003

Chapter 1

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Endocrinolog & Metabolism

Abnormal thyroid function Abnormal thyroid function tests Test
Possible cause
High TSH + low free T4
Primary hypothyroidism Low TSH + elevated free T4 and free T3 Primary hyperthyroidism
Low or normal TSH + low T4 Secondary hypothyroidism Low TSH and normal free T4 T3 toxicosis (approximately 5% of thyrotoxicosis) Low TSH and normal free T4 and free T3 • Subclinical hyperthyroidism
• Recovery from thyrotoxicosis
• Excess thyroxine replacement
• Non-thyroidal illness
High TSH and high free T4 and free T3 • TSH-secreting pituitary tumour (2ry poor compliance) High TSH and Normal free T4 • Poor compliance with thyroxine • Subclinical hypothyroidism High free T4 and low normal free T3, normal TSH Low or normal TSH and low normal free T4 and free T3 • Non-thyroidal illness
• Central hypothyroidism
• Isolated TSH deficiency Normal TSH and low free T4 • Steroid therapy Low TSH and low free T4 • Sick euthyroid syndrome (non-thyroidal illness)

_Post-partum thyroiditis Definition
• thyroid dysfunction occurring within the first 6 months after delivery. Course of disease

• Hyperthyroid status followed by a hypothyroid phase at three to six months, followed by spontaneous recovery in one third of cases. In the remaining two-thirds, a single-phase pattern or the reverse occurs. Features • characteristic sequence of three phases: hyperthyroidism, followed by hypothyroidism, and then recovery Pathophysiology
• The exact aetiology is unknown but lymphocytic infiltration of the thyroid is typical, suggesting auto-immunity. Prevalence • occurs in approximately 5-7% of females
Risk factors • Common in whom thyroid peroxidase (TPO) antibodies were positive prior to delivery
• twice common in patients with type 1 diabetes mellitus. Notes & Notes for MRCP

hyperthyroidism) • Thyroid hormone resistance
• Heterophile antibodies, leading to spurious measurements of free T4 and free T3
• Thyroxine replacement therapy (including • Amiodarone

Investigations • Thyroid peroxidase (TPO) antibodies are found in 90% of patients Management • the thyrotoxic phase is not usually treated with anti-thyroid drugs as the thyroid is not overactive. Symptomatic treatment using beta-blockers for relief of tremor or anxiety. Propranolol is typically used for symptom control • the hypothyroid phase is usually treated with thyroxine withdrawal period after 6 months to measure recovery of thyroid function. Stop thyroxine and reassess thyroid function in approximately one month. Prognosis • Recurrence of thyroiditis is common in subsequent pregnancies
• in up to 40% permanent hypothyroidism develops.

Subacute (De Quervain's) thyroiditis

Basics • Subacute thyroiditis also known as De Quervain's thyroiditis and subacute granulomatous thyroiditis
• It is associated with HLA-B35

Pathophysiology • Occur after viral infection
• thyroid inflammation drives increased release of stored thyroid hormone, rather than the clinical picture being due to overproduction of T3 and T4.
Features Tender goitre, hyperthyroidism and raised ESR + globally reduced uptake on technetium thyroid scan is typical (De Quervian) • typically presents with hyperthyroidism symptoms triphasic course of transient thyrotoxicosis, followed by hypothyroidism, followed by a return to euthyroidism.
 The thyrotoxic phase is due to thyroid follicular damage and release of preformed hormone • painful goitre,
 The thyroid enlargement is typically rapid, occurring over a period of days. The thyroid gland will be firm, enlarged bilaterally or unilaterally due to extravasation of colloid from the follicles causing a granulomatous reaction.
• raised temperature (e.g. flu-like symptoms)

Investigations • Hyperthyroidism
 As the condition resolves patients become hypothyroid and then euthyroid.
• raised ESR (>50 and usually 100) , elevated CRP. • Thyroid ultrasound: shows
 areas of hypoechoic echotexture
 decreased or normal vascular flow by Doppler. Thyrotoxicosis with tender goitre = Subacute thyroiditis (De Quervain's thyroiditis)

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• thyroid scintigraphy: globally reduced uptake on iodine-131 scan the most helpful investigation in establishing the diagnosis Radioactive iodine uptake scan Radioiodine uptake is typically less than 1% at 24 hours (Tc 99m uptake is similarly low).

Management • usually self-limiting - most patients do not require treatment • symptomatic control.
 Symptoms of hyperthyroidism: should be managed with beta blockade as required,
 no role for thionamides. thyroid pain may respond to aspirin or other NSAIDs • steroids (Prednisolone)
 in more severe cases, particularly if hypothyroidism develops Prognosis • The hypothyroidism is usually mild but persists for 2 - 4 months.
• return to normal thyroid function in >90% of patients • A few patients (~5%) remain hypothyroid and need long-term thyroid hormone replacement.
• Recurrences are uncommon.

Subclinical hyperthyroidism

Definition
• normal serum free thyroxine and triiodothyronine levels • with a thyroid stimulating hormone (TSH) below normal range (usually < 0.1 mu/l) Causes • usually occurs in the setting of thyroid overactivity due to Graves' disease or autonomously functioning thyroid nodules sufficient to suppress pituitary TSH secretion but insufficient to cause an elevation of circulating hormones.
• multinodular goitre, particularly in elderly females • excessive thyroxine may give a similar biochemical picture Complications • Cardiovascular (atrial fibrillation)
• Bone metabolism (osteoporosis) • impact on quality of life • increase the likelihood of dementia Patient with subclinical hyperthyroidism with measurable TSH and no features of exogenous thyroid dysfunction can be managed conservatively Subclinical hyperthyroidism: normal FT4 and FT3 with a suppressed TSH level with nonspecific symptoms In De Quervain’s thyroiditis, treatment is aimed at reducing inflammation with NSAIDS or steroids in severe cases (e.g. prednisolone 20–40 mg/day for two weeks and titrated down). T3 levels should be performed where tests show normal T4 with suppressed TSH

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Management • Observation Repeat measurement of TSH (with serum FT4 and FT3) TSH levels often revert to normal - therefore levels must be persistently low to warrant intervention • therapeutic trial of low-dose antithyroid agents for approximately 6 months in an effort to induce a remission • indication for definitive therapy: presence of an unmeasurable TSH (sustained TSH suppression (<0.1 mU/l)) and/or
 exogenous thyroid dysfunction symptoms of hyperthyroidism,
 osteoporosis a DEXA scan is appropriate next line management to quantify the osteoporosis

risk and inform the decision as to whether or not to treat the sub-clinical hyperthyroidism. atrial fibrillation, or
 unexplained weight loss The American Association of Clinical Endocrinologists recommends that treatment is considered in patients with a persistently low TSH level if they are older than 65 years or are at risk of osteoporosis or heart disease. Prognosis
• Progression to overt hyperthyroidism occurs in 1-3 % of elderly patients per year.

