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J. H. BRYANT, M.D., F.R.C.P. LOND.

ASSISTANT PHYSICIAN AND PATHOLOGIST TO GUY'S HOSPITAL.

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THE VALUE OF BLOOD EXAMINATIONS AS AN AID TO DIAGNOSIS AND PROGNOSIS.[1]

I HAVE been greatly interested in blood examinations for some time and am much impressed with the important information which can be derived from this method of investigation. I have therefore ventured to hope that a few remarks on the value of this form of clinical examination as an aid to diagnosis and prognosis will be of interest. During the last few years the number of workers in this field of clinical pathology has increased enormously and some very important papers and text-books have been published which deal with the subject and I would mention in particular the works of Ehrlich and Lazarus, Cabot and Ewing. A further impetus has been given to this fascinating form of research by a greater perfection in the methods, by the introduction of more reliable instruments, and by a simplification of the manner of fixing and staining films for microscopical examination. For many years it has been customary both in hospital and general practice to examine the urine of every patient when first coming under observation. The tendency at the present time is certainly in hospital practice to make also an examination of the blood of every in-patient, and in this respect the Johns Hopkins Hospital at Baltimore has been the pioneer, for every patient admitted to this institution, irrespectively of the diagnosis, has the blood examined in a routine manner. At Guy's Hospital many more examinations are made than hitherto; in the clinical wards which I have recently had under my charge the blood of every patient was examined as soon as possible after admission. It would be a matter of impossibility for a busy medical man engaged in general practice to use this aid to diagnosis in anything like a systematic manner on account of the length of time it requires to conduct a satisfactory examination of this kind. The

[1] A paper read before the West Kent Medico-Chirurgical Society.

technique is also a stumbling block ; this, however, can easily be overcome by a little practice. The scope of this paper must necessarily be small as the subject is so large, but I shall endeavour by reference to a few of my cases to draw your attention to some important and practical points and to give you an indication of the class of case in which a clinical examination of the blood is likely to prove of value.

There are several different methods of examining the blood, but I shall confine myself to a consideration of the following : (1) the estimation of the number of red and white blood corpuscles and the percentage amount of hæmoglobin ; (2) an examination of stained blood films in order to determine the relative proportion of different kinds of leucocytes, the form and character of the red blood corpuscles, and the presence or absence of protozoa and micro-organisms ; (3) the determination of the agglutinating power of the blood on certain bacilli—e g., in typhoid fever and Malta fever ; and (4) the bacteriological examination of the blood.

Before considering these methods of examination I will first of all remind you of the condition of the blood in health and of the abnormal corpuscles which may be found in disease. The normal number of red blood corpuscles per cubic millimetre is from 5,000,000 to 6,000,000 in men and about 4,500,000 in women. The average number of white blood corpuscles per cubic millimetre is about 8000 in adults and 10,000 in children. The varieties of white corpuscles and their relative proportions in health are : polymorphonuclear leucocytes, from 70 to 72 per cent. ; lymphocytes, from 22 to 25 per cent. ; large mononuclear leucocytes, 1 per cent. ; eosinophiles, from 2 to 4 per cent. ; transitional, from 2 to 3 per cent. ; and mast cells, 0·5 per cent. Myelocytes are present in leukæmia but not in normal blood. In health, the red cells are more or less uniform in shape and size, but in disease there may be smaller or larger forms and also nucleated cells of various sizes. The varieties of red corpuscles found are : normal red blood corpuscles, small red blood corpuscles (microcytes), large red blood corpuscles (macrocytes), normal-sized nucleated cells (normoblasts), small-sized nucleated cells (microblasts), large-sized nucleated cells (megaloblasts), enormous sized nucleated cells (giantoblasts), cells which stain irregularly (polychromatophilic), and cells altered in shape (poikilocytes). The estimation of the number of the red and white blood corpuscles is best accomplished by the Thoma Zeiss hæmocytometer and of the hæmoglobin by

Haldane's hæmoglobinometer. The technique of the making and staining of films, the estimation of the agglutinating power of the blood on certain bacilli, and the bacteriological examination I will endeavour to explain at the end of my remarks should time permit.

