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Complement

THE

DIAGNOSTIC AND PROGNOSTIC IMPORTANCE  
OF LEUCOCYTOSIS.

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## THE DIAGNOSTIC AND PROGNOSTIC IMPORTANCE OF LEUCOCYTOSIS.<sup>1</sup>

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THE material for this paper consists largely of blood-counts, 332 in all, which I have made at the Massachusetts General Hospital within the last year; and for all of it I am indebted to the kindness of the visiting physicians and surgeons of the hospital, who have given me the freest access to their cases at all times. I am under special obligations to Dr. F. C. Shattuck and Dr. R. H. Fitz.

It is important to know exactly what leucocytosis is before we attempt to estimate its diagnostic or prognostic value. It is a very difficult idea to define. Not one of the authors whom I have consulted have seemed to me to give a satisfactory definition, that is, one which sufficiently distinguishes it from leucæmia. Von Jaksch,<sup>2</sup> for instance, distinguishes it from leucæmia by its transitoriness, but it may last as long as leucæmia. Virchow defined it as an increase in the white cells of the blood due to a stimulation of the lymph glands, but in typhoid the increased glandular activity causes no leucocytosis.

Eichhorst, Jürgensen, Seifert, Müller, Strümpell, Vierordt and Pée<sup>3</sup> in their text-books give it to be understood that leucocytosis is transitory, symptomatic, and less in degree than leucæmia; but counts as large as those in leucæmia have repeatedly occurred in cases

<sup>1</sup> Read before the Section for Clinical Medicine, Pathology and Hygiene of the Suffolk District Medical Society, January 17, 1894.

<sup>2</sup> Von Jaksch: *Klinische Diagnostik*, 1889.

<sup>3</sup> Pée: *Untersuchungen über Leukocytose*; Inaug. Dissert., Berlin, 890.



where none of the characteristic lesions of leucæmia were present, especially in connection with malignant disease and the anæmiæ of children (Von Jaksch).

Very probably many of the reported cases of acute leucæmia where nothing was found at autopsy, were simply leucocytosis. The reported developments of pseudo-leucæmia into leucæmia were probably all leucocytosis. At any rate, I have not been able to come across a single such case where the crucial test of the differential count was applied. The mere increase in the white was held to constitute leucæmia.

On the whole, the best definition that I have been able to arrive at is this: Leucocytosis is the presence in the blood of an increased number of white cells of the same varieties morphologically as those in normal blood, a plurality and generally an overwhelming plurality being polynuclear.

In leucæmia many of the varieties of white cells present have never yet been found in normal blood, although every one of them has now been found in diseases other than leucæmia.

In leucæmia the polynuclear cells are never increased, and are generally in minority. In leucocytosis the polynuclear cells are generally much increased, and are never in a minority.

But we cannot say, as Friedländer<sup>4</sup> does in his short and pregnant definition, that: "Leucocytosis is an increase in the polynuclear or other varieties of white cells present in normal blood"; for in pure lymphatic leucæmia there are no varieties other than those found in normal blood, the diagnosis being made on the overwhelming majority of lymphocytes, or small mononuclear white cells, taken in connection with the other physical signs.

Practically, 90 out of 100 leucocytoses are perfectly

<sup>4</sup> Friedländer: *Microscopische Technik*.

easily distinguishable from leucæmia by their enormous percentage of the polynuclear varieties, 90 to 98 per cent. being the rule.

We cannot, then, make the distinction from leucæmia simply by the count. As an example of this, let me cite a case occurring in the wards of Dr. Maurice H. Richardson last summer, in which a mistaken diagnosis was made for lack of a differential count.

A. M., single, age twenty-one, entered with a diagnosis of malignant tumor. She was so pale that an examination of the blood was made. This showed an overwhelming number of white cells, 1 to 39 red; and taking this fact in conjunction with the position and nature of the tumor, a diagnosis of leucæmia was made. The tumor was in the region of the spleen, projecting below the left ribs, and it was thought that a notch was felt upon its upper surface. The patient was transferred to a medical ward; and here, after considerable delay, a triple stain and differential count of the blood was made, which at once showed that the case was not leucæmia, for 95 per cent. of all the white cells present were of the polynuclear type. Not long after this, the tumor began to assume a position near the median line, and a zone of resonance appeared between the left ribs and the tumor. During her stay on the medical side she had several well-marked chills. She was transferred to the surgical wards again, and the tumor was tapped in several directions, nothing but a little fecal matter being obtained.

