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MEETING ABSTRACTS

A1

The risk of malignancy of the thyroid nodule/focal lesion – an assessment by ultrasound, based on our own scoring system

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Thyroid Research 2013, 6(Suppl 2):A1

Ultrasoundography (US) is the most commonly performed test used to visualize the thyroid. This examination is safe and readily available, hence it is very often carried out. Ultrasound observations allow the description of structural abnormalities of the thyroid gland evaluated in whole, or of nodules/focal lesions present in the thyroid. An ultrasound examination measures the acoustic density of tissues. The image is displayed on the apparatus screen in grayscale (B-mode). An assessment of blood flow, showing the location and intensity of thyroid vascularity is a newer US technique that uses the Doppler effect for measurements. In turn, elastography is the latest application of US, i.e. the examination which is based on the assessment of the, so-called, stiffness of lesions in comparison with the stiffness of normal thyroid tissue (i.e., the tissue of morphologically normal appearance). A common performance of US of the neck region, often carried out because of the indications that are not related to the thyroid gland (e.g., evaluation of salivary glands, assessment of blood flows in carotid and vertebral arteries) leads to the disclosure of a number of lesions detected incidentally in the thyroid gland itself. In turn, it results in the need for proper interpretation of US images in order to optimize further diagnostic and therapeutic procedures. Previous studies on the use of US to determine the nature of focal lesions/thyroid nodules in terms of their benign vs. malignant character did not allow to give a clear answer. These studies have not led to the general acceptance of cancer risk US patterns. Thus, at the present stage of knowledge, it is not possible to accept the categorical and definitive determination of the nature of lesions in terms of “malignant” vs. “benign” – on the basis of US image only. However, the studies have helped to determine the characteristics of a group of US image features, the presence of which is associated with a higher risk of cancer diagnosis. Endocrinologists diagnosing the patients with thyroid diseases are expecting to have exact guidelines and recommendations that would make easier to decide on the appropriate management. This applies in particular to answer the question: what is a greater risk to the patient – whether to undergo a surgical treatment, or abandon it? Analysis of data from the medical literature and our personal experience indicate the possibility of assigning certain patterns of US appearance to the risk of lesion malignancy. The multiplicity of possible combinations of co-occurrence of different US characteristics indicates that the most appropriate way of an objective assessment of the image is the introduction of an appropriate scoring system which reflects the accumulation of suspicious US features and the category of US risk of malignancy expressed by a number of assigned points. This is precisely our issue that we have decided to propose; our scale divides the patterns of US image risk into 3 levels: high, intermediate and low risk. In our scoring system, the finding of pathologically altered lymph nodes (usually enlarged) and/or a confirmation of the fast growing lesions/thyroid nodules (augmentation) is equal to granting 3 points for each of these characteristics. Hypochoagenicity, the presence of microcalcifications, shape of lesion - close to the rotational ellipsoid with the longest axis of a vertical (shape of an egg in upright position), as well as the presence of abnormal vascular flows (the increased and chaotic blood flows centrally located in the lesion, or totally absent blood flows in hypochoegenic lesions) is equal to the grant 1 point for each of the features. The absence of a regular thin “halo”, solid structure (composition) of the lesion, the focus/ nodule diameter of 3 cm and more and its uneven, blurred outlines (margins) are associated with granting 0.5 points for each of the features. The sum of granted points, resulting from the presence of US features specified above, is the basis of qualification for US risk levels. The score ranging from 0 to 4 points, awarded on the basis of thyroid US, speaks for a low risk of thyroid cancer, the score from 4 to 7 points – corresponds to intermediate risk, and the granting of 7 points or more qualifies to the group of US high-risk of malignancy. The use of this scoring system can help make the right clinical decisions, especially in patients with non-diagnostic smears (category I of The Bethesda System for Reporting Thyroid Cytopathology - TBSRTC), also in patients with the smears, in case of which it is impossible to determine the nature of the smear (category II TBSRTC, being also called “category of exclusion”), as well as in patients with benign lesions (category III TBSRTC) when such a cytological diagnosis seems unlikely in combination with the US image indicating a high risk of malignancy.

A2

Medullary carcinoma of the thyroid: an update

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Thyroid Research 2013, 6(Suppl 2):A2

Medullary carcinoma of the thyroid (MTC) represents 5-10% of differentiated thyroid cancers. It derives from the thyroid C-cells which produce calcitonin...
and are of neuroendocrine origin. It is a rather rare tumour and is accompanied by considerable mortality as it has frequently already metastasised at diagnosis and is not sensitive to either radiation or chemotherapy. Recently it has been shown that MTC is not infrequent in multinodular thyroid disease and thus universal calcitonin screening has been suggested in the diagnostic workup of thyroid nodules. The prognosis of the disease has recently improved as many of the newly diagnosed cases are now small, non-invasive tumours, that probably were previously missed. MTC is an interesting tumour as it occurs in a familial form in >25% of the cases, as part of the multiple endocrine neoplasia 2 syndromes (MEN2). When familial MTC may occur in combination with pheochromocytomas and, more rarely, with primary hyperparathyroidism. Recent advances in MTC management include preclinical diagnosis using molecular techniques in the case of familial disease and prophylactic thyroidectomy in asymptomatic gene carriers. The gene responsible for transmission of the MEN2 is the ret proto-oncogene, which is a membrane receptor tyrosine kinase; its physiological role is the transmission of neural signals during development. Most of the mutations which are found in MEN2 syndromes are clustered in the cysteine rich extracellular domain of the protein and either cause dimerisation or ligand-independent activation. Novel previously unknown ret mutations across many regions of the gene are currently being recognized. Mutation analysis should be performed in all cases of MTC before these somatic mutations represent unrecognized familial disease. When a mutation is identified, family members are screened and carriers are offered prophylactic thyroidectomy at a young age. The type of mutation is classified into more or less aggressive and it is important for the penetrance of the disease. The majority of experts suggest prophylactic surgery at 5-10 years, especially when the specific mutation associates with risk for earlier MTC development and more aggressive disease. Several recent publications have examined the success/cure rate of prophylactic treatment.

One important development in the field of MTC concerns the use of newer antineoplastic agents, including agents targeting the molecular pathways involved in its pathogenesis. Novel multi targeted tyrosine kinase inhibitors are being tested in advanced disease in the context of clinical trials. Recent publications indicate that a substantial proportion of patients with advanced disease will stabilize with the use of these promising agents. Patients with familial disease appear to respond better to therapy with tyrosine kinase inhibitors. Combination therapies are also being tested.

A4 Combined glucocorticoid and orbital radiation therapy – literature review and clinical experience
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Thyroid Research 2013, 6(Suppl 2):A4

The aim of immunosuppressive treatment of Grave’s orbitopathy (GO) is to limit acute inflammation and congestion of orbital tissues. Application of intra-venous glucocorticoid (GCS) pulses is presently the treatment of choice in active (CAS3/7), moderate-to-severe, and severe GO. Randomised trials (RTC) have proved this treatment to be more efficient than oral glucocorticoid therapy. The response rate of this regimen is about 80%. However, exact schedules of GCS treatment have not yet been uniquely established and depend on the experience acquired in different centres.

According to the EUGOGO (2008) Consensus, to avoid acute liver damage, the total GCS dose should not exceed 80 g in a single therapy cycle. Typically, in current schedules, the applied GCS dose per pulse per week is limited and the duration of therapy extended to 12 weeks to deliver a total methylprednisolone dose of 4.5 g. While this may not always be the optimum dose, according to the EUGUGU (2012) randomised trial of the efficacy and safety of three different cumulative doses of intravenous methylprednisolone (2.5; 5.0 or 7.5 g) for moderate to severe and active GO, the dose of 7.5 g was found to be most effective. It appears therefore that intravenous methylprednisolone treatment should be individualised depending on the severity of GO (NOSPECS criteria) and inflammation activity (CAS).

Orbital radiotherapy (RT) is less efficient in GO than in GCS but, as based on rather scarce RTC reports, oral glucocorticoid therapy combined with orbital radiotherapy (20 Gy) appears to give better results than GCS alone (efficacy of about 70-80%). Again, no single schedule of combined GCS and RT has been established since no randomised trials with intravenous glucocorticoid have been conducted.

According to our experience of over a decade, GCS pulse treatment followed by orbital irradiation improves the treatment outcome, especially in patients with eye muscle involvement, and reduces the frequency of recurrences. Restoring permanent euthyroidism is very important in GO therapy.Radiotherapy and orbital radiotherapy should be considered in patients with poorly controlled hyperthyroidism. Oral GCS should be given to patients with risk factors or active GO for radiodiode use, however no randomised clinical trials have been performed to ascertain the optimum GCS dose. According to our experience, ablative 131-I doses should be applied to efficiently control thyroid function.

Radioiodine therapy can also take place while GCS pulses are delivered, with RT supplied after completion of methylprednisolone treatment. Randomised prospective trials are also necessary to assess the efficacy of these treatment schedules. In our investigations, we have found that the group of patients who, following 131-I therapy, have reported to our Department with severe GO, demonstrated significantly higher levels of TSH and TRAb, than patients treated with anti-thyroid drugs. It is for this reason that to avoid hypothyroidism, early control of Grave’s disease patients treated with 131-I is essential.

According to the Amsterdam Declaration, detailed knowledge of the course of disease, avoiding recurrences of hyperthyroidism, and prompt qualification for well-selected treatment by an experienced endocrinologist-ophthalmologist team will improve the efficacy of GO treatment and protect the patient against severe orbitopathy.

A5 Thyroid hormones – obesity and metabolic syndrome
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Thyroid Research 2013, 6(Suppl 2):A5

Metabolism provides new information on the changes occurring in thyroid tumours
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Thyroid Research 2013, 6(Suppl 2):A3

Metabolomics is a part of systems biology dealing with the determination of qualitative and quantitative profile of low molecular weight compounds (metabolites) present in body fluids and tissues of living organisms. Metabolic composition is strongly dependent on the state of homeostasis and any deregulation should affect it. For this reason, there is now increased interest in metabolomics as a potential tool to support cancer research. At the same time the analysis of metabolic pathways involved in the process of carcinogenesis provides the possibility of a more complete understanding of the mechanisms that are critical for tumour biology.

In this study, 1H NMR measurements were performed for thyroid tumour tissue and healthy tissue homogenates and analyzed by chemometric manner. Multivariate analysis of the data using the PCA, PLS-DA and OPLS-DA methods allowed a precise separation from normal thyroid tissue of all tumours originating in both benign and malignant lesions. In addition, classification of nodular goiter, follicular adenoma and malignant tumours was possible with comparable efficacy.
Recently there has been increased interest in the association between thyroid function and obesity. Based on the notion that triiodothyronine (T3) controls metabolic and energy homeostasis and influences body weight, thermogenesis, lipolysis and metabolism of cholesterol, and that thyroid-stimulating hormone (TSH) via receptors in fat tissue, induces differentiation of preadipocytes in to adipocytes and expansion of adipose tissue (adipogenesis), thyroid function has been extensively investigated in obese adults. An elevated level of TSH with normal peripheral thyroid hormone concentration suggesting sub-clinical hypothyroidism has been consistently found in obese subjects. Several mechanisms leading to hyperthyrotopinemia have hypothesis including sub-clinical hypothyroidism caused by iodine deficiency, autoimmune thyroiditis or mutations in TSH-R gene. TSH production is also regulated by neurotransmitters and hormones that influence body weight such as neuropeptide Y and alpha-melanocyte-stimulating hormone related peptide, that innervate hypothalamic TRH neurons. These neurotransmitters and hormones are also influenced by leptin. Thyrotropin also directly induces the synthesis and release of adipokines. Some of them control appetite by acting on the brain. Metabolic syndrome (MS) is clustering obesity, hypertension, dyslipidemia and insulin resistance. MS is a status where most features of hypothyroidism can be seen. TSH increase was shown to be associated with increased cholesterol and triglycerides and with decreased HDL-C. Thyroid hormones are important determinants of glucose homeostasis. Increased thyroid hormone levels impair the ability of insulin to suppress hepatic glucose production and increase glucose uptake in muscles. An association between TSH and fasting insulin and insulin sensitivity has been reported in adults with obesity. The increased TSH and peripheral hormone levels, which are usually in the upper normal range in obese subjects may be adaptation process to increase energy expenditure in order to reduce further weight gain. The changes of thyroid hormones concentration may be regarded as a consequence rather than a cause of obesity. MS is cluster of metabolic abnormalities with insulin resistance as a major component. The patients with MS have significantly increased thyroid volume and nodule prevalence and insulin resistance is an independent risk factor for nodule formation. The prevalence of insulin resistance would be an important risk factor for developing thyroid cancer and some other non-thyroid cancers.

### A7

**MicroRNAs in thyroid function and pathology**

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**Thyroid Research 2013, 6(Suppl 2):A7**

MicroRNAs (miRNAs) are short (19-25 nucleotides), non-coding RNA transcripts regulating gene expression by binding to their 3’ untranslated regions and causing inhibition of translation or mRNA cleavage. They appear to regulate multiple biological processes, including cell growth, differentiation and apoptosis. MicroRNAs are transcribed by RNA polymerase as primary longer transcripts, which are then processed by Dicer and Drosha ribonucleases into mature miRNAs.

The importance of miRNAs for normal function of the thyroid gland has been demonstrated in mouse models with inactivated DICER gene. This mutation resulted in development of thyroid gland with follicular hyperplasia which led to inhibition of thyroid hormone production probably through significant downregulation of PAX8, FOXE1, NIS and TPO expression. In consequence, severe hypothyroidism was gradually developed.

It was demonstrated that aberrant expression of miRNAs can be deregulated in different types of thyroid cancers, and could be responsible for tumour initiation and progression. Most studies have focused on analysis of miRNA expression in papillary thyroid carcinoma (PTC) and upregulation of several miRNAs (including miR-21, miR-146a, miR-181a and miR-221) was observed. Further functional studies have determined the role of these molecules in PTC pathogenesis. It was shown that miR-221 and miR-222 negatively regulate p27Kip1 (regulator of cell cycle progression) as well as KIT gene (a tyrosine kinase receptor involved in cell growth and differentiation). Interestingly, our recent studies revealed that miR-21, miR-146a, miR-181a and miR-221 contain binding sites in 3’UTR of THRB gene, coding for thyroid hormone receptor β which is an important tumour suppressor. We have demonstrated that the expression of this miRNAs is regulated by thyroid hormone - triiodothyronine (T3). Theses results suggest a new feedback control mechanism within the thyroid hormone signaling pathway.

Recent studies confirmed negative regulation of miRNAs expression by T3 in liver of hypothryoid mouse compared with euthyroid animals. Significant overexpression of miR-206 and downregulation of its target genes in mouse with low thyroid hormone levels was observed.

In summary, microRNAs play key role in thyroid gland development, thyroid hormone synthesis and proper function of T3 signal path. Aberrant expression and function of these molecules leads to thyroid pathologies including cancers. Current research is focused on the potential applications of microRNAs as novel diagnostic markers and therapeutic targets in thyroid cancers.

### A8

**Role of Th17 cells and IL-17, IL-23 cytokines in pathogenesis of autoimmune thyroid disease in children**

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**Thyroid Research 2013, 6(Suppl 2):A8**

**Introduction:** Up till now, altered balance of Th1 and Th2 immune cells has been postulated to play an important role in the pathogenesis of autoimmune thyroid diseases (AITD). However, recent studies on thyroid diseases suggest a new role for Th17 (T helper 17) cells that have been classified as a new lineage, distinct from Th1, Th2 and Treg cells. Despite wide interest, the role of Th17 cells in the pathogenesis of inflammatory and autoimmune diseases is still being debated. Th17 cells are involved in immune responses against extracellular pathogens and have the ability to secrete cytokines; IL-17, IL-17F, IL-21 and IL-23. Th17 cells can be
characterized by several surface markers, i.e. CCR6 (CD196), IL-23R, IL-12Rbeta2 and CD161.