Thyrotoxicosis

Causes • Graves' disease (50-60% of cases of thyrotoxicosis) • Toxic nodular goitre • Toxic adenoma (Plummer's disease) • Thyroiditis Subacute granulomatous thyroiditis (de Quervain thyroiditis) Subacute lymphocytic thyroiditis (e.g., postpartum thyroiditis) • Acute phase of Hashimoto's thyroiditis (Hashitoxicosis): later results in hypothyroidism.

1. Transient thyrotoxicosis in patients with early Hashimoto's disease resulting from the initial destruction of the thyroid gland and subsequent release of thyroid hormones.
2. Positive thyroid peroxidase antibodies and negative TSH receptor antibody • Amiodarone therapy • β-hCG-mediated hyperthyroidism (hydatidiform mole, choriocarcinoma) • Secondary thyrotoxicosis : thyrotoxic with an abnormally 'normal' TSH.
   TSH-producing pituitary adenoma Ectopic TSH (e.g. struma ovarii, ovarian teratomas can produce exogenous TSH causes secondary hyperthyroidism. can be visualized with a pelvic ultrasound or abdominal CT.) Negative neck ultrasound and neck exam in the setting of hyperthyroidism and low radioiodine uptake.

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• Factitious hyperthyroidism: Exogenous thyrotoxicosis, diagnosed by:
 Undetectable thyroglobulin (a precursor of thyroid hormones, indicates an external source of thyroid hormone)
 Radioactive uptake thyroid scan
 endogenous causes of thyrotoxicosis → increased radioactive uptake In thyrotoxicosis factitia, uptake is globally reduced. • T3 thyrotoxicosis
 associated with 5% of cases of thyrotoxicosis.
 suppressed TSH , low or normal T4 and fT4, high fT3

• Excess iodine ingestion Kelp is a very rich source of iodine. Treatment is withdrawal of the kelp with monitoring of thyroid function. Iodine excess • Jod-Basedow phenomenon:
 Hyperthyroidism following iodine excess (e.g., after IV contrast administration, due to intake of amiodarone or other iodine-containing drugs, etc.) Mechanism: occurs due to either overactivation of the entire thyroid gland or, more commonly, autonomous nodules within the gland after iodine repletion without adequate feedback control from the pituitary gland. • Wolff-Chaikoff effect Hypothyroidism following iodine excess (opposite effect to Jod-Basedow phenomenon) Mechanism: excess iodine inhibits thyroid peroxidase → decreases T3/T4

production

Thyrotoxicosis factitia (thyroxin abuse): The combination of low thyroglobulin, decreased uptake on scintigraphy and raised T4

Feature • General
 Heat intolerance Excessive sweating because of increased cutaneous blood flow Weight loss despite increased appetite Frequent bowel movements (because of intestinal hypermotility) Weakness, fatigue Onycholysis: a separation of the nail from the nail bed. Infiltrative dermopathy, especially in the pretibial area (pretibial myxedema) • Goiter: Diffuse, smooth, nontender goiter; often audible bruit
• Eyes Lid lag: caused by adrenergic overactivity, which results in spasming of the smooth muscle of the levator palpebrae superioris Lid retraction: “staring look” Lid retraction and lag are signs of sympathetic overactivity, and occur in any thyrotoxic state (thyroxine potentiates the action of catecholamines). Graves ophthalmopathy (exophthalmos, edema of the periorbital tissue) T3 thyrotoxicosis should always be considered in patients with suppressed TSH and normal T4 levels, especially when patients are symptomatic.

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• Decreased libido
• Cardiovascular Palpitations, tachycardia , irregular pulse (due to atrial fibrillation/ectopic beats) caused by increased beta-adrenergic tone.
 Atrial fibrillation (AF) occurs in 10% to 25% of patients with hyperthyroidism Hypertension with widened pulse pressure Systolic pressure is increased due to increased heart rate and cardiac output. Diastolic pressure is decreased due to decreased peripheral vascular resistance.
• Endocrinological Female: oligo/amenorrhoea, anovulatory infertility, dysfunctional uterine bleeding
 Male: gynecomastia, decreased libido, infertility, erectile dysfunction • Musculoskeletal Fine tremor of the outstretched fingers Hyperthyroid myopathy: Typically affects proximal muscles (e.g., hip flexors, quadriceps) more than distal muscles. Serum creatine kinase levels are most often normal Osteopathy: osteoporosis due to the direct effect of T3 on osteoclastic bone resorption • Neuropsychiatric Anxiety, Restlessness, Insomnia Hyperreflexia

Investigations • Thyroid function tests: low TSH, plus high T4 and T3. The most sensitive test to diagnosis hyperthyroidism is TSH level (initial screening test). In primary hyperthyroidism the TSH should always be suppressed by negative feedback Non-suppressed (TSH) suggests → excessive TSH production by the pituitary gland → the possibility of a thyrotroph adenoma → do MRI scan pituitary gland T3 is more sensitive because occasional cases of isolated T3 toxicosis can occur. • TSH receptor antibody (TRAb): for suspected Graves disease without characteristic features
• Thyroid ultrasound with Doppler first-line for pregnant/lactating patients, palpable nodules or suspected thyroiditis Increased perfusion: either diffuse (Graves’ disease, toxic adenoma) or nodular (toxic MNG) Decreased perfusion: destructive causes of hyperthyroidism (e.g., subacute thyroiditis or postpartum destructive thyroiditis) • Thyroid scintigraphy: Radioactive iodine uptake

measurement (RAIU test) first-line for most patients with uncertain diagnoses, e.g., suspected thyroid adenoma or toxic MNG Assess functional status of thyroid nodules Hot nodule: Hyperfunctioning tissue takes up large amounts of radioactive iodine
 Cold nodule: Non-functioning nodules do not take up any radioactive iodine and appear "cold", but the surrounding normal thyroid tissue takes up radioactive iodine and appears "warm" Identify ectopic thyroid tissue Contraindications: pregnant or breastfeeding women

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• General laboratory findings
 Serum glucose levels typically increase in patients with hyperthyroidism. Hypocholesterolemia due to increased LDL receptor expression. Serum cholesterol: decreased total cholesterol, LDL, and HDL CBC in thyrotoxic Graves' disease is most likely to show: Mild leukopenia with relative lymphocytosis (mild neutropenia and lymphocytosis)
 Normochromic anaemia
 Rarely, thrombocytopenia. High bone turnover and osteoporosis may be associated with thyrotoxicosis. Bone turnover involves increased osteoclastic and osteoblastic activity, leading to elevated alkaline phosphatase levels derived from bone. Increased levels of sex hormone-binding globulin (SHBG)

