P2-07-08
PROGNOSIS OF PAPILLARY THYROID CANCER WITH EXTRATHYROIDAL EXTENSION ACCORDING TO THE LOCATION OF PRIMARY TUMOR
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1Thyroid Cancer Center, Gangnam Severance Hospital, Seoul, Korea, Rep. of South

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.

P2-07-09
PATIENT WITH HIGH-MALIGNANT B-CELL LYMPHOMA AND INFILTRATION INTO THE THYROID
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1Gemeinschaftspraxis, Nuklearmed, Praxis, Fulda, Germany
2Gemeinschaftspraxis, Fulda, Germany

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 Thyroiditis de Quervain because of a pain in the left lobe a corticoid 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 hypoechochogenic 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.
P2-08-01
A NEW ROLE FOR MONOCARBOXYLATE TRANSPORTER 8: REGULATION OF THYROID HORMONE AVAILABILITY DURING RETINAL DEVELOPMENT
Pieter Vancanneyt1, Veerle Darras1
1Laboratory Comparative Endocrinology, Biology Department, Ku Leuven, Leuven, Belgium

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 layer displays a high expression of MCT8 and plays a crucial role in the development of retinal neurons. We hypothesized that MCT8 is required for the transport of thyroid hormones across the blood-brain barrier and that its absence will lead to a decreased availability of thyroid hormones during retinal development.

Method: We generated Mct8 knockout (ko) mice to study the role of MCT8 during retinal development. Immunohistochemical staining for TH and parvalbumin were performed on E6 and E8 retinas, and the expression of these markers was compared to wt controls. Additionally, we performed in situ hybridization using probes specific for Mct8 and Oatp1c1 to analyze their expression pattern in the developing retina.

Results: We found a 2-fold reduction in retinal ganglion cells at E6, indicating also a diminished 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 photoreceptor motors 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
Lisbeth Hanzer1, Susi Duday-Gralia2, Heike Heuer2, Jens Mittag2
1Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany, 2Karolinska Institutet, Department of Cell and Molecular Biology, Stockholm, Sweden, 3Leibniz Institute for Environmental Medicine (Ifu), Leibniz Institute for Aging, Fritz Lipmann Institute (Fl), Düsseldorf, Germany, 4Universität Lübeck, Ccbm, Lübeck, Germany

Thyroid hormones (THs) are essential for brain development and maintenance. In humans, hypothyroidism, a disorder characterized by reduced TH signaling in newborns, if not treated immediately, 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 TRα1 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
Beate Hermann1, Lisbeth Harder2, Jiesi Chen3, Rebecca Oelkrug2, Heike Heuer2, Jens Mittag2
1University of Lübeck, Center of Brain, Behavior and Metabolism, Lübeck, Germany, 2Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany, 3Leibniz Institute for Environmental Medicine (Ifu), Leibniz Institute for Aging, Fritz Lipmann Institute (Fl), Düsseldorf, Germany, 4Universität Lübeck, Ccbm, Lübeck, Germany

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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1Institut für Biochemie und Molekularbiologie, Universität Bonn, Bonn, Germany, 2Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany

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 T3 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 mutations 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 MCT8G495A and MCT8G282C mutants. The administration of these compounds might point to a new direction for the therapy of MCT8.

P-20-08-05
TRANSMEMBRANE MCT8-MEDIATED T3 TRANSPORT IS INHIBITED BY SOME COMMONLY USED DRUGS AND BY L-CARNITINE

Caterina Di Cosmo¹, Giuseppina De Marco¹, Patrizia Agretti¹, Eleonora Ferrarini¹, Antonio Dimida¹, Salvatore Benveniga¹, Paolo Viti¹, Massimo Tonacchera¹
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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-labelled TH. Transfected cells were exposed to increasing concentrations of hydrocortisone, dexamethasone, prednisone, prednisolone, valproic acid and L-carnitine and [125I] T3 uptake and efflux were measured.

The mode of inhibition was also determined.

