Shree H. N. Shukla Institute of Pharmaceutical Education and Research, Amargadh, Bhichari

Material

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THYROID GLAND

NORMAL STRUCTURE ANATOMY. Embryologically, the thyroid gland arises from a midline invagination at the root of the tongue and grows downwards in front of trachea and thyroid cartilage to reach its normal position. Failure to descent may produceanomalous lingual thyroid. The thyroglossal duct that connects the gland to the pharyngeal floor normally disappears by 6th week of embryonic life. In adults, its proximal end is represented by foramen caecum at the base of the tongue and distal end by the pyramidal lobe of the thyroid. Persistence of the remnants of thyroglossal duct in the adults may develop into thyroglossal cyst (page 520). The C-cells of the thyroid originate from the neuroectoderm. The thyroid gland in an adult weighs 15-40 gm and is composed of two lateral lobes connected in the midline by a broad isthmus which may have a pyramidal lobe extending upwards. Cut section of normal thyroid is yellowish and translucent. HISTOLOGY. The thyroid is composed of lobules of colloidfilled spherical follicles or acini. The lobules are enclosed by fibrovascular septa. The follicles are the main functional units of the thyroid. They are lined by cuboidal epithelium with numerous fine microvilli extending into the follicular colloid that contains the glycoprotein, thyroglobulin. The follicles are separated from each other by delicate fibrous tissue that contains blood vessels, lymphatics and nerves. Calcitoninsecreting C-cells or parafollicular cells are dispersed within the follicles and can only be identified by silver stains and immunohistochemical methods. FUNCTIONS. The major function of the thyroid gland is to maintain a high rate of metabolism which is done by means of iodine-containing thyroid hormones, thyroxine (T4) and tri-iodothyronine (T3). The thyroid is one of the most labile organs in the body and responds to

numerous stimuli such as puberty, pregnancy, physiologic stress and various pathologic states. This functional lability of the thyroid is responsible for transient hyperplasia of the thyroidal epithelium. Under normal conditions, the epithelial lining of the follicles may show changes in various phases of function as under: 1. Resting phase is characterised by large follicles lined by flattened cells and filled with deeply staining homogeneous colloid e.g. in colloid goitre and iodine-treated hyperthyroidism. 2. Secretory phase in which the follicles are lined by cuboidal epithelium and the colloid is moderately dark pink e.g. in normal thyroid. 3. Resorptive phase is characterised by follicles lined by columnar epithelium and containing lightly stained vacuolated and scalloped colloid e.g. in hyperthyroidism. The synthesis and release of the two main circulating thyroid hormones, T3 and T4 are regulated by hypophyseal thyroid-stimulating hormone (TSH) and involves the following steps: 1. Iodine trapping by thyroidal cells involves absorbing of iodine from the blood and concentrating it more than twentyfold. 2. Oxidation of the iodide takes place within the cells by a thyroid peroxidase. 3. Iodination occurs next, at the microvilli level between the oxidised iodine and the tyrosine residues of thyroglobulin so as to form mono-iodotyrosine (MIT) and di-iodotyrosine (DIT).

4. Coupling of MIT and DIT in the presence of thyroid peroxidase forms tri-iodothyronine (T3) and thyroxine (T4). The thyroid hormones so formed are released by endocytosis of colloid and proteolysis of thyroglobulin within the follicular cells resulting in discharge of T3 and T4 into circulation where they are bound to thyroxine-binding globulin. A number of thyroid function tests are currently available. These include the following: Determination of serum levels of T3, T4 by radioimmunoassay (RIA). TSH and TRH determination. Determination of calcitonin secreted by parafollicular C cells. Estimation of thyroglobulin

secreted by thyroid follicular cells. Assessment of thyroid activity by its ability to uptake radioactive iodine (RAIU). Assessment whether thyroid lesion is a nonfunctioning ('cold nodule') or hyperactive mass ('hot nodule'). Diseases of the thyroid include: functional disorders (hyperthyroidism and hypothyroidism), thyroiditis, Graves' disease, goitre and tumours. The relative frequency of some of these diseases varies in different geographic regions according to the iodine content of the diet consumed. One of the important investigation tools available in current times is the widespread use of FNAC for thyroid lesions which helps in avoiding a large number of unwanted diagnostic biopsies.

