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Part I.—Original Articles.

Bacteriological and Clinical Observations on the Blood of Cases suffering from Acute Continuous Mania.

By LEWIS C. BRUCE, M.D., Murthly, Perthshire.

TWO years ago, when the toxic theory of the causation of insanity was attracting attention in this country, I made a series of observations on the blood of acute recent cases of insanity with the object of ascertaining whether organisms were ever present. In no case, with the exception of one of general paralysis, did I ever find an organism in the blood. It occurred to me, however, that if I could make an aseptic necrotic area subcutaneously, the serum and pus in such an area would be a suitable nidus for the growth of organisms circulating in the blood, and that by aspirating the serum and pus and placing it in suitable nutrient media one should be able to grow such organisms, if present. Acting upon this theory, I took a case of acute mania—an adult woman—and, with antiseptic precautions, injected into the soft tissues of the flank 2 c.c. of turpentine.(1) An abscess formed, and on the third day after the injection I aspirated some fluid, consisting

of blood-serum and pus. A couple of drops of this fluid were then added to each of four tubes containing 8 c.c. of sterile nutrient broth. These tubes were incubated for forty-eight hours, when they showed slight turbidity, and upon microscopical examination the broth was found to contain a pure growth of a small diplo-bacillus.

Since then I have made twenty-four similar observations, and have isolated this diplo-bacillus in seven cases. Table I shows the varieties of mental disease in which the observations were made. It will be noticed that this small diplo-bacillus has been obtained almost exclusively in cases of acute continuous mania in adults.

Dr. Houston kindly examined the organism, and gives the following description:—"A small, short bacillus occurring singly, in couples and short chains; stains very feebly by Gram's method. A stroke culture on agar shows a white growth with no special characters; later acquires a yellow tint; on gelatine the growth tends to remain somewhat circumscribed, with sinuous edges. Later, it becomes pitted and wrinkled and skin-like in character; eventually assumes a pale yellow colour, and later slow liquefaction sets in. In broth it forms a uniform turbidity, but the growth is not very abundant. In litmus milk at 37° C. it gives a slow alkaline reaction. It is not fatal to guinea-pigs in doses of 5 c.c. broth culture inoculated subcutaneously."

My own observations on the organism are as follows:

The method of obtaining the diplo-bacillus is as follows:—A small quantity of the serum and pus from the necrotic area is extracted with a hypodermic needle and syringe, and a few drops are added to each of four tubes containing 8 c.c. sterile broth. The tubes are incubated for forty-eight hours at 37° C., at the end of which period they show a slight turbidity if the bacillus is present. I have seen the bacillus take seventy-two hours to show in the broth. If a hanging-drop culture of the broth be now examined, it will be noticed that the bacillus tends to grow in chains and also in clusters, and that it is slightly motile. If stroke cultures be now made from the broth upon agar, the bacillus grows in from thirty to forty hours in the form of little gelatinous colonies, which later become opalescent. If a sub-culture be made again on agar from these colonies, the growth appears as a thin whitish line

in about twelve hours. The bacillus holds Gram's feebly, and does not take up any of the commoner dyes well. A stab culture in gelatine grown at 20° C. liquefied the gelatine in sixty days.

I am indebted to Mr. Richard Muir, of Edinburgh University, for much valuable assistance and instruction in this part of my work.

The organism is not fatal to rabbits, guinea-pigs, or white mice. Two kittens were fed every second day for four months upon 4 c.c. of broth cultures. Their growth was slow, and they were thin and poorly nourished. When the cultures were no longer added to their food they improved in appearance, and are now apparently healthy and well developed.

Agglutination tests were made with the blood of five patients suffering from acute mania. The results were unsatisfactory, but partial agglutination seemed to occur in every case. The blood-serums of five members of the nursing staff were used in controls, and in only one of these was there any clumping of the bacillus, even at the end of twelve hours. . The dilution used in all the agglutination tests was 1 in 10.

I have examined bacteriologically the skins of ten cases of acute insanity, and have never isolated the diplo-bacillus. I have also made plate cultures from the fæces of six cases of acute insanity. In one I isolated an organism presenting all the characters of the diplo-bacillus, and in two of the other five cases I saw an organism corresponding to the diplo-bacillus in size and staining reaction, but failed to isolate the growth.