**Aim of the study:** To estimate the proportions of circulating CD4+CD161+CD196+ and CD4+IL-17+ Th17 cells and serum concentrations of IL-17 & IL-23 in patients with Graves’ disease (GD, n=22, mean age±SEM 14.3 ± 4 years), Hashimoto’s thyroiditis (HT, n=37, mean age ± SEM 15 ± 2 years) and in healthy controls (C, n=25, mean age ± SEM 15.2 ± 2 yrs).

**Material and methods:** Polychromatic flow cytometry and several fluorochrome-conjugated monoclonal antibodies were applied to delineate Th17 cells with either CD4+CD161+CD196+ or CD4+IL-17+ phenotype using apparatus FACSCalibur (BD Biosciences). The expression of IL-17 and IL-23 were analyzed by Bio-Tek ELx800 ELISA reader. Thyroid anti-TSH receptor immunoglobulins (TRAK), anti-thyroglobulin (anti-TG) antibodies were measured in all the samples using electrochemiluminescence “ECLIA” with Modular Analytics E170 analyzer (Roche Diagnostics, Poland).

**Results:** In untreated HT children we observed an increased percentage of CD4+CD161+CD196+ (7.1 ± 3.5 vs. 3.7 ± 1.8; p < 0.04) and CD4+IL-17+ (3.7 ± 2.7 vs. 1.4 ± 0.4; p < 0.01) Th17 lymphocytes in comparison to the healthy controls. In GD children we did not reveal such abnormalities in the population of these cells. In cases with HT, a positive correlation between the percentage of CD4+IL-17+ and CD4+CD161+CD196+ T cells and serum level of anti-TPO antibodies (r=0.49; p < 0.025; r=0.65; p < 0.01; respectively) was detected. In untreated patients withAITD we observed an increased levels of IL-23 in comparison to control group (GD:156.29 ± 118.22 vs. 69.04 ± 38.23, p=0.004, HT:135.04 ± 140.19 vs. 69.04 ± 38.23, p=0.046). Methimazole treatment in GD led to decrease of these cytokine levels in a period of 6-12 months. However, during 6-24 months of L-thyroxine therapy in HT there wasn’t any reduction of IL-23 concentration compared with HC. IL-17 was elevated only in HT patients in comparison to the controls (17.17 ± 10.49 vs. 11.38 ± 2.99, p=0.021), which normalized during therapy.

**Conclusions:** We conclude that the increased percentage of Th17 cells and elevated level of IL-17 and IL-23 cytokines in children with HT can suggest their role in initiation and development of immune and inflammatory processes in this endocrinopathy.

**A9**

**Interactions of metabolic syndrome and thyroid hormones**

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**Thyroid Research 2013, 6(Suppl 2):A9**

The prevalence of metabolic syndrome worldwide is high and rising (Alexander Diabetes 52: 1210, 2003; Cameron Endocrinol Metab Clin North Am 33: 351, 2004). According to all definitions visceral obesity, increased blood pressure are part of the definition. Thyroid hormones impact all these factors. In a large Chinese case control study all components of the metabolic syndrome were associated with systematically higher TSH levels (Lai Endocr J 58:23, 2011). Recent data on TH replacement following thyroid surgery further strengthen the close relation between TH status and body weight. Total thyroidectomy despite full replacement with T4 increases body weight by a mean of 2 kg above controls within 1 year (Jonklaas Thyroid 2011). When patients are treated with T3 instead of T4 to TSH body weight decreases by more than 2% (Ittermann JCEM 97: 828, 2011). Thus, all components of the metabolic syndrome are altered by thyroid hormone status. Measurement of thyroid hormone status ought thus to be considered in any patient with metabolic syndrome or diabetes mellitus to rule out an easily manageable cofactor of the disease.

**A10**

**Do thyroid peroxidase antibodies influence risk of cardiovascular diseases before and after treatment of hyperthyroidism?**

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**Thyroid Research 2013, 6(Suppl 2):A10**

We have evaluated how levels of predictors of the cardiovascular risk such as: glucose, insulin, total cholesterol, high-density cholesterol, low-density cholesterol and triglycerides as well as adiponectin, fibrinogen, D-Dimers and CRP changed 24-28 weeks after treatment of hyperthyroidism in women with low and high titer of antibodies, and if their levels were different in these groups before and after treatment of hyperthyroidism. We compared also T4 level before and after treatment in study groups. We investigated 15 postmenopausal women (non-smoking, aged 51-69 years) with subclinical and overt hyperthyroidism. We divided them into two groups according to titer of thyroid peroxidase antibodies: with low titer of antibodies (27 women) and high titer of antibodies (8 women).

Statistical analysis revealed no difference in lipids profile, coagulation-fibrinolytic system, glucose, insulin, CRP and adiponectin level (before and after treatment) between groups with low and high titer of antibodies. No difference in T4 level before and after treatment was found. In women with low titer of antibodies significant decrease was observed only in T4 level (20.38 vs. 13.23 ng/ml). Levels of other factors did not differ before and after treatment. Triglycerides level decreased (133.00 vs. 89.13 mg/dl) and CRP level increased (2.95 vs. 4.48 mg/l) significantly after treatment in women with high titer of antibodies.

Data suggest that it is more difficult to become euthyroid for women with hyperthyroidism and high titer of antibodies (there is no significant difference between T4 level before and after treatment). Changes in metabolic profile and increase in inflammatory process are observed in women with hyperthyroidism and high titer of antibodies.

**A11**

**Expression mRNA pattern of retinoid acid and retinoid X nuclear receptor subtypes in thyroid carcinomas**

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Retinoid receptors (RARs) upon a proper ligand binding act as all-trans retinoic acid-inducible transcription factors interacting as heterodimers with retinoid X receptors (rexinoid receptors, RXRs).

The objective of this study was to evaluate all retinoid/rexinoid nuclear receptor subtypes (RARalpha, RARbeta, RARgamma, RXRalpha, RXRbeta, RXRgamma) expression pattern in thyroid tumour tissue of patients with different types of thyroid cancer in order to compare it with that of the intact thyroid tissue of the corresponding patient. The expression of the retinoid/ rexinoid nuclear receptor subtypes has been analyzed by the semi-quantitative RT-PCR technique.

Papillary thyroid carcinoma (PTC) patients expressed RXRgamma when compared to non-neoplastic thyroid tissues of the corresponding patients that were lacking to express RXRgamma or its expression was very low. Moreover, we have found significantly increased expression of RARbeta and RARgamma in overall group of FTC patients. This increase was detected in cases with positive lymph node metastasis (LNM), but not with negative LNM. On the other hand, RARbeta was significantly reduced in the subgroup of classic variant (CV) of papillary carcinoma. Expression of RXRgamma in the patient with anaplastic carcinoma was found to be lower than that of patients with papillary carcinoma. Follicular adenoma or malignant lymphoma, and also nonmalignant follicular nodules
were expressing all RAR and RXR subtypes. On the other hand, hyperplastic
tissue was found to express all RAR or RXR subtypes, except RARgamma.
In conclusion, the data on the differences in RAR and RXR subtype mRNA
expression patterns in various thyroid carcinomas might thus enhance
therapeutic potentialities, and thus they may find exploitation in clinical oncology, predominantly, in the differential diagnostics of human thyroid neoplasms.

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A12 Thyroid surgery – intraoperative localization and protection of
important structures of the neck
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Nodular thyroid disease affects 500 to 600 million people worldwide.
Tumours of the thyroid account for about 1% overall human cancers.
Thyroidectomy is the most common endocrine operation. Surgical
management for benign thyroid nodules is recommended for: progressive
increase in nodule size, substernal extension, compressive symptoms in the
neck region, the development of thyotoxicosis and in case of preference of
that kind of treatment reported by the patient. In Poland thyroidectomy is
the fourth surgical procedure and concerns 25000 operations yearly.
Reduction of surgical injury with simultaneous retention of current safety
and radical nature of surgical procedure forces the work in a relatively small
operating field. Electric devices enabling the achievement of full and lasting
haemostasis during thyroidectomy supplant traditional surgical method
(ligature, haemostatic sutures) with no impact on the incidence of
perioperative complications, while at the same time allowing to shorten
the duration of the procedure. The haemostatic effect is associated with
regeneration of heat, which apart from the intended result may bring about
thermal tissue injury. During the surgical procedure important is to
determine the thermal spread around the active tip of electric devices in the
operating field during thyroidectomy, and the safe temperature range
during the operation to protect important structures of the neck. The mean
safe distance of the active tip of an electric device from important anatomic
structures is 5 mm minimally and depends on the device type, time of using
and its power settings. All the modern techniques of vessel sealing are
associated with generation of heat and its spherical spread, which causes
thermal injury to the surrounding tissues. Their mode of operation through,
among others, structural changes in collagen and elastin, leads to lasting
joining of sealed vessel walls and tissue structures. These systems enable a
safe sealing of vessels of up to 7 mm in diameter.

In conclusions: In the cases analysed by the author concerning the
thyroidectomy techniques, it is recommended to replace to electric devices
with ligatures or clips or human fibrinogen in place near the laryngeal
nerves, parathyroid glands and the trachea. The decision on the change of
the method of haemostasis maintenance in the vicinity of crucial structures
belongs to the surgeon.

A13 The proteins of iodine metabolism in the pathophysiology of the
thyroid gland
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Thyroid Research 2013, 6(Suppl 2):A13

Iodide (I-) is a trace element (0.0001% lithosphere) that is an important
constituent of thyroid hormones. The iodide-containing T3 and T4 are
crucial for normal development and the proper functioning of numerous
metabolic pathways in probably all adult tissues. The biosynthesis of T3
and T4 involves thyroid specific proteins, found predominantly but not
exclusively in the thyroid tissue. The process requires the presence of
iodide (I-), a peroxidase (TPO), a supply of H2O2, and an iodine acceptor
protein (Tg). The active trapping I- from the blood by basolateral iodide
transporter NIS and concentration in the thyroid gland is a first step of
hormonogenesis. Then I- is translocated across apical membrane to the
follicle lumen by apical anion transporter pendrin. Once the I- reaches
the colloidal lumen it is quickly oxidized by TPO, the key enzyme of
biosynthesis. Thyroperoxidase is localized as a dimer at the apical
membrane – colloid interface where the catalytic sites are exposed to the
colloidal lumen, and where the main steps of hormonogenesis take place.
Then oxidized iodide is further bound to tyrosyl residues in Tg – a
precursor and storage form of thyroid hormones. The hormonogenic
monoiiodotyrosine (MIT) and diiodotyrosines (DIT) are subsequently
coupled to form of T3 and T4. These key proteins engaged in the process
of thyroid hormone synthesis are involved in pathological autoimmune
response and genetic abnormalities in each of these proteins are
responsible for some of thyroid disorders.

A14 Perspectives in the management of thyroid orbitopathy
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Despite the huge progress in the understanding of the pathomechanism
of thyroid orbitopathy (OT) done during recent years this extrathyroidal
manifestation of Graves’ disease still remains one of the most complex
problems of clinical endocrinology. The outcome of the management is not
satisfying neither for patient nor for physicians. Some likelihood of the
improvement of the results may be expected from innovative treatment
options basing on the progress in understanding of mechanisms of
autoimmunity and inflammation. On the other hand an effort must be done
for the progress in the existing treatment regimes.
Glucocorticoids have been used in the treatment of severe OT for over
50 years but irrespectively of therapeutic regime any improvement in eye
changes may be achieved only in ca. 70% of patients. Numerous schemes of
glucocorticoid use should be validated, optimized and meet an individual
approach as well as adhere to the local capabilities. The common
adjuvant treatment with selenium in Graves’ disease patients may prevent from a development of eye symptoms and possibly
will improve the quality of life. The mode of management of hyperthyroidism has an influence on OT. Medical and surgical therapy seem not to deteriorate the course of OT while
radioiodine therapy may worsen eye symptoms. OT patients at high risk
should get the preventive glucocorticoid treatment. The access to a surgical treatment procedures as orbital decompression and
rehabilitative surgery must be assured for OT patients and techniques of
surgical procedures should be developed. The results of anticytokine therapy are promising and the progress in this
field may be expected while the value of newly developed TSH receptor
blocking molecules needs further observations. The frequency of circulating CD40(+) fibrocytes is markedly increased in
patients with OT, suggesting that this receptor might represent a
therapeutic target for OT. An increase in a local steroidogenesis documented within orbital tissues in
an active phase of OT rises the idea of the use of 11β hydroxysteroid
dehydrogenase-1 inhibitors in OT patients. These drugs are under intensive
clinical investigation for the treatment of type 2 diabetes. Since
recommendations basing on EBM according to the pivotal problems of
the management OT are still lacking, the system of care for OT patients
should be based on centres of excellence with proper experience and
multidisciplinary approach.

A15 Recent progress in thyroid surgery
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Thyroid Research 2013, 6(Suppl 2):A15

The management of thyroid disease has evolved rapidly within the past
decade. The history of thyroid surgery starts in the second half of XIX
Introduction: Thyroid papillary carcinoma represents 75% of all thyroid cancer cases. It is more prevalent in the young and middle age group of patients. Distant metastases occur in 10% of cases. Metastases to lymph nodes can be the first sign of micrometastases. This is a case report where thymus is the most common and pulmonary embolic disease appeared to be the first manifestation of the carcinoma. The chest CT scan showed mediastinal lymphadenopathy representing metastases of papillary thyroid cancer. The 18F-FDG PET/CT scans had a major diagnostic and prognostic value in the overall management.

Case: A 36-year-old man was diagnosed with thymus papillary thyroid carcinoma. In September 2011, the chest CT scans showed mediastinal lymphadenopathy. The neck ultrasound imaging was unremarkable. On 29th September 2012, the EBUS/TNB confirmed a papillary lesion. The 18F-FDG PET/CT scans showed an increasing FDG uptake in mediastinal lymph nodes and in the left lobe of thyroid gland. The FDG level of 7 mm diameter thyroid nodule detected. In December 2012, a total strumectomy with Transcervical Extended Mediastinal Lymphadenectomy (TEMLA) was performed. The treatment included cardiac tamponade. The treatment included cardiac tamponade therapy. In the 131I scintigraphy scan, there was no uptake of 131I. The CT scans suggested recurrence of the carcinoma. In January 2013, the 18F-FDG PET/CT scans showed an increasing FDG uptake in several lymph nodes, in the left lung and the subcutaneous lesion of chest.

Conclusions: The 18F-FDG PET/CT proved a sensitive and specific imaging modality, useful in assessing the progression of a thyroid papillary carcinoma with suspected recurrences suggested by radiologic imaging.

Methods: Basal and stimulated CT levels were measured 3 months after the surgery. The follow-up was continued for average 7.2 years (1-16 years). In the event of increasing CT levels, imaging studies were performed to detect metastases. Correlation between the occurrence or lack of metastases and CT levels 3 months after the surgery was assessed.