FUNCTIONAL DISORDERS Two significant functional disorders characterised by distinct clinical syndromes are described. These are: hyperthyroidism (thyrotoxicosis) and hypothyroidism.

HYPERTHYROIDISM (THYROTOXICOSIS) Hyperthyroidism, also called thyrotoxicosis, is a hypermetabolic clinical and biochemical state caused by excess production of thyroid hormones. The condition is more frequent in females and is associated with rise in both T3 and T4 levels in blood, though the increase in T3 is generally greater than that of T4. ETIOPATHOGENESIS. Hyperthyroidism may be caused by many diseases but three most common causes are: Graves' disease (diffuse toxic goitre), toxic multinodular goitre and a toxic adenoma. Less frequent causes are hypersecretion of pituitary TSH by a pituitary tumour, hypersecretion of TRH, thyroiditis, metastatic tumours of the thyroid, struma ovarii, congenital hyperthyroidism in the newborn of mother with Graves' disease, hCG-secreting tumours due to mild thyrotropic effects of hCG (e.g. hydatidiform mole, choriocarcinoma and testicular tumours), and lastly, by excessive doses of thyroid hormones or iodine called jodbasedow disease. CLINICAL FEATURES. Patients with hyperthyroidism have a slow and insidious onset, varying

in severity from case to case. The usual symptoms are emotional instability, nervousness, palpitation, fatigue, weight loss in spite of good appetite, heat intolerance, perspiration, menstrual disturbances and fine tremors of the outstretched hands. Cardiac manifestations in the form of tachycardia, palpitations and cardiomegaly are invariably present in hyperthyroidism. The skin of these patients is warm, moist and flushed. Weakness of skeletal muscles and osteoporosis are common. Typical eye changes in the form of exophthalmos are a common feature in Graves' disease. Serum levels of T3 and T4 are elevated but TSH secretion is usually inhibited. A sudden spurt in the severity of hyperthyroidism termed 'thyroid storm' or 'thyroid crisis' may occur in patients who have undergone subtotal thyroidectomy before adequate control of hyperthyroid state, or in a hyperthyroid patient under acute stress, trauma, and with severe infection. These patients develop high grade fever, tachycardia, cardiac arrhythmias and coma and may die of congestive heart failure or hyperpyrexia.

HYPOTHYROIDISM Hypothyroidism is a hypometabolic clinical state resulting from inadequate production of thyroid hormones for prolonged periods, or rarely, from resistance of the peripheral tissues to the effects of thyroid hormones. The clinical manifestations of hypothyroidism, depending upon the age at onset of disorder, are divided into 2 forms: 1. Cretinism or congenital hypothyroidism is the development of severe hypothyroidism during infancy and childhood. 2. Myxoedema is the adulthood hypothyroidism.

Cretinism A cretin is a child with severe hypothyroidism present at birth or developing within first two years of postnatal life. This is the period when brain development is taking place; in the absence of treatment the child is both physically and mentally retarded. The word 'Cretin' is derived from the French, meaning Christ-like because these children

are so mentally retarded that they are incapable of committing sins. ETIOPATHOGENESIS. The causes of congenital hypothyroidism are as follows:

1. Developmental anomalies e.g. thyroid agenesis and ectopic thyroid. 2. Genetic defect in thyroid hormone synthesis e.g. defect in iodine trapping, oxidation, iodination, coupling and thyroglobulin synthesis. 3. Foetal exposure to iodides and antithyroid drugs. 4. Endemic cretinism in regions with endemic goitre due to dietary lack of iodine (sporadic cretinism, on the other hand, is due to developmental anomalies and genetic defects in thyroid hormone synthesis described above). CLINICAL FEATURES. The clinical manifestations usually become evident within a few weeks to months of birth. The presenting features of a cretin are: slow to thrive, poor feeding, constipation, dry scaly skin, hoarse cry and bradycardia. As the child ages, clinical picture of fullydeveloped cretinism emerges characterised by impaired skeletal growth and consequent dwarfism, round face, narrow forehead, widely-set eyes, flat and broad nose, big protuberant tongue and protuberant abdomen. Neurological features such as deaf-mutism, spasticity and mental deficiency are more evident in sporadic cretinism due to developmental anomalies and dyshormonogenetic defects. Characteristic laboratory findings include a rise in TSH level and fall in T3 and T4 levels.

Myxoedema The adult-onset severe hypothyroidism causes myxoedema. The term myxoedema connotes non-pitting oedema due to accumulation of hydrophilic mucopolysaccharides in the ground substance of dermis and other tissues.

ETIOPATHOGENESIS. There are several causes of myxoedema listed below but the first two are the most common causes: 1. Ablation of the thyroid by surgery or radiation. 2. Autoimmune (lymphocytic)

thyroiditis (termed primary idiopathic myxoedema). 3. Endemic or sporadic goitre. 4. Hypothalamic-pituitary lesions. 5. Thyroid cancer. 6. Prolonged administration of antithyroid drugs. 7. Mild developmental anomalies and dyshormonogenesis.

CLINICAL FEATURES. The onset of myxoedema is slow and a fully-developed clinical syndrome may appear after several years of hypothyroidism. The striking features are cold intolerance, mental and physical lethargy, constipation, slowing of speech and intellectual function, puffiness of face, loss of hair and altered texture of the skin. The laboratory diagnosis in myxoedema is made by low serum T3 and T4 levels and markedly elevated TSH levels as in the case of cretinism but cases with suprathyroid lesions (hypothalamic-pituitary disease) have low TSH levels. The clinical appearance of these three major forms of functional disorders of the thyroid gland is shown in Fig. 27.6.

THYROIDITIS Inflammation of the thyroid, thyroiditis, is more often due to non-infectious causes and is classified on the basis of onset and duration of disease into acute, subacute and chronic as under: I. Acute thyroiditis: 1. Bacterial infection e.g. Staphylococcus, Streptococcus. 2. Fungal infection e.g. Aspergillus, Histoplasma, Pneumocystis. 3. Radiation injury II. Subacute thyroiditis: 1. Subacute granulomatous thyroiditis (de Quervain's thyroiditis, giant cell thyroiditis, viral thyroiditis) 2. Subacute lymphocytic (postpartum, silent) thyroiditis 3. Tuberculous thyroiditis III. Chronic thyroiditis: 1. Autoimmune thyroiditis (Hashimoto's thyroiditis or chronic lymphocytic thyroiditis) 2. Riedel's thyroiditis (or invasive fibrous thyroiditis). While acute infectious thyroiditis is uncommon, some of the morphologically important forms of thyroiditis from the above list are discussed below.

HASHIMOTO'S (AUTOIMMUNE, CHRONIC LYMPHOCYTIC) THYROIDITIS Hashimoto's thyroiditis, also called diffuse lymphocytic thyroiditis,

struma lymphomatosa or goitrous autoimmune thyroiditis, is characterised by 3 principal features: 1. Diffuse goitrous enlargement of the thyroid. 2. Lymphocytic infiltration of the thyroid gland. 3. Occurrence of thyroid autoantibodies. Hashimoto's thyroiditis occurs more frequently between the age of 30 and 50 years and shows an approximately tenfold preponderance among females. Though rare in children, about half the cases of adolescent goitre are owing to autoimmune thyroiditis. Hashimoto's thyroiditis is the most common cause of goitrous hypothyroidism in regions where iodine supplies are adequate. Regions where iodine intake is highest have higher incidence of Hashimoto's thyroiditis e.g. in Japan and the United States.

