Endocrine Therapy and the Psychoses. By CHARLES B. MOLONY, M.B., Ch.B., Assistant Medical Officer, District Mental Hospital, Limerick.

IN 1913 the late Sir William Osler made the prophetic statement that the glands of internal secretion would open up many fields of endeavour in the science of medicine within the next two decades. In view of subsequent events it must be acknowledged that he thereby displayed even more than the usual vision for which he was famous.

In the fourth edition of Leonard Williams's handbook, *Minor Maladies*, the following passage appears :

"Still more earnestly do I believe that the study of the whole field of the internal secretions will enable us to detect and correct morbid tendencies with a degree of success which has been denied to the older methods. The microbe—the seed—has ruled the immediate past; the future is with the soil, the endocrine glands."

In relation to a subject more germane to this article, Prof. Robertson, in his Maudsley Lecture on "The Prevention of Insanity" (1), lays great stress on the importance of disorders of the ductless glands in the ætiology of mental abnormalities. He says :

"Just as heredity is a factor to be reckoned with to a greater or less extent in every case of insanity, so we are beginning to recognize that disturbance of the internal secretions plays a more or less important part in all forms of mental disorder. Any future great therapeutic discovery in the domain of mental disease will probably be found in a knowledge and control of the internal secretions."

The above are general statements, and, proceeding from the sources from which they do, are entitled to command our attention and respect. It is when we endeavour to apply the well-known and carefully elaborated principles of physiological endocrinology to the treatment of the more elusive and consequently less well-known pathological entities that it behoves us to be critical, to curb our imagination and enthusiasm, and to substitute for these latter the maximum amount of common sense and cold logic in our assessment of the degree of success we can legitimately claim for such treatment. The number of pathological conditions which endocrine therapy claims to ameliorate or cure is already legion; the grounds for such claims are, I am afraid, in many cases anything but well-founded, and it is not the aim of this article to add the psychoses to this list without unimpeachable clinical evidence.

Physiological endocrinology has made huge strides in the present century, but more particularly within the last decade. The corresponding applied science has more than kept pace with it—in fact

it may be said to have pursued its own reckless course irrespective of the steadying hand of experimental work. This particular phenomenon invariably follows the transition from a pure to an applied science, but in this case more especially do we see its ill-effects, and the disrepute into which it has led honest attempts at scientific organotherapy.

In claiming that any particular drug can be credited with curing any particular disease I maintain it should be the aim of the clinician to observe three cardinal principles, *viz.*:

(1) To eliminate spontaneous recovery.

(2) Long periods of unsuccessful treatment by other methods—this obviously strengthens the case immensely; and—

(3) By long-continued clinical after-observation to show that the particular therapeutic agent did, in fact, have the desired curative or ameliorative effect.

Bearing these fundamentals carefully in mind, I hope to show that, in my hands, endocrine therapy applied to carefully selected cases of mental disease has been remarkably successful. From the point of view of a rapid, complete and permanent cure of a psychosis, the discovery by the psychiatrist of an underlying basis of glandular insufficiency or dyscrinism points directly to a hopeful therapeutic agent at his command—I refer, of course, to substitutive or homo-stimulative organo-therapy. To appeal for a more general recognition of the possibility, the probability, nay the certainty, in many cases, of this direct causative association between such dyscrasias and certain of the psychoses is the prime object of these pages.

In this field, of course, I cannot claim to be a pioneer, but, looking over the literature of mental disorder on the one hand and endocrinology on the other, the dearth of observations on the successful use of extracts of the ductless glands in the treatment of mental derangement has struck me as being rather remarkable. In my more critical moments this has often moved me to question whether my results, reported, and, I hope, critically analysed below, can, after all, be genuine. By which I mean to convey, Can organotherapy, *per se*, be credited with the undoubted cures? Further on I hope to show that, by carefully selecting one's cases, by accurately and impartially reporting their progress, and by reasonably close after-observation, one can conscientiously draw conclusions of definite clinical and scientific value, even in such ætiologically obscure conditions as the psychoses, and such physiologically complex entities as the ductless glands.

In the following descriptions of cases I do not propose to attempt

a classification based on the influence of defects of the secretion of individual glands in producing individual psychoses, because I believe in most cases there is a pluriglandular deficiency manifesting itself in an infinite variety of ways. The term "psychoses," therefore, is here used in its broadest sense to indicate any form of mental aberration, although indeed there has been a remarkable uniformity of symptoms in one group—the climacteric insanities; while it is only very isolated cases which have responded in a satisfactory manner to uniglandular, as opposed to pluriglandular, therapy.

