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## Part I.—Original Articles.

### HYPERTHYROTIC CATATONIA: A SCHIZOPHRENIC SYMPTOM-COMPLEX *

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THE thyroid, as one of the glands of internal secretion to be studied first and subsequently most intensively, was early regarded with interest in relation to mental disorder. Its role in the production of cretinism and in myxoedema in which the activity of the gland is diminished, as well as the association of thyrotoxicosis with psychic changes, suggested that anomalies of this organ might be linked with some forms of mental disease.

The very extensive research in endocrinology that has been conducted in recent years has shown that a synergism exists between the thyroid and other endocrine organs, and that symptoms formally attributable to thyroid disturbances may have their origin in some other gland. The establishment of the thyrotrophic principle of the pituitary has made it necessary to reconsider and perhaps recast many old ideas on the physiology of the thyroid, and has made even the picture of toxic goitre or myxoedema less simple than before.

On the subject of the responsibility the thyroid bears in the development and maintenance of mental illness there is an abundant and scattered literature. Psychic disturbances accompanying exophthalmic goitre were cited as far back as 70 years ago (Andrews, 1870; Cane, 1877), and have been noted in every textbook on thyroid disease since. The mental symptoms described as occurring in hyperthyroidism do not form a consistent picture, nor is there any agreement between authorities as to whether this is to be expected or not.

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Anxiety is generally believed to be basically responsible, unless the picture is coloured by delirium derived from excessive thyroid intoxication. No doubt this is true for normal subjects, but the importance of thyroid hyper-function in true psychotic illnesses is very obscure, and the unsatisfactory opinion usually expressed is that a constitutional predisposition determines the form of a psychosis activated by hyperthyroidism.

Certain relevant literature dealing with attempts to influence psychoses by the administration of thyroid extracts will be referred to later, but at this juncture it must be emphasized that these measures, which in themselves are potentially therapeutic, have been conducted on psychotic subjects, and that there is no evidence at all to suggest that the administration of thyroid hormone to normal or pre-psychotic individuals can activate latent psychic traits and produce the picture of a new psychosis. Furthermore, mental symptoms have been studied and reported largely in subjects who came under notice because of a pathological degree of thyroid hyperfunction, and in whom the mental symptoms were of secondary interest. If hyperthyroidism can activate a latent psychosis by operating on constitutional factors, it is reasonable to suppose that amongst mental patients many examples derived from this source will be available for study.

This paper is devoted to an investigation of the incidence of hyperthyroidism in mental patients and its distribution amongst recognizable types of mental illness. Its role in the development of a form of schizophrenia will be referred to, and discussed at some length. The case material consists of 2,096 male and 2,654 female patients, a total of 4,750, treated at the Bristol Mental Hospital between the years 1930 to 1940. Nearly all these patients have been examined by the writer, and every case of hyperthyroidism to which reference is made has been investigated by him. Established cases of mental deficiency are not included in this census, and no note has been made of slight degrees of hyperthyroidism such as frequently accompany adolescence, menstrual periods and the menopause.

The simple classification of goitres into two types, toxic and non-toxic, has been adopted because the numbers involved are small, and it is difficult to interpret satisfactorily the significance of primary and secondary toxic, colloid and adenomatous goitres and the like—a difficulty experienced by most authoritative writers on thyroid diseases. This classification is convenient for the purpose of this paper, as hyperthyroidism rather than goitre is here the elected subject. All the cases of catatonic schizophrenia with hyperthyroidism, on which special interest is centred, suffered from primary thyrotoxicosis.

The distribution of endemic goitre varies with the locality. According to Campbell (1927), Stocks (1928), afterwards confirmed broadly by Joll (1932), the highest incidence of goitre amongst school children in Great Britain occurs in the south-west of England, including Somerset and Gloucester, and then follows a belt extending roughly north through the Cotswolds towards the

Pennine and Chiltern Hills. Females are affected more than males, in some districts in the ratio of as much as 18 to 1. This ratio lessens after puberty, but seems to be preserved to some extent throughout life and does not usually drop below 2 to 1. The incidence of exophthalmic goitre, a disease of adult life, cannot be so easily estimated. It seems to correspond in this country with non-toxic goitre, but recently Read (1939) has shown that in U.S.A. it has not the same distribution as endemic goitre and he considers that the two conditions are unrelated. The use of iodized salt as a prophylaxis has lessened the occurrence of goitre in certain parts of the world, but has been ineffective in others, New Zealand for example. These considerations should be borne in mind when attempting to correlate figures derived from different sources. On the whole it is probable that the incidence of goitre, toxic and non-toxic, should be higher among the population from which the patients of the Bristol Mental Hospital are drawn than from those outside the goitrous belt.

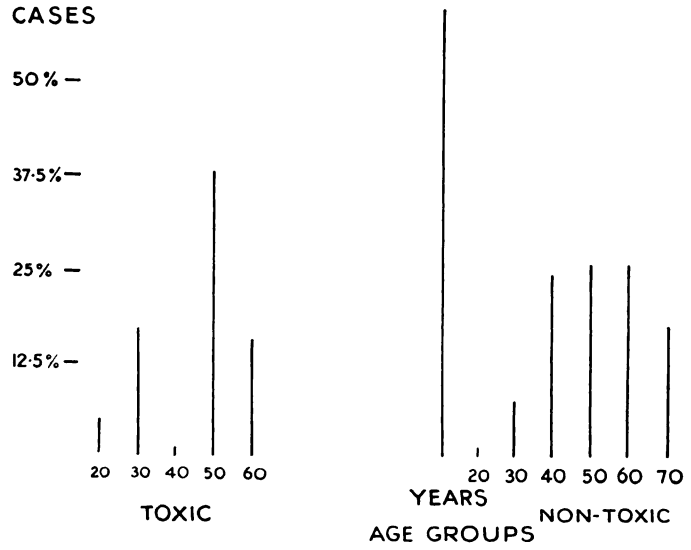
Lord (1930) reported that amongst 1,793 women at Horton Hospital there were 13 toxic and 65 non-toxic goitres. There were no goitres in 271 males. By comparison with the Bristol census the incidence of toxic goitres is about

TABLE I.—*Distribution of Goitres, Toxic, Non-toxic and Thyroidectomies, in 2,096 Male, 2,654 Female = 4,750 Patients.*

| | Number of goitre cases. | | Type of goitre. | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Toxic. | | Non-toxic. | | Thyroidectomy. | |
| | Male. | Female. | Male. | Female. | Male. | Female. | Male. | Female. |
| Epilepsy | 2 | 1 | – | – | 2 | 1 | – | – |
| Mania | 1 | 7 | 1 | 1 | – | 6 | – | – |
| Depression | – | 17 | – | 4 | – | 13 | – | 2 |
| Involutional melancholia | – | 4 | – | – | – | 4 | – | – |
| Schizophrenia : Simplex | – | – | – | – | – | – | – | – |
| ,, Hebephrenia | – | – | – | – | – | – | – | – |
| ,, Paranoid | – | – | – | – | – | – | – | – |
| ,, Catatonic | 1 | 3 | 1 | 3 | – | – | – | 1 |
| ,, Periodic | – | 1 | – | – | – | 1 | – | 1 |
| Paraphrenia, Paranoia | – | 9 | – | – | – | 9 | – | – |
| Dementia, senile and organic | 1 | 2 | – | – | 1 | 2 | – | – |
| Delirium (toxic) | | 6 | – | 6 | – | – | – | – |
| Anxiety | – | 1 | – | 1 | – | – | – | 1 |
| Obsessional | – | 1 | – | 1 | – | – | – | – |
| G.P.I. | – | 2 | – | – | – | 2 | – | – |
| Totals | 5 | 54 | 2 | 16 | 3 | 38 | 0 | 5 |

Total of both sexes in 4,750 cases = 59.

TABLE II.—*Age Distribution of Goitres, Toxic and Non-toxic.*




the same, while that of non-toxic is considerably higher. Twelve of Lord's 13 toxic cases occurred in schizophrenia and melancholia; her diagnostic classification makes any further comparison between the two tables invalid.

Reviewing the distribution of goitres in female patients, the first table shows that toxic hyperthyroidism was associated chiefly with three forms of mental disorder, namely, catatonic schizophrenia, depression and toxic delirium. Non-toxic goitres predominated in the manic-depressive psychosis and in delusional insanity.

These facts deserve some comment. All cases of toxic delirium were admitted in an advanced state of exhaustion, whether from general physical effort or from thyrotoxicosis is not clear; the mental symptoms were those of restless delirium devoid of specific features. Hyperthyroidism appears to be no more than an incidental accompaniment in the manic-depressive group. Some of these patients had had previous manic or depressive attacks, evidently not notably influenced by the thyroid state. Exacerbations of mania and depression are not very infrequent in hyperthyroidism, and the thyroid condition does not seem to impede remission nor make the prognosis much graver. Mental improvement, but not recovery, was recorded by Joll (1932) in three cases of melancholia with thyrotoxicosis successfully operated on by him.