She failed rapidly, decided to go home, and was lost sight of; but her death was reported in the papers within a few weeks. No autopsy. This was probably a case of large malignant new growth and the count, 1 to 39, was not higher than has been repeatedly found in large abdominal tumors. I have collected eight cases of malignant growths from literature in which the count was 1 to 50 or greater.

On the other hand, we may have leucæmia with no increase in the number of white cells. A few months ago Dr. Hubbard, of Taunton, sent me some blood-slides from a case of leucæmia, Mrs. S., which I had seen and counted in the hospital a year before in the service of Dr. Shattuck and which is now under Dr. Hubbard's care in Taunton. *They showed no increase at all in the white cells*; but on making a differential count, a large proportion of the white cells present were found to be myelocytes, so large a proportion as could only occur in leucæmia. The patient has still all the other signs and symptoms of leucæmia. In leucocytosis then, as distinguished from leucæmia, we have only those varieties of white cells present which are found in normal blood.

We have said that leucocytosis is an increase in the white cells over the normal number. This normal number has been somewhat disputed; but the majority of careful observers in late years agree in placing it at or near 7,500. Any variation, of more than 1,500 above or below this number is to be considered abnormal.

Now, leucocytosis is found in a considerable number of physiological conditions. This must be carefully borne in mind if we are to rightly interpret its significance in disease.

*Digestion.* — We have in the first place leucocytosis during digestion. This has been doubted by many authors; but the weight of authority is in favor of it, at any rate under certain conditions. Two and one-half hours after a meal rich in proteids the blood of most normal persons shows an increase of white cells varying from 1,000 to 7,000 above the normal.

Rieder,<sup>5</sup> who has made a most thorough investigation of the subject, says that in adults the digestion

<sup>5</sup> Rieder: Beiträge zur Kenntniss der Leukocytose, Leipzig, 1892.

leucocytosis rarely if ever goes above 13,000. Von Jaksch states that it may be so great as to cause a ratio of 1 white to 100 red, but he gives no cases in support of his assertion; nor does Klein,<sup>6</sup> who asserts that the white cells may reach 20,000 simply from digestion.

In children it may be a good deal higher, but never, I think, so high as the estimate of von Jaksch. My own investigations of this matter agree entirely with those of Rieder. In 21 cases, on various diets, I have never seen it rise above 13,000. In 13 of these it was absent altogether.

*Pregnancy.* — Next may be mentioned the leucocytosis of pregnancy and the puerperal state, which occurs in about two-thirds of all cases; it is generally moderate, not over 14,000. The leucocytosis of pregnancy might be of value in excluding those cases of phantom tumor simulating pregnancy. This has not been done as far as I know.

*Children.* — New-born children have a very considerable leucocytosis; which falls gradually, until at the sixth year the count becomes normal. At no time during the first year is 12,000 abnormal. Besides these physiological conditions, we must bear in mind hæmorrhage, which, if large, may cause considerable increase soon after the loss of blood; also the leucocytosis occurring just before death, so-called leucocytosis of agony. If these causes are excluded, any leucocytosis may be called pathological.

*Typhoid.* — Taking up now the diseases in which the count of leucocytes is important, I shall begin with typhoid. Most febrile diseases are accompanied by leucocytosis; and Strümpell, in the edition before the last, of his "Text-Book of Medicine," makes the mistake of saying that leucocytosis is present in typhoid.

<sup>6</sup> Klein: Volkmann's Sammlung Klinische Vorträge, Dec., 1893.

In this he only follows the lead of such authorities as Virchow, Vierordt and others, who, judging apparently from *a priori* considerations, have stated that in all diseases accompanied by increased activity of the lymph glands, increase of white cells should be found. As a matter of fact, however, the overwhelming majority of observers, and almost all the facts, are on the other side. As mentioned in Osler's text-book, Thayer has counted nearly 150 cases, not reported in detail as far as I know, in which no increase was found. Rieder, v. Limbeck,<sup>7</sup> Pick<sup>8</sup> and others have come to similar conclusions. Leucocytosis occurring in typhoid points to some complication, such as thrombosis, pneumonia, abscess. The diagnosis between relapse and some of these causes of temporary rise of temperature may, perhaps, be assisted by the blood-count. In a patient of Dr. Shattuck's, who had just recovered from a thrombosis during convalescence of typhoid, the temperature began to rise again. The question arose, whether this was due to the smouldering remains of the thrombosis (which, when active, had caused both fever and leucocytosis), or whether the patient was having a relapse. The blood-count was normal; two days later rose-spots appeared, and the subsequent course of the case confirmed the diagnosis of relapse as indicated by the blood-count.

