2011 Thyroid Board Review Answers

1. Answer D). This patient presented initially with thyrotoxicosis, which over the next 6 weeks evolves to overt hypothyroidism. Her course suggests that of a destructive thyroiditis. She has positive thyroid peroxidase antibodies (TPO Ab) and a family history of hypothyroidism. The most likely diagnosis in this case is painless or silent thyroiditis. Patients with this disorder typically have positive TPO Ab, and the disorder is closely linked to postpartum thyroiditis. Occasionally hypothyroidism persists, but most return to euthyroidism. The patient did not have clinical stigmata of subacute thyroiditis, such as anterior neck pain, malaise, or a recent upper respiratory illness (option A). Patients with Graves’ disease occasionally present with fluctuating thyroid function due to changes in stimulating or blocking antibodies (option B), but the time course of 6 weeks is relatively short for such as change in this patient. Acute thyroiditis (option C) and thyroid abscess present with fever, pain and fluctuance over the affected thyroid lobe. The abrupt change in thyroid function does not occur in patients with toxic multinodular goiter (option E).

2. Answer E). Incidental thyroid uptake on PET scanning has been the subject of multiple case reports and small series. Focal nodular uptake has a higher risk of malignancy than nodules without PET uptake in some studies, yet diffuse uptake, as in the current case is more typical of generalized thyroid abnormalities such as Hashimoto’s thyroiditis. As summarized nicely by Katz and Shaha, approximately 3% of PET-scans show incidental thyroid uptake; this uptake is focal in approximately 40% and diffuse in approximately 60%. When subjected to further investigation such as thyroid FNA or thyroidectomy 14-47% of patients with focal or unilateral uptake have a thyroid malignancy, compared to 1.4-12% in patients with diffuse PET uptake in the thyroid.

References:


3. Answer C). Oral estrogen therapy results in elevation of the principal thyroid hormone binding protein, thyroxine-binding globulin (TBG), but transdermal estrogen appears to have little to no effect on TBG. It may be surprising that an increase in TBG in a hypothyroid patient should lead to an increased levothyroxine dose requirement. It would make physiological sense for disassociation to occur until the free T4 level and TSH were normal, but it appears that there is an obligatory binding of T4 to TBG, even at the expense of serum free T4 levels in the face of hypothyroidism.
4. Answer E). The CT scan shows a substernal goiter without mass effect on the trachea. The patient is asymptomatic, however, a positive Pemberton’s sign, which is pronounced facial flushing and distension of superficial veins in the head and neck when keeping the arms raised above the head, suggesting a positional occlusion of great vessels at the thoracic inlet would indicate significant obstructive defect that if coupled with rapid expansion due to nodule hemorrhage could prove critical. The remaining options are relatively commonplace and do not in of themselves warrant thyroidectomy in this octogenarian with comorbidity. Since most substernal goiters represent multinodular goiter, it is expected that there will be nodules inaccessible to fine needle aspiration, or nodules that appear hypofunctional on radioisotope imaging, which in general is hampered by the substernal location. Thyroglobulin elevation to this degree is not predictive of cancer in a patient with a nodular goiter.

5. Answer B). In the setting of familial medullary thyroid cancer (MTC), C-cell hyperplasia (CCH) is considered a premalignant condition. A more common occurrence is secondary CCH, which occurs in a variety of circumstances such as chronic lymphocytic thyroiditis (Hashimoto’s thyroiditis), hypergastrinemia, hyperparathyroidism, adjacent to follicular-derived tumors, and with aging. The absent family history of thyroid cancer in this patient in addition to the negative RET protooncogene testing is reassuring, making secondary CCH more likely.

References:

6. Answer C). AJCC-7 staging for this patient first takes into account that she is ≥ age 45. If she were less than age 45, she could only be stage I or II. Her thyroid cancer is 3.5 cm, which by size would be a T2 lesion but since there is also microscopic invasion through the thyroid capsule, the tumor is a T3 lesion. Next you see that she has lymph nodes outside of the central compartment, making her lymph node status N1b and therefore, since she has no indication of distant metastases on post-treatment scan, her TNM status...
is T3N1bM0. Her staging is stage IVA, due to the lymph node status N1b (had her involved lymph nodes been confined to the central compartment, her staging would have been stage III).

7. Answer A). The correct answer to this question is best arrived at by exclusion of the nodules with benign ultrasound appearances. The nodule in B is a simple cyst. The nodule in C has a spongiform appearance, which has been shown to be very low risk for malignancy. The nodule in D is hyperechoic relative to the surrounding thyroid parenchyma, making it most likely a benign lesion. That leaves the nodule shown in A. This nodule has somewhat irregular borders, but also has the “taller than wide” feature in the transverse view shown, which is an independent predictor of malignancy.

