

SCHIZOPHRENIA

A SURVEY OF THE PROBLEM WITH  
THE RESULTS OF TREATMENT.

THE S I S

Submitted for the

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by

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INTRODUCTION

The schizophrenic problem is a many-sided one and easily the most outstanding and important of this era. In the field of preventive psychiatry it offers many complexities and difficulties. The fundamental concepts of medical science are inadequate to its full understanding - an inadequacy that may be due to their impersonality.

The study of mental disorders in general is to-day a very complicated one: one may consider exclusively the principles which dominate the study of the organic psychoses, or use the point of view which has thrown so much light on hysteria and the other psychoneuroses or try to correlate both. Symptoms may be considered as defects or anomalies dependent on some structural or toxic damage to the nervous system, or each symptom and syndrome may be regarded as possibly having some significance, and as being part of an attempted adjustment to a life situation. The one attitude does not necessarily exclude but should supplement the other. A symptom may have its origin in certain hereditary structural or toxic factors, while at the same time it may be utilised for adaptive purposes: the severity and duration of the symptom may only be intelligible in the light of the

Hebephrenia is the most definitely age-bound of the four groups. It appears at an early age, often at puberty, and is marked by incoherence in the train of actual situation and of the strivings of the individual, marked emotional disturbance, periods of excitement alternating with periods of tearfulness.

Despite the fact that schizophrenia has been known under one or other name for centuries, the nature of the disorder, even at the descriptive level, remains in no small measure yet to be determined. The progress made in the study of the psychoneuroses stimulated a revival of the study of the functional psychoses, and the stimulus given to this revival by the formulations of Adolf Meyer and of Jung on the schizophrenic group has done much to direct the work of the last two decades.

The technical difficulties in the accurate analysis of material are considerable and while the main principles were clearly outlined twenty years ago, the schizophrenic group of psychoses is by no means easy to delimit, and there is no general consensus of opinion as to the exact criteria which entitle a case to be included in this group. It has been divided into four sub-groups by Kraepelin (1), (1) simple, (2) hebephrenic, (3) catatonic, (4) paranoidal.

The simple type consists essentially of a slow, undramatic withdrawal from close contact with reality. Kraepelin (2) describes an "impoverishment and devastation of the whole psychic life". The patient gradually reaches a level at which he can no longer act as a functioning social unit.

Hepephrenia is the most definitely age-bound of the four groups. It appears at an early age, often at puberty, and is marked by "incoherence in the train of thought, marked emotional disturbance, periods of wild excitement alternating with periods of tearfulness and depression and, frequently, illusions and hallucinations". (3)

The catatonic sub-group is the most obvious and dramatic of all, and is characterised by the presence of catatonic stupor, perseveration, mannerisms, negativism and sudden outbursts of apparently causeless excitement, often with suicidal impulses.

In the paranoid type there is much less "devastation". The personality is maintained to a greater, sometimes a considerable degree. A delusional system is evolved, of a fantastic widespread nature, which may be persecutory, depressive or grandiose. The age-incidence is commonly later than in the other types.

All four groups show the general symptomatology of schizophrenia, but the question is still open as to which of the deviations are essentially characteristic of the psychosis. In the picture as presented by the patient we have to deal with pathologic phenomena of several different categories, for the abnormalities may comprise the effects of heredity, home influences, bad hygiene, environment and training. The need, therefore, remains for an adequate definition of the psychosis, a definition

which should delimit it from other disorders, broad enough to include all of the subvarieties and which should include none but characteristic attributes.

The position is put in a less rigid way by Bleuler (4), "schizophrenia does not appear to us as a disease in the narrower sense, but as a disease group, about analogous with the group of organic dementias - one should, therefore, really speak of schizophrenia in the plural.

According to Kraepelin, who has done much in recent years to define the condition, the characteristic features are weakening of those emotional activities which permanently form the mainsprings of volition, so that the essence of the personality becomes destroyed. There is a loss of the inner unity of the activities of intellect, emotion and volition in themselves and among one another". This weakening, I believe to be due primarily to an inborn instability, (94.8 per cent. of my cases were "highly strung" in childhood), plus the later influence of environmental and other extraneous factors.

Therefore the deterioration in schizophrenia is dependent on the emotional and volitional factors,

the defect in memory being only secondary to a primary defect of attention and interest, whereas in the dementia of general paresis and chronic senility, there is an inability to retain and elaborate impressions.

The term "schizophrenia" is now used, rather than the alternative "dementia praecox", for schizophrenia in its sense of "mind split" is more aptly descriptive of the condition.

Stoddart states "the aim of the malady appears to be to retreat from the world of reality". Under stress and strain human nature, even when adequately equipped by heredity, can go very far in the way of deviation from rational thought and action in an evasive, imaginative and regressive direction with no definite evidence of any primary structural damage or intoxication. In many cases regarded as normal, the disturbance of conduct and utterances is so profound that some take for granted that there must be some definite break and some irreparable damage to allow of such degradation of human behaviour, and yet one may see the return from such a condition to complete previous normality with no indication of anything having been permanently lost.

attention The human mind is among the functions of the organism to which is intrinsically bound the conception of progress. According to Soury (5), "Life is only a dynamism of which intelligence is merely the subjective side". Intelligence is the consciousness of life and is manifested through the wonderful mechanism of the nervous system. Just as no movement is co-ordinated and rational and capable of attaining a preconceived end, so no thought expresses a purpose, no mentalisation is the reflex of external circumstances. Man is controlled by two things, heredity and environment. The entire being, with the relations, from the most elementary movement to the most complex conception of which the individual is capable, is unstable and sometimes dispersed in a series of useless and valueless products which have all the same significance - the temporary liquefaction of the nervous system in its two fold and correlative manifestation of somatic and psychic functions.

In schizophrenia every aspect of the patient's life must be given its due share of consideration, for mere enumeration of traits is a method of research of strictly limited utility. In addition to an evaluation of various methods of treatment, before arriving at any conclusions, I obtained a life history of each patient in as great details as possible. Special

## II. HISTORICAL OUTLINE.

attention was given to the parents - their attitude towards one another and towards the child - for I consider the former relationship of equal importance with the latter. Environment, school life, friendships, habits, and hygiene are other points of much importance. According to Pavlov, "the brain itself is a product of heredity alone. Without mechanical aids no brain can develop. The mechanical aids thereto develop through environment, stimulating in turn the growth of mental power".

These cases, and called them "idiocy", and Esquirol used the term "accidental or acquired idiocy" (*Des Maladies Mentales*). Later, however, idiocy became limited to early and congenital defects, while dementia was confined to acquired deteriorations and these non-organised deteriorations began to be divided into partial and total insanities, into which were incorporated mania, melancholia and confusion. About the middle of the nineteenth century Morel first used the term "démence précoce" and described it as "stupidité", making of his concept the picture of a familial degeneration. Later came the use of the term "démence" or total insanity, first used by Lavergne and Gullen. Under this heading were included mania, melancholia, confusion, paranoia and dementia, to which were later added neurasthenia as a psychomotor disorder, the term being used as descriptive of a fatigue syndrome.

## II. HISTORICAL OUTLINE.

The evolution of the conception of dementia praecox as a definite disease with characteristic features has been a gradual one and it has been said with truth that "the history of dementia praecox is really that of psychiatry as a whole". (6)

In 1674, the dementia type of deterioration was described by Willis (*De Amina Brutorum*), who recognised a progressive descent into hebetude dating from adolescence. Pinel described similar cases, and called them "idiotism", and Esquirol used the term "accidental or acquired idiocy" (*Des Maladies Mentales*). Later, however, idiocy became limited to early and congenital defects, while dementia was confined to acquired deteriorations and these non-organised deteriorations began to be divided into partial and total insanities, into which were incorporated mania, melancholia and confusion. About the middle of the nineteenth century Morel first used the term "démence précoce" and described in it a "stupidité", making of his concept the picture of a familial degeneracy. Later came the use of the term "vesania" or total insanity, first used by Lavages and Cullen. Under this heading were included mania, melancholia, confusion a paranoia and dementia, to which were later added neurasthenia as a prodromal symptom, the term being used as descriptive of a fatigue syndrome.

Magnan (7) at this time described a "délire chronique à évolution systématique" which was the equivalent of a paranoid type of dementia praecox.

In 1863, Kahlbaum made a considerable advance along the lines formulated by Morel, having in mind unity of cause, course and outcome in cases of this disease. He attempted a much more complete attitude to the patient in which there were both comprehensive-ness and comprehension. In his conception, the general clinical findings of whatever kind were given equal value with the psychic symptoms, and here we find the first frank attempt to regard the patient's illness as a dysfunction of a psychobiological unit - that is to say, a disorder of the entire organism. He described four groups of disorder:

1. Vesania, equivalent to dementia praecox, but including in it a progress of the type already mentioned.
2. Vecudias (wrong-heartedness), the affective psychoses of the manic depressive type.
3. The dysphrenias, equal to our toxic ex-haustive reactions.
4. The paraphrenias, psychoses determined by age: neophrenia in infancy, hebephrenia in youth; presbyophrenia in old age.

This classification was criticised as being impossible to square with chemical evidence.

Hecker described as hebephrenia one of Kahlbaum's paraphrenias, the age-bound disorder. At about the same time Kahlbaum described katatonia as a

Vesania similar to paresis with motor symptoms.

Therefore, in this way, the grouping that he had set up was rendered less firm. had been brought forward.

Thereafter, there occurred what Meyer calls a "paranoification of psychiatry" by Westphal, Krafft-Ebing and Seliute, during which paranoias of various types came to occupy the place of dementia praecox. This was in response to a psychology of emotion, which tended to create a separation between affective and intellectual disorder. The manic-depressive group was included in the affective series, and under the paranoias were included part of the older vesania with paranoia as a primary state. At the same time, in America, Spitzka, Hammond and Pick began to describe a progressive primary dementia, and about this time also began Kraepelin's work in this connection.

In 1893, he described dementia praecox as synonymous with hebephrenia (Hecker), and also included katatonia and dementia paranoides, while in a review of Ziehen's work, which was full of a series of paranoias, he grouped all primary and secondary dementias in a progressive deteriorative dementing process. Thus dementia praecox made its début at the hands of Kraepelin in 1898 as a result, to some extent, of the work of Morel, Kahlbaum and Hecker. The aim of Kraepelin, as of the others, was to show a uniformity of cause, course and outcome. At the time the description

met practically none of these requirements, but at any rate a definite concept had been brought forward.

While up to this point the object had been to secure a disease entity, from now on attention began to be directed to attempting an understanding of the condition. In 1896, Meyer, working at the Worcester Hospital, developed a general analytic-synthetic principle, which was gradually expanded into "a conception of dementia praecox as depending on a special personality and constitution, on habit disorganization: leaving the internal working and development of the functional and structural deficit as possibly incidental, still to be worked out."

Among the first to traverse the "royal road to knowledge of the unconscious" (Freud) among schizophrenic patients was Jung (8) in 1907. He developed the determination of symptoms by complexes and hinted at special personality types, demonstrating also that the products of schizophrenic thought activity are akin to normal dream activities. In 1911, Bleuler endorsed this opinion. Since then a number of excellent contributions have appeared to substantiate the view that schizophrenic thought processes are primitive processes. Among them are the works of Freud (Totem and Taboo), of Jung (Wandlungen und Symbole der Libido), of Schilder (Wahn und Erkenntnis), of Storch (The Primitive and

Archaic Forms of Inner Experiences and Thought in Schizophrenia). About this time many contributions from various points of view were made. Stransky developed the conception of an "intra psychic ataxia" as an explanation of the affect disharmony, and in 1914 Berze suggested a primary insufficiency of mental activity - another way of stating the case for a constitutional defect. Previous to this, however, Freud had described a case of hallucinatory paranoia, and in 1912, he published a paranoia study. His dynamic attitude was followed by Kempf, who, in 1920, introduced a classification based not so much on formal grouping as on the astrological process, problems of repression, regression to more primitive thought processes, and fixation. In Germany, during the period of Kempf's work, investigation was being carried out along unimaginative and almost purely descriptive lines, but, at the same time, Kretschmer took up, in a new and stimulating way, the constitutional factor; and Kahn developed the heredity factor to the point of postulating two inheritable factors: first, a disposition to the disease, and second, the actual progressive process. Among the other lines of investigation pursued at this time were the Abderhalden tests, Mott's

on gonadal influences, Von Monakow's suggestions as to lesions of the choroid plexus, and the work of Bruce and Cotton on focal sepsis as an aetiological factor.

At the same time, advances were being made along other lines by Meyer and Kirby in America and by Hoch in Germany. The lines of discussion and theory pursued by these workers led to the recognition of schizophrenia as a condition in which the aetiology was, if not uniform in quality or quantity, yet constant in its method of activity, so that it produced a group of recognisably similar cases. Now began to be formulated the principle of mental illness as a definite purposive reaction to stresses of a very varying nature. To some extent Kahlbaum had hinted at this and the principle was accepted by Kraepelin.

Turning from the various psychological conceptions of the disease, reference may be made to its pathology.

The subject of endocrinology has been from time to time in the foreground of science and also has suffered an alternating lack of attention and even disrepute.

Some older theories of medicine, among them Galen's "humoral" theory, might be considered in some respects to be the forerunners of present-day theory. Galen, without any knowledge of the circulation of the

blood and lymph, regarded a faulty mixing, proportion of the four juices (gall, phlegm, blood and pancreatic juice) of the body as the cause of disease. In his work of extending and confirming this theory, Theophile de Borden, in 1775, was probably the first to clearly formulate a general theory of internal secretions, in many respects very similar to the theory as now understood. In 1801, Legallois suggested that the blood undergoes a change as a result of acquiring substances from the organs through which it passes. A. R. Berthold, in 1849, furnished experimental evidence of the production of substances in the internal secreting tissues which exerted profound effects on the animal by his experiments and observations in grafting and transplanting the testis of cocks. Berthold was perhaps the first to furnish actual experimental data, correctly interpreted, demonstrating the internal secretions, for he showed that, even after severance of all the nerves to the gonads, the sex impulse was not destroyed.

In 1855, Claude Bernard coined the words "internal secretion" as distinguished from external secretion. He regarded glycogen as the internal secretion of the liver and definitely showed the synthetic capacity of the body cells to produce new compounds. Now, it is convenient to restrict the term to secretions containing specific organic substances such as the active chemical agents which are produced

by certain ductless glands.

In 1856, the first work by M. Schiff of thyroid-ectomy in animals was performed and suggested internal secretion effects.

In 1873, Gull of London described hypothyroidism and hyperthyroidism. Ord, in his study in 1878, gave the name myxoedema to conditions which were accompanied by deposits of mucin in the subcutaneous tissue and which were associated with thyroid gland deficiency. The condition was being investigated in France at the time by Morran and by Charcot.

In 1882, J. Reverdin showed that the affection described by Gull in adults and by Bourneville in children could occur in either case after a thyroid-ectomy for goître. This was a very important discovery which led to the pathogenic treatment of the myxoedema - thyroid organo-therapy. In 1886, Moebius attributed exophthalmic goitre to hyperthyroidism.

The actual beginning of the subject is almost universally considered to be June 1st, 1889, the date of the famous lecture of Brown-Séquard before the Société de Biologie of Paris, when he announced the results of the injection of testicular extracts in his own person. He maintained that the internal secretion of the testicle keeps up physical and sexual strength. When these decrease under the influence of age or disease they can be stimulated by means of injections of the extracts. These ideas had an immediate application - the intro-

-duction of testicular extract in therapeutics and an enormous variety of conditions were treated by this medication. The results, however, did not come up to expectations and the theory of Brown-Séguard as regards the testicular extract was abandoned.

In 1886, Pierre Marie described the disease now known as Acromegaly, and, four years afterwards, his pupil, Louza-Leite, showed that it had some relation to disturbances of the pituitary.

The syndrome known as "dystrophis-adiposo-genitalis" was first described by Babinski in 1900, then by Frölich in 1901. It is found either in infancy or in the adult, sometimes even at the menopause.

The pineal gland was described by Testut as a "degenerated gland with only rudimentary functions or none at all", mentioning that Descarte considered the gland to be the centre of the soul, while Magendie believed that it regulated the circulation of C. S. F. It was first studied in 1908 in the investigation of tumours of the pineal gland by Marburg and by Frankl-Hochwart. Observations by French writers are still more numerous: those of Raymond and Claude, Apert and Porak being the most important.

The labours of Pighini (9) and others of the Italian school failed to discover any single fact in the metabolism that was directly characteristic of dementia praecox and allied psychoses. In 1914,

Cuneo, (10) an Italian observer, claimed that by diminishing or increasing the protein fraction of the diet he was able to produce either a calm or an excited phase in a schizophrenic patient.

From time to time various workers in mental disease have formulated ideas regarding the connection of the glands of internal secretion with the different types of psychosis, and literature contains many references to the changes of the endocrine glands in schizophrenia.

Kraepelin (11) in 1881 first called attention to the relation of this disease to the endocrines, especially to the sex glands.

Dercum (12) states that in schizophrenia the various glands of internal secretion have suffered in the course of development of the organism so that their respective functions are subsequently imperfectly and aberrantly performed. He believes that it is not at all unlikely that, while a number of glands, perhaps the entire chain, are involved in most cases, e.g. the gonads may dominate the picture, in others again it is the thymus, in still others it is the system of the pituitary, thyroid and adrenals. He regards the thymus as most likely to be involved, because cases of schizophrenia frequently betray in childhood the forerunners of the affection.

From an histological study of two cases Kojima (13) concludes that the thyroids have an opposite appearance in the male and female; a tendency

to hypofunction in the male and hyperfunction in the female. He states that in schizophrenia the glands on the whole are small, especially in the female. In the male, the parathyroids contain watery, clear cells and a few eosinophile cells, and in the female, on the contrary, many eosinophile cells. The sexual glands and adrenals are small in the female. Striking changes are seen in the sexual glands, i.e. very slight spermatogenesis in the testis and an appearance of early involution of the ovaries. Frankel (14) found the infantile type of genitalia in 72% of 176 cases of schizophrenic cases examined. Mott (15) showed pathological changes in the testis and semen, defective maturation of the primordial follicles, degeneration of the nucleus and proliferation of the stroma so that he believed that schizophrenia results from deficient productive energy of the generative organs based on congenital insufficiency of the gonads. He found a primary regressive atrophy in 27 cases of schizophrenia in which the testes were examined. Pézard (16) states that apparently the testes in the schizophrenic cease growing about the age of puberty or soon after, thus allowing sufficient time in most cases for secondary sexual characteristics to develop, although these are always fully determined. Morse (17) studied 12 male and 15 female schizophrenics dying under 45 years of age and concluded that 16

patients had active gonads. She used as criteria the presence of spermatogenesis and maturing follicles and corpora lutea. She stated that there was no correlation between atrophy of the sex glands and the duration of the mental disease or the degree of psychic deterioration. The conditions in the sex glands of the controls were essentially the same as in the schizophrenic cases for the same terminal diseases. The pituitaries in nearly half the cases showed a fibrosis which could be correlated to some extent with a similar condition in the gonads. This fibrosis of the pituitary is not peculiar to schizophrenia but depends rather on the nature and duration of the terminal disease. She stated that the lesions in the adrenals were such as are usually found in the diseases to which the patients succumbed. The thyroid showed changes less frequently than the other endocrines. There was occasionally a mild glandular hyperplasia or increase of connective tissue. From the pathological side Morse feels that there is very little evidence of primary atrophy of the gonads in schizophrenia with the possible exception of those cases developing on a basis of mental defect.

Matsumoto (18) in a study of the relation between the reproductive organs and schizophrenia, and Lewis (19) after a careful review of the autopsies of 143 cases of this disease as compared to 458 other autopsies, concludes that gonadal atrophy is more

commonly found in schizophrenic cases than in other individuals. Further, that in these cases, the adrenal cortex as a whole is thinned out and pale in colour. The zona glomerulosa is rudimentary and sclerotic and the zona fasciculata shows acinal and cellular alterations.

Geller (20) attempted to show the close relations between the body and psyche in schizophrenia on the basis of sexual function. He found considerable anatomic and functional hypogonitalism in 7 of 8 cases of schizophrenia in women, and agrees with Mott, Fraenkel, Hanck and Kohler that the disorder is intimately associated with deficient genital function. Serologic tests in these cases were formed by Geller to show destruction of the brain, testis, ovary and often also of the thyroid substrates, more frequently than in other psychoses. In 26 women, his most important finding was that, at the age of sexual maturity, the genital organs were hypoplastic. Therefore, he feels justified in assuming a connection between inferior ovarian function and schizophrenia.

According to Sippel (21) a more or less pronounced hypoplasia and hypofunction of the sex glands is found in a considerable percentage of schizophrenic cases. In a few cases he tried transplantation of ovaries in treatment of schizophrenia. In one case he obtained no results. Three subjects improved to a

surprising extent.

Tsubura (22) in 1923 reported that individuals without gonads showed a lowered tolerance for sugar and that if these individuals were given subcutaneous injections of either adrenalin or pituitrin, a marked hyperglycemia followed. He also found that if gonads were transplanted into these individuals, the above conditions were eliminated. Walker (23) states that the pituitary and adrenals are most important in the determination of the sex characteristics, and that the interstitial cells of the gonads are trophic rather than secretory. The following year (1925) Korenshevsky (24) reported that 60% of castrated individuals became obese, while the remaining 40% are usually thin. He found that in these cases the nitrogen metabolism is decreased. Lipschütz (25) states that the morphological and physiological changes which follow absence or deficiency of the gonads vary according to the age at which the deficit arose. He found that the thyroid of the hypogonad subject was usually small, and that the hypophysis was larger and heavier than in normal individuals.

In order to prove whether the ovaries play a part in schizophrenia, Pötzl and Wagner (26) removed the adnexa in two cases of long standing. Fibrosis such as described by Fraenkel in the testis of male schizophrenics was formed in the ovaries. Hypothetically, a delay in the retrogression of the corpora

lutea may be assumed as a manifestation of injury to the genital glands in female schizophrenics, they state, which is to a certain extent comparable to a pregnancy action. They had no favourable results from castration combined with homeoplastic ovarian grafts in schizophrenic women. They attribute the menstrual aggravation to increased permeability of the meninges during these periods.

Gibbs (27) found that some disturbance of lipid metabolism may occur in schizophrenia and may involve the suprarenal cortex as suggested by the following:

- (a) Previous observations on the sexual development and behaviour of these patients.
- (b) The evidence that the suprarenal cortex is involved in these disturbances of sexual development.
- (c) The evidence that the suprarenal has both an embryologic and functional relation to the gonads on the one hand and to the brain on the other.
- (d) Substances of a lipid nature play an essential part in the functional metabolism of each of these organs.
- (e) The female sex hormone and the vitamine for reproduction are both of a lipid nature.
- (f) The low basal metabolism rate frequently observed in schizophrenia suggests an involvement of the suprarenals.

He also found that in many patients with schizophrenia the blood cholesterol was unusually low, and may be more directly correlated with the psychosis and with sex than with any other recognised factor.

Münzer described in detail the case of

a man of 25 years who quite suddenly developed a schizophrenic state with delusions, chiefly in the sexual sphere, and after three months committed suicide. The chief gross post mortem changes consisted of the thymus which weighed 50 grams and showed marked increase in the number and size of Hassall's corpuscles: enlargement of the spleen and of the lymph follicles of the tongue and small intestines. The testis weighed 32 grams and showed marked atrophy and degeneration and abundant Lubarsch-Charcot crystals. The adrenals weighed 17 grams with rather hypertrophic cortex and persistent undifferentiated cells of the zona glomerulosa of the cortex. There was reduction of the islands of the pancreas, and the thyroid presented a polymorphic picture with good evidence of function, even hyperfunction, but also degenerated foci resembling terose seen in idiots and cretins. One of the parathyroids lay within the thyroid, there was diminution of eosinophile cells and on the whole, these glands had preserved the characters seen in children. There was an apparent increase in the eosinophilic cells in the hypophysis and an adenoma like formation. Münzer maintains that abnormalities of the endocrines are constant in this psychosis.

One of the most complete studies is by Langfeldt (29) who reports a detailed clinical examination

of 40 unquestionable cases of schizophrenia. He used every known diagnostic test of any value. His cases fell into three groups: 16 catatonic, 11 hebephrenic, and 13 mixed. In the catatonic group he found the following essential disturbances present, in both the acute and the quiescent cases:- slow pulse, low blood pressure, lymphocytosis, glandular swelling, positive pilocarpin test, positive Aschner reflex (vagatonic disposition), and reduced basal metabolism. In the acute cases he noted also certain sympathicus signs such as dilated pupils, tachycardia, exophthalmos and reduced glucose tolerance. In the hebephrenic cases, in the acute as well as in the chronic phases, only sympathicus symptoms were found: tachycardia, exophthalmos, tumor, dilated pupils and reduced glucose tolerance. These symptoms were, however, found most pronounced in the acute phases. In the schizophrenics he also found large firm testes. Finally it may be of interest to mention the findings of James L. MacCarthy, who in China in 1925 - 27 examined twenty Chinese eunuchs abandoned after the dissolution of the Imperial Court in Peking, and three Skopees driven from Russia and taking refuge in China. The former type of eunuchs have been known in China as long as history and were used as servants in the Imperial Palace. Many of these were castrated in youth and were completely deprived of external genitals (30).

The Skopees were castrated because of their religious teachings, and it is said that there were at least 150,000 members of this sect before the intolerance of the Soviet scattered them out of Siberia. This sect has been in existence since 1757, and many of the subjects were castrated in childhood. Two of the Skopees examined had their external genitals completely removed, while the third had only been castrated. All of the twenty-three eunuchs examined showed certain general characteristics: 15 tended to be obese, and 8 were emaciated, probably due to starvation. The larynx was infantile. The extremities were proportionately larger than normal. In all cases it was found that the body height: leg length ratio was 1.75, whereas in an equal number of normal individuals it was 2.0. The pelvis was juvenile. There was an acrocyanosis and the nails were spotted. Several showed a rather general cyanosis of the body, while the remainder were very pale. The skin was clammy, rather puffy, doughy and creased. The subcutaneous fat in the gluteal region, under the breasts, in the trochanters, abdominal wall and especially under the mons veneris was more abundant than in normal men. The middle of the upper lip, the submental skin, the cheeks and the upper part of the neck were hairless. The perineum, axillae and extremities did not have the abundant hair that is commonly found in the normal male. The pubic hair

line was horizontal, or, in two or three of the individuals, concave. s of what is considered "dementia praecox".

Psychologically, these individuals were found to all have good intelligence, were all orientated, but had been living a hand to mouth existence since they had been thrown on their own resources. They all appeared very introspective and apathetic. Although they could talk quite intelligently when questioned, they never volunteered any information and appeared very stupid. They seemed methodical in their actions and only two showed any purposeful efforts. There was a distinct lack of affect: they were cold and passive, although in dire straits financially. At least half of the eunuchs had got into trouble because of their tempers and two had been sentenced because of murder. They all appeared moody. Most of the eunuchs who still retained the penis stated that they had often indulged in sexual intercourse with prostitutes although they had found that their erections were always of short duration. They all said that they indulged in homosexual practices and other perversions. Ten of them had had gonorrhoea and one of them had an active chancre. No blood examinations or basal metabolism tests could be made on these subjects, but Shen and Lin (31) have reported the nitrogen metabolism of eunuchs examined by them and it conforms to the general picture. The ex-

## III. NATURE OF THE DISORDER.

-amination of these eunuchs showed them to be almost typical prototypes of what is considered "dementia praecox".

of the personality developing during the period of adolescence or maturity. It occurs in individuals of defective organization who break down under ordinary strains and stresses. A great number of them have shown for years before the break, clear signs of coming trouble, many of them being brought to notice by the occurrence of behaviour of a simple psychoneurotic character. Attempts at hysterical incapacitations not only precede many psychoses, but actually make up much of the psychotic picture in some cases. Reactions by obsessive substitutions are seen in some to have preceded for years definite schizophrenic phenomena, and the gradations from the neurasthenic picture into schizophrenia might be easy to observe, were it possible to attend to the mental state of quasi-normal adolescents. Our difficulty is that we see too many end states and too few of the prepsychotic.

Jung believes that fundamental to the disorder in each case is a lack of nervous energy leading to a feeling of inadequacy and a consequent flight from reality. It can develop in a relatively strong person as a result of overwhelming difficulties and in a weak person from relatively trivial difficulties. The chief

III. NATURE OF THE CONDITION.

Schizophrenia is regarded as a disorganisation of the personality developing during the period of adolescence or maturity. It occurs in individuals of defective organisation who break down under ordinary strains and stresses. A great number of them have shown for years before the break, clear signs of coming trouble, many of them being brought to notice by the occurrence of behaviour of a simple psychoneurotic character. Attempts at hysterical incapacitations not only precede many psychoses, but actually make up much of the psychotic picture in some cases. Reactions by obsessive substitutions are seen in some to have preceded for years definite schizophrenic phenomena, and the gradations from the neurasthenic picture into schizophrenia might be easy to observe, were it possible to attend to the mental state of quasi-normal adolescents. Our difficulty is that we see too many end states and too few of the prepsychotic.

Janet believes that fundamental to the disorder in each case is a lack of nervous energy leading to a feeling of inadequacy and a consequent flight from reality. It can develop in a relatively strong person as a result of overwhelming difficulties and in a weak person from relatively trivial difficulties. The chief

significant changes observed in their scholastic factor in determining the occurrence seems to be a constitutional object.

The debate whether the disorder is of organic or psychogenic origin is on a par with a discussion whether tuberculosis is due to the presence of tubercle bacilli or the susceptibility of the patient. It disregards the nature of causality. Most schizophrenics have shewn evidences enough to excite even lay curiosity during more or less extended periods before mental disease was diagnosed.

In many young people there are periods of apathy, a tendency to seclusiveness, negativism, tricks or mannerisms, which for the most part are outgrown. If, however, these persist and are accentuated, it becomes evident that there is a real disorder. Although the patients who suffer from schizophrenia are of a neuropathic type, and many, as a rule, exhibit definite stigmata of degeneration, it is by no means the case that they have been of defective intelligence. At school, many cultivate their studies carefully and books are their closest companions. They may be described as juvenile recluses; their judgment is warped and at certain stages they prefer to be by themselves. They are not gregarious and do not keep pace with children of their own age at games and other forms of amusement. The 'shut in' type of personality is stated to prevail from early childhood in the majority.

Significant changes may be observed in their scholastic conduct at puberty. They may progressively fail in interest after exhibiting intelligence and become unwilling to apply themselves. They turn into day dreamers. Their unstable nervous organisation may have flared up with comparative brilliance during their schooldays with the result that an endeavour may have been made by teachers and others to spur them on to further efforts, little realising that their bolt has been shot, so that instead of progress there is retrogression. Not all, however, are equally endowed intellectually, for all grades of intelligence from feeble-minded to genius are found among them. They have, however, one factor in common - the asocial character. Among the outstanding symptoms a generalised restriction of interests from environmental situations appears with much regularity. The result is they have no outlet for their instinctive cravings, therefore conflicts ensue, and symptoms of morbid significance are felt which may not be recognised by those in contact with them for months, for they do not appear in the outward behaviour. The primary changes are for the most part emotional. Kraepelin (32) said that in schizophrenia "the connection between thinking, feeling, deliberation, emotional activity and practical work is lost". The patient loses the interests that formerly sustained him and becomes more passive towards affairs

in general. There is therefore a diminution of the effective response, emotion being lacking and introversion occurs. This inadequacy is not demonstrable in the intellectual field but expresses itself in an inability to react as the normal well-balanced personality does to the difficulties encountered during the course of educational, economic, sexual, emotional, domestic or social life of the individual. The inadequate personality may evince itself in any of these spheres. Psychologically it is the reaction of an inadequate personality to the difficulties of his environment. A splitting of the psychic life occurs with a failure of psychic synthesis and a loss of the inner unity of the activities of intellect, feeling and volition. The clinical picture in the beginning is generally free from the abnormal manifestations characteristic of the more advanced stages. The original causes of conflicts in the incipient phases are thinly disguised. The highly symbolic expressions of the advanced stages have not yet been formed. The early schizophrenic does not focus her difficulties. She spreads them over the entire environment and for a considerable time the patient's libido is often without any object. Stages, however, are by no means sharply defined. Psychotic manifestations may stop at any point and the patient may afterwards adjust his existence to the level at which he stopped. If he continues to regress to the infantile level, emotional

without any definite organic basis - the reaction of an

responses are correspondingly reduced and a state of emotional apathy results. Macdougall interprets schizophrenia as a disturbance of the sentiment of self-regard; self-regard being built of the sentiments of self-assertion and self-submission. In schizophrenia these two component parts do not function smoothly but remain in rigid balance and lead to an embarrassment resulting in no effective action or expression. The sentiment of self-regard cannot dominate the psychological system because the various parts of the system function in relative independence and are apt to come perpetually into conflict with one another. Therefore, there is a loss of emotional and effective contact with society and emotions do not correspond to ideas. Freud, on the other hand, believes there is fixation at the first oral stage and that the symptoms are an attempt at self-cure.

Stransky emphasises the lack of co-ordination between the neopsychic (intellectual, receptive) and the thymopsychic (affective) functions of mentation. This lack of co-ordination results in intra-psychic ataxia. "The allopsychic resonance (relationship to the external world) becomes obliterated before the autopsychic." (Kretschmer).

Schizophrenia is therefore characterised by inco-ordination of the mental mechanisms and is associated sooner or later with intellectual deterioration without any definite organic basis - the reaction of an

inadequate personality to the difficulties of his environment. The defence reactions, infinitely diverse in their combinations, individual goals and explanatory rationalisation, these are the processes of maladjustment which can be seen to form a gradient from mere poses and trifling evasion of the obvious to the essential schizophrenia. They all show themselves to be the unwitting evasions and distortions of simple experience, means by which the organism interposes something artificial and relatively abstract in the complex of the individual and his environment. The barrier sub-variety of defence reactions, especially, are of a piece with schizophrenia. It is never easy to say just when the schizophrenic patient has crossed the line into actual psychosis. Psychopathic maladjustment is a product of the pre-adolescent phase of personality development; the adolescent upheaval in these individuals includes destructive phenomena of distinctive character.