I have been tempted to place these results before you in the hope that the same organism may be detected by other workers. If it is obtained by others exclusively from cases of acute mania, there may be grounds for believing that there is some connection between the organism and the disease.

What was the effect of the abscesses upon the patients? 1. In twenty-three out of the twenty-four cases the abscess induced a febrile attack within twenty-four hours after the injection of the turpentine. In several cases the temperature rose as high as 102° F. 2. In no case was the patient the worse physically for the abscess, and in many cases there was marked benefit.

To refer again to Table I, it will be seen that the patients who benefited most were those suffering from acute mania.

The only patient among the ten suffering from acute mania who did not recover or improve had been ill for over six months before the abscess was made. The average duration of the illness in those who recovered was three and a half months. Some of the results in cases of acute mania were so satisfactory from a recovery point of view that I never hesitate to induce an abscess in every case of acute mania which does not rapidly improve under ordinary treatment. Out of the whole twenty-four abscesses I only had to open one which became septic accidentally. A few of the abscesses ruptured, but the majority became absorbed, and I am of the opinion that the abscess should not be evacuated, as even after all acute symptoms have subsided it apparently acts as a stimulant to leucocyte production, which is Nature's method of assisting recovery in these cases. I do not wish you to think that I ignore the effect of the febrile attack and the subsequent stimulus to nutrition which follows febrile attacks, but I am satisfied that it is through the leucocyte action of the blood that Nature effects recovery in all cases of acute mania. I have examined in the last two years the blood, and especially the leucocytes, in fifty cases of acute insanity. The observations in each case were not single ones, but made continuously for weeks and months. To assist in this work I have trained several members of the nursing staff, who have been of great service in preparing slides and cover-glasses, making and staining films, and even, in some cases, of counting leucocytes by means of Thoma Zeiss's hæmocytometer.

To-day I propose to describe the changes which occurred in the leucocytes in fourteen acute continuous cases of mania occurring in adults. I start on the hypothesis that anything between 6000 and 10,000 leucocytes per cubic mm. of blood is normal, and that the usual percentage of the polymorphonuclear leucocytes is about 70 *per cent.* The numerical counts were made with Thoma Zeiss's hæmocytometer, and thirty or forty fields were counted upon each enumeration, and the results were frequently checked by duplicate counts and control counts on healthy blood. The films were stained with eosine and methylene blue—eosine and hæmatoxylin—Leishman's stain and Jenner's stain. At each differential count never less than 200 leucocytes were counted. I have divided my observations as follows :

1. The leucocytosis which occurs in a patient who recovers without interference. (Chart I.)

2. The leucocyte changes which occur in a patient who does not recover, but becomes chronic. (Chart II.)

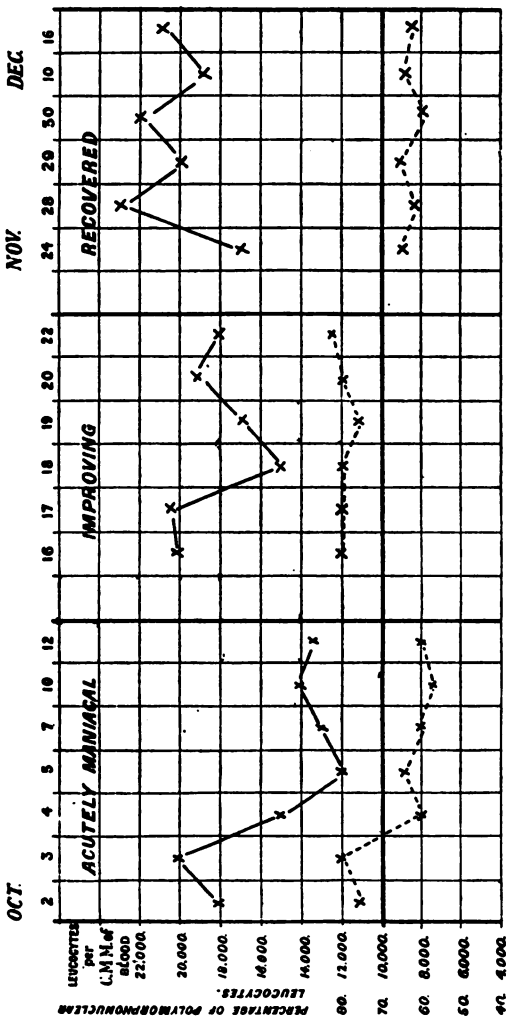

CHART I.—Showing the leucocyte changes in a case of acute continuous mania which recovered. The leucocytes per c.mm. of blood are indicated by the continuous line; the percentage of polymorphonuclear cells by the dotted line.

