

MANIC DEPRESSIVE PSYCHOSES

With Special Reference to the Lymphatic Reaction

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By

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Much work has been done within recent years towards elucidating the causation of mental diseases and it is now recognised by the physiogenic school of psychiatrists that certain forms of mental disorder are due to toxins, many of which are microbic in origin. ⁽¹⁾ There does not appear to be, however, any uniformity of opinion that one particular organism or group of organisms is the exciting cause in any particular mental syndrome and this is perhaps only to be expected when one considers how varied and different are the clinical manifestations encountered in any form of mental disorder. The object of this thesis, therefore, is to emphasise the importance of leucogenesis in the psychoses and to attempt to correlate the various mental states with the haemopoietic changes which occur. The cases selected and referred to are drawn exclusively from the Manic Depressive Group of the psychoses, but sufficient research has been carried out in certain of the other psychoses to demonstrate, that in these cases also, leucogenesis plays an essential part. Its importance cannot be overrated and is a valuable link in elucidating some hitherto inexplicable alterations in the clinical picture. Various causative and predisposing factors are recognised in the

Manic Depressive Group of psychoses but beyond this, we are unable to account for the various alternating states or for the sequelae of events in a given case or to explain satisfactorily why the clinical picture so often alters dramatically from the condition of mental and motor activity to the quiescent state or even to the depressed and inactive state and eventually to the chronic condition. Furthermore, we experience difficulty in ascertaining the terminal condition in most cases and in these can only give a very tentative prognosis. It is manifest that the continually changing panorama of clinical features observed in the Manic Depressive psychoses cannot be adequately explained by psychological or by exogenous factors alone and must, of necessity, be determined by underlying pathological processes. In this thesis, the more striking alterations from the normal have been investigated and it is to be hoped that a more extensive research will elucidate much that has hitherto remained unrecognized in the psychoses.

In the psychiatric field, the study of leucogenesis with reference to mental disorder is by no means a recent innovation, dating back to the close of the previous century when the leucocytic responses were investigated

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by Lewis Bruce and others. Since then, many advances have been made in the realm of Haematology, more scientific technique has been employed and various therapeutic and biochemical measures have been utilised in conjunction with the blood determinations. It cannot be over-emphasised however that such advances have been made practically exclusively in the study of somatic diseases, while little if any attempt has been made to correlate the underlying pathological processes with the mental disorder; hence there has been but little advance towards determining the basis of the characteristic mental and physical features of the psychoses. With the introduction of artificial methods of producing pyrexia, we possess a potent weapon in procuring alterations in the haemopoietic system, but there still remains the fact that, in mental diseases proper, as ascertained by laboratory investigations we are dealing with conditions characterised by a complexity of alterations from the normal out of all proportion to those found in somatic disorders, given the same subjective and objective clinical picture. Bearing these considerations in mind, it will be readily understood that any real advance in the subject will only be obtained, not by casual leucocytic

determinations at irregular and infrequent intervals but only by systematic and prolonged serial counts. This appears an involved and somewhat laborious method which at first seems to furnish no indication of a relationship between the mental features and the leucogenic responses, but, after a series of such counts have been performed, a definite and distinctive relationship can readily be appreciated. It seems superfluous to emphasise the importance of regularity in the estimations since the blood picture is so susceptible to exogenous influences, that uniformity ^{is} much be achieved as far as possible in the conditions under which the successive counts are taken before any relationship or distinctive features can be unequivocally demonstrated.

In the psychoses, the chief interest from a pathological point of view lies rather in the important lymphocytic changes which occur than in the neutrophile variations, to which attention has mainly been directed in the past. ⁽³⁾ That important neutrophile changes do occur in the psychoses cannot be disputed but they are rather of a generalised tissue reaction mechanism, whereas the lymphatic reaction may be regarded as of a highly specialised nature. In the psychoses, the lymphatic reaction is not usually present to such a marked degree

as in certain of the somatic disorders, e.g. Glandular Fever; where special infective agents are causative of a pronounced lymphatic tissue stimulation. This statement however, must not be accepted as a hard and fast rule, since certain psychotic conditions are encountered where the lymphatic response not only approximates but even surpasses that which is commonly found in the various somatic diseases; a reaction which at once suggests the possibility of a definitely specific infective origin for the psychoses. At present, we can only state that in the psychoses there is present a "lymphatic reaction syndrome" and we can only assume the existence of a systematic infection by analogy. From serial counts, however, the tissue attacked can be shown to be that of the lymphatic system, either in the nature of stimulation or of inhibition, as in a very virulent infection, a fact which further emphasises the possibility of an infective agent being the causative factor.

From a physiological and psychological point of view, the lymphatic reaction is of considerable importance as it occurs during a phase of temporary exhaustion and metabolic auto-intoxication associated with an in-

definite factor, the nature of which is at present not clearly understood. This unexplicable factor may possibly be intimately linked with the lymphatic response in some manner giving rise to a picture suggestive of chronic infection and toxic action. It, therefore, seems reasonable to advance the suggestion that this factor must be of infective origin and while capable of inhibiting neutrophile response to a marked degree, will necessarily attract little or no somatic reaction. This combination of toxic action and reaction, when found in the psychoses, is suggestive of the presence of a specific neurotoxin, capable of causing lymphatic stimulation while simultaneously producing neutrophile inhibition and paresis. The power of the lymphatic response must necessarily depend upon the degree of inter-relationship between these antagonistic factors.

By the term "lymphatic reaction" is meant an anomalous response of the haematopoietic tissues to infection. The name was first used by Tuerk who recorded a case of acute sepsis in which a relative lymphocytosis replaced the normal neutrophilia which is the characteristic response to infection. Several other workers have in-

investigated this condition and while some regard the reaction as being constitutional in nature, Naegeli advances the theory that special infective agents are causative of a lymphatic tissue stimulation. The blood picture of this lymphatic reaction shows great variations, from 2700 leucocytes of which 74% were lymphocytes to Koenigsberger's case of 23,600 leucocytes of which 64% were lymphocytes. These figures serve to indicate the extreme variations which may be encountered in investigating the lymphatic reaction. If the responses of the lymphatic system to well recognised pathological states are considered, certain interesting observations are encountered. In typhoid fever, the infective etiology of which is well established, there is usually a hyperplasia of the lymphatic tissue in the portal tract associated with an early relative and later absolute lymphocytosis. The lymphatic reaction is important in this condition, protecting the tissues against toxic bacillary infection and the prognosis may be accepted as varying directly with the extent of lymphocytic response. Similarly, it has been demonstrated that hyperlymphocytosis in Dysentery and Tuberculosis is of favourable prognostic significance while neutrophilia and leucocytosis are both bad signs. Further Jackson,

as a result of prolonged investigations upon general paralysis of the insane, demonstrated that the production of an artificial lymphatic reaction by small doses of Tuberculin prolonged the remission periods. These observations emphasise the part played by the lymphatic system as a defence mechanism and upon the recuperative powers of this system, recovery often depends.

In the Manic Depressive Psychoses, there are definite indications that the lymphatic system is being acted upon to a degree that is pathological in its intensity and this fact is important if only on account of the infrequent references to its occurrence in the literature. Numerous investigators have noted persistent slight variations from the normal in many of their cases but as these observations have been made at irregular and infrequent intervals in the course of routine examinations, it is not surprising that little or no importance has been attached to those results. As emphasised earlier in this paper, a true indication of the importance of these persistently abnormal variations in the haemopoietic system can only be appreciated if an investigation be carried out upon a selected number of cases by means

of serial counts. This factor has not been fully appreciated by several other workers in this field of Psychiatry and accounts for their misinterpretation of these variations. Thus, until the importance which it merits is assigned to this branch of research, the real meaning of any blood alterations from the normal in the Psychoses will remain hidden and any progress in a therapeutic direction will of necessity be thwarted.

In considering the actual clinical material employed, great difficulty has been experienced in determining the most satisfactory avenue of approach, both from a technical and a therapeutic point of view as well as on account of the difficulties to be overcome as regards the time involved, the variability of the different cases from a clinical point of view and the important part played by exogenous influences. Manifestly, on account of the time and labour involved in doing serial counts, it is impossible to employ this method in all the Manic Depressive cases under observation. On the other hand, however, it is of little value to consider isolated and unconnected estimations on a number of cases in an attempt to determine a uniform factor, since, under these conditions,

one would be dealing with various phases of psychotic reaction, from all states leading to recovery or chronicity and those intermediate in type. Furthermore, as stated earlier, the extreme susceptibility of the haemopoietic system to exogenous factors necessitates the selection of a uniform time of examination for all cases, so that the effect of digestion will not influence results. Finally, the presence or otherwise of possible hidden gross organic disorders, and to what extent these will influence the haemopoietic system, must also be taken into account. With these various points in view an attempt has been made to classify the clinical material under review into three groups.

GROUP I comprises those cases upon whom a single systematic blood count for erythrocytes, leucocytes, haemoglobin, colour index, diameter of corpuscles etc, was performed as part of the ordinary routine examination upon admission and upon discharge, either recovered, relieved, or otherwise. In some of these cases, intermediate examinations were carried out at irregular intervals as circumstances demanded. It will be readily appreciated that the majority of these cases gave vague and indeterminate results from which no definite con-

clusions could be deduced. In some, however, sufficient evidence was obtained to justify the value of the method in isolated cases, as will be seen later, when for example, if a marked difference is found between the blood picture before and after treatment, then this alteration should be carefully interpreted in correlation with the patient's mental condition. This method of investigation must however, be regarded as a poor substitute for the more accurate method of serial counts, and it is by laying undue stress upon the results obtained under these conditions that several other workers have erred fundamentally in their interpretation of the
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leucogenic response.