Bleuler (33) considered the development of the secondary signs on the structure of the primary lesions as due to normal environmental initiations and to normal psychologic and physiologic mechanisms. This conception of schizophrenia may be compared with the general conception of medical disease, e.g. in rickets the lack of calcification and changes in blood chemistry represent primary signs and the various deformities due to mechanical influences on the tender bones represent secondary signs.

Professor Adolf Meyer (34) stated that all mental reactions are to be regarded as a particular type of biological reaction, their characteristic being found in their occurrence within a system of symbolization. In normal thinking one has to choose constantly from among an immense number of possible associations that have been created by custom, similarity or causality. This selection is guided by a goal idea, which is loaded with affectivity, or rather, it is guided by a multiplicity of these goal ideas. In schizophrenic thinking the associations no longer seem to follow the same principles as in normal thinking. They are no longer connected by a final aim and suddenly and without apparent reason they deviate from the direction which in a normal person is given precedence by the topic and aim of the central thoughts. They are apt suddenly to leave the primary topic and to wander off in hidden pathways. Disorders of association are present in nearly all cases of schizophrenia, but they differ greatly in degree. The degree varies not only from patient to patient, but in the same patient from day to day, from hour to hour and from topic to topic. Disorders in affectivity are also among the primary signs in schizophrenia. Bleuler believes that associative and affective disorders are identical but seen from different angles. He regards indifference

Not only is reality split off but the patients'

to environment and lack of affective modulation as not due to a primary destruction of all feeling, for in most he finds at all times the evidence of strong, natural and well modulated feelings, even in chronic and demented cases. A special kind of splitting of the feelings is much more general and characteristic and finds its clearest expression in ambivalence. Complexes of feelings can be split off so far that they seem strange to the patient and he can no longer recognise them as part of his own personality. Therefore, it is a frequent complaint of the schizophrenic patient that someone else feels or thinks in him, that someone else takes possession of his tongue to speak with it or of his face to laugh with it.

This splitting off of complexes of feelings is regarded as the basis of the voices that are the most common kind of hallucination in schizophrenia. In the explanation of the secondary signs such as autism, delusions, delusions of memory, illusions of memory, negativism, stereotypic<sup>s</sup>, mannerisms and most of the catatonic signs, Bleuler has utilised the mechanisms that are true also for the secondary elaborations of normal psychology and based on the primary trouble. The root of autism he regards as a tendency to make reality inoffensive - the patient splitting reality off from his consciousness and escaping into imagination.

most probable physiologic cause of schizophrenia is the

Not only is reality split off but the patients fulfil their conscious and unconscious wishes in their secondary signs. This explanation is applicable to phenomena that at first sight seems to contradict it: delusions of persecution, which can be a direct fulfilment of sex wishes, particularly in women, or they may interpret the patient's problems in such a way as to render her innocent and worthy of sympathy. On the other hand, there are certain symptoms which he considers as more or less primary, and in which he is inclined to deny the importance of psychogenic roots. Among them are certain kinds of stupor and confusion, which give the impression of being organic. There are also certain forms of hallucinations which seem to have a more direct organic basis, especially the auditory hallucinations of simple sounds and some somatic hallucinations which seem to represent a more direct expression of an organic schizophrenic process.

Janet was the first to draw the parallel between dreams and schizophrenia - that if a man can walk and talk in his dreams his total behaviour would be in no way different from that of a patient with schizophrenia. Although sleep and schizophrenia are not identical, they have many points in common. This view has found expression in Pavlov's (35) paper on "The Excursion of a Physiologist into the Field of Psychiatry," in which he stated the belief that the most probable physiologic cause of schizophrenia is the

overdevelopment of the process of inner inhibitions which are also overdeveloped in hypnosis and sleep.

Kempf (36) questions whether there is such a thing as inherited predisposition and takes the view that peculiarities in the child are more likely caused by an unconscious imitation of the peculiarities in the parent or the moulding of the child by the parent, that emotional stresses are just as infective and harm producing as bacteria and that they may produce even grave physical lesions has been demonstrated by Pavlov and Cannon.

In everyday life the schizoid is a person who preserves his independence to the environment; he endeavours to withdraw from its influences and to follow out his own aims. In the pathological state such behaviour assumes active, hostile or passively dereistic attitudes. In the milder forms it leads to a turning away from reality or to an active transformation of it for his own aims, or to an adaptation to reality through inventions, thus changing it in some ways for his own ends.

Insidious temperamental changes, especially apathy and indifference in adolescents and young adults, hallucinations and delusions which may be at variance with the emotional tone, accesses of mental confusion, a tendency to automatic reactions, all these are

important from the diagnostic point of view, especially if a family history of mental disorder or "nervousness" is obtainable.

The purpose of inner inhibitions, including sleep, consists in cessation of contacts with the outside world. Therefore, autism, withdrawal and shutting oneself off from reality, are results of a special state of the central nervous system of patients with schizophrenia. The loss of contact with the outside world is not the result of schizophrenia but an expression of the protective forces of the organism reacting with inner inhibitions to the weakness of the central nervous system. All higher psychologic functions, including speech and conceptual thinking, are of social origin, and it is significant that in dreams there is a cessation of contacts with that social self which forms the foundation of the normal personality.

One might centre one's efforts on the analysis of the psychic difficulties and on attempting to remove them or re-educating the patient to conquer them, or on detecting and removing the organic causes of feelings of inadequacy. While this part should be given due consideration and not neglected, this study is based on the assumption that schizophrenia is a reaction to a sense of personal failure, arising primarily from a feeling of inadequacy to meet the issues of life as they actually present. Any

outstanding resemblance between dissociations and "split" seems to be that they both serve the purpose of therapeutic efforts, therefore, should be directed towards restoring the feeling of adequacy.

Further, might not the so-called catatonic stupor of the schizophrenic be at the far end of the Hysterical Dissociations? In hysteria the splitting of the personality quantitatively speaking may be 4 to 1, 3 to 5, 8 to 2 and so on. Might not the stupor of schizophrenia be regarded as an hysteria with a quantitative formula of say 1000 to 1, the 1000 being the split off part, the complete "belle indifférence," and the 1 being the main personality such as it is? Jung has already in 1903 emphasised certain similarities between dementia praecox and hysteria. Since then the concept of dissociation has by numerous authors been used to explain the schizophrenic condition. Macdougal points out that he often has found hysterical traits in cases of dementia praecox, but as he believes that hysteria and schizophrenia are fundamentally different disorders, he speaks of these cases as mixed disorders.

It might be suggested that the obvious hysterical features of the schizophrenic be considered, not as due to a mixture of disorder, but to the fact that the predisposing agent to schizophrenia, the schizoid trait, is the same as the trait that predisposes to hysteria, that consequently the "split" of the dementia praecox patient is allowed for by the same constitutional factor as the dissociation of the hysteric. The most

outstanding resemblance between dissociations and "split" seems to be that they both serve the purpose of relieving mental pain. In cases of repression without dissociation marks are always found of the continued conflict in a continuing distress of some kind of the patient. This is not characteristic of the "split" dementia praecox case; it is found in the period before the reality criterion has become entirely devoid of significance, due to dissociation of the inclination to test reality. When, on the other hand, this inclination is definitely "split off", or dissociated from the self, every route is opened to the patient for wish fulfilment in the fused reality sphere, and no conflict with mental pain exists any longer. What there may occur of suffering after the "split" is not due to inner conflict but to external friction with environment. Reality is here extensively distorted to fit fantasy, its resistance factor is very much lowered, and thus its power of seriously injuring comparatively small. The slow development of the "split", together with numerous other features of the onset of schizophrenia, would indicate that the decline of the reality criterion is due to repression. This is in a large number of hysterical cases also true of the dissociation, particularly when this follows a period of incubation. Any dissociation is the dissociation of a function. The outstanding difference between the simple hysterical diss-

ociations and the dissociation of the dementia praecox patient is that in the later the dissociation involves a thinking, striving disposition that is all important for any well-adjusted higher mental activity, while in the hysteria the dissociation is often of a very simple order - a simple paralysis or a simple amnesia. The hysterical patient before the disorder gets along fairly successfully, in general, with her fellow beings. Then she meets the injury that breaks her, but this injury is only on one front of activity, a part of one, and the dissociation that relieves her is consequently of narrower and more circumscribed reach than in the dementia praecox patient and does not impair her activity on other parts of the field of life. She does not need a total subjective decline of the reality criterion for her protection.

He conceives his physical types as existent among normal and psychotic individuals (10) and emphasizes the relationship of psychoses to the normal temperaments which he describes as primarily schizothymic or cyclothymic. He further describes the asthenic, athletic, dysplastic physical types which he relates to the schizothymic temperament and to schizophrasia, and the cyclic physical type, which he

IV. PHYSICAL DISORDERS AND THEIR RELATIONSHIP  
TO SCHIZOPHRENIA.

1. Abnormal growth of the skeleton.

Kretschmer's emphasis of physical types and his attempt at formulation of a relationship between physical type and psychosis has given new impetus to the study of constitution in relation to mental disorder.

Kretschmer (39) states: "The important idea about a type is that it possesses a firm center but not hard and fast boundaries. Types as a rule can only be determined intrinsically; we cannot mark their boundaries. By 'type' we mean a nucleus of more distinct and among themselves quite firm formations which have been deliberately lifted out from a sea of progressive transitions. This holds good for a racial type as well as a personality or clinical reaction type."

He conceives his physical types as existent among normal and psychotic individuals (40) and emphasises the relationship of physique to the normal temperaments which he describes as primarily schizothymic or cyclothymic. He further describes the asthenic, athletic, dysplastic physical types which he relates to the schizothymic temperament and to schizophrenia, and the pyknic physical type, which he

considers of significance in relation to the cyclothymic temperament and which need not be considered here.

According to Holmgren's (41) studies, the psychic development of the child seems to have a certain relation to the development of the body, and is besides dependent on the economical circumstances. As the development of the body is regulated by the endocrine organs, we may conclude that they are also of importance for the development of the brain. In connection with such physiological influences, Kretschmer's (42) examinations seem to show that certain body structures are connected with certain characters. A number of after examinations of these measurements by Henschel (43), Manz (44), Oliver (45) and Wyrsh (46), have, as far as the conditions in psychoses are concerned, mainly confirmed these. Bleuler (47) and Lioli (48), on the other hand, warn against being too schematic in the classification of normal individuals in fixed, so-called schizoid and cyclothymic, types. Kretschmer based his views upon exact anthropological investigations and the study of psychological types as revealed in the biogenetic psychoses. He found statistical relational frequencies between the asthenic and athletic body builds and the schizophrenic personality. As regards the asthenic type, the essential character-

istic of the type of the male asthenic is taking the general total impression, a deficiency in thickness combined with an average unlesened length. This deficiency in the thickness development is present in all parts of the body - face, neck, trunk, extremities - also in all the tissues - skin, fat, muscle, bone and vascular system. On this account, the average weight, as well as the total circumference and breadth measurements, is found to be below the average. The individual looks taller than he actually is, has narrow shoulders and delicately boned hands, a long, narrow, flat chest, on which the ribs can be counted, with a sharp angle. The lower limbs resemble the upper ones in character.

The athletic type is recognised as having particularly wide projecting shoulders, a well-developed chest and a trunk which tapers in its lowest region, so that the pelvis and the legs sometimes seem almost graceful compared with the size of the upper limbs, and particularly the hypertrophied shoulders. The head, long and solid, is carried upright on a free neck, so that the linear contour of the trapezius looked at from the front gives the part of the shoulder nearest the neck a peculiar shape. The bone relief is specially prominent in the shape of the face. The coarse boning throughout is to be seen especially in the collar-bones, the hand and foot joints and the hands. The extremities in some cases may be reminiscent of acromegaly.

Turning to another 'type' not yet mentioned, it is to be noted that Kretschmer proposes in his classification a 'dysplastic' type, and states there is a clear biological affinity between the psychic disposition of the schizophrenes and the bodily disposition characteristics of the asthenics, athletics and certain dysplastics. Vice versa he finds only a weak affinity between schizophrene and pyknic on the one hand and between asthenics, athletics and dysplastics on the other.

Wertheimer (49) calls attention to the fact that this physical form can hardly be considered in relation to the other physical forms described, the athletic, asthenic and pyknic. These three latter are dependent upon what may be best considered 'normal' variables, while the dysplastic type includes forms recognisable as products of endocrine gland disturbance, or possibly as dependent upon accidental hindrances to the normal developmental process or disease processes. Functional disturbance as well as structural variation is interjected; qualitative rather quantitative distinctions are utilised.

Kretschmer, however, is emphatic in closely relating the dysplastic form to schizophrenia. The characteristics of this class are: the extreme length of the extremities in relation to the height of the body, the obliteration of the sexual characteristics in the proportions of the trunk, so that we find in

the male 'asexual' pelvis, which, to the casual observer, has a tendency to femininity. In ten of his group anomalies of the genitalia were noted: hypoplasia of the testicles, four times; severe hypoplasia, four times; hypoplasia of the genital organ, twice.

As regards the female eunuchoid, Kretschmer refers to seven cases of schizophrenic women in whom the most striking characteristics was a distinct variation in the secondary characteristics from the female type, while certain of them resembled the male eunuchoid, particularly as regards the excessive length of the extremities. He further observes that it would seem idle to collect together all the cases of hypoplasia of the genitalia among schizophrenic women, because such anomalies are so common among them that it would be necessary to include practically the majority of all the female schizophrenics.

Other investigations agree in this, and too, in noting that dysplastic forms are not found among manic depressive patients. The implication of various functional deficiencies or peculiarities among schizophrenic patients has been the subject of much study from many angles of approach. It is important to make a distinction between the results of faulty development and these abnormalities which appear to be the result of acquired dysfunction of

of the endocrines. Naturally the endocrine glands have been most vigorously attacked as offering possibilities for explanation of supposed structural or functional peculiarities specific for schizophrenia. It is therefore of interest to enquire to what extent cases of schizophrenia are of degenerate type as evidenced by poor development, stigmata of degeneration and atavistic signs. Stoddart (50) lays stress on the 'ape hand', which he has found in many instances. He describes this as "long, thin and delicate with flattening of the thenar and hypothenar eminences; the thumb looks more or less forward like the other digits being rotated outwards instead of looking across the palm. If the terminal phalanx of the thumb be flexed, it may be observed that it fails to undergo the normal amount of internal rotation on the proximal phalanx. Another common feature is abnormal laxity of the ligaments of the metacarpo-phalangeal joints so that the fingers can be passively hyperextended, almost to a right angle." As these conditions are also sometimes found in idiocy, especially of the Mongol type, he regards schizophrenia as a "failure in evolution, as an atavism or reversion to an ancestral type". He also finds that the other physical stigmata are common, such as abnormalities of the palate and pinnae. Kraepelin (51), on the other hand, does not lay stress on the frequency of such signs in schizophrenia.

As regards hypoplasia, Kretschmer regards the hypoplastic as being also a dysplastic in whom the growth has been disproportionate, in that the hypoplasia is only found in isolated parts of the body, so that there is a striking disproportion in the measurements of those parts in relation to other better developed, and even hyperplastic, parts of the body. Instances of hypoplasia, to any marked degree, are, according to Kretschmer, often found among schizophrenes. The hypoplasia shows a preference in these cases for the face, and particularly the middle part of the face, the extremities of the limbs, particularly the hands and also the pelvis. The general impression of infantilism is shown by him to be justified when accurate anthropological methods are employed. He points out that by 'infantilism' is meant, not merely smallness of form, but also a modelling of such morphologically separate regions as the lower stomach and the pelvis, which is imitative of the proportions of such regions in childhood, where, not only the size, but also the shape, is typically childish. The term 'infantilism' is especially appropriate where the morphological signs are associated with dysgenital stigmata, which suggest as the cause of the infantile formation a lack of pubertal development in the part of the body in question.

Kretschmer considers that individuals showing

predecessors', who since the days of Hippocrates a tendency to pronounced fatness are in the minority among schizophrenics. While the pyknic fatness only rarely reaches an abnormal and outstanding degree, and even then is confined to certain localities, particularly the cheeks, neck and trunk, among schizophrenics are found types of fatty deposition which may, morphologically, be grouped under eunochoid fat abnormalities, and from which transitional stages may be discriminated to a kind of fatness which cannot yet be clearly delineated, but which is probably of a polyglandular nature. There are found here and there disposition of fat, according to the eunochoid plan, among the schizophrenic men of all groups, with and without the correlative symptoms in the formation of the skeleton. Kretschmer refers to the case of a young hebephrenic, who exhibited, together with an otherwise asthenic physique, an isolated layer of fat round the buttocks, making them stand out and quite obliterating the normal modelling of muscle and bone.

The general results of these studies have but tended to show that like all such similar generalisations there is a nucleus of truth behind the general idea that leptosome (asthenic, athletic, dysplastic) habitus individuals are more often found among those with the schizophrenic reaction type. Kretschmer's study may be said to represent a more detailed and minute series of measurements than his

predecessors', who since the days of Hippocrates have attempted similar generalisations of relations between bodily form and personality traits.

## 2. Pupillary Anomalies.

Much has been written about the condition of the pupils in schizophrenia, Kraepelin stating that their behaviour is of much significance. He found them dilated, especially during the first stages and during excitement, Schüle (52) found frequently dilated pupils, while Schültz (53) and Weiler (54) stated that in cases of schizophrenia, the pupils are larger than in normal cases, without however stating the type or phase of the disease. Weiler explains this as due to an increase caused by the morbid process of that cortical excitement, which reduces the tone of the sphincters. Meyer (55) found permanent dilation only in a fraction of his cases, medium sized frequently and small seldom. Among 238 cases he found mydriasis in 10% and very small in only 3 cases. Knapp (56) found especially in hebephrenia dilated pupils, both constant and variable according to the condition of the mind. Evensen (57) states that both during catatonic excitement and stupor dilated pupils are frequently to be found. In 1906 Bümke (58) described the absence of a triad of pupillary reactions in 60% of patients with schizophrenia in the Freiburger Clinic: "psychic reflex,



pupillary unrest, and reflex dilatation on sensory stimulation". By the psychic reflex, he refers to the pupillary reaction on psychic stimulation (fear, anger, etc.), and by pupillary unrest, the normal oscillation of the iris. He regarded this triad as almost pathognomonic of early schizophrenia, and many subsequent writers have confirmed his observation - Bach (59), Hubner (60), Lioli (61), Wassermeyer (62), Weiler (63) and others. In 1907, Westphal described 'katatonische pupillenstarre' in catatonic stupor: a transient loss of the light and convergence reflexes, sometimes in one eye and then in the other, sometimes in both, as well as changes in the outline of the pupil from oval to round and the reverse. Many subsequent observations have demonstrated temporary loss or slowing of the reaction in many cases. On the basis of this work, the opinion was not infrequently expressed that schizophrenia was to be regarded as an organic disease. Meyer's (65) work first published in 1910 and elaborated (66) in 1912, showed that changes in the pupillary reaction, even to complete inactivity, can be induced by localised abdominal pressure. In 1914, Reichmann (67) investigated the subject in 215 cases of schizophrenia, and concluded that a definite explanation is not yet determined: but it appears probable that there is a connection between certain



vasomotor disturbances and disturbances of the innervation of the iris. In Table I are summarised the more important pupillary symptoms of other kinds in schizophrenia, which brings out the individual equation in the observation of the same phenomena. There is, however, a wide variation in the types of schizophrenia as well as many stages in the progress of the illness, and the variations shown in these figures by different observers depend not only on the individual interpretation of the various phenomena but also on the type of cases included. Consequently, these figures have questionable value, except to point out that various pupillary anomalies are frequently seen in persons with schizophrenia.

(c) Irregularity in Contour.

Analysis of Anomalies found.

(a) Size of Pupil.

The percentages obtained in my series of 200 cases agree in general with those of other observers that the dilated pupil is much more frequently encountered than the contracted pupil.

(b) Inequality.

This anomaly was present in 12.5 per cent. Lewis (68) found 11.0 per cent in a series of normal persons and Triberger (69) found that 44.6 per cent of normal persons show anisocoria. Consequently it

seems questionable whether it occurs any more frequently in persons with schizophrenia than in apparently normal persons. It is generally agreed that inequality may be hereditary (Wilbrand and Saenger (70), Fuchs (71), Piltz (72); in the adult it is regarded by many as being always pathological (Hansell and Sweet (73), De Schweinitz (74), and by others as physiological in many cases (Barrie (75), Schmidt-Rimpler (76), Lewis (77), Firth (78).

In Schizophrenia, it may be possible that its occurrence may be regarded as either pathological or physiological, its physiological importance being nil, while its pathological importance seems to point to only a local regressive or degenerative change.

(c) Irregularity in Contour.

Irregularity was divided into slight and marked with 23.5 per cent showing slight and 5.0 per cent showing marked changes in contour. The figures of others observers vary between 10 and 50 per cent.

(d) Sight reflex.

Of the total series 52.5 per cent showed some disturbance of the reaction to light. Of this number 29.5 per cent showed a moderate impairment of the light reflex, either in the speed of the reaction or in the radius of the reaction arc. An additional 16.0 per cent showed a marked impairment in the light reaction, many of this group showing only a slight response to light. 4.5 per cent showed the typical

Argyle- Robertson reaction, which, in the absence of a positive Wassermann or Meinicke reaction, in schizophrenic cases may possibly be due to organic disease of the central nervous system other than syphilis.

(e) Impairment of the Convergence Reflex.

In this series there was impairment of the reflex in 19.5 per cent of the cases. The so-called paradoxical Argyll Robertson reaction (entire absence of the convergence reflex with the retention of some degree of the light reflex) as mentioned by Kestermann (79), Schwartz (80), Levinsohn (81), and others, was not present in any of my cases.

3. The Blood Pressure in Schizophrenia.

Much attention has also been given to the blood pressure in schizophrenia. Kraepelin (82) stated that the blood pressure in this condition is, as a rule, lowered, but that it fluctuates, however, considerably. Besta (83), in an investigation of the methylene blue excretion in this psychosis, noted that the arterial pressure is below normal. Gibson (84), conducting an examination of the pathological features of schizophrenia, found the mean systolic pressure in 44 male patients to range between 113 and 118 mm. of mercury among the various types, with 4 catatonic, 2 hebephrenic and 2 paranoid subjects having a systolic tension less than 100. Dawson (85) reported 50 cases of schizophrenia in males in which the mean systolic level was 116.9 mm. with 10 cases

of catatonia and 4 of hebephrenia in which it was below 100; the diastolic reading was between 55 and 65 mm. in all cases. In 25 male schizophrenic patients, whose pressure was reported by Kanner (86), the mean systolic point was 116.8 mm. Weber (87), cited 15 male patients, whose mean systolic pressure was 108.5 mm. with a pulse pressure of 45.1. An interesting case was presented by Raphael, Parsons and Woodwell (88) of a boy, who, during an acute catatonic phase, had a systolic pressure of from 90 to 100 mm. which on recovery rose to 120. Five catatonic patients, studied by Walther (89), had a mean systolic level of 110.2 mm. In Langfeldt's (90) monograph the mean pressure in 28 male schizophrenes was reported to be 116.2, while that of the controls was 125.2 mm. Also, Cornell (91) stated that in 25 cases the average systolic pressure was 115 mm. while sitting and 95 mm. while reclining. Parkin's (92) observations in 89 cases showed a mean systolic pressure of 123.3 mm. and in Paddle's (93) 90 schizophrenic males the mean systolic pressure was 134.6. Most statisticians consider the mean systolic pressure of the general population to be round about 125 mm. and the mean diastolic about 80. It is of interest to note that Hunter (94) stated that between the ages of 17 and 32 the systolic pressure varies between 120 and 126 mm. The relatively few

claimed any importance for this factor. Larimore (101)

in a study of factory workers, recorded a difference comparable studies in schizophrenia place these figures at about 115 mm. systolic and 65 mm. diastolic. Of late, however, the observations of several investigators that the blood pressure varies directly with age, have been shown to be not entirely true. In children up to the age of 15, there has been shown to be a distinct correlation between age and both systolic and diastolic pressures (95). The case is rather different for adults. Alvarez and Stanley (96) found no change in the systolic pressure up to the age of 40, and, after that, a direct tendency to rise. Symonds (97) agreed with this view, but, in addition, an analysis of his figures shows a steady rise in the diastolic level beginning at 20 years. Hüber (98) stated that age has "no statistical significance" in the determination of systolic pressure, while Dunham's (99) systolic levels vary but 5 mm. from the second to the fourth decade. It seems, therefore, that while there is a rise in systolic pressure in childhood and after the onset of middle age, there is little change between these periods but that the diastolic level tends to increase throughout.

The rôle of the constitutional factor in the maintenance of blood pressure has been reviewed by Alvarez and Stanley (100) who found no difference in the tensions of the various bodily types and disclaimed any importance for this factor. Larimore (101)

in a study of factory workers, recorded a difference of 20 mm. between the systolic tensions of sthenics and asthenics. Fossier (102) also, stated that the hypotension is usually found in the asthenic or splanchnoptotic type. In schizophrenia, the patients are, according to Raphael, Ferguson and Searle (103), predominantly of this type.

Freeman (104) made a study on the effect of "habituation" on the blood pressure in schizophrenia. He made a study of the systolic and diastolic blood pressures in 50 cases of schizophrenia in three periods, three months apart, the patients becoming habituated to daily laboratory procedures. He found the systolic and diastolic pressures to be lower in the second than in the first period. The systolic pressure stayed at approximately the lower level in the third period, but the diastolic pressure rose to an intermediate level. The mean values of the systolic pressures in the three periods were 105.2, 99.6, and 100.3 mm. of mercury. The diastolic pressures were 65.5, 55.5 and 60.8 mm. respectively. Season, nutrition, anaemia and oxygen consumption rates were excluded as factors causal in the production of the lower pressures, and he did not regard sedentary life as a significant factor. He ascribed the fall in systolic pressure on repeated determinations to habituation to the environmental situation and stated

that the observations served further to emphasise vascular hypotension as a characteristic of the schizophrenia psychosis.

Kraspelin (105) found, as a rule, that the frequency of the pulse could at one time be slow and at another rapid. Mayer (106) also speaks of the existence of both bradycardia and tachycardia. Klipstein (107) and Knapp (108) mention tachycardia as a symptom in the hebephrenic type and Evensen (109) found it in acute cases. Goldstein and Reichmann (110) found that bradycardia was very characteristic of catatonia, whilst the frequency of the pulse in hebephrenia was normal.

Morgenthauer (111), on the other hand, found nothing characteristic of schizophrenia. The reports regarding these conditions during stupor seem to be more in agreement, as Knapp (112), Raphael and Parsons (113), Eber (114), Dawson (115), and also Knebuske (116) have all mentioned a slow pulse and most of them a low blood pressure during this phase of the disease.

With regard to the temperature of the body, Kraspelin (117) usually found the temperature low, sometimes subnormal with a small range of the daily fluctuations. Schulte (118) has mentioned frequent variations of temperature. Lukas (119) invariably found hypothermia in 33 schizophrenic cases. Hypothermia is also mentioned by Sæll (120) and Knapp (121) during stupor, while Bechterew, Müller (122) and Specht (123) have mentioned a rise of temperature

#### 4. Subnormal pulse, temperature.

Kraepelin (105) found, coincident as a rule with low blood pressure, that the frequency of the pulse could at one time be slow and at another rapid. Meyer (106) also speaks of the existence of both bradycardia and tachycardia. Klipstein (107) and Knapp (108) mention tachycardia as a symptom in the hebephrenic type and Evensen (109) found it in acute cases. Goldstein and Reichmann (110) found that bradycardia was very characteristic of catatonia, whilst the frequency of the pulse in hebephrenia was normal.

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With regard to the temperature of the body, Kraepelin (117) usually found the temperature low, sometimes subnormal with a small range of the daily fluctuations. Schüle (118) has mentioned frequent variations of temperature. Lukas (119) invariably found hypothermia in 30 schizophrenic cases. Hypothermia is also mentioned by Snell (120) and Knapp (121) during stupor, while Bechterew, Müller (122) and Specht (123) have mentioned a rise of temperature

for which they found no reason.

Cameron (124) in a study of the temperature in schizophrenic patients came to the conclusion that the internal temperature in the schizophrenic group was throughout the day slightly lower than that in the non-schizophrenic psychotic group, both groups being at room temperature. There was also evidence to show that at room temperature, the mechanism of heat control in the schizophrenic group is more active than in the non-schizophrenic group, while findings on exposure to extreme cold suggested that the mechanism of heat control acts more strongly and more sharply in the schizophrenic than in the non-schizophrenic group. Exposure to extreme heat revealed no weakness in the mechanism of heat control, while the response to the ingestion of food was more marked but less well sustained in the schizophrenic than in the non-schizophrenic group. From this one gains the impression of an intact and active mechanism of heat control in the schizophrenic reaction. This is of special interest because mechanisms of heat control depend largely on the sympathetic nervous system, and one still observes in the literature attempts to correlate the schizophrenic reaction with vagotonia.

with hearts weighing less than 300 gm. is larger than

5. Sluggish Circulation. Cold Cyanotic extremities.

the figure of Lewis, (75.5). Fulstow came to the conclusion that hearts of psychotic patients grouped together undergo the same changes with increasing age, as do those of sane persons, and that schizophrenics were no exception to this rule. Especially is noticed cyanosis of the hands, less of the feet, the nose and the ears; from the deep blue colour of the skin, dilated arterial areas may sometimes be distinguished as bright red, sharply circumscribed spots, which can be artificially produced by pressure. These circulatory phenomena have brought the cardiovascular system into prominence (130).

Lewis (131), from a large number of necropsies performed at St. Elizabeth's Hospital, concluded that, "generally speaking, a small circulatory system was discovered to be characteristic of the schizophrenic group, this constitutional factor being independent of age, colour, sex, duration of psychosis or associated diseases". In a series of 90 cases, he found that 75.5 per cent of the cases diagnosed as schizophrenia showed at necropsy hearts weighing less than the average, while a much smaller percentage of such hearts was found in other psychosis. He takes the average heart weight to be 300 gm. In Fulstow's (132) series, the percentage of schizophrenic patients

with hearts weighing less than 300 gm. is larger than in any other group, (56), but it does not approach the figure of Lewis, (75.5). Fulstow came to the conclusion that hearts of psychotic patients grouped together undergo the same changes in weight with increasing age, as do those of sane persons, and that schizophrenia was no exception to this rule, maintaining a middle course throughout as compared with other psychoses.

The cardio-vascular system in schizophrenia has recently been studied by the Schneider method (133). This test purports to afford a measure of cardio-vascular fitness and was elaborated from a somewhat similar test devised by McCurdy. The highest score possible is plus 18, and the lowest, minus 11. Bauer (134) graded the results as follows: from 14 to 18, excellent; from 11 to 13, very good; from 9 to 10 fair; from 7 to 8, doubtful, and below 7, unsatisfactory. Trentzsch (135) seems to have been the first to report on the application of the Schneider test to psychotic patients. His data show a mean score for the entire schizophrenic group of 8.4 with 57.6 per cent scoring below 10. For the sub-groups, the mean scores were: paranoid, 10.5; mixed, 11.3; catatonic, 6 and hebephrenic, 6.3. By roentgen study Trentzsch noted also a higher percentage of "tubular" hearts in the catatonic and hebephrenic than in the paranoid patients. He commented on the relationship of these findings to the type of psychotic reaction;

the catatonic and hebephrenic groups he took to represent "purely regressive" and the paranoid a "compensatory projecting reaction". Trentzsch further noted that the paranoid patients showed some improvement of score with a months training by standard exercises, but the catatonic and hebephrenic patients showed no response.

Lenton, Hamelink and Hoskins administered the test to 25 members of the hospital staff and to 99 schizophrenic patients. The mean score of the patients was 11.9 and of the controls 13.4 - a difference two and one-half times its standard error. Correcting the score of the patients in relation to the initial lower pulse rate would reduce their score to 11.3, a value 19 per cent below that of the controls. The pulse rates and the systolic blood pressures were slightly lower in the patients than in the controls, but the ranges among individuals were notably greater, as were also the Schneider scores. The different sub-types of schizophrenia showed substantially equal scores. The conclusion arrived at was that "the Schneider score indicates a significant lowering of physiologic fitness in the schizophrenic patient, but apparently mirrors the degree of physical activity rather more than the intrinsic degree of normality".

He found in two male catatonic cases pronounced axillary pubic hair, at the same time there was a lack of hair round the trunk. In addition to these, he found the hair on the trunk lacking in the case of

6. Trophic changes in the hair and nails.

Cannon (136) states that in females the pubic hair often extends up to or above the umbilicus, while hair is also found on the breasts and on the chin. In males there is usually only a weak growth of beard on the chin, while the pubic hair is scanty and of female distribution. The hair of the head is often curiously erect. Anomalies in the disposition of hair in female schizophrenics are also referred to by Hegar (137).

The normal disposition of the hair is specific for the sex: the typical female hair disposition covering only the regio pubis with horizontal limits upwards, and also the regio axilla; in the adult man, on the other hand, there is abundant growth on the chest, thighs and legs, besides the axillary and pubic regions, where the hair at an adult age should stretch upwards towards the umbilicus, in the shape of a triangle with its base against the symphysis pubis. Langfeldt (138) states that in younger patients, probably up to the age of about 25, no importance can be attached to the so-called feminine or semi-feminine pubes. That can only be done when these are found in adult age. He found in two male catatonic cases pronounced asexual pubic hair, at the same time there was a lack of hair round the trunk. In addition to these, he found the hair on the trunk lacking in the case of

two grown men. The nails were brittle and lustreless in most of the acute cases as well as the chronic cases.

In the hebephrenic group he found the disposition of hair scanty in two male patients, in the remainder typically masculine. In one female case typically masculine pubic hair was present and slightly hairy mammae. The nails in several cases were lustreless and atrophied.

Regarding the distribution of hair in his mixed cases, in three male cases he found a typical asexual pubis and in two cases extremely scanty hair covering.