I. *What can be learnt from an estimation of the number of red blood corpuscles and of the amount of hæmoglobin.*—An examination of the blood is often necessary before an accurate diagnosis can be made, when anæmia is the most important and prominent indication of the patient being ill. Anæmia may be due to a deficiency of red blood corpuscles or of hæmoglobin or of both. It is of great importance to note the relation between the reduction in the number of the red blood corpuscles and of the percentage amount of hæmoglobin and it is at once obvious that there are three possible types of change which may occur—viz. : 1. A much greater reduction in the percentage amount of hæmoglobin than in the number of red blood corpuscles—viz. : with 3,500,000 (e.g., 70 per cent.) red blood corpuscles to the cubic millimetre 25 per cent. of hæmoglobin—the colour index being therefore considerably under 1. This is the chlorotic type of blood. 2. A very great diminution in the number of red blood corpuscles with a relative higher percentage of hæmoglobin—e.g., 1,000,000 (i.e., 20 per cent.) red blood corpuscles to the cubic millimetre with 25 per cent. of hæmoglobin—the colour index being therefore above 1. This is the pernicious anæmia type. 3. An equal or approximately corresponding reduction of the number of red blood corpuscles and percentage amount of hæmoglobin—e.g., with 2,500,000 (i.e., 50 per cent.) blood corpuscles to the cubic millimetre 45 per cent. of hæmoglobin—the colour index being just under 1. This is the type of a secondary anæmia. If the anæmia, however, is very severe it may approach nearer to the chlorotic type. It is by carefully noting the relationship between the number of red blood corpuscles and the percentage amount of hæmoglobin that a secondary anæmia can be distinguished from a primary anæmia when the cause is not apparent after a careful physical examination. A primary anæmia is a form of anæmia in which the cause is either unknown or there is no sufficient pathological change found to account for it. A secondary anæmia may be defined as a form of anæmia which is the result of some recognisable pathological change or lesion. Chlorosis and pernicious anæmia are classed as primary anæmias. Secondary anæmia may be caused by an

actual loss of blood, from diminished and defective nutrition, and from increased consumption or loss of albumins ; it may therefore result from severe hæmorrhages, from wasting diseases such as phthisis, cancer, &c , from syphilis, malaria, plumbism, intestinal parasites, and many other causes.

I will now tell you about three patients who were sent to me as cases of pernicious anæmia in order to have the diagnosis confirmed or refuted by an examination of their blood.

Case 1.—A man, aged 40 years, was brought to me for pernicious anæmia. He had been ill for three months and had been unable to work. His friends kept asking him why he was looking so pale and this was the first indication of the commencement of his illness. He had always enjoyed good health before. He had never had anything to do with lead. He had gradually been getting weaker and during the last three months had lost over a stone in weight. He had not vomited or passed any blood. He had had no pain. There had been neither sickness nor diarrhœa. He was intensely anæmic. His pulse was 124 and he was rather dyspnœic. The examination of the blood showed : red blood corpuscles, 3,750,000 ; white blood corpuscles, 12,000 ; and hæmoglobin, 25 per cent.—a chlorotic type of blood, the colour index being under 0·5, which at once showed that he was not suffering from pernicious anæmia, and further it was not likely that his condition could be explained by chlorosis for this disease is most unusual—in fact, almost unheard of—in men of this age. I therefore concluded that it was a secondary anæmia and after making a careful, systematic, physical examination found a tumour in the right lumbar region. It was tender, did not extend far back into the loin, was not connected with the liver, and was resonant on percussion. The urine was healthy. A diagnosis of carcinoma of the ascending colon was made which was subsequently verified by an operation and later by a post-mortem examination. This tumour gave rise to no local symptoms and was not discovered until the blood examination had proved that he was not suffering from pernicious anæmia, for which he had been treated.

Case 2.—A man, aged 72 years, was brought to me for cough and bladder trouble. He had enjoyed good health until about six months before when he was noticed to be ailing. He had suffered from bleeding hæmorrhoids,

frequent micturition, and looseness of the bowels. He had lost flesh and his appearance suggested malignant disease. A careful and systematic physical examination was made but nothing abnormal was found to account for his weakness. His urine was normal. A few weeks afterwards he went to the Riviera, became weaker and very anæmic, and consulted a medical man who felt what he considered to be some enlargement of the spleen. He diagnosed pernicious anæmia and treated him with arsenic. I saw him again about four and a half months after first seeing him, and found that he was intensely anæmic and very much like a case of pernicious anæmia in appearance. A blood examination showed 4,500,000 red blood corpuscles, 5000 white blood corpuscles, and 38 per cent. hæmoglobin—i.e., a chlorotic type of blood, the colour index being low, which at once excluded pernicious anæmia. A careful physical examination of the abdomen and of the tumour which was stated to be the spleen showed that it was more characteristic of an enlargement of the kidney or of a carcinoma of the colon. The former was considered to be most likely and a subsequent post-mortem examination proved it to be so.

These two cases illustrate the marked changes which take place in the blood as a result of carcinoma, but in both, the hæmoglobin index was remarkably low. Case 2 also is an example of what is usually found in most cases of malignant disease—viz., that in the early stages the anæmia is not a prominent symptom. The blood in carcinoma has a closer resemblance to chlorosis than any other form of secondary anæmia, for the hæmoglobin index is always low. In Osler and McCrae's monograph on malignant disease of the stomach, accurate blood counts were made in 59 cases: the average number of red blood corpuscles was 3,712,186 (over 70 per cent.), the average percentage of hæmoglobin was 49·9, and the average number of white blood corpuscles was under 8000 to the cubic millimetre.

