Thyreopathies during pregnancy and in newborns

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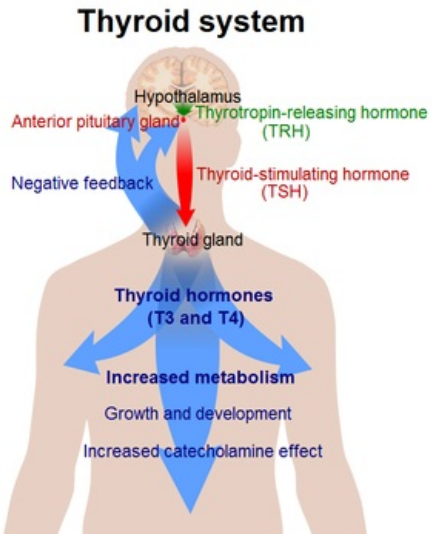
Thyreopathy or thyroid disorders affect a significant proportion of women of childbearing potential. Untreated thyroid disorders can cause infertility, complications in pregnancy (abortions, premature births, etc.) and can contribute to the delay of the child's psychomotor development. Therefore, early detection and treatment of thyroid disorders in pregnancy is necessary. According to the recommendations of the Czech Society of Endocrinology from 2018, thyroid stimulating hormone (TSH), free thyroxine (fT4) and antibodies against thyroid peroxidase (TPOAb) should also be taken during the first blood collection during pregnancy (i.e. usually in weeks 9-11). According to some international professional associations, this examination is not necessary for women without risk factors (see below). Iodine supplementation (150-200 ug of elemental iodine per day over and above normal dietary intake) is recommended for all pregnant and lactating women (except those with hyperthyroidism).However, beware of excessive iodine intake (> 500 ug per day), which can lead to fetal hypothyroidism.[1]



Hormonal regulation of the thyroid gland

Risk factors for thyreopathies in pregnancy

- Tyreopathy in personal or family anamnesis;
- Symptoms of thyroid dysfunction or goiter;
- Type 1 diabetes mellitus or other autoimmune diseases;
- History of abortion or premature birth;
- Positive TPOAb;
- History of head and / or neck irradiation;
- Obesity with BMI ≥40 kg / m2;
- Use of amiodarone, lithium, application of cytokines, recent application of iodine X-ray contrast agent;
- Infertility;
- Living in an area with moderate or severe iodine deficiency.[1]

The most common endocrine disease in women is autoimmune thyroid disease – especially chronic lymphocytic thyroiditis (CLT) a Graves' disease (GB).[2]

Physiology (effect of pregnancy on the thyroid gland)

- during pregnancy, the volume of plasma increases along with the plasma pool of thyroxine (T4) and triiodothyronine (T3);
- the renal clearance of iodine increases and part of the iodine passes through the placenta into the fetal circulation;
- acceleration of metabolic inactivation of T4 and T3 by deiodination on the inner ring by the enzyme deiodase 3, which is overexpressed in the placenta (quantitatively the most important factor);
- the above changes result in an overall increased need for iodine and thyroid hormones in pregnancy - women with normal iodine stores in the thyroid gland and with normal gland function easily adapt to these changes with increased synthesis of T4 and T3;

- at the beginning of pregnancy the concentration of thyroxine-binding globulin (TBG), which is the main binding protein for T4 and T3, increases due to the increase in estrogens → therefore the free fraction of T4 and T3 is temporarily decreased → after the synthesis increase, FT4 normalizes and bound (therefore the overall) T4 remains increased;

- at the beginning of pregnancy, chorionic gonadotropin (hCG) rises sharply, which, among other things, stimulates the thyroid gland (similar to TSH - together they share a large part of the molecule - alpha chain) → T4 and T3 secretion increases (FT4 and FT3) and by negative feedback the secretion of TSH is partially or even completely suppressed, especially in conditions with high hCG (eg twins) - a transient and clinically insignificant condition.[3]

The synthesis of thyroxine (T4) and triiodothyronine (T3) is dependent on iodine supply. These hormones are necessary both for the preconception period and for fertilization and throughout the pregnancy up to several months after birth. In hypothyroidism, increased prolactin levels cause fertility problems. The fetus is completely dependent on the mother's production of thyroxine, especially until the 12th to 16th week, after which the fetal thyrocytes begin their own synthesis of T4, but the mother's supply of T4 is important throughout the whole pregnancy.[2]

Thyreopathy in pregnancy

Hypothyroidism

- moct common cause: autoimmune thyroiditis, failure to increase the replacement dose at times of increased demands, and relative iodine deficiency; central hypothyroidism (decreased serum FT4) is rare;
- treatment: levothyroxine substitution (target TSH values are <2.5 mIU / l) and iodine supplementation.[4]

