THE HÆMATOLOGY OF CONVULSIONS.

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THE theme of this essay is not new. It is humbly suggested that the method involved in it, while not original, is not usual. We have employed no original technique and formulated no new doctrine. We claim to have approached the subject in the appropriate, inevitably laborious fashion.

The tendency of modern medicine is towards group research, an inevitable sequel of the transference of its spiritual home from the temple of Æsculapius to the medical counterpart of the Woolworth Building. Group research is an admirable technique when applied to unchangeable norms. It must inevitably attain considerable employment at present, since our knowledge of the individual variations composed by personality is so meagre. One must insist, however, that in epilepsy it is misapplied. Whatever the reaction investigated, it is easy to find innumerable examples of a group of 50, or 100, epileptic beings, submitted to some particular test, on some particular occasion, and either recovering from, anticipating, or actually in the throes of convulsions. These are the most salient features of epilepsy. There is a multiplicity of precipitating factors. This must inevitably be so, since the best opinion avers that epilepsy is less a disease than a response on a lower teleological plane. We are therefore dealing not with a fixed condition, but with vastly varying personality types, with the incidence of convulsions as possibly their only common principal characteristic. It may even be that blood changes previously described in epilepsy are due less to some fixed pathological tendency on the part of the individual concerned than to the transient cumulative dyscrasia which manifests itself in the convulsion. It is for this reason that our title has been so circumspectly chosen.

Besides the general principles outlined above, epileptics are particularly unsuited to group research for other reasons. The multiple causation indicates the great variability of epileptic types. Epilepsy may or may not be associated with considerable biological abnormalities of structure and function. Most important of all, the great variation in the incidence of convulsions is a bar to efficient sub-grouping. An epileptic, in his convulsive phenomena, may present an almost mechanical precision, but where such a state of affairs exists, the subject is a law to himself and it may be impossible, for comparative purposes, to find his counterpart.

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We therefore confined ourselves to a small group of subjects and studied their hæmatological findings from day to day. We thought it wiser not to limit our procuring of the samples of blood to any particular time of the day, our subjects not being such as presented any considerable regularity in the production of their convulsions, besides which it was advisable, where possible, to take samples as near to the time of the fit as could be managed. Furthermore, over a long period of time, the taking of samples day by day, but at irregular times, is much more likely to provide us with information as to the blood changes concomitant with the occurrence of convulsions, when these occur at irregular and, as was the case in the patients here considered, unpredictable intervals.

Most important of all, in inducing us to concentrate our efforts from day to day, on a limited number of patients, is the fact that the most scientific of the recent researches performed on the cell-contents of the blood indicate how fluctuating, in the same person at different times of the day, are the numbers of the blood cellular elements. We are referring in particular to the work of Sabin and Cunningham in America, and that of Bernard Shaw in England. The latter's article establishes the prevalence of daily mass fluctuations in the leucocyte count. This being so in normal individuals, it is of special importance in epileptics in whom it is recognized that, whatever their nature, considerable changes in the hæmatological indices do occur in relation to the seizures. It is therefore essential that this should be allowed for in assessing variation in epileptics, and that its presence be particularly sought for. Furthermore, we consider that the methods of Shaw are, wholly apart from any practical result he may have obtained, a model of what hæmatological research should be.

Literature.

We do not propose to deal at any great length with the literature on the subject of the blood changes in epilepsy. The very variability of the results obtained precludes this, though the statement that the seizure was preceded by a leucopenia and followed by a leucocytosis has been considered so much in the nature of a classical observation as actually to have been employed in the argument that the epileptic disturbance is an anaphylactic problem. Possibly so much discrepancy in the voluminous literature has resulted from the very misconceptions we have hinted at in the last section. At the cost of making this essay fatiguing by too constant reiteration, it must be emphasized that we are trying to seek some change in the blood concomitant with the incidence of convulsions, and that where these latter are precipitated by such a divergence of causes it is to be expected that the effects will likewise vary. We therefore propose to outline the hæmatological biography of a few epileptics from day to day. We are prepared to find no constancy in the results, but

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we hope to show that there are undoubted effects of convulsions reflected in the blood-counts of the individual, and endeavour to outline their nature. As for the obtaining of results which will be axiomatic for epilepsy as a whole, it seems to us that the very expectation of common denominations in such a condition may be unscientific, seeing that epilepsy is not a disease, but an innate hinterland of personality which may or may not achieve the foreground conspicuousness of disease.

Patterson and Weingrow comment on the variability of the leucocyte count, indicating a leucocytosis in most cases, for which the lymphocytes were mostly responsible. They found no relation between the leucocytosis and the convulsion. Their research has the defects of the group system. Kroumbmiller said the convulsion was associated with a leucocytosis which reached its maximum an hour after the attack, and that a few hours afterwards the eosinophil count increased. Pugh conducted an investigation of the blood changes in epilepsy, involving several factors. Unfortunately the excellent regime of day to day counts which he employed in estimating the alkalinity of the blood was not maintained in dealing with the leucocyte count. His general conclusions suggest that in the majority of cases a drop in the leucocyte count precedes the paroxysm, and that afterwards there is a leucocytosis, the greatest factor involved being the lymphocytes. He, too, postulates a delayed eosinophilia. Ostmann concurs with these views. Onuf and Lograsso conducted an excellent regime of daily counts on two epileptics. The most definite result was the variability in the leucocyte count. As to its relation to the paroxysms, opposite results were obtained in both cases. An interesting fact is that, though this investigation occurred as far back as 1906, something in the nature of an afternoon tide of leucocytes was observed, thereby antedating Sabin and Cunningham's work by some years. Spangler points out the great variability in the white cell-count when the attacks are occurring. Wuth regards a leucocytosis and an eosinopenia as the commonest findings associated with convulsions, but says that they are not always uniform in the same or different individuals, and that they are not specific for the convulsive reaction, being inducible by physical exertion. A valuable feature of Wuth's paper is his classification of results obtained by different authors for the periods before, during and after fits. The general inference is that white-cell elements increase with, and following the fit. Their exact nature is not clearly specified.

Most investigators are concerned merely with blood changes in association with fits, but do not clearly distinguish between the periods, before, during and after fits. The most general conclusion to be derived is that there is a leucocytosis in relation to the fit. This statement seems remarkably bald. Anything more specific would seem unscientific.

In the past less attention has been paid to the erythrocytes than to the white-cell elements. Macphail, Smyth, Pearce and Boston and South point

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out a tendency to lowering of the hæmoglobin percentage, while Féré described an increase in the red cells in seizures, an increase with which the hæmoglobin did not keep pace. Ostmann found an increase in red cells during fits.

It is unfortunate that the red-cell and hæmoglobin counts have not attracted more attention. This is strange in view of the widely extant opinion that there is a direct connection between deficient oxygenation, such as might accrue from a deficiency of red-cell elements, and convulsive phenomena, of which the production of fits by hyperpnœa is only one example.

Material of the Thesis.

Ten cases were chosen. These included two non-epileptic controls. In some cases a complete blood-count, comprising the number of red-cells, the hæmoglobin content, the number of white cells, and a differential white count was performed. The white count involved the assesment of the polymorphs, lymphocytes, eosinophils, large mononuclears and mast cells. In other cases the elements calculated were somewhat different. These factors are outlined in Table I.