Galant (139) describes Alopecia Areolata, which he regards as a trophic disturbance, probably a type of alopecia areata. The difference between alopecia areolata and alopecia areata seems to lie in the size of the spots. In the former they are much smaller and elliptoid in shape. The surface is smooth and pale. They usually cover the occipital region, giving a mottled appearance to the head. He believes it is a trophic disturbance and probably a disturbance in the function of the vegetative nervous system. The relationship with the patient's psychotic state is not clear, except that it is of frequent occurrence in schizophrenia.

## 8. Obesity.

The presence of obesity should also be noted in schizophrenia, as here anomalies are frequently met with in complaints of the endocrine organs. The dis-

7. Altered action of the Sweat and other Glands.

Disposition is chiefly in the abdomen, in females chiefly in the breasts.

Increased secretion of the saliva and perspiration are mentioned by Hüffler (140) and Antheaume (141) as being specially common in catatonia, whilst Schüle (142), Meyer (143) and Specht (144) only relate to the frequent appearance of these symptoms as a rule in schizophrenia. Knapp (145) found increased salivation and perspiration chiefly in hebephrenia, while these secretions were reduced in catatonia.

Langfeldt (146) states that the skin has in most of the chronic catatonic cases, an oily, shiny appearance; in one case pronounced vitiliginosities. In the hebephrenic group the skin did not present changes worthy of mention - there was no increased secretion of tallow - but frequently increased sweat production.

Heredity undoubtedly accounts for many cases of obesity. Bauer (148) says "most of the cases of endogenous obesity are only to be explained by a constitutional anomaly - about 90 per cent showing marked heredity - that is to say they originate from an abnormal gene bringing about a constitutional destiny of the tissues to store fat on account of some anomalies in the intermediate metabolism". He also refers to

## 8. Obesity.

The presence of obesity should also be noted in schizophrenia, as here anomalies are frequently met with in complaints of the endocrine organs. The disposition of fat is specific for the sex: in males the disposition is chiefly in the abdomen, in females chiefly in the mammary, pubic region, and around the hips. The influence of the sex gland on the fat deposit also emerges from the feminine (or asexual) localisation of fat in the castrated and eunuchs, also from the increasing obesity of women at the climacteric.

Pathological fat deposits are also found in complaints originating from the hypophysis cerebri, (dystrophia adiposogenitalis).

According to Curschmann (147), adiposity is a concomitant symptom of many cases of myxodema both in adults and children, and occasionally appears as the chief or only apparent symptom of thyroidal insufficiency, and indeed as "one form - though certainly an uncommon one - of partial benign hypothyrodism".

Heredity undoubtedly accounts for many cases of obesity. Bauer (148) says "most of the cases of endogenous obesity are only to be explained by a constitutional anomaly - about 90 per cent showing marked heredity - that is to say they originate from an abnormal gene bringing about a constitutional destiny of the tissues to store fat on account of some anomalies in the intermediate metabolism". He also refers to

experimental evidence of heredity as shown by Danforth's strain of fat mice, which transmitted this special characteristic to their offspring as a dominant Mendelian unit".

Laurence and Moon (149) in 1866 reported a family group of four of eight brothers and sisters, who showed retinitis pigmentosa, adiposity, genital dystrophy and mental deficiency: three of these also showed imperfections of bony and muscular development leading to defective gait. Biedl (150) in 1922 and Raab (151) in 1924 report a family of six, two of whom showed retinitis pigmentosa, adiposity, genital dystrophy, polydactylism and mental deficiency.

Solis-Cohen and Weiss (152) in 1925 reported four of eight brothers and sisters who exhibited marked adiposity with mental deficiency, and genital dystrophy, the fat distribution being largely of the girdle, mons and mammary type.

Bernhardt (153) states "it is impossible to accuse a particular endocrine gland of being the cause of obesity: disturbances of the endocrine glands are often involved, but they do not play the first role. The decisive factor is the function of the hypothalamic regulative center".

## SUMMARY OF FINDINGS.

1. General development and Stigmata.

Careful examination of the bodily development, stature, measurement of the skull together with the stigmata of degeneration and atavistic signs, in a series of 200 cases, (all women), does not point to the conclusion that schizophrenics are generally of a degenerate physical type. The physical findings in the total group were not greatly abnormal. The weight was commonly low, and only a few patients in the series were significantly overweight.

Though it may be quite possible to detect the physical types as described by Kretschmer, these cannot be differentiated with any degree of precision, and there seems to be a progression of physical characteristics from those that define the asthenic, through those of the pyknic build. It would seem then that Kretschmer's concept of type should not be adhered to, as there is no evidence of there being anything but a progression of characteristics in accordance with a normal distribution. In my series, in no catatonic were the lower extremities longer than the trunk, nor were there any other signs of eunuchoid proportions. In the hebephrenic group, the skeleton on the whole was clean built, this being specially noticeable in the

hands and feet. In 4 per cent, however, open epiphyseal lines were present.

In four patients of the other groups, the lower extremities were longer than the trunk - 33 had stigmata of degeneration - but doubtless these stigmata have been grossly exaggerated in importance in the past and it must be admitted there is a wide range of normal variation. According to the late Professor Robertson, we are "all blessed with at least one of ten stigmata"!

In view of the regressive changes that have been demonstrated in the gonads, it is remarkable that more cases do not approximate to the eunuchoid type. 22 per cent of the series showed reduced subcutaneous fat, while only a few cases showed increased deposition of fat, these being mainly hebephrenics in the later stages. Two paranoid cases showed collars of fat on the neck and shoulders, a protuberant abdomen and pads of fat above the pubis.

In two hebephrenic cases there was typically masculine pubic hair and slightly hairy mammae. The nails in several cases were lustreless and atrophied, but the skin did not present changes worthy of mention, as especially here is there no increased secretion of oil, no cyanosis but frequently increased sweat production.

In the catatonic group the pubic hair was lacking in two cases; in other two the hair was erect, like a wire brush, while the skin, especially in the

chronic cases, had the well-known oily, shiny appearance. Increased salivation was noted in 7 of this series, all chronic cases, and cyanosis of the peripheral parts is striking and characteristic also of the chronic group.

**BLOOD PRESSURE.**  
The hands also become swollen and oedematous, especially in the chronic type. Alopecia Areolata was noted in three cases, one catatonic, two paranoid.

The blood pressure was taken in all cases, nurses being used as controls. It was found that the mean systolic pressure was 11.3 mm. lower than that of control subjects, while the diastolic pressure was 17.8 mm. below that of the controls. Nutrition plays no significant rôle in the determination of the height of the blood pressure, nor has it any correlation with height, and there is no constant variation with the season. The results were:-

Catatonic, 54 cases - average blood pressure - 115 mm. Hg. (97 - 133); Hebephrenia, 103 cases, 123 mm. Hg. ; Paranoid, 11 cases, 150 mm Hg. (115-186); Simple schizophrenia, 33 cases, 118 mm. Hg. (104-129).

BLOOD PRESSURE.

The blood pressure was taken in all cases, nurses being used as controls. It was found that the mean systolic pressure was 11.8 mm. lower than that of control subjects, while the diastolic pressure was 17.2 mm. below that of the controls. Nutrition plays no significant rôle in the determination of the height of the blood pressure, nor has it any correlation with height, and there is no constant variation with the season. The results were:-

Impairment of Reflex	Catatronics, 54 cases - average blood pressure - 115 mm. Hg. (97 - 133);	
Moderate light reflex	Hebephrenics, 102 cases, 122 mm. Hg. ;	
Ma	Paranoid, 11 cases, 120 mm. Hg. (115-136);	
Impairment	Simple schizophrenia, 33 cases, 118 mm. Hg. (104-129).	32 18.0
Argyll Robertson reaction		9 4.5
Absolute fixation		5 2.5
No anomaly		68 36.0

The pupils in 66 per cent of 200 cases of schizophrenia showed some pupillary anomaly. Dilatation occurred in 16.5 and contraction in 6.0 per cent. Inequality of the pupils was found in 12.5 per cent.

While slight irregularity occurred in 23.5 per cent, there was marked irregularity in 5 per cent. The light reflex was disturbed to some degree in 52.2

### Pupillary Anomalies.

#### Summary of Pupillary Anomalies in 200 cases of Schizophrenia

	<u>No. of Cases</u>	<u>Percentage</u>
Dilatation	33	16.5
Contraction	12	6.0
Inequality	25	12.5
Slight Irregularity	47	23.5
Marked Irregularity	10	5.0
Impairment of Convergence Reflex	39	19.5
Moderate light reflex impairment	59	29.5
Marked light reflex impairment	32	16.0
Argyll Robertson reaction	9	4.5
Absolute fixation	5	2.5
No anomaly	68	34.0

The pupils in 66 per cent of 200 cases of schizophrenia showed some pupillary anomaly. Dilatation occurred in 16.5 and contraction in 6.0 per cent. Inequality of the pupils was found in 12.5 per cent.

Changes in weight are likely to be due to changes in the assimilation of food. Such changes

While slight irregularity occurred in 23.5 per cent, especially in the assimilation of protein food, in there was marked irregularity in 5 per cent. The light reflex was disturbed to some degree in 52.2 per cent, 29.5 showing moderate impairment, 16.0 marked impairment, 4.5 fixation to light and retention of convergence reflex and 2.5 per cent fixation to both light and convergence. The convergence reaction was disturbed in 19.5 per cent.

The hypothesis of an inferior constitution in the patient and the fact that the dementia is so often precocious might lead one to expect to find a certain degree of inhibition of further development, both physical and mental, before full development had been reached, which is subsequently followed by regressive changes. Along with other more delicate functions of the nervous system, which are unquestionably impaired, one might conceive that a relatively sensitive organ like the eye would show some indication of change from the hypothetic normal as regards functional efficiency and anatomic structure.

Studies in recent years have shown that the schizophrenic psychosis is marked by certain displacements of metabolic levels of performance and, what is probably of greater importance, that the relationships among various functions are seriously abnormal.

Changes in weight are likely to be due to changes in the assimilation of food. Such changes

Shortly after Kraepelin attempted to define the mental disorder which he called dementia praecox, especially in the assimilation of protein food, in now more generally known as schizophrenia, there followed not only a general awakening of clinical interest, but gradually a more rational therapeutic attitude began to manifest itself in psychiatry. This condition was brought about in a relatively short time, following the more or less adoption of the Kraepelin nomenclature.

There is still doubt that the internal secretion exert an important influence on the development of the hair. Those glands which, at present, seem most important are the suprarenals, the gonads, the thyroid and the pituitary, though in the last two instances it is possible that the effect is not direct, but that their disturbances react on the suprarenals, which, in turn, influence the hair. One theory is that the male type of hairiness is latent in all persons, but that its development over the greater part of the body is suppressed by the action of the ovary; second, that the hairiness of the male is due to stimulation by testicular secretion in the absence of which body hair remains undeveloped except within narrow limits.

in 1931, stated, "in a recent publication entitled 'Schizophrenia (1928)' issued by the Association for Research in Nervous and Mental Diseases, there are articles by thirty-one authors. The symposium contains 460 pages, of which only 13 are devoted to treatment. Does the ratio of

V. TREATMENT.

Shortly after Kraepelin attempted to define the mental disorder which he called dementia praecox, now more generally known as schizophrenia, there followed not only a general awakening of clinical interests, but gradually a more rational therapeutic attitude began to manifest itself in psychiatry. This condition was brought about in a relatively short time, following the more or less adoption of the Kraepelin nosology. In 1903, within a decade of Kraepelin's classification, Adolf Meyer was already inculcating a hopeful standpoint towards the reaction types included in the dementia praecox group. Even yet, it is only a little over a quarter of a century ago that therapeutic interests began to assume a positive character. Every year since that time enquiries into the various aspects of schizophrenia have taken on an added significance, to the extent that the condition is no longer enshrouded in abject hopelessness, but, on the contrary, is viewed with encouragement. Results that were previously unattainable have cast a favourable ray of hope in the direction of therapy, quite apart from the still obscure aetiology. Rudolf (154) in an article on the experimental treatment of schizophrenia in 1931, stated, "in a recent publication entitled 'Schizophrenia (1928)' issued by the Association for Research in Nervous and Mental Diseases, there are articles by thirty-one authors. The symposium contains 460 pages, of which only 18 are devoted to treatment. Does the ratio of

ready to take advantage of this knowledge. Later this  
 18 to 460 represent the relative interest existing in  
 topic will be enlarged upon.  
 the treatment as compared with other aspects of the  
 disease"?

The psychobiological doctrines of Meyer and  
 of Hoch have contributed a means by which something of  
 a positive and favourable nature may be accomplished.

A somewhat analagous situation is presented in patients  
 with general paralysis, in that successes of varying  
 grades are encountered under the malarial form of  
 therapy; a certain number of subjects with general  
 paralysis gain states of remission and a certain per-  
 -centage of schizophrenic individuals are likewise  
 restored to their prepsychotic level of adaptation.

It is only a short time ago that the fatalistic attitude  
 towards general paralysis and schizophrenia was render-  
 -ed untenable. It is now well recognised that patients  
 with definite schizophrenic syndromes may and often do  
 gain states of remission, some of them "spontaneously",  
 others in association with various therapeutic measures.  
 However, too often it is said that a schizophrenic  
 subject recovered "spontaneously" without an evaluation  
 of the significance of environmental changes. The  
 latter are known to be highly instrumental in the pro-  
 -duction of a patient's mode of reaction, the schizo-  
 -phrenic subject being delicately keyed to her surround-  
 -ings, alterations therein often provoking decided  
 changes. This is particularly true regarding the  
 personalities she encounters and one should always be

ready to take advantage of this knowledge. Later this topic will be enlarged upon.

In the last five years I have carried out increasing therapeutic experiments in the women's department of the mental hospital, my plan of treatment being largely influenced by the various outlines given by Rudolf.

Table I gives a list of treatments by various authors to a sufficiently large number of cases to give an approximate estimation of the values of the methods.

TABLE I.

Method	No. of Cases	Improvement per cent.	Authors
Salicylates	76	75	Margulies (1927)
Aseptic Meningitis	64	57.8	Carroll, Barr, Barry and Matzke (1925)
Sodium Nucleinate	32	39.7	1. Douath (1913), 2. Lundval.
Sulfosin	59	39	1. Schroeder (1929) 2. Salinger (1929) 3. Marcuse & Kallmann (1929)
Manganese Chloride	308	35.26	1. English (1929), 2. Reed (1929), 3. Schrizer, 4. Reiter & Bisgaard (1927)
Occupational Therapy	20	35	Main (1923)
Malaria	48	33.3	1. Yakubovsky (1929) 2. Rudolf (1927), 3. Wizel and Markusze- weiz (1927)

Method	No. of Cases	Improvement per cent	Authors
Ringer-Locke Solution	49	28.6	1. Morokowa (1927), 2. Ikeda (1926), 3. Sato & Morita (1918).
Somnifen	26	25.33	Klasi (1922)
Calcium	30	23.3	1. Dodel, 2. Rudolf, 3. Berndt & Kollé (1926)
Removal of Sepsis	35	22.8	1. Kirby (1923), 2. Holmes (1921)

TABLE II.

This table shows some methods used on smaller groups of cases.

Method	No. of Cases	Improvement per cent.	Authors
Assisted Respiration	12	83.3	Peters (1930)
Lectures	10	80	Lazell (1930)
Vitamin D.	12	50	Rudolf
Thyroid	16 (selected)	88	Hoskins & Sleeper (1930)
	15 (unselected)	0	Walker (1924)
T. A. B. Vaccine	15	0	1. Berkley (1929) 2. Raphael & Gregg (1921)

Owing to the small numbers treated these results are of less statistical value.

view to success only when it is continued over a period of months; occasionally it must be given throughout

Technique and Remarks on Methods.1. Glandular Therapy.

A few leading principles have guided investigators to seek a remedy that might prove of value in the treatment of schizophrenia. Among these is the consideration that the endocrine system is in part at least responsible for some of the factors associated with the clinical picture. In the majority of clinics, however, endocrine therapy had been reported as ineffective. Kraepelin and Bleuler, for instance, employed this form of therapy in an extensive and intensive manner without the production of any clinical changes, save in those instances in which organotherapy has proved of value independent of the presence of a mental disturbance.

Among the first more promising communications was that of Kanders (155), who, believing that the germinal glands are in a state of dysfunction in schizophrenia, used the products Testosan and Ovosan with favourable results. He stressed the point that heretofore the dosage has been too small to induce results. Under the use of Testosan he reported that in two patients with schizophrenia, extensive remissions were produced, one in a patient under observation for five years, and another for seven years. As a result of large experience, he concluded that organotherapy with the glands of reproduction is to be undertaken with a view to success only when it is continued over a period of months; occasionally it must be given throughout

the patient's adulthood as a substitutive form of treatment.

Stanley (156) carried out testicular implantation one thousand times in the treatment of 656 human individuals. Among the 656 persons there were eight patients with schizophrenia of which seven were regarded as not having been benefited, while one was favourably influenced.

As regards ovarian preparations, Sippel (157) recorded good results in three early cases of schizophrenia by ovarian transplantation. Each of the patients exhibited a mild degree of hypogenitalism. Climenko (158) administered corpus luteum to schizophrenic patients early in the course of their illness and concluded that the substance was inert in these cases.

Berkeley and Follis (159) studied the effect of thyroid administration in schizophrenic patients and reported their observations on the influence of thyroidectomy and thyrolecithin in the treatment of catatonia. They concluded that, on account of the small number thus far thyroid-ectomised, they were not in a position to give any conclusions of a definite character. They suggested that partial ablation of the gland might be a factor in the return of the reflexes to a natural state, in the decrease of the mechanical muscular irritability, as well as of the dermatographia, the loss of pigmentation and of the doughy, pasty character of the skin. They felt also that the operation might in some way be

associated with the return to the normal both of the mental and physical state. They reported the results of thyroidectomy in eight successive cases of catatonia, claiming that it would be difficult to find similar beneficial results under any other form of treatment. They came to the conclusion that thyrolecithin gave constant results only in the prodromal state, adding, "it probably acts by increasing constructive metabolism, but may also act by nullifying the thyroid hormone, just as iodine increases its activities".

Fay (160) stated that there seemed to be some connection between schizophrenia and endocrine disorders. In his experimental work he selected only those patients who had recognisable endocrine disorders. No selection was made on the basis of mental disorder. He came to the conclusion that "the treatment may possibly be of great value in breaking into the so-called vicious cycle of mental disease, particularly in the early stages. A combination of thyroid stimulation and psycho-analysis might be an excellent method of attacking incipient schizophrenia".

Hübner (161) treated 10 cases with anti-thyreodin (Mökins) by mouth, administering from one to three tablets daily. He observed improvement in some of the patients and in others an alteration of their clinical condition. He stated he had secured the same results with thyroid tablets and concluded that thyroid did not exert a specific action in these

patients. Hudovering (162) reinforced the action of the thyroid extracts by the infection of foreign proteins, using 5 to 10 c.c. of milk every five days. By the use of the latter, he was able to induce a temperature of at least 104°F. The earlier the patient is treated, the better the results are apt to be. He did not state that any of the three cases had been cured, but preferred to infer that they had attained restitution and integram, a state that they would not have achieved in the absence of such combined therapy.

Walker (163) treated 15 cases, of which three were catatonics, with thyroid extract. None of these cases showed evidence of thyroid deficiency and none improved. Hoskins and Sleeper (164) treated 16 cases of schizophrenia, all suffering from thyroid deficiency, and obtained improvement in 88 per cent. Five (31.25 per cent.) were discharged to their homes. These authors state that no improvement can be expected unless the cases are selected.

Smith and Hill (165) administered orally for two months thyroid and whole pituitary extract to 7 cases. No mental improvement took place, although improvement in the circulation and gains in weight were recorded. Each patient showed a low blood sugar curve before treatment, but a higher one, more nearly approaching the normal, after.

Ludlum and Corson-White (166) reported excellent results in the administration of thymus gland

extract in three of six patients. The three who were not especially benefited were old patients and much demented.

Sajous (167) felt that thymic function was associated with schizophrenia, in that the thymus supplies nucleins "to the organ of mind". He claimed that there was a marked reduction of the lymphocytes in this disease and that the therapeutic use of thyroid gland corrects this reduction. Bentley (168) recorded the summaries of three cases of schizophrenia treated by hormotone. Two of the patients were discharged as recovered; the third improved. The younger patients responded to this form of therapy more effectively than the older ones did.

Lingjaerde (169) of the Dikemark Asylum in Norway, started his therapeutic investigations on the basis of Wigert's observation that in schizophrenia running a comparatively favourable course, the thyroid is slightly enlarged or at any rate definitely palpable, whereas in cases running an unfavourable course, this gland is not palpable. The basal metabolism being the best index to the functional condition of the thyroid the author has investigated the basal metabolism in about 130 cases, and he has never found it above normal in any case of schizophrenia. In many attempts to treat with thyroid extract, he suggests that many of the failures have been due to inadequate dosage. Using the Norwegian thyroid preparation 'nyco' standardised by the aceto-nitril method, each tablet corresponding in action to 0.10 mg. of pure thyroxin and containing the equi-

-valent of 0.30 gram of the fresh gland, he exceeded the timid dosage of one or two tablets daily and has pushed the treatment until the basal metabolic rate was over 110-115 and the pulse rate had risen from 80 to 100, at which stage he had kept the patient in many cases for several months.

Among 20 cases of schizophrenia thus treated, there were 8 in which great improvement or freedom from symptoms was achieved and 5 in which there was marked improvement. In May, 1927, experiments were begun with a diet of liver in certain cases, but on this treatment alone the improvement observed was limited to the purely physical conditions of the patients. Very good results were obtained in some cases with a combination of thyroid and liver treatment; 9 out of 13 cases of schizophrenia showed great improvement or freedom from symptoms, 2 other patients being markedly benefited. He does not claim that these substances act as a specific on a well-defined morbid entity, but he believes they may support the body's natural recuperative powers. There are many other references to the value of endocrine therapy in the literature, but they are either not of promising character or they are too ill-defined to warrant repetition.

Details of Treatment.

In addition to securing as complete family and personal history as possible and of making careful

routine physical examinations, various metabolic studies were made on each patient. A quantitative analysis of two twenty-four hour samples of urine was made for total solids, total nitrogen, and residual nitrogen. In actual practice, the total solids, total nitrogen, and residual nitrogen are the three data of most significance. The ammonium nitrogen gives an index of possible loss of urea through ammoniacal decomposition, and thus casts a light on the dependability of the reported residual nitrogen, which is a derived figure, dependent largely for validity on an accurate determination of the urea. In dealing with psychotic patients there is always an element of uncertainty as to whether an actual twenty-four hour sample is secured. Catheterization as a routine measure is inadvisable because of its unfavourable psychological effect. The creatinin value is therefore of particular importance as affording a rough indication of the success in obtaining a true representative specimen. The total solids give an indication of the general level of metabolism, and the total nitrogen of protein metabolism. Even in a partial twenty-four hour sample, some idea of the level of protein metabolism can be obtained by comparison of the relative proportions of total nitrogen and creatinin nitrogen. A TN/CN ratio is calculated. In the normal subject, with average protein intake, this ratio is about 28. Marked lowering of the ratio is indicative of protein inanition.

basal level. During the course of the

In addition to quantitative analyses, qualitative tests are also made for albumen, reducing substances and urobilinogen, and microscopic studies are made of the urinary detritus. These may give an indication of serious disturbances of carbohydrate metabolism, of liver dysfunction, and particularly of nephroses or pseudo-nephroses suggestive of thyroid or adrenal deficiency. This diagnostic system requires the interpretation of each datum in the light of the presence or absence of all factors that may influence it in a quantitative way, with due regard to the limitations of the test. The phenolsulphonphthalein output is determined on each patient as an index of the condition of the kidneys, which is potentially able to cause marked displacement of the levels of the various nitrogenous bodies. In the presence of nephritis, the interpretation of the urinary, as well as the blood chemical findings, is quite different than in a case without this complication.

Basal metabolism is carefully determined in each case. No little patience is required at times to obtain reliable readings in the case of psychotic subjects, and in the same case, for the time being, a satisfactory determination cannot be made. There are various checks on the actual validity of the tests. Usually, with each successive rehearsal, the oxygen consumption is lowered until an approximately constant level is reached. This is likely to be at the true basal level. During the course of the determination,

both the pulse rate and the respiration rate are determined at brief intervals. In a true basal state, these figures remain essentially constant throughout the test. Any irregularity, therefore, is interpreted as indicating upward displacement from the true basal level. Further, the nurses record the early morning pulse rates of each patient. A comparison of the ward pulse rate and that obtained during the basal metabolism test indicates whether or not the patient is in a state of actual repose. When the first tests are unsatisfactory, repetitions are made, until either convincing evidence of their true basality is secured or it becomes evident that it is not then possible to secure a representative test. The blood pressure and temperature are routinely determined at each basal metabolism test.

The blood morphology is studied in each case. The three data of special endocrine significance are presence or absence and degree of secondary anaemia, of lymphocytosis and of eosinophilia. Secondary anaemia is much more characteristic of thyroid than of pituitary deficiency, which conditions may present confusingly similar pictures. Lymphocytosis is likely to be found in any type of endocrinopathy. Eosinophilia points towards pituitary rather than thyroid deficiency.

A chemical analysis of the blood is made for non-protein, urea, uric acid and creatinin nitrogen, as well as for sugar. The non-protein, as well as the urea nitrogen, is normal in pituitary and ovarian deficiency,

but trends upward in thyroid and adrenal deficiency. Uric acid, on the other hand, is typically high in pituitary and adrenal deficiency, but is normal in thyroid and ovarian deficiency. The blood sugar trend is low in adrenal and thyroid deficiency, but normal in pituitary and ovarian deficiency. The most useful single datum is high blood uric acid, as differentiating pituitary from thyroid deficiency. Further, especially significant in this regard is the galactose tolerance. A high galactose tolerance accompanying other signs of glandular deficiency, practically always means pituitary involvement.

The "lung volume" is determined by the spirometer method. This datum is of considerable importance, especially as an index of thyroid involvement. Shallow respiration is a wellknown sign of thyroid disease. In significant degrees of thyroid deficiency, in which the oxygen consumption is materially lowered, the patient appears to establish such a deep-seated habit of restricted respiration, that his spirometer reading is characteristically affected. It is an empirical fact that "lung volumes" substantially below prediction are highly indicative of thyroid rather than of other glandular deficiencies. The normal volume is calculated to both the Dryer and the West standards and the average deviation is taken as representing the condition actually present.

nearly similar as possible in age, duration of hospitalization, psychiatric type, background and mental symptomatology. A further control is obtained by a consideration of antecedent possibilities and the degree of consistency with which the data correlate with these. It is a matter of common experience that periods of improvement or even "spontaneous" cures are not infrequently encountered in dementia praecox - even occasionally in patients with a poor prognosis.

(A) 1. Thyroid: Before starting this method of treatment, the patient's weight should be such that she can afford to lose up to about 4 lbs. during the treatment as this often happens. Prior to the administration of the thyroid, nourishing diet should be given - eggs and milk in addition to the ordinary diet, and the condition of the intestinal tract should be made as satisfactory as possible.

On the first day of the treatment an initial dose of 15 grs. is given and this is raised by 5 grs. daily until a maximum of 70 - 80 grs. is being given daily. This dose is then continued from one to three weeks provided that the patient's condition is satisfactory. As a rule, reaction to the drug is early and distinct: in most cases the temperature rises a little and the pulse begins to quicken. The pulse-rate must be carefully watched and any irregularity must be long as the pulse remains regular there is no cause for anxiety, but any marked irregularity should act as a danger-signal to stop the treatment. I do not allow

No special comments on the technique employed in the various tests are necessary, as accepted standard methods were used. The various data having been secured and analysed, the patient, if her condition is not already well-known, is placed under observation without treatment for one to three months. She is then either dismissed from further study or is subjected to one or more courses of gland therapy, with usually about three months' intervals between courses. At intervals of about six weeks one or more data such as the basal metabolic rate or others regarded as especially significant as indicating progress in the given case are re-determined and at intervals of about three months the complete series of vital function tests are repeated.

Daily records of the patients' mental state are made by the nursing staff while each week during the entire study, I fill in a report of the mental condition. An element of personal judgment is un-escapable in the assessment of degree of improvement or regression. In this study, whenever the changes for better or for worse are in doubt, the statement recorded is, "Not significantly changed". In evaluation of the various reports that make up the evidence, attention is directed predominantly to specific facts rather than to the impression of the observers. The special necessity of a critical attitude is constantly to be kept in mind.

Formal controls are used as far as possible. Ideally, patients should be dealt with in pairs, as

nearly similar as possible in age, duration of hospitalization, psychiatric type, background and mental symptomology. A further control is obtained by a consideration of antecedent possibilities and the degree of consistency with which the data correlate with these. It is a matter of common experience that periods of improvement or even "spontaneous" cures are not infrequently encountered in dementia praecox - even occasionally in patients with a poor prognosis.

(A) 1. Thyroid: Before starting this method of treatment the patient's weight should be such that she can afford to lose up to about 14 lbs. during the treatment as this often happens. Prior to the administration of the thyroid, nourishing diet should be given - eggs and milk in addition to the ordinary diet, and the condition of the intestinal tract should be made as satisfactory as possible.

On the first day of the treatment an initial dose of 15 grs. is given and this is raised by 5 grs. daily until a maximum of 70 - 80 grs. is being given daily. This dose is then continued from one to three weeks provided that the patient's condition is satisfactory. As a rule, reaction to the drug is early and distinct; in most cases the temperature rises a little and the pulse begins to quicken. The pulse-rate must be carefully watched and any irregularity noted. As long as the pulse remains regular there is no cause for anxiety, but any marked irregularity should act as a danger-signal to stop the treatment. I do not allow

the kidneys. It acts as the determinant of the level the pulse rate to exceed 100 - 120. A striking observation in this series is that schizophrenic patients, apparently have, as a rule, a remarkably high tolerance for thyroid substance. There may be profuse sweating and the lobes of the thyroid frequently become thickened. Patients who have reacted to the treatment usually look somewhat ill and have lost weight up to 14 lbs. It is therefore necessary to stimulate the patient and attempt to quickly rebuild the tissues. The diet should be nourishing and liberal, milk with the addition of glucose being taken in abundance. In addition the patient should be given a strychnine tonic, and kept in bed, preferably in the open air. The preparation used throughout for this treatment was Burroughs, Wellcome & Co's "Tabloid" Thyroid Gland, standardised, each representing 5 grs. (0.324 gm.) of fresh healthy gland substance and not 5 grs. of desiccated thyroid, equivalent to  $1\frac{1}{2}$  grs. dry thyroid, B.P., which contains 0.1 per cent iodine in combination as thyroxine.

Thyroid exerts a powerful effect on metabolism; following its administration by mouth, the metabolic processes proceed more rapidly and a reduction in body weight occurs. There is an increase in the consumption of oxygen, and increased destruction of fats and protein. The administration of thyroid increases the available energy, increases the appetite and brightens the mental outlook. Following large doses there is also an increased excretion of water by

the kidneys. It acts as the determinant of the level of catabolic activity in the body.

The basal metabolic rate as indicated by oxygen consumption in given time is a measure of thyroid activity and varies less than 10 per cent. normally, but in hyperthyroidism the rate is increased 20 to 50 per cent. or more above normal, and in thyroid deficiency is reduced similarly below normal. The active principle may be absorbed from the alimentary tract.

Thyroxine is a complex organic compound containing iodine, which possesses the characteristic action of thyroid gland on oral administration. One milligramme of thyroxine orally raises the B.M.R. about 2 per cent. at the height of its action. 'Tabloid' thyroxine is prepared synthetically by the process of Harington and Barger and agrees physiologically and clinically with the earlier natural thyroxine isolated from the thyroid gland by Kendall. It possesses the characteristic action of thyroid gland on oral administration. Notwithstanding the popularity of some of the more recently introduced glandular preparations, thyroid medication still occupies the foremost place in organotherapy. The aim of thyroid therapy is to bring the rate of metabolism up to normal. The therapeutic effects of the gland are generally attributed to the iodo-albuminous matter which it contains.

2. Thyroid with Liver. The thyroid was given as above, and the liver either as  $\frac{1}{2}$  lb. liver daily, or as injections of Hepatex, which is a pre-

-paration similar to Extract Hepatis Liquidum, one fluid drachm being equivalent to 2 ounces of fresh liver.

3. Ovarian Therapy. For several years ovarian therapy has been in a state of flux due to broadening of our concept of the physiological function of the ovary and to the discovery, isolation and purification of definite chemical substances produced by the ovary. The older miscellaneous ovarian extracts have been replaced by standardised products, the activity of which has been fully demonstrated in lower animals, and to a lesser degree in man. Up to the present time the clear cut striking results obtained in animals have not been reproduced in human subjects, the two outstanding reasons why results of animal experimentation cannot be used as criteria for human therapy, being differences in sexual cycles between man and other animals, and psychological factors. Psychological factors are unimportant in animal experimentation, but they play an important rôle in many functions of the human body and therefore must be excluded before the efficiency of any therapeutic agent administered to the human being can be fairly judged. Products of the ovary have not been shown to have any stimulating effect on that organ. They merely supply a deficiency.

The ovarian extract was used in two forms:-

1. Subcutaneously in 1 c.c. ampoules every fourth day, 1. c.c. equalling 30 grs. of whole fresh ovary, the patient having in all from 20 to 30 injections.
2. Tabloid Varium, grs. v. (Burroughs Wellcome & Co.), each product representing the stated weight of fresh ovarian substance.

This was used for the secondary amenorrhoea, so common in cases of dementia praecox. This type of amenorrhoea would seem to indicate a real deficiency of ovarian internal secretion, which could be supplied by introducing the hormones into the body. Inasmuch as there is no way of measuring the amount of deficiency, the necessary dosage is uncertain. However, it seems obvious that in some instances the deficiency would be so slight that even a small dose would be inefficient. This assumption corresponds with the clinical results. Some patients in whom all extraneous factors have been removed, have been followed carefully over a period of a few years, and they have responded well to this form of therapy. Reports of a single menstruation following therapy, should be excluded as inconclusive. Such a menstruation is more probably a coincidence.

