A STUDY OF THE BLOOD IN GENERAL PARALYSIS.¹

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SINCE attention has been given to the study of the blood in general a number of observers have written upon the blood in the insane; and more particularly is this true with reference to general paralysis, partly because of its frequency and partly because the diagnosis can be made with greater definiteness in this than in most other forms of mental disease.

As early as 1846 Erlenmeyer² made investigations upon the globules and fibrin of the blood in the insane, finding an increase in either to be rare.

Hittorf,³ in 1847, also arrived at the conclusion that in mania there is a diminution in the number of red globules and fibrin, and that the blood is in a watery condition.

To Michea⁴ (1848) belongs the credit of having first studied the blood in general paralysis, in which he noted an increase in the globules. He also speaks of a change in the character of the blood in convulsions and cataleptic seizures, though what this change is he does not say.

Sutherland⁵ (1873) considered a great increase in the white cells and an absence of rouleaux-forming power as an indication of low vitality with a grave prognosis. He found a leucocytosis in the insane generally, but most marked in general paralysis.

The conclusions of Voisin⁶ (1879) on the condition of the blood in general paralysis are more interesting historically than of actual value. He states that the blood of general paralytics spreads on a cover-glass with less pressure than normal blood; that the red cells make peculiar rouleaux with white corpuscles between them; that the coagulability is greater; that in the last stages in some cases vibrions and bacteria appear.

MacPhail⁷ (1884), in his valuable contribution on the blood of general paralytics, studied the subject more thoroughly and with better apparatus than any of his predecessors. In fifteen cases examined he found the hæmoglobin low on admission, higher in the quiescent period, and

¹ From work done in the laboratory of McLean Hospital under the supervision of Dr. Edward Cowles.

² Quoted by Dagonet, in *Traité des Maladies Mentales*, 1894, p. 103.

³ Quoted in Bucknill and Tuke's *Psycholog. Medicine*, 4th ed., p. 597.

⁴ *Recherches cliniques sur le sang dans les névroses*. Rev. in *Zeitschrift für Psychiat.*, vol. v. p. 485.

⁵ "On the Histology of Blood in the Insane." *Journal of Ment. Scien.*, vol. xxxi. p. 147.

⁶ *Paralyse General des Allenes*, 1879, p. 160.

⁷ "Clinical Observation of Blood in the Insane." *Journ. of Ment. Scien.*, vol. xxx. p. 378.

low again during the paralytic stage. The red corpuscles "deteriorat;" in quantity and quality coincident with the progress of the disease; "small granule-cells" are not present in the last stage; the relative proportion of white to red corpuscles is increased, and this increase is likewise coincident with the progress of the disease.

Lewis¹ (1889) observed practically the same condition in a series of cases of general paralysis, namely, a reduction in the hæmoglobin and number of red corpuscles and an increase in the white. In 7 of 21 cases, however, the white count was 10,000 or under, while in a few the leucocytosis was very marked.

Smyth² (1890), in his analysis of 40 cases, states that the hæmoglobin in general paralysis is within physiological limits, though it may be very high in the exalted stage of the disease. There was much less falling off in the red corpuscles than in other forms of insanity. The specific gravity he found increased.

D'Aundo³ (1891) has experimented upon the toxicity of the blood in the insane, and has demonstrated that the blood of general paralytics injected into animals is more toxic than normal blood.

According to Winckler,⁴ the hæmoglobin and red corpuscles in general paralysis vary with the body-weight, the hæmoglobin, however, diminishing more than the red cells. They both decrease in the early stage, are stationary in the so-called second stage, and fall again in the third. He noticed, along with a fall in body-weight, that a paralytic attack has a deteriorating influence on the blood.

Agostini⁵ has investigated the "isotonia" of the blood, or the power of resistance of the globules to solution. In typical general paralysis the isotonia is little altered, and the hæmoglobin and red cells usually normal, while all are diminished in periods of long excitement. During apoplectiform attacks the isotonia is reduced, with but little change in the hæmoglobin or red corpuscles.

The earliest attempt to study the variety of leucocytes was made by Krypiakiewicz,⁶ who devoted his attention to the eosinophiles. He observed no increase in these cells in any case or in any stage of the disease. The variation in the eosinophiles was between 1 and 5 per cent., and was without relation to any peculiarity, course, or stage of the disease; they never entirely disappear from the blood. In some cases the leucocytes were sufficiently increased to justify the name of leucocytosis.

¹ Text-book of Mental Diseases, p. 257.

² Journal of Mental Science, vol. xxxvi. p. 504.

³ "Sull' azione tossica e battericida del siero di sangue del Pazzi." Rivist. speriment. di Freniatria, vol. xvii. F. iv. and vol. xviii. F. 2, p. 322.

⁴ "Über Blutuntersuchungen bei Geisteskranken," Inaug. Dissert., 1891, Bonn, p. 39.

⁵ "Sulla isotonia del sangue negli alienati." Rivist. speriment. vol. xviii. F. 3 and 4, p. 492.

⁶ Einige Beobachtungen über das Blut der Geisteskranken. Wien. mediz. Wochenschrift, Nr. 25, 1892.

The hæmoglobin and red corpuscles were diminished, and there was poikilocytosis.

Zappert¹ (1892) reports two cases of general paralysis in which the red corpuscles were decreased, the leucocytes normal, and the eosinophiles slightly below the normal number.

Excitement and motor restlessness in general paralysis were found by Vorster² to cause a lowering of the specific gravity and hæmoglobin. Sometimes after paralytic attacks an increase in specific gravity and hæmoglobin was observed, but following light attacks no change took place. These alterations had no relation to the temperature.

Houston³ gives the result of the blood-examination in four cases of general paralysis; in all the hæmoglobin and red corpuscles were below normal. The white corpuscles he considered, without counting them, about normal.

Roncoroni,⁴ in his study of the leucocytes in general paralysis, was concerned only with the eosinophiles. These he found to vary, at times very scarce, rarely in normal frequency, in extremely agitated cases with a tendency to violence they increase from 8 to 18 per cent., and, in one instance, even to 25 per cent. of the total number of leucocytes.

More recently Burton⁵ has published his results in four cases of general paralysis. The red corpuscles averaged 5,177,500, the white 10,250, and the hæmoglobin 73 per cent. The differential counts are of little value, no percentages being given.

From the foregoing we see that all observers are almost unanimous in finding the red corpuscles and hæmoglobin either normal or decreased, except in excitement or after a paralytic attack. The specific gravity has been investigated by only two men, one of whom claims that it is always high in general paralysis; the other, that it becomes so after some paralytic attacks. By all who accurately counted the white corpuscles an increase was noted except by Zappert, who made but two observations, and Burton, who made four; both found the number about normal. Very little has been done in making differential counts of stained specimens, since Krypiakiewicz, Zappert, and Roncoroni were only interested in the eosinophiles, and Burton gives no figures whatever.

¹ "Über das Vorkommen der eosinophilen Zellen im menschlichen Blut." *Zeitschrift für klin. Medicin.*, Bd. xxii. H. 3 and 4.

² "Über d. Hæmoglobingehalt u. d. spec. Gewicht des Blutes bei Geisteskrank." *Allgemeine Zeitschrift für Psychiatri*, 1894, Bd. xv. H. 3 and 4, p. 740.

³ "On the Examination of Blood in the Insane." *Bost. Med. and Surg. Journ.*, Jan. 18, 1894.

⁴ "Studi sui leucociti nel Pazzi." *Archiv di Psichiat. Scienze, etc.*, 1891, vol. xv. F. III. p. 293.

⁵ "The Blood in the Insane." *Am. Journ. of Insanity*, 1895, vol. li. p. 495. We cannot refrain from criticising the inaccuracy of statement in this article, *c. g.*, the classification of lymphocytes and large mononuclear cells under the head of neutrophils; the statement that the leucocytes are "markedly decreased" in general paralysis, when his average was 10,250 and in no case fell below 9000; the statement that no mononuclear cells were present in one case, the illustration of which plainly shows several of both large and small varieties.

In the light of these facts it seemed very desirable to examine the blood in all these particulars at the same time; and not only once in each case, but to follow each through the various phases of the disease over as long a period as possible, to see what changes, if any, take place, and whether the presence of certain mental and physical symptoms is attended by any constant alteration in the blood.

Methods. To obtain the blood the lobe of the ear was pricked with a fine-pointed lancet after the skin had been cleansed with alcohol. The corpuscles were counted with the Thoma-Zeiss apparatus, Toison's solution being used to stain the white corpuscles in a dilution of 1 to 100. For estimating the red corpuscles, with but few exceptions, 50 squares were counted in never less than three drops, or 150 squares in all. The whole ruled area was counted for leucocytes in four different drops, except in four instances, frequently in more when there was much disparity between the several results. Considerable time was saved by employing two or three counters.

The hæmoglobin was taken with Fleischl's hæmometer, and the average of four readings obtained in each case.

For determining the specific gravity, Hammerschlag's¹ method was used of suspending a blood-drop in the middle of a cylinder containing a mixture of benzol and chloroform, the specific weight of this mixture being that of the blood.

Cover-glass preparations were then dried for several hours in a thermostat at a temperature of 100° C. and stained with Ehrlich's triple stain, as modified by Gollasch and Biondi, and a differential count made of 1000 leucocytes in nearly every instance.

