GOITRE

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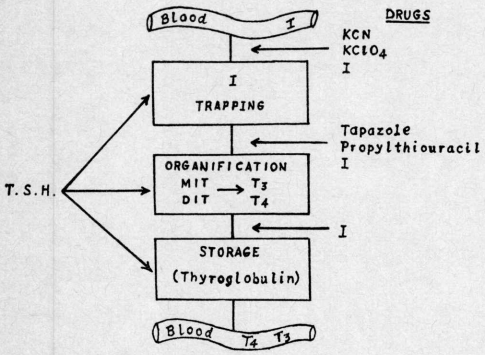
It has been my impression that students stop thinking once they make the "diagnosis" of goitre. In fact goitre is not a diagnosis, it is a sign, which in most cases, is readily detectible by any individual with 20 - 20 vision. It is proper at this time to outline some of the more important causes of goitre and relate them to thyroid pathophysiology.

By definition (Dorlands) "goitre is an enlargement of the thyroid body causing a swelling in the front part of the neck". The normal thyroid may weigh up to 30 gms., the ease with which it can be palpated depends on the amount of subcutaneous tissue present between the skin and the thyroid gland. In order to understand the causes for this swelling one must first have an elementary grasp of thyroid physiology.

The thyroid can be divided into three major compartments: (1) Trapping, (2) Organification (3) Storage.



We consume approximately one hundred to two hundred micrograms of iodine per day. This is converted to iodide and carried in the blood. The thyroid gland can concentrate iodide up to 50 times the concentration present in the circulating blood. Within seconds, the trapped iodide is converted to iodine possibly by the enzyme peroxidase. This iodine combines with tyrosine, a protein, to form monoiodotyrosine (MIT) and diiodotyrosine (DIT) under the influence of certain enzymes these combine to form triiodothyronine (T_3) and tetraiodothyronine (T_4). This stage is called organification. The T_3 and T_4 compounds are then bound to globulin and stored in the thyroid follicle as thyroglobulin.

When the thyroid is stimulated by thyroid stimulating hormone (TSH), all of the above functions are accelerated, that is, iodine uptake is enhanced, organification is accelerated and thyroxin output increases. When TSH decreases, the reverse holds true. You are also aware that the control of TSH is almost completely under the influence of circulating thyroxin so that a lowering of thyroxin will cause an increased output of TSH and a rise in thyroxin will cause a decreased output of TSH. It has been shown experimentally that any condition which leads to increased production of TSH will eventually cause enlargement of the thyroid gland, provided the gland is capable of responding.

We are now in a better position to understand what may cause thyroid enlargement.

A. Compensatory - any condition leading to a decreased output of thyroxin.

B. Hyperfunctioning toxic states - diffuse thyroid enlargement and nodular thyroid enlargement.

C. Thyroiditis - Acute, subacute and chronic thyroiditis can all lead to thyroid enlargement secondary to oedema, infiltration with lymphocytes or replacement by fibrosis.

D. Neoplastic - either primary, arising from

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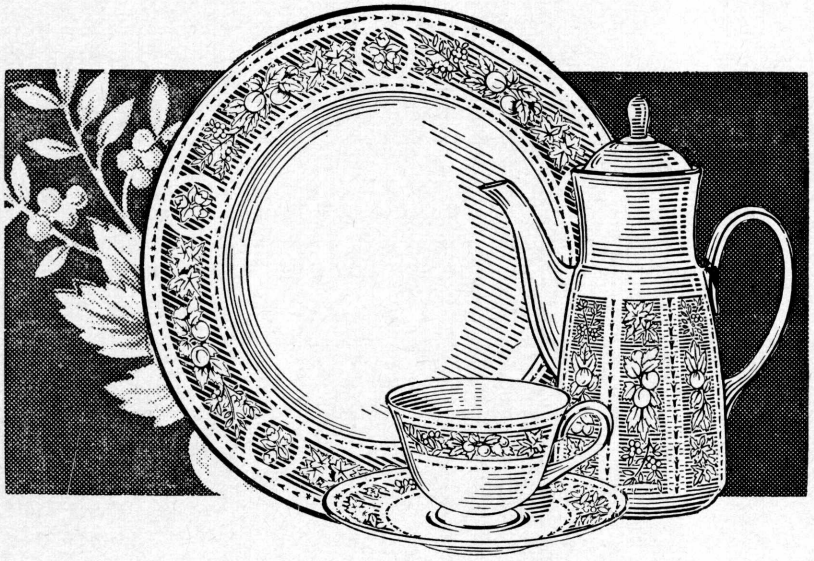

thyroid tissue or secondary metastatic deposits.

A. COMPENSATORY GOITRES

1. **Iodine deficiency** - this is extremely rare in this part of the country because of our nearness to the salt water plus the fact that all our table salt is supplemented with iodine giving us a daily requirement of four to five times the daily needs.
2. **Enzymatic Defects:**
   (a) Failure of the thyroid gland to trap iodide.
   (b) Failure to convert trapped iodide to iodine - thought to be due to deficiency of peroxidase enzyme.
   (c) Failure to conserve iodine during the organification phase - felt to be due to lack of enzyme dehalogenase.
   (d) Failure of MIT and DIT to combine to form T_3 and T_4 - felt to be due to defective "coupling enzymes".
   (e) Abnormal thyroid hormone produced - giving a normal PBI, but having no metabolic effect.
3. **Antithyroid Drugs** divided into two groups:

(a) Those that block trapping: Potassium thiocyanate (KCN), Potassium Perchlorate ($KCLO_4$) and iodine.

