roid hormone overproduction. It is the most common cause of hyperthyroidism, with 20—50 cases per 100 000 persons annually. The incidence peaks at 30—50 years. The annual incidence of Graves' ophthalmopathy is 18/100 000 women and 3/100 000 men yearly. The diagnostic work-up of hyperthyroidism is presented below (Smit and Hegedus, N Engl J Med, 2016). Treatment of hyperthyroidism is initiated by an antithyroidal drug (methimazole/carbimazole is first-line, propylthiouracil is an alternative option). The final choice of treatment (12—18 months of antithyroid drug therapy, radioiodine or total thyroidectomy) should be individually tailored. Patients should be advised to stop smoking. In this session, we will discuss these different treatment options, treatment of hyperthyroidism during pregnancy, as well as the diagnosis and treatment of Graves' ophthalmopathy.

KEYWORDS: Graves' disease, thyroid-hormone receptor antibodies, hyperthyroidism.

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ADRENAL INSUFFICIENCY

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Adrenal insufficiency (AI) is a condition associated with decreased secretion of steroid hormones from adrenal cortex resulting in a decrease of their biological effects on cells, tissues and organs of human body. Primary AI is a consequence of destruction of the entire adrenal cortex resulting wit loss of both, glucocorticoid and mineralocorticoid activity. By contrast, secondary adrenal insufficiency reflects an inability to sufficiently stimulate adrenal cortex by ACTH that results mainly in glucocorticoid deficiency whereas mineralocorticoid secretion is largely preserved. Among peripheral (primary) causes autoimmune destruction of adrenal cortex is most frequent in developed countries. Other possible peripheral causes of AI are: infections, bilateral metastases, bilateral adrenalectomy, adrenoleukodystrophy, amyloidosis, hemochromatosis, vascular causes (bilateral adrenal hemorrhage or thrombosis). Central (secondary) causes of adrenal insufficiency are: structural lesions of the hypothalamus or pituitary gland (tumours, infiltrating disorders, irradiation, lymphocytic hypophysisits) and some other rare conditions. One of most frequent causes in clinical practice is functional suppression of HPA axes caused by exogenous glucocorticoids. Proper replacement therapy is essential for patients' survival and also for maintaining their quality of life a normalizing morbidity and mortality.Treatment of acute AI should be performed and ICU setting with a close monitoring of patients. It has to start with immediate intravenous application of 100 mg of hydrocortisone followed by daily dose 200—400 mg continuously or divided in 3—4 partial doses. At the same time volume resuscitation with intravenous saline infusion and hypoglycaemia correction with intravenous glucose has to be carried out. Treatment of chronic AI of all causes consists of oral administration of glucocorticoid, commonly hydrocortisone in basal doses in approximate dose of 10—15 mg/m^2. Basal dose has to be adjusted before and during stress conditions properly. In primary AI patients usually require an addition of mineralocorticoid (Fludrocortisone in oral dose of 0,5—2 mg daily). On the other hand in cases with secondary AI hydrocortisone could be replaced by selective glucocorticoid in equipotent dose (e.g. prednisone or prednisolone). Proper and careful education of patients is essential and patients have to be equipped with steroid emergency card.

KEYWORDS: adrenal insufficiency, replacement therapy, exogenous glucocorticoids.

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MALE HYPOGONADISM

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The scientific and medical topic of male hypogonadism is one of the most growing and discussable problems in endocrinology in our days. Hypogonadism in male patients defined as testosterone level decrease in serum associated with specific symptoms and/or signs can be observed in case of abnormal changes in testes and/or pituitary such as Klinefelter syndrome, Kallmann syndrome and also in male patients with idiopathic, metabolic or iatrogenic disorders resulting in androgen deficiency. Among the classical reasons pointed above the growing number of hypogonadal elderly men are now in focus of clinicians. The main guidelines' for diagnosing and treatment options of hypogonadal adolescents and adults will be discussed. Also the introduction into Russian Guidelines for diagnosing and treatment of testosterone deficiency will be discussed during the talk.

KEYWORDS: male hypogonadism, Klinefelter syndrome, Kallmann syndrome, testosterone deficiency.