The absolute number in a cubic millimetre was calculated for the sake of clearness. A Leitz mechanical stage was found to be of great convenience and value in traversing a large area without recounting any field as well as for locating cells for future reference. The lens was a Zeiss 1/12" oil immersion with a No. 6 compensating ocular.

The classification is essentially that of Ehrlich.

1. Lymphocytes, as large or somewhat larger than the red corpuscles, with a round, deeply stained nucleus almost filling the cell-body.

2. Large mononuclear leucocytes, of greater size, with a large nucleus faintly stained. The protoplasm is more abundant than in the lymphocytes, and is without granulations.

3. Transitional² forms, including those cells which in the evolution of the large mononuclear into the neutrophile cells with polymorphous

¹ Described by von Limbeck in *Grundriss einer Klin. Path. des Blutes*, 1892, p. 9.

² Ehrlich's definition takes in all the large mononuclear forms with indented nuclei without reference to the affinity of the protoplasm for coloring-matter. Ouskow lays more stress on the color of the protoplasm. (See review by Thayer, *Johns Hopkins Hosp. Reports*, 1894, vol. iv. No. 1, p. 102.)

nuclei, have not only irregularly shaped nuclei, but some evidence of beginning granulation in the protoplasm.

4. Polymorphonuclear neutrophiles (polynuclear neutrophiles), with nuclei of various shapes and having a protoplasm filled with neutrophilic granulations.

5. Eosinophiles, cells with polymorphous nuclei, but containing large granulations staining with eosin or acid fuchsine.

Excluding those taken in cases with convulsions, nearly all the specimens of blood were obtained between 3 and 5 P.M., or from two and one-half to four and one-half hours after dinner. The time of day is important, especially in its bearing upon digestion leucocytosis. Rieder¹ states that after a proteid diet there is, in most persons, an increase in the white corpuscles, which reaches its maximum from three to four hours after eating, and on an average is about 33 per cent. above the normal count. Reinert's² conclusions are practically the same.

Nearly all the following examinations, therefore, were at a time when digestive leucocytosis is active. To ascertain what the physiological leucocytosis amounts to, and by learning our own personal equation to have a basis for comparison, blood-specimens were obtained from ten male adults in health at the same length of time after eating. These persons were nurses and others living in the hospital, with diet similar to that of the patients.

From the table one can see that the red corpuscles and hæmoglobin are about in the proportions commonly accepted. The normal specific gravity is not so well determined, variations depending on the method, age of individual, and probably also on the time of day. Smyth, in the work referred to above, took as his normal 1056, which is certainly much lower than most recent observers have found it in adult males. Hammerschlag³ obtained a range from 1056.5 to 1066, with an average of 1060.5. Perhaps our result is made a little higher through the influence of meals.

The average number of leucocytes is decidedly above the normal as given by most authors, but not high considering the effect of digestion.

An important thing to observe in the differential count is that in spite of the wide variations in the number of leucocytes in these cases, the proportion of the cellular elements to each other does not change materially. In other words, in the leucocytosis following proteid digestion the relation of the polymorphonuclear to the mononuclear cells remains the same,⁴ a fact that distinguishes it from the inflammatory leucocytoses. The eosinophile cells, according to Rieder,⁵ tend to diminish in all leucocytoses, whether physiological or pathological.

¹ Beitrage zur Kenntniss der Leukocytose, 1892, pp. 53 and 201.

² Die Zählung der Blutkörperchen, 1891, p. 95.

³ Cited by Vierordt in his "Daten und Tabellen," 1893, p. 126.

⁴ Rieder, Beitrage zur Kenntniss der Leukocytose, 1892, p. 63.

⁵ Loc. cit., p. 65.

Throughout this paper the results in these healthy individuals will be taken as a basis for comparison, since they were examined under as nearly as possible the same conditions as the paralytics.

CASE I.—S. E. S., aged thirty-five years, married, admitted October, 1892. No heredity. Since having influenza two years ago has been nervous and irritable. Has always overworked. Pupils unequal, talks slowly, tremor of tongue and hands, knee-jerks absent, Romberg's symptom, well-developed delusions of wealth, excited, unreasonable, and extravagant. When the blood was first examined, ataxia and dementia were very pronounced, and he was having convulsions at frequent intervals.

Upon studying the table it is evident that the red corpuscles are about normal and the specific gravity and hæmoglobin diminished. There is a leucocytosis amounting to 35 per cent. above the normal. The differential count shows that this lies chiefly in the polymorphonuclear cells, the lymphocytes falling relatively and absolutely. The relative increase in the large mononuclears is greater than in any other element. No abnormal variation is present in the eosinophiles. These examinations were made at a time sufficiently distant from convulsive seizures to be little if at all influenced by them, the nearest being 14 hours after a light attack. During the nine months over which the examinations were made not much change in the blood took place save a slight drop in the red corpuscles and specific gravity.

CASE II.—F. E. C., aged thirty-four years, admitted in October, 1892. Syphilis ten years ago. For several months previous to entrance made business blunders and was absent-minded. Impairment of moral sense, restless, and at times violent, extravagant ideas of grandeur and power. Speech imperfect, staggering gait, writing faulty, knee-jerks increased. Later on he became more paralyzed and demented, losing control of the voluntary muscles. At one time he had a convulsion. Died October 13, 1894.

A general reduction in the red corpuscles, specific gravity, and hæmoglobin is apparent. The augmentation in the leucocytes is too slight to be considered abnormal. Aside from the increase in the polymorphonuclear neutrophile cells, the differential count reveals a low number of lymphocytes.

CASE III.—J. N., aged fifty years, admitted December, 1889. No heredity. Naturally of a nervous temperament. A change in character was first noticed eighteen months before entering the hospital. Memory poor. Grand ideas of his own greatness and importance. Delusions of wealth, emotional. Inequality of pupils, fibrillary tremor of tongue, Romberg's symptom present, knee-jerk absent. Subsequently was suspicious, and acquired delusions and hallucinations of sight. Ataxia of gait and dementia. Died October 20, 1894.

The red corpuscles are apparently little affected; the specific gravity and hæmoglobin are both subnormal. The leucocytes are most interesting; with but one deviation the number steadily rises as the termination of the disease draws near. This agrees in part with the conclusion of McPhail¹ that the increase in the white corpuscles is coincident with the progress of the affection, but later observations fail to bear it out. With this progressive leucocytosis the absolute number of the different varieties remains practically stationary excepting that of the polymorphonuclear cells, in which alone the increase takes place.

CASE IV.—C. C. B., aged forty-two years, married, admitted April, 1892. The onset was sudden. Three days ago became excited, talked loudly, and acted in an unusual manner, doing many senseless things. Has extravagant schemes. Pupils react sluggishly to light; tongue shows a fibrillary tremor; twitching of facial muscles; speech often hesitating, words being repeated. Knee-jerks diminished. Romberg's symptom present. The physical and mental condition grew constantly worse, as manifested by his unsteady walk and dementia.

This is a man in the demented stage who underwent comparatively little change in the nine months during which the blood was taken, although the disease had progressed rapidly prior to this.

The hæmoglobin, always below normal, was as high at the end as at the beginning. The specific gravity was not far from the normal and was quite constant. In the red corpuscles there is a considerable loss. The average of white corpuscles gives a gain of about 20 per cent. over the normal average, but the variation at different times has no especial relation to any state of mind or body. In the differential count one notices a diminution in the lymphocytes and a rise in the large mononuclear and polymorphonuclear cells. The eosinophiles are within physiological limits.

CASE V.—F. C., aged forty-three years, married, admitted September, 1893. Dissipated in his youth. A year before admission he had an attack of speechlessness without loss of consciousness, which was followed by others of a similar nature. For many months has been irritable and unreasonable. Memory poor. Delusions. Hallucinations of hearing and sight. Fine tremor of tongue, slurring of syllables, tremor of lips and facial muscles. Knee-jerks absent. Romberg's symptom present. At times ataxia of gait and mental confusion. April 22, 1895, died in an apoplectic seizure.

The red corpuscles are below the standard, and a tendency can be detected to decrease with the advance of the disease. Both the specific gravity and hæmoglobin are diminished constantly. The leucocytes are slightly increased and do not fluctuate in the course of the disease to any extent except in one instance, where the leucocytosis reached

¹ Loc. cit.

18,000. This unexpected result at once brought up the question of cause. Three days previous he had an apoplectic attack with subsequent paralysis of the face and inability to articulate, the temperature being 104° . At the time of the blood-examination the temperature had fallen to 100° . Had this marked increase in the leucocytes, specific gravity, and hæmoglobin any dependence on the seizure? A relation of cause and effect was more strongly suspected on finding, three days later, the blood had recovered its usual condition, and with this clew further and more systematic examinations were made later on. In the production of the leucocytosis the polymorphonuclear neutrophils and the lymphocytes both play an important part, but the large mononuclear cells are relatively most increased. The average of the other counts shows only a little drop in the lymphocytes and a rise in the number of large mononuclear cells.

CASE VI.—W. H. P., aged forty-nine years, admitted February, 1894. Overwork. For five years past his friends have noticed an unnatural nervousness and irritability of temper. There is a history of a "fainting spell," for which he was in bed several days. Delusions of wealth and grandeur, memory poor, sense of propriety impaired. Pupils do not react to light. Fibrillary tremor of tongue and muscles of the face. Articulation faulty. Romberg's symptom, inco-ordination, ataxic gait. Knee-jerks absent.

