Pediatric Endocrine Society (PES) Board Review Course in Pediatric Endocrinology – 2025
"Thyroid Disorders"

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****Below is a copy of the ABP content specification outline. If the information was reviewed in the presentation, then the slide number from the talk is listed after each specification (and at times with some additional information). Specifications that were not covered in the talk are expanded on below if necessary.****

c. Acquired Hypothyroidism

1. Pathophysiology

a. Be aware of the intracranial abnormalities (and their treatments) which may affect TRH and TSH production
--- *see the pituitary/hypothalamus section for discussion of acquired hypopituitarism from masses or infiltrative disorders*
b. Be aware that thyroid hormone deficiency may develop during treatment of growth hormone deficiency – **slide 34**
c. Know which drugs may interfere with thyroid function (eg, iodides, lithium, and amiodarone) and the clinical correlates of these drugs in thyroid physiology – **slides 16-21**
d. Be aware that neck irradiation can cause hypothyroidism and thyroid neoplasia – **slide 15**
e. Know that some chromosomal disorders (Down syndrome, Turner syndrome) predispose a patient to the development of autoimmune endocrine diseases – **slide 27**
f. Recognize the importance of iodide deficiency as a cause of hypothyroidism in some parts of the world – **slide 18**
g. Know the frequency and manifestations of thyroid disease in cystinosis – **slide 22**
h. Recognize that iodine excess in topical anti-sepsis therapy (eg, betadine to open umbilical wounds), medications, radiographic dyes, and other forms can inhibit thyroid function – **slides 15-18**

2. Clinical implications

a. Clinical manifestations
1. Be aware of the clinical findings of acquired hypothyroidism including typical impact on growth patterns – **slides 23-24**
2. Recognize the unusual type of sexual precocity which may accompany severe acquired primary hypothyroidism and the pathophysiology of this problem – **slide 25**
3. Recognize the characteristics of the thyroid gland on physical examination or imaging studies in autoimmune acquired hypothyroidism – **slide 26**
4. Be aware of association of the autoimmune acquired hypothyroidism with other autoimmune endocrine diseases, including the autoimmune polyglandular syndromes – **slide 28**
5. Know the clinical significance of the changes in thyroid hormone concentrations that occur during severe illnesses such as euthyroid sick syndrome – **slide 61**
6. Know that clinical features of secondary or tertiary hypothyroidism are milder than primary hypothyroidism – **slide 24**

b. Diagnosis

1. Be aware of the laboratory measurements for documentation of primary hypothyroidism as well as the antibody determinations which will indicate its autoimmune nature – **slide 29**
2. Understand that a substantial fraction of the population has measurable thyroid auto-antibodies, and that if T4, TSH, and thyroid exam are normal, treatment is not indicated for antibody titer alone – **slide 30**

c. Treatment

1. Know the dosage of thyroxine for replacement therapy for acquired hypothyroidism – **slide 31**
2. Know the techniques for monitoring the adequacy of thyroid hormone replacement in primary hypothyroidism and in central hypothyroidism, including the need to delay thyroxine monitoring for at least five half-lives (5 weeks) after dose adjustment – **slide 32**
3. Know the effects of age and size on thyroid hormone replacement dosage in patients with secondary or tertiary hypothyroidism – **slide 32**
4. Be aware of the effects on thyroid function tests of treatment with large doses of thyroxine
--- *large doses of LT4 will result in low TSH and elevated T4 and T3 levels*
5. Know the effects of medication on thyroid function tests – **slides 16-17**
6. Know that thyroid hormone is not indicated as a weight loss drug in individuals with normal thyroid function test results

d. Prognosis

1. Be aware of the effects of the treatment of acquired hypothyroidism on the patient's school performance and be able to counsel parents – **slide 33**
--- *children with profound primary hypothyroidism are often quiet, well-behaved, and docile. After starting a hypothyroid child on levothyroxine, they may "come alive" and be more talkative, less attentive, and have behavioral problems at school*
2. Be aware that delay in the treatment of acquired hypothyroidism and overzealous replacement therapy may have an adverse effect on ultimate height – **slide 33**
3. Be aware of ultimate outcome of acquired hypothyroidism, including impact of the disorder on the patient's growth and mental development – **slide 33**
4. Recognize that treatment of acquired hypothyroidism may be required indefinitely
5. Recognize the occurrence of pseudotumor cerebri in some hypothyroid children treated with thyroxine – **slide 33**

d. Thyroid hormone resistance

1. Pathophysiology

a. Be aware that mutations in the thyroid hormone receptor beta are associated with thyroid hormone resistance – **slide 36**
b. Be aware that the presence of different thyroid hormone receptor types in different tissues produce variable effects of this condition upon different tissues of the body – **slide 37**

2. Clinical implications

a. Clinical findings

1. Be aware of the clinical findings in thyroid hormone resistance, including attention deficit hyperactivity disorder – **slide 38**
b. Diagnosis
1. Be aware of the diagnostic approach to thyroid hormone resistance – **slide 39**
c. Treatment
1. Be aware of the treatments for thyroid hormone resistance – **slide 40**

