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HORMONES AND BEHAVIOUR PATTERN*

BY

S. LEONARD SIMPSON, M.A., M.D., F.R.C.P.

Consultant Endocrinologist to St. Mary's Hospital, London

Endocrinology is at least 100 years old, if we accept as a landmark Addison's discovery of suprarenal disease in 1849, the year in which Berthold studied castration and its reversal in the cockerel. For the last quarter of a century people have speculated on the influence of the endocrines on the psyche—often with unbridled imagination and incomplete knowledge both of endocrinology and of psychology. The invitation of your Society has induced me to return, albeit with some trepidation, to this fertile field of merging fact and fantasy in which I made my first incursion some twenty years ago.

Historically we might go back to the Psalms xxvi, 2, "Try my reins and my heart" and the Sancino editorial commentary, "In the Bible the reins are the seat of the emotions; with the heart they determine character and actions." Reins being archaic English for loins, or kidneys, we approximate to modern knowledge of the adrenals and the emotions.

In a symposium at the Royal Society of Medicine in 1937 I advanced the following thesis: "Apart from the well-defined psychoneuroses, the endocrine balance of an individual, either grossly abnormal, or merely constitutional and familial, or physiological (puberty, pregnancy, or the climacteric), has an important influence on the character, behaviour pattern, and emotional reactivity. Such endocrine disturbances are exceedingly common, and if, instead of psychiatric labels, one uses the wider conception of behaviour pattern, or characteristics of conduct, one could not fail to recognize a close association." With more recent knowledge, we will consider this thesis under three headings: (I) Psychoneuroses, psychoses, and behaviour patterns in major endocrine disorders; (II) the evidence for types of endocrine constitution in normal individuals; (III) the applicability of knowledge gained from the endocrinopathies to accepted normality.

I. Major Endocrine Disorders

Gonads

Male eunuchoids are usually placid, docile, and apathetic, although they may "flare up" at times, and show sensitivities. Apart from ineffective coitus, they are usually incapable of the warmth or intensity of other relationships between husband and wife. As to the dramatic effect of testosterone, I have recorded (Simpson, 1938, 1948) that "psychological and personality changes after testosterone are remarkable. Shyness and diffidence are lost. Patients become extroverted, creative, energetic, and sometimes aggressive. They develop

initiative and are capable of assuming responsibility. Depression and apathy disappear and may be replaced by euphoria." I have no experience of males castrated before puberty, but those castrated after puberty have behaviour patterns comparable to those of eunuchoids. One male patient, aged 20, was previously an exemplary intellectual and athletic leader at public school, but changed completely in character after bilateral castration at 16, following unusual torsion and strangulation in a fall while sprinting. He slept a great deal during the day; was discharged from every job because of laziness; and failed to get on with other people. During the consultation, as at other times, he cried easily without obvious cause. He was said to have changed to a "female" type and to be like a temperamental "female." He showed considerable charm of manner at times. Another surgical castrate was listless and apathetic, had no initiative, felt like someone dying, and showed lack of application and concentration.

On the other hand, a woman, completely castrated in infancy by an operation on an inguinal hernia containing both ovaries strangulated in the inguinal sac, showed none of the above characteristics. She was a charming and successful woman, of many interests and obvious ability and normal sexual activity, after a minor dilatation of the introitus.

Sexual precocity and pseudo-sexual precocity in the male, associated with relatively high 17-ketosteroids, is often characterized by aggressiveness, physical as well as pseudo-sexual, courage, and enterprise, as well as great physical strength.

The "differences" between the sexes, physiological as well as pathological, are complicated by two considerations. Although the testes contribute roughly one-third of the total androgens, the adrenal androgens in any one woman may be greater than the total adrenal and testicular androgens in any one male. Further, the chromatin sex patterns (skin, mucous membrane) may be the opposite of the somatic sex—for example, in ovarian agenesis and Klinefelter type of male eunuchoidism.