Following these examinations over a period of eight months we find the specific gravity quite unchanging throughout, and a steady decrease in the hæmoglobin and number of red corpuscles. The leucocytosis, always present, is sometimes very pronounced, at other times small. Unlike some of the preceding cases, the late counts were lower than the early ones. The absolute number of lymphocytes is nearly normal, that of the polymorphonuclear neutrophils considerably increased, while the large mononuclears are more than doubled.

CASE VII.—M. W. C., aged forty-six years, married, admitted March, 1894. Heredity in family. Syphilis twelve years ago. Has always overworked. About two months since formed delusions of possessing a great fortune, was confused, and sometimes violent. Now more quiet and contented. Does not appreciate his condition or whereabouts. Pupils unequal. Knee-jerks much decreased. Romberg's symptom. Speech slow and hesitating, ataxia of gait. Died January 6, 1895, after a hemiplegia followed by convulsions that recurred frequently until his death.

The only noteworthy deviation from the normal is in the number of white corpuscles, which are decidedly increased. This increase is entirely in the neutrophilic polymorphonuclear cells.

CASE VIII.—A. F. S., aged thirty-two years, admitted July, 1894. Naturally a keen man, he became a year ago less attentive to business and gave it up. More recently wandered away from home in

a state of mental confusion. Memory for recent events much impaired. Judgment and power of attention poor. Tremor of tongue and lips. Articulation decidedly defective. Knee-jerks increased. Marked ankle-clonus, inco-ordination of movement.

This case is of interest because seen in the early stage, soon after his entrance into the hospital. A general diminution in the red corpuscles, specific gravity, and hæmoglobin is apparent. There is no leucocytosis; in fact, the count is below the average normal. The count of stained specimens is essentially a normal one.

CASE IX.—J. M. R., aged forty-three years, married, admitted March, 1894. Syphilis eight years ago. For seven months has been nervous and depressed. Afterward became exhilarated and developed delusions of wealth and grandeur. Moral sense apparently lost. Memory poor. Emotional. Tremor of tongue and lips. Speech hesitating. Romberg's symptom. Knee-jerks diminished. Handwriting characteristic with omissions of letters and words. At the period when the latter observations were made he was breaking down very rapidly.

We have here a good example of the general paralytic who runs a rapid course, the mental and physical impairment being more marked at each successive examination. The red corpuscles and hæmoglobin show a tendency to decrease. In contrast to the previous cases the specific gravity is never below the normal, and at times is extremely high. Speaking roughly, the specific gravity is higher during periods of motor excitement than at other times, but the correspondence is neither constant nor accurate.

The leucocytosis is always of fair proportions, and at one time even reached 20,000. This was taken when the mental and physical disturbance had attained its climax, and the degree of excitement and confusion was more pronounced than at any other examination. The polymorphonuclear neutrophils make up the greater part of the excess of leucocytes, but relatively the large mononuclears increase much more, their actual number sometimes being three times the normal. The lymphocytes are low throughout. At the beginning the eosinophiles were more numerous than afterward. It is worth mentioning that the eosinophiles were fewest when the leucocytosis was greatest.

CASE X.—G. P. E., aged thirty-five years, admitted February, 1894. Syphilitic history questionable. After a period in which he was irritable and forgetful, he became excited and showed marked delusions of grandeur. On admission, pupils unequal and facial tremor. Diminished knee-jerks. During the subsequent year he progressed to profound dementia with great impairment in speech and gait.

A feature in the analysis of this case is the evenness of the various examinations, not only in the leucocytes, but in the red corpuscles, hæmoglobin, and specific gravity as well. The last three are diminished, the white corpuscles above normal. His condition at the several times of observations was very similar except on November 8th, when he was

declining with unusual rapidity. The leucocytes alone were affected, reaching 13,500. In the differential count the lymphocytes, as usual, were abnormal. The eosinophiles were at all times very high, but without apparent relation to any physical or mental condition.

CASE XI.—C. F., aged fifty years, admitted March, 1894. No syphilis. Drank alcohol freely. Disease began rather abruptly with failure of memory and thickness of speech. This was soon followed by unsteadiness of gait, delusions of grandeur, and excitement. Pupils unequal, react slightly to light. Fibrillary tremor of tongue and face. Knee-jerk diminished. Steady progress during the year to high-grade dementia.

All the observations were made in the stage of contentment and physical well-being. The blood is quite normal, save a low percentage of hæmoglobin. The analysis of the white corpuscles shows a fall in the lymphocytes with a great rise in the large mononuclear cells.

CASE XII.—A. G., aged forty years, admitted November, 1894. No syphilis. Violinist. For a number of months before admission it was noticed that he was losing his skill in playing, that his speech was affected, and that he was careless in keeping appointments. Three weeks previous to entrance became extravagant and excited. Full of schemes. Tremor of tongue and face, slurring of speech, slight inequality of pupils and slow reaction to light. Since then has failed steadily in mind and body, and has frequently been very restless. Is demented and easily excited.

This patient was followed along from the excited stage at the beginning, with restlessness and incessant talking, to the later period of quiet and contentment. No change in the blood coincident with the alteration in the mental condition can be discovered aside from a fall in the hæmoglobin. The range of the specific gravity is physiological and the red corpuscles likewise. A constant leucocytosis is present of fairly high grade, in which the lymphocytes and transitional cells are normal and the polymorphonuclears increased, but much less relatively than the large mononuclears and eosinophiles, both of which in actual numbers are more than doubled.

CASE XIII.—S. A. H., aged sixty years, admitted January, 1894. For a year previous to admission slight mental changes, slight tremor of face, and slight slowing of speech. Later became depressed and was brought to the hospital profoundly melancholy. There was marked tremor of face and tongue, increased knee-jerks, and Romberg's symptom. With the depression some delusions of grandeur—he is the "king of sinners." He failed mentally and physically with extreme rapidity and died four weeks after admission.

Unfortunately, but one specimen was obtained in this case, which was of such short duration. When the blood was taken three days before death, the patient was in bed with a temperature of 100.4°. The blood is evidently concentrated since the specific gravity, hæmoglobin, and red corpuscles are very high for a man pale and emaciated as he

was. A distinct leucocytosis was found, consisting chiefly of polymorphonuclear neutrophile cells.

CASE XIV.—F. W., aged forty-four years, admitted January, 1894. History of syphilis and excesses. Optic atrophy for eight years. For six months before admission, irritable, forgetful, and unmanageable. On admission, confused, apprehensive, suspicious, hallucinations and delusions, emotional. Pupils unequal, reaction to light slow. Tremor of tongue, speech slurring, knee-jerks absent. One fainting attack in which he became very pale. In September, restless and noisy, since then more quiet and happy, failing mentally. On April 1st had a small hedsore with slight discharge. April 12th, hedsore healing, no discharge. May 1st, hedsore well.

The red corpuscles, hæmoglobin, and specific gravity are all somewhat diminished, but are not affected particularly at any period of the disease. The leucocytosis, though sometimes inconsiderable, is fairly constant; it attains a maximum of 14,500 at a time when the patient had a small hedsore.

The differential count is remarkable in several respects. Previous to April 3d, the lymphocytes were diminished and the large mononuclear and eosinophile cells markedly increased. Upon this date, when the stained specimens were examined, the large mononuclears numbered four times the normal, and the eosinophiles more than ten times the normal. The patient was restless and noisy; on physical examination the only thing to be discovered was a hedsore the size of a five-cent piece, with a little discharge. Eleven days later when the abrasion had cleaned up and was rapidly healing, another specimen was taken. Instead of a falling-off in the eosinophiles, they were still further increased, amounting to 2671 in a c.mm. Two weeks later, although the lesion had entirely healed, the eosinophiles were still over five times the normal, the large mononuclears also remaining high. Such a great number of eosinophiles is very unusual.

Excluding leukaemia¹ and the results of injections² of bacterial products,³ in both of which the absolute number may be enormous, the highest counts of eosinophiles that we have been able to find in a hurried review of the literature are as follows:

Author.	Disease.	Number of leucocytes.	Per cent. of eosinophiles.	Absolute number of eosinophiles.
Zappert ⁴	Ankylostomiasis,	4,300	27.9	1200
Zappert	Asthma,	7,120	12.36	880
Zappert	Pemphigus,	16,400	29.28	4800
Zappert	Lymphosarcoma,	11,964	17.76	2077
Roncoroni ⁵	Gen. par. excited,	-----	25	

¹ Von Limbeck: *Grundriss einer klin. Pathologie des Blutes*, p. 160.

² Rieder: *Loc. cit.*, p. 183.

³ Zappert: *Zeitschrift für klin. Medizin*, Bd. xxiii., Heft 3 and 4, p. 293.

⁴ *Loc. cit.*, pp. 257, 260, 271, and 280.

⁵ *Archivo di Psichiatria, Scienze Penale, etc.*, vol. xv., F. III. p. 293.

