DR. R. S. ROWLAND, Detroit, Mich., has been doing a limited amount of work with the Wright theory, but it is too early, he said, to draw any conclusions. Several interesting facts were brought out by some of the other workers in Detroit. One patient with tuberculous peritonitis, too bad for operation, was given tuberculin as a last resort and improved rapidly. The appetite improved first, then the general condition, and the fluid disappeared from the abdomen. The condition was so good that operation was delayed, and now it is not thought necessary to operate. Dr. Rowland saw a postoperative case beginning to show improvement, but whether or not this was due to the opsonic treatment or to the time in the disease, he is unable to say. However, the opsonic index has been higher than it was before this treatment, and the patient's condition is much better. Two facts have been brought out by this treatment. One that may be of value in the future, and which he thinks worthy of consideration, is the fact that in tuberculous peritonitis if the index is low before treatment, it can be raised so as to have the patient in better condition for operation. He thinks that operation is indicated as well as the opsonic treatment in most cases. After operation the opsonic index goes down and remains low for a long time, and this shows possibly that operation may be simply an autogenous method of producing vaccine. It may be that this is the reason why operation is of value. Dr. Rowland's observations lead him to believe in smaller doses of vaccine for therapeutic purposes than Dr. Rotch has given, from 1/3,000 to 1/4,000 mg. of tuberculin (T. R.) is a sufficient initial dose. This is gradually worked up as the patient can stand it. He also mentioned a case of meningitis —diplococcus meningitis. He saw the case late and after securing the vaccine the child had improved to such an extent that he was not allowed by the parents to use it. If he had given the vaccine he would probably have thought the improvement due to it.

DR. T. M. ROTCH, Boston, said that he has been using entirely Koch's original preparation. So far as he knows there is no great difference in the efficacy of the two preparations, only care must be exercised if using a new preparation to give much smaller doses. In these cases he investigated he gave the tuberculin without diluting. Those two children had enough to kill cows. As to the danger, he said that besides what has been done at the Children's and Infant's Hospital and at the Massachusetts General Hospital, a large number of children are being treated every day in this way. It is routine treatment to discover early tuberculosis. The work is done efficiently by Dr. Floyd of Boston. Dr. Rotch said that if tuberculin is given properly, there is no more danger than in giving opium, strychnin or arsenic. The dose for children is from 2 to 5 mm. He has never given 10 mm. That amount has been given at the Massachusetts General Hospital, but he thinks that from 2 to 5 mm. is the best dose. One milligram very seldom gives reaction. If one wishes to get a slight reaction, the interrupted treatment, one can begin in that way, but if a reaction is desired in one dose more should be given. Dr. Rotch can see no reason for not using this measure in private practice. It is taking a shorter time to determine the disease. Ordinarily he has an exceedingly intelligent class of people to deal with, and they are glad to know, because if it is beginning tuberculosis there is opportunity for cure. From 2 to 5 mm. is given as a diagnostic dose. For therapeutic measures he starts with small doses, going over a period of weeks and months. In adenitis they have had favorable results at the Massachusetts General Hospital. In the wards there were 25 cases of cerebrospinal meningitis in which he used antitoxin. It looked as though it might cure these patients at first. The final conclusions, however, were that it probably was not curative, but they have been using diphtheria antitoxin with the meningococcus vaccine, and this will carry up the opsonic index. Then they stop the antitoxin and go on with the vaccine. In the last ten or twelve years children that come into the Children's Hospital, no matter what appears to be the trouble, are given diphtheria antitoxin. This has given opportunity of comparison with other vaccines. Dr. Rotch has just reported a series of cases of cerebrospinal meningitis. He thinks that it is doubtful indeed whether or not the vaccine treatment is going to be any more curative than antitoxin, but it is worth trying. A case which was brilliant, but which he does not think proves anything, was that of a child 5 years old in private practice attacked within twenty-four hours; there was high temperature and the child could not swallow. Dr. Rotch gave it a dose of 50,000,000 organism; the next day it recognized its mother, ate and swallowed, and in two weeks it was sitting up; not cured, but with subacute symptoms of contractures. He said that he should not have stopped there, but should have known when to give another dose. This physicians have yet to learn.

THE DIAGNOSIS OF ANEMIA.*

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We may be concerned either with the fact, or with the type. Is anemia present? If so, what kind?

