# ENDOCRINOLOGICAL PROBLEMS : WHAT CAN BE LEARNED AT THE BEDSIDE*

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With the many new technological advances and therapeutic weapons which have become available in various fields of medicine in recent years, the responsibility of the doctor towards his patient becomes greater than it has ever been before. Only by the continual process of self-education can the physician engaged in the practice of medicine best fulfil his role in caring for the sick. By remaining abreast of new information with regard to the basic sciences and by integrating them with his observations and examinations at the bedside, it is possible to bring to the patient the maximum amount of intelligent medical assistance.

The field of endocrinology is only one of many in which such principles apply and it is the purpose of this paper to show how some of the problems may present themselves to a clinician at the bedside without recourse in the first instance to the various laboratory or other investigative procedures which may be necessary in their more exact elucidation. In the limited time available it will not be possible to deal with more than a very few of the various clinical pictures which may present themselves.

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## HYPERTHYROIDISM

The thyrotoxic individual, usually a female, is nervous or irritable, restless and fidgety. Commonly when one approaches the bedside, she jumps into an upright position and throws off the bedclothes. She may wish to cooperate but rather overdoes it. Such behaviour constitutes a pattern which is almost pathognomonic. The patient feels hot and likes to be in a cold environment. Handshaking gives a nearly diagnostic impression; the hand is very hot and moist—sometimes actually dripping wet. Whilst occasionally such hands may be found in other conditions, the converse—the finding of a cold hand, dry or moist—almost excludes hyperfunction of the thyroid. Redness of the elbows, first noted by Plummer, is very frequently present and also of the knuckles and thenar and hypothenar eminences. The fingernails tend to leave the nail-bed, giving a concave or wavy margin to the terminal portion in contact with the nail-bed. Pigmentation of a more or

less Addisonian variety is met with occasionally, but the mucous membranes remain free. Then there are, of course, the eye signs, which may be related either (1) to lid retraction, causing the wide palpebral aperture or the lid lag or the staring or frightened expression, or (2) to extrinsic muscle weakness, causing limitation of movement of the eyeball, especially in a upward direction, or diplopia, or (3) to swelling—chemosis of the conjunctiva or swelling of the lids. It is important to know that these eye signs vary independently of the intensity of the thyrotoxicosis and that in certain cases they may get worse when the thyrotoxicosis is subsiding. Burning, photophobia, epiphora, corneal ulceration and marked blepharitis may occur. Often exophthalmos is obvious with the patient upright but is almost unnoticeable when the patient lies on his back. The tongue, apart from exhibiting a definite tremor, is often red and smooth owing to achlorhydria.

The neck, of course, often shows the goitre, but it is possible for marked thyrotoxicosis to exist without visible or palpable goitre. The carotid arteries are often to be seen violently throbbing. Various muscular phenomena are frequently observed. A useful test for the demonstration of muscular weakness was described by Lahey in 1926: If a thyrotoxic patient seated in a chair is asked to hold one leg out straight in a horizontal position, he can do so for 25-30 seconds only, whereas most normals can go over 60 seconds. Myasthenia gravis occurs in some, and other degrees of weakness in 75% of all cases of thyrotoxicosis. Acute bulbar palsy is sometimes seen. In a considerable number of cases wasting of the temporalis muscles and the interossei of the hands is seen; in a few cases, wasting of all skeletal muscles. Vitiligo, alopecia and decrease of the auxillary hair, and premature graying of the scalp hair are other features which are sometimes observed. Not infrequently neuropsychiatric manifestations may be the presenting features—paraphasia, acalculia, psychosis with hallucinations, bulbar palsy, coma, myo-encephalopathy, choreo-athetotic movements—and often these indicate the presence of the so-called 'thyroid crisis'. Then there are the easily recognized disturbances referable to the cardio-vascular system which may be elicited on examination—the tachycardia which is present during waking and sleeping hours, premature beats or paroxysms of auricular fibrillation, a forceful cardiac apical impulse, a systolic murmur heard all over the praecordium, a raised systolic blood-pressure and a slightly decreased diastolic pressure with a resultant high pulse-pressure.