GROUP II comprises those cases in whom the method of serial counts was adopted as a means of further investigating the lymphatic response over a fixed period which of necessity varied with the type of case under consideration. The routine method adopted was as follows:- estimations were carried out at 4 hourly intervals during the 24 hours - the hours of these counts being determined so that the possible changes following digestion were eliminated and also that a definite correlation of the early morning state of the

patient with that of the latter part of the day should be ensured and emphasised. Throughout the investigation, short notes of the patient's mental condition at the time of the count were taken in every case. The estimations were made with the ordinary diluting pipettes, the Buerker "double chamber" haemocytometer and a Hearson Daylight Lamp. Leishman's stain was used for the blood smears and the Schilling differential technique was employed in ennumerating the cells.⁽⁶⁾

It is to this group of cases that attention is mainly directed since, by adopting the serial count method, the influence of exogenous factors is reduced to a minimum and also because an isolated abnormal result will not, of necessity, receive the undue prominence which is attached to it when investigation by single count is adopted. In this method, all results were double-checked and, if any abnormal variation to a marked degree were noted, a control estimation was performed to ensure the accuracy of the initial determination.

GROUP III comprises those cases in whom a serial count was performed at intervals when the mental state showed a definite trend in either a direction of mental

activity or in a direction of depression. The alterations between the clinical pictures were then correlated with the blood findings.

Out of these groups of cases the most striking types have been selected for the purposes of this thesis as demonstrating various degrees of lymphatic reaction. In the three groups, selected cases have been further investigated at intervals, as far as possible, subsequent to their discharge and the results obtained have been correlated with those obtained while under treatment.

With reference to these cases, a digression for a moment is justified to consider what constitutes the normal blood picture since some uniform standard must be adopted in order to compare different cases satisfactorily. The various authorities are not entirely agreed as to what constitutes the normal blood picture and this is to be regretted since a "normal" blood picture to some investigators will, under these conditions, appear "pathological" to others. In this investigation, Schilling's figures have been accepted as the standard in determining any deviation from the normal.

Neutrophiles	60 - 70%
Lymphocytes	23 - 35%
Eosinophiles	2 - 4%

Monocytes 4 - 8%

The lymphocytic values, according to this observer, vary directly as the total number of leucocytes; the normal number of lymphocytes forming 23 - 35% of the total number of cells where the total does not exceed 8000 cells per c.mm., and being reduced to 23 - 30% where the total number of cells exceeds this figure. Throughout, attention has been paid to this variation in estimating the degree of variation from the normal. Furthermore, the normal range of the total counts has been accepted as being 6000 - 8000 cells per c.mm. and in determining the absolute and relative values to be assigned to the various results the following figures have been accepted.

Hyperleucocytosis 8000 cells and over per c.mm.

Normal 6000 - 8000 cells per c.mm.

Hypoleucocytosis 5000 - 6000 cells per c.mm.

Leucopenia 500 cells and under per c.mm.

With these points in mind, the consideration of the characteristic features of the individual groups is most clearly demonstrated by means of haemograms.

GROUP I (1).

Example of a hyperlymphocytic reaction in a patient who made a good recovery.

Male. Married. aet. 54 years. Labourer. Admitted 15th June, 1933. 1st. Cert.

Synopsis of Case History.

Family: Mother suffered from some "nervous trouble" from age of 45 years - was never certified and died at age of 60 years from Cerebral Haemorrhage. Father was a chronic alcoholic and was drowned in 1916 aged 61 years.

Personal: Fairly bright and up to the standard at school. Commenced work at 14 years. Joined army in 1914 and was discharged, wounded in left leg in 1918. Married in 1920 and has no family.

From 14 until 48 years of age, he appears to have led a well adjusted life. At 48 years of age, he lost his employment through inattention and experienced difficulty in obtaining a situation from this period onwards. A holiday failed to produce any alteration in the state of mild depression which affected him at this

time and in May 1933, he became definitely exalted and restless. He was certified and removed to the mental hospital on 15/6/33.

On Admission:

Physical State: Height 5 ft. 5 ins; weight 9 st. 4 lbs; general vitality and nutrition very poor. A few enlarged glands in posterior triangle of both sides of the neck. Gums edentulous.

Circulation: Heart action slightly irregular and rapid. Pulse irregular and low of tension. B.P. 124 mms Hg Systolic; 90 mms Hg. Diastolic.

Lungs: No abnormality detected. Radiograph of chest negative.

Muscular System: Poor in tone.

Nervous System: Pupils equal and regular. React both directly and consensually to light and to accommodation.

Abdomen: Examination failed to reveal any abnormality.

Urine: Pale Amber; Acid; S.G.1024. Nil abnormal.

Mental State.

On examination he presented a self-satisfied, complacent appearance, being mildly grandiose and elated in his demeanour. He talked incessantly in an incoherent

manner rambling from one subject to another and giving no clear impression of his meaning. His attention was difficult to obtain and impossible to retain for any length of time. If his wishes were thwarted, he became noisy, abusive and impulsive.

Course and Treatment.

Following a course of colonic irrigation and ultra-violet light treatment, the patient became gradually more composed and improved physically. This improvement continued from the beginning to July onwards.

Case Reviewed 26/7/33: Weight 10 sts. 4 lbs. Appetite, sleep and bowel action good.

Patient is well orientated and composed and shows a marked degree of insight into his condition, both now and previous to admission. He realises clearly his mental illness and now volunteers the information that he feels better than he has done for years past. He displays initiative and intelligence and is usefully employed in the Occupational Department.

Patient was put on 3 weeks' trial on 7/8/33 and was finally discharged recovered on 28/8/33.

The following haemograms demonstrate the alteration in the blood pictures which occurred while the patient was under treatment.

	Mental Condition	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
15/6/33	Hypomania mild exaltation, grandiose and rapid flight of ideas.	10,200	<u>Per c.mm.</u> 5,600		<u>Per c.mm.</u> 4,580 + 1940	
15/7/33	Slightly improved Much more settled but still garrulous and mildly excited	11,000	5,350	48.5%	5,650 + 3010	51.5%
7/8/33	Much improved mentally and physically. Put on pass.	13,000	5,850	45%	7,150 + 4510	55%

Remarks:

The above case shows both a relative and an absolute lymphocytosis, gradually progressive and associated with a corresponding improvement in the patient's mental condition, finally terminating in complete mental recovery. An interesting point of note is that the lymphocytic values have constantly been pathological in their numbers through-

out the period of investigation and have never approached normal limits. This relative and absolute lymphocytosis has persisted subsequent to the patient's discharge and although the absolute numbers have decreased slightly, the relative values still persist, while the patient shows no signs of any recurrence of his mental disorder.

GROUP I (2).

Example of a sustained hyperlymphocytic reaction in a patient with no improvement in the mental condition.

Male. Single. Aet. 32 years. Joiner. Admitted 1st. April, 1932. 1st Cert.

Synopsis of Case History.

Family: No psychotic history elicited. Both parents alive and healthy.

Personal: Normal child, youngest of family of 4 males, his brothers are all alive and healthy, displaying no psychopathic tendencies. Reached highest standard at school, leaving at 16 years, and worked as apprentice joiner until 21 years and has remained in steady employment up to a short time before admission. He was always cheerful and "full of life", interested in his work and ambitions, made social contacts readily and has been described as "the life of a party". At irregular and infrequent intervals he suffered from mild transient attacks of depression. These appear to have been caused

by his success in life not being sufficient to satisfy his super ego.

The onset of his mental symptoms was gradual. About six weeks previous to admission he showed undue activity and restlessness - failed to return for his meals - became irritable and aggressive in his conduct - his manner and conversation became "strange" and he commenced to go for long walks at night. Immediately previous to admission, he became unduly elated and boisterous in his behaviour, speech becoming rapid and unintelligible; eventually he was certified and admitted to the mental hospital on 1/4/32.

On admission:

Physical State: Height 5 ft. 8 ins. Weight 8 sts. 2 lbs.

Patient appears emaciated. Skin is loose and hangs in folds. Several carious teeth.

Heart: Shows some shortening of cardiac diastole.

Pulse: Rapid and irreular. B.P. 112 mms. Hg
Systolic; 90 mms. Hg. Diastolic.

Lungs: Examination failed to reveal any abnormality.

Nervous System: Marked facial asymmetry. Pupils equal

and regularly contracted. React both directly & consensually to light and to accommodation.

Abdomen: Examination of all major viscera failed to reveal signs of any gross lesion.

The general physical state was suggestive of toxæmia.

Mental State.

The patient was unduly elated, grandiose and garrulous. His assertions with regard to his physical achievements were not supported by his physical state, although his claims were within the bounds of possibility. His speech was rambling and at times incoherent; his statements followed each other with extreme rapidity and were irrelevant to the topic under discussion. He was restless, and excited and showed a tendency to divest himself of his clothing. When remonstrated with, he became abusive and impulsive.

Course and Treatment.

In spite of medicinal treatment, the patient showed an aggravation of all his mental symptoms during the first week following his admission. He became restless, excitable, and resistive to nursing. His conversation was rambling and incoherent and confusion increased pro-

gressively; he was easily distractible and could not engage in even simple ward work. The flight of ideas evident upon admission, became more pronounced and were followed by the onset of mild persecutory ideas which have persisted until the present time. With the exception of a few slight transient attacks of depression the condition of Hypomania has continued uninterruptedly and shows no signs of an early improvement. The following haemograms indicate the blood condition upon admission and at intervals throughout the illness.