Which blood tests is most sensitive in establishing whether there is excess thyroid activity? • Free T3 level Management • Treatment of hyperadrenergic symptoms: beta blockers (first line) Propranolol is effective in controlling all symptoms prior to initiation of specific therapy (e.g. carbimazole, which will have a more delayed effect on symptoms). If there are contraindications to beta blockers, e.g., severe asthma, Raynaud phenomenon , consider CCBs: verapamil OR diltiazem • Antithyroid drugs (ATDs) Most patients: methimazole
 Thyroid storm or first trimester of pregnancy: propylthiouracil Duration of therapy for Graves' disease: typically 12–18 months Contraindications to ATDs, e.g., liver disease • Radioactive iodine ablation (RAIA) destruction of thyroid tissue via radioactive iodine (iodine-131) Indicated for Toxic MNG, toxic adenoma and failure of antithyroid drugs (ATDs) in Graves disease.
 Contraindicated in pregnant/breastfeeding women and moderate to severe Graves ophthalmopathy. • Thyroid surgery The efficacy of antithyroid drugs and RAIA has reduced the need for thyroid surgery. Indications: Large goiters (≥ 80 g) or obstructive symptoms, suspected thyroid malignancy and Graves ophthalmopathy.

Secondary thyrotoxicosis:
• Thyrotoxic with an abnormally 'normal' TSH.
• Pituitary adenoma
• Prior to pituitary surgery → restoration of euthyroidism with somatostatin analogues.

In acute thyrotoxicosis, stop aspirin as it can worsen the storm by displacing T4 from thyroid binding globulin Thyrotoxicosis is associated with reversible cardiomyopathy

Management of thyrotoxicosis in pregnancy
Suspect a molar pregnancy or choriocarcinoma if severe hyperthyroidism manifests during pregnancy

Transient thyrotoxicosis and/or hyperemesis gravidarum
• Supportive therapy • Management of dehydration, and hospitalization if needed.
• Anti-thyroid drugs (ATDs) are not recommended, though β-blockers may be considered.

• Early pregnancy (1st trimester) → Propylthiouracil (PTU) Due to the small risk of fetal abnormalities with carbimazole it is recommended to use PTU in the first trimester during organogenesis and then carbimazole in trimester 2 + 3. Propylthiouracil (PTU) is highly protein bound making it less likely to cross the placenta or breast milk.
 Carbimazole has rarely been associated with aplasia cutis of the neonate • Late pregnancy (2nd + 3rd trimester) → Carbimazole
 Propylthiouracil associated with hepatotoxicity
 Despite this the BNF states both drugs may be used in pregnancy.
• Postpartum Patients Carbimazole is recommended by European Thyroid Association Guideline during lactation, given the concerns about PTU-mediated hepatotoxicity.
• Contraindications Block-and-replace regimes should not be used in pregnancy Radioiodine therapy is contraindicated • Monitoring and targets Maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism In women being treated with anti-thyroid drugs (ATDs) in pregnancy, FT4/TT4 and TSH should be monitored approximately every 4 weeks. • Thyroid-stimulating hormone receptor antibodies In a patient with a past medical history of Graves' disease who is clinically and biochemically euthyroid who is planning pregnancy: check thyroid-stimulating hormone receptor antibodies (as it can cross the placenta and cause foetal problems.): If they are positive, then treatment should be initiated to control the antibody levels, despite the normal TSH and T4.

Due to the small risk of fetal abnormalities with carbimazole it is recommended to use PTU in the first trimester during organogenesis and then carbimazole in trimester 2 + 3.

A 10 weeks pregnant C/O anxiety and an inability to sleep. Blood results show: total thyroxine (T4) 160 nmol/l (normal range 70–140 nmol/l), free T4 27 pmol/l (9–25 pmol/l) and thyroid-stimulating hormone (TSH) 0.2 mU/l. Which management of choice in this patient?
• Observe and repeat thyroid function tests in one month • Diagnosis: Physiological hyperthyroidism

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Hyperthyroidism with non-suppressed TSH • Elevated free T4 and free T3 + non-suppressed TSH (normal or elevated) = think of either :

 TSH-secreting pituitary tumour OR Thyroid hormone resistance

• TSH-secreting adenoma
 ↑Alpha subunit: the next investigation to differentiate it from thyroid hormone resistance. elevated alphaSU: TSH ratio (usually 1:1). A molar ratio of Alpha - subunit to TSH of > 5.7 is considered diagnostic. Pituitary MRI should be done to look for a pituitary mass. Treatment: Trans-sphenoidal resection of the tumour is the therapy of choice. • Thyroid hormone resistance Mechanism: THB gene defects, Features: Usually clinically euthyroid with only goitre. Sometimes: goitre with short stature, hyperactivity, attention deficits, learning disability, Diagnosis: gene sequencing (sequencing the thyroid hormone receptor gene) can confirm diagnosis in 85%. Treatment: Most cases require no treatment. If needed, it is usually B-adrenergic blockers

MRCPUK-part-1-September 2007 exam: Pregnant lady investigated for excessive sweating and tremor. Blood tests reveal the following: TSH < 0.05 mu/l. T4 =188 nmol/l. What is the most appropriate management? Propylthiouracil

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Toxic multinodular goitre (TNG) (Plummer's disease)

Definition • multiple autonomously functioning thyroid nodules that secrete excess thyroid hormones.
Epidemiology • second most common cause of hyperthyroidism in the Western world, after Graves disease.
• most common cause of hyperthyroidism in elderly and in areas of endemic iodine deficiency. • Develops in 10% of patients with a long-standing nodular goiter
• Sex: ♀ > ♂
• Age: often > 60 years Pathophysiology • Iodine deficiency → ↓ T4 → thyroid cell hyperplasia to compensate for the low levels of T4 → ↑thyroid cell replication → somatic mutations of the TSH receptor → further growth →
clonal proliferation → multiple nodules. • Somatic mutations of the TSH receptors and G α protein → activation of cyclic adenosine monophosphate (cAMP) cascade of the inositol phosphate pathways → functional autonomy of the thyroid
• Multiple somatic mutations of TSH receptor occur in long-standing goiters (> 60% of cases) → autonomous functioning of some nodules (toxic MNG) → hyperthyroidism (due to ↑ release of both T3 and T4) Features • goiter with multiple palpable nodules • thyrotoxicosis

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• Pemberton sign is the obstruction of the thoracic inlet by extending the arms over the head, and can be positive in cases of multinodular goiter.