Only in pemphigus and possibly the case of general paralysis during excitement, in which the extent of the leucocytosis was not given, is the absolute number greater than in this patient. To determine what effect, if any, a bedsore might have, two paralytics with open abrasions on the buttocks were examined:

Case.	Per ct. of lymphocytes.	Per cent. of large mononuclear.	Per cent. of transitional.	Per cent. of neutrophile polymorphonuclear.	Per cent. of eosinophiles.	No. leucocytes counted.	
A	10.6	8.0	0.8	80.2	0.4	500	Sore open, but clean. Slight purulent discharge.
B	7.2	6.4	0.6	83.2	2.2	500	

The absence of any increase in the eosinophiles in these two cases indicates that probably the bedsore was not the cause of their increase in the patient under discussion. Moreover, the maximum number was present not during the active stage, but after it was nearly healed.

In view of these facts, it is fair to presume that this great augmentation of the eosinophiles has no dependence on the bedsore.

The mental condition of the patient was one of restlessness and irritability, but without the excitement that existed in Roncoroni's case, which had 25 per cent. of eosinophiles.

CASE XV.—J. F., aged forty-three years, admitted April, 1895. For two years before entrance a gradual failure of memory and intellect made evident by numerous business mistakes, hallucinations, and delusions, the latter changing frequently. He is considerably demented, often confused, very forgetful; pupils unequal; tremor of facial muscles; speech good, except for an occasional dropping of a word.

A diminution in the red corpuscles and hæmoglobin is evident with a low degree of leucocytosis. The specific gravity is about normal. The large mononuclear cells are rather high; otherwise there is no noteworthy alteration in the proportion of the various kinds of leucocytes.

CASE XVI.—J. A. H., aged thirty-three years, admitted January, 1895. Successful business man, hard worker. No syphilis. A month prior to admission irritable, extravagant, and reckless. On entrance, tremor of tongue, diminished knee-jerk. Romberg's symptom. Feels well. Exalted ideas of his ability, delusions of wealth. Distinctly demented. Argyll-Robertson pupil. Failed rather rapidly mentally and physically. At times much excited and emotional.

The case is of more value because the blood was obtained within three months of the appearance of the first symptoms of general paralysis. The red corpuscles and hæmoglobin were low, while the specific gravity and white corpuscles are what one would expect in health. The lymphocytes are the only cells that give evidence of any alteration in

the differential count. The highest number of leucocytes was found during a period of excitement.

CASE XVII.—E. D. M., aged thirty-one years, admitted July, 1888. A year before this had a fainting attack with affection of speech. Delusions of persecution. Homicidal and suicidal. Dementia gradually came on. Speaks little. Constant stereotyped motor activity. Pupils unequal, tremor of facial muscles and tongue. Resistive. Speech very much impaired. Several convulsions.

April 21. Owing to a fall, has an abscess on elbow. Opened March 20th. Wound healed. Mind lately rather clearer. Much demented.

Standing out in contrast with the preceding case, the disease in this patient was of seven years' duration. A considerable leucocytosis characterizes the earliest examination, in which the large mononuclear element relatively plays the greatest part, though the polymorphonuclear increase is absolutely greater. The second specimen was taken after an abscess had formed near the elbow as a result of trauma. The leucocytosis reached 20,330. The difference between the inflammatory leucocytosis and that which was present before the accident is the preponderance of the polymorphonuclear element in the former. The lymphocytes suffered an actual loss of numbers, while the eosinophiles entirely disappeared. In this instance the character of the differential count was sufficiently changed to make the diagnosis of pus extremely probable. When the incision had entirely healed the count resumed in all essential respects its former proportions.

CASE XVIII.—S. M. H., aged fifty-one years, admitted December, 1894. Heard voices telling him to kill himself and family. Violent and threatening. Frequent fainting spells for a year past. *Tabes dorsalis* for six years. Ptosis of left lid. Argyll-Robertson pupil. Knee-jerks absent on right, slight on left. Sensation diminished all over. Passes urine and feces involuntarily. Constantly grinds his teeth. Mentally dull and apathetic.

The leucocytosis on an average is 35 per cent. above the normal, but does not vary much from the physiological proportion of cellular constituents excepting in an increased number of large mononuclear and a scarcity of eosinophile cells. The highest leucocytosis corresponds to a time of restlessness and excitement.

CASE XIX.—H. M., aged forty-two years, admitted July, 1894. History of syphilis(?) and overwork. For a year had been irritable, and in the past month unusually emotional. Brought to hospital because he suddenly developed the most absurd business schemes on a large scale. Diminished knee-jerks, tremulous tongue, Argyll-Robertson pupils. Incoherent, excited, destructive, and aggressive. Delusions of grandeur. More recently has been quiet and contented, and it was during this period that examinations were made.

CASE I.		Date.	Hour.	No. of white count.	No. of red count.	White.	Hed.	Sp.gr.	Hb.	Lymphocytes.			Large mononuclear.			Transitional.			Neutrophils polymorphonuclear.			Eosinophiles.			No. leucocytes count.	Remarks.
										Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	Pr. et.	Ala. No. in 1 c. mm.	
		July 10	3.00 P. M.	4	100	13,750	4,950,000	1002	84	14.0	1918	7.6	1023	1.0	137	70.5	10,480	1.0	137	70.5	10,480	1.0	137	70.5	300	No convulsions for 14 hours.
		Aug. 10	3.30 "	4	160	14,500	5,215,000	1000	86	11.3	1638	6.6	942	1.6	218	70.2	11,484	1.6	218	70.2	11,484	1.6	218	70.2	1000	" " 17 "
		Sept. 10	4.00 "	4	160	10,000	5,300,000	1000	90	10.9	1625	4.4	669	1.0	150	82.1	12,318	1.0	150	82.1	12,318	1.0	150	82.1	1000	" " 6 days.
		Oct. 18	4.00 "	4	160	13,750	4,960,000	1001	85	11.7	1629	4.8	660	1.2	105	86.3	11,011	1.2	105	86.3	11,011	1.2	105	86.3	1000	" " 11 "
		Nov. 23	3.30 "	4	160	12,000	4,160,000	1038	84	15.0	1809	0.9	702	1.0	228	73.6	8,820	1.0	228	73.6	8,820	1.0	228	73.6	1000	" " 3 1/2 "
		Apr. 2	4.30 "	0	160	12,500	4,810,000	1059	81	13.6	1700	9.7	1212	1.0	200	72.0	6,000	1.0	200	72.0	6,000	1.0	200	72.0	1000	" " 24 hours.
		Average	3.49 "	4 1/4	141	13,676	5,031,700	1050	86.6	12.7	1717	6.0	882	1.4	183	77.3	10,623	2.0	230	78.0	10,623	2.0	230	78.0	880	
CASE II.																										
		July 19	3.00 P. M.	3	100	8,000	4,492,000	1055.5	80	13.6	1080	6.0	480	2.0	160	70.5	6,040	3.0	240	70.5	6,040	3.0	240	70.5	400	Falling steadily.
		Aug. 10	3.00 "	3	100	11,000	4,690,000	1050	82	12.3	1350	4.0	690	0.8	104	70.6	8,745	3.1	311	70.6	8,745	3.1	311	70.6	1000	" "
		Sept. 15	3.00 "	4	160	12,750	4,770,000	1051	82	13.0	1657	4.3	618	1.3	158	73.8	10,021	2.8	361	73.8	10,021	2.8	361	73.8	1000	" "
		Average	3.00 "	3 1/4	119	10,683	4,617,600	1058	81	12.0	1363	5.0	511	0.7	139	71.9	8,268	3.0	312	71.9	8,268	3.0	312	71.9	1000	
CASE III.																										
		July 25	4.00 P. M.	4	100	13,000	5,228,000	1055	90	13.8	1794	9.6	846	1.3	169	78.0	9,038	1.8	234	78.0	9,038	1.8	234	78.0	1000	Ataxia, dementia.
		Aug. 13	3.30 "	4	125	9,000	5,264,000	1061	89	13.6	1216	7.6	676	1.6	135	78.8	6,822	1.7	160	78.8	6,822	1.7	160	78.8	1000	Irritable, stuporous.
		Sept. 14	1.00 "	4	160	14,500	5,160,000	1038	90	13.0	1855	0.9	870	1.0	201	71.8	11,735	1.4	203	71.8	11,735	1.4	203	71.8	1000	Loosing strength. Temp. 99°.
		Oct. 10	4.00 "	4	160	18,500	4,980,000	1060	85	9.5	1768	3.3	610	1.3	210	86.9	10,725	0.9	160	86.9	10,725	0.9	160	86.9	1000	
		Average	3.55 "	4	130	13,760	5,151,000	1058.6	87 1/4	12.4	1633	6.8	760	1.6	201	78.8	10,910	1.5	190	78.8	10,910	1.5	190	78.8	1000	