Date	Mental Condition	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
1/4/32	Hypomania. Mildly elated, grandiose and garrulous with flight of ideas.	12,100	7,850	65%	4250 +1610	35%
10/6/32	Hypomania more pronounced. Restless, excited, abusive and impulsive.	12,800	8,100	63%	4700 +2060	37%
7/8/32	Depression (transient) Morose, Sullen monosyllabic. Refuses food.	12,500	8,500	68%	4000 +1360	32%
12/4/33	Hypomania. Mildly elated, grandiose and garrulous.	12,650	8,250	65%	4400 +1760	35%
9/3/34	Hypomania. Elated, grandiose, garrulous. Restless and excited.	12,200	8,100	66%	4100 +1460	34%

Remarks:

The above case demonstrates the persistence of both relative and absolute hyperlymphocytosis over a period of

22 months with no appreciable alteration in the mental symptoms. The lymphocytic response, in this case, although exhibiting a pathological response to a functional demand, both relatively and absolutely, is however, insufficient to produce an alteration in the mental state. The picture suggests a failure of the defence mechanism; where the response has succeeded to a certain degree but is not sufficient to promote recovery. The results, when compared with those of the previous case suggest that if recovery is to occur, then lymphocytic regeneration to a more advanced degree is apparently necessary. In this case, however, the probability of an early recovery must further be rendered unlikely by the fact that associated with the unduly prolonged period of failure of response, there is the additional feature in the later estimations showing a lymphocytic decrease, both relatively and absolutely as compared with those in the early part of the illness. Those observations emphasise more definitely the possibility of a defence mechanism failure in this case.

GROUP I (3).

Example of a mild hyperlymphocytic response with a marked reactive increase preceding the change from the depressive to the maniacal state.

Female. Single. aet. 48 years. Factory Worker. Admitted 11th October 1931. 1st. Cert.

Synopsis of Case History.

Family: Mother suffered from Epilepsy and died at age of 27 years. Sister suffers from depression. Father alive and healthy.

Personal: Normal birth and early childhood - patient is the younger of two sisters. At age of 5 years, patient contracted Scarlet Fever with right Otitis Media following which the right ear continued to discharge until she reached the age of 7 years, when the discharge ceased. She was "backward" at school, quiet and reserved in her manner and inclined to be asocial and egocentric, not making social contacts easily. Left school at 15 years to obtain employment in a factory and has remained in steady employment up to the time of admission. She lives alone in a single rented room, cooks her own meals and rarely goes out at night;

states that she has "few if any friends" and is not connected with any church or social organisation. Her reaction time has always been slow and this became more marked previous to admission. She always experienced difficulty in attempting new work and appears to have performed her duties in an automatic fashion. She was admitted on 11/10/31 in a profoundly depressed condition.

On Admission:

Physical Condition: Height 5 ft. 2 ins. Weight 6 sts. 3 lbs. Anaemic appearance. Blood count. Erythrocytes 3,600,000/c.mm. Leucocytes 4,800/c.mm. Hb.55%

Heart: Slightly dilated. Haemic murmurs at mitral and aortic areas. No evidence of any valvular organic disease.

Pulse: Poor in volume and of low tension. B.P. 115/80 mms.Hg.

Lungs: Examination failed to reveal any abnormalities except diminished expansion.

Mouth: Soft palate inflamed. Tongue raw and red. Several carious teeth.

Nervous System: Reflexes difficult to elicit and sluggish in reaction. Pupils equal and regular, react both directly and consensually to light and to accommodation.

Menstruation: Regular 4-5/28 days. Ceased two months before admission. No disease of the nasal or oral passages could be demonstrated upon examination although this was suspected upon admission.

Mental Condition.

She is profoundly depressed and complains of severe bitemporal headache. During the last two years there have been several similar attacks of lesser severity. She is fairly well orientated but is morbidly depressed and her mind is occupied with ideas of a persecutory nature. Difficulty is experienced in concentration and her attention to personal and business affairs is of a fleeting nature. She has a certain degree of insight into her condition, realising her depression and irritability nevertheless she is unable to throw off the idea that she is unworthy to live. She displays a listening preoccupied attitude when her attention is not being fixed but she denies hearing voices.

Course and Treatment.

During the first month subsequent to admission, there

was little improvement in the mental condition. Her posture was dropping, her gait and movements were slow, her facial expression remained fixed and there was complete absence of variation. She appeared to understand questions but her replies remained persistently monosyllabic and were given in a low monotone after a prolonged latent period. She remained well orientated but her association of ideas was markedly retarded.

Several blood estimations were performed at this stage, but these failed to show any appreciable variation from those obtained on admission as shown below.

Date	Total No. of Cells	Neutrophiles		Lymphocytes	
		Actual	%	Actual	%
	<u>Per c. mm.</u>			<u>Per c. mm.</u>	
11/10/31	4,800	2,950	61.5%	1,850 +120	38.5%

On 28/6/32, she appeared to make a sudden recovery, altering dramatically, in the space of a few hours from a depressed and inactive state to a condition of hypomania, showing both mental and motor activity. On the following day, she became violent, abusive and impulsive in her behaviour. She was elated, excited and garrulous,

spacing up and down the ward, and interfering with the patients and staff. She was totally inaccessible and violently refused any form of treatment. This condition continued until her transfer on 1/7/32. On 26/6/32, examination of the blood revealed a picture which contrasted markedly with that obtained upon admission.

Date	Total No. of Cells	Neutrophiles		Lymphocytes	
		Actual	%	Actual	%
		<u>Per c.mm.</u>		<u>Per c.mm.</u>	
28/6/32	6050	2,900	48%	3,150 +410	52%

Remarks:

The above case shows the definite reactive hyperlymphocytosis coincident with the onset of the hypermaniacal condition. During the depressive phase, there was a marked degree of leucopenia associated with a slight degree of both relative and absolute hyperlymphocytic values and this remained constantly present over a prolonged period. With the advent of the hypomaniacal condition, the lymphocytic values became increased to the extent of 72% of their former values absolutely and their relative percentage being increased by 13.5%. It is to be regretted that, in this case, a serial count was not performed on

27/6/32, immediately preceding the dramatic change in the clinical picture but here the alteration was so sudden and unexpected that no premonitory indication of any change in the mental picture could be appreciated. This example, further serves to demonstrate the value of the serial method of investigation, since if this method had been utilised here, the alteration in the clinical picture could have been more fully appreciated.

GROUP II (1).

Serial counts demonstrating the restoration of the "normal" leucocytic balance coincident with mental recovery.

Female. Single. Aet. 21 years. At home. Admitted 12/12/31. 1st Cert.

Synopsis of Case History.

Family: Father - twice under certification, first at age of 45 years, second at 61 years. Alcohol was the causative factor of these attacks of confusion. Discharged recovered at 63 years, dying from Pneumonia at 65 years.

Mother - no psychotic history available, dying when patient was 8 days old.

Mother's brother died of Cerebral Syphilis.

Personal: Patient is an only child, normal intelligence and affection. Never suffered from attacks of depression or excitement. Made social contacts easily and was a good mixer. Upon leaving school, entered business and kept her situation until the age of 18 years when she left to keep house for her father, who had recently been discharged from hospital. Father died when patient was 20 years of age. She

remained healthy until July 1931 when she became "nervous". Rapidly becoming excited, garrulous and restless, she commenced to go for long periods without food and walked about the streets at night on account of insomnia. Her bodily health became markedly impaired and on 2/12/31, she collapsed in the street and was removed to a general hospital. Upon admission her mental condition became apparent; she was excited, noisy and restless and could not be quieted. She was admitted to the mental hospital on 12/12/31.

On Admission.

Physical State: Height 5 ft. 3 ins. Weight 7 stones.

General vitality and nutrition very poor.

Thyroid mildly palpable. Teeth carious.

Circulation: Heart action rapid and slightly irregular.

Pulse irregular and of low tension. B.P.120/80

mm. Hg. Face extremely pale and extremities mildly cyanosed.

Mouth and Throat: Mouth dry, tongue furred; slight de-

gree of gingivitis.

Lungs: Appeared normal except for diminished expansion.

Abdomen: Examination failed to reveal any gross lesion.

Muscular System: Tone very poor. Mild degree of asthenia present.

Nervous System: Some degree of facial asymmetry present. Right eyebrow slightly elevated; right palpebral fissure narrowed; right nasolabial fold more prominent than left, slight ptosis of right upper eyelid. Pupils equal and regular, react both directly and consensually to light and to accommodation.

Blood: Erythrocytes 3,200,000/c.mm; Leucocytes 10,100/c.mm; Hb.55% Radiograph of skull revealed no abnormalities.

Mental State.

Patient was excited, exalted and restless. She showed accelerated mental activity with flight of ideas too rapid to be followed.. She was unable to concentrate and was easily distractible. The emotional tone was one of extreme exaltation, combined with irritability and obstinacy if her wishes were thwarted. Gradually she developed an increasing antagonism to those around her and showed

a tendency to impulsiveness, although during her period in hospital there is no history of a definite impulsive act. Throughout her illness there were short periods during which she became mildly depressed. These phases never exceeded 4 hours in length and were well remembered by the patient.

Course and Treatment.