A great deal is said about the interrelation and the balance of the glands of internal secretion. The fact of the dependence of the ovary upon the thyroid is well demonstrated clinically. The theory as to the manner in which it acts is a matter of discussion. It would seem that when the thyroid functions normally, the hormone is secreted in the blood almost continuously. It is carried by the blood to all parts of the body and may be used by any tissue or organ which has the ability to withdraw it from the blood stream. Unquestionably, a certain amount of this thyroid hormone is necessary, directly or indirectly, for normal function of the ovary. It can be readily understood that if the

thyroid hormone is below normal that the function of the ovary might be below normal and bringing the thyroid to its normal level would have a similar effect on the ovary. The dependence of the ovary upon the thyroid is so striking that in all clinical treatment of ovarian deficiency it seems important to first stabilise the individual on thyroid. This should be done over a long enough period so that it can be determined whether or not the condition treated is due purely to thyroid deficiency before any specific ovarian therapy is begun.

In all cases treated with thyroid I have found it necessary to continue the therapy in order to maintain the improvement. From 10 - 15 grs. daily is usually necessary.

Before one can render a definite decision it must be shown that the gland substance selected was the one indicated in the individual case, that a potent preparation was used, that the dosage was adequate and that treatment was continued for a sufficiently long period. The history of each patient is obtained, and the patient then subjected to a careful physical examination. Then a series of special tests are made, first to determine the presence or absence of endocrine disorders, then to differentiate among the various glands that might be at fault.

(B) (a) "Opojex" Lymphoid Solution (B.O.C.)  
(formerly Lymph Serum).

(b) "Opocaps" Lymphoid Co. (B.O.C.)

These products have proved efficacious in several thousands of cases of functional nervous disorders and degenerative conditions since their introduction to the medical profession in 1909.

## Opocaps Lymphoid Compound contains:-

Spermin	}	gr. 2. sicc.
Lymphatic gland		
Brain		
Spinal cord		
Iron		gr. $\frac{1}{2}$
Sodium		gr. 1
Calcium		gr. 1
Aloin		gr. $\frac{1}{20}$

which are conveyed in the form of soluble gelatine capsules.. They may also be obtained without aloin or without glycerophosates and aloin when desired, but I have always employed the above combination. The dosage is: one capsule half an hour before meals thrice daily.

The Lymph serum for hypodermic injection contains:-

Spermin	}	gr. 2. sicc.
Lymphatic gland		
Brain		
Spinal cord		
Bi-chloride of gold		
Chloride of sodium		

The usual and maximum dosage I gave in all cases was 20 minims per injection. One injection was given daily. When "Opocaps" Lymphoid Compound capsules were employed conjointly an injection was only given on alternate days. The solution should not be exposed to light or extremes of temperature and should be well shaken before each injection. The injection should, when possible, be made in the gluteal region, or along the region of the spinal column, and may be given hypodermically or intermuscularly. Pressure massage should be applied for thirty seconds after each injection.

Lymphoid Compound and Lymph Serum are scientific combinations of animal substances, but the word "pluriglandular" is not perhaps an accurate name to apply to them. The various ingredients are all utilised by the body to serve different purposes. In their value and importance they have an unusually wide range of action and do not depend to any extent on any hormonal influence. Still they are strictly organo-therapeutic products and no convenient word has yet been coined to denote the combination of two or more extracts of animal substances other than glandular substances. Lymphoid Compound and Lymph Serum conform to the rules laid down for pluriglandular compounds in that the animal substances contained in them have no antagonistic interaction and to none of them are there

any contra-indications. Each ingredient, as well as undertaking its own share of therapeutic labour is able to supplement and assist the others. Given singly, the ingredients will not produce such satisfactory results as those obtained by their use in combination. The brain and spinal cord extracts supply highly organised phosphorus, nucleins, lipoids and other essential food materials for the nerve cells. The orchic extract aids the assimilation of these and by its spermin content exerts a definite tonic and regulating effect on the metabolism of the cells of the body, particularly promoting the health and balance of the endocrine glands, while the lymphatic gland extract materially raises the defensive powers of the body and of the individual cells, encourages phagocytosis and assists normal cellular metabolism.

Modern organotherapy has greatly advanced in the knowledge of intracellular activities and of the chemical processes involved in anabolic and catabolic metabolism. The presentation to the nerve cell of phosphorus in a perfectly assimilable form has long been an object of chemical research and has furnished the raison d'être of a variety of nerve tonics and nerve foods from crude phosphorus to combinations of lecithin, nuclein and other complex organic substances. In Lymphoid Compound and Lymph Serum this object has been attained. These preparations contain the actual organic living phosphorus elaborated by the vital pro-

-cesses of the cells of animals into the delicate proteins only to be found in nerve cells, and are rich in lecithin, nuclein and cell albumins. Modern synthetic chemistry has produced substances as high in the scale as polypeptids, but bodies of more complex molecular structure can still only be obtained from the actual cells as contained in these preparations. Cells crippled by disease or lowered in vigour by fatigue can thus be restored to health, because assimilation of the ready-made proteins is easy, whereas reconstruction from cruder, less elaborated material is difficult and generally beyond their weakened anabolic capacity. There is direct laboratory evidence that cells possess a selective affinity for material harmonious to their structure, i.e. for their own proteins, so that brain cells help to rebuild brain cells, the cells of the spinal cord help spinal cells and so on. Lymphoid Compound and Lymph Serum are:-

1. Powerful alternatives, influencing the inherent processes of cell metabolism.
2. Active cell nutrients.
3. Powerful direct tonics and reconstructors, acting most markedly on the cells of the cerebrum and spinal cord.
4. Correctors of impaired or weakened cell functioning, restoring normal metabolism.
5. Direct tonics to the cells of the endocrine glands, restoring the hormone balance when upset.

In all cases in which there are present

defects of glandular functioning, subnormal functioning of the nervous mechanism, incapacity for physical or mental endurance and malnutrition the Lymphoid Compound and/or Lymph Serum will generally greatly aid in a rapid restoration to the normal. They are held to effect recoveries partly by restoring metabolic equilibrium in the nerve cells, supplying them with the specific proteins they require and aiding assimilation, and partly by re-establishing the hormonal balance by their tonic and stimulating effect on the endocrine glands. also mentioned Atophan preparations. Margulies (1931) gave salicylates in the following forms to different patients:

(a) 20% solution of sodium salicylate.  
100 c.c. intravenously twice a day for five days or more.

(b) Strontisal (strontium salicylate), 40 c.c. intravenously. 5% solution with four .5 gm. tablets orally.

(c) Atophenyl in smaller doses than of sodium salicylate.

The three methods appeared equally efficacious. Of 67 females and 9 male patients, 23.9 per cent. female and 33.3 per cent male were discharged. Temporary improvements, such as loss of stupor and the calming of excited cases, occurred in 50 per cent. Repetition of the treatment gave no improved results.

#### Details of Treatment.

(a) A 20 per cent. solution of sodium salicylate was used, two intravenous injections of 10-15 ccm being given daily. The smallest number of injections

## 2. Salicylate Treatment.

At the forty-ninth travelling meeting of the South-Western Germany Neurologists and Alienists at Baden-Baden in May, 1924, Weichbrodt (170) of Frankfurt-on-the-Main in a lecture of "Therapeutic Experiments in Endogenous Psychoses" drew attention to the success of intravenous injections of a 20% solution of sodium salicylate in quietening excited patients. Among the preparations tested for their effect he also mentioned Atophan preparations. Margulies (171) gave salicylates in the following forms to different patients:-

- (a) 20% solution of sodium salicylate.  
100 c.c. intravenously twice a day for five days or more.
- (b) Strontisal (strontium salicylate), 40 c.c. intravenously. 5% solution with four .5 gm. tablets orally.
- (c) Atophanyl in smaller doses than of sodium salicylate.

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### Details of Treatment.

(a) A 20 per cent. solution of sodium salicylate was used, two intravenous injections of 10-15 ccm. being given daily. The smallest number of injections

given with improvement in the patient was 12, the largest 33. Subjective troubles were not outstanding. Two patients showed a toxic erythema with accompanying urticaria which spread over the whole body and lasted  $1\frac{1}{2}$  and 4 days respectively.

(b) Atophanyl. A particularly intensive and rapid effect is obtained by the simultaneous administration of Atophan and Salicylic acid = Atophanyl. This preparation may be given:-

1. By intravenous injection, ampoules of 10ccm. being used, containing 0.5 grm. ( $7\frac{1}{2}$  grains), of sodium atophan and an equal amount of sodium salicylate in sterile aqueous solution. Five patients stated that they felt a burning sensation along the vein into which the injection had been made. With regard to the vasomotor symptoms that occasionally occur, it is advisable at the first injection to administer only 2-3 ccm. by way of trial and to make the injection slowly, repeatedly drawing back the piston of the syringe so as gradually to mix the Atophanyl with the aspirated blood. In my experience the intravenous administration is here, as always, to be preferred to any other.

2. By intramuscular injection - ampoules of 5ccm. - containing 0.5 grm. ( $7\frac{1}{2}$  grs.) of sodium atophan

### 3. Calcium Treatment.

and an equal amount of sodium salicylate in sterile aqueous solution. Separate ampoules containing 0.025 grm. of novocain (R.T.M.) are included in order that the injections may be painless. As a general rule, the action of atophanyl, particularly the analgesic effect, persists for several hours. One injection daily is usually sufficient, but, if necessary, the dose may be increased to two ampoules per day. The variation in colour of the atophanyl in different ampoules is due to the fact that the contents of some ampoules deepen in colour more than in others. The difference, however, does not effect the quality of the preparation and there is no consequent alteration in either the effect or tolerance of atophanyl.

The action of the salicylates shows itself in two ways. The protein metabolism is increased and thus more carbon dioxide is formed, and, in addition, salicylic acid is formed. This possesses germicidal qualities. (Hall White)

by mouth, for 4, 5, and 6 months. The duration of the disease before treatment was 5, 7, and 3½ years respectively. One patient became less frequently incontinent, but otherwise showed no change. One patient after 4 months of treatment became quieter while the third became definitely less excitable. When treatment was stopped for 16 days this patient

### 3. Calcium Treatment.

From Sägel's (172) investigations on "Intracutaneous reaction of ox-albumin in catatonia and hebephrenia", which in these two forms of disease regularly gave a positive, but in idiots, imbeciles, paralytics and paranoics a negative result, there arose the question of the mode of action of calcium in schizophrenic affections. In Sägel's opinion anaphylactic processes play a significant part in their pathogenesis.

Up to 30 intravenous injections of 10 c.c. of afenil were given to 14 cases by Dodel. (173) The treatment was administered every second or third day. Striking results were reported and in 28.6 per cent. of cases there was mitigation, or prevention, of periodical confusional attacks of excitement. Berndt and Kolle (174) gave the same treatment to 13 cases of all types. Only 15.4 per cent. improved and once case relapsed 9 months later. Rudolf treated 3 female paranoidal cases with collosol calcium with lecithin by mouth, for 4, 5 and 6 months. The duration of the disease before treatment was  $6\frac{2}{3}$ , 9 and  $3\frac{1}{2}$  years respectively. One patient became less frequently incontinent, but otherwise showed no change. One patient after 4 months of treatment became quieter while the third became definitely less excitable. When treatment was stopped for 16 days this patient

again became excitable and renewal of the treatment did not lessen the excitability.

Details of Treatment.

1. Afenil, or calcium-chloride-urea is a preparation of calcium for intravenous administration. It is a double combination of one molecule of chloride of calcium (31.6%) and 4 molecules of carbamide (68.4%) and is sold in ampoules each containing 10 c.c.s of a 10 per cent solution = 0.11 gm. calcium. It will keep indefinitely and is a well tolerated preparation. A few injections, according to the makers, Messrs. Knoll-Ludwigshäfen, bring about the same results as those produced by taking calcium chloride for weeks and even months at a time. It is given intravenously, and if the technique of the injection be scrupulously attended to, it may be regarded as free from pain and risk. The typical burning sensation which frequently accompanies the injection can be almost entirely avoided by carrying out the injection very slowly. Special warning, however, must be given of the risk of necrosis if there is any leakage into the intramuscular or subcutaneous tissues. I have found improvement set in as early as the seventh injection, and that, in cases showing improvement, 30 injections were rarely needed. The injections are given every second day. I have found the intravenous application of Afenil to be always well tolerated, no disturbances being observed apart from an occasional access of heat to the head,

sensation of heat in the mouth or slight cerebral pressure. Variations in blood pressure were of the slightest. Alterations in the urine were not seen, nor was there any noteworthy acceleration of the pulse beat during the injections. These are subjective symptoms, for the rest were merely of a passing nature and disappeared almost immediately on the termination of the operation.

2. Collosol Calcium with Lecithin. In this preparation collosol calcium is combined with lecithin, 1 per cent. It is given by injection, hypodermically, or preferably intramuscularly, 0.5. c.c. to 2 or 4 c.c. daily, or at longer intervals as the case improves.

3. Opocalcium. In cases where it is desirable to prolong the calcium therapy after the course of injections, I have found opocalcium tablets invaluable.

Opocalcium is described as "the most active recalciifying agent in endocrine mineral association. By means of its endocrine mineral composition, optimum remineralisation is ensured, decalcification and demineralisation of the organism being not only due to the lack of minerals in the diet, but also to a deficiency of the endocrine glands. Patients lose their calcium less as a result of a low calcium content of the diet, than as a result of deficient functioning of the organs which control the metabolism of this mineral in the tissues. This deficiency is such that not only

does the patient cease to retain calcium but she actually eliminates the minerals which had previously accumulated in her body.

Therefore to achieve the remineralisation of the body it is necessary to supply it with all the minerals which it may need, not only calcium, but also phosphorus, manganese, fluorine, silicon, magnesium, etc. It is also essential to supply it with the minerals which it can use in totality, and therefore with organic minerals with a biological tendency, and to supply it at the same time with the substances which it needs for the retention of these minerals. Opocalcium fulfils these essential conditions. It contains all the necessary minerals and extracts of parathyroid, adrenal, and thymus glands in addition. It consists of an association of parathyroid suprarenal, thymus, calcium, fluorine, glycerophosphate of lime, triple calcium phosphate, carbonate of lime, magnesium phosphate and manganese nucleinate.

Opocalcium by means of its endocrine mineral composition ensures an optimum remineralisation, decalcification and demineralisation of the organism being not only due to the lack of minerals in the diet, but also to a deficiency of the endocrine glands. Opocalcium tablets are given two tablets thrice daily before meals.

In explanation of the action of Afenil and the other calcium preparations, one might ascribe to the

(control ionisation of calcium)

calcium a checking influence on conditions of excitation of the nervous system. Calcium ions have a general sympatheticotonic effect.

Acidosis generally lowers the calcium level in an organism and also produces hyperexcitability of the central nervous system, which may be countered by alkalinizing the blood. Experimental acidosis also causes histological changes in the cells.

It has been proved that Afenil applications were followed by some decrease in the calcium contents of the blood: it is possible therefore that Afenil transfers some of the calcium in the blood into the tissues.

It has been contended that an acid diathesis predisposes the individual to juvenile ailments.

The investigations of Jansch (175) on the eidetic constitution and of Peritz, who traces a part of the schizothymic dispositions of Bleuler and Kretschmer to spasmophile dynamics of the organism, suggest that the calcium therapy acts by the route of the epithelial bodies. Since the discovery of the parathyroid glands and the isolation of their active principle by Collip, these glands are often considered to be the sole regulators of calcium metabolism. Metabolism as a whole, as well as calcium metabolism, is regulated by an equilibrium between all the members of the ductless gland chain. Briefly the relationship can be summarised in tabular form:-

Parathyroids  
(control ionisation of calcium)

(a) Anabolic group  
(promote retention of calcium)

Anterior lobe of Pituitary  
Thymus  
Gonads  
Suprarenal Cortex?

(b) Katabolic group.  
(increase excretion of calcium)

Thyroid  
Adrenal Medulla?  
Posterior lobe of Pituitary?

The calcium requirements of adult females are somewhat higher than that of males.

Pyrethrotherapy

4. Sodium Nucleinate.

In 1907 Lundvall (176) reported that under ordinary circumstances in schizophrenia there is no decrease in the erythrocytes or increase in the leucocytes, but that there are what are termed "blood-crises" which make their appearance during periodic states of excitement. In the crises the number of red blood corpuscles is reduced and there is an increase in the white-blood cells. In his search for a drug that would promote leucocytosis, he finally selected sodium nucleinate, but because the human organism generally becomes immune to the drug after a few injections, he incorporated other constituents to insure the desired results and gave the following formula:

improvement which very possibly might have occurred later on without treatment".

Quassinisicci	
Depurati (Merck)	g.m40.0
Sodii Nucleatis	gm. 200.0
Acidi arsenosi	gm. 0.1.
Aquae destillatae g.s. ad	c.c. 1000.0

From 2 to 15 c.c. of the above solution were injected hypodermically twice daily. Lundvall did not take into consideration the possible effects of the rise of temperature, other than to show that ordinarily a leucocytosis runs parallel with it. The object of the treatment is to sustain by the smallest possible dosage a leucocytosis for as long a period as possible. During the treatment the patient is put on a highly nutritious diet. The contra-indications for the employment of this form of therapy are cardiac and pulmonary diseases.

Of 25 schizophrenic patients treated in the above manner by Lundvall, 11 were discharged as clinically cured, 2 were regarded as "not quite cured but able to work", 5 patients improved and 7 remained uncured.

Itten (177) in a series of 9 "serious" cases treated by the Lundvall method, observed temporary improvement in 3.. In 1913 Donath (178) reported on 14 cases treated and stated that 57.1% improved and 28.5% recovered. Read (179) recorded his results in the treatment of 10 unselected patients, concluding that "in certain cases it seemed to precipitate an improvement which very possibly might have occurred later on without treatment".

Keatly and Bobbitt (180) "were impressed by the absolute lack of mental improvement" in 4 of 5 patients, the fifth having improved a little for a short period. Kielholz (181) modified the procedure of Lundvall to the extent of employing a 10 per cent solution of sodium chloride. He began treatment with an injection of his solution, the equivalent of 0.5. to 1 gram, gave injections at four to five day intervals until 4 to 5 grams were administered in a single dose. In all from 6 to 12 injections were made, depending upon the temperature and leucocytosis. He summarised the effects in 17 schizophrenic patients. Severe cases of the catatonic type, of more than two years' duration were only temporarily benefited (2 cases) or were not influenced at all (2 cases). Of 9 cases of the catatonic type of less than two years' duration, 4 were discharged as capable of working, shorter remissions were observed in 2 cases and an extensive improvement in 1. Two were uninfluenced. One patient of the paranoid type achieved sufficient improvement to permit his discharge for a short time. Two patients of the hebephrenic form attained states of remission and one improved markedly and was able to work.

#### Details of Treatment.

Nucleinate of soda has for its active ingredient a substance which is a derivative of starch and has the property, when introduced into the body, of increasing the number of polymorphonuclear cells in the

produces. The dose should be regulated according to the degree of the leucocytosis found before injecting and by the subsequent results. The patients selected were examined and a quantitative and a qualitative blood-count made of the white cells. The dose of sodium nucleinate varied from 20 grs. to 1 drm. The drug was dissolved in water and the solution was boiled in order to render it sterile. The strength of the solution was usually half a drachm to one ounce of water. After cooling, the fluid was injected into one or both arms of the patient, the syringe, the operator's hands and the patient's skin being rendered sterile by the usual means.

The result of the injection of an aqueous solution of nucleinate of soda in the skin shows itself in two ways, a local reaction and a general reaction. About three hours after the injection there is a certain amount of discomfort which gradually increases to a maximum at the end of twelve or fourteen hours at which time there is some tenderness, redness, heat and swelling, but reaction is a sterile one, and usually subsides at the end of 36 or 48 hours. Constitutional disturbance was shown by a rise in temperature in every case. The state of the blood and the febrile temperature were evidences of the general constitutional disturbance and a leucocytosis, more or less marked, was found to be produced in all cases.

The disadvantage of the drug is the amount of reaction and consequent pain and tenderness it

produces. The dose should be regulated according to the degree of the leucocytosis found before injection and by the subsequent result.

Introduced by Schroeder in the treatment of general paralysis and other syphilitic infections of the nervous system and later its use was extended to the treatment of schizophrenia. He injected the preparation deeply into the muscles on the outer side of the thigh, preferably between the upper and middle thirds. The quantity used was calculated from the result of previous injections, a rise of temperature of  $104^{\circ}\text{F}$ . or more being desirable. Ten injections were given in each series, the doses being administered twice a week. Two weeks after the termination of the first series, a second was commenced. Two or three series are usually sufficient. Of 3 cases whose treatment was completed, all had returned to their previous work. "One with perfectly normal mentality." He stated that this method of treatment was worthy of an extended trial. Minski (193) treated 20 cases of schizophrenia with sulfosin, 2 of whom recovered, 1 was much improved & had a short remission, 1 became much worse and 15 showed no change.

McGowan and Harthoits (194) gave a report of the results of treatment with sulfosin in a group of 21 cases. The final result was that 15 (71%) was quite unimproved, this including two patients who had shown temporary improvement for a few weeks; five were slightly improved, in that their asocial habits were less pro-

5. Sulfosin.

Sulfosin was first introduced by Schroeder in the treatment of general paralysis and other syphilitic infections of the nervous system and later its use was extended to the treatment of schizophrenia. He injected the preparation deeply into the muscles on the outer side of the thigh, preferably between the upper and middle thirds. The quantity used was calculated from the result of previous injections, a rise of temperature of 104<sup>0</sup>F. or more being desirable. Ten injections were given in each series, the doses being administered twice a week. Two weeks after the termination of the first series, a second was commenced. Two or three series are usually sufficient. Of 3 cases whose treatment was completed, all had returned to their previous work. "One with perfectly normal mentality." He stated that this method of treatment was worthy of an extended trial. Minski (183) treated 20 cases of schizophrenia with sulfosin, 2 of whom recovered, 1 was much improved 1 had a short remission, 1 became much worse and 15 showed no change.

McCowan and Northcote (184) gave a report of the results of treatment with sulfosin in a group of 21 cases. The final result was that 15 (71%) was quite unimproved, this including two patients who had shown temporary improvement for a few weeks; five were slightly improved, in that their asocial habits were less pro-

-nounced, while one recovered clinically and was discharged. This aqueous preparation appears to be capable. From his investigations at the Ranchi Mental Hospital, Dhunjibhoy (185) concluded that there can be no doubt that injections of sulphur in olive oil invariably produce pyrexia, the average temperature obtained being 102.1°F. Pain at the site of injection in every case was unavoidable but certainly bearable. The injections are perfectly safe and can be used for young and old alike. Earlier cases respond better to treatment than the old chronic cases and the earlier the treatment is instituted the greater is the chance of recovery. Out of 44 schizophrenics, 20 improved, 4 recovered, and 20 showed no change. On the other hand, Ceroni (186) states that in schizophrenia little improvement is obtained with sulphur therapy and often none at all.

#### Details of Treatment.

The preparations used have been those of the Crookes' Laboratories, the first product employed being sulphur in olive oil, "Colsul". As the intramuscular method caused some local discomfort, the question arose as to whether this could be reduced by the use of preparations in which the olive oil was replaced by other oils, e.g. peach kernel, cod liver and rape oils, as the suspensory vehicle for the sulphur. Crookes' laboratories are now able to prepare a one per cent aqueous colliodal suspension of sulphur and this,

having been found satisfactory, is now used for sulphur therapy. This aqueous preparation appears to be capable of inducing pyrexias as high as those following the use of sulphur in oil and the local discomfort does not appear to be any more severe. The other general effects of this agent have also been similar. The aqueous has certain advantages over the oily preparation: it is more easy to manipulate into and out of the syringe and the possibilities of oil emboli are eliminated. The scale of doses for the aqueous has been the same as that used for sulphur in oil. A series of injections, generally ten in number, usually at 48 hourly intervals, if the temperature by then has returned to normal, comprise a course of this treatment.

The initial dose given was  $\frac{1}{2}$  c.cm. and increased each time by  $\frac{1}{2}$  c.cm. thus rising to a maximum of 5 c.cm. The outer side of the thigh has been the usual site for injection. A second series of injections has been given in some cases, within three weeks. As a rule the temperature rises gradually, reaching its maximum in about 12 hours and returns to normal in periods varying from 12 - 72 hours.

Temperature charts seem to show that with the later doses of the series, there is an increase of pyrexia, but this is not constant, probably because of the individual peculiarities of response of the thermogenic centres. The duration of the pyrexial period

depends also on the individual. As in other forms of pyretotherapy, many of the charts show secondary rises of temperature following what appears to be the fall from the acme induced by the agent itself. The extent of the pyrexial swing from the subnormal or normal level at the time of injection was also found to vary with corresponding injections in different patients. No bowel disturbance was noted and vomiting, even when it occurs, is of a mild character. Profuse sweating was present in most of the cases. There was very little disturbance of the circulation with such elevations of temperature and this is a very valuable property of this preparation. In all the cases treated, oral sepsis was attended to and obvious local reactions in relation to chronic septic foci were not apparent: rarely does herpes appear with sulphur therapy.

The fact that this stronger aqueous preparation is capable of evoking pyrexias, shows that in these preparations it is the sulphur in colloidal form which is the responsible agent.

I do not employ this form of treatment, for improvement was only temporary and the results are not outstanding. Pyrexia and leucocytosis are not in themselves sufficient to cause mental improvement. It is possible that the treatment is largely, if not entirely, psychological, the physical illness with its pain and discomfort and the incidental nursing attention, interrupting the phantasy life of the patient and forcing reality upon him.

about a week after the termination of the treatment.

6. Malaria.

It was considered that the empiricism which justified the use of malarial therapy in general paralysis was quite as applicable to schizophrenia, particularly if one inclined to the toxæmic hypothesis of its aetiology. It was believed that even a negative result would be of value.

Templeton (187) treated 20 cases of schizophrenia with artificially inoculated malaria of the benign form. He observed a "complete return to normal" in the majority of patients during, and for a short time after, the course of malarial therapy, but at the end of two months, "there were few who had not materially relapsed". He concluded that the results of this form of treatment in schizophrenia were of no lasting benefit.

Hinsie (188) reported that among 13 selected schizophrenic patients of the hebephrenic type, who were subjected to the same technique of malarial therapy, that had been followed in patients with general paralysis, there was no permanent beneficial results in the general clinical picture of any of them. On the contrary, the ill-effects were outstanding. The clinical condition in two patients was rendered worse and two others died.

Aguglia and D'Abundo (189) apparently treated several schizophrenic patients with benign malaria, but they were in a position to report on only one - a catatonic patient, who attained a state of remission

about a week after the termination of the treatment. Wizel and Markuszewicz (190) treated 27 cases. Of these 19 were chronic, and included hebephrenic, catatonic and paranoidal types. No satisfactory results were obtained in the chronic cases, but remissions persisting for several months were obtained in the intermittent types. Successful results were obtained in the 4 acute cases.

Yakubovsky advises therapeutic malaria for early cases only, although one case, with a history of  $4\frac{1}{2}$  years' duration, was able to leave the hospital. This writer obtained remissions in 30 per cent.

Varena treated one hundred and seven cases of dementia praecox with malarial therapy. Of these 32 showed some improvement during the course of treatment, which ceased when the latter came to an end. Two were considered to be much improved and to continue so. In all the others, the method was a failure.

#### Details of Treatment.

The method adopted was that of Wagner-Jauregg. The blood was drawn from the vein of a patient suffering from benign tertian malaria and injected into the subcutaneous tissue in the area between the spine and the scapula of the patient.

As a rule, it is advisable to leave the patient in bed during the incubation period, which is usually 12 days, but may be only 10 days or as long as 26 days. The reasons are: 1. Warmth favours the development of the injection. 2. Rest in bed prevents

It is desirable to abort the attack; this is irregular non-specific rises of temperature. All patients were put on a four-hourly temperature chart from the fifth day after injection. Routine daily blood examination was commenced from the day on which the first febrile temperature was noted. From the day of the first rise of temperature the instructions for taking the temperature were as follows: 1. Note the hour of the day or night at which the rise of temperature occurred on the first day. 2. On the next day, about an hour before that time, begin to take temperatures every half hour. 3. As soon as a rise above normal is observed take the temperature every fifteen minutes and continue to do so throughout the febrile paroxysm until it has fallen to normal. 4. Then resume the four-hourly rule until the next rise. It is only in this way that a correct chart of temperatures can be obtained, and that "anticipation" or "retardation" of the daily paroxysms can be accurately ascertained and recorded. During the developed stage the temperature should be taken every fifteen minutes and if the temperature reaches 105°F. cold sponging should be begun and repeated as often as may be necessary to keep it at or below the above temperature. During this stage, also, blood examination must be made at least once a day, in order to ascertain that the number of parasites is not increasing beyond a safe limit - a thin blood-film stained with Leishman's stain being examined daily.

It is desirable to abort the attack; this is effected by giving one dose of 5 gr. of quinine, the result being usually cessation of fever, with almost complete disappearance of parasites from the peripheral blood, to be followed in from ten to twenty days by recrudescence. No untoward results were experienced during the course of the fever. Epistaxis and vomiting were present in a few cases and herpes ferbrilis in quite a number.

The patients were allowed to have from 8 to 12 rigors.

The attack may be terminated either by giving 10 gr. of quinine three times a day for five days or 5 gr. three times a day for ten days.

Malaria is a disease which primarily affects the red blood corpuscles. The leucocytosis following malaria is of a wholly different nature from that which follows sulfosin, being much smaller in degree and bearing no evident relation to the pyrexial paroxysms. It has been shown that the leucocytosis which follows sulfosin involves a profound stimulation of the bone-marrow and that many of the newly formed corpuscles originate from the reticulo-endothelium. In malaria the haemolysis brought about by the parasites leads to haematopoietic demands of a totally different nature. If it is conceded that the reticulo-endothelium is the ultimate source of the red blood corpuscles then it will follow that with malaria, as well as with sulfosin, this

system is affected. Stress has been laid on a single aspect of sulfosin and malarial therapies in an endeavour to find a factor which is common to them both and the argument has been advanced that both sulfosin and malaria strongly affect the reticulo-endothelium and that possibly other fever-producing agents act in the same way.

Clinical improvement, when this occurs, may be due to changes in bodily metabolism of a general nature than to the development of specific influences inimical to the pathogenic organism.

In sulfosin therapy the resulting neutrophile leucocytosis is a prominent feature of the reaction, while in malarial injection no leucocytosis but a leucopaenia is the rule.

that small doses of the metals have no stimulating action on the injecting organisms and that larger doses do stimulate the pathological process; therefore the deduction is that there is an optimum dose which is not to be exceeded. He has also shown that the more complex salts are inert. The mechanism is thought to be a catalysis of the biochemical defences of the body. Considering the marked effect of salts on proteins and colloid solutions, this explanation seems plausible.

Reiter and Risgaard of Denmark, and Schrijer of Holland each reported fifty cases of dementia praecox treated with manganese chloride with 50 per cent of the cases improved. Stenberg in Sweden, obtain-

## 7. Manganese Chloride.

The earliest reference to this salt in the treatment of the psychosis was published by Reiter and Bisgaard (192) (1927) in Denmark, whose work was inspired by the experiments of Walbum (193), the latter at the state Serum Institute of Denmark, found that the simple salts of heavy metals, increased the antibodies in the blood and that in animals manganese cured or prevented diseases due to staphylococci, and to paratyphoid, Shiga-Kruse, diphtheria and tetanus bacilli. He suggested that cases of schizophrenia should be treated with metallic salts and particularly with manganese chloride.

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-ed the same results but reserved drawing definite conclusions. G. E. Reed (194) treated cases of schizophrenia by intravenous injections of manganese chloride and observed a substantially higher discharge rate among the cases with manganese, than in similar cases not receiving treatment.

#### Details of Treatment.

The patients were put to bed under observation for two weeks: a physical examination, urinalysis, blood count and sedimentation test were made and a clinical record kept. The treatment was then begun and consisted in an intravenous injection of from two to eight c.c. of a 0.02 molar solution of manganese chloride. Thirty injections in all were thus given to every patient in the course of fifteen weeks. They were given 0.3 grams of manganese chloride by mouth twice a day for a month after the intravenous injection was stopped. The amount given was determined by the appearance of a slight reaction, noted by former investigators. This consists in a transitory erythema of the face and conjunctivae associated with a feeling of warmth but not accompanied by any change of the pupils, blood-pressure or pulse rate. A sedimentation test was done during and after the treatment; this is of value in estimating the optimum dose. The clinical record was stopped at the end of the treatment. There was not any marked variation from the normal pulse or

B. Ringer-Locke Solution.

3.

temperature, prior to or during the treatment, which could not be accounted for by some evident condition.

The mechanism of the treatment is thought to be a catalysis of the biochemical defences of the body, an explanation which seems probable considering the marked effects of salts on protein and colloid solutions.

In April 1916 at the annual meeting of the Japanese Neurological Association, held Tokyo University, he published some results of his experience in psychoses with the Ringer-Locke's solution. In the following year (1917) he read a second report dealing with 30 cases of psychoses. By this time he had greatly improved the technique of the method and had constructed a large sterilizing boiler for the preparation of Ringer-Locke's fluid, under high pressure, in order to prevent decomposition of the sodium bicarbonate. The boiler was also furnished with an oxygenating apparatus.

In 1917 Merowaka treated a second series of 14 cases and obtained recoveries in 35.3 per cent.

In 1918 Sato and Morita (196) treated 14 catatonic cases and obtained 35.7 per cent improvements, but there was no improvement in 2 cases of hebephrenia.

In 1922, Ikeda, Superintendent of Tokyo Mental Sanatorium, published an extensive study on the therapeutic effects of Ringer-Locke's solution on the psychoses. He stated the treatment did not produce any effect until after the ninth injection in catatonia and the sixth in hebephrenia.