Diagnosis • Ultrasonography is a highly sensitive to detect nodules
• Thyroid scintigraphy → patchy uptake Increased radioiodine uptake by multiple hyperfunctioning (hot) nodules Decreased uptake (suppression) by the rest of the gland and intervening parenchyma • CT of the chest → is the investigation of choice to determine the degree

of retrosternal involvement • Histopathology of resected tissue: patches of enlarged follicular cells distended with colloid and with flattened epithelium

Thyroid nuclear scintigraphy • Toxic nodular goiter (TNG) → patchy uptake. • Graves’ disease → homogeneous diffuse uptake. • Thyroiditis → low uptake.

Treatment • The treatment of choice is radioiodine therapy Recurrence of multinodular goitre after RAI → The next best step is a further dose of RAI after 6 months of the first RAI therapy. • Surgical therapy is usually reserved for young individuals, patients with 1 or more large nodules or with obstructive symptoms, patients with dominant nonfunctioning or suspicious nodules, patients who are pregnant, patients in whom radioiodine therapy has failed, or patients who require a rapid resolution of the thyrotoxic state.

Toxic thyroid adenoma (solitary toxic nodule) Overview • Typically, a single large thyroid nodule accompanied by clinical and biochemical hyperthyroidism. • This nodule is almost always benign Pathophysiology • Gain-of-function mutations of TSH receptor gene in a single precursor cell → autonomous functioning of the follicular cells of a single nodule → focal hyperplasia of thyroid follicular cells → toxic adenoma • The autonomous nodule overproduces thyroid hormones → hyperthyroidism → decrease in pituitary TSH secretion → suppression of hormone production from the rest of the gland Diagnosis • Thyroid iodine uptake scan:
 Hot area surrounded by extranodular thyroid tissue. Thyroid tissue surrounding a toxic adenoma typically has suppressed function. • In the absence of any thyroid auto-antibodies which argue against both Graves' disease and Hashitoxicosis, the most likely diagnosis is a solitary toxic nodule.

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Treatment • Initial treatment Control symptoms with beta-blockers and thioamides until euthyroidism is achieved, followed by tapering of beta-blockers
• Definitive treatment
 Non-pregnant, non-lactating adult with no mass effect: 1st line → Radioactive iodine therapy
 2nd line → subtotal thyroidectomy
 Non-pregnant, non-lactating adult with mass effect: 1st line → subtotal thyroidectomy
 Pregnant or lactating; 1st line → anti-thyroid drugs
 2nd line → subtotal thyroidectomy

Graves' disease

Overview • Graves' disease is the most common cause of thyrotoxicosis.
• typically seen in women aged 30-50 years. • associated with the presence of HLA-DR3 and HLA-B8 • 50% of patients with Graves disease have a family history of autoimmune disorders • Triggers: Physical or psychological stress and pregnancy

Pathophysiology
• B and T cell-mediated autoimmunity → production of stimulating immunoglobulin G (IgG) against TSH-receptor (TRAb; type II hypersensitivity reaction) → ↑ thyroid function and growth → hyperthyroidism and diffuse goiter
• there are antibodies to the TSH receptor mimicking the action of endogenous TSH. Binding to the TSH receptor then activates adenyl cyclase and results in increased secretion of thyroid hormones (Antibodies overstimulating adenyl cyclase)

Features • General features of thyrotoxicosis • Specific features seen in Graves' but not in other causes of thyrotoxicosis Eye signs (30% of patients): exophthalmos, ophthalmoplegia Pretibial myxedema (commonly described as orange peel skin present on both shins) → pathognomonic raised, indurated pinkish patches. may appear years before, or after, hyperthyroidism. Thyroid acropachy (a dermopathy characterized by soft-tissue swelling of the hands and clubbing of the fingers). Radiographic imaging of affected extremities typically demonstrates periostitis, most commonly the metacarpal bones. Thyroid bruit: presence of goitre is not necessary, although usually there is a small palpable goitre. Anti-TSH receptor stimulating antibodies (90%) → specific for Graves' disease

 Globally increased uptake on thyroid scan.

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The most likely associate of Graves' disease is vitiligo occurring in approximately 7% of cases.

Triad of Graves disease

1. Diffuse goiter (smooth, uniformly enlarged goiter)
2. Ophthalmopathy (Exophthalmos)
3. Dermopathy (pretibial myxedema): non-pitting edema and firm plaques on the anterior/lateral aspects of both legs

Management • Treatment of hyperadrenergic symptoms → Beta blockers: first line: propranolol • Anti-thyroid drugs (ATDs)
 ATD titration carbimazole is started at 40mg and reduced gradually to maintain euthyroidism typically continued for 12-18 months fewer side-effects than those on a block-and-replace regime Long-term remission following antithyroid drugs is of the order of 15%, with the vast majority relapsing. Thus, frequently, radio-iodine is advocated as a primary treatment - particularly for multi-nodular or toxic solitary nodules. Block-and-replace carbimazole is started at 40mg thyroxine is added when the patient is euthyroid treatment typically lasts for 6-9 months this approach is associated with 50% long term remission rate (the relapse rate after treatment is 50%) • Radioiodine iodine (RAI) treatment: in refractory cases to medical management • Surgery: less commonly used and usually reserved for patients with large goitre, compressive symptoms or intolerance to antithyroid drugs and difficulties in administering radioiodine

The principal test used to follow the immediate effect of treatment of hyperthyroidism is the serum free T4 concentration. Measurement of serum TSH can be misleading in the early follow-up period

because it can remain low for weeks or even months, even when the patient is biochemically euthyroid or even hypothyroid,

Which factor can be used as a predictor of relapse of hyperthyroidism before pharmacologic treatment is discontinued? Positive thyroid-stimulating autoantibody test. (This is a good predictor of relapse, but rates of relapse are still high when thyroid-stimulating autoantibodies disappear). Pregnant woman with a history of Grave's disease should have thyroid stimulating hormone binding antibody titres measured even if euthyroid as the antibodies can cross the placental barrier