The acute symptoms leading up to certification did not abate after admission. During December 1931 and the first 3 months of 1932, she continued excited, uncontrollable and noisy, restless and abusive in spite of sedative therapy. Six carious teeth were extracted on 28/3/32 under Gas and Oxygen anaesthesia. In June there was a marked reduction in the intensity of her symptoms but she remained restless and uncertain in her conduct. During the last week of August 1932, a definite exacerbation was noted during which she became very noisy, restless and abusive. From this period onwards, she remained in a condition of Hypomania. In the early part of 1933, her mental symptoms were considerably aggravated in intensity. On 6/2/33 her case was reviewed with the following serial count.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
6/2/33	8 am.	9,000	6,200	69%	2,800	31%
	12 noon	9,200	6,300	68.5%	2,900	31.5%
	4 pm.	9,000	6,300	70%	2,700	30%
	8 pm.	9,400	6,000	63.5%	3,400	36.5%
	12 midn.	9,100	5,900	65%	3,200	35%
	4 am.	9,700	6,300	65%	3,400	35%
Average		9,235	6,165	66.5%	3,065 + 425	33.5%

Serial counts were performed from 6/2/33 until 14/2/33 and during this period the patient showed a remarkable and progressive degree of mental improvement.

Case reviewed 13/2/33. She is well orientated, her demeanour is calm and composed, she is able to converse rationally, and her attention is well maintained and not readily distracted. She shows a surprising degree of insight into her present illness and realises her marked improvement. Her conduct is satisfactory and she performs her duties in a methodical and satisfactory manner. The physical condition is also markedly improved,

normal colour greatly restored and her muscular tone is increased. The serial investigations from 5/2/33 until 12/2/33 presented no noteworthy features but those of 13/2/33 and 14/2/33 are interesting on account of the sudden change in the lymphocytic picture which occurred within a period of 48 hours.

Date	Time	Total No. of Cells.	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
			<u>Per c.mm.</u>		<u>Per c.mm</u>	
13/2/33	8 am.	10,300	6,500	63%	3,800	37%
14/2/33	12 noon	10,250	6,750	65.5%	3,500	34.5%
	4 pm.	9,700	6,000	62%	3,700	38%
	8 pm.	9,100	5,900	65%	3,200	35%
	12 midn.	9,700	6,500	67%	3,200	33%
	4 am.	9,900	6,400	65%	3,500	35%
Average		9,816	6,335	64.6%	3,486	35.4%
14/2/33	8 am.	9,300	6,500	70%	2,800	30%
15/2/33	12 noon	9,500	6,600	68%	3,000	32%
	4 pm.	9,000	6,500	72%	2,500	28%
	8 pm.	8,300	6,200	74.5%	2,100	25.5%
	12 midn.	8,000	6,000	75%	2,000	25%
	4 am.	7,800	5,800	74%	2,000	26%
Average		8,650	6,250	72.25%	2,400	27.7%

Remarks:

The above haemograms show the striking fall in both relative and absolute lymphocytic values occurring in a space of 48 hours. The normal lymphocytic balance has now been restored while the neutrophile values still remain slightly above the normal range. The patient was discharged recovered on 16/2/33.

Termination of Case:

20/4/33. Patient reported at hospital and appears to have progressed satisfactorily both mentally and physically. She has remained in steady employment since her discharge and with the exception of a few incidents, she remembers little of her early period of residence in hospital. A blood examination showed that the normal lymphocytic balance continued to be present.

18/11/33. The patient's doctor reports that her physical and mental condition are very satisfactory. Her weight has improved by 20 lbs. since her discharge and her conduct is exemplary.

GROUP II (2).

Serial counts demonstrating well marked hyperlymphocytic reaction with ultimate recovery.

Female. Single. Aet. 28 years. Factory worker. Admitted 28/10/32. Voluntary.

Synopsis of Case History.

Family: No psychotic history elicited. Mother suffers from Migraine and Asthma. Patient is eldest of family of 7, 4 males and 3 females; remaining members are alive and healthy.

Personal: Full term, easy, non instrumental delivery. As a child, healthy, bright, alert and intelligent. Chickenpox at 7 years. Progressed satisfactorily at school but was asocial and did not make friends readily. Upon leaving school, obtained employment as message girl and continued to perform her duties satisfactorily until she commenced factory work at 16 years. In this latter employment, her progress was rapid, she was an efficient and careful worker and at age of 24 years was promoted to charge of her flat where she continued to give every satisfaction. In 1930, she felt

that she was becoming lethargic and commenced to be troubled by occipital headaches, which necessitated frequent absence from duty and this worried her considerably. Her home life was happy and she had no financial difficulties. In June 1931, she became definitely depressed and following advice, she went for a 6 weeks' holiday. On returning she became progressively more depressed and apprehensive, work appearing distasteful and her headaches increased in severity and duration. She left her employment in May 1932 and resided at home. From this period until her voluntary admission on 28/10/32, the symptoms have become progressively worse and she volunteers that on several occasions she has contemplated suicide as being the only solution to her problems.

On Admission.

Physical State: Height 5 ft. 8 ins. Weight 8 sts. 2 lbs. Muscular tone is poor. Drooping posture and carriage. A few scattered septic spots on the face and chest.

Circulation: Second aortic sound accentuated. Arteries palpable. B.P. 108/80 mms.Hg. Peripheral circulation very poor.

Lungs: No abnormality detected except diminished expansion.

Abdomen: No gross lesion of the major viscera detected upon examination.

Nervous System: Reflexes sluggish. Pupils equal and regular, react both directly and consensually to light and to accommodation. Radiograph of skull revealed no abnormalities.

Mental State.

The patient is markedly depressed, presenting a dull, listless and at times apprehensive appearance. She is retarded and slightly amnesic. She possesses no insight into her present condition and complains of persistent occipital headache. There is also an absence of emotional feeling leading to a sense of unreality, accompanied by generalised slowing and blunting of all her faculties. No spontaneity is displayed and there is failure of response to stimuli.

28/10/32. An examination of the blood was carried out with normal findings

Case Reviewed 11/2/33.

The patient remains profoundly depressed, displaying mutism and great retardation. In appearance she is thin and ill-looking with marked loss of weight. Her expression suggests dejection and great misery. She takes no interest in her surroundings and is totally inactive. She requires to be fed constantly. Serial counts performed at this period, failed to reveal any abnormalities in the haemopoietic system.

Case Reviewed 7/4/33.

There is practically no alteration in the mental symptoms from those of the previous review. She is reticent and monosyllabic and her association of ideas is definitely retarded. Conversational capacity is much reduced as she is obsessed with depressed ideas e.g. that she is sinful; that she will never be well; that she would be better dead etc. The blood examination which had persistently shown values comparable with those of the normal state, revealed a marked change in the relative percentages of the constituent cells as shown below.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
		Per c.mm.	Actual	%	Actual	%
7/4/33	8 am.	9,200	6,800	74%	2,400	26%
8/4/33	12 noon	9,000	6,500	72%	2,500	28%
	4 pm.	9,000	6,200	68.5%	2,800	31%
	8 pm.	9,200	6,200	67%	3,000	33%
	12 midn.	8,600	5,800	67%	2,800	33%
	4 am.	8,000	5,000	75%	2,000	25%
Average		8,835	6,416	70.6%	2,585	29%
8/4/33	8 am.	8,200	6,200	75.5%	2,000	24.5%
9/4/33	12 noon.	8,400	5,500	65%	2,900	35%
	4 pm.	8,600	5,300	64%	3,300	36%
	8 pm.	8,000	5,500	68.5%	2,500	31.5%
	12 midn.	8,400	5,600	66.5%	2,800	33.5%
	4 am.	8,600	5,800	60%	2,800	40%
Average		8,365	5,650	66.6%	2,716	33.4%

Remarks :

The above serial counts demonstrate the sudden alteration of the lymphocytic values from the persistently normal range, which have continued over a period of 6 months, to figures which now fall within pathological

limits. This sudden onset of hyperlymphocytosis is associated with a corresponding fall in the neutrophile values while the total number of cells has not appreciably altered. In this case, the presence of both an absolute and relative lymphocytic response enabled the probability of recovery to be predicted at a phase when the clinical features of the case were definitely in favour of chronicity and suggested that any early recovery was unlikely. The correctness of this assumption was later established.

Termination of Case.

The clinical picture showed no improvement for a period of 3 weeks following the last review but from 1/5/33 onwards, a steady improvement was noted and on 5/5/33, she appeared much improved mentally. She was fairly well orientated, showing a fairly good conversational capacity and volunteering information concerning her illness. Her replies to questions were intelligent and brisk and in appearance she was bright and cheerful. The appetite has improved and she sleeps well at night. Her conduct is now satisfactory and she is able to engage in simple ward work, while her headaches are of lesser severity and occur at prolonged intervals.

On 28/5/33 she appeared bright, cheerful and alert, working well and showing interest and initiative. She was given parole and displayed good conduct.

On 5/6/33 she volunteered that she now felt sufficiently well to resume work and was finally discharged on 8/6/33. A serial count performed on 7/6/33 demonstrated the following results.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
7/6/33	8 am.	8,400	5,700	67.5%	2,700	32.5%
	12 noon	8,300	5,600	67.5%	2,700	32.5%
	4 pm.	8,200	5,800	70.5%	2,400	29.5%
	8 pm.	8,400	5,500	65.5%	2,900	34.5%
	12 midn.	8,500	5,200	61%	3,300	39%
	4 am.	8,200	5,400	66%	2,800	34%
Average:		8,335	5,535	66.5%	2,800	33.5%

The patient has not returned to report since discharge but a visitor's report concerning her progress is of interest. She reports that the patient resumed her former employment 14 days after discharge and that she

has successfully retained her position. She is now bright, alert and efficient and confesses to "feeling better now than ever before." The headaches are no longer troublesome; she is taking an active interest in social activities, as advised, and is making social contacts readily.

GROUP II (3).

Serial Counts demonstrating a progressive hypolymphocytosis associated with a steady decline in the bodily and mental condition.