3. The leucocyte changes which occur when an abscess is made in a recent case, and is followed by recovery. (Chart III.)

4. The leucocyte changes which occur when an abscess is made in a chronic case which does not recover. (Chart IV.)

1. The leucocyte changes which occur in a patient who recovers.

If you are fortunate enough to observe the leucocytes in a

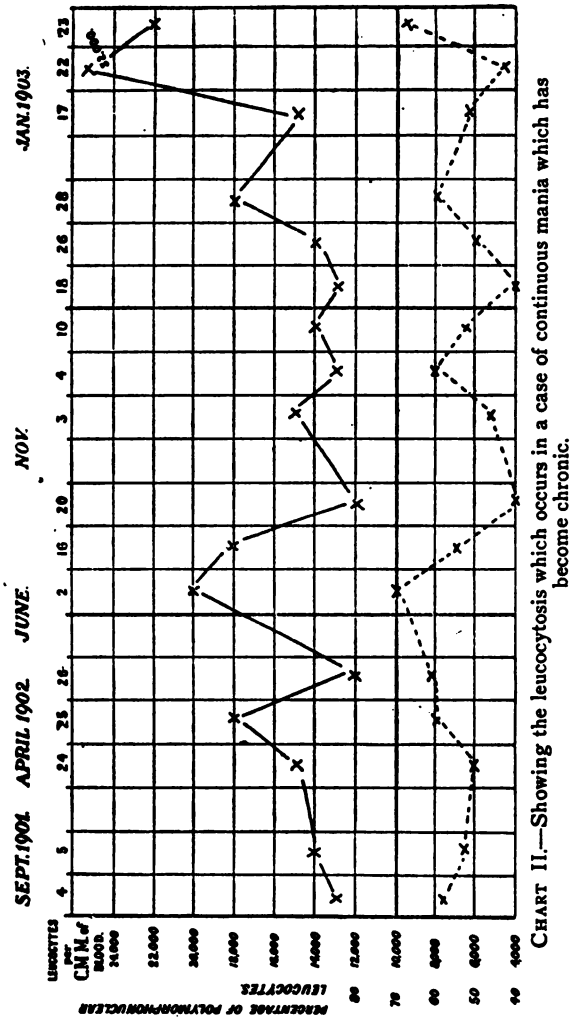

CHART II.—Showing the leucocytosis which occurs in a case of continuous mania which has become chronic.

recent case of mania from the very commencement, you find during the first few days of the disease that the leucocytosis is high, say 18,000 to 20,000 per c.mm. of blood, and that the percentage of polymorphonuclear cells is 70 or above 70 *per*

cent., and never lower than 60 *per cent.* Nature apparently makes a vigorous effort at the commencement of the disease to counteract the toxæmia by pouring leucocytes into the system. The higher the leucocytosis, within certain limits, and the higher the percentage of polymorphonuclear cells, the better is the prognosis. If the patient does not recover at once the leucocytosis falls slightly to anything between 12,000 and 16,000 leucocytes per c.mm. of blood, and the polymorphonuclear cells rarely reach 70 *per cent.* This state of affairs may last for weeks, and gradually leads into the stage of recovery. When the patient shows signs of recovering a curious change sets in in the leucocytosis. Instead of the leucocytosis diminishing, it increases, and the percentage of polymorphonuclear cells rises. In a favourable and rapidly recovering case these cells may be as high as 80 *per cent.* A still more curious thing occurs when recovery is actually complete—the leucocytosis persists, but the percentage of polymorphonuclear cells again falls to between 60 and 70 *per cent.* It is impossible to say how long this leucocytosis persists, because one cannot keep a recovered patient indefinitely under observation. All I can record is that all the recovered cases of mania discharged since these observations were begun have been discharged with a high leucocytosis. Is this leucocytosis a protective leucocytosis?