Exposure to each glucocorticoid caused 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, 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 glucocorticoid caused 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, desethylamiodarone, dronedarone, buspirone, carbamazepine, valproic acid and L-carnitine and [125I] T3 uptake and efflux were measured. The mode of inhibition was also determined.

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.

P-20-06
MCT8 MUTANTS F287V AND S313A SEVERELY IMPACT THYROID HORMONE TRANSPORT

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¹Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany

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 of 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 125I labelled thyroid hormone uptake- and efflux experiments. Furthermore, KI 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.

P-20-08-07
THYROID FUNCTION IN PSEUDOHYPOPARATHYROIDISM TYPE 1A

Slavica Savić¹, Tijana Lalić², Marija Barać³, Mirjana Stojkovic², Tanja Nidžić², Bјlana Belesteni³, Milоš Stejnović³, Jasmina Cirić¹, Milоš Žarković¹
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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 – pseudohyoparathyroidism 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 characteristics of TSH resistance are high serum TSH, normal/low serum thyroid hormones, and normal/hyperplastic 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 osteodystrophy 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)

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</tbody>
</table>
thyroid 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 dihydroxycholecalciferol 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 thyroidecotomy, 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 euthyroidism. 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 euthyroidism, 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.

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### P3-01-01

**A COMPARISON OF LEVELS OF T4 AND TSH FROM SERUM AND WHOLE BLOOD ON FILTER PAPER**

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1Population Health Sciences, Medical School, University of Dundee, Dundee, UK, 2University of Dundee, Population Health Sciences, Dundee, UK, 3Academic Medical Centre, Amsterdam, Netherlands

**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.

\[
\text{T4/TSH serum correction factor} = \text{[constant + (gradient of line* T4/TSH in DBS)] ± residual standard deviation.}
\]

**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.

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**Table 1. Linear regression of T4 and TSH in DBS on T4 and TSH in serum (for abstract P3-01-01)**

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardised coefficients</th>
<th>Standardised coefficients</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>std error</td>
<td>beta</td>
</tr>
<tr>
<td>Constant</td>
<td>41.286</td>
<td>6.971</td>
<td>5.923</td>
</tr>
<tr>
<td>T4 DBS</td>
<td>1.841</td>
<td>0.097</td>
<td>0.882</td>
</tr>
<tr>
<td>R = 0.882, R² = 0.778, Adjusted R² = 0.776, residual standard deviation = 24.979</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>1.810</td>
<td>0.427</td>
<td>4.238</td>
</tr>
<tr>
<td>TSH DBS</td>
<td>1.602</td>
<td>0.053</td>
<td>0.950</td>
</tr>
<tr>
<td>R = 0.950, R² = 0.902, Adjusted R² = 0.902, residual standard deviation = 3.912</td>
<td></td>
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</tr>
</tbody>
</table>
CIRCULATING FREE TRIODOOTHYRONINE 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 is 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, eGFR and hypothyroidism were associated with SPPB score. eGFR was positively related 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 is 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.

Conclusion: Our data suggest an inverse association between eGFR and risk of hypothyroidism.
Results: In 23 patients over 803 consecutive thyroidectomy procedure (2.8%), V2 signal was missing after first lobe excision (loss of signal LOS <150 mcV). In 20/23 cases we stopped the surgical procedure (staged 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 laryngoscopy 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 multi-disciplinary 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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11st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy, 2Department of General Surgery, The Chinese People’s Liberation Army General Hospital, Beijing, China, 3Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South, 4Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

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 (1st-2nd-3rd clinical pathways) and vocal fold permanent paralysis after six months until one year without and with phono-surgery (4th-5th 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, 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
Tanu Soni1, Sandeep Bhalla2, Deepak Monga3, Anirudh Gaurang3, Varnyata Bagre4, Arshit Koundal5, A.G. Unnikrishnan6, Shailesh R. Deshpande7, Anjali Bhat8, D. Prabhakar9
1Gurgaon, India, 2Public Health Foundation of India, Gurgaon, India, 3Chellaram Diabetes Institute, Pune, India

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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1Hospital Garcia de Orta, Almada, Portugal