Results: Metastases to cervical lymph nodes were found in 6 patients 1 to 10 years after the surgery. In the second case of PTU intolerance, the CT levels were slightly above. The recommended medication in the first trimester is propylthiouracil (PTU) because its use is not associated with congenital abnormalities. Alternatively methimazole (MMI) can be instigated in the case of PTU allergy. In the second and third trimester, the use of MMI is preferred because it is not associated with PTU hepatotoxicity. Serum TSH, and free TH should be monitored every 2-6 weeks. Surgery is indicated in the second trimester in case of severe adverse reactions to ATDs, when high doses of ATDs are persistently needed or when patient is not compliant with ATD therapy. Radioiodine therapy is forbidden in pregnancy because of potential teratogenic effects.
The thyroid hormone (TH) system is involved in many important physiological processes, including regulation of energy metabolism, growth and differentiation, development and maintenance of brain function, thermo-regulation, osmo-regulation, and axis of regulation of other endocrine systems, sexual behaviour and fertility, cardiovascular function. Therefore, concern about TH disruption (THD) has resulted in strategies being developed to identify THD chemicals (THDC). Information on potential of chemicals causing THD is typically derived from animal studies. However, for most chemicals, this information is often limited or even unavailable. It is also unlikely that animal experiments will be performed for all TH relevant chemicals in the near future for ethical, financial and practical reasons. In addition, typical animal experiments often do not provide information on the mechanism of action of THDC, making it harder to extrapolate results across species. Relevant effects may not be identified in animal studies when the effects are delayed, life stage-specific, not assessed by the experimental paradigm (e.g., behaviour) or only occur when an organism has to adapt to environmental factors by modulating TH levels. Therefore, in vitro and in silico alternatives to identify THDC and quantify their potency are needed. THDC have many potential mechanisms of action, including altered hormone production, transport, metabolism, receptor activation and disruption of several feedback mechanisms. In vitro assays are available for many of these endpoints, and the application of modern ‘omics’ technologies, applicable for in vivo studies can help to reveal relevant and possibly new endpoints for inclusion in a targeted THDC in vitro test battery. Within the framework of the ASAT initiative (Assuring Safety without Animal Testing), an international group consisting of experts in the areas of thyroid endocrinology, toxicology of endocrine disruption, neurotoxicology, high-throughput screening, computational biology, and regulatory affairs has reviewed the state of science [1] for (1) known mechanisms for THD plus examples of THDC; (2) in vitro THD tests currently available or under development related to these mechanisms; and (3) in silico methods for estimating the blood levels of THDC. Based on this scientific review, the panel recommends a battery of test methods to be able to classify chemicals as of less or high concern for further hazard and risk assessment for THD.

Reference

of an exon 33 SNP (p.R1999W), together with the presence of 1 or 2 copies of the susceptibility allele of one of the 10-12 exons SNP cluster seems to confer the strongest association with AITD for this gene. However, none of the mentioned genes has an effect which would be large enough to explain the predisposition to HT on its own. It is currently accepted that it is rather interaction of a couple of altered genes rather than one single gene, which triggers the phenotype of disorder. In contrast to many other autoimmune diseases, it was impossible to unaniuously associate HT with one HLA-DR type. It has but been found that a specific amino acid signature in exon 2 of the HLA-DRB1 gene is important for HT susceptibility. Additional presence of the exon 33 SNP in the TG gene causes a synergistic effect on disease susceptibility. This co-existence probably causes the preferred presentation of mutated TG to autoreactive T-cells by the altered HLA pocket, which then lead to AITD development.

Other mutations could partially explain the impact of environmental factors on HT susceptibility. Carriers of the susceptibility allele at position -1623 of the TG promoter region are prone to produce high amounts of TG when encountering IFNα.

In summary however, it is impossible to identify a single etiological polymorphism or even gene, which would be responsible for the etiopathology of Hashimoto’s thyroiditis. It seems that there are at least a couple of genes responsible for this disease and that different mutations could be responsible for the different phenotypes of this disorder like the age of symptom onset, occurrence of postpartum thyroiditis, presence of goitre, or a coexisting thyroid carcinoma.

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**A22**

**Treatment of advanced thyroid cancer refractory to therapy**

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Thyroid Research 2013, 6(Suppl 2):A22

Radioiodine treatment constitutes the most effective therapeutic option of advanced differentiated thyroid cancer. Unfortunately, about 30% cancers do not show radioiodine uptake or do not respond to therapy. Thyroid kinase inhibitors (TKI), among them axitinib, cabozantinib, lenvatinib, motesanib, pazopanib, sorafenib, sunitinib and vandetanib, constitute a new group of drugs implemented to therapy of both differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC). They inhibit growth factor receptors which play crucial role in processes of growth, differentiation and maturation of neoplastic cell. Detailed information related to mechanism of action of each drug as well as to conducted clinical trials are given in the table below:

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Mechanism of action</th>
<th>Clinical trials (phase)</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOTESANIB</td>
<td>VEGFR1, 2, 3, PDGFR, c-KIT, RET</td>
<td>II</td>
<td>MTC, DTC</td>
</tr>
<tr>
<td>SORAFENIB</td>
<td>B-RAF, VEGFR1, VEGFR2</td>
<td>II/III</td>
<td>MTC</td>
</tr>
<tr>
<td>AXITINIB</td>
<td>VEGFR, c-KIT, PDGFR-B</td>
<td>II</td>
<td>DTC</td>
</tr>
<tr>
<td>SUNITINIB</td>
<td>VEGFR1, 2, PDGFR, c-KIT, FLT3, RET</td>
<td>II</td>
<td>DTC</td>
</tr>
<tr>
<td>LENVATINIB</td>
<td>VEGFR1, 2,3, FGFR1, PDGFR</td>
<td>II/III</td>
<td>MTC</td>
</tr>
<tr>
<td>CABOZANTINIB</td>
<td>MET, VEGFR2, RET</td>
<td>III</td>
<td>DTC</td>
</tr>
<tr>
<td>PAZOPANIB</td>
<td>VEGFR, PDGFR, c-KIT</td>
<td>II</td>
<td>MTC</td>
</tr>
<tr>
<td>VANDETANIB</td>
<td>RET, VEGFR, VEGFR2, EGFR</td>
<td>II</td>
<td>DTC</td>
</tr>
</tbody>
</table>

was obtained in DTC patients treated with pazopanib (49%). Whereas, in phase II clinical trials with cabozantinib, motesanib and sorafenib carried out in MTC, disease control was achieved in 90%, 83% and 94% patients, respectively. The most common side effects are skin reactions such as photosensitivity, rash, hand-food syndrome, arterial hypertension, gastrointestinal – diarrhoea, nausea, vomiting, stomatitis and decrease in body weight. Majority of them have slight or moderate intensiveness (G1 and G2 according to Common Terminology Criteria for Adverse Events). The tolerability of TKI is acceptable and does not affect the quality of life.

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**A23**

**Amiodarone and the thyroid dysfunction**

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Thyroid Research 2013, 6(Suppl 2):A23

Amiodarone, a class III antiarrhythmic agent, is a benzofuran derivative containing 75 mg iodide per 200 mg tablet. During the metabolism of 200 mg of the drug approximately 6-8 mg of inorganic iodine is released into the systemic circulation. Amiodarone is very lipophilic and concentrates in various tissues and organs such as adipose tissue, skeletal muscles, myocardium, liver, lung and thyroid. Amiodarone is dealkylated in the liver to its major active metabolite desethylamiodarone. Amiodarone therapy is associated with a number of side effects, including thyroid dysfunction – thyrotoxicosis in 2-15% and hypothyroidism in 5-20% of patients, respectively. The effects of amiodarone on thyroid function depend on underlying thyroid status and dietary iodine intake. Patients with autoimmune thyroid disease are more likely to develop hypothyroidism due to failure to escape from Wolff-Chaikoff effect. In patients with multinodular goiter or latent Graves’ disease hyperthyroidism may occur. Amiodarone may also cause destructive thyroiditis in patients without underlying thyroid disease. Thyrotoxicosis may be a result of increased synthesis of thyroid hormones (type 1) or of their excessive release due to a direct damage of thyroid cells caused by amiodarone, its metabolite desethylamiodarone or iodine (type 2). The distinction between type 1 and type 2 thyrotoxicosis is crucial, since therapy is different in these two types. The differential diagnosis is based on the presence of goiter, evaluation of thyroid autoantibodies, colour flow Doppler image, thyroid uptake and on the response to steroids or perchlorate. Patients with type 1 thyrotoxicosis require thiocionamides or potassium/sodium perchlorate, while those with type 2 – corticosteroids. Hypothyroidism is treated with L-thyroxine. The signs and symptoms of amiodarone-induced thyrotoxicosis and hypothyroidism can be scanty. Therefore, all patients treated with amiodarone need periodic examination of thyroid function. Apart from inducing thyroid dysfunction, amiodarone causes hypercholesterolemia due to decreased expression of the LDL receptor gene, which is regulated by T3. Adverse effects of amiodarone have led to the search for analogues with the same efficacy but safer profile. Dronedarone is structurally related to amiodarone but does not contain iodine atoms and does not increase the incidence of thyroid disease. Dronedarone appears to be less-effective but may be beneficial for patients with atrial fibrillation or flutter who are at risk of developing amiodarone induced thyroid dysfunction.
A24
What is the best therapeutic approach if the initial glucocorticoids therapy of active Graves’ orbitopathy fails?

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Thyroid Research 2013, 6(Suppl 2):A24

Glucocorticoids are the first-line treatment for active moderate-to-severe and sight-threatening Graves’ orbitopathy. Glucocorticoids treatment, by exerting antiinflammatory and immunomodulatory effects, reduces pain, injection and edema of orbital tissues and provides a substantial relief from optic nerve compression. Although efficiency of both oral and intravenous glucocorticoids is proven, the randomized clinical trials revealed that intravenous therapy is more effective and better tolerated. However, 20-40% of patients respond only partially or do not respond to immunosuppressive treatment. The effectiveness of treatment may be improved by proper selection of patients suspected to have beneficial results, i.e. those with a high degree of disease activity, with orbitopathy of recent onset or recent progression. Corticotherapy may cause major side effects which make treatment continuation impossible. Orbital radiotherapy exerts nonspecific antiinflammatory effect and suppresses radiosensitive lymphocytes infiltrating the orbital space. Orbital radiotherapy remains an effective and safe second-line treatment preferably used in association with glucocorticoids. The combined therapy is more effective than either treatment alone. Sight-threatening Graves’ orbitopathy due to compressive optic neuropathy or corneal ulceration requires immediate intervention. High-dose daily intravenous glucocorticoids are the first-line treatment and if the response is absent or poor within 1-2 weeks the orbital decompression should be performed. Corneal breakdown should be additionally treated with topical lubricants, and sometimes, to provide eyelid closure, with blepharorrhaphy or tarsorrhaphy. Unsuccessful oral glucocorticoid treatment of active Graves’ orbitopathy should be an indication for orbital radiotherapy, preferably combined with glucocorticoids, or to a 3 month intravenous methylprednisolone course. If intravenous methylprednisolone was the first treatment and the response is not satisfactory, the intravenous course should be repeated combined with orbital radiotherapy. An alternative approach is combination of oral or intravenous glucocorticoids with cyclosporine for 3-6 months. It was demonstrated that the combined treatment of cyclosporine with oral glucocorticoids resulted in substantial improvement and was useful to reduce the dose of glucocorticoids. In steroid unresponsive Graves’ orbitopathy, biological agents as anti-lymphocyte antibody (anti-CD 20, rituximab) and anti-cytokine antibody (anti-TNFα, etanercept) have shown promise. Theoretically somatostatin analogue pasireotide, with a wider than octreotide or lanreotide binding affinity for various somatostatin receptor subtypes could be also a treatment option. As far as the randomized clinical trials are not available, the use of biological agents and somatostatin analogues is experimental. We hope that the future treatment will be based on pathogenic mechanisms of Graves’ orbitopathy. Small molecule “drug like” TSH receptor neutral antagonists were shown to antagonize TSHb activation of TSH receptor on retroorbital preadipocytes and possibly could be used to treat Graves’ orbitopathy. Currently their effects were determined in the model of orbit cells.

A25
The ATA guidelines of thyrotoxicosis

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Thyroid Research 2013, 6(Suppl 2):A25

The authors of guidelines provide 100 recommendations describing many intensively discussed issues. Among them is hepatotoxicity of PTU and limitations of PTU treatment mainly to the first trimester of pregnancy. Methimazole becomes first line ATD for patients with new onset of Graves’ disease. Graves’ orbitopathy (GO) is classified according to its clinical activity and severity. Deterioration of GO after radioactive iodine (RAI) treatment and beneficial effects of steroids to prevent RAI induced exacerbation of GO are described. All patients with subclinical thyrotoxicosis who are older than 65 years and those who are below age 65 and have risk factors or hyperthyroid symptoms should be treated. It is proposed to measure TSH receptor autoantibodies in pregnant women with a previous history of autoimmune thyroid disease. The information about thyroid ultrasonography with the colour-flow Doppler for the rapid differentiation between the two main types of amiodarone-induced thyrotoxicosis, and its help for accurate treatment of these conditions is provided.

A26
Thyroid disorders and pregnancy

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Thyroid Research 2013, 6(Suppl 2):A26

During pregnancy specific changes in thyroid physiology occur, resulting in such consequences as different course of thyroid disorders and difficulties in diagnostics of thyroid disorders. Pregnancy is characterized by the increased formation of thyroid hormones. This is associated with the substantial increase in the requirements for dietary iodine – according to current recommendations to 250 micrograms/day. Therefore, additional iodine supplementation is advised at the level of 150 micrograms/day to be administered to every pregnant and lactating woman, and also to women who are planning to be pregnant. Another physiological change during pregnancy is thyroid hyperstimulation, caused by human chorionic gonadotrophin (hCG) in the first trimester. Quite frequently it takes the form of gestational transient thyrotoxicosis. Thyroid dysfunctions, i.e. hyper- and hypothyroidism, both are predominantly of autoimmune etiology in pregnant women. Thus, hypothyroidism is usually associated with Graves’ disease, whereas hypothyroidism – with Hashimoto’s thyroiditis. The diagnosis is based on abnormal values of thyroid hormones and thyrotropin concentrations, with some difficulties in the interpretation of results occurring mainly in the first trimester. The increased concentration of thyroid antibodies can be helpful to diagnose thyroid dysfunction of autoimmune origin, therefore they should always be measured. Medical treatment in hyperthyroid pregnant women is the management of choice, with propylthiouracil being the preferred antithyroid drug in the first trimester and thiarmazole being recommended in the second and third trimesters. Careful control of maternal thyroid function is required during antithyroid drug treatment to avoid fetal hypothyroidism. In turn, hypothyroidism, especially its subclinical form, relatively frequently occurs during preconception period and gestation. Replacement therapy with levothyroxine (L-T4) is the treatment of choice in hypothyroidism. Hypothyroid patients on L-T4 replacement should be carefully monitored to keep TSH and thyroid hormone concentrations in recommended ranges before conception and during pregnancy. Patients with pre-existing hypothyroidism generally require increased L-T4 doses during pregnancy. Discussing the diagnostic procedures used in pregnant women constitutes the separate issue. For example, not free thyroid hormones but their total fractions are recommended for the diagnosis of thyroid dysfunction during gestation. Another separate issue relates to screening for thyroid dysfunction before and during pregnancy. According to current guidelines, universal screening is recommended in individuals at high risk for thyroid illness. Summing up, the diagnosis and management of thyroid disorders during pregnancy differ substantially from those in general population.

A27
Effect of triiodothyronine on hyperandrogenism in women

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Thyroid Research 2013, 6(Suppl 2):A27

Introduction: The imbalance of thyroid hormones can cause the dysfunction of the reproductive system. The aim of our study is to evaluate the thyroid hormone triiodothyronine’s (T3) influence on women’s hyperandrogenism.

Methods: 42 women aged 18-35 were randomly selected with FAl > 4.5 or one of the following signs of hyperandrogenism: hirsutism, acne, menstrual disorder, with normal thyroid function. Patients were divided into two
groups. The first group (n=23) received 12.5 μg of T3 for 6 months and the second group (n=19) – placebo. After the 6-month course the treatment was changed accordingly. We estimated hirsutism by using the Ferriman–Gallwey score system, acne, testosterone (T) levels, sex hormone binding globulin (SHBG) and free androgen index (FAI) and we also examined ovarian volume changes.