The cases of catatonia will be described in detail later in this paper, and their peculiar features will form the subject of a special discussion. It is very noteworthy that in such a large series of patients no case of goitre, toxic or non-toxic, was met with in any schizophrenic psychosis of early life apart

from the catatonic group. It is the impression of the writer that depressive illnesses in women are unusually common in Bristol. This impression is shared by other workers. If so, it is not remarkable that the distribution of non-toxic goitres predominated in depression and melancholia.

In significant contrast to hyperthyroidism, simple or non-toxic goitre was not represented in any of the early schizophrenic reaction types, but its incidence in paranoia was second only to that in depression. These small figures do not justify positive conclusions. Individual cases of paranoia showed no constant features that seemed to be influenced by non-toxic goitre. Probably as depression, involutional melancholia and paranoia form a large part of the psychotic illnesses of the middle or later period of life, the majority of non-toxic goitres in older patients would be distributed amongst them. But the negative finding that simple or non-toxic goitre failed to occur at all in young schizophrenics is striking and important and may suggest a special endocrine constitution in schizophrenia. Goitre, toxic or non-toxic, appears to develop very rarely in established psychoses. The writer has been unable to find in the case material of this hospital, and a large number of patients seen elsewhere, a single case in which a goitre or thyrotoxicosis made its appearance after a schizophrenic illness had been in existence for a year or more. In about 2,000 chronic hospital patients of various types goitre has not developed during the period of hospitalization. This is all the more interesting as the peak of the age distribution of toxic goitre is in the third and fourth decade (Means, 1937), and the majority of patients are hospitalized at or before this time.

Information is not so complete about recurrent or alternating attacks of mania and depression. If goitre or thyrotoxicosis set in between relapses they do so in the minority of cases. The majority of cases of this sort seen by the writer were already goitrous before the onset of the first psychotic illness.

The male census, though very much smaller, agrees generally with the female ; the sole case of schizophrenia was of the catatonic type.

A study of the distribution of the goitres in the age groups merely shows the age at which the first known mental illness set in, for, except in the young patients and toxic cases, it has not been possible to discover reliable information about the duration of the goitres. Between the ages of 20 and 35 non-toxic goitres occurred twice in mania, four times in depression, thyrotoxicosis in three cases of catatonic schizophrenia alone. As all cases of toxic hyperthyroidism occurring in the second, third and fourth decades belong to the group of catatonic schizophrenia, these figures suggest, but can do no more, that when hyperthyroidism occurs in psychotic patients in early life it results in a specific type of psychotic reaction. The accompanying curve indicates the general distribution of goitres in patients of various ages, the age group being determined by the onset of the mental illness.

It was hoped to ascertain what proportion of patients who had undergone thyroidectomy in Bristol during the years 1930-40 had subsequently been

mentally ill and if there was any recognizable post-operative mental reaction. Unfortunately all the records were not available as a result of the war. The numbers of patients operated upon must have been considerable, for at one of the smallest of the six general hospitals, 155 thyroidectomies were performed in nine years. None of these 155 cases came under review at the Bristol Mental Hospital, nor its out-patients' clinic. The table shows that of the 17 cases of thyrotoxicosis, thyroidectomy had been performed on five. In two cases of depression and one of anxiety, either the operation had not been sufficiently complete, or thyroid hyperactivity had recommenced. These three patients presented symptoms of hyperthyroidism, but the mental picture had not been noticeably influenced by the operation. The two cases of schizophrenia will be considered later. The operation may have determined the onset and form of the schizophrenic illness in one.

Detailed psychiatric examinations of patients treated in the great surgical clinics are somewhat scanty and incomplete, so that meaningless and unprovable statements to the effect that toxic goitre is an agent that sets off a psychosis waiting to be brought to light have their place in the literature.

Crile (1932) believes that toxic delirium is the commonest psychic reaction. He asserts categorically that all the psychoses he has seen are toxic in origin, and that any relationship between thyrotoxicosis and mental disorder is a coincidence. In his experience operative measures have aggravated pre-operative psychotic symptoms. Quoting Kmosch he classifies psychic reactions as neurotic, paranoid schizomanic and toxic delirious. In the schizoid group, restlessness, confusion and visual hallucinations are common. McCarrison (1917) has dismissed the psychic reactions briefly as based on a state of physiological fear mediated perhaps by the adrenal apparatus.

Freeman (1935) considers that the mental pattern of the patient determines the form of the psychosis. He suggests that a potentially schizophrenic patient becomes frankly schizophrenic under the influence of thyrotoxicosis. If this was so there would be undoubtedly many more hyperthyrotic schizophrenics in mental hospitals, for as Jung (1939) points out, an amazing number of potential or real schizophrenics exist who never enter a psychiatric hospital. Dunlap and Moersch (1935) investigated the psychotic aspects of hyperthyroidism from the Mayo Clinic records for ten years. In this great material they found 134 psychotic patients which they classified as follows:

| | |
|---|---|
| Toxic exhaustion psychosis | 54 |
| Acute delirium | 48 |
| Manic-depressive reactions | 26 |
| Other types | 6 |

In their opinion there was no psychic reaction characteristic of hyperthyroidism.

Once more it must be stressed that the case material studied was supposedly

normal, coming under notice because of hyperthyroidism ; and as such one is struck by the small number of true psychotic reactions reported, namely 32 apart from states of exhaustion and delirium occasioned by a high degree of toxaemia, of which less than 6 of the vast case material could have belonged to the schizophrenic group. When schizophrenic reactions in hyperthyroidism have been detected, the form appears generally to have been catatonic, with changes of mood and action, and the presence of hallucinations. One such case is reported by Means (1937) where thyroidectomy was followed by an aggravation of the psychosis.

Henderson and Gillespie (1940) quote Falta for the statement that catatonic reactions occur in hyperthyroidism, but fail to give a clear picture of the precise nature of these reactions.

Falta (1923) himself mentions delirium as a terminal state and says that only occasionally does a true psychosis occur. He quotes the survey of Sattler in which of 150 cases of mental disease associated with thyrotoxicosis, 70 were of the manic-depressive type.

Joll (1932) has operated on three cases, all of melancholia suffering from thyrotoxicosis. He does not refer to any examples of schizophrenia in his large case material. The evidence then drawn from several sources seems to be that schizophrenia is but an infrequent accompaniment of hyperthyroidism, and that when it does occur catatonia may be a reaction.

It will be regrettably evident that the authors of these generalizations on psychotic reactions in hyperthyroidism overlooked the possible existence of a rare symptom-complex because it was not immediately apparent.

Summarizing the findings in the foregoing survey and census the following facts are significant :

There is a great preponderance of female to male goitres in mental patients. This is in accordance with general experience in non-mental subjects.

Non-toxic goitre was not found in a single case of early schizophrenia, and hyperthyroidism was not seen in chronic schizophrenia.

There is no record that a goitre has appeared in any chronic psychotic after the psychosis had been well established.

The association of thyrotoxicosis with a catatonic type of reaction only was noted in every relevant case of early schizophrenia.

These are positive findings based on observation and devoid of decorative deduction. They may be coincidences, but until such can be proved from surveying a very much larger series of patients they are sufficiently significant to merit investigation in the light of recent researches in schizophrenia and of what is known of thyroid function to-day.

## Thyroid Extract in Schizophrenia.

Although it is not possible to produce the identical clinical picture of thyrotoxicosis in normal subjects by administration of thyroid hormone,

well-known physiological and metabolic effects can be produced in this way. Feeding mental patients with thyroid extracts has been extensively practised; the results claimed are varied and somewhat unsatisfactory.

Hoskins and Sleeper (1929) believed that they could influence favourably hebephrenia by thyroid feeding. Their findings have not been generally confirmed.

Thyroid extract does not always operate in schizophrenia in the same way as in normal subjects. It does not in all cases influence the metabolic rate nor have a consistent effect upon the mental symptoms. Some schizophrenics, especially those showing obvious nutritional and sympathetic anomalies, respond with improved health, gain of weight, better muscle tone, and generally a less vegetable existence. But not infrequently schizophrenics become extremely irritable. That the metabolic response of many schizophrenics is abnormal is demonstrated by their habitual low body temperature and slight or negligible pyretic reaction to bodily infection such as tuberculosis.

In myxoedema and forms of cretinism undesirable mental reactions sometimes follow ingestion of thyroid extract. The writer has observed a case of myxoedema who became suspicious, excitable, very irritable and violent, only during periods of thyroid medication. Means (1932) reports a case of a cretin girl who responded to thyroid on several occasions by psychotic episodes of somewhat similar form, the psychotic symptoms disappearing when thyroid extract was withheld. It is clear that even in subthyroid cases there are examples where the brain and nervous system are unable to adjust themselves to a state of increased metabolism and who therefore respond in an unexpected way.