The question whether or not anemia is present can be decided only and sufficiently by testing the hemoglobin. We should never assume that anemia is present either from the symptoms alone, or from the appearance of the patient, or from both taken together. Mistakes from this cause are many. On the other hand, there can be no mistake in supposing that the patient who has a low hemoglobin is anemic, and practically no mistake in supposing that the patient whose hemoglobin is normal, or nearly so, is not anemic.

Diagnoses of anemia are very much more frequent than the facts justify. Patients are frequently treated for anemia when nothing more than a pale skin substantiates the diagnosis. The treatment does no harm except in so far as it may prevent us from taking measures more appropriate for whatever disease does genuinely exist. On the other hand, the mistake of assuming that a patient is not anemic, because there is a good color in the face, may lead to more serious consequences.

When the hemoglobin is normal, then, we need go no further in our blood examination, and may rest satisfied that anemia is not present. If the hemoglobin is low, we must endeavor, both by a general physical examination and by a study of the blood, to determine what type of anemia is present.

The important types of anemia may be classified as follows:

1. Chlorosis.
2. Pernicious anemia.
3. Secondary anemia, including:
   (a) Parasitic types.
   (b) Other types.

Rarer varieties are:

4. Myelophthisic anemia.
5. Aplastic anemia.

The first two types mentioned above are distinguished from the others by the fact that we have no idea of their cause. In this sense they may be and have been called "primary." The other types of anemia are "secondary" in the sense that they would not exist but for the presence of other diseases of one or another organ.

In the practical work of distinguishing these types of anemia the history of the case is of value to us chiefly when it points to some disease to which we can attribute the anemia as a result. If there is a history of recent malaria, dysentery or hemorrhage, this is important, though not conclusive, evidence that the anemia be-

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longs to the type called secondary. If the history gives presumptive evidence of the presence of malignant disease, of nephritis, or syphilis, it may afford us a useful hint regarding the type of anemia present. But so far as the symptoms of anemia itself are concerned, they are quite indistinctive and almost useless to us in differential diagnosis, because they do not differ essentially from those which may be produced by cardiac disease (organic or functional), or by a variety of debilitated states. The pallor and weakness, the dyspnea, the stomach troubles, the slight edema of the ankles, the throbbing arteries and disturbed sleep are all non-characteristic of the anemia to which they are due, because perfectly similar symptoms may be produced by other diseases.

On the other hand, considerable aid is given us by taking account of the age and sex of the patient and by taking a good look at him. Thus anemia existing in a girl between 17 and 25 is generally of the type known as chlorosis, while severe anemias in persons past 45, who do not complain of any special local symptoms but chiefly of general weakness, are very apt to turn out pernicious.

It is, therefore, on the physical examination of the body generally, and the blood in particular, that we must depend for definite diagnosis. To this subject I now turn.

The most important differential point in the physical examination of cases found to be anemic is the determination of the presence or absence of some organic disease known to be capable of producing anemia. On the other hand, a negative physical examination, including a negative examination of the urine, is a most important piece of information. Provided we know that anemia is present, a negative physical examination in a young girl points strongly to chlorosis, and in a person past 40 points strongly to pernicious anemia. I do not think there is any type of anemia which can be positively determined by the blood examination alone. Consequently, in the description of the different types to which I now turn, I shall group together all symptoms, physical signs and hematological data, which together determine diagnosis.

I. CHLOROSIS.

There is no such thing as chlorosis in boys, and if it occurs in a woman past 30 it is almost invariably a relapse or recurrence of a chlorosis established earlier. The typical age, as has already been stated, is from 17 to 25, that is, during the years immediately succeding those in which the function of menstruation is established. Though the patients complain of weakness, dyspnea and the other symptoms common to all anemias, they are usually not emaciated, but rather plump. Physical examination is negative or shows nothing more than systolic murmurs at all the valvular orifices of the heart, with perhaps slight edema of the ankles. The menses are often suppressed, and dyspepsia in one or another type is almost always present. The blood shows a reduction of hemoglobin to a point which averages 40 per cent. of the normal, while the red cells are not far from the normal point, averaging about 4,000,000 to the cubic millimeter. This discrepancy between the reduction of red cells and the reduction in hemoglobin means that each cell contains only about half the amount of hemoglobin present in a normal red cell. This fact is technically known as a "low-color index," and is further revealed in the stained film by the striking pallor of the centers of the corpuscles and the general tendency to a diminution in the diameter of the cells. There is nothing remarkable about the white cells. The disease seems to be getting rare—rarer than pernicious anemia.