CASE IV.									
July 27	3.30 P. M.	4	100	14,000	5,004,000	1000	85	12.3	1862
Aug. 10	4.00 "	4	150	10,000	4,812,000	1058	78	16.0	1670
Sept. 16	4.00 "	4	150	12,000	4,720,000	1059	82	13.9	1668
Sept. 13	3.00 "	4	150	12,750	4,680,000	1060	84	12.3	1668
Dec. 18	3.30 "	0	150	13,000	4,800,000	1061	85	13.0	1660
1895									
Feb. 0	2.00 "	0	150	12,100	4,920,000	1060	80	12.8	1628
Feb. 6	4.00 "	0	150	11,500	4,221,000	1061	83	12.8	1628
Apr. 24	4.00 "	0	150	10,600	3,772,000	1064	86	16.4	1643
Average	3.30 "	5	145	12,027	4,402,000	1060½	82½	13.0	1622
CASE V.									
July 20	1.00 P. M.	4	100	11,000	4,072,000	1058	88	16.0	1620
Aug. 20	4.30 "	3	110	10,000	4,660,000	1059	90	12.3	1620
Sept. 18	3.30 "	4	150	15,000	4,900,000	1063	103	12.0	1630
Sept. 21	3.30 "	4	150	10,600	4,701,000	1063	92	14.0	1630
Nov. 10	3.30 "	4	150	10,000	4,020,000	1060	85	18.0	1650
Dec. 11	3.15 "	4	150	10,000	4,051,000	1064	90	18.5	1650
Mar. 27	3.30 "	0	150	12,000	4,632,000	1060	86	17.8	2225
Average	3.45 "	4½	137	10,750	4,750,000	1060½	87½	16.0	1769
CASE VI.									
July 30	3.00 P. M.	4	100	15,000	4,021,000	1059	94	10.1	2405
Sept. 4	4.00 "	4	150	13,000	4,800,000	1060	94	15.5	2016
Nov. 0	3.00 "	4	150	10,750	4,700,000	1062	87	9.0	1708
Dec. 11	3.15 "	4	150	12,000	4,860,000	1058	78	13.5	1629
Mar. 10	3.30 "	0	150	11,000	4,550,000	1060	75	13.0	1430
Average	3.40 "	4½	140	13,550	4,724,000	1060	80½	13.5	1833
CASE VII.									
July 31	3.00 P. M.	4	100	13,000	4,900,000	1060	100	14.7	1837
Aug. 25	4.00 "	4	150	14,250	5,161,000	1060	98	14.0	1985
Sept. 17	4.00 "	4	150	14,000	5,080,000	1058	100	13.6	1904
Average	3.40 "	4	133	13,750	5,045,000	1059½	99	14.1	1837

Three days after an apoplectic attack,

This examination is not included in the average.

Contented, Restless, deluded, Quiet, confused.

CASE VIII.		No. fields of view	No. white corpuscles	White.	Red.	Sp-gr.	Hb.	Lymphocytes	Large mononuclear.	Transitional.	Neutrophile polymorphonuclear.	Eosinophiles.	No. leucocytes	Remarks.
Date.	Hour.							Pr. ct.	Pr. ct.	Pr. ct.	Pr. ct.	Pr. ct.	Pr. ct.	
Aug. 10	3.00 P. M.	4	125	8,300	4,800,000	1055	75	17.1	0.1	660	73.9	0.333	2.4	100
Sept. 1	3.00 "	4	200	9,760	4,600,000	1055	83	19.1	7.3	711	70.1	0.831	2.2	100
Sept. 20	4.00 "	4	160	8,250	4,020,000	1060	80	10.6	0.4	628	71.0	0.867	2.0	100
Nov. 10	3.00 "	4	160	10,000	4,520,000	1054	85	10.7	0.8	650	74.7	0.740	0.6	100
Average	3.15 "	4	133	9,075	4,539,000	1057½	81	18.1	0.6	610	72.4	0.503	1.8	100
CASE IX.														
Nov. 15	3.00 P. M.	4	150	14,250	5,000,000	1057	92	12.5	8.9	1268	70.6	10.040	0.1	100
Dec. 31	3.10 "	5	160	10,000	4,604,000	1065	82	11.5	10.7	1685	71.6	10.740	0.7	100
Mar. 20	3.30 "	6	160	12,600	4,772,000	1062	78	10.2	12.6	1675	73.0	9.125	3.0	100
Apr. 20	5.00 "	5	160	11,000	4,888,000	1067	85	12.0	11.1	1721	74.0	8.140	2.1	100
May 4	3.30 "	7	160	20,550	4,840,000	1064	78	8.1	16.9	8.4	229	81.4	0.8	100
Average	3.40 "	5½	160	14,720	4,800,800	1065	83	10.0	10.3	1484	74.1	11.103	3.1	100
CASE X.														
Aug. 22	3.00 P. M.	5	160	11,000	4,750,000	1059	84	12.4	4.5	495	73.7	8.107	7.0	100
Aug. 29	4.00 "	4	160	10,700	4,680,000	1060	81	14.7	4.8	491	71.0	8.607	5.1	100
Sept. 24	3.00 "	4	160	13,000	4,900,000	1058	82	13.0	6.4	492	71.0	8.607	5.1	100
Oct. 10	3.00 "	4	160	13,000	4,900,000	1058	80	12.6	5.0	525	71.0	10.395	4.6	100
Mar. 10	3.45 "	6	160	11,100	4,704,000	1055	72	14.2	3.4	377	76.2	8.347	4.7	100
Average	3.55 "	4½	140	11,060	4,686,000	1058½	79½	13.5	4.8	505	73.0	8.592	0.4	100
CASE XI.														
Jan. 10	4.30 P. M.	0	160	7,000	6,008,000	1053	90	16.5	12.0	612	70.1	5.328	0.0	100
Mar. 20	4.30 "	0	160	8,500	6,040,000	1052	82	15.6	11.0	625	70.9	0.927	1.2	100
Apr. 10	4.45 "	0	160	9,300	6,200,000	1059	85	17.2	14.9	1385	64.0	0.108	2.2	100
Average	4.35 "	0	160	8,467	6,044,000	1051½	85½	16.4	12.6	1077	68.0	0.821	1.4	100

Falling.

"

"

Excited.

Very excited; breaking down

CASE XII.					
	4	100	12,000	5,320,000	1055
Nov. 22	3.30 P.M.				
Dec. 22	3.30 "	4	150	17,750	1058
Mar. 20	4.30 "	0	150	17,750	1063
May 2	5.00 "	0	150	6,150,000	1002
Average	4.05 "	5	150	14,020	1052
Temp. 100.4°					
CASE XIII.					
Feb. 13	4.30 P.M.	0	150	14,420	1065
CASE XIV.					
1891					
Aug. 10	4.30 P.M.	4	800	9,250	5,200,000
Sep. 6	4.30 "	4	150	11,750	1061
Oct. 25	4.10 "	4	150	12,500	5,020,000
Nov. 23	3.30 "	4	180	12,500	5,160,000
1895					
Jan. 1	4.20 "	4	150	11,250	1055
Apr. 1	4.30 "	0	150	14,500	4,804,000
July 14	4.30 "	0	150	12,000	1062
May 1	3.30 "	0	150	10,160	4,882,000
Average	4.10 "	4½	150	11,821	4,937,000
CASE XV.					
Apr. 18	4.30 P.M.	0	150	11,830	1062
May 14	5.00 "	0	150	10,800	1050
Average	4.45 "	0	150	11,315	1061
CASE XVI.					
Feb. 14	4.30 P.M.	0	150	8,500	1062
Mar. 22	4.00 "	7	150	11,750	4,930,000
Apr. 27	3.15 "	0	150	7,350	4,450,000
Average	3.50 "	0½	150	0,150	1062

CASE XVII.		No. fields of white count.	No. of red count.	White.	Red.	Sp. gr.	Hb.	Lymphocytes.		Large mononuclear.		Transitional.		Neutrophils polymorphonuclear.		Eosinophiles.		Remarks.	
Date.	Hour.							Pr. ct.	Ala. No. in 1 c.mm.	Pr. ct.	Ala. No. in 1 c.mm.	Pr. ct.	Ala. No. in 1 c.mm.	Pr. ct.	Ala. No. in 1 c.mm.	Pr. ct.	Ala. No. in 1 c.mm.		No. leucocytes count.
Apr. 17	2.30 P.M.	0	160	14,830	4,580,000	1063	04	12.2	1809	7.7	1142	2.0	297	75.3	11,167	2.8	416	1000	Traumatic abscess. 1 The examination on April 21st is not included in the average.
Apr. 21	3.30 A.M.	0	160	20,330	4,875,000	1061	81	5.7	1159	5.4	1698	0.6	122	88.3	17,051	0	0	1000	
May 20	2.15 "	0	160	11,600	4,540,000	1059	90	16.7	1020	13.0	1698	2.3	205	63.0	7,314	3.6	400	1000	
Average	3.30 "	0	160	13,166	4,660,000	1061	02	14.6	1864	10.8	1370	2.1	281	66.5	0,840	3.1	409	1000	
CASE XVIII.																			
Feb. 16	4.00 P.M.	7	160	11,450	9,024,000	1049	00	16.2	1832	4.7	637	1.2	137	77.1	8,813	0.8	01	1000	
Mar. 28	4.30 "	0	160	12,880	4,004,000	1053	82	14.9	1809	8.0	1142	0.0	116	73.7	0,468	1.7	218	1000	
May 1	6.00 "	0	160	19,568	4,590,000	1065	88	10.7	1705	6.6	1022	1.2	108	81.3	13,415	0.3	24	1000	
Average	4.30 "	0 2/3	160	13,666	4,898,000	1062 2/3	89 2/3	13.0	1859	6.7	017	1.1	150	77.4	10,601	0.0	120	1000	
CASE XIX.																			
Apr. 25	4.00 P.M.	0	160	14,000	4,760,000	1065	86	17.3	2422	12.1	1604	2.0	280	67.0	0,380	1.0	224	1000	
May 18	6.00 "	7	160	11,300	4,020,000	1065	92	21.6	2450	13.6	1625	3.1	350	60.3	0,814	1.0	181	1000	
Average	4.30 "	0 2/3	160	12,650	4,390,000	1065	89	10.4	2420	12.8	1609	2.6	305	63.0	8,097	1.0	152	1000	

TABLE OF AVERAGES.