Cohen and Fierman (1938) investigated the response of a number of schizophrenics to daily administration of 15–18 gr. of thyroid extract. They found that toxic symptoms were absent, psychic changes did not occur, and that in spite of great increase in oxygen consumption the pulse-rate began to fall after reaching a maximum of 110.

A classification of schizophrenia based on the reaction of the subject to thyroid hormone should be possible; that such a classification does not exist in any workable form is an admission of technical incompetence, especially as this hormone has been so widely advocated in the therapy of this complex and many-sided group of disorders.

Angyal, Freeman and Hoskins have studied psychic withdrawal in schizophrenia from the response of the patient to a variety of physiological stimuli such as thyroxine and vestibular irritation. Their conclusions were that the reduction of responsiveness to a number of physiological agents is not uniform and one physiological factor may undergo a greater reduction than others, some being unchanged, apparently depending on some property of the individual patient. This has contributed to the knowledge of the behaviour of the individual rather than to a classification of schizophrenia.

The great difficulty of forming such a classification is in establishing objective standards for physiological activity and resting states. In the census recorded earlier hyperthyroidism has been diagnosed on clinical grounds without resort to laboratory methods. The methods for estimating thyroid function in non-mental subjects are several, and all open to much individual variation both from patient to patient and operator to operator. They suffice to show a fair degree of hyperthyroidism, but only a much greater degree of hypofunction, and by themselves are of no more than confirmatory value for variations close to the normal. The great objection to most of these methods is that they supply indirect information about some but not all of the effects of a gland which is itself influenced by other factors, and whose activity is not necessarily constant on successive occasions when the experimental conditions have been laid down as identical according to the standards set by the operator. Well-known laboratory methods are :

*The basal metabolic rate.*—For this measurement to be approximately accurate it is necessary to ensure the usually accepted conditions about rest, relaxation and diet. This demands a high degree of collaboration, and successive measurements in difficult subjects have shown that the results cannot be relied upon in mental patients.

*Blood iodine.*—The determination of the protein-bound alcohol-insoluble iodine in the blood furnishes information about thyroid activity at a particular time, the blood iodine being increased in hyperthyroidism. Estimation of total or alcohol-soluble iodine is unreliable, being affected by the iodine in food, excreta and sweat, and the premenstrual rise (Green, 1941). A comprehensive study of iodine metabolism and its problems has been made by Elmer (1938). The delicate biochemical technique involved renders this estimation difficult and specialized. It cannot be easily employed at present for establishing differential diagnoses in mental patients.

*Blood cholesterol.*—It is related to the basal metabolic rate, and according to Hurxthal (1934) *et al.* is significantly raised in myxoedema. It bears approximately an inverse relationship to the blood iodine. Hypercholesterolaemia is not always found in myxoedema nor is it exclusively confined to thyroid hypofunction.

*Skin capillaries.*—Their architecture has been studied by Redisch (1924), Jaensch and Wittneben (1927), who have demonstrated that the capillary formation is radically different in Graves's disease and myxoedema. Their work shows that capillary structure, like the skin and other tissues, is special in these two opposite extremes of thyroid functioning. The difficulty of establishing an adequate classification for slight deviations of the normal, and of attributing capillary changes only to the action of the thyroid when perhaps these changes are but one part of a general structural type, of which the thyroid is itself a controlled and not a controlling member, is immediately apparent. Hoepfner (1928) surmounts the disadvantages sufficiently to claim

that hypothyroid mental defects can be accurately diagnosed from other forms of idiocy on capillary formation alone.

As an index to the architecture of a system intimately related to cellular formation and cell metabolism on which the integrity of the body depends, the study of the capillary picture may provide a valuable basis for the classification of types of schizophrenia, especially those in whom somatic symptoms are prominent. It is interesting to note, especially with reference to thyroid feeding in schizophrenia, that Jaensch and Wittneben (1927) have demonstrated a characteristic capillary picture in sub-thyroid types of mental deficiency which may be altered by feeding with thyroid extract, and that in certain cases this change can be correlated with mental and intellectual improvement.

*Impedance angle.*—The electrical properties of the body in relation to thyroid function were studied by Brazier (1933), who showed that after establishing a normal value by investigating many normal subjects, the impedance angle was raised above this normal in hyperthyroidism and diminished in hypothyroidism. The value of this measurement has been questioned on theoretical grounds. Horton and Van Ravenswaay (1935) and Robertson and Wilson (1934) deny that it has any diagnostic significance. Nevertheless, Brazier has shown that in normal subjects the impedance angle does not change appreciably over a period of months, perhaps longer, but that in certain schizophrenics the impedance angle value is variable, showing readings that fluctuate to some extent with the clinical state. Furthermore, she showed that in normal subjects the impedance angle value could not be raised except by administration of thyroid extract. Sargant, Fraser and Brazier (1938) have treated a number of patients whose mental condition exhibited periodic fluctuations with thyroid extract and endeavoured to control the dosage by correlating the mental changes and physiological effects with impedance angle measurements.

The description of their case material is not such that a clear picture of the significant psychological features of the cases relative to their response to thyroid or their impedance angle values can be recognized. Like other workers, they found that the response of individual cases to thyroid extract was not uniform, and that it did not correspond to the behaviour of normal subjects. As the impedance angle is a property of the intimate relationship between body cells, its variability in schizophrenia when compared to normal suggests that in some cases or types of schizophrenia there is an unstable or abnormal state of cellular integration.

It will be seen, therefore, that there is some evidence for the existence of types of schizophrenia in which manifestations of normal thyroid activity are inconstant, and whose response to thyroid medication is irregular, and perhaps in which the form and relationship of the physical units, which make up the body, are abnormal. It is necessary to consider the outstanding work of Gjessing in this connection.

### Catatonia with Periodic Disturbances of Somatic Function.

This is a small group believed by Gjessing (1933) to comprise not more than 2 or 3 per cent. of schizophrenics. These patients show phases of excitement or stupor of fairly acute onset alternating with phases of normality. Attacks occur at intervals of several months or less. The phases of excitement or stupor are associated with a variety of abnormal mental symptoms with schizophrenic features. Gjessing (1938, 1939), after investigating the biochemistry of more than 30 of such male patients, found that in periodic catatonia there are alternative phases of retention and over-excretion of nitrogen. In some patients when the nitrogen retention has reached a certain maximum level, stupor or excitement sets in and continues until the nitrogen store is depleted. Retention and storage then recommences. The impedance angle showed a resemblance to the hypothyroid state in the reactive phase. Gjessing distinguishes two groups in which the so-called reaction syndrome sets in at the negative or the positive end of the nitrogen balance respectively. His investigations were exceptionally complete, and entailed much specialized work to eliminate sources of error in the estimation of the nitrogen balance. As a preliminary to every investigation all ascertainable foci of sepsis were cleared up. Gjessing investigated the possibility of depleting the nitrogen store or of preventing nitrogen accumulation by administration of adequate doses of thyroxine and thyroid extract. He found that by applying this measure at the right moment in the phase of nitrogen retention, attacks would be aborted and the patients kept well. In most cases it was necessary for the patient to continue to take a maintenance dose of thyroid extract indefinitely. In some cases this appeared to be unnecessary, for it seemed as if the patient's own thyroid had been influenced in the direction of increased activity. Gjessing's work, therefore, shows that haphazard administration of sufficient quantities of thyroid extract to schizophrenics may produce occasional therapeutic successes, if by chance his type of periodic catatonia is represented in the series treated. The mechanism responsible for the nitrogen disbalance cannot be stated. Gjessing himself imagined that some product of protein metabolism acting irritatively on the vegetative and myostatic centres in the diencephalon might be a factor. Probably the cause does not lie in the thyroid, but thyroid malfunction resulting from a faulty control of thyroid activity may be one link in a vicious chain. It seems probable that a severe degree of hyperthyroidism or Graves's disease could not co-exist with this type of periodic catatonia. Gjessing stresses that there is no method of discovering nitrogen retention except by daily nitrogen determination. The psychiatric picture of his cases seems to be largely coloured by the periodic nature of the illness, and as pointed out by Watterson (1939) after visiting Gjessing's clinic, the psychological features of the cases are not very clear, but they vary and generally are devoid of special symptomatology. Perhaps the greatest importance of Gjessing's

work is to link the phases of one form of periodic insanity with aberrations of biological activity.

The cases of catatonia associated with hyperthyroidism referred to in the survey of the Bristol patients have significant mental features common to all. They do not necessarily coincide with any of Gjessing's cases, and in contrast to those he has investigated, all of which were males, although this does not necessarily exclude the other sex, they are female. They will now be described in sufficient detail to bring out the essential facts of each case. For the sake of brevity anything but relevant events in the case histories will be omitted.