In the last few months I have counted 79 cases of typhoid fever. In only one was leucocytosis present, and that in a child of four, where the normal number of white cells is so great that the count in this case, 1 to 300, may not be really leucocytosis at all. In 49 of my cases the number of white cells was less than the normal, and this agrees with most of the

<sup>7</sup> Von Limbeck: Grundriss einer Klin. Path. des Blutes, Jena, 1892.

<sup>8</sup> Pick: Klin. Beobachtungen über die Entzündl. Leukocytoes Prag. Med. Wochenschrift, 1890, No. 24.



latest observations. Lack of time prevented my making more than one count in each case of typhoid.

Cold baths, as recently observed by Thayer, may produce a temporary increase. In two of my cases I was able to confirm this observation.

Now this fact, the absence of leucocytosis in typhoid, is a very important one in the diagnosis of that disease, for a large number of affections with which typhoid is likely to be confounded *do* show leucocytosis. Local suppurations, for instance, which are sometimes difficult to distinguish from typhoid fever, almost always produce leucocytosis. Purulent meningitis has shown in every case which I have been able to find in literature (only seven in all) a very marked leucocytosis. I have only one case to add to this.

Last September, a man entered the Massachusetts General Hospital with a diagnosis of typhoid fever. He had the typical "typhoidal" aspect. Low, muttering delirium, heavy coated tongue, temperature 104.2°, pulse 115, respiration 22. He could give no account of himself, and complained of nothing in particular. Physical examination was generally negative. No rose-spots were present, no spleen was felt, and there was no distention. The diazo reaction was present. In the absence of any other obvious diagnosis, the case was considered one of typhoid. The blood-count, however, showed 22,000 white cells. Next morning the patient's brother arrived, and stated that the patient had been suffering for years with middle-ear catarrh. There was no discharge from the ear; but Dr. Green found purulent otitis with perforation in the left ear, and made a diagnosis of meningitis. The patient became unconscious within a few hours, and died two days later. No autopsy.

Ewing reports a number of cases in the *New York Medical Journal*, December 16, 1893, where the diag-

nosis was very difficult between pneumonia and typhoid until an examination of the blood cleared it up. No such difficulty has occurred in the cases I have seen, but, should it arise, the blood would undoubtedly decide in the great majority of cases.

*Typhoid vs. Appendicitis.*— A diagnosis between typhoid and appendicitis has presented considerable difficulty in several cases which I have seen at the hospital this year. As is well known, the pain of appendicitis may be very slight, and the tenderness no greater than is occasionally found in typhoid. The histories in a certain number of cases are not markedly different. In two such doubtful cases where I have found no leucocytosis, a diagnosis of typhoid has been confirmed by the subsequent course of the disease.

Three years ago, I saw in the hospital, in the service of Dr. Shattuck, a case in which the diagnosis between typhoid and some internal suppuration was for several weeks doubtful, until at last an abscess of the liver came to the surface and was opened. In such a case as this I think the blood examination would have settled the difficulty at once.

*Grippe.*— Between grippe and typhoid the blood does not help us, for in neither are the white cells markedly changed. I have counted but five cases of uncomplicated grippe, but in none of these, and in but few of those which I have found in literature, has increase been present.

*Sepsis.*— Between general sepsis and typhoid a blood-examination was of value in a case occurring this autumn in Dr. Shattuck's service. Patient presented symptoms and signs of acute polyarticular rheumatism with fever. The fever came down under salicylates, but soon rose again, and the man became wildly delirious. His delirium persisted after the salicylate was stopped. Several joints continued swollen and tender. The

fever was very moderate, ranging between 99° and 101°. There were no rose-spots and no spleen. The question arose as to whether it was a case of sepsis with localization in the joints, or whether it was a case of typhoid supervening on an arthritis of some kind. The blood-count, which was repeated several times, showed always a perfectly normal blood except for a slight anæmia. The subsequent course of the case, during which he remained for nearly three weeks more or less delirious, convinced Dr. Shattuck that it was a case of typhoid fever.

*Tuberculosis.* — As between typhoid and incipient pulmonary tuberculosis or tubercular meningitis, the blood does not give us any help. For in pulmonary tuberculosis all observers agree that leucocytosis is present only in advanced cases with high fever (that is, I suppose, in those where the infection is mixed) and in tubercular meningitis there is no leucocytosis, so far as observed. My own counts in tuberculosis in eleven cases have coincided with the results obtained by others. In two cases of galloping consumption and two cases of empyema with phthisis, leucocytosis has been present. In the other cases, consisting of two cases of tubercular peritonitis, two of early phthisis, two of tuberculosis of the kidney and one of general miliary tuberculosis, no increase has been present. I have only been able to find four cases of miliary tuberculosis in literature where counts have been made. In none of these was there any increase, so that in those cases of tuberculosis which would be likely to be confounded with typhoid the blood does not help us. The same is true of malaria, where a normal blood-count is found.