Case.	No. of examinations.	Horr. P. M.	No. fields of white counted.	No. sq. res. of red counted.	White.	Red.	Sp. gr.	Hb.	Lymphocytes.		Large mono-nuclear.		Transitional.		Neutrophils polymorpho-nuclear.		Eosinophiles.	
									Per ct.	Abs. No. in 1 c.mm.	Per ct.	Abs. No. in 1 c.mm.	Per ct.	Abs. No. in 1 c.mm.	Per ct.	Abs. No. in 1 c.mm.	Per ct.	Abs. No. in 1 c.mm.
I.	0	3.45	4%	141	13,575	5,654,700	1064	80%	12.7	1707	4.6	882	1.4	183	71.3	10,023	2.0	236
II.	3	3.06	4	110	10,583	4,017,000	1058	81	12.6	1363	5.0	511	0.7	130	77.9	8,268	3.0	312
III.	4	8.65	4	130	13,750	5,164,000	1059	87%	12.4	1663	5.8	720	1.6	201	78.8	10,040	1.5	190
IV.	8	8.30	0	141	12,027	4,492,000	1069	82%	13.0	1622	0.8	890	1.2	145	75.7	7,686	2.3	270
V.	0	8.45	4	117	16,750	4,701,300	1065	87%	16.6	1768	8.9	875	1.9	182	71.0	7,702	1.0	116
VI.	5	8.40	4	140	13,650	4,724,000	1060	80%	13.6	1833	8.8	1101	1.5	105	73.7	10,092	2.6	339
VII.	4	3.40	4	133	13,750	5,045,000	1060	89	14.1	1037	4.1	514	0.6	127	78.1	10,751	2.8	390
VIII.	4	3.16	4	136	6,075	4,530,000	1057	81	18.1	1642	6.6	916	1.1	89	72.4	9,653	1.8	157
IX.	5	3.40	5%	150	14,720	4,800,800	1065	83	10.0	1501	10.3	1184	1.5	223	74.1	11,103	5.1	440
X.	0	3.55	4%	140	11,650	4,080,000	1058	70%	13.5	1694	4.8	743	1.7	195	73.0	8,533	0.4	743
XI.	3	4.35	0	150	8,407	4,010,000	1061	85%	10.4	1393	12.6	1077	1.0	83	68.0	6,821	1.4	125
XII.	4	4.06	6	150	14,020	4,889,000	1062	87%	13.7	1618	8.2	1160	1.1	165	73.4	10,201	3.0	549
XIII.	1	4.30	0	150	14,330	5,400,000	1065	61	12.0	1720	3.5	501	0.0	129	83.6	11,065	0.1	14
XIV.	8	4.10	4%	150	11,821	4,057,000	1069	81	10.9	1265	10.4	1248	3.2	383	50.8	7,011	8.7	1675
XV.	2	4.40	0	150	11,315	4,684,000	1061	70%	15.0	1812	7.6	807	1.8	105	75.1	8,290	1.0	176
XVI.	3	3.50	6%	150	6,130	4,106,000	1062	73%	14.2	1289	8.1	730	1.9	92	75.0	9,952	1.1	99
XVII.	2	3.20	0	150	13,105	4,000,000	1061	92	14.5	1804	10.8	1370	2.1	281	69.5	6,240	3.1	409
XVIII.	3	4.30	0%	150	13,960	4,808,000	1062	80%	13.9	1839	6.7	917	1.1	100	77.4	10,501	0.0	120
XIX.	2	4.20	0%	150	12,650	4,390,000	1065	86	16.4	2426	12.8	1099	2.0	305	63.0	8,097	1.0	162
Final average.		3.55	4.0	144	12,202	4,750,000	1060	84.0	14.2	1748	7.8	992	1.5	182	73.0	8,744	2.6	414

One sees a loss in the red corpuscles and hæmoglobin with a high specific gravity. The leucocytosis is different from most of the other cases. The number of lymphocytes is even above normal, and the large mononuclear and transitional cells are much more abundant than normally.

CONCLUSIONS. In looking over the final table of averages we see that as a whole the hæmoglobin in general paralysis ranges from 73 to 92 per cent., never falling below 70 per cent. The percentage is usually higher several months after entrance than on admission, which is probably due more to hospital care and abundant good food than to any change in the disease.

The specific gravity varies from 1058 to 1066, a difference that may be found in healthy individuals. The average falls somewhat below the normal, but the tendency is not pronounced enough to make it of any practical importance.

Much more constant is the diminished number of red corpuscles, which in only 4 cases reaches 5,000,000. Nevertheless they maintain a much better average than some observers have stated.

The leucocytosis is never very great, but considering that it is present in some degree in the great majority of a large number of observations, we are led to believe that *in most cases of general paralysis there is a slight leucocytosis, amounting on an average to about 22 per cent. increase over the normal.* Of three cases examined within four months of the beginning of the disease, two had no leucocytosis; a third, of longer duration and rapid in its progress, exhibited a decided increase in the white corpuscles. From these few results it seems that *early cases of general paralysis may have no leucocytosis whatever unless accompanied by excitement or running a rapid course.* Nothing further can be said with regard to a correspondence between the degree of leucocytosis and the stage of the disease, since in many instances the leucocytes are more abundant in the earlier than in the later stages.

In the analysis of the leucocytes, the lymphocytes in every case but one are found to fall below the normal average. The large mononuclear cells, on the other hand, are generally increased, sometimes to three times the usual number. Roughly speaking, the average increase in the large mononuclears offsets the diminution in the lymphocytes, so that the total mononuclear element is little altered from the normal. The transitional forms nearly always vary with the large mononuclears. The polynuclear cells as a rule vary directly with the leucocytosis, as with but few exceptions they are the predominant variety.

The eosinophiles are more changeable than any other form, varying from 14 to 1075 in a c.mm. They are inclined to be more plentiful in the cases that are restless and show motor excitement, although sometimes the reverse is true.

CASE I—CONVULSIONS.

Date.	Hour.	No. fields of white count.	No. segs of red count.	White.	Red.	Sp-gr.	Hb.	Lymphocytes.				Large mono-nuclear.				Transitional.				Neutrophils polymorpho-nuclear.				Eosinophiles.		No. leucocytes count.	Remarks.
								Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.	Pr. ct.	Abn. No. in 1 c.mm.		
July 10	3.00 P.M.	4	100	13,790	4,020,000	1052	84	14.0	1018	7.5	1028	1.0	137	74.5	10,480	1.5	137	300									
Aug. 10	5.30 "	4	160	14,660	5,218,000	1060	88	11.8	1055	6.5	942	1.6	218	79.2	11,484	2.5	218	1000									
Sept. 10	4.00 "	4	160	15,000	5,200,000	1060	90	11.7	1609	4.4	660	1.0	160	82.1	12,316	1.0	210	1000									
Oct. 18	4.00 "	4	160	13,760	4,060,000	1061	88	11.0	1609	4.6	660	1.2	165	81.3	11,911	2.0	270	1000									
Nov. 23	4.30 "	4	160	12,000	3,600,000	1058	86	7.5	1800	0.6	702	4.9	228	73.6	8,520	3.0	140	1000									
" 20	0.00 A.M.	4	160	28,000	5,160,000	1058	83	7.7	1046	5.1	983	2.0	410	88.2	21,700	0.0	0	1000									
" 20	12.00 "	4	160	28,000	5,170,000	1058	83	7.7	1046	5.1	983	2.0	410	88.2	21,700	0.0	0	1000									
" 20	5.00 A.M.	4	160	17,660	5,238,000	1058	84	4.0	805	6.0	980	1.1	170	88.1	12,510	0.1	17	1000									
" 27	10.00 A.M.	4	160	17,660	5,238,000	1058	84	4.0	805	6.0	980	1.1	170	88.1	12,510	0.1	17	1000									
" 30	7.45 P.M.	4	160	13,750	5,204,000	1057	81	11.8	2931	18.1	3258	3.0	472	73.0	11,358	3.6	148	1000									
Dec. 1	0.15 "	4	160	13,750	5,198,000	1060	85	8.5	1393	11.2	1640	3.0	472	73.0	11,358	2.4	330	1000									
" 1	0.15 "	4	160	13,750	5,198,000	1060	85	8.5	1393	11.2	1640	3.0	472	73.0	11,358	2.4	330	1000									
" 7	0.25 "	4	160	10,600	4,908,000	1060	83	18.3	1399	18.9	1134	4.3	450	68.2	7,103	5.4	357	1000									
" 7	0.25 "	4	160	13,250	5,100,000	1057	85	14.1	1868	15.7	1415	3.5	461	65.6	8,072	3.2	424	1000									
" 8	1.15 A.M.	4	160	11,000	4,988,000	1055	80	10.5	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 16	8.40 P.M.	4	160	11,750	4,934,000	1057	83	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 21	11.10 "	4	160	13,000	4,884,000	1058	78	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 21	8.45 A.M.	4	160	12,500	4,884,000	1060	80	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 27	0.00 P.M.	4	180	11,250	4,908,000	1058	80	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 28	1.00 A.M.	4	160	10,800	4,400,000	1059	80	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 28	0.00 "	4	160	11,000	4,390,000	1061	80	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 28	1.45 P.M.	4	160	8,600	4,228,000	1062	84	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 28	3.45 "	4	160	8,600	4,140,000	1057	78	13.0	1608	6.0	720	2.3	275	73.2	8,796	4.5	510	1000									
" 28	10.45 "	4	160	13,000	4,110,000	1059	74	14.2	1605	7.3	647	0.7	28	72.1	6,408	5.7	427	1000									
" 29	2.15 A.M.	4	160	17,500	4,180,000	1062	80	10.0	1185	11.5	1253	2.3	253	73.2	8,072	2.5	275	1000									
" 29	0.15 "	4	160	10,800	4,200,000	1062	81	8.0	929	18.1	1052	2.6	462	67.0	7,809	2.6	287	1000									
" 29	0.15 "	4	160	11,500	4,125,000	1060	84	8.0	929	18.1	1052	2.6	462	67.0	7,809	2.6	287	1000									
" 29	6.00 "	4	160	10,800	4,000,000	1059	77	4.0	497	16.2	2088	2.8	392	74.8	8,708	1.6	173	1000									
" 29	9.00 A.M.	4	160	10,800	4,000,000	1064	82	6.0	1636	78.6	2088	2.8	392	74.8	8,708	1.6	173	1000									
" 30	8.750	4	160	10,000	4,200,000	1064	88	6.0	1636	78.6	2088	2.8	392	74.8	8,708	1.6	173	1000									
" 30	4.00 "	4	160	18,000	4,100,000	1062	88	6.0	1636	78.6	2088	2.8	392	74.8	8,708	1.6	173	1000									
" 30	7.50 "	4	160	18,000	4,100,000	1064	84	6.0	1636	78.6	2088	2.8	392	74.8	8,708	1.6	173	1000									
" 30	4.00 "	4	160	10,600	4,100,000	1062	77	8.0	1636	78.6	2088	2.8	392	74.8	8,708	1.6	173	1000									
" 30	3.00 P.M.	4	160	10,600	4,600,000	1062	77	8.0	1636	78.6	2088	2.8	392	74.8	8,708	1.6	173	1000									
Apr. 2	4.30 "	6	160	12,000	4,840,000	1059	81	13.0	1709	9.7	1212	1.0	200	72.0	9,009	3.1	388	1000									