Here, at the risk of being discursive, I must endeavour to establish the fact that pluriglandular therapy is based on rational principles, which have received abundant support from recent physiological, pathological and clinical investigation. No one will now deny that there is a very well-marked physiological endocrine inter-relationship, and that disturbance of one gland inevitably affects one or more of the others. To take a specific example which has been experimentally proved up to the hilt—the influence of the ductless glands on carbohydrate metabolism. The predominant hormone in regulating the amount of sugar in the blood is that derived from the B cells of the islets of Langerhans in the pancreas. Experimental removal of three-fifths of the pancreas, by producing hyperglycæmia and diabetes, establishes this fact. Adrenalin, the active principle of the suprarenals, when injected, causes hyperglycæmia and glycosuria, thereby demonstrating an antagonistic relationship between the adrenals and the pancreas as far as carbohydrate metabolism is concerned. Experimental injection of extract of the posterior lobe of the pituitary has been shown directly to antagonize the action of insulin, and to cause hyperglycæmia. In exophthalmic goitre, which is characterized pathologically by excessive secretion of the thyroid, increase of blood and urine sugar has been repeatedly observed; in the opposite condition — myxœdema — hypoglycæmia and high carbohydrate tolerance are invariably present. Here then we have an interacting quartette of endocrine activity, balanced to a nicety in the normal individual; but, by the very fact of such a delicate poise, alteration in the activity of one member will inevitably result in a proportionate positive or negative secretory disturbance in one or more of the remainder. I merely mention this well-known experimental work to establish a presumption in favour of the probability of endocrine disturbance in psychotic conditions being, in most instances, polyglandular, and therefore demanding, at the hands of the clinician, appropriate pluriglandular therapy.

Some quotations on this point from contemporary sources may not be amiss at this juncture:

"It should be recognized that when one gland is malfunctioning others are also disturbed, and may cause atypical conditions" (Osborne, *Principles of Therapeutics*, Part 4, p. 400).

"The most remarkable fact about the internal secretions is that they are correlated with one another. Not only has it been abundantly demonstrated by experiment, but in many cases pathological lesions of the individual glands cause some disturbance in the functional relations of other glands—the so-called pluriglandular syndromes" (Fielding H. Garrison, *Endocrinology and Metabolism*, i, p. 70).

"The theory of a correlation between the glands that constitute the endocrine system, though only vaguely understood, is, nevertheless, essentially well established. It may be stated in general that the ductless glands are normally so correlated as to form a perfect physiologic balance, which is preserved by a proper distribution of harmony and antagonism between the functions of the various glands. If one of the glands is diseased or injured, or extirpated, the normal balance is upset, and the organism of the individual may be affected by the abnormal action of one or more distant glands of the group" (Graves, *Gynæcology*, p. 45).

Certain correlationships between the individual glands have been definitely established both in experimental physiology and clinical medicine. Take the case of the thyroid and pituitary. Most investigators agree that the pituitary hypertrophies after thyroidectomy—on histological examination increased secretory activity, especially of the anterior lobe, is apparent. What practical conclusions can we draw from this fact? I admit it has yet to be proved that the pituitary can function for the thyroid. But is it unreasonable to assume, in cases where the thyroid secretion is diminished, that it *does* make a valiant attempt to do so? A constant symptom in many of my climacteric cases has been headache. Cannot this be interpreted, without unduly stretching the imagination, as due to increased activity of the pituitary compensatory to decreased ovarian, and probably thyroid, secretion, resulting in hyperæmia and enlargement of the first-named gland in its unyielding sella turcica? The fact that I have found the administration of a combined thyropituitary-ovarian extract of immense benefit for this otherwise intractable symptom convinces me that this explanation is well founded.

At the same time it brings me to another relationship, likewise experimentally and clinically well established. I refer to that between the thyroid and the ovaries. The thyroid hypertrophies during puberty, menstruation and pregnancy—obviously an attempt to help the sex-glands over these periods of stress and strain. Experimentally, thyroidectomy results in marked loss in the development of the ovary and uterus (2). Pathologically, abnormal menstrual conditions and atrophy of the gonads are fairly constant findings in Graves' disease. Clinically I have yet to see a case with well-marked hypothyroidism in which amenorrhœa was not a prominent symptom, and more important still, in which the administration of thyroid did not re-establish the flow in a remarkably

short time, and often after all other measures had failed. A typical case of this kind which exhibited an exceptionally striking endocrine psychosis is reported *in extenso* below.

Finally we can work round the circle to the reciprocal secretory relationship between the pituitary and the gonads. Experimentally the well-known syndrome of dystrophia adiposo-genitalis has been produced by numerous physiologists (Cushing, Biedl, Paulesco, Bell, etc.) by *partial* ablation or injury of the anterior lobe of the pituitary. Biedl concludes: "The anterior hypophysial lobe represents the vital portion of the organ, the complete extirpation of which is followed by death; its partial extirpation by disturbance of growth and metabolism and by derangement of the activity of the sexual organs"—the derangement consists of very pronounced atrophy. In pathological conditions such as acromegaly we get amenorrhœa in the female and impotence in the male. Clinical successes are claimed for the administration of pituitary in amenorrhœa, but of this I have no personal experience—in amenorrhœa occurring in endocrine mental disorders I invariably use a pluriglandular formula.

So much for the experimental and clinical basis of multiple-gland medication. The reports, on the one hand, of dramatic clinical successes in any particular form of uniglandular therapy, and hopeless failures in the same morbid conditions treated by the same gland on the other, seem to me to be often attributable to one or more of the following circumstances:

(1) Faulty diagnosis of the dyscrinism present, (2) the use of inert gland products, or (3) failure to recognize the existence of multiple associated dyscrasias.

The aim of the physician who wishes to achieve success in the domain of organotherapy should therefore be threefold: (1) Accurate diagnosis of the underlying endocrine deficiency, (2) treatment with what he knows to be reliable and potent gland products, and (3) to allow for the possibility of the dyscrinism being multiple—in other words to employ pluriglandular therapy when indicated, or where thyroid, ovarian, etc., medication alone, fail.