## Cases.

Case 1.—Lily V. H—, aged 23, single, occupation typist, admitted 7.ii.40. Early history: Family history normal; good education and intelligence; believed to have had sleepy sickness at 8 years; was treated at home. There were no residual symptoms and the patient was unaware that there might be until the present illness commenced.

1.viii.39: Noticed some difficulty in using the left hand normally at the typewriter. At the same time she became moody, slept badly, was depressed, spoke little and expressed doubts as to whether she could or would marry her fiancé.

1.i.40: Was noticed to have a small goitre. During January she attended a psychological out-patients' clinic not connected with the mental hospital. She is reported to have become progressively more depressed and more disjointed in her conversation during this month.

4.ii.40: There was some acute episode. She became very restless, wandered from the house, saying she was in a daze and that her sex had been changed. She shouted out and could not be managed by her parents.

7.ii.40: Entered hospital as a voluntary patient. On admission her condition was as follows: She said that she felt she was in a haze, that her mind was "full of imaginations of sex." She thought and dreamed that she was "both a man and a woman." Sometimes she thought she was her "own brother," at other times she "might be her father." She felt that she had been "changed" and that "people had altered" her by looking at her, and that she "could alter people by her thoughts." Her eyes seemed "strange"; through them everything looked different from what she used to see. Sometimes voices spoke to her accusing her of having sexual intercourse with her father. These voices were experienced at first on the left side, and subsequently on either or both sides.

She was unreal and was afraid of the world around her because she did not know "if she belonged to it." Sometimes she felt that her arm was being "cured"; "red hot needles shot down to the wrist" leaving the hand "uncured." She lay in bed in a semi-stuporose condition, only conversing when spoken to. She showed slight rigidity of the left hand and left leg with a Parkinsonian tremor of the left hand. There was no ascertainable disorder of sensation, no ataxy, no loss of position or joint sense, no apraxia, no aphasia and no agnosia; apart from the particular personal dysgnosia described, there were no other abnormalities of the central nervous system. All movements were executed rather stiffly and the general expression and posture were of catatonic stupor although there was no true catalepsy. There was a small goitre with exophthalmos and clinical hyperthyroidism. She became more stuporose and silent until 14.ii.40, when, following a lumbar puncture which yielded a normal fluid with 1·2 cells per c.c. not under pressure, she appeared brighter, alert and relatively free from psychotic symptoms. She said the "voices" had lessened and that her "body felt more her own." 21.ii.40: Her condition was much the same as on admission. She complained that her eyes were not her own and that her whole body felt

unreal, and that parts of it looked different so that she was not sure which was her right hand, which was her left leg, or arm. As before, voices came on the left or the right side.

During the next month she was silent and more stuporose but would make unprovoked attacks on members of the staff, giving no reason for so doing, and, lapsing into silence immediately afterwards. Her conversation was fragmentary, and related chiefly to disturbances in the parts of her body similar to what has been described.

19.iv.40: She was discharged at her own request and at the request of her relatives. It has not been possible to establish contact with her since.

*Summary of Case* 1.—In this case a schizophrenic reaction developed without exciting cause in a young woman who had a slight residual defect from encephalitis lethargica contracted 14 years previously. Three months later an exophthalmic goitre developed, to be followed by an acute schizophrenic reaction with periods of excitement and catatonic stupor. Special symptoms noted were the inability to distinguish between parts and sides of the body, a marked degree of depersonalization with loss of identity, the idea that she might be someone else, the feeling that voices and hallucinatory experiences operated independently on various parts of the body, and an abnormal conception of visual percepts and of the sensory function of the eyes. These special psychotic symptoms did not endure, the picture two months later being a silent, catatonic stupor, interrupted by impulsive acts.

CASE 2.—Monica G. C—, aged 23, single, shop assistant, admitted 25.ix.40 Early history: No family history; normal education and upbringing; a sociable, rather highly strung girl.

4.vii.39: Operation for acute appendix. Shortly after leaving hospital she became depressed, unsociable, and broke off her engagement. She attended the psychiatric out-patients' clinic in January, 1940. She then complained that she felt "wicked"; that a voice whispered this in her ear. She thought that she could not work because people talked about her, but said she would be all right if the voices left her alone. Her feeling of guilt related to sexual episodes three months previously. There had been amenorrhoea since. Her manner suggested early schizophrenia; advice for treatment was neglected. She returned home, did not report again at clinic, apparently made a spontaneous recovery. She went back to work in March and April.

6.v.40: She developed acutely an exophthalmic goitre, but she continued to work apparently free from mental symptoms until 24.vii.40, when she was admitted to a general hospital.

17.viii.40: Thyroidectomy was performed. After operation she became restless, rather excitable and talked in a disjointed fashion. No precise psychiatric information about the onset of this phase is available.

5.ix.40: She was admitted to the Bristol Mental Hospital as a certified patient.

On admission her condition was as follows: She stated that she felt changed; both sides of her body felt "different," one leg being "shorter" than the other. She said, "I do not know who I am; I feel different." "Voices tell me I am a German, so I must be in Germany." "I am unhappy; no, I am not unhappy." "I want to go home on my two feet to prove that I have feet." "My feet are here and I can see them." "One feels shorter than the other." She could not say which was her right or left hand, did not know which she should offer when she normally shook hands. She would look at her hands and say that they could not be hers, or that they could not be right or left hands because they "looked the same," although they "felt different." She would turn her hands so that both her thumbs pointed to the same side and try to determine to which side they belonged by the direction in which the thumb was pointing. She could converse fairly sensibly about events of the previous winter, and when reminded that she had seen the writer at the clinic, she described accurately what she had worn and said, "Thank God you recognize me; now I know that I used to be real; that you can believe me and

prove that it is true when I say that my body and limbs are not the same. You know I used to be different." Between examinations she was semi-stuporose, would lie in bed in a stiff posture, and at times showed a degree of flexibilitas cerea.

She was rather fat, her hair was thin and coarse. The skin was not moist, the pulse rate was constantly raised and there was a marked degree of exophthalmos. The impedance angle reading indicated a pathological degree of hyperthyroidism. The central nervous system was normal, there was no apraxia, aphasia nor agnosia.

For about six weeks she remained in the same condition. She would converse only when spoken to, and, as at first, appeared to have lost the idea of her identity and was still puzzled to know the right or the left hand. This form of dysgnosia appeared to be quite genuine; she always seemed to be trying to orientate the parts of her body and herself relative to her limbs. Sometimes it almost seemed as if she saw a mirror image of her hands and that on this account she could not tell her right from her left, although she had no difficulty in indicating correctly the parts and relative sides of the examiner's arms and hands. She was extremely grateful for any reassurance by people who had known her before her illness that she had existed in the form she used to remember, and she would discuss readily dresses she had worn on particular occasions, and even the way her hair was done and her slim figure. She then became uncommunicative, dull and stuporose, the stupor being interrupted by unexplained outbursts of violence or aimlessly restless behaviour.

5.i.41 until 13.ii.41, when she was discharged by order of the Petitioner, she looked after herself, helped in the sewing ward, and gave no further trouble. She no longer expressed the earlier psychotic ideas, but showed much retardation and no initiative. She said that voices whispered to her sometimes, but she did not know what they said. She was able to tell the parts of her body correctly, but expressed her views about right or left with no confidence, prefacing her remarks with, " I suppose it is my right hand or my left," as the case may be. She had no idea of time and showed no desires nor ambitions for the future. The picture was one of mild confusion with considerable inhibition. This picture has not changed substantially in the last six weeks.

*Summary of Case* 2.—In this case, a girl of 23, a schizophrenic reaction followed an abdominal operation. There was a complete remission. Four months later an exophthalmic goitre developed acutely.

Thyroidectomy three months later was followed by an acute schizophrenic psychosis in which the prominent features were a gross disturbance of body sense and of the inability to identify parts of the body by sight, a high degree of depersonalization with auditory hallucinations relating to the identity of the subject. There were phases of catatonic stupor and wild impulsive outbursts. Three months after admission a state of chronic retardation with mild confusion, inhibition of initiative, and loss of the early psychotic ideas developed. The physical appearance on admission was that of partial myxoedema and exophthalmos with hyperthyroidism.

Case 3.—Eva Rose B—, aged 32, single, shop assistant, admitted 12.ii.41. Early history: No family history of insanity; well educated, intelligent girl.

Autumn, 1939, developed exophthalmic goitre; was able to work until summer, 1940. She then " rested " for three months; there was no suspicion of mental abnormality up to this time. She returned to work from August to October when her mental state first showed signs of change. She became irritable, quarrelled with her family, broke off her engagement, said that she had been " tricked," and one evening in November stopped a passing car, telling the occupants that she was being followed. At times she was violent, and would dash out of the house, knocking down members of the family who tried to stop her. She was treated for seven weeks in a private nursing home. She recovered to some extent and returned home for two weeks, but she became unmanageable once more. Her relatives could furnish no reliable information about the precise form of the psychotic

symptoms, except that " at times she would seem very quiet and suddenly become violent."