Immuned, after very severe conv.
 2 hours " " " "
 24 " " " "
 24 " " " "
 12 hours " " " "
 12 hours " " " "
 6 hours before light conv.
 25 min. " " " "
 Immuned, after light conv.
 4 1/2 hours later,

10 min. after severe conv.
 2 hours after severe conv.
 19 min. after second conv.
 11 hours after convulsion.

CONVULSIONS AND APOPLECTIFORM ATTACKS. Several times during the course of the examinations it was suspected that convulsions and apoplectic attacks might have an influence on the blood. Accordingly,

CHART I.

Showing the condition of the blood before and after convulsions of general paralysis in Case I.

CASE I. (For history see Case above.)

The temperature was taken after every attack and was never above 99°.

It is evident in studying this series of convulsions that the number of red corpuscles rises uniformly, if not greatly, at the occurrence of a seizure, and that it afterward diminishes as a rule.

The variation in the hæmoglobin is perhaps too small to give it much importance, but in two of three cases it rose slightly and always remained high for some time later.

The lack of agreement at various times in the results on specific gravity does not justify any definite conclusion.

A glance at Chart I. shows a well-marked leucocytosis after Convulsions I. and II., lasting many hours. They do not indicate, however, whether this augmentation takes place gradually or suddenly. Twenty-five minutes before Convulsion III. the leucocyte count was 10,500, being 13,500 afterward. This was a very light attack with but little increase. Preceding Convulsions IV. and V. the counts were low and rose abruptly at the seizure to 16,000 and 18,000, respectively. None of these were preceded by any leucocytosis; although it was present immediately afterward. In general terms the degree of leucocytosis corresponded to the severity and duration of the fit, being highest after the most severe and very slight after a light convulsion. The effect of a series of attacks is apparently to intensify the leucocytosis, as the highest count was the fourth of a succession of convulsions. Moreover, No. V. is greater than No. IV., notwithstanding that they were of similar intensity and duration.

A tendency is noticeable for the leucocytes to fall even below their usual number before an attack. Two hours after No. IV. the white corpuscles were low, while usually the leucocytosis persists for several hours. The explanation may lie in the fact that it preceded by one hour a second seizure, which again produced a leucocytosis.

Twenty-four hours before the above-mentioned convulsion there was a distinct rise in the white as well as the red corpuscles. On this evening, a long deferred attack was expected and indicated by his actions. No muscular spasm, however, was seen at this time. One naturally wonders whether this might not have been an abortion of an attack.

As would be expected, the polymorphonuclear element predominates, not, however, to the extent it does in the inflammatory leucocytoses; in fact, the increase is in the absolute count rather than in the percentage. Just before each attack they diminish and subsequently fall steadily. The rôle of the lymphocytes is peculiar. Previous to a convulsion, even many hours before, they decrease in number to become more numerous again at the time of onset; even then the absolute count rarely reaches and never surpasses the normal. Following the convulsion also they become subnormal again, and slowly recover their usual proportions.

Most remarkable of all is the action of the large mononuclears; unlike the polymorphonuclears their rise begins before and rapidly progresses until the attack, when the maximum is attained. The count preceding a seizure on an average was double the normal, although there was as yet no increase in the leucocytes as a whole; the number of large mononuclears just after the fit was over four times the normal, being in one case nearly 4000 in a c.mm. Subsequently they fell quite rapidly.

An interesting point is the inverse variation between the lymphocytes and large mononuclears. In proportion as the latter increase, the former diminish. The large mononuclears apparently multiply at the expense of the small mononuclears or lymphocytes. It should be added, however, that a great excess of large mononuclear cells remain unaccounted for in this way.

In every respect the transitional forms go hand in hand with the large mononuclears.

No change was observed in the eosinophiles before convulsions, nor immediately afterward, except perhaps a slight increase. Several hours following they had a tendency to become less numerous.

CASE XX.—W. B. R., aged forty-nine years, admitted March, 1892. Had felt nervous and run down for a year before coming to the hospital. Could not grasp simple problems. Gradually lack of judgment came on, delusions of grandeur, hallucinations. Pupils equal, do not respond to light. Knee-jerks absent. Dementia became pronounced. Speech thick and gait ataxic.

December 28. Had three convulsions this morning, involving chiefly the right side, with twitching of the eyelids, facial muscles, right arm and leg. Ten minutes after the last the blood was examined and the examination repeated at intervals for two days.

January 17. This morning had another apoplectic seizure, the convulsive twitchings lasting for two hours. During all this time there was a clonic spasm of the muscles and partial paralysis.

18th Swallows with difficulty. Only partially conscious. Pulse, respiration, and temperature rising.

19th. Rapidly failing. Temperature rising.

20th. Died at 8.40 A.M.

Autopsy. Leptomeningitis, granulations in ependyma, atrophy of the cortex, also a lobular consolidation in one lung, probably due to inhalation.

CASE XX.—APOPLECTIC ATTACKS.

Date.	Hour.	No. fields of white count.	No. erys red count.	White.	Red.	Sp. gr.	Hemo-globin.	Lympho-cytes.		Large mono-nuclears.		Transitional.		Neutrophile polymorpho-nuclear.		Eosinophiles.		No. leuco-cytes count.	Remarks.
								Fr. ct.	Abn. No. in 1 c.mm.	Fr. ct.	Abn. No. in 1 c.mm.	Fr. ct.	Abn. No. in 1 c.mm.	Fr. ct.	Abn. No. in 1 c.mm.	Fr. ct.	Abn. No. in 1 c.mm.		
Dec. 28	11.45 A.M.	4	160	15,500	4,248,000	1062	77	7.8	1209	12.3	1007	2.5	387	74.0	11,020	0.5	77	1000	Temp. 98.0°, 10 min. after attack.
" 28	3.45 P.M.	4	160	21,250	4,200,000	1068	83	1.7	391	4.5	656	1.0	213	92.8	10,720	0	0	1000	Temp. 99°, 4 hours after attack.
" 29	8.30 "	4	150	20,000	4,080,000	1064	94	2.7	540	5.0	1000	1.2	240	91.1	18,220	0	0	1000	Temp. 99°, 8½ hours after attack.
" 29	11.00 A.M.	5	100	17,200	3,810,000	1064	78	2.6	448	4.8	825	1.0	172	91.6	15,765	0	0	1000	Temp. 102.5° 23¼ hrs. after attack.
" 30	6.45 P.M.	5	150	13,200	3,746,000	1062	77	8.6	1135	7.5	000	2.4	316	81.0	10,750	0	0	1000	Temp. 100.0°, 2¼ days after attack.
Jan. 17	8.05 A.M.	4	150	23,000	4,624,000	1065	93	6.7	1276	21.0	4035	4.1	063	94.0	16,650	1.0	377	1000	Temp. 99.5°, 10 min. after attack began.
" 17	10.30 "	5	150	37,000	4,486,000	1058	80	2.0	740	13.9	6143	3.2	1184	90.8	29,805	0.1	38	1000	Temp. 100.0°, end of attack.
" 17	12.30 "	4	150	26,000	4,320,000	1064	88	3.2	832	9.2	2392	1.2	312	86.4	22,464	0	0	1000	Temp. 99°, 2 hours after end of attack.
" 17	5.50 P.M.	5	150	16,500	3,612,000	1062	83	2.5	412	6.5	1072	1.7	281	89.3	14,735	0	0	1000	Temp. 100°, 1½ hrs. after end of attack.
" 18	8.30 A.M.	4	150	12,000	4,240,000	1061	87	5.7	684	9.6	782	0.2	24	87.5	10,500	0	0	1000	Temp. 101.4°, 22 hours after end of attack.
" 19	1.00 "	6	150	8,000	3,740,000	1057	99	5.2	424	4.7	376	0.4	33	89.6	7,168	0	0	1000	Temp. 100°, 3½ hours after end of attack.
" 20	8.00 "	7	150	18,250	6,632,000	1076	116	7.3	1332	3.9	712	0.2	37	88.3	16,114	0.3	55	1000	Temp. 101.2°, nearly 2 days after end of attack.

