A SHORT OVERVIEW OF DISEASES AND SYNDROMES INVOLVING THE ENDOCRINE SYSTEM

The pituitary

Underaction

Simmond's disease

This rare disorder is due to destruction, partial or total, of the anterior lobe of the pituitary.
It may result from thrombosis of the vessels supplying the gland in association with post-partum haemorrhage (Sheehan's syndrome) or from the presence of a pituitary tumour.

Apathy, weakness, loss of libido, amenorrhoea and atrophy of breasts and testes result. There is pallor from loss of pigment and the hair is scanty. Significant loss of weight is unusual.

Thyroid activity is reduced and is shown by thyroid function estimations and the urinary 17-ketosteroids are reduced often to less than 2 mg. per day (Normal Values p. 523). A lateral X-ray of the skull may show enlargement of the sella turcia.

Diabetes insipidus

This disorder is also rare. It results from destruction of the posterior pituitary lobe, idiopathic or from local inflammation or neoplasm.

The striking feature is gross polyuria, up to 10 litres of low specific gravity urine being passed daily with consequent intolerable thirst, dehydration, constipation and loss of weight unless sufficient fluid is drunk to balance the loss.

Overaction

Pituitary tumours

Acromegaly is usually associated with a pituitary tumour. Symptoms may be due to the presence of the tumour or to oversecretion of the growth hormone. Fatigue but not loss of weight may be complained of but is not prominent. Hypothyroidism may develop later.

Arising in the growth period it takes the form of *gigantism*. Secondary diabetes develops in about 25 % of cases.

Other disorders of the pituitary glands and its hypothalamic control include Forbes-Albright syndrome (galactorrhea-amenorrhea caused by chromophobe adenoma of the pituitary), Chiari-Frommel syndrome (persistent galactorrhea and amenorrhea after pregnancy), panhypopituarism, SIADH (syndrome of inappropriate secretion of antidiuretic hormone), iatrogenic pituitary disorders, and some other unspecific pituitary disorders.

Thyroid

Underaction

Hypothyroidism

Etiology – Deficient secretion in the thyroid gland is seen in:
Congenital goiter or *cretinism*
Simple parenchymatous goiter occasionally.
Lymphadenoid goiter or *Hashimoto's disease*, which appears to result from an autoimunie response to thyroglobulin.

Patients treated by partial *thyroidectomy*, following which the incidence of hypothyroidism has been found to rise to 6 per cent after 10 years.
After I^{131} therapy the incidence is as high as 29 per cent after 10 years.

The incidence is largely among women (8-1), and chiefly in middle life. Myxedema is fairly rare but mild hypothyroidism is not uncommon though often overlooked.

Characteristics and Associated Symptoms – These are the reverse of those of thyrotoxicosis. All activities, mental and physical, are slowed down. The basal metabolic rate is lowered and there is sympathetic underaction. Thought and speech are slow and somnolence is noticeable; headache is common. Debility is marked but may be more apparent to friends than to the patient and there is no loss of weight. Cold is disliked, just as the thyrotoxic case dislikes heat. Many complain of paraesthesae of the hands of the carpal tunnel syndrome type.

Examination – It should be our endeavour to detect the early case. When fully developed the face is heavy and expressionless with yellowish pallor and a malar flush. The eyes are puffy, the skin harsh and dry, the hair dry and falling, the nails brittle, the legs swelled but without true edema, and where the condition has advanced to a state of myxedema the hands become thickened and spade-like. The temperature is low. Anaemia is often present but is not severe; it may respond only to treatment with thyroid substance.