12.ii.41: Admitted to the Bristol Mental Hospital as a voluntary patient. On admission she was in a state of partial stupor, lay quietly in bed, and would not speak unless addressed. She said that people talked about her and that she could hear her own thoughts, and so thought that she was a film star. Other people discussed this and their talk annoyed her so that she made violent attacks upon them. She heard " thoughts like voices " which were unreal. She herself felt " unreal;" she could not decide which was her right hand or which was her left hand. Various parts of her body did not feel the same. Her body seemed to be changed;" it was full of blood." Her arms felt like " someone else's." When she looked at people they looked back through her eyes so that their appearance changed constantly. Her eyes had altered as her " eyelids were distended by the war." She spoke in a slow drawling voice; she refused food. She had an enlarged thyroid and clinical signs of exophthalmic goitre. There was no aphasia, apraxia nor agnosia, and the only abnormal findings in the central nervous system were a doubtful extensor plantar response on the right side and rather brisk knee jerks. The temperature was slightly raised. Two days after admission she became stuporose, would not speak and would not eat.

Lumbar puncture yielded a normal fluid not under pressure. During the next week she became much clearer, would converse spontaneously and eat, wash and clothe herself.

One month after admission, at the time of writing, she was still much retarded, maintained a statue-like attitude, and, while the ideas characteristic of the acute stage of her illness were no longer apparent, she felt that her identity was mistaken and that people thought that she was " some other patient." She recollected that her body and limbs had felt unreal, and that she had had some difficulty in realizing who and where she was. She sometimes heard voices whispering about her, and her eyes felt " distended and very strange."

In contrast to the two preceding cases, the phase following the acute symptoms appears to be associated with less confusion, and the tendency to turn towards normal life rather than to regress towards dementia is at present noticeable.

*Summary of Case* 3.—In this patient, a girl of 32, without previous illness, exophthalmic goitre appeared about twelve months before the development of a schizophrenic psychosis. The psychosis took the form of phases of catatonic stupor with occasional violent and restless outbursts.

At what appeared to be the peak of the illness just before passing into inaccessible stupor the prominent symptoms were depersonalization, with a feeling of unreality and the inability to distinguish clearly between the two sides of the body. Visual impulses were distorted and the eyes became, to some extent, part of the outer world, in that external people looked through them at the patient.

CASE 4.—Fanny Y—, aged 41, married, admitted 27.xi.39. Early history: Her mother, brother and uncle had been treated in mental hospitals. The father was an alcoholic. She had had rather a poor upbringing with an unhappy life. She was of suspicious, asocial and hard-working nature. She had one son. In 1935 thyroidectomy for thyrotoxicosis of rather acute onset was performed. Since the operation the menses had been irregular. The operation was successful; following it she was free from thyrotoxic symptoms and gained weight.

October, 1939: She began to sleep badly, was restless, and thought she heard the voices of her neighbours slandering her. She would see the devil looking out of her husband's eyes, and his (her husband's) face would appear " like the devil's " if she stared at him. When her doctor examined her " his face swelled up and took the form of the devil." Through the five openings of a boil on her face she could see the heads of five Members of Parliament. When she touched the boil the faces disappeared. A healing cruciform burn on her finger appeared as " Christ on the Cross " in her flesh as she looked at it.

29.xi.40: She was admitted to hospital after these symptoms had been present

for a few weeks. They had apparently become more intense just before the date of admission, and the appearance of individuals " through " her eyes was constantly " changing."

On admission she was very depressed, but showed good insight. She substantiated the above history, and said that these phenomena made her very frightened so that she felt inclined to take her life. Voices whispered threats to her which she tried not to hear.

Physically she was a thin woman with a very dry skin and hair, the nails and hair were brittle, there was no exophthalmos and no palpable thyroid behind the thyroidectomy scar. The impedance angle measurement indicated hypothyroidism—a finding that agreed with the appearance of the skin and hair. Other symptoms of thyroid disturbance were not apparent, although the loss of weight following the post-operative gain may have been significant. There were no notable abnormalities in the central nervous or other systems.

The menses were scanty and irregular.

A fortnight after admission she was much more cheerful and stated that the hallucinatory experiences had completely disappeared.

3.iii.40: She was discharged free from symptoms.

After discharge she remained well for three months, when she again became depressed. Voices whispered to her saying that her husband was " on fire " and that she ought to be killed. A voice told her to kill herself and to persuade her husband to kill her son.

6.vi.40: She was readmitted to the Bristol Mental Hospital as a certified patient. On this occasion, as before, she showed good insight. She was frightened at her mental state. She thought she was going to die, and that she would commit " some wickedness."

As before she experienced peculiar visual phenomena. People looked " different " if she stared hard at them, and when she looked in the mirror she saw " the face of God like a big man " looking at her, and sometimes she saw the devil. She said that recently anything she looked at " seemed different and changed " because of some property of her eyes. She had once more seen important people, whose picture she knew from newspapers, looking at her through a skin wound. These symptoms had developed fairly rapidly during the three weeks before admission to hospital. She was very quiet and asocial. As before, she was highly co-operative, showing good insight, asserting that she felt safe in hospital.

Her condition showed little change for about twelve weeks, when, following a course of electrically-induced convulsions, she became brighter and interested in her surroundings; she stated that the characteristic hallucinations and delusions had disappeared. During the next three months her mental state seemed unstable. At times she seemed depressed and would be seen weeping to herself, but there was no recurrence of hallucinations. Three months later she was discharged from hospital free from symptoms. She is still in normal mental health.

*Summary of Case* 4.—This case has been described because of the unusual nature of the somatic hallucinations and their association with a disorder of the thyroid. The patient was a married woman of 41 whose thyroid had been removed six years previously. An acute schizophrenic psychosis set in, lasting for about four months. A psychosis recurred after a remission of about five months. Its form was similar to the first, and its duration approximately six months. Remission seems to have been complete after each attack. There was no true catatonia; the patient's insight was very well preserved. The interesting symptoms were the inability of the patient to preserve the unity and the integrity of the body surface relative to the external world, and the intrusion of elements from that external world through wounds or openings in the skin surface. In addition, there was a great distortion and projection of visual experiences, and as in the early cases reported, the opening of the eye seemed to serve as an interruption in the boundaries of the individual surface through which the outer world might pass. The relationship of this case to the preceding cases will be discussed later.

CASE 5.—Ernest R—, aged 19, male, single, admitted to the Bristol Mental Hospital 12.viii.39. Early history: No family history of insanity; normal education and upbringing.

March, 1939: Became irritable and moody, kept to himself, and when questioned said that he was walking "round in circles." He had an idea that his mother was in a plot against him, and would laugh and chatter to himself if he thought he was unobserved. He continued to work until August 7, 1939, when he refused to speak and would only stand and stare into space.

12.viii.39: He entered hospital as a voluntary patient. On admission he was semi-stuporose. He could scarcely speak, and expressed the belief that people were whispering about him and that they had affected his head and eyes. He would give no further account of himself, and during the next week he passed into a state of rigid catatonia with flexibilitas cerea. He had, from admission, an enlarged thyroid with some exophthalmos, and an elevated pulse rate. Being unfit to remain in the voluntary class he left hospital three weeks from the date of admission.

## COMMENT.

The last case is reported as being the only male in the series reviewed showing clinical hyperthyroidism. The hyperthyroidism was associated with a catatonic schizophrenic illness, and it apparently was not obvious until after the catatonic symptoms made their appearance. The examination and history of this case is too incomplete to permit further discussion.

The four female cases have the following common symptomatology: After an initial period in which the usual signs of early schizophrenia appeared, special symptoms developed acutely. Visual hallucinations of similar form appeared in each case, and in all hallucinations referring to a change in the form or representation in the body. The invariable complaint was that the body as a whole and parts of it relative to one another both looked and felt subjectively different from normal. There were no executive or other disabilities to suggest that any special brain lesion was responsible. In the more severe cases a catatonic phase developed, and when prolonged in two cases terminated in dementia. One case is recovering; Case 4 has had two complete and mild cycles.

## A HYPERTHYROTIC FORM OF SCHIZOPHRENIA.

It will be apparent that the course and psychic symptoms of three of the four cases described are very similar and that the fourth has many points in common with the other three. As these were the only schizophrenic cases in which hyperthyroidism existed, the question must be asked, do these cases belong to a clinical subtype of schizophrenia in which the thyroid abnormality bears a causal relationship to the psychosis, or are the psychic and physical components of the picture coincidentally associated? If the thyroid disorder is related to the psychic reaction, great issues are involved, for the aetiology of the thyrotoxicosis and the psychosis may be the same, both having a common origin; and if so, an approach to the nature of one form of schizophrenia may be possible. These questions cannot be answered with certainty, involving,

as they do, problems of schizophrenia and of the causation of thyrotoxicosis, but some relevant evidence can be produced and discussed.