8. Answer D). This patient has thymic hyperplasia concomitant with Graves’ disease. There have been multiple case reports and small series regarding similar patients, including unfortunately some who underwent thymectomy by median sternotomy, for what is in fact a benign and reversible disorder. Since anatomic distinction of hyperplasia from a thymoma is difficult using cross-sectional imaging, it is important that patients with apparent hyperplasia have follow-up imaging to show resolution as the Graves’ disease is treated.

References:


9. Answer D). The photograph shows a patient with onycholysis, which results from a separation of the fingernail (or toenail) from the nailbed. It can occur in thyrotoxicosis from any cause. The differential diagnosis includes psoriasis, trauma, and fungal infection.

10. Answer A). This patient has nephrotic syndrome as an explanation for the progressive increase in levothyroxine dose, due largely to loss of thyroid binding proteins (with thyroid hormone attached) in the urine. Clues to this etiology include her lower extremity edema on examination, low albumin, and high lipid levels. This case and similar cases have been reported in the literature. In cases of reversible nephrotic syndrome, levothyroxine dose requirements return to baseline as the proteinuria resolves.
Reference:


11. Answer A). A low thyroglobulin level (provided thyroglobulin antibodies are negative) is the most specific test for surreptitious thyroid hormone ingestion among those listed. A low RAIU can also be seen with various forms of thyroiditis, as can a low or normal vascular flow pattern on Doppler ultrasound. An elevated T3 with normal T4 can be seen with T3 thyrotoxicosis, as is seen in some patients with nodular thyroid disease and thyrotoxicosis or in areas of iodine deficiency. A negative TSH-receptor antibody test does not exclude non-Graves' forms of thyrotoxicosis, and patients with mild Graves' disease may have high-normal, rather than elevated values with this test.

References:


12. Answer E). This patient is being treated with antithyroid drugs during pregnancy. The goal of therapy for these patients is to keep the TSH slightly suppressed and the free T4 at the upper limit of normal (subclinical hyperthyroidism). The rationale behind this goal is to minimize fetal exposure to the effects of antithyroid drugs which can cause fetal goiter and fetal hypothyroidism. In light of this goal, the remaining options are not appropriate.

Reference:


13. Answer B). This patient is admitted to the ICU for urosepsis and would be expected to have classic changes in thyroid hormone levels that occur as a result of an acute nonthyroidal illness (NTI) of this severity. The most prevalent and pronounced change of thyroid function during NTI is a depression in the serum total and free T3 levels and a concurrent elevation in reverse T3. A low T3, present in 70% or more of hospitalized patients, may be considered, with a few notable exceptions, the sine qua non of the euthyroid sick syndrome. Total T4 is frequently low in patients with severe NTI and a very low T4 portends a poor prognosis. Free T4 generally remains in the normal range. TSH is frequently normal, but may be slightly suppressed or elevated, particularly during the recovery stages (but generally < 20
mIU.L). Using the process of elimination, only options A, B, and D have a low T3, and only B and D have an elevated rT3. Option D is eliminated due to the high total T4 and free T4.

Reference:


14. Answer A). Xerostomia is a relatively common sequelae of high dose radioactive iodine therapy, and is frequently reversible. Approximately 4-5% of patients with have persistent xerostomia which predisposes them to excessive caries. One study showed a 40% reduction in parotid gland function following doses of 270 mCi $^{131}$I. The use of sialogogues following radioiodine therapy in order to increase clearance of isotope from the salivary glands was found in an early article to actually increase the rate of xerostomia, but a recent well-performed study showed that lemon drops given several times daily do in fact reduce salivary gland exposure to radioiodine. The other options are much less likely. Specifically, an alteration of taste, which occurs commonly after radioiodine therapy, is typically transient rather than permanent. Patients may complain of a metallic or chemical taste, which may occasionally persist for months after therapy. Permanent hypoparathyroidism is a very rare consequence of radioiodine therapy, with only 2 cases described in the literature to date. Transient depression of sperm counts occurs following radioiodine, and a cumulative effect on the testes occurs, manifested as an elevation in serum FSH and slight decreases in sperm count, but not azospermia. It is recommended that men desiring future fertility and receiving radioiodine doses of $> 400$ mCi utilize sperm cryopreservation. Leukemia is a potential consequence of receiving very high doses of radioiodine with a frequency of 0.3%, typically occurring in older patients receiving a cumulative dose of $> 800$ mCi. Patients who received the highest doses over the shortest intervals were the ones most likely to develop this rare complication, with a latency period of $< 10$ years. Ideally patients requiring repeated treatments with radioiodine should receive this at intervals of at least one year, but patients with aggressive radioiodine-avid disease should not be denied therapy at shorter intervals when appropriate.