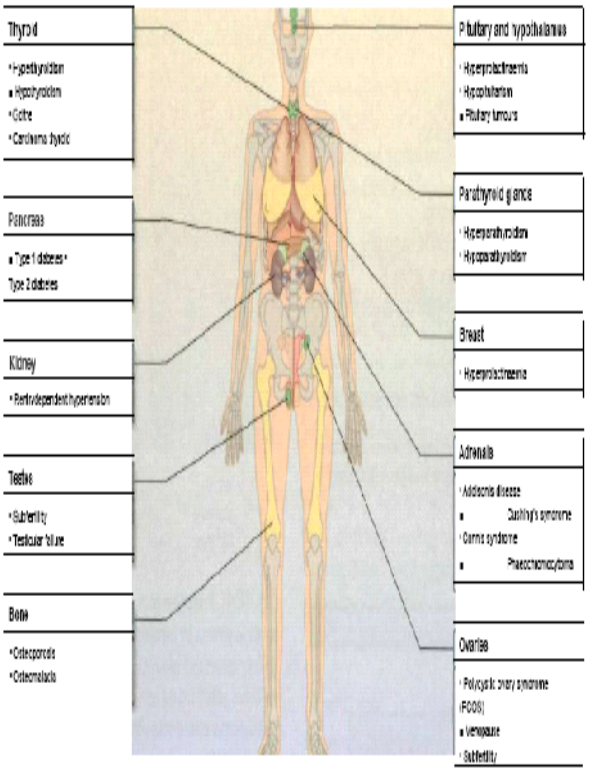
Investigations – Estimation of the plasma cholesterol, which is raised in hypothyroidism, is of value. The B.M.R. may be lowered to as much as 60 per cent below normal. Radio-active iodine uptake estimation (Normal Values, *p.* 525) is useful. In Hashimoto's

disease, the E.S.R. is raised and flocculation tests are abnormal because of increased gamma globulin.

Overaction

Thyrotoxicosis

Etiology – It occurs chiefly (6-1) in females, usually young women, but it may first become active at the menopause. Its frequency in certain hilly regions, such as Devonshire and Derbyshire, Switzerland, the Himalayas and the Great Lakes of Canada, is striking. Psychological factors are of some importance in precipitating the condition.



Characteristics and Associated Symptoms – The symptoms result from a raised metabolic rate and sympathetic overactivity. Exhaustion and debility are early and often the first symptoms. Loss of weight is striking and often severe. Palpitation, excessive sweating and occasionally diarrhea are prominent. "Formes frustes" occur in which loss of weight or fibrillation may be the only signs; here the enlargement is often retrosternal and dyspnae is usually present. It has been said in discussing atrial fibrillation (Tachycardia *p.* 306) that 20 per cent of all patients with toxic goiter develop fibrillation and that 80 per cent of cases over 60 years do so. In the absence of heart failure or mechanical narrowing of the trachea from retrosternal enlargement dyspnea is not a prominent symptom, but because of increased pulmonary ventilation, it may be present. The patient is often restless and irritable, psychoneurosis is common and insanity may occur.

Examination – The prominent eyes, flushed, excitable appearance, moist skin and the rapid heart, often fibrillating at the menopause, are characteristics.

The thyroid gland is usually visibly and as a rule palpably enlarged but sometimes the enlarged portion lies behind the sternum. It may then sometimes be felt filling up the suprasternal notch. In retrosternal goiter dialted veins may be visible on the upper thorax. Tremors of the extended hands are fine, regular and rapid; they are increased by excitement or movement of the hands.

Investigations – Where retrosternal goiter is suspected X-rays may show narrowing or displacement of the trachea. The diagnosis should be able to be made without an estimation of basal metabolic rate which may be raise to more than 100 per cent above normal but figures such as plus 30 per cent to 60 per cent are usual. The sleeping pulse rate remains raised and is useful in differentiating thyrotoxicosis from nervous tachycardia. A rate consistently above 80 makes the diagnosis highly probable but definite cases may have slower rates. Estimation of the uptake of radioactive iodine is the best guide to diagnosis (Normal Values *p.* 525). Glycosuria consequent upon hyperglycaemia is common. Regular weighing is important in estimating progress and all the effects of treatment.

Jod-Basedow phenomenon; a complication of iodine therapy including inflammation of the salivary glands, conjunctivitis, and skin rashes. In addition, induction of a transient hyperthyroidism in patients with non-toxic goiter.

Euthyroid sick syndrome (ESS); abnormal thyroid function in clinically euthyroid patients. suffering from severe non-thyroidal systemic illness.

Disorders of thyrocalcitonin secretion; hypersecretion of calcitonin or thyrocalcitonin.

Parathyroid

Underaction

Hypoparathyroidism

Destruction of operative removal of the parathyroid glands may result in tetany and less often in convulsive attacks resembling epilepsy. Other effects are abdominal cramps and vomiting, laryngeal spasm as in the spasmophilia of rickety children, and the early appearance of senile cataract.

These manifestations are due essentially to a lowered blood calcium level resulting from parathormone deficiency.