**Results:** The hirsutism score decreased from 11.86 ± 6.17 to 8.44 ± 5.02 (p=0.009). A significant decline of acne score was observed from 1.66 to 0.58 (p=0.02). The testosterone serum level dropped from 2.85 ± 1.29 ng/l to 2.28 ± 0.87 ng/l (p=0.03) and SHBG serum concentration during the 6-month period increased from 34.99 ± 15.34 nmol/l up to 44.52 ± 19.69 nmol/l (p=0.03). FAI decreased from 10.11 ± 7.29 to 6.48 ± 6.62 (p<0.007). The TSH level after 3 months of treatment decreased from 1.69 ± 0.93 mIU/l to 0.82 ± 0.69 mIU/l (p<0.001) and after 6 months it was 1.15 ± 0.9 mIU/l (p<0.01). The FT4 level dropped from 15.52 pmol/l to 10.51±12.12 pmol/l (p<0.05). The FT3 level increased from 4.73 ± 0.69 pmol/l to 7.57 ± 1.86 pmol/l (p<0.05). The thyroid gland volume during the treatment remained stable. The ovarian volume over 6 months changed from 25.3 ± 9.3 to 18.36 ± 6.25 (p=0.002). A positive correlation was found between the ovarian volume and T serum level r=0.47 (p<0.001) together with FAI level r=0.429 (p<0.001). The weight loss was observed in some of the women during the T3 treatment course. In this group the weight and ovarian volume remained stable after six months of not receiving drug treatment. Also in this group the decrease of oestrogen was seen during and over half a year after treatment. The oestrogen level for the group of women whose weight was stable or increased during the treatment, at the beginning, was lower, and during the course increased from 165.1 ± 80 pg/ml to 205.7 ± 99.4 pg/ml. Finally the oestrogen level significantly increased to 288.9 ± 223.5 pg/ml (p<0.03) after six months of no T3 treatment. The difference in ovarian volume between these two groups according to the weight changes was statistically proven p=0.008. The ovarian volume decreased only during the treatment of women with the same or bigger weight, compared with the group with weight loss where the ovarian volume remained smaller after discontinuation of the treatment. Also the T3 impact on androgens after discontinuation of treatment was determined only for women with weight loss.

**Conclusions:** Hirsutism, acne, androgens and ovarian volumes are decreased due to the increase of the triiodothyronine level in blood of women with hyperandrogenism signs. The long-term (6 months) clinical effect of T3 is observed in women with weight loss during treatment.

**A28**

**Vitamin D and thyroid cancer**

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**Thyroid Research 2013, 6(Suppl 2):A28**

**Introduction:** The vitamin D system includes a group of fat-soluble hormones and their respective metabolites. Reduced levels of vitamin D3 are linked with various forms of cancer, including breast, colon, prostate, and skin cancer. The most common form of vitamin D is 25(OH)D3, which is converted to its active metabolite, 1,25(OH)2D3, in the liver and kidneys. The 1,25(OH)2D3 hormone is also synthesized in the placenta during pregnancy. The 1,25(OH)2D3 hormone is a vitamin that regulates the calcium metabolism, supports the immune system, and is essential for bone health.

**Patients and methods:** Vitamin D2 (25(OH)D2, and 1,25(OH)2D3), PTH and calcium serum levels of 50 consecutive patients with epithelial thyroid cancer; 27 cases of papillary cancers (PTC), 16 follicular cancers (FTC), seven cases of anaplastic cancers (ATC), and 4 multinodular nontoxic goiter (MNG) were measured by specific immunoassay. The control group consisted of 26 healthy volunteers.

**Results:** The results revealed significantly lower 1,25(OH)2D3 concentration in the PTC group (22.67 pg/ml ± 8.12; p<0.05), FTC group (16.09 pg/ml ± 6.15; p<0.02) and ATC group (9.48 pg/ml ± 5.18; p<0.02) versus controls. Levels of 1,25(OH)2D3 varied by cancer stage and were also significantly different. A significant decrease in circulating 1,25(OH)2D3 concentration was found in patients with stage I (24.12 pg/ml ± 6.77; p<0.05), stage II (16.93 pg/ml ± 4.55; p<0.05), stage III (12.44 ± 8.98; p<0.02) and in stage IVa (6.18 ± 2.22; p<0.01) of cancer. There were no differences when comparing serum levels of 25(OH)D3, PTH or calcium concentrations among individuals with multinodular goiter, thyroid cancer and age- and sex-matched control volunteers.

**Conclusions:** Our study revealed that impaired vitamin D3 metabolism may play an important role in thyroid follicular cell oncogenesis.

**A29**

**Picture of thyroid cancer in 2012**

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**Thyroid Research 2013, 6(Suppl 2):A29**

Thyroid cancer (TC) is the most common tumour of the endocrine system. In Poland, the standardized incidence rate in 2010 was 6.7 for women, 1.5 for men and it is characterized by a constant increase. Patients with thyroid cancer make up a very heterogeneous group with a differential clinical course - from an indolent to a fast progressing which is the cause of a patient's death. As our studies indicate, in recent years papillary thyroid cancer with a diameter of less than 10 mm dominates among the cases of differentiated thyroid carcinoma (DTC). Such situation requires the verification of the approach to the diagnostic process - moving the diagnostic burden from a palpable examination to an ultrasound method and indicating an outbreak to cytological and molecular examination. The open problem is reducing the diameter of lesions displayed in ultrasonography, which should be subjected to further assessment.

Surgical treatment with a total thyroidectomy with central lymph node dissection is a common procedure. Supplementary treatment with [131I] has a documented value in the cases of advanced TC. Controversy arouses with the usage of [131I] in patients with a lower stadium. The results of ESTIMABL and HiLo studies indicate high effectiveness of ablation with the use of an isotope with an activity of 30mCi, regardless of endogenous or exogenous TSH stimulation. While monitoring the patients with DTC, the main tool is an ultrasound examination of a neck and thyroglobulin (TG) measurement. High hopes are connected with the use of ultrasonotensive TG measurements under endogenous or endogenous TSH stimulation.

Isotope imaging is reserved only for patients with the suspicion of a relapse or metastases. To examinations used in these cases, a PET technique with the use of [124I] or FDG was joined. Due to a very differentiated clinical course of TC, prognostic indicators of worse prognoses requiring more aggressive measures are searched for. High expectations were connected with a BRAF mutation. Many studies have indicated that the BRAF mutation can correlate with a more aggressive clinical course of papillary thyroid cancer and with a worse prognosis. The results of our studies seem not to confirm this opinion - the high mutation frequency (72.5%) in papillary thyroid cancer of very good prognosis with a diameter of less than 10 mm.

Recent years have brought new therapeutic possibilities for the patients with the spread of the disease and with the lack of iodine uptake. A new group of medications are tyrosine kinase inhibitors out of which Vandetanib owns a registration to treat patients with medullary thyroid cancer. The other agents are in the course of clinical studies. The most important problems for the future are: in the field of diagnostics - the development of molecular methods which improve the accuracy of cytological diagnosis; in the field of therapy - the identification of prognostic indicators of a worse disease course and a more aggressive treatment of this group of patients; seeking new medications aiming according to the pathway of oncogenesis.
**Introduction:** The incidence of thyroid cancer (TC) is increasing constantly. A standardized incidence rate in 2010 was 6.7 for women, 1.5 for men. The observed situation seems to be affected by the improvement of thyrological diagnosis and cancer detection.

**Purpose of the study** was to analyze the histological type and the diameter of TC and their variation over a twelve-year observation.

**Material:** The study involved 1158 patients with newly diagnosed TC in the years 2000 to 2012, treated in Holy Cross Cancer Centre in Kielce.

**Methods:** In all cases, the histological types and the diameter of cancer lesions were examined over the years. The statistic analysis of records was based on Chi-square test, Kruskal Wallis test, with the use of Med-Calc 12.4.

**Results:** Histological types of TC in the entire group: papillary - 87.1%; follicular - 3%; oxyphilic - 1.2%; medullary - 4.9%; poorly differentiated - 1.9%; anaplastic - 1.6%; lymphoma - 0.3%. The median of cancer diameter was 19.3 mm in year 2000 and 8.0 mm in year 2012. A statistically significant decrease in diameter of diagnosed cancer was observed over years (p < 0.05).

**Conclusions:** Papillary thyroid carcinoma (PTC) is definitely the most frequent type of TC. 2. The difference in the percentage of different cancer types in the following years was observed due to the increase of the incidence of PTC. 3. The diameter of majority of recently diagnosed cancers is less than 10 mm.

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**A31 Metastasis to the thyroid gland as the first clinical manifestation of lung cancer – case report**

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**Thyroid Research 2013, 6(Suppl 2):A31**

**Introduction:** The incidence of metastatic thyroid tumours range from 2 to 3% of all thyroid cancer cases. Histological and immunohistochemical examination plays a decisive role in metastasis recognition. Metastases to the thyroid gland are rarely identified in cytological diagnostics. Patients who were postoperatively recognized with metastasis to the thyroid gland were diagnosed in cytological results as follicular tumour, cancer or atypical cells. We present a case of a 64-year-old male, who was diagnosed with lung adenocarcinoma based on diagnostics of a nodular change in the thyroid gland.

**Case report:** A 64-year-old man was admitted to our Outpatient Clinic in 2009 with a chief complaint of a palpable nodule on the right side of the neck. Thyroid ultrasonography revealed a 40 mm solid change in the right lobe of the thyroid gland, therefore an ultrasound-guided fine-needle aspiration biopsy (FNAB) of the thyroid nodule followed by a cytological examination was performed. Because there was a suspicion of a follicular tumour a right-side thyroidectomy was done. Histopathological and immunohistochemical examinations suggested a metastasis to the thyroid gland, most probably from a kidney. An abdominal CT scan which also included bases of the lungs revealed cortical cysts in both kidneys and was showing progression of subpleural tumour in the right lung in comparison to the chest CT scan obtained in 2009. The patient was directed to the Department of Lung Diseases where he was diagnosed with adenocarcinoma typos bronchiolevolaris. The patient was treated with chemotherapy. In 2011 metastases to the bones were discovered. In January 2012 ultrasonography revealed: three solid lesions in the left lobe of the thyroid gland, the largest of 15 × 10 mm solid hypoechoigenic lesion on the right side of the neck. FNAB of the largest nodule in the thyroid gland disclosed benign cells while FNAB of the lesion on the right side of the neck - cellulae carcinomatosa. Since March 2012 there was no more further information about the patient.

**Conclusions:** 1. A metastasis to the thyroid gland may be the first clinical manifestation of another organ cancer; 2. a suspicion of a follicular tumour in cytological material does not exclude recognition of a metastasis of another organ cancer to the thyroid gland in postoperative histopathological examination.

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**A32 Diagnosis of follicular thyroid cancer based on the presence of a metastasis in the vertebral column – case report**

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**Thyroid Research 2013, 6(Suppl 2):A32**

**Introduction:** Follicular thyroid cancer, similar to follicular adenoma, usually takes the form of a round, encapsulated tumour. Cytological examination does not allow a firm diagnosis of follicular thyroid cancer to be made. Follicular thyroid cancer may be diagnosed by histopathological examination only after demonstrating the infiltration of the capsule by the tumour and/or vessel invasion. The tumour spreads mainly through the bloodstream causing metastasis to the lungs and bones. We present a case of a 70-year-old woman who has been diagnosed with a follicular thyroid carcinoma based on the presence of a metastasis to the bones.

**Case report:** A 70-year-old woman who had undergone a subtotal thyroidectomy in 2007 because of a nodular goiter, diagnosed as struma nodosa on the histopathological examination, was admitted to the Clinic of Orthopedy and Traumatology with a pathological fracture of the first lumbar vertebra (10.2012). The spine MRI scan revealed a 30 mm pathological mass in the L1 vertebral body; therefore a removal of the L1 vertebral body was performed, followed by a histopathological examination. The result revealed metastasis carcinomatosa, carcinoma folliculae glandulae thyroideae. The patient was directed to the Department of Surgery, where a total thyroidectomy with the removal of lymph nodes was performed (12.2012). Based on the histopathological result, the patient was diagnosed with struma macro et microfolllicularis and reactive lymph nodes. The histopathological result of the material from the corpus vertebrae was verified, and the previous diagnosis of follicular cancer was confirmed. Accordingly, specimens from the thyroid gland obtained during the first thyroidectomy in 2007 were verified, yielding the following result: encapsulated follicular thyroid cancer with infiltration of the capsule; infiltration of the vessels was not demonstrated - minimally invasive follicular carcinoma. 18F-Fluoride PET/CT was performed which revealed metastatic metabolically active lesion in L1 vertebral body. The patient will be treated with radioactive iodine.

**Conclusions:** Diagnosis of follicular thyroid cancer, especially its minimally invasive forms, may pose difficulty even when based on post-surgical histopathological specimens.

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**A33 The assessment of side effects of tyrosine kinase inhibitors (TKI) applied in patients with advanced thyroid cancer (TC) - one centre experience**

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**Thyroid Research 2013, 6(Suppl 2):A33**

TKI constitute a new group of drugs evaluated in TC patients. The efficacy of some of them in prolongation of progression free survival has been recently documented. However, possible side effects may affect the quality of life as well as limit their clinical use. Only drugs which were known to inhibit VEGFR were considered. In the study adverse effects were evaluated in patients treated in our centre within the prospective clinical trials phase II and III. The aim of the study was to analyze the frequency and severity of side effects related to TKI in TC patients. Thus, we retrospectively re-evaluated side effects on the basis of Common
Table 1(abstact A33) Frequency and severity of the most common treatment-related side effects.

<table>
<thead>
<tr>
<th></th>
<th>G1 / G2 / G3</th>
<th>Total</th>
<th>Treatable</th>
<th>Dose reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin reactions</td>
<td>16 / 8 / 2</td>
<td>26 (70.3%)</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>3 / 7 / 17</td>
<td>27 (73.0%)</td>
<td>yes</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7 / 9 / 4</td>
<td>20 (54.1%)</td>
<td>yes</td>
<td>4</td>
</tr>
<tr>
<td>Weight loss</td>
<td>4 / 13 / 3</td>
<td>20 (54.1%)</td>
<td>yes</td>
<td>5</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>15 / 1 / -</td>
<td>16 (43.2%)</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

For years it was regarded that testis was unresponsive organ to thyroid hormone (TH). Recent studies have changed this view by demonstration that triiodothyronine (T3), beside follicle stimulating hormone (FSH) from pituitary, plays an essential role in testes maturation.

Experimental hypothyroidism during sexual development: Testes size and number of spermatzoa in adulthood are determined by postnatal/ pubertal proliferation of seminal tubule somatic cell constituents, the Sertoli cells. Cessation of proliferation of Sertoli cells during early development occurs concomitantly with formation of their terminaly differentiated population. Transient experimental hypothyroidism in newborn rats evokes prolongation of Sertoli cell proliferation period and retards their maturation. In adulthood it results in increased Sertoli cell number, doubled final testis size in comparison to normal values, and animals produce more spermatzoa. However, prolonged hypothyroidism depresses testicular development and induces germ cell degeneration.

The influence of T3 on seminiferous tubule development: Expression of TH receptor (TR) in rat’s Sertoli cells evolves during proliferative/ maturation phase of Sertoli cells and is minimal thereafter. We have shown that T3 exerted a biphasic effect on Sertoli cell number in rats. Stimulatory influence was present before initiation of seminal tubule maturation, whereas inhibitory one appeared during initiation of pubertal development. Simultaneously, before pubertal development T3 evoked differentiation of the earliest precursors of spermatozoaa, gonocytes, resulting in precocious initiation of spermatogenesis. In turn, prolonged exposition to T3 with high serum level of the hormone normalized initiation of spermatogenesis with increased cell apoptosis, together with the signs of hyperthyrodisism.

Unexpected interaction: We have shown that both T3 and FSH when given alone stimulated, whereas given in combination inhibited testes maturation. It has been shown that T3 caused disturbance of the cell cycle by controlling cyclin-dependent kinase inhibitors. This may partially explain reduced ability of Sertoli and germ cells to proliferate after combined administration of T3 and FSH.

Clinical correlates: Hypothyroidism initiated in infancy may occur in association with macroorchidism without virilization, with impaired spermatogenesis in adulthood. When adequately treated boys with congenital hypothyroidism progress through puberty normally. Among 3369 men aged 40-79 years overt hypothyroidism was not frequent (0.2-0.3%) but produced erectile dysfunction in 60% of cases with no affection of sex hormone levels. Both α and β nuclear TR have been described in human corpora cavernosa cells. Hyperthyroidism impairs penile nitric oxide synthesis via direct effect and treatment of hyperthyroidism restores erectile functioning.