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Antithyroid drugs Agents
• Methimazole, Carbimazole, Propylthiouracil • Methimazole is the active metabolite of carbimazole Mechanism of action • Inhibits thyroid hormone production via inhibition of thyroid peroxidase → blockade of iodide oxidation, organification, coupling (Inhibition of the iodination of tyrosine) • Propylthiouracil also lowers peripheral conversion of T4 to T3 by inhibiting 5'-deiodinase. Onset of action • Slow onset of action (3–4 weeks) • Methimazole has a faster onset of action and fewer side effects than propylthiouracil Adverse effects • Carbimazole-induced agranulocytosis (the major complication) defined as neutrophil count less than 0.5 ×109/L
 the incidence of leukopenia/neutropenia with carbimazole is less than 1%. should be stopped if neutrophil count below 1.5 ×109/L (1.5-7). In fact, a mild decrease in WBC can also occur with hyperthyroidism. If neutrophil count are just below normal →The most appropriate treatment would be to continue the carbimazole. Treatment
 thionamides should be withdrawn
 appropriate antibiotics (broad spectrum cephalosporin)
 occasionally, granulocyte colony-stimulating factor (G-CSF) is required when white count fails to respond. • Hepatotoxicity (seen with propylthiouracil use) • Teratogenicity: increased risk of congenital malformations with carbimazole and methimazole (e.g., aplasia cutis) Neonatal hypothyroidism will occur in approximately 10% of babies, because carbimazole crosses the placenta and switches off the fetal thyroid axis. The goitre that occurs is transient and will disappear following delivery also, propylthiouracil cross the placenta but less freely than carbimazole , although thyroxine does not. • Allergy/hypersensitivity pruritic rash (particularly with methimazole) ANCA-associated vasculitis (propylthiouracil) As methimazole and carbimazole are teratogenic, propylthiouracil is recommended in the first trimester. After the first trimester, switch back to carbimazole or methimazole because of the hepatotoxic effects of propylthiouracil. Interaction • Carbimazole effect is potentiated by the liver enzyme-inhibitor (eg: erythromycin)

Carbimazole (CBZ) VS Propylthiouracil (PTU)

Carbimazole (CBZ) Propylthiouracil (PTU) Action
↓thyroid peroxidase ↓thyroid peroxidase + ↓51 deiodinase type 1 → ↓peripheral conversion of T4 to T3 Potency

More (15 times as potent as PTU) Less

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Carbimazole (CBZ) Propylthiouracil (PTU) Structure
less protein bound, more transfer across placenta more protein bound, less transfer across placenta Teratogenicity Associated with aplasia cutis Less associated with aplasia cutis Major side effects
Agranulocytosis Hepatotoxicity use in pregnancy
2nd and 3rd trimester
1st trimester

Radioactive iodine therapy (RAI)

Definition: destruction of thyroid tissue via radioactive iodine (iodine-131) Indications • Graves' disease refractory to medical management • Toxic multinodular goitre

Preparation before RAI
• Anti-thyroid drugs is often used prior to RAI due to the risk of early deterioration of thyrotoxicosis. This depletes the intrathyroidal stores of hormone to prevent reexacerbation of thyrotoxicosis in the weeks following treatment due to release of preformed thyroid hormone. • Carbimazole needs to be stopped at least 7 days prior to radioiodine to ensure appropriate uptake.
• Avoid excess iodine for 7 days prior to RAI.

Procedure • Single oral dose of iodine-131 • The recommended dose of RAI is typically between 500 - 800 MBq

Advice post procedure
• Patients should be advised to keep babies, children under five, pregnant women and pets at arm's length for two to three weeks • Females are advised to avoid pregnancy for at least 6 months after radioactive iodine treatment • Males are advised not to cause a pregnancy for 6 months after radioactive iodine

Advantages

• Goitre shrinkage may occur in up to 30% following RAI.

Adverse effects
• Thyrotoxic symptoms
 Mild thyrotoxic symptoms after radioiodine occur in about one-third of patients,
 About 4% of patients develop a clinically significant radiation-induced thyroiditis. Should be treated symptomatically with beta blockers. • Hypothyroidism Early post-radioiodine hypothyroidism might be transient. Hypothyroidism is the most common adverse effect.
 Proportion of patients who become hypothyroid
 depends on the dose given, but as a rule the majority of patient will require thyroxine

supplementation after 5 years

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 approximately 80% will have long-term hypothyroidism following radioiodine. • Flare of Graves' eye disease (↑↑ thyroid eye disease in 15% of patients with Grave's disease) patients with thyroid eye disease should be treated with steroids for one to two weeks prior to starting radioiodine therapy. Contraindications • Pregnancy • Breastfeeding • Active thyroid eye disease (unless providing steroid cover)
• Radioiodine therapy should be avoided until 8 weeks following CT contrast administration. the iodine in the CT contrast medium competes with the radioactive iodine (I131) for binding sites →↓ thyroid uptake of radioiodine.

Thyroidectomy

Indications • Large goiters (≥ 80 g) or obstructive symptoms • thyroid malignancy • Graves' disease with severe ophthalmopathy

Complications
• Transient hypoparathyroidism due to local trauma at the time of surgery
 occur in 8 – 10% of cases (the most likely post-operative complication) Rarely becomes permanent hypoparathyroidism in fewer than 1% of patients. Usually presents 24-48 hours postoperatively
• permanent hypoparathyroidism seen in 1-2%
• Infection is seen in 1-2%
• Bleeding is less common, seen in around 0.5% or less
• Permanent recurrent laryngeal nerve palsy occurs in 1% of patients; Recurrent laryngeal nerve injury leads to a hoarse voice, because of paralysis of the posterior cricoarytenoid muscle, which is responsible for opening the vocal cord. superior laryngeal nerve palsy affects more patients (3-4% in case series).

Which structures is most closely related to the recurrent laryngeal nerve? • Inferior thyroid artery • The superior thyroid artery runs closest to the superior laryngeal nerve.

Radioiodine therapy is the treatment of choice for patients with a relapse of Graves' disease in the absence of contraindications, such as pregnancy and active severe Graves ophthalmopathy

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Amiodarone and the thyroid gland

Overview
• Amiodarone, a class III antiarrhythmic drug can induce thyroid dysfunction (both hypo- and hyperthyroidism), which is due to amiodarone's high iodine content and its direct toxic effect on the thyroid. Amiodarone contains 75 mg of iodine per 200 mg tablet (40% iodine by weight).
• Around 1 in 6 patients taking amiodarone develop thyroid dysfunction • Amiodarone has a wide tissue distribution, very long half-life (100 days) , very lipophilic,
and can result in prolonged effects even after stopping therapy for several months.

Amiodarone-induced hypothyroidism (AIH)

• Epidemiology Amiodarone-induced hypothyroidism is the commonest side effect associated with amiodarone treatment in iodine replete areas (in contrast to amiodarone induced thyrotoxicosis more commonly seen in iodine depleted areas). • Pathophysiology
 High iodine content of amiodarone causing a Wolff-Chaikoff effect (an autoregulatory phenomenon where thyroxine formation is inhibited due to high levels of circulating iodide) Amiodarone inhibits the peripheral conversion of T4 to T3 (normal T4 , ↓ T3 , ↑ TSH). • Management Same as for primary hypothyroidism. Doses larger than normal, is often required Amiodarone should only be discontinued if it fails to control the underlying arrhythmia.