ETIOPATHOGENESIS. Hashimoto's thyroiditis is an autoimmune disease is well established. Hashimoto, a Japanese surgeon, described it in 1912 as the first auto

immune disease of any organ. Autoimmune pathogenesis of Hashimoto's thyroiditis is explained by the following observations: 1. Other autoimmune disease association: Like in other autoimmune diseases, Hashimoto's disease has been found in association with other autoimmune diseases such as Graves' disease, SLE, Sjögren's syndrome, rheumatoid arthritis, pernicious anaemia and Type 1 diabetes mellitus. 2. Immune destruction of thyroid cells: The sequence of immune phenomena is initial activation of CD4+ T helper cells. These cells then induce infiltration of CD8+ T cytotoxic cells in the thyroid parenchyma as well as activate B cells to form autoantibodies, which bring about immune destruction of thyroid parenchyma. 3. Detection of autoantibodies: The following autoantibodies against different thyroid cell antigens are detectable in the sera of most patients with Hashimoto's thyroiditis: i) Thyroid microsomal autoantibodies (against the microsomes of the follicular cells). ii) Thyroglobulin autoantibodies.

iii) TSH receptor autoantibodies. iv) Less constantly found are thyroid autoantibodies against follicular cell membranes, thyroid hormones themselves, and colloid component other than thyroglobulin. 4. Inhibitory TSH-receptor antibodies: TSH-receptor antibody seen on the surface of thyroid cells in Hashimoto's thyroiditis is inhibitory to TSH, producing hypothyroidism. Similar antibody is observed in Graves' disease where it causes hyperthyroidism. It appears that TSH-receptor antibody may act both to depress or stimulate the thyroid cells to produce hypo- or hyperthyroidism respectively. Thus, these patients may have alternate episodes of hypo- or hyperthyroidism. 5. Genetic basis: The disease has higher incidence in firstdegree relatives of affected patients. Hashimoto's thyroiditis is seen more often with HLA-DR3 and HLA-DR5 subtypes. MORPHOLOGIC FEATURES. Pathologically, two varieties of Hashimoto's thyroiditis are seen: classic form, the usual and more common, and fibrosing variant found in only 10% cases of Hashimoto's thyroiditis. Grossly, the classic form is characterised by diffuse, symmetric, firm and rubbery enlargement of the thyroid which may weigh 100-300 gm. Sectioned surface of the thyroid is fleshly with accentuation of normal lobulations but with retained normal shape of the gland. The fibrosing variant has a firm, enlarged thyroid with compression of the surrounding tissues. Histologically, the classic form shows the following features (Fig. 27.7): 1. There is extensive infiltration of the gland by lymphocytes, plasma cells, immunoblasts and macrophages, with formation of lymphoid follicles having germinal centres. 2. There is decreased number of thyroid follicles which are generally atrophic and are often devoid of colloid. 3. The follicular epithelial cells are transformed into their degenerated state termed Hurthle cells (also called

Askanazy cells, or oxyphil cells, or oncocytes). These cells have abundant oxyphilic or eosinophilic and granular cytoplasm due to large number of mitochondria and contain large bizarre nuclei. 4. There is slight fibrous thickening of the septa separating the thyroid lobules. The less common fibrosing variant of Hashimoto's thyroiditis shows considerable fibrous replacement of thyroid parenchyma and a less prominent lymphoid infiltrate.

CLINICAL FEATURES. The presenting feature of Hashimoto's thyroiditis is a painless, firm and moderate goitrous enlargement of the thyroid gland, usually associated with hypothyroidism, in an elderly woman. At this stage, serum T3 and T4 levels are decreased and RAIU is also reduced. A few cases, however, develop hyperthyroidism, termed hashitoxicosis, further substantiating the similarities in the autoimmune phenomena between Hashimoto's thyroiditis and Graves' thyrotoxicosis. There is no increased risk of developing thyroid carcinoma in Hashimoto's thyroiditis but there is increased frequency of malignant lymphoma in these cases.