(b) Those that prevent organification: - Propylthiourocil, Tapazole and Iodine. Iodine also works in another sphere preventing the release of thyroxin from thyroglobulin. Approximately 2 mgms. of iodine per day is sufficient to inhibit the hyperactive thyroid gland, that is, one tenth of a drop of Lugol's Solution or one-thirtieth of a drop of Saturated Potassium Iodide Solution.

4. **Goitrogenic Substances** - those of the Brassica Family responsible for goitre are mainly cabbage and turnip, therefore, unusual eating habits are necessary before one develops goitre secondary to ingestion of these substances.

One can see that all of the above lead to a decreased production of thyroid hormone thus causing a compensatory rise in TSH which both stimulates and enlarges the thyroid gland causing goitre. The gland may vary considerably in size increasing from a few grams to several hundred grams in weight. In the beginning it will usually be diffuse and smooth but in long standing cases is usually irregular and nodular.

B. FUNCTIONAL (TOXIC) GOITRES

1. **Diffuse enlargement** (Graves', Parry's, or Basedow's Disease). It is now generally accepted that in this condition the thyroid is stimulated by a TSH - like substance called long-acting thyroid stimulator (LATS). It has been identified as a 7 S Gamma Globulin and has been demonstrated attached to the thyroid follicular cells. There is overwhelming evidence to show that LATS does not arise in the pituitary but just where it comes from is uncertain. Could it be that Graves' Disease is another so-called "auto-immune process"? The thyroid is diffusely enlarged - about 30 - 60 gms., smooth, firm, nontender and has an audible bruit.
2. **Adenoma (Plummer's Disease):** On occasions an adenoma can produce excess thyroxin causing a hyperthyroid state. These adenomas are autonomous, that is, not under the influence of thyroid stimulating hormone. Thyroid size varies considerably; a small gland with a single nodule or a large gland with multiple nodules are the most common findings.

C. THYROIDITIS GOITRE

1. **Acute thyroiditis:** This is secondary to a bacterial infection usually staphylococci, streptococci or pneumococci which causes inflammation, oedema and on occasions suppuration. The gland may be soft or firm, tender, and the overlying skin hot and erythematous.
2. **Subacute thyroiditis:** (Acute nonsuppurative). This is felt to be viral in origin. The patient presents with diffusely swollen gland, firm, and tender. The overlying skin is not hot or erythematous. Pain may radiate up the neck and into the ears. Initially the patient may be toxic secondary to the release of thyroglobulin, and this is followed by a transient phase of hypothyroidism because the injured gland is unable to produce more thyroxin. Complete recovery is the rule.
3. **Chronic thyroiditis:** (a) Infective such as tuberculous and fungus infections.
   (b) Non-infective such as Hashimoto's and Riedl's thyroiditis. Hashimoto's thyroiditis (Struma Lymphomatosa) is a disease affecting mainly middle aged women involving the thyroid diffusely, leading to firmness without tenderness of the thyroid gland. Antibodies have been demon-

strated against thyroglobulin, non-thyroglobulin colloid and thyroid cellular antigen, thus putting this disease high on the list of the "Autoimmune Disease" par excellence. Riedl's thyroiditis: this affects both sexes starting at about the fourth decade, causes minimal thyroid enlargement: the gland is usually firm to stony hard and bound to the underlying structures giving the clinical impression of carcinoma.

D. NEOPLASTIC GOITRE

The pathogenesis of carcinoma of the thyroid remains uncertain. However, it seems clear that from animal experiments and clinical observation, TSH significantly influences development and growth of thyroid neoplasms. The sequence of events is possibly as follows: Hyperplasia followed by adenoma and then carcinoma. In the early phases, the changes may be reversed by giving thyroxin, thereby decreasing TSH, but after neoplasm has become hormonally independent (autonomous) it grows irrespective of thyroxin therapy.

Carcinoma of the thyroid as a cause of death is rare accounting for approximately one per two hundred thousand population and only 0.4% of all deaths due to cancer. The estimated new cases per year is in the vicinity of 2.5 per hundred thousand population, that is, about four per year for Halifax and vicinity.

Neoplasms of the thyroid are best classified according to their clinical course rather than their pathological picture:

1. Slow growing - papillary and follicular types. Both of these types occur in the younger age groups and are usually very benign. They present mainly as a nodule, not as a diffuse enlargement.
2. Fast growing - small cell, giant cell and spindle cell types. These occur mainly in the older age groups, characterized by progressive unilateral or bilateral enlargements, with recurrent laryngeal nerve palsy and dysphagia as significant findings. Necrosis with cystic formation in tumour is common. There is a rapid downhill course.

As you can see, I have attempted only to point out the major causes of goitre. No attempt has been made to give all of the clinical features or any of the management of the above conditions. However, if the etiology is understood, and an approach to goitre is based on an understanding of the pathophysiology, then the management, although still controversial in some respects, becomes much simplified.

The illustration (1400 A.D.) shows the demise of an Aztec warrior who, having endured fear and pain, is finally devoured by the Death God . . .
Nowadays, there are available very valuable drugs to combat pain, anxiety, depression and psychotic conditions.

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