When I first began to use gland extracts in the treatment of mental disease, I must confess it was with the profound scepticism I watched for results from oral administration. I recognized, of course, that if I could establish an unequivocal diagnosis of thyroid insufficiency in any particular case, I might expect a positive result with practically the same certainty as I should in giving antidiphtheritic serum in a case of diphtheria, because thyroxin, the active principle of the thyroid, has been proved to be so stable that it passes into the blood unaffected by the digestive enzymes. I had

been so often told, and the text-books insisted so much, that this is the *only* internal secretion to escape from the stomach in a potent form, that I regarded the question as settled. A large portion of my experimental work involved prescribing ovarian extract plus pituitary or thyroid or both, for psychoses associated with the menopause. Consequently this problem loomed large in my mind.

Let us see what the experimental physiologists have to say on the subject. Unfortunately this is very little. I have come across the following reference by Hoskins. He distinguishes between the hormones proper and the protein contents of the extracts, and says:

"The hormones, on the other hand, are, so far as known, much simpler bodies. They are crystallizable and dialyze freely. They withstand boiling, and, according to Abderhalden, are not destroyed by the action of the digestive juices" (3).

I have not been able to trace the source of the reference to Abderhalden's work on this point, but presumably it is authentic. Feeding experiments with anterior pituitary, to mention only one, go to show that very definite results on growth processes and development in general, together with apparently selective stimulation of the sex-glands, can be experimentally produced, despite the alleged destructive influence of the gastro-intestinal tract on hormones of unknown chemical constitution. As Robertson says:

"The results obtained with pituitary (anterior lobe) tissue which have been cited tend to indicate that the active material in this instance is not totally destroyed by digestive juices, nor totally unassimilable from the digestive tract, but either of these factors, nevertheless, may have contributed to *reduce* the effect of the administration" (4).

The influence of the parathyroids in controlling the blood calcium is well known, and affords an experimental means of determining whether this influence is manifested when the gland substance is orally administered. In tuberculosis or sprue the blood-calcium is very much below normal; one-tenth of a grain of parathyroid two or three times daily by the mouth for a few weeks will increase the blood-calcium without any other treatment. I recently had to deal with a very obstinate varicose ulcer of the leg on which no treatment had the slightest effect. The calcium content of the patient's serum was 5 mgrm. per 100 c.c. The normal figures are said to be between 9 and 11 mgrm. per 100 c.c. (5). Parathyroid extract by the mouth increased the blood-calcium to 13 mgrm. per 100 c.c. by the end of a month, and the ulcer was almost healed.

I have already drawn a distinction between homo-stimulative and substitutive organotherapy; the *modus operandi* of the former is well summarized in "Hallion's Law": *The extract of an organ administered in suitable amount has an elective stimulating action on the functional activity of the same organ in the patient to whom it is administered.*

I believe that this is the way in which all extracts (not even excluding thyroid), orally administered, cure minor degrees of insufficiency of the homologous organs, and, as a clinician, I do not concern myself greatly with the problem whether it is the hormone itself, the lipoids, or the specific proteins of the prepared substance which achieves the satisfactory results. After all, when the physiologists, the bio-chemical purists and other laboratory workers have exhausted the possibilities, there still remains to us clinicians one very sound way of knowing whether or not the endocrine preparations which we prescribe are worth the paper on which the prescriptions are written, and that is that in 99 out of 100 selected cases we *do* achieve unimpeachable therapeutic successes by the oral route.

As far as my experience goes, psychoses associated with endocrine dyscrasias occur roughly at two well-marked periods in the lives of females—puberty and the menopause. These correspond to two of what Prof. Robertson calls the "Three Critical Periods of Life." I quote from a report of his recent lecture on "The Prevention of Insanity":

"Coming to the three critical periods of life, all connected with sex, Professor Robertson remarked that during pubescence and adolescence the balance of the internal secretions of the body was disturbed by the intrusion of the internal seecretions from the sexual glands. For all practical purposes insanity occurred for the first time at this period of life. Leaving on one side the effect of heredity, there was, in insanity, almost always a physical basis, but usually combined with mental causes. The physical cause in adolescent insanity was the physiological disturbance produced by the internal secretions. The mental cause was the change in the social status of the young adult or adolescent. He had to adjust himself to the problems of life, and of these the most disturbing during these early days were those connected with sex.

"The next critical period was the climacteric, occurring between 45 and 50. This was the age when the powers first began to fail; an age when, to keep abreast of younger competitors, increased effort was needed. When the climacteric was surmounted the incidence of insanity for a period fell steadily" (6).

Sir Frederick Mott has left behind an extensive work done on the pathology of mental disorder occurring at puberty and adolescence. He investigated in particular dementia præcox, and, from the constancy of certain findings in the sex-glands, he strongly inclined to the opinion that in them is to be sought the most probable physical basis for this disease. Unfortunately, attempts at endocrine therapy on those lines have so far met with very little success, so I shall not pursue the matter further, but proceed to report and discuss some interesting cases in which disturbed internal secretions undoubtedly laid the foundations of very severe psychoses.