II. PERNICIOUS ANEMIA.

The onset of this variety is strikingly insidious. Patients can rarely tell within a year or two when it was they began to feel the general weakness and incapacity for the relief of which they seek advice. There are usually no striking local symptoms, and physical examination in the early stages of the disease may be absolutely negative. It is only relatively late that we see the pale yellow tint of the skin, or find any changes in the function of the spinal cord. Patients are usually well nourished, for their digestive functions are rarely disturbed except for relatively short periods of time. The red cells are usually reduced to 2,000,000 or less at the time the patient first consults a physician. This reduction is in striking contrast to the absence of severe pain or other local symptoms. The hemoglobin is usually reduced relatively less than the number of corpuscles, that is, with a count of 2,000,000 red cells we may have 50 per cent. of hemoglobin. The white cells are usually subnormal. In the stained specimen we see that each cell contains as much hemoglobin as it ought. There is no pallor of the centers and the cells are strikingly oversized. This is the most important single point in the diagnosis of the disease. Less important are the great deformities, the changes in staining reaction, or the presence of nucleated red corpuscles.

This blood picture is not absolutely characteristic of the disease, but, when taken in connection with the history and the physical examination as above outlined, it is almost pathognomonic.

The diseases most likely to be confused with pernicious anemia are cancer of the stomach, myxedema, nephritis, cardiac disease and one or another of the parasitic anemias. Each of these will now be discussed, as types of secondary anemia.

III. SECONDARY ANEMIA.

1. *Malignant Disease and Pernicious Anemia.*—In the vast majority of cases malignant disease produces no anemia that is at all likely to be mistaken for pernicious anemia, but now and then we see cases, especially of gastric cancer, in which the count of red corpuscles will not distinguish the two diseases. Here the presence of marked and especially of continuous digestive troubles, together with a considerable degree of emaciation, a low-color index, and the presence of small-sized, poorly-stained red cells, with relatively few megaloblasts, or none at all, points to cancer of the stomach. Of course where a tumor can be felt the difficulty of diagnosis is not likely to arise. If, on the other hand, the patient is relatively well nourished, has periods of weeks or months during which digestion is good, and if the blood shows a high-color index and large-sized red cells—greatly deformed, abnormally stained and often nucleated—the disease is probably pernicious anemia.

2. *Myxedema.*—A clinical history and picture identical with that of pernicious anemia may be found in myxedema, except as regards to the data afforded by blood examination. The age of the patient, the insidious onset, the good nutrition, the general symptoms of anemia, the digestive disturbances (occasional, not continuous), may be the same in both diseases. But here the blood examination sets us right, for the blood of myxedema is never strikingly similar to that of per-

nicious anemia, but presents the characteristics of other types of secondary anemia, as described in the last paragraph.

3. *Nephritis.*—Only the external aspect of the patient and the general complaints are confusing here. The blood is quite unlike that of pernicious anemia, and the examination of the urine should help us to a speedy differentiation of the two diseases. It should be remembered, however, that pernicious anemia can and often does coexist with a considerable degree of those senile changes in the kidney which receive the name of interstitial nephritis when they become extreme. This coexistence of the two diseases should not be interpreted as anything more than coincidence. The nephritis is in no sense the cause of the anemia, for in the vast majority of cases this type of nephritis runs its course without any anemia whatever.

4. *Cardiac Disease.*—This malady is similar to pernicious anemia only in the symptoms which it presents, and sometimes in the pallor which accompanies it—a pallor due presumably to the imperfect filling of the subcutaneous blood vessels. The absence of any considerable anemia easily distinguishes the two diseases as soon as the hemoglobin test is made.

5. *Myelitis*—Diffuse or patchy sclerosis of the spinal cord accompanies a large proportion of all cases of pernicious anemia. In some of these cases the cord symptoms are so prominent and the symptoms of anemia so mild that the diagnosis of myelitis is made—the anemia being altogether overlooked. The blood examination, however, is usually as characteristic as in the cases without cord symptoms, and if we do not forget altogether to examine the blood the diagnosis is easy. The importance of differentiating simple myelitis from pernicious anemia with cord changes lies in the fact that the latter usually runs a much shorter course than the former.

6. *Parasitic Anemias.*—The fish tapeworm (*Dibothriocephalus latus*) is often carried by an individual without any anemia resulting. In other cases the blood is more or less diseased, and in a considerable group the blood may be absolutely identical with that of pernicious anemia, as has been shown by the minute and careful studies of Schaumann among the Finnish fishermen.