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BONE BIOLOGY AND FUTURE TARGETS FOR OSTEOPOROSIS TREATMENT

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Novel therapeutic approaches to osteoporosis have not only provided better treatment modalities but also shed new light on the cellular and molecular mechanisms by which trabecular and cortical bone skeletal homeostasis is regulated. Skeletal homeostasis is ensured by the balanced activities of bone resorption and bone formation in bone remodeling. Osteoclasts are responsible for the resorption of bone, but also for the local recruitment

of osteoblasts at resorption sites (coupling) ensuring repair of resorbed areas. In turn, osteoblasts are responsible for the formation of new bone at these sites but also for the differentiation of osteoclasts, mostly through the local production of RANKL and OPG, also secreted by osteocytes. Consequently, inhibition of osteoclast differentiation leads to a decrease in both resorption and formation, with suppression of bone remodeling. Denosumab treatment nevertheless allows a continued increase in bone density and reduction in fracture risk over time. The mechanisms by which bone mass continues to increase despite very low remodeling activity appears to involve bone modeling activity, during which bone formation continues independent of bone resorption, particularly in cortical bone. Although not pursued anymore as a therapeutic target, inhibition of cathepsin K in humans decreases bone resorption while maintaining bone formation, allowing cross-talk between osteoclasts and osteoblasts and a robust and prolonged increase in BMD at trabecular and cortical sites. The other, most promising approach involves not the inhibition of resorption but the stimulation of bone formation with osteo-anabolics. Bone formation occurs in the context of bone remodeling or bone modeling, and activation of the PTH and/or Wnt signaling pathways increase bone formation by osteoblasts via both processes. Daily PTH1-34 (Teriparatide) injections increase bone formation but also bone resorption, increasing bone turnover, albeit with a positive balance. Although bone density is efficiently increased, the secondary increase in bone resorption may affect intracortical remodeling and increase cortical porosity, limiting the benefits of PTH treatment. Weekly administration of PTH1-34, the use of PTHrP analogs (Abaloparatide) or the combination of PTH with Denosumab may avoid in part the increase in resorption and increasing bone density further. Other osteo-anabolics target the Wnt signaling pathway, which is a key regulator of the differentiation and function of osteoblasts as well as their ability to cross talk with osteoclasts. Inhibition of endogenous inhibitors such as Sclerostin, secreted locally by osteocytes, leads to massive increases in bone formation and production of OPG, thereby also reducing resorption. Sclerostin antibodies (Romosozumab and Blozosumab) enhance locally, at the level of osteoblasts and osteocytes, Wnt signaling. These compounds have both an anabolic and an anti-resorptive effect that, albeit limited in time, increase very quickly and efficiently bone density at trabecular and cortical sites, in large part via bone modeling. Taken together, these new therapeutic developments provide not only promising prospects for the future treatment of osteoporosis but also important insights into bone biology.

KEYWORDS: osteoporosis, osteoclasts, Denosumab, PTHrP analogs.

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OSTEOPOROSIS: HOW AND HOW LONG TO TREAT

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Osteoporosis is the most prevalent bone disease and a major health-economic problem worldwide. It is defined as a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. The disease is still underdiagnosed and undertreated in spite of rich armamentarium of different drugs. The aim of treatment is to prevent a fracture. Each patient with osteopenia or osteoporosis should take cholecalciferol 1,000—2,000 IU daily or 7,000—14,000 IU once weekly in addition to food rich in calcium (dairy products) or calcium supplements. Patients who sustained an osteoporotic fracture or those who are at high risk of a major osteoporotic fracture (>20% in next 10 years) or hip fracture (>5%) as assessed by FRAX or other fracture risk assessment algorithm, should receive an antiosteoporotic medication. The most commonly used drugs are antiresorptive medications such as the nitrogen-containing bisphosphonates (BPs) and the receptor activator of nuclear factor kappa B ligand inhibitor denosumab. Whereas both BPs and denosumab inhibit osteoclastic bone resorption (and, to a lesser degree, bone formation), they do so by different cellular and molecular mechanisms. The skeletal effects of denosumab resolve quickly and completely when treatment is stopped while BPs can stay in bone for years. Less commonly used and generally reserved for patients with severe and established osteoporosis are the anabolic agents PTH [PTH-(1—84)] and teriparatide [PTH-(1—34)]. These peptides potently stimulate osteoblastic bone formation but also stimulate bone resorption. The treatment is limited to two years. Immediately after anabolic treatment an antiresorptive medication should be introduced to sustain the benefits. Concomitant teriparatide and denosumab therapy increases BMD more than therapy with either medication alone and more than has been reported with any current therapy. The combination of these agents might be an important treatment option in patients at very high risk of fracture. In case there is a need for prolonged treatment the effect is better when starting with the anabolic drug teriparatide for two years and following with an antiresorptive like bisphosphonate or denosumab. There are new medications in the pharmaceutical pipeline: anti-sclerostin monoclonal antibodies, anti katepsin K monoclonal antibodies, PTHrP analog abaloparatide. How long treatment should last depends on the individual fracture risk assessed by FRAX. This is performed before and every two to three years during the treatment. Continuous long-term therapy with antiresorptive drugs can cause late complications like osteonecrosis of the jaw or atypical femur fractures.