CASE I.—Female, æt. 25, admitted December 29, 1924, suffering from a rather severe form of psychosis, manifested by great restlessness, insomnia, profound depression, some degree of confusion of ideas, suicidal tendencies, with hysterical interludes during which she became very excited, and at times violent. Hallucinations of sight and hearing being a prominent feature, a history of recent influenza,

the case was at first looked upon as acute confusional insanity or exhaustion psychosis, although the patient, on admission, exhibited no obvious bodily disease, but was well nourished and in fairly robust health. The usual rest and forced alimentation treatment for exhaustion states was tried for three months without any success whatsoever—in fact by this time the patient had become almost stuporose. She was put on thyroid co. with almost immediate beneficial result, and, as menstruation had been absent for some six months before admission, thyro-ovarian co. was substituted after a fortnight. Result: Menstruation recommenced (before the compound ovarian substance was begun), and patient was discharged completely recovered on May 13, 1925. Pluriglandular therapy was ordered to be continued, patient to report in one month.

Let us analyze this case more fully. When admitted the psychosis was already well established—she had been drifting along without treatment for over twelve months, and there was a history of amenorrhœa of six months' duration. There was no history of heredity, and I must confess I was not at all satisfied at the time with my provisional diagnosis of exhaustion psychosis, more especially when I found, on closer investigation, that the initial mental symptoms actually antedated the attack of influenza. Such exhaustion psychotic states are well-recognized entities in psychiatry—very many supervened on the influenza epidemic of 1918—but they invariably respond to mental hospital treatment after three months at most. In this case the patient seemed to get steadily worse, so much so that I began to consider the possibility of dementia præcox, and to regard the prognosis as hopeless. One morning I happened to feel her pulse—the rate was 54 per minute. Her hands felt cold and looked bluish. The skin of the face seemed unduly coarse and dry. We see such vasomotor and dermatological conditions very often in mental hospitals. They are not always manifestations of hypothyroidism. But to me, on that particular morning, there seemed to be something very suggestive about this lady's facies. It appeared coarser, duller and more puffy than usual, and I seemed to get a general impression, perhaps more intuitive than anything else, that her bodily metabolism was below par.

Being now convinced that the clinical picture, if not altogether due to, was undoubtedly complicated by hypothyroidism, I decided to try her on small doses of thyroid—½ gr. of the dried gland three times a day. Hand-in-hand with a hastening-up of the metabolic processes there followed a most remarkable clearing up of the mind. Within a fortnight her personality had altered beyond recognition, and she made a rapid and uninterrupted recovery. I saw her as recently as July 8, 1926 (14 months after her discharge), and she continues to enjoy physical and mental health.

A word about the pluriglandular formula, thyro-ovarian co., which, as mentioned in the notes, I thought wise to substitute for the plain thyroid after two weeks trial of the latter. Each tablet contains 2½ gr. of ovarian substance, with corpus luteum, $\frac{1}{15}$ gr. thyroid, and ¼ gr. total pituitary, and is made up to 5 gr.

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with a mixture of the phosphates of magnesium and calcium, glycero-phosphates, and potassium and sodium bicarbonate. The salts are designed to help neutralize the acidosis so commonly found in conditions of reduced metabolism, of which hypothyroidism is the classical prototype.

As I shall have occasion to refer to the use of this formula often hereafter, I may anticipate events by saying that I regard it as a very rational combination, and personally have found it to give uniform results, which justify the high price charged. Needless to say the potency of the extracts used is of paramount importance.

CASE 2.—J. M—, female, æt. 22, admitted July 6, 1925. First acute attack one and a half years ago. Mental condition more or less abnormal since. Acute exacerbations eight months, six weeks and two days ago respectively. Severe pelvic peritonitis nine months ago. Appendicitis and complicating oöphoritis at laparotomy—appendix and right ovary removed; psychosis subsequently very much aggravated, necessitating certification to private asylum, where followed eight months' treatment on the usual lines with little or no improvement. No history of heredity.

On admission restless, hysterical and spasmodically violent. Fits of crying and laughing. Delusions of persecution elicited. History of progressive insomnia, refusal to remain in bed, constipation, very irregular menstruation, followed more recently by total amenorrhœa, capricious taking of food, and repeated attempts at assault on the neighbours. Physical condition poor, but no obvious signs of disease.

July 13, 1925: Suggestive of manic-depressive psychosis—now in the depressed phase. No symptoms or physical signs referable to the abdomen (including pelvis), if we except amenorrhœa.

January 20, 1926: Six months of routine treatment without appreciable change. Remissions have occurred during which the patient has approached normality, but a mild degree of stupor and dementia, with vacant expression, have persisted. Menses still in abeyance despite hæmatinics. Mental equilibrium unstable, and the prognosis, as far as complete recovery is concerned, appears hopeless. Blood-pressure persistently low (systolic, 90–95 mm. Hg) and general metabolism obviously subnormal. Hence, the next day, put on adreno-ovarian co. Improvement may be described as immediate. Menstruation re-established in three weeks; intelligence brightened and wits sharpened. Patient now began to live instead of to vegetate. (Habits had been "wet and dirty" at intervals.) Systolic blood-pressure 110 mm. Hg. Skin (previously rough, dry and scaly) cleared up and she has not looked back since. Discharged "recovered" on April 14, 1926; she has since been under the continuous observation of her brother (a medical man with some experience of mental disease), who reported (May 18, 1926) that past failures with various methods of treatment had rendered him totally unprepared for such a complete restoration of mental faculties. Patient, to his knowledge, had never previously, even before puberty, been, as now, 100% normal. Advised to recommence glandular therapy on any re-appearance of untoward signs.