A36

Rare thyroid diseases
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Thyroid Research 2013, 6(Suppl 2):A36

In general, rare thyroid diseases can be divided into neoplastic and non-neoplastic.

Neoplastic rare thyroid diseases include the following:
1. primary thyroid lymphoma (1-5% all malignant neoplasms of the thyroid; 21 000 000 per year);
2. metastases to the thyroid gland (2-3% malignant thyroid neoplasms; 0.5-2.8% in autopsy) from various primary cancers such as breast carcinoma, renal carcinoma, colon carcinoma, melanoma and others;
3. others (ie: sarcoma).
On the contrary, non-neoplastic rare thyroid diseases include the following:
1. congenital defects of thyroxine binding proteins, particularly partial and
total congenital TBG deficiency (1:5 000), congenital TBG excess (1:25 000)
(both caused by TBG gene mutations) and familial dysalbuminemic hyper-
thyroxinemia (1:25 000, more frequent in some populations, such as the
Spanish and Portuguese);
2. congenital resistance to thyroid hormones (with frequency about 1:40
000) as a result of THR8 gene mutations;
3. rare cases of congenital thyroid hormones biosynthesis defects, for
instance: Pendred syndrome (with frequency of 7.5-10:100 000) resulting
from PDS gene mutations, total iodide organification defects (1:46 000; TPO
and THOX2 gene mutations);
4. congenital defects of the thyroid gland development, which constitute
about 85-90% causes of primary congenital hypothyroidism. About 2% of
these are associated with the presence of other nonthyroid congenital
anomalies and are caused by genetic mutations: for example, in the
PAK, TTF1, TTF2, GNAS 1 genes;
5. congenital nonautoimmune hyperthyroidism as a result of TSH receptor
gene mutation (TSHR) (until now 55 various mutations and over a dozen
cases of de novo germlinal mutations have been described);
6. hyperthyroidism associated with McCune-Albright syndrome (in about
30% of patients with this syndrome; McCune-Albright syndrome frequency
of occurrence is estimated - 1:10 000-1:1 000 000; background - mutation in
the GNAS 1 gene);
7. an association of the thyroid autonomous nodule and Graves’ disease
(4,1%), and the thyroid cancer and Graves’ disease (1.1%-6.5%).

The latest data on the etiopathogenesis of rare thyroid diseases, diagnostic
criteria and possibilities for their treatment will be discussed. In addition, information obtained from PUBMED database concerning patients with rare
thyroid diseases detected in the Polish population, particularly the data on
molecular-genetic results, will be presented.

A38

The correct interpretation of thyroid FNA cytological result by
the endocrinologist as a basis for further optimal diagnostics
and treatment
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Adopted by the Polish Society of Endocrinology and the Polish Thyroid
Association American system of the classification of FNAB cytological smears -
the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)
determines exactly how to run diagnostics and therapy for each category of
smears. Cytopathologist establishing a diagnosis should provide it in such a
way as to include a detailed description of both the observed specimen
(existing types of cells, their abundance (their number) and the spatial
arrangements (layout) which they form, as well as other components of the
smear, such as, e.g. colloid protein masses) and a diagnostic conclusion which
assigns a smear to one of six (6) categories TBSRTC. In order to avoid
unintentional mistake during the process of assigning in question, the
endocrinologists should have a basic idea of what kind cellular and/or
acellular components determine and prejudge the qualification of cytological
smear to a specific TBSRTC category. It should be noted that having this
skill is not to control the description of cytological result as morphological
diagnostics (within the meaning of the direct microscopic evaluation of
slides) is beyond the reach of an endocrinologist and other doctors who
are not cytopathologists, just check whether there is compliance of the
diagnostic conclusion and morphological description of the smear, because
it is TBSRTC category which decisively determines further medical
management. As shown by us in the proposed algorithm, the assignment of
the specimen to each category, together with the, so-called, US risk pattern
(which is defined in a 3-stage as a pattern of high, intermediate or low risk)
are decisive for the recommendation of surgical treatment or abandonment
of such treatment and further follow up; they also are decisive as regards the
frequency of repeat US and FNAB cytology. Thus, the essence of the present
lecture is to familiarize endocrinologists with the significance of individual
components of the smear, as described in cytology, in determining the
appropriate TBSRTC category. In practice, the most important issue is to
properly differentiate categories II, III and IV, because there is little doubt as
regards treatment of patients with other smear categories (I, V and VI).
Therefore, it is necessary to remember that the normotopic thyroid follicular
cells (fcf), both dispersed and arranged in large and/or medium-sized spatial
patches and groups, and sometimes nests, are characteristic rather for benign
lesions. On the other hand, small spatial layouts, especially arrangements of
rosettes type are characteristic for category IV (follicular neoplasm or
suspicious for a follicular neoplasm). It should be added, however, that large
spatial layouts may also be present in papillary thyroid carcinoma; undoubted
high in case of detection of this cancer is, however, characteristic appearance
of cells and their typical cytological features. Cytological smears obtained
from benign lesions may contain cells with different abundance, and also a
variety of other cells can be the smear components, such as, e.g. cells typical
for inflammatory processes (lymphocytes, neutrophils, multi- and mono-
nucleated macrophages), anisocytosis is frequently observed (sometimes
anisocaryosis), and - which is particularly characteristic - considerable

A37

Odd thyroid function tests results: interference versus non-compliance
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Despite the advent modern immunoassays, particularly with regards to TSH
measurements, clinicians still encounter seemingly inexplicable results of
thyroid function tests, for instance raised concentrations of free hormones
(free T4 and/or free T3) in the setting of high, or at least not suppressed TSH
concentrations. Though cases of TSH-oma or thyroid hormone resistance do
exist, they are in fact rare, while some

quantities of colloid are present in the smear. In contrast to the above components, “follicular neoplasm” in cytological smear has no colloid at all or its trace amount, monomorphic tfc occurring usually in large numbers and arranged in small layouts, which characteristically take the form of the, so-called, rosette. Anisocytosis generally does not occur, cell types other than monomorphic tfc and larger spatial arrangements are very rare. In case of smears collected from oncocytic lesions, the assignment to the category IV is determined by the percentage of oncocyes in the smear (above 75%). Oncocytic cells should have described the presence of nucleoli, anisocytosis may occur in this case and spatial arrangements can be of any type. Finally, it is noted that smears of category III, called by some authors as “a category of exclusion”, contain both components characteristic for category II and may also include elements of morphological smears of category IV, but in a such proportion that would not allow to categorically qualify them as benign lesions or as “a suspicion of follicular neoplasm”.

A39 Ability of proper application of ultrasound (US) and a fine needle aspiration biopsy (FNAB) in the management of thyroid nodules/focal lesions in patients with coexisting additional worrying clinical signs and symptoms Andrzej Lewiński1, Anna Polakiewicz2, Bogusław Skowron2, Włodzimierz Lisiewicz1
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Thyroid Research 2013, 6(Suppl 2):A39

Application of the main principle - that therapeutic decisions should be taken only on the basis of FNAB result, while US is used to assess qualification of patients for FNAB and to decide on the selection of lesions that should be submitted to FNAB - may be associated with the risk of taking the wrong decision, based on erroneous assumptions. We must remember - especially in the era of dominance of various recommendations and guidelines, pointing to the need for thyroid US and FNAB diagnostics in every single patient with thyroid tumour/lesion, the principles of common sense in thought and deed. It is our patient and his/her future is the most important to us, and not getting the results, especially when the clinical context indicates clearly the need for urgent surgery. Repeat testing or performance of time-consuming diagnostic procedures - is a mistake. The results will not - in a majority of circumstances - alter therapeutic management but can only delay introduction of effective treatment.

We cannot forget that the patient has the right to demand surgical treatment and a doctor cannot refuse to perform surgery in all cases when the presence of thyroid lesion is confirmed - regardless of US risk patterns and FNAB results and of initial diagnosis. Despite technological development and the use of modern diagnostic equipment, basing for the time being, the diagnoses on preoperative tests, e.g. on the assignment to each TSRTC category - does not provide 100% certainty of confirmation (positive verification) in postoperative histopathological examination.

We are aware of the fact that our proposals of optimal management, like many others developed previously in order to assess the nature of thyroid lesions, do not solve all the possible clinical problems. However, it is important to take into account the most essential features visualised in US examination which are related to an increased risk of malignancy and by considering them in combination with the results of cytological assessment.

We urge that stress be laid on the importance of other potentially compounding clinical signs and symptoms and believe that our scheme of management with thyroid nodules/US focal lesions will fulfill its role in everyday medical practice and will facilitate to make the right diagnostic-therapeutic decisions.

A40 Effects of radioiodine administration on serum concentrations of matrix metalloproteinases, adiponectin and thrombospondin Andrzej Lewiński1, Anna Brona2, Diana Jędrzejuk2, Anna Bohdanowicz-Pawłak2, Krzysztof C Lewandowski3, Malgorzata Bieńkiewicz1, Andrzej Milewicz3
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Introduction: In order to assess long-term safety of radioactive iodine administration in treatment of thyrotoxicosis, we assessed concentrations of selected markers of risk cardiovascular disease, i.e. matrix metalloproteinase 2 (MMP-2), its main inhibitor TIMP-2, matrix metalloproteinase 9 (MMP-9), its main inhibitor TIMP-1, as well concentrations of anti-inflammatory adiponectin and pro-inflammatory thrombospondin.

Material and methods: The study involved 23 patients (3 males) age 53 ± 12 (mean ± SD) years treated with radioiodine for thyrotoxicosis. Serum concentrations TSH, FT4, FT3, MMP-2, MMP-9, TIMP-1, TIMP-2, adiponectin and thrombospondin were measured just before radioiodine administration (visit 1), and subsequently, after 7 days (visit 2), 3 months (visit 3), six to eight months (visit 4) and 15-18 months after radioiodine administration (visit 5).

Results: There were no acute changes in serum concentrations of MMP-2, MMP-9, TIMP-1 and TIMP-2 adiponectin and thrombospondin (visit 1 versus visit 2). Subsequently, however, there was no change in serum MMP-9 or thrombospondin, but an increase in MMP-2 (from 393 ± 196 mg/ml to 774 ± 424 ng/ml), TIMP-1 (from 177 ± 76 mg/ml to 296 ± 118 ng/ml), TIMP-2 (from 136 ± 44 ng/ml to 168 ± 41 ng/ml), and adiponectin (from 16442 ± 774 ± 424 ng/ml to 23518 ± 9840 ng/ml). TIMP-1 ratio, but there was a significant increase in MMP-9/TIMP-1 ratio (p < 0.05), suggestive of possible decrease in concentrations of free MMP-9. Further analysis, however, revealed no significant change in MMP-2/TIMP-2 ratio.

Conclusions: Our data reveal a significant and sustained increase in serum adiponectin as well as possible decrease of concentration of free MMP-9 after radioiodine administration. This might indicate overall safety of radioiodine treatment of thyrotoxicosis in terms of the risks of cardiovascular disease.

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A41 Natural history of subclinical hypothyroidism in children and adolescents Ewa Matecka-Tendera Departement of Pediatrics, Pediatric Endocrinology and Diabetes, Medical University of Silesia, Katowice, Poland
Thyroid Research 2013, 6(Suppl 2):A41

Introduction: Diagnosis of subclinical hypothyroidism (SH) is based on interpretation of biochemical tests in the absence of the evident clinical symptoms. Mildly elevated TSH with normal fT4 are common in adults and the prevalence of this finding is reported to be 1-10% of general population, being higher in the elderly. In pediatric population its prevalence is lower than 2%. Moreover in about 60% of subjects the natural course of SH is a reversal of the elevated TSH to normal values. Only 3% of them progress to overt hypothyroidism with TSH values above 10 mIU/l. The risk of progression is higher in patients with elevated anti-thyroid antibodies and higher degree of hypoechogenicity at thyroid ultrasound. Increased prevalence of SH is described in obese and overweight subjects, children with Down’s syndrome, with diabetes type 1 and in girls with Turner’s syndrome. Studies regarding the natural history of SH and its consequences in children are scarce and their conclusions are controversial. Meta-analysis of 39 potentially relevant articles showed that SH in children seems to be a remitting process with a low risk of progression toward overt hypothyroidism regardless of the LT4 treatment. There was also no clear evidence of the beneficial effect of LT4 treatment on psychological and physical development. Replacement therapy did not seem to be justified in children with SH and TSH values between 5 -10 mUI/l, no goiter and physical development. Replacement therapy did not seem to be justified in children with SH and TSH values between 5 -10 mUI/l, no goiter and negative anti-thyroid antibodies. Therefore decision regarding the treatment of the young patient with elevated TSH but normal fT4 value continues to be controversial.

A42 The flow of genetic information – the role of thyroid hormones in the regulation of gene expression Alicja Nauman Department of Biochemistry and Molecular Biology, The Centre of Postgraduate Medical Education, Warsaw, Poland
Thyroid Research 2013, 6(Suppl 2):A42
Human genome encodes about 25 000 protein coding genes, among which some are constitutively expressed in all cells of the organism while the others are activated in response to specific extra- and intracellular signaling. Gene expression is regulated on multiple levels in a spatiotemporal manner. These levels include: genome, which contains all cellular DNA sequences (nuclear and extranuclear - mitochondrial), transcriptome, which contains all sequences of RNA synthesized in the cell (including long: pre-mRNA, mRNA, ncRNA, and short: snRNA, miRNA, and piRNA), proteome, which contains all proteins synthesized in the cell, metabolome, which includes all metabolic pathways in the organism, localizome, which includes all possible subcellular localizations of macromolecules in the organism, phenome, which is defined as a set of all phenotypes of the organism and establishes enabling of the real effects of particular genes and external environment on the phenotypic variability in humans.

Thyroid hormones, 3,5,3'-triiodothyronine (thyroxine) and 3,5,3'-triiodothyronine (T3) participate in the regulation of key cellular processes, including proliferation, differentiation, apoptosis and metabolism. Together with other factors they initiate variable cellular processes, starting from activation of the flow and amplification of genetic information (via DNA-RNA-protein), and ending with elicitation of specific phenotypic traits of the cell. The action of thyroid hormone, is mediated mainly by interactions with nuclear receptors (THR), which belong to the superfamily of ligand dependent nuclear transcription factors. TR bind to specific sequences of response to thyroid hormone (TRE) in promoters of target genes and regulate their expression. Apart from classic, genomic mechanism of action, THR can also act via non-genomic mechanism in which regulation of target genes is mediated by interactions with other receptors – located in plasma membrane or cytoplasm. THR are encoded by two genes, THRA (ERBA) and THR8. These genes, located in chromosome regions 17q21 (THRA) and 3p21-3p24 (THR8), encode for three functional receptors: TR1, TR11, and TR12, and the receptor TR2 which does not bind T3 and acts as an antagonist of the other receptors. TR1 and TR11 are expressed in all tissue types and their expression and ratios at which they are expressed depend on tissue type and developmental stage. In most tissues and organs only one of the receptors is responsible for T3 mediated regulation of genes. For instance, TR1 is the main receptor acting in bones, TR1 acts in liver and kidney, while TR2 acts in pituitary and hypothalamus where it regulates HPT axis. In the genomic mechanism THR regulate expression of target genes via binding to the sequences of response to thyroid hormone (TRE) located in their promoters. Typical TRE consists of two repeats of AGGTCA/ACA sequence. The presence of so called positive TRE results in induction of gene expression after binding of TR and T3, while binding of THR without T3 results in inhibition of gene expression. Thus, deficiency of T3 in the cell will result in inhibition of expression of a given gene, for instance GH or a gene coding for iodothyronine deiodinase type 1. The genes with negative TRE are regulated in an opposite manner: binding of T3 to the receptor results in inhibition of gene expression. The negative regulation of gene expression via T3 enables, among others, the mechanism of feedback regulation of expression of THR and TSH via T3.