Chvostek's sign – the production of contraction of the facial muscles by tapping the cheek – and *Trousseau's sign* - carpal spasm when pressure in the

sphygmomanometer is kept above systolic level for 1-5 minutes – are confirmatory.

Investigations – The *serum calcium* (normal 9-11 mg./100 ml) is reduced below 8 mg/100 ml) and may be 5 mg or lower.
The s*erum inorganic phosphorus* (normal: 2.4-4.5 mg per 100 ml, children 4-6 mg per 100 ml) may be above 10 mg/100 ml. It is normal in *rickets* and in *steatorrhea* in which tetany may be seen.

Overaction

Hyperparathyroidism

This is as a rule primary and is due to an adenoma. The increased secretion of parathormone may cause generalized *osteitis fibrosa* (von Recklinghausen's disease) or *renal calculi*. In Massachusetts General Hospital 5 per cent of all renal calculi were associated with hyperparathyroidism. As Dent says, "stones and bones" are the mainstay of diagnosis.

Characteristics and Associated Symptoms – The onset may be insidious or sudden in the form of renal pain or a spontaneous facture; peptic ulcer symptoms are not uncommon.
Asthemia and loss of flesh may be the only manifestations for some time.

Examination– X-rays may show rarefaction and cyst formation of bones and renal calculi. The *fasting serum calcium* level is often above 11 mg/100 ml and the *serum inorganic phosphorus* level is usually below 2.5 mg/100 ml provided that the blood urea is normal.

Thymus

It is likely but not established that the thymus has an endocrine function. It is likewise not firmly established that thymic tumours or overaction are responsible for myasthenia gravis but the frequent amelioration of symptoms following thymectomy may be held to justify its inclusion here.

Myasthenia Gravis

This disorder is seen more in women than in men and chiefly between 20 and 50 years.
The striking feature is weakness and undue fatigability of skeletal muscles. This is shown by a drooping of the eyelids, an expressionless face, nasal voice and difficulty in chewing and swallowing all becoming more apparent as the day goes on.

Di George syndrome

Congenital absence of the thymus and parathyroid glands without agammaglobulinemia but with frequent infections and delayed development.

Pancreas

Underaction

Diabetes

Etiology – Joslin states that diabetes is 100 per cent hereditary. It is not sex-linked but appears to depend upon a Mendelian recessive trait. A family history of diabetes is found in half to one-third of cases.
Diabetes may remain latent or potential so that we may think of a vulnerable pancreas. This may be acted upon by various stresses, early in life when it is more severe or later when it may be mild in degree.
Such stress includes:
Infection: Any infection, tuberculosis, urinary tract, influenza, tonsillitis but particularly staphylococcal infection may suffice.
Pregnancy: It may be that increase in the diabetogenic or growth hormone not only depresses the insulin activity of the pancreas but explains the frequently large infant.
Obesity: This is by far the most important precipitating factor. It has been estimated that 80 per cent of all diabetics over 20 years are obese; three-quarters of these are women. It seems that the fat depots finally refuse to accept any more glucose which therefore accumulates in the blood.

The secondary type of diabetes as opposed to the primary form, accounts for 10 per cent of all cases and result from disorder of other endocrine glands.
In the pituitary *acromegaly* is accompanied by diabetes in 25 per cent of cases.

In the Adrenals, *phaeochromocytoma* and *Cushing's syndrome* are also diabetic in 50 per cent of cases.
In Thyrotoxicosis, 4 per cent are diabetic.
In Pancreas itself diabetes is seen in *chronic pancreatitis* (25 per cent) in *cancer* (25 per cent) and in *haemochromatosis* in 75 per cent.

Characteristics and Associated Symptoms – These depend to some extent upon age, sex and the acuteness or otherwise of the condition. In the young (under 40 years) an acute onset is common with loss of weight and ketosis.
In the middle-aged (40-65 years) the symptoms are mild and have commonly been present for months. Obesity is usual and pruritus vulvae is common.
In the elderly (over 65 years) symptoms may be milder as a rule.

Diabetes may present in many ways:

1. *Symptomless glycosuria* glucose being found on testing of recruits, for life assurance, among relatives of diabetics or as part of a routine examination. This may not of course be diabetes but due to a low threshold (renal glycosuria) or a lag effect.