Note that the mental disorder had been about two years in existence at the time endocrine therapy was begun. As in the first case reported, alternative methods of treatment had been given a fair and exhaustive trial—thus has been fulfilled the second of the three cardinal desiderata on which I have laid stress in the earlier portion of this article. In this case, also, I think we may eliminate the element of spontaneous recovery: I need not dwell on the significance of the "wet and dirty" habits in establishing the apparently bad prognosis. So that we may safely credit endocrine therapy with the cure—when last seen on July 10, 1926, she was normal in every way.

An interesting point is the adverse effect on the mental disorder of the oöphorectomy performed about nine months before she came under my care. Contrary to what one should expect, the removal of the septic foci in the appendix and ovary, instead of ameliorating, very much aggravated the mental condition. I would suggest that the surgical ablation of one ovary, resulting, of course, in the *complete* loss to the body of its internal secretion, served to accentuate the existing pluriglandular syndrome—a syndrome in which the diseased and defectively secreting organ doubtless played an important part; in view of the response to treatment, it cannot be denied that the multiple dyscrinism indicated must have been the predominant, nay, the sole factor in this psychosis.

The existence of a subnormal blood-pressure influenced me in the choice of *adreno*-ovarian co.—½ gr. adrenal gland substance, added to the thyro-ovarian co. formula already alluded to. In this connection it is interesting and suggestive to know that adrenal dysfunction as well as actual adrenal pathology have been often found in insane persons, and the late Sir Frederick Mott reported that, in 143 cases of dementia præcox, the average blood-pressure was comparatively low, and in 100 cases examined *post-mortem* " the adrenals were smaller than in any other class of cases studied to date." (7)

I would draw the reader's attention to the remark somewhat casually thrown out by the patient's (J. M—) brother that her mentality had, previously to endocrine therapy, never been perfect: there had always been, apart from the major disturbance which eventually supervened, a slight want noticeable to an acute observer. It occurs to me that a minor dysfunction, manifested in this way, is much more common than has been suspected, and the importance of its recognition should be ever present to the psychiatrist. Mental dullness, "slowness of apprehension, accompanied by slowness of execution" (8), no matter how slight in degree, should always be regarded with suspicion, and a careful search made for physical stigmata of dysthyroidism, dyspituitarism, etc. As evidences of the former condition I find the following particularly helpful—they are doubtless well known, but often overlooked, or have not the full significance attached to them:

(1) Lowered temperature with cold and blue extremities: the patient feels chilly, and is never warm.

(2) Loss of, or scanty, brittle, dry, hair: in children particularly this condition is very suggestive.

(3) Hertoghe's sign—thinning of the outer third of the eyebrow.

(4) A slow and small-volume pulse.

I have selected the above two cases from my series, because they

offer proof of the truth of my contention that disturbed endocrine secretion, usually polyglandular—but it may be of only one organ —will be found in practice, more particularly at or soon after puberty, to have an immense ætiological significance in the production of severe psychoses. They are two such cases as, in the absence of a recognition of this fact, might have been diagnosed as dementia præcox, or perhaps manic-depressive psychosis, and considered, from that view-point, incurable.

I now pass on to a more definite group, in which I think I may claim to have had unusual success with organotherapy, namely, the climacteric psychoses. Here we are on more solid ground as regards ætiology, and the literature is more generous. I have been fortunate in securing a typed translation of an exhaustive article on "Climacteric Difficulties," by Dr. Erwin Graff, which recently appeared in a German paper—the *Wiener klinischen Wochenschrift*. Other contributions which I have had from the same source are "A Review of the Action of Ovarian Preparations," by Dr. Michael Floris, and "Experimental and Clinical Research on the Dosage Question of Generative Gland Treatment," by Dr. Otto Kauders, Departmental Assistant to Prof. Wagner-Jauregg. I can commend the articles to anyone interested in the subject, but shall here only make use of that by Graff, which bears most directly on the subject of this dissertation. He says:

"The ultimate cause of all these difficulties is the reduced ovarian activity, and the consequent disturbances of the hormone balance. In what method the other endocrine glands are involved is not exactly determined, but it appears that the adrenals produce more secretion, while the thyroid is in a condition of hypofunction, which means less secretion introduced into the circulation. The *rôle* of the pituitary is not altogether understood, notwithstanding the beneficial effect of radio-treatment to the hypophysis for climacteric trouble."

On reading the above I was confirmed in my belief that the dyscrinism at the menopause is scarcely ever purely ovarian, but polyglandular. Graff states that he employs the preparations of the Sanabo works of Vienna, called polyhormone (feminine), whose ingredients are ovarian substance, thyroid and pituitary. Climacteric disturbances of polyglandular origin respond very favourably to 2–3 tablets daily. The reader will note that thyro-ovarian co., which I have been using in these cases for the past four years, has practically an identical composition.

I think the following summary, by the same author, of the consequences of disturbed ovarian activitiy, is very comprehensive, and I shall not attempt to improve on it:

(1) Diminished menstrual flow; (2) tendency to protracted hæmorrhage in consequence of changes in blood coagulability (perhaps also degenerative processes in the vascular walls); (3) plethora and retention of metabolic products after

commencement of the menopause; (4) obesity of thyroidal and perhaps of pituitary origin; (5) *psychoses* [italics mine]; (6) the numerous climacteric disturbances of the senses which manifest themselves in abnormal irritability of the vegetative system and especially of the sympathetic.