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 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 thyroid...
P3-01-09
A REVIEW AND CLINICAL ANALYSIS OF 12 CASES OF PRIMARY THYROID LYMPHOMA
Yang Zhang1, Ying Gao2, Zhenfang Yuan1, Yan Ming Gao1, Xiaohui Guo1
1Peking University First Hospital, Peking, China, 2Peking University First Hospital, Beijing, China

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 suctioned. Seven patients were hypothyroid 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 goiter in older 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 CONTINUOUS INTRAOPERATIVE NEUROMONITORING (CIONM) THYROID SURGERY
Cesare Carlo Ferrara1, Vincenzo Pappalardo1, Alberto Mangano1, Davide Inversini1, Andrea Leotta1, Matteo Lavazza1, Francesco Frattini2, Stefano Rassei2, Wen Tian2, Hoon Yub Kim3, Che-Wei Wu4, Gianlorenzo Dionigi1
11st Division of General Surgery, Research Center for Endocrine Surgery, Department of Surgical Sciences and Human Morphology, University of Insubria (Varese-Como), Varese, Italy, 2Department of General Surgery, The Chinese People’s Liberation Army General Hospital, Beijing, China, 3Department of Surgery, Division of Breast and Endocrine Surgery, Minimally Invasive Surgery and Robotic Surgery Center, Korea University, Anam Hospital, Seoul, Korea, Rep. of South, 4Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

Background: To determine the rate and predictors of failure of planned total thyroidectomy (TT).


Result: 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.
P3-02-02

CONGENITAL SUBCLINICAL HYPOTHYROIDISM IN CHILDREN – TO TREAT OR NOT TO TREAT?
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2Endocrinology Research Centre, Moscow, Russian Federation

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 mU/l by the end of observation remained elevated (25.5), while T4 levels was normal (16.5 pmol/l). In sister 2: TSH levels ranged from 25.1 to 11.9 mIU/l by the end of observation remained elevated (25.5), while T4 level of 11.9 mIU/l. Correlated to the background observations indications of thyroid hormone (T4 and periodically controlled FT3) remained within the reference range, there were no complaints 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.
P3-02-04

GENE EXPRESSION PANEL TO MARK THERAPEUTIC EFFICACY ON LEVOTHYROXINE-TREATED PATIENTS WITH PRIMARY HYPOTHYROIDISM

Valdelena Alessandra da Silva, Robson José de Almeida, Patrícia Varella Lima Teixeira, Leonardo Martins da Silva, João Bosco Pesquero, Cleber Pinto Camacho

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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 make 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 ≤5.7 pmol/l; Group III >5.7 pmol/l.

Results: There were no difference in TC, LDL, 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 LDL, 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, increasing 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 Cmax 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 AUC0–72,adj was 99.3% (90% CI: 95.6–103.2) and the Cmax,adj was 101.7% (90% CI: 98.8–104.6). Bioequivalence can therefore be established as the CI for lie within the predefined 0.9–1.1 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/I) 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
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 demographic, 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 most frequently prescribed doses were 50 (31.5%), 100 (24.2%), 25 (23.2%), 75 (20.1%) and 15 (18.1%) 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 esophagastroduodenoscopy.

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 choledolithiasis – 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 cytotologically 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-
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% at 43% in Bethesda V nodules. For scores TIRADS 2 and 5, the risk was 0% and 100% respectively in all cases.

**Conclusion:** TIRADS 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.

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**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 severe 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.

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**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 randomised 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 < 10-4 for both TSH, T4, T3, fT4 and fT3). The amiodarone group had higher TSH, fT4 and fT3 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.

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**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.

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**Results:** The treatment duration was similar in both groups. We found a significantly elevated thyroid density in AIT2 as compared to AEth (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 AEth. 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 AEth 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.

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**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.

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**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 (9%). TSH was not different between the two groups. UE was 134 ± 17 μg/l in Th and with 104 ± 13 borderline in EA, while Se was 74 ± 14 μg/l (Th) and 65 ± 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.

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**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 a pro-inflammatory 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 vegetarians 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.

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**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 immunoochemiluminiscent 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.