1 Several neutrophile mononuclear cells. 2 12.0 per cent. of neutrophile mononuclear cells. 3 11 per cent. of neutrophile mononuclear cells.

Both of these seizures were apoplectiform in nature, characterized by muscular twitchings, partial paralysis, some temperature throughout, and prolonged unconsciousness. The first lasted over ten minutes, from

CHART III.

Showing the changes in the blood during and after two apoplectic attacks in general paralysis, Case XX.

the effects of which he was in bed two days with little temperature. The second attack continued for two hours, from which he never entirely recovered consciousness, and died. Unfortunately it was not possible to examine the blood before the onset. But in the two-hour attack a

with a view of getting light on the subject, Case I. was selected for the purpose, because his convulsive seizures were frequent and came with more regularity than is usual. Not much difficulty was experienced in securing the blood immediately after a seizure, but it was quite different with the specimen preceding an attack, on account of the uncertainty of the onset. Since the ante-convulsive examination is quite as important

CHART II.

Showing the absolute number of the different varieties of leucocytes before and after convulsions in Case I.

as the post-convulsive, an effort was made to learn the condition of the blood just before the spasm as well as after. This was done in the following manner: beginning at a time when an attack was expected, examinations were made continuously at about four hour intervals until it occurred. Thus the blood was secured three hours before Convulsion IV. and one hour before Convulsion V. We were fortunate in getting a specimen only twenty-five minutes previous to Convulsion III.

specimen was obtained at the beginning and at the end, thus throwing some light on changes occurring during the seizure.

Both attacks were followed by a diminution in the red corpuscles that did not soon disappear.

The hæmoglobin sustained only a slight reduction during the long attack, which tended to continue for some time afterward.

The specific gravity fell during the progress of the attack and later rose again.

In contradistinction from this general lowering of blood-values, the white corpuscles were enormously augmented during the attack. In one instance the leucocytosis began to fall immediately after the seizure, and gradually disappeared; whereas in the other the maximum was not reached until four hours after the spasm had ceased. The highest count was obtained at the termination of the more severe attack, when it amounted to 37,000.

The temperature cannot be considered as a factor in leucocytosis. It has been shown by Carter,¹ Winternitz, and others that fever in itself will not produce leucocytosis. Moreover, in this case no correspondence whatever exists between the height of the temperature and the degree of leucocytosis, since the lowest count was present at the time of the highest fever. The influence of the inhalation-pneumonia, which was most likely contracted a short time before death, cannot be held responsible for the leucocytosis, as will be shown in the discussion of the differential count.

At the last examination, thirty minutes before death, it will be observed that the red and white corpuscles, specific gravity, and hæmoglobin all attained an unusual height. The face was cyanosed, breathing difficult and stertorous, and the whole appearance that of a dying man. This increase in white cells has been described by Rieder² and Litten³ under the name of "premortal" or "agonal" leucocytosis. They found it fairly constant and dependent in its intensity upon the duration of the agony.

The polymorphonuclear cells were almost doubled in number during the prolonged attack, while subsequently they either fell gradually or attained a maximum a few hours later and then diminished.

The lymphocytes were subnormal at the beginning of the attack and fell still lower at its termination, notwithstanding the leucocytosis was greater. Their number underwent even further depletion in the hours following, the absolute count being only one-third to one-quarter of the normal. Restoration to the normal took place more slowly in the lymphocytes than in any other element.

¹ University Medical Magazine, December, 1894, p. 159.

² Loc cit. p. 104.

³ "Zur Pathologie des Blutes." Berlin. klin. Wochens., 1883, p. 27.

The influence of the long attack on the eosinophiles was to reduce their number exceedingly, while in slides taken several hours afterward none at all were present.

When the seizure had just begun there was a decided increase in the large mononuclears, which became even greater at its termination, amounting to over 5000 in a c.mm. in one instance. The return to the normal was comparatively rapid. What has been said of the large mononuclear is true also of the transitional cells.

a, Lymphocyte; b, large mononuclear; c, polymorphonuclear neutrophil; d, mononuclear neutrophil.

A striking feature of the stained preparations was the variation in the character of the large mononuclear cells at different times. Soon after an attack cells with a small, round, deeply staining nucleus like that of a lymphocyte, but with a large body of clear protoplasm, predominated. Several hours later larger cells with irregular, faintly staining nuclei, that almost filled the cell-body, made up the prevailing type.

More particularly do we wish to call attention to a variety of cell that was present in this patient alone, namely, a cell as large or larger

than the polymorphonuclear neutrophile, with a round or ovoid nucleus, deeply stained, and having a protoplasm thickly sprinkled with neutrophilic granules. These neutrophile mononuclear cells first appeared twenty-two hours after the last prolonged attack and forty-eight hours before death, but only a few were found at this time. At the next examination, thirty-one and one-half hours before death, they constituted 12.6 per cent. of the total number of leucocytes, although those cells having much irregularity or a distinct indentation of the nucleus, were not included in this class. The absolute number in n c.mm. was 1008. Finally, in the last specimen, obtained thirty minutes before death, the total number reached 2000 in a leucocytosis of 18,250.

The origin and nature of these cells are somewhat obscure. They certainly come under the definition of myelocytes, since granulations are as distinct and as abundant in them as in the polymorphonuclear neutrophiles, but it does not follow that they arise from the bone-marrow.

A much simpler explanation presents itself. It is now quite commonly accepted as probable, if not proved, that all the varieties of the leucocytes, excepting, perhaps, the eosinophiles, are but different forms in the growth of the leucocytes. As Ouskow¹ claims, it is likely that the lymphocyte is the youngest cell, and that by the growth of its nucleus and protoplasm it becomes a large mononuclear; this, in turn, by a change in the shape of its nucleus and by a granulation of the protoplasm, passes through the transitional form into the polymorphonuclear neutrophile cell. Physiologically in the evolution of the large mononuclear into the polymorphonuclear neutrophile the nucleus becomes irregular and polymorphous *before* the granulation is well marked. Now in this specimen (see illustration) every stage of this nuclear change can be followed from the perfectly round or ovoid or slightly indented forms to the typical horseshoe nucleus, in all of which the granules are equally distinct and numerous. Why, then, is it not easier to explain these unusual forms by supposing that the granulation, process has preceded the changes in the nucleus instead of appearing subsequently?

These cells might have been due to the apoplectic attack itself or to the influence of the death-agony. If the former were true, we should expect that such cells would have been found in his first attack, which was not the case. We have been able to get a stained specimen in one other case three hours prior to death, but no abnormal leucocytes were present. It should be added, however, that the cyanosis and dyspnoea so pronounced in Case XX. were absent in this patient. The cause for the presence of these cells cannot be assigned.

¹ Loc. cit.

GENERAL CONCLUSIONS.

GENERAL PARALYSIS. 1. The hæmoglobin and red corpuscles are always diminished.

2. The specific gravity falls slightly below the normal.

3. Most cases show a slight leucocytosis, amounting on an average to about 22 per cent. above the normal. Early cases may have no leucocytosis whatever.

4. In the differential count a decrease is found in the lymphocytes along with a marked increase in the large mononuclear cells. The eosinophiles in a few cases are very numerous.

CONVULSIONS AND APOPLECTIFORM ATTACKS. 1. The red corpuscles and hæmoglobin are usually increased at the time of a convulsion. During an apoplectic attack of long duration they are both somewhat diminished.

2. The specific gravity is variable, sometimes increasing, sometimes diminishing, at the time of an attack.

3. There is a leucocytosis after convulsions and apoplectic attacks which is as sudden as it is usually pronounced. It certainly does not appear until within a very short time preceding the convulsion, probably not before it actually takes place.

4. The degree of leucocytosis and the period of its continuance, as a rule, vary directly with the length and severity of the attack.

5. In the production of the leucocytosis the large mononuclear cells are increased relatively more than any other variety.

6. The fact that after convulsions and apoplectic attacks in general paralysis there is not only an increase in the number of white cells, but a change in their character, as shown by the differential count, and that abnormal cells appear, is an argument against the theory that leucocytosis is merely a change in the distribution of the white corpuscles.

I wish to take this opportunity of thanking Dr. Cowles and Dr. Hoch for their assistance, and especially to acknowledge my indebtedness to Dr. Hibbard for aid in the bibliography.