Schizophrenia is a psychological conception and although, psychologically, schizophrenic disorders are related, it must not be expected that schizophrenic reactions are linked with the same clinical conditions. The tendency to regard schizophrenia as a disease *per se* is largely responsible for the contradictory results of therapy and experiment. In classifying cases for this paper, schizophrenic illnesses of early life of various forms, paraphrenia and paranoia, illnesses in which the morbid psychological processes may be theoretically allied to the other schizophrenias, but in which the course and general form are not the same, have been distinguished.

The present census and the figures of others agree that early schizophrenia and thyrotoxicosis are rarely found together—so rarely that their association might well be a chance one. On the other hand, thyrotoxicosis is relatively common in the third and fourth decade, yet its accompanying mental disorders are most frequently toxic delirium and manic-depressive insanity. Mere chance could hardly explain the aversion of thyrotoxicosis from general schizophrenic reactions, in spite of their similar age distribution, and its predilection in this series for schizophrenia of a special form only.

The psychic symptoms common to all the cases reported were a disturbance of the conception of various parts or even sides of the body and a variety of visuo-psychic aberrations, and in the three youngest, catatonic reactions. In two cases it was noted that even by sight the right hand could not be distinguished from the left, and that parts of the body felt different, both from one another and from what they used to be.

Disturbances of the body image and gnostic failure for right and left are not common mental symptoms and are usually related to organic brain lesions. The writer has rarely seen symptoms of this kind in non-organic cases of his experience, and has not encountered the special catatonic symptom-complex apart from the cases here described. Experienced members of the staff and colleagues are in agreement ; case sheets of several thousand patients fail to record it.

Visual hallucinations are comparatively uncommon in schizophrenia and are more characteristic of toxic states. It can be claimed therefore with some certainty that three of the four female cases fall into one rare symptomatic group, with the same incidence in the 4,070 cases studied in this paper as the accompanying hyperthyroidism found in early schizophrenia.

The fourth case, presenting some of the significant psychic features, can be regarded as a slightly atypical example of the same group. There therefore appears to be a form of schizophrenia specifically related to hyperthyroidism of which the features have been described above, rarely seen, but in itself a clinical entity. In the writer's knowledge such a syndrome has not been recorded hitherto in the literature.

Having established the existence of this symptom-complex, it is necessary to consider in what way it may arise, and whether the psychic picture is a reaction to hyperthyroidism acting in a susceptible constitution, or is with the thyroid malfunction the expression of a deeper process. The problem may be clarified by considering the psychopathology of this hyperthyrotic schizophrenic reaction.

### *The Psychopathology of Hyperthyrotic Catatonia.*

The psychotic course of Cases 1, 2 and 3 is much as follows :

First there is a stage of early undifferentiated schizophrenic symptoms in which the affective relationship between the individual and the social environment is undergoing change; ideas of reference and auditory hallucinations appear. After a period of some weeks an acute episode takes place in which the patient shows extensive motor activity, to be followed by degrees of catatonic stupor. Before the stupor deepens the specific symptoms appear. There are then fluctuations between stupor and excitement followed by confusion with a degree of dementia and loss of the specific symptoms. This course is also true for Case 2, except that the first psychotic phase underwent remission and the acute episode followed shortly after thyroidectomy. The final stage of Case 3 seems to be in the direction of recovery; of the other two cases towards dementia. Case 4 can be regarded as a milder form of the other three, showing a pre-psychotic phase, a phase of special symptoms with visual aberrations and then recovery, to be succeeded some months later by a recurrence of an almost identical cycle. In Case 4 the thyroid had been removed six years before the first attack, but there is a suspicion that its activity was altering prior to the first psychotic illness possibly with the onset of the menopause.

All these special symptoms may be regarded psychologically as the result of changes taking place in the barrier between the ego and the outer world. If this intermediate barrier which consists of the skin surface and the bodily tissues, forming the internal environment, be interrupted, the internal environment of the ego, as it were, is interfered with and the relationship of the ego to the external environment is altered.

The integration of the psycho-somatic pattern in normal subjects is such that even though a limb is removed or a large portion of the skin surface broken, the identity and orientation of the ego are preserved.

Afferent impulses are actually productive of movement, and are responsible for the continual adjustments in the internal environment made necessary by changes in the external, or by physiological processes going on within. Motion, conscious or unconscious, from whatever level it is directed is the effort of the ego to orientate itself relative to the external environment by conditioning the activities of its body.

Catatonia may be regarded as the effort or lack of effort of the ego to orientate itself in response to chaotic afferent impulses. The immobility, the stupor, and the wild changes of kinesis followed by stupor, indicate attempts at ego orientation and the acceptance of their failure. Catatonia occurs in a variety of conditions ; it accompanies brain damage, as seen in encephalitis lethargica, and can be induced by drugs such as bulbocapnine. It is probable that in these types of catatonia the pathological process responsible for the akinesis operates centrally. In the cases described in this paper the evidence is that the process operates through the relationship between individual cell units of the body.

In hyperthyroidism, as shown by the altered electrical properties of the body, by the structure and the distribution of the capillaries and by the increased oxygen consumption, even in a state of minimal activity, the functioning and therefore the relationship between the body cells is altered.

Thyroid hormone has manifold effects on the animal organism. It is concerned in the production of heat, the distribution of salts, colloids and fluids, and acts on the circulatory, nervous and endocrine systems. With regard to individual cells, it alters the physical condition of the cell surface and the permeability of its membrane. It is thought to act directly on the cell surface ; (Means, 1937 ; Zondek, 1935). For this reason the internal environment, even when at rest, undergoes a change in hyperthyrotic states.

Specific symptoms common to the cases have been described. It must not be supposed that these symptoms furnish positive evidence about the state of the patient or her body. We are no more entitled to deduce truths about what a schizophrenic patient experiences from what she says, than we are to discover the religion and creed within wide limits of a preacher from his broadcast sermon. Our knowledge of sensory impressions and what they mean to others is negligible unless they are linked with familiar and common concepts.

The value of afferent stimuli may vary with the duration of application ; percepts lose in vividness as they grow old. We attach the most importance to a pain at its onset, and in many cases disregard it after enduring it for a short while. The sole disturbance in the internal environment which makes the subject increasingly aware of it is a sudden change of metabolism, as occurs during the incubation of malaria and acute fevers ; such a state, familiar to all, renders the individual " different " from what he was previously, and if severe, makes him unresponsive to calls of the external world, so occupied is he with the internal changes.

The most striking of the special psychotic symptoms was the repeated assertion in every case that the body had been " changed," that it did not " feel the same," and that even parts of it, such as one limb, did not " feel the same " as other parts, or as they used to.

In normal subjects there is little conscious awareness of the body until, as described, altered metabolism attracts interest to the internal environment,

causing the idea of personal change. It may well be then that in these schizophrenic cases the unexpected changes of metabolism related to thyrotoxicosis produced an awareness not of self, but of change of self.

The first argumentative quality to appear in the child is that of denying. The child learns to deny before it does to assert. Its earliest denials are in the field of sameness or difference. The infant refuses a bottle or a toy on the ground that they are not its own, or that they are unfamiliar, long before it learns to express a preference or to make assertions.

When the catatonic says that she is " changed " she may be believed, for she is denying that she is the same. It is her idea of the nature, origin and form of the change that is subject to psychotic interpretation. It is possible, though improbable, that the changes in the presentation of the body image may be the result of a local disturbance in the brain. Schilder (1934) has shown that loss of the awareness of the existence of one half of the body or of its members is sometimes seen in large lesions of the left supramarginal and angular gyri. Gerstman *et al.* (1924, 1940) have investigated finger agnosia or the inability to recognize individual fingers from one another or even from someone else's. This syndrome has not been seen in an isolated form, but may occur as part of an aphasia. While it is not impossible to exclude such local factors, the absence of aphasia, or of disturbances in the central nervous system and the transitory nature of the symptoms, almost certainly rule out local cortical disturbance. None of the patients were left-handed, nor were they capable of performing mirror writing.

Lhermitte (1938) discusses cases in which the vaguely appreciated body image may be presented more strongly in consciousness. His studies in phantom limbs and similar phenomena make him favour a central and not peripheral origin, located in the parietal lobes.

Some authorities believe that hyperthyroidism does not affect all parts of the body uniformly, and cases have been reported in which local myxoedema and exophthalmic goitre co-existed in the same patient (Haines, 1928; Rolleston, 1936). Such a circumstance in these schizophrenic cases might decide the relative disturbances in the presentation of units of the body. In some schizophrenics there develops a specific reaction to interruptions in the body surface or to intrusion of external objects within the body. The reaction, instances of which have been described by Hemphill (1939) and Hemphill and Stengel (1940), consists of a psychotic interpretation being drawn from certain forms of external stimuli, and the tendency to incorporate external objects within the body through a break in its surface. This reaction is noted in some patients only, and at some acute phase in the development of the psychosis. What determines the susceptible period is not known, but coincidental bodily illnesses seemed to be responsible to some extent. If so, such cases react in a parallel way to the hyperthyrotic schizophrenics at the period of metabolic change.

