TYSON (Jas.)

THE

PRIMARY OR ESSENTIAL ANÆMIAS.

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THE results of the application of staining methods to the study of the blood by Ehrlich and his pupils, supplemented by the more recent studies of Von Jaksch, Löwit, Limbeck, Müller, Rieder, and others, have already modified to some extent our views as to the constitution of the blood in various diseases, and it is probable that there will be further changes. It seems, however, not an inappropriate time to review the conditions constituting the anæmias and the management which modern clinical experience has determined to be most successful, even though it may involve a repetition of some existing knowledge.

The broadest definition of anæmia—impoverished blood—is correct, but, more definitely, it is any state of the blood in which there is a diminution in its total bulk, its hæmoglobin, its albumen, or the latter two. The first is the condition which ensues from a large hemorrhage of any kind, as from the bursting of an aneurism, erosion of a blood-vessel in an ulcer of the stomach or in a tuberculous lung, as well as from traumatism. In all of these instances, however, where the hemorrhage is not fatal, the original bulk of the blood is rapidly restored by the absorption of water and salts from the tissues, while the hæmoglobin and albumen remain deficient. The hæmoglobin in blood may be diminished by a reduction in the total number of red corpuscles, or in the proportion of coloring-matter in each corpuscle.

Anæmias are further divided into *primary* or *essential* and *secondary* anæmias. The former are the direct result of a defect in the blood-making apparatus, while secondary anæmias are those resulting from the loss of blood, or some one of its important constituents, or of a defective supply of blood-making material.

Among primary anæmias are commonly included chlorosis, pernicious anæmia, leucocythæmia, lymphatic anæmia or Hodgkin's disease, and splenic anæmia. It is not conceded by all observers that pernicious anæmia is the result of a defect in blood-making. By some, as Quincke and Hunter, it is regarded as a hæmolysis or disintegration of the red blood-corpuscles in the circulation or certain parts of it, especially in the liver. While admitting that the facts adduced by Hunter, and more recently by Griffith and Burr, favor such a view, the evidence to me is not sufficiently conclusive to demand its transfer from the essential anæmias.

The secondary anæmias are numerous, including those due to hemorrhages, the action of poisons on the blood,—the toxanæmias,—viz., lead-poisoning, uræmia, drains of various kinds on the economy, inadequate food, and defects in the digestive apparatus. The present paper will be confined to the consideration of the primary or essential anæmias.

I.—CHLOROSIS.

Blood Changes.—At once one of the easiest recognized yet least distinctive of the anæmias in its morbid anatomy, chlorosis scarcely admits of a definition. A disease of overworked young women occurring most commonly at the age of completing sexual development, sixteen to twenty years, the most marked and constant change in the blood is a reduction in the hæmoglobin, associated with a moderate *oligocythæmia* or diminution in the red blood-corpuscles. The hæmoglobin value of each corpuscle is therefore reduced. Certain cases are, however, reported in which the eruthrocytes have been as low as one million one hundred and ninety thousand to the cubic millimetre. It is, moreover, true that the number is always somewhat below the normal, the maximum in one of fifteen cases observed by Limbeck being three million six hundred thousand, the normal for women being four million five hundred thousand. The hæmoglobin I have found as low as fifteen per cent., but such a fall is extreme. This disproportionate fall in the hæmoglobin, while not invariable, remains, however, a tolerably constant feature, producing sometimes a recognizable paleness of color when the blood is seen *en masse*.

Along with the lowering of hæmoglobin, as would be expected, since it is a constituent of the hæmoglobin, the iron of the blood falls. An increase of alkalescence, announced by Græber[1] as a constant symptom, has not been found by Kraus[2] in his more exact methods of testing.

As to remaining changes, the red corpuscles may be altered in shape to a moderate extent, constituting a small degree of *poikilocytosis*, or they may be larger than in health, when they are known as *megalocytes*. But even the slighter degrees of these conditions are not constant. More frequent is an undue reduction in size of the corpuscles,—a *microcytosis*. A very slight degree of *leucocytosis* may be rarely present, while the *blood-plaques* in severe cases may also be increased.

Morbid Anatomy.—Other than the changes in the blood there is no essential morbid anatomy to chlorosis. Many years ago Virchow pointed out an imperfect development of the circulatory apparatus as more or less characteristic,—that the heart was small, the aorta and its larger branches poorly developed and thin-walled. Such a state of affairs, when present, is probably an accidental coincidence. There is no enlargement of the spleen or lymphatics.

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[1] Zur klin. Diagnostik d. Blutkrankheiten. Leipzic, 1888.

[2] Zeitschrift f. Heilkunde, Bd. ii.

Symptoms.—While the blood-alterations in chlorosis are scarcely distinctive enough to be considered diagnostic, the symptoms are quite the reverse. The patient is invariably a girl, generally between sixteen and twenty, who, although she may have been overworked, does not seem badly nourished; certainly she is not emaciated. She is, however, characterized by a peculiar pallor, often exhibiting a yellowish-green tinge, which is especially marked on the mucous membranes, and is responsible for one of the names of the affection, green sickness. She is extremely weak, especially on exertion, and short of breath. She is subject to vertigo, palpitation of the heart, and even irregularity of the heart's action. Physical examination will sometimes discover functional cardiac murmurs. Rarely a compensatory hypertrophy of the left ventricle has been noted, but never valvular disease. Epigastric pain is also a symptom at times.