I stated before that the majority of cases of typhoid show by the second week leucopenia, or lack of white cells. Cases of debility with fever, and with or with-

out gastro-intestinal symptoms, which are sometimes difficult to tell from typhoid, may, perhaps, be distinguished from it in some cases by their normal count. Two cases of acute gastro-intestinal catarrh with fever, which I counted with a view of finding out the cause of the fever, both showed a decided increase in white cells. This might be of use in a diagnosis of typhoid.

*Pneumonia.* — It has long been known that pneumonia shows a marked increase in white cells. I published the blood-counts of 48 cases last summer, in all but 5 of which leucocytosis was present.<sup>9</sup> I dwelt then upon the prognostic significance of the absence of increase in the white cells, for all of the 5 which had no increase died. Since then I have counted 24 more, or 72 in all.

I will speak first of the diagnostic importance of blood in pneumonia. In the cases that I have seen it has helped mostly in distinguishing pneumonia from gripe, or rather in anticipating the complication of pneumonia in gripe. In three cases seen last month where no physical signs of pneumonia were present, where the history might do either for gripe or pneumonia, the high leucocyte count made me suspect pneumonia, and this was verified in each case by the appearance of signs of consolidation within thirty-six hours.

It is important before any treatment or any prognosis to make this distinction between gripe and pneumonia as early as we can, especially if we are in the habit of treating gripe with phenacetine.

Ewing, in the article mentioned above, says that he found a connection between the count and the amount of physical signs, and also between the count and the vigor of the systemic reaction. In my cases I have not been able to establish any such connection. High counts have been present in sthenic and in fatal cases

<sup>9</sup> Cabot: Boston Medical and Surgical Journal, August 8, 1893.

repeatedly; low counts in those with much lung substance involved. Of the 24 new cases since my last report on pneumonia, two have had no leucocytosis. One of these died. The other did not; but the course of the case was so interesting that I think it will be worth reporting a little more in detail.

The patient, L., was seen in Dr. Fitz's wards a few weeks ago, and was evidently a very mild case of pneumonia. Temperature and pulse were not high; there was no cyanosis, and but little lung involved. The man was perfectly sensible; and after the count, which showed a normal number of leucocytes, I felt as if the theory were certainly at fault in this case. The man was evidently going to get well. But within twelve hours the temperature rose to  $105^{\circ}$ ; the pulse to 160, and became so weak as to be almost uncountable. The man became much cyanosed and wildly delirious. He seemed almost moribund, and remained in this condition for forty-eight hours. At the end of this time he began to improve a little. The count was repeated, and found to show a marked increase in the white. He ultimately recovered. Now here was a case where from ordinary appearances at the time of the first count a good prognosis would have been given; but if we could have anticipated what his condition would be twenty-four hours afterwards, the prognosis would have been the very reverse. *The blood did anticipate it*; so that this case does not seem to me to be one which tends to upset the prognostic importance of the absence of leucocytosis in pneumonia. Of my 72 cases, 7 had no leucocytosis; 6 of these have died; and the other came so near it that if it had been foreseen what his condition would be, a very unfavorable prognosis would have been given. It is interesting here to see that when his condition began to improve, the leucocyte count rose.

*Phthisis* and *Pneumonia*. — Between pneumonia and phthisis in the early stages the blood-count might be of value, but it is not in this stage of phthisis that the difficulty of diagnosis would be likely to occur.

*Pleurisy*. — Pleurisy with serous effusion shows, according to v. Limbeck and Pick, moderate leucocytosis in febrile stages, none in the quiescent afebrile stage. I have counted six cases, two in the febrile stage and four in the afebrile stage; and my results are entirely in accord with those of the writers above mentioned. Rieder thinks (on the evidence of a very small number of counts) that tubercular effusions give no increase in leucocytes, even when febrile.

In three cases of empyema, I have found moderate leucocytosis, but not greater than that present in the febrile stages of serous effusions, so that no help is given by the blood-count, as between empyemas and serous effusions in the febrile stage.