It is noteworthy that Jaensch (1921), in studying eidetic imagery, maintains

that there is a constitutional form known as the Basedow type, in which the imagery is most susceptible to modification by external and internal factors.

The visuo-psychic aberrations may be explained in several ways. Some, such as the appearance of changing faces of the devil and the like, may be of toxic origin, and akin to the hallucinations of acute toxaemia as seen in mescaline poisoning. More probably they are related to the general metabolic disturbance, and show how the ego limitations are insecure at the ocular point of entry to the body.

Disorders of muscles and ophthalmoplegias of various orders have been noted in thyrotoxicosis even after thyroidectomy, the change being sometimes fairly severe with a lymphocytic infiltration of the orbital muscles (Brain and Turnbull, 1938). The visual aberrations may be dependent to some extent on such changes in the ocular muscles and apparatus itself.

From a psycho-pathological point of view, therefore, the catatonic phases, the disturbance in the identity and the relationship of parts of the body, the visuo-psychic phenomena and especially the sense of altered individuality can be related to a general, and not necessarily uniform, disturbance of the integration and functioning of the cell units of the body such as may be caused by thyroid hyperfunction. This interpretation applies equally whether the disturbances in bodily representation are of central or peripheral origin, or whether the thyroid hormone exerts a direct influence on cells or indirectly through sympathetic channels.

That such reactions are not met with in normal subjects indicates either that the reaction develops only in a specific type of constitution or that the type of thyrotoxicosis is itself special. This problem must now be approached.

### *The Mental Constitution in Hyperthyrotic Schizophrenia.*

Mental illness made its first appearance in three cases at 23, 23 and 32 respectively. There is no particle of evidence to suggest that any of these three patients had abnormal prepsychotic mental traits. They were known to be intelligent, sociable and stable. There was no history of insanity in any member of the family. In the eldest, Case 3, the goitre ante-dated the mental illness by about a year. In Case 1 it approximately synchronized with it, and in Case 2 it appeared during the first remission.

It is, perhaps, significant that a mild schizophrenic illness set in after an abdominal operation in Case 2, for marked hyperactivity of the thyroid usually follows major surgical operations, as shown by an increase in blood iodine (MacCullagh and MacCullagh, 1936). There were no prepsychotic symptoms in this case before this first operation.

The trace of encephalitis lethargica unsuspected during 16 years from the time of infection cannot reasonably be related to the clinical syndrome in Case 1.

In Case 4, known to be an asocial and rather paranoid individual with an extremely bad family history of insanity, no psychosis of any kind developed until six years after thyroidectomy performed at 35.

There is no evidence, then, that in this small group of cases hyperthyroidism acting on a special mental constitution produced the psychic symptoms. The well-known attempts of Kretschmer (1925, 1934) and others to establish constitutional and endocrine types in mental diseases are based on too wide generalization to throw light on this question. The hyperthyroid constitution, if it exists, seems to be incompatible with what is generally regarded as the schizophrenic personality ; schizophrenics tend to show hypo- rather than hyper-plastic endocrine anomalies, as evidenced by the absence of non-toxic goitre in schizophrenia noted in this paper.

### *The Patho-physiology of Hyperthyrotic Schizophrenia.*

While there appears to be no doubt that hyperthyroidism can be of pituitary or thyroid origin, authoritative opinions are not in harmony about the existence of several forms of thyrotoxicosis. The important question whether there is a psychogenic form of thyrotoxicosis is beyond the scope of this paper, and it is only possible to mention some developments in endocrinology which bear on the subject. Marine (1935) considers that some forms of exophthalmic goitre are of pituitary origin ; support of this is found in the experimental work of Smelser (1937), who produced exophthalmos without thyrotoxicosis in thyroidectomized guinea-pigs by administration of an extract of the anterior pituitary. Spence (1937), although denying the existence of more than one form of Graves's disease, held that when acromegaly is a complication, the pituitary function is the prime cause of hyperthyroidism.

Moorhead (1940) describes a case of severe thyrotoxicosis with exophthalmos in which there was no palpable thyroid. It was thought to be of primary pituitary origin.

It is believed that an equilibrium is preserved between the anterior pituitary and the thyroid through the concentration of thyrotrophic and thyroid hormones in the blood. Thyrotrophic hormone increases the secretory activity of the thyroid, but thyroid hormone inhibits the thyrotrophic activity of the anterior lobe of the pituitary. There is a limit to this inter-relation, for the continued administration of thyrotrophic hormone to an animal is eventually followed by a falling off of thyroid activity, so that the initial thyrotoxicosis may be replaced by hypothyroidism (Means, 1939). The intimate relation between the anterior pituitary and other endocrines, such as the gonads, makes possible a general endocrine disbalance in which the activity of the anterior pituitary is affected with an indirect influence on thyroid function.

In the special type of catatonia described in this paper the psychic picture

and the periodic course of the illness may not depend upon thyroid function but upon cyclical disturbances, arising elsewhere and perhaps influencing the activity of the anterior lobe of the pituitary. Hyperthyrotic catatonia appears to the writer to be one form of a disturbed endocrine and neuro-psychic pattern, in which the changes of endocrine equilibrium are rapid, and if severe seem to produce psychic damage which is beyond repair.

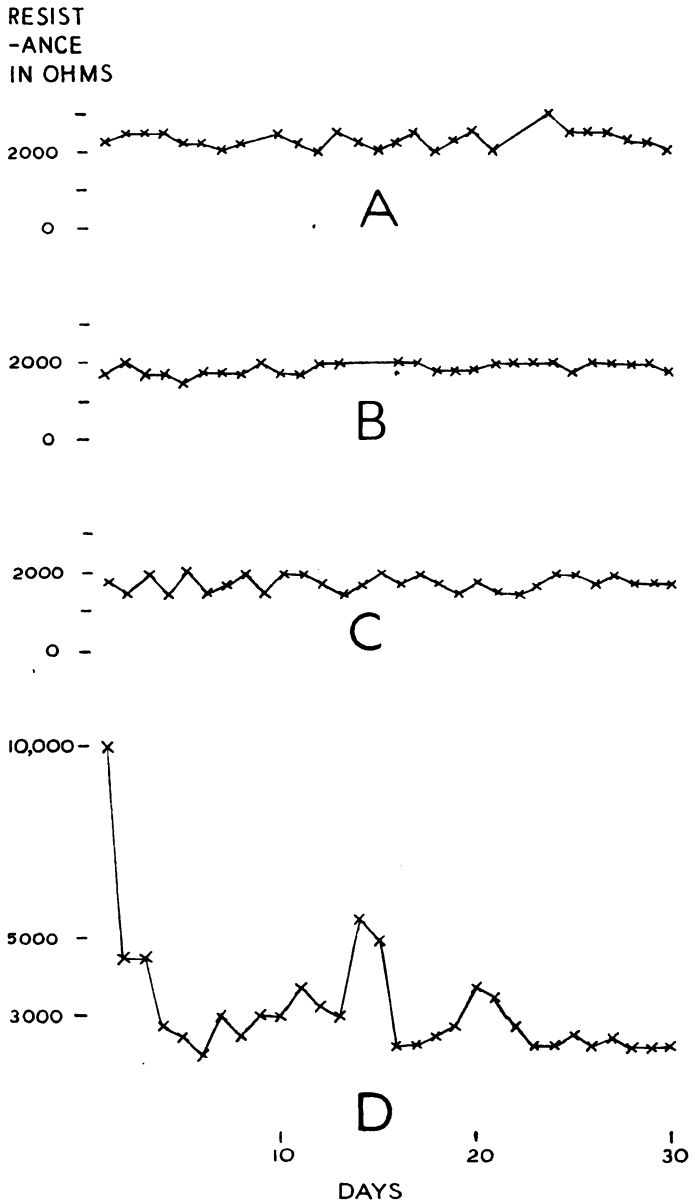
Nothing was ascertained to account for the onset of the illnesses. Anxiety, mental shock and focal sepsis, often cited as provoking factors in Graves's disease, did not appear ; nor did the war seem to contribute.

It is possible that some of the symptoms of hyperthyrotic catatonia are related to altered brain metabolism, for it has been shown in hypophysectomized animals that thyrotrophic hormone affects the oxygen consumption of cerebral cortex in a different way than certain other bodily tissues (MacLeod and Reiss, 1940). In this connection the electro-encephalogram of Case 3 may be recorded ; it obviously cannot be commented on here. " This patient showed an abnormally quiet record in which there was no trace of rhythmic activity whatever, either with the eyes open or shut. This finding is peculiar in that it is not associated with any pathological category. The total absence of the alpha rhythm is usually taken to mean full normal activity of the cortex, but there can be no question of this in this patient, and the abnormal quiet in all areas is hard to interpret, since inactivity of the organic pathological type would be associated with a slow delta discharge. It is possible that such finding indicates a biological rather than pathological variation." (Grey Walter.)

