ETIOLOGICAL FACTORS

AND

ENDOCRINE THERAPY

IN

INVOLUTIONAL MELANCHOLIA.

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SELECTION OF CASES.

Involutional melancholia is that form of mental disorder characterized by depression without retardation, anxiety, self-accusatory and self-depreciatory trends, hypochodriacal and nihilistic delusions, and feelings of unreality. Only those cases where there is no previous history of mental disorder may qualify for the term involutional melancholia. This syndrome is usually prone to develop at the involutional period which, in women, has been roughly fixed at the age 40 to 55, but which may occur before this.

In the origin of the psychosis various factors are involved. The climacteric itself is frequently implicated and heredity and environment may play a part. Psychic and physical factors may bulk largely in the etiology, whilst physical type and personality make their contribution. Different authorities stress different factors. According to some, endocrine changes are more important, whilst others emphasize more the psychic aspect. The varied etiology of involutional melancholia can be illustrated by reference to the cases examined at the Glasgow Royal Mental Hospital where psychic factors were paramount in 57% of the women and physical in 21% (1), and by reference to William Mabon's figures, where psychic factors were causal in 47%, physical in 34%, and a combination of these in 17% (2).

In the present series twenty cases were examined including one who developed her psychosis subsequent to artificial menopause. This latter was the youngest, thirty-three, and the oldest, at the commencement of psychosis, was fifty-one. The material was accumulated from the hospital population after eliminating those cases where the disorder presented features more in consonance with paraphrenia, manic-depressive, or organic psychoses. Furthermore, cases over sixty years of age at initiation of treatment were left out as being less likely to be profitable subjects for investigation. All the cases presented depression without retardation, anxiety, and the typical trends or delusions. Three of them showed a hallucinatory tendency during the initial acute phase.

INFLUENCE OF HEREDITY.

The difficulty of obtaining accurate information about the presence of mental disorder in family histories is notorious, and the present series is no exception.

Information has been culled from patients' relatives and friends - generally the most illuminating - and where possible from case records and from direct observation of abnormal relatives, and of these twenty cases twelve were found to have abnormal heredity in the direct, collateral, or atavistic line.

In two cases, Jane A. and Isabella J. the mothers were involutional melancholic and moral defective, respectively; in one, Jane B. the father was a chronic drunkard, and in a fourth case, Maud P. the mother was

an involutional melancholic, whilst the father was an alcoholic. In Jane A's case a sister of her mother died in a mental hospital, whilst in Jane B's case her father's sister was a schizophrenic and both her father's brother and cousin died in mental hospitals.

Alcoholism was in evidence in two of these ancestries. It has been pointed out that alcoholism is itself often a symptom of mental instability (3), and undoubtedly with reference to the father of Jane B. the family history would indicate that in this case alcoholism was such a symptom. In the instance of Maud P. not only was there the alcoholism of the father, but there was the more definite involutional melancholia, and suicide of the mother. This event occurred when the mother was 45, and the fact that her daughter developed the same psychosis nine or ten years earlier might be due to anticipation. Mott has pointed out in his investigations that insanity tended to occur at a much earlier age in the offspring than in the parents (4), and Paterson, whilst disagreeing with some of Mott's work, has agreed that the rule applies where the patients became affected later in life (5).

Purely collateral heredity was present in seven cases and embraced mental deficiency in two instances, involutional melancholia, schizophrenia, neurasthenia, and marked eccentricity, respectively in four, whilst the nature of the psychosis could not be ascertained in the remaining case. In the one case of atavistic heredity the psychosis was senile dementia.

In two more cases the mothers suffered from apoplexy and subacute combined degeneration respectively.

Koller in her examination of 370 psychotic cases found that hereditary tainting with insanity, nervous diseases, apoplexy, alcoholism, senile dementia, abnormal character and suicide, occurred in 76.8% of the psychotic series, whilst Diem, working on a much larger series, found an hereditary taint in 77%, and found further that direct inheritance took place in 50 - 70% (6).

In the above series of twenty involutional melancholics, if apoplexy and nervous disease be included, heredity, direct, collateral and atavistic, insofar as could be ascertained, was therefore present in 70% of the material, and to this extent approximating to the figures of Koller and Diem. Direct inheritance, however, took place in only 30% of these cases. In these latter cases it was borne out that mother-daughter transmission was commonest (7). Four were definitely of this type, one was father-daughter transmission, whilst in the remaining case, Maud P., both father and mother were implicated but with the more likely involvement of the mother.

EFFECT OF ENVIRONMENT.

The county of Northumberland embraces a large and sparsely populated rural area, an extensive mining area along the southern half of its coastal strip, and the industrial region on the north bank of the Tyne.

Northumberland Mental Hospital draws its admissions from the entire rural area, from the mining area, and from the industrial region north of the Tyne, with the exception of that part drained by the City of Newcastle.

The usual finding of the greater rural incidence of involutional melancholia also applied in the cases under investigation. Twelve cases came from the agricultural areas or from the small mining villages, whilst only eight derived from the industrial towns on the Tyne or from the few moderate sized towns elsewhere in the county. Of the twelve cases drawn from a rural environment one was a native of a country district in North Devon.

There appeared to be an increased tendency towards recovery in the rural group, eight out of twelve, compared with the urban group, four out of eight, and the average duration of the illness in the former group was considerably less than in the latter, 3.8 years compared with 5.1 years. Moreover, the average age at the commencement of the psychosis was 44.3 years in the rural compared with 42.7 years in the urban series. Lest this should be a coincidence, all discharges of female involutional melancholics for the preceding three years, 1938 - 1940, were examined. The case records were scrutinised and only those patients between the ages of thirty-five and sixty presenting the clear-cut clinical picture, were accepted. Although the higher rural recovery rate was not substantiated, the other findings appeared to be borne out, for in the rural group the average duration was 1.15 years and in the urban 1.5 years, whilst the average age at onset in the rural was 45.6 years compared with 42.4 years in the urban group. From the above data the psychosis, whilst it was more common in rural patients, not only developed at an earlier age in the urban patients, but tended to last longer in those of this latter group who recovered.

In the case of these patients then, investigations were made to see if there were any factors operating earlier or with greater intensity in the urban group. The definite factors which emerged were that the bulk of the urban women were single, and therefore lacked the stabilising effect of a happy marriage; that four out of the eight urban cases had faulty home conditions during their childhood, or suffered considerable repression, and that in two cases the abnormal home conditions were due in considerable part to the alcoholism of the fathers. In this latter connection Bevan Lewis has pointed out the higher incidence of alcoholism in maritime, mining, and manufacturing communities (8).

From a study of these cases it seems not impossible that patients predisposed to involutional melancholia by their personality may have found more adverse, and more severe conditions in the more intricate society of an urban environment and broke down earlier than they might have done in purely rural surroundings.

RACIAL TYPES AND BODILY HABITUS.

The causes of Involutional Melancholia were investigated from the point of view of Racial Type and of Bodily Habitus.

Kretschmer has attempted to differentiate various physical types and to correlate them with types of mental disorder (9). As the individuals most prone to affective disorders he ranks those of pyknic type. Of ethnologists, Günther, amongst others, has pointed out that this pyknic type corresponds to the Alpine race, whilst the asthenic type finds its counterpart in the Nordic race (10). Von Verschuer showed further that the predominantly Alpine South Germans tended to a cyclothymic temperament, whilst the predominantly Nordic North German tended to be schizothymic (11).

Wertheimer and Hesketh have stated that the influence of race on bodily habitus seems negligible (12). From a study of their monograph this statement would be hard to substantiate. In the section dealing with Race (13) they state: "That racial distribution is not a causal factor for these morphological types as has been claimed by Stern-Piper is apparent from our material which is an example of the racially heterogenous American population. In most cases both maternal and paternal extraction could be obtained. Our patients represent parental extraction of the following character: Scotch, Irish, English, Dutch, French, Norwegian, North German, South German, Welsh, Swedish, Canadian, Portuguese, Russian, Italian, Polish, and Czecho-Slovakian". But this is a catalogue of peoples and not of races! These peoples are made up of different proportions and blends of the three main European races - Nordic, Alpine, and mediterranean - and range from the predominantly Nordic Swedes in the north, through the predominantly Alpine South Germans to the predominantly Mediterranean Southern Italians. Later on (14) these writers compare the descriptions and illustrations of Don Quixote and Mr. Pickwick and seek to give these as prototypes of asthenic and pyknic types. But the Spanish nobility in Cervantes' time was mainly a Nordic ruling class, and illustrations of Don Quixote would not appear to make him an exception, whilst Houghton's illustration of Mr. Pickwick on page 66 of the monograph could scarcely show a more typical Alpine!

Examination was made according to the criteria laid down in Stibbe's Physical Anthropology (15) and in Günther's Rassenkunde des deutschen Volkes (16). Thus the Nordic tall, fair, blue-eyed, long headed and long faced, contrasting with the Mediterranean small, dark, dark-eyed, long headed, and of slight build, and with the Alpine medium stature, thick-set, round headed, and broad faced. Only where the type was clear cut Nordic was it entered as such. Any broadness of face or skull, or shortness of stature, combined with thick-setness was regarded as indicating Alpine characteristics, and from the point of view of Kretchmer's classification such cases belonged more to the pyknic group. Out of the twenty cases there were twelve predominantly Nordic, three predominantly Mediterranean, and five of the preceding types, three Nordic and two Mediterranean,

presenting Alpine characteristics. These latter approximated to the Pyknic type. Surveying these now from the angle of Kretschmer's classification the Nordics would be represented by the Asthenics, and those with Alpine attributes with the Pyknics, whilst the Mediterranean might possibly, from their slender build and small size, rank with the Infantile group of his Dysplastics. Thus we obtain the following percentages - Asthenic 60%; Pyknic or Pyknoid 25%; Dysplastic 15%; Bearing in mind the greater diversity of racial types in the United States, these may be compared with the figures obtained at the Central Islip State Hospital, from the investigation of 272 cases where the findings were - Asthenic 43%; Pyknic 37%; Dysplastic-athletic 20% (17).

Reverting to the strictly ethnological grouping of these Involutional Melancholias the following facts emerge. There were twelve of predominantly Nordic race, three predominantly Mediterranean, and none predominantly Alpine. There were, however, three Nordics and two Mediterraneans with Alpine characteristics, and of these the Nordic Alpine blends were much more Nordic than Alpine. The preponderance of Nordics or Asthenics in this group is at variance with the findings usually given for the Manic-Depressive group.

When Kretschmer founded his views on the connection between constitution and character it was on the basis of Continental and mainly Central European population where the predominant type is the Alpine. To the Asthenic type, or according to ethnologists, the Nordic type, he ascribed a Schizoid personality and frequently associated it with Schizophrenia.

The ratio of Nordics to Alpines in Germany is about 50:40, whilst in Britain it is 60:10. If the same conditions held good in this country one would expect to find some sort of correspondence between the proportion of Nordics and the incidence of schizophrenia on the one hand and the proportion of Alpines and the incidence of affective psychosis on the other hand. In this part of England, and certainly in Scotland, this does not hold good, although Northumberland and Scotland are ethnologically amongst the most Nordic parts of Britain.

In this hospital in the course of the past five years the average admission rate of melancholics alone, is almost twice that of schizophrenics. Female melancholics for the period May 1940 to May 1941 numbered thirty-one out of a total of ninety-three admissions, and of these thirty-one there were twenty-one of the involutional type, thirteen being the clear-cut psychosis, as described by Henderson and Gillespie. These authorities stress the prevalence of involutional melancholia in Scotland and quote the figures for the Royal Glasgow Mental Hospital for the period June 1915 to December 1919, where out of two hundred and ninety-nine admissions between the ages of forty and seventy there were ninety-seven showing anxiety states characteristic of the involutional period (18). Since the Nordic type is the prevalent one in Scotland and Northumberland, and since the Nordic, or asthenic type is elsewhere regarded as the type prone to Schizophrenia rather than to Melancholia, one would expect so high an incidence to be of Schizophrenia rather than of Melancholia. That this is not the case leads one to speculate on possible

reasons for this regional difference. One question that arises is whether the Nordic type here differs in any way from the same type in Europe, and probably in other parts of England as well. That different peoples are more prone to some psychoses than to others has been ascertained, and the high incidence of general paralysis in the American negro, and of epileptic psychoses in the Italians, has been pointed out (19). Is it not possible, therefore, that some such racial tendency is in evidence here?

It is generally accepted that the original Celts were a branch of the Nordic race (20), and comparative philology locates their original home in the valley of the upper Danube, in what is now South Germany (21). The first wave, that of the Gaels, passed into Scotland and Ireland where it blended with the pre-existent Mediterranean race. In Ireland, the Mediterranean race, favoured possibly by a climate more congenial to it, gradually came more to the fore than in Scotland. In Scotland the Nordic wave remained purer, and in course of time further blending was largely with the subsequent Teutonic wave of the same race, especially the Scandinavian sub-division. If Involutional Melancholia were prone to attack those people of Celtic origin then the larger proportion of this blood in the modern Scottish population might account for the special prevalence of this psychosis in Scotland. Conditions in Wales were rather different. The second Celtic wave, the Brythonic, forming a ruling caste over a large Mediterranean and Alpine population and ultimately types representative of these latter races tended to prevail (22). Of the Continental Celts the race apparently remained purest in South West Germany, and one of the leading authorities on German ethnology was forced to admit that many a Nordic German might just as easily be of Celtic as of Teutonic origin. "Mancher nordische Deutsche könnte ebensowohl von Kelten wie von Germanen abstammen" (23). In view of the considerable shifts of population in Germany at the time of the Wandering of the Peoples, it would be difficult to substantiate the effect of this strain on the incidence of Involutional Melancholia in that country.

It is a commonplace that there is a considerable difference in temperament between the more Anglo-Saxon and the more Celtic elements in the population of the British Isles. To take only one instance, the essentially matter of fact, practical, and not very imaginative Anglo-Saxon may be compared with the idealistic, somewhat impractical, and definitely imaginative Irishman. Moreover, the peoples of Celtic origin share with the Slavs a certain vein of melancholy, plainly evident in their folklore, music, and perhaps even religion. It seems not altogether impossible that a tendency to Involutional Melancholia might exist in people of such origin. There are the rather high figures for Scotland, both rural and urban, whilst of the Irish immigrants in America, the Central Islip State Hospital has put it on record that of the various Non-American peoples the Irish, or people of Irish origin, contribute fully 25% of their admissions of Involutional Melancholia (24). Nor may it be without significance that in 1938, to take only one year, in the out-patient department at Cardiff Mental Hospital

out of 153 psychoses seen, 55 were melancholics (25).

Viewed in this light the percentages of Melancholics in English Hospitals might be capable of bearing a fresh interpretation. The counties of Bedford, Hertford, and Huntingdon, are predominantly Anglo-Saxon and have probably had little admixture of Celtic blood, and the latter would certainly apply to Kesteven County and Grantham Borough in the south-east of the country. The mental hospitals in these counties in 1939 and 1940 had melancholia admission rates of 19.6% (26), and 17.7% (27), respectively. In Somerset, whether or not the original Celtic population was destroyed, there has been a steady stream of immigration, not only from Wales, but from Cornwall, over at least several centuries, and this blood undoubtedly permeates the population. When the percentage of Melancholics in the Somerset and Bath Mental Hospital is examined, it is found to reach 32.8% (28), whilst the high incidence of Involutional Melancholia in Bristol, a Nodal point of Welsh, and to a lesser extent of Irish immigration has been stressed in a recent paper (29).

In Northumberland, as in most border regions, racial admixture has taken place with the people on the other side of the border over many centuries. Moreover, Scottish blood has entered in increasing quantity since the Union, and as one indication of the amount of this contribution is the fact that fully 20% of the hospital population here have Scottish names. More recently, the development of the Ashington coalfields and of the Tyne industrial area has been a strong factor in altering the original population, and amongst other, considerable Irish and Welsh blood has been drawn to this area. It is possibly no coincidence that out of these twenty cases, five have Scottish, Irish, or Welsh ancestry in the preceding generation alone.

The same Celtic element which would appear to be associated with Involutional Melancholia is, therefore, in evidence in this population, and it is at least not impossible that the presence of this strain may account for the high incidence of an affective disorder in people of Asthenic or Nordic type.

PREPSYCHOTIC PERSONALITY.

A connection between the personality of an individual and the type of psychosis that that individual develops has often been traced, and the importance of investigating the prepsychotic personality of patients with mental illness is generally conceded.

It has been observed that some types of personality have some or all of the essential attributes of particular psychoses, and that the differences between personality and psychosis in these cases seems to be one of degree, and moreover the more pronounced the abnormality of personality the more probable the

tendency to the corresponding psychosis (30). It has been found in the manic-depressive psychosis that many who developed it were habitually of a hypomanic or depressive nature and the accentuation of these tendencies led to the development of the illness (31), whilst in the case of schizophrenia Meyer and later Hock, pointed out the influence of what Hock termed the "shut-in" personality, identified with Kretschmer's schizoid type, the following have been stressed: reticence, seclusiveness, difficulty of adaptation, sensitiveness, restricted interests, secretiveness, shyness, and " a tendency to live in a world of fancies" (32). Treadway has also stressed the lack of social adaptability in the sexual sphere (33).

The prepsychotic personality in those people who develop involutional melancholia has been studied by various investigators. Titley studied ten cases and claimed to establish the presence of a constant reaction pattern characterized by narrow interests, difficulty in making adjustments, poor sexual adjustment, lack of sociability, intolerance, extreme reticence, anxiety, proclivity for saving, pronounced sensitiveness, stubborness and over-conscientiousness (34). Palmer and Sherman investigated fifty cases from this aspect and found constantly a definite reaction type wherein were featured marked introversion, sexual maladjustments, strong obsessional character, and hyperreligious trends (35). These writers believed it was possible to demonstrate an abnormal rigidity in the life history of the involutional melancholic, and claimed that the degree of this could be utilized in giving a prognosis (36). From a study of eighty cases Wittson (37) found that a strong predisposition to involutional melancholia existed in the personalities of those women who developed the psychosis He found the predominant characteristics to be quietness, sensitiveness, anxiety, overconscientiousness, inability to confide in others, submissiveness, and sometimes stubbornness and jealousy.

The personality in the present series would appear to conform more to the type just described than to that prevalent in the manic-depressive psychosis. On the one hand, a tendency to be easily worried was definitely present in fourteen cases, and in fact there were only two instances where it could be ruled out with any degree of certainty, in the cases of Isabella R., and Gladys T. Restricted interest, sensitiveness, reserve, marked conscientiousness, and lack of sociability were prominent as also was timidity. Hyperreligious trends were only marked in one case, Elizabeth S., whilst an abnormal proclivity to saving was possible present in two cases, whilst jealousy coloured two personalities. On the other hand a definitely depressive nature was present in only two cases, Mabel M. and Hannah S., and in these there were in addition a tendency to be easily worried, coupled with sensitiveness. Pronounced egotism was an additional feature in Irene T.

INFLUENCE OF MARITAL STATUS.

Stoddart has stated that insanity is at least twice as common in the single as in the married, and has attributed this fact to the "evil influence of a

single life", and "enforced repression of the sexual life and complexes" (38). On the other hand, Aubrey Lewis and Mapother, whilst recognising the influence of sex, have deprecated the tendency to put undue stress on this aspect alone (39).

Investigation was made into the marital status of the present series, and four groups were found - single, married and childless, married and with family, and widowed. Eight of the cases, or 40%, were single; four, or 20%, were married and childless; seven, or 35%, were married and with family; whilst one, or 5%, was widowed. In the case of the single patients the love interest had not been entirely absent: two had had prospects of marriage and the loss of this had probably been contributory to their illness, whilst the promiscuity of a third, Jane B., was undoubtedly contributory to her delusions of sin and unworthiness. Of the four childless married patients, three were poorly adjusted, and in these three cases marriage had taken place later in life, two of them had had lovers earlier on whilst the third had formed her conception of the perfect husband from a previous employer, and the shortcoming of her husband was a factor in the onset of her psychosis. The fourth of this group became ill following ovariectomy. Of the seven married women with one or more children six were happily married, although one of them had an invalid husband, whilst the seventh had been happy until she came to doubt the faithfulness of her husband, an event preceding the onset of her illness. In the case of the widow, about four years elapsed after the bereavement before her psychosis blossomed.

When the age at onset of illness and the duration of the psychosis at the commencement of treatment were compared in the first three groups, the following facts emerged. Average age at onset and average duration at beginning of treatment:- Single, 43.8 and 4.8 years; married and childless, 38 and 5.8 years; married and with family, 45.5 and 1.9 years. The single women in this series would appear to give some support to Stoddart's views on the "evil influence of a single life", since they developed their psychosis earlier than the happily married woman with a family, but on the other hand the pernicious effect of an unhappy marriage could be deduced even more from the above figures.