2. Thyroid hormone excess

a. Neonatal Graves disease

1. Pathophysiology
a. Understand the mechanism of neonatal Graves disease in relation to maternal thyroid disease – **slide 43**

2. Clinical implications
a. Know the clinical presentation of neonatal Graves disease – **slides 44-45**
b. Know the course of neonatal Graves disease – **slide 46**
c. Be aware of the management of neonatal Graves disease – **slide 47**

b. Childhood Graves disease

1. Pathophysiology
a. Know about the autoimmune mechanisms involved in the pathogenesis of Graves disease including the various types of TSH receptor antibodies – **slide 42**
b. Recognize the relationship of Graves disease to other autoimmune diseases of the thyroid with and without hyperthyroidism
---other autoimmune diseases are found in ~9% of individuals with Graves (vs. ~15% in Hashimoto) – for example, rheumatoid arthritis, pernicious anemia, SLE, Addison disease, celiac disease, vitiligo)

2. Clinical implications
a. Clinical manifestations – **slides 48-49**

b. Diagnosis
1. Differentiate between Graves disease and other conditions involving hyperthyroidism – **slide 57**
2. Know the usefulness of the measurement of T4, free T4, and T3 concentrations in hyperthyroidism – **slide 57**
3. Recognize and identify the various forms of nonthyrotoxic hyperthyroxinemia – **slides 55 and 57**
4. Understand that low iodine uptake in the face of negative stimulatory antibodies with high T4, T3, and low TSH may be indicative of a temporary form of hyperthyroidism, such as subacute thyroiditis – **slide 57**
5. Understand that, after the neonatal period, children's serum T3 concentrations exceed those of adults, and that with normal TSH do not indicate hyperthyroidism, and that obese children may have slightly increased serum T3 concentrations --- ***see slide 10 of Thyroid Physiology/CH talk***
6. Understand that the reference ranges for thyroid function tests provided by many laboratories are often specific to adults, and not children --- ***see slide 10 of Thyroid Physiology/CH talk***
7. Understand that a mildly increased TSH concentration with normal T4 and T3 concentrations cannot account for excessive weight gain or other symptoms

---*studies have shown that a moderate elevation of TSH between 4 and 10 occurs in up to 23% of obese children and adolescents. Abnormalities in thyroid function and TSH often normalize after weight loss, suggesting that these biochemical alterations are reversible and treatment is often not necessary. Various theories exist as to why this occurs, and it appears to be most likely due to leptin mediation. In human studies, there are direct correlations between TSH and leptin concentrations in cross sectional studies. Leptin stimulates TSH production by acting through the hypothalamic-pituitary axis (i.e. production of pro-TRH). The elevated TSH seems to be a consequence of obesity rather than the actual cause of obesity.*
8. Understand the usefulness of measuring TSH receptor antibodies and the different tests available – **slide 42**

c. Treatment
1. Understand the medical management of Graves disease with antithyroid drugs, including dosage, monitoring, and side effects – **slide 51**
2. Understand the medical management of Graves disease with antithyroid drugs including pharmacologic actions
--- *inhibits thyroid hormone synthesis by interfering with and blocking the enzyme thyroid peroxidase in thyroid follicular cells; PTU (but not methimazole) can also block conversion of T4 to T3. Methimazole is 10-20 fold more potent than PTU, and methimazole has a longer half-life.*
3. Understand the medical management of Graves disease with antithyroid drugs including indication for seeking alternative treatments – **slide 52**
4. Know how to use beta-blocking agents for immediate control of the symptoms of Graves disease – **slide 50**
5. Know the indications for surgery to treat Graves disease – **slide 54**
6. Know the medical preparation for surgery to treat Graves disease – **slide 54**
7. Know the intra and post-operative complications of surgical treatment of Graves disease – **slide 54**
8. Know the risks of radioactive iodine therapy – **slide 53**
9. Know the indications and use of radioiodine in the treatment of Graves disease – **slide 53**
10. Know the likelihood of remission with medical management and the duration of therapy required for this to occur – **slide 53**

d. Prognosis
1. Understand that stimulatory antibodies may persist for years after treatment in a subset of women with Graves disease, and be unrecognizable if thyroid ablation has occurred, increasing the risk for neonatal hyperthyroidism in their offspring – **slide 53**

c. Hyperthyroidism--other causes

1. Pathophysiology
a. Be aware of the occurrence but rarity of the "hot nodule" as a cause of thyrotoxicity – **slide 55**
b. Be aware of the occurrence of thyrotoxicosis following ingestion of ground beef with a high thyroxine content due to inclusion of neck strap muscles – **slide 55**
c. Be aware of subacute thyroiditis (silent thyroiditis) as a cause of hyperthyroidism and of its clinical cause – **slides 12, 55, and 57**
d. Be aware of activating mutations of the TSH receptor as a cause of familial (autosomal dominant) congenital or acquired hyperthyroidism – **slide 56**