Male. Single. Aet. 24 years. Shop Assistant. Admitted 16th July, 1933. 1st. Cert.

Synopsis of Case History.

Family: No psychotic history available. Both parents alive and healthy.

Personal: Only child, happy disposition, showing normal intelligence and affection. He was well adapted socially and had no peculiarities, and did not suffer from attacks of depression. He was bright, alert, and showed intellectual promise at school, which he left at 14 years to serve as "errand boy" in grocer's establishment. Later he commenced his apprenticeship at 16 years in same employment and retained his situation until shortly before admission. From the age of 19 years, a change in his mentality was observed by his parents and friends. He became of a reserved and uncommunicative disposition and showed a liking for solitary

pleasures, finding conversation progressively more difficult until his speech became almost monosyllabic in character although with an effort he could engage in animated conversation. His employment became irksome to him and he confessed to his parents that he felt "at a dead end" and that "he would die a grocer's help." Efforts were made by his friends to stimulate him but these were unsuccessful. Gradually he became more and more solitary and regarded his employment as an irritating necessity. About 1931 he came to be regarded as "peculiar" by his friends on account of his mode of life but he strenuously opposed seeking advice. In August 1933 he attempted suicide by gassing himself and was admitted to the mental hospital on 16/7/33.

On Admission:

Physical State: Height 5 ft. 1 in. Weight 10 sts. 8 lbs.

General nutrition and vitality is poor. Skin is seborrhoeic.

Circulation: Area of cardiac dulness within normal limits. Apex beat diffuse and heaving in character.

Cardiac sounds normal. Pulse poor in volume and of low tension. B.P. 112/90 mms. Hg.

Lungs: No abnormality detected except diminished expansion.

Mouth: Tongue furred: 4 carious teeth.

Abdomen: No abnormality detected upon examination.

Nervous System: Left pupil slightly larger than right.

Both pupils react both directly and consensually to light and to accommodation.

Mental Condition.

The patient presents a dull apathetic appearance, being depressed, lethargic and reticent, taking little interest in his surroundings. His attention is difficult to obtain and is easily distracted. The conversational capacity is much reduced, his replies to questions being monosyllabic with a much delayed reaction time. His judgment is in abeyance and his association of ideas is retarded. He cannot be stimulated in any fashion and he appears to be potentially suicidal.

Course and Treatment.

The patient became progressively more depressed and presented a dejected appearance. His posture and gait was drooping and his attitude one of immobility. His speech continued slow, monotonous and monosyllabic while he

showed progressive mental retardation and appeared to be completely absorbed with morbid ideas. His bodily conditions became progressively impaired being unaffected by physical treatment. Marked delusions of a self accusatory nature gradually developed and at times he became emotional and begged to be "put out of his misery". From 28/9/33 until the present there has been no appreciable alteration in either his physical or mental condition.

Several serial counts were performed at various stages of the illness and the salient features of these investigations are demonstrated in the following haemograms.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
		Per c. mm.	Actual	%	Actual	%
18/7/33	8 am.	7,300	5,200	71%	2,100	29%
19/7/33	12 noon	7,200	5,000	70%	2,200	30%
	4 pm.	8,200	5,800	63%	2,400	37%
	8 pm.	7,800	5,600	71.5%	2,200	38.5%
	12 midn.	7,000	5,000	70%	2,100	30%
	4 am.	6,800	5,000	73.5%	1,800	26.5%
Average:		7,383	5,266	69.8%	2,133	30.2%

The above serial count is characteristic of the blood picture, which persisted with slight and indeterminate variations during the first two months of residence and showed normal lymphocytic values both relatively and absolutely with slightly raised neutrophile values. No appreciable deviation from the above picture was noted until the beginning of November 1933 when a progressive decline in the lymphocytic percentages became apparent and persisted over a prolonged period. An impression of the alteration in the absolute and relative figures is demonstrated below.

Date	Time	Total No. of Cells.	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
			<u>Per c. mm.</u>		<u>Per c. mm.</u>	
24/11/33	8 am.	7,200	5,200	72%	2,000	28%
25/11/33	12 noon	6,800	5,100	75%	1,700	25%
	4 pm.	7,100	5,300	74.5%	1,800	25.5%
	8 pm.	7,400	5,400	73%	2,000	27%
	12 midn.	7,200	5,300	73.5%	1,900	26.5%
	4 am.	7,100	5,300	74.5%	1,800	25.5%
Average		7,133	5,266	73.75%	1,866	26.25%

The marked fall in the lymphocytic values is readily appreciated from the above haemogram. An interesting observation, can be made in this case, in that the lymphocytic values have been at their maximum both absolutely and relatively in the late afternoon and this has throughout been associated with a mild degree of mental improvement of transitory duration.

In January 1934, the fall in the lymphocytic totals and percentages become more pronounced while the mental condition progressively deteriorated. A serial count typical of this period presents the following features.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
			<u>Per c. mm.</u>		<u>Per c. mm.</u>	
22/1/34	8 am.	7,200	5,400	75%	1,800	25%
23/1/34	12 noon	7,100	5,300	74.5%	1,800	25.5%
	4 pm.	7,800	5,600	71.5%	2,200	28.5%
	8 pm.	7,000	5,700	81%	1,300	19%
	12 midn.	7,000	5,500	77.5%	1,500	22.5%
	4 am.	7,200	5,700	79%	1,500	21%
Average:		7,216	5,365	76.4%	1,683	23.5%

Termination of Case.

From this period onwards, there has been no appreciable change in the mental symptoms and at the present time, 1/3/34, the patient is in a condition of profound depression and passes an almost vegetative existence. The failure in the lymphocytic response has progressively increased and there seems to be no suggestion of an early alteration in the clinical features. The following serial count gives an impression of the state of the haemopoietic system at this period.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
			<u>Per c. mm.</u>		<u>Per c. mm.</u>	
1/3/34	8 am.	7,100	5,600	74%	1,500	21%
2/3/34	12 noon	7,200	5,400	75%	1,800	25%
	4 pm.	7,400	5,500	74.5%	1,900	25.5%
	8 pm.	7,400	5,900	80%	1,500	20%
	12 midn.	7,100	5,800	81.5%	1,300	18.5%
	4 am.	7,200	5,800	80.5%	1,400	19.5%
Average:		7,235	5,665	78.4%	1,500	21.6%

Remarks:

The above investigation demonstrates the progressive decline in both bodily and mental activity associated with a progressively increasing tendency towards hypolymphocytic reaction both relatively and absolutely. When this is correlated with the fact that there has at no time been an indication of a stabilised lymphocytic picture since 19/7/33, it would strongly suggest the possibility of an increasing failure of a vital mechanism. Both the clinical features and the leucocytic picture in this case suggest that the patient is losing any chance of an early and satisfactory recovery.

GROUP II (4).

Serial Counts demonstrating
failure of lymphocytic response.

Female. Married. Aet. 64 years. Housewife. Admitted
5/6/32. 1st Cert.

Synopsis of Case History.

- Family:** Mother's brother died in a mental hospital. Mother suffered from Bronchitis and Asthma and died from these conditions in 1907. Father died from Uraemia in 1901. Patient is eldest of family of 4 daughters; youngest suffers from Imbecility and other two sisters are married and healthy.
- Personal:** Instrumental delivery at full time. Contracted Scarlet Fever at 5, Measles at 7, Diphtheria at 13 and Rheumatic Fever at 23. Has suffered from Migraine since she was 17 years of age. Progressed well at school and left at 16 years to help with household duties. Married at 29, childless - home life very comfortable with no domestic or financial difficulties.
- Present Illness:** The patient's conduct is reported as being very unstable, her husband describing her as being one day "up in the heights" and

next day "down in the depths." She appears to have had periods of undue activity lasting several weeks and associated with Insomnia, followed by periods of mild depression when her household duties annoyed her and she became morose and irritable. These attacks commenced early after her marriage in 1898 but no significance was attached to them. She has undergone several courses of physical treatment including changes of climate without appreciating any benefit. Menopause ensued in 1916 and from this time onwards, her attacks of depression have become progressively more severe and of longer duration. Since 1928 she has been more or less constantly in a depressed condition and on 4/6/32 she attempted suicide by gas poisoning. She was certified and removed to the mental hospital on 5/6/32.

On Admission:

Physical Condition: Height 5 ft. 2 ins. Weight 7 sts.
Mildly anaemic. Skin cold, dry, rough and there were several septic spots on the face

and over the scapular regions.

- Heart:** Slightly dilated. Mitral systolic murmur conducted well into the axilla. No murmurs at the other areas.
- Pulse:** Regular in rate and rhythm and of good volume. B.P. 138/90 mms. Hg.
- Lungs:** Examination failed to reveal any abnormalities.
- Mouth:** Lips and tongue were dry, furred and cracked.
- Muscular System:** Well developed but poor in tone.
- Nervous System:** Pupils equal, regular, react both directly & consensually to light and to accommodation.
Coarse rhythmical tremor of hands.
- Abdomen:** No gross abnormality revealed upon examination.
History of long standing constipation.
- Urine:** Pale amber; Acid; S.G.1022. Nil.abnormal.

Mental State.

Patient was profoundly depressed and apprehensive in appearance. She took no interest in her surroundings, and was suspicious of the actions of those around her. Her attention was difficult to obtain and was easily distracted, while she presented an appearance of abject misery and at times was emotional, weeping for no obvious reason. Her replies to questions were monosyllabic and

were elicited after an unduly prolonged latent period. She persistently refused her food, saying she wished to die and did not want to keep herself alive. She suffered from persistent insomnia and was potentially suicidal.