Adrenals

Cushing's syndrome, in which there is excessive secretion of cortisone (used for convenience as a comprehensive term for the various adrenal glucocorticoids) is frequently associated with depressive states, but maniacal agitation and violence have been recorded (Hertz *et al.*, 1955). Phases of euphoria are less usual, but I have met with this condition in the mixed type of adrenal hyperfunction, in which sufficient androgens are secreted to prevent a negative nitrogen balance. Starr (1952) has made a special study of personality changes in Cushing's syndrome. He writes: "It is the purpose of this paper to record the relevant findings gleaned from a scrutiny of 53 proven cases of Cushing's syndrome and to determine the incidence and nature of the mental and emotional aberrations. Most of these cases have been

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reported elsewhere. In the earlier report, however, no specific reference was made to psychotic disturbances except when suicide was the cause of death. It is noteworthy that personality changes were present in 60% of these cases. Severe depression was the most frequent finding. Euphoria, which often occurs with A.C.T.H. therapy, was a rare finding in this series. Thirteen (24.5%) of the patients showed such severe personality disturbances that 8 were institutionalized as insane and 5 others attempted suicide. An additional 19 patients (35.8%) had marked or moderate mental symptoms, but isolation was not necessary. The suicide rate in our series is 1,000 times that of the general population."

Cortisone, or corticotrophin, has been given in large doses for a number of non-endocrine disorders. In the majority of cases euphoria results from cortisone therapy, at least initially, although depressive states may follow. Excitement, restlessness, and insomnia are also met with, and even behaviour approximating to the maniacal. One circumspect, dignified patient of mine, successfully adrenalectomized for Cushing's syndrome, found that moderate doses of cortisone accelerated and intensified his intellectual and emotional reactions, caused him to drive his car very fast and recklessly, and to develop an irrepressible compulsion to join any game of football he might be passing, without the consent of the players, and in a black formal jacket, striped trousers, and a bowler hat. All these features, he found, could be abolished by reducing the dose of cortisone and would reappear on increasing it. Sprague *et al.* (1950), of the Mayo Clinic, record the case of a boy of 2½ with macrogenitosomia who became wildly excited and maniacal after 50 mg. of cortisone, injected daily for some days.

Addison's disease may be regarded as the opposite of Cushing's syndrome, and I have frequently (Simpson, 1948, 1952) drawn attention to the apathy, negativism, and irritability of chronic Addison's disease, and the disorientation and delirium of crises. Desoxycortone and (or) cortical extract both favourably influenced these personality changes, but to a far less extent than cortisone, which restores personality to normal, reversing at the same time abnormal encephalogram patterns. Cleghorn (1952) has met with depressive psychosis and delusions, but these must be regarded as rarities.

Pituitary

Gigantism and mild acromegaly are often associated with great physical strength and energy, restlessness, courage, exploratory drive, and social or economic aggressive persistence. When accompanied with good intellect, the physical presence and booming voice (large laryngeal cords) constitute a formidable combination. With the addition of charm, with or without the subtraction of intellect, we get the typical film male hero. Harvey Cushing pointed out the considerably enlarged adrenals in this condition. In the later-phases of severe gigantism and acromegaly, weakness may supervene, and it is many years since I suggested that David defeated Goliath in his "weak" phase, with the added disadvantage of optic atrophy from a pituitary tumour.

Simmonds-Sheehan disease, or panhypopituitarism, may be considered the opposite of acromegaly, and is characterized by the development of weakness, apathy, inertia, lack of social drive and pride, lack of interest in the home, in children, and in personal appearance (Simpson, 1948, 1952). Whereas thyroid and testosterone are helpful, particularly testosterone, the improvement in behaviour pattern is not comparable to the dramatic change produced by cortisone. Depressive states and delusional insanity are also met with in patients where the diagnosis has been missed for some time.