Case 3.—The patient was a man, aged about 40 years, who was sent to me on account of his extreme anæmia and weakness, pernicious anæmia having been diagnosed. He had all the typical symptoms of anæmia and the general appearance of pernicious anæmia. For a long time he had been suffering from bleeding hæmorrhoids. The only abnormal condition, discovered after a careful physical examination, was the presence of large bleeding internal hæmorrhoids. The blood examination showed that he was not

suffering from pernicious anæmia, for he had 2,950,000 red blood corpuscles, 12,187 white blood corpuscles, and 22 per cent. of hæmoglobin, which indicated a marked secondary anæmia of the chlorotic type. The hæmorrhoids were treated by operation and the loss of blood stopped. Alginate of iron and arsenic were administered and after a few months he appeared to be perfectly well.

CASE 4. *Chlorosis.*—A girl, aged 18 years, was admitted into Guy's Hospital under my care for syncopal attacks, restlessness, and vomiting. She had led a sedentary life and had been under extremely bad hygienic conditions. There was no history of any loss of blood. She had suffered from amenorrhœa and constipation for some time. She was intensely anæmic and very short of breath on admission. There were loud hæmic bruits at the base of the heart and a well-marked venous hum in the neck. There were no physical signs or symptoms of disease of the lungs, liver, spleen, kidneys, or any of the abdominal viscera or of organic disease of the heart. A diagnosis of chlorosis was made and confirmed by the blood examination. There were 3,000,000 (67 per cent.) red blood corpuscles, 16,000 white blood corpuscles, and 25 per cent. of hæmoglobin. The leucocytosis was caused by some suppuration under the nail of her big toe. She was treated by rest in bed and with ten-grain doses of alginate of iron three times a day. Three and a half weeks afterwards a blood count showed rapid improvement. The red blood corpuscles numbered 3,875,000 and the percentage of hæmoglobin was 50 per cent.

The blood in chlorosis in marked cases is very pale and it rapidly coagulates. The average number of red blood corpuscles is 4,000,000 to the cubic millimetre when the patient first comes under observation and it is extremely rare to find a case with the red blood corpuscles as low as 1,000,000. The leucocytes are not increased. A blood examination alone will therefore not be sufficient to differentiate a case of chlorosis from a severe secondary anæmia. The diagnosis can only be correctly made when the result of the blood examination and the physical examination of the patient are considered together. If leucocytosis is present and the polymorphonuclear cells are increased chlorosis without any complications can be excluded. In the case of chlorosis alluded to above the leucocytosis was accounted for by the suppuration under the big toe-nail.

CASE 5. *Pernicious anæmia.*—A woman, aged 50 years, was under my care for pernicious anæmia, the third occasion on which she had been in the hospital for treatment for this condition. She was first admitted on April 4th, 1901, for vomiting and palpitation. She had been under treatment for acute dyspepsia. She had not been able to do any work since October, 1900, and her chief symptom had been vomiting. On admission she was markedly anæmic and her skin had a peculiar light yellowish tint. A blood examination showed 650,000 (13 per cent.) red blood corpuscles to the cubic millimetre and 26 per cent. of hæmoglobin, the colour index therefore being 2, which is exceptionally high ; there were 7000 leucocytes to the cubic millimetre. She was treated with liquor arsenicalis, five minims three times a day. Her mouth was in a very septic condition and there was well-marked pyorrhœa alveolaris. Cultures were taken and various bacilli, cocci, and streptococci were found. On the 13th she was ordered one-minim keratin coated tabloids of creasote and later was treated with injections of anti-streptococcic serum. She improved and on May 14th the blood showed 1,800,000 red blood corpuscles and 41 per cent. of hæmoglobin. She left the hospital much improved but was readmitted two months afterwards. She was intensely anæmic, the blood count being red blood corpuscles 750,000 and hæmoglobin 20 per cent. The blood film showed poikilocytosis and a number of normoblasts. She gradually became worse and died. At the post-mortem examination the only abnormal change which was found was an excess of iron in the liver.