2. The leucocyte changes which occur in a patient who does not recover.

The changes which occur are slow, and go on for months with many fluctuations, but shortly they are as follows:—The leucocytosis tends to remain between 12,000 and 16,000 per c.mm., with occasional rises and falls, but the percentage of polymorphonuclear cells tends to fall until finally, after the disease has lasted for one or two years, the proportion of polymorphonuclear cells may be anything from 20 to 50 *per cent.* There is always a proportionate increase of lymphocytes. With an exacerbation of the disease there may be increased leucocytosis, with a rise in the percentage of the polymorphonuclear cells, but such an increase is very temporary.

3. The leucocyte changes which occur when an abscess is made in a recent case and is followed by recovery.

Within six hours after the subcutaneous injection of the turpentine the polymorphonuclear cells may show a marked

relative increase. In twenty-four hours the leucocytosis is distinctly increased, and the percentage of polymorphonuclear cells remains high, *i. e.* they are both actually and relatively increased. In forty-eight hours the leucocytosis is still higher, rising in various cases to 30,000, 40,000, or even 60,000

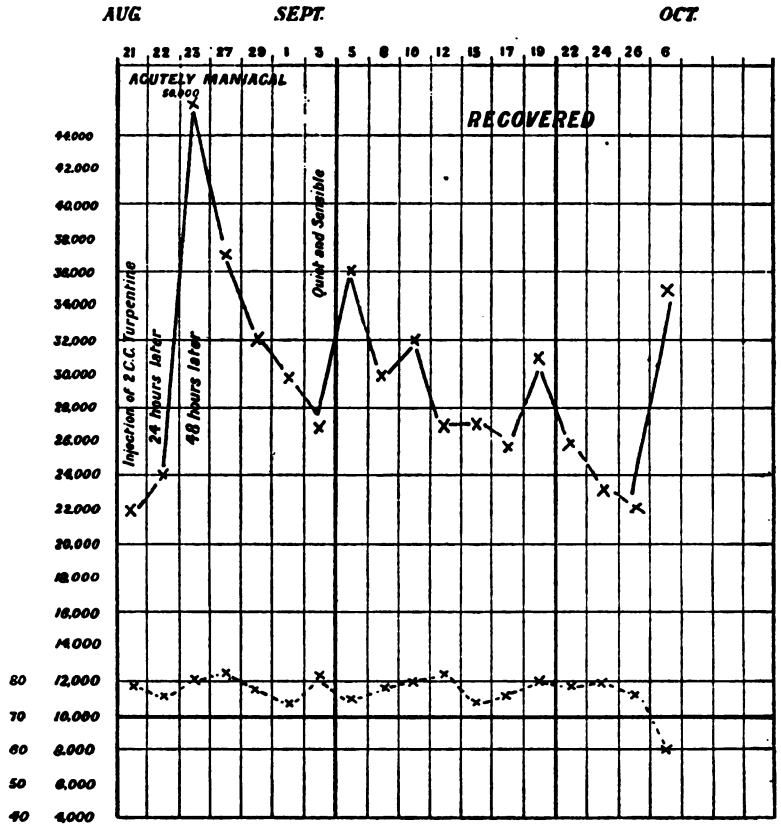

CHART III.—Showing the leucocyte changes in a recent acute case of continuous mania in which a turpentine abscess was induced, and which recovered rapidly.

per c.mm. of blood, while the percentage of polymorphonuclear cells remains above 80 *per cent.*, and this is generally the maximum of the leucocytosis.

Mental improvement appears to be in proportion to the leucocytosis, *i. e.* the higher the polymorphonuclear element the more marked is the mental improvement. For a varying

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period after the forty-eight hours the leucocytosis remains high. For instance, in one case in which an abscess was induced on August 21st the leucocytosis by the end of September had never fallen below 22,000 per c.mm. This patient made a rapid and excellent recovery. As recovery advances, however, the percentage of polymorphonuclear cells generally falls until it reaches somewhere about 60 *per cent.*, and the lymphocytes are slightly increased.