Finally, I wish to mention the condition of pretibial myxoedema, which occurs almost invariably in patients with severe or malignant exophthalmos and often after subtotal thyroidectomy. It appears in painless symmetrical patches of variable size but of definite outline on the anterior aspects of the lower half of the legs or the dorsal surfaces of the feet. It has also been described on the face, the eyelids and the scrotum. The skin overlying the lesions is thickened and pigskin-like in appearance, and red cyanotic or yellow-white in colour. It does not pit on pressure but will dimple after the local injection of hyaluronidase, and its cause is probably related to an excessive production of thyrotropic hormone.

## HYPOTHYROIDISM

*Myxoedema.* In the adult case of hypothyroidism also, interestingly enough, the patient is generally a female. Myxoedema is, in fact, 4 times as common in females as in males. It is well to remember that the disease is extremely insidious in its onset and many years of thyroid insufficiency or deficiency may be required before myxoedema becomes manifest. It would be pertinent to mention at this stage that if the thyroid gland of a person with standard metabolism is extirpated, it will take 20 days for the metabolic rate to decrease to approximately minus 20, when mild clinical manifestations of hypothyroidism begin to appear. After 40 days the rate will be about minus 30 and frank myxoedema begins to appear. Within 80 days the disease is full blown. Decreased sweating and increased sensitivity to cold are the early manifestations. The patient wants more clothes, more cover and more heat in his room. Drowsiness and slowing of mental and physical activity appear, soon followed by lack of energy and ambition, and puffiness of the skin. Peri-orbital puffiness is particularly striking. Mucus collects in the eyes and the lids often are found on waking to be stuck together. The skin becomes pallid and may have a yellow hue. The soft tissues of the body become thickened, particularly noticeable in the face and hands. The nose, ears, lips and other portions of the face appear large. The face looks somewhat expressionless. The tongue is large and the voice husky, leathery and low-pitched. The speech is slow, deliberate, without inflection. Some words sound slurred or otherwise inarticulate. The patient may lose some of the body hair and develop constipation, meteorism, deafness, oedema, dyspnoea, cardiac enlargement. Menorrhagia occurs very frequently. The pulse rate is slow. The blood pressure is generally raised.

*Cretinism.* Hypothyroidism which develops before birth and produces cretinism either of the endemic or the sporadic type is an entity which can often be recognized at the bedside in the latter half of the 1st year of life and sometimes as early as the 3rd month. The segment of the body above the symphysis is distinctly longer than that below. The head is large in comparison to the body and closure of the fontanelles is considerably delayed. The forehead is short, the nose broad, the eyes wide apart, the eyelids puffy and wrinkled, the mouth open, the lips and tongue thick, and the voice deep and husky. The teeth appear late, the neck is short and thick, and the hands and feet are puffy, short and broad. The abdomen is large and protuberant; an umbilical hernia is often present. The skin is dry and cool, pale and thick, and roughened. The hair is sparse, coarse and dry. Sitting, walking and talking are considerably delayed. Most important of all, when one wishes to confirm one's diagnostic impression by means other than bedside observations, it must be remembered that the appearance of the ossification centres is markedly delayed.

*Juvenile myxoedema.* When hypothyroidism develops after birth, the condition of juvenile myxoedema results,

and its characteristics are midway between those of cretinism and adult myxoedema; growth and development, though normal in the early stages of life are retarded, and dwarfism and delayed sexual development become apparent. The extremity-trunk ratio is infantilistic, i.e. the ratio of the distance from the symphysis to the head to that from the symphysis to the feet remains 1·7/1 as it is at birth. This is a simple yet valuable bedside observation to make which, when elicited, will readily lead one to perform all the other investigations —biochemical and radiological—for the definitive diagnosis of this condition.

### HYPERFUNCTION OF THE SUPRARENAL CORTEX

Before describing the features in any detail, it would be as well to clarify the terms and nomenclature used at the present time:

*Cushing's syndrome* refers to the clinical picture designated by Cushing as pituitary basophilism; it is encountered chiefly among young women, although it does of course occur in men and in children of either sex. Its salient features are a distinctive habitus characterized by wasting of muscle and obesity or an abnormal distribution of fat, the combination of which makes the trunk, face and neck appear obese and the extremities thin; hirsutism; diabetes either latent or frank; ecchymoses; and amenorrhoea or impotence. Except for the presence of hirsutism, there is little or no evidence of masculinization. Usually there is a pad of fat over the cervico-thoracic part of the spinal column. The upper lids and corners of the mouth droop. The cheeks may be fiery red and so full that they obscure the ears when the face is viewed squarely from the front. In children, the normally short neck may be completely obscured by a drooping double chin. As the fat cheeks roll forward and hang down, the mouth appears unduly small and set deep in the face. Almost always there is an easily demonstrable muscular weakness, sometimes of a degree seen in moderately advanced muscular dystrophy or atrophy. Acne of varying intensity is fairly common. Generally the skin is thin, mottled and high coloured, and there are distinctive purplish striations in it.