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**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 hypertriglycerideremia (P = 0.001), decreased HDL-C (P = 0.001) but no assoc...
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 indicate 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 starting to collect 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 fatigue.

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-month data and the comparisons to controls will spread further lights on the brain involvement in GD.
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 macroalbuminuria rather than decline of the eGFR. Our study suggests that subclinical hypothyroidism might be a risk factor for progression of diabetic nephropathy.

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**P3-04-06**

**ADIPOCYTOKINES, INSULIN RESISTANCE 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:** 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, aged 43 ± 11 years) were divided into 4 groups: gr.A - obese hypothyroid patients (BMI-36 kg/m²), gr.B - obese euthyroid (BMI-38 kg/m²), gr.C - hypothyroid (BMI <25 kg/m²), gr.K (control) – euthyroid (BMI 22.3 kg/m²). 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 ng/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 correlation between BMI, visceral fat%, cholesterol, ApoB, insulin, HOMA-1 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.

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**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 thyroiditis (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 which were 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 pmol/L, thus significantly higher than in those with sPAP values <36 mm Hg (10.7 ± 1.3 pmol/L, \(P = 0.04\)). Moreover, serum FT4 directly correlated with sPAP in the whole group of SSc (\(r = 0.011\), 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.

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**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 IG; folate acid and vitamin B12 levels. Two groups were defined: euthyroid group (\(n = 185, \text{TSH} 0.35–2.50 \mu\text{UI/mL}\)), and subclinical hypothyroid (SH) group (\(n = 66, \text{TSH} 2.50–10.00 \mu\text{UI/mL}\) 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, \(P = \text{NS}\)) and BMI (27.23 ± 5.12 vs 26.04 ± 5.29 kg/m², \(P = \text{NS}\)) between euthyroid and SH groups. In the total group, T3 variations were negatively correlated with HOMA-IR (\(r = -0.222, P = 0.003\)), IG (\(r = -0.184, P = 0.012\)) 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-\(\beta\) (\(r = 0.310, P = 0.043\)) 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 (\(r = 0.368, P = 0.003\)). 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 β1-adrenoreceptors gene and Ser33Gly 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 = 0.03. 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 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 were 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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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 DIAGNOSTICITY

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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 diagnosticity.

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 diagnosticity rates were 56.9% in AS and 74.8% in NAS technique (p < 0.001) (Table 1).

Conclusion: Diagnosticity 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 commun- nal 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 clonogenic assay. Ethidium bromide/acridine orange (EB/AO) staining and Tunel were used for apoptotic cell detection. The observations were tabulated and ana- lyzed 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 at 24, 48, and 72 hrs respectively. Also results showed that IC50 of Paclitaxel was 11.60, 6.831 and 0.670 μg/ml at 24, 48, and 72 hrs respectively. The EB/AO staining showed 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 beneficial 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 thy-roid cancer were enrolled. As primary surgery, all patient underwent total thy-roidectomy 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 histopatho- logical 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 con- firmed 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, medul- lary 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 appearance, 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 thy-roid nodules in 84 patients were examined prospectively with B-mode US, color Doppler, strain elastography (SE) and fine needle aspiration biopsy

Eur Thyroid J 2016;5(suppl 1):57–176
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(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 5) 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 79.3%; 94.3%; 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 NPV 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.

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**P3-05-06**

**EFFECTS OF BODY MASS INDEX ON THYROID CANCER AGGRESSIVENESS AND RECURRENCE**

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**Background:** 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 associated with aggressiveness and recurrence of thyroid cancer.

**Methods:** A total of 970 patients with papillary thyroid cancer (PTC) over 20 years 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, extrathyroidal 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-thyroglobulin antibody levels every 3–6 months and neck ultrasonography, computed tomography or 123I whole body scan every year.

**Results:** When we analyzed the relationship between body weight 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. 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.
**P3-05-09**

**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 hemithyroidectomy 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 of yellowness of nails, slightly expressed tiredness and tachycardia, with past medical history of hemithyroidectomy 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 5×5×5.5 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 it would 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.

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**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 parangangioma-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, immunohistochemical, and biochemical 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 THV-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 Levothyroxin 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.