In consequence, all disturbances of thyroid hormone signaling pathways can directly result in deregulation of homeostasis of the organism.

**A43**

**Etiopathogenesis of Graves-Basedow disease; where we are and where we are going**

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**Thyroid Research 2013, 6(Suppl 2):A43**

Graves-Basedow disease (GBD) since late fifties has been considered to be autoimmune thyroid disorder where the presence of thyroid stimulating antibodies (TSAb) may lead to hyperthyroidism, thyroid orbitopathy and thyroid dermopathy. During last years it was generally accepted that development of Graves-Basedow disease is dependent on the presence of two or three groups of factors - genetic and environmental or genetic, environmental and endogenous. Familial clustering of GBD, familial presence of thyroid autoantibodies and high concordance in the incidence and clinical course of the disease in monozygotic siblings all suggested that several genes decided about susceptibility to this disorder and its phenotypes. On the other hand environmental agents and endogenous factors served as triggers important to the development of the disease, its clinical course and response to given therapy. It was believed that finally, development of GBD (and other autoimmune disorders) is a consequence of lack of balance between the formation of self reactive T cells and central and peripheral tolerance. As a result thyroid was infiltrated by self reactive T cells that in turn affected B cells and led to the production of thyroid stimulating antibodies.

Most recently etiopathogenesis of GBD became further complicated by both clinical and molecular findings. First, GBD can be clinically presented as a hypothryroidism depending on the switch of TSAb production to thyroperoxidase blocking antibody (TBAb) production as well as vice versa. Some findings suggest that in prone clinically hyperthyroid patient the administration of methimazole can provoke switch off of TSAb generation and start of TBAb followed by block of thyroid hormones biosynthesis and quite rapid morphological damage of thyroid cells. It is a pity that in other hypothyroid patient administration of thyroxine can switch on the generation of TSAb and switch off the production of TBAb. Second, it is more and more obvious that autoimmune thyroid disorders and differentiated thyroid cancer (DTC) especially of papillary type (PTC) share some genetic factors (RET/PTC1) and environmental and epidemiological features. In addition presence of GBD disease in patients with DTC leads to increased mortality of cancer patients. Third, microarray DNA analysis of thyroid from GBD patients with severe coarse of the disease led to the identification of seven additional genes either overexpressed or underexpressed that may be responsible for high level of TSH-R Abs, large goiter size and high free T3/free T4 ratio, features characteristic for patients that poorly respond to anti-thyroid drug therapy. In addition to these clinical observations, the pathogenesis of GBD during the last two-three years was strongly affected by studies suggesting that non sufficient peripheral tolerance was a key to autoimmunity in general, including mechanisms leading to development of Graves-Basedow disease. In a way we returned to Volpe hypothesis developed in the 70-ies of the previous century that pointed out the role of T-suppressor cells. At present the name suppressor cells was postponed and we know that control of self reactive T cells is a function of T regulatory cells (Tregs). It has been proven that block of activation of Tregs both in experimental animals and humans led to the development of generalized fatal autoimmunity. The mechanism of appropriate Tregs activation concerning first signal (MHC-TCR) and especially second costimulatory signals (CD28-B7-1(CD80) or CD86-B7-2 (CD86)) will be presented and their role for the thyroid autoimmunity discussed. The progress in our knowledge concerning autoimmunity as a whole and GBD as a thyroid autoimmune disorder clearly shows that pathogenesis of this disorder is more complex than previously expected and that personalized approach to given patient based on clinical and molecular findings is more important than the hope that single finding (light in corridor) brings a positive solution for all patients with Graves-Basedow disease.

**A44**

**Subclinical hypothyroidism in population of aging Polish women and men over 65s old and cardiovascular risk factor, endogenous vitamin D levels and its gene receptor polymorphisms – PoSenior Study**

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**Thyroid Research 2013, 6(Suppl 2):A44**

Clinical consequences of subclinical hypothyroidism (SH) are still controversial, especially in aging persons. Recently the pleiotropic action of vit. D, also the influence on immune system, was shown and discussed. On the basis of randomly selected 723 women and men (382 men) over 65 yrs old from PoSenior Study we developed the frequency of SH in Polish aging population, and we compared the metabolic profile of cases with SH in comparison to healthy controls according to cardiovascular risk factors (CRF). The serum vit. D and its receptor (VDR) gene polymorphisms Fok-I and Bsm-I in both these groups were estimated. The elevated serum TSH level (over 4.5 mU/ml) with FT4 range: 10.3-25.7 pmol/l and elevated anti-TPO (over 200.0 IU/ml) this disorder affect 20.6% of men and 4.4% of men the CRF profile: waist circumference, BMI, serum total cholesterol, HDL and LDL cholesterol,
triglycerides, fasting glucose, insulin and HOMA were comparable in both groups. Also the endogenous vit. D serum levels were comparable between the group of patients with elevated anti-TPO and elevated or decreased TSH in comparison to controls with euthyroidism. However the analysis of Fok-I and Bsm-I polymorphisms of VDR and thyroid immune status showed higher frequency of recessive genotype bb in person with elevated TSH and anti-TPO (p=0.0334). Conclusions: aging people with subclinical hypothyroidism don’t present higher risk for CVD. The relation between vit. D and its receptor gene polymorphisms and thyroid immune status needs further study.

A45
Non-autoimmune hyperthyroidism caused by thyroid-stimulating hormone receptor germline mutations - 2012 European Thyroid Association Guidelines

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All cases of familial thyrotoxicosis with absence of evidence of autoimmune and all children with persistent isolated neonatal hypothyroidism should be evaluated for familial non-autoimmune autonomous dominant hyperthyroidism (FNAAH) or persistent sporadic non-autoimmune hyperthyroidism (PSNAH). First, all index patients should be analysed for the presence/absence of a thyroid-stimulating hormone (TSH) receptor (TSHR) germline mutation, and if they display a TSHR germline mutation, all other family members including asymptomatic and euthyroid family members should also be analysed. A functional characterization of all new TSHR mutations is necessary. Appropriate ablative therapy is recommended to avoid relapses of hyperthyroidism and its consequences, especially in children. Therefore, in children the diagnosis of FNAAH or PSNAH needs to be established as early as possible in the presence of the clinical hallmarks of the disease.

Reference:

A46
Aberrent expression of follicle stimulating hormone receptors (FSHR) in thyroid neoplasia

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Introduction: In normal conditions FSHR are expressed in the ovary and the testis. It is well known that they can also be expressed in gonadal tumours. However, recently we have found FSHR immunopositivity in tumoral tissues of other endocrine tumours, namely pituitary adenomas, adrenal tumours and neuroendocrine gut and lung tumours (carcinoids). The aim of this study was to see whether the same phenomenon occurs in thyroid neoplasia.

Material and methods: Twenty three samples of surgically excised thyroids were examined. FSHR immunostaining was performed on paraffin sections using the rabbit anti-human FSHR polyclonal antibody raised against 1-190 amino acid sequence from the human FSH-R (sc-13935, Santa Cruz).

Results: Normal thyroid follicles do not show the immunopositivity for FSHR. The same concerns the majority of benign lesions, diagnosed as hyperplasia nodularis or follicular adenoma. However, the FSHR immunostaining is partially positive in the minority of follicles. In thyroid cancers (13 papillary cancers and one case of anaplastic thyroid cancer) the majority of tumoral cells exhibit the positive FSHR immunostaining. In about one third (9/23) samples FSHR immunoreactivity can be observed also in the endothelia of the intrathyroidal blood vessels. This immunopositivity was more frequent in the samples of thyroid cancers (6/14) than in the benign lesions (3/9).

Conclusions: The positive FSHR immunostaining is present in thyroid cancers, and, to a lesser degree, in benign thyroid lesions but not in normal thyroid tissues. It suggests that aberrant expression of FSHR is connected with thyroid neoplasia.

A47
Permanent and transient congenital hypothyroidism in full-term and preterm born infants

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Congenital hypothyroidism (CH) is one of the most common endocrine disorders in the infant population. It is also one of the most important causes of foreseeable brain damage and severe mental impairment. Current views on CH pathogenesis, screening schema and treatment standards have been presented. Also outlined have been the newest reports on the impact on CH epidemiology and classification generated by the introduction of low TSH cut-off (6 mU/l). The use of low TSH cut-off allowed the detection of an unsuspected number of children with neonatal hypothyroidism, evolving in mild permanent thyroid dysfunction later in life. Constantly growing, especially in developed countries, number of preterm infants is a separate group of children, mainly with transient fluctuations in thyroid function. Thyroid gland function develops and matures during fetal life, with production of serum thyroxine (T4) beginning around 12 weeks gestation and increasing to term. Infants born prior to term have lower cord serum T4 concentrations which correlate with gestational age or/and birth weight. This is partially a result of lower thyroxine-binding globulin (TBG) concentrations. The cord serum free thyroxine (FT4) concentrations also correlate with gestational age, but they are not proportionately as low as cord T4 concentration. Preterm infants have a postnatal thyrotropin (TSH) surge and rise in serum T4 and triiodothyronine (T3), which is qualitatively similar to, but quantitatively smaller than term infants. In contrast to term infants, preterm infants often experience a fall in serum T4 and T3 in the first week of life to below birth levels. This drop appears to be the result of many factors, including nutritional problems and decreased hepatic TBG production, immaturity of hypothalamic-pituitary control of the thyroid gland, immaturity of the thyroid gland itself, and increased tissue utilization of T4. Several studies have correlated different measures of morbidity and mortality in the preterm infant with lower serum T4 concentrations. This has led to speculation that T4 treatment might be beneficial in improving these complications of prematurity, in particular the neurological outcome. Latest studies do not confirm that hypothyroidism in preterm infants is for them harmless. Many factors, however, influence mental development of those children. Thus, treatment strategies, including thyroid hormone substitution, should consider both the etiology of the hypothyroidism and the impact of aforementioned factors. There is no “hard evidence” to support introducing thyroid hormone supplementation in preterm infants as a rule.

A48
Molecular mechanism of thyroid hormone action in carcinogenesis

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Thyroid hormones, 3,5,3’-triiodothyronine (thyroxine) and 3,5,3’-tetraiodothyronine (T3) contribute to the regulation of key cellular
processes, including proliferation, differentiation, apoptosis and metabolism. Thus, deregulation of thyroid hormone pathway can result in serious disturbances of cellular physiology such as those observed in tumoral transformation. The intra- and extracellular concentrations of thyroid hormones (TH) are regulated by three types of iodothyronine deiodinases (DIO1, DIO2, and DIO3). These enzymes catalyze two types of reactions: deiodination in position 5’ of iodothyronines (catalyzed by DIO1 and DIO2), resulting in activation of thyroid hormones, and deiodination in position 5 of iodothyronines (catalyzed by DIO1 and DIO3), which results in inactivation of thyroid hormones. Changes in expression and activity of iodothyronine deiodinases result in modulations of thyroid hormone concentrations and thus influence cellular processes. The actions of thyroid hormone are mediated by thyroid hormone receptors (TRs) which influence intracellular processes via modulation of expression of target genes. In this process, known as genomic mechanism of TH action, thyroid hormone receptors act as transcription factors whose activity is modulated by the presence of ligand, T3. TH can also influence cellular processes via non-genomic pathways in which TH modulate activity of membrane or intracellular receptors and activate different intracellular signaling pathways, involving protein kinases, for instance PI3K, and Akt/PKB.

In the process of carcinogenesis the signaling pathway of thyroid hormones is disturbed. This is illustrated by observations of mutations and deregulated expression of thyroid hormone receptors, altered expression and activity of iodothyronine deiodinases as well as decreased intracellular concentrations of T3 in tumours. Whether these changes play a causative role in the process of carcinogenesis is currently a matter of discussion. In vitro studies in cancer cell lines and mouse models showed that increased expression of DIO3 together with enhanced proteasomal degradation of DIO2 in basal cell carcinoma stimulates tumoral proliferation. Moreover, thyroid hormone receptor beta-1 was shown to act as a powerful suppressor of tumour invasiveness and metastasis in mouse models of breast cancer and hepatocarcinoma. These studies suggest that local tissue hypothyroidism may rather support tumoral transformation and even initiate enhanced cancerous proliferation. In contrast, studies on the effects of systemic hypothyroidism and cancer risk show opposite or conflicting results. For instance, hypothyroidism was associated with increased risk of hematopoietic malignant, and cancers of lung and prostate. In case of breast cancer, different studies reported that hypothyroidism was linked to reduced risk of the disease in humans while when studied in mice, hypothyroidism reduced tumour growth but enhanced metastasis. Finally, studies performed on cell line and mouse xenografts of thyroid and kidney cancers showed that inhibition of integrin-mediated thyroid hormone signaling can effectively result in inhibition of tumour growth. All these studies show that the role of thyroid hormones in carcinogenic process is complex and presumably depends on type of cancer and extra- or intracellular effects of TH signaling. The results showing benefits from the use of TH pathway genes in cancer treatment and diagnosis suggest that further and more in depth studies are needed.

A50

Imaging techniques in diagnostics, differentiation and monitoring of different types of thyroiditis

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Thyroid imaging is nowadays an essential part of thyroid disease evaluation. Different types of thyroiditis may share some parallel clinical and biochemical features, what might lead to diagnostic difficulties, while thyroid imaging may aid in establishing proper diagnosis. In the lecture, usefulness of several imaging techniques (conventional ultrasonography, Doppler examination, sonoelastography, scintigraphy and other) in diagnostics, differentiation and monitoring of different types of thyroiditis are presented according to up-to-date guidelines. The most commonly applied modality in evaluation of thyroiditis is conventional ultrasonography. Chronic autoimmune thyroiditis typically presents with decreased, heterogeneous echogenicity of the whole gland, signs of fibrosis and decreased blood flow in Doppler examination. More often than in other types, in silent thyroiditis the most hypechoegenic area is the anterior part of the thyroid. Subacute thyroiditis presents with an enlargement of the gland, especially in depth. The ill-defined hypechoegenic regions of thyroid parenchyma of different size and shape, change smoothly into those of normal echogenicity. Most commonly, one lobe is involved. Anti-inflammatory treatment results in remission with no residual changes. Initially, acute thyroiditis resembles subacute type. However, gradual resolution can be observed with formation of abscesses with dense content. On ultrasound picture, Riedel’s thyroiditis presents as a hypechoegenic region with ill-defined margins and marked fibrosis. Signs of trachea compression and displacement may be seen. Moreover, features of post-radioiodine and most common drug-induced thyroiditis are presented. These typically present with heterogeneous echogenicity and signs of fibrosis, while may differ according to blood flow picture. Lately, sonoelastography appeared to be useful in evaluation of various types of thyroiditis. Acute and subacute thyroiditis were found to be associated with decreased elasticity of thyroid tissue, which is restored to normal with treatment. Chronic thyroiditis is associated with a minimally decreased elasticity of thyroid parenchyma, which remains unchanged.