Of these we are only concerned with No. 5, or at least with those cases of menopausal difficulties in which psychotic manifestations preponderate, and it was peculiarly gratifying to me as a psychiatrist to find this aspect of the question elaborated and given more space (small though this be) than I have yet seen in a general paper on the subject, as follows:

"It is rare for the mentality of a woman to remain undisturbed at the climacteric. The temper is variable: irritability, excitability, anguish and depression alternate, but states of depression predominate. As a rule this condition is not permanent, but during the climacteric period there is undoubtedly an increased tendency for the development of temperamental disturbances."

I think Dr. Graff, in common with the majority of writers, rather understates the case, and dismisses it more cursorily than its importance would seem to warrant by the somewhat mild conclusion, "during the climacteric period there is undoubtedly an increased tendency for the development of temperamental disturbances." In my experience climacteric temperamental disturbances are common, their severity and importance as a social problem are exemplified by the frequency with which they require certification, and often prolonged asylum treatment. They tend to become permanent, although the purely physical concomitants of this regressive period of woman's life have passed away. We must remember that the highly specialized cerebral tissue, on whose integrity depends the normal functioning of the mind, is infinitely more liable to damage by many adverse influences, metabolic or otherwise, than is the rest of the body, while the tendency to repair or regeneration is excessively weak. Of such importance do I regard endocrine disorders in producing certifiable insanity in women between the ages of 40 and 50 that I think it wise to spare no trouble in elucidating the minutest details of the history of these patients' past and present ovarian function, even should this entail a less thorough examination in other respects. I have mentioned that the dyscrasia is usually multiple, but to take the thyroid aspect only, is it not highly significant that 90% of cases of myxœdema (with its invariable mental syndrome) occur in women, and of these 90% are between the ages of 40 and 50?

Before I go on to report cases in this group, let me sum up my convictions thus: *To treat any menopausal disorder otherwise than by organotherapy is unscientific, and, in most cases, unnecessary; to modify the abnormal condition by supplying extracts containing the*

deficient hormone or hormones is rational in theory, and, I maintain, successful in practice.

CASE 3.—D. C—, female, æt. 45½; first seen October 13, 1925. Previous history: Unipara; no complications during pregnancy, parturition, or puerperium; child now aged 10 years. Sustained a severe fall and injury to the head in 1922 (three years ago); unconscious one day and a half. Was "unwell" at the time; has "never seen anything" since. Short time afterwards got a thorn stuck in right eye: lens had to be evacuated; sight now poor, but other eye healthy. Had tonsillar trouble simultaneously with ocular; incision made in one tonsil; doctor advised removal of tonsils, which has not since been done.

For the past year and a half has become very much changed in manner; from being quite placid and even-tempered has become very irritable, worries about trifles and flies into a rage at the slightest or no provocation (husband's information). Feels depressed and "down-and-out," especially in the morning; improves towards evening; restless at night; sleeps but poorly. Appetite good, bowels fairly regular. Has a *dull sensation at vertex—feeling of weight on top of head;* imagines her head has never been right since accident. Worries about her throat unnecessarily; tonsils are now normal. Does not care to mix in company, or, in fact, to leave the house at all; will not even go to church on Sundays. *Extremities always cold*—more so on right side. *Thyroid slightly enlarged and tender to touch*; says her swallowing is affected, she thinks by tonsils, but obstruction and pain occur in *middle* of throat. Pulse-rate 62 per minute.

Diagnosis.—Climacteric psychosis; general endocrine imbalance.

Treatment.—Three bromides with capsicum three times a day and at bedtime. Thyro-ovarian co.—one tablet *t.i.d.*

Progress.—October 19, 1925: Seen again. Somewhat improved. Feels calmer and steadier. Sleeps better. November 11, 1925: Improvement maintained. Feels more cheerful and no longer worries about trifles. Is getting rid of the idea that she may become insane. Normal in every way. Reports herself rid of objectionable symptoms, except very occasional and "short-lived spells of the blues," intensity of which has decreased.

May 24, 1926: Has been seen three times since last report. Only once since then has she felt not quite up to the mark. Advised to repeat short course of thyro-ovarian co. should such recur. May be regarded as permanently cured.

The possible influence of shock in determining the endocrine disturbance in this case required careful consideration, especially from the point of view of the thyroid. As is well known, the usual response of this gland to severe emotional disturbances is in the nature of a hypersecretion. Consequently, before thyroid medication could be considered, anxiety neurosis complicating exophthalmic goitre had to be carefully excluded. Although the thyroid was slightly enlarged and tender, there was no exophthalmos, while the *pulse-rate at no time exceeded 64 per minute.* The patient was, if anything, obese and rather phlegmatic. Then we have the coldness of the extremities, which, when complained of even in a warm atmosphere, as in this case, is, to my mind, highly suggestive of hypothyroidism. That a *non*-exophthalmic goitre may occasionally result from shock is well known, and Dr. Primmer recently reported two such cases in the *British Medical Journal.*

It will have been noticed that D. C— had been menstruating normally up to 42½ years of age, and the sudden and complete cessation was closely connected with the shock of the accident.