Table I.

Subject.	Period of research.	Number of counts made.	Fits.	Red cell-count.	Hæmo-globin.	Total white count.	Poly-morphs.	Lympho-cytes.	Eosino-phils.	Mono-nuclears.	Mast cells.
Cont. 1	39 days	30	..	No	No	Yes	Yes	Yes	Yes	Yes	Yes
„ 2	..	28	..	„	„	„	„	„	„	„	„
No. 3	21 days	4	14	Yes	Yes	„	„	„	„	„	„
„ 4	64 „	17	67	„	„	„	„	„	„	„	„
„ 5	24 „	8	13	„	„	„	„	„	„	„	„
„ 6	23 „	15	12	„	„	„	„	„	„	„	„
„ 7	60 „	48	12	„	„	„	„	„	„	„	„
„ 8	38 „	32	5	No	No	No	„	„	„	„	„
„ 9	50 „	36	3	„	„	„	„	„	„	„	„
„ 10	27 „	27	28	„	„	Yes	„	„	„	„	„

Technique.

Red cells.—Leitz hæmocytometer pipettes, with an error guaranteed not more than 2·5%, were used in conjunction with a Thoma-Hawksley counting chamber. The patient's blood was diluted 1 in 200 with Hayem's fluid and two counts of 100 squares were made, the chamber being freshly charged for each count, the maximum error allowed for these counts was 3%, that is, if either count varied by more than 3% a third or fourth preparation was made until two counts were found to be within the prescribed error.

Hæmoglobin.—Estimated by the colorimetric method, using Newcomer's

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standard disc. For conversion into %, 15·6 grm. were taken as equivalent to 100%.

White cells.—Leitz pipettes, with an error of not more than 2·5%, were used, and the patient's blood diluted 1 in 20 with 5% acetic acid coloured with gentian violet. A single count of 160 small squares was made in a Fuchs-Rosenthal counting chamber.

Differential count.—Smears for the differential count were made on cover-glasses, and stained by Leishman's method; 200 cells were counted, 100 on each cover-glass.

(For details of technique see "Alleged Hæmoclasia in the Insane", by Dr. T. D. Power and A. W. Pettit, *Journ. Ment. Sci.*, January, 1932.)

Results.

The interpretation of the results obtained is a matter of very great difficulty. A study of the charts appended will convince one that there is a definite hæmocytic variation with the incidence of the convulsions. It is not, however, uniform in tendency in all cases, which seems to indicate, at the outset, the truth of our early contention, that there are characteristic pathological variation for epileptics, but not for epilepsy. We tried to construct graphs secondary to those printed here, in which we might derive average blood variations as occurring at average periods from the time of the convulsions, but it seemed illogical and unscientific where so much variation in individual cases was obvious at first sight, to calculate average values where these might have no strict justification. We could find no more satisfactory method than the laborious interpretation of each chart in turn, but before embarking on this it is as well to point out that there are certain unescapable general conclusions that can be drawn from a mathematical summary of each graph.

We will now proceed to the interpretation of each of the charts in turn.

Chart 1: *E. G*— (*Control*).

Period 39 days; blood-counts 30.

White cells oscillate between 5,000 and 8,000, the greatest variation being a drop from 8,000 to 6,000.

Polymorphs oscillate between 54% and 63%, the greatest variation between two counts being 8%, from 63% to 55%. The average is 58·2%.

Lymphocytes oscillate between 31% and 42%, the greatest variation between two counts being 7%, from 32·5% to 39·5%. The average is 37·5%.

Eosinophils are present throughout. They vary between 0·5% and 3·5%. The average is 1·71%.

Large mononuclears are present on all but one occasion. They vary between 0·5% and 4%. The average is 2·27%.

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Mast cells are present on 14 occasions. They vary between 0·5% and 1%, the average being 0·75%.

The graph cannot give evidence of an a.m. and p.m. tide. Yet even though the counts were all taken in the early morning there is a considerable variation. The count is high on the 6th, 9th, 14th, 17th and 22nd days. There seems to be a 3- or 4-day periodicity in these elevations. In between these high-count periods the number of leucocytes seems to rise more or less evenly. The highest rise is from the 4th to the 6th day, being 2,200.

The polymorphs fluctuate about the 60% level. The variability of the lymphocytes is greater. The elements of smaller incidence, mast cells, large mononuclears and eosinophils, show variations more appreciable than would appear at first in view of their usual small incidence.

Chart 2: J. G— (Control).

Period 35 days; blood-counts 28.

White cells oscillate between 4,900 and 8,120. The greatest variation between two counts is a rise from 5,000 to 8,000.

Polymorphs oscillate between 55·5% and 74%. The greatest variation between two counts is 17%, being a rise from 55·5% to 72·5%. The average is 65·5%.

Lymphocytes oscillate between 23% and 38%. The greatest variation between two counts is 14·5%, being a fall from 38% to 23·5%. The average is 30·6%.

Eosinophils are present on 25 occasions. They vary between 1% and 5·5%. The average is 2·1%.

Large mononuclears are present throughout. They vary between 1% and 3·5%. The average is 2·1%.

Mast cells are present on 21 occasions. They vary between 0·5% and 2%. The average is 0·8%.

The white cells show a greater variability than in Case 1. The five highest counts recorded in the series occurred in the afternoon. There is a tendency for the lower counts to be those taken in the morning. Again the lymphocytes seem the most varying factor, their range of oscillation being 15% as compared with 18·6% for the leucocytes, which is more considerable seeing how much smaller a proportion of the total white cell count the lymphocytes normally supply.