In regard to the controversial problem of adiposity, I wrote in 1938: "A pituitary type of adiposity as typified by the fat girl or woman, with slender limbs, a beautiful and lovable face, good teeth, and a fascinating smile; wide social leanings, loving and loved, perhaps made fun of but extremely popular, a good dancer in spite of corpulence, very

musical and often gifted, a warm quality voice, artistic temperament, romantic nature, with alternating phases of happiness and depression that may recall to mind a lesser grade of maniacal-depressive psychosis." This condition I subsequently called adipose gynism (Simpson, 1950), in so far as the patients are intensely "feminine" in regard to certain physical and mental characteristics. They have some clinical features also met with in Cushing's syndrome, and an excess of adrenal glucocorticoids has been indicated by chromatographic assays (Gray *et al.*, 1956), but, owing to their height being above average, an excess of pituitary growth hormone has also been postulated. A comparable condition in males I termed adipose gynandria, to indicate an admixture of male and "female" physical and mental characteristics; and the behaviour pattern as recorded above is comparable.

In addition to adiposity of the face, buttocks, thighs, breast, and abdomen, true gynaecomastia may be present, puberty and descent of the testes delayed, the voice may break late or persist as a high voice, particularly in excitement, body hair may be absent or late, and facial hair may always remain scanty. The patients are sensitive and loving, and particularly attached to their mother. They may be talented musicians, opera-singers, and artists, and are often sentimental and social. In many, in their late teens, an adrenal androgenic phase may change the physical and behaviour pattern, but residual indications may be detected. Both types are usually valuable and gifted members of the community, and, in so far as the mild forms are so numerous, these are more correctly regarded as varieties of normal than as examples of minor endocrinopathies.

Thyroid

Thyrotoxicosis is frequently associated with anxiety neurosis, but it can be argued that thyrotoxicosis is a complication of an anxiety state in a patient with a labile thyroid gland; and, further, that toxic adenomata do not present the same personality pattern as Graves's disease. However, an excess of thyroid by mouth often produces restlessness, apprehension, and hyperacute sensory and intellectual processes. Prior to the era of controlled thyroidectomy, acute mania, hallucinations, and delusions were frequent complications of severe thyrotoxicosis (Rogers, 1904; Jameison and Wall, 1936). It is of interest that Dunlap and Moersch (1934), of the Mayo Clinic, reporting on the "Psychic Manifestations of Goiter," recorded acute delirium reactions in a high percentage of the cases of hyperfunctioning adenomatous goitre, whereas, in exophthalmic goitre, toxic psychosis was the more frequent complication.

The opposite condition of untreated myxoedema may present as an apathetic mentally slow and dull-witted vegetative hibernating individual, the condition sometimes complicated by dementia or delusions, as recognized by the Clinical Society of London in 1888 and more recently by Asher (1949) in a clinical paper with the dramatic title "Myxoedema Madness." Changes in the electroencephalogram occur both in myxoedema and in thyrotoxicosis.

Parathyroids

Hyperparathyroidism does not appear to be associated with characteristic personality changes, but hypoparathyroidism is often associated with irritability, excitability, irascibility, and explosive reactions, which seem to parallel in the mental field the neuromuscular irritability associated with low serum calcium. Associated abnormal encephalograms are met with. Greene and Swanson (1941) reported psychoses, with delusions and hallucinations, in five patients with hypoparathyroidism, and refer to the report of Shannon on eight children with hypoparathyroidism, who suffered from convulsions, depression, irrational speech, night terrors, and acute maniacal excitement with screaming, fighting, and tearing of clothes.

Hyperinsulinism

The disorders of feeling and behaviour associated with overdosage of insulin are well known—apprehension, irrita-

bility, argumentativeness, disorientation, mental confusion, and sometimes aggressive bellicosity. These features are present in minor degree when some normal people are kept from eating, giving rise to the old adage "feed the brute" and the custom of prefacing delicate negotiations with a good meal. Functional endogenous hyperinsulinism is found to be more intense with pre-existing emotional instability and following some types of gastrectomy and gastro-jejunostomy (Skillern and Rynearson, 1953). Much more severe symptoms are met with in pancreatic islet-cell tumours; these may present in psychiatric clinics as anxiety states, as hysteria, and as psychotic states with mania and delusions. Widespread necrosis of the cerebral cells and multiple minute cerebral haemorrhages have been observed (Richardson and Russell, 1952). The disturbance of cell carbohydrate metabolism, with low blood-sugar concentrations, appears to be the essential disturbing factor, initially, and is also met with in pituitary and adrenal insufficiency. The cerebral changes are apparently reversible in the milder or earlier phases but irreversible later.