References:


15. Answer A). This patient has malignant struma ovarii with evidence of metastatic disease. She should be treated in the same manner as any other patient with metastatic thyroid cancer; namely, removal of both the tumor and normal thyroid tissue followed by radioiodine therapy. In a recent review of 24 cases of malignant struma ovarii, 16 patients were followed conservatively postoperatively while 8 received varied additional therapy (4 received $^{131}$I). There were 8 recurrences and all occurred in the conservatively managed patients. $^{131}$I for recurrent disease provided an initial complete response in 7 women with recurrent disease. Struma ovarii generally presents as a pelvic mass, but may present with thyrotoxicosis in up to 10% of cases. Occasionally patients with previously treated Graves’ disease have stimulation of the ectopic ovarian tissue by persistent TSH-receptor antibodies. Approximately one third of struma ovarii cases have histological evidence of malignancy, such as nuclear features of papillary thyroid cancer, and of these, approximately 5% have metastatic disease. The remaining options are incorrect. High dose radioiodine would be taken up largely by the normal thyroid gland. Suppressive therapy with thyroid hormone is insufficient in this circumstance, and more aggressive chemotherapy is not warranted.

References:

b. DeSimone CP, Lele SM, Modesitt SC. Malignant struma ovarii: a case report and analysis of cases reported in the literature with focus on survival and $^{131}$I therapy. Gynecol Oncol. 2003 Jun;89(3):543-8.

16. Answer A). Absorption of levothyroxine (LT4) occurs in the small intestine. Patients with short bowels due to surgery or extensive small bowel disease malabsorb LT4. One study of 5 patients with surgically shortened small bowels, who had previously undergone removal of portions of jejunum and ileum, found diminished LT4 absorption in each patient, despite the presence of an intact duodenum. Another study demonstrated an increased dose requirement to as high as 600 mcg daily in a patient following a jejunoileal bypass procedure, with a diminished requirement following surgical reversal. It is likely therefore that the distal small bowel is the most important site for absorption of LT4. The patient in this question needs a higher dose of LT4. The remaining options ignore the basic problem of malabsorption (B,C,and D) or are unnecessarily aggressive (E).

References:

17. Answer E). This infant has a father with a clinical syndrome consistent with MEN 2B, which includes the most aggressive form of medullary thyroid cancer. Due to the complete penetration of MTC in this syndrome and the propensity for early metastases, it is recommended that infants in MEN 2B families who test positive for a RET protooncogene mutation undergo thyroidectomy in an experienced tertiary care setting as soon as feasible in the first year of life. However, since approximately 50% of MEN2B patients have a de novo germline mutation (i.e. they are the first affected member in their family), this syndrome is frequently not recognized in the first year of life.

Reference:


18. Answer B). Resistance to thyroid hormone is inherited in an autosomal dominant pattern. Statistically speaking, one half of this mother’s offspring will have the disorder and the other half will be unaffected. Since the mother’s thyroid hormone levels are chronically elevated, an unaffected fetus is exposed to high thyroid hormone levels, to which it is sensitive. Conversely, a fetus with the gene for thyroid hormone resistance will be insensitive or resistant to the high thyroid hormone levels crossing the placenta, and will have a lower risk of miscarriage. Tachycardia is a common manifestation of THR and will not distinguish an affected from unaffected fetus. It has been postulated that cardiac sensitivity to thyroid hormone is dependent more on TRα than TRβ, and in addition, there may be tissue-specific differences in the relative expression of wild type and mutant TRβ, accounting for the apparent cardiac sensitivity to thyroid hormone in patients with THR.

References:


19. Answer D). Familial dysalbuminemic hyperthyroxinemia (FDH) is the most common cause of inherited hyperthyroxinemia in Caucasians. Patients with FDH are generally overlooked these
days with the widespread measurement of TSH alone or in conjunction with free T4. The disorder is the result of mutations in the albumin gene that greatly increase the affinity of albumin for T4 but generally not T3. As a result, reliance on the total T4 (elevated) or a free thyroxine index (also elevated, since this is the product of a normal T3RU and an elevated T4) may be misleading. A defect in 5'-monodeiodination due to selenium deficiency is much less common than FDH. This is not a TSH-adenoma given the familial pattern and the fact that the patient is clinically euthyroid. This is not familial TBG excess or thyroid hormone resistance, since the total T3 is normal rather than elevated; an elevated total T3 would be expected in each of these disorders.