This was a typical case of pernicious anæmia. The blood in this disease is pale and watery and coagulates slowly. There is a remarkable decrease in the number of the red corpuscles. The average in 52 cases examined by Cabot was 1,200,000 per cubic millimetre and the lowest count which has been recorded is in a case reported by Quincke in which only 143,000 red blood corpuscles to the cubic millimetre were present. The examination of a blood film shows in this disease a large proportion of macrocytes and the presence of nucleated red blood corpuscles. The diagnosis must rest on the small number of red blood corpuscles, the relatively higher percentage of hæmoglobin, and the presence of a large number of macrocytes and megaloblasts. The bad prognostic signs in this disease are an extreme reduction of the red cells—e.g., to 600,000 per cubic millimetre,—a high colour index, the presence of a large number of

megaloblasts, and an increase in the number of lymphocytes.

II. *Some practical points to be learnt from an estimation of the number and of a differential count of the various forms of leucocytes.*—The average number of white corpuscles in healthy adults is 8000 to the cubic millimetre. Certain physiological and pathological states are associated with an increase of leucocytes, whereas in other diseases the number of these cells may be diminished. Leucocytosis is the term used to indicate the former condition and leucopenia the latter. The degree of leucocytosis varies between very wide limits, from 10,000 or 12,000 to 1,000,000 or more cells per cubic millimetre, and cases have been recorded in which the white have equalled and even exceeded the red in number. Leucocytosis may be caused by a large number of conditions and it may be either physiological or pathological. Physiological leucocytosis occurs in the newly born, after digestion, during pregnancy, after parturition, after cold baths, violent exercise, massage, &c. Pathological leucocytosis may occur after hæmorrhage, as a result of inflammatory and septic conditions, from certain toxic states, in malignant disease, as a result of certain therapeutic influences, and in leukæmia. I shall confine my remarks to a few of the pathological conditions characterised by leucocytosis. When estimating the particular significance of the presence of leucocytosis in any given case it is not only necessary to find the number of white blood corpuscles per cubic millimetre, but also to know the percentage number of each variety of cell, which can be most satisfactorily ascertained by the examination of a stained film. The following case illustrates the importance of attending to these points.

Case 6.—A woman, aged 56 years, came to my out-patients' department on account of a painful swelling in her left side below the ribs. About a month before, as she was feeling ill and on account of the pain, she consulted her medical attendant who, after examining her, told her she was suffering from an enlargement of her left kidney. When I examined her abdomen I found a large tumour occupying the left hypochondriac, left lumbar, and left half of the umbilical region. It was tender and had a fairly well-defined, hard, rounded edge extending downwards from the right costal margin towards the umbilicus and reaching to a point about half an inch below it. It yielded a dull percussion note which was continuous in front with the

usual area of normal spleen dulness. It could be felt to extend well into the loin, so that from the physical signs it was difficult to say whether the tumour was splenic or renal. I examined a fresh specimen of blood under the microscope and found an enormous increase in the white blood corpuscles, for there appeared to be about one white to seven or eight red and this suggested a diagnosis of spleno-medullary leukæmia. She was admitted into the hospital and a few days afterwards a more careful examination of the blood showed a moderate leucocytosis with the polymorphonuclear cells predominating and no myelocytes. A subsequent post-mortem examination showed that the tumour was a peri-nephritic abscess, secondary to a calculous pyonephrosis which had discharged into the colon.

This case shows that a too hasty opinion must not be expressed before a satisfactory blood examination has been made. In cases of enlargement of the spleen a correct diagnosis cannot be made until the blood has been examined and this applies in particular to enormous enlargements of the spleen such as may be due to spleno-medullary leukæmia, chronic malaria, splenic anæmia, and spleno-megalic cirrhosis.

CASE 7.—A man, aged 30 years, came to my out-patients' department for anæmia, shortness of breath, and enlargement of the abdomen. He was markedly anæmic. His abdomen was distended and the spleen was enormously enlarged. It was found that the blood was pale and that it clotted very readily. There were 3,000,000 red blood corpuscles, and 300,000 white blood corpuscles to the cubic millimetre, and 42 per cent. of hæmoglobin. The differential count of the leucocytes showed—polymorphonuclear cells, 49 per cent.; myelocytes, 44 per cent.; lymphocytes, 4 per cent.; and eosinophiles, 3 per cent. The large percentage of myelocytes pointed with certainty to a diagnosis of spleno-medullary leukæmia.

CASE 8.—A girl, aged 23 years, was sent to the hospital for enlargement of the abdomen which was thought to be due to an ovarian tumour. A careful physical examination revealed enormous enlargement of the spleen which was considered to be due to spleno-medullary leukæmia. The blood examination showed a diminution in the number of red blood corpuscles and of the amount of hæmoglobin, but no leucocytosis. As she was not suffering from any inter-

current disease and had not been abroad her condition was considered to be due to either splenic anæmia or splenomegalic cirrhosis, and certainly not to spleno-medullary leukæmia. A few days afterwards she died from hæmatemesis and at the post-mortem examination the enlargement of the spleen was found to have been due to cirrhosis of the liver.