### 8. Ringer-Locke Solution.

In 1915 Morowoka (195) treated 18 cases and obtained 16.7 per cent recoveries by the subcutaneous injection of 1.000 c.c. of the solution. In acute cases a few injections only were necessary, but the treatment was continued up to two years in some cases. In April 1916 at the annual meeting of the Japanese Neurological Association, held Tokyo University, he published some results of his experience in psychoses with the Ringer-Locke's solution. In the following year (1917) he read a second report dealing with 30 cases of psychoses. By this time he had greatly improved the technique of the method and had constructed a large sterilizing boiler for the preparation of Ringer-Locke's fluid, under high pressure, in order to prevent decomposition of the sodium bicarbonate. The boiler was also furnished with an oxygenating apparatus.

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The catatonics become less irritable, slept better, were better nourished and their delirious states and confusion cleared up when of slighter degree. The hebephrenics also were less irritable, better nourished and often an hallucinosis cleared up. No effects, however, were observed in the paranoidal dements.

Details of Treatment.

The Ringer-Locke's solution was prepared as follows:

Na	9.0
K Cl	0.42
Ca C/2	0.24
Na HCO <sub>3</sub>	0.1
Glucose (Merck)	0.1
Aqua destillata	1000 .0

The solution has to be specially made up in this country, though in Japan, where this form of treatment has achieved much popularity, it is stocked by the drug-stores in ampoules of 500 c.c. sterilised, oxygenated, sealed and ready for use.

I have been in communication with Dr. T. Morowoka, concerning this form of therapy and he specially emphasises the importance of giving large quantities of the Ringer-Locke's solution and of making many injections. My method has been to give 1000 c.c. subcutaneously, twice weekly, the duration of the treatment depending on each case. The site of injection may be changed, for example, from the groins to the back or the flank. As a matter of fact, such large

quantities are absorbed very quickly but the utmost patience is required in making the injections.

So far as is known at present, Ringer-Locke's fluid is the ideal medium for washing and nourishing living tissue, and especially that of the central nervous system. Halliburton has shown this to be the case, and the practical value of the solution - as an artificial cerebro-spinal fluid - has been indicated by its use by students of biology in the cultivation of nervous tissue in vitro.

For a short time prolonged narcosis occupied a position of pre-eminence in the treatment of schizophrenia. Somnifaine was the drug of choice but opinions varied as much as to the propriety of its administration that it was used, if at all, with extreme caution. It was claimed that particularly in states of schizophrenic excitement, the induction of prolonged narcosis proved highly beneficial in quietening the excitement and also in producing, in some cases, a remission of the symptoms. Many investigators, however, soon turned their attention to the

method gradually fell into disrepute and prolonged narcosis as a form of treatment remained in abeyance until 1929. An attempt at revival was made in 1915 by Eklund (1915) with sodium luminal but it was not until Klasi's (1929) work on somnifaine narcosis was published that the treatment was put on a firmer basis.

### 9. Narcosis Treatment.

principle, rather than to the drug itself, because of the harm.

Treatment of mental disorder by prolonged narcosis was originated as long ago as 1901 by Wolff (197). In that year he published a paper in which he described the results obtained in 3 cases of acute confusional insanity using trional over a period of twelve days. His work had, on the whole, a poor reception, partly owing to the toxic risks that were encountered, and partly also on account of the inherent prejudice of the medical profession at that time, against the use of narcotics for such purposes. The method gradually fell into disrepute and prolonged narcosis as a form of treatment remained in abeyance until 1920. An attempt at revival was made in 1915 by Epijanio (198) with sodium luminal but it was not until Kläsi's (199) work on somnifaine narcosis was published that the treatment was put on a firmer basis.

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principle, rather than to the drug itself, because of the harmful effects that were observed in the use of somnifaine. The drug has been rejected by several because of its unreliability of action and its harmfulness, it being claimed that its effect on the heart is sometimes extremely severe.

In 1920 Liebmann (200) of the Zürich Medical Clinic, had begun to use somnifaine in the symptomatic treatment of such disorders as delirium tremens, tetanus and insomnia and had found it of great value, the drug proving safe for these purposes and showing little tendency to accumulate. This led Kläsi to try the drug for prolonged narcosis in schizophrenia. In 1922 he published the results of treatment of 26 cases, and claimed that one quarter to one third of the cases improved to such an extent that they were either discharged or transferred to convalescent wards. This assertion from a man of Kläsi's reputation caused many notable psychiatrists on the Continent to give somnifaine narcosis a trial, and during the following years a wealth of literature on the subject appeared. The opinions expressed therein were somewhat at variance. Some authors, Werner (201), Moser (202), and Möllenhoff (203) regarded the treatment as unreliable and dangerous, whereas others, notably Demole (204), Wyler (205), Furrer (206) and Gjessing (207) and Lingjaerde were enthusiastic and reported good results.

Müller (208) in 1925 published a critical

survey of the literature up to that date and included therein an account of 24 cases personally treated. His attitude towards the somnifaine treatment was severe and he endorsed the view of other observers that Kläsi was far too optimistic. He agreed that with prolonged narcosis, one obtained results which no other remedy gave, but stated that, while the principle of this form of treatment undoubtedly had ensured for itself a place in psychiatric therapy, somnifaine could not be regarded as the ideal remedy owing to its dangers. He also pointed out that prolonged narcosis and somnifaine are not inseparably linked, and stated that prolonged narcosis as a principle is valuable for the reduction of marked states of excitement, but in cases of long standing the results are less likely to be effective. It was claimed that those schizophrenic patients who exhibited periodicity in their reactions, were the ones in whom the better results were to be expected.

Against this view came the work of Oberhölzer (209), who, during a period of three years, carried out 186 narcoses on 92 patients in the Burghölzli Clinic in Zürich. In his opinion prolonged narcosis had at that time (1927) fallen into disrepute largely because its therapeutic significance had in many places been overlooked and its dangers overestimated. Complications, however, were abundant in Oberhölzer's cases, and, although no fatalities occurred, he was compelled to cut

short the treatment in many of them. In England somnifaine therapy was first tried at the Maudsley Hospital in 1924, the results being published by Dawson and Barkas (210).

Since the introduction of sodium amytal in about 1926 it has gained wide spread use in medicine. Its use in psychiatry was investigated shortly after its introduction by Bleckwenn (211) in 1930 as a producer of narcosis. He records his experience in the treatment of 15 catatonics. Palmer and Paine (212) treated a number of psychotic patients, employing two techniques:

1. With pheno-barbital.
2. With sodium amytal.

Their aim was to produce deep unconsciousness approaching so far as possible normal profound sleep. The first consisted of the administration of pheno barbital and sodium barbital, followed by a course of chills and fever induced by typhoid vaccine. The preparations of barbital were given both orally and intravenously in a dosage sufficient to produce narcosis for a week or ten days. The second regimen consisted in giving 15 grains (1 gm.) of sodium amytal in a 5 per cent solution intravenously, at a rate of injection of 1 c.c. a minute. The injection was given daily at 9 a.m. and the same preparation was administered orally in tablet form during the day, in order to ensure persistence of the narcosis. Twice a day the patient was permitted to remain awake for feeding and evacuation. The in-take of

fluid is maintained at 3 litres daily and the amount of food at 3,000 calories daily. Narcosis was continued for from 7 to 10 days, with the exception of the two and a half hours' intervals daily for the purpose of attending to nutritional needs and evacuations.

Bleuler, Bohn and others also speak of the beneficial action of drug produced "narcosis" and "semi-narcosis" in the treatment of psychiatric cases. In 1933, Meerloo (213) collected sufficient clinical material regarding barbital intoxication to make it possible to draw conclusions, while sifting the complications, in regard to the action, point of contact and so forth, of the barbitals. Within the limits of psychopathology, this sedative must be considered as a specific poison, which induces and affects local biological processes, but at the same time as a non-specific factor which only lays bare a more deeply buried psychic structure. Clinically speaking, we may resolve the action of the barbitals to the action on the sub-cortical brain centres, the brain stem in its widest sense. Pathologico-anatomical discoveries support this. The secondary phenomena produced by barbitals, such as catatonia, epilepsy, hallucinations, etc., are of interest to psychopathology in that they constitute a contribution to our knowledge of the function of the space encephalon. Meerloo states that prolonged treatment of psychotic patients with barbitals is of great therapeutic value.

therapeutic value. The effect of this may be compared with that of non-specific stimulant therapy. Sudden disintoxication is an important factor here and sleep constitutes no very real element. A dangerous secondary action is to be guarded against.

Efforts to induce extended narcosis with other drugs have been made. Oppler (214) reported his results in the case of trional in 12 cases of catatonia in their first attacks. Each was given as much as 20 grains a day, for from five to eight days. In only six patients, however, was he able to induce sleep: the remaining six patients were too restive to be given a sufficient quantity. Three of the satisfactorily treated patients attained quiet states for a long period and three improved sufficiently to leave the hospital. Oppler felt that trional was a safe drug with which to produce protracted narcosis.

Wright (215) reported that resistive highly negativistic and disturbed patients were rendered co-operative and were in a much better condition for the introduction of further therapeutic measures ( e.g. occupational therapy), by the use over a considerable period of sodium bromide to the point of producing a state of drowsiness. He said: "When one regards the drug as an aid to therapy rather than as a panacea, a better appreciation of its value will be had".

Details of Treatment.

Details of Treatment.

1. Somnifaine. This drug is an aqueous solution of a combination of diethylamine with diethyl dipropenyl barbituric acid. The usual preparation of somnifaine is in the form of 2 c.c. ampoules and the method of treatment is as follows. In the pre-narcotic stage the patient is put to bed in a quiet darkened room. It should be borne in mind that sustained narcosis temporarily lowers the body resistance when accidental contaminations may possibly endanger life. A physical examination is made in order to rule out pulmonary or renal involvements. Minor cardiac insufficiencies, if present, call for a digitalizing regime before sustained sleep is begun. Likewise rectal disorders need corrective measures to facilitate homogenous retention of medications and feedings. An enema is given before treatment is started. Intelligent co-operation of the nursing staff is essential and measures must be taken to ensure quietness. Specimens of urine are collected daily and sent to the laboratory for examination. It is essential that such specimens should be as fresh as possible owing to the importance of detecting acetone bodies. Temperature and pulse readings are recorded every four hours. The blood sedimentation is estimated. The diet throughout the course should be entirely fluid. The reasons for this are obvious;

as variable, some persons require comparatively small doses of morphine and sleep well the greater part of the time, or they may develop toxic symptoms after only a few injections. Others require larger quantities to induce a satisfactory narcosis, and, despite this, may remain practically free from complications. Constant observation is necessary and the dosage must largely depend on the amount of sleep obtained and the physical condition of the patient. Restless and excited patients, as a rule, require larger doses than quiet and cooperative ones; in fact, in some cases, it may be impossible to induce a satisfactory narcosis at all. In such instances it is advisable to cut short the treatment rather than continue injecting large quantities of the drug. No hard and fast rule can be laid down about maximum dosage, this depending to a great extent on individual sensitiveness, but more than 3 c.c. in 24 hours must be regarded as dangerous. The duration of the treatment averages 14 days, but shorter periods were used in milder cases. The length of narcosis then on, an average of 5 to 6 c.c. in twenty-four hours were administered to subjects in robust health, a quantity which was adequate for the production of a fairly deep narcosis. Injection at regular intervals is not advocated; indeed, such a practice would be impossible, because the reaction of each individual to the drug is

Treatment was commenced with a dose of 2 c.c. which proved quite sufficient to induce sleep. From then on, an average of 5 to 6 c.c. in twenty-four hours were administered to subjects in robust health, a quantity which was adequate for the production of a fairly deep narcosis. Injection at regular intervals is not advocated; indeed, such a practice would be impossible, because the reaction of each individual to the drug is

The following are conditions necessitating

so variable, some persons require comparatively small doses of somnifaine and sleep well the greater part of the time, or they may develop toxic symptoms after only a few injections, others require larger quantities to induce a satisfactory narcosis, and, despite this, may remain practically free from complications. Constant observation is necessary and the dosage must largely depend on the amount of sleep obtained and the physical condition of the patient. Restless and excited patients, as a rule, require bigger doses than quiet and co-operative ones; in fact, in some cases, it may be impossible to induce a satisfactory narcosis at all. In such instances it is advisable to cut short the treatment rather than continue injecting large quantities of the drug. No hard and fast rule can be laid down about maximum dosage, this depending to a great extent on individual sensitiveness, but more than 8 c.c. in 24 hours must be regarded as dangerous. The duration of the treatment averages 14 days, but shorter periods were used in milder cases. The length of narcosis aimed at was ten to fourteen days, this being prolonged to sixteen days in a few cases. Frequent and careful observation of the patient is necessary in order to detect the premonitory signs of serious intoxication, but if insulin and glucose are given serious complications do not as a rule occur.

The following are conditions necessitating

## 10. Vitamin Therapy.

The progress made in recent years in the study of vitamins has been phenomenal in that many disorders previously regarded as of infective origin have been shown to be due to a deficiency of one or more of the vitamins. The immediate stoppage of the drug, whether temporary or permanent.

1. Tachycardia with a fall of more than 25 mm. in the systolic blood pressure: premonitory of circulatory collapse.
2. Ketonuria.
3. Pyrexia over 100°F., in which case stopping the drug for 6 to 12 hours usually suffices.
4. Persistent vomiting. In such cases ketosis and other toxic symptoms readily supervene.
5. Dusky complexion, shallow breathing and extreme drowsiness.

Simultaneously with each dose of somnifaine 10 - 15 units of insulin are injected hypodermically and an ounce or more of glucose given by the mouth.

on the skin have been shown to arise from the capacity of the cells of the sebaceous glands of the skin to manufacture under these influences, from the various sterols they contain, a substance - Vitamin D - which is then picked up by the blood stream and distributed throughout the body. The second source is the fat taken in the diet, butter and cream being particularly rich in this respect. It has also been proved that food exposed to ultra-violet radiation acquires in an added degree the capacity to ward off the ill-effects of the Vitamin D deficiency. The third, and from the point of view of accurate laboratory control, the most important source, is that in the form of ergosterol, a compound related to cholesterol, produced by

## 10. Vitamin Therapy.

The progress made in recent years in the study of vitamins has been phenomenal in that many disorders previously regarded as of infective origin have been shown to arise from deficiency of some particular item of the diet, which quantitatively is infinitesimal in relation to the total bulk of food taken. Vitamin - fat soluble D - has been isolated in pure form and has acquired a chemical formula. This vitamin has a powerful influence in the prevention and cure of rickets; and its relation to dentition and caries of the teeth has been established by careful and prolonged experiment. Vitamin D can be obtained by the body from at least three different sources. The effects on health of sunlight and ultra-violet rays on the skin have been shown to arise from the capacity of the cells of the sebaceous glands of the skin to manufacture under these influences, from the various sterols they contain, a substance - Vitamin D - which is then picked up by the blood stream and distributed throughout the body. The second source is the fat taken in the diet, butter and cream being particularly rich in this respect. It has also been proved that food exposed to ultra-violet radiation acquires in an added degree the capacity to ward off the ill-effects of the Vitamin D deficiency. The third, and from the point of view of accurate laboratory control, the most important source, is that in the form of ergosterol, a compound related to cholesterol, produced by

substance, but is probably a mixture of substances of similar nature. They found that, if after irradiation extraction from yeast and other substances. Ergosterol can be obtained in more or less pure form, and after being subjected for a definite time to irradiation by ultra-violet rays becomes converted into a substance which has all the effects of Vitamin D.

At present little is known of the causative relation of any vitamins to mental and nervous disorder, but it is known that a form of multiple neuritis is part of the symptomcomplex of beri-beri, arising from deficiency of the water-soluble vitamin B.

Vitamin D is not to our knowledge associated with any dysfunction of the nervous system, unless it be that the irritability and general nervous restlessness arising from prolonged exposure to sun-light or ultra-violet rays is due to excess production of it in the skin, with possible toxic effects. The pressure of cholesterol in all cells of the body, and especially in the cells of the brain and nervous system, has for a number of years focused our attention on this substance. On the whole, the results of these investigations have been unsatisfactory, but perhaps the most significant observations in this connection have been the finding of cholesterol or excess of cholesterol in the cerebrospinal fluid in destructive brain affections.

Rosenheim and Webster have shown that ordinary cholesterol as we know it, is not a pure chemical

substance, but is probably a mixture of substances of similar nature. They found that, if after irradiation, cholesterol was subjected to a separation process, a highly active fraction could be identified which would effectively prevent or cure rickets in rats, and that the cholesterol residue had no such effect. It is possible therefore that the previous work on cholesterol would have been more productive of results in relation to mental disorder had it been possible to take other, more known, similar chemicals, into account. Glen-Duncan states that "therapeutically induced diminution of blood-cholesterol acts on the nervous system, in some cases at least, as a stimulant, causing increased mental activity. Therapeutic raising of the blood-cholesterol acts on the nervous system, in some cases as a sedative, causing diminished mental activity". It is concluded, therefore, that cholesterol is one of the controlling factors of cellular metabolism, and that nerves are susceptible to quantitative changes of this substance in their environment.

Although irradiated ergosterol cures rickets, the practical importance of Vitamin D is by no means limited to the prevention of dental caries, but applies also to other ill-defined conditions causing greater or less ill-health and suffering. The undoubted effect of sunshine on general health, nervous stability and mental ease is too well known to be emphasised here.

It has been demonstrated that Vitamin D has

a definite effect on certain blood reactions that occur in mental disorders, more especially in schizophrenia. Not only is this so, but the same effect is found when there is an apparent sufficiency for the normal body needs of Vitamin D obtained from natural sources. These observations were made by testing the effect of certain substances on the haemoclastic crisis which is found to occur in a proportion of cases of mental disorder. Rees Thomas (216), from many careful experiments, concluded that irradiated ergosterol causes a reversal of the abnormal blood reaction known as the haemoclastic crisis, in cases of schizophrenia and that the dose required to establish a permanent reversal is 2 mgrm. (1.33 gr.). There was no evidence in control cases of any deficiency of Vitamin D obtained from the skin and from the food supplied. He found that ultra-violet radiation does not increase the production in the body of Vitamin D sufficiently to produce a reversal of the reaction, and the quantity thus provided appeared to be roughly equivalent to 1 mgrm. of irradiated ergosterol. The vital significance of this vitamin to the body economy suggests the possibility of some relation between it and mental disorder, either directly or through some yet unknown function of the liver.

The results obtained at the Maudsley Hospital, showed that a haemoclastic crisis occurred in 94

per cent of schizophrenics.

In 1927, Rudolf (217) treated 10 female and 2 male cases with Vitamin D the substances used being radiostol, radiostol with liver extract, irradiated milk and ultra-violet irradiation. Two female paranoidal cases were treated with 10 drops of radiostol thrice daily for 2 months. In one patient, with a history of  $3\frac{1}{4}$  years, no change occurred. In the other, of  $3\frac{1}{2}$  years' duration, a definite change took place, in that the patient became more noisy and impulsive and refused to work. Noisy and impulsive behaviour occurred whilst under the treatment, on the cessation of same, she returned to her previous condition.

Radiostol (10 drops thrice daily) with liver extract representing  $\frac{1}{2}$  lb. of liver once a day, was given for 2 months to one female paranoidal case with a history of 9 years and to one female catatonic case with a history of  $5\frac{1}{2}$  years' duration. The paranoidal case showed no change. The catatonic, who was previously mute, became brighter and answered when addressed after one month's treatment. The brighter outlook persisted after the termination of the treatment.

One catatonic female and two paranoidal female cases (duration  $4\frac{1}{4}$ ,  $5\frac{2}{12}$  and  $7\frac{11}{12}$  years, respectively) were treated for 2 months with irradiated milk. No

change taking place. A female catatonic patient (duration 6 years) was treated for 4 months and became brighter, beginning to work and to speak. Towards the end of the treatment, she gradually reverted to her former condition. The changes observed were only temporary.

Two male patients, one hebephrenic, and the other paranoidal, were treated by exposure to a four arc ultra-violet lamp with iron-cased electrodes. The improvement, again, was only temporary.

#### Details of Treatment.

1. Radiostol. Radiostol was originally the total product of the irradiation of ergosterol, but as a result of later investigations (Proc. Roy. Soc. B. 1932, 109, 488), it was isolated from this total product in the form of pure Vitamin D, a substance of definite crystalline structure and chemical constitution, possessing 40 million international units of antirachitic activity per gramme. This pure substance is employed in making Radiostal Solution and Radiostol Pellets. In the B.P. 1934, irradiated ergosterol which finds a place under the name *Liquor Ergosterolis Irradiati*, is standardised to contain 3000 international units of anti-rachitic activity per gramme. Radiostol Solution is now in exact conformity with the B.P. preparation: moreover, as it is prepared with the pure crystalline substance, its activity is adjusted much more precisely than is possible when

ordinary irradiated ergosterol is employed.

Radiostol was given:

1. In the form of pellets, each equivalent to millilitre 15 minims of the solution. One pellet was given twice daily.
2. Liquor Ergosterolis Irradiati, made by submitting a solution of ergosterol to the action of ultra-violet rays from mercury vapour lamp. This was given in ʒ dram doses, thrice daily.

2. Cavodol. Cavodol is copralated cod liver oil extract tablets containing colloidal copper and metallic iron with the concentrate of cod liver oil biologically assayed to a potency of 1,000 vitamin A units and 500 vitamin D units. The fact that copper favours the utilisation of iron by the blood has been frequently demonstrated. It acts as a catalyst in the chemical combination of iron with haemoglobin. A superiority is achieved in Cavodol Tablets by the use of colloidal copper in association with iron, rather than the commonly used copper salts. Colloid metal solutions act in the same manner as true ferments, they are indeed highly effective catalyzers. They are stored by the liver and other organs and exert a slow continuous action over long periods. Due to the slow diffusibility of colloids and their lower rate of excretion, a smaller dosage is sufficient than is required with the salts of the metal. Colloids are substances not foreign to the human organism. Indeed, enzymes are colloids, and the living cytoplasm is mainly composed of negative charged colloids. With the administration of Cavodol Tablets the patient is

is assured maximum utilisation of the iron content of the tablet. In addition, Vitamin A, the so-called anti-infective vitamin, serves to build resistance and increase bodily vigour, while the anti-rachitic vitamin D prevents abnormal conditions of the bones and teeth. Cavodol tablets are supplied in two forms:

1. Cod liver oil extract tablets containing A and D Vitamins, iron and colloidal copper.
2. Cavodol cod liver oil compound tablets with A and D vitamins. One to two tablets are given thrice daily.

In two Cavodol tablets the patient receives the equivalent of one tablespoonful of finest cod liver oil. Each tablet contains 1000 units Vitamin A and 500 Units Vitamin D; stimulating bone and tissue metabolism and strengthening the defence forces of the organism.

The anti-infective powers of Vitamin A have been demonstrated particularly by Mellanby. Cramer also pointed out that this vitamin maintains the mucous membrane in a state of physiological efficiency, preventing bacterial invasion. Vitamin D, the "anti-rachitic vitamin", is stated by Mellanby to be the master key to bone calcification.

In addition to their vitamin content, Cavodol tablets provide calcium iodide to guard against deficiency of this mineral and to ensure proper calcification and growth; berberin sulphate for its alternative properties, so valuable in the treatment

of cachexias; reduced iron, a readily absorbable chalybeate; and extract of gentian for its stimulation of gastric digestion. These accessory nutritional factors favour the complete absorption and utilization of the vitamin element by the organism.

Therefore, Cavodol tablets are a reconstructive and tonic of the first order. They restore vigour and strength, give needed stimulation to nutritional processes, accelerating the work of repair; they alter pathological courses and effect a salutary condition without adding to the digestive burden.

3. Ultra-Violet Radiation. The use of actino therapy in mental treatment was debated at the Royal Society of Medicine in 1929 (218) by officers of mental hospitals. According to Dr. Cormac "actino therapy is a very necessary adjunct to the treatment of mental cases. It is employed as a routine for convalescent cases, whose recovery is thereby hastened". Open carbon arc lamps were used, by which light baths were given to the skin directly without the intervention of filters. Care was taken to avoid pigmentation of any degree. The carbons were generally about three feet from the ground, on a level with the chins of the patients seated on chairs in front of them. The distance of the individual patients was, on an average, about 18 inches.

The general effect of sunlight on the body is to stimulate metabolism, improve both the appetite and digestion, cause an increase in the body weight and to act as a general tonic. The general blood-pressure

and the force of the heart-beat are increased by it and the pulse is slowed. It is held by some authorities that the exhibition of these rays is even more beneficial to the body than those of the sun itself, in as much as they can be administered with greater accuracy and contain a greater intensity of the beneficial rays with an absence of any harmful rays.

Mennesheimer (219) explains the process as follows: "The skin is conceived as a gland with internal secretions which are of importance in the defensive mechanism of the body, ('esopylaxis'). Under the stimulus of actino rays the walls of the skin cells in the absorbed layers become permeable and substances pass from the activated cells outwards into the blood. These substances (the so-called 'detoxin') consist of tyrosin and other amino-acids. They promote increase of antibodies in the blood. Other substances transmitted from the irradiated skin-cells into the blood resemble histamine in their action". The general systemic changes were summarized by Professor W. E. Dixon of Cambridge as follows: "mild stimulation of the medullary centres, slight increase of the pulse rate and stimulation of respiration." There is an increased activity of the tissues as shown by an augmented power of phagocytosis of the leucocytes, and, as mentioned by Leonard Hill (220) the haeme-bactericidal power of the blood is enhanced. Lastly, actinic irradiation creates Vitamin D in the human body, raises

11. Removal of Sepsis, etc.

I propose to only touch briefly on this subject here the serum content of calcium and phosphorus and promotes the fixation of these minerals in the body.

In certain cases of nervous diseases and especially in insanity, it has been shown that the phosphate ratio is lowered. As the exposure of the whole body to ultra-violet radiation raises the phosphorus content, it would appear that there are definite uses for it in the nervous system. A familiar local effect produced is pigmentation and this may be a reaction in some way related to endocrine balance.

The mercury vapour lamp was used for a certain percentage of cases. While the carbon arc was used mainly for its effects on the nutrition of debilitated patients, the mercury vapour lamp was used for affection of the skin and for debilitated cases which were too ill or otherwise unsuitable for transport to the principal treatment centre.

The alleged "proven relationship" of sepsis and mental disorder, which among whom are Henderson and Menzies. The fact that chronic sepsis is as common in the sane as the insane, and the difficulty of determining in any particular case whether a focus of sepsis is causative or incidental, constitutes the core of the problem. Henderson says: "It is very dangerous to state that because something (a septic focus) existed in a given mental case, that something was the specific agent". Also, "many a healthy abdomen has been mutilated and many a serviceable tooth removed as the result of ill-grounded theories of the aetiology of mental illness".

11. Removal of Sepsis, etc.

I propose to only touch briefly on this subject here. The theories are many and varied and the subject has derived a wide range of publicity from the efforts of Cotton in America and Graves in this country. The rôle of focal sepsis as a causative factor has received increasing attention since Cotton (221) published his results in 1923. He reported on "the successful treatment of 1400 cases during the years, 1918-1921, with only 42 return cases now in hospital".

In England workers in this branch of medicine, while unable to report the striking therapeutic results of Cotton, have confirmed his main contention that many acute and subacute psychoses seem to be intimately related to some focus of sepsis. This confirmation has come from Graves (222), Chalmers Watson (223) and Hunter and Moynihan (224). On the other hand prominent psychiatrists have called in question the results claimed and alleged "proven relationship" of sepsis and mental disorder, chief among whom are Henderson and Menzies. The fact that chronic sepsis is as common in the sane as the insane, and the difficulty of determining in any particular case whether a focus of sepsis is causative or incidental, constitutes the core of the problem. Henderson says: "It is very dangerous to state that because something (a septic focus) existed in a given mental case, that something was the specific agent". Also, "many a healthy abdomen has been mutilated and many a serviceable tooth removed as the result of ill-grounded theories of the aetiology of mental illness".

Holmes (225) stated that there is a "toxic molecule in the calcium, which molecule, by a selective process, acts upon the brain to produce the mental symptoms and later the histopathologic lesions of dementia praecox". Holmes cited one case at length to support his theory.

Robertson (226) was of the definite opinion that dementia praecox patients formed "a special type of inherent defective resistance to the action of bacterial toxins". He reported his results as "very encouraging" and attempted therapeutic immunisation against the bacterial toxins.

There are many others in support of the theory whose views need not be referred to here. Bleuler (227) was exceedingly ambiguous in reference to this subject. "Neither the grip nor the war has added to the existence of schizophrenia.

#### Method of Treatment.

1. Dental Treatment. All new patients are examined as soon after admission as their condition permits. Increasing use is being made of radiography to localise buried roots and unerupted teeth and in several cases these have been found in mouths otherwise apparently edentulous. At times these buried roots, when they are related to the antrum of Highmore, have been proved to be, in the mentally disordered, as well as in normal persons, the cause of continued suppuration within that cavity. The use of antistreptococcal serum has been continued in the treatment of the mouths of several cases,

with satisfactory results.

Many of the patients' mouths showed acute gingivitis, large deposits of hard and soft calculus, pyorrhoea - either general or localised - and dental caries. As regards the last named, there is not noticed the rapid type in the chronic cases of mental disease, in spite of the fact that the patient is, in many cases, unable to pay due attention to oral hygiene. The chief pathogenic feature is the unhealthy gums leading up to suppurative inflammatory conditions, and, in some cases, to stomatitis, occasionally of the ulcerative type. Dental radiographs are very useful in the diagnosis of doubtful and obscure cases of oral sepsis. Films of the Bite-Wing type are also taken, as these show up deep interstitial caries six months or more before it would otherwise be discovered.

Investigation for and treatment of diseased conditions of the ear, nose, and throat, is also carried out. In the case of gynecology, patients who have required it, have been examined and reviewed in connection with their gynecological treatment. Conditions of chronic endocervicitis have been treated with the electric cautery for multiple punctures and radial cauterisation and this has produced excellent results. Routine antiseptic douches and pessaries have also been used.

Bowel Lavage. Treatment in general is carried out on the following lines. An initial dose of calomel, given in a single dose of 2 gr. at night, followed by

a morning saline repeated on one or two occasions. In two or three days, intestinal lavage is commenced, from two to three pints of plain water being employed at blood heat. It may be employed as a single wash-out for a day or two, or as a double wash-out, this procedure having diagnostic value, as well as being therapeutically beneficial. The frequency and duration of lavage depends upon the results observed. In some cases the condition rapidly improves, when the lavage may be dispensed with or adopted intermittently after a few days or a week or so. The success of the treatment has to be judged by its influence on the reduction and disappearance of the foetor of the stool, the double wash-out by its influence on the urine and especially on the bacteriuria and the general condition of the patient. Autogenous vaccines may be prepared with benefit from the organisms obtained from the culture.

Similar methods of investigation were carried out by Langenbrass (231). Twelve stuporous tetanics were treated by the Loewenhart method. Five patients only showed a transient period of responsiveness that lasted from twenty to thirty minutes. In these cases no lasting improvement of the clinical picture was observed.

D' Elmosux and Galozon (232) administered gaseous mixtures containing from 5 - 35 per cent of carbon dioxide and from 20 - 40 per cent of oxygen, the remainder being nitrogen. They stated that no single

## 12. Carbon Dioxide Mixture.

In 1916, Loevenhart (228) found that sodium cyanide, an intravenous injection, stimulated the respiratory centre in man. In one case of schizophrenia, a patient who had been mute for several months, made a few relevant and coherent responses to simple questions. In 1929 cerebral stimulation (229) was produced by a mixture of 10 per cent carbon dioxide and 90 per cent oxygen and the strength was increased until a final concentration of 30 to 40 per cent of carbon dioxide was reached. Patients who had been mute and inaccessible for long periods of time carried on conversations. Loevenhart observed that these investigations can be linked up with the work of Golla, Mann and Marsh (230) which shows that in certain psychotic subjects there is a marked reduction in the sensitivity of the respiratory centre to carbon dioxide. Similar methods of investigation were carried out by Langenstrass (231). Twelve stuporous catatonics were treated by the Loevenhart method. Five patients only showed a transient period of responsiveness that lasted from twenty to thirty minutes. In these cases no lasting improvement of the clinical picture was observed.

D' Elseaux and Solomon (232) administered gaseous mixtures containing from 5 - 35 per cent of carbon dioxide and from 20 - 30 per cent of oxygen, the remainder being nitrogen. They stated that no single

factor, whether it be acidosis, CO<sub>2</sub> tension, etc., appeared sufficient to explain the temporary arousal from stupor. The fact that the procedure is a shock to the system appeared to play a part; several patients expressed a wish not to die. They consider that a variety of psychological factors enter into the problem and may alter the response.

Hinsie and others (233) treated cases of schizophrenia by continuous oxygen administration in chambers and oxygen and carbon dioxide inhalations. Five patients resided continuously for  $2\frac{1}{2}$  months in an oxygen chamber at a concentration of approximately 50 per cent oxygen. During this time they received treatments of carbon dioxide and oxygen daily. After each carbon dioxide inhalation, attempts were made to establish communication with the patients. Two of the five gained a state of remission and the clinical history of these had indicated a favourable prognosis. A second group of five patients were treated similarly except that no attempts at communication were made. None of these showed improvement. A third group of five resided in the oxygen dormitory without carbon dioxide treatment and without attempts at communication. None of these showed any improvement.

A fourth group of five living under normal atmospheric conditions were given daily inhalations of carbon dioxide and oxygen. Here one showed a clinical improvement but did not gain a remission. The blood

After  $\text{CO}_2$  inhalation there is an increase of chemical studies showed no effect of long continued oxygen inhalation on the urea nitrogen, uric acid or blood sugar content of venous blood. Basal metabolic determinations varied so much that no consistent conclusions could be drawn. Under various psychological tests no consistent improvement was observed in the patients who did not gain a remission. From observations made, it does not appear that oxygen and carbon dioxide treatment of catatonic dementia praecox patients is to be advocated as a general therapeutic procedure.

#### Details of Treatment.

The patients were allowed to breathe a mixture of 40%  $\text{CO}_2$  and 60%  $\text{O}_2$  for a matter of 2 - 3 minutes. They were then allowed to breathe room air or  $\text{O}_2$  mixed with room air and their responses noted.