Of the third group, five have left the hospital as recovered. This tends to be in keeping with the investigations of Palmer and Sherman in fifty cases of involutional melancholia, in which they found that all patients who had children and whose relation to them was good, were in the group that recovered. They concluded that normal family life had a definite influence in diminishing the malignancy of the psychosis (40).

PREDISPOSING AND PRECIPITATING FACTORS.

The problem of causation is necessarily complex since it depends on the interaction of several variable factors, such as the psychic make-up of the patient, her inherited tendencies, her physiological state, and the situations to which she reacts.

The present series is no exception and in most cases there are factors, the cumulative action of which could reasonably be inferred as causative in producing the psychosis in individuals whose prepsychotic personality, not to mention physical type, revealed an underlying predisposition.

Nearly all of the cases showed a combination of psychic and physical causes, and indeed in only one case did the physical cause appear paramount. This was in the case of Isabella R., where undernourishment occurred previous to the onset of the psychosis, and it is noteworthy that she is of the type of polyglandular insufficiency.

In eleven cases the menopause coincided with the onset of the psychosis, in one the artificial menopause, and in another a probable menopause, whilst in three cases childbirth was implicated. In twelve cases the history revealed abnormal heredity, and in at least three of these, Jane A., Jane B., and Maud P., appears to have been of major import.

In eight cases physical ailments or operative procedures played a part, thus: Mary D. - deformed foot and subsequent operation: Rose E. - undernourishment: Elizabeth G. - scarlet fever: Jane I. - ovariectomy: Isabella J. - measles: Mabel M. - hypertension: Hannah S.- deafness and cholecystectomy: Edith T. - influenza and bronchitis.

In sixteen cases psychic factors were in evidence, and included financial worries and worry over future security, illness and death of relatives, unsatisfying or unhappy marriage, unsatisfactory childhood environment, and effects of war as manifested in air-raids and calling-up or loss of relatives. In one case promiscuity and alcoholism were additional features.

An adverse or unsatisfactory childhood played a part in six cases but in five of these heredity was also implicated. In the case of Elizabeth G., childhood environment may have been the most important factor.

The effects of war were evident in seven cases and in three, Mary B., Gladys T., and Elizabeth S., provided the final factor.

It is noteworthy that of the five patients who responded most quickly and most satisfactorily to Theelin, Jane A., Ada A., Jane I., Elizabeth S., and Gladys T., there were fewer factors involved, in none of them was there an adverse childhood and in only one was heredity a factor. Of the five patients who failed to respond to treatment, Jane B., Mary D., Irene T., and Edith T., it is equally noteworthy that a number of factors were implicated - abnormal heredity in three, adverse childhood conditions in three, severe physical disability in one, late childbirth in two, and additional psychic factors in all.

Investigation into the history of these patients revealed then that not one but several factors, physical and psychic, contributed to the onset of their psychoses. Furthermore, those cases where factors such as heredity, and adverse childhood were present and where marked

psychic trauma could be postulated, were those wherein the psychosis was severest, and most resistant to treatment. Conversely, those cases where the menopause was partially causal but where other factors were less operative, tended to be of shorter duration and more responsive to treatment.

RELATION TO THE MENOPAUSE.

It has been pointed out that in a certain proportion of involutional melancholics the involutional period itself appears to be the most important factor in the aetiology (41), and the importance of this period as a time when anxiety normally mounts has been indicated (42).

In the present series the psychosis coincided with this period in eleven cases, in two cases it followed the menopause, and in five it preceded. In one case it set in after the artificial menopause, and in the remaining case the patient presented signs suggestive of an early menopause coincident with her psychosis. If the psychosis following artificial menopause be included this would give 60% of cases coincident with the menopause. In a series of 100 cases Wittson found that the psychosis developed during the menopause in 47% (43).

McCurdy has given it as his opinion that physical change during involution cannot be the only factor (44), and this is borne out in the cases under investigation. In all of the twelve cases other factors were definitely present, and the menopause was only the last factor of a series.

Of those patients in whom the psychosis preceded the menopause the precipitatory factor appears to have been late childbirth: two were primiparae of thirty-seven, Elsie C. and Irene T., and the third a multipara of forty-four, Edith T. In none of these, however, were pregnancy and labour the only factors operative.

ENDOCRINE FACTORS IN INVOLUTIONAL MELANCHOLIA.

An endocrine factor has been postulated in the etiology of various psychoses, but the evidence in most instances has been somewhat conflicting. In Dementia Praecox, for instance, Mott believed there was a general atropy in all the main glands (45), whilst Dunlap and Morse from their investigations were unable to confirm this (46). Frederic and Florence Wertham, from the examination of almost a thousand cases came to the conclusion that they had sufficient evidence to implicate the endocrines in certain psychoses. They found a high percentage of what they termed "growth disorders" in their material, involving anomalies of the sex and other glands, and whilst such disorders were present in 63.4% of schizophrenic psychoses, they could only establish their presence in 1.7% of clear-cut cases of affective psychoses (47). At the same time the authors were careful to point out that such factors did not denote a pathological constitution, but that they could be regarded as characteristics of biological types.

That primary endocrine disorders may cause pathological changes in the brain has been suggested in the case of certain degenerative conditions, such as Pelizaeus-Merzbacher's disease (48), whilst Lotmar demonstrated malformed and displaced Purkinje cells in the cerebellar cortex in cretinism (49).

Clinically, malfunction of the endocrines, such as the thyroid and the pituitary, is sometimes associated with psychoses. Myxoedema is sometimes associated with a chronic paranoidal psychosis (50), and Hayward and Wood have emphasized the importance of hypoactivity of the thyroid in producing psychotic symptoms, presumably from the resultant mal-functioning of the brain cells (51). Hermann Zondek believed the pituitary to be especially capable of influencing the mind (52), whilst von Frankl-Hochwart considered that in cases of pituitary tumour a definite "pituitary temperament" could be made out (53). Zondek further stressed the importance of the interplay between hormones and tissues as a factor in the formation of personality (54), and considered the endocrines as the body's intermediaries between the somatic and psychic functions. This authority, however, took care to indicate that disturbance of the mind could, in its turn, affect the hormonal glands, and that, moreover, structural changes demonstrated in the endocrines in cases of psychosis, did not necessarily have a causal relationship with the latter. He considered that at least some cases exhibiting psychic and endocrine changes should be viewed as manifesting a common degenerative tendency (55).

In involutional melancholia the psychosis frequently coincides with a period of marked glandular change, and it might be of advantage to recapitulate the salient features of endocrine activity in the preceding period of recurrent cyclic change.

The anterior pituitary produces two gonadotropic hormones, follicle stimulating hormone, and luteinizing hormone, formerly called prolans "A" and "B" respectively. Follicle stimulating hormone promotes the growth and maturation of the ovarian follicles, which in turn secrete the oestrogenic hormone. This is oestradiol (56), with a similar intensity of action as the synthetic oestrogens stilboestrol and hexoestrol (57). Oestradiol is soon broken down to the less active oestrone, known also by the trade name of Theelin, and further degradation products, such as oestriol, or Theelol, are formed. The oestrogens produce hypertrophy of the uterus and cervix and increased growth of the mammary ducts, and are responsible for uterine contractibility and sensitivity to oxytocics. Increasing concentration of oestrogens in the blood acts on the pituitary, inhibiting the production of follicle stimulating hormone and thus diminishing its action on the ovary, with a consequent fall in oestrogen production. Thus there is a definite cycle of alternate activity and quiescence of the anterior pituitary and of the ovarian follicles. The luteinizing hormone brings about formation of the corpus luteum, the main product of which is progesterone, a hormone inducing secretory changes in the endometrium and growth of alveolar tissue in the mammary gland.

It has been estimated that the human ovary produces per month the equivalent of 25 to 30 mgm. of oestradiol

and 20 to 25 mgm. of progesterone (58). With regard to the pituitary hormones it has been ascertained that after the menopause, or following ovariectomy, the urine of women contains only follicle stimulating hormone. (59)

The climacteric in women is a time characterized in many instances by nervous irritability, psychic instability, diminished mental efficiency and a tendency to fits of depression. Extensive changes occur in the body. Ovulation becomes exhausted and menstruation consequently ceases. The process is gradual, the interval between successive periods increases and their intensity diminishes. The ovaries atrophy, become permeated with connective tissue, and subsequent atrophy occurs in the uterus, vagina, and vulva. The body generally is much affected and changes in metabolism find expression in the tendency to increased deposition of fat. The assumed inhibitory action of the ovaries on the sympathetic nervous system is weakened and vasomotor changes assume prominence. On this basis Kuntz explained the characteristic hot flushes, "The sudden hot flushes, so common during this period, probably are the result of the shifting of large volumes of blood from the splanchnic area towards the periphery by reason of sympathetic stimulation. This at once explains the flushing of the skin as well as the sensation of warmth. Adler also regards the severe headaches associated with the menopause as the result of hyperirritability of the cranial sympathetic nerves" (60). All the autonomic symptoms, however, do not appear explicable on this basis, and Sevringhaus gave it as his opinion that the mechanism whereby the endocrine changes affected the autonomic system was still obscure. (61)

Werner, from a comparative study of fifty-three castrated women, ninety-six menopausal women, and forty-eight involutional melancholics, concluded that their symptoms were accompaniments of ovarian hypoactivity, or non-activity. (62)

In a more recent communication than this Sevringhaus investigated three hundred cases of menstrual disorder, and found that a surprisingly large proportion of these women had symptoms characteristic of those undergoing the menopause syndrome. He grouped their symptoms into an autonomic and a psychic series and ascertained the percentage occurrence of these. The results were as follow:-

Autonomic Group.	Present in following percentage of cases.
Nervous Irritability.	55
Hot Flushes.	34
Sweating Attacks.	22
Palpitation.	43
Dyspnoea.	38
Vertigo.	38
Headache.	47

Psychic Group.	Present in following percentage of cases.
Melancholy or Weeping Attacks.	45
Morbid Worrying.	37
Insomnia.	33
Paresthesias.	22
Self-Depreciation.	16
Jealousy.	2
Ideas of Self Destruction.	5

Sevringhaus concluded that the occurrence of these symptoms indicated not so much the climacteric as a disturbance of the ovarian and pituitary mechanism (63).

The close relationship between the symptoms and signs of the climacteric and ovarian dysfunction was emphasized by Scherf, who reported the finding of the same disturbances in young women with hypofunction of the ovaries (64).

That the pituitary plays a part in the causation of such disturbances has often been claimed. During the climacteric definite changes occur in this gland and a new equilibrium appears to be slowly set up between the ovaries and pituitary hormones. From hormonal analysis of the urine, B. Zondek believed he could establish three phases in the establishment of this equilibrium, viz: (1) the poly-oestrin phase; (2) the oligo-oestrin phase, and (3) the poly-prolan phase. "During the first phase the uterus is found to be slightly enlarged and softer than normal; haemorrhages are not rare. An excess of follicular hormone is produced: as compared with the premenstrual period, when there are many follicles, its yield may be increased 10 - 20 fold. The first phase may last for weeks or months; it is followed by the second with its typical precipitate fall of the hormone. During it practically no more oestrin is produced. That is the stage characterized by the signs of vasomotor insufficiency. After the ovaries have ceased to function, increased activity of the anterior pituitary lobe sets in, as manifested by a considerable secretion of prolan, which may last for the rest of life. Not always are these stages sharply separated, they may merge imperceptibly into one another" (65).

Recent work by Nathanson, Rice, and Meigs, agrees with the above in its essentials, but lays greater stress on the influence of the pituitary. These authors studied the changes in the hormonal content of the urine where artificial menopause had set in after irradiation of the ovaries. They found that symptoms occurred with low oestrogen content but were inclined to believe that low oestrogen content in itself was insufficient and that a rise in gonadotropic hormone as well was necessary for the production of these symptoms. In some of their patients they believed the gradual cessation of symptoms could be correlated with the gradual diminution of gonadotropic hormone, and in three cases where menstruation recurred, a cessation of symptoms was associated with the rise in urinary oestrogen and fall in gonadotropic hormone. They

concluded that the symptoms of the climacteric were accompanied by hyperactivity of the anterior pituitary, and that when the quantity of oestrogen reached a threshold level it depressed this gland and alleviated the vasomotor symptoms (66). This depression of the gonadotropic hormone by excess production of ovarian hormone has been established (67), probably after an initial stimulation (68). Commenting on the views of Nathanson, Sevringhaus pointed out that other investigators, employing assay methods just as sensitive as those used here, were able to show that climacteric symptoms could be held in complete abeyance by doses of oestrogen which did not cause a significant reduction in urinary gonadotropic hormone, and he concluded that there was no justification for assuming a necessary connection between the pituitary secretion and the symptoms (69).

The relationship between changes in the ovaries and pituitary on the one hand, and the occurrence of climacteric symptoms on the other is obviously complex, and whilst the consensus of opinion would appear to agree on the importance of ovarian dysfunction, the manner in which the pituitary contributes to the causation of climacteric symptoms is less apparent.

This vexed question is further complicated by the work of Zondek and Bier on the metabolism of bromine. They discovered that the pituitary contained 10 to 20 times as much bromine as any other endocrine, mainly in its anterior lobe, and believed this was of significance in the light of the frequent association of pituitary disturbances with emotional affections (70). It has been pointed out that only a third of the normal amount of bromine is present in the pituitary of a woman aged forty-five, whilst the quantity in the male remains more constant up to a much later age, and it has been suggested that this difference has a bearing on the greater incidence of affective psychoses in women after the menopause (71).

Apart from the changes in the ovaries and pituitaries, involvement of other glands in the upset of the climacteric has been noted. Hypertrophy of the adrenal cortex has been observed, and according to Zondek may have a bearing on the tendency to hypertension common at this period (72), whilst the frequent onset of myxoedema at about this time has been remarked on (73). In a series of thirty involutional melancholics Hemphill and Reiss found an appreciable number of cases with adrenal and thyroid dysfunction (74).

The boundaries between mental health and mental disorder, like those between bodily health and disease, are indefinite, and in involutional melancholia this indefiniteness is exemplified. On the psychic plane, many women at the climacteric stage are afflicted with a mood of depression, a sense of inadequacy, and a tendency to worry, and in many cases a mere exaggeration of this state of mind, symbolical perhaps of the somatic changes associated with the climacteric, results in a picture recognizable as that of involutional melancholia. Werner indeed stressed the remarkable parallelism between the symptoms of the climacteric and those of involutional melancholia (75), and if Sevringhaus' figures are again

refered to, further exemplification of this parallelism may be found. Thus in 45% of his cases he found melancholy or weeping attacks, in 37% morbid worrying, in 16% self-depreciation and in 5% ideas of self-destruction.

As numberless women undergo the menopause without developing involutional melancholia the possibility has been mooted of a more intense endocrine reaction in those women who develop this psychosis, and indeed, this is what one would expect if the etiology was purely glandular.

Such a hypothesis has found no substantiation in the quantitative investigations carried out on the hormone content of the urine. Carlson was unable to find any difference between the endocrine status of involutional melancholics and of normal women at the climacteric (76), and more recently Neustadt and Myerson were unable to establish a pathogenetic relationship between hormone excretion and involutional melancholia (77).

It is therefore not unreasonable to infer that for the development of the psychosis of involutional melancholia purely endocrine factors are insufficient. That they play a part, and that they may be an important factor, is possible and even probable. It has been pointed out how Scherf found, even in young women, ovarian dysfunction to be associated with symptoms characteristic of the climacteric, and how B. Zondek established three phases of endocrine activity at this stage, involving both ovaries and anterior pituitary. For the transition from the syndrome of the climacteric to the psychosis of involutional melancholia, however, these factors appear inadequate, else the incidence of involutional melancholia would have assumed titanic dementions and the gravity of the climacteric as a phase in woman's life would have been magnified out of all proportion.

TYPES OF ENDOCRINE DISORDER ENCOUNTERED.

For the endocrine examination of the cases the general plan laid down in Zondek's book was followed (78). Skin and hair were examined for texture, pigmentation, dryness or otherwise, and in the case of the hair any abnormal distribution was noted. The presence and distribution of fat deposits was observed, as was also the size, consistency and power of the muscles. The circulatory system was investigated, more particularly from the point of view of tachycardia, extra-systoles and abnormal blood-pressure, whilst in the gastro-intestinal system, the presence of constipation, nausea, vomiting or diarrhoea was considered with reference to the general setting. Enquiry was made about possible alterations in weight. Obvious change in the thyroid to inspection and palpation were noted, the presence of tremor, or von Graefe's sign looked for, or, on the other hand, such signs as subnormal temperature, sensitiveness to cold, somnolence and lethargy. Presence or absence of menses and any other abnormality connected with them received attention.

Where indicated, further investigations, such as blood- sugar, blood-sodium, response to adrenaline, and basal metabolism were carried out. In the case of basal metabolism the method adopted, by reason of necessity rather than choice, was that of Read's Formula. The pulse-rate and pulse-pressure were obtained from patients who had fasted for twelve hours. These patients were not allowed to read or write, were instructed to empty their bladders an hour before examination, and in bed as comfortable a posture as possible was arranged. The rate was determined on two consecutive mornings. The formula B.M.R. = 0.75 (P.R. + 0.74 P.P.) - 72, where P.R. is the basal pulse-rate and P.P. the basal pulse-pressure has been tested by Beaumont and Dodds who found it usually corresponded with the B.M.R. as actually estimated (79). Since Odén found the formula of dubious value in neurotics (80), it was felt that in the present series too great stress could not be laid on it.

Employment of the above scheme of examination, whilst simple, was found to be of sufficient use to establish definite types of endocrine upset. From the endocrinological aspect the patients could be classified in three groups: those where no upset other than that characteristic of the menopause was present; those where hyperthyroidism was present in addition to ovarian dysfunction, and a group of pluriglandular insufficiency.

The first group, by far the largest, was characterized by increase of fat, and vasomotor instability, as shown by such signs as flushes and dermographism. Those patients who were past the acute phase of glandular change and who did not evince signs implicating glands other than the ovaries, were included here. The case of artificial menopause, Jane I., belonged to this group and the initial severity of her psychosis was possibly conditioned by operative interference (81).

Those in the second group presented the usual signs of mild hyperthyroid activity, such as, tremors, von Graefe's sign, profuse perspiration, marked vasomotor instability with tachycardia and extra-systoles, tendency to subfebrile temperatures, and increased basal metabolism. There were two patients in this group, Ada A. and Edith T., of these the former was a clear-cut case presenting the typical signs and symptoms. These characteristics while present were less prominent in the latter case, in whom, however, repeated estimations of the basal metabolism showed an increased rate, whilst injections of adrenaline subcutaneously (82), and its instillation into the eye - Loewi-Cord's test (83) produced marked response. Volhard's water test (84) was attempted but the agitation of the patient prevented proper administration. Blood sodium showed some reduction, 308 mgm. per 100 c.c.s, of interest in view of the observation of E. Schneider that the sodium content of the blood is reduced in hyperthyroidism (85). Blood sugar was not apparently disturbed, 0.07%, but Zondek has pointed out the compensatory action of the pancreas in cases of hyperthyroidism (86).

In the third group there was evidence of hypoactivity not only of the ovaries, but of other glands as well. Three cases of mild polyglandular insufficiency occurred, two being hypothyroid and the third hypoadrenal. The two former corresponded to Zondek's thyro-ovarian

insufficiency (87), and were characterized by dryness and roughness of the skin, diminished perspiration, dry scanty and brittle hair, sensitiveness to cold, bradycardia, and a certain slowness of movements. Basal metabolic rate was reduced in both. In one case, Mary D., there was almost a cassowary neck (88), and the signs and symptoms approached nearest to myxoedema, and her B.M.R. was -15.5, with reference to which one may cite Lahey's finding that frank myxoedema was the rule under -25 (89).

The remaining case, Isabella R., was in many ways the most interesting, presenting, as she did, a suggestive picture of hypoadrenia. She was lean, with a poorly developed musculature, marked debility and fatiguability, and had lost considerable weight. Anorexia and gaseous distension were marked on admission, and her skin was pigmented a light brownish shade, particularly noticeable on the face. Blood pressure was reduced, 108.76, and the pulse of diminished volume. The picture was in keeping with the mild and comparatively benign form of the syndrome to which the term "Addisonism" has been applied (90). In addition an extensive psoriasis was present, of interest from the aspect of a postulated suprarenal dysfunction in this condition, and a profound depletion of the body's store of vitamin C was demonstrable (91). Subcutaneous injections of adrenaline evoked only a very slight response, whilst the withdrawal of sodium, and the administration of potassium salts produced a pronounced worsening of her symptoms (92).

METHODS OF TREATMENT AND RESULTS OBTAINED.

In the treatment of involutional melancholia the administration of oestrogenic substances has for years been a feature. The results claimed for this form of therapy have varied, some writers claiming unqualified success and others being unable to substantiate these claims, or even finding the treatment detrimental.