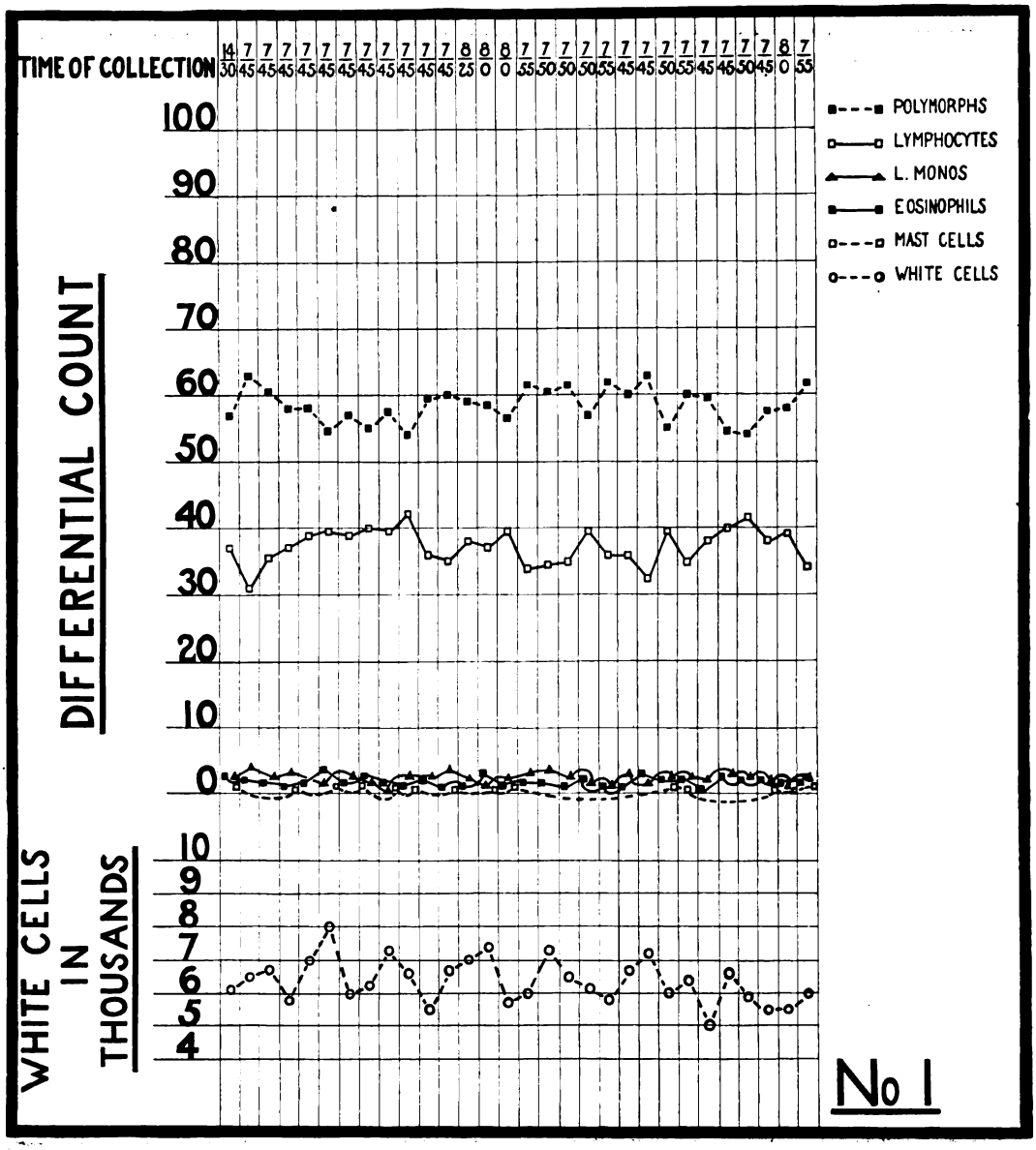
Chart 3: F. S—.

Period 21 days; blood-count 4; fits 14.

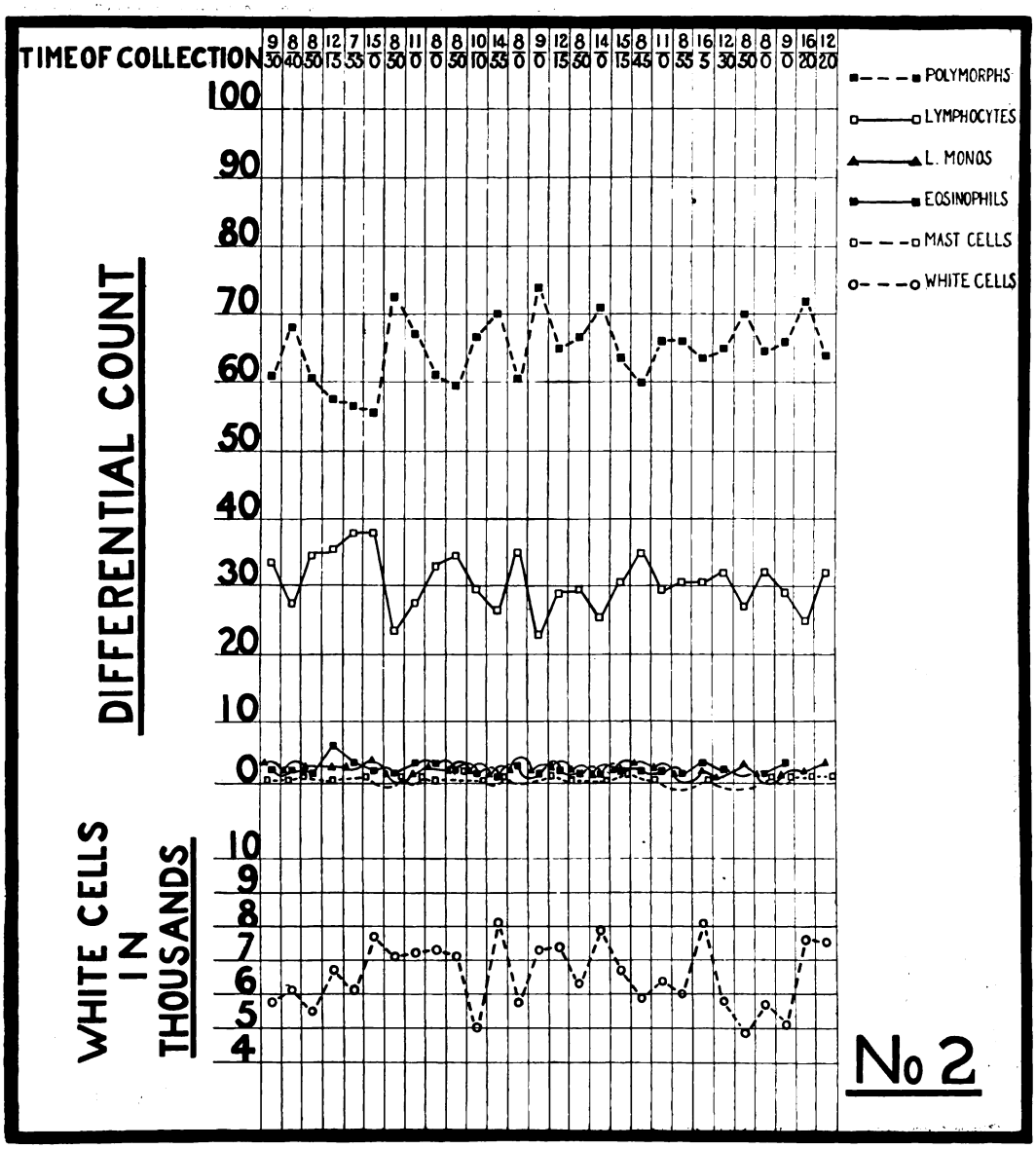
Red cells oscillate between 4,900,000 and 5,300,000.

White cells oscillate between 9,000 and 13,300.