The experiments of Cobb and Forbes have shown by the use of a glass window put into the skull of an animal, that when relatively small percentages of  $\text{CO}_2$  are breathed, there is a marked dilation of the cerebral vessels. Similar effects have also been shown to be produced by the use of higher concentrations of  $\text{CO}_2$ . It may therefore be concluded that, by the use of this method, there is stimulation of the medullary centre of respiration, an increase of the  $\text{CO}_2$  and  $\text{O}_2$  content of the blood, an increased flow of blood, dilation of the cerebral vessels and an increase of the intracranial pressure.

After  $\text{CO}_2$  inhalation there is an increase of the  $\text{CO}_2$  content of the blood, the  $\text{CO}_2$  content being 69.27 volumes per cent, which compares with the average normal content of 40 to 45 volumes per cent. Therefore, there is a marked increase in the  $\text{CO}_2$  content. The blood also showed an  $\text{O}_2$  saturation of 97.10 per cent which compares with the theoretical normal  $\text{O}_2$  saturation of about 95% breathing room air. The  $P_{\text{H}}$  of the arterial blood was 7.08. The average normal  $P_{\text{H}}$  of the blood is 7.3 to 7.5, whereas a  $P_{\text{H}}$  of 7.0<sup>0</sup> or less is not consistent with life. Therefore this mixture produces a marked drop in the  $P_{\text{H}}$  of the blood, and there is therefore rapidly produced a condition of acidosis associated with an increase in the  $\text{O}_2$  and  $\text{CO}_2$  content of the blood, one effect of this acute acidosis being the unconsciousness which is comparable to the unconsciousness occurring in diabetic acidosis.

The hypothesis of the action of  $\text{CO}_2$  is based on the assumption that in stuporous patients there is a reduced activity of the cerebral neurones, and that this possibly is dependent upon an interference with the normal metabolic activity of the cell, either in the anabolic or catabolic phase. When  $\text{CO}_2$  is inhaled there is possibly a further lessening of this metabolic activity in the lessened activity of the neurones and in the clinical manifestation of a loss of consciousness. With the cessation of the administration of  $\text{CO}_2$  the processes referred to are released from interference with the result that they seek the point

### 13. Miscellaneous Forms of Therapy.

In this section are described various of equilibrium maintained previous to CO<sub>2</sub> inhalation. In so doing they are necessarily speeded up and may overslip the previous point of equilibrium, i.e. approximate or more normal degree of metabolic activity with a consequent more normal degree of nervous activity shown by more normal contact with their environment. As the effects are only temporary, the original point of metabolic equilibrium of the cells would again ensue when the effects had passed off. CO<sub>2</sub> may also have a direct stimulant effect on the cellular structure because it is reported to act as a specific stimulant to the cells of the respiratory centre, and may therefore likewise act as a specific stimulant to cerebral cells.

The general posture of any of the patients so closely resembles that seen in disorders of the extra-pyramidal system together with the tendency of the CO<sub>2</sub> mixture to produce movements similar to those seen in such syndromes followed by a return to more normal posture leads one to consider the possibility of the disorder being subcortical.

enjoying remissions. Insight is often gained." Barr and Barry (256) found mental improvement of varying degree in a large percentage of cases, and concluded that younger cases were more responsive and their

### 13. Miscellaneous Forms of Therapy.

In this section are described various other methods of experimental treatment, which I, myself, have not attempted.

1. Aseptic Meningitis. Acting on the probability that in schizophrenia the choroid plexus might be involved to the extent of interference "with normal chemotaxis and that, perchance, dementia praecox might prove to be a food - chemico - deprivation rather than a toxic destructive process", Carroll (234) introduced inactivated horse serum into the sub-arachnoid space through a lumbar puncture, then 25 c.c. of cerebrospinal fluid were withdrawn and an equal amount of horse serum injected. His reports were based on the results obtained in five patients, each of whom improved under this form of treatment. "A minimum of two, a maximum of five injections have succeeded in producing either temporary or permanent lucidity in every dementia praecox case thus treated."

In a later communication, Carroll (235) reported, "that the mental condition of 66 per cent of cases of dementia praecox so treated, show improvement which has lasted from two to eleven months, several enjoying remissions. Insight is often gained."

Barr and Berry (236) found mental improvement of varying degree in a large percentage of cases, and concluded that younger cases were more responsive and their

improvement more lasting. ~~Simon, Perelman (236)~~  
~~decided to~~ Kubitschek and Carmichael (237) decided that  
 the intraspinal injection of horse serum produces a  
 strong stimulation of the body defensive mechanism,  
 the intensity of the reaction being localised to the  
 cerebro-spinal system. They found the incidence  
 and degree of permanent improvement was much greater in  
 dementia praecox of early stages than in the chronic  
 deteriorated types. ~~Twelve patients were treated.~~

2. Typhoid - Paratyphoid Vaccines. Lamenting the lack  
 of progress in schizophrenia, Berkley (238) was led to  
 try the effects of typhoid - paratyphoid vaccines since  
 they favourably influence the course of cerebro-spinal  
 syphilis. One c.c. of the sterilized vaccine selected  
 represented 2 billion germs. The initial dose was  $\frac{1}{10}$   
 of 1 c.c. increased by degrees to .15 c.c. according to  
 the reaction produced. The vaccine being injected  
 intravenously every other day for 10 days. The  
 average rise in temperature was  $102.4^{\circ}$ . The results  
 were all unfavourable. Raphael and Gregg (239) and  
 treated 7 male cases with durations of disease from 1  
 to 22 years. No mental improvement occurred.

3. Cocain Hydrochloride. Cocain hydrochloride in doses  
 of 0.025 to 0.05 gram was employed by Berger (240) in  
 eight cases of the catatonic form of schizophrenia. He  
 concluded that the method was without value.

in their inner lives.

4. Light Alcoholic Intoxication. Perelman (241) decided to use alcohol in schizophrenia, basing the treatment on Pavlov's theory of schizophrenia, as a state of inhibitions. Two or three hours before lunch the patients were given 25 c.c. of a 50 per cent. solution of absolute alcohol. If no results were obtained in fifteen minutes, the dose was repeated. Another dose was given fifteen minutes if no signs of intoxication appeared. Twelve patients were treated in this way. Inaccessible stuporous patients were chosen for the experiment. There was a great variability in a patient's willingness to drink the alcohol as well as in his susceptibility to it. Only in two cases did the alcohol not produce intoxication. There was a marked change in the psycho-motor states of the patients. The faces were more expressive and in most of them there was a marked vasomotor reaction. The movements became more alert and definite with a marked stimulation of motor areas. All patients took a great interest in their environment. They also became more communicative and accessible. The moods varied from crying to euphoria or outbursts of anger. A few hours after the intoxication the patients lapsed into the previous state. The author thinks that alcohol is a useful adjunct in the study of schizophrenia, because it stimulates the patients and also gives a good idea of what is going on in their inner lives.

5. Physiotherapy. Reports in the literature on physiotherapy in schizophrenia are few. Prengoroski (242) in the belief that schizophrenic disturbances are related to changes in the vasomotor system, recommended that hot compresses be applied to the spinal region. He also advised massage of the entire surface of the body. At other times he employed high pressure douches and hot baths. Finally, he prescribed small doses of iodine. Among 48 patients treated by one or more of the above measures, he reported 14 patients as cured, 18 essentially improved, 9 as somewhat improved and 7 as uninfluenced.

6. Haemotherapy. On the assumption that the injection of normal human serum might produce an anti-toxin or might in some other way give rise to a "defensive ferment", Jacobi (243) treated 10 patients of the schizophrenic form over a period of three months. From 200 to 250 c.c. of blood was withdrawn under sterile conditions from patients with hysteria. The blood was centrifugalised and partly inactivated by heating to 56°C. The latter step was subsequently regarded as unnecessary. Each patient received an intravenous injection of from 50 to 70 c.c. of the serum at intervals of eight days. Five of the patients were classified as hebephrenic and five as catatonic. No conspicuous improvement was seen in the hebephrenic group, save a slight transitory improvement during the course of the treatment. Two of the catatonic patients

catatonic. Two recovered and three improved temporarily.

7. Assisted Respiration Peters (247) treated 42 exhibited a decided improvement and in a third there was a questionable improvement in the clinical picture. Two patients remained unaffected.

Josephy (244) treated five schizophrenic patients by the intramuscular injection of the patient's own blood. He regarded the treatment as highly beneficial, three of the five patients, treated early in the course of their illness, having responded in a favourable manner from three to five days after the injections had been given.

Stoker and Vasilii (245) who claimed that they selected patients who were "on the road to recovery" to act as donors of blood serum for schizophrenic patients in an acute stage, reported the results of their experiments on one patient who was "not very far advanced pathologically". Every two or three days for about a month they injected from 5 to 35 c.c. of blood from a patient whose clinical condition was similar to that of the recipient. The latter improved.

Pascal and Davesne (246) gave each patient 6 intramuscular injections of whole blood taken from cases of insanity during remissions after haemotherapy or shock from turpentine and sodium nucleinate. These injections were given on alternate days and consisted usually of from 5 - 10 c.c. as the first dose and from 15 - 20 c.c. as subsequent doses. Six cases were treated, of which 3 were acute forms of hebephrenic or catatonia. Two recovered and three improved temporarily.

14. Psychotherapy  
7. Assisted Respiration. Peters (247) treated 12 females by means of artificial respiration, using Silvester's method for 15 minutes daily. The duration of the disease before treatment varied from 6 months to over 9 years. Four cases showed great improvement, 3 of these maintaining their improvement up to the time of writing, nearly 6 months after treatment. Six cases showed slight improvement which was maintained.

14. Psychotherapy.

Although much has been written on the analytical treatment of schizophrenia, there is still much diversity of opinion regarding its use in this condition.

Hoch (248), under the influence of psychoanalytic conceptions stressed the likeness between the neuroses and dementia praecox, asking, "whether the dissimilarities are so great that we have to disregard this parallelism and take refuge in a totally different kind of interpretation of the disorder". He pointed out as Freud, Jung and Bleuler had previously done, that the symptoms of dementia praecox were not to be regarded as scattered and bizarre productions, but rather as representations of a definite meaning to the individual. Moreover, "the meaning is sometimes more transparent in dementia praecox than in the neuroses". Hoch maintained that the precipitating factors must be known "in their setting, their background and their relationship to various trends in the patient's mind. We must know the internal development of peculiar attitudes in the patient's mind which determine the reaction". In the same communication Hoch further states that, "both the pathological personality, with its milder manifestations and the psychosis, with its more complete break of compensation, may be looked upon as determined by constitutional factors, in the sense that when demands for adaptation arise, the individual is found unfit to meet them, unfit through inherent weakness, but also at times through false attitudes which have

developed through lack of proper training. In this last direction lies our hope for modifying these effects."

Campbell (249) indicates in a concrete manner the various methods of approach, depending upon the stage of the mental disease. He encourages intensive study of the constitutional traits of the patient, of his habits and ideals, emphasising that "the special treatment of a case, as opposed to the general hygiene management, consists in the interpretation of the individual symptoms, in their resolution into component forces and in dealing with these component forces in a healthy manner". He outlines definite procedures with respect to therapy and assumes a broad psycho-biological approach. Freud has expressed himself as unfavourably inclined to recommend the application of his system in the treatment of schizophrenia. He groups this mental disease with the narcissistic neuroses, a class that ordinarily, he thinks, is not responsive to the psycho-analytic form of treatment. Other investigators are not as categorical in this respect as Freud is: they feel that schizophrenic patients show a wide divergence in their syndromes, that some are capable of understanding the nature of their conflicts when it is shown to them and they thereby gain an insight that enables them to re-establish themselves on their prepsychotic level. Kirby (250), for example, characterised Freud's attitude toward the analytic treatment of schizophrenia as one that fosters too much pessimism because of its all-inclusiveness. Maeder (251) reported considerable

success in the psycho-analytic treatment of two cases of the paranoid form of schizophrenia. Kempf (252) claimed that the "psycho-analytic treatment of repressed, perniciously repressive, dissociated personalities produces astonishingly reconstructive results". Clark (253) devised the "phantasy method" of analysing narcissistic neuroses and claims that "the displaced primary personality of the narcissist is enabled to gain the power of insight into the intricate pattern of the narcissian, which has been built up from the identification with the mother".

Coriat (254) observed that marked improvement "may be noted in early cases through a complete psycho-analysis, which procedure lays bare the unconscious disturbing complexes".

Lazell (255) outlined a plan for the group treatment of dementia praecox patients selecting "only such patients as presented the same fundamental problem and were solving their difficulties in the same manner". He did not regard his patients as recovered, "but all left the hospital later as social recoveries".

Kogerer (256) is optimistic about the treatment of schizophrenic patients in an out-patient clinic, but only to the extent that many patients may be prevented from developing more intense manifestations of their symptomatology.

Bull (257) states that analysis gives good results and gives examples of individual cases, stating that his experience extends over many years. He gives no figures, however, of the number of cases

treated either successfully or unsuccessfully.

Some investigators consider that the application of psycho-analysis to patients with schizophrenia is a harmful procedure. No greater voice in respect to this attitude could be heard than that of the founder of the system, Freud. His opinion should make us doubly wary of advancing a contrary or a qualified stand, unless the reasons for so doing are strongly fortified by clinical evidence. Trämer (258) cites the case of a latent schizophrenic man, who through psycho-analysis was rendered a manifest case. He believes that when the psychological splitting is pronounced, psycho-analysis is contra-indicated. Strasser<sup>(259)</sup> is of the opinion that "one cannot emphasise too strongly the danger and falsity of psycho-analysis in the treatment of dementia praecox". Culpin (260) holds the view that "as a therapeutic measure little is at the present claimed for it". (Psycho-analytic treatment of schizophrenia). "In regard to dementia praecox..... analysis is impossible when once the disease can be diagnosed with certainty, but it has in a few cases proved curative when the diagnosis seemed only probable".

The majority of psycho-analysts at present seem to consider the concepts of psycho-analysis most helpful for understanding the meaning and structure of schizophrenia, but feel at the same time that an adequate therapeutic technique has not yet been developed.

The application of psycho-analysis to schizophrenia is still definitely in an experimental stage. The general contra-indications seem to be that because of the impossibility to bring about any transference of the narcissistic libido it is useless to treat psycho-analytically dementia praecox, paranoia and of special schizophrenic states in general. patients interest in activities away from himself. He is already so little concerned in environmental circumstances to ensure a healthful outlook and anything that can be done to encourage an externalization of his interests will of help.

Occupational therapy should be regarded as a means to an end, the latter constituting the establishment of rapport with the patient so that psychotherapeutic measures may be established. Even though the etiology of schizophrenia is obscure, it is certain that there are psychical elements in almost every patient that are amenable to a greater or lesser extent to a psychotherapeutic approach. One of these psychical elements comprises the attitude that the patient assumes towards the various personalities in the surroundings. Therefore, the relationship of the occupational teachers and the other patients in the class to the patient under consideration should be looked upon with special care, for schizophrenic subjects are prone to embody at least a part of their psychical life into that of others.

White (251) states that occupational therapy is a "naive conception of psychotherapy." He maintains

15. Occupational Therapy. "individualizes the patient, centres" Probably one of the most influential adjuncts in the management of schizophrenic patients comprises industrial therapy. Among this group of patients in particular the restoration to a working capacity is highly important. This is considered to be of special merit in the attempts to keep the patients interest in activities away from himself. He is already so little concerned in environmental circumstances to ensure a healthful outlook and anything that can be done to encourage an externalization of his interests will of help.

group. Occupational therapy should be regarded as a means to an end, the latter constituting the establishment of rapport with the patient so that psychotherapeutic measures may be established. Even though the etiology of schizophrenia is obscure, it is certain that there are psychical elements in almost every patient that are amenable to a greater or lesser extent to a psychotherapeutic approach. One of these psychical elements comprises the attitude that the patient assumes towards the various personalities in the surroundings. Therefore, the relationship of the occupational teachers and the other patients in the class to the patient under consideration should be looked upon with special care, for schizophrenic subjects are prone to embody at least a part of their psychical life into that of others.

White (261) states that occupational therapy is a "naive conception of psychotherapy." He maintains that occupational therapy "individualises the patient, centres his interest and attention upon his specific problems, sets up a wholesome type of transfer, starts the flow of interests to outside realities and socializes his tendencies in useful occupations.

The first thing which it seems worth while to work for is to preserve, as far as possible, contact with normal life. In this way, occupational therapy will prove of incalculable benefit to the patient as well as to the country.

Attempts are also worth making to rehabilitate chronic demented patients and fit them into some social group. Their degeneration may be mainly due to habit deterioration. The principles of the treatment are therefore:

1. By training to prevent the formation of vicious habits before they become fixed.
2. To form new and better habits.

The play instinct is the best opening for most, and in the case of chronic demented patients, I find gymnastic classes invaluable.

The well-balanced occupational therapy programme should cover activities from habit training and the simplest kindergarten guidance, up through various grades to work carried on under conditions closely stimulating the community life.

With psychotics, two closely correlated objectives are to be considered - first, social adjustment, and, second, institutional adjustment. The first is always to be desired, but often is not possible of attainment. Social adjustment may be complete or partial, permanent or temporary. Hospital adjustment should be made on the highest plane attainable by the individual patient. She should, so far as possible, be made an interested, satisfied and efficient member of the institutional community in which she must live. Work, exercise, recreation and special treatment must be so arranged as to assist in accomplishing this result. Previous experience, training, the mental and physical ability and the aptitude of the patient, should all be given due weight in prescribing occupational therapy. Occupations which assist in the upkeep of the hospital will often furnish the best form of treatment, and should always be given consideration for patients who will be institutional cases over extended periods. Even in cases where deterioration is inevitable, this will not occur so rapidly in the interested, busy patient, as with the one who is unoccupied. Through a change to better surroundings where work is done, the instinct of imitation may be stimulated. The acquisitive and constructive instincts properly directed, bring wonderful results, while sympathy is of great aid. Further, the dilapidated patient may, by painstaking

Entertainments must also be regarded as a treatment, be brought back, so, that instead of being destructive and untidy, she takes active part in simple occupations and recreations, resumes passable personal habits, and ceases to be a disciplinary problem. It is essential in treatment to have the hospital environment, simulate, so far as is practicable, community life with some of its drawbacks eliminated. The patient is protected from the keen competition of industry and from social domestic disturbances. She has enforced regularity of habits, mild competitive stimulus in occupation and recreation is added after the individual's productive reaction is established. Manual activities are indicated for a large percentage of the patients. To make occupational therapy a success, it is necessary to have proper co-operation between medical officers, instructors and the other employees who come in contact with the patient; to make a careful study of the individual characteristics, and to place the patient correctly; to have close supervision of the patient while employed and to change occupations as indicated to prescribe practical tasks, and to take a human interest in the patient, always having in view her advancement.

Goss (262) says: "We have at the present time many cases of dementia praecox that have remained stationary for years, where, in our opinion, further degeneration has been prevented by steady congenial occupation."

Entertainments must also be regarded as a definite form of treatment, and so regulated and supervised, they are of considerable therapeutic value, every effort being used to encourage the patient to exercise her neglected social instincts.

Encouragement is also given to recoveries to wear their own clothing, and every effort is made to avoid the provision of clothing made to a pattern. This may seem a very small matter, but the principle underlying it is of considerable importance, i.e. to avoid the danger of institutionalising our patients, and this can only be done by a careful study of each patient's individuality. She had this individuality before coming to Hospital and it is in the interests of her mental health that it should be fostered, or, if lost restored.

Stanford Read, after a visit to the Belgian town of Gheel, where for many centuries large numbers of the insane have lived a life of comparative liberty in care of the inhabitants but under medical supervision, was stimulated to recognise the fact that institutional care was not needed to anything like the extent usually supposed. Though the marvellous success of the Gheel colony is due largely to the effects of tradition, there is reason to think that much more could be accomplished in this country in the familiar treatment if only the public were slowly but surely educated up to it. Unconsciously, or at any rate,

## VI. RESULTS OF TREATMENT.

the, "lunatic is still regarded as something alien and a subject of awe and fear, and home segregation away from society is thought to be the necessary treatment!" Jung believes that the worst catatonic states and the most complete dementias are in many cases products of the lunatic asylum, brought about by the psychological influence of the milieu.

One therefore gathers from the observations presented thus far, that patients with schizophrenia, form a wide and varied group, and that a single therapeutic approach is illadvised. The group is entirely too complex in its symptomatology to warrant any but an individualistic method of therapy.

The task of the clinical psychiatrist, therefore, is to unravel the component forces and estimate their relative importance. It must be clearly understood that occupational therapy is a method of treatment, its purpose being a cured patient and not the production of a well-made piece of workmanship. Occupational therapy is therefore a distinct entity.

Individual case are summarized and an endocrine diagnosis made. At intervals of one to two months the case is again summarized and modifications in the treatment made in accordance with the results of later tests and of the patient's history.

VI. RESULTS OF TREATMENT.1. Endocrine Therapy.

In Table I. is shown the "Summary Sheet" that is employed in tabulating the data. It serves in this connection to indicate the data secured. The general plan is to make a thorough initial study, securing data as complete as possible, not only on the features scheduled in the Table but also on the history and physical conditions of the individual patient. Table II. reproduces the form used by me in securing and recording data. The nurses also report their impressions of the patient each three days, every day when actually under treatment, as well as whenever anything unusual occurs. Occasionally significant observations are reported by workers in the Occupational Therapy Department. Table III. reproduces the form used to secure uniformity in these examinations.

I further find that a valuable method of estimating the patient's mental state is letter writing. If possible, the patient is persuaded to write a letter shortly after admission and from time to time during the course of treatment. The initial data on the individual case are summarised and an endocrine diagnosis made. At intervals of one to two months the case is again summarised and modifications in the treatment made in accordance with the results of later tests and of the interim history.

In all 69 cases have been studied with sufficient thoroughness to permit an endocrine diagnosis, either definite or probable. The outstanding findings in the entire series are set forth in Table IV.

The most difficult phase of the undertaking is to determine in each case the prognosis - "slight improvement", following the use of endocrine medication in a case where the prognosis appears particularly hopeless is correspondingly more significant than would be a marked improvement in a case of initially good prognosis.

Further, I have found that cases of schizophrenia, where there is an element of congenital mental deficiency do remarkably well on thyroid medication and I now invariably adopt this method of treatment in all such types.

All the patients reported in this series were females, the ages ranging from 18 to 38 years, and the period of hospitalization from 1 month to 11 years. Some had suffered from one to three previous attacks. Of the 69 cases studied, all have received various forms of gland treatment. The distribution of endocrinopathies among the various types of dementia praecox as shown in Table IV. of the entire group, 49.2 per cent. have been diagnosed "not endocrine", 28.9 per cent. "definitely endocrine", 21.8% "probably endocrine". The occurrence of 16 definite and probable instances in 23 catatonics is striking and correlates with the fact that the incidence of improvement is highest in this group.

The composite results of specific and non-specific treatment in various types are set forth in Table V. The highest incidence of significant improvement, 69.5 per cent. occurred in the catatonic group, and the lowest, 11 per cent., in the paranoid group. In all but one of 11 cases of thyroid deficiency unquestionable improvement occurred. This ranged in degree from greater co-operation and better contact to apparently complete freedom from the psychosis. The improvement was especially well-marked in the excited, negativistic, badly behaved type, who grew much quieter during the course of treatment and gradually became co-operative and amenable to discipline.

In Table VI. are shown the results of substitutive gland treatment in cases in which definite or probable diagnosis of specific gland hypo-function were made. This group includes only cases of thyroid and pituitary deficiency. In pituitary medication there is a relative lack of potency of this substance when taken by the mouth. It is now my practice to give in such cases Multigland Tablets, containing:-

Corpus luteum	$\frac{1}{4}$ gr.	)	Sicc.
Ovarian, W.9.	$\frac{1}{2}$ gr.		
Pituitary		)	
whole gland	$\frac{1}{8}$ gr.		
Thyroid, B.P.		)	
1932.	$\frac{1}{4}$ gr.		

In Table VII is shown the incidence of improvement in 29 cases diagnosed as not demonstrably endocrine. In 14 of these patients thyroid was used without any significant improvement, whereas, all but one of 11

patients initially suffering from definite or probable thyroid deficiency profited by its use.

In 24 cases, as indicated by Table VII. the deviations in the vital function tests were sufficient in degree and number to justify a diagnosis of endocrine deficiency, but the pictures were not sufficiently characteristic to permit the allocation of any one gland. Therapy, therefore, had considerably more of the random element, than in the case of the preceding series. In 6 instances thyroid proved efficacious and in 4 multi-glandular treatment. It is possible that these cases might be allocated to the thyroid component.

Endocrine deficiencies as they occur in schizophrenic patients are seldom of sufficient degree to produce the classic stigmata of these conditions. In few cases were sufficient degrees of obesity noted to raise even a suspicion of endocrine involvement and in no case was myxodoema present. On the other hand, depressed basal metabolism occurred with notable frequency, as did low temperature and blood pressure, in the "non-endocrine" as well as the "endocrine" cases. These latter evidences of metabolic depression proved amenable to thyroid therapy in various instances, but corresponding mental improvement occurred only in the "endocrine" group.

In a few instances adjuvants to the gland substance were used, namely, liver, and Halmagon, containing the halogen salts of magnesium crystalline. These substances do not act as a specific on a well-

been isolated in a crystalline form and some of which defined morbid entity, but they may support the body's natural recuperative powers. In several instances the symptoms became more acute following the administration of gland substances. Since schizophrenics are characteristically subject to ups and downs, a certain number of such instances might be expected irrespective of gland treatment. Whether the treatment was actually a factor in such exacerbations, it is not possible to decide. Perhaps the most ominous feature in a schizophrenic psychosis is the passive acceptance of it by the patient. When she is no longer troubled by continued delusions or hallucinations she is well on the way to dissolution. The recurrence of evidences of acute conflict therefore, could theoretically be regarded as a favourable rather than unfavourable development. As a matter of fact, whether as a coincidence or not, in several cases in which marked improvement occurred, it dated from the subsidence of a state of increased mental tension marked by irritability, noisiness, etc., endocrine glands, stimulating or It is concluded that endocrine deficiency plays a significant rôle in dementia praecox and that in properly selected cases specific endocrine therapy is of value in the treatment of this disorder. Dodds classifies hormones under two headings. The first are complex protein bodies formed by the anterior pituitary which act on the other endocrine glands causing them to form the secondary type of hormones which are bodies of comparatively small molecular weight, most of which have

been isolated in a crystalline form and some of which have been prepared synthetically. All hormones of the secondary types contain benzene rings. It has been shown that oestrin and the male sex hormone contain this condensed ring, which is also found in Vitamin D. Further, it has been shown that the chemical organiser or the evocator which determines certain developments of the embryo, belongs to the same group; a series of facts of far-reaching significance. Dodds has further shown that rings of simpler structure than the ones found in nature can produce the appropriate response. The simplest form which can turn the biological lock he terms the skeleton key. He also finds that in some instances the effects are non-specific, i.e. one chemical substance can produce more than one hormonal effect. To such substances he gives the name of pass keys. Therefore, we arrive at the conclusion that the integration of the endocrine system is based on the influence of the diencephalon upon the anterior pituitary, which through complex hormones acts on the other endocrine glands, stimulating or inhibiting the production of simpler hormones in them. These substances are closely related chemically to other substances concerned in normal activities such as the growth of the embryo and the growth of bone and calcium metabolism.

My final suggestion is not to lay too much stress upon the endocrine therapy alone. Attention to the patient, re-education, suggestion and persuasion all play important rôles. Further, the form of treat-

ment adopted must be continued in order to maintain the improvement.

Endocrinology is a field in which great benefit may be wrought by the correct usage of its powerful therapeutic agents and even greater damage done by their misuse.

TABLE I.Ward Observations.

Name of Patient.....Place.....Date

Appearance and General Behaviour: (Neatness, output of energy, mannerisms, postures, etc.).

Mood: Placid, complacent, cheerful, euphoric, elated, silly, facetious, boastful, irritable, suspicious, sad, hopeless, bitter, gloomy, anxious, perplexed, thoughtful, indifferent, apathetic, stuporous, variations.

Social Attitude: Co-operative, amiable, submissive, self-assertive, antagonistic, sociable, seclusive, fault-finding, self-pity, ego-centric.

Work Period: Kind of work - voluntary or compulsory.

Actual work: Efficiency, steadiness, interest.

Leisure Period: Social intercourse, attitude, interest, reading, writing, games.

Day Dreaming: Facial expression, physical posture, evidences of response to hallucinations, evidences of erotic indulgences.

Response to Special Situations: Visitors, letters, transfers, church, etc.

Significant utterances and behaviour of Patient.

TABLE 11.Scheme for Staff Review of Cases.General Appearance and Behaviour:

Gait:

Clothing:

Attitude:

Facial Expression:

Mannerisms:

Speech:

Spontaneous or not:

Tone of voice:

Normal, coherent, relevant  
or abnormal:

Volubility:

Circumstantiality

Verbigeration:

Distractibility:

Slowing:

Neologisms:

Retardation and  
Blocking:Orientation:

Time:

Place:

Person:

Mood:

Placid:

Bitter:

Cheerful:

Sad:

Elated

Hopeless

Diagnostic Summary:

Boastful

Gloomy

Timorous

Anxious

Prognosis:

Irritable

Perplexed

Indifferent

Apathetic

Suspicious

should be used for patients who will recover and be able to resume their place in the world. They should

Memory:

Recent

become self-supporting and without trace of former symptoms.

Remote

Hallucinations:

Full information as to: either fully or partly

When heard: will retain some of his symptoms

Men's or Women's voices:

Do they talk to each other or to the patient?

Content of hallucinations: no useful work, but

Hallucinations other than auditory: retain her

Compulsive Phenomena:

Impulses, compulsions, etc.

Insight:

How far does the patient understand what is wrong?

Delusions:

When possible get full information relative to former ideas. Have the patient give an explanation of her conduct since the preceding progress note.

Diagonostic Summary:

Open to revision if necessary.

Prognosis:

Should be recorded in the following terms:-

A. Complete Recovery: This classification should be used for patients who will recover and be able to resume their place in the world. They should become self-supporting and without trace of former symptoms.

B. Social Recovery: The individual can return to the community, become either fully or partly self-supporting, but will retain some of his symptoms under good control.

C. Institutional Social Adjustment: The patient may be given parole, do some useful work, but cannot return to community life. She will retain her symptoms but have them under good control in the environment of the Hospital.

D. Institutional Adjustment: The patient will not be able to be trusted with any liberty but will remain clean and tidy, get along with other patients in the ward and do simple work.

E. Deterioration: The patient will gradually become untidy, antisocial or aggressive and violent, and do no useful work in the institution. She will remain inaccessible.

TABLE III.

Catatonic Type.

Patient Age	No. of Attack	Duration Years	Pronosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
H.R. 26	2nd	4	Doubtful	Thyr. Def.	Thyroid and Liver	Improved	At home Apparently Well
M.S. 32	2nd	5	Fair	Thyr. Def.	Thyroid	Marked Improvement	At Home
A.M. 25	1st	$\frac{1}{4}$	Fair	End. Def. unclassified	Thyroid	Improved	At home
A.K. 29	1st	$\frac{1}{4}$	Poor	Not End.	Thyroid	Not Improved	Discontinued
L.L. 23	1st	$\frac{1}{2}$	Bad	End. Def. unclassified	Thyroid & Pituitary	Moderate Improvement	Continued
C.H. 18	1st	2	Poor	Not End.	Thyroid Thyr. & A.L. Pituitary	None Moderate Improvement	Continued
I.R. 17	1st	$\frac{1}{2}$	Poor	Thyr. Def.	Thyroid & Halmagon	Marked Improvement	At Home
G.T. 31	1st	2	Poor	Pit. Def.	A.L. Pituitary & Halmagon	Improved	At home Apparently Well
M.L. 28	2nd	5	Bad	Not End.	Thyroid Thyroid & Pituitary Ovarian	None Slight Improvement	Continued

Catatonic Type.

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat.	Present Status
M.H. 28	1st	$\frac{3}{4}$	Bad	End. Def.	Thyroid Ovarian	No change	Discon- -tinued
M.K. 25	1st	$\frac{1}{2}$	Poor	End. Def.	Thyroid	Marked Improvement	At home
F.G. 26	1st	$\frac{1}{4}$	Poor	Pit. Def.	A.L. Pituitary & Halmagon	Marked Improvement	At home
B.M. 23	2nd	4	Bad	Thyroid Deficiency	Thyroid	Improved	At home
M.M. 28	1st	$\frac{1}{12}$	Bad	Pituitary Deficiency	A.L. Pit. & A.L. Pit. & Thyroid	None Improved	At home
M.S. 19	1st	$\frac{5}{12}$	Bad	Not. End.	Thyroid Ovarian	No change Slight Improvement	Continued
A.P. 23	1st	$\frac{5}{12}$	Fair	End. Def. unclassified	Multigland	Improved	At home
B.E. 24	1st	1	Poor	Not End.	Thyroid Pituitary	No change	Discon- -tinued
G.S. 19	1st	3	Bad	End. Def. unclassified	Thyroid & Pituitary Ovarian	None	Discon- -tinued

Catatonic Type.