Werner, Kohler, Ault, and Hoctor, in 1936 treated twenty-one patients with Theelin over a period of six months and claimed thirteen to be markedly improved (93). Using oestradiol benzoate, Jones, MacGregor, and Todd treated seventeen cases and found that six recovered with an average stay in hospital of three months (94). Incidentally gonadotropic examination was made before and after treatment in this series but with no definite correlation between the laboratory findings and the clinical results. Schube and his colleagues treated ten cases with Theelin, and not only obtained negative results in all cases, but actually found three of their cases to be worse both physically and mentally (95). Ault, Hoctor, and Werner, in 1937 treated a further fourteen cases with Theelin and claiming favourable results in all were emboldened to state "For all practical purposes Theelin seems to be a specific in involution melancholia" (96). Again, on the debit side, Notkin, Dennes, and Huddart treated fifteen cases and at the end of treatment stated that three patients could still be considered somewhat improved whilst two others were showing signs of improvement. Improvement in all cases was purely institutional, no patient being sufficiently well to resume life outside, and furthermore, at a recheck three years afterwards the entire

group was found to have relapsed (97). Nevertheless, Ault in 1940 was claiming a recovery rate of over 90% in uncomplicated involutional melancholia, although he now recommended the employment of a much larger dosage (98).

Wittson, in a series of cases with a total dosage of Theelin varying from 72,000 to 500,000 international units, over a period of three to thirteen months, recorded the following results:- Recovered 8.7%; improved and paroled 21.7%; improved but not sufficiently for parole 8.7%; unimproved 60.9% (99). He criticised the results claimed by Werner, Ault, and colleagues and pointed out that the high recovery rate was obtained by eliminating from the series patients who failed to respond to Theelin. Since a history of previous mental illness in their cases did not exclude the diagnosis of involutional melancholia, he wondered how many of their recoveries were manic-depressives. Moreover he believed excessive dosage of oestrogen to be harmful and stated that one of his series died of carcinoma following administration of the hormone.

This latter aspect has attracted considerable attention, and, whilst an element of risk may be present, the experience of most would not rate this as a very great likelihood during ordinary treatment. Chronic oestrogenic stimulation of the post-menopausal endometrium possibly predisposes to adenocarcinoma (100), whilst experiments on rats have demonstrated both uterine metaplasia and the occurrence of adenomata in various endocrine glands as a consequence of such activity (101). Auchincloss and Haagensen believed that oestrogens were contraindicated in patients with carcinoma, chronic mastitis, or any form of breast neoplasm, or where there was a family history of breast cancer. They considered that large or prolonged doses should be avoided and that treatment should be preceded by clinical examination of both breasts (102). Bernhard Zondek found that very large doses, six million international units spread over sixty days, causes an erosion of the portio, but on the other hand he could find no carcinomatous change (103). Commenting on this subject Sevringhaus mentioned that over a period of more than thirteen years' employment of oestrogens in his clinic he could attribute no case of carcinoma to this therapy. An initial examination for neoplasm was carried out and a minimal dosage was employed (104). Cramer considered the therapeutic value of oestrogens to be so high that risk of inducing carcinoma should not preclude their use. In any case he considered there was no risk of causing cancer where the hormone was administered over short spells of several months in a dosage just sufficient to produce the desired therapeutic effect (105).

In the present series of patients examination did not reveal evidence of neoplasm in any, and in none was there prolonged administration of oestrogens. The average individual dose was 10,000 units, whilst in the most resistive cases so large a dose as 100,000 units was employed in view of Ault's claim for the efficacy of heavy dosage. Of the total dosage the minimum employed was 32,000 units and the maximum was 2,100,000 units. Depending on the effect of treatment the patients could be arranged in four groups: those where

it was slight; those with no change; and the group that was worse after treatment.

There were five patients where the effect of Theelin therapy was pronounced, and where the oestrogen could reasonably be regarded as an important factor in their recovery. These were Jane A., Ada A., Jane I., Elizabeth S., and Gladys T.

Jane A. was fifty-seven when treatment was started, her psychosis had lasted six years, and she was depressed, occasionally agitated, and stated she was to be burnt in a furnace. It was, however, recorded that she was a little brighter and could be employed in the ward. She received an injection twice weekly of 2,000 units, and after a few weeks was very much brighter and appeared to have lost her agitation. She became anxious to be of use in the ward and for the first time showed an active interest in her family and asked to go home. Her delusions receded and she was paroled after having received a total of 32,000 units. A month after cessation of treatment she appeared fully recovered, showed no sign of relapse, and was consequently discharged. It is certain that amelioration had occurred in this patient prior to treatment, but for the rapidity of improvement during treatment considerable credit must be given to the oestrogen.

Ada A. was fifty-one and her psychosis had lasted four years, although she only sought admission to hospital as a voluntary patient shortly before the commencement of treatment. She presented a picture of hyperthyroidism, her basal metabolic rate was estimated to be +21.35, and anxiety was a prominent feature. During the first week she received only 2,000 units, and on account of the insomnia and agitation was given sulphonal gr. 5 at night and potassium bromide gr. 15 thrice daily. The following week this was discontinued, and she received three injections of 4,000 units Theelin, as an apparent result of which her depression and agitation diminished and she complained less of her ideas of unworthiness. She still remained unstable however, and easily upset. In an effort to combat the hyperthyroidism more effectively, ascorbic acid 50 mgs. daily, was commenced, and one week later an injection of 10,000 units Theelin was administered. The result was more impressive, and a short time after injection the patient was reported as being brighter and showing little trace of agitation. The next day she had relapsed slightly and resort was again had to ascorbic acid: an initial dose of 300 mgs. was given, followed by further 50 mgs. two-hourly till a total of 600 mgs. had been administered. On the following day a more marked improvement physically and mentally was observed. She was hungry and relished her meals for the first time, her features were restful and no sign of nervousness was apparent, and she no longer shrank from contact with other patients. An optimistic outlook on her troubles appeared and she insisted on leaving hospital. Her doctor was informed of her progress, the treatment found successful in hospital was carried on outside, and she continued to receive Theelin 10,000 units weekly and vitamin C, 100 mgs. daily. Any tendency to relapse appeared to be checked by an additional 10,000 units of Theelin whenever necessary, and four months after she had left

hospital she appeared to be remaining normal. In this patient a dosage of 2,000 units made little impression whilst 10,000 units were followed by a definite if transient improvement, an improvement possibly connected with the depressant action of oestrogens on the thyroid (106).

In this connection it may be mentioned that eight cases of hyperthyroidism, including five arising with the climacteric, were successfully treated with large doses of oestrogen, by Goldman and Kurzrok (107). At the same time the possibility cannot be ruled out that the injected oestrogen acted by merely replacing a supply deficient as the result of an inhibitory action of the overactive thyroid on the ovary (108) or deficient as the result of the normal atrophic process at this period of life.

Equally notable was the effect of soaking this patient's tissues with ascorbic acid, a vitamin credited not only with a depressant action on the thyroid (109), but believed also by Monauni to be of value in depressive psychoses (110). On weighing up it was, not unjustifiably felt that in this case if the main credit were due to Theelin the part played by the vitamin was at least considerable.

Jane I. was thirty-four when treatment began and her psychoses was of six months' duration. As a result of ovariectomy artificial menopause had set in, the early onset of which probably accounted for the severity of her symptoms (111). She was acutely depressed and agitated, and prior to admission had attempted suicide. She was given two injections of 2,000 units and appeared slightly brighter after each. A larger dose was tried and in the course of five weeks she received eleven injections and a total dosage of 110,000 units. After the first 40,000 units improvement was sufficiently marked to allow her to be paroled and at the end of the course she was bright and happy and ready to face life with renewed vigour. A month later she was discharged recovered and in view of the early onset of the menopause was advised to visit her doctor regularly for further treatment as required.

Elizabeth S. was forty-nine at the commencement of her illness, which had lasted one month before treatment was begun. Her agitation was extreme, auditory hallucinations of a terrifying character were present, and she was convinced she had been brought to the hospital to die. The first injection, one of 4,000 units, noticeably diminished her agitation, but in a transient fashion. A dosage of 6,000 units was more effective, whilst the maximum effect was attained with 10,000 units. A tendency to relapse was present when treatment with the smaller doses was left off and this disappeared when the larger dosage was substituted. After a total of 80,000 units of Theelin she was fully recovered and left hospital.

Gladys T. was thirty-eight at the beginning of treatment and her psychosis had lasted for a year. Prior to treatment she was markedly depressed and miserable with pronounced suicidal tendencies. An initial course of Theelin with injections of 2,000 units and a total dosage

of 24,000 made little or no impression. Benzedrine likewise was of little avail. A heavier dose of Theelin being adopted, more progress was made and after she had received 60,000 units in the course of a week, she was less depressed and began to converse spontaneously. A deficiency of vitamin C having been revealed earlier, a considerable quantity was administered over the course of a week, following which there was a more marked improvement. The patient became brighter, more confident, and expressed a wish to be employed in the handicrafts department. When she had had, during the second course of Theelin, a total dosage of 130,000 units, she was recorded as continuing to improve, as showing more power of concentration, and as showing more interest in her surroundings and in those around her. Unfortunately an attack of acute cholecystitis supervened, and this was accompanied by a slight deterioration in her mental state. Following this she received a third and more concentrated course of Theelin, receiving 100,000 units in five days, and made a rapid recovery. She was paroled, tried home first for an afternoon and then for a weekend, events which all were of definite value in increasing her confidence, and finally discharged on trial.

In these five cases there was a definite correlation between the clinical improvement and the administration of Theelin, and where a small amount of the latter was insufficient, increase of dosage was associated with more pronounced improvement. In the first case, Jane A. the first steps towards recovery had been taken prior to treatment, and it is possible that this is the reason why such small doses were effective; moreover, it seems probable that the oestrogen accelerated her recovery. In two patients, Ada A., and Gladys T., the value of vitamin C as an adjuvant appeared established.

Of these patients, obvious signs of endocrine upset were present in four out of five, and fewer additional factors were ascertainable in this group than in any of the others. The action of Theelin appeared to have a specific quality here. Certain features in these cases are of interest. With the exception of the patient with artificial menopause none of these women was childless, and their relation to their children was good. In none of them had there been an adverse childhood environment with its stultifying effects and in only one could direct inheritance be implicated - and that incidentally in the case of longest duration. Evidence of financial strain was provided in not more than one instance, and bereavement figured in none. The onset, coinciding with the menopause, was rapid in four of them. It seems likely that endocrine dysfunction was of major import in this group and that the improvement of the internal milieu consequent on the provision of oestrogen resulted in betterment of the mental state.

Coming to the second group, there were eight patients in whom oestrogen could be accredited with a slightly beneficial effect. Although three of these patients were discharged, two others granted voluntary status and yet another paroled, it would be an exaggeration to attribute all to the oestrogen they received.

Eleanor B. was fifty-five when treatment started and her psychosis was of twelve years duration. On admission in 1929 she had been depressed and agitated, believed herself guilty of sinning deeply, and was suspected of suicidal tendencies. In 1937 improvement had already occurred and patient was brighter and had been granted parole, whilst in 1939 she was recorded as being cheerful, showing insight, and obviously thinking about the outside world since it was noted that she worried over the absence of a home to go to. Before Theelin treatment was employed she was recorded as being much improved, showing more confidence in herself, and only slightly depressed. After a total of 110,000 units of Theelin, given during the course of a month, the last trace of her depression vanished and she was discharged recovered. It is highly probable however than the successful element was due, not to the oestrogen, but to the discovery, shortly before the completion of treatment, of a relative willing to take her out, and one cannot help but feel that if this object could have been attained previously she might possibly have been able to leave hospital perhaps two years earlier. It is probable that the action of Theelin was in the nature of a tonic in this instance.

Mary B. was fifty-two at commencement of treatment and her illness was of two years duration. Before treatment was started she was only mildly depressed and a certain element of resignation was present. She expressed a hypochondriacal delusion, but was apparently not greatly concerned about it, and was well enough to be on parole. A course of 100,000 units of Theelin was given, following which she was observed to be more energetic and cheerful, but still believing in her cancer. A further 110,000 units was followed by further improvement, although slight, and she would have been considered for a period of trial had not her home been in a danger zone. In assessing the effect of treatment in this patient it must be remembered that on two previous occasions when apparently recovered, she had returned to hospital after only a few days on trial, with a picture similar to that on her first admission: moreover the clinical picture she presented appeared to be only an exaggeration of her normal prepsychotic personality with its hypochondriacal trend, timidity, and tendency to be easily worried. One cannot help feeling that were she discharged, the first strain that tried her would produce a similar reaction.

Elsie C. was fifty-two at commencement of treatment and her psychosis was of fifteen years duration. Restlessness and agitation were marked features and were reported with monotonous frequency from 1926 till 1937, whilst in 1929 an attack of typhoid was recorded. She continued to be infective till 1937 when drastic treatment was adopted, her gall-bladder and appendix being removed. The removal of the source of infection initiated the first improvement in her condition. Five weeks afterwards she was noticeably less restless and agitated, whilst eight months later although delusions of poverty were noted, it was observed that she was quieter and more cheerful.

A year later it was entered that she has been quiet and sensible for the preceding nine months, had uttered no complaint or delusion, and was occupying herself in

the ward. When she was examined prior to treatment she appeared to be practically recovered. Following the course of 100,000 units of Theelin, she appeared to have more confidence in herself, and took more interest in the consideration of her future. As this patient had almost recovered before administration of oestrogen it would be incorrectto assign a major role to its effect, which was comparable to that on Eleanor B. Of particular interest is the dating of improvement from the removal of toxic foci, the original source of which remained undiscovered. It seems probable that its removal was the immediate inniator of the recovery process, and not unlikely that its persistence was causative in prolonging the psychosis.

Rose E. was forty-eight at the onset of her illness, which lasted a month before treatment was instituted. She received a short course of 16,000 units Theelin and was discharged on trial within two months. Of undoubted benefit however, was the plentiful nourishment she received after a period of semi-starvation, and the quiet and peace she was able to enjoy away from an environment fraught with worry, and it may be that these factors were of as much importance as the oestrogen she received. This seems likely as after her relapse on trial, due to a return to conditions of overwork and undernourishment, improvement began before Theelin was given, and emphasis was laid chiefly on rest and diet. Credit seems nevertheless due to tne oestrogen for the complete recovery of confidence that was observed after a considerable dosage had been given. She was again discharged on trial, this time arrangements being made to ease her burden at home, and according to latest reports she is doing well.

Elizabeth G. was forty-six, and her psychosis of two years duration. In February of the current year she had recovered and it was intended to discharge her on trial. Unfortunately, whilst visiting friends she slipped and fractured her femur, and within a week had relapsed into her previous state. She became depressed, agitated, and miserable, and believed her case was hopeless. A month later she began to improve, and after this Theelin therapy was commenced; she received a total of 180,000 units of Theelin. She became brighter, and gradually reaching the degree of improvement she had previously attained, was discharged on trial.

The impression conveyed in this case was that after the wearing off of the first shock of her fracture with the attendant blasting of her hopes of an immediate return home, she became reconciled to the new situation and improvement set in. Oestrogen may have accelerated her recovery, but was probably not essential to it, and it may be significant that the latest report (26.7.41) indicates a definite tendency to relapse, in face of outside conditions.

Isabella J. was forty-four and her illness of six years standing when treatment was begun. The acute phase of her illness had subsided soon after admission and she had remained ever since in a state of mild depression, whilst latterly a tendency to jealousy and spitefulness appeared more prominent. A course of 120,000 units of Theelin was administered over a period

of a month with some resultant benefit. The patient appeared brighter, a higher standard of work was attained, and she showed less tendency to be spiteful. Nevertheless, as she still appeared lacking in confidence, a further course of oestrogen was prescribed, and in the course of a fortnight received 28 mgs. Hexoestrol, of the same order as oestradiol, and the equivalent of 1,120,000 international units (112), but in spite of this no further improvement occurred, or has occurred since. In this patient Theelin obviously had a slight effect but in no way produced a sufficient improvement to warrant a change in her status. The reappearance of spiteful tendencies is interesting in view of their recorded presence during her school days, and in view also of the adverse prognosis imputed to a psychosis thus complicated (113).

Mabel M. was fifty and had been ill for five years. Initially she had presented the usual picture. Still, amelioration had occurred during the past year, and before treatment was given she was only mildly depressed, although easily worried and rather apprehensive of anything in the nature of a change. She was given 110,000 units of Theelin over a period of a month, and this certainly seemed to hasten the final phase of her recovery. She became brighter, showed a greater desire to arrange her own life and for the first time since admission developed a decided turn for wit. Here again the oestrogen appeared to give that feeling of confidence noticed in other cases and although the patient had gone a long way to recovery before this, credit seems due to Theelin for the acceleration of her recovery. This patient is now on parole and whenever her husband can make the necessary arrangements she will return home.

Hannah S. was fifty-five and her psychosis was of four years duration. Right up to the inception of treatment she had shown little change and was depressed and agitated, miserable and believing herself to be utterly hopeless. A course of 100,000 units of Theelin was followed by an improvement in her physical as well as in her mental state, and she became noticeably brighter despite the fact she still retained her delusion. An effort was made to ameliorate her state still further and she received 500,000 units Theelin together with the equivalent in Hexoestrol of a further 1,000,000 units. In spite of this large dosage no advance was made on the improvement coinciding with the administration of the much smaller course. It seems possible that several factors contributed to the improvement in this case. To begin with, she was moved from the chronic atmosphere she had been in for years to a better ward, and considerably more interest was taken in her case by medical and nursing staff. A deficiency of vitamin C having been revealed by the appropriate test, a liberal supply was provided not only of this but of other vitamins as well, and her diet in general improved. That these factors were at least to some extent operative might be inferred from the fact that the administration of a much greater dosage of oestrogen failed to result in any advance in the physical or mental sphere.

In this second group comprising eight cases, no spectacular results were observed. In some instances

the impression was obtained that oestrogens accelerated a convalescence already in evidence, inducing a sense of increased confidence; in others it coincided with an improvement in their condition. The operation of additional factors could be traced in most of these cases, and on the whole it seemed incorrect to assign all the credit to oestrogenic substances. In one case rest and an abundant diet together with liberal vitamins were of considerable importance, whilst in another the removal of avitaminosis together with yet other factors, coincided with improvement. The removal of toxic foci heralded recovery in one patient. Another patient, apparently recovered, relapsed as the result of physical injury, and on recovery from this and discharge was later reported as reacting abnormally to the more complex situations she encountered outside.

At the time of treatment the physical concomitants of the menopause had passed off in five of the eight cases; in two, Elsie C., and Rose E., they were in process of passing off, whilst in only one, Isabella J. were these disturbances marked. Moreover in the case of Elsie C. recovery from her psychosis was almost complete before she had oestrogenic therapy, and improvement in her state could be dated from the eradication of typhoid from her system, an event preceding the onset of the menopause, whilst in the instance of Rose E. the removal of starvation together with the easing of her home burden appeared to be paramount factors. In Isabella J's case the acute phase of this psychosis preceded the menopause by five years and the onset of this period was not attended by any deterioration in her psychosis, unless it could be held responsible for the reappearance of spiteful and jealous trends which had seemingly been in abeyance for many years.

In this group of cases it therefore seemed probable that in their psychosis a purely glandular dysfunction was not the essential element.

Coming now to the group where oestrogens were without effect, four patients were found to be in this category.

Jane B. was sixty and her psychosis was of eleven years duration. When examined prior to treatment little improvement had taken place since admission; She was slightly less depressed, was no longer considered suicidal, but retained much the same delusions. She believed herself to be riddled with syphilis, reproached herself for the evil life she had led, and often burying her face in her hands would say, "It's a terrible end to come to". Nothing could convince her she was not afflicted with disease, even when specimens of blood were taken and their purpose explained. She blamed herself for mixing with decent people in the ward when she was only fit for the gutter. An initial course of 100,000 units of Theelin was given but as it was without effect, a heavier dosage was employed, 600,000 units in all, and of this the last two injections were each of a strength of 100,000 units. As no improvement was observed she now received, within the space of a fortnight, the equivalent of a further 1,000,000 units.

Since no change took place in her state with this it was not considered advisable to continue treatment. It may be added that other means of treatment were adopted simultaneously - transfer to a better ward, encouragement given to talk about herself and an attempt made to combat her delusion of disease, attempts to employ her in simple occupations, and an increase in diet together with a liberal supply of vitamins. At the end of treatment she remained in the same state as before, nor has she since made any advance on this.

Irene T., aged forty, has had her psychosis for three years. The onset was rapid and followed a difficult instrumental delivery complicated by retained placenta. Patient on admission was acutely depressed and agitated, suicidal and expressed delusions of unworthiness, and although the agitation and depression diminished with the passage of time her delusions remained unchanged. A first course of Theelin, 24,000 units in all, being without avail, a second course of 100,000 units was given over a period of a fortnight. This in its turn failing to make any impression she was given the equivalent of 2,000,000 units in the same space of time. At the end of treatment no improvement was discernible, and none has since been recorded.