Amiodarone is most likely to cause a false increase in which of these laboratory values? Free T4. (Amiodarone can cause a reduced peripheral conversion of T4 to T3).

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Amiodarone-induced thyrotoxicosis (AIT) Amiodarone-induced thyrotoxicosis (AIT) may be divided into two types: Differentiating between the two forms of Amiodarone-Induced Thyrotoxicosis (AIT)

AIT type 1 AIT type 2 Epidemiology
Most often seen in iodine-deficient areas. Most common in Europe and North America Pathophysiology Amiodarone contains↑ iodine → ↑ thyroid hormone synthesis (JodBasedow effect) ↑ release of T4 and T3 due to a destructive thyroiditis history Occurs in patients with underlying thyroid pathology, such as a nodular goitre or Graves’ disease. Occurs in patients without underlying thyroid disease.
Goitre Present Absent Color Doppler ↑ Blood flow ↓ Blood flow Iodine-131 uptake scan normal or high Minimal or none IL-6 levels Low or normal
Markedly elevated Management Carbimazole
Corticosteroids ± Antithyroid

Differentiation between type 1 and type 2
• Colour flow Doppler is most likely test to differentiate between Amiodarone induced thyrotoxicosis (AIT) type 1 and type 2. It appears to be superior to IL-6 which may be markedly elevated in AIT type 2, however may also be raised by concurrent non-thyroidal illness.

AIT initial management
• Usually Type 1 AIT is treated with high doses of anti-thyroid drugs to block thyroid hormone synthesis. Type 2 thyrotoxicosis is treated with glucocorticoids.
• Due to practical difficulties to distinguish between the 2 types, often a combination of steroids and thioamides is the best first-line management used for treatment of AIT. A rapid response suggests type 2 AIT; thionamides can be tapered.
 A poor initial response suggests type 1 AIT; the steroids can be tapered, and the patient can be treated for type 1 AIT.

Withdrawal of the amiodarone in AIH & AIT • For AIH: continue amiodarone , treat with thyroid hormone. Amiodarone should only be discontinued if it fails to control the underlying arrhythmia. • For type I AIT: Amiodarone should not be discontinued until hyperthyroid symptoms are well controlled with thionamides, since worsening hyperthyroid symptoms due to increased T3 levels may occur when the amiodarone is discontinued. • For type 2 AIT:
 Amiodarone should be stopped, if possible (if the patient does not have a lifethreatening arrhythmia that requires amiodarone therapy. In cases such as VT, this decision should be considered carefully in conjunction with a cardiologist, so the next management step will be Start carbimazole 40 mg od. Discontinuation of the drug has no immediate benefit. Even if amiodarone is stopped, thyrotoxicosis persists for up to 8 months because of the drug's long half-life.

The presence of markedly elevated serum IL-6 and low thyroidal radioiodine uptake in a patients without underlying thyroid disease suggests the presence of amiodarone-induced thyroiditis as the etiology of thyrotoxicosis.

Thyroid eye disease

Feature Assessment Frequency Lid lag / lid retracted Measure lid fissure width 50-60% Grittiness, discomfort, periorbital oedema, pain, excessive tears. Proptosis (aka exophthalmos) this is where the eye bulges out of its socket. Extraocular muscle dysfunction –typically causes diplopia (double vision) when looking up and out. Corneal involvement, causing exposure keratitis Flourescin staining <5% Loss of sight due to optic nerve compression Visual acuity tests, visual field tests. CT/MR scan

Overview
• Also called Graves’ Ophthalmopathy or Graves’ eye disease • Graves' eye disease can occur in euthyroid, hypothyroid or hyperthyroid setting. • Thyroid eye disease affects between 25-50% of patients with Graves' disease. • In about 10% of patients, the signs will only be unilateral.
• Ophthalmopathy may occur before the onset of hyperthyroidism, or as late as 20 years afterward.
• Risk factors for the development of Graves' orbitopathy include genetics, female sex, smoking, and prior radioiodine therapy.

Graves' eye disease can occur in euthyroid, hypothyroid or hyperthyroid setting. Definitions • Exophthalmos (also known as proptosis) is the protrusion of one eye or both anteriorly out of the orbit. • Lid retraction: When looking at the patient from the side, you see that the eyes are

proptosed. • Lid lag: When the patient follows your finger, moving downwards from above, the sclera can temporarily be seen above the iris.
Pathophysiology • TSH autoantibodies are present in the orbital cavity; bind TSH receptor antigen (autoimmune reaction) on cells; lymphocytic infiltration into the orbital tissues → inflammation and release of cytokines from CD4+ T cells → stimulates fibroblasts to secrete glycosaminoglycans (hyaluronic acid); expansion of retro-orbital tissue → infiltrative ophthalmopathy (exophthalmos). the most likely underlying pathogenesis → Excessive fibroblast proliferation • in case of reduced vision with colour desaturation, the most likely mechanism is → Optic nerve compression

• Hyperthyroidism → stimulates the beta receptors of the third cranial nerve → stimulates the levator palpebrae superioris muscle →Pull up the eyelid →lid lag and lid retraction Notes & Notes for MRCP
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Self-assessment score by patient 40% Exophthalmometry or evaluation on MR/CT scan. 20% Hess chart + CT/MR to detect muscle size 10% <1%

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Which eye signs are specific to Graves' disease? Eye signs specific to Graves' disease Eye signs found in most thyrotoxic states • Proptosis • Ophthalmoplegia • Chemosis • Periorbital oedema Both lid lag and lid retraction reflect enhanced sensitivity to circulating catecholamines and may therefore be found in most thyrotoxic states.

Prevention • Avoid smoking
• Patients with thyroid eye disease are generally treated with steroids for one to two weeks prior to starting radioiodine therapy. Radioiodine treatment →↑↑ thyroid eye disease → malignant exophthalmos. Prednisolone may help reduce the risk.
• In patients with thyroid eye disease undergoing radioiodine treatment, post-radioiodine hypothyroidism should be avoided, because of the risk of worsening Grave's eye disease. For this reason, patients are stabilised on a block replace regimen before moving to radioiodine therapy.

Smoking is the most important modifiable risk factor for the development of thyroid eye disease

Investigations • Thyroid function tests: ↓ TSH and ↑ free T3/T4; ↑ TSH receptor antibodies • Noncontrast CT scan of the orbits: the initial image of choice
 assess the risk of future optic nerve compression by enlarged extraocular muscle at the orbital apex. measure the of proptosis and retroocular fat accumulation helpful in the differential diagnosis • MRI of her orbits: certainly demonstrate retro-orbital and extraocular muscle inflammation.