- **Manifested hypothyroidism**: TSH elevation and decreased FT4 or TSH elevation> 10 mIU / l and normal FT4 - indicated for levothyroxine treatment;
- **Subclinical hypothyroidism:** TSH elevation ≤10 mIU / l and normal FT4 - indicated for levothyroxine treatment;
- **Isolated positive antibodies**: Positive TPOAb and normal TSH and FT4 - levothyroxine treatment should be considered (especially in women with abortions, premature births, infertility, decreased FT4, etc.);
- **Isolated hypothyroxinemia**: Decreased FT4 and normal TSH and negative TPOAb - consider levothyroxine treatment if no adjustment is made after iodine supplementation.[1]

Hashimoto's thyroiditis – chronic autoimmune thyroiditis

- one of the most common autoimmune diseases, affects about 5% of women of reproductive age;
- arises in part from a genetic basis;
- it develops very slowly as chronic lymphocytic inflammation, mediated mainly by cellular immunity directed against follicular cells of the gland;
- it is also manifested by the production of circulating autoantibodies against glandular structures, of which antibodies against thyroperoxidase (TPOAb) are of the greatest importance for diagnosis;
- limits the gland's secretory reserve - functional impairment varies in severity;
- functional impairment of the gland can be assessed by an increase in TSH and, in the case of a more severe disorder and / or iodine deficiency, also by a decrease in free T4;
- ultrasonographic image: coarse structure (dispersive → diffuse), hypoechogenic and hypervascularized.[3]

Hyperthyroidism

- physiological pregnancy can mimic hyperthyroidism clinically and laboratory (increased cardiac output, peripheral vasodilation, increase in total and partially free thyroxine, mild goiter, physiological TSH suppression due to chorionic gonadotropin);
- however, the prevalence of true peripheral hyperthyroidism in pregnancy is up to 10 times lower than in the general population;
- the most common cause is Graves's disease (in 85% of cases), other causes are rare (hyperfunctional phase of autoimmune thyroiditis, iodine excess, thyroid hormone overdose, toxic adenoma, polynodose toxic reconstruction / goiter);
- untreated or inadequately treated hyperthyroidism in pregnancy increases the risk of preterm birth and miscarriage;
- overdose of thyrostatics in pregnancy leads to fetal hypothyroidism with negative consequences for CNS development and fetal goiter;
- thyrostatic treatment - in the 1st trimester propylthiouracyl (increased incidence of VVV after methimazole and carbimazole), from the 2nd trimester change to methimazole (higher incidence of hepatopathies after propylthiouracyl), during breastfeeding methimazole;
- The most serious side effects of thyrostatics: agranulocytosis and hepatopathy (monitoring of liver enzymes is indicated).[4]

- **Manifested hyperthyroidism**: Decreased TSH, increased FT4 and confirmed thyroid etiology (examination of antibodies against TSH receptor (TRAK) and ultrasound), significant clinical signs - indicated for treatment with thyrostatics (propylthiouracil in the 1st and methimazole in the 2nd and 3rd trimester), not iodine supplementation indicated;
- **Subclinical hyperthyroidism**: Decreased TSH, normal FT4 and confirmed thyroid etiology, minimal or no clinical signs - not indicated for thyrostatic treatment or iodine supplementation;
- **Transient gestational suppression of TSH:** Decreased TSH and normal FT4 of non-thyroid etiology - not indicated for thyrostatic treatment but is indicated for iodine supplementation;
- **Isolated hyperthyroxinemia**: Elevated FT4, normal TSH and negative TPOAb - not indicated for thyrostatic therapy but is indicated for iodine supplementation.[1]

- **Newly diagnosed node** by palpation or by ultrasound (> 1 cm) - endocrinological examination indicated.[1]

Consequences of untreated thyroid diseases in pregnancy

- Abortions;
- Gestational arterial hypertension;
- Preeclampsia/eclampsia;
- Placental abruption;
- Preterm birth;
- Higher frequency of caesarean sections;
- Low birth weight;
- Embryo, fetal, neonatal and child developmental disorders - especially in the central nervous system;
- Postpartum thyroid dysfunction (postpartum thyroiditis).[4]

Postpartum thyroiditis

- a variant of autoimmune thyroiditis that occurs in the first year after delivery (even after abortion);
- cause: "rebound" phenomenon of immunotolerance, induced in pregnancy by the presence of an antigenically different fetus in the mother's body;
- risk factors: positive TPOAb, type 1 diabetes mellitus and other autoimmune diseases;
- in women with TPOAb and type 1 DM positive, TSH screening is recommended 3 and 6 months after delivery;
- clinical manifestation:
  - hyperfunction with a transition to hypofunction (about 1/3 of cases),,
  - hyperfunction followed by permanent normalization (about 1/3) - hyperfunction is caused by the destruction of thyroid follicles and the release of thyroid hormones into the circulation, so that thyrostatics are not effective; resolves spontaneously in 4-6 weeks,
  - hypofunction (about 1/3) - levothyroxine substitution and iodine supplementation during breastfeeding.[4]