Maud P. was thirty-six and her psychosis of nine months' duration. She was acutely depressed and agitated, believed she was hopeless and was convinced that she would never leave hospital. An initial course of Theelin, 160,000 units, being ineffective, a further course of 300,000 was given. This made as little impression, and it was decided to give her the equivalent of 1,000,000 units, which she had during the space of three weeks. Avitaminosis had meantime been corrected. In spite of treatment the patient was as little improved after as before.

Edith T. the fourth of this group, was fifty-four at the commencement of treatment. The duration of her psychosis was said to be four months, but there had been an earlier attack at the age of forty-five entailing seven months detention in hospital, and a mild depression had persisted till conditions proved favourable for the development of a more acute reaction. On her first admission she was depressed, agitated and suicidal, and expressed the delusion that she had "no inside"; improvement slowly occurred till she was sufficiently well to leave hospital. Readmission took place almost ten years later and she presented an almost identical clinical picture, with the same hypochondriacal trend, and the same delusion that she had "no inside". In addition, however, her physical state had deteriorated, she was emaciated, partially starved, and showed signs of hyperthyroidism. A nourishing diet was provided and as a marked deficiency of vitamin C was demonstrated she received large doses of this vitamin. An improvement occurred in her physical state and was accompanied by betterment in the mental sphere. Thereupon Theelin, 130,000 units in toto, was given, but with no improvement. Within a month she had relapsed and a further course of Theelin, 190,000 units prescribed, but without effect. Vitamin C in large doses was then resumed but an intercurrent broncho-pneumonia carried off the

patient before any possible effect could be ascertained. Post-mortem examination revealed the presence of extensive fatty degeneration of the myocardium together with cystic kidneys.

Consideration of these four cases shows the involvement of a considerable number of factors.

To take the last first, physical factors revealed post-mortem were myocardial degeneration and cystic kidneys, whilst clinically there was the evidence of hyperthyroidism and prolonged malnutrition. A severe influenzal attack had heralded her return to hospital, whilst a hereditary factor was to be seen in the mental deficiency of her sister and daughter. Then there was also the effect of air-raids, with nightly dashes to shelter, sleeping in pit-shafts, and the shock of near-by explosions. Moreover the chronicity of her illness could be gathered from the persistent mild depression residual from the first appearance of her psychosis. The untimely decease of this patient prevented the employment of larger doses of Theelin and it is therefore impossible to say how she would have responded. The presence of the above factors, however, could scarcely be regarded as providing grounds for optimism in this connection.

Of interest is the temporary improvement, physically and mentally, resulting from the exhibition of vitamin C.

In the three remaining cases factors bearing on their illnesses had been operative over many years, extending back to their childhood.

The home Jane B. came from was made wretched by the drunkeness of her father and by parental squabbles, and the child was left mostly to her own resources. Her early history bore witness to screaming attacks and enuresis into her 'teens. Profitting by parental example she became a drunkard and later added promiscuity. The strength of heredity was apparent also in the crop of psychoses on the paternal side of the family. The bitter self-reproach and delusions of disease become more understandable on this foundation.

The seeds of Irene T.'s psychosis can likewise be traced far back. As a child, an only child, she was spoiled by her mother and got more or less all she wanted, and became somewhat selfish. Later, an unfortunate obstetric accident made her mother an invalid for the remaining twenty years of her life. When Irene was aged twenty she fell in love and formed an illicit association which she kept up for two years. Many years later her father married again and the step-mother proved unsympathetic to the daughter. As much to get another home as for any reason of affection she accepted a suitor and married him when she was thirty-five. Her marital life was not happy and her mother's invalidism had given her an intense dread of pregnancy. Pregnancy nevertheless ensued, subsequent delivery was difficult, placenta was retained, and the child did not long survive. The psychosis blossoming forth after this was strongly tinged with egotism - she was the most wicked woman in the whole world, and her sin was

of incredible enormity. Her former liaison she was convinced, had riddled her with syphilis and this had killed her child. In this case a faulty adaptation to life was manifest while in the preceding instance a misspent life was revealed.

An unhappy childhood environment could also be seen in the case of Maud P. There was considerable clash of parental temperaments, the mother strict and religious, and the father lazy and a drunkard. The child was partly neglected and emerged from this phase somewhat wayward and wilful. When she was aged twenty-two her mother, who had in the meantime developed involutional melancholia, took her life by swallowing Lysol. This proved a severe shock, and she was unable to continue with her job. Some months later she found employment in the laundry of a general hospital, life went past in a smooth even tenor, and she ultimately rose to be in charge of her department. At the age of thirty-four the first of a series of shocks occurred to shake her. A man from who she had anticipated marriage was called up for service with the Army and she no longer saw him. Shortly afterwards she resigned her job because of disagreement with her new superior, and this was followed by unemployment and financial insecurity. To augment her worries she realized she could not obtain so senior a position as she had vacated and she was forced to look for a junior appointment. When she was accepted as a laundrymaid in the hospital where her mother had been a patient the reanimation of early and painful associations was soon detrimental. She pictured herself as working in the same spot where her mother had been and relived the events leading up to her suicide. In this depressed frame of mind Maud came face to face with an old schoolmate, now practically demented, and this acted as a further shock. On leaving hospital she went to stay with relations who were soon bereft of their daughter in an air-raid, and thereafter the patient's psychosis was not long in coming to a head.

In this group particularly adverse factors appeared to be operating, and it seems not unreasonable to assume that a possible endocrine factor in these cases was outweighed by these others, and this may therefore be the reason why there was no response to treatment.

The final group, wherein a deterioration followed oestrogen therapy, comprised three members.

Elizabeth C. was forty-five and her psychosis of six months duration. She was acutely depressed and agitated, expressed delusions of poverty, and showed suicidal tendencies. She presented, however, one atypical feature which at first sight would appear to cast doubt on the validity of the diagnosis - she had a definite localised amnesia for certain recent events, those relating to the death of her fiancé. Over a period of ten days she was given 100,000 units of Theelin, and at the end of this treatment she was more agitated, and on two occasions she had difficulty in identifying her bed. Because of her hypothyroidism she was put on Thyroid 3 grains daily, and by the end of three weeks was much improved. She became bright

and cheerful, her delusion of poverty faded, she obtained employment in the handicrafts department, her bodily movements increased in agility, and the hiatus in her memory narrowed. This latter is of particular interest. Formerly she had refused to admit the death of her fiance, and during the earlier part of her stay in hospital spent much of her time talking about her wedding, which she believed was imminent; she now remembered his death, and as her general condition improved was able to talk calmly of this event. The dose of thyroid was reduced to ? grains daily and in a further six weeks she had lost her delusion and the happy, sociable and energetic personality that had been hers appeared restored, and she was discharged on trial.

Mary D. was forty-four at the beginning of treatment, and she had been ill for two years. She was miserable, agitated, and expressed delusions of unworthiness. There appeared to be little change in her state, but thirteen months later a slight improvement was recorded, and on the husband's application she was discharged "relieved". This relief was short-lived. After one week at home she became as depressed as ever, and even a most devoted family was forced to send her back after four months. From then until oestrogen was tried she showed little change, apart from being employed in occupation therapy. After she had received 110,000 units of Theelin over a period of three weeks her condition was definitely worse. She was more agitated and wept more frequently whilst her work in the handicrafts department showed a distinct deterioration. Thyroid treatment was commenced, 4 grains daily, but apart from a return to her previous state no improvement occurred. Lest the hormone was not encountering in the tissues the best conditions for its action an attempt was made to increase the susceptibility of the tissues by protein therapy, following Zondek's recommendation (114). Nevertheless no change was thereafter obvious although the dose of thyroid was increased to ten grains daily, and a course of anterior pituitary extract given. She has made no progress over the past two months in spite of this treatment. In an effort to throw light on the different reactions, investigation was made into the probable psychic and somatic factors involved.

In the case of Elizabeth C. who recovered, the operation of adverse factors could only be ascertained within a period of four years before her admission to hospital. In that time she lost her parents, and her fiance, and experienced the strain of air-raids. The loss of the parents, both over seventy was not a particularly severe shock and the main strain appears to have been the nursing effort. It was different however, when she lost her fiance, and with him her last chance of marriage. She was mildly depressed for several months but apparently got over the disappointment, and kept bright and energetic till a German plane, in a hurry to get away, jettisoned its bomb-load in a field beside her cottage. She was considerably agitated, and her relations believed they could date the onset of her depression from then.

It is possible that the death of her fiancé was of considerable importance as a causal factor, and the amnesia relating to this event which she subsequently developed is suggestive.

The influence of heredity might be traced from the presence of a schizophrenic cousin, but on the credit side the normal personality of this patient was better balanced than most in this series and included such qualities as cheerfulness, sociability, and energy.

The other patient, who did not improve, had been deformed from birth and as a child had been something of a butt, because of her infirmity; partly because of this, marked sensitiveness and asociability had developed. Shortly before the onset of her illness her father-in-law attempted suicide in her house, and she experienced the onset of the climacteric.

The one factor that was outstanding in both cases was hypothyroidism, slight in the one who recovered, and more marked in the other. Oestrone has been shown to produce hypofunction in the thyroid, and the still further depression of an already underactive organ may well have been associated with the deterioration in the state of these patients following Theelin therapy. The administration of thyroid was followed in one case by so definite an improvement that it appeared justifiable to assume a connection between the exhibition of the hormone and the improvement in the mental state. The other patient failed to react to much larger doses of thyroid and to anterior pituitary extract given in an attempt to induce increased production of the patient's own thyroid secretion (115).

It is not impossible that the conditioning factors were of a psychic nature. The first patient had normally a well-balanced and healthy outlook on life, and was thus with assistance able to weather the storm, whilst the second case had had to battle from childhood against the disadvantages that beset a cripple, and when the shock of her father-in-law's suicide was quickly followed by thyroid dysfunction, the difficulty of readjustment produced a psychosis comparable in its chronicity with those of that group who failed to respond to oestrogens.

The remaining patient, Isabella R. was forty-eight when treatment, began and her illness was of two years duration. On admission she was depressed and agitated, believed her food turned to water and was of no benefit to her, and declared that her life was unbearable because of her misery. Physically she had lost weight, was easily fatigued, and presented a brownish pigmentation, and an extensive psoriasis. A small course of Theelin, 2,000 units weekly and 12,000 units in all, produced little change. Because of a pronounced C avitaminosis she was given 50 mgs. of vitamin C daily, and at the end of the month was considerably improved. There was a diminution in her depression and agitation, her hypochondria was less pronounced and she took an interest in her appearance. A parallel improvement was noticed in her physical state. To assess the value of the

vitamin therapy no further treatment was given for a month: at the expiry of this period the patient had definitely relapsed into her state on admission.

Theelin therapy in much larger dosage was resumed, and after 110,000 units had been given, the mental and physical state were much worse. She was in a wretched state, restless, destructive, picking her skin, and having to be spoonfed because of the accentuating of her hypochondriacal belief in the uselessness of her food. Physically she was more easily fatigued, the pigmentation of her skin more noticeable and her psoriasis more extensive, whilst numerous furuncles developed on her trunk and abscesses developed on the extremeties.

Oestrogen was stopped and in view of the previous improvement with vitamin C, 300 mgs. of the latter were given daily for ten days. By the end of this period a bettering of her condition had occurred. The vitamin, in a dosage of 100 mgs. daily was kept up and the effect of suprarenal cortex hormone was tried, since she furnished evidence of hypoadrenia. An injection of 2 c.c.s caused a transient but striking improvement: the patient became brighter, smiled, carried on a conversation, and behaved fairly normally. A dose of 2 c.c.s appeared to give the optimum effect, which however, seldom lasted longer than twenty-four hours.

From the point of view of expense it was frankly impossible to continue with cortical extract, particularly as the patient was rate-aided and could never keep it up outside. Sodium salts have been prescribed with success in hypoadrenia, since there is here an increased excretion of sodium, and in some instances have alone maintained good health for a time (116).

It was therefore decided to give the patient 2 drams sodium bicarbonate daily together with increased salt in her diet. She meanwhile continued to receive the vitamin C which had earlier proved of value. This was satisfactory up to a point. The physical advance was maintained, but the mental state never reached the degree of wellbeing attained with Eschatin, although it was better than on admission.

After she had been having vitamin C for three months and sodium bicarbonate for two months, she was given a course of anterior pituitary extract, Antuitrin S., and towards the end of this became brighter, conversed normally and even displayed a whimsical sense of humour. For the first time since admission she has begun to menstrate. It is, of course, too soon to claim recovery in this patient, but the general trend is suggestive, and a vast improvement is undeniable.

The interrelationship between psychosis and glandular upset is of peculiar interest in this case. In her prepsychotic history she had been characterized by an abnormal proclivity for saving,

which latterly was exercised upon her diet with resultant production of long-standing chronic malnutrition. Defective supply of vitamins is known to produce secondary changes in the production or secretion of hormones (117), and it is at least feasible that this may have been the essential etiology in the pathogenesis of the mild hypoadrenia observed.

In passing it may be noted that Udaondo and Gonalons have described a syndrome of adrenal insufficiency, similar to the present case, where the cause was "emotional disturbances either of intense or unexpected, or depressive slow and continuous type", and where disappearance of the syndrome was produced by giving cortical hormone (118).

The establishment of this state would tend to produce a vicious circle. Diminished production of the cortical hormone causes upset of the sodium-potassium balance with increased excretion of sodium chloride, leading to diminished blood volume and to hypochlorhydria with its sequelae, such as nausea and gaseous distension, whilst the loss of the antiseptic action of hydrochloric acid results in the formation of a favourable soil for the development of gastritis, duodenitis, and enteritis. These digestive disturbances in their turn aggravate the dietary position and lead to increased loss of weight.

Additional symptoms of hypoadrenia are asthenia and fatiguability, diminished resistance to infection, and pigmentation of the skin. In a predisposed subject gastro-intestinal derangement and asthenia might be regarded as a fruitful breeding-ground for hypochondriacal delusions and this patient's delusion that her food turned to water and did her no good may have arisen from such a substratum - indeed the prevalence of hypochondriacal tendencies in hypoadrenia has been remarked upon (119). The further distaste and refusal of food arising from her delusion could not but augment the malnutrition.

The physical deterioration apparent after the course of oestrogen seemed due to a still further depression of cortical function, and in fact the likelihood of this is borne out by the knowledge that prolonged oestrinization results in a specific degeneration of the innermost zone of the cortex (120). If her increased asthenia and pigmentation, together with lowered resistance to infection were consonant with such an etiology, as seemed certain, the fact that this period of worsened physical health was accompanied by a corresponding phase of worsened mental health would argue in favour of an inter-dependence of these two aspects. Confirmation of this is to be sought in the patient's reaction to potassium - the administration of which still more upsets a disturbed sodium-potassium balance - where an extreme wretchedness was produced. Conversely, injection of cortical hormone was followed by a pronounced improvement, and while under its influence the patient came near normality. It is possible that continuous treatment with this would have brought about recovery. If, however, she were to be forced to keep up such treatment indefinitely as in the case

of a diabetic with insulin, the question of expense would weigh heavily with her. Sodium salts were found beneficial, but not specific, and vitamin C had a definite value. As anterior pituitary extracts possess in virtue of the adrenotropic hormone a stimulating action on adrenal cortices not irreparably damaged (121), the patient was tried with this, and the most permanent benefit hitherto has accrued. It seems likely that a prolongation of this treatment, accompanied by adequate diet and vitamins, such as she has had from admission, will prove the most fruitful line to follow.

The amelioration associated with the provision of adequate vitamin C in this patient further emphasized its value as an adjuvant to endocrine therapy. This patient had the most profound avitaminosis of all, not altogether surprising in view of a postulated faulty storage mechanism for this vitamin in adrenal insufficiency (122), and the improvement noted after considerable doses had been given may have been due to an indirect action on the adrenal cortex. It is known that vitamin C is stored mainly in the adrenal cortex and anterior pituitary, and it seems likely that it takes part in the formation of their hormones (123). In conclusion, the parallelism shown in Isabella R. between her general state and the extent of her psoriasis is in favour of the assumption that in some instances at least, a definite connection exists between the condition of the adrenal cortex and the presence of psoriasis, and brings her case into line with those described by Grüneberg, where the optimum results were obtained from cortical extracts or from pituitary extracts containing the adrenotropic hormone (124).

GENERAL SUMMARY.

In this series of twenty cases the latest analysis shows that nine patients have been discharged, recovered, six have manifested various shades of improvement, four are not improved, and one is dead.

From this it would follow that a recovery rate of 45% has been attained, whilst improvement has ensued in an additional 30%

The means employed have included oestrogens, anterior pituitary extract, adrenal cortex extract, thyroid and vitamin C.

In the preceding study an attempt has been made to evaluate endocrine therapy in relation to the recovery and improvement rate, and the results have tended to show that in most cases a favourable outcome could not be attributed to any one factor. With regard to oestrogens it was felt that a classification of patients according to the response to treatment could be made out and that this gave more accurate information of the relative importance of the part played by oestrogen in improvement or recovery. It was found possible to form four groups: those where oestrogen led to a pronounced improvement; where a slight improvement resulted; where no change occurred, and the group that was worse after oestrogen. In

five cases the administration of oestrogen was followed by a marked advance and ultimate recovery, and it seemed equitable to attribute to this treatment a large share of the credit. In 25% therefore recovery appeared due mainly to oestrogen.

Eight cases were benefited, the effect being apparent either in a slight lessening of depression, or in the removal of slight residual depression in a convalescing and otherwise recovered patient. In four patients of this group who had almost recovered oestrogen appeared to impart a feeling of increased confidence, and two of these were able to leave hospital. Although three of this group were discharged recovered, several factors were operative in all, and the part played by oestrogen in no way corresponded to the more dramatic role conceded it in the first group.

Four patients showed no improvement even though receiving much larger doses than had the cases who recovered. Further comparison showed that adverse factors other than those of an endocrine nature reached their maximum in this group, and it appeared reasonable to regard the lack of response to oestrogen as due to the malignancy of these factors. Conversely, those cases which responded well to oestrogen belonged to that group where the minimal number of such factors could be ascertained, and where in consequence the relative importance of an endocrine upset would be enhanced. It would therefore appear unreasonable to expect a specific action from oestrogens in patients where the endocrine factors appear so much overshadowed as in the above cases.

Claims for the efficacy of larger dosage could not be substantiated from this series. The patients of the first group, all of whom recovered, received a total dosage varying from 32,000 to 254,000 international units, and in the latter case spread over months. Those cases who remained unimproved received much greater doses, one patient getting as much as 2,000,000 units in the space of a fortnight. In the present series the impression was conveyed that if a patient did not respond to a moderate dosage the exhibition of massive dosage was unlikely to be more successful.

Three patients were worse after treatment and here an endocrine mechanism appeared definitely implicated. Polyglandular insufficiency was shown to be present, and it seemed that oestrogen by upsetting still further the hormonal balance brought about the deterioration in their state. The adverse results reported by others are explicable on such a basis. Recovery resulted in one of these from the administration of thyroid, and another improved with suprarenal cortex hormone and anterior pituitary extract.

The value of vitamin C as an adjuvant to treatment appeared established in cases where avitaminosis was present. Not every case showed appreciable improvement but in four patients the effects were obvious in both the physical and mental sphere. Of these, two presented the features of hyperthyroidism, a condition

where avitaminosis readily arises and where improvement has followed the administration of vitamin C (125), and a third had developed hypoadrenia, where again a gross deficiency of the vitamin occurs. It seems not unlikely that conditions such as these might constitute the most suitable criteria for the use of the vitamin in depressive states.

Of the twenty patients then, six or 30% appear in the final analysis to owe the maximum credit for their recovery to endocrine therapy, mainly oestrogenic.

This study further illustrates the complex etiology of involutional melancholia. An element of endocrine dysfunction was definitely present in a number of cases and where this assumed the extent seen in polyglandular insufficiency the impression was given of increased prominence of the glandular disturbance in contributing to the full development of the psychosis. Nevertheless, investigation revealed the presence of other factors, the aggregation of which appeared likely to be of as much predisposing influence as the purely endocrine aspect. Throughout the normal personality of these patients there kept recurring a tendency to be easily worried, sensitiveness, reserve, marked conscientiousness, lack of sociability, and timidity, so that these seemed characteristic of the usual prepsychotic personality. The prevalent physical type encountered was the asthenic, in contrast with the general findings in manic-depressive psychoses, and an attempt was made to associate a proneness to involutional melancholia with a definite racial stock.

Heredity and Environment also played their part. Taking heredity in a broad sense its influence could be seen in fourteen family-histories, or in 70% of the cases, whilst direct parent-daughter transmission including two instances of involutional melancholia could be ascertained in 30%. A preponderance of cases developed in a rural setting but it seemed that those arising in an urban environment commenced earlier and lasted longer, a feature which if not of general application might indicate some regional peculiarity.

The good prognostic value attributed to a happy family life seemed justified from the increased recovery rate in the patients belonging to this group.