2. *Debility* which justifies the inclusion of diabetes in this chapter is usual and the weight may fall from polyuria and deranged metabolism.
3. *Thirst, polyuria* and frequency of micturition result from osmotic dieresis.
4. *Skin manifestations* such as boils, carbuncles, pruritus vulvae, perforating ulcer of foot or gangrene of a toe.
5. *Peripheral neuritis* with pain, numbness and pins and needles felt in the extremities.
6. *Ocular* – cataract, retinitis, and disturbed vision from alterations in intra-ocular tension.
7. *Ketosis* – This may manifest itself by epigastric pain and vomiting, dyspnea, drowsiness and actual coma.

Examination – The first step is to confirm or exclude diabetes by blood sugar estimations Obesity is frequently present but the juvenile cases are thin and all may have lost weight.
Dehydration result in a dry tongue, inelastic skin, cramps and constipation. The fundi, reflexes, heart, blood pressure and lungs must be examined.

Investigation – A blood sugar curve is unnecessary as a rule and a burden to patient and pathologist. A fasting blood sugar, followed by a carbohydrate meal and a further estimation in one and a half hours usually suffices. A blood urea may be of value and the urine may contain, as well as sugar, acetone and protein and may be infected. The heart and lungs should be X-rayed.
Other disorders of the pancreas include abnormality of secretion of glucagons in which there is hyperplasia of the pancreatic alpha islet cells, abnormality of secretion of gastrin, Zollinger-Ellison syndrome, and other unspecific disorders of pancreatic internal secretions.

Adrenals
Underaction
Addison's Disease
Etiology – There is a diminution or absence of the hormones produced by the cortex, in particular hydrocortisone and aldosterone. Destruction of the cortex may be due to tuberculosis or fibrosis which is now thought to result from an autoimmune process. This links with *Hashimoto's thyroiditis* and *Sjogren's syndrome*, which affects the salivary and lachrymal glands. Infiltration of the adrenal glands by *secondary amyloidosis* is a rare cause of adrenal failure.

Characteristics and Associated Symptoms – It is characterized by increasing weakness and pigmentation. Anorexia is marked, there is great loss of weight and bouts or cries occur in which all the symptoms are increased with vomiting and diarrhea and marked fall in blood pressure. The vomiting and diarrhea result in a further loss of sodium, which is the primary condition; muscular cramps occur and a state resembling shock ensues.

Examination – The pigmentation is characteristic and affects exposed parts, axillae and groins and areas where friction occurs, it is seen in the lines of the hands; the mucous membrane of the mouth shows pigmented areas. The weight falls progressively as does the systolic blood pressure, which may fall to 90 or even 70mm. of mercury.

Investigations - X-rays may show calcification of suprarenals and lesions in the lung.
The serum electrolytes may undergo alteration, the sodium and chloride being low, the potassium raised. The blood urea is frequently raised to 50-7- mg. per cent.

The urinary 17- ketogenic steroids are characteristically low (Normal Values *p.* 523). They normally rise after giving corticotrophin (A.C.T.H.), a failure to do so being good evidence of adrenal failure.

Overaction
Cushing's syndrome
Etiology – this syndrome is due to an excessive secretion of hydrocortisone by the adrenal cortex. It is most frequently seen today in a minor form in persons undergoing corticosteroid therapy.

The primary form results from hyperplasia, adenoma or, uncommonly, carcinoma of the adrenal cortex.
The hyperplasia is thought to result from an excessive production of corticotrophin (A.C.T.H.) and a pituitary tumour can sometimes be demonstrated. Hyperplasia accounts for 80 per cent of cases. Cushing's syndrome is four times as frequent in women as in men and the onset is usually in early adult life.

Characteristics and Associated Symptoms – It is included in this chapter despite the obesity which is a feature, because of the marked fatigability resulting from muscular wasting.

Amenorrhea or oligomenorrhea is present, back pain from osteoporosis is frequent and secondary diabetes is common. There may be an alteration of the personality in the direction of depression.

Examination – In a typical case diagnosis may be made on sight. The face is plethoric, purplish and moon-like.

A patchy cyanosis is seen over the trunk and limbs and purple striae are visible, especially over the lower abdomen in about 30 per cent of cases.
Height is diminished and the posture is stooping with dorsal kyptosis resulting from osteoporosis of the vertebrae.
Hypertension is usually present.