Management • Eye protection: local measures (e.g. artificial tears (saline eye drops), raising the head of the bed at night). topical lubricants to prevent corneal inflammation caused by exposure • Mild orbitopathy: local measures are usually effective to relieve eye symptoms, and no additional

treatment is needed. • Moderate-to-severe orbitopathy → glucocorticoids is the initial therapy. • Avoid smoking • Treat hyperthyroidism (if present): by thionamides, radioiodine, or surgery. Radioactive iodine ablation (RAIA) can be used for patients with active mild disease. Moderate-to-severe is a contraindication to radioiodine therapy.
 Although radioiodine could exacerbate Graves' ophthalmopathy, radioiodine treatment can safely be given to patients with inactive Graves' ophthalmopathy with steroid cover, provided hypothyroidism is avoided. • For sight-threatening (malignant exophthalmos, diplopia and loss of colour vision) The initial treatment is IV glucocorticoids (dexamethasone, 4 mg IV) Surgical orbital decompression may be necessary: performed 1-2 weeks after IV glucocorticoids if the response is poor.

Indications of urgent review by an ophthalmologist • Unexplained deterioration in vision • Awareness of change in intensity or quality of colour vision in one or both eyes
 Impaired perception of colour implies → acute progressive neuropathy. • History of eye suddenly 'popping out' (globe subluxation) • Obvious corneal opacity • Cornea still visible when the eyelids are closed • Disc swelling

If there is active Grave's eye disease, then radioiodine therapy is not recommended as it can worsen the eye disease

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Thyroid storm (crisis)

In a patient with thyroid storm with high heart rate over 170bpm and low blood pressure the most urgent management is IV beta-blocker

Overview Thyrotoxic storm is treated with beta blockers, propylthiouracil and hydrocortisone • An acute exacerbation of hyperthyroidism that results in a life-threatening hypermetabolic state.
• Thyroid storm is a rare but life-threatening acute exacerbation of thyrotoxicosis.
• Associated with a significant mortality rate (30-50%) • It is typically seen in patients with established thyrotoxicosis and is rarely seen as the presenting feature. • Iatrogenic thyroxine excess does not usually result in thyroid storm.

Precipitating factors • Any acute stressful condition such as surgery or trauma • Acute infections • Acute iodine load e.g. CT contrast media

Clinical features include • Altered mental status (confusion,
agitation) • Fever > 38.5C • Tachycardia • Nausea, vomiting, and diarrhea • Jaundice
• Hypertension • Multisystem decompensation: heart failure, respiratory distress, prerenal failure, abnormal liver function test.

Diagnosis • Low/undetectable TSH, elevated free T3/T4 (but may not be grossly elevated)

• Postpartum
• When antithyroid drugs are being withdrawn.

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Management • Transfer the patient to the Intensive Care Unit
• Symptomatic treatment Tachycardia: beta blockers, first-line → propranolol Hypotension and hypovolemia: fluid resuscitation
 Hyperpyrexia → Paracetamol Agitation → chlorpromazine (also can be useful in treating the hyperpyrexia
because of its effect in inhibiting central thermoregulation) • Antithyroid drugs in thyroid storm Inhibition of thyroid hormone synthesis: First line → propylthiouracil Inhibition of thyroid hormone release (through the Wolff-Chaikoff effect): First line → Potassium iodide solution given at least 1 hour after antithyroid drugs
 Inhibition of peripheral conversion of T4 to T3: Glucocorticoids → First line: hydrocortisone, alternative: dexamethasone
 Inhibition of enterohepatic circulation of thyroid hormones: bile acid sequestrants → cholestyramine Plasmapheresis and peritoneal dialysis may be effective in cases resistant to the usual pharmacological measures.

In thyroid storm, treat acutely with propylthiouracil rather than carbimazole

Treatment of thyroid storm, five ‘Bs’:
1. Block synthesis (i.e. antithyroid drugs);
2. Block release (i.e. iodine);
3. Block T4 into T3 conversion (i.e. high-dose propylthiouracil, propranolol, corticosteroid);
4. Beta-blocker.
5. Block enterohepatic circulation (i.e. cholestyramine).

_Thyroid cancer

Epidemiology
• accounts for <1% of all cancer
• commonest in adults aged 40–50
• ♀ are affected more than ♂. Causes • Genetic factors Medullary carcinoma: associated with MEN2 (RET gene mutations) Papillary carcinoma: associated with RET/PTC rearrangements and BRAF mutations Follicular carcinoma: associated with PAX8-PPAR-γ rearrangement and RAS mutation Undifferentiated/anaplastic carcinoma: associated with TP53 mutation • Ionizing radiation; associated with papillary carcinoma

Iodine in CT contrast media can precipitate thyrotoxicosis or thyroid storm

Classification
• There are five main types of thyroid carcinoma and their properties are given below:

Cell type Frequency Behaviour Spread Prognosis Often young females present as "cold nodules" on isotope scanning Papillary 80% Follicular 10% More common in females Haematogenous Good Often familial.
Cancer of parafollicular cells (c cell), secrete calcitonin, part of MEN-2 Medullary cell 5% *almost always non-Hodgkin lymphomas

- Associated with Hashimoto's *often elderly women. lymphoma 2% Aggressive, Not responsive to treatment, can cause pressure symptoms
  Anaplastic ~ 1–2%

Papillary carcinoma is the most Prevalent type of thyroid cancer, it features Palpable lymph nodes, and it has the best Prognosis compared to all other types of thyroid cancer. Medullary thyroid carcinoma (MTC) • C cells derived from neural crest and not thyroid tissue • Systemic effects of calcitonin

→

flushing/diarrhoea • The best screening and diagnostic test: pentagastrin stimulation test . It measures calcitonin levels at 2 and 5 minutes after pentagastrin infusion , and a rise in calcitonin is suggestive of medullary thyroid carcinoma. • Investigations to exclude MEN 2 should be done: serum calcium to exclude hyperparathyroidism metanephrines to exclude phaeochromocytoma. Exclusion of phaeochromocytoma is crucial before thyroidectomy → abdominal MRI, because any major surgery can precipitate hypertensive crisis due to release of massive amounts of catecholamines. genetic testing for RET mutation
• Need geniting screening. Germline RET mutation carriers should undergo thyroidectomy before 5 years of age.