The existence of adverse psychic and physical factors could be demonstrated in the majority of the series and their cumulative effect might well have been of considerable importance in the origin of mental illness. From the study of this series of cases it would appear that no one factor, whether glandular or otherwise, was capable of inducing the typical picture of involutional melancholia and that in most cases there was present a constellation of factors including endocrine upset, a particular physical type, hereditary weakness, unhelpful personality trends, and adverse physical and psychic conditions.

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CASE RECORDS.

J A N E A.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 51 years.
Age on admission - 52 years.
Age when treatment initiated - 57 years.

HEREDITY.

Mother was an involutional melancholic.
Mother's sister died in a mental hospital after suffering from a depressive psychosis.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion slightly sallow; hair originally brown, long and fine; skull dolichocephalic; face long and features prominent; nose high and narrow; eyes blue-grey; average stature; medium build.

PREPSYCHOTIC PERSONALITY.

Her nature was essentially a reserved one, and although she took part in various activities she was nevertheless rather sensitive and apt to brood over real or fancied criticism. A certain stubbornness was present, and whilst as a rule moderately cheerful, she was described by her husband as being sometimes moody and difficult to manage.

MARITAL STATUS.

Happily married and with three children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Apart from the menopause there is nothing definitely ascertainable in the role of precipitating factors.

She was happily married had three healthy children with whom she was on the best of terms, and her financial position was secure. After a short period of insomnia there was a rapid onset of depression and agitation accompanied by marked delusions of poverty and suicidal tendencies.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her features and posture betray a general sadness, and her speech, whilst it shows no slowing, is short and brief. Orientation is in no way impaired, and her memory appears normal. She is depressed and expresses nihilistic delusions, stating that she is fit only to be cast into a furnace and that this will happen to her. There is no clouding of consciousness, but insight is lacking. A slight improvement is evident upon her previous state: she sleeps well and can now be employed in ward-work.

PHYSICAL STATE.

In the C.N.S., articulation is normal, and no abnormality is detectable in the cranial nerves, motor and sensory systems, and superficial and deep reflexes are present.
In the cardiorenal system there is commencing hypertension, 180/100, and a faint mitral systolic murmur is present. No obvious signs of embarrassment.
Respiratory system shows nothing abnormal nor does the alimentary.
Wasserman reaction negative.

ENDOCRINE STATE.

Skin is of normal texture, colour and moistness.
Hair normal in texture and distribution, whilst hair of scalp is grey and rather fine.
Muscles are normal in size, consistence and power.
Thyroid is normal in size and there is no evidence of dysfunction.
Menses ceased seven years ago at age 50; typical fat deposits of ovarian type; no signs of vasomotor instability.

EXTRACTS FROM CASE-SHEETS.

11.7.34. Admitted in a state of extreme wretchedness. She is depressed and anxious, and expresses the delusion that she will have no money to live on. She is restless, is too agitated to answer questions, and frequently weeps.

8.3.35. She is less depressed, more energetic, and is more employable in the ward.

11.5.35. Improvement maintained. Discharged "relieved" on application of husband.

14.5.35. Readmitted to-day. She is depressed as on first admission.

15.4.36. She is depressed and miserable. States she is sure she will be crucified and then burnt. Sleep impaired.

14.4.39. She is depressed and miserable, wanders about wringing her hands and states that she is worthless and will be burnt in a furnace.

18.7.40. She is silent but slightly less depressed and is capable of employment appearing to take an interest in working in the ward-kitchen.

18.10.40. A course of Theelin, 32,000 units, in 2,000 unit doses twice weekly, has been given. Improvement has been pronounced. After the sixth injection she was much brighter, and showed an interest in her family and home, and at the end of the course was able to have parole and appeared recovered. She was to-day discharged recovered.

A.D A A.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 47 years.
Age on admission - 51 years.
Age when treatment initiated - 51 years.

HEREDITY.

Sister is a neurasthenic.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Mediterranean.
Complexion dark; hair originally dark and fine; skull dolichocephalic; face long and features prominent; nose prominent; straight and narrow; small stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was of a worrying disposition and always rather timid and fearful of new experiences. The main interest in life was her family, and her relatives described her as having been thoroughly spoiled from the time of her marriage by an indulgent husband and later by her older children. She was very sensitive, and occasionally petulant. She was generally fairly active and busied herself continually about her home.

MARITAL STATUS.

Happily married and with three children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

In addition to the menopause there was a period of

strain preceding her illness when her husband changed his occupation to that of market gardening. He had been unemployed for some time, and as the new venture did not prosper at first, the domestic situation promised to become acute. Although conditions subsequently improved, the patient became increasingly depressed and after several months developed the full syndrome.

CONDITIONS AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

The patient looks anxious and apprehensive and is in a constant state of movement. She is constantly turning and twisting and frequently wrings her hands. Her speech is rapid and at times almost voluble. Orientation and memory are unimpaired. Her affect is one of sadness strongly tinged with anxiety. Nihilistic delusions are present, the patient believing she has been a useless mother to her children and that she must have done something wrong in her life to deserve the feeling of depression that has come upon her. An obsessional element is also in evidence, patient stating that "horribly sexual thoughts - thoughts too horrible to talk about" are often troubling her.
Consciousness is unimpaired but insight is lacking.

PHYSICAL STATE.

In the C.N.S. no abnormality of articulation, cranial nerves or sensation; fine tremor of fingers present. Deep reflexes show a slight increase; plantar response flexor.
Cardiorenal system shows increased pulse rate, 90, and presence of extra-systoles. B.P. not increased. No evidence of arteriosclerosis.
Nil abnormal detected in respiratory or alimentary system.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is of normal texture but shows a faint brownish pigmentation and a marked tendency to perspiration is present.
Hair of scalp is of rather fine texture, grey in colour, whilst distribution of body hair appears normal.
Muscles are slightly diminished in size and power.
Menses became irregular about four years ago and have been absent for the past two years.

Vasomotor system is unstable, pulse rate varies considerably, average rate being about 90; occasional extra-systoles; pronounced dermographism.
Thyroid gland appears slightly increased in size; von Graefe +; Fine tremor of outstretched fingers.
B.M.R. +21.35.

EXTRACTS FROM CASE-SHEETS.

22.1.41. Patient reported as slightly less restless and agitated, but frequently weeping, ideas of unworthiness pronounced and complains of sexual thoughts occupying her mind. She has received sulphonal gr. 5 nocte, and potassium bromide gr. 15 t.i.d. One injection of Theelin, 2,000 units, given.

29.1.41. During this week 12,000 units Theelin given. Depression and agitation diminished and ideas of unworthiness less marked but still easily upset, and avoids contact with the other patients.

6.2.41. Agitation again pronounced. Theelin 10,000 units given, with improvement of symptoms.

12.2.41. Improvement maintained but patient still irritable and easily upset. Theelin 2,000 units given. Ascorbic acid, 50 mgs. daily commenced.

18.2.41. Relapsed again to condition of restlessness and anxiety. Theelin 10,000 units.

19.2.41. Patient bright and cheerful, feels capable of managing her affairs, and shows little trace of agitation.

20.2.41. Ascorbic acid 300 mg. followed by 50 mg. two-hourly.

21.2.41. She is better to-day than at any time since admission. She shows no sign of nervousness and her features are more restful. Her appetite is good and she states she is looking forward to her meals with greater relish than she has experienced for months. She feels confident and optimistic and no longer shrinks from social contact.

23.2.41. B.M.R. estimated at +8.2. Left hospital following voluntary resignation.

ELEANOR B.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 43 years.
Age on admission - 43 years.
Age when treatment instituted - 55 years.

HEREDITY.

Patient's only niece is a high-grade mental defective

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair light brown, long and fine; skull dolichocephalic; face long and features prominent; nose prominent, straight and narrow; eyes blue; average stature; thin build.

PREPSYCHOTIC PERSONALITY.

Patient was always easily worried, conscientious, and sensitive to the opinions of others. She was quiet, reserved, and seldom mixed much with others. Her interests were restricted and when she had finished her day's work, housekeeping for her brother, she spent the evening knitting and very rarely went out.

MARITAL STATUS.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Her childhood and early life were uneventful. She always remained at home, and when her parents died, kept house for her brother. The latter developed a chronic illness when the patient was aged forty-two, and a steady deterioration in his health took place. She realized how dependent she was on her brother, and began to worry about her own future. Shortly after this

the menopause commenced, and within a few months she, apparently quite suddenly, developed acute depression and agitation, and was certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

A slight sadness is apparent from her expression, but her movements are normal. Orientation and memory show no impairment. Her affect is one of slight sadness tinged with apprehension. She fears she will have to spend her life here since no relative has been willing to have her and as she herself lacks sufficient confidence to go out on her own. She has apparently no delusions and shows considerable insight into her illness. She employs herself in the laundry.

PHYSICAL STATE.

No abnormality detected in C.N.S.
Cardiorenal system shows increased blood pressure 170/90 but is otherwise normal.
Nil abnormal in respiratory or alimentary systems.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is normal in texture colour and degree of moistness.
Hair is greyish but of normal texture; no abnormal distribution.
Muscles normal in size, consistence and power.
Thyroid appears normal and there is no sign of dysfunction.
Menopause set in twelve years ago; no vasomotor instability; increased fat deposits over hips.

EXTRACTS FROM CASE-SHEETS.

8.2.29. She is restless and agitated and keeps moaning "I want to die". She says she is very wicked and has no right to live because she has slandered her family so grievously. Sleeplessness is prominent and suicidal tendencies have been suspected.

1.5.29. She is described as slowly improving, as quiet, reserved, and less depressed.

6.1.31. She is depressed and emotional, hangs her head and weeps when asked questions. Her answers are almost inaudible and she blames herself for committing an unforgivable sin. She pays little attention to her surroundings but can be employed under supervision in the laundry.

6.1.33. She is depressed and silent and does not answer questions unless urged to do so. She is emotional, weeps for no obvious reason, and shows no desire to return home. She is employed in the laundry.

6.1.36. She is depressed, self-effacing, and lacking in initiative. Says she is doubtful of ever being able to live an independent existence again, but cannot say why and weeps when pressed with questions.

7.8.37. She is a little brighter, and much more settled since a niece came to visit her. Patient is on parole and continues to employ herself usefully in the hospital.

19.10.38. She is more cheerful lately, enjoys parole and all social amenities available, and works well.

30.11.39. She is quite cheerful and enjoys the dances. She realizes that she used to worry about imaginary things. Now she is just slightly worried about having no relative to whom to go. She still is emotional and easily upset.

8.1.41. Her state is much improved. She tends to worry unduly over incidents in the past but her mood is now on the whole one of only slight depression. She is employable and is tending to regain a greater degree of confidence in herself.

23.4.41. In the course of the past month she has received a total of 110,000 units of Theelin. There is no trace of depression, she has been home for a weekend for the first time since admission, following the unearthing of a niece who was willing to take an interest in her.

19.5.41. Discharged on month's trial.

J A N E B.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 49 years.
Age on admission - 49 years.
Age when treatment instituted - 60 years.

HEREDITY.

Father was a chronic alcoholic.
Father's sister was a schizophrenic.
Father's brother and cousin died in mental hospitals.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion originally fair; hair originally brown, long and fine; skull dolichocephalic; face long and features prominent; nose prominent, straight, and narrow; eyes grey; tall stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was the youngest of six children whose childhood environment was deplorable. The father, irritable and unstable, was a chronic drunkard, and frequently the children had to help to defend the mother from his drunken rage. Later the mother took to drink and finally the couple separated. Meanwhile the children were allowed to do much as they pleased. The younger children received no home care or religious training, and as the patient bitterly remarked "were not brought up but dragged up". Jane was an intelligent and imaginative child, who had inherited some of her father's temper, which she frequently displayed. After being naughty she would lie and scream in order to escape punishment. Until the age of fourteen she was addicted to enuresis. When she grew up she was friendly, cheerful and sociable, with considerable interests apart from her work. Her intelligence was above the average, she was highly imaginative and could display considerable temper on occasion. Reserve and reticence were conspicuous by their absence - she told everyone her business and soon knew everyone else's business. She was very sociable, and if left alone felt uncomfortable

and tended to be introspective and worried. In later years this tendency became more prominent and a mild depression developed.

MARITAL STATUS.

Single, but with one illegitimate child.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

When nineteen years of age she became a bar-maid and at twenty-one, while still in this occupation, was seduced by a married man whom she had believed single and who had spoken of marriage. When he refused to marry her and she discovered the state of affairs the shock was considerable; she threw up her job and later went to another town where she worked as a waitress. At the age of thirty she obtained a post as canvasser for Lyon's Tea, and held this for fourteen years. The lack of social contacts while travelling depressed her, and she started drinking and began a series of affairs with men. When she was forty-four she either lost or gave up this employment, and opened a second-hand clothes shop. This never prospered and her addiction to alcohol hastened its failure. This occurred at the age of forty-nine, coinciding with the onset of the menopause. The patient lamented her wasted life, acute depression and agitation appeared, and she had to be restrained to prevent suicide.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her facial expression is one of sadness. She sits by herself as a rule and her posture is generally bowed, although on occasion she will talk with other patients. She generally speaks in low tones. Orientation and memory are unimpaired. She is depressed and miserable and at times covers her head with her apron.

On the subject of her former life she shows considerable disgust. Delusions of sin and of unworthiness are prominent. She believes she is completely hopeless and has ruined herself beyond redemption, and that a terrible end lies ahead.

She shows no insight into her condition.

PHYSICAL STATE.

In the C.N.S. no abnormality detected in cranial nerves, motor sensory, and reflex systems. Articulation normal.
In the cardiorenal system there is slight hardening of the peripheral arteries, otherwise nothing abnormal.
Respiratory system appears normal.
Apart from chronic constipation the alimentary system appears normal.
Wassermann reaction normal.

ENDOCRINE STATE.

Skin is wrinkled and sallow; no undue dryness or perspiration.
Hair is normal in texture and distribution; hair of scalp is grey and thin.
Muscles slightly diminished in size, consistence, and power.
Thyroid of normal size; no signs of dysfunction.
Menopause set in at age 49 and was associated with very severe headaches. No vasomotor instability.

EXTRACTS FROM CASE-SHEETS.

7.10.30. She is very agitated and depressed and is firmly convinced she has contracted syphilis and that she will be burnt alive. She is acutely suicidal and to-day made an attempt to choke herself by pushing her lower denture down her throat.

31.7.33. To-day received from hospital where she has been since certification. She is depressed and miserable, her sleep is disturbed, she is restless and agitated, and states she has no desire to live as her case is so hopeless.

23.7.36. There has been little change. She is depressed and miserable, sits by herself with head bent and covers her face with her apron when approached, and states she is too wicked to mix with the people around her.

11.6.40. A slight improvement has been noted. She is less depressed but is restless and idle. She talks freely of her past life and says she is too far gone to be good for anything. She is careless in her dress and confesses she has no interest in her appearance.

7.5.41. She is depressed and at times agitated. She is less solitary than of old and talks more with other patients. She constantly bemoans her wasted life and is firmly convinced that her wicked life has ruined her beyond redemption. She states she is riddled with syphilis, that she should never be allowed near decent people, and that she will come to an awful end.

18.6.41. Patient has had an extensive course of Theelin. Smaller doses being without effect she ultimately received injections of 100,000 units, but with as little action. She has received in all 600,000 units of Theelin.

20.7.41. A further course of oestrogens, Hexoestrol 25 mgs, the equivalent of 1,000,000 units Theelin, has been given in the course of a fortnight without effect.

M A R Y B.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 50 years.
Age on admission - 51 years.
Age when treatment initiated - 52 years.

HEREDITY.

Nothing abnormal detected.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type Mediterranean-Alpine.
Complexion dark; hair dark-brown and short; skull mesocephalic; face short, lower jaw light; nose small and short; eyes dark brown; low stature; medium build.

PREPSYCHOTIC PERSONALITY.

She was essentially shy and timid, quite lacking in confidence, never associating much with others - except children, of whom she was very fond. When she went for a motor run with relatives she usually sat in the car whilst the others wandered off. Her interests were restricted and she was easily worried, although superficially cheerful. She tended to magnify aches and pains into definite complaints, and it was noticed that this tendency became stronger as she got older. Indeed, for ten years preceding the onset of her psychosis she was increasingly hypochondriacal.

MARITAL STATUS.

Widowed, and with two children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Occurred ten years after onset of menopause.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Her husband died of rectal carcinoma, in harrowing circumstances, four years before the onset of her

illness. She was left in a difficult financial position, and as her husband had been an official with a coal-company, and was provided with a house, the widow had to seek other accommodation. This was at a time when houses were difficult to get, and she only succeeded in her quest shortly before the period of grace expired. She was able to scrape along, but her relatives noticed that she became quieter, more self-effacing and more hypochondriacal. At about this time she was heard to express the view that she might have cancer of the womb, a disease from which an aunt had died. When war broke out she became apprehensive lest her elder son, aged twenty, should be taken from her. She became depressed and agitated and her ideas of cancer developed into a definite delusion. Suicidal tendencies showed themselves, although it is doubtful if her constitutional timidity would have permitted her to give effect to them, and she was certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her expression is one of mild resignation, and she talks little and in low tones.
Orientation and memory are unimpaired. She is depressed, and on questioning readily breaks into tears. She is firmly convinced she has cancer of the womb and that this is slowly eating away her life. Anything in the nature of a change - change of ward, for instance - causes marked apprehension and deepening of her depression.
She sleeps fairly well, occupies herself in a routine fashion, and is quiet and orderly. She shows no insight into her state.

PHYSICAL STATE.

Nil abnormal detected in C.N.S.
In the cardiorenal system there is slight hardening of the peripheral arteries.
Respiratory and alimentary systems appear normal.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is of rather coarse texture but shows no abnormal pigmentation or dryness.

Hair is thin on scalp and is almost grey but is of average texture. Slight tendency to hypertrichosis present on face.
Muscles are normal in size, consistency and power.
Menopause set in ten years ago. No vasomotor instability. Fat deposits on breasts, hips, thighs and buttocks.
Thyroid appears small. Temperature normal and no undue sensitiveness to cold. Pulse rate 74.

EXTRACTS FROM CASE-SHEETS.

9.1.40. She is depressed and miserable. She has been unable to rest owing to worry about her health. She believes she has cancer of the womb and admits telling her sister she intended to drown herself because there was no hope for her recovery.

20.1.40. She is bright and cheerful, conversing freely with other patients and helping in the ward. She says she no longer feels she has cancer.

19.2.40. Progress has been maintained and patient to-day discharged on a month's trial.

27.2.40. She was brought back to-day. Her sister said that yesterday she became restless and to-day was found wandering near the river. The patient states she was untruthful when she denied having cancer and only denied it in order to get home. At home she could not sleep, and the feeling in her body got worse in the course of the last two days, especially after she had witnessed a street accident when a girl was run over by a bus. She is depressed and agitated.

9.3.40. She settled down very quickly and appears bright and cheerful as before her discharge on trial.

3.5.40. She states she has lost all her trouble. She helps in the ward and converses freely with the other patients.

17.6.40. She appears recovered and has been discharged on a month's trial.

20.6.40. Patient returned to hospital to-day; her son states they could do nothing with her. She is depressed and agitated, complains of her womb, and has been put to bed.

26.6.40. She is up and about and appears cheerful. She states that her womb gives her very little trouble now.

9.12.40. She is mildly depressed and her attitude tends to be one of resignation. She believes she has cancer of the womb but that it is not causing her any trouble at present. She expresses vague ideas of unworthiness, hinting that life does not hold much for her. She is on parole.

17.3.41. During the course of the past fortnight patient has had 100,000 units of Theelin. She is more energetic in her walk, more cheerful and assists more in the ward; she has not been emotional or depressed. She still believes she has cancer but no longer weeps when discussing it.

30.5.41. A further 110,000 units of Theelin have been given. Patient appears bright and cheerful in a rather restrained fashion, and no longer discusses her delusion about cancer with other patients. She has been granted voluntary status and would have been tried home had not her home been in a danger area. In addition to Theelin this patient had vitamin C during past three months, a deficiency having been shown to exist, but without appreciable benefit.

E L S I E C.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 37 years.
Age on admission - 37 years.
Age when treatment initiated - 52 years.

HEREDITY.

Paternal grandfather was a senile dement.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair originally light brown, long, fine and wavy; skull dolichocephalic; face long and features prominent; nose prominent and narrow; eyes grey; tall stature; medium build.

PREPSYCHOTIC PERSONALITY.

She was cheerful and friendly and it was her greatest pleasure to be amongst children, with whom she felt most at home. Sensitiveness was pronounced, and she responded quickly to favourable or adverse criticism, the latter inducing considerable worry. At home and in her employment she led a sheltered life and never required to do any manual work, an activity which her upbringing caused her to regard as degrading. She had artistic tastes, was fond of music and dabbled in French and literature.

MARITAL STATUS.