4. The leucocyte changes which occur when an abscess is made in a chronic case.

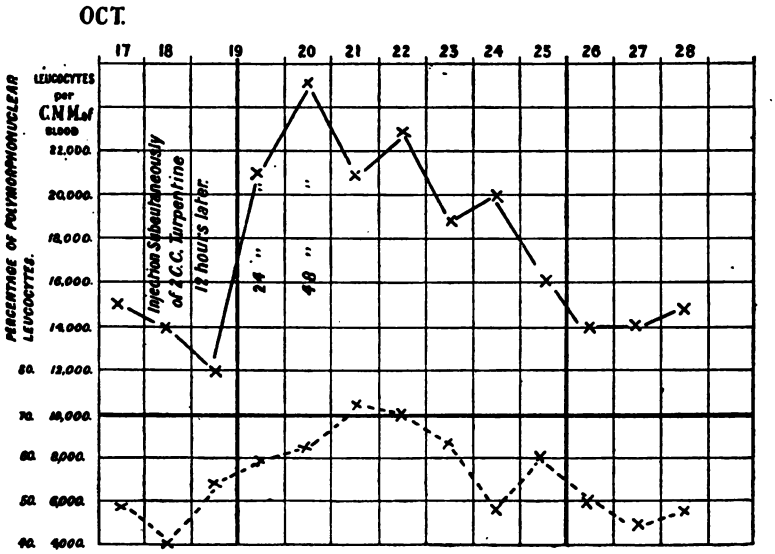

CHART IV.—Showing the leucocyte changes occurring in a case of chronic continuous mania after the subcutaneous injection of turpentine.

Twelve hours after the subcutaneous injection of the turpentine there may be a fall in the leucocytosis with a slight relative increase of the polymorphonuclear elements. Twenty-four hours after the injection there is a decided rise in the leucocytosis, but the polymorphonuclear cells show a very slight relative increase. In forty-eight hours the leucocytosis is markedly increased, but the increase of polymorphonuclear cells may not reach 70 *per cent.* By the end of seventy-four hours in the case shown in the chart, the leucocytosis was showing a tendency to fall, but the polymorphonuclear cells

were relatively increased, and by the end of 122 hours the leucocytosis was distinctly falling and the polymorphonuclear cells were again below 70 *per cent.* Thereafter there was a steady fall of both the leucocytosis and the percentage of the polymorphonuclear elements. This patient showed no mental improvement. By comparing Charts I and III it will be seen how the formation of an abscess simulates and surpasses the leucocyte production which naturally occurs when a patient recovers, and a comparison of Charts III and IV illustrates graphically the differences in the resistive powers of a recent acute curable case of mania and a chronic case, whose energies have been sapped by long-continued disease.

These observations do not apply to the condition of mania in patients suffering from "folie circulaire," nor to mania the result of alcoholic poisoning.

1. If these blood observations are correct, they practically prove that acute continuous mania is an acute infective condition, and that when recovery takes place a condition of immunity is established.

2. They prove that, although the patient apparently recovers, the disease remains latent; hence the persistent leucocytosis, a point which might be of great importance in life-insurance examinations.

3. An examination of the blood is a valuable aid to prognosis.

Let us say a case of mania has lasted for a month, and remains maniacal and sleepless. The blood examination gives a leucocytosis of 14,000 per c.mm. of blood, with a percentage of 60 or below 60 of the multinucleated cells. The chances of an immediate or early recovery are poor. On the other hand, if the blood examination gives a leucocytosis of 18,000 or 20,000, with the multinucleated cells in a percentage of 70 or above 70, the prognosis is good. It is as well, when examining the condition of the blood to aid prognosis, to examine the blood on at least two consecutive days.

TABLE.

Cases.	Sex.	Age.	Mental disease.	Organisms.	Remarks.
1	F.	64	Adolescent mania	Diplo-bacillus	Arrested the attack.
2	F.	64	,, ,,	,,	Very temporary benefit.
3	F.	36	,, ,,	Diplo-bacillus and cocci	Recovery.
4	M.	53	,, ,,	Diplo-bacillus	Recovery.
5	F.	62	,, ,,	Sterile	Arrested the attack.
6	F.	46	,, ,,	Diplo-bacillus and cocci	Recovery.
7	F.	47	,, ,,	Diplo-bacillus and cocci	Recovered, then became depressed.
8	F.	53	,, ,,	Sterile	No immediate benefit, but patient made good recovery.
9	F.	32	,, ,,	,,	Slightly less excited.
10	F.	62	,, ,,	,,	No immediate benefit, but made good recovery.
11	F.	28	Puerperal mania	,,	Marked benefit; rapid recovery.
12	F.	28	Adolescent epileptic mania	,,	Arrested the attack.
13	F.	27	Adolescent mania	,,	No benefit.
14	F.	34	Chronic mania of adolescent	Cocci	Very slight benefit.
15	M.	24	Adolescent mania	Sterile	Recovery.
16	F.	18	,, ,,	Diplo-bacillus	Temporary benefit.
17	M.	35	General paralysis	Sterile	No benefit.
18	F.	47	,, ,,	,,	,,
19	F.	38	,, ,,	,,	,,
20	F.	50	,, ,,	Cocci	,,
21	M.	37	,, ,,	Sterile	Marked improvement.
22	F.	35	Excited melancholia	,,	Temporary benefit.
23	F.	54	,, ,,	,,	No improvement.
24	M.	54	,, ,,	,,	,,

(1) Dr. Ford Robertson points out to me that G. Albertotti (*Annali di Freniatrice*, 1896, pp. 23 and 147) has already utilised turpentine abscesses as a method of treatment. I utilised the turpentine in the first place to induce an aseptic abscess for bacteriological observation.

DISCUSSION

At the Meeting of the Scottish Division, December, 1902.

Dr. IRELAND.—I regret that Dr. Clouston has had occasion to go away on some business, and he has asked me to take the chair. I must say that by his absence we will miss some very pregnant observations, which he no doubt would have made. I remember in the first edition of his book on mental diseases he pointed out the probability of a cure for insanity from the consideration of cases which recovered after certain fevers which he had observed. Now here we have Dr. Bruce, who has experimented with a similar idea and reduced it to an exact form, and I think that some of our members should repeat these observations made by Dr. Bruce. I have got some hopes that they will be confirmed, and we

all ardently wish that that should turn out to be the case. The only suggestion I could make is that Dr. Bruce apparently has only employed turpentine to create the abscess.

Dr. BRUCE.—Yes.

Dr. IRELAND.—He might try some other substance. Turpentine has very peculiar properties, and it is possible that this might have a certain effect on the blood. I therefore think that if there was an abscess formed in some other way it would confirm the conclusions which Dr. Bruce has come to if the results were identical. I have no doubt that a number of gentlemen will have remarks to make on this very pregnant paper.

Dr. YELLOWLEES.—I have nothing to say except to express my emphatic admiration for the work done and my very hopeful views as to what may come out of it. If I were a young man like Dr. Bruce I would work at this with all my soul. I am sorry I have not time to offer any remarks, as I have to go to the same meeting as Dr. Clouston has gone to. I have pleasure in proposing a hearty vote of thanks to Dr. Bruce for his admirable paper.

Dr. EASTERBROOK.—I have much pleasure in seconding Dr. Yellowlees' vote of thanks to Dr. Bruce, and know that his inquiry has involved much time and work. I have not made any observations myself from the same point of view as Dr. Bruce. He lays great stress on the connection between the leucocytes in the blood and the mental condition of the patient, as if the one had almost a dominating relationship with the other. I am not prepared to exactly contradict that statement, but I must say that from certain observations I have made, I would be more inclined to ascribe the changes in the mental condition to changes in the cell metabolism of the brain and body generally. For example, when a patient recovers, one of the most striking things is a gain in weight, and improved colour and circulation. If one tries to get at the explanation of the loss in weight followed by the gain in weight, there is one explanation which seems pretty apparent, and that is going back to the condition of affairs in the cells of the body. According to the views of Hering and other physiologists, the more catabolism that takes place in the cell the greater is the resistance to that catabolic condition going on in the cell—there is a tendency for anabolism to assert itself. So in acute mania, where you have very advanced catabolism going on, that stage continues for a certain period, and then the tendency to anabolism asserts itself, and when the patient recovers it is increased. It seems as if one would have to go to the protoplasm of the brain neurons as explaining the condition and recovery in the patient. I would rather be inclined to say that it was the protoplasm of the cells of the brain and body generally that held the secret. With regard to the leucocytes, there may be some connection between the two, and whether they stimulate this anabolism or not I do not know.

Dr. MACDONALD.—Have you attempted any experiments in the way of injecting the turpentine into presumably healthy individuals?

Dr. BRUCE.—I have not found any individuals who would offer themselves for such an experiment.

Dr. MACDONALD.—You might find some. No matter what chemical you may introduce under the skin, it will certainly tend to the production of an abscess, granted that there are pus-producing organisms in the body. It is not correct to talk of that collection of matter which Dr. Bruce produces as an abscess. He must first show that it contains pus-producing organisms. This diplo-bacillus may be a pus-producing organism, but it may not be. It is most important to have these contrary experiments.

Dr. FORD ROBERTSON said he was of opinion that the observations that Dr. Bruce had brought before them were of much value. They illustrated the importance of uniting the study of the pathology of insanity with clinical investigation. It was from researches of this nature that important advances in the treatment and prophylaxis of insanity would chiefly come. It was easy to criticise work such as Dr. Bruce had been doing, and he supposed that in a discussion of this kind it was right to be critical. He agreed with Dr. Macdonald that Dr. Bruce had not laid before them any evidence that went to prove that this bacillus had anything to do with the causation of acute mania. The treatment of certain forms of insanity by the artificial production of abscesses by turpentine had been advocated several years ago in Italy (see *Journal of Mental Science*, July, 1897, p. 612), and the results recorded

had been excellent, but he believed he was right in stating that the treatment had been abandoned in that country now. He would like to know if Dr. Bruce had ascertained if the bacillus he had isolated was identical with that found by Bianchi and Piccinino in acute delirium. He was surprised that Dr. Bruce had not attributed any importance to disorders of the gastro-intestinal tract in the causation of acute mania. There was now satisfactory evidence that a large proportion of such cases were really dependent upon toxic infection from the alimentary tract.

Dr. URQUHART.—Dr. Bruce's paper has not been a simple one to write; it is a paper which evidently has cost him much trouble, and there must have been a great deal of arithmetical work in counting up these leucocytes in all these cases. It is somewhat difficult for anyone to follow Dr. Bruce's observations properly without going to Murthly and seeing the work that is done there. Lately I had the advantage of having one patient examined there, and if the case could have been followed up to the end it would have shown results similar to those in the fourth chart. I hope that you will accord a very hearty vote of thanks to Dr. Bruce for making this elaborate investigation.

Dr. IRELAND.—Yes. We are, I am sure, extremely grateful to Dr. Bruce. (Applause.)—If you have anything to say in reply, Dr. Bruce, we will be glad to hear you.

Dr. BRUCE.—I don't know that there is much to reply to. In regard to Dr. Easterbrook's observations, I must say from my observations of leucocytes that I believe their action to be just as important as changes in the protoplasm of the cell. As to the remarks about pus-producing, it is nonsense to say that you cannot talk of the necrotic area produced by turpentine as an abscess. You can produce an abscess by irritants; if what you call an abscess is a thing full of pus, then you get it. Then as to people coming forward to have abscesses made: I shall be glad to make abscesses in anyone who will volunteer. It is a very striking point that out of twenty-four abscesses sixteen were absolutely sterile.

Dr. MACDONALD.—A sterile abscess?

Dr. BRUCE.—Yes. What you are arguing about is the definition of an abscess. My definition is a dead area caused by a toxin or irritant, and that is a view now very generally held. As my paper threatened to be too long, I shortened it, and I did not tell you that I had made observations on the skin of acute cases and never got this bacillus. I examined the intestinal tracts of six cases, and I got the bacillus in three. I agree with Dr. Ford Robertson that changes or toxins formed in the intestinal tract have something to do with the production of acute mania, but in a whole lot of diseases, such as phthisis, you always get intestinal symptoms. In my opinion the intestine is the point of attack of organisms if such organisms are the cause of mania. The bacillus does not resemble the bacillus of Bianchi. Turpentine is the only substance which produces a prolonged leucocytosis. I have tried other substances, such as nucleic acid and cinnamate of soda, but I have not been able to produce the same leucocytosis as with turpentine. Turpentine is not so inhuman as you would think; out of twenty-four cases I have only had three that complained of the pain. The great majority of these cases of acute mania are very insensible to pain; they don't seem to feel it. I take a small quantity of carbolic acid, which makes the skin anæsthetic and purifies it at the same time, and I inject the turpentine at this spot. After three or four days the pain and inflammation are gone, and you have a big swelling which acts as a stimulant to leucocyte formation. I don't think that there is anything more I can say to the criticisms you have so kindly made.

The Case of an Unrecognised Degenerate punished by the Law. By EDWIN GOODALL, M.D.

THE case here dealt with is that of a man æt. 35, now a patient at Carmarthen Asylum, formerly a ferryman. He was