Reference:


20. Answer A). This vignette provides a classic description for thyroid lymphoma—a rapidly growing goiter in an elderly woman with a history of Hashimoto’s thyroiditis. Initial fine needle aspiration may be suggestive of lymphoma, but frequently a repeat aspiration with flow-cytometry or open biopsy is needed for confirmation. Encircling of the trachea by a thyroid lymphoma on cross-sectional imaging is referred to as the “donut” sign. The remaining choices are less likely in this clinical scenario. Anaplastic thyroid cancer presents with a discrete invasive mass rather than diffuse thyroid enlargement. Metastatic breast cancer would appear as discrete thyroid masses, and the rapid growth is not suggestive of benign adenomatous hyperplasia. Sclerosing or Reidel’s thyroiditis is very uncommon and presents as a fixed, wood-hard thyroid mass.

References:


21. Answer E). This patient has a fairly typical presentation for Riedel’s thyroiditis, which is a rare fibrotic disease of the thyroid also known as invasive fibrous thyroiditis. In a series of Riedel’s patients seen at the Mayo Clinic, 32% presented initially with hypothyroidism, 4%
with destructive hyperthyroidism, and 64% were euthyroid. Women are four times more likely than men to be affected, and most the disorder occurs most commonly between 30 and 50 years of age. Approximately one third of Riedel’s patients develop extracervical manifestations of multifocal fibrosclerosis, including retroperitoneal fibrosis, mediastinal fibrosis, and sclerosing cholangitis. Tamoxifen has been found beneficial in treating desmoid tumors, retroperitoneal fibrosis, and more recently, Riedel’s thyroiditis. The mechanism of action is unclear in this circumstance, but may relate to inhibition of cytokine-mediated fibrosis. Surgery is sometimes used to treat respiratory compromise, but generally a limited procedure is utilized in order to minimize damage to adjacent tissues. Chemotherapy with adriamycin, radiation therapy, and radioiodine therapy are not indicated to treat Riedel’s thyroiditis.

References:


22. Answer D). Inadvertent exposure to radioiodine during pregnancy is a dreaded event with potentially devastating consequences. Every effort should be made to avoid this circumstance utilizing a combination of careful history, patient education, and laboratory testing to exclude pregnancy prior to the administration of radioiodine. The nature of the detrimental effects is determined by the timing and dose of the fetal exposure. Exposure during the first 2 weeks of gestation, as in this patient, is more likely to lead to miscarriage than fetal malformations. Later, during the period of organogenesis at 2-7 weeks gestation, exposure to 5-50 rads leads to a slight increased risk of malformations, and higher exposures lead to a substantial increased risk of major malformations. During the period of fetal thyroid development (10-12 weeks gestation), exposure to 5-50 rads leads to depressed or absent thyroid function at birth and doses > 50 rads lead to complete fetal thyroid ablation. Exposure at this stage leads to the detrimental effects associated with congenital hypothyroidism including impaired neurological development and mental retardation, intrauterine growth retardation. Induction of malignancy is also a concern after radioiodine exposure in utero.

References:


23. **Answer B**). This patient likely has a disorder of organification, due to an inherited defect in thyroid peroxidase as the source of familial goiter. Dietary goitrogens such as those present in the cassava plant roots and in yellow turnips and cabbage do not generally lead to clinically apparent goiters in regions of iodine sufficiency, but may augment the effect of iodine insufficiency on thyroid size in regions of endemic iodine deficiency. The most common cause of a euthyroid diffuse (non-nodular) goiter in the North America is Hashimoto’s thyroiditis (worldwide the most common cause of goiter is still iodine deficiency). However, this patient has negative thyroid peroxidase antibodies, which has only rarely been described in patients with histologically proven Hashimoto’s thyroiditis, and the thyroid echotexture is homogeneous rather than heterogeneous as would occur with Hashimoto’s thyroiditis. Pendred’s syndrome is characterized by deafness and goiter due to mutations in the pendrin protein, which controls apical iodine uptake in thyrocytes; this patient does not fit this syndrome. Resistance to thyroid hormone would be associated with elevated rather than normal thyroid hormone levels.

**References:**


24. **Answer B**). Minocycline is the classic cause of a “black thyroid.” The mechanism is believed to be oxidation of the drug by thyroid peroxidase. Other causes of thyroid discoloration include hemochromatosis, ochronosis, and bruising (such as after a seat belt injury).