Unhappily married; no children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Preceded menopause by twelve years.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

She was married when she was thirty-six to a man she had known only a few months. The marriage was not particularly happy. She lived in

furnished rooms instead of in a house of her own, such as she had pictured, and she had to do much of the coarse work she disliked. Her husband was very frequently ill, and, as he changed his employment several times, the financial position was never good. Her people disapproved of the marriage, and this was an additional source of worry. When she became pregnant, after a few months, these conditions caused her greater worry. The lack of money was increasingly bitter and it is possible that in her conception of marriage an assured and peaceful existence, such as she had enjoyed in her parents' home, formed a considerable part of the picture. She soon found she had little in common with her husband, who, in addition to his other failings, was coarse and a heavy drinker. Her ideal of a husband had been formed when she was about twenty-eight. At that time she was a teacher in a small private school, and in the evenings she took on typing for a local landowner. This man was a middle-aged bachelor, artistic in his tastes, kindly and courteous, and a lover of music, for whom his richly furnished home provided a suitable setting. When a few months of married life had shown that her husband came nowhere near her ideal, the disillusionment was shattering. The final factor was a difficult labour, resulting either in a stillbirth or a child who died soon after, and the onset of her psychosis was rapid.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her features are mobile and pleasant and her speech is normal. Her general attitude is one of a rather restrained cheerfulness. She is generally bright but at times a mood of mild sadness comes over her and she feels that life has been in vain and that she is a misfit. She is rather easily upset and lacks confidence. Orientation is perfect and her memory is unimpaired except for the events immediately preceding her admission to hospital. She shows considerable insight into her condition. She is employed in the handicrafts department and takes an interest in her work and in her fellow patients.

PHYSICAL STATE.

Nothing abnormal detected in C.N.S.
Cardiorenal and respiratory systems appear normal.
Old cholecystectomy scar present.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is normal in texture, colour, and degree of moistness.
Hair of scalp is thin and grey, having changed colour at the beginning of her illness.
Muscles are normal in size, consistence and power.
Menses ceased six months ago following a period of menorrhagia of six months' duration. She has frequent headaches and occasional dizziness and hot flushes; dermographism marked; typical ovarian fat deposits.
Thyroid is of normal size; no apparent dysfunction.

EXTRACTS FROM CASE-SHEETS.

14.3.28. She was admitted as a transfer from Bristol Mental Hospital where she had been for two years. Transfer sheet stated she had made no improvement. On admission here she was restless and agitated, and wept for no obvious reason.

20.12.29. There has been little change in her mental state. Physically has presented signs suggestive of typhoid and Widal reaction positive.

18.1.30. She is reported as now convalescent from typhoid.

30.8.37. Reports have not varied much up to date. She is described as being restless agitated and even destructive, whilst repeated tests have revealed the presence of B. Typhosus.
To-day she underwent operation and had her gall-bladder and appendix removed in an attempt to eradicate the infection.

6.9.37. Patient has done remarkably well since her operation, is cheerful, asks for food, and already desires to get up.

5.10.37. No evidence of enteric organisms in stools. Mentally she is mildly depressed and at times emotional, but is less restless and agitated.

4.5.38. She is quieter and more cheerful, but still expresses delusions of poverty stating that she has no food and is in rags.

28.5.39. She has been quiet and sensible for the past nine months, and has uttered no complaint or delusion. She does some work in the ward and is tidy in her appearance.
Some insight into her condition appears to have been acquired about this time.

27.3.40. She is quiet, is employed in the handicraft department, and is now on parole.

10.5.41. She keeps cheerful but admits that life is rather empty and that at times she is overcome by a feeling of hopelessness. She is sensitive and easily upset. She occupies herself in handicraft work.

12.6.41. In the course of the past month she has received 100,000 units of Theelin. She was more or less recovered before this, but treatment seems to have given her a feeling of increased confidence as she has written to her relatives asking them to take her, and has even made enquiries about resuming her old employment. A period of trial would have been considered but as her husband has no settled home at present, and as her mother's home is taken up with evacuees, voluntary status instead was granted until such time as a home could be found.

E L I Z A B E T H .C.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 45 years.
Age on admission - 45 years.
Age when treatment initiated - 45 years.

HEREDITY.

Mother suffered from subacute combined degeneration.
Cousin is a schizophrenic.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type Mediterranean-Alpine.
Complexion dark; hair dark brown and profuse; skull brachycephalic; face broad and features prominent; nose fine and prominent; eyes black; small stature; light build.

PREPSYCHOTIC PERSONALITY.

She was always cheerful and active and found something to do from morning till night. She was not easily worried and showed no tendency to brood. There was a certain reserve in her manner and she preferred to busy herself at home rather than go out. She was of a kindly disposition, although capable of considerable obstinacy, and was very conscientious in what she did. Her interests were mainly restricted to the household.

MARITAL STATUS.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Psychosis has preceded menopause.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

No adverse features appears in her history until four years ago, and her life till then had been smooth and happy. During these latter years

her parents died after having been bed-ridden for a spell, and she acted as nurse. Three years ago she became engaged to a man twenty years her senior and a chronic diabetic. She experienced considerable opposition from her brothers, and to their expostulations generally ended up with "Other people get married, so why shouldn't I?" The fiancé, however, died after a year and this seems to have been the first real shock sustained by the patient. A little more than twelve months ago air-raids became frequent in her district, and the onset of her depression appeared related to an occasion, six months before admission, when five bombs exploded in an adjacent field.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

The patient is miserable, sits by herself, and frequently buries her face in her hands; at other times she wanders in a slow aimless fashion about the ward. She is acutely depressed and repeats over and over again that she has no money and that she has ruined her brother. She states she ought to be dead and that if only she had had the courage she would have killed herself. A certain slowness is present in her speech, but no retardation of thought. Orientation is unimpaired but there is a localized amnesia for a short period two years previously during which her fiance died. She believes him still to be alive and on questioning says she is going to be married. Sleep has been much disturbed. There is no insight.

PHYSICAL STATE.

In the C.N.S. articulation is normal and nil abnormal detected in cranial nerves, sensory or reflex systems; bodily movements are rather slow.
In the cardiorenal system pulse rate 60 and B.P. 108/60 otherwise nothing worthy of note.
Respiratory system normal.
In alimentary system there is chronic constipation.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin rough and dry. Hair of scalp is grey, scanty and moderate in texture.
Muscles appear normal in size, consistency and power.
Menses appear to be regular. Deposit of fat however is taking place in ovarian sites. No vasomotor

instability. Pulse rate 60.
Thyroid appears normal in size, but temperature is consistently subnormal and patient states she is always cold; lethargy present.
B.M.R. shows slight reduction -1.36.

EXTRACTS FROM CASE-SHEETS.

29.3.41. Admitted to-day in a condition of acute depression and agitation. She is miserable and restless, states that she has no money, which is incorrect, and that life is not worth living. She has been regarded as suicidal. There is a definite localized amnesia for recent events, in particular those concerning her fiancé whom she still believes to be alive. There is some slowness of speech and of movements.

10.4.41. In the last ten days she has had 100,000 units of Theelin. Her condition has deteriorated. There is no increase in her depression, but an increase in agitation. On two occasions she had difficulty in identifying her bed.

27.5.41. For the past three weeks she has had Thyroid grs 3 daily. She is much improved. Not only is she bright and cheerful but her delusions of poverty are receding. Her memory is much improved, she now remembers that her fiancé is dead and she can contemplate this fact more calmly now. She is employed in the handicrafts department and is showing increasing willingness for work and greater ability in following a pattern. Her movements are much quicker.

29.6.41. Improvement has been maintained. There is no trace of her former delusion, she is bright, happy, sociable and energetic. Now receiving Thyroid grs 2 daily.

21.7.41. To-day discharged on trial.

M A R Y D.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 42 years.
Age on admission - 42 years.
Age when treatment initiated - 44 years.

HEREDITY.

No abnormal heredity detected.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type Nordic-Alpine.
Complexion fair; hair brown and originally long and fine; skull dolichocephalic; face long and features prominent; nose prominent; eyes blue; low stature; heavy build.
The low stature and heavy build are indicative of Alpine strain.

PREPSYCHOTIC PERSONALITY.

As a child she was lame, and because of her infirmity came to be left out of childrens' games and was considered timid and shy. As she grew up she became bright and cheerful, sympathetic and kind, and willing to help anyone. Her husband described her as willing to give away her last penny. She was exceedingly conscientious in the care of her family to whom she was very loyal and devoted, and it is possible that the desire to show appreciation of her husband's action in marrying a cripple contributed to this social contacts were not readily made, largely due to sensitiveness about her deformity, and apart from her home, her church was the only other interest.

MARITAL STATUS.

Happily married and with two children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Four months before her admission to hospital she had a severe shock when her father-in-law, who had been staying with her for five years. Attempted suicide by cutting his throat, being thereupon taken to hospital where he died some time after. About this time the menopause set in. From the day of the tragedy she became increasingly depressed, would not go out with her husband, blamed herself for not looking after her father-in-law, and began to lament the loss of her deformed foot at operation twelve years previously. Depression increased, suicidal tendencies were suspected, and she was certified.

CONDITION AT COMMENCEMENT

OF TREATMENT.

MENTAL STATE.

Her expression is one of misery and her general posture is bowed. She sits by herself and pays little attention to what is going on around her. Her voice is low and toneless. There is no impairment of orientation or memory. Her affect is one of deep sadness tinged with anxiety. Nihilistic delusions are prominent. She states she should never have been born and that she ought to be dead and away from everyone since she is so useless and has been nothing but a source of constant trouble. She seldom speaks without bursting into tears and bemoaning her wretchedness. She is capable of simple employment, but this is often interrupted by weeping. She shows no insight into her condition.

PHYSICAL STATE.

Apart from slight slowness of movements nothing abnormal in C.N.S.
Heart action is regular, pulse rate 56.
Respiratory system appears normal.
Chronic constipation present. Artificial foot.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is firm and exceptionally dry: patient has noticed the diminution in perspiration and states that "her pores are all closed now".
Hair of scalp is thin and brittle.
Muscles are of normal size, but their power appears diminished.

Menstrual irregularity was noticed at the beginning of her illness, menses becoming irregular and gradually ceasing. Patient has occasional flushes.

Thyroid is reduced in size; temperature is consistently subnormal and patient complains of coldness; general lethargy present; pulse rate 56; B.M.R. -15.57.

Fat deposits are present not only in ovarian sites but also in the back and clavicular regions, whilst there is almost a "cassowary neck" appearance from the deposits in the cervical region.

EXTRACTS FROM CASE-SHEETS.

14.11.38. Admitted to-day. She is depressed, agitated and apprehensive. She sits weeping and wringing her hands; says she has no worries but is always miserable, and repeats over and over again, "What have I done to be punished like this?"

14.10.39. She is depressed and miserable. She has delusions of unworthiness and says everything she has done in her life was a mistake; she should never have married. She weeps freely and takes little interest in her surroundings.

19.12.39. She has shown a slight improvement and is less depressed although still emotional. On family's application was to-day discharged "Relieved".

23.4.40. Readmitted to-day. Husband states she was somewhat brighter during first week at home, but thereafter relapsed into depression and agitation. She is miserable and wretched and weeps continually. Her old delusions of unworthiness are again apparent: she says she should never have been born, that she has brought great trouble on her family, and that it is time she were dead and away from everybody as she is such a source of trouble.

20.2.41. There has been little change in her state. She is depressed and agitated, weeps freely and says repeatedly she should never have been born because she is such a source of trouble to everybody. She is employable in handicrafts.

26.3.41. During the preceding three weeks she has received a total of 110,000 units of Theelin. Her condition is definitely worse. She is more agitated, weeps more frequently, is less able to concentrate and there has been a distinct falling-off in the standard of her work in the handicrafts department.

16.4.41. In the course of the past three weeks she has had Thyroid, grs 4 daily. She is once again in the condition prior to the administration of Theelin.

3.5.41. Course of Haemoprotein, 5 c.c.s in all, given during past week. Thyroid resumed.

1.6.41. No improvement in her state. She received Thyroid grs 6 daily, and is now getting grs 10. Antintoin S. 5 c.c.s weekly has been injected.

10.7.41. No improvement has been observed.

R O S E E.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 48 years.
Age on admission - 48 years.
Age when treatment initiated - 48 years.

HEREDITY.

No abnormal heredity detected.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Mediterranean. Complexion dark; hair dark brown, strong and straight; skull dolichocephalic; face long, lower jaw light; nose rather short; eyes dark brown; low stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was always shy and timid and fearful of new experiences. Her education was much below the average, she took little interest in current affairs, and showed little desire for social contacts or for interests outside her own home. She was unambitious and apparently content to be a drudge. Imagination was poorly developed.

MARITAL STATUS.

Married and with three children. Husband an invalid.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided, developing during the phase of menopausal upset.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

There has been continued strain over several years. Her husband lost his job through chronic illness and for two years has been a complete invalid.

Also about two years ago the patient reached the climacteric phase. Owing to the husband's condition, the financial position, never very good, deteriorated, and the family just managed to exist. A little assistance was given by the eldest daughter, who was married, and by the next eldest who was a domestic servant. The patient worked hard to maintain her husband and youngest daughter, became overworked, and as the result of the lack of proper food, a state of undernourishment developed. About the time of the Dunkirk Evacuation her son-in-law was reported missing, and the daughter's grief added to the burden of the mother who by now was semi-starved and already in a state of mild depression. The husband's illness appeared to render him impotent, and the necessary readjustment, coming as it did at so critical a period of her life, seems to have been an additional factor. A month before admission she became hallucinated, complained of electric shocks being administered to her, and her increasing depression and anxiety led to certification.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

She moves about in a constant state of activity, wringing her hands and weeping. She is acutely depressed and is very apprehensive about what is going to happen to her. Hallucinatory voices are present and threaten her with death for having been a wicked woman. She complains also of feelings of electricity going through her. She believes she is going to be killed and that she has been brought to hospital to make the final expiation for her sins. Orientation and memory are not impaired. Insight is quite lacking.

PHYSICAL STATE.

Patient is in a state of semi-starvation, and is emaciated. Apart from this there is no organic change in her system.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is slightly dry and of loose texture (due to general state).
Hair of scalp is thin and commencing to turn grey but texture is normal.
Muscles are diminished in size, consistence and power.
Menstrual irregularity set in two years ago; patient has occasional hot flushes and slight vertigo.
Thyroid normal or slightly small in size; no signs of dysfunction.

EXTRACTS FROM CASE-SHEETS.

3.12.40. She is acutely depressed and agitated and is in a state of apprehension on account of hallucinatory voices that inform her she is going to be killed.
Physically she is in a poor condition, has lost considerable weight, and is to all intents and purposes in a state of starvation. Theelin therapy, 2,000 units twice weekly, commenced.

13.12.40. Considerable improvement has occurred. Patient is brighter and taking an interest in her surroundings, and is no longer troubled by hallucinatory voices although she still believes in the existence of these latter.

27.12.40. Patient is bright and cheerful, willing to help in the ward, and shows no signs of delusion or hallucination. With regard to the latter she is now convinced she imagined everything.
She has had eight injections of Theelin with a total dosage of 16,000 units.

20.1.40. Physically she shows a great improvement, her tissues have filled out, and the starved and care-worn appearance has been lost. She was discharged to-day on a month's trial.

9.2.41. Patient brought back from trial. She is depressed and agitated but less so than on her first admission. Hallucinatory voices are again present which threaten to choke her and prophesy her death because of the sins she has committed.
She has been overworked and underfed since she left here.

13.2.41. Patient has quickly settled down, is much brighter, has lost her hallucinations and no longer believes she is going to die.
Two injections of Theelin, 6,000 units in all have been given. Nevertheless improvement had begun before this.

17.3.41. Patient has only had 4,000 units Theelin in course of past month. In view of undernourishment she has been given all extras - eggs, milk, malt, and a liberal supply of vitamins.
She mixes with others, helps in the ward and shows no sign of agitation, hallucination or delusion. She is bright when spoken to but in repose her features betray a mild sadness or resignation which she does not admit.

19.5.41. In the course of the past month she has had 100,000 units of Theelin. She has quite regained her confidence and has been discharged on a month's trial. In order to diminish the burden of work on the mother the daughter has been recalled from service and is to stay at home to help.

E L I Z A B E T H G.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 44 years.
Age on admission - 44 years.
Age when treatment initiated. - 46 years.

HEREDITY.

Mother was an apoplectic.
The entire family was regarded as eccentric.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair with tendency to sallowness; hair originally brown long and straight; skull dolichocephalic; face long and features prominent; nose prominent, long and curved; eyes grey; tall stature; medium build.

PREPSYCHOTIC PERSONALITY.

Patient was timid and shy, reserved and sensitive. She was very conscientious in her work and her interests were restricted to her work and her mother. A worrying tendency became pronounced after the death of her mother.

MARITAL STATE.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

She was the youngest of three children and the only girl. Her mother was a domineering and ambitious woman of whom the easy-going father stood in some awe. The daughter was very much under maternal control and became shy and timid, whilst her will-power was sapped and she came to rely more and more

on her mother. When Elizabeth was grown up her mother exerted a strong influence over her and was instrumental in discouraging suitors. When she was aged thirty-five her mother had the first of a series of strokes that was to make her a complete invalid. The mother proved as exacting in illness as she had been in health, and the daughter had to give up her work to nurse her. This endured for six years, till pneumonia terminated the illness. After the loss of this strong personality the patient was like a ship without a rudder, and her brothers noticed she was getting "jumpy" and easily worried. This was three years before her admission to hospital, and about this time she obtained employment away from home. A year before admission she had a severe attack of scarlet fever and was fairly ill for two months. Shortly after her recovery she invested her entire savings in shares that almost immediately started to fall. Realization that she had made a serious mistake and jeopardized her future security caused increasing depression, and this was not improved by the onset of the menopause. Within three months she was certified and admitted to hospital.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

She lies quietly in bed, where she has been kept because of her fracture. Her expression is now one of slight sadness and the anxious look that formerly characterized her is no longer so obvious. She is quiet and when she speaks it is in a low voice. Orientation and memory are unimpaired. Her affect is one of mild depression, but she no longer expresses her former delusions of unworthiness. She appears to show increasing insight into her condition.

PHYSICAL STATE.

Patient has an intracapsular fracture of neck of left femur.
In C.N.S. no impairment detected.
Cardiorenal and respiratory systems appear normal, as does also the alimentary system.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is normal in texture and humidity. Hair is of normal distribution and texture, while hair of scalp has been grey for several years.

Muscles normal in size, consistence and power.
Menopause two and a half years ago, at onset of illness; no vasomotor instability; fat deposits on hips, thighs, and breasts.
Thyroid appears normal in size; no signs of dysfunction.

EXTRACTS FROM CASE-SHEETS.

17.9.38. She is depressed and agitated, wanders aimlessly about wringing her hands, moans and weeps and is in acute misery. She refuses food, her sleep is disturbed, and she has attempted to strangle herself. It is her belief that she has committed an unpardonable sin and that she has a foul disease which she transmits to others.

30.5.39. Little change. She does not talk and takes no interest in her surroundings. Her expression is one of extreme misery. Skin condition is poor owing to patient's habit of picking it. She is restless and agitated, apprehensive, and resistive to attention.

14.8.40. She is depressed and taciturn, emotional and weeps and moans freely, is unable to concentrate and is completely idle. She wishes she were dead and believes she is responsible for all the patients being here.

8.12.40. Considerable improvement has taken place during the past three months. She is less depressed and more controlled, has stopped picking her skin and no longer expresses her delusions.

20.2.41. No trace of her former delusions, her features are composed, she mixes freely with other patients, and shows no sign of depression or agitation. She is on parole, and has on several occasions visited friends in town. She is being considered for discharge.

22.2.41. While visiting a friend in Morpeth patient slipped and sustained a fracture of neck of left femur.

1.3.41. Patient has relapsed. She is depressed and agitated, weeps copiously, looks miserable and speaks in low tones, and says there is no hope for her.

7.4.41. There is a slight improvement in her state. She is less agitated and depressed, looks happier and does not express any delusions of unworthiness.

27.5.41. During the past month she has had 180,000 units of Theelin. Improvement has been maintained. She is brighter and takes a definite interest in herself.

16.6.41. She has attained the degree of improvement recorded on 20.2.41. and has been discharged on trial.

J A N E I.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 33 years.
Age on admission - 34 years.
Age when treatment initiated - 34 years.

HEREDITY.

No abnormal family history elicited.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type Nordic-Alpine.
Complexion mainly fair; hair brown and rather coarse; skull mesocephalic; face broad and features rather flat; nose strong and prominent; eyes blue; tall stature; heavy build.

PREPSYCHOTIC PERSONALITY.

She was reported by her husband as being very conscientious, reserved and rather sensitive. He described her as being highly strung, and very sensitive. He described her as being highly strung, and very easily upset if he spoke roughly. Her intelligence was rather below the average and she showed no interest in current affairs. As a rule she was bright and cheerful, but sometimes appeared to be sulky. She did not feel at home in company, except in that of children, of whom she was very fond. There was a definite lack of initiative and self-reliance.