This, then, is a clear case of climacteric psychosis with a well-marked endocrine basis, seen sufficiently early to respond rapidly and completely to appropriate therapy. The rapidly-induced, steady, and finally permanent improvement in both physical and mental condition was most striking, and, to my mind, must be chiefly attributed to the pluriglandular therapy. Neither suggestion (only employed for very short periods, and at long intervals), the bromides (discontinued after two mixtures), nor the natural wane of the menopause can adequately explain such a rapid amelioration.

CASE 4.—M. D—, female, æt. 45. Seen May 17, 1925. Married eleven years; never pregnant. Menstruation irregular for past few years; absent last seven months. No history of heredity Psychosis evident for six weeks. Peculiar in manner, suspicious; thinks people are jibing at her; imagines her sister-in-law is poisoning eggs intended for her consumption and that she has recourse to witchcraft in doing so. Is restless, sleepless and obstinately constipated. There is myocardial degeneration and she has passed no urine for eighteen hours. Resents all medical interference; obstinately refused an enema. Is taking only small quantities of liquid food.

A hypodermic injection of $\frac{3}{200}$ gr. of hyoscine hydrobromide being given, a large enema was administered while patient was under the influence of the drug; successful result—urine was subsequently passed. The following were prescribed: Nujol (1 oz., night and morning), paraldehyde (2 drm.) for two successive evenings and afterwards as required, bromide mixture and thyro-ovarian co. (two tablets *t.i.d.*, to be commenced when the bowels became regular).

May 24, 1925: Considerable improvement. More amenable and tractable. Still somewhat resistive, but nurse was able to give enema with some assistance. Sleep broken up to last night, when she had a good rest. Bowels still sluggish, but general condition much improved. Heart better. There is a short, ineffectual cough; temperature normal. More rational and talking.

May 31, 1925: Patient very much improved. More amenable and communicative. Bowels now free (daily motion). Sleeps fairly well; appetite better. Still reluctant to be examined, but enjoys a joke and is more optimistic. Mentality nearly normal; her friends think she is as well as ever, but a certain amount of psychotic condition remains.

July 24, 1925: After having been very well for six weeks had a bad relapse, profound depression with suicidal tendencies, delusions and periodic fits of restlessness and subacute excitement. *The bowels were regular*, but insomnia was a marked feature. I found that the thyro-ovarian tablets, contrary to my instructions, had been discontinued three weeks after my last visit. On resuming them the patient showed a remarkable improvement within two weeks and finally became normal, and has continued so, to my certain knowledge, up to July 6, 1926, when I last saw her.

The endocrine aspect of this case may not be apparent at first sight, but I think I have not included it under this heading without justification. It may be contended that the improvement in the first instance might be attributed to general measures, such as energetic treatment of constipation. I do not deny the possibility of this, at least as an accessory factor, and have often seen very early cases of mental disorder respond to this simple procedure. On the other hand, I doubt whether intestinal or other toxæmia, in the absence of a strong hereditary predisposition or neuropathic taint, can ever, *per se*, initiate a psychosis—it is my belief that constipation is a result rather than a cause of insanity. In this

case heredity could be with certainty excluded. There appeared to be a direct connection between the discontinuance of the endocrine therapy and the recurrence of the acute melancholic symptoms. The frequent response of these latter to ovarian extract convinces me that melancholia occurring at the menopause, and manifested by symptoms ranging from slight temporary depression to strongly suicidal impulses, is a definite ætiological entity. It is well known that a similar condition exists in men between 50 and 60. Whether this type of case responds as well to testicular extract as the former undoubtedly does to ovarian I cannot definitely say, but my results in regard to the former, so far, have not been discouraging.

Depressed states, occurring in women or men, at a time when their respective sexual powers are on the wane, may be aptly grouped under the heading "involutional melancholia," and, in my opinion, a regressive change in the gonads, supervening in some unusual fashion, is the predominant factor in their causation. Just as the intrusion of the internal secretions from the sex-glands into the system at puberty predisposes the individual to mental instability at that period, so will their extrusion (so to speak) in the pre-senile epoch render her or him correspondingly liable to psychical aberration. In the former case, with the mind at the threshold of its development, states of excitement will be the rule; in the latter, with the whole system, and more particularly the mental powers, on the down grade, depression will predominate.

CASE 5.—The patient was a multipara aged about 41 years. There was a history of insanity in the family, and the onset was closely connected with shock, the sudden death of the husband, aggravated subsequently by financial worries. At an early stage she had a fixed delusion that she was developing cancer of the breast. When I first saw her in her own home she had recently returned from a private asylum, where she had undergone eleven months' treatment. She was practically in a state of chronic dementia—lay like a log in bed, would not speak, eat, or attend to her person, which was consequently in an indescribably filthy condition. I have scarcely ever seen a worse case. As she obstinately resisted all attempts at examination or medical interference, and skilled nursing facilities were not available, I had her certified and conveyed to Limerick Mental Hospital. Here she spent five months without appreciable improvement beyond the fact that she could be persuaded to take her food without artificial feeding (this had had to be resorted to for the first six weeks). She sat all day long in the day-room without moving or opening her lips, was dull, apathetic, and took no interest whatever in her surroundings; in fact she was just one of those apparently incurable dements who fill the wards of mental hospitals. At this stage I decided to try compound ovarian extract. In one month the patient was able to sew and knit; in two she played the ward piano in an accomplished manner, and I discharged her nine months from the date of her admission as "improved"—a conservative estimate of her mentality occasioned by the fact that she still exhibited a certain amount of sluggishness of perception and ideation. She continued to take the extracts, and the final result will be fully appreciated when I state that, on June 9 of this year, I had no hesitation in giving her a certificate of complete recovery and ability to resume her duties as assistant teacher in a National school. Only last week I had a letter from the manager of the school reporting that in the performance of those duties she has justified the certificate.