*Adrenal virilism and androgenital syndrome* are more or less synonymous terms denoting a clinical picture which usually occurs among young women, but again it may occur at any time of life and in either sex. It is characterised by most of the physical attributes of masculinity, namely vigour, muscularity, enlargement of the larynx and hirsutism of the type normally occurring in men. When this syndrome occurs prenatally in a foetus having ovaries, it is associated with anatomic defects of the genital system, and the clinical picture is then known as feminine pseudo-hermaphroditism. When it occurs postnatally among children, the syndrome is characterized usually by somatic and sexual precocity. Among boys this sexual precocity is homologous, i.e. masculine in type; in the case of girls, the puberty is heterologous, which means that it proceeds along masculine lines. Among children of either sex a distinctive habitus appears as the child grows older. The arms and legs are short and the trunk is relatively elongated. The muscles bulge conspicuously, the shoulders are broad and the hips are narrow. When the syndrome occurs in a woman she becomes more or less masculinized. Menses cease and the breasts become smaller.

To amplify some of the features of the *Cushing's syndrome* from the point of view of their importance at the bedside: The hypertension which occurs may be relatively benign. On the other hand it may be so severe that it may be associated with heart failure or cerebrovascular accident, or blurring of vision or blindness. The obesity will be very extreme when the disease occurs in childhood. The diabetes which sometimes occurs may be an insulin-resistant type. Osteoporosis may manifest itself to the clinician as severe backache with root pains associated with compression fracture. Attacks of renal colic may draw attention to the hypercalciuria which is the sequela of the osteoporosis. Muscular weakness occurs in the Cushing's type and is particularly noticeable when the patient tries to climb stairs. It should be remembered, however, that the actual atrophy of the muscle may be hidden by the overlying fat. In the adreno-genital type there is increased strength and vigour. The purple striae of the skin (see above) occur in the lower part of the abdomen, the anterior lateral aspect of the thighs, the upper part of the arms, the axillae, the pectoral regions, and even the breasts. They are roughly parallel and depressed and vary in size from 0·5 to 5 cm. in width and 5 to 15 cm. in length. They may become necrotic and infected. In addition to the striae, the entire skin of the body often becomes thin and transparent, so that the superficial veins are unduly prominent. Keratosis pilaris in the region of the buttocks makes the skin of this area feel like sandpaper. Ecchymoses and petechiae appear after the slightest trauma and are often prominent symptoms. The face may be fiery red and the skin of the extremities may be mottled and somewhat cyanotic (see above). Beneath the clavicles and over the sternum there is often a semilunar area containing tiny whitish papules, between which the skin is red and flushed. This has been referred to as the 'androgenic flush'.

In connection with the *adreno-genital syndrome*, I should like to make a few points which may be of assistance to the clinician at the bedside in helping him to formulate an assessment of the picture: Simple hirsutism in the absence of virilism rarely proves to be adrenal cortical in origin. Patients with hirsutism plus obesity and amenorrhoea deserve further diagnostic study, even though few of them prove to have recognizable organic adrenal cortical disease. Patients with both hirsutism and milder degrees of virilism are more likely to have organic adrenal cortical disease. A feminine pseudo-hermaphrodite almost always has adrenal cortical hyperplasia rather than tumour. Most patients who show all the features of Cushing's syndrome and nothing else prove to have adrenal cortical hyperplasia rather than adrenal cortical tumour. Patients who present mixed clinical pictures of both the adreno-genital syndrome and Cushing's syndrome are likely to have adrenal cortical tumours rather than hyperplastic cortical lesions. An enlarged clitoris in a patient who seems to have nothing but Cushing's syndrome indicates adrenal cortical tumour; however, an enlarged clitoris

in a patient who has the adreno-genital syndrome may indicate either tumour or hyperplasia.