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**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/PPARG 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.
CERVICAL LYMPH NODE METASTASES AFTER THYROIDECTOMY FOR PAPILLARY THYROID CARCINOMA USUALLY REMAIN STABLE OVER YEARS

Chisato Tomoda1, Kiminori Sugino1, Yuna Ogimi1, Chie Masakii, Junko Akaishi1, Kyiomy Y. Hamae1, Akitumi Suzuki1, Kenichi Matsuzu1, Takashi Uruno1, Keiko Ohkawa1, Hiroshi Shibuya1, Wataru Kitagawa1, Mitsuji Nagahama1, Koichi Ito1
1Ito Hospital, Tokyo, Japan

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.

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.

IMPACT OF PREOPERATIVE DETECTION OF SODIUM-IODIDE SYMPORTER EXPRESSION LEVEL ON DIFFERENTIATED THYROID CANCER (DTC) PROGNOSIS

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

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 quantitatively by FC method.

Results: According to the results of routine histology examination: 58 patients needed radioiodine ablation (RIA). During 48 months of observation reurrences were detected in 24 cases. All reurrences 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.

NATURAL HISTORY OF CONTRALATERAL NODULES AFTER LOBECTOMY IN PATIENTS WITH PAPILLARY THYROID CARCINOMA

Amit Ritter1, Gideon Bachar2, Orna Katz2, Nadav Kochen2, Dania Hirsch3, Carlos Benbassat4, Eyal Robenstok1
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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 of 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.

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**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)**

**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 had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%). Notable regional differences in the treatment history were observed; average dose per RAI treatment had distant metastases primarily in the lung (76%).

**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.

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**Table 1.** (for abstract P3-06-07)

<table>
<thead>
<tr>
<th></th>
<th>USA (n = 26)</th>
<th>Japan (n = 44)</th>
<th>ROW* (n = 30)</th>
<th>Total (n = 100)</th>
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<tr>
<td>Median cumulative dose of RAI, Gbq (mCi)</td>
<td>12.63 (341.35)</td>
<td>11.96 (315.57)</td>
<td>15.71 (424.59)</td>
<td>7.40 (200)</td>
</tr>
<tr>
<td>Average dose of RAI, Gbq (mCi)</td>
<td>5.83 (157.57)</td>
<td>11.96 (315.57)</td>
<td>5.43 (146.76)</td>
<td>3.80 (102.70)</td>
</tr>
<tr>
<td>Median time from RAI-refractory classification to initial visit (mo)</td>
<td>23.60</td>
<td>1.30</td>
<td>11.15</td>
<td>8.40</td>
</tr>
</tbody>
</table>

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**Poster Presentations**

Eur Thyroid J 2016;5(suppl 1):57–176
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.

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 bilateral 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 psammomatosus 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.

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 μg/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). Thirteen 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 counseling 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.

OPTIMAL CUTOFF VALUE OF AGE PREDICTING CANCER SPECIFIC SURVIVAL FOR PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

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1Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South, 2Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Rep. of South, 3Anam Medical Center, Department of Oncology, Seodaemun-kun, Seoul, Korea, Rep. of South

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 over staging. 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%, 92.1%, 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 undetermined 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 lobectomy 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-effectiveness 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-off 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.
**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.

<table>
<thead>
<tr>
<th>Category</th>
<th>FNAB (n = 993)</th>
<th>Surgical diagnosis (n = 133)</th>
<th>CNB (n = 912)</th>
<th>Surgical diagnosis (n = 219)</th>
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<tr>
<td></td>
<td></td>
<td>benign (n = 14)</td>
<td>malignant (n = 119)</td>
<td>benign (n = 49)</td>
</tr>
<tr>
<td>Nondiagnostic</td>
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<td>3</td>
<td>18</td>
<td>6 (0.6)</td>
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<td>5</td>
<td>609 (66.6)</td>
</tr>
<tr>
<td>AUS/FLUS</td>
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<td>37</td>
<td>25 (2.7)</td>
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<tr>
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<td>92 (10.0)</td>
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<td>Malignancy</td>
<td>54 (5.4)</td>
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</table>

*Data are number of nodules, with percentages in parenthesis.*

**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 N0 (39.0%) and 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.