This is certainly a striking case. Endocrine therapy was tried empirically, if you like, but the result cannot be questioned. Neither can it be regarded as an isolated example of what gland extracts can do in the treatment of climacteric psychoses.

I propose, therefore, to give statistics detailing my experience of this line of treatment.

Since June, 1922, I have treated 53 cases of psychoses by endocrine therapy. Of these, 11 belonged to the adolescent group, and exhibited many features in common with Cases 1 and 2 described. There was not a single failure in this group, but I must emphasize the fact that this small series was very, very carefully selected, and includes only those who exhibited undoubted signs of glandular insufficiency. Any case in which pluriglandular therapy was empirically prescribed has been rigidly excluded here. 5 were private patients, all of whom were spared the ordeal of certification —4 completely recovered, the fifth is very much improved. There were 6 hospital cases, and all were discharged, after varying periods of detention, "recovered."

The climacteric group is naturally much larger—42 cases in all. Of the 27 private cases included in this number, only 2 required certification during the course of the treatment, and they eventually made perfect recoveries (Case 5 is one of them). Of the total (42), 34 were completely cured, 2 very much improved, 3 improved, while there were 3 total failures to record—possibly because of mistaken diagnosis or long-standing disease, and are the only ones at present in a mental hospital.

Percentages work out as follows: Treated, 53; recovered, 44 (83%); improved, 6 (11%); not improved, 3 (6%).

These figures are, to say the least, satisfactory, and taken in conjunction with the critical analysis I have endeavoured to make of individual cases, afford proof of what I set out to establish, and which I shall, in conclusion, thus summarize:

(1) No case of mental disorder, more particularly if it supervenes at puberty or the menopause, however advanced or hopeless, should be considered incurable until disordered endocrine function has been definitely excluded, whether this be done by the absence of characteristic symptoms or by the failure of response to organotherapy.

(2) Endocrine therapy fulfils a very important and useful *rôle* in the treatment of psychoses in carefully selected cases.

(3) Compound ovarian extract, in private practice, will obviate the necessity for certification in many cases.

(4) Polyglandular dyscrasias are the rule in the endocrine psychoses, and pluriglandular therapy should give the highest percentage of satisfactory results.

(5) The fact that physiologists have not yet succeeded in isolating the hormones or chalones of certain of the ductless glands, and therefore cannot *prove*, by experiments on animals, whether these hormones or chalones are or are not absorbed unaltered from the digestive tract, is no justification for our denying to our patients the benefits clinically proved to accrue from the oral administration of extracts of these endocrine organs.

(1) *Journ. Ment. Sci.*, lxxii, October, 1926, p. 482.—(2) F. S. Hammett, *Amer. Journ. Anat.*, xxxii, July 15, 1923.—(3) Hoskins, *Endocrinology and Metabolism*, i, p. 8.—(4) T. Brailsford Robertson, *The Chemical Basis of Growth and Senescence.*—(5) Beaumont and Dodds, *Recent Advances in Medicine*, p. 50.—(6) *Brit. Med. Journ.*, July 24, 1926, p. 151.—(7) *Ibid.*, July 21, 1923, p. 95.—(8) F. L. Golla, "Early Mental Disease," *Lancet*, extra numbers, No. 2, p. 156.—(9) *Brit. Med. Journ.*, July 24, 1926, p. 151.

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*Observations on the Prison Psychoses.** By H. T. P. YOUNG, M.B., Ch.B.Edin., Medical Officer, H.M. Convict Prison, Parkhurst.

FROM time to time in convict prisons examples are seen of certain morbid mental states which are described as distinct disease forms under the name of "prison psychoses." These states may be defined as special types of mental reactions developing upon conflicts which arise as the result of imprisonment, and possibly from the shock attending the criminal act, trial and conviction. They have been the subject of much inquiry, but, on account of the variation in the material which was available and in the conditions under which the studies were pursued, some confusion of thought appears to exist as to what may or may not be regarded as belonging to this class of disorder, and whether, in fact, the classification is not redundant. The sole justification for the use of the term "true prison psychosis" lies in the ability to establish the disorder as a separate entity, lest the name should be applied to conditions which are adequately described under other titles, as has been the case with shell-shock and "barbed-wire" disease.

The problem is one of much interest on account of the relation borne by the condition to the psychoses on the one hand and the psycho-neuroses on the other, and in order that the existence of a separate and distinct disease may be demonstrated, it is essential that all those cases in which the chief external cause cannot be attributed to the effect of prison surroundings should be eliminated.

* A paper presented at the Annual Meeting held in London on July 16, 1926, and published with the sanction of the Directors of Convict Prisons, although it does not necessarily represent their views.