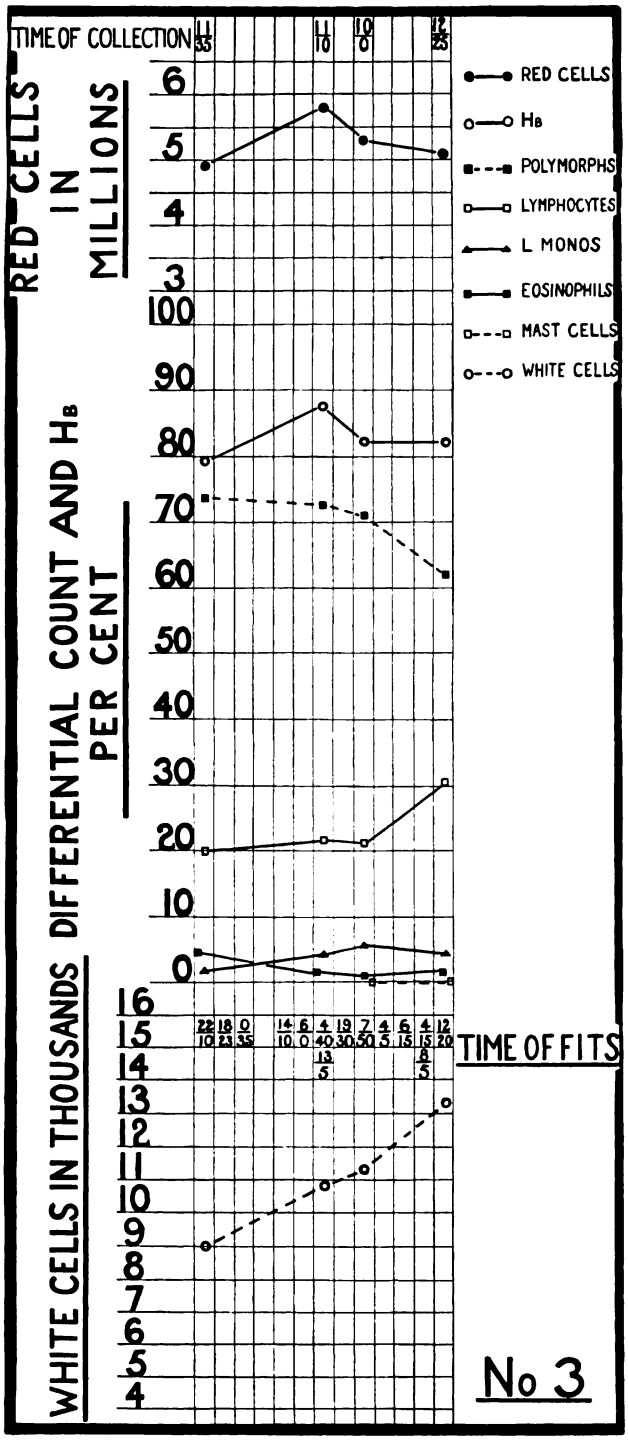
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Polymorhps oscillate between 62% and 73·5%. The average is 72%. The greatest variation between two counts occurs during a fit, being a decrease of 9%.

Lymphocytes oscillate between 20% and 32·5%. The average is 23·2%. The greatest variation, 9·5%, during fit.

Eosinophils oscillate between 1% and 4·5%. The average is 2·1%. They are present on each occasion.

Large mononuclears are present throughout. They oscillate between 2% and 5·5%. The average is 4%.

Mast cells are present on two occasions, 0·5% on each occasion.

During fit: Maximum white cells, maximum lymphocytes, minimum polymorphs.

A study of the chart will show that the more closely the time of collection approximates to a fit the higher is the leucocytic count.

Where the blood was collected five minutes after a fit (see right extremity of Chart 3) the polymorphs exhibited unmistakably their lowest, and the lymphocytes their highest value.

The data pertaining to the other white cells are inadequate for scientific deduction.

The interesting feature of this chart is the close correlation of the total red cell and hæmoglobin curves. The second count, taken at 11.10, i.e., 2 hours before seizure at 13.5, shows a rising value in each of these factors. The count taken immediately subsequent to a fit shows the lowest recorded figure for each.

Chart 4: *W. B*—.

Period 64 days; blood-counts 17; fits 67.

Red cells oscillate between 3,500,000 and 4,550,000.

White cells oscillate between 9,700 and 19,000.

Polymorphs oscillate between 70·5% and 85%. The greatest variation between two counts is 10% from 85% to 75%. The average is 77%.

Lymphocytes oscillate between 11·5 and 24%. The greatest variation is 8%, from 24% to 16%. The average is 15·8%.

Eosinophils are present throughout. They oscillate between 0·5% and 5%. The average is 1·78%.

Large mononuclears are present on all but one occasion. They oscillate between 2% and 10%. The average is 4·92%.

Mast cells are present on 6 occasions only. The average is 0·75%.

This case considered in relation to that preceeding well illustrates the futility of attempting to derive any comparative standard common to all the cases, by working out average counts at average times before and after fits. A given interval before or after fits must obviously, because of their very number, have a different significance in this case than in the preceeding one. Indeed,

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in the case of the total white cells, it cannot be found that there is any relationship between the blood-count and the occurrence of any particular convulsion, when the whole group is being considered.

A study of the curve for the whole period reveals that, during the time when the convulsions are of the greatest incidence, in the middle portion of the graph, there is a tendency for the total white cell-count to be at its lowest. On the other hand, the first count taken was coincident with a fit and showed the figure 16,400, and the last count, some two hours odd before a couple of fits, shows a count of 15,900.

The variations in the white cell elements are irregular, though an increase in the white cell-count in connection with the convulsions, seems most dependent on the lymphocytes. It is of interest that the highest eosinophilia recorded was on a day free from fits, following a convulsion at 10.25 the previous evening.

During a three days' remission following the period of maximal fit-incidence, the total red blood-count shows the sudden considerable drop of 2,000,000. During the few days previous to this depression the hæmoglobin curve steadily rose. The hæmoglobin percentage is lowest in the centre of the chart, i.e., corresponding with the maximum fit-incidence.

Chart 5 : *J. H—.*

Period 24 days ; blood-counts 8 ; fits 13.

Red cells oscillate between 4,500,000 and 5,800,000.

White cells oscillate between 6,000 and 17,500, the greatest variation being a rise of 7,000, from 10,500 and 17,500. This occurred at 9 a.m. the previous fit being at 5 p.m. on the evening of the day before.

Polymorphs oscillate between 55·5 and 78%, the greatest variation between two counts being 12%, from 67·5% to 55·5%. This latter was present one hour before a fit. The average is 71·5%.

Lymphocytes oscillate between 16·5% and 39%, the greatest variation between two counts being a rise of 13%, from 26% to 39%. The average is 22·8%.

Eosinophils are present throughout. The average is 13·1%.

Large mononuclears are present throughout. The average is 4·1%.

Mast cells are present on one occasion only, 0·5%.

This case is interesting because the maximal and minimal white-cell values both occurred on a day on which there were no convulsions.

The first count, taken fifteen minutes after a fit, is 11,500. This is the most proximal count obtained. Of more significance, perhaps, is the fact that the period of highest fit-incidence, on the first to the third days, is associated with a low white count. There is, then, a rising white count, extending to the seventh day. On the 18th day of the experiment, at 12 noon, there is an elevated count of 14,000, following a fit at 4.15 the previous evening. The maximum

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variation in the leucocytes is a rise from the 22nd to the 23rd day, following a fit on the former evening. The indications here are that there is a leucocytosis following seizures.

This leucocytosis is due mainly to the lymphocytes. The less common white cell elements reveal no indubitable finding.

On the whole the excursions of the red cells and the hæmoglobin are generally similar. The highest elevations of each occur six and a half hours before a fit. The next highest excursion of each occur on days when there are no fits. The variations of the hæmoglobin percentage are more considerable than those of the red cells.

Chart 6 : *L. C—.*

Period 23 days ; blood-counts 15 ; fits 12.

Red cells oscillate between 3,700,000 and 4,700,000.

White cells oscillate between 4,400 and 12,500, the greatest variation being a rise of 6,000 from 6,500 to 12,500. The patient had a fit between these counts being made. The 12,500 count was collected ten hours after the fit.

Polymorphs oscillate between 58·5% and 75·5%, the greatest variation between two counts being a drop of 13%, from 75·5% to 62·5%. The first count was collected at 14.20 and the second twenty hours later. During this period the patient had three fits, the last one being eight hours before the count was collected. Average 68·2%.

Lymphocytes oscillate between 17·5% and 34%, the greatest variation between two counts being a rise of 11%, from 17·5% to 28·5%, at the same time as the 13% drop occurred in the polymorphs. Average 25·33%.

Eosinophils are present throughout. Average 1·5%.

Large mononuclears are present throughout. Average 3·9%.

Mast cells are present on all but two occasions. Average 0·96%.

This case was one in which fits were infrequent, though at the time of the test she was having more than usual. The highest count, 12,500, occurred ten minutes after a fit. The difference between this count and the one preceding it, represents the maximum rise shown by this patient. The previous count was taken twelve hours after a seizure.

This elevation mainly involved the polymorphs. The greatest variation in the polymorphs was observed from the 2nd to the 3rd day of the experiment, when the count varied between 75·5% and 62·5%. During this time three fits occurred. The last of these was eight hours before the next count. It appears as though the fit is accompanied by a leucocytosis, soon after which there is a leucopenia.

Of the less frequently occurring elements the eosinophils reached their maximum value in the count taken ten minutes after a fit.

The red count was irregularly variable.

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The hæmoglobin percentage showed its lowest value in the count immediately succeeding the fit. There was a tendency for the highest hæmoglobin percentage to occur in the period free from fits.

Chart 7: *R. T—.*

Period 60 days; blood-counts 48; fits 12.

Red cells oscillate between 3,800,000 and 5,900,000.

White cells oscillate between 4,700 and 11,000, the greatest variations between two counts being a drop of 4,600 from 11,000 to 6,400, twenty-two hours after a fit.

Polymorphs oscillate between 49·5% and 82%, the greatest variation between two counts being a drop of 25·5% during a fit, from 75% to 49·5%. The average is 66·9%.

Lymphocytes oscillate between 13·5% and 45%, the greatest variation between two counts being a rise of 24% during a fit, from 21% to 45%. The average is 27·89%.

Eosinophils are present in 38 counts. Average 1·55%.

Large mononuclears are present throughout. They oscillate between 0·5% and 8%. The average is 3·58%.

Mast cells are present on thirty occasions. Average 0·75%.

On the 14th day of the test a sample taken five minutes after a fit revealed the highest leucocyte count, the increase mainly affecting the lymphocytes, the polymorphs being correspondingly decreased. The maximum variation in the white cell count occurs between this count and the one taken twenty-two hours later. On the other hand, a count taken one hour and twenty minutes after a fit on the 30th day of the experiment gave a low figure, 7,600. Where the fits occurred in the early morning counts taken seven to eleven hours afterwards yielded low figures. More significant than the relation of any individual count to a seizure is the fact that during the non-fit period, from the 30th to the 43rd day, the white cell count remained low.

The increase in white cells, on the above mentioned 14th day, involved an elevation of the lymphocytes, and a compensatory depression of the polymorphs.

There is a definite elevation of the large mononuclears with the fit on the 14th day. These cells show, in addition, conspicuous variations which seem independent of the occurrence of convulsions. The eosinophils vary more than normally; their maximum variations occur in non-convulsive intervals.

The red cell-count shows a steep descent on the occasion of the count five minutes after a fit. The curve of the hæmoglobin percentage reflects accurately that of the erythrocytes. There are considerable variations in these two curves independent of the occurrence of convulsions. On the other hand, their least varying period is that between the 33rd and 46th days, during which time there were no seizures.

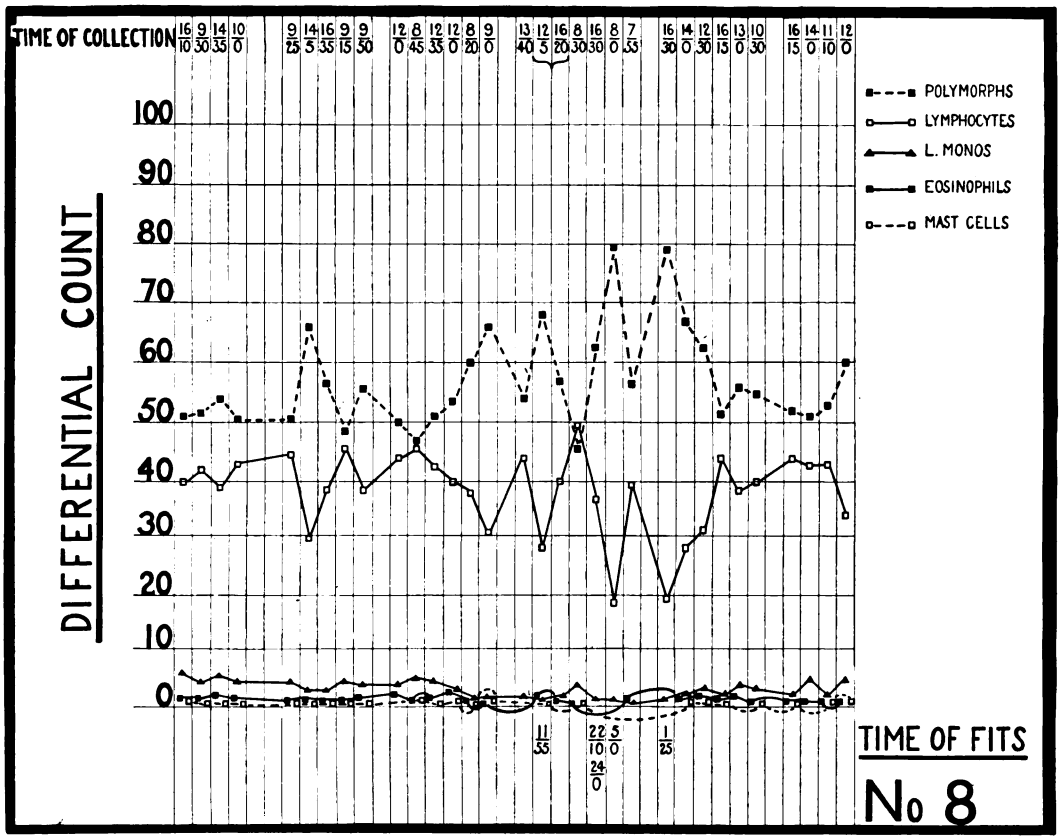
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Chart 8 : *G. D—.*

Period 38 days ; blood-counts 32 ; fits 5.

Period of Fits 5 *Days.*

Polymorphs oscillate between 45·5% and 79·5%. The greatest variation between two counts is 23%, from 56·5% to 79·5%. The average is 64·3%.



Lymphocytes oscillate between 19% and 49·5%. The greatest variation between two counts is 20%, from 19% to 39%. The average is 32·4%.

Eosinophils are present on six occasions. They oscillate between 0·5% and 2%. The average is 1·3%.

Large mononuclears are present throughout. They oscillate between 1% and 3·5%. The average is 1·93%.

Mast cells were present on four occasions. The average is 0·87%.

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Period of Quiescence, 24 Days.

Polymorphs oscillate between 47% and 66%. The greatest variation between two counts is 15·5%, from 50·5% to 66%. The average is 54·46%.

Lymphocytes oscillate between 29·5% and 45·5%. The greatest variation between two counts is 15%, from 29·5% to 44·5%. The average is 39·97%.

Eosinophils were present on twenty-three occasions. They oscillate between 9·5% and 2%. The average is 1·36%.

Large mononuclears were present throughout. They oscillate between 2% and 6%. The average is 3·7%.

Mast cells were present on twenty occasions. The average is 0·67%.

Cases 8, 9 and 10 differ from those previously considered in that the fit incidence is less frequent.

There are far greater oscillations in the polymorphs and lymphocytes during the fit periods than at other times.

Chart 8.—On the 21st day the polymorphs were highest ten minutes after a fit; four and a quarter hours later they had dropped by 11% and next morning by 23%. On the 23rd day a count taken five hours forty minutes before a fit showed them to be rising. On the 24th day a count taken three hours after the last fit of the group showed the maximum score of 79·5%, whereas a count on the 25th, a fit-free day, showed a steep drop to 56·5%. A further fit on the 27th is associated with a rise to 79%, even though the count was made more than eighteen hours afterwards.

These polymorph elevations associated with fits are accompanied by depressions in the lymphocyte count.

On the 21st day the eosinophils were raised, with the polymorphs, ten minutes after the fit. Throughout the test the eosinophil variation was not much marked. The large mononuclears are more valuable. There is a tendency for them to be lowest at the time the fits occur.

Chart 9: *W. S—.*

Period 50 days; blood-counts 36; fits 3.

Period of Fits, 14 Days.

Polymorphs oscillate between 57·5% and 89·5%, the greatest variation between two counts being a rise of 32% two hours after a fit, from 57·5% to 89·5%. The average is 76·9%.

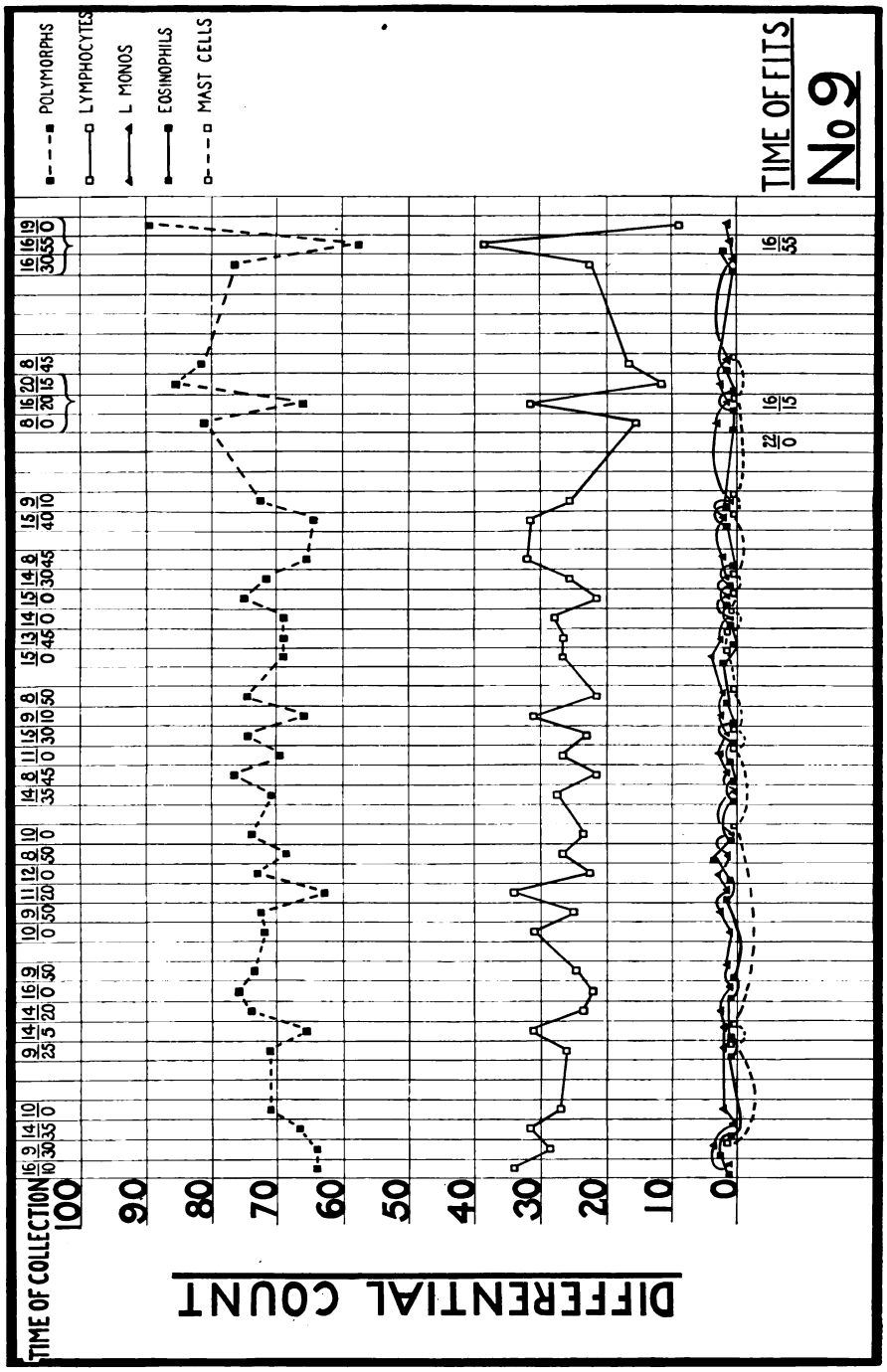
Lymphocytes oscillate between 19% and 48·5%, the greatest variation being a drop of 29·5%, from 48·5 to 19% two hours after a fit. The average is 20·7%.

Eosinophils are present on all but two occasions. The average is 0·9%.

Large mononuclears are present throughout. The average is 1·64%.

Mast cells are present on four occasions only. The average is 0·5%.

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Period of Quiescence, 36 Days.

Polymorphs oscillate between 63% and 76·5%. The greatest variation between two counts is 10%, from 63% to 73%. The average is 70·22%.

Lymphocytes oscillate between 21·5% and 34%. The greatest variation between two counts is 11·5%, being a drop from 34% to 22·5%. The average is 26·8%.

Eosinophils are present on 25 occasions. The average is 1·18%.

Large mononuclears are present throughout. The average is 1·8%.

Mast cells are present on fourteen occasions. The average is 0·78%.

Again the maximum oscillations in the chief white-cell elements occur in relation to the fits.

This chart is of considerable interest when compared with the previous one. A count taken on the 39th day of the test, five minutes after a fit, showed the polymorphs to be low (and the lymphocytes correspondingly raised). Counts taken eight hours before the fit and four hours after the fit showed the polymorphs to be raised again, the lymphocytes showing a complimentary distribution.

This finding is confirmed by the occurrence on the 44th day of a further lowering of the polymorphs at the time of a fit, with their elevation in counts taken twenty-five minutes and two hours fifteen minutes after the fits.

During the long period in which there were no fits there were less considerable fluctuations in the polymorphonuclear and lymphocytic counts.

The eosinophils remained steady on the 39th day, but rose from 0·5% to 2% with the fit on the 46th day.

On the 39th day the large mononuclears dropped with the polymorphs at the time of the fit.

Chart 10: *R. U—.*

Period 27 days; blood-counts 27; fits 28.

White cells oscillate between 5,700 and 20,300, the greatest variation being a rise of 9,500.

Polymorphs oscillate between 53% and 84·5%, the greatest variation being a rise two hours after a fit, of 26%, from 53% to 79%. The average is 70·44%

Lymphocytes oscillate between 13% and 41·5%, the greatest variation between two counts being a drop of 23·5% two hours after a fit, from 41·5% to 18%. The average is 26·5%.

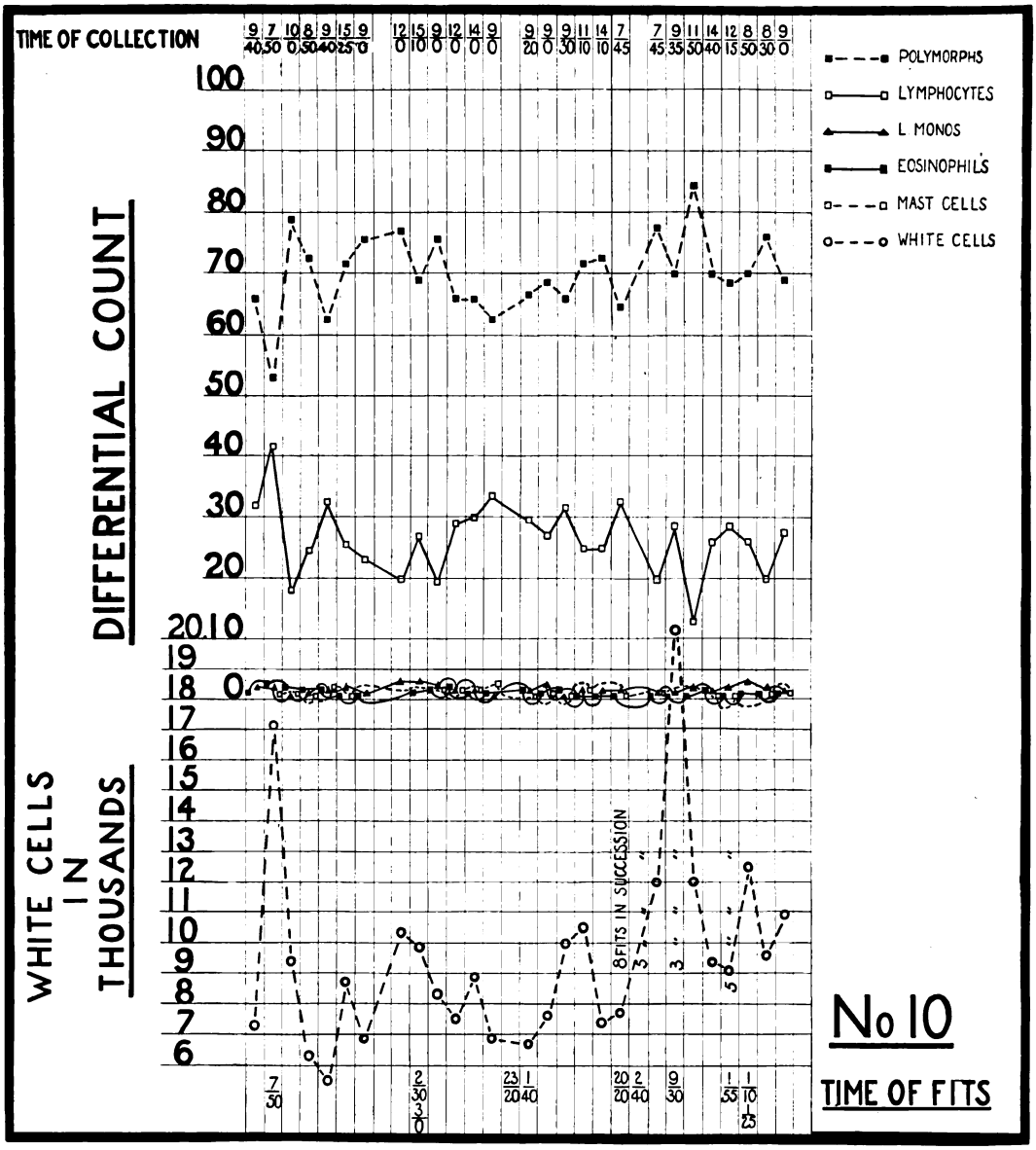
Eosinophils are present on all but one occasion. They oscillate between 0·5% and 2·5%. The average is 1·68%.

Large mononuclears are present throughout. They vary between 0·5% and 3%. The average is 1·68%.

Mast cells are present on twenty occasions. The average is 1·1%.

Again the maximum white cell excursions occur in association with fits. This case is of especial interest in that a very definite variation during and

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after a fit was to be observed, and secondly because, in the course of the experiment, the patient was afflicted with a succession of fits.

On the second day of the test a count taken during a fit showed a considerable elevation of the total white count, the height attained being 17,100, whereas on the day previous, when no fit occurred, the count was 7,300. A further count, taken two hours after the fit, showed a very considerable reduction to 9,400.

The elevation referred to was effected chiefly by the lymphocytes, the polymorphs being reduced.

On the 8th day of the test a count taken ten minutes after a fit showed a white cell count of 9,000 with a similar distribution of the polymorphs and lymphocytes. On two succeeding days, free from fits, the count fell.

During a period of greater incidence of convulsions, when these occurred in series as shown in the chart, the total white count tended to maintain itself at a high level, culminating in a count of 20,300 taken five minutes after a succession of three fits. During the two days following this the curve falls steeply until, on the twenty-fifth day, if fell to 9,300. The lymphocytes were mainly instrumental in the elevation.

Far less considerable fluctuations occur in the total white count, and in the differential count of the two main varieties of leucocyte, apart from the incidence of the fits.

There were no variations in the other white-cell elements comparable to those observed in the total count, and the polymorph and lymphocyte percentages as described above.

Discussion.