**References:**


25. **Answer C**). Type 3 deiodinase is an inactivating enzyme located in the placenta and brain. This enzyme inactivates T4 to reverse T3 and to 3, 3’-T2, and likely serves a major role in modulating the thyroid hormone status of the early fetus. Conversely, both D1 and D2 are activating enzymes, converting T4 to T3. Ectopic or paraneoplastic expression of type 3 deiodinase has been described in hepatocellular carcinoma, and recently in patients with hepatic hemangioblastomas. Patients with paraneoplastic synthesis of this enzyme require very large amounts of exogenous T4 and T3 to keep up with the enhanced deactivation occurring...
through tumor expression of type 3 deiodinase. This process has been referred to as “consumptive hypothyroidism.”

References:


26. Answer C). The rationale for completion thyroidectomy is to remove additional foci of tumor and to allow radiiodine remnant ablation (RRA) when appropriate. Current guidelines of the American Thyroid Association for the management of thyroid cancer suggest that patients with a finding of medullary thyroid cancer (MTC) at the time of a lobectomy, who are RET negative with no adenopathy, no family history of MTC, and a normal level of calcitonin, may be managed with observation alone. Likewise, patients with follicular thyroid cancer and capsular invasion alone, without vascular invasion have no increased mortality due to disease and may generally be managed without RRA. Patients with papillary thyroid cancer who have unifocal tumors less than 1 cm in size do not need RRA, whereas those patients aged 45 years or older with larger tumors are expected to have a reduction in the risk of recurrence and death with the use of RRA.

References:


27. Answer E). The association between overt hypothyroidism and hyperlipidemia is well known. More controversial is the association between subclinical hypothyroidism and enhanced cardiovascular risk or the presence of coronary artery disease. No intervention trial has demonstrated a consistent improvement in sense of well being or energy level, weight reduction or improvement in cardiovascular risk with treatment of subclinical hypothyroidism. Although recent studies have identified an association between mild TSH elevation and thyroid
cancer in patients being evaluated for thyroid nodules, there is no evidence that treatment with thyroid hormone affects this association. Whereas substantial improvement in lipids is seen with correction of overt hypothyroidism, the results with treatment of subclinical hypothyroidism are less impressive. A meta-analysis including 13 published studies in this area found a mean LDL decrease of 10 mg/dL, but no significant change in HDL or triglycerides values overall with correction of subclinical hypothyroidism.

References:

a. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, Franklyn JA, Hershman JM, Burman KD, Denke MA, Gorman C, Cooper RS, Weissman NJ. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA. 2004 Jan 14;291(2):228-38.


28. Answer B). This question involves recognition of various cytology patterns and synthesis with current clinical guidelines regarding management of thyroid nodules suspected preoperatively as being thyroid cancer. The picture labeled “B” has the appearance of papillary thyroid cancer, with a papillary frond of cells showing nuclear crowding and nuclear clearing, known as Orphan Annie eyes. Picture “A” shows a colloid nodule; “C” shows follicular neoplasm (hypercellular, microfollicle formation with minimal colloid), and “D” shows numerous polyclonal lymphocytes consistent with lymphocytic thyroiditis. A near-total thyroidectomy would generally be performed for a 3 cm papillary thyroid cancer, and a lobectomy would be generally performed after an FNA finding of follicular neoplasm.

29. Answer C). This pregnant woman’s fetus has a large goiter and advanced hypothyroidism. The goiter increases the risk for fetal asphyxia at the time of birth and fetal hypothyroidism increases the risk of developmental abnormalities. A treatment for fetal hypothyroidism and associated goiter is intraamniotic administration of thyroid hormone. Typical doses in the literature include 150-300 micrograms of levothyroxine injected into the amniotic fluid on 2-4 occasions. Both cord blood sampling and intraamniotic levothyroxine therapy pose a risk of pregnancy loss, so a careful consideration and discussion of benefits versus risks is required.

References:


30. Answer A). TSH-receptor antibody testing will reveal Graves’ disease. The thyroid scan in the picture shows unilateral increased uptake on the right and no uptake on the left. This finding can be due to either a hot nodule with suppression of the contralateral lobe or due to thyroid hemiagenesis with a superimposed Graves’ disease. The ultrasound demonstrates an intact right lobe and an absent left lobe, clinching the diagnosis. The positive family history of autoimmune thyroid disease was given as a hint. T3-suppression testing is not used due to the risk of aggravating thyrotoxicosis (as would administration of rhTSH), and would not help with the distinction of a hot nodule from unilateral Graves’ disease. A CT scan with contrast could also aggravate the thyrotoxicosis. Thyroid FNA is not necessary and there is nothing to biopsy on the left!

References: