DISORDERS OF THE THYROID

Disorders of the thyroid can be divided into basic pathological categories:

- Developmental abnormalities
- Inflammatory or autoimmune disorders
- Hyperplastic and metabolic disorders
- Neoplasms

PHYSIOLOGY OF THE THYROID GLAND

The thyroid gland is situated just below the larynx on the lower anterior aspect of the neck. The glandular tissue comprises closed follicles, which are lined by simple cuboidal epithelium (follicular epithelium). Outside this epithelium, dispersed – are the parafollicular cells or "C" cells. The thyroid gland produces three main hormones: thyroxine, tri-iodo-thyronine and calcitonin (C cells). The follicles contain colloid material.

Iodine is taken up by the thyroid via active transport, & combines with the amino acid tyrosine. If 3 iodine atoms are involved, you get formation of: tri-iodothyronine (T3). If 4 iodine atoms are involved, you get formation: thyroxine (T4). T3 & T4 are stored in the thyroid bound to thyroglobulin. When the hormones are released from the thyroid gland, they bind to thyroid-binding globulin (TBG), a plasma protein.

What controls the production and secretion of T3 & T4? The anterior pituitary gland secretes thyroid stimulating hormone (TSH), which acts on the thyroid to release more T3 & T4. The effects of T3 & T4 are identical, but the difference is T3 is more potent and acts much faster.

The effects of these thyroid hormones are to **up-regulate** the body. Therefore you get increase in heart rate, respiratory rate, basal metabolic rate, gastrointestinal motility/secretion/absorption. A way of measuring thyroid function is the see how much of a radioactive isotope of iodine (I-123) is actually taken up by the thyroid gland. Usually 35-40% is taken up within 24 hours.

PATHOPHYSIOLOGY VS CLINICAL FEATURES OF BENIGN DISEASES OF THYROID

Developmental abnormalities

1. **Thyroglossal cyst**: Pathophysiology: During embryological development, the thyroid gland descends in front of the pharyngeal gut, and remains connected to the tongue via the thyroglossal duct. Later, this duct disappears. A cyst can develop anywhere along this pathway of descent therefore termed: thyroglossal cyst. Usually the cyst forms along the midline. Clinical Features: A smooth rounded swelling, with fluid consistency. Occurs anywhere between the submental areas to isthmus of thyroid gland.

2. **Thyroglossal fistula:** Pathophysiology: A thyroglossal cyst can be excised to let the fluid out. If this is done incompletely, then you can have a fistula formation between the cyst and the skin. Clinical Features: There is a small opening in the midline of the neck, and there is discharge coming out of it – usually intermittently. Because there is a connection, infection can develop – so you might also get some pus discharge.
3. **Ectopic thyroid:** Pathophysiology: Due to the descent of the thyroid during embryological development, you can have thyroid forming anywhere along this descending pathway. Therefore forming an ectopic thyroid. Note that only parts of the thyroid can form here as well, and the rest forming in the normal area. Clinical Features: Because the thyroid gland is connected to the tongue, you might get some unusual lumps at the junction of the anterior 2/3 and posterior 1/3 of the tongue.

Inflammatory & autoimmune disorders

1. **Hashimoto's thyroiditis:** Pathophysiology: The immune system (antibodies against thyroid) attacks the thyroid tissue, destroying the thyroid follicles and architecture. There is diffuse lymphocytic infiltration and over a period of years, the thyroid gland is destroyed, becomes atrophied and fibrosis occurs. Due to a lack of functional thyroid tissue, the level of thyroid hormones decreases over time, although increasing at the outset. Because there is a feedback loop between TSH and thyroid hormone production, the body realizes there isn't enough thyroid hormone in the system. Therefore, the anterior pituitary secretes TSH, but there is not much thyroid gland left, so TSH accumulates producing an enlarged thyroid gland. Clinical Features: Often the thyroid is not enlarged, but presentation can include enlarged tender thyroid gland. Patient is euthyroid or hyperthyroid at outset (i.e.: body reacts to the destruction by trying to compensate for the loss of thyroid hormone/tissue) but later the patient because hypothyroid (i.e.: body cannot keep up with thyroid tissue destruction).
2. **Graves' disease:** Pathophysiology: Usually, TSH binds to its receptor on thyroid tissue therefore producing more thyroid hormone. In this disease, there is a circulating immunoglobulin called: "Long acting thyroid stimulator" (LATS). This binds to TSH receptor and mimicks the normal response. The body does not recognize this as a potential different hormone to TSH. The thyroid keeps producing the thyroid hormone as if nothing has ever happened. Clinical Features: Main feature on clinical examination is the marked hyperthyroidism (thyrotoxicosis). Patient shows all the systemic features of this condition. There is also diffuse thyroid enlargement.
3. **De Quervain's acute thyroiditis:** Pathophysiology: A viral infection of the thyroid causes diffuse inflammation and its associated features. Inflammatory cells infiltrate the gland to get rid of the virus. This causes further inflammation. Clinical Features: The virus may destroy some thyroid tissue, and the inflammation will do some damage too. Initially, the thyroid responds to this by compensating for the loss of thyroid hormone. This may cause symptoms of hyperthyroidism initially. Later on, the thyroid hormone levels become normal – patient is euthyroid. The thyroid gland itself may be swelled up a little on the outside, and will be very tender due to the infection. Patient may also show signs of infection systemically: pyrexia, loss of weight, lethargy, tachycardia etc.

4. **Riedl's thyroiditis:** Pathophysiology: No one knows for sure, but they think its an autoimmune process then causes dense fibrosis of the thyroid gland. Clinical Features: The swelling is extremely hard due to presence of fibrous tissue, and often presents in an asymmetrical fashion.

Hyperplastic and metabolic disorders

1. **Simple non-toxic colloid goitre:** Pathophysiology: A minor abnormality of thyroid hormone synthesis may cause benign, diffuse, multinodular hyperplasia of the thyroid follicles. Clinical Features: There is a diffuse multinodular thyroid enlargement.
2. **Endemic goitre:** Pathophysiology: Thyroid gland takes up iodine to produce T3 & T4. If there is iodine deficiency, then the level of thyroid hormone will decrease. Therefore there is no inhibitory feedback, and the anterior pituitary will keep producing more TSH. This will cause thyroid to hypertrophy. It is endemic in developing countries, mountainous areas, Australia, Switzerland, Pacific islands etc. Clinical Features: Massive enlargement of the thyroid gland, and often becomes multinodular. The patient is euthyroid, or can suffer from low T4. Thyroid function tests show elevated TSH levels.
3. **Drug induced goitre:** Pathophysiology: Certain drugs interfere with the thyroid hormone synthesis pathway. Carbimazole is an example of such a drug. Carbimazole is usually used in thyrotoxicosis. This is to reduce the level of thyroid hormone in the body. But, the thyroid gland may react to this by hyperplasia. Clinical Features: Diffuse thyroid enlargement. The patient is euthyroid. This can be prevented by giving a 'block and replace' dose regimen.

PATHOPHYSIOLOGY VS CLINICAL FEATURES OF MALIGNANT DISEASES OF THYROID

Adenocarcinomas

Remember, adeno = glandular appearance, carcinoma = epithelial in origin.

1. **Papillary carcinoma:** This form of thyroid cancer is very common in adults, accounting for about 66%. In children, almost all cases are of such sort. Pathophysiology: Histologically, you can see a fibro-vascular stroma containing calcified "psammoma bodies", and the neoplastic cells can range from poorly differentiated to well differentiated. The growth of the tumour is slow. The tumour can invade locally to the trachea or oesophagus. Metastasis is to the cervical lymph nodes. Histology of the involved lymph nodes, will show thyroid tissue. Prognosis of papillary carcinoma is very good, with only 10% mortality rate after 10 years. The cancerous tissue does not product thyroid hormone. Clinical Features: A solitary thyroid nodule is palpable, and also enlarged cervical lymph nodes may be involved. Radioisotope scanning shows no uptake into the cancerous tissue. Diagnosis is made by fine needle aspiration cytology. Management: Total thyroidectomy with associated lymph nodes. Oral thyroxine is given after operation to keep TSH levels down.

2. **Follicular carcinoma:** Peak incidence is 50 years of age, older than for papillary carcinoma. Pathophysiology: Histologically, you see a follicular pattern of the neoplastic cells that are usually well differentiated. Metastasis occurs via the blood stream. Clinical features: A solitary thyroid nodule, without any lymph node involvement. Management: A tumour with only microinvasion into the local tissues will only require a thyroidectomy of that lobe. If the tumour has invaded the capsule or entered the blood stream – then total thyroidectomy is required. This means, the metastatic lesions will uptake more iodine, which is easily seen by the radioisotope test.
3. **Anaplastic carcinoma:** Extremely aggressive with high mortality rate within 1 year. Tumours are more common among elderly. Pathophysiology: Poorly differentiated cells just proliferate rapidly, and you get a diffuse enlargement of the thyroid gland. The tumour tissue will spread beyond the thyroid capsule. It soon invades the trachea and oesophagus. It also spreads to blood and lymph nodes. Clinical Features: Diffuse hard thyroid enlargement, often with tracheal or oesophageal obstruction. Recurrent laryngeal nerve involvement causes hoarseness of voice. Management: Poor prognosis. Tracheal obstruction can be treated with a metal thyroid stent. Cancer does not respond to radiotherapy or chemotherapy.
4. **Medullary carcinoma:** This tumour is often associated with MEN II. Pathophysiology: This is a malignancy of the C cells. The tumour tissue secretes calcitonin, therefore making this a marker for diagnosis. Tumours can also secrete serotonin and ACTH-like peptide. It is usually transmitted genetically as part of MEN II. It is associated with tumours of APUD cell origin, particularly phaeochromocytoma and parathyroid adenomas. The stroma contains excessive amounts of amyloid, making the mass stony hard to palpate. Growth is slow, and metastasis is usually to regional lymph nodes → liver etc. Clinical Features: Stony hard thyroid lump with possible associated lymph node involvement. Calcitonin in blood is a good marker. Management: Thyroidectomy and clearance of regional lymph nodes. Does not respond to radiotherapy.