II. Constitutional Endocrinology or Endocrine Constitution

The experience gained from psychological and behaviour studies of major endocrinopathies would be of little value to our main thesis if we failed to demonstrate that there was such a thing as endocrine constitution and that its physical expression resulted in the recognition of physical types. The answer by an endocrinologist, in regard to the existence of endocrine constitution, is in my opinion an unequivocal positive, but let us be less credulous, or more sceptical, and examine the problem from two angles: (a) Do endocrine disorders, in major and minor forms, occur in families, their incidence being genetically determined? (b) Can types of normal physical constitution, as recognized by the anthropologist, be correlated with a preponderance or relative deficiency of one or more hormones?

A. Occurrence of Endocrine Disorders in Families

The adreno-genital syndrome, manifest at puberty or in adult life, is undoubtedly familial in incidence, sometimes transmitted through females and sometimes through hairy males (Simpson, 1948, 1953). To the endocrinologist interested in paediatrics, as well as in adults, indications of the tendency can be found in early childhood. This is not to be confused, however, with congenital virilism (adrenal pseudohermaphroditism) in females and adrenal pseudo-sexual precocity in males, obvious at birth, or infancy, occurring in families, and apparently due to a genetic chemical inability to convert 17-hydroxyprogesterone into 17-hydroxycorticosterone (Bartter *et al.*, 1951; Jailer, 1953); although a puberty or adrenarche type of adreno-genital syndrome may yet be shown to be due to an inherent metabolic abnormality. Cushing's syndrome, in its classical form, is usually not familial, but mixed types of adrenal hyperfunction, with hypersecretion both of androgens and of glucocorticoids, are often familial. In one family, grandfather, father, and two adult sons suffered from this disorder, and steroid diabetes was present in both sons and in the grandfather. In adipose gynism and gynandrisms, conditions associated with clinical and chromatographic assay evidence of adrenal glucocorticoid hyperfunction, a familial incidence is usually present (Simpson, 1950, 1951).

Diabetes mellitus has been divided by Lawrence (1951) into lipoatrophic and lipoplethoric (adipose), the former being due primarily to insulin deficiency and the latter to an excess of pituitary and (or) adrenal diabetogenic hormones (steroid diabetes). Considering both types, Oakley (1955-6) concludes that "there is general agreement that heredity is the most important single factor in the aetiology of diabetes mellitus."

Atkinson (1932, quoted by Rolleston, 1936) collected 12 examples of hereditary or familial incidence of acromegaly. A sister, 55 years old, of three tall big-boned prognathic normal brothers, was sent to me with classical acromegaly

and a pathologically enlarged sella turcica. Professor Seligman (1931), in a letter to *Nature*, described acromegaly among the old Northmen, and Michael Perkins (1931) followed this with a description of a genealogical tree through several generations of the Egil Norse family, and concluded that "gigantism seems to have become endemic in the Fyrdafjord district of Sogn (Norway)—men more like giants in growth and seeming than mortal men." He incidentally refers also to their "bent of mind, courage and fits of uncontrollable rage." The opposite condition of familial dwarfism, with or without other features of infantilism, is frequently met with, and has a parallel in congenital strains of dwarf mice, with few eosinophil cells in the anterior pituitary.

Some other major endocrine disorders which are not hereditary on a large scale, but which are associated with a genetic familial incidence in a limited way, are cretinism due to a genetic chemical defect with inability to synthesize thyroxine (Hutchison and McGirr, 1956); eunuchoidism in twins (Simpson, 1948; Ellenbogen and Ryan, 1955); familial diabetes insipidus (Levinger and Escamilla, 1955); and familial Addison's disease with spastic paraplegia (Harris-Jones and Nixon, 1955).