SUBACUTE LYMPHOCYTIC THYROIDITIS Subacute lymphocytic (or painless or silent or postpartum) thyroiditis is another variety of autoimmune thyrioditis. Clinically, it differs from subacute granulomatous thyroiditis in being non-tender thyroid enlargement. It is seen more often 3-6 months after delivery.

Microscopically, the features are as under: 1. Dense multifocal infiltrate of lymphocytes and plasma cells in the parenchyma. 2. Collapse of thyroid follicles. 3. Rarely, presence of lymphoid follicles with germinal centres, simulating Hashimoto's thyroiditis.

SUBACUTE GRANULOMATOUS (DE QUERVAIN'S) THYROIDITIS Granulomatous thyroiditis, also called de Quervain's or subacute, or

giant cell thyroiditis, is a distinctive form of selflimited inflammation of the thyroid gland. Etiology of the condition is not known but clinical features of a prodromal phase and preceding respiratory infection suggest a possible viral etiology. The disease is more common in young and middle-aged women and may present clinically with painful moderate thyroid enlargement with fever, features of hyperthyroidism in the early phase of the disease, and hypothyroidism if the damage to the thyroid gland is extensive. The condition is self-limiting and shows complete recovery of thyroid function in about 6 months.

MORPHOLOGIC FEATURES. Grossly, there is moderate enlargement of the gland which is often asymmetric or focal. The cut surface of the involved area is firm and yellowish-white. Microscopically, the features vary according to the stage of the disease: Initially, there is acute inflammatory destruction of the thyroid parenchyma and formation of microabscesses. Later, the more characteristic feature of granulomatous appearance is produced. These granulomas consist of central colloid material surrounded by histiocytes and scattered multinucleate giant cells. More advanced cases may show fibroblastic proliferation. Morphologically similar appearance may be produced in cases where vigorous thyroid palpation may initiate mechanical trauma to follicles, so-called palpation thyroiditis.

RIEDEL'S THYROIDITIS Riedel's thyroiditis, also called Riedel's struma or invasive fibrous thyroiditis, is a rare chronic disease characterised by

Figure 27.7 Hashimoto's thyroiditis. Histologic features include: lymphoid cell infiltration with formation of lymphoid follicles having germinal centres; small, atrophic and colloid-deficient follicles; presence of Hurthle cells which have granular oxyphil cytoplasm and large irregular nuclei; and slight fibrous thickening of lobular septa.

MORPHOLOGIC FEATURES. Grossly, the thyroid gland is usually contracted, stony-hard, asymmetric and firmly adherent to the adjacent structures. Cut section is hard and devoid of lobulations. Microscopically, there is extensive fibrocollagenous replacement, marked atrophy of the thyroid parenchyma, focally scattered lymphocytic infiltration and invasion of the adjacent muscle tissue by the process.

GRAVES' DISEASE (DIFFUSE TOXIC GOITRE) Graves' disease, also known as Basedow's disease, primary hyperplasia, exophthalmic goitre, and diffuse toxic goitre, is characterised by a triad of features: Hyperthyroidism (thyrotoxicosis) Diffuse thyroid enlargement Ophthalmopathy. The disease is more frequent between the age of 30 and 40 years and has five-fold increased prevalence among females. ETIOPATHOGENESIS. Graves' disease is an autoimmune disease and, as already stated, there are many immunologic similarities between this condition and Hashimoto's thyroiditis. These are as follows: 1. Genetic factor association. Like in Hashimoto's thyroiditis. Graves'disease too has genetic predisposition. A familial occurrence has been observed. Susceptibility to develop Graves' disease has been found associated with HLA-DR3 (Hashimoto's thyroiditis has both HLA-DR3 and HLA-DR5 association, page 804), CTLA-4 and PTPN22 (a T-cell regulatory gene). 2. Autoimmune disease association. Graves' disease may be found in association with other organ-specific autoimmune diseases. Hashimoto's thyroiditis and Graves' disease are frequently present in the same families and the two diseases may coexist in the same patient. 3. Other factors. Besides these two factors, Graves' disease has higher prevalence in women (7 to 10 times), and association with emotional stress and smoking. 4. Autoantibodies. Autoantibodies against thyroid antigens are detectable in the serum of these patients