The chief characteristics of the blood in spleno-medullary leukæmia are: a reduction in the number of red blood corpuscles to about 3,000,000 per cubic millimetre, and an enormous increase of the white cells to between 200,000 and 500,000, of which over 30 per cent. are usually myelocytes.

In cases of enlargement of the glands, especially if associated with enlargement of the spleen, a blood examination is necessary before a correct diagnosis can be made. The disease which can, in particular, be diagnosed by this means is lymphatic leukæmia.

CASE 9.—A boy, aged 15 years, had no illness until a week before he was admitted into the hospital when he felt pains in the neck, axillæ, and groins, and on the following day he noticed lumps which quickly enlarged to the size found when he was admitted. On admission enlarged glands were found in the submaxillary, submental, cervical, axillary, suboccipital, and inguinal regions. A diagnosis of acute tuberculosis of the glands or of acute lymphadenoma was made. A blood count showed that the correct diagnosis was lymphatic leukæmia, for there were 3,800,000 red blood corpuscles and 43,750 white corpuscles, of which 95·6 per cent. were lymphocytes. Subsequent examinations showed a great increase in the number of white cells to 116,875 and 126,000. He died from hæmoptysis.

The chief characteristics of lymphatic leukæmia are therefore enlargement of the glands with or without enlargement of the spleen, but, when it is enlarged, never reaching the enormous size it does in spleno-medullary leukæmia. The red blood corpuscles are diminished in number as a rule to about 3,000,000 to the cubic millimetre; the percentage of hæmoglobin is reduced as in spleno-medullary leukæmia. The white blood corpuscles are much increased, but do not as a rule exceed 150,000 to the cubic millimetre and the percentage of the lymphocytes is enormously increased, on an average to about 96 per cent. Such an enormous lymphocytosis as this serves to distinguish it from lymphadenoma

and other diseases characterised by enlargement of the glands or spleen.

In suppurative and inflammatory conditions a leucocytosis may occur which does not often exceed 50,000 to the cubic millimetre. A differential count usually shows that the polymorphonuclear cells are in excess and may amount to 90 per cent. of the leucocytes. Klein has described a case of hæmorrhagic septicæmia in which 40 per cent. of eosinophiles were found in the blood. This occurrence of leucocytosis as a result of suppuration has a very important bearing on diagnosis, treatment, and prognosis, and is well exemplified in cases of appendicitis. Last year I had two male patients admitted on the same day suffering from appendicitis and each had a tumour in the right iliac fossa. After a careful physical examination and a consideration of the state of the abdomen and of the general condition of the patients I came to the conclusion that in one the tumour would subside and he would get well without an operation and in the other that a surgical procedure would be necessary. I had a blood examination made and found in the former 8500 leucocytes and in the latter 25,000 leucocytes. I asked my surgical colleague, Mr. L. A. Dunn, to see the two cases, and he decided to operate at once on the patient with the marked leucocytosis and to leave the other. He found an abscess and drained it and the other patient recovered without an operation. I do not mean to claim that a blood examination will tell you when to operate and when not to operate, but it will be an additional indication should the state of the abdomen and the general condition of the patient point to the advisability of immediate surgical interference.

Case 10.—Three months ago I hurriedly had to make a journey to the west of England to see one of my sisters who was suffering from a typical attack of appendicitis and it was left to me to decide whether she should be immediately operated on or not. Her pulse was 100, the temperature was 103° F., and there was a large tender swelling in the right iliac region. From a physical examination alone it was almost impossible to say whether pus was present or not I made a blood examination and found between 11,000 and 12,000 leucocytes and on the strength of this I decided to defer the question of operation. The opinion thus formed was justified by her recovery, the tumour gradually diminishing in size until it finally disappeared. I mention this case to emphasise further my opinion of the importance of blood examination in such cases.

Cabot's experience is that a marked leucocytosis—i.e., over 25,000—usually means a large abscess or peritonitis. A catarrhal appendicitis rarely causes leucocytosis. Very mild cases and very severe cases may show no leucocytosis, so that, as I have already stated, a blood examination must not be relied on alone as an indication of the pathological changes which have taken place or as an absolute guide to operation. With regard to differential diagnosis, if there is a difficulty in determining whether a patient is suffering from appendicitis or typhoid fever a leucocytosis would practically exclude typhoid fever. In pneumonia blood examinations are of very great importance both from the point of view of diagnosis and prognosis, for leucocytosis is a constant accompaniment of it, very mild and fatal cases being excepted. The increase in the number of white blood corpuscles can be found a very short time after the initial rigor and when the case ends by crisis the leucocytes do not fall to their normal number with the temperature but take two or three days to do so. When the temperature falls by lysis the leucocytosis falls with it and the normal number to the cubic millimetre is, as a rule, recorded when the temperature remains normal. If there is a difficulty in making a diagnosis, the presence of leucocytosis would point to pneumonia and exclude typhoid fever, influenza, and malaria. If the case is obviously pneumonia and the patient is very ill with a considerable area of lung involved, an absence of, or a very slight degree of, leucocytosis is an extremely grave prognostic sign. If the leucocytosis remains for several days after the temperature has fallen, and then a further rise of temperature and an increase in the number of leucocytes occur a relapse or empyema is indicated. Dr. H. A. Gaitskell has recently been working in the wards of Guy's Hospital on this subject and has published his results.[2]