A49

Changes of the hypothalamic-pituitary-thyroid axis in aging

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Study of healthy aging of the hypothalamic-pituitary-thyroid axis is difficult, since aging is accompanied by the increased frequency of various thyroid diseases and of extrathyroidal disease, as well as by the increased intake of medicines modulating the function of this axis. Nevertheless, researchers managed to determine that in the paraventricular nucleus of age-related changes in the number of neurons synthesizing TRH are observed. In the pituitary, the number of thyrotrophs also increases, and the cells are commonly hypothyphrophic. In the thyroid, epithelial cells are smaller, the amount of colloid decreases, and the whole gland becomes smaller and denser. It is still not known how aging affects secretion of TRH. Healthy aging is accompanied by the slight increase of concentration of TSH (highest concentrations of this hormone were detected in centenarians), and the night peak of its secretion is lower. In healthy aging humans, concentrations of T3 and of T3 decrease, concentration of T3 increases, and concentrations of T4 and of T4 remain stable. According to the current theory of aging, the direct cause of aging is the accumulation of stochastic damage to DNA, and to proteins and lipids. The most important (albeit not only) damaging factors are the reactive oxygen species (ROS), by-products of the cellular metabolism, especially of the respiratory chain in mitochondria. Most likely, the function of the hypothalamic-pituitary-thyroid axis influences the rate of aging, since the function of the respiratory chain and, therefore, the rate of production of ROS, remain under the control of T3. Consequently, slowdown of the T3-dependent metabolism might promote longer life through slower production of ROS. This hypothesis is supported by the above described epidemiological observations showing that healthy aging is accompanied by the decreased activity of the hypothalamic-pituitary-thyroid axis and by the fact that in long-lived humans (whole 85+ group and, especially, centenarians) the activity of this axis is lowest compared to younger age groups. Because of this, subclinical hypothyroidism in 65 years old or older humans might be, in fact, a manifestation of healthy aging of the thyroid gland, and this is why in these individuals this condition should not be “automatically” treated. Instead, the patient should be regularly examined (if we do not want to omit the overt hypothyroidism), and decision to treat should be taken individually, based on the biological age, the clinical state, the presence of other diseases, the results of biochemical tests, etc.

The percentage of aged humans with anti-TPO and anti-TG auto-antibodies is much higher compared to young individuals, but above the age of 80 the percentage of such individuals decreases. Aging is accompanied by the increased frequency of hypothyroidism, hyperthyroidism, and of thyroid cancers. Their symptoms are commonly untypical and, because of this, might be confused with signs of aging per se or with symptoms of other diseases. Nevertheless, all these diseases should be adequately diagnosed and treated.
A51 The role of the transcription factor - Prosper homeobox 1 (Prox1) in the biology of differentiated thyroid cancer - the effect of the expression of Prox1 on migration and invasiveness of thyroid cancer cells

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The feature of malignancy is its ability to infiltrate and metastasize. The differentiated thyroid carcinoma (DTC), which constitutes more than 80% of all thyroid cancers is spread by two major paths: papillary carcinoma (PTC) usually by the lymphatic vessels, and follicular cancer (FTC) mainly through the circulatory system. It was proposed that the cancers microenvironment induced by lymphangiogenesis could be an important factor affecting the expansion of primary tumour cells to lymph nodes. The aim of our work was to investigate signaling pathways associated with migration and invasiveness of thyroid cancer cells. We were especially interested in the role of Prosper homeobox 1 (Prox1) protein, an important element of the lymphangiogenesis.

The studies were performed in a series of thyroid cancer FTC and PTC cell lines. The protein expression level and intracellular localization of the Prox1 gene was determined using molecular biology methods including: Q-RT-PCR, Western Blot and immunocytochemistry. The tumour cells' dynamics and invasiveness were monitored by microscopic observation assay and using invasion test, respectively. Additionally, the cells phenotype under Prox1 gene overproduction and silencing conditions was investigated. We observed significant differences in the level of expression Prox1 between tested thyroid cancer cell lines. Additionally, protein subcellular localization was also variable and correlated with the tumour type. The protein concentration was not directly combined with mRNA level and even under small mRNA concentration in some tissue culture lines, the Prox1 protein was cumulated in the cells over the time. We noticed that the increased expression level of Prox1 gene resulted in a lower rate of cell migration. Interestingly, a similar effect was demonstrated under overexpression conditions of the Prox1 gene, but uniquely, the lower dynamic rate of cells was additionally accompanied by a significantly higher invasive potential of the tested cells.

The differences in the expression level and localization of Prox1 protein in various DTC lines may suggest an important role of it in the spreading of follicular and papillary carcinomas. We showed that Prox1 is a factor that has a significant effect on the migration and invasiveness of thyroid cancer cells, and thus affects the spread of the tumour. We propose that Prox1 may lead to changes in the signaling pathway controlling cytoskeleton dynamics in the tumour cells and the turnover of invasiveness. Further on-going studies will precisely determine the role of Prox1 lymphangiogenesis factor in DTC propagation.

A52 Maintenance of iodine intake

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Dietary iodine status is routinely assessed by measuring urinary iodine excretion (UI). In most European countries iodine intake is maintained at WHO recommended levels by iodisation of table salt [1]. Exceptions to this practice include Ireland and the UK where only 5% (approximately) of table salt sold is iodine supplemented. However despite the finding of relatively low median UI values in study populations in both Ireland and the UK [2-4] there is little evidence of an increased prevalence of hypothyroidism, overt or subclinical, of non autoimmune pathogenesis [5-8]. In this communication studies on iodine status in the Irish population over the years 1988-2007 are reviewed, as are investigations into how in the absence of salt iodisation, factors such as proximity to the sea or placental iodide transport/storage have a role in providing sufficient iodine to maintain euthyroid status in the study population.

Subjects were not selected on a systematic basis but were a combination of available findings from different Irish populations studied over the years specified. Although most study groups were comprised of adult females, where these were not available, findings from female schoolchildren were assessed. Median values for UI in study populations ranged from approximately 50-140 µg/l. In the absence of iodised salt availability, milk and dairy products constitute a major iodine source but their content shows seasonal variation with a higher iodine content when cattle in winter housing are fed dietary supplements including iodine [9,10]. Thus UI values were lowest during the summer months (April to September) and highest during winter (October to March). The low values in Irish subjects were supported by recent findings in a study of UK female schoolchildren [4] where a median UI value of 80 µg/l corresponded to the most recent Irish value of 79 µg/l [11]. Interestingly the lowest regional value in the UK study came from Northern Ireland where Belfast children had a median UI of 62 µg/l with 30% having values < 50 µg/l. Despite the relatively low UI values obtained in the Irish study populations, findings for neonatal TSH assessed over the years 1995-2006 did not exceed 3%, a cut off point indicative of iodine deficiency. However a small but significant trend to higher TSH, within the reference range, was observed [6]. In the absence of iodine supplementation of table salt, dietary iodine intake is entirely opportunistic. Consumption of milk and dairy products obviously plays a part but this communication reports on the investigation of possible other modes of iodine intake aimed at establishing if living near the sea in a seaweed abundant environment, and therefore exposed to gaseous I2 ingestion by respiration, may confer advantages in terms of iodine intake. Also, as adequate iodine nutrition for the foetus depends not only on maternal iodine supply, but also on the ability of the placenta to successfully transport iodide to the foetal thyroid for use in thyroid hormone biosynthesis, it is proposed to report on placental uptake and possible storage of iodine as a means of maintaining adequate iodine intake in utero.

Ireland has traditionally been regarded as an area of borderline iodine deficiency which might not be expected on an island where few live more than 200 Km from the sea. However as has become apparent in recent times, availability of iodine in the diet is dependent on many factors, of which the presence of thyroiditis in certain cases may be influenced by seaweed abundance rather than proximity to the sea. Atmospheric I2 was also variable and correlated with the tumour type. The protein concentration was not directly combined with mRNA level and even under small mRNA concentration in some tissue culture lines, the Prox1 protein was cumulated in the cells over the time. We noticed that the increased expression level of Prox1 gene resulted in a lower rate of cell migration. Interestingly, a similar effect was demonstrated under overexpression conditions of the Prox1 gene, but uniquely, the lower dynamic rate of cells was additionally accompanied by a significantly higher invasive potential of the tested cells.

The differences in the expression level and localization of Prox1 protein in various DTC lines may suggest an important role of it in the spreading of follicular and papillary carcinomas. We showed that Prox1 is a factor that has a significant effect on the migration and invasiveness of thyroid cancer cells, and thus affects the spread of the tumour. We propose that Prox1 may lead to changes in the signaling pathway controlling cytoskeleton dynamics in the tumour cells and the turnover of invasiveness. Further on-going studies will precisely determine the role of Prox1 lymphangiogenesis factor in DTC propagation.
perchlorate inhibition [unpublished observations]. RNA was isolated from placental trophoblasts and real-time RT-PCR performed using sodium iodide symporter (NIS) and pendrin (PDS) probes. Trophoblastic cells expressed both NIS and PDS. 125I uptake in primary cultures from placental tissues was enhanced by individual pregnancy-related hormones, particularly hCG and oxytocin, with synergism between hormone combinations. These incremental responses were mirrored by increased expression of NIS but not PDS when measured by real-time PCR suggesting that the increased iodide uptake was solely due to increased NIS expression. Measurement of placental tissue iodine content (mean 40ng/g tissue), while not approaching thyroid levels (~1,000 ng/g tissue), is significantly greater than that of other non-thyroidal tissues and appears to be directly proportional to iodine intake as determined by UI [11,15].

Conclusions: The above findings demonstrate that in the absence of an iodine supplementation through iodisation of salt or otherwise, the study population appears to be only borderline iodine deficient. Even this apparent deficiency depends on the applicability to the definition of iodine deficiency of the WHO recommended UI cut off point (Median UI 100 µg/l) as it has been suggested that using the Recommended Daily Allowance (RDA) of the Institute of Medicine (95 µg) would lower this cut off point from 100 µg/l to 63 µg/l [16]. Investigating alternative pathways of iodine intake such as gaseous I2 ingestion or placental iodide transport in utero may help to explain maintenance of adequate iodine intake. However calculation of the potential exposure to gaseous I2 ingestion in children residing in a seaweed abundant coastal area is difficult to reconcile with the relatively high UI values observed. On the basis of measured atmospheric gaseous I2, extremely preferential I2 absorption would be required to make a significant contribution to daily iodine intake. Although living near the sea may not in itself be sufficient to maintain satisfactory iodine intake, findings in this study do not exclude the possibility of a significant role for iodine inhalation in influencing iodine status.

Iodine (125I) uptake in primary cultures from placental tissues was enhanced by individual pregnancy-related hormones, particularly hCG and oxytocin with synergism between hormone combinations. These incremental responses were mirrored by increased expression of placental NIS. As only up to 30% of 125I uptake by placental cells was blocked by perchlorate, it is likely that passive diffusion as well as active transport is involved. However iodide uptake does appear to involve placental storage as placental tissue had a significantly higher iodide content than other non-thyroidal tissues. Also it has been demonstrated that maternal urinary iodine (UI) excretion in the immediate antenatal and early postpartum periods showed a precipitous fall in median values from 93 µg/l antenatally to 36 µg/l at delivery which could be possibly explained by placental loss [17]. It therefore appears that iodide uptake and transport from other than conventional dietary sources may assist in maintaining normal thyroid function even dietary intake is apparently deficient.

References

AS53
Long-term thyroid hormone replacement therapy
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In recent years the number of patients with hypothyroidism has significantly increased. It is the result of increased prevalence of autoimmune thyroid disease, increased frequency of total thyroid resections and also common radiodine thyroid ablation in patients with hyperthyroidism or differentiated thyroid cancers. The treatment of hypothyroidism is considered by many physicians as effortless, simply based on L-thyroxine substitution. Universal access to therapy and to laboratory tests supports their approach. Is it true? Nowadays, both the development of diagnostic methods and current knowledge concerning pathomechanism of thyroid disorders enable to establish a diagnosis much earlier, in clinico pathological phase, before typical symptoms appear. The question is, whether a patient should be treated at this early stage. If a doctor decides to start a hormonal therapy, next questions concerning a dose of medication and treatment monitoring must be answered. The dose of L-thyroxine should be individually adjusted, based on both clinical and laboratory findings. Moreover, the age of patient, weight, physical activity, profession and general health state should be borne in mind. It is widely established, that the monitoring of TSH level is sufficient. However, in many cases even if TSH level is within the reference range, the patient’s complaints, symptoms and quality of life are not satisfying. Therefore, assessment of other parameters of hormonal balance might be helpful. Observations of patients treated for hypothyroidism bring new clinical dilemmas, unresolved despite of long-term experience. There are still questions, whether the laboratory test should be performed before or after taking medication? Should L-thyroxine be taken on the empty stomach every morning, or there are other options? How should results of hormonal tests be interpreted? What factors modify the therapeutic approach (age, pregnancy, coexisting disorders, elective surgery and other)? To conclude, the treatment of hypothyroidism requires multifaceted approach. Therefore, medical care for patients cannot be limited only to monitoring of TSH level, what unfortunately is common in medical practice.
A54 Clinical experience in the management of patients with Graves' orbitopathy treated according to the novel protocol of glucocorticoid therapy designed in the Department of Endocrinology, Metabolism and Internal Medicine of Poznan University of Medical Sciences
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Introduction: Graves’ orbitopathy, despite of the results of recent research concerning pathomechanism of the disease, is still a therapeutic challenge. Corticosteroids are the treatment of choice for active, moderate to severe Graves’ orbitopathy.

The aim of the study is to evaluate the effects of treatment of patients with GO with novel protocol of steroidotherapy designed and introduced in Department of Endocrinology, Metabolism and Internal Medicine. The management protocol consists of 3 g of methylprednisolone administered intravenously followed with methylprednisolone injected intramuscularly in divided doses every 3 weeks (total dose of methylprednisolone is 36 g).

Material and methods: The study group consisted of 50 patients. Assessment of efficacy of therapy was performed before and immediately after the therapy and 6 months later. Thyroid function parameters (TSH, FT4, FT3), titers of thyroid autoantibodies (TRAb, TPOAb, TgAb), thyroid volume (V) were analyzed. Moreover, ophthalmological findings (soft tissue involvement, proptosis, diplopia, clinical activity score, visual acuity) and disease activity on magnetic resonance imaging of orbits were evaluated.

Results: The therapy significantly improved the degree of soft tissue involvement, CAS, diplopia and decreased the autoimmune disease activity in oculomotor muscles. Moreover, significant decrease of TRAb titer was observed.

Conclusions: To conclude, novel protocol of glucocorticoid therapy is effective and safe.

A55 Various types of autoimmuneinmunological diseases of thyroid gland
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Thyroid gland disease of autoimmune origin presents wide spectrum of pathologies, Graves’ disease from one side and chronic thyroiditis with fibrosis and atrophy of gland parenchyma from the other one. Among them the highest number of misunderstandings is observed in pathological reports of chronic thyroiditis in pre-operative cytological as well as in post operative histological examinations. There are numerous classifications of chronic thyroiditis, however they are not widely accepted. Histochemical classification which correlates elements of microscopic examination with clinical course of the disease seems to be ideal but still does not exist. FNAB of thyroid gland is a method of the greatest importance in the diagnosis of chronic thyroiditis however that fact is not widely understood in every day routine of clinicians and pathologists.

A56 Curiosa in fine needle aspiration biopsy of the thyroid gland
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Thyroid Research 2013, 6(Suppl 2):A56

The great importance of cytological examination in diagnostic procedures of thyroid gland pathological lesions is widely known. Unfortunately, cytology as a diagnostic method presents many limitations due to possible presence of elements abnormal for thyroid gland physiology and histology. Especially difficult in cytological diagnosis appear: among non-neoplastic lesions - dys hormonogenous and amyloid goiter and Riedel disease and among neoplastic lesions - rare microscopic variants of tumours, neoplasms arising from ectopic tissues and nonepithelial tumours.

A57 Local renin-angiotensin system in the thyroid – myth or fact?
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Beside the basic control system associated with the hypothalamus-hypophysys-thyroid axis and thyrotropin, a growing evidence suggests that thyroid function is influenced by a vast spectrum of locally produced factors. Renin-angiotensin system (RAS) is considered as one of the most powerful and effective regulatory systems in humans. In the “classical” cascade of RAS, angiotensinogen is enzymatically converted to the most active element of RAS – angiotensin (Ang) II. Ang II exerts its effects via two main receptors: AT1R and AT2R. The understanding of RAS biological function was significantly changed by the discovery of new enzymatic cascades leading to the production of molecules with different than Ang II functional properties – for instance Ang (1-7), molecule reacting with its specific receptor – Mas. Beside the growing complexity of RAS-structure, diverse expression patterns of RAS components in various tissues formed a basis for a concept of “local RAS” in many organs including brain and immune system. It was shown that many organ-specific effects of hormonal factors, including the influence of thyroid hormones on cardiovascular system, were dependent on the modulation of local RAS components. However, very little is known about the role of RAS in the control of thyroid function. In our immunohistochemical analysis of operative specimens we observed for the first time expression of RAS components in human thyroid. Interestingly, although our recently published findings suggest a direct regulatory influence of thyroid function on the phenotype and activity of immune cells in humans, no studies regarding the influence of human RAS on the course of such common inflammatory process as thyroiditis are available. Flow Cytometry analyses performed in our laboratory on thyroid fine needle aspiration biopsy material allowed us to assess quantitatively and phenotypically the immune cell populations of local thyroid blood. The comparison of results obtained with paired peripheral blood and local thyroid blood samples suggested differences in the structure of antigen presenting cell populations, e.g. monocytes, known to be the main source of RAS components in the immune system. Interestingly, RAS positive immune cells have been shown to correlate with clinical course of various inflammatory and malignant diseases.