Thyreopathy in newborn

Congenital hypothyroidism

- the most common congenital endocrine disease (prevalence 1: 3000–4000);[5]
- thyroid hormones play a key role in brain development, especially by 8 months of age (slightly less so by 3 years of age);
- without substitution treatment, irreversible brain damage occurs - at the clinical diagnosis, the brain is already irreversibly damaged;
- since 1985, nationwide neonatal screening has been introduced - for TSH level determination;
- etiopathogenesis: in 75–80% **thyroid dysgenesis** (agenesis, aplasia, hypoplasia, hemithyroidism, cystic malformation, ectopy) or **dyshormonogenesis** (disorder of any stage of hormone synthesis or secretion; neonatal goiter), or rare **isolated congenital central hypothyroidism** (congenital TSH defect - cannot be detected by neonatal screening);
- clinical picture without treatment: initially only prolonged neonatal jandice (due to transplacental transmission of thyroid hormones from the mother), later (in the first 2 - 3 months of life) failure, delayed growth rate and bone maturation - late closure of the fontanelle, delayed eruption of dental dentition muscle hypotension, omphalocele, constipation, hoarseness, thermoregulation disorders, anemia; even later growth failure, psychomotor retardation, sensorineural hearing loss;
- neonatal goiter or thyroid gland of normal size;
- 2-5 times increased risk of associated congenital malformations compared to other populations → ultrasound examination of the heart, kidneys and CNS is recommended;
- laboratory findings: ↑ TSH, ↓ fT4; (for the central form ↓ TSH and fT4);
- therapy: lifelong levothyroxine replacement therapy (started as soon as possible); intestinal absorption of L-thyroxine is impaired by concomitant ingestion of fiber, soy milk, calcium or iron preparations, and malabsorption as such.[6][5]

Transient hypothyroidism

- causes:
  - in neonates of some mothers with autoimmune thyroid disease, it may develop on the basis of transplacentally transferred maternal antibodies that inhibit the TSH receptor;
  - iodine deficiency of the mother;
  - excess iodide in the perinatal period.[5]

Congenital hyperthyroidism

- a rare disorder, thus can be life-threatening for newborns;
- etiopathogenesis: transplacental transmission of maternal IgG antibodies stimulating the TSH receptor (aTSHR, TRAK, TRAb) in maternal thyrotoxicosis of the Graves-Basedow type but also after conditions after thyroidectomy or radioiodine treatment, as the antibodies may persist (autoimmune neonatal thyrotoxicosis);
- clinical picture in the fetus: tachycardia, arrhythmia, growth retardation (IUGR), goiter;
- clinical picture in the newborn: goiter, increased irritability, tachycardia, more frequent loose stools, failure to thrive despite normal or increased appetite, insomnia, hypertension, hyperthermia, exophthalmos, hepatomegaly and / or splenomegaly, smaller large fontanelle, accelerated bone maturation;
- risk of metabolic breakdown and heart failure;
- in a newborn at risk of transplacental transmission of TRAb, it is recommended to examine the thyroid profile (T4, TSH, fT3) and TRAb from umbilical cord blood and then again during the first and second week of life[5]
- llaboratory findings: ↑fT_4;
- therapy: antithyroid treatment (thiamazole) until the disappearance of maternal antibodies, ie in a descending dose for 2-3 months; beta-blockers may be required to affect tachycardia and adrenergic stimulation; long-term dispensary is necessary after the end of treatment.[5][6]

Peripheral resistance to thyroid hormones

- peripheral tissue resistance to thyroid hormones → significant elevation of total and free T4 and T3, with TSH levels slightly elevated or normal;
- the most common cause: a genetic defect in the β subunit of the nuclear thyroid hormone receptor;
- clinical manifestations very variable: only biochemical abnormalities, picture of hypothyroidism or hyperthyroidism;

- can be detected by neonatal screening (TSH elevation); otherwise, the cause of the examination is goiter, tachycardia and hyperactivity.[5]

Iodine deficiency

- our natural diet is low in iodine → iodination of table salt since the 1950s (now potassium iodate), supplementation of pregnant and lactating women, enrichment of infant and toddler nutrition products;
- mild iodine deficiency → decreased production of thyroid hormones → ↑ TSH → iodopenic goiter → discrete cognitive impairment → poorer school performance;
- the most severe form: endemic cretinism - eradicated (severe iodine deficiency of pregnant and lactating women → reduced production of thyroid hormones in the fetus and later in the newborn with serious consequences for CNS development).[5][6]

Links

Related articles

- Thyroid diseases
- Children's goiter
- Examination of the function of the thyroid gland

External links

- Doporučení České endokrinologické společnosti pro screening tyreopatií v těhotenství (2018) (http://www.endokrinologie.cz/upload/doporuceni-pro-prevenci-endokrinologove-nahled.pdf)

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