B. Types of Physical Constitution

Anthropologists (Sheldon, 1940; Tanner, 1955) divide types of physical constitution into three major groups—endomorphs, mesomorphs, and ectomorphs. Briefly and crudely expressed, the mesomorphs are the muscular athletic type (male and female); the endomorphs the adipose type, with some feminine physical characteristics in the male; and the ectomorphs the thin wiry nervous type. Each individual is classified by three arbitrary figures, indicative of the degree of each component.

There is no difficulty in correlating the mesomorphs with a high-level secretion of pituitary growth hormone and (or) an excess of adrenal androgens. In clinical language, as one aspect of this, a trained observer will not fail to notice square massive lower jaws, with mild prognathism, among a good proportion of men in rugby teams and among boxers of the heavier weights. Height is determined not only by the time phase and the extent of pituitary-growth-hormone secretion, but also by the early or late closure of the epiphyses, which depends upon androgens and (or) oestrogens, as well as thyroxine. A heavyweight boxer under my care was found to be excreting 38 mg. of androgens, measured as 17-ketosteroids, in 24 hours, about twice the average. Surprisingly, according to conventional ideas, I found that a very strong, tall, muscular woman excreted nearly as much as this male—namely, 34 mg.—which means that her adrenals were probably secreting more than the adrenals of the boxer. Neither was ill, and their only complaint was their heavy weight. Another group of powerful athletes, including rugby players and boxers, are of mesomorphic build but somewhat plethoric in facies, often with red or purple lineae distensae, because their adrenals are simultaneously secreting an excess of adrenal glucocorticoids. Sometimes the relatively early closure of their epiphyses renders them stocky and broad rather than tall.

Correlation of endocrinology with endomorphism is equally probable on the background of my endocrine experience and interpretation, but appears more controversial and indefinite to many of my colleagues. Without denying the importance of psychogenic and hypothalamic adiposity, I must content myself with referring briefly to a few of the numerous clinical and experimental observations indicating the role of hormones in adiposity (Simpson, 1948, 1953); to Young (1945, 1951) and Salter and Best (1953) on the protein and fat anabolism of pituitary growth hormone and of insulin, separately or in combination, endogenous or exogenous; to the finding of hyperplasia of the pancreatic islet cells in hereditary obese-hyperglycaemic mice (Wrenshall *et al.*, 1955); to the effect of cortisone in non-endocrine states, coupled with gross obesity in some

patients with Cushing's syndrome, particularly in children, and considered in conjunction with Kendall's (1945) experimental studies of the relative and absolute increase in fat content of the carcass of mice treated with various adrenal glucocorticoid hormones; to the close resemblance between endomorphism in the male and adipose gynandrm; to clinical examples of hyperinsulinism; and to the loss of fat in some women with virilism and its return with removal of an adrenal virilizing tumour. Experiments have shown that augmented appetite is one aspect of this complex metabolic problem; but, again from the pragmatic angle, augmented appetite determined by endogenously secreted hormones is just as important as metabolic abnormalities leading to augmented fat deposition. Further, it is necessary to remember that the relative percentage of fat and protein in the body can be changed dramatically by hormones in the absence of change in body weight (Kendall, 1945).

The possible relationship between the ectomorph type and endocrine constitution is admittedly nebulous, and I shall not attempt to substantiate it on the scanty evidence that might be put forward. It might be more easily explained, if at all, by relative deficiency of some pituitary and adrenal hormones. However, the whole field of minor deficiency of hormones, in accepted normality, is itself a much less obvious and difficult field than that of hormone excess.

III. Applicability of Knowledge Gained from the Endocrinopathies to Accepted Normality

The answer to the question of the validity of correlating endocrinopathy behaviour pattern with varieties of normality depends upon the degree of acceptability of the evidence, deductions, and considerations advanced up to this point, as outlined above in I and II. In so far as I have consistently propounded the thesis, based mainly on clinical observations and interpretations, that endocrine disorders, or syndromes, are met with in varying degrees of intensity and completeness, or rather incompleteness, and are manifested frequently in minor degree in accepted normality, I have no personal difficulty in drawing a positive inference on the applicability of knowledge gained from a study of major endocrinopathies. Absolute proof, if such could be forthcoming, is obviously dependent upon a large and comprehensive investigation by a team of experts, including psychologists, psychiatrists, and anthropologists.