There is considerable evidence from the scattered literature to show that in some schizophrenics the thyroid function is atypical, as evidenced by the irregular response to thyroid hormone and the inconsistent behaviour of the electrical impedance of the body. In Case 3, the capillary picture and the impedance angle agreed with the clinical symptoms of thyrotoxicosis.

The electrical resistance of the skin to a direct current has been shown by Vigouroux (1888) to be low in exophthalmic goitre. Golla (1921) has confirmed this, and has demonstrated that administration of thyroid extract diminishes the mean value of the skin resistance. The accompanying curves show the daily values of the skin resistance in Case 3 for 30 days, commencing when the reactive stupor was passing off, a case of depression with thyrotoxicosis, a stationary retarded schizophrenic acutely catatonic 12 months previously, and a normal female (not a patient) for the same period. The approximate range of the skin resistance for a number of female subjects in a series at present under investigation was 2,000–3,500 ohms. It will be noted that Case 3 has behaved quite differently from the others, and in contradiction to what Vigouroux demonstrated. The significance of the skin resistance cannot be discussed here, but these measurements are at least suggestive that the hyperthyroidism of hyperthyrotic schizophrenia has some special physiological features.

FIG. 3.—*Electrical Resistance of the Skin to Direct Current, daily for 30 Days in Four Subjects.*




Subjects: A = Normal female, aged 20. B = Chronic schizophrenia, formerly catatonic, aged 20. C = Depression with thyrotoxicosis, aged 48. D = Case 3, hyperthyrotic catatonia, aged 32. The first day marks an early period in the emergence from stupor as patient was beginning to co-operate. All four patients were measured at the same time early each day. The period of 30 days was of the same date for all patients. With apparatus employed the approximate fluctuation attributable to local conditions and errors in technique is ± 400 ohms.

*The Relationship between Periodic Catatonia as Described by Gjessing and Hyperthyrotic Schizophrenia.*

Gjessing's group of cases were male, females being deliberately excluded because of the complication of the menstrual cycle. The biochemical changes he describes can be accounted for by cyclical hypo-activity of the thyroid mechanism, ranging between various extremes of sub-thyroidism. These periodic changes suggest the automatic functioning of a system no longer under control, and out of physiological harmony with related systems.

In the cases of hyperthyrotic catatonia the illness has a periodic nature, but the thyroid disturbance appears to be a fluctuation between extremes of hyperthyroidism. If these extremes are great it seems as if irreparable damage has been done, and, as two of the three cases show, the end result after the phase of stupor is retardation and dementia. Case 3 and Case 4, the two eldest, do not seem to have been affected in such an extreme degree, Case 4 having made two full remissions, and Case 3 at present showing a tendency towards recovery.

It is not impossible that Gjessing's type of case is met with in females or that hyperthyrotic catatonia occurs in males. Investigations in large numbers of schizophrenics will alone decide this question. But apart from the great preponderance of hyperthyroidism in females, the gonadal factors special to the sexes may determine a difference.

Psychologically the catatonia and disturbances of kinesis seen in both types can be regarded as derived from alterations in the internal environment. In hypothyroidism the psychic components of these alterations may be less striking, while the evidence that hyperthyroidism renders the individual more susceptible to external and internal influences would account for the more vivid reaction. The colourful and arresting picture in hyperthyrotic catatonia may have its drab counterpart in hypothyrotic catatonia.

Although the cases described were few, they represent only an extreme form of an illness in which hyperthyroidism was well marked. It is not impossible that hormone analyses coupled with a careful study of symptomatology in fluctuating cases would demonstrate mild examples of hyper- or hypothyrotic catatonia.

In formulating a hypothesis on the nature of these special schizophrenic illnesses, the incompleteness of the data in this paper is lamentably evident. Hormone analyses, biochemical and electrical estimations could have dispelled much of the obscurity. As it is, such facts as are available are subject to personal variations of interpretation.

There appears, from diverse sources, evidence of groups of schizophrenias in which a loosely integrated endocrine and neuro-psychic constitution exists. For some cause, neural, psychic, infective, or possible from a vitamin deficiency,

a chain of pathological events is set in motion in this constitution. The nature of the ensuing activity depends on the order in which disturbances of endocrine balance take place. In the acute phase there may be notable psychic phenomena, but irreversible changes in nervous tissues may lead to dementia masking the psychic consequences of subsequent physiological activity. Through the synergism that exists between endocrines, the eventual endocrine picture may be quite different from what it was at first. If irreversible changes do not take place, the psychosis may have a cyclical form.

Catatonia can be attributed to chaotic alterations in the internal environment. Forms of shock treatment which sometimes produce a dramatic improvement in catatonic schizophrenia, probably as lumbar puncture did in Cases 1 and 3, bring about favourable, if temporary, adjustments in the internal environment.

Some may find it tempting to postulate a mid-brain disturbance influencing the vegetative system, the nervous control of the thyroid and by local spread inducing catatonic phenomena. Histological changes of the same order have been demonstrated not very convincingly in the brains of catatonic cases of dementia praecox and of bulbocapnine poisoning (Pero, 1932; Buscaino, 1932; Wilson, 1940).

At present successful elucidation of the problem of periodic schizophrenia seems to depend on investigating the functions of the anterior pituitary. Occasional biochemical estimation of solitary functions is inadequate. Only from studying the acute stages of schizophrenic illnesses before irreversible changes have occurred and from repeated determinations of every assayable hormone will clarification emerge. It is important that cases should be investigated early. The psychosis of acute onset that has run a progressive course towards dementia frequently shows a variety of endocrine abnormalities, sometimes not unlike those of a hypophysectomized animal. In one chronic patient, not a schizophrenic, under the writer's care, no thyrotrophic hormone could be demonstrated in the urine. The cause of these physiological abnormalities will not be found until their nature and significance can be made clear. This is a task for the psychiatrist and the endocrinologist together.

## Summary.

From an investigation of 4,750 cases of mental disease, the distribution of toxic and non-toxic goitre was ascertained. This and relevant factors and findings have been discussed. Goitres predominated greatly in female subjects.

Apart from toxic delirium and the special psychosis mentioned below, hyperthyroidism did not appear to be a significant factor in the production of mental disease. There is no typical post-operative reaction. Simple or non-toxic goitre occurred in no case of early schizophrenia.

Hyperthyroidism in schizophrenia was very infrequent and was only found

to be associated with a particular form of reaction: this has been named hyperthyrotic catatonia.

The clinical features of this disorder are briefly a period of varying schizophrenic symptoms with auditory hallucinations, an acute episode when visual hallucinations appear, with distortion of the body-image, inability to differentiate clearly parts of the body and other evidences of instability of the boundaries of the ego.

This phase is succeeded by catatonic stupor. In severe cases the end result is dementia, in others towards recovery with repetition of the cycle.

The psychopathology and relationship of this condition to other disorders, and especially to the periodic catatonia described by Gjessing, have been considered and discussed in some detail.

There appear to be types of schizophrenia derived from special physical and endocrine constitutions.

Systematic determination of the anterior pituitary hormones may provide the key to these schizophrenic illnesses.

## NOTE.

Since the above paper was written six months ago, it has been possible to observe to some extent the progress of Case 1, Case 2 and Case 3:

CASE 1 (L. H—).—Information has been supplied by this patient's mother that about three months after her discharge from hospital she began to improve, being less stuporose and more communicative. Three months later she appears to have been free from psychotic symptoms and was able to resume her occupation. She now works in a Corporation office and is even able to take her turn at fire watching. She refuses to attend the Out-patient Clinic.

CASE 2 (Monica G. C—).—During the three months following discharge she became more talkative, quicker on the uptake, and able to look after herself. Three months later she was well enough to be able to look for employment. She put on weight, and from the description seems to be myxoedematous. This information has been supplied by her mother.

CASE 3 (Eva Rose B—).—She has left hospital and has attended the Out-patient Clinic. There is no trace of the earlier psychotic symptoms at present. The thyroid is less prominent, she has gained 2 st. in weight, there are no tremors and her pulse rate is within normal limits. She is shortly to resume work. The electro-encephalogram, which during the acute stage of her illness was highly abnormal, is now " normal in every respect " (Grey Walter).

It is necessary, therefore, to revise the conclusions suggested in the preceding paper that the termination of the illness of Case 1 and Case 2 was towards dementia. It seems as if in all the cases reported there has been remission of symptoms with a return of almost complete working capacity and a restoration of affective life.

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