The examination of the blood which was carried out upon the day after admission gave the following results.

Average of 6 Counts over a period of 24 hours.

Date	Total No. of Cells	Neutrophiles		Lymphocytes	
		Actual	%	Actual	%
	<u>Per c.mm.</u>			<u>Per c.mm.</u>	
6/6/32	8,000	5,800	72.5%	2,200	27.5%
				Normal	

Course and Treatment.

The depressed state rapidly passed off subsequent to admission. She gradually became more communicative and took an interest in the ward work. The emotional tone, however, remained slightly depressed and there was some associated retardation. She appeared fairly well mentally when her interest was stimulated, but when she considered herself to be unobserved she became listless, dull and apathetic. During her period of residence on no occasion did she give any indication of suicidal tendencies and volunteered on several occasions that she

regretted her "foolish act". The degree of mental improvement was fairly well maintained from the beginning of September and she was discharged to the care of her friends on 12/9/32. At this period, the blood picture showed the following characteristics.

Average of 6 counts over a period of 24 hours.

Date	Total No. of Cells	Neutrophiles		Lymphocytes	
		Actual	%	Actual	%
	<u>Per c. mm.</u>			<u>Per c. mm.</u>	
12/9/32	8,400	5,800	69%	2,600 High Normal.	31%

Second Attack:

Patient was readmitted on 1/2/33 in a mildly maniacal state. She was exhilarated and considerably elated, becoming aggressive and domineering in her manner, and if her wishes were thwarted, noisy and argumentative. During the period of convalescence from her first attack she appears to have progressed satisfactorily for the first three months subsequent to discharge but during the week previous to her readmission she passed through rapidly alternating phases of excitement and depression.

On 1/2/33 she became extremely violent in her behaviour, shouting and singing and running from room to room, banging the doors violently. She neglected her ordinary duties and could not be persuaded either to eat or sleep. Subsequent to admission she rapidly became more composed and on 2/2/33 she was in a mildly depressed condition presenting similar features to those which characterised her first attack. A blood estimation presented the following results.

Average of 6 counts over a period of 24 hours

Date.	Total No. of Cells	Neutrophiles		Lymphocytes	
		Actual	%	Actual	%
	<u>Per c.mm.</u>			<u>Per c.mm.</u>	
1/2/33	10,400	6,500	62.5%	3,900	37.5%
				+1260	

On 3/2/33 she was in a profoundly depressed and apathetic mental state. Gradually persecutory ideas supervened and she became emotional, depressed and asociable. She persistently refused her food and was resistive to nursing attention, saying that she was unworthy to live. At intervals she was impulsive and violent in behaviour but these periods were only

momentary and the prevailing emotional tone throughout was that of depression. On two occasions the 7/2/33 and 14/2/33, she attempted suicide by tying articles of clothing around her throat, and when discovered, became emotional and begged to be killed. The following haemograms give an indication of the state of the haemopoietic system during this period.

Averages of 6 counts over a period of 24 hours.

Date	Total No. of Cells	Neutrophiles		Lymphocytes.	
		Actual	%	Actual	%
	<u>Per c.mm.</u>			<u>Per c.mm</u>	
6/5/33	8,700	6,800	78%	1,900	22%
				Low Normal.	
20/5/33	8,900	7,850 _m	88%	1,050	12%
				-320	

The mental condition showed a transitory improvement on 18/5/33 while the blood estimations were progressively lower and on 20/5/33 the patient was discharged" unrecovered", against advice, at her husband's request.

Remarks:

The above case shows a striking alteration in the

leucocytic balance, the picture varying between a condition of relative and absolute hyperlymphocytosis on 1/2/33 while the patient was in a hypomaniacal state, and hypolymphocytosis on 20/5/33 while the patient was in a depressed state, the prevailing values being that of both relative and absolute loss to an advanced degree. This case is further interesting on account of the fact that the hypolymphocytic reaction obtained on 20/5/33 was out of all proportion to what would have been expected, judging from the mental condition. As enumerations on the days immediately preceding this date were also of the hypolymphocytic type, the results were interpreted in the light of a defence mechanism failure and the outlook was thus considered unfavourable although the clinical features of the case suggested a marked degree of improvement. This prognosis was later substantiated in a tragic fashion as on 9/6/33, the patient committed suicide by drowning. This example serves to emphasise the importance of careful leucocyte examination on all doubtful cases previous to discharge and the necessity for correlating the clinical condition with the type of underlying leucogenic response.

GROUP III (1).

Serial Counts demonstrating a hyperlymphatic reaction during the hypomaniacal state with a return to "normal" values at onset of mild depression.

Female. Single. Aet. 32 years. Shop Assistant. Admitted 1/1/33. 1st Cert.

Synopsis of Case History.

Family: Mother was a highly strung neurotic woman who worried excessively over trifles and died when patient's sister was born in 1904. Father succumbed to injuries received in train accident in 1907.

Personal: Patient was reared by her paternal grandparents from the age of 3 years. During early childhood, there is an indefinite history of Measles and Diphtheria. She progressed fairly well at school and made social contacts easily. Left school at 16 years of age and commenced work in a draper's firm; appears to have been a careful and efficient saleswoman and retained her situation until her admission to the mental hospital. She showed a stabilised personality until 1924.

The exact details of her mental state are lacking but it would seem that from 1924 until 1928 she passed through alternate periods of mild elation and depression, during which she became morose and sullen if thwarted in her desires. Her grandmother's death from Influenza in 1928, affected her, and from this period she appears to have encountered financial difficulties, in having to support her sister. These two factors resulted in a "nervous breakdown" in August 1928, which lasted for a period of 8 weeks. She remained well from this time until 1929 when she passed through a state of mild confusion, characterized by a tendency to wander from home and be unable to give a clear account of her actions. In 1930, she became further depressed over the death of her fiancée. Throughout 1930 and 1931 she was frequently absent from work on account of "nervous exhaustion" and she found that her work was causing her anxiety. Her employer noted

that she was morose and sullen at times and commented upon this, an incident which seems to have increased the depression. In December 1933 she became more depressed and emotional and was admitted to the mental hospital on 1/1/33.

On Admission.

Physical State: Height 5 ft. 3 ins. Weight 7 sts.

Skin dry and loose. General vitality and nutrition very poor. Thyroid palpable.

Circulation: Heart action slight, irregular and rapid. Pulse irregular and of low tension
B.P. 126/90 mms. Hg.

Lungs: No abnormality was detected except diminished expansion.

Abdomen: No lesion of major viscera detected.

Muscular System: Drooping posture and gait, Muscular tone very poor.

Nervous System: Reflexes sluggish and difficult to elicit on account of the patient's resistiveness and failure of cooperation. Pupils equal and regular, react both directly and consensually to light and to accommodation.

Mental Condition.

She was depressed and apathetic. She was mildly agitated and her emotional level was low. Her attention was difficult to obtain and she was readily distractible. She was reticent and self absorbed and replied in a monotone after a prolonged reaction period. She maintained that she would never recover and became morose and sullen when reasoned with.

Numerous serial counts were performed during her period of residence, which showed marked variations at different stages of her illness. The most pronounced of these changes are given later in tabular form for purposes of comparison.

Course and Treatment.

For the first 5 weeks subsequent to admission, the patient remained in a condition of mild depression, presenting features similar to those found initially. In February, 1933, the extreme depression and lassitude which characterised her early mental state rapidly subsided and were replaced by a hypomaniacal state with no intervening period of normality. From this period, onwards, as demonstrated by the succeeding reviews of the case, her mental state alternated at irregular

intervals between hypomania and depression until her transfer on 18/7/33.

7/3/33. The patient is mildly depressed. In the emotional field, there is depression, sadness and mental pain with a feeling tone of misery. She is reticent, monosyllabic and inactive. She shows marked mental retardation but is well orientated and possesses a definite degree of insight into her condition.

25/3/33. She shows excessive motor activity constantly directed towards several goals. She is exalted and over confident of her abilities. She exhibits mild flights of ideas and at times is incoherent in speech. Her attention is fleeting in character and is readily distractible. She is unable to control her emotions and irritability is shown when her desires are thwarted.

17/6/33. She is profoundly depressed and amnesic. There is no spontaneity and marked mental and physical retardation are present. She persistently refuses food on account of hypochondriacal ideas.

18/6/33. Sudden onset of euphoric phase in which she shows great pressure of activity in many directions,

her conduct being excited, garrulous and noisy. She is constantly divesting herself of her clothing. There is marked insomnia and a coarse tremor of the face and hands can be made out.

The following haemograms which summarise the average results of serial counts extending over a period of 24 hours, demonstrate the marked alteration between the periods of depression and those of hypomania.

Averages of 6 counts over a period of 24 hours.

Date.	Mental Condition.	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
11/2/33	Hypomania	8,000	4,200	52.5%	3,800	47.5%
					+1160	
7/3/33	Mild Depression.	6,400	5,800	69%	2,600	31%
					Low Normal	
25/3/33	Hypomania	8,100	4,400	54%	3,700	46%
					+1260	
18/7/33	Profound Depression	8,300	5,900	71%	2,400	29%
					Low Normal	

Remarks:

The above haemograms show the striking alteration between the states of depression associated with a mild degree of hypolymphocytosis and the states of hypomania associated with both a relative and absolute hyperlymphocytosis. This example satisfactorily demonstrates the sudden alteration from marked hyperlymphocytic phases to values falling within the normal range in a relatively short space of time. Single counts would not possibly have shown the periodicity of leucocytic response corresponding to the cycles of mania and depression.

GROUP III (2).