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
G.M. 25	2nd	2	Bad	Thyroid Def.	Thyroid	Apparently Improved	At home
L.D. 32	2nd	7	Bad	Not End.	Thyroid	No change	Discontinued
C.C. 38	3rd	9	Bad	Not End.	Thyroid Ovarian Multigland	No change	Discontinued
T.M. 26	1st	1/4	Fair	Pit. Def.	A.L. Pit. Thyroid	Improved	At home
A.P. 21	1st	1/12.	Poor	Thyr. Def.	Thyroid	Improving	Ready for discharge
M.O. 29	1st	5	Bad	Pit. Def.	A.L. pit-uitary	Improvement	At home
A.R. 24	1st	2 1/2	Fair	Thyr. Def.	Thyroid	Improved	At home
M.B. 37	2nd	1/2	Poor	Not End.	Ovarian Thyroid	No change	Discontinued
A.R. 27	2nd	1 1/3	Bad	Not End.	Ovarian	No change	Discontinued
M.A. 25	1st	4	Bad	Not End.	Thyroid Multigland	No change	Discontinued

Hebephrenic Type

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
E.W. 28	2nd	$1\frac{1}{2}$	Poor	Not End.	Thyroid	None	Discontinued
H.D. 18	1st	$\frac{1}{2}$	Fair	Thyr. Def.	Thyroid Halmagon	Marked Improvement	At home
F.G. 28	2nd	7	Poor	Not End.	Thyroid Multigland	None	Discontinued
A.C. 22	1st	1	Poor	Pit. Def.	A.L. Pit- -vitary	Improved	At home
A.C. 28	1st	$\frac{1}{2}$	Poor	Not End.	Thyroid Ovarian	More acute No Change	Discontinued
M.T. 26	1st	$\frac{1}{2}$	Poor	End. Def. unclassified	Thyroid Multigland	No change Improved	Ready for home
M.C. 29	1st	$\frac{5}{12}$	Bad	Pit. Def.	A.L. Pit- -vitary	Slight Improvement	At home
A.R. 24	1st	$10\frac{1}{2}$	Fair	Thyr. Def.	Thyroid	Improved	At home
M.B. 37	2nd	$1\frac{1}{2}$	Poor	Not End.	Ovarian Thyroid	No change	Discontinued
A.R. 27	2nd	$1\frac{1}{3}$	Bad	Not End.	Ovarian	None	Discontinued
M.A. 25	1st	$\frac{3}{4}$	Bad	Not End.	Thyroid Multigland	None	Discontinued

S.M. 38 1st

Poor

Thyr. Def.

Thyroid

Improved

At home

Hebephrenic Type.

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
M.C. 19	1st	$\frac{1}{2}$	Bad	Not End.	Ovarian Multigland	None	Discontinued
A.S. 23	1st	$\frac{1}{4}$	Poor	Thyr. Def.	Thyroid Liver	Improved	At home
M.H. 23	1st	$\frac{2}{4}$	Poor	Pit. Def.	A.L. Pit. Thyroid	None	Discontinued
M.B. 20	1st	5	Poor	End. Def. unclassified.	Multigland Thyroid Halmagon	Marked Improvement	At home
M.H. 19	1st	$1\frac{1}{4}$	Poor	End. Def. unclassified	Multigland	None	Deteriorating
G.P. 26	1st	$\frac{1}{4}$	Poor	Not End.	Thyroid Halmagon	None	Other treatment adopted
S.W. 20	1st	5	Poor	Not End.	Thyroid A.L. Pit.	None	Discontinued
G.M. 28	1st	2	Bad	Pit. Def.	AL. Pit. A.L. Pit. & Thyroid Thyroid	Moderate Improvement	At home
J.K. 32	2nd	9	Poor	Thyr. Def.	"	None	Discontinued
S.M. 38	1st	$\frac{1}{2}$	Poor	Thyr. Def.	Thyroid	Improved	At home

Paranoid Type

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
M.T. 36	1st	1 1/2	Bad	Not End.	Ovarian Multigland	None	Discontinued
D.K. 31	2nd	1	Poor	Not End.	Thyroid	None	Discontinued
E.H. 37	3rd	4	Bad	End. Def. unclassified	Ovarian Multigland	Improved	At home
H.T. 30	1st	4	Bad	Pit. Def.?	A.D. Pit. Thyroid	None	Discontinued
E.H. 33	1st	1 1/2	Poor	Not End.	Multigland	None	Discontinued
J.R. 37	1st	1 1/2	Poor	End. Def. unclass.	Ovarian Hormotone	None Slight Improvement	Works in hospital
C.S. 29	1st	5	Bad	Not End.	Thyroid	None	Discontinued
M.R. 38	2nd	11	Bad	Not End.	Hormotone	None	Discontinued
T.M. 31	1st	1 1/3	Poor	Not End.	Multigland Thyroid	None More acute	Discontinued
J.D. 20	1st	1/2	Poor	Not End.	Multigland Ovarian	None	Discontinued

Simple Type.

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
J.T. 25	1st	2	Poor	Not End.	Thyroid Halmagon	None	Discontinued
E.F. 18	1st	$\frac{1}{2}$	Poor	Pit. Def.	A.L. Pit. Thyroid	Moderate Improvement	At home
R.M. 29	2nd	$\frac{1}{12}$	Poor	Not End	Thyroid Ovarian	None	Discontinued
J.D. 22	2nd	$\frac{1}{4}$	Poor	End. Def. unclass.	Thyroid Multigland	Moderate Improvement Worse	At home
A.K. 24	1st	$\frac{1}{2}$	Poor	Not End.	Multigland	None	Discontinued
A.M. 27	2nd	$\frac{3}{4}$	Poor	Not End.	Thyroid Ovarian	None	Discontinued
S.H. 20	1st	$\frac{1}{12}$	Poor	End. Def. unclass.	Multigland Thyroid	None	Discontinued
M.D. 17	1st	$\frac{1}{12}$	Poor	Not End.	Ovarian A.L. Pit. Thyroid	None	Discontinued
A.S. 19	1st	$\frac{1}{4}$	Poor	Not End.	Thyroid	None	Discontinued
J.D. 20	1st	$\frac{1}{12}$	Poor	Not End.	Multigland Ovarian	None	Discontinued

Simple Type.

Patient Age	No. of Attack	Duration Years	Prognosis	Endocrine Diagnosis	Treatment	Psychiat. Results	Present Status
A.M. 24	2nd	3	Bad	Not End.	Thyroid Multigland	None	Discontinued
S.R. 22	1st	1 1/2	Poor	Not End.	Ovarian Hormotone	None	Discontinued
E.D. 18	1st	1 1/4	Poor	End. Def. unclass.	Thyroid Multigland	Slight Imp.	Discontinued
S.T. 24	1st	2 1/4	Poor	Not End.	Multigland Ovarian	None	Deterioration
R.C. 20	1st	1 1/2	Poor	Not End.	Ovarian Thyroid	None	Discontinued
D.M. 19	1st	1 1/2	Poor	Not End.	Multigland Ovarian	None	Deterioration

Types	Not Endocrine	Definitely Endocrine	Probable Endocrine
Hebephrenic	5	1	1
Catatonic	7	1	0
Paranoid	3	0	0
Simple	12	0	0
TOTALS	27	2	1
Percentages	49.2%	3.7%	1.7%

Type	Number Treated	Thyroid	Ovarian	Multigland	Psychiat.	Present Status
Hebephrenic	21	1	1	1	1	Discontinued
Catatonic	23	1	1	1	1	Discontinued
Paranoid	3	0	0	0	0	Discontinued
Simple	12	0	0	0	0	Discontinued

TABLE IVEndocrine Distribution.

<u>Types</u>	<u>Not Endocrine</u>	<u>Definitely Endocrine</u>	<u>Probably Endocrine</u>	<u>Total</u>
Hebephrenic	9	9	3	21
Catatonic	7	10	6	23
Paranoid	6	0	3	9
Simple	12	1	3	16
TOTALS	34	20	15	69
Percentages	49.2%	29%	21.7%	100%

TABLE VIITABLE V.Results of Treatment in Different  
Psychiatric Types

<u>Type</u>	<u>Number Treated</u>	<u>Number Improved</u>	<u>Percentage Improved</u>
Hebephrenic	21	9	42.8
Catatonic	23	16	69.5
Paranoid	9	2	22
Simple	16	2	18

TABLE VI.Results of Specific Therapy.

	<u>Treated</u>	<u>Improved</u>	<u>Percentage</u>
Thyroid Deficiency	11	10	90.9
Pituitary Deficiency	9	7	77.7
Pituitary	—	—	—
Total	20	17	85.00

TABLE VII.Results of Gland Treatment in Non-Endocrine Cases.

<u>Gland Material</u>	<u>Treated</u>	<u>Improved</u>	<u>Percentage.</u>
Thyroid	14	0	0
Pituitary	4	2	50
Multigland	4	0	0
Ovarian	7	2	28.5
<u>Total</u>	<u>29</u>	<u>4</u>	<u>13.00</u>

TABLE VIII.Results of Treatment in Unclassified  
Endocrinopathies.

	<u>Treated</u>	<u>Improved</u>	<u>Percentage.</u>
Thyroid	10	6	60
Pituitary	2	1	50
Ovarian	4	1	25
Multigland	8	4	50
<u>Total.</u>	<u>24</u>	<u>12</u>	<u>50</u>

Cases Illustrating Results of Endocrine Therapy.CASE 1.

M.H. Admitted 14.5.34.

Confused and excited with marked flight of ideas. Was influenced by auditory hallucinations and expressed bizarre delusions. At times was dull, emotional and self-absorbed. Was restive and troublesome to treat - very impertinent at times and required much personal attention.

Made a good recovery on thyroid treatment.

Discharged 26.2.35.

Weight on admission 6 st. 13 lbs.

Weight on discharge 8 st.

CASE 2.

M.C. Admitted 11.9.33. Mother insane.

Simple, irresponsible, negativistic, abusive, stubborn. Became restless and excitable at times, striking other patients. Habits faulty. Wrote numerous love letters. Was very restive to treatment and required much personal attention. Thyroid treatment commenced 28.7.34.

Discharged 12.10.34.

Weight on admission 6 st. 6 lbs.

Weight on discharge 9 st. 1 lb.

Cases Illustrating Results of Endocrine Therapy.

Case 1.



Before



After

Case 2.



Before



After

Cases Illustrating Results of Endocrine Therapy.

Case 3.



Case 4.



Cases Illustrating Results of Endocrine Therapy.

Case 3.



Case 4.



Cases Illustrating Results of Endocrine Therapy.

Case 5.



Before



After

Case 6.



Before



After

Cases Illustrating Results of Endocrine Therapy.

Case 5.



Before



After

Case 6.



Before



After



Case 9 before and after treatment with Atophanyl.



Case 12 before and after treatment with Afenil.

2. Opojex Lymphoid Solution (B.O.C.) and 'Opocaps'  
Lymphoid Co.

These preparations are of special value in early or borderland cases, when serious and permanent mental derangements appear to be frequently averted. The nutrition and functioning of the brain cells is said to be improved and their normal metabolism and capacity restored.

Twenty four cases received treatment - 10 hebephrenics, 8 catatonics, 2 paranoids and 4 simple. The most outstanding improvement was in the hebephrenic group. Of the ten cases treated, 9 showed marked improvement, 7 being discharged home 'recovered'; the two remaining in hospital doing useful work in the occupation department. Striking objective improvements were (1) restoration of ability to work, (2) complete insight and restoration of judgement, (3) severe speech and writing disturbances cleared up. I have found the improvement, in this form of therapy, to be of a sudden and dramatic nature, and the course of treatment requires to be prolonged usually for 6 - 12 weeks, before definite signs of improvement set in. The physical condition improved as the mental balance was regained.

Of the catatonics 4 showed no improvement, 2 improved sufficiently to take an interest in their surroundings, read books, write letters and do simple tasks, 2 were discharged home 'recovered'. Three out of 4 of the simple type showed improvement, 2 being fit to be discharged to the care of their friends. The paranoids showed no improvement from this form of treatment.

Cases illustrating results of treatment with Opojex  
Lymphoid Solution and Opocaps Lymphoid Co.

CASE 7.

C.H. Admitted 26.4.34.

Was wildly excited and emotional, rambling and inconsequent in her talk, had visual hallucinations and stated she had no brain. Became depressed at times. Was very resistive and troublesome to treat, and required much personal attention.

After 30 injections made an excellent recovery, and was discharged on 27.11.34, having gained over a stone in weight; still remains well.

CASE 8.

F.H. Admitted 13.7.34.

Was very excited, restless and impulsive, rambling and incoherent in her talk and faulty in her habits. Was acutely hallucinated. At times she became depressed, self-absorbed and inclined towards cheerfulness. Required much personal attention, suggestion and persuasion.

Made a good recovery after 38 injections and was discharged 28.3.35, having gained 16 lbs in weight. Still remains well.

204.

Cases Illustrating Results of Treatment with  
Opojex Lymphoid Solution and Opocaps Lymphoid Co.

Case 7.



Before



After

Case 8.



Before



After

3. 35% Solution of 204. a Salicylate.

Twelve cases of dementia praecox were given this form of treatment - 4 hebephrenics, 4 catatonics and 4 paranoid - of which 9 were chronic cases and

TABLE IX.

Results of Treatment with Opojex Lymphoid Solution and 'Opocaps' Lymphoid Co.

treatment, 10 of the 4 chronic patients were favourably effected, inasmuch as their habits were improved and they began

	<u>Number treated</u>	<u>Number improved</u>	<u>Percentage</u>
Hebephrenic	10	9	90
Catatonic	8	4	50
Paranoid	2	0	0
Simple	4	3	75

The result occurred after the first injection. In case of the paranoid case hallucinations were not observed. Turbulent patients became quieter, some even going to sleep. This quietening effect occurred in all the cases. The beginning of the effect seems to be connected with the presence in the circulation of a certain quantity of medication, since it does not occur until the third day. The states of excitement gradually returned after cessation of the injections and reached their former height again after three to four days. The results of the sodium salicylate injections, although satisfactory at the time, proved to be only transitory.

TABLE X.

	<u>Treated</u>	<u>Recovered</u>	<u>Improved</u>
Hebephrenic	10	9	9
Catatonic	8	4	4
Paranoids	2	0	0
<u>Total</u>	<u>20</u>	<u>13</u>	<u>13</u>

3. 20% Solution of Sodium Salicylate.

Twelve cases of dementia praecox were given this form of treatment, 4 hebephrenics, 4 catatonics and 4 paranoids - of the 12, 4 were chronic cases and 8 recent admissions. The latter responded best to the treatment, though 2 of the 4 chronic patients were favourably effected, inasmuch as their habits were improved and they began to show some interest in their surroundings. The result occurred after the fourth or fifth injection. In one of the chronic cases, auditory hallucinations which had persisted for years disappeared. Turbulent patients became appreciably quieter, some even going to sleep for a time after the injection. This quietening effect occurred in all the cases. The beginning of the effect seems to be connected with the presence in the circulation of a certain quantity of medicament, since it does not occur until the third day. The states of excitement gradually returned after cessation of the injections and reached their former height again after three to four days. The results of the sodium salicylate injections, although satisfactory at the time, proved to be only transitory.

TABLE X.

	Treated	Recovered	Improved.
Hebephrenic	4	0	4
Catatonic	4	0	4
Paranoids	4	0	4
<u>Total.</u>	<u>12</u>	<u>0</u>	<u>12</u>

4. Atophanyl.

Ten cases were treated, 4 hebephrenics, 4 catatonics and 2 paranoids. Atophanyl showed in all a definite sedative, in some cases also an hypnotic effect. The patient experienced a subjective feeling of well-being, fell into a restful euphoria and 4 of their own accord asked for a continuation of the injections. Of the 4 hebephrenics, 1 showed no permanent improvement, while 3 improved sufficiently to work in the occupational department. Two of the 4 catatonics were discharged 'recovered'. It is interesting to note that both suffered from head injuries prior to admission. No appreciable improvement was noted in the paranoids.

Salicylates, therefore, have a quietening effect upon excited states in dementia praecox. The results, however, are only transitory in the majority of cases. Atophanyl is to be recommended in acute attacks. If permanent improvement is desired, it is advisable to combine the treatment with some other form of therapy, each case being judged on its own merits. I have found thyroid very useful in combination.

TABLE XI.

Results of Treatment with Atophanyl.

	<u>Treated</u>	<u>Recovered</u>	<u>Improved</u>
Hebephrenic	4	0	3
Catatonic	4	2	2
Paranoid	<u>2</u>	<u>0</u>	<u>0</u>
<u>Total</u>	<u>10</u>	<u>2</u>	<u>5</u>

5. 3/21/11.  
Cases Illustrating Results of Treatment with Atophanyl.

Case 9.



Before



After

Case 10.



Before



After

5. 2011.

Cases Illustrating Results of Treatment with Atophanyl.

most outstanding of all obtained from the patients

Case 9.



Before



After

Case 10.



Before



After

## 5. Afenil.

The results from this form of treatment were the most outstanding of all obtained from the various forms of therapy employed. I now use Afenil exclusively in the hebephrenics and in the acute phases of catatonia, unless otherwise indicated. It has been shown that the creatine content of the blood of catatonic patients showing marked rigidity was considerably increased above the value found in a group of normal controls, and that some of the patients showed a tendency to bleed for some time after the needle was removed. Creatine is a derivative of guanidine, and in 1922 Bayer showed a decrease in the calcium content of the blood in guanidine poisoning. In 1921, Noel Paton demonstrated that in guanidine poisoning the hyperexcitability to electrical stimulation, the clonic eclamptic attacks, the laryngo-spasms and the carpalospasms were very similar to those found in tetany. It would appear therefore that there is an interrelation between the lowering of the calcium of the blood and the simultaneous increase in guanidine and that both are factors in the production of tetany. A quick and easy method of determining calcium deficiency is by the enumeration of blood platelets in a blood film. The blood platelets were all decreased in the cases treated, and all showed an increase after treatment. From our point of view the most important group of symptoms due to calcium deficiency are those developed from the nervous system. Investigations have shown that both the central nervous system and

the vegetative - with a blood calcium deficiency - gave evidence to stimuli, the lowered threshold probably being at the synapses. At any rate, it was found that children, and adolescent particularly, thus affected, reacted with marked rapidity to all types of stimuli and at the same time more intensely than the average. These patients were inordinately affected by environmental changes, temperature variations, noises and disturbances of all kinds; opposition and criticism irritated them and they reacted rapidly to them. In the domain of vegetative nervous system likewise objective symptoms as well as subjective make their appearance. The calcium sub-utilization condition does not specifically affect the true sympathetic to the exclusion of the parasympathetic divisions of the system, but it accentuates the individual predilection of the patient. Thus, if a so-called vagotonic state is present ab initio, the lack of calcium makes a markedly vagotonic status of a moderately latent one; and similarly, with sympathetic type, the calcium disturbance accentuates all its symptoms. It is, therefore, the utilization of the calcium that is of tantamount importance. A few years ago I tried injections of parathormone. Injections, varying in strength and time of administration suitable to the cases, caused almost an immediate change in the varying symptomatology which I had looked upon as dependant on a low calcium utilization. The subjective sensation of a lack of muscular tension with attendant relaxation was stated to have occurred shortly after the first injection. As a consequence

of this lessened tension irritability decreased, fatigue disappeared and sleep became more normal. The conduct disturbance became much modified, and, in some cases after a week or two of treatment practically disappeared. To control these results treatment with the injection was discontinued for weeks at a time and some other bland injection substituted. The irritability with its attendant symptoms returned within a fortnight of the discontinuance. On the other hand, I have had no relapses in the cases treated with Afenil.

In reference to other calcium mobilization agents, notably with those containing Vitamins B and D, some of these latter medicaments were substituted with practically no success at all. Viosterol produced increased irritability in many cases and greater tenseness, though it probably enhanced the good effect of parathormone injections when given in combination.

A total of 26 cases have been treated so far, 12 hebephrenics, 2 paranoids, and 12 cases of periodic confused excitement of acute onset and equally rapid disappearance, with pronounced catatonic features.

Cases Illustrating Results of Treatment with Afenil.

Case 11.



Before



After

Case 12.



Before



After

Cases Illustrating Results of Treatment with Afenil.

Case 11.



Before



After

Case 12.



Before



After

In the catatonic group I found:-

1. That by using this preparation, a state of confused excitement that had already broken out, could be not exactly abated, but diminished in its severity, both as regards the motorium and the confusion.

2. That the onset of the excited states which were, with great probability to be expected, was prevented or reduced to rudiments.

3. That the better the free intervals, the better also are the prospects of a complete disappearance of the states of excitement - the less the deterioration of personality is noticeable during the quiet phase, the more likelihood is there of a complete remission.

4. In two catatonic final conditions, there was a marked increase of the extroversion, the connection with her surroundings to which the patients reacted even during their excitement in a way that had never been so noticeable before.

5. In 2 cases also, the attack of excitement did not occur in its catatonic form after Afenil and manifested itself only rudimentarily as a fluctuation of mood and activity, i.e. the endogenous waves of emotion again influenced the whole personality and no longer discharged themselves autonomously. However, the more advanced the schizophrenic dementia is,

the less apparently is the possibility of this connection between the personality and its control, and this perhaps explains why in the most severely demented final condition the autonomous catatonic movements keep on breaking through alongside the excitement which approximates to the symptom complex of simulated mania. In the purely paranoid type, the effects of Afenil are much less certain and the attitude in some of the chronic cases to their environment and their reaction to illusions and hallucinations becomes more active after Afenil.

6. In many fresh cases, however, of schizophrenic affection, the process comes to a standstill or can be rendered latent by Afenil. My most outstanding results in this series were in the hebephrenic group.

7. It also seems a noteworthy fact that many patients, even when at first they are distrustful or even antagonistic to the injections, after a few injections asked directly for a repetition, because they said they found their effect quietening and beneficial, and that even the patients in the advanced stage generally ceased all opposition to the injections after the third or fourth administration, and therefore felt their effect to be only pleasant.

Therefore the earliest possible application of Afenil is to be highly recommended in schizophrenic patients, especially in the hebephrenic type and in

those with periodic confused excited conditions, which, in my experience, respond directly in a striking manner to this treatment. The effect of Afenil upon the schizophrenic process is unmistakable, and, although it cannot be called a specific remedy for it, (yet, what can?), its employment is to be urgently recommended for its undoubtedly favourable effect upon the course of the cure. The possibility of having at hand, for our cases hitherto inaccessible to any medicinal therapy, a remedy which without even doing any harm may be relatively useful, does at least throw a hopeful light upon the treatment of mental diseases and opens up new prospects for the undertaking of their pathogenesis.

TABLE XII.

Results of treatment with Afenil.

	<u>Treated</u>	<u>Improved</u>	<u>Recovered</u>
Hebephrenic	112	22	90
Catatonic	112	13	77
Paranoid	12	0	0
<u>Total</u>	<u>236</u>	<u>35</u>	<u>167</u>

Cases Illustrating Results of Treatment with Afenil.

Case 13.



Before



After

Case 14.



Before



After

Cases Illustrating Results of Treatment with Afenil.

Case 13.



Before



After

Case 14.



Before



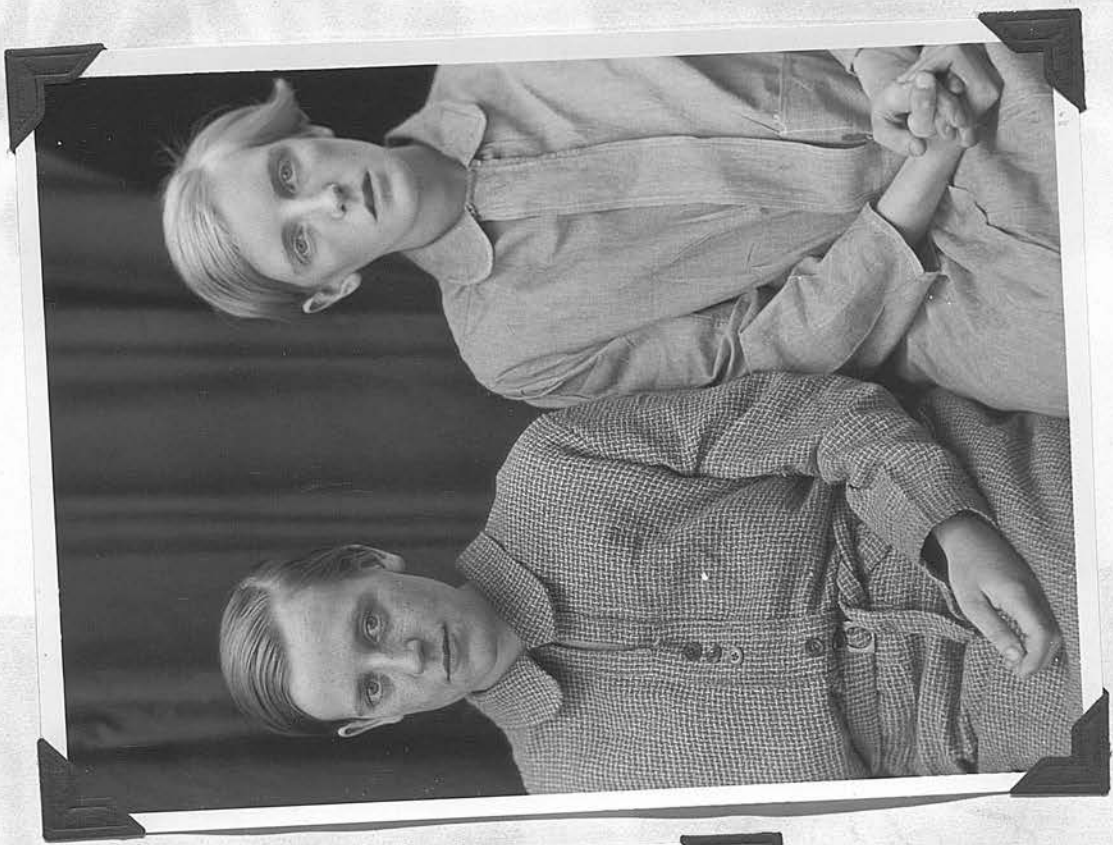
After

Case 8 before and  
after treatment  
with Opocaps  
Solution



After

Before



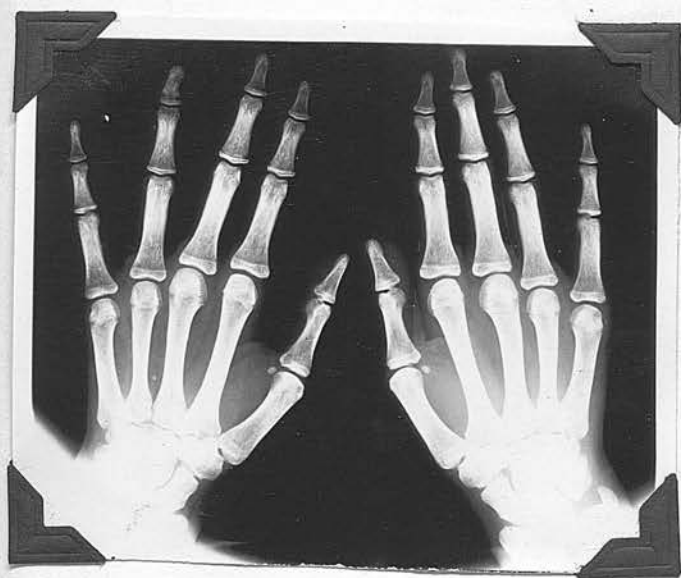
Before

Case 14 before and  
after treatment  
with Afenil

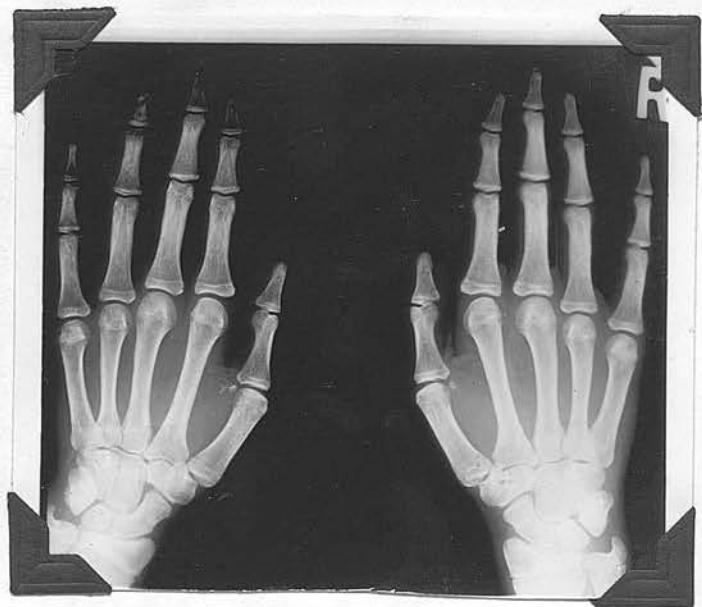


After

Before and After Treatment with Afenil.



Before



After



Before



After

Case Illustrating Result of Treatment with  
Collosol Calcium with Lecithin.

CASE 15.

E.G. Admitted 4.5.34.

Noisy, excited, troublesome and resistive.

Dirty and destructive in her habits. Negativistic and abusive. Said she was Lady Macbeth and had a vision of Christ on the Cross. Rambling and inconsequent in her talk.

Made a satisfactory recovery.

Discharged 28.8.34.

Weight on admission 8 st.

Weight on discharge 10 st.

Case Illustrating Result of Treatment with Collosol Calcium with Lecithin

Case 15.



Before



After

6. Collosol Calcium with Lecithin.

Eight cases received this form of treatment, 3 hebephrenics, 3 catatonics and 2 paranoids. The paranoids showed no change. The catatonics became more alert, showed some interest in their surroundings, and occasionally spoke. They relapsed on the treatment being discontinued. Of the hebephrenics all three became less excited, two improved sufficiently to occupy themselves in the occupational department, and one was discharged 'recovered'. Fig. 15 This patient was noisy, excited, impulsive in her actions and very mischievous. Her habits were dirty. Treatment was started one month after admission and she was discharged 'recovered' three months later, twelve injections having been given. All of the patients in this series showed physical improvement, but I do not regard the mental improvement of sufficient merit to warrant the adoption of this form of treatment.

TABLE XIII.

	<u>Treated</u>	<u>Recovered</u>	<u>Improved</u>	<u>No change</u>
Hebephrenic	3	1	2	0
Catatonic	3	0	3	0
Paranoid	2	0	0	2
<u>Total</u>	<u>8</u>	<u>1</u>	<u>5</u>	<u>2</u>

7. Sodium Nucleinate.

Six patients were treated by this method, all being of the excited type. Following the first injection all the patients became quieter and less restless, but there was no improvement in their conversation which remained rambling and incoherent. On each occasion following the injection of the nucleinate of soda an increased leucocytosis was found, but this, when not influenced by the drug, showed a tendency to fall quickly. The patients slept better and were generally less excited when under the influence of the artificial leucocytosis, but four of the six patients immediately relapsed in to their earlier restless, noisy state when the injections were discontinued. A high eosinophile percentage was, as a general rule, a sign of good prognosis. Of the two cases which recovered, I do not consider that it can be claimed that the injections had any effect upon the ultimate issue.

In excitement with confusion, there is a never-ending flight of ideas, a restless crowding out of consciousness of one thought after the other, hallucinations may arise to further embarrass the patient, and the mind is unable to concentrate its attention upon any one mental factor. However, if there be created

aphasic	3	3	0
Catatonic	3	3	0
	—	—	—
Total	6	6	0

C. Sulfosin:

In this series 13 patients were treated. Only a physical condition, such as can be produced by artificial means, which by its persistence demands the attention of the patient, and this will be accompanied for a short period by a cessation of the rapid flow of thought, and a concentration on the reality of a physical state, rather than on the changing scenes of an unstable psychical condition. A certain amount of attention is drawn to the affected area, and the patient is by force made to do a corresponding amount of self-examination, during which time she tries to concentrate her attention upon her present condition.

The disadvantage of the drug is the amount of reaction and the consequent pain and tenderness it produces. There is thus a danger that the patient may regard the treatment as a form of punishment. There is the greater danger that the staff will think the same.

All I can say is that in excited, noisy cases of acute mental disturbance it is useful as a means of allaying excitement and encouraging rest, and may therefore thus produce a state of mind which is, at an earlier stage than would otherwise be the case, ready to receive further treatment by other methods.

TABLE XIV.

	<u>Treated</u>	<u>Improved</u>	<u>Recovered</u>
Hebephrenic	3	3	0
Catatonic	3	3	0
<u>Total</u>	6	6	0

8. Sulfosin: There was loss of weight varying from 5 to 15 lbs. In this series 18 patients were treated. Only cases of doubtful prognosis were selected, cases with an undoubtedly good prognosis being purposely omitted. Stuporose patients showed the greatest degree of pyrexical reaction, and in all these patients temperatures varying from  $103^{\circ}$  to  $104^{\circ}$ F. were recorded. In 5 patients even with the maximum doses of sulfosin the highest temperature recorded was  $102.6^{\circ}$ F, but Schroeder states that good results may be obtained in schizophrenia even with the lower temperatures. In 8 of the cases it was found that a higher temperature was obtained with a moderate dose of sulfosin (5 c.c.) than with the subsequent larger doses (10 c.c.). This suggests that the patients developed a tolerance to the sulfosin after the first three or four injections. The temperature usually began to rise ten to twelve hours after the injection, in some cases within six hours and in others not till 18 hours. The pulse rate rose coincidentally with the temperature and returned to normal with the fall in temperature.

The leucocytosis was always polymorphonuclear in type, and counts ranging from 20,000 to 56,000 were obtained. Red counts showed a tendency to a mild secondary anaemia. The blood picture, however, soon returned to normal on the cessation of the injections.

All the patients treated complained of nausea, loss of appetite and severe pain at the site of injection, the muscles around becoming indurated and remained so

for some time. There was loss of weight varying from 5 to 14 lb. which was quickly regained after the injections had been discontinued. Of the 18 cases treated, 2 recovered, 3 were much improved, 3 had short remissions and 11 showed no change.

TABLE XV.

Results of Treatment with Sulfosin.

	<u>Improved</u>	<u>Recovered</u>	<u>Remission</u>	<u>Not Improved</u>
Hebephrenic	2	0	0	3
Catatonic	1	2	1	3
Paranoid	0	0	1	2
Simple	0	0	1	2
<u>Total</u>	<u>3</u>	<u>2</u>	<u>3</u>	<u>10</u>

was there any extreme excitement. There was, however, failure to maintain the improvement. At the end of two months there were few who had not relapsed, and it seems only a matter of time before all or most will have resumed their former mental state. In some cases periodical attacks of excitement were alleviated for a short period, while others showed a temporary improvement of bad habits.