**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)

<table>
<thead>
<tr>
<th>Category</th>
<th>FNAB (n = 993)</th>
<th>Surgical diagnosis (n = 133)</th>
<th>CNB (n = 912)</th>
<th>Surgical diagnosis (n = 219)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>benign (n = 14)</td>
<td>malignant (n = 119)</td>
<td>benign (n = 49)</td>
</tr>
<tr>
<td>Nondiagnostic</td>
<td>160 (16.1)</td>
<td>3</td>
<td>18</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Benign</td>
<td>609 (61.3)</td>
<td>4</td>
<td>5</td>
<td>609 (66.6)</td>
</tr>
<tr>
<td>AUS/FLUS</td>
<td>146 (14.7)</td>
<td>7</td>
<td>37</td>
<td>25 (2.7)</td>
</tr>
<tr>
<td>FN/SFN</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
<td>92 (10.0)</td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
<td>24 (2.4)</td>
<td>0</td>
<td>18</td>
<td>9 (0.8)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>54 (5.4)</td>
<td>0</td>
<td>41</td>
<td>171 (18.7)</td>
</tr>
</tbody>
</table>

Data are number of nodules, with percentages in parenthesis.
**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 ultrasonic 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 (73.7-78.5)%), 23.8 (18.1-29.5)%), 97.0 (96.2-97.7)% and 76.0 (74.3-77.7)%). 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 morphological 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 thyrotopinoma. 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.

This study was funded by PN-II-PT-PCCA-2011-3.2.no.135/2012.

**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 CEA. 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 ultrasound, 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 immunohistochemistry 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 PCC13 cells using specific siRNA.

The results showed that Sox9 is expressed in the nucleus of thyroid adult mice and in PCC13 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 ophthalmopathy. 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+CD24+HCDCD27-IL-10+ AND CD19+IL-10+ BUT NOT CD19+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 (phenoype CD19+CD24+CD27-IL-10+, CD19+IL-10+) in regulation of immune response.

Table 1. Final outcome in 1653 PTC patients according to N status (for abstract P3-08-02)
The aim of the study was to estimate the expression of CD19+CD24+CD27-IL-10- and CD19+IL-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 controls (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+CD27-IL-10- (p < 0.033 for GB and p > 0.05 for HT) and CD19+IL-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 auto-immune diseases to the healthy controls.

We conclude that the reduction number of Breg cells with expression of CD19+CD24+CD27-IL-10- and CD19+IL-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 radiodiode 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 recovery 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 NIS expression; we observed that TAZ protein is mainly located in the nucleus under treatment with this cytokine and its silencing induces a partial recovering of NIS expression in thyroid cells. Given the fact that this protein has been characterized as over-expressed 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**

**MICRONRNAS IN THYROID TISSUE AND SERUM IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE**

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_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 gene we have shown that the carriers of A allele and A4 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.

**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.
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, 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.

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+ 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.
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Zygmunt, A. 101
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
DISCOVERING TOMORROW

We are united by our passion for curiosity and new ideas. Over 5,000 Merck researchers are dedicated to discovering pioneering health solutions and developing new technologies. In 2015 our research and development investment totaled €1.7 billion.

MERCKgroup.com
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?

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
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
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
**ETA Industry-Sponsored Satellite Symposium 4**