Case 11.—The patient was a woman, aged 24 years, suffering from pneumonia. Dr. Gaitskell found no increase of leucocytes, the whole of the patient's left lung was consolidated, and in spite of the fact that her condition appeared to be satisfactory a bad prognosis was given and was confirmed by the death of the patient on the eighth day.

If pneumonia complicates typhoid fever an absence of leucocytosis or even a leucopenia does not necessarily mean a bad prognosis. A case of this nature was investigated by Dr. Gaitskell.

[2] Guy's Hospital Reports, vol. lvii.

CASE 12.—The patient was a boy, aged nine years, whose leucocytes did not rise above 10,937 per cubic millimetre. After the first examination, on account of the absence of leucocytosis, a bad prognosis was given, but two days afterwards a typical Durham (so-called Widal) reaction was obtained, and the absence of leucocytosis being thus explained a more favourable prognosis was given and justified by the boy's subsequent recovery.

In typhoid fever the most important characteristic of the blood is an absence of leucocytosis and in the later weeks of the disease the presence of a leucopenia. The differential count shows a progressive increase in the number of the lymphocytes with a corresponding decrease in the polymorphonuclear cells. I have already pointed out that diseases characterised by suppuration are usually associated with a polymorphonuclear leucocytosis, so that an absence of leucocytosis would be a point in favour of typhoid fever and much against appendicitis, perinephric abscess, hepatic abscess, suppurative pylephlebitis, and other forms of intra-abdominal suppuration, and it would also be against pneumonia.

CASE 13.—There has recently been a case of pyosalpinx in the hospital admitted for typhoid fever. The absence of a positive Durham reaction and the presence of a marked leucocytosis helped to exclude typhoid fever and to indicate the presence of intra-abdominal suppuration.

CASE 14.—A few weeks ago a patient under the care of Dr. E. C. Perry (who has kindly allowed me to mention this case) suffering from a typical attack of typhoid fever, suddenly, on the fifteenth day of the disease, complained of severe abdominal pain, became collapsed, and appeared to be suffering from hæmorrhage or perforation. The question of hæmorrhage was soon decided. The specific gravity of the blood was found to be 1053, which indicated that there had been no serious loss of blood. The red corpuscles were enumerated and found to be 3,750,000 per cubic millimetre, which also pointed to the same conclusion. This view was subsequently confirmed by no blood being passed per rectum. It seemed much more likely that perforation had occurred. On the previous day he had bitten off and swallowed the bulb of a thermometer which had injudiciously been placed in his mouth ; it was in the third week of the disease ; he had suffered from marked twitching of his hands which is said to denote that the ulceration was deep ; the abdomen was

full, rigid, and tender, and there was very little movement during respiration. The pulse was 128 and running in character. The leucocytes were counted and found to number 8250 per cubic millimetre, a result which was very much against perforation having occurred. It was decided not to operate at once, but that laparotomy should be performed if there was an ingravescent leucocytosis, so a leucocyte count was therefore made every hour for the next 12 hours, the number being found to vary between 7500 and 9000 per cubic millimetre. From a consideration of the result of these blood counts taken together with the improving condition of the pulse it was decided not to operate, and the decision has been justified by his complete recovery.

Malaria is a disease which is often confounded with typhoid fever, for in addition to pyrexia and other symptoms it is also characterised by an absence of leucocytosis. This difficulty does not often arise in this country unless patients have returned to it from a malarial district abroad. The presence of the malarial parasite in the blood is the absolute and decisive test of the presence of malaria. Tuberculosis cannot be distinguished from typhoid fever by a blood examination alone.

Eosinophilia.—I have alluded to a disease in which the lymphocytes are enormously increased, to conditions characterised by an increase in the polymorphonuclear cells, and to another disease in which a large number of myelocytes are present. I shall now say a few words about eosinophile cells. The examination of a blood film and the finding of a large number of eosinophiles were instrumental in clearing up a very difficult case.