However, little or no permanent improvement can be expected from this line of treatment. Perhaps the fitting results of this treatment in schizophrenia

9. Malaria.

Ten cases were treated with malaria, 3 hebephrenics, 4 catatonics, 2 paranoids and 1 simple. Most of the cases showed some degree of mental improvement, even during the course of the fever. In 3 cases there was no change whatsoever - the 2 paranoids and the 1 simple - in whom there was not the slightest deviation from their own particular mental state prior to inoculation.

In those cases which improved there was brightening of intellectual interest, desire to converse and to read, and in some a complete return to normal as far as could be judged. The patients began to write letters and there occurred a general transformation of interest. In some this improvement was preceded by a period of extreme irritability, though in no case was there any extreme excitement. There was, however, failure to maintain the improvement. At the end of two months there were few who had not relapsed, and it seems only a matter of time before all or most will have resumed their former mental state. In some cases periodical attacks of excitement were alleviated for a short period, while others showed a temporary improvement of bad habits.

However, little or no permanent improvement can be expected from this line of treatment. Perhaps the fleeting results of this treatment in schizophrenia,

19. Manganese Chloride.

Nineteen patients received this form of treatment as opposed to the seemingly permanent and progressive improvement in G.P.I. may be regarded as indirect evidence against the parasitic nature of dementia praecox, but even here it must be considered how far the biological relationship between the Plasmodium malariae - a protozoon and the spirochaete pallida explains the successful results obtained in the malarial treatment of G.P.I.

Regarding the blood picture, during the last week of the incubation period there was a definite lowering of the leucocytic level, with some evidence of leucocytic stimulation during the rigors, which disappeared when convalescence had been established by the administration of quinine. This leucocytosis was of a different nature from that following sulfosin, being much smaller in degree and bearing no evident relation to the pyrexial paroxysms.

TABLE XVI.

Results of Treatment with Malaria.

	<u>Improved</u>	<u>Recovered</u>	<u>Remission</u>	<u>Not Improved.</u>
Hebephrenic	3	0	0	0
Catatonic	4	0	0	0
Paranoid	0	0	0	2
Simple	0	0	0	1
<u>Total</u>	<u>7</u>	<u>0</u>	<u>0</u>	<u>3</u>

#### 10. Manganese Chloride.

Nineteen patients received this form of treatment, the duration of the disease being from two months to eleven years. The catatonic patients did not respond in any instance to the treatment, while two out of five paranoids showed improvement. The improvement rate was most marked in the hebephrenia type. Further, a far greater rate of improvement was obtained in cases treated comparatively early.

The weight chart and sedimentation tests proved the most valuable indices of the general condition of the patients and for ascertaining the optimum dose. The temperature and pulse variations were not of any special value in this respect. 73.6 per cent. gave an accelerated sedimentation test before treatment. This improved in 57.9 per cent of cases as treatment progressed. Manganese chloride may be expected to improve the physical condition of many patients with dementia praecox. No case was recorded as improved physically unless there was a sustained gain in weight during treatment. The salt, however, is contraindicated in larger doses than recommended, if given repeatedly as it will cause an exacerbation of physical symptoms if any major organic disease is demonstrable or even suspected. One of the essentials would appear to be that the optimum dose must not be exceeded. Therefore, it is not desirable to use it in a routine manner. An improvement in the physical condition

does not always mean mental improvement. It must be remembered that a gain in weight in patients presenting a praecox syndrome often accompanies the onset of psychical degeneration, even when not treated by this method. Of those who improved mentally, 5 were discharged, 2 recovered, and 3 improved. Two remain in hospital, working usefully, two years after treatment.

TABLE XVIII.

Results of Treatment with Manganese Chloride.

	<u>IMPROVED</u>	<u>RECOVERED</u>	<u>REMISSION</u>	<u>NOT IMPROVED.</u>
Hebephrenic	2	2	0	2
Catatonic	1	0	0	5
Paranoid	0	0	2	3
Simple	0	0	0	2
Total	<u>5</u>	<u>2</u>	<u>2</u>	<u>10</u>

Cases Illustrating Results of Treatment  
with Manganese Chloride.

Case 16.



Case 17.



### 11. Ringer-Locke Solution.

Fourteen cases received this form of treatment, 6 catatonics, 4 hebephrenics, 2 paranoids and 2 simple. I found that the most encouraging results were obtained when the cases were young, recent and acute, in whom the lesions had not progressed to any great extent. In the catatonic type recovery is only hopeful up to a year's illness and in the hebephrenic up to two years. Results are not to be expected in a short time and the greatest patience is required for this form of treatment, therefore the recoveries might have occurred spontaneously if waited for long enough, though it must be admitted that Ringer-Locke solution is an ideal medium for washing and nourishing living tissue, especially that of the central nervous system.

No effect was observed until after the seventh injection in catatonia, and the eighth injection in hebephrenia.

In the catatonics there was often some slight febrile reaction. They became less irritable and unsettled, less confused, slept better, and two cases the auditory hallucinations disappeared. The hebephrenics became less irritable, were better nourished, and in one case an hallucinosis cleared up.

This treatment is good for improving general nourishment and for sedative purposes; a good Diuresis is obtained, the appetite is stimulated and the patients become cleaner and more active. The general behaviour is, on the whole, improved. It had no effect on the paranoids and the simple type.

I do not, however, consider that this treatment is alone responsible for the improvements seen. It is undoubtedly of great value in all cases where there is any evidence of an associated toxæmia, and I now use it for all such, especially of the catatonic type, combining this treatment with whatever other form of therapy is indicated.

The treatment requires a maximum of personal attention to the patient. In a slowly advancing adolescent insanity, a good result is hardly to be expected in a short time; in hebephrenia there is a general breakdown in the mental life, which requires a total re-education of the deranged personality.

In the toxic case which is exhausted and refusing food, I believe there is no better form of treatment. Ringer-Locke's solution dilutes and washes away the exogenous toxins as well as the endogenous waste products present in the whole organism, it removes the irritating toxins from the cerebral hemispheres, and thus permits the general nourishment of the nervous system and all the other organs. Therefore the irritability, hallucinations and illusions are cleared up, and therefore the patients become less emotional and sleep and eat better as the general nourishment is gradually improved.

18. Somnifaine.

Twenty-seven patients were submitted to a prolonged somnifaine narcosis for a period of eight to fourteen days. In TABLE XIX. each injection of 2 c.c.

produced periods of sleep varying from four to eight hours. It is important to exercise the greatest

Results of Treatment with Ringer-Locke Solution.

possible care during the first three days, and to

investigate Improved Recovered Remission Not Improved

Investigate	<u>Improved</u>	<u>Recovered</u>	<u>Remission</u>	<u>Not Improved</u>
Hebephrenic	4	0	0	0
Catatonic	6	0	0	0
Paranoid	0	0	0	2
Simple	0	0	0	2
<u>Total</u>	<u>10</u>	<u>0</u>	<u>0</u>	<u>4</u>

there might not be a warning indication against the treatment. When evaluating the results, it is necessary to have a clear conception of the criteria used. Two phases may be distinguished:

1. The condition after completion of the treatment.
2. The condition after completion of the treatment.

In this discussion only the second category need be considered. "Improvement" is here meant to signify that a patient, within a few days of the termination of treatment, had passed into a better phase, i.e. established contact with the environment and on the way to becoming employable. About a week is often necessary for withdrawal symptoms to subside. Temporary amelioration during the first week or two after completion of the course was not considered as improvement. No patient was considered to have recovered unless there was complete restoration of her normal mental health, resulting in her discharge from hospital or being rendered fit for discharge.

12. Somnifaine.

Twenty-seven patients were submitted to a prolonged somnifaine narcosis for a period of eight to fourteen days. In most cases each injection of 2 c.c. produced periods of sleep varying from four to eight hours. It is important to exercise the greatest possible care during the first three days, and to investigate whether, because of some physical defect, there might not be a warning indication against the treatment.

When evaluating the results, it is necessary to have a clear conception of the criteria used. Two phases may be distinguished:

1. The temporary influence on the patient during narcosis and
2. The condition after completion of the treatment.

In this discussion only the second category need be considered. "Improvement" is here meant to signify that a patient, within a few days of the termination of treatment, had passed into a better phase, i.e. established contact with the environment and on the way to becoming employable. About a week is often necessary for withdrawal symptoms to subside. Temporary amelioration during the first week or two after completion of the course was not considered as improvement. No patient was considered to have recovered unless there was complete restoration of her normal mental health, resulting in her discharge from hospital or being rendered fit for discharge.

The clinical picture of catatonia is often altered by somnifaine treatment; during the course they showed an increased contact with reality and were able to converse. The results on the whole, however, in catatonic stupor were disappointing, for as soon as the narcosis was interrupted they relapsed into their former state of stupor. Two patients in a violently exalted condition, hallucinated, singing, screaming and cataleptic, during treatment became quiet and reacted satisfactorily, the catalepsy disappearing. They very soon, however, relapsed into their old condition upon the cessation of treatment.

In the depressed forms of hebephrenia showing tearfulness and depression with delusions of reference and hypochondriacal ideas, the results were, on the whole, encouraging. Four became free from depression and were able to interest themselves in occupational therapy, while two had good remissions and were fit to be discharged recovered.

Many of the exacerbations of excitement were due to the development of an acute hallucinatory phase. This phase was much less in evidence or had disappeared after treatment, these patients passing into a quiet amenable and co-operative state.

Patients who refused to employ themselves and exhibited negativism, employed themselves usefully in the occupational department following treatment and their contact with reality was greatly improved. It is here essential to commence occupational therapy

at the earliest possible opportunity in order to follow up any advantage gained by the narcosis. This is particularly essential in autistic and stuporose patients who have been temporarily extricated from their phantasy life and gained an increased feeling of freedom from conflict. Prolonged narcosis should form only a part of an organised scheme of therapy, its purpose being to make some attempt to break through the faulty habit of thought into which the patient has fallen, first, by putting her mind completely at rest, and secondly, the post-narcotic period should be made a starting-point for the formation of new habits of thought. In the twilight states of prolonged narcosis the suggestibility of the patient is markedly increased; therefore the constant use of reassurance and suggestion is indicated. In this group of mental disorder the prolonged narcosis might act in two ways.

1. By controlling motor excitement.
2. By causing a shift of the symptoms towards a condition of facility.

Success is most easily achieved with the early cases. The period of therapeutic narcosis must be continuous and it should be emphasised that there is an essential difference between this form of therapy and the routine administration of sedatives given in fixed doses, and at fixed times, merely to control turbulence.

Of the toxic symptoms which frequently accompany the narcosis, the most important are ketosis, albuminuria, fall of blood pressure, circulatory collapse,

tachycardia, pyrexia, difficulty in swallowing and skin eruptions of an erythematous nature.

A disturbance of the carbohydrate metabolism of vital organs occurs during prolonged narcosis with somnifaine, clinical evidence of which is seen in the development of ketonuria, which is a contra-indication for further treatment. It has been shown that narcotics inhibit the oxidation by the brain, liver and heart of substances such as glucose and lactic acid, which are important in carbohydrate metabolism, the inhibitions being much greater with the brain than with the other organs. Ketonuria is the outward manifestation of this disturbance, but it is claimed that other symptoms, such as circulatory collapse can be ascribed to the same fundamental cause.

This knowledge that carbohydrate metabolism was effected by narcotics led to the adoption of the administration of insulin and glucose during narcosis with a view to eliminating dangerous symptoms.

Narcosustained therapy is not without danger. The dangers are lessened by carefully eliminating contra-indications and by employing a carefully trained nursing personnel. In the post-narcotic stage lasting for three days or over, the patient is conscious but her memory for recent events remains clouded and retention is poor. Long-standing deteriorated cases respond slightly, if at all.

The mechanism of recovery or improvement seems to be psychological rather than biochemical. A psychodynamic formulation seems not only more reasonable and more tenable but is readily correlated with, and supported by well-founded psychological and psychiatric observations. All afferent stimuli are excluded, thus giving the organism an opportunity to regain its equilibrium.

TABLE XX.

Results of Treatment with Somnifaine Narcosis.

	<u>Improved</u>	<u>Recovered</u>	<u>No change</u>	<u>Total.</u>
Hebephrenic	2	4	2	8
Catatonic	5	.1	2	8
Paranoid	3	0	4	7
Simple	1	0	4	5
<u>Total.</u>	<u>11</u>	<u>5</u>	<u>12</u>	<u>27</u>

14. Ultra-violet Radiation.13. Vitamins.

(i) Radiostol. Ten cases, 3 hebephrenics, 3 paranooids and 4 catatonics were treated for three months but the results being disappointing, other forms of therapy were resorted to. The hebephrenics showed no change, one paranoid became less impulsive and excited, but the change was only temporary. Two of the catatonics became brighter, answered when addressed, and one began to work. Towards the end of the treatment, however, they all gradually reverted to their former condition.

It will be admitted that most mental cases have a greater chance of recovery when their physical condition is good, and ultra-violet radiation is a valuable aid to this end. The more usual therapeutic aids must, however, on no account be omitted. Further, I believe that part, at least, of the beneficial results obtained with this treatment are due to psychological effects in suggestible patients.

13. CO<sub>2</sub> Mixture.

While breathing the gaseous mixture there occurred a marked increase in the depth of respiratory movements

14. Ultra-violet Radiation.

This treatment is employed as a routine in convalescent cases, for light baths are of obvious utility in improving metabolism. It is a useful adjunct to other forms of treatment, appetite, nutrition, weight and sleep being improved. An improvement, however, in the physical state is all that can be expected, if discount is made of suggestive influences.

It will be admitted that most mental cases have a greater chance of recovery when their physical condition is good, and ultra-violet radiation is a valuable aid to this end. The more usual therapeutic aids must, however, on no account be omitted.

Further, I believe that part, at least, of the beneficial results obtained with this treatment are due to psychological effects in suggestible patients.

minutes the original state was regained. Repeated experiments always produced the same results.

Catatonia breathe more slowly than other schizophrenics, it may be, therefore, that the shallow breathing of schizophrenics is ordinarily compensated for by the increased rapidity of respiration, but that when the rate falls during an increase in the catatonic state then failure of oxidation ensues, with cyanosed extremities and increased torpor of mind. Increase of

15. CO<sub>2</sub> Mixture.

While breathing the gaseous mixture there occurred a marked increase in the depth of respiratory movements, although not a great increase in their rapidity. The face became suffused and red. At times a more general convulsive picture with movements of the hands and feet occurred. When the gas mask was removed, the respiration continued deep for approximately a minute. The face took on a more normal expression with a tendency to smile. Several of my patients struggled and requested the mask to be removed - others sat up, walked about and obeyed requests, all movements being lively. The majority talked freely, some coherently and intelligently, others a word salad with obscenity. This period of lucidity and more or less spontaneous activity lasted, on the average fifteen to twenty-five minutes. At the end of about fifteen minutes, a somewhat startled, amazed and confused expression came over the face. The patient began to move more slowly, responses to questions were delayed and at the end of another five to fifteen minutes the original state was regained. Repeated experiments always produced the same results.

Catatronics breathe more slowly than other schizophrenics, it may be, therefore, that the shallow breathing of schizophrenics is ordinarily compensated for by the increased rapidity of respiration, but that when the rate falls during an increase in the catatonic state then failure of oxidation ensues, with cyanosed extremities and increased torpor of mind. Increase of

breathing from administration of  $\text{CO}_2$  seems to improve the condition. Observations of patients receiving the  $\text{CO}_2$  mixture show that there is an increase in the depth of respiration with an increase in the alveolar tension and a consequent increase in the amount of  $\text{O}_2$  and  $\text{CO}_2$  received into the blood stream. There is an initial increase of heart rate, the systolic blood pressure is raised, the superficial vessels of the face are dilated and there is also an increase in the C.S.F. pressure. Patients with long-standing schizophrenic symptomatology show less response to the  $\text{CO}_2$  and  $\text{O}_2$  mixture than do the patients in more acute attacks. The most that happens is an odd word salad-like response, leading us to question if this is not the full capacity of their cerebral process at the time.

2. Carious teeth with infections.

3. Apparently healthy teeth with periodontitis.

4. Periapical granulomata.

5. Gingival granulomata in apparently vital teeth.

6. Extensively filled teeth, with evidences of infection at the root.

7. Devitalized teeth with either Richmond or gold shell crowns.

Unerupted and impacted third molars or wisdom teeth occurred in 13 per cent. of the cases. When there are clinical evidences of septic infection and intoxication present, these teeth should be extracted, for they are nearly always infected, and this infection

16. Removal of Sepsis.

The incidence of sepsis in my series of cases, with the exception of infected teeth, was not large.

Two cases suffered from chronic suppurative otitis media with a persistent perforation and evidence of recent discharge. Such cases may be described as residua of otitis media. Both cleared up in about three months, Ringer Locke solution, 1,000 c.c. being given weekly, in addition to local treatment. It is interesting to note that toxæmia resulting from chronic aural suppuration is very rarely seen.

Eighty-eight per cent. of the patients had infected teeth, which may be divided into:-

1. Unerupted and impacted teeth, especially third molars.
2. Carious teeth with infections.
3. Apparently healthy teeth with periodontitis.
4. Periapical granulomata.
5. Gingival granulomata in apparently vital teeth.
6. Extensively filled teeth, with evidences of infection at the root.
7. Devitalised teeth with either Richmond or gold shell crowns.

Unerupted and impacted third molars or wisdom teeth occurred in 49 per cent. of the cases. When there are clinical evidences of septic infection and intoxication present, these teeth should be extracted, for they are nearly always infected, and this infection

appears to be in some way related to the fact that the tooth has not erupted in a normal manner. The X-ray pictures of these teeth will not show evidences of infection, but cultures made from the cavities nearly always show pure cultures of streptococci. All crowns and fixed bridge work are to be condemned; all devitalised teeth should be extracted and no suspicious teeth allowed to remain. This is not a radical doctrine and does not mean necessarily that all patients must have all their teeth extracted, but a thorough elimination of oral sepsis can only be obtained by extraction.

In all cases intestinal lavage was used. It may be employed as a single wash-out for a day or two, or where not contra-indicated, a double wash-out is employed, this procedure having diagnostic value, as well as being therapeutically beneficial. The extent to which the second wash-out returns rich in faeculent matter with a very offensive odour and an abundant bacterial flora, is a definite indication of the degree of excessive putrefaction present in the bowel. The frequency and duration of treatment by lavage depended upon the results observed. In some cases the condition rapidly improved, and the lavage was dispensed with or adopted intermittently after a few days or a week or two. Care and good judgment are required in the handling of patients in regard to this treatment. The success of the treatment has to be judged by its influence on the reduction and disappearance of the foetor

of the stool and double wash-out, by its influence on the urine and on the general condition of the patient. With the exception of charcoal, I have not found drugs of the intestinal antiseptic class of any particular value as an aid to treatment.

The effect of the removal of focal infections on the course and outcome of the psychoses in individual cases cannot be judged unequivocally because of the many factors that enter into the recovery and improvement of psychotic patients. I have, however, except in the two cases mentioned of chronic aural suppuration, failed to note any evidence that would lend support to the belief that the course of the psychosis is directly influenced by the elimination of focal infection. This is not to say that it is unnecessary to eliminate focal infection in psychotic patients. On the contrary, psychiatry owes Cotton a lasting debt for directing attention to the neglect of certain physical conditions in those suffering from mental diseases, therefore all focal infection that can be adequately demonstrated should be eliminated. There are many intermediate products of chemical decomposition in the intestinal tract which may have a toxic effect and perhaps contribute to a psychosis. Also, problems of metabolism, endocrine disturbances, etc., may involve a consideration of toxins other than those of a specific bacterial nature, but I consider that there is no relation of

TABLE XXI.

cause and effect between specific bacterial toxins coming from focal infection and dementia praecox. The isolation of organisms from an area in which contaminants are present, as in the case of the teeth or cervix cannot be considered as establishing the presence of focal infection. The mere definition of infection is open to various interpretations. For example, Cotton considered the presence of bacteria in the stomach contents as a criterion of infection. The mere presence of bacteria does not necessarily imply infection; it is at least necessary for the bacteria to multiply and probably necessary that they should invade the tissues. While it is desirable to treat the patients by any means that will improve their physical condition, it is not to be expected that this will, per se, clear up the psychosis.

Method	No. Treated	Recovered	Improved	Percentage
Endocrine	59	25	4	42
Opojex Lymphoid	54	11	9	33
with Iodine	5	1	5	75
Sodium Chloride	4	0	0	50
Sulfur	18	2	5	50
Solution	14	0	14	50
Somifaine	27	5	11	39
TOTAL	243	67	67	

A total of 243 patients have received various forms of treatment. I have only classed outstanding cases as recoveries. Under the heading 'improved' are classed what I regard as 'social recoveries'. These patients have been discharged however, as 'recovered' and have been able to resume their normal every day existence. Therefore the total recovery rate in this series is 63.3 per cent.

Discussion.

TABLE XXI.

Summary of Results of Various Methods of Treatment.

<u>Method</u>	<u>No. Treated</u>	<u>Recovered</u>	<u>Improved</u>	<u>Combined Percentage</u>
Endocrine	69	25	4	42
Opojex Lymphoid Solution	24	11	9	83
Sodium Salicylate	12	0	12	50
Atophanyl	10	2	5	70
Afenil	26	17	5	84.6
Collosol Calcium with Lecithin	8	1	5	75
Sodium Nucleinate	6	0	6	50
Sulfosin	18	2	6	50
Malaria	10	0	7	35
Manganese Chloride	19	2	7	47
Ringer Locke Solution	14	0	14	50
Somnifaine	27	5	11	59
<b>TOTAL</b>	<b>243</b>	<b>67</b>	<b>87</b>	

A total of 243 patients have received various forms of treatment. I have only classed outstanding cases as recoveries. Under the heading 'improved' are classed what I regard as 'social recoveries.' These patients have been discharged however, as 'recovered' and have been able to resume their normal every day existence. Therefore the total recovery rate in this series is 63.3 per cent.

VII. CONCLUSIONS.Discussion.

Dementia praecox in the past has been more or less placed in the class of incurable and hopeless diseases, and anything that offers a possible amelioration is worthy of support. Much suggestive work on the subject has been done in the past, but without proper co-operation and without being brought to a satisfactory conclusion.

The symptomatology of the large provisional group of dementia praecox is now sufficiently familiar. Much work has been done in differentiating this group from other groups and in dividing it into sub-groups, also in giving further definition to individual symptoms. The psychology of the disorder has received much study and attention has been drawn to the two main factors, the disorders of volition and the dissociation of the emotional from the intellectual life. On the other hand, the physical symptoms have been emphasised and histopathology has contributed some facts with regard to cortical changes.

In endeavouring to find out the nature of any disorder, the line of investigation is often already determined by the nature of the clinical data. Thus in the presence of a fever, one thinks of working along the lines of ordinary bacteriological technique. When one endeavours to find out the essence of a complex disorder of the biological economy like dementia

praecox, the line of investigation is not so clear; the few facts available are often interpreted not so much in the light of clinical experience as in the light of a priori theories. When it is a question of formulating a conception of dementia praecox, two widely divergent attitudes are encountered. One set of investigators consider that the most hopeful line of investigation is to be found when we regard dementia praecox as essentially similar to general paresis, where nerve tissue is destroyed by undetermined poisons and where in the slow deterioration of the nervous system many mental pictures may crop up. These mental pictures may be of diagnostic help but are considered as irrelevant features from the dynamic standpoint and not as important guides to the pathogenesis of the disease. A very different point of view is that of those who do not a priori rule out the dynamic importance of psychological factors, nor believe that it is only in hysteria that this principle is available. They do not divorce psychological reactions from the other reactions of the individual, but consider them merely as the most complex of human biological reactions. The tendency of those who adopt the former point of view, i.e. that general paresis is the paradigm of dementia praecox, is to remain content with rather formal clinical differentiations, to refer to the presence of mannerisms, stereotypes, odd reactions, delusions, hallucinations, etc. without paying much attention to their content, and without

endeavouring to ascertain what relation such content bears to the life history of the individual. It is assumed that such reactions are more or less meaningless, not to be psychologically analysed, and that one must look away from them to the various pathological laboratories for further light on the pathogenesis of the disorder. It is important to note that this assumption depends upon a general philosophical attitude rather than upon any established body of observations.

In dealing with a disorder that has been discussed from so many and such diverse points of view, it is necessary that one defines somewhat definitely the conceptions upon which the experimental attempts and the interpretations are based. The diagnosis of schizophrenia is, in many cases, difficult, and cases diagnosed as such by one observer, may not be similarly diagnosed by another. Dementia praecox is a reaction trend and an entity only and to a lesser degree that headache and fever is an entity. It is a disorder of multiple causation, as amongst the "causes" demonstrated of the psychosis are puerperal and other sepses, trauma, fevers and unresolved psychic conflicts.

Studies on metabolism in dementia praecox have been numerous: the blood has received attention: every constituent of the urine has been estimated and wide reaching conclusions drawn. The various glands with internal secretions have furnished ready material for hypotheses, and an endocrine theory has received much support in some quarters. While there is no doubt  
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that endocrine preparations do much good in many cases, the findings are not consistent with the constant presence of any definite endocrine disorder, and do not suggest that a simple glandular dysfunction of a constant type is an etiological factor in schizophrenia. Rather they suggest that many functional disorders, closely linked up with the endocrine system, are frequently found and that schizophrenia is not a specific endocrine disease but may arise on a number of different bases. Endocrine dysfunctions frequently occur without psychoses, and another alternative has to be borne in mind, viz. that the organic changes in the brain and endocrine glands are secondary to the mental disorder.

Pituitary dysfunction has been held to be very common in dementia praecox. I have not found this in my series, nor have I been impressed with the results of treatment with pituitary extracts. Sajous (263) holds that the pituitary is a nervous centre: the anterior lobe acts as a sensory structure or test organ for the detection of toxic substances in the blood, and may, through the intermediary of the thyroid and adrenals stimulate the defensive functions of the body. The posterior or neural lobe is believed by Sajous to be the nucleus of the sympathetic nervous system. Other investigators have recognised the importance of differentiating assumed internal secretion effects due to a nervous mechanism. Baily and Bremer (264) found

that polyuria and even genital atrophy and adiposity, usually held to be symptoms of disturbed internal secretion of the pituitary, result from even minute lesions of the para-infundibular region of the hypothalamus.

The stress which has been put upon certain disturbances in calcium and lipoid metabolism, (cholesterol, lecithin, etc.), and offered as a possible etiological factor, does not seem to be justified, as the deviations for calcium and lipoids in such overt endocrinopathies are minimal. The enormous social and economic importance of the functions of these glands, coupled with the usual assumption of interdependence upon the internal secretory activity, has inevitably coloured thought and influenced trends of study.

The story of evolution is that of the attempts of organisms to adapt themselves to their ever-changing environments. In the response of organisms to environmental stimuli, the nervous and endocrine systems play an all important part. The two systems are intimately connected both as regards structure and function, the nervous mechanism controls and co-ordinates the more primitive chemical mode of response.

Centuries ago Lucretius (265) pointed out that the "mind is begotten with the body, grows up together with it and becomes old along with it". "The psyche", says Kempf (266), "is not something which has been added in the course of evolution, its history is

that of the history of the body".

Sex implies phylogenetic differentiation; reproduction the fusion of the differentiated parts. It is the external manifestations which are the prime factor in reproduction, which is, after all, the one essential. However, conservative interpretation of experimental evidence, regards a concomitant endocrine function as one essential for the proper development of those portions in which the outward capacities have their origin. The true sequence of the stages of development leading first to maturity and later to the recessions incident to the decline of reproductive power, are intrinsic, seemingly, in the proper functional adjustments, not only of the gonads themselves, but of a number of other centres of endocrine activity. Degenerative changes do not rigorously exclude all traces of the parts of endocrine function. When one realises how fractional residua are capable of maintaining function, it would seem wise to maintain a scepticism towards the comprehensive generalisations based on partial experiments.

That the endocrine glands are among, though not the only, potent regulators of growth and development will be conceded by all, many of their effects being mediated through and by that vastly complex series of interrelated mechanisms, which are conveniently grouped under the title metabolism. The inference warrantable from the foregoing, is that agencies,

- in some cases probably both. Here again, the presence of the two components need not necessarily which affect metabolic levels, be it directly or indirectly, through the hormone control of the endocrine glands or through the manifold intrinsic functions of the nervous system, through one or both, working independently or together, that such agencies may be associated with the mental status.

In the child with the behaviour problem, in the patient with mental disease, there is no inevitability in an association with endocrine malfunction. Even more is there an equal or even greater lack of unvarying sequence of mental disease following or occurring with functional disorders of the ductless glands. On the other hand, high degrees of correlation have been recorded. That the great majority of the larger series with like metabolic derangements fail to show equivalent mental disorders, implies the presence of at least another deciding factor in the equation. That a tendency to mental disease is transmissible from generation to generation is a well-documented and generally accepted belief. In my series an hereditary element was present in 87.6 per cent. Such a constitutional tendency to mental disease, derived either from heredity or from other predisposing factors of the nature or even existence of some of which we are to-day ignorant, could furnish a soil fertile to outside influences. These could be psychogenic or physiogenic

live only if the summation of their several indices exists a critical boundary. The difficulty of distin-

- in some cases probably both. Here again, the presence of the two components need not necessarily produce an end result of a psychosis. In the study of human fertility we recognise to-day what may be called a fertility index for each partner. This is a quantity which is the elaborate summation of a wide variety of favourable and opposing agencies, intrinsic in, and characteristic of the individual possessing them. Fertility of union results when the combination of these two indices of the two partners, thus constituting a "mating index", is superior to a certain critical zone or boundary. Therefore, fertility is usually a relative term falling between the limits of absolute fertility and absolute sterility. The partners in an infertile union will both frequently demonstrate power to reproduce when mated with other partners of a higher relative fertility. Dementia praecox, further, is not infrequently seen in the only child of a union.

adult an It may thus be the same with the causal factors in the psychosis. One could conceive of the two necessary components, one a constitutional tendency of diverse and varied origins, endocrine, etc., the other the outside agent, simple or complex, psychological or physiological, one or both, these two acting together to produce the end result of the mental disease. In such a concept there is again no inevitability. All of the factors may be present, but they become productive only if the summation of their several indices exceed a critical boundary. The difficulty of distin-

guishing between hereditary and acquired traits, of saying what is constitutional and what is not, is the "correlative unity of those morphological, physiological developments of the individual, which are definitely more influenced by heredity than by environment", Draper's view or definition being "a set of basic unit characters predetermined by heredity and influenced to some extent by environment".

While the schizophrenic disorder is to a large extent intelligible as the reaction to the life-situation the latter need not be of any dramatic quality. In the history of the patient, one may note no outstanding event or situation which seems to involve undue strain, and conditioning factors of importance in early life may have escaped notice. When one scrutinises the symptoms of the psychosis and when one reviews with the patient the various steps in her experience, one appreciates better the rôle which the actual life-situation has played in the whole development. The adult environment may be of very normal appearance and the early moulding forces of the patient's life may seem to have been little different from those of her fellows, but the unobtrusive forces of the environment may have subtly and profoundly influenced her adjustment to the insistent demands of sex, to the bond between parent and child, to the opinion of others, and may have modified the vulnerability of the personality

observations on metabolism and other bodily functions. ability. Psychological reactions must be looked upon as merely the most complicated biological reactions. In such reactions there is always a somatic component of more or less relative importance. The disorder of the biological economy in dementia praecox in terms of a lower denominator than one which includes psychological reaction would be to fail to do justice to the facts of observation. Unhampered by empty hypothesis as to the mutual relationship of mind and body, and refusing to express the facts of observation by an inadequate denominator, we are able to direct our activities wherever facts can be modified.

When we understand better the development of cases of dementia praecox, the soil upon which it is most likely to arise, the educational and social factors which appear to influence it, the nature of the troubles which seem to precipitate it, the physical disorders which accompany it, we shall perhaps be able to aid more effectively in the development of these individuals who give evidence of ominous constitutional traits, and be able to contribute more guidance towards the mental health of the community. Treatment shows that even when the disorder has been established, a bad prognosis is no longer inevitable. Rather should we weigh all the facts in the development, consider how far the circumstances are modifiable

in relation to the tests of adult life. This vulnerability, partly determined by congenital endowment, is also influenced by a long series of situations and experiences, the significance of which is apt to be overlooked.

The overt series of reactions which constitute the psychosis, is often but the later stage of a maladjustment, which stretches far back to the childhood of the patient. The study of the etiology of a schizophrenic psychosis is the study of the action and interaction of an individual, congenitally predisposed, and her environment over a long period, and throws light on many phases and varieties of human maladjustment.

When, therefore, we see the symptoms of this mental disorder consist in the outcropping in a peculiar distorted frequently symbolic form of the thoughts and ruminations and longings of the individual, and when we find these elements have been a disturbing factor throughout the patient's life, and that this disorder appears to arise in individuals of certain temperamental peculiarities, our conception tends to gravitate towards the psychological side. In doing this, we in no way neglect the importance of the physical symptoms incident to the disorder. The fact that one attributes importance to hereditary and psychological factors does not mean that one neglects

observations on metabolism and other bodily functions.

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In these comments which I have offered there is a complete elimination of supporting references from the literature, as much of the material offered must be regarded as still in the process of its evolution and the final generalisations no more than the hoped for outcome of the future.

Each member of the community is an entity, combining in her person the summation of the great vital forces of heredity, of environment, both external and internal, and of nutrition, of growth, of development and such others as may be regarded as intrinsic in the stuff of which we are compounded. In our daily lives we act and are acted upon by our environment and similar agencies and no two of us respond in straitly identical terms to a common stimulus. Likewise, within the individual body with its myriad of homeostatic adjustments, its personal characteristic degrees of tolerance, and its limitless possibilities, seemingly common end results may and do arise from a wide variety of causes. As the inevitable corollary it follows that like or identical agencies operating in the medium of the individual body may equally engender terminal conditions of which the imperfect knowledge of to-day forbids an interpretation in terms of equality or even parity.

The keynote to-day in dementia praecox is one of warranted optimism. From the incomplete seemingly contradictory and inconsistent mass of material which we at present possess, the work of the future, be it near or far, will gradually resolve into the ordered system which

to-day we but imagine in the shadowy and amorphous outline lighted from afar by our meagre knowledge.

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