Thyroid lymphoma • Associated with preexisting chronic autoimmune (Hashimoto's) thyroiditis
• The best choice of therapy is combined chemotherapy with local radiation therapy.
Features • May be asymptomatic • Thyroid nodule: Firm to hard, Typically painless • Features of local infiltration or compression: recent onset of: hoarseness of voice, dyspnea or dysphagia

Local – Lymph node mets predominate excellent
Local and mets Poor Locally invasive Poor
Haematogenous Very Poor

Diagnosis
• Thyroid ultrasound:
 the initial investigation of choice in small non-symptomatic thyroid mass sonographic signs of thyroid cancer Solid or mostly solid hypoechoic nodule(s) Irregular margins Microcalcifications taller than wide • Fine-needle aspiration cytology (FNAC): Confirmatory test The appropriate investigation after ultrasound • Thyroid scintigraphy → decreased or no radiotracer uptake (i.e., hypofunctioning or nonfunctioning nodules, referred to as cold nodules) • Thyroid cancer tumor markers Follicular or papillary thyroid cancer: Thyroglobulin (Tg): precursor of thyroid hormones; produced exclusively by the thyroid gland. Indicated after total thyroidectomy or RAIA therapy Medullary carcinoma: Calcitonin: A hormone secreted by parafollicular cells, which is the tissue of origin of medullary carcinoma supportive diagnostic marker monitor response to therapy

Follicular thyroid carcinoma VS follicular adenoma. • Fine-needle aspiration (FNA) biopsy alone cannot distinguish
• The actual diagnosis of follicular thyroid cancer requires histologic evaluation of the thyroid after surgery and the identification of tumor capsule and/or vascular invasion.
• Follicular carcinoma invades the thyroid capsule and vasculature, unlike a follicular adenoma.

Pathology • Papillary thyroid carcinomas:
 Psammoma bodies (concentric lamellar calcifications) “Orphan Annie” eyes nuclei (empty-appearing large oval nuclei with central clearing) Nuclear grooves • Follicular carcinoma Uniform follicles Vascular and/or capsular invasion • Medullary carcinoma Ovoid cells of C cell origin and therefore without follicle development Amyloid in the stroma (stains with Congo red) • Anaplastic thyroid carcinoma Undifferentiated giant cell (i.e., osteoclast-like cell) “Papi and Moma adopted Orphan Annie:” papillary thyroid cancer is histologically characterized by psammoma bodies and Orphan Annie-eye nuclei.

Medullary thyroid cancer - calcitonin is used for screening, prognosis and monitoring

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Medullary carcinoma is composed of C-cells producing Calcitonin and is characterized by amyloid aCCumulation staining with Congo red.

Which proto-oncogenes is most associated with papillary carcinoma of the thyroid? • Trk is a proto-oncogene, mutation of which leads to activation of tyrosine kinase receptors. • Trk activation is thought to play a role in the pathogenesis of papillary thyroid carcinoma

Management: Surgical resection is the primary treatment for thyroid cancer. • Total thyroidectomy +/- neck dissection as needed (e.g., in patients with regional lymph node spread) • Hemithyroidectomy: Indications Small, well-differentiated thyroid carcinoma with all of the following characteristics: Intrathyroidal tumors (i.e., no evidence of extrathyroidal extension) No nodal or distant metastasis No high-risk patient factors Preferred option in tumors < 1 cm in size An alternative to total thyroidectomy in tumors 1–4 cm in size Contraindications

Intrathyroidal tumor ≥ 4 cm Extrathyroidal spread Distant or nodal metastasis

• Adjuvant therapy
 Well-differentiated thyroid cancer Radioactive iodine ablation (RAIA): conducted 4– 6 weeks after total thyroidectomy to destroy remaining thyroid tissue or metastases TSH suppression therapy: → thyroxine after completion of RAIA Poorly differentiated thyroid cancer: adjuvant radiation therapy and/or chemotherapy • Post-operative thyroid replacement therapy (thyroxine)
 The aim: titrate the thyroxine dose to suppressed TSH levels: in high risk thyroid cancers: TSH levels should be less than 0.1 mU/L
 In intermediate risk cancers: TSH can be maintained between 0.1- 0.5
 In low risk thyroid cancer target TSH to be in 0.5-2.0 range.
 Most patients will require 175 or 200 µg daily. • Post-operative follow-up yearly thyroglobulin (Tg) levels to detect early recurrent disease (thyroid is the only source of thyroglobulin).
 The most appropriate investigation at annual follow-up for papillary thyroid cancer.
 Ultrasound scan is the most sensitive investigation for the detection of locally recurrent papillary carcinoma.
 Other investigations should be considered if ultrasound scan is negative or distant metastases are suspected. (SCE. Questions sample. Mrcpuk.org).

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Thyroid cancer treatment → Thyroidectomy and neck dissection with postoperative radioiodine ablation

Thyroid cancer associated with Graves' disease is not uncommon and usually due to papillary carcinoma and must be considered in suspicious/expanding nodules rather than attributing purely to Graves' disease. • hyperthyroidism with prominent nodule which is 'cold' on uptake scanning is highly suggestive of thyroid carcinoma and the mostly likely diagnosis is Graves' disease (periorbital puffiness and thyroid bruit) associated with papillary thyroid carcinoma.

The association of Horner's syndrome and a thyroid nodule suggest invasion of the sympathetic chain and suggest that this thyroid nodule is malignant.

Which familial condition carries an increased risk of papillary carcinoma of the thyroid ? • Gardner's syndrome (intestinal tumours & lipomas. Also Osteomas & fibromas). carries an increased risk of papillary carcinoma

Which test is most useful in the assessment of airflow obstruction due to the retrosternal goitre? • Flow volume curve

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Thyroid nodule and fine-needle aspiration Epidemiology • About 50% of the general population have single or multiple thyroid nodules, whereas the incidence of thyroid malignancy is 2–4%. Thyroid ultrasound

• Ultrasonographic criteria associated with higher risk of malignancy:

1. Low echodensity (Hypoechogenicity)
2. Microcalcifications: the most predictive feature of malignancy
3. Irregular borders (poorly-defined margin)
4. Increased intranodular vascularity: (↑↑marginal blood flow → benign adenoma, ↑↑ intranodular blood flow → thyroid cancer)
5. Absence of a halo
6. Taller-than-wide configuration on transverse view • Referral of a thyroid nodule: (British Thyroid Association (BTA) guidelines) Same day Urgent Non-Urgent Managed by GP Stridor associated with thyroid lump Palpable cervical lymph nodes

Rapidly enlarging (days-weeks)

Presence of risk factors for thyroid cancer

Hoarseness of voice

Nodule in a child

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Patient with hyper or hypothyroidism refer to endocrinologist No change in size over years Lump enlarging over months No known risk factors Sudden pain and enlarged mass (bleeding in a cyst) <1cm, incidental thyroid nodule

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