Case 15.—The patient was a man, aged 25 years, who was admitted under my care for cough and attacks of dyspnœa. He had been invalided home from India. He had been seen by a physician who had diagnosed aneurysm and in consequence of this diagnosis he would have had to retire from his appointment. He was sent to me by Dr. C. S. Pantin of Douglas who had diagnosed asthma. I failed to find any positive evidence of aneurysm and an examination under the x rays did not show any sign of this condition. A blood examination showed red blood corpuscles, 6,587,500; white blood corpuscles, 10,625; and hæmoglobin, 90 per cent. The differential count showed 24 per cent. polymorphonuclear cells, 59 per cent. eosinophiles, 4 per cent. large lympho-

cytes, and 13 per cent. small lymphocytes. Eosinophilia in asthma has been noted by many observers and its occurrence in this case was undoubtedly an important diagnostic sign in favour of this disease. The blood examination saved this patient from compulsory retirement.

Eosinophilia occurs in a good many diseases and especially in certain skin diseases—viz., pemphigus, eczema, sclerodermia, psoriasis, urticaria, &c. ; also in some of the diseases due to animal parasites—e.g., bilharzia hæmatobia, ankylostomum duodenale, &c.

Malaria is a disease which cannot be diagnosed with certainty until the parasites have been demonstrated in the red blood corpuscles and this is best accomplished by staining thin films with carbol-thionin blue, eosin and methylene blue, or with Jenner stain. Not only can malaria be diagnosed but the particular kind of parasite may be demonstrated and from the examination of a blood film the type of fever predicted. The demonstration of the parasite is sufficient to distinguish it from other febrile diseases. The spirillum of relapsing fever may be demonstrated by means of blood films. Streptococci, pneumococci, typhoid bacilli, and other organisms are not usually found in stained films and their presence cannot be relied on as an aid to diagnosis.

III. *What can be learnt from the addition of blood serum to living motile cultures of certain bacilli.*—The diagnosis of two diseases—viz., typhoid fever and Malta fever—may be very materially helped by noting the agglutinating power of the serum of a patient suffering from either of these diseases on recent motile cultures of their respective bacilli. If a few cubic centimetres of blood serum from a patient suffering from typhoid fever are added to a recent actively motile broth culture of the bacillus typhosus the bacilli are precipitated in flakes, leaving the upper part of the fluid clear, and if the sediment is examined under the microscope the bacilli will be found to be no longer motile but to be agglutinated into compact non-motile masses. The agglutinating power of the blood is tested by mixing some blood serum with a recent culture of the typhoid bacillus and examining the mixture under the microscope. Authorities differ as to the degree of dilution and the time limit which constitute a positive reaction. It is customary in the Bacteriological Laboratory at Guy's Hospital to use a 50 per cent., 5 per cent., and 0·5 per cent. dilution, and the reaction is not considered positive unless clumping and

immobility of the bacilli occur with the 1 in 200 dilution within half an hour. Examinations made before the eleventh day of the disease with a negative result are of little value. That the result of the reaction is of great value is shown by Mr. W. C. C. Pakes's analysis of 304 consecutive cases in which the error was only 3·03 per cent. In doubtful cases a morphological examination of the blood should be made, and if, in addition to a slight or indefinite serum reaction, there are an absence of leucocytosis and a relative lymphocytosis the disease is, without much doubt, typhoid fever. A negative serum reaction does not necessarily prove that the patient is not suffering from typhoid fever. If the clinical evidence is sufficient to make the diagnosis certain a negative serum reaction should in many cases be looked upon as a warning of the possibility—in fact, I might say of the probability—of a relapse.

CASE 16.—Last year I had under my care a boy who was undoubtedly suffering from typhoid fever. Repeated attempts at obtaining a positive serum reaction failed until the beginning of the tenth week of his illness, when a third relapse was commencing.

CASE 17.—Lying in the bed opposite to the patient in the preceding case was another boy suffering from the same disease whose serum did not give a positive reaction until the middle of a second relapse.

The following case illustrates the value of the reaction in making a diagnosis of typhoid fever.

CASE 18.—A male, aged 25 years, was admitted on Sept. 11th, 1901, for debility resulting from diarrhœa. He commenced to feel ill a month before admission and complained of headache, diarrhœa, pain in the abdomen, and sickness. The diarrhœa continued and he could not check it with medicine. He became weaker and lost weight, but did not have to keep to his bed. On admission his temperature was 98° F., his pulse was 72, and his respirations were 24. The abdomen was not distended and the spleen was just palpable. There were no spots. The stools were liquid and pale. The possibility of ambulatory typhoid fever was considered and three days after admission his blood serum gave a positive reaction when diluted to 1 in 200, the temperature being 97° (*vide* Chart). A week after admission the temperature began to rise and he had a relapse. The diagnosis of this case as one of typhoid fever was much helped by the positive serum reaction.