**Pregnancy and Hypothyroidism**

Chairpersons: *George J. Kahaly*  
*Elizabeth N. Pearce*

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<tr>
<th>Time</th>
<th>Session Title</th>
<th>Speaker(s)</th>
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<tbody>
<tr>
<td>18.15–18.20</td>
<td>Welcome and Introduction</td>
<td><em>George J. Kahaly</em>, Mainz, Germany</td>
</tr>
<tr>
<td>18.20–18.45</td>
<td>Hypothyroidism and Infertility</td>
<td><em>Kris Poppe</em>, Brussels, Belgium</td>
</tr>
<tr>
<td>18.45–19.10</td>
<td>Diagnosis and Treatment of Hypothyroidism during Pregnancy</td>
<td><em>Elizabeth N. Pearce</em>, Boston, USA</td>
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<tr>
<td>19.10–19.35</td>
<td>Fetal and Neonatal Consequences of Maternal Hypothyroidism and Hypothyroxinemia</td>
<td><em>Robin P. Peeters</em>, Rotterdam, The Netherlands</td>
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<tr>
<td>19.35–19.45</td>
<td>Discussion and Conclusions</td>
<td><em>Elizabeth N. Pearce</em></td>
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</tbody>
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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
Monday, 5th September 2016

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
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
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.

Evidence of Life
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

<table>
<thead>
<tr>
<th>Member Category</th>
<th>before 30th June</th>
<th>1st July – 25th August</th>
<th>on site</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETA Ordinary and ETA Senior</td>
<td>150 €</td>
<td>175 €</td>
<td>200 €</td>
</tr>
<tr>
<td>ETA Junior &lt;35 yrs</td>
<td>60 €</td>
<td>80 €</td>
<td>100 €</td>
</tr>
<tr>
<td>ETA Corresponding</td>
<td>250 €</td>
<td>300 €</td>
<td>350 €</td>
</tr>
<tr>
<td>Non-Member</td>
<td>500 €</td>
<td>550 €</td>
<td>600 €</td>
</tr>
<tr>
<td>ATA, LATS, AOTA, JTA Members</td>
<td>250 €</td>
<td>300 €</td>
<td>350 €</td>
</tr>
<tr>
<td>Students/Res. Fellows &lt;30 yrs</td>
<td>125 €</td>
<td>160 €</td>
<td>200 €</td>
</tr>
</tbody>
</table>

Pre-Conference Events Fees

<table>
<thead>
<tr>
<th>Event</th>
<th>Fee</th>
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</thead>
<tbody>
<tr>
<td>ETA Ultrasound Course</td>
<td>150 €</td>
</tr>
<tr>
<td>ETA-CRN Symposium</td>
<td>50 €</td>
</tr>
<tr>
<td>Iodine Global Network Meeting</td>
<td>40 €</td>
</tr>
<tr>
<td>ETA Basic Educational Course</td>
<td>free</td>
</tr>
<tr>
<td>ETA Clinical Educational Course</td>
<td>free</td>
</tr>
</tbody>
</table>

Available Day Tickets

<table>
<thead>
<tr>
<th>Category</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary Members</td>
<td>100 € per day</td>
</tr>
<tr>
<td>Junior Members</td>
<td>50 € per day</td>
</tr>
<tr>
<td>Members of the Danish Endocrine Society</td>
<td>50 € per day</td>
</tr>
<tr>
<td>Non-Members</td>
<td>250 € per day</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>Event</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welcome Reception at the ‘Carlsberg Brewery’ on Saturday, 3rd September</td>
<td>free for registered participants</td>
</tr>
<tr>
<td>Network Dinner at the Teaterkaelderen Det Ny Teater on Monday, 5th September</td>
<td>80 €</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Day</th>
<th>Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friday, 2nd September</td>
<td>16.00–20.00</td>
</tr>
<tr>
<td>Saturday, 3rd September</td>
<td>07.00–19.00</td>
</tr>
<tr>
<td>Sunday, 4th September</td>
<td>06.30–19.00</td>
</tr>
<tr>
<td>Monday, 5th September</td>
<td>06.30–19.15</td>
</tr>
<tr>
<td>Tuesday, 6th September</td>
<td>07.00–15.00</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Day</th>
<th>Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturday, 3rd September</td>
<td>09.00–18.00</td>
</tr>
<tr>
<td>Sunday, 4th September</td>
<td>09.00–18.00</td>
</tr>
<tr>
<td>Monday, 5th September</td>
<td>09.00–18.00</td>
</tr>
<tr>
<td>Tuesday, 6th September</td>
<td>09.00–13.30</td>
</tr>
</tbody>
</table>
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.
Social Programme

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 €