There are so many variations in the counts of cell elements, which do not occur in relation to the incidence of the convulsions, that it may be profitable to study whether they are to be explained by some such daily variation as workers like Sabin, Cunningham and Shaw believe. To this end we will study each chart in turn. In the cases given below we will consider the time of incidence of the lowest and highest counts for each individual. As the cases vary considerably in their average values for each of the different elements, to adopt a fixed average value for each element, to apply right through the series appears to be a definitely unscientific procedure.

The vitiating effect of fits is excluded as far as possible.

Chart 1: E. G—. All the counts, except the first one, were taken in the early morning, between 7·45 and 8.15 a.m. Even under such conditions the difference between the maximum and minimum counts in the polymorphs is 8% and in the lymphocytes 7%.

Chart 2: J. G—. In this case all the occasions when the leucocyte count rose above 7,500 occurred between 2 and 4.20 in the afternoon. Counts below 6,000 were all, except one, obtained in the early morning, at times between

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TABLE II.

Chart No.	Patient.	Average during period of fits.		Average during period of quiescence.		Control patient.		Polymorphs %.		Lymphocytes %.		Greatest % of variation between two counts.	
		Polymorphs %.	Lymphocytes %.	Polymorphs %.	Lymphocytes %.	Polymorphs %.	Lymphocytes %.	Minimum.	Maximum.	Minimum.	Maximum.	Polymorphs.	Lymphocytes.
1	Control	..	..	..	..	58·2	37·5	54	63	31	42	8	7
2	Control	..	..	..	..	65·5	30·6	55·5	74	23	38	17	14·5
3	Frequent fits (14 in 21 days)	72	23·2	..	..	..	..	62	73·5	20	32	9	9·5
4	Frequent fits (67 in 64 days)	77	15·8	..	..	..	..	70·5	85	11·5	24	10	8
5	Frequent fits (13 in 24 days)	71·5	22·8	..	..	..	..	55·5	78	16·5	39	12	13
6	Frequent fits (12 in 23 days)	68·2	25·33	..	..	..	..	58·5	75·5	17·5	34	13	11
7	Infrequent fits (12 in 60 days)	66·9	27·89	..	..	..	..	49·5	82	13·5	45	25·5	24
8	Occasional fits (5 in 38 days)	64·3	32·4	54·46	39·97	..	..	45·5	79·5	19	49	23	20
9	Occasional fits (3 in 50 days)	76·9	20·7	70·22	26·8	..	..	57·5	89·5	19	48·5	32	29·5
10	Frequent fits (28 in 27 days)	70·44	26·5	..	..	..	..	53	84·5	13	41·5	26	23·5

8 and 10 a.m. The exception was at 12.30 p.m. This would seem to lend some slight support to the view that a morning and evening variation occurs, but, considering that it is held that a variation in the total white count in the proportion 1 : 2 is observed, that noted here is inconsiderable.

Chart 3: F. S—. Here the counts were all taken at the same time of day, they were few, and fits were regular. It is, therefore, considered that the case provides insufficient data.

Chart 4: W. B—. The fits are many and occur at all times of the day. This chart is, therefore, unsuitable for examination for our purpose.

Chart 5: J. H—. In this case the fits were more or less distributed as in Chart 4.

Chart 6—L. C—. There is a fit-free interval of eight days which shows no evidence of an a.m. and p.m. variation. Similar intervals in Chart 7 give the same result.

Charts 8, 9 and 10 are better material for investigation, in that considerable periods of quiescence occur, but no signs of a morning and evening tide showed themselves in the graphs.

Summary.

A mathematical excerpt of the results is shown in Table II.

We will first summarize the general findings for the total white cell and erythrocyte counts, and the hæmoglobin percentage, apart from their temporal relationship to the convulsions.

Table III.—*Range of White-Cell Oscillation.*

Subject.	Lowest count.	Highest count.
Control 1	5,000	8,000
,, 2	4,900	8,000
Epileptic 3	9,000	13,300
,, 4	9,700	19,000
,, 5	6,000	17,500
,, 6	4,400	12,500
,, 7	4,700	11,000
,, 10	5,700	20,300

This gives an average range of variation of 9,017. This is much more than that encountered in the control cases (3,100).

It must be understood clearly that the figures above represent the differences between the highest and lowest counts obtained during the whole period of the investigation. Differences between consecutive counts are often much less. (See Charts.) We must bear in mind that Turk postulates a variation in the total count of from 5,000 cells in the early morning to 10,000 cells in the early afternoon, and that Sabin and Cunningham indicate that during the

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day it is possible for the whole white count to vary in the proportion 1 : 2. Even then it will be seen that such changes as those outlined in Table III, are more, except in Case 3 and possibly Case 4, than could be explained by means of the daily variation.

The figures quoted above reveal an unmistakable tendency to leucocytosis.

TABLE IV.—*Range of Red-Cell Oscillation.*

Case.	Lowest figure.	Highest figure.
3	4,900,000	5,300,000
4	3,500,000	4,550,000
5	4,500,000	5,800,000
6	3,700,000	4,700,000
7	3,800,000	5,900,000

Were these figures derived from non-epileptic subjects the oscillations would be held to have considerably greater significance. As it is, we do not consider that these changes, as considered above, i.e., not in temporal relation to the convulsions, are of sufficient significance for discussion.

TABLE V.—*Range of Hæmoglobin Oscillation.*

Case.	Lowest percentage.	Highest percentage.
3	79	87·5
4	63	82
5	83	105
6	71	87
7	75·5	104

The above figures show a surprising variation in the hæmoglobin index. It is interesting to compare these figures with those derived elsewhere. Macphail said the hæmoglobin percentage was much below normal, his average figure being 72·8%. South's figure was 63%. Spangler placed it higher, at 84%. The point to be derived from this research is not the lowness of the figure, but the great variability of the hæmoglobin percentage.

TABLE VI.—*Relation of Fits to Different Elements.*

Case.	Red cells.	Hæmoglobin %.	Eosinophils.	Large mononuclears.
3	+	+	..	..
4	+	—	..	..
5	+	+	..	..
6	..	..	+	..
7	..	..	..	+
8	..	..	+	—
9	..	..	+	—

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The above results are indubitable and definite. Further findings, more tentative, and less indisputable, are given in Table VI.

Conclusions.

Main Results.

(1) The white cell count is very variable in epilepsy, its greatest variability being at the time of the convulsion.

(2) There is a definite leucocytosis.

(3) This leucocytosis is associated with the occurrence of fits.

(4) It is due, in practically all cases, to a relative increase in the lymphocytes.

(5) Eosinophilia, traditionally associated with epileptic convulsions, occurred but rarely.

Subsidiary Findings.

(1) Eosinophilia is found in that minority of cases where the increased white count, associated with fits, is due to the polymorphonuclears.

(2) When fits occur in groups there is a tendency for a low count to be associated with a period of fits.

(3) The red cell-count and hæmoglobin percentages vary, in association with the convulsions, but to a less degree than the leucocytes.

(4) There is an increase in the erythrocyte count at the time of the fits. This may, or may not, be accompanied by an increase in the hæmoglobin percentage.

(5) There appears to be no very definite relation between the type of cell count and the degree of frequency of the fits.

No real evidence of a daily leucocyte tide is afforded by a study of the charts of the control patients, or of the epileptic subjects in a quiescent phase.

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