*Scarlet Fever* and *Measles*. — Between these two diseases the blood is said by several authors to be of greater diagnostic importance, leucocytosis being present in scarlet fever and not in measles. I have had no personal experience in these diseases. According to Koczetkow, leucocytosis is present in scarlet fever in the incubation stage early as six days before the eruption.

In *Rheumatism* but few counts have been made. In the febrile stages the white cells are apparently increased. The same is true of erysipelas. In two cases I have found marked increase.

*Diphtheria* shows as high a count as any febrile disease. According to v. Limbeck the higher the count the worse the prognosis.

In *Follicular Tonsillitis* Halla has found moderate leucocytosis; and I have found the same in three cases, all febrile ones.

Experiments in the inoculation of animals with cultures of various pyogenic cocci show that those animals in which no leucocytosis is present generally die. This has been observed in a number of cases in the inoculation experiments at the Pasteur Institute last year.

*Malignant Disease.*—Leucocytosis occurs in a certain proportion of cases of malignant disease. Just what that proportion is and what relation the count bears to the presence of the disease in one or another organ, or to the kind of disease, does not seem to me to have been settled as yet.

V. Limbeck found it most frequently in soft, growing tumors, and constantly in osteo sarcoma. Here the count may be of great importance in helping the diagnosis between malignant disease or some other form of joint affection. Tuberculosis, for instance, as before mentioned, does not cause an increase in the white cells; nor does chronic arthritis sicca., nor gonorrhœal arthritis.

*Gastric Cancer and Ulcer.*—Schneider has, during the last year of two, maintained the thesis that the examination of the blood is of great importance in the diagnosis between cancer and ulcer of the stomach. He has found leucocytosis in all of 12 cases of cancer of the stomach and failed to find it in a number of ulcers. It is important here, however, to rule out all cases of ulcer where profuse hæmorrhage has taken place, or where a long-standing chlorosis is present, for chlorosis and hæmorrhage both may cause leucocytosis. In cases of ulcer not dependent on these causes, it seems that the count might be of diagnostic value. I have counted only two cancers of the stomach, and there leucocytosis was present. I have counted no ulcers. In the diagnosis between anæmia secondary to malignant disease, and the simple primary or pernicious anæmia, the count is certainly of importance;

for in these latter forms of anæmia, no considerable increase is often found, and although the absence of leucocytosis would not be of any great diagnostic importance, its presence might be. Moreover, Klein, the latest and most enthusiastic writer on the subject, states that in malignant disease, even where no leucocytosis is present, a differential count shows a marked increase in the percentage of polynuclear cells. In cancers of the uterus it has been found less often, and in cancer of the gullet it apparently does not occur, the white cells being decreased.

I have counted 19 cases of malignant disease and found leucocytosis in 12. In my cases a leucocytosis was present wherever cachexia was present, without any particular reference that I can trace to the position or nature of the tumor. The 7 cases where no increase has been present have been mostly small tumors, and all in persons where no cachexia was present. Thus, in a small cancer of the lip, a sarcoma of the testis, and a sarcoma of the abdominal wall, there was no increase. In all of these cases the tumors were small, and there was no cachexia. In one case of cancerous growth filling the whole pelvis, and in another case of very large sarcoma, probably of both suprarenal capsules, both without cachexia, there was no increase. The last of these two cases became cachectic, and several months after the first count the leucocytosis rose proportionally. In one case of multiple sarcoma of the skin where the tumors were very small, although fairly numerous, there was a large increase; but here again the patient was markedly cahectic.

*Appendicitis.* — I have counted 24 cases of appendicitis, and have been specially interested in these counts, because leucocytosis if constant in appendicitis would be a diagnostic factor of some value. In every case except two where pus was found at operation,



leucocytosis was present, the size of the count having, as far as I could judge, no relation to the amount of pus found. In three cases of appendicitis proved at operation to be catarrhal, no increase was present, as was the case in several others whose course made the diagnosis of catarrhal appendicitis probable, although this was not actually verified by operation. The count has seemed to me of real value in some cases where the diagnosis was difficult, between simple colic due to constipation (with or without gastro-intestinal symptoms) and true appendicitis. Two cases where symptoms and signs pointed decidedly towards appendicitis, but where no leucocytosis was present were relieved of all these symptoms within forty-eight hours, by clearing the bowels. The count may be of use, it seems to me, in deciding us whether an enema ought to be given. It is sometimes desirable to give an enema in cases simulating appendicitis to help clear up the diagnosis, but some physicians are afraid to do so for fear of causing a walled-off abscess to break into the general peritoneal cavity. In such cases, if no leucocytosis were present, we might go ahead with a clearer conscience.