Another aspect of this problem is how far physical constitution and appearance, however determined, influence behaviour pattern. I am not attempting to answer this complex problem with any dogmatism, but if the answer is not a complete negative it is worth while bearing in mind that the endocrine glands determine, or at least considerably influence, physical strength, height, breadth of shoulders and hips, hair and skin in regard to thickness, greasiness, dryness and pigment, plethora or pallor of face, strength and pitch of voice, and some forms of adiposity.

However, the main thesis of this paper deals with the more direct influence of various hormone concentrations, or resulting metabolic changes, on cerebral processes. In attempting to apply the deductions from major endocrine disorders we should also consider the applicability of the following generalizations in regard to an excess or deficiency of specific hormones. An excess of androgens (adrenal or testicular) appears to be associated with positive personalities, with energy, drive, enterprise, restlessness, courage, and positive achievement. A severe deficiency of androgens is usually associated with apathy, passivity, negativism, and lack of enterprise. The associated physical strength, or weakness, probably plays a part in determining these attitudes, which latter, however, are more intense and characteristic than those caused by variations of physical strength due to non-endocrine illness. A deficiency of adrenal glucocorticoids is similarly associated with a negative apathetic personality, and cortisone therapy appears to have a remarkable influence on personality changes and

emotions, both in Addison's disease and in Simmonds's disease. In general, the glucocorticoids appear to be more specifically concerned with the emotions, sensibilities, artistic expressions, and social relations than do the androgens. Cushing's syndrome, with an excess of adrenal glucocorticoids, is paradoxically more often associated with depression than with the excitement or euphoria that follows cortisone therapy, but maniacal excitement and restlessness do occur; and, in the mixed types of adrenal hyperfunction, as well as with mild increases of adrenal glucocorticoids (adipose gynandrm and gynism), euphoria, high spirits, great social activities and successes, artistic creative achievements, and an emotional successful drive are in dramatic contrast to the apathy and withdrawal attitudes associated with deficiency of adrenal glucocorticoids. Since alternative phases of excitement and depression (mild manic-depressive states) are also met with in these states, a varying relative level of adrenal glucocorticoid might be as important as an average concentration above normal.

Deficient thyroid secretion results in a general slowing of mental and physical activities, approximating to a vegetative existence, whereas excessive thyroid secretion is associated with the opposite—namely, rapidity of thought and action, anxiety and apprehension, urgent anticipation, intellectual penetration and awareness, and, in milder degrees, with a dynamic vivacious personality. A deficient secretion of parathormone results in a low blood calcium with resulting well-known irritability of neuromuscular tissue but less well known psychogenic irritability and irascibility, an electrolyte influence on cerebral cells.

An excess of insulin, with resulting hypoglycaemia, leads to disorientation, irrational behaviour, sometimes violent, and ultimate coma—degenerative changes in the cerebral cells and multiple minute cerebral haemorrhages being found in fatal cases. Initial changes in the cerebral cells, associated with low blood sugar, appear reversible, but severe and prolonged effects irreversible. Endogenous compensatory adrenaline secretion plays a part in the more immediate symptomatology.

The pituitary gland manifests its influence on personality by its controlling relationship with the adrenals, thyroid, and sex glands; but in addition the growth hormone is nitrogen-anabolic, as is testosterone, prolactin hormone influences maternal behaviour in animals, and the gonadotrophins in excess appear to be a factor in climacteric disturbance.

It is of interest that abnormal electroencephalograms are found in many major endocrine disorders and that they return to normal with appropriate organic therapy. There is as yet no evidence to indicate detectable aberrations in the encephalograms of normal individuals who might be regarded as having a variety of endocrine constitution.

As regards the psychoses, it is noteworthy, and perhaps challenging to hormone theories, that there is no consistent relationship between the type of psychosis and the type of endocrine disorder. This may suggest that hormones do not determine but only precipitate, or reveal, an underlying psychotic disease or tendency. However, the response to therapy is often convincing from the limited pragmatic angle, not unimportant to the clinician and patient.