too but their sites of action are different from that of Hashimoto's thyroiditis. In Graves' disease, TSH-receptor autoantigen is the main antigen against which autoantibodies are directed. These are as under:

i) Thyroid-stimulating immunoglobulin (TSI): It binds to TSH receptor and stimulates increased release of thyroid hormone. ii) Thyroid growth-stimulating immunoglobulins (TGI): It stimulates proliferation of follicular epithelium. iii) TSH-binding inhibitor immunoglobulins (TBII): It is inhibitory to binding of TSH to its own receptor. Depending upon its action as inhibitory or stimulatory to follicular epithelium, it may result in alternate episodes of hypo- and hyperthyroidism. However, it is not quite clear what stimulates B cells to form these autoantibodies in Graves' disease. Possibly, intrathyroidal CD4+ helper T cells are responsible for stimulating B cells to secrete autoantibodies. The pathogenesis of Graves' infiltrative ophthalmopathy is also of autoimmune origin. The evidence in support is the intense lymphocytic infiltrate around the ocular muscles and detection of circulating autoantibodies against muscle antigen that cross-react with thyroid microsomes. MORPHOLOGIC FEATURES. Grossly, the thyroid is moderately, diffusely and symmetrically enlarged and may weigh up to 70-90 gm. On cut section, the thyroid parenchyma is typically homogeneous, red-brown and meaty and lacks the normal translucency. Histologically, the following features are found (Fig. 27.8): 1. There is considerable epithelial hyperplasia and hypertrophy as seen by increased height of the follicular lining cells and formation of papillary infoldings of piled up epithelium into the lumina of follicles which are small. 2. The colloid is markedly diminished and is lightly staining, watery and finely vacuolated. 3. The stroma shows increased vascularity and accumulation of lymphoid cells. However, the pathologic changes in gross specimen as well as on histologic

examination are considerably altered if preoperative medication has been administered.

CLINICAL FEATURES. Graves' disease generally develops slowly and insidiously. Patients are usually young women who present with symmetric, moderate enlargement of the thyroid gland with features of thyrotoxicosis (page 802), ophthalmopathy and dermatopathy. Ocular abnormalities are lid lag, upper lid retraction, stare, weakness of eye muscles and proptosis. In extreme cases, the lids can no longer close and may produce corneal injuries and ulcerations. Dermatopathy in Graves' disease most often consists of pretibial (localised) myxoedema in the form of firm plaques. Like in Hashimoto's thyroiditis, there is no increased risk of development of thyroid cancer in Graves' disease.

GOITRE The term goitre is defined as thyroid enlargement caused by compensatory hyperplasia and hypertrophy of the follicular epithelium in response to thyroid hormone deficiency. The end-result of this hyperplasia is generally a euthyroid state (in contrast to thyrotoxicosis occurring in diffuse toxic goitre or Graves' disease) though at some stages there may be hypoor hyperthyroidism. Two morphologic forms of goitre are distinguished: A. Diffuse goitre (simple nontoxic goitre or colloid goitre). B. Nodular goitre (multinodular goitre or adenomatous goitre).

Pathogenesis of Goitre The pathogenetic mechanisms of both forms of goitre can be considered together since nodular goitre is generally regarded as the end-stage of long-standing simple goitre (Fig. 27.9). The fundamental defect is deficient production of thyroid hormones due to various etiologic factors described below, but most common is dietary lack of iodine. Deficient thyroid hormone production causes excessive TSH stimulation which leads to hyperplasia of follicular

epithelium as well as formation of new thyroid follicles. Cyclical hyperplastic stage followed by involution stage completes the picture of simple goitre. Repeated and prolonged changes of hyperplasia result in continued growth of thyroid tissue while involuted areas undergo fibrosis, thus completing the picture of nodular goitre.