In conclusion, better knowledge about local RAS in the thyroid seems to be of great importance for the understanding of both: thyroid physiology and pathological processes associated with inflammatory and malignant disorders of this gland.

A58 Evaluation of ultrasound-guided fine needle aspiration biopsy (USG-FNAB) of thyroid nodules: 12 years of accepted diagnostic algorithm in Holycross Cancer Centre (HCC) in Kielce
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Introduction: Role and place of USG-FNAB in diagnosis of thyroid lesions were confirmed in recently published algorithm proposed by the recommendations of Polish Group of Endocrine Tumours.

Aim of the study: Presentation of parameters describing thyroid USG-FNAB in HCC in Kielce.

Material: Since year 2000 all FNABs, including thyroid gland, were performed and evaluated according to the accepted diagnostic algorithm.
Between 2001 and 2012 FNAB was performed for 26361 patients, in 28079 biopsy sessions with 40815 ultrasonographically selected and biopsied thyroid lesions. Since year 2001, all data about subsequently surgically treated patients along with pathology reports and with previous FNAB data were currently gathered. Each correlated case gained true positive (TP), true negative (TN), false positive (FP) or false negative (FN) status. There were overall 1453 cases of thyroid malignancies of all 10142 correlated FNABs vs. subsequent surgical specimens in CORRELATION DATABASE between 2001-2012. In that period of time there were 343 TP, 1026 TN, 5 FP and 74 FN correlated cases of thyroid malignancies. On the basis of these data, sensitivity, specificity and overall accuracy for thyroid USG-FNAB were calculated.

Methods: On the basis of annual data for true and false cases, overall sensitivity (OS), overall specificity (OSP) and overall accuracy (OA) were estimated. The trend for those values was evaluated. Results: For whole analyzed period of time (2001-2012) FNAB's OS was 0.85, ranging from 0.68 to 1.0 and OSP was 1.0, ranging from 0.97 to 1.0. OA was 0.95, ranging from 0.9 to 1.0. In graphical analysis there was a strong gradual trend of increase in sensitivity since year 2007, with maintaining specificity approaching 1.0. Statistically significant strong positive trend of sensitivity value (R=0.76, p=0.004) was shown for each year, separately from the flow of time, in analyzed period of time.

Conclusions: Applied in our department USG-FNAB method was characterized by statistically significant and regular increase of correct malignant tumour diagnoses (sensitivity) and overall accuracy with stable high level of correct benign lesions diagnoses (specificity).

Effectiveness analysis of papillary thyroid carcinoma (PTC) diagnostics in Holy Cross Cancer Centre (HCC) in Kielce according to fine needle aspiration biopsy quality assurance program in pathology department between years 2001 and 2012
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Introduction: Commonly accepted evaluation of diagnostic test usefulness is based on the basis of such factors as sensitivity, specificity and overall accuracy is a prelude to more profound statistic deliberations. Practical meaning of those factors depends on many elements like representativity of FNAB smear and also final microscopic evaluation, tumour type or diameter.

Aim of the study: To evaluate detection of PTC by ultrasound-guided fine needle aspiration biopsy (USG-FNAB).

Material: Between years 2001 and 2012, a group of 26361 patients had thyroid lesions diagnosed by USG-FNAB. At least one carcinoma was diagnosed (including two metastases) in 343 patients. Surgical specimens (SS) revealed 419 malignancies, with 335 PTCs. A diameter of histologically diagnosed PTC was between 0.5 mm and 170 mm. Number of false negative (FN) cases ranged from 0 to 16 each year.

Methods: A correlation was sought between mean diameter of PTC, FN cytocologic cases and whole number of PTCF found in surgical specimens, each year, in analyzed period of time.

Results: On the basis of numerical and proportional results of assessed parameters three periods of time can be distinguished in analyzed 12 years. The first period is between years 2001 and 2002. Mean PTCs greater diameter were diagnosed with USG-FNAB and the percentage of FN diagnoses was higher than in the rest of the whole analyzed period. Since year 2008 till 2012 the number of FN diagnoses stabilized and reached the percentage value interval between 0 and 5. Strong negative correlation was statistically shown between the percentage of FN diagnoses and elapsed time (R=−0.7591, p=0.0042) as well as between the mean PTC diameter (R=−0.6011, p=0.387) and elapsed time.

Conclusions: Presented data showed that, in the course of time, smaller diameter of PTCs was diagnosed by USG-FNAB and more rarely false diagnoses were given in Holy Cross Cancer Centre.

Hashimoto’s disease - from theory to practice
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Hashimoto’s thyroiditis is the most prevalent autoimmune thyroid gland disease. It is now over a century since the first description of the disease by the Japanese doctor Hakaru Hashimoto in 1912, yet the etiopathogenesis of the disease is still discussed. At present it is thought that Hashimoto’s disease is provoked in genetically susceptible individuals by both environmental and endogenous triggers. Genetic predisposition to development of the autoimmune thyroid diseases was established on the basis of the epidemiologic studies indicating increased prevalence of such diseases in some families, especially in twins. According to current knowledge appearance of Hashimoto’s disease in Caucasians is associated with some gene alleles: human leukocyte antigens (HLAs), mainly class II HLA DR3 and DR 5, cytotoxic T lymphocyte antigen-4 (CTLA-4), protein tyrosine phosphatase nonreceptor – type 22 (PTPN22), thyroglobulin (Tg), vitamin D receptor (VDR) and cytokines. Among environmental factors triggering the thyroid autoimmunity the following should be mentioned: excessive iodine intake, treatment with certain drugs (interferon α, IL-2, lithium, amiodarone), infections, mainly viral and exposure to many chemicals such as polyaromatic hydrocarbons and phenyls. Female sex, rebound phenomenon in postpartum period and fetal microchimerism are essential endogenous factors in the etiopathogenesis of Hashimoto’s disease. Above mentioned factors are responsible for the development of autoimmune response in thyroid gland. It leads to increased antigen presentation by antigen presenting cells (APC), inappropriate presentation of HLA antigens class II by thyroid follicular cells and reduced immune tolerance. Developing autoimmune process, predominantly Th1-type, is responsible for the increased production of TNF-α, IFN-γ and IL-1 cytokines. Destruction of thyroid tissue with subsequent development of fibrous tissue is mediated by apoptosis process, CD8+ cytotoxicity, change of cell junctions and complement activation. On clinical examination Hashimoto’s disease may present as classical, atrophic, focal or juvenile form. Additionally, there are two variants of Hashimoto’s disease: silent, painless thyroiditis and postpartum thyroiditis. Natural course of Hashimoto’s disease leads to hypothyroid state. High antithyroperoxidase and antithyroglobulin antibodies concentrations and hypochoegonic structure of thyroid gland on ultrasonographic examination confirm the diagnosis of Hashimoto’s disease. Fine-needle aspiration biopsy is rarely needed to confirm the diagnosis. The treatment of Hashimoto’s disease includes an administration of substitutive doses of levothyroxine, but the time of treatment beginning is still the matter of discussion.

The risk of iodine deficiency in the current model of iodine prophylaxis in Poland
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Poland is an iodine deficient area. Polish Council for Control of Iodine Deficiency Disorders (PCCIDD) as a multicenter group of experts in the field, was set up in 1991 at the Department of Endocrinology, Jagiellonian University, Collegium Medicum in Kraków. PCCIDD organized in 1992/1993 epidemiologic survey which confirmed iodine deficiency and endemic goiter on the population level and applied to the Ministry of Health for introducing an obligatory model of iodine prophylaxis based on the household salt iodization. In 1996 the Ministry of Health issued such disposition with 20-40 mg KI per 1 kg of household salt. The council detailed also other elements of iodine prophylaxis, including to the model an iodization of newborn formula (0.10-0.15 mg KI/kg) for children not being breastfed, and
A63 Feasibility and efficacy of neck dissections in patients with thyroid cancer

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Introduction: The aim of the study was to assess (1) the feasibility and the outcomes of secondary neck dissections in well differentiated, medullary and poorly differentiated thyroid cancer and (2) to evaluate complications associated with surgical treatment.

Material and methods: We assessed the results of secondary neck dissections in 51 patients previously operated for thyroid cancer: 33 well differentiated thyroid cancer, 15 medullary cancer, 3 poorly differentiated thyroid cancer.

Results: Reoperations covered I–VII neck levels. Radical neck dissection was performed in 20 patients, selective neck dissection (SND) in 31 patients. These included 16 central compartment (CC) and 10 mediastinal excisions. Postoperative complications were stated in 13 patients: 4 chyle leaks, 3 massive bleedings, 8 injuries of RLN, hypoparathyroidism in 2 patients died in perioperative period. Stimulated Tg<2mg/ml was observed in 7 patients with WDTC during the first control after neck dissection; in 6 patients Tg level decreased after operation; 7 patients had still notably elevated Tg levels (>30 ng/ml). None of the patients with medullary cancer achieved calcitonin level lower than 10 pg/ml; 9 patients developed distant metastases.

Conclusions: Patients with nodal metastases deriving from thyroid cancer present a challenging group for surgeons. The policy is to operate due to strong indications. It is important to be aware of possible complications. The outcomes of neck dissections in patients with medullary and poorly differentiated thyroid cancer were unsatisfactory.

A64 The role of somatostatin analogues in treatment of TSH secreting pituitary adenomas

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Introduction: TSH-secreting tumours are extremely rare case of hyperthyroidism. Most important clinical feature is preserved TSH level in subjects with apparent thyrotoxicosis. Possible misdiagnosis of primary thyroid hyperfunction could lead to mistreatment with anti-thyroid medications. This worsens disease course and outcome. Neurosurgery success rate is limited by tumour size and its extrasellar expansion. Native somatostatin is key negative regulator of TSH secretion. In most cases tumour cells express somatostatin receptors. This feature creates potential use of somatostatin analogues for medical treatment of TSH-secreting tumours.

Aim of the study: The aim was to determine potential value of somatostatin analogues in primary TSH-oma treatment. Secondary objective was to evaluate efficacy of long-acting somatostatin analogues in cases after unsuccessful neurosurgery.

Material: Material comprised of 17 patients with secondary thyrotoxicosis, 7 women and 10 men, aged 20 to 69 years (mean 39), presenting with pituitary macroadenoma (16) and one with microadenoma and empty sella. Before diagnosis was established 8 out of 17 patients received antithyroid medications. The most severe complication of GO is optic neuropathy. Exophthalmos. The most severe complication of GO is optic neuropathy.

Conclusion: High dose IV MP pulse therapy is a highly effective immunosuppressive treatment used in various inflammatory and autoimmune diseases e.g. active, moderate to severe GO and neuropathy due to GO. It remains to be proven, whether in some cases, the administration of MP can cause orbitopathy as well as may lead to the deterioration of its severity, including optic nerve neuropathy, probably as a result of the proliferation of adipose tissue.
medication, in 2 cases strumectomy was performed and 2 patients received 131I therapy.

**Intervention:** Somatostatin analogue octreotide long acting repeatable (LAR) administration at least 3 months (3 injections) before surgery, and in cases of unsuccessful surgery stable octreotide LAR therapy.

**Results:** Initially, all patients had elevated T4 and a-SU levels (mean 29.3 pmol/l SD 4.3, and 6.2 ng/ml SD 4.9). 3 months of octreotide LAR therapy led to significant T4 reduction (to mean 12.2 pmol/l) and TSH reduction from mean 6.5 mIU/ml to 0.3 mIU/l. In all cases clinical improvement was observed.

In 14 out of 17 pre-treated with octreotide LAR decreased tumour volume and in 2 improvement in visual field was observed. Patients in euthyroid state were referred to neurosurgery department. Transsphenoidal adenomectomy was successful 13 out of 17. In four cases after unsuccessful neurosurgery intervention stable euthyroidism was achieved with octreotide LAR treatment. In one case secondary thyrotoxicosis relapsed 2 years and now is controlled by octreotide treatment.

**Conclusions:** Somatostatin analogue treatment is efficient in TSH-secreting tumours in the terms of TSH secretion, thyroid function and clinical improvement. In cases of surgery failure prolonged octreotide treatment could be safe and efficient option of disease management.

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**A66**

**Endoscopic intranasal orbital decompression in the course of Graves’ orbitopathy**

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The authors present the endoscopic intranasal orbital decompression, one of the surgical techniques used for orbital decompression. It can be applied for various indications. The most common indications are: maxillo-facial trauma, orbital haemorrhage, subperiocular abscess as the complication of sinusitis, optic neuropathy, thyroid-associated orbitopathy (Graves’ orbitopathy). The authors conclude that the endoscopic transnasal orbital decompression is a valuable and safe operational technique for patients requiring orbital decompression.

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**A67**

**Obliteration of thyroid arteries as a new method of treatment of thyroid diseases**

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Standard methods including pharmacotherapy, radioiodine and surgery cannot always be applied in treatment of thyroid diseases. The limitations of these methods are: drug intolerance and their side effects, too low radioiodine uptake, high risk of surgery. The obliteration of thyroid arteries seems to be an alternative method which could be used in the situation of ineffective standard treatment. It is based on shut down of blood flow in chosen thyroid arteries by injection of embolizative material (histoacryl or particles of polyvinyl alcohol) into the vessels. The consequence of acute ischemia is a septic necrosis of the glandular tissue in a field being supplied by this particular artery. Further repair processes and fibrosis lead to the reduction of an active thyroid hormone synthesis and decrease of thyroid volume. Effects of the embolization on apoptosis induction and modulation of autoimmune reactions are also observed. Preoperative selective embolization of a huge goiter or thyroid cancer improves surgery outcomes, reduces the risk of haemorrhage and damage to surrounding tissue. Palliative use of embolization in advanced stages of thyroid cancer reduces symptoms and improves quality of life. Little invasive nature of this procedure in comparison to surgery, the lack of serious undesirable coincidence makes the embolization of thyroid arteries an attractive form of therapy, which may become a therapeutic option in many difficult clinical situations and may improve the effectiveness of treatment of thyroid disease. The authors present the experiences gained in their institution with conclusions as follows:

1. As a result of using embolization of thyroid arteries in the treatment of selected thyroid diseases the following observations have been made: a significant reduction in goiter volume with resolution of compression symptoms of adjacent organs, reduction of the concentration of thyroid antibodies characteristic for patients with Graves’ disease (TRAb), cure of hyperthyroidism in 71% of patients with thyrotoxicosis. Embolization procedure was not associated with the occurrence of undesirable side effects, such as the clinical symptoms associated with increased concentration of free thyroid hormones, and induction or exacerbation of pre-existing autoimmune thyroid disease.

2. Thyroid artery embolization had no significant influence on activity of the parathyroid glands, regardless of the number and quality of closed vessels.

3. Thyroid artery embolization is an effective and safe treatment of selected thyroid diseases as an alternative to conventional forms of therapy.

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*Cite abstracts in this supplement using the relevant abstract number, e.g. A66: Kamiński G, Jaroszuk A. Obliteration of thyroid arteries as a new method of treatment of thyroid diseases. Thyroid Research 2013, 6(Suppl 2):A66*