Summary

In so far as major endocrine disorders, with a preponderant excess or gross deficiency of one or more hormones, are frequently associated with characteristic behaviour patterns, as well as with psychoneuroses and psychoses, it seems reasonable to conclude that the excess or deficiency of hormones is causative or influential, and not merely coincidental—a view which is further supported by successful organic treatment but which does not necessarily exclude the existence of non-endocrine genetic factors modifying the response of individuals to hormonal stimuli, excessive or deficient.

In so far as major endocrine disorders, particularly those of hyperfunction, are frequently familial and genetically determined, and in so far as many major endocrine disorders have their representation, but with less intensity, in accepted normality, observations in regard to the association of major endocrine disorders with characteristic behaviour patterns are relevant to a consideration of the varieties of normal behaviour pattern among normal individuals.

Classifications of physical build, as used by anthropologists, bear some relationship to classifications of endocrine constitution, and the evidence put forward suggests an endocrine basis for two of the anthropological groups, the muscular mesomorphs and the adipose endomorphs, thus giving further support to the previous two conclusions.

I qualify my conclusions by an unqualified admission of the importance of non-endocrine factors in determining behaviour patterns, and even more so in the case of the psychoneuroses and psychoses, the majority of the latter of which are not due to endocrine disorders.

REFERENCES

- Asher, R. (1949). *Brit. med. J.*, 2, 555.
 Atkinson, F. R. B. (1932). Quoted by Rolleston (1936).
 Barter, F. C., Albright, F., Forbes, A. P., Leaf, A., Dempsey, E., Carroll, E. (1951). *J. clin. Invest.*, 30, 237.
 Cleghora, R. A. (1952). *Ciba Foundation Colloquia on Endocrinology*, 3, 141. Churchill, London.
 Dunlap, H. F., and Moersch, F. P. (1934-5). *Amer. J. Psychiat.*, 91, 1215.
 Ellenbogen, B. K., and Ryan, G. M. S. (1955). *Brit. med. J.*, 2, 712.
 Gray, C. H., Lunnon, J. B., Pond, M. H., and Simpson, S. L. (1956). *J. clin. Endocr.*, 16, 473.
 Greene, J. A., and Swanson, L. W. (1941). *Ann. Intern. Med.*, 14, 1233.
 Harris-Jones, J. N., and Nixon, P. G. F. (1955). *J. clin. Endocr.*, 15, 739.
 Hertz, P. E., Nadas, E., and Wojtkowski, H. (1955). *Amer. J. Psych.*, 112, 144.
 Hutchison, J. H., and McGirr, E. M. (1956). *Lancet*, 1, 1035.
 Jailer, J. W. (1953). *Bull. N.Y. Acad. Med.*, 29, 377.
 Jameison, G. R., and Wall, J. H. (1936). *Psychiat. Quart.*, 10, 464.
 Kendall, E. C. (1945). *Josiah Macy Foundation Metabolic Conference*, New York, p. 81.
 Lawrence, R. D. (1951). *Brit. med. J.*, 1, 373.
 Levinger, E. L., and Escamilla, R. F. (1955). *J. clin. Endocr.*, 15, 547.
 Oakley, W. (1955-6). *Trans. med. Soc. Lond.*, 72, 232.
 Perkins, M. (1931). *Nature (Lond.)*, 128, 491.
 Richardson, J. E., and Russell, D. S. (1952). *Lancet*, 2, 1054.
 Rogers (1904). Quoted by Jameison and Wall (1936).
 Rolleston, H. D. (1936). *The Endocrine Organs*. Oxford University Press, London.
 Salter, J., and Best, C. H. (1953). *Brit. med. J.*, 2, 353.
 Seligman, C. G. (1931). *Nature (Lond.)*, 128, 221.
 Sheldon, W. H. (1940). *The Varieties of Human Physique*. Harper, New York.
 Simpson, S. L. (1938). *Major Endocrine Disorders*, 1st ed., 1938, 2nd ed., 1948. Oxford Univ. Press, London.
 — (1950). *Postgrad. med. J.*, 26, 201, 417.
 — (1951). *Bull. N.Y. Acad. Med.*, 27, 723.
 — (1952). *Ciba Foundation Colloquia on Endocrinology*, 3, 123. Churchill, London.
 — (1953). *Proc. roy. Soc. Med.*, 46, 39.
 Skillern, P. G., and Ryncarson, E. H. (1953). *J. clin. Endocr.*, 13, 587.
 Sprague, R. G., et al. (1950). *Arch. Intern. Med.*, 85, 199.
 Starr, A. M. (1952). *J. clin. Endocr.*, 12, 502.
 Tanner, J. M. (1955). *Growth at Adolescence*. Blackwell Scientific Publ., Oxford.
 Wrenshall, G. A., Andrus, S. B., and Mayer, J. (1955). *Endocrinology*, 56, 335.
 Young, F. G. (1945). *Biochem. J.*, 39, 515.
 — (1951). *Brit. med. J.*, 2, 1167.