Investigation – The urinary 17- ketogenic steroids are often increased but high normal levels are sometimes found Normal Values *p.* 523.
An intravenous pyelogram and presacral oxygen insufflations may demonstrate a tumour. X-rays of the spine show osteoporosis, wedging and sometimes fractures. In some 50 per cent, glycosuria and in 75 per cent a diabetic blood sugar curve are found.

Conn's syndrome
This rare syndrome is mentioned for completeness' sake. It is due to an excessive secretion of a sodium-retaining hormone, possibly aldosterone, from the adrenal cortex.
A tumour is usually found but occasionally it is associated with hyperplasia.

Characteristics and Associated Symptoms – Hypertension is present and is associated with muscular weakness. This may be minimal but sometimes the patient presents with episodic muscular paralysis due to severe intracellular potassium depletion.

Examination – Hypertension will be found and latent tetany can sometimes be demonstrated.

Investigations – The serum potassium will be low (less than 3.5 mEq per litre) and the bicarbonate is usually raised. The serum calcium is normal. Metabolic studies will demonstrate excessive sodium retention and increased potassium loss.
An intravenous pyelogram and prescral oxygen insufflations may demonstrate a tumour.

Phaeochromocytoma
This rare tumour of the adrenal medulla is considered along with other causes of hyoertension. It is not a cause of debility or loss of weight.

Bartter's syndrome
A combination of fluid, electrolytes, and hormonal abnormalities characterized by renal potassium, sodium, and chloride wasting; hypokalemia; hyperaldosteronism; hyper-reninemia; and normal blood pressure. The syndrome usually appears in childhood either as a sporadic or a familial, usually autosomal recessive, disorder.

Oversecretion of adrenal androgens is associated with adrenogenital syndromes (adrenal virilism). These syndromes include congenital adrenal hyperplasia, Achard-Thiers syndrome (one form of a virilizing disorder of adrenocortical origin in women characterized by masculinization and menstrual disorders, in association with manifestations of diabetes mellitus such as glucosuria), female adrenal pseudo hemaphroditism, macrogenitosomia praecox, and sexual precocity with adrenal hyperplasia.

Kidneys
The kidneys have endocrine and autocrine functions which include the renin-angiotensin system, erythropoetin and vitamin D metabolism.
Autocrine functons are mediated by endothelins and prostateglandins. Renal natriuretic peptide particiaptes in the intrarenal regulation of sodium and chloride transport. Nitric oxide synthesized in the kidneys is involved in the regulation of renal haemodynamics and tubuloglomerular feedback.

Ovaries
The Menopause
Etiology **-** The irregular diminution of eotrogen, perhaps with a secondary overactivity of the anterior pituitary gland at the menopause which usually begins in the late forties or after double oophorectomy frequently produces symptoms. It is important to realize that these symptoms do not necessarily coincide with the cessation of the menses but persist for or arise years after it. The picture is complicated by the fact that there may be imbalance of other hormones.

Characteristics and Associated Symptoms – The emotional state is unstable and there is readily induced dyspnea, fatigue and debility; insomnia and depression are common.

Characteristic and perhaps a *sine qua non* of the menopausal origin of the condition are hot flushes which may be dry or accompanied by sweating, giddiness, headaches and variations in the blood pressure are other evidences of vasomotor instability. Thoracic pain, sterna or praecordial, and sometimes felt in the left arm may be complained of and resemble angina pectoris. The existence of other symptoms characteristic of the menopause and their relief by the giving of oestrogen will, however exclude this.

The thyroid may be disturbed in the direction of overaction with palpitation, tremor and weight loss or there may be thyroid deficiency with scantiness and dryness of the hair. Pruritus vulvae and arthritis are common.

Ovarian dysfunction is also seen in hyperestrogenism, hypersecretion of ovarian androgens, ovarian failure (primary, iatrogenic, postirradiation, or post surgical), polycystic ovaries (isosexual virilization, Stein-Levanthal syndrome), and unspecific or idiopathic ovarian dysfunction.

Testes

Hyper and hypo secretion of testicular hormones. Hypofunction may result from defective synthesis of testicular hormones or post ablative testicular hypofunction due to iatrogenic, postirradiation, or postsurgical procedures.

The endocrine system is closely linked with metabolic, nutritional, and neurological regulation and function. Dysfunctions that result from these associations are too vast and numerous to fit into this short overview of clinical diseases involving the endocrine system.