### ADDISON'S DISEASE

Turning from hyperfunction of the suprarenal cortex to hypofunction, or Addison's disease, the clinical description given by Addison himself exactly one hundred years ago is still the best: 'An insidious onset of a feeling of languor and debility, a remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change in the colour of the skin.'

The classical symptoms and signs are the profound asthenia, the gastro-intestinal symptoms, particularly anorexia, nausea, vomiting, constipation or diarrhoea and occasionally relatively severe abdominal pains, marked weight loss, pigmentation, and hypotension. There is a slow but continued loss of weight and the patient either becomes aware himself or is told by others of a change in the colour of his skin. Curious mental changes characterized by marked irritability and personality alterations often severe enough to suggest an underlying psychosis of a persecutory character frequently appear. Occasionally the first presenting evidence of the disease is the development of the so-called Addisonian crisis, precipitated by an acute infection or some surgical procedure. It is well to remember that pigmentation and hypotension may be present for months or years—even 15 years—before gastro-intestinal symptoms and weight loss appear. The pigmentation, which is invariably present but not always so, often begins as a sun-tan which persists and becomes permanent and with the passage of time becomes progressively darker.

The occurrence of pigmentation in unexposed portions of the body is of great clinical significance. First in importance and frequency are the unshapely patches of brown-grey, grey-black or blue-grey pigmentation observed on the mucous membrane of the oral cavity, particularly on the lips, gums and tongue, and occasionally on the posterior pharyngeal wall. It is to be borne in mind that oral pigmentation occurs in argyria and that it is a normal occurrence in the Bantu. The areolar, peri-anal and genital pigmentation shows an increase in its intensity; also, operation scars, pressure points such as the elbows, the hat-band region, and places where a restraining or tight-fitting garment has caused pressure, will show the appearance of this pigmentation. The folds of the axillae, the palms of the hands, and the knuckles of the fingers are other frequent sites. In addition to the diffuse pigmentation, many patients develop scattered jet-black spots or freckles. Infrequently mahogany-coloured longitudinal bands of pigmentation appear in the finger nails. Addison himself also called attention to areas of vitiligo or leukoderma which were observed as small decoloured patches on the back and trunk.

The hypotension frequently has a postural component and the symptoms associated with it thus constitute a considerable part of the symtomalotogy. The dizziness, blurring of vision, sense of faintness, cardiac palpitation and tachycardia, and occasionally even angina, occur particularly with change of posture and most frequently on rising in the morning. The loss of weight may be considerable and yet the patient does not appear to be Cachectic. This was also commented on by Addison in his original description. *The asthenia* is profound. The patient both looks and acts unutterably wearied even when lying in bed. He may be completely incapable of any effort and no amount of rest in itself produces any improvement in this symptom. The crisis is heralded by an intensification of all the previously mentioned symptoms and signs. The weakness is more profound, the blood pressure falls, the skin colour assumes a darker hue with a superimposed dusky slaty cyanosis. Nausea, vomiting and diarrhoea becomes severe, and sometimes intractable abdominal pain may develop. A thready, feeble pulse, distant and muffled heart-sounds, a markedly dehydrated skin, soft and sunken eyeballs, all indicate the state of circulatory collapse which has developed.

### PHAEOCHROMOCYTOMA

A clinical syndrome concerning the chromaffin tissue of the medullary portion of the suprarenal gland may be mentioned here, viz. that produced by the pheochromocytoma. If recognized, it presents one of the remediable causes of hypertension. It manifests itself frequently in the form of attacks of *palpitation*, headache, dizziness, blurring of vision, epigastric and thoracic pain, pain in the extremities and back, dyspnoea, choking sensations, nausea, vomiting, diarrhoea, profuse sweating, shakiness, and fear. The face and extremities may be pale or cyanotic. The pulse is small and hard. The blood pressure during the attack may be more than 300 mm. mercury. The attack may last minutes or days. Change of posture, mechanical pressure on one or other kidney area, hyperventilation, pain, emotion, micturition, may bring on an attack. Between attacks, the patient enjoys a sense of ordinary health. Sometimes, the elevation of blood pressure is persistent.