The hospital waiting-list for cases of tuberculosis in Northern Ireland virtually disappeared in 1956, according to the eleventh Annual Report of the Northern Ireland Tuberculosis Authority. In consequence, when the Waringfield Chest Hospital becomes available for the reception of patients, the chest hospitals at Armagh and Downpatrick will be used for other types of cases. The number of people given B.C.G. vaccination was 32,669. The number of patients examined by the mass radiography service was 124,459; of 10,622 people referred by general practitioners in Belfast, 438 were diagnosed tuberculous.

ENDOCRINE ACTIVITY IN PSYCHIATRIC PATIENTS WITH MENSTRUAL DISORDERS

BY

J. H. REY, M.D.

U. NICHOLSON-BAILEY, B.A.

AND

A. TRAPPL, B.Sc.

From the Institute of Psychiatry, the Maudsley Hospital,
London

Though psychiatric literature is full of references to the relationship of mental illness and disorders of the sexual and reproductive systems, few studies have been carried out of gonadal activity in mental disorders. This is partly due to the great difficulties encountered in its proper assessment. The methods available are laborious and time-consuming. This applies both to bioassays and to chemical methods, especially serial investigations.

The need for such studies arises, firstly, because of the high incidence of menstrual abnormality in mental illness (Hause, 1923; Allen and Henry, 1933; Strachan and Skottowe, 1933; Ripley and Papanicolaou, 1942); secondly, because psychological changes are observed during the cycle and certain periodic syndromes and events occur at specific times during the cycle (Cooke, 1945; Reifstein, 1946; Kroger and Freed, 1951; Mackinnon and Mackinnon, 1956); and, thirdly, because of the complexity of the psycho-physiological processes which produce normal and abnormal cycles (Kroger and Freed, 1951).

The Experiment

An experiment was designed to obtain information primarily with regard to gonadal activity in psychiatric patients with menstrual disorders. Information was also obtained with regard to gonadotrophic, thyroid, and adrenal activity.

Material.—Patients were chosen from amongst the in-patient population of the hospital. They suffered from: (1) amenorrhoea (below age 45); (2) irregular periods; (3) menstrual disturbances (above age 45); (4) puerperal amenorrhoea. The only other factor affecting the choice of patients was the willingness to show sufficient co-operation in the collection of biological specimens—for example, urine and vaginal smears.

Definitions.—Arey (1939) has summarized the results of 10 different investigations and has found for the length of the cycle a mean of 28 days, with a standard variation of 4.92. This was adopted as a measure of the normal cycle. Any variation of more than twice the standard deviation each way but less than twice the normal cycle was defined as an irregular cycle. Amenorrhoea was taken to be present when a full cycle had been missed—that is, twice the length of a cycle.

Methods Used for Hormonal Estimations.—(a) Gonadal activity was assessed by the vaginal-smear method (de Allende and Orias, 1950; Pundel, 1952; Wachtel, 1954). Smears can be repeated over a long period of time, and the information obtained from such a procedure is fairly extensive. Oestrogenic activity can be measured quantitatively by the cornification index count, and indications of ovulation and pro-