Diagnosis.—The diagnosis is based chiefly upon the age and sex of the patient, the peculiar greenish-yellow color, the paleness of the lips, and the decidedly diminished hæmoglobin, unaccompanied, as a rule, with a proportionate reduction in the number of eruthrocytes, although these are always somewhat diminished, and sometimes extremely so. The same lost normal ratio between the hæmoglobin and the corpuscles is also a characteristic of lead-poisoning, which has, however, superadded its own characteristic symptoms, and is almost restricted to adult males.

The epigastric pain mentioned as occurring in chlorosis resembles that more common in ulcer of the stomach. The anæmia which so constantly attends ulcer of the stomach, often in a high degree, is, however, different from that of chlorosis, there being a corresponding decline in the eruthrocytes and their coloring matter.

A not infrequent error of diagnosis in connection with chlorosis is the mistaking it for a "decline," a pulmonary consumption, which it resembles in the pallor, the feebleness, and shortness of breath of the patient. The absence of cough and of the physical signs of consumption will aid in a diagnosis between the two conditions.

Prognosis.—The prognosis is nearly always favorable when the disease is recognized and the proper treatment afforded. There are few results more satisfactory in therapeutics than those of a properly-treated case of chlorosis. Time is, however, required, and too rapid a cure must not be promised, several months to a year being usually required. The question whether a chlorosis will be transformed into that more serious variety of anæmia known as pernicious anæmia has been raised. This seems not impossible. Both are failures in the cytogenetic apparatus to produce a proper cellular blood. In the one, chlorosis, the coloring-matter is chiefly wanting, although associated with this is usually found a less degree of cell-defect. In pernicious anæmia both cells and coloring-matter are defective. Both embarrass the oxygen-carrying office of the blood, and thus interfere with important vital processes, the total suspension of which must be fatal.

Treatment.—The treatment is pre-eminently by iron, and it matters not

very much what preparation is used. The carbonate of iron, in the shape of Blaud's pill, made by a double decomposition between the carbonate of potassium and the sulphate of iron, is at this day very popular, one to three being given at a dose three times a day. But the tincture of the chloride of iron or reduced iron or one of the vegetable salts may be given. Iron is given in too large doses in the majority of cases for which it is prescribed. Most of it is unabsorbed, and therefore wasted; nay, worse, that which is unabsorbed locks up the intestinal secretions by its astringency, produces headache, and makes the patient otherwise uncomfortable. But chlorosis is one of the few diseases in which large doses of iron are well borne. The reason is plain. It is the iron-holding constituent of the blood which is wanting, and the iron is needed to replace it. The blood is, as it were, hungry for it. Next to iron comes arsenic. The efficiency of iron is greatly aided by union with arsenic, which should be given in increasing doses, but short of toxic effect.

But to give these drugs is not alone sufficient. Rest in bed, at first continuous, is imperative to secure a rapid result, and this must be associated with an abundance of good food. Daily massage, except during menstruation, is also a useful adjuvant. There is no condition in which the so-called "rest cure" is more efficient than in chlorosis. With a return of color to the lips, or, better, with the growing increase in the hæmoglobin as measured by the hæmoglobinometer, the patient should be permitted to be out of bed at first a half-hour to an hour only, but this should be gradually increased until she is up most of the day. For a long time, however, fatigue should be avoided. To those who can afford it a residence at the sea-side materially aids convalescence. Indeed, I know of no condition so rapidly improved at the proper time by sea-air as chlorosis. To the poor a well-regulated hospital treatment is a boon for which there is scarcely a substitute.

II.—PROGRESSIVE PERNICIOUS ANÆMIA.

A second variety of essential anæmia is *pernicious* or idiopathic anæmia, originally described by Addison in 1855, in his celebrated paper on "Diseases of the Supra-Renal Capsules." Biermer again drew attention to the subject in 1868, and since then numerous others have studied it anatomically and clinically. It is, however, still the least understood of all the anæmias. Fortunately, it is a rare disease.

Etiology.—The etiology of pernicious anæmia is almost unknown. The pregnant state seems to be responsible for a certain number of cases of true pernicious anæmia, the first of which were described by Channing and Gusserow. Other causes are cited, such as atrophy of the stomach, but I prefer to include under pernicious anæmia what Addison has characterized as a "general anæmia, occurring without any discoverable cause whatever, —cases in which there had been no previous loss of blood, no exhausting diarrhœa, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease." It can be best explained as a primary defective hæmogenesis, although some, led by Quincke, ascribe the state

of the blood to a hæmolysis, in proof of which they point to the enormous accumulation of iron in the liver noted by Quincke in 1876, and confirmed by Rosenstein in 1877. To these Hunter added a pathological increase of the urobilin in the urine. In a recent noteworthy paper Griffith and Burr take the same view.[1]

The disease affects mostly those beyond middle age, but children also have it, and Griffith mentions ten cases occurring under twelve. It is also more frequent in males.