MARITAL STATUS.

Married. Patient's husband was of a coarse and unsympathetic nature, but in spite of this she did not appear to be unhappy.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided with artificial menopause.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Nothing of an adverse nature appeared in her childhood or adult life. Six months before admission she had an ovarian cyst removed. This cyst was of considerable size and pregnancy had been assumed. She earnestly desired a child, and when the cyst was removed refused to believe she had not been

pregnant. This disappointment was a severe blow. She became depressed and blamed herself for causing the death of her child by consenting to operation. Signs of ovarian insufficiency set in, her depression rapidly deepened, and after several attempts at suicide she was certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Patient wears a sad and anxious expression, and is restless and agitated. She is acutely depressed, weeps when questioned, and states that she wants to die. She believes that the operation she underwent caused the death of the child she thought she was bearing, and she bitterly accuses herself for having killed it. She states she has no justification for living on, and indeed, she has made two suicidal attempts, one an attempt to cut her throat and the other an attempt to drown herself.

Her sleep has been much disturbed. Orientation and memory appear normal. There is no insight.

PHYSICAL STATE.

Patient has had a large right-sided ovarian cyst removed.

In the C.N.S. cranial nerves, motor and sensory systems are normal. Deep reflexes are slightly increased.

Cardiorenal, respiratory and alimentary systems appear normal.

Wassermann reaction negative.

ENDOCRINE STATE.

Condition of skin is normal and there is no pigmentation.

Hair is rather dry and grey.

Muscles are normal in size, consistency and power.

Menses have been scanty and irregular since operation.

Pronounced vasomotor instability as shown by hot flushes, vertigo, sweating attacks and frequent headaches. Dermographism is pronounced and fat is being increasingly deposited over the breasts and hips.

No change apparent in thyroid; no tremors, exophthalmos, or abnormal temperature.

EXTRACTS FROM CASE-SHEETS.

20.2.41. She is depressed and miserable and constantly worrying. She feels life is empty and bitterly reproaches herself for causing the death of her child.

26.2.41. Theelin 2,000 units.

27.2.41. Patient slightly brighter and less miserable.

19.3.41. Theelin 10,000 units.

24.3.41. She has now received 40,000 units of Theelin. Improvement is marked. She is bright, no longer expresses nihilistic ideas or delusions of unworthiness, and is now on parole.

23.4.41. A total of 110,000 units Theelin given in course of past five weeks. She is bright and happy, mixes with other patients, is described as being lively and full of fun, and has adopted a healthy attitude towards life.
With regard to her former delusion, she still believes she was pregnant, but states that it is over and done with and she must now face the world.

19.5.41. Discharged recovered on month's trial.

I S A B E L L A J.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 38 years.
Age on admission - 38 years.
Age when treatment initiated - 44 years.

HEREDITY.

Mother was a moral defective.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair medium brown; skull dolichocephalic; face long and features prominent; nose straight and narrow; eyes grey; average stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was easily worried, lacking in self-reliance, and very timid. She was sensitive, and suspicious of strangers, kept at least superficially bright, and carried out her work to the best of her ability.

MARITAL STATUS.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Psychosis commenced five years before onset of menopause.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

She was an illegitimate child and nothing is known of the father. At first she lived with her mother, a selfish, callous and cruel woman, who thought only of her own gratification. The child was harshly treated and became timid and dispirited. At the age of six years the mother got rid of her to a childless couple who adopted her outright. For the first time she received loving care and became deeply attached to her foster-mother, while the memory of her own mother became fainter. The latter married soon after, and it sheds a light on her character that the daughter born in wedlock was also driven from home at an early age, and like her step-sister, ceased to exist as far as her mother was concerned. At school the patient

was of fairly average intelligence but was not liked by her schoolmates because of spiteful and jealous tendencies. On leaving school she went into domestic service, and after changing her employment once or twice, found a congenial post. In 1934, three months before admission, her foster-mother died and she learned for the first time she was illegitimate. This proved a double shock and she became moody and depressed. She appeared to develop gastritis soon afterwards, and hypochondriacal trends appeared. Following this she had an attack of measles, her depression deepened, agitation developed, and she was certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Patient's expression is one of mild sadness tinged with resignation. She is quiet and keeps to herself.

Orientation and memory are unimpaired. Her mood is one of mild depression and she tends to be suspicious of others. Occasionally she shows herself jealous and spiteful towards her ward-mates, although she is usually shy and retiring. She is easily worried and is lacking in initiative. Hypochondriacal trends are present, the patient complaining on the slightest provocation of bowel upset, headaches, or of numerous vague aches and pains. There is no pronounced delusion, but nihilistic tendencies are in evidence, and she frequently states she feels doubtful about showing her face in the World again.

She occupies herself in the sewing-room.

PHYSICAL STATE.

Nil abnormal detected in C.N.S.

Soft mitral systolic murmur present: no symptoms of cardiac ambarrassment.

Respiratory and alimentary systems appear normal.

Wassermann reaction negative.

ENDOCRINE STATE.

Skin is of normal texture and colour and there is no dryness of the skin.

Hair is of slightly coarse texture, but is not brittle and is of normal colour and distribution.

Muscles are small and poorly developed.

Menses ceased nine months ago. Vasomotor instability is marked, patient having frequent hot flushes, vertigo and headaches, whilst dermographism is pronounced and the pulse is variable.

Thyroid does not appear to be altered: no tremors, tendency to exophthalmos or abnormal temperature.

EXTRACTS FROM CASE-SHEETS.

9.8.34. She is depressed and miserable. She states she has a constant fear of something dreadful happening to her, and she feels there is no hope. She is agitated and apprehensive and her state has been made worse by auditory hallucinations telling of impending doom.

5.9.34. She has made a marked improvement, is brighter, occupies herself in the ward, and writes cheerful letters. No evidence of hallucinations.

27.1.35. She no longer appears to have periods of agitation. She is quiet, industrious, and amiable.

5.5.35. She is recorded as being depressed and lacking in confidence.

4.5.38. She is mildly depressed, shy and retiring, and lacks initiative. Says she cannot face the world.

19.4.40. She is quiet and sensible but nervous and retiring, slightly hypochondriacal and unsettled.

5.4.41. Patient is mildly depressed, worries over trifles, and is of a rather jealous nature. Hypochondriacal trends are present.

26.5.41. She has had a course of Theelin, 120,000 units in all, during the past month. She is slightly brighter and less irritable but still displays spiteful tendencies towards other patients.

30.6.41. There is little change from last month. She remains slightly brighter but lacks initiative and is easily upset, in spite of the fact that she has just had a course of hexoestrol equivalent to 1,120,000 units of Theelin.

M A B E L M.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 45 years.
Age on admission - 46 years.
Age when treatment initiated - 50 years.

HEREDITY.

Mother's cousin died in a mental hospital.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair medium brown, long and fine; skull dolichocephalic; face long and features prominent; nose straight and rather wide; eyes blue; tall stature; medium build.

PREPSYCHOTIC PERSONALITY.

She was reserved, sensitive, and easily worried. She was lacking in confidence and initiative, and was rather afraid of new experiences. In company she was diffident. Latterly she tended to be pessimistic and hypochondriacal.

MARITAL STATUS.

Unsatisfactory marriage. No children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Her father spent most of his life at sea and the patient and her sister were brought up by the mother, who though kindly, was yet strong-willed and exacted unswerving obedience. At the age of eighteen the patient became engaged, but the engagement was broken off on the mother's insistence. Later, at the age of thirty-eight she married a seafaring man whom she seldom saw, and as she said wistfully, she spent most of her married life writing to her husband. With the passing of time she came to realize she was unlikely to have any children, and pessimistic trends appeared or became more marked. When she was aged forty-three hypochondriacal tendencies appeared, she began to worry over trifles and took to bed on the slightest

pretext. At age forty-five the menopause commenced, and possibly about the same time, hypertension showed itself. For nine months she was depressed and moody, and after a further three months marked by severe menorrhagia, her depression deepened, agitation appeared, and on the advice of her doctor sought admission as a voluntary patient.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

There is a mild air of sadness about the patient, but she appears brighter when conversed with. She occupies herself in handicraft work. A tendency to be easily worried is present and she is upset by any suggestion of a change in her position.

Memory and orientation are normal. Her mood is one of mild depression tinged with apprehension. Hypochondriacal tendencies still remain and possibly a trace of her former delusion can be seen in the care with which she watches her bowels. She shows considerable insight into her condition.

PHYSICAL STATE.

Considerable hypertension is present: B.P. 210/116, some thickening of peripheral arteries, second aortic sound accentuated, and deep cardiac dullness slightly increased to left; no symptoms of decompensation. No albumen in urine. Blood urea 34 mg. per 100 c.c.s.

No abnormality detected in nervous or respiratory systems.

Occasional constipation.

Wassermann reaction negative.

ENDOCRINE STATE.

Skin tends to be dry but is well nourished and of good texture. Hair is of fine quality and of normal colour and distribution.

Menopause set in at onset of her illness and was preceded by severe haemorrhages; menses ceased altogether three years ago; fatty deposits of ovarian type present; no vasomotor instability.

Muscles normal in size consistency and power.

Thyroid appears normal and no apparent signs of dysfunction.

EXTRACTS FROM CASE-SHEETS.

4.5.37. Patient sought admission to-day in a voluntary capacity. She is depressed, restless and agitated, saying that a terrible calamity is going to befall her and that she is sure she is going to lose her eyes.

9.6.37. She remains miserable and depressed.

5.5.38. She is depressed and occasionally agitated and has developed the delusions that her food goes no further than her neck, and that her bowels never move. Considerable persuasion is necessary to induce her to eat.

31.5.40. She is brighter, complains less about difficulty in swallowing and has apparently forgotten her delusion about the bowels. She is taking much more interest in her surroundings and is beginning to think about her home.

5.3.41. Patient is only mildly depressed, expresses no delusions, and occupies herself in handicrafts.

25.4.41. During past month patient has had 110,000 units of Theelin. She is bright, takes a livelier interest in her work, does not complain in any way, and is described as showing a sense of humour. She is anxious to get home and has every confidence that can now manage. Her husband however, is on war work and has no settled home, so that she is waiting on for the present. Parole has been granted.

M A U D P.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 35 years.
Age on admission - 35 years.
Age when treatment initiated - 36 years.

HEREDITY.

Mother was an involutional melancholic who committed suicide at age forty-five.
Father was a chronic alcoholic.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair brown, long and fine; skull dolichocephalic; face long and features prominent; nose prominent; eyes light brown; average stature; medium build.

PREPSYCHOTIC PERSONALITY.

She was of average intelligence and was bright cheerful and sociable. She had wide interests, and took up various forms of sport. To her subordinates she was domineering and short-tempered. In performing what she conceived to be her duty she was very conscientious, and at times she could display considerable stubbornness. She was rather easily worried, and frequently retired to her room to weep over trifles that had assumed abnormal proportions.

MARITAL STATUS.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

An early menopause appears to be setting in.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Childhood was unhappy. Her father and mother were unsuited, the father being lazy and a drunkard, whilst the mother was very strict and religious. Maud was said to be very wilful as a child. When she was about twenty-two, her mother, an involutional melancholic, committed suicide after a short spell in a mental hospital, This was a severe shock and made a profound impression upon her.

She gave up her job, and after a short time at home, obtained a post as laundrymaid in a general hospital. She was capable and conscientious and with the passage of years was put in charge of the laundry. At age thirty-four she became friendly with a man, and an engagement seemed imminent, when the romance was interrupted by his calling-up. Shortly after this a new matron was appointed who proved a martinet and proceded to make considerable changes. The patient clashed repeatedly with her superior, and in an outburst of pique, resigned. From having led a more or less sheltered hospital existence she was plunged into unemployment and soon realized the difficulty she would have in finding a post as senior as that she had vacated. She was reduced to seeking a junior position and fate led her to the very mental hospital her mother had been in before her suicide. From the beginning the revival of painful memories had a depressant effect. Her work was unsatisfactory and she was abstracted and emotional. A fortnight later she saw a chronic dement and recognized in her a former schoolmate. As the result of this further shock she could not continue her work, and went to stay with relatives. She was depressed, could not sleep, felt incapable of occupying herself, and wept frequently. Whilst there, her cousin, with whom she had been very friendly, was killed in an air-raid, and the home was plunged in gloom. Her depression deepened and she became acutely agitated. It was in this condition that the police found her standing beside a river, and she was sent into hospital for observation, where, after an unsuccessful attempt at suicide, she was certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Patient is extremely wretched and her expression is one of utter misery. At times she sits in a bent position and hardly lifts her head, and at others she moves up and down the ward in a restless, agitated fashion. Her voice is low and sometimes amounts to little more than a whisper. She is acutely depressed and expresses delusions of unworthiness, stating that she must have done something very wicked to deserve the extreme misery she feels. She asks anxiously over and over again if she will be kept here all her life and moans "Let me go". "Oh! I know you will keep me here always. I am behind bars for the rest of my life." She has to be coaxed with food, and before admission made a serious attempt at suicide. There is no evidence of insight.

PHYSICAL STATE.

She is undernourished as the result of prolonged

refusal of food and has lost three stones in weight over the past six months.
C.N.S. appears normal. In the Cardiorenal system there is no abnormality detectable apart from an increase in blood pressure, 140/100.
Respiratory and alimentary systems appear functionally normal.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is normal in texture and colour and there is no abnormal perspiration; skin is somewhat loose, owing to emaciation.
Hair is rather fine and dry, and of normal distribution.
Muscles are partially atrophied and of diminished power.
Menses have been scantier during the past six months.
Pronounced vasomotor instability shown by occasional hot flushes, vertigo, and sweating attacks; dermographism is marked.
Thyroid appears normal in size; no tremor, tendency to exophthalmos, or abnormality of temperature.
Adrenaline reaction, 1 c.c. subcutaneously, was pronounced. P.R. rose from 80 to 100 and B.P. from 140/100 to 180/120; patient became pallid, dizzy and complained of throbbing in the head; her pupils dilated and the dermographic response was increased both in rapidity and extent; glycosuria present.
Loewi-Cords reaction ++.

EXTRACTS FROM CASE-SHEETS.

18.4.41. Admitted to-day from Newcastle Mental Hospital where she has been for four months. She is extremely depressed and agitated, and can scarcely speak for weeping. She feels she has done something far wrong but is rather vague about it. She states that there is no hope for her and that she will be shut up here all her life. Marked suicidal tendencies are present.

3.5.41. She has had a course of 160,000 units of Theelin but with no apparent effect. She remains miserable and depressed and moans and weeps.

18.6.41. No improvement. She is solitary, agitated and restless, and continually moans "Let me go home", then "I know you won't let me go home. I am behind bars for the rest of my life". A slight deficiency of vitamin C has been corrected by large doses of this, but with no change in her mental state.

30.6.41. A further course, 300,000 units Theelin just concluded. No improvement.

20.7.41. Hexoestrol, 25 mgs, given during past three weeks. No improvement. She is still acutely depressed and miserable, feels she is hopeless, and will be kept here for life.

I S A B E L L A R.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 46 years.
Age on admission - 48 years.
Age when treatment initiated. - 48 years.

HEREDITY.

Apparently nothing abnormal in family history.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion originally fair; hair light brown, long and wavy; skull dolichocephalic; face long and features prominent; nose prominent and straight; eyes blue; average stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was always reserved, never mixed much in company, and was noticeably less sociable than other members of her family. She was conscientious, hard-working, and with definitely restricted interests. Frugality was a virtue with her, and she saved every possible penny. A certain peevishness was sometimes observable.

MARITAL STATUS.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Her childhood and early adult life were normal. Later she spent many years in London as a waitress, and adverse factors may have been operative. Possibly lack of company and restricted interests tended to accentuate her proclivity for saving. In recent years this tendency was outstanding and extended to her diet. She would often starve herself, partly to avoid spending money on food, and partly to hoard the food itself. About two years ago a mild depression showed itself, and as it gradually deepened, the patient became more solitary and retiring.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Patient is acutely depressed. Her expression is anxious and apprehensive and she wanders about in a state of agitation, frequently weeping. On questioning she says she is in a terrible state and that life is unbearable. Hypochondriacal delusions are pronounced, patient believing that her food turns to water and is of no use to her, and stating that her stomach is completely ruined by the food she has eaten. Considerable difficulty is experienced in getting her to take nourishment, and she is apprehensive of all such attempts. Orientation and memory are unimpaired but insight is quite lacking. A definite tendency towards hoarding is present, an exaggeration probably of an already marked prepsychotic trait.

PHYSICAL STATE.

Patient has lost two stones in weight in the course of the past two years.
No detectable abnormality in the C.N.S. apart from asthenia, or in the respiratory system.
B.P. reduced 108/76. P.R. 70 and pulse soft.
Patient is constipated and has frequent nausea and considerable gaseous distension.
A widespread psoriasis covers her trunk and limbs.
Very marked avitaminosis C. An intradermal injection of 0.01 c.c. 2:6 dichlorophenol indophenol showed incomplete decolourisation after two hours and ten minutes, instead of within the normal five minutes.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is pigmented or light brownish shade, most noticeable on the face; texture of skin appears normal in those areas not affected by psoriasis.
Hair appears normal in texture colour and distribution.
Muscles are poorly developed and are unduly fatiguable.
Menstrual irregularity was noted at the beginning of her illness and there has only been one slight bleeding, immediately after admission. There is no sign of vasomotor irritability.
Thyroid is normal or slightly small in size; no evidence of dysfunction.
Blood sodium 324 mg. per 100 c.c. serum.
Blood sugar .110%.
Adrenaline 1 c.c. subcutaneously, had no appreciable response apart from an increase of 8 in the pulse-rate.
Loewi Cords reaction - .

EXTRACTS FROM CASE-SHEETS.

17.10.40. Patient admitted to-day in a state of marked depression, and agitation. She bursts frequently into tears and declares that life is unbearable. She has been refusing her food because she believes it turns to water and does her no good. An extensive psoriasis covers her trunk and limbs.

18.12.40. She has had a course of Theelin, 12,000 units in all. At the beginning of the course the impression was conveyed of diminished agitation but this was not maintained and she is now in the same state as on admission.

20.1.41. During the past month the patient has had vitamin C 50 mgs. daily. There has been a marked improvement. Her depression and agitation have diminished, she takes more interest in herself, has asked to have herhair attended by the hair-dresser, has occasionally been observed to smile, her delusions are less prominent, and her skin condition is less extensive.

24.2.41. No treatment has been given during the past month. Patient has lapsed into her original state. She is depressed and miserable, refuses her food, and says that something terrible is going to happen to her.

26.3.41. A course of 110,000 units of Theelin has been given, three injections of 10,000 units weekly. Her condition is much worse physically and mentally. Her psoriasis is more extensive, pigmentation of skin more pronounced, asthenia noticeably increased, and general resistance to infection lower as evidenced by presence of numerous furuncles on her trunk and two abscesses on her left heel and arm. Mentally she is completely wretched, and is restless, destructive, and constantly picking her skin, whilst her hypochondriacal delusion is more marked and she has to be spoonfed.

7.4.41. Daily for the preceding ten days she has received 300 mgs. vitamin C, and improvement is again obvious. She is no longer spoonfed and takes her food voluntarily, her colour is better and a diminution in her pigmentation and psoriasis has begun, asthenia has decreased and her agitation is abating.

24.4.41. Vitamin C, 100 mgs. daily has been maintained and patient has also received suprarenal cortex hormone (Eschatin). The most marked benefit hitherto has been derived from this. About an hour after each injection the patient became brighter, carried on a conversation, smiled, and acted fairly normally, and at night she slept soundly.
This effect required a minimum of 2 c.c.s and lasted approximately twenty-four hours; after 1 c.c. there was a less marked improvement.

On one occasion 4 c.c.s was given, with no greater benefit than accrued from 2 c.c.s. Intensive sodium therapy has begun, patient receiving increased common salt and 2 drams sodium bicarbonate daily. Vitamin C, 100 mgs. daily is being continued.

8.5.41. Patient keeps well physically: she is stronger, suffers less from fatigue, her skin is clear and the pigmentation and psoriasis have now completely disappeared. Mentally she has not been able to maintain the advance she made under Eschatin: she is mildly depressed, occasionally emotional, usually when she has to take her sodium mixture, which she believes is a purgative, but apart from this no longer expresses any hypochondriacal delusion and eats and sleeps well.

30.5.41. Potassium bicarbonate was substituted for the sodium salt and she received 30 grs. four-hourly By the third day she was utterly wretched, more so than after Theelin, and made an ineffectual effort to strangle herself.
Potassium has been discontinued, sodium resumed, and Eschatin 4 c.c.s injected.

18.6.41. She keeps moderately well but remains mildly depressed and is occasionally emotional. She continues to take an interest in her appearance and is generally in better state.