Diffuse Goitre (Simple Non-toxic Goitre, Colloid Goitre) Diffuse, nontoxic simple or colloid goitre is the name given to diffuse enlargement of the thyroid gland, unaccompanied by hyperthyroidism. Most cases are in a state of euthyroid though they may have passed through preceding stage of hypothyroidism due to inadequate supply of iodine. TSH levels are invariably elevated. In general, goitre is more

common in females. Simple goitre often appears at puberty or in adolescence, following which it may either regress or may progress to nodular goitre.

ETIOLOGY. Epidemiologically, goitre occurs in 2 forms: endemic, and non-endemic or sporadic. Endemic goitre. Prevalence of goitre in a geographic area in more than 10% of the population is termed endemic goitre. Such endemic areas are several high mountainous regions far from the sea where iodine content of drinking water and food is low such as in the regions of the Himalayas, the Alps and the Ande. Of late, however, the prevalence in these areas has declined due to prophylactic use of iodised salt. Though most endemic goitres are caused by dietary lack of iodine, some cases occur due to goitrogens and genetic factors. Goitrogens are substances which interfere with the synthesis of thyroid hormones. These substances are drugs used in the treatment of hyperthyroidism and certain items of food such as cabbage, cauliflower, turnips and cassava roots. Sporadic (non-endemic) goitre. Non-endemic or sporadic simple goitre is less common

than the endemic variety. In most cases, the etiology of sporadic goitre is unknown. A number of causal influences have been attributed. These include the following: Suboptimal iodine intake in conditions of increased demand as in puberty and pregnancy.

Genetic factors. Dietary goitrogenes. Hereditary defect in thyroid hormone synthesis and transport (dyshormonogenesis). Inborn errors of iodine metabolism.

MORPHOLOGIC FEATURES. Grossly, the enlargement of the thyroid gland in simple goitre is moderate (weighing up to 100-150 gm), symmetric and diffuse. Cut surface is gelatinous and translucent brown (Fig. 27.10). Histologically, two stages are distinguished: 1. Hyperplastic stage is the early stage and is characterised by tall columnar follicular epithelium showing papillary infoldings and formation of small new follicles. 2. Involution stage generally follows hyperplastic stage after variable period of time. This stage is characterised by large follicles distended by colloid and lined by flattened follicular epithelium (Fig. 27.11).

Nodular Goitre (Multinodular Goitre, Adenomatous Goitre)

Classification of Intracranial Tumours. I. TUMOURS OF NEUROGLIA (GLIOMAS) 1. Astrocytoma 2. Oligodendroglioma 3. Ependymoma 4. Choroid plexus papilloma

II. TUMOURS OF NEURONS 1. Neuroblastoma (page 800) 2. Ganglioneuroblastoma 3. Ganglioneuroma

III. TUMOURS OF NEURONS AND NEUROGLIA Ganglioglioma

IV. POORLY-DIFFERENTIATED AND EMBRYONAL TUMOURS 1. Medulloblastoma 2. Neuroblastoma

V. TUMOURS OF MENINGES 1. Meningioma 2. Meningeal sarcoma

VI. NERVE SHEATH TUMOURS 1. Schwannoma (neurilemmoma) 2. Neurofibroma 3. Malignant nerve sheath tumour

VII. OTHER PRIMARY INTRAPARENCHYMAL TUMOURS 1. Haemangioblastoma 2. Primary CNS lymphoma 3. Germ cell tumours

VIII. MISCELLANEOUS TUMOURS 1. Malignant melanoma (page 787) 2. Craniopharyngioma (page 796) 3. Pineal cell tumours 4. Pituitary tumours

IX. TUMOUR-LIKE LESIONS (epidermal cyst, dermoid cyst, colloid cyst)

X. METASTATIC TUMOURS