Serial Counts demonstrating a mild hyperlymphocytic reaction during hypomania with the onset of a profound hypolymphocytosis during the depressive state.

Female. Married. Aet. 48 years. Housewife. Admitted 16th May, 1933. 1st Cert.

Synopsis of Case History.

- Family:** Mother died in mental hospital of Maniac Depressive Psychoses. Father died of cerebral haemorrhage at age of 72 years. 3 sisters and 2 brothers alive and healthy.
- Personal:** Early life appears to have been normal and uneventful. Attended school until 16 years of age and appears to have progressed satisfactorily. Married at 23 years, marital relationships have been happy and she has had no domestic or financial difficulties. She has no children.
- Present Illness:** The present illness began 2 years ago when she suddenly became depressed and potentially suicidal. She was removed to a nursing home for observation and the main

features of her case at this period appear to have been mild depression associated with persistent occipital headache. She left after 7 weeks' residence and from this time her headaches have become more frequent and of greater severity and she appears to have been in a more or less depressed condition in spite of all attempts to stimulate her. There has been no change in attitude to her husband or friends but she has become progressively more solitary in her habits and restricted in her conversation. On the evening previous to admission, she suddenly became noisy and abusive to her neighbours. It appears that she was acutely maniacal and could not be restrained. Certification and removal to the mental hospital was necessary on 16/5/33.

On Admission.

Physical State: Height 5 ft. 7 ins. Weight 12 sts. 2 lbs.

General nutrition good.

Circulation: Cardiac sounds pure in quality. B.P.152/90.

mms.Hg.

Lungs: Examination failed to reveal any abnormalities.

Abdomen: No gross lesion of the major viscera detected upon examination.

Nervous System: Coarse tremor of hands and face present with mild degree of hyperaesthesia of limbs. Reflexes hyperactive. Pupils equal and react both directly and consensually to light and to accommodation.

Mental State.

The patient is markedly euphoric, her mood being exalted and grandiose. Motor activity is excessive, and ideation rapid, with a flight of ideas too rapid to be followed. Her attention is fleeting and distractibility marked, while emotionally she lacks control, exhibiting undue irritability and impulsive behaviour. She refuses to remain in bed and is constantly divesting herself of her clothing. A serial estimation presented the picture of absolute and relative hyperlymphocytosis as shown below.

Date	Time	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
18/5/33	8 am.	8,400	5,500	65%	2,900	35%
	12 noon	8,200	5,800	70.5%	2,400	29.5%
	4 pm.	8,200	5,400	66%	2,800	34%
	8 pm.	8,600	5,800	67%	2,800	33%
	12 mid.	9,200	6,700	73%	2,500	27%
	4 am.	8,500	5,600	66%	2,900	34%
Average:		8,516	5,800	68%	2,716	32%
					+316	

Course and Treatment.

During her period of residence in the mental hospital the mental condition alternated in a very regular manner between hypomania and depression over a period of several months with no intervening period of normality and finally she remained in a constant state of mild depression which persisted uninterruptedly until her discharge to the care of friends on 17/9/33. The various changes in the haemopoietic system throughout her illness have been summarised in the following tables, which demonstrate the average of six counts each extending over a period of 24 hours.

Averages of 6 counts over a period of 24 hours.

Date	Mental Condition	Total No. of Cells	Neutrophiles		Lymphocytes	
			Actual	%	Actual	%
18/5/33	Hypomania	8,500	5,800	68%	2,700 +300	32%
20/6/33	Hypomania	8,400	5,600	66.5%	2,800 +400	33.5%
11/7/33	Mild Depression	8,400	7,200	85.5%	1,200 -60	14.5%
15/7/33	Mild Depression	8,550	6,800	79.5%	1,750 Low Normal.	20.5%
12/8/33	Mild Depression	8,200	6,600	80%	1,600 Low Normal.	20%
12/9/33	Mild Depression	8,600	6,700	77.5%	1,900 Low Normal	22.5%
17/9/33	Mild Depression	8,400	6,300	75%	2,100 Low Normal	25%

Remarks:

The striking alteration from mild hyperlymphocytosis to that of marked hypolymphocytosis is demonstrated in the above haemograms. A sudden fall in both absolute and relative lymphocytic figures coincided with the onset

of mild depression, and these negative lymphocytic values have progressively increased up to the time of the patient's discharge. The relatively low lymphocytic figures in the depressive stage would appear to be of poor prognostic significance and this view is further substantiated by the after history of the case which shows that the patient while at home has failed to make satisfactory progress and has constantly remained in a mildly depressed state which shows no signs of an early improvement, since discharge.

GROUP III (3).

Serial Counts demonstrating Hyperlymphocytosis during the state of Hypomania and Hypolymphocytosis during the state of Depression.

Female. Single. Aet. 41 years. Book-keeper. Admitted 11th August, 1933. 1st Cert.

Synopsis of Case History.

Family: No psychotic history available. Mother died at Chronic Bronchitis; father died of Pneumonia.

Personal: Early life appears to have been uneventful. Patient progressed well at school and left when in highest standard at 14 years. Commenced work in thread mills and by evening tuition qualified herself for the position of book-keeper which she held satisfactorily from the age of 20 until her admission. She has had no business, family, or financial difficulties; appears to have made social contacts easily and to have been an efficient and trustworthy worker. The exact details of her mental state, leading up to certification are lacking but it appears that 3 days previous to admission she

became morose, sullen and depressed. The onset of this attack was sudden and unexpected. She locked herself in her bedroom and said she wanted to die. Her friends became anxious with regard to the possibility of suicide and had her certified and removed to the mental hospital on 11/8/33.

On Admission:

Physical State: Height 5 ft. 6 ins. Well developed and moderately nourished. Psoriasis of both legs.

Circulation: Cardiac sounds appear normal. Pulse regular and of good tone. B.P. 138/mms.Hg.

Lungs: No abnormalities detected upon examination.

Nervous System: Pupils equal and regular. React both directly and consensually to light and to accommodation. Superficial abdominal reflexes equal and sluggish.

Mental Condition.

The patient presents a vacant appearance with no emotional variation. In mood she is depressive and apprehensive, taking no interest in her surroundings

and cannot be aroused out of her lethargy. She is reticent almost to the extent of mutism and her association of ideas is markedly retarded. There is constant pre-occupation with morbid thoughts and she confesses that she feels herself sinful and a burden to the world. She is resistive to treatment and potentially suicidal.

Course and Treatment.

Since admission she has remained in a depressed condition with rare and irregular transient exacerbations of hypomania. She remained morbidly depressed and displayed no spontaneity. Her already limited conversational capacity became progressively impaired to the extent of complete mutism. Delusions of a hypochondriacal nature rapidly supervened and as a result of these she persistently refused her food.

On 18/1/34 a mild hypomaniacal state dramatically occurred and lasted for a period of 36 hours, followed by a reversion to the depressed state. During this period excessive psychomotor activity was manifest, her speech becoming rapid and incoherent. Coincidentally she became elated and excited and resistive to treatment.

On 12/2/34 she showed a similar change in her mental

state to the above. With the exception of these two phases of transitory duration, the clinical picture has been persistently that of mild depression and this state has continued up to the present time, with no intervening period of normality. The average of the serial counts during the various stages of the illness are contrasted below.

Averages of 6 counts over a period of 24 hours.

Date	Mental Condition	Total No. of Cells	Neutrophiles		Lymphocytes.	
			Actual	%	Actual	%
			Per c.mm.		Per c.mm.	
12/8/33	Mild Depression	9,400	8,200	87%	1,200 -180	13%
12/12/33	Mild Depression	9,000	7,800	86.5%	1,200 -180	13.5%
18/1/34	Hypomania	9,800	5,800	59%	4,000 +1600	41%
12/2/34	Hypomania	9,000	5,200	57.5%	3,800 +1400	42.5%
1/3/34	Mild Depression	9,000	7,200	80%	1,800 Low Normal	20%

Remarks:

The above haemograms demonstrate similar features to those of the previous case, but to a more advanced

degree. The low absolute and relative hypolymphocytic values which are persistently manifest during the state of depression are unfavourable but the striking feature is that during the condition of hypomania, these figures increase well beyond normal limits, but these values are not sustained for any length of time. A leucocytic reaction of this type can be interpreted in the light of a defence mechanism failure where a certain degree of activity has been attained but the intensity of which has neither been sufficiently adequate nor prolonged to allow recovery to ensue.

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From a combined clinical and haematological study of these cases, the advantages of the serial count method of investigation will be readily appreciated since the state of the haemopoietic system may vary from hour to hour and any deviation from the normal range may be missed or fail to have its proper importance attached to it if isolated counts are employed. Further, it is only by the utilisation of this method that evidence of a persistent pathological process can be obtained, and the possibility of gross technical errors eliminated. Minor discrepancies and apparent changes in the blood estimation are so often encountered in the course of routine investigations that there is always interest in determining the actual significance of these small variations. This is particularly so in regard to ascertaining how many of these variations can be attributed simply to the chance variations which are unavoidable in the estimation of a relatively small number of different objects and how many are of actual pathological significance. Ratcliffe, as a result of a mathematical analysis of the elements of uncertainty in blood estimations has demonstrated conclusively,

that by the ordinary method of isolated enumerations there is an ever present and appreciable element of indetermination. He points out that if the true neutrophile percentage is 70%, the possibility of estimating to within 5% if 200 cells are counted is only 71.5% while the chances of estimating to within 10% is 80%. Similarly if the true lymphocytic percentage is 20%, the possibility of estimating to within 3% and 5% when 200 cells are counted, is respectively only 54% and 67.5%. This demonstrates a decidedly striking element of error and thus great clinical importance cannot necessarily be attached to white cell variations of small dimension, when the ordinary method of examination is employed. By the serial method of investigation, as adopted in this research, the possibility of error is reduced considerably. Calculations based on the present technique show that if the true neutrophile percentage is 70% then the possibility of estimating to within 5% and 10%, if 200 cells are counted is 95.3% and 96.7% respectively. The diminution of error is even more closely demonstrated in the lymphocytic figures, where, if the true lymphocyte percentage is 20%, then the

chances of estimating to within 3% and 5% by the enumeration of 200 cells, is raised to 92.4% and 94.7% respectively. These figures demonstrate clearly the accuracy and advantages of the serial method of investigation as compared with single routine investigations. It seems superfluous to emphasise the erroneous impression which must be obtained if a number of cases are compared by the ordinary routine method since the hyperlymphocytic values over a period will necessarily be adequately balanced by hypolympocytic values at another stage of the investigation or by these values occurring in a different case, thereby giving a range of values within normal limits. Manifestly, a totally erroneous impression of the variability of the haemopoietic function is thus obtained and the minor variations from normality in a given case fail to be appreciated.