30.7.41. Patient has had a course of Antuitrin S. 40 c.c.s in all, and towards the end began to show an improvement on her previous condition. She appears to have reached the state she attained under Eschatin, but in contrast with the latter it has been kept up since her last injection three days ago.
Menstruation has occurred for the first time since admission.

E L I Z A B E T H S.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 49 years.
Age on admission - 49 years.
Age when treatment initiated - 49 years.

HEREDITY.

No adverse factors ascertained.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair originally fair, long and fine; skull dolichocephalic; face long and features prominent; nose straight and narrow; eyes blue; low stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was shy and retiring but kept bright and cheerful. Apart from her home and church she had no interests. Always very conscientious, her home had to be spick and span at all times, and she worked from morning till night, leaving off reluctantly on her husband's half-day. Strong religious tendencies were present and she was a strict observer of the Sabbath.

MARITAL STATUS.

Happily married and with seven children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Her childhood, youth, and married life were happy. There is no history of strain until six weeks before the onset of her illness, when her brother became seriously ill with pneumonia and just managed to pull through. The patient was very upset and when this was followed by the calling-up of three sons in quick succession there was a rapid development of depression and agitation.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her expression is constantly changing and varies from one of acute misery to one akin to sheer terror. She is in a state of great restlessness and agitation and it is impossible to hold her attention for more than a few seconds. She is hallucinated and hears terrifying voices which tell her she is to "be dead for all time" for having been a miserable sinner; at times these voices become unbearable and she shouts out "Lord God of Israel, save me, a sinful woman". She reiterates there is no hope for her and that even death cannot make up for what she has done. Her sleep has been much disturbed. There is no insight.

PHYSICAL STATE.

Her tissues are well nourished.
Nil abnormal detectable in the C.N.S. as verified later.
Cardiorenal, respiratory and alimentary systems appear normal.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is of normal texture and colour and is not unduly moist.
Hair of scalp is grey and of normal texture.
Muscles are normal in size, consistence, and power.
Menses became scanty and irregular six months ago; patient is depositing fat over hips and thighs; vasomotor instability does not appear to be prominent, and is most obvious in nocturnal hot flushes.
Thyroid is of normal size and there is no evidence of dysfunction.

EXTRACTS FROM CASE-SHEETS.

12.2.41. She is extremely agitated and depressed, crying out that there is no hope for her and that such a sinner is eternally damned.
Theelin 4,000 units given.

13.2.41. Following injection she was quieter and less agitated but this effect only lasted a few hours.
Theelin 4,000 units.

14.7.41. She is less agitated and depressed and more rational conversation can be held with her.

17.2.41. She has completely relapsed and her condition is as on admission.
Theelin 6,000 units given.

18.2.41. Further 6,000 units administered.

19.2.41. For the first time she is quiet and composed and no longer appears to hear the hallucinatory voices that castigated her for her wickedness.

5.3.41. She has received 12,000 units of Theelin in the course of the past fortnight and is quiet and well-behaved, although mildly depressed and quite lacking in confidence.

7.4.41. No Theelin has been given for three weeks. For the past three days she has been restless, excitable, and unable to sleep. Menstruation has occurred for the first time in eight months and patient perspires very freely, shows pronounced dermographism, and complains of hot flushes, headache, and dizziness.
Theelin 10,000 units administered..

8.4.41. Theelin 10,000 units.

12.4.41. She is now free from the physical symptoms of which she complained, and is bright and cheerful, and willing to assist in ward work. She has been put on parole. In an effort to improve her physical state treatment with liver extract and insulin 5 units daily has been commenced.

29.4.41. A further 30,000 units of Theelin, together with 12 c.c.s liver extract. She appears to have no residual depression and there is no trace of her former delusions.

19.5.41. Discharged recovered on a month's trial.

H A N N A H S.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 51 years.
Age on admission - 51 years.
Age when treatment initiated - 55 years.

HEREDITY.

Father's brother was an involutional melancholic who committed suicide.

ENVIRONMENT.

Urban environment.

RACIAL TYPE.

Racial type predominantly Mediterranean.
Complexion dark; hair originally dark brown, long and fine; skull dolichocephalic; face long and features prominent; nose prominent; eyes brown; average stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was described as being always pessimistic, easily worried, and having few interests. When she was aged forty she became increasingly seclusive and asocial, and practically isolated herself from her relatives.

MARITAL STATUS.

Single.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Psychosis set in six years after the menopause.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Since the age of twenty she has been somewhat deep and this appeared to be accentuated about the age of forty. Considerable worry was caused, she withdrew more and more into herself, reduced her social contacts to a minimum and became mildly depressed. When she was aged fifty-one she had a cholecystectomy performed, and on discharge from hospital could not sleep, became depressed and agitated, and talked of suicide. Three months later, after an almost successful attempt to cut her throat, she was certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

She is solitary and for preference sits huddled up in the darkest corner of the ward, paying no attention to what is going on, apparently sunk in her own misery. Occasionally she moans and weeps and states she is utterly hopeless. There is sometimes difficulty in making contact with her, but no evidence of retardation is present. Hypochondriacal delusions are present and she says she has no blood. When pressed for elucidation she becomes agitated and weeps. Memory and orientation seem unimpaired. Insight is lacking.

PHYSICAL STATE.

Pronounced deafness is present, apparently as the result of old otitis media. Other cranial nerves appear normal and no impairment found in motor, sensory, or reflex systems.
Cardiac action regular, but evidence present of slight arteriosclerosis.
Nil abnormal detected in other systems.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin is of normal texture and shows no unusual dryness.
Hair is of normal distribution and hair of scalp is grey and scanty, but of normal texture.
Muscles are slightly diminished in size, consistence, and power.
Menses ceased nine years ago; no signs of vasomotor instability. P.R. 70. B.P. 130/90.

EXTRACTS FROM CASE-SHEETS.

7.9.36. Patient is restless agitated and depressed. She is constantly moaning and pays no attention to anything said to her. Recent suicidal attempts have left her with scars on throat, wrists, and abdomen.

30.9.36. Miserable and depressed, and to-day made an ineffectual attempt to burn herself.

8.8.38. She is depressed and wretched, pays no attention to her surroundings, is unoccupied, and frequently moans and weeps for no apparent cause.

9.6.39. She is miserable and depressed, moaning and weeping. Sometimes she expresses the wish to die.

21.5.41. There is little change in her state. She is miserable and depressed, emotional at times, and states that she is utterly hopeless.

6.6.41. A course of 100,000 units of Theelin has been given. Several days after the last injection she was noticeably brighter and it was possible to hold a short conversation. She had been transferred to a better ward before commencement of treatment, and her constant plaint had been that it was too good for so hopeless a case. Following treatment her skin shows more colour, her appetite is better, and she sleeps better. She is no longer feeling she is unworthy of her new ward, and sits outside basking in the sun instead of hiding herself in a corner. She still says there is no hope for her, but there seems less conviction in her statement.

10.7.41. In an attempt to improve her condition she has received during the past month 500,000 units of Theelin together with 25 mgs. hexoestrol. There is no change in her state.

I R E N E T.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 37 years.
Age on admission - 37 years.
Age when treatment initiated - 40 years.

HEREDITY.

No abnormal heredity elicited.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type Nordic-Alpine.
Complexion fair; hair light brown, long, and slightly coarse; skull mesocephalic; face broad; nose prominent; eyes brown; average stature; heavy build.

PREPSYCHOTIC PERSONALITY.

She was timid, easily worried, and lacking in self-reliance, whilst her interests were few. As a child she had been pampered and spoiled, and when she grew up there was a definitely selfish trend in her character.

MARITAL STATUS.

Married but poorly adjusted; no children.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Psychosis preceded menopause by three years.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Patient was an only child, brought up in a sheltered environment, and spoiled by her mother. At the age of twenty she fell in love with a youth and indulged in intimacies but broke off this relationship after two years. When she was thirty-five her father married again and the step-mother was not at all sympathetic to Irene. Apparently to get away from this environment she accepted a suitor after a brief acquaintance. Her married life was not happy, tinged as it was with a dread of pregnancy. This dread was attributable to the fact that her mother had been an invalid for twenty years following a stillbirth. Marital relations were difficult, and the spectre of her earlier experiences added a feeling of guilt to

the fear she felt. Two years later she gave birth to a child, delivery being difficult and placenta retained, and child dying within a short period. This was the final stress. She became depressed, agitated and suicidal, with marked feelings of guilt and developed the delusion that she had syphilis, acquired from her former lover, and that this disease had been transmitted to her husband and child. Later she expressed the delusion that she was the most sinful woman in the world because she had brought into it a child rotten with disease.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

She is superficially bright, mixes with the other patients, and occupies herself with needlework. Her delusions appear to be unchanged, and on questioning she reveals all her previous thought content, becomes depressed and anxious, and breaks into tears. She states she has committed an unpardonable crime and that she is the most wicked woman in the whole world. She believes her body is riddled with syphilis and it was because of this that she lost her child. Her agitation becomes more pronounced when any proposal is mooted of sending her to her husband for a weekend, and she gives the impression of being capable of rapidly developing suicidal tendencies.
Orientation and memory are unimpaired. There is no insight.

PHYSICAL STATE.

No abnormality detected in C.N.S.
Cardiorenal, respiratory and alimentary systems appear normal.
Wassermann reaction negative.

ENDOCRINE STATE.

Skin and hair are normal in texture, colour and humidity.
Muscles normal in size, consistency, and power.
Menses are fairly regular, but hot flushes are becoming increasingly pronounced, and fat has been deposited in ovarian sites.
Thyroid appears normal and no evidence of dysfunction.

EXTRACTS FROM CASE-SHEETS.

4.6.38. She was admitted to-day in a condition of agitation and depression. She frequently bursts into tears, states she is the most wicked woman in the world and that she has committed an unpardonable crime in bringing into the world a child to whom she had, with fatal results, transmitted the syphilis that she was certain riddled her body. She is acutely suicidal.

29.6.38. She is employed in the ward and states she must keep on working to prevent her thoughts making her utterly miserable. Now and then she breaks out into a paroxysm of weeping.

28.6.39. Appears to be more contented, although still mildly depressed, occupies herself with needle-work, and is sociable. When questioned she voices the same delusions as before: there has never been so wicked a woman, she has committed an unpardonable sin, she is full of disease, and will never recover.

12.3.41. She is superficially cheerful, but still expresses the same delusions, and on questioning breaks down and weeps. When treatment was suggested she became exceedingly agitated, saying she was too worthless to deserve treatment and that she was only fit for a life-time in hospital.
Her letters are strongly tinged with egotism: they deal entirely with herself, the food she is getting, or not getting, and the hardship she thereby undergoes, how worthless she is, and how she must spend her life here; possibly also egotism is to be seen in her belief that no one has ever been as wicked as she.

10.4.41. A course of 24,000 units Theelin given but without effects.

2.5.41. A further course of 100,000 units given. No apparent change.

20.6.41. She has had 50 mgs. Hexoestrol, equivalent to 2,000,000 units Theelin, but with no improvement.

G L A D Y S T.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 37 years.
Age on admission - 38 years.
Age when treatment initiated - 38 years.

HEREDITY.

Nothing adverse elicited.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion fair; hair light brown, long, and straight, skull dolichocephalic; face long and features prominent; nose straight and narrow; eyes blue; average stature; thin build.

PREPSYCHOTIC PERSONALITY.

She was reserved and sensitive. Her interests were confined to her house, of which she was inordinately proud, and to her husband and daughter. She was always reserved, kept much to herself, and made few friends. She was sensitive to the views of others, and to adverse criticism from her family she reacted by making unpleasant remarks. The achievements of others made her envious and she always claimed to be able to do better.

MARITAL STATUS.

Married and with one child.
Marriage was happy until a year before onset of psychosis.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Coincided.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

Her childhood and early life were uneventful. She was happily married and her life was smooth until about a year previous to the onset of her illness. Her husband travelled in connection with his work, and there was a strong suspicion that his wife was not the only woman in his life. This information eventually reached the patient

and caused a certain coolness towards her husband. Six months after this, just as the menopause was commencing the husband was called up. A rapid change took place in her state. She became depressed and agitated, suicidal tendencies appeared, and in spite of her relatives' efforts to keep her at home she had to be certified and was admitted within six months.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her expression is miserable, she wanders about the ward in a hopeless sort of way, and her voice is low and toneless. Frequently she weeps quietly or brushes away tears. Memory and orientation are normal. Her mood is one of extreme sadness. She answers questions freely and without hesitation. Sleep is disturbed, patient stating that she often wakens with a vague but intense feeling of fear. She can give no reason for her depression and says that she feels as though a ton weight were pressing down on her brain. She is suicidal and has attempted strangulation, whilst at other times feeding has been difficult. She is unemployable and shows but little insight.

PHYSICAL STATE.

No abnormality in cranial nerves, motor, sensory, or reflex systems.
Cardiorenal, respiratory and alimentary systems, appear normal.
Wassermann reaction negative.
Considerable avitaminosis C. Intradermal injection of 0.01 c.c. 2:6 dichlorophenol indophenol decolourized in twenty-six minutes.

ENDOCRINE STATE.

Skin is normal in texture, colour and degree of moistness.
Distribution of hair is normal, and hair of scalp is of normal texture, but somewhat scanty.
Slight diminution in size of muscles but no asthenia.
Thyroid appears normal; no evidence of dysfunction.
Menses were noted to be irregular shortly after admission; vasomotor instability seen in alterations in pulse rate, palpitations, slight sweating attacks and headaches. B.P. 126/84. P.R. varies from 70 to 94.
Adrenaline reaction produces marked response with considerable pallor, sweating, glycosuria and increase in B.P. and P.R.

EXTRACTS FROM CASE-SHEETS.

4.7.40. She is depressed and agitated, somewhat sullen in manner and shows no improvement in her state.

20.11.40. A course of Theelin, twelve biweekly injections of 2,000 units, has been given but with little effect.

1.1.41. She has remained in a state of depression, asking only in a hopeless sort of way to be allowed to go home. Suicidal tendencies remain. On one occasion she attempted strangulation and on another she tried to induce a parole patient to obtain poison for her.

28.2.41. Her state is one of depression with agitation. She is miserable and says she feels as though a ton weight were pressing her brain down. A course of Benzedrine caused a slight improvement at the beginning but soon lost effect and she lapsed into her original state.

5.3.41. Theelin therapy begun; injection of 10,000 units given. On account of coincident vitamin A deficiency, as revealed by her skin condition, extra supply of vitamin provided.

12.3.41. Theelin 60,000 units now given. Patient is slightly brighter and converses spontaneously with others.

10.4.41. Considerable deficiency of vitamin C having been revealed by the 2:6 dichlorophenol indophenol test, patient has in the course of the past week received 300 mgs. of the vitamin daily. Her condition appears to have improved; she has evinced a desire to work in the handicrafts department, is obviously brighter, and has been transferred to a better ward.

17.4.41. A total of 130,000 units of Theelin has now been administered. She continues to improve, her work in the handicrafts department shows considerably more evidence of care and concentration, she talks more freely and can now sustain a conversation. Her countenance is much brighter and there is almost the beginning of insight.

30.4.41. An attack of cholecystitis has developed and patient's mental state has lapsed. She is again rather depressed and states she feels she will be here for the rest of her life.

26.5.41. Patient has now recovered from her cholecystitis but remains slightly depressed. Treatment with Theelin has been resumed.

30.5.41. In the course of the past five days she has received 100,000 units of Theelin.

2.6.41. Following treatment she has been much better. She is brighter, shows no tendency to agitation, and co-operates willingly in ward work. No apparent evidence of suicidal tendencies, and her outlook is much healthier, although she is still rather thankless for anything that is done for her. She has now been tried on parole.

5.6.41. Patient remains bright and cheerful. She has been allowed home for an afternoon in the care of her relatives and following this was was noticeably happier and better composed.

16.6.41. She has spent a weekend at home with her husband, who was on leave, and with her daughter, and from all accounts was bright and happy and seemingly recovered.
Patient has now been discharged recovered on a month's trial, and a letter has been forwarded to her doctor to whom she has been advised to report for further treatment as required.

E D I T H T.

ETIOLOGICAL FACTORS.

AGE.

Age at onset of psychosis - 45 years.
Age on admission - 45 and 54 years.
Age when treatment initiated - 54 years.

HEREDITY.

Sister is a mental defective.
Daughter is a mental defective.

ENVIRONMENT.

Rural environment.

RACIAL TYPE.

Racial type predominantly Nordic.
Complexion p ale; hair originally brown, long, and straight; skull dolichocephalic; face long and features prominent; nose straight and narrow; eyes blue; average stature; thin build.

PREPSYCHOTIC PERSONALITY.

Her intelligence was rather below the average, and she never displayed much interest in current affairs, being seemingly content to spend her life in domestic drudgery without compensating interests. She was shy and retiring and easily worried. Latterly a tendency to depression appeared.

MARITAL STATUS.

Married and with one child.

RELATION OF PSYCHOSIS TO MENOPAUSE.

Psychosis preceded menopause by several months.

OTHER PREDISPOSING, AND PRECIPITATING FACTORS.

There is little trustworthy information about her childhood or early life. Her married life seems to have been uneventful and her role appears to have been that of drudge. At age forty-five a stillbirth resulted in acute depression and agitation and she was certified. The menopause apparently set in several months after this late pregnancy. Eight months from admission she was discharged recovered.
According to her niece she remained mildly depressed until war conditions and acute influenza brought about a recurrence of acute depression. Patient

lived beside an aerodrome which for a year had been subject to spasmodic bombing. A few months before admission raids became more frequent and she was compelled to spend the nights in shelters, generally disused pit-shafts. Insomnia resulted and she became noticeably depressed. About six weeks before admission a period of exposure during a raid led to influenza followed by bronchitis. Subsequently she became extremely depressed and agitated, suicidal tendencies reappeared, and she had to be certified.

CONDITION AT COMMENCEMENT OF TREATMENT.

MENTAL STATE.

Her features register acute misery, she is restless and in constant movement, wringing her hands, and weeping freely. Her mood is one of acute depression tinged with anxiety. Hypochondriacal delusions are prominent, the patient believing she has no insides and that it is useless to take food. She states also that she has been doing wrong for years. Considerable difficulty is experienced in feeding her. Memory and orientation are unimpaired, but insight is lacking. The patient's agitation does not permit of employment.

PHYSICAL STATE.

She is in moderate general health. An element of malnutrition has been present before patient's admission to hospital.
Deep reflexes are slightly exaggerated and pupils are unusually brisk.
Cardiac sounds are of poor quality, P.R. 100, B.P. 140/100.
Scattered rhonchi are present in chest from recent bronchitis.
In the alimentary system pyorrhoea and constipation are present.
Wassermann reaction negative.
Avitaminosis C present; reagent decolourized in twenty-five minutes.

ENDOCRINE STATE.

Skin is of normal texture but shows increased perspiration.
Hair is fine, and white in colour.
Muscles are diminished in size, consistence and power.
Menses ceased about eight years ago.
Thyroid does not appear enlarged, there are no eye signs but a definite fine tremor is present in the outstretched fingers. P.R. is 100 and there is an occasional extra systole.

B.M.R. estimated to be +25.2.
Blood sodium 308 mg. per 100 c.c.s.
Blood sugar 0.07%.
Volhard's Water Test indecisive because of patient repeatedly vomiting.
Adrenaline reaction has had fair response with pallor, sweating, glycosuria, marked dermographism, increase in pulse-rate of 18 and in pulse-pressure of 20.

EXTRACTS FROM CASE-SHEETS.

5.12.31. She is acutely depressed and agitated, restless and unable to sleep, and states there is no possible hope of her recovery. She has twice attempted suicide.

30.3.31. Depressed and hypochondriacal and states she has "no inside".

18.7.31. Has been much improved over the past two months, and to-day discharged on trial.

22.3.41. Admitted to hospital to-day. She is depressed agitated and very restless. She states she has been doing everything wrongly for years and that she had "no inside". In conformity with this latter delusion she is resistive to feeding.

4.4.41. Patient's diet prior to admission has been very faulty and some emaciation was present on admission. Pronounced C avitaminosis was shown to be present. To remedy these defects she has been given plentiful nourishment, and during the past ten days has also received 1,300 mgs. vitamin C. She is sleeping better, eating better, her features are more composed and there is some lessening of her agitation. This improvement is reflected in the reduction of the pulse-rate from 100 to 90 and in a slight diminution of tremor. Extra vitamin C now stopped.

23.4.41. She has now received a course of 130,000 international units of Theelin. No improvement on previous state.

10.5.41. Patient has steadily relapsed and is as agitated as on admission.

30.5.41. A further course of 190,000 units Theelin given. No improvement in mental state. Vitamin C resumed 100 mg. daily.

7.6.41. Patient died of an intercurrent broncho-pneumonia and post-mortem examination revealed in addition extensive fatty degeneration of heart, and cystic kidneys.