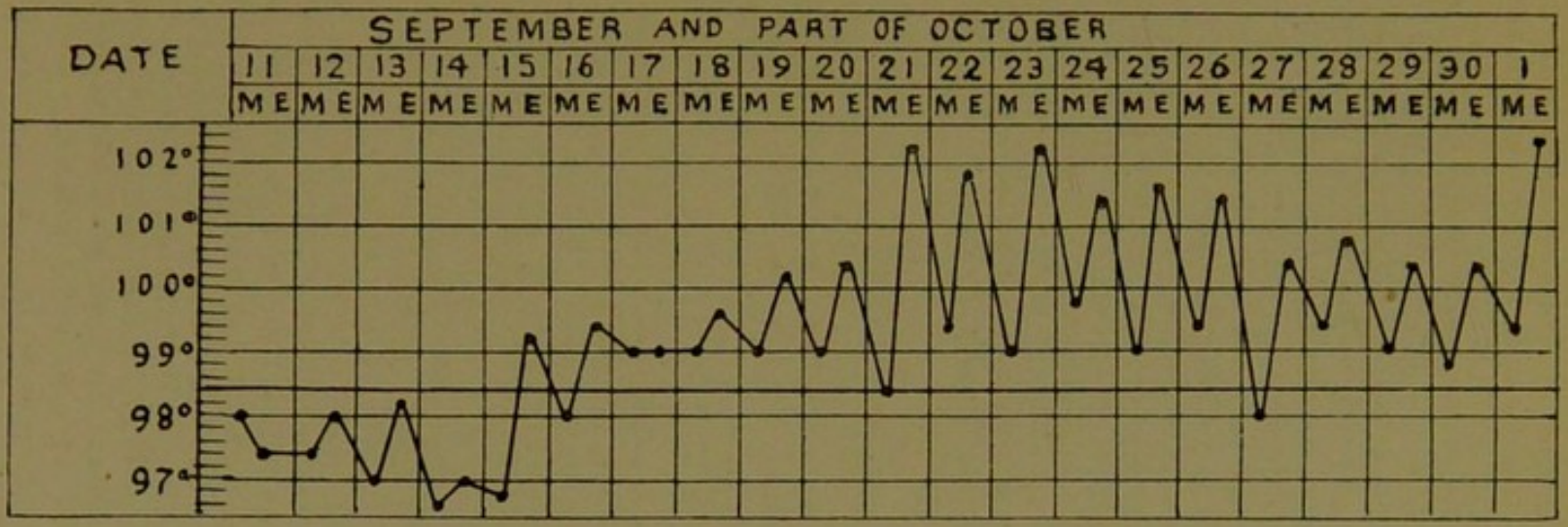

Chart of temperature in case of ambulatory typhoid fever with relapse. Positive serum reaction on Sept. 14th.

Malta fever may be diagnosed by means of a similar serum reaction if a culture of the bacillus Melitensis is mixed with the serum from a patient suffering with this disease.

IV. *The bacteriological examination of the blood.*—Great care must be exercised to prevent the possibility of the blood which is obtained for bacteriological examination being contaminated. The staphylococcus albus, if found, is due to contamination and is not the specific cause of the disease from which the patient is suffering. The micro-organism which is most frequently obtained by cultivating the blood is the streptococcus pyogenes. I have obtained it in a good many cases of infective endocarditis. If a patient is suffering from some valvular lesion, has an irregular temperature, is anæmic, and streptococci are obtained by cultivating the blood a diagnosis of infective endocarditis can be made and the indication for treatment is the injection of anti-streptococcic serum. A question which is often asked is—Is infective endocarditis invariably fatal? The following case bears on this point.

CASE 19.—A boy, aged 15 years, was admitted to hospital suffering from mitral disease. He had had several attacks of rheumatism. His temperature was varied and was running an irregular course, ranging between 98° and 101·5° F. When he first came under my care he had been in the hospital for nearly two months and during the whole of this time his temperature had been raised and he had not had any manifestation of rheumatism or of tonsillitis. A bacteriological examination of the blood showed the presence of streptococci in pure culture. A few days afterwards the temperature dropped to normal and remained normal. A subsequent bacteriological examination of the blood was negative. I considered that this boy was suffering from infective endocarditis, that the acute process had subsided, and the streptococci had died out.

I have endeavoured to show in this paper what can be learnt by examination of the blood in certain diseases. It is only a sketch of the subject which is one of very great interest to me. I hope I have not given the impression that I believe blood examinations are infallible as an aid to diagnosis and prognosis. I fully indorse what Ewing writes, "The examination having been performed *its results are to be interpreted only in the light of the fullest possible clinical information.*"

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No available reprint of Dr. Bryant's
paper on "Algoid vion."

Vide,-

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