When considering the significance of hyperlymphocytosis at certain stages of the Manic Depressive state, several difficulties are encountered. It is well known that the usual reaction to the presence of infection is a Polymorphonuclear leucocytosis and it has been suggested that the hyperlymphocytic reaction

is merely an individual variation of the usual response. This view, however, has been negatived by two facts. Firstly, as demonstrated by Cottrell,⁽⁹⁾ the increased lymphocytic response cannot necessarily be regarded as a special and individual tissue reaction to infection since the presence of a marked degree of hyperlymphocytosis in one of his Manic Depressive cases was followed by the usual polymorphonuclear leucocytosis with the onset of Acute Follicular Tonsillitis. Secondly, as reported by various observers, particularly Dods Brown, Ross, Pilcz,⁽¹⁶⁾ Hussels and McDowall, a lymphocytic reaction can be altered to a high grade polymorphonuclear leucocytosis by an injection of various substances such as Sodium Nucleinate, Nucleic Acid, Argentum Colloidale and Tuberculin.

Further it is well known that a number of physiological states can cause a pronounced neutrophilia in the absence of infection but there is no available evidence in favour of a persistent hyperlymphocytosis under these conditions. The former phenomenon can be satisfactorily accounted for on the assumption that the bone marrow acts as a reservoir for mature cells to

cope with the body's physiological demands and that any increase in the blood constituents must be regarded as being due to increased functional demand. In correlation with this theory, it is of value to consider the available evidence as to the presence or otherwise of the phenomena of "digestive leucocytosis".

(11)
Szabuniewicz, as a result of animal experiments, regards the phenomenon as of the nature of a "conditioned reflex" and had demonstrated its presence even in the absence of food in dogs who were fed at a set hour on successive days. (12)
Rosenow, by electrical experiments regards the phenomenon as being dependent upon nervous stimulation of the bone marrow and not simply to a redistribution of the circulating cells. On the other hand, (13)
Shaw advances considerable evidence in favour of its non-existence. According to this observer, the total number of leucocytes exhibit two "daily tides" which are uninfluenced by food, rest, sleep or exercise. The "day tide" begins in the forenoon and gradually increases, reaching its peak in the late afternoon and ebbing to its initial level towards evening. The "night tide" in a similar fashion begins shortly after the final ebb of the "day tide",

reaches its flood shortly after midnight and slowly falls away towards morning to be succeeded by the slowly rising "daily tide". It is apparent that these variations must influence the relative blood estimations to a considerable extent depending upon the time of the day. The essential feature of note, however, is that this tidal condition although exerting an influence on the absolute values of the different blood constituents, does not alter the relative percentages to an appreciable degree and thus any high relative values cannot necessarily be accepted as being due merely to the presence of these daily fluctuations. Further, although this normal variation may considerably affect a single determination its influence, upon a serial count is definitely lessened and in the group of cases under review can be ignored, especially in regard to the relative figures. (14)

The more recent work of Lepskaia and Goldberg, regarding the effects of mental and physical work upon leucocytic activity serves to indicate the participation of the lymphatic system in this reaction. According to these observers, any increase in the neutrophile

values takes place at the expense of the lymphocytes while the contrary also holds good with the proviso that, if the work be unduly severe or prolonged, and especially if it is mental rather than physical in character, there is a complete disappearance of eosinophiles from the circulation with the appearance of immature neutrophils and increased lymphocytosis. It is interesting to note the correlation between the observation of these authors who have advanced the theory of an auto-intoxication to account for the phenomenon with the results obtained in this research. The maniacal phase may be accepted as one of severe mental effort and is associated with an increase in lymphocytic response while the depressive phase, associated with diminished lymphocytic values, may be regarded as a period of mental inactivity.

(15)

Investigating, along similar lines, Ackermann and Lebrecht have demonstrated the effects of measured exercise upon the circulation and found that in trained athletes no appreciable changes occurred even following upon prolonged or strenuous exercise while in untrained persons or in those unaccustomed to pro-

longed exertion, a progressive decrease in neutrophiles with a concomitant increase in lymphocytes followed. These experiments serve to emphasise the importance of the lymphatic system as a "second line of defence" against either infection or fatigue. The bone marrow undoubtedly shows a predilection for the production of neutrophiles which is so pronounced that the other varieties are physiologically speaking neglected by the reticulo-endothelium. If an excessive number of cells are required for any reason, infective or otherwise, an immediate hyperplasia of the bone marrow results with a consequent increased production of neutrophiles and a corresponding reduction in intensity of lymphocytopoiesis. Upon the subsidence of the causative agent, however, the neutrophile values rapidly return to normal while the lymphocytic values increase both relatively and absolutely so that a "post infective lymphocytosis" results. No satisfactory explanation of this phenomenon has been as yet advanced but it would seem that the lymphocytic response must be regarded as an attempt by the economy to equalise the production of the neutrophilic and lymphocytic elements

in response to infection and as the neutrophile reaction occurs primarily and is unduly pronounced, the lymphocytic reaction must be regarded as secondary both in time of occurrence and in importance. On the other hand, the lymphocytic response may be interpreted as the "second line of defence" which serves as the system's sole protection against further impairment during the convalescent period and which if it fails, must of necessity be followed by severe and far reaching effects. ⁽¹⁶⁾ Hickling, as a result of his observations upon the production of "sterile abscesses" has advanced the theory that this hyper-lymphocytic response is concerned rather with tissue repair than with direct reaction and it may be that the two-fold function of protection and tissue repair is the real explanation of the lymphocytic response. Thus, the presence of this phenomenon may be regarded as an indication that the infective lesion or other factor causative of the mental symptoms has been overcome or, at least is being held in check and its presence is to be interpreted as a sign of the onset of bodily reparative processes. This response serves

as an index to the capacity of the patient to progress satisfactorily or otherwise and, from the cases examined, it has been noted that the prognosis in those with a well marked hyperlymphocytosis has been definitely better than in those showing either no response or a failure of response. The investigation of over 2000 such estimations has lead to the following conclusions.

1. That the serial count technique is the only satisfactory method available for determining the variations in the haemopoietic system over a prolonged period and should receive precedence over the usual single estimation common to routine procedure.

2. That the presence of marked lymphocytic variations cannot be attributed to morbid psychological factors alone and must be governed by underlying pathological processes.

3. That the presence of marked and persistent variations from the normal indicates that the causative pathological process is one of considerable intensity and duration.

4. That a persistently normal range is indicative

of a condition of stability, if not to say chronicity, and if at all prolonged must affect recovery to an unfavourable degree.

5. That the mental states show an intimate parallelism with the blood pictures, rendering the latter valuable in prognosis.

6. That, as a general rule, the alterations in the haemopoietic system precede the alteration in the mental symptoms and may be regarded as predetermining their form and characteristics.

7. That the presence of a hyperlymphocytic reaction is indicative of improvement in the mental state and conversely hypolymphocytosis especially if at all prolonged, is of unfavourable prognostic significance.

8. That, in doubtful cases, the serial method of estimating the balance between the defence mechanism and the causal factors should receive precedence over the clinical features or at least should result in the case being carefully reviewed if the clinical state and the underlying pathological processes fail to correspond.

9. Normal range average findings may be the product of the extremes of normality and, as such, are of very distinct value as an index of stability. This index to the stability or otherwise of the responses is of value in estimating the balance between defensive activity and attack.

Sufficient evidence has been advanced to indicate that, both from a physiological and a psychological point of view, the subject is of great importance. In the Manic Depressive Psychoses there are definite indications that the lymphocytic system is being acted upon to a degree that is pathological in intensity. The whole question appears to depend upon the inter-relationship of reaction to the presence of infection between the two great haemopoietic systems, the myeloid and the lymphoid systems. When this is correlated with the fact that an increased lymphocytic reaction occurs subsequent to fatigue or strenuous exercise, it seems possible that in the Manic Depressive Psychoses, we are dealing with an intermediate phase of mental and physical exhaustion which if prolonged indefinitely must necessarily result in complete asthenia of mind

and body. What factor is instrumental in producing this condition must remain at present hypothetical but it appears logical to assume that it must be of toxic origin, whether metabolic, bacillary, auto-toxic or otherwise and it is probable that it is influenced to a distinct and variable degree by the mental and physical characteristics of the individual. In concluding, it follows that if the presence of a specific neurotoxic element can be satisfactorily associated with the mental state, then the somatic basis of Manic Depressive Psychosis is well established.

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