2. Clinical implications
a. Be aware of the biochemical findings in various types of hyperthyroidism – **slide 57**

b. Recognize clinical and laboratory findings suggesting hyperthyroidism – **slide 57**
c. Know the radiographic and MRI findings associated with longstanding primary hyperthyroidism --- *prolonged hyperthyroidism can result in craniosynostosis in infants and young children; bone age advancement; CT and MRI findings in Graves disease allow for characterization of eye disease: exophthalmos, extraocular muscle enlargement, and fatty attenuation*
d. Know the diagnostic evaluation of patients with hyperthyroidism due to TSH excess – **slides 39**

3. Other

a. Thyroid hormone binding protein abnormalities

1. TBG deficiency
a. Be aware of the clinical significance of low total thyroid hormone concentrations due to a low thyroxine-binding globulin (TBG) – **slides 60 and 62**
b. Know the changes in thyroid hormone concentrations in blood which suggest a deficiency of TBG – **slide 62**
--- *free thyroxine index (which is an indirect way of looking at free T4) = total T4 x T3U, with the T3U being roughly equal to 1/TBG. The T3 uptake (T3U) test is a way to diagnose TBG deficiency or excess without directly measuring TBG. Radiolabeled T3 is added to a tube containing the patient's serum and a resin. TBG has a single binding site for both T4 and T3. The radiolabeled T3 binds to the TBG in the patient's serum, and the remaining unbound radiolabeled T3 binds to the resin, which is reported by the lab as the T3 uptake (T3U). In TBG deficiency, the T3U is high. In TBG excess, the T3U is low. The calculated free thyroxine index (like the free T4 level) is normal in both TBG deficiency and in TBG excess.*
c. Know the genetics of TBG deficiency and how to apply the genetics of TBG deficiency when counseling families – **slide 62**
d. Be aware of the impact of nonthyroidal illnesses, which alter protein concentrations, on thyroid hormone binding by proteins such as in nephrosis – **slides 60-61**
e. Know that certain drugs and hormones will alter the concentration of thyroid binding proteins with subsequent impact on laboratory measurements of total thyroid hormones – **slide 60**

2. TBG excess
a. Recognize the characteristic findings on laboratory measurements which suggest increased concentrations of TBG – **slide 63**
b. Know the clinical significance of excess TBG – **slide 63**
c. Know the genetics of TBG excess and how to counsel families – **slide 63**
d. Know the common clinical conditions (e.g., estrogen therapy, oral contraceptives, pregnancy) that will increase TBG concentration – **slide 60**

3. Dysalbuminemia
a. Know the clinical significance of dysalbuminemia and the characteristic laboratory findings – **slide 64**

b. Thyroiditis

1. Acute suppurative
a. Be aware of the clinical and laboratory findings in acute suppurative thyroiditis – **slide 10**
b. Know the appropriate treatment of acute suppurative thyroiditis – **slide 10**

2. Subacute (de Quervain)
a. Pathogenesis
1. Recognize the relationship of subacute (de Quervain) thyroiditis to viral diseases such as mumps – **slide 11**
2. Recognize the rarity of subacute (de Quervain) thyroiditis in children – **slides 9 and 11**
b. Clinical implications
1. Be aware of the clinical picture of subacute (de Quervain) thyroiditis – **slide 11**
2. Understand the natural course of subacute (de Quervain) thyroiditis – **slide 11**
3. Know how to manage subacute (de Quervain) thyroiditis – **slide 11**

3. Subacute (lymphocytic)
a. Be aware that subacute (lymphocytic) thyroiditis may be a cause of transient hyperthyroidism followed by transient hypothyroidism and then by euthyroidism – **slide 12**
b. Be aware of the propensity for transient abnormalities caused by subacute (lymphocytic) thyroiditis to recur in affected individuals – **slide 12**

4. Chronic
a. Be aware of the variable clinical course of chronic thyroiditis including the effects of pregnancy and the postpartum period – **slide 13**

d. Diffuse enlargement

1. Pathophysiology
a. Know that diffuse enlargement of the thyroid is most commonly due to chronic lymphocytic thyroiditis – **slide 13**
b. Be familiar with the mechanisms of diffuse enlargement of the thyroid – **slides 4-5**
c. Be aware of causes of diffuse thyroid enlargement other than chronic lymphocytic thyroiditis – **slide 5**
d. Know that lymphoma and teratoma may rarely involve the thyroid gland – **slide 5**
e. Know that Hodgkin disease and other infiltrative hematologic diseases (eg, histiocytosis) and their treatment may involve the thyroid gland – **slide 5**

2. Clinical implications
a. Be familiar with the clinical methods for diagnosis of diffuse enlargement of the thyroid – **slide 6**
b. Be familiar with the laboratory tests used to evaluate diffuse enlargement of the thyroid – **slide 6**
c. Know the indications for treatment of diffuse thyroid enlargement – **slide 7**