Mr. B. entered the Massachusetts General Hospital September 20th, with a diagnosis of appendicitis. For twenty days he had been having pain and tenderness in the region of the appendix, pain being controlled by morphia. The bowels had been loose, he said. There was dulness, tenderness and a distinct tumor in the region of the appendix, with slight pyrexia. The blood-count showed only 8,000 leucocytes. He was given a compound cathartic pill, had a large movement of the bowels, and all symptoms and signs disappeared. V. Limbeck, Rieder, Pick and Koblanck<sup>10</sup> all state unconditionally that leucocytosis is present in general

<sup>10</sup> Koblanck : Inaugural Dissertation, Berlin, 1889.

septic peritonitis with fever. But in three cases of general peritonitis, two of them with appendix pus present, no increase of white cells has been present. I do not know how to explain these cases. It is possible that they may be explained in the same way as the absence of leucocytosis in some fatal cases of pneumonia. All these three cases of peritonitis died within twenty-four hours. It may be that the lack of leucocytes is a point in prognosis, pointing to a feeble systemic reaction. It is interesting also that in none of these three cases was there any pain, while in every one of those cases where I found leucocytosis, pain was a marked feature. This would suggest that pus under tension is more likely to cause leucocytosis than where free.

*Felons.*—The same thing is suggested by counts that I have made in felons and small abscesses in the Out-Patient Department. In three felons, one of which contained less than half a drachm of pus, I found well-marked leucocytosis, the blood being drawn as usual from the ear. In a paronychia with great pain, but without pus, no increase was present.

*Pus-Tube.*—In 15 cases of pus-tube or pelvic abscess I have never once failed to find leucocytosis. This fact may serve to help in the diagnosis between pus-tube and pelvic abscess, on the one hand, and those pelvic pains with no anatomical basis, and other non-suppurative and non-malignant pelvic affections, such as extra-uterine pregnancy, pelvic hæmatoma, and small ovarian cyst, on the other. In two cases of extra-uterine pregnancy I have found a normal blood-count. I may mention here two interesting cases of severe inflammation under the scalp, following scalp wounds. In one of these I found normal blood-count; and at operation no pus was found, only boggy, water-soaked tissue. In the other I found leucocytosis, and

plenty of pus appeared on making a cut. The external appearances of the two cases were almost exactly similar.

*Septic Hands, etc.*—I have counted three septic hands and one septic foot, and always found leucocytosis. The same is true of three buboes and two small abscesses of the neck. One case of mumps showed normal count.

*Osteomyelitis, etc.*—Two cases of osteomyelitis with deep seated suppuration (as proved by subsequent operation) showed marked leucocytosis, while one with similar symptoms, but normal blood-count, turned out to be rheumatism. Three cases of otitis media were counted. Two of them were purulent and had leucocytosis; one was serous and had none. In one case of housemaid's knee in which the general constitutional symptoms were more marked than usual, so that the presence of pus was thought of, I found large increase in leucocytes; a few hours after pus was found at operation. Two joint cases, one of the elbow and one of the knee, where before operation the question of pus was seriously entertained, showed normal counts, and no pus was found in either. Besides the three cases of general peritonitis mentioned above, where the indication of the blood-count was wrong, there should be mentioned a large abscess, apparently originating in the liver, which burrowed forward and was evacuated in the epigastrium, and which showed a normal blood-count. I have no idea why the blood-count failed in this case.

*Obstruction.*—In three cases of intestinal obstruction, one of them so closely simulating appendicitis that it was sent in by a surgeon of the Massachusetts General Hospital with that diagnosis, no leucocytosis has been found.

*Carbuncle.*—Two cases of carbuncle showed, as was expected, marked leucocytosis.

*Cystitis, etc.* — Two cases of cystitis, and three cases of endometritis showed normal count, as did two cases of so-called urethral fever following operation on bladder.

*Healing Wounds.* — On the whole, the cases where the blood has seemed to me of greatest importance have been those where after the operation, the wound having been sewed up tight, the question has arisen whether pus was forming inside. I shall speak of these somewhat more in detail.

CASE I. Frank B. was a case of appendicitis operated on by Dr. Richardson at the end of an attack. A little pus was found, the appendix was excised, and the wound nearly closed, a small strand of gauze, however, being left in. Several days after the operation, there being at the time no external discharge, the temperature rose. The wound seemed perfectly clean. The man was very nervous about himself, and much stirred up at each dressing; and as the temperature never went higher than  $101^{\circ}$ , there seemed to be considerable doubt as to what the cause of the temperature was. The blood-count in this case showed 52,000 leucocytes; on opening the wound a large amount of broken-down blood-clot was evacuated, and the temperature came down to normal.