Hookworm disease, on the other hand, while often producing a very severe type of anemia, rarely produces a blood picture similar in all respects to that of pernicious anemia, for in hookworm disease, even when the red corpuscles are reduced to 1,000,000 or less, the color index usually remains low, the corpuscles small or of normal size, palely stained and less deformed than in pernicious anemia. Abnormal staining reactions and the larger types of nucleated red cells are less frequent, while the increase of white cells, and especially of eosinophiles, is usually distinctive.

In both the parasitic anemias just described, however, an examination of the feces is the mainstay of diagnosis, for in cases severe enough to produce a profound anemia the eggs of the parasites responsible for the disease are sure to be easily found.

IV. MYELOPHTHISIC ANEMIA.

As a result of a leukemic overgrowth of white cells in the bone marrow, as in the latter stages of leukemia, the red-cell-forming tissue of the marrow is apt to become so much compressed that a pressure atrophy occurs. As a natural result of this the supply of red corpuscles sent out into the blood stream becomes progressively diminished, and a grave anemia develops. This happens in almost every case of leukemia, both of the so-called lymphatic and the so-called myelogenous type, provided the patient lives long enough for the development of the pressure atrophy above described. In conditions other than leukemia, myelophthisis anemia is not often seen, but a few cases have been recorded resulting from malignant disease affecting the bone marrow.

The diagnosis of this type of anemia must depend wholly on its cause, that is, on the recognition of an overgrowth of cells of one or another variety, which drive the red-cell-forming tissue into a corner. This means in most cases the recognition of the disease leukemia, one of the easiest of all diseases to recognize.

In practical diagnosis, therefore, this type of anemia raises no considerable difficulty; it is here introduced merely because from the point of view of pathogenesis it deserves to be distinguished from the other varieties above described.

V. APLASTIC ANEMIA

Most of the recorded cases of this rare disease have occurred in young girls and have been accompanied by severe purpura. The blood is like that of pernicious anemia, except that the erythrocytes are smaller and rarely contain nuclei, while all the granular varieties of leucocytes are greatly diminished. Postmortem we find fatty marrow in the long bones, with no trace of regenerative effort.

ELEMENTS OF DIAGNOSIS IN ANEMIA.

	Chlorosis.	Pernicious Anemia.	Secondary Anemia in General.	Parasitic (Secondary) Anemia.	
				Due to a Fish Tapeworm.	Due to a Hookworm.
Cause...	0	0	+	+	+
History..	Not helpful.	Not helpful.	Very helpful.	Helpful.....	Helpful.
General physical examination.	Not helpful.	Not helpful.	Very helpful.	Eggs in stools.	Eggs in stools.
Blood...	Small cell type.	Large cell type.	Small cell type.	Large cell type (sometimes).	Small cell type (usually).

SUMMARY AND CONCLUSIONS.

1. In the diagnosis of anemia it is essential to take account of all the facts in the case. The etiologic factors and the data of general physical diagnosis are as important as the hematologic findings. Especially is this true in the types of anemia known as secondary.

2. There are but two important types of anemia, if we are to distinguish by blood examination alone. To the first type (the small cell type) belongs the anemias secondary to hemorrhage, malaria, nephritis and other diseases which lead to increased destruction of red corpuscles. So far as the blood picture is concerned, chlorosis is identical with the types just mentioned. It is distinguished wholly by the absence of etiologic factors and by the age and sex of the patient.

3. Pernicious anemia usually, but not invariably, can be recognized by the blood picture alone. If the data of blood examination are combined with those obtained by a careful history and physical examination the diagnosis is one of the clearest and surest in medicine. The most important single fact in the blood examination is the great reduction in red corpuscles, with a relative increase in the amount of hemoglobin per corpuscle (large cell type of anemia).

4. The parasitic anemias are not always to be recognized by blood examination, but present no difficulties of diagnosis if the eggs of the responsible parasites are sought. Myelophthisic anemia is easily recognized by the evidences of its cause and offers no difficulties in diagnosis.

THE TREATMENT OF ANEMIA.*

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I do not intend to read a paper on the details of the treatment of anemia. All are familiar with the chief measures and remedies employed in this treatment: Iron, arsenic, rest, nutrition, fresh air and other dietary and hygienic measures. As to the particulars, any of the many good text-books will give the desired information. But to do some justice to the task assigned to me, which at a weak moment I have thoughtlessly accepted, I shall discuss briefly some points in the treatment of anemia which, to my mind, mark a distinct progress. I do this with special pleasure, since the underlying work of some of these points was done in this country by men to whom the medical profession of this country owes a debt of gratitude for their continued splendid activities in the fields of science and practice of medicine.

