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Part I.—Original Articles.

Quantitative and Qualitative Leucocyte Counts in various forms of Mental Disease.

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THE following observations are the result of three years' work in examining the leucocytes in the various patients admitted to the Perth District Asylum. During this period the blood of 150 patients has been systematically examined, not on one or two occasions only, but often for weeks and months at a time. We have observed in medical literature observations recorded on the leucocytosis occurring in various forms of insanity in which the observer had made many observations on different patients, but as a rule limited the observations made on each individual patient to one, two, or at most three occasions. Such records are of little or no value, and would be on a par with the observations of, let us say, an astronomer who, having examined the heavens on two nights out of the 365, and having found both nights cloudy, reported that no such things as stars existed. With regard to the technique employed for the estimation of the number of leucocytes per c.mm. of blood, we have throughout employed Coles' system of counting "fields" with the counting slide of a

Thoma Zeiss' hæmocytometer. Never less than thirty fields were counted for each enumeration, and frequently sixty and eighty fields were counted when extra accuracy was deemed necessary.

The differential counts were made from films stained at first by eosine and hæmatoxylin, Leishman's stain, but latterly entirely by Louis Jenner's stain. This stain, especially when home-made from tabloids, is the most satisfactory we have had for general use. Never less than 200 cells were enumerated in each count. An oil immersion lens is almost necessary for this work.

In differential counts we recognise the following varieties:

1. Polymorphonuclear leucocytes with neutrophile granules.

2. Small lymphocytes; cells about the size of a red blood corpuscle with a deeply stained nucleus which occupies nearly the whole of the cell, the perinuclear protoplasm being of very limited extent and staining with basic dyes.

3. Large lymphocytes; cells larger than a red corpuscle with a nucleus which stains less darkly than in the ordinary lymphocyte; the perinuclear protoplasm being well marked and staining with basic dyes. We also include under large lymphocytes the hyaline or large mononuclears, cells which vary from 8–12μ in diameter. The nucleus is large and stains faintly. The cell protoplasm also stains very faintly with the basic dyes.

4. The eosinophile leucocyte.

5. Mast cells with large basophile granules.

For purposes of comparison we made numerous control counts from the blood of various members of the staff. We found in these control cases that the leucocytes per c.mm. of blood varied from 6000 to 9000 in young healthy men and from 6000 to 13,000 in women. Several of the women were anæmic.

The average percentage of the different forms of cells in the control men were as follows: Polymorphonuclear, 70 *per cent.*; small lymphocytes, 20·5 *per cent.*; large lymphocytes, 8 *per cent.*; eosinophiles, 1·5 *per cent.*; and in the control women, polymorphonuclear, 60 *per cent.*; small lymphocytes, 30·5 *per cent.*; large lymphocytes, 7·5 *per cent.*; eosinophiles, 2 *per cent.*

Mast cells occurred occasionally, and a percentage of ·5 to 1

was met with in the control bloods. For purposes of description we have divided our cases under the various forms of mental disease. Under melancholia we have—simple melancholia, acute melancholia, excited melancholia, and delusional melancholia.

All the cases of simple melancholia which we have examined eventually became excited, and we describe their leucocyte counts therefore under " folie circulaire."

In pure cases of acute melancholia—a disease which I tried to describe, as I saw it, in the *Journal of Mental Science* for October, 1900—we have never found a leucocytosis. The leucocytes per c.mm. of blood varied from 7000 to 13,000, the polymorphonuclear cells from 55 to 70 *per cent.*, the small lymphocytes from 31 to 20 *per cent.*, the large lymphocytes from 5 to 10 *per cent.* The eosinophiles never exceeded 1 *per cent.*, and in a few cases an occasional mast cell was seen. This observation is of practical value, because when one is asked to examine an early case of melancholia which has not fully developed, and one finds a hyperleucocytosis, and especially if the polymorphonuclear percentage is above 70, the prognosis must be guarded. On the other hand, when you examine a case and find the leucocytosis below 10,000 the prognosis is good, but it is always well to remember that the onset of some cases of delusional insanity cannot be distinguished from acute melancholia, and in these cases also there is no hyperleucocytosis, so far as we have been able to observe.

Every case of excited melancholia which we examined presented a high leucocytosis early in the disease. Taking one of our typical cases, we found on admission January 3rd, 1902, a leucocytosis of 15,000 ; on January 5th, 14,000 ; on January 7th, 10,000 ; and on January 9th, 17,000. Early in the disease also, and coinciding with the hyperleucocytosis the percentage of polymorphonuclear cells was frequently above 70 ; later in the disease during relapses it is quite common to get a hyperleucocytosis of 20,000 or 30,000 with a polymorphonuclear percentage of 80, or even higher. A relapse generally is preceded by a fall of the leucocytosis to 10,000 or 13,000 with a low polymorphonuclear percentage. As the excitement increases, the leucocytosis gradually rises, and the percentage of polymorphonuclear cells also rises until the attack reaches its height. When such a case recovers the leucocytosis remains high, but

the percentage of polymorphonuclear cells generally falls to 60, or below 60. The leucocytosis of a case of excited melancholia is exactly similar to that of acute continuous mania.

There appear to us to be two types of delusional melancholia, one resembling acute melancholia in the physical symptoms in which a delusion or delusions constitute the outstanding mental symptom. In all such cases there is a high leucocytosis which resembles the leucocytosis in excited melancholia. The second type is more like simple melancholia physically, but there are fixed delusions, and the patient is frequently suicidal. As a rule, in such case the leucocytosis is below 13,000, and the polymorphonuclear percentage rarely touches 70.

States of mental excitement.—All the cases of simple mania which we have been able to examine eventually proved to be cases of "folie circulaire," and the leucocyte counts are enumerated under that disease.

The leucocytosis of acute continuous mania and recurrent mania in adolescent cases have been described by me in the *Journal of Mental Science*, April and July, 1903. The leucocytosis exactly resembles that of excited melancholia, and a notable feature in all three diseases is the fact that upon recovery taking place a hyperleucocytosis is persistent for months and even years after discharge from the asylum. In cases which do not recover, but become chronic, the leucocytosis falls, and the percentage of polymorphonuclear cells is often below 50. If recovery does eventually take place in these chronic cases, it is invariably accompanied by a rise of the leucocytosis and an increased polymorphonuclear percentage. This observation is also of practical importance, because if, on examining the blood in a case of continuous mania, you find a leucocytosis of, say, 10,000, with a polymorphonuclear percentage of, say, 50, the prognosis is bad. Artificially raising the leucocytosis can be readily accomplished by injecting 1 or 2 c.c. of turpentine subcutaneously into the flank. Some cases of mania recover at once under this treatment, but others are not benefited, and it is noticeable in these cases refractory to treatment that there is apparently a failure in the production of a leucocytosis for a sufficient length of time to simulate the leucocytosis which occurs during natural recovery.

Recurring mental states.—All the cases of "folie circulaire" which we have so far been able to examine exhibited depression

or excitement of the simple melancholia or simple mania type. During the depressed stage we invariably found a high leucocytosis, with a polymorphonuclear percentage between 60 and 70. If a period of apparent sanity followed the depression, the leucocytosis still remained high, but the polymorphonuclear percentage fell to about 60. When excitement set in the leucocytosis at first fell to 10,000, 11,000 or 12,000, and the percentage of polymorphonuclear cells was also low, generally about 50. As the excitement increased the leucocytosis gradually rose, culminating at the height of the excitement, and then gradually fell to normal. Two typical cases were, however, discharged still showing a hyperleucocytosis of 16,000 or 17,000. These observations strongly point to the fact that the depression and excitement of cases of "folie circulaire" are quite different from ordinary attacks of mania and melancholia.

Cases of recurrent mania—in which class we do not include alcoholic cases—have a persistent leucocytosis which first rises and then falls somewhat as an attack comes on, rises gradually with the attack and then falls slightly as the attack passes off, but rarely falls to normal for more than a few days. The polymorphonuclear percentage follows the general curve of the hyperleucocytosis. Between the excited periods the large lymphocytes and hyaline cells are much increased, often reaching 20 *per cent.* One of our cases of recurrent mania suffered from severe facial erysipelas, which induced a hyperleucocytosis of 28,000, with a polymorphonuclear percentage of 89, and following this illness there was a cessation of mental attacks for four months.

Alcoholic insanity.—We have never had the opportunity of examining a case of delirium tremens; but the leucocytosis of acute continuous alcoholic mania follows in every detail that of cases of acute continuous mania of non-alcoholic origin, and leads us to suggest that the alcohol was merely an exciting cause, breaking down the resistive power of a patient predisposed by heredity to the infection of this type of disease.

The delusional alcoholic cases never exhibited any leucocytosis whatever.

We have never been able to examine a true case of dipsomania.

Hebephrenia.—Cases of hebephrenia vary a good deal. For the most part the leucocytosis is about 12,000 to 14,000, but

every now and then they present a marked hyperleucocytosis, with little or no increase of the polymorphonuclear percentage, the increase being chiefly due to the hyaline or large mononuclear cells, which may vary between 20 and 30 *per cent.* Only one of our cases has recovered, and in his case the leucocytosis never rose above 14,000, and upon recovery fell to normal.

We described the leucocytosis of katatonia in the *Journal of Mental Science*, October, 1903, and the only fact we have to add to these observations is that in all the cases which recovered, during the period of recovery the patients exhibited a distinct but transient eosinophilia, the eosinophile cells rising to 5 or 10 *per cent.*

All cases of delusional insanity, whether cases of paranoia or occurring later in life, were entirely free from hyperleucocytosis.

General paralysis of the insane.—Three years ago in the *Brit. Med. Jour.*, June 29th, 1901, I described the leucocytosis of general paralysis, and later results have confirmed these early observations. The leucocytosis of general paralysis largely depends upon the character of the particular case. In a classical case at the onset there is always a hyperleucocytosis with a high polymorphonuclear percentage, and the higher the leucocytosis, *i. e.* the more vigorous the reaction to the poison causing the disease, the more marked is the apparent remission which follows. In the second stage the leucocytosis follows the course of the disease—if there is a febrile attack up goes the leucocytosis; the polymorphonuclear percentage also rises somewhat. During the third stage the leucocytosis becomes very irregular—one day up to 30,000 and the next below 10,000 per c.mm. of blood. The polymorphonuclear percentage may fall very low—40 or even lower—and there is a great increase of lymphocytes. Transient eosinophilias are quite common, especially during the second stage of the disease.

If a patient recovers, or enters upon a marked remission equivalent to recovery, the leucocytosis invariably falls to normal, but the polymorphonuclear percentage is generally very low—between 40 and 50. So far we have only been able to examine three such cases.

Epileptic insanity.—Every case of epilepsy has shown hyperleucocytosis, not only during periods when the patients were suffering from epileptic seizures, but even in the intervals

when the patient was quite free from attacks. The most marked period of hyperleucocytosis follows a fit or occurs during the period when the patient suffers from a series of seizures. We have had one case of "masked epilepsy" and one case of "convulsive melancholia" under observation, which both showed marked hyperleucocytosis.

Of drug insanities we have had no experience, but I examined a case of mania for Dr. Urquhart which was supposed to have been induced by poisoning with thyroid extract. I made only two observations, but on both days there was a hyperleucocytosis with an average percentage of polymorphs.

The leucocytosis of cases of puerperal insanity does not differ from that of acute mania. In the only two cases of lactational insanity we have been able to examine the leucocytosis was similar to that of an ordinary anæmic woman.

All cases of senile insanity presented a high or low leucocytosis according to the disease from which they suffered.

It will be noticed then that, with the exception of one variety of melancholia and all cases of delusional insanity, all types of acute mental disease present more or less this symptom of hyperleucocytosis, and the persistence of this symptom, after apparent recovery in some cases and during the whole course of the disease in others which do not recover, is an interesting fact, and demonstrates what hardly requires demonstration, that as yet we know very little about the causes, course, and termination of the various diseases called "mental."

The differences which occur in the character of the individual cells is often very striking. In young strong patients the polymorphonuclear cells are large and well formed with well-marked granules. In old or debilitated patients the polymorphonuclear cells tend to be smaller, and the granules are small and often stain badly.

Distinctly degenerated, vacuolated and breaking down cells occur sometimes in acute and debilitated cases. We practically never found marrow cells, nor did we ever find a cell exhibiting distinct evidences of phagocytosis.

Large lymphocyte cells—excluding the hyaline variety—are said to be uncommon in healthy blood. They are frequently increased in the various forms of mental disease, but most markedly in hebephrenia, katatonia, recurrent mania, and any case which is much debilitated.

Discussion

At the Quarterly Meeting of the Medico-Psychological Association in London, May 18th, 1904.

Dr. Robert Jones admitted he had not been able to work much in the particular field which Dr. Bruce had just demonstrated. It showed marked vigour on the part of a young superintendent that he was able to combine with so much success the administrative and the scientific aspects of the work. He (Dr. Jones) had often thought that there was a considerable amount of information to be obtained from the examination of the blood, and it had now become a very simple matter. One used the little instrument designed by Thoma-Zeiss, only a small quantity of blood was necessary, and the Jenner soloids or tabloids from Burroughs and Wellcome completed the equipment, and the matter was carried through without much trouble. The interest which blood examinations would have was probably great, and the observations could be carried out *in corpore* or *in vitro*. One could verify for oneself that there must be a good deal of reason for the theories about blood immunity, agglutinins, precipitins, haptophores, and the various technical terms with which the literature of the subject abounded. Toxins, such as that of tetanus, could be mixed with the nerve matter outside the body, and the antitoxin demonstrated. Unless one kept up actively with the chemical and microscopical literature of the present day, medical men would find themselves very quickly out of touch with the best work which had been done in their own particular branch. Coming to a more practical point, there were certain drugs which were known to definitely increase certain cells in the blood; pilocarpine, for instance, was said to increase the lymphocytes particularly; again, cinnamate of soda and camphor, both vaunted remedies for cancer and tuberculosis and such like ailments, possibly because these, to some extent, altered the leucocytes, which Dr. Bruce pointed out as occurring in some cases when convalescing, are said to increase the polymorphs; he would like to ask Dr. Bruce if he had tried the effects of these drugs. The question of immunity again was a very large one, and he would not prolong the meeting by discussing it; but the Association was greatly indebted to Dr. Bruce for his demonstration.

Dr. Bruce, in reply, said Dr. Peebles and he had tried cinnamate of soda and other drugs, and found that though they increased the lymphocytes they did not increase the polymorphs. Leucocyte examinations gave a certain amount of assistance in prognosis, and a forecast was often asked for in the cases which one was called upon to examine. Some time ago he saw a patient in regard to whom it became necessary to say whether he would be likely to make an early recovery or not. It was a case of melancholia. The leucocytosis was 20,000 and the polymorphs nearly 80 *per cent.* The patient had had one previous attack. There was no possibility of that patient recovering under months, and perhaps longer. A case of melancholia with a high leucocytosis might be looked upon as absolutely certain to have a prolonged attack, in the present state of knowledge of the treatment of those forms of disease. There was another case which he would like to cite. The friends were very badly off, and they were keeping the patient in the country in charge of a nurse, straining their resources to the utmost in doing so. He made a blood count, and found the proportion of leucocytes high. The patient looked as if she would make a good fight against the disease, which was excited melancholia. He said at that time he thought it would be well to continue the treatment. Two months later he examined the blood again, and the polymorphs were down to 40 *per cent.*; there were many transitional forms and many were vacuolated. When that was observed one could conclude that the resistive force was failing. He therefore advised that the patient should be placed in an asylum. So far as he knew that woman would never recover, and he did not think she had improved at all. Since she was admitted to the asylum she had become dirty in her habits and demented. In cases of mania, however, one was very apt to be mistaken. He was asked to see a case of acute mania which showed a leucocytosis of 20,000 and polymorphs over 70 *per cent.*, on the strength of which he said the patient would be well in three months. That was two years ago, but she was now as grave a case as he had ever seen. So what he had pointed out did

not help the forecast in every case. Still, it afforded a great deal of assistance in a large number of cases in giving a tentative prognosis.

Dr. A. R. URQUHART said he would like to add a word to what Dr. Bruce had said with regard to prognosis. In a case to which he referred a young lady had overdosed herself with thyroid for a considerable time, and Dr. Bruce, after an examination of the blood, concluded she was on the high road to recovery, and he proved correct in a very difficult set of circumstances. The tables exhibited represented years of most arduous labour on the part of Dr. Bruce and his assistants, and he was sure no body of men would be keener to give every credit to workers in the speciality than the members of the Medico-Psychological Association. Members were more interested in the results than in the methods; some of them had scarcely time, or inclination, or even ability to prosecute such very difficult and long-drawn inquiries, but the Association included a number of active and willing workers who had demonstrated the value of those methods, and none had done so up to date more than Dr. Lewis Bruce.

A Statistical Note on the Social Causes of Alcoholism.

By W. C. SULLIVAN, M.D., Deputy Medical Officer, H.M. Prison, Pentonville.

THE object of this paper is to draw attention to the nature of the social conditions that lead respectively to drunkenness and to chronic alcoholism, and to point out that these two phenomena are in great measure related to two distinct types of drinking, differing in origin, differing enormously in social gravity, and corresponding to quite different statistical measures.

The two types of drinking referred to may be conveniently distinguished as luxury drinking and misery drinking. By the former is meant the drinking that belongs to relative well-being, temporary or permanent. It will include, for instance, all the forms of convivial drinking, the drinking connected with social and religious celebrations, and the like. Misery drinking, on the other hand, indicates the drinking that goes with conditions of relative ill-being, when what is sought from alcohol is the relief of painful emotional states, or the capacity to react to stresses which the drinker would otherwise feel to be in excess of his powers. This form of drinking, therefore, includes the drinking related to overwork, insufficient or unattractive food, overcrowding, bad hygienic conditions of all sorts. Having regard to what is the chief factor in either variety, we may also describe these opposed forms of drinking as convivial drinking and industrial drinking. To take a concrete instance, the workman who carouses with his comrades on a Saturday night is a type of the convivial drinker; the labourer who, before a