CASE II. Mrs. S. was a case of pus-tube shelled out and sewed up tight. Ten days after the operation the temperature began to look a little like pus. Here again the patient was exceedingly nervous; and, as so often happens, the question was asked and re-asked, whether she was keeping up her own temperature by the state of her mind. The blood-count, however, showed marked leucocytosis, which led to a careful ether examination, revealing a fluctuant mass behind the uterus, from which pus was obtained by puncture.

CASE III. Mr. R. entered the Massachusetts

General Hospital in December, under the service of Dr. Porter, with a compound fracture of the thigh. Some days after it had been put up, the temperature began to look like pus, the wound, however, remaining perfectly clean. I counted the blood, and found a marked leucocytosis. A more thorough exploration of the wound revealed a pocket of pus, the evacuation of which brought down the temperature. I was not sure in this case whether the absorption of the blood-clot, such as takes place, I suppose, after any compound fracture would be sufficient to cause leucocytosis. I therefore counted several cases in which there was fever and presumably blood-clot absorption, namely, a hæmothorax, a pelvic hæmatocele, two compound fractures and a crushed foot; in none of these was any leucocytosis present.

CASE IV. Mr. S. was operated on by Dr. Warren for traumatic epilepsy. Nothing special was found, and the wound was closed. Ten days after the operation the temperature rose to  $104^{\circ}$ , and the patient complained of severe headache and pain in the back. I counted the blood, and found no leucocytosis. Next day the temperature was down. The patient apparently had the grippe.

There is no time to report more cases in detail, but these last cases have seemed to me to be very suggestive and interesting.

#### CONCLUSIONS.

Only in typhoid and in pneumonia does the number of counts which I have made warrant any conclusion. The absence of leucocytosis in typhoid and its presence in pneumonia (except in the severest cases) seem to me fairly well established and of some diagnostic and prognostic importance.

The number of cases counted among the surgical af-

fections is too few to warrant any conclusions; but they are sufficient, it seems to me, to make it important that the subject of leucocytosis in surgical cases should be studied much more carefully, with a view to its practical diagnostic value. If a felon with half a drachm of pus in it will cause marked leucocytosis, it certainly seems as if the diagnosis of deep-seated suppurations of larger size might be helped out by blood-examinations, as apparently it was in some of the appendix and osteomyelitis cases I have quoted.

Into the interesting and possibly important subject of the diagnostic importance of qualitative changes in the varieties of white cells, which is being so eagerly pushed in Germany just now, I have not undertaken to enter. Its advocates say it is even more important than the quantitative variations dwelt on in this paper.

#### TECHNIQUE.

In most of the cases reported above I have used the Thoma-Zeiss counter with Hayem's or Gower's solution and a dilution of 1 to 200. So great a dilution is condemned by German writers, as affording too small a number of leucocytes for computation, and so increasing the chance of error. To avoid in part this difficulty, I measured the field of my microscope, using always the same lenses. It happens to measure almost exactly one-quarter of a square millimetre, so that four fields of my microscope are almost exactly equal to the whole four hundred ruled squares of the Thoma-Zeiss instrument. By taking four fields in each of the four directions away from the sides of the ruled space of the instrument, we have counted as many leucocytes as we should have done by taking four additional drops from the pipette and counting only the ruled space. As the lines extend out some distance beyond the squares on each side, we can use them as a guide to start us in the

right direction; and by using a movable stage, we can be sure of not getting off the track and into fields already counted. After counting one field, the eye is fixed on a corpuscle at the side of the field most distant from the central ruled squares, and then by means of the moving stage the slide is moved until that corpuscle is on the inner edge of the field, that is, that nearest the ruled squares. By counting four fields in four directions, I had with the central ruled space twenty thousand squares as a basis of computation. In each count I did the whole process over with a second drop as well, making forty thousand squares in all. This gives us in most cases from fifty to one hundred leucocytes as a basis of computation, which makes the error considerably smaller.

I have used also the one-third per cent. acetic-acid solution, which makes the red corpuscles invisible, and can therefore be used with much less dilution than the other solution, 1 to 20 being that generally used abroad. I have used generally 1 to 50, and found the results obtained by counting the same blood first with Gower's solution (1 to 200) and then with the acetic acid to be so nearly the same that I have fallen back onto the 1 to 200 dilution, which has the advantage (besides that of needing less blood) that it does not deprive us of the count of red corpuscles, whereby we may check any mistake in our mixing by reference to the ratio of red to white. If the red are invisible (as with the acetic-acid method) we are deprived of this advantage.