The first point I wish to bring out refers to the progress made in the method of transfusion. In secondary anemias, especially in those following acute or chronic hemorrhages, the best measure of treatment of the anemia would be to replace the lost blood. But a century of attempts to carry out blood transfusion proved futile. Alien blood, or defibrinate blood of the same species, is harmful to the recipient, and the method introduced by Von Ziemssen, namely, the rapid withdrawal of blood by a syringe from the vein of a spender and its immediate injection, without defibrination, into the vein of the receiver, had very little success in practice. The method generally in vogue at present is, as you know, the venous infusion of one form or another of a so-called physiologic salt solution. Obviously these solutions do not replace the essential element of the blood, the red cells.

Within this year, however, the problem of transfusion has been brought nearer its solution by a bound, through the experimental and clinical efforts of George W. Crile. Using the improved technic of Carrel, he established an end to end union between a vein of a donor and an artery or a vein of a receiving animal, thus establishing a transfusion in which the blood of one animal is flowing directly into the vessels of another animal free from the dangers of intermediary manipulations. In a long series of experiments, that surgeon-physiologist has studied the effect of such a direct transfusion on the receiving animal and obtained most gratifying results. Even after complete exsanguination of an animal, with complete stoppage of respiration and with only a barely perceptible auricular heartbeat, a direct transfusion led invariably to a complete recovery of that animal. Crile next tested that method in a desperate post hemorrhagic case of anemia in a human being, brothers lent themselves as spenders, and obtained the same blissful result. In a recent communication before the Society for Experimental Biology and Medicine, Crile summarized his present clinical results by stating that the direct transfusion is a positive cure in all acute hemorrhagic anemias, and that in pathologic hemorrhages not only is the anemic condition invariably benefited but also the hemorrhages themselves are, in most instances, controlled without special treatment.

Permit me to point out that the experiments which that admirable man of Cleveland has carried out on seventy dogs will, undoubtedly, save thousands of human lives, and I feel called on to add that the so-called humane societies, which direct their agitation against animal experimentation and which just now, in their libelous circulars, are dragging the good name of Crile into mire, are engaged in a criminal activity which moral men, and especially physicians, should strongly resent.

The second point I wish to bring out concerns a simple method of treatment of pernicious anemia based on an advance made in the understanding of its etiology. The pathology of this disease, which is also designated as primary or idiopathic anemia, is admittedly obscure, but it was generally assumed that the cause is probably within the blood itself. During the past few years several writers have advanced the view that the disease is caused by an infection or an intoxication from the gastro-intestinal canal. These surmises had not much significance, since no facts were available showing a connection between the anemia and some definite form of infection or intoxication. Recently, however, in a profound and extensive study of the chemistry of the feces and the urine and of the bacteriology of the feces of fifteen cases of pernicious anemia, Christian A. Herter made a discovery that within the intestinal tract of such patients certain specific putrefactions are going on which are caused by the activity of anaërobic bacteria and that the *Bacillus capsulatus aerogenes,* discovered by Welch, is greatly in evidence in the feces of these patients. With the recovery of the patients from their anemic condition the predominance of this anaërobic bacillus in the feces disappears. Here we have a definite, well-established fact that at least in a certain number of cases of pernicious anemia, the anemic symptoms run parallel to the presence of well-defined anaërobic bacteria in the intestinal tract, and are probably caused by them. Among other measures of treatment in these cases, Herter recommends frequent and thorough irrigation of the colon, since it is the chief thriving place of these bacteria. Following this suggestion, Dittmar and Hollis were able to report a few months ago cures in two cases of pernicious anemia by irrigation of the colon which resisted all other methods of treatment. A few years ago Grawitz reported several cures of pernicious anemia treated by lavage, irrigation, restricted proteid diet of animal origin and other merely dietetic measures. It may be that lavage, as well as the restriction of the proteid diet, are unessential to the success. At any rate, the discovery that a good many cases of pernicious anemia are due to intestinal putrefaction, caused by anaërobic bacteria, and that some of these patients can be cured simply by efficient irrigation of the colon, present surely a valuable scientific and practical progress.

The third point I wish to touch on very briefly relates to the rôle of iron in the animal organism and its use in the treatment of anemia.

It is an old, well established clinical observation that inorganic iron is a most efficient remedy in chlorosis. For the last two or three decades, however, its use was

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