#### DISCUSSION.

DR. M. H. RICHARDSON: I should like to say a word in regard to the application of this method to surgical diseases. Dr. Cabot examined the blood in many of my cases this past summer, and his conclusions were almost invariably correct. Several of the cases

which he has quoted were in my wards. With one exception we found pus every time the blood-count indicated it. Of course, in many instances we can tell well enough whether there is pus present or not without any such investigation; in other cases we cannot be sure, especially in the secondary abscesses which sometimes follow the drainage of appendicitis, in which one is very unwilling to stir up the abdomen without good reason. In one case referred to by Dr. Cabot, in which an appendix was removed at the end of the attack, there was a small amount of pus. Dr. Cabot is mistaken in regarding this case as aseptic. The patient, a young man, had developed very serious symptoms some time after the appendix had been removed. There was nausea and vomiting, with pain and tenderness. The pulse and temperature were elevated. Yet beyond the probability of pus deeply seated somewhere, we could form no definite opinion. Dr. Cabot examined the blood, and found a leucocytosis that indicated pus. We therefore felt justified in exploring the wound — an operation which should be undertaken only when clearly indicated. Dr. Conant operated for me twice, and the boy recovered. The amount of pus was very large; it was deeply seated and gave no physical evidence of its situation. The only instance in which we were mistaken was a case of general peritonitis following appendicitis. My diagnosis the first day was appendicitis, and I advised immediate laparotomy. The others thought it was some acute condition not demanding interference; moreover, Dr. Cabot found no leucocytosis. Inasmuch as he had been invariably correct in previous cases, I decided not to operate. On the following day, for other reasons, we opened the abdomen. Dr. Shattuck on that day made the correct diagnosis of appendicitis with general peritonitis; I, meantime, changed my



opinion. The patient's abdomen was distended with a very septic fluid; there was a gangrenous and perforated appendix, with a general purulent peritonitis. He died in the course of twenty-four hours.

From the surgical standpoint this subject is a very promising one. There is a very intimate connection between a leucocytosis and the presence of pathogenic micro-organisms. From the valuable work that Dr. Cabot has done, the treatment of patients has already been very materially improved. Further researches will undoubtedly give this method of investigation a still greater value in its practical application.

A question that arises frequently is, whether or not there is pus in the abdomen or in some of the closed cavities beyond reach. Now, if by such an examination as this we can be sure that, for instance, there is a perforation of the appendix or pus deeply seated in the abdomen, the vexed question of interference is decided at once. Moreover, if an expert examination of the blood is able clearly to demonstrate a condition of septic absorption; if, in connection with other symptoms, it can show unmistakably that there is a deep-seated focus of pus in the abdomen, in the thorax, in the head, or in a joint, it seems to me that we have added to our resources in diagnosis one of the most important and valuable aids of recent years.

Personally, I feel much indebted to Dr. Cabot for the work which he has done.

DR. F. C. SHATTUCK: I cannot forbear adding a word in expression of my appreciation of and interest in this paper. As I have watched Dr. Cabot's work in my ward and among my patients, I have learned to attach much value to this study which seems to me to promise great things for us in the future when thoroughly worked up.

DR. MASON: The very great interest of this subject

is certainly apparent, and I have listened with great pleasure to the paper. There are one or two questions I should like to ask. In speaking of purulent meningitis, I suppose that would include the epidemic cerebrospinal form?

DR. CABOT: I have seen counts of only two such cases. Both showed leucocytosis.

DR. MASON: In that affection there is a good deal of purulent secretion within the head and spinal canal. Cases are rare with us now; sometimes there is difficulty in determining the diagnosis with accuracy. I should think that blood examination would be very valuable. In one other affection I lately have been interested in having the blood counted; that was in a case of Graves's disease; and I should like to ask Dr. Cabot if, in his researches, he came across any statement with regard to that affection. Of course, it is pretty well known that internal abscesses give rise, as a general thing, to a greater or less degree of leucocytosis. In one case last year, or the year before, a liver abscess was explored for two or three times, and finally found, the blood-count having shown a high degree of leucocytosis. In the one case of Graves's disease I have observed there was no increase in the white elements.

DR. CABOT: I have counted only one case of Graves's disease, and in that the blood was normal. In those about which I have read the blood has been normal as far as the quantitative changes of the red to white were concerned.

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