Symptoms.—The symptoms of pernicious anæmia are most insidious, and begin with a gradual progressive weakness. What is first interpreted as a causeless weariness or languor grows slowly into an extreme debility with faintness on the slightest exertion, and thence into a state of thorough muscular weakness, which ultimately prostrates the patient, rendering him unable to rise from bed. To this succeeds a mental hebetude and state of general torpor. Yet there is no emaciation. The body-bulk is well preserved. The skin acquires gradually a yellowish hue, and sometimes an actual jaundice, whence, in connection with the symptoms, the disease has been mistaken for the slower form of yellow atrophy of the liver. In fact, the jaundice is similarly caused. It is a hæmatogenous jaundice, although it has also been ascribed to defective action of the liver-cells due to the accumulation of pigment in them. The mucous membranes, on the other hand, are blanched, as may be noted in the lips, gums, and mouth.

Cardiovascular symptoms are especially conspicuous in progressive pernicious anæmia. Hæmic murmurs, visibly pulsating and throbbing arteries, even pulsating veins, have been noticed. The large but soft jerky pulse was mentioned by Addison. The capillary pulse is also frequently seen, and hemorrhages, cutaneous and retinal, occur.

Digestive derangements also form a part of the symptomatology of pernicious anæmia. Indisposition to take food, nausea, vomiting, and diarrhœa are troublesome symptoms. Moderate elevation of temperature, irregular and intermittent, is also noted, while nervous symptoms, including numbness, languor, and even paralysis, sometimes occur.

The urine exhibits no constant changes, being sometimes pale and sometimes dark-hued. The dark color is ascribed by Mott and Hunter to an excess of urobilin.

Blood Changes.—The changes in the blood are more distinctive than in chlorosis, although it is true also that there is no single constant characteristic feature. The most constant is, however, a very decided oligocythæmia unaccompanied by a proportionate reduction in the hæmoglobin, although the hæmoglobin, as a whole, may still be less than in health. On the other hand, it is sometimes increased. Quincke found as few as one hundred and forty-three thousand corpuscles in a cubic millimetre of blood, while it is

[1] Pathology of Pernicious Anæmia, Transactions of the Association of American Physicians, vol. vi., 1891.

not uncommon to find them less than half a million. Frederick P. Henry found three hundred and fifteen thousand a few hours before death, and Laache three hundred and sixty thousand.

The inevitable conclusion from such a state of affairs is that either the hæmoglobin value of each corpuscle must be increased or there is a hæmoglobinæmia which has its seat in the plasma. This latter view Silbermann[1] has adopted, because he has been able to produce in animals by the administration of blood-corpuscle dissolving substances, as pyrogallol, a complex of symptoms like those of pernicious anæmia. If pernicious anæmia be a hæmolysis, as held by Hunter, rather than a defective hæmatogenesis, we would expect such a hæmoglobinæmia to result.

A further striking peculiarity in the blood of pernicious anæmia is the increase in the size of the red corpuscles. They become megalocytes, from ten to fifteen micro-millimetres in diameter, as compared with a normal of from six and five-tenths to nine and four-tenths. The majority may be so enlarged. On the other hand, there are also microcytes and poikilocytes, characterized by great irregularity in shape, being crescentic, conical, and otherwise distorted. While these irregular shapes were first demonstrated in connection with pernicious anæmia, and although they are more or less characteristic, cases of the disease have been described by Grainger Stewart, Lepine, and Hermann Müller in which poikilocytosis was absent.

There are also sometimes found in the blood numerous minute highly-colored spherical bodies, called Eichhorst's corpuscles. Eichhorst regarded them as pathognomonic, but they, too, are sometimes absent. When present they contribute to the hæmoglobin in the blood, but as they are not included in the blood-count they get no credit for their effect. The relative excess of the hæmoglobin may, in a measure, be thus accounted for. Nucleated *red* corpuscles are a constant constituent of the blood of pernicious anæmia, and have also been regarded by their discoverer, Ehrlich, as almost distinctive. Two kinds are found: first, the small normal-sized corpuscle with its deeply-stained nucleus, and certain large forms with pale nuclei. Blood-plaques, according to Osler, are either absent or very scanty. Leucocytes are usually slightly diminished in number, while there is a tendency to an increase of the mononuclear white cells as compared with health.

F. P. Henry[2] has called attention to a fact which, while it does not aid us in the solution of the problem of pernicious anæmia, is interesting and deserves to be mentioned. He says that in this disease the red corpuscles "approach those of the lower animals in many, if not all, of their chief characteristics, namely, in their number, their size, their shape, and the amount of hæmoglobin they carry."

Morbid Anatomy.—Various tissues have been studied in the effort to find a morbid anatomy for pernicious anæmia. In the absence of lymphatic or

[1] Berliner Klinische Wochenschrift, 1886, page 472.
[2] Anæmia, Philadelphia, 1887.

splenic enlargement, the marrow of bones has claimed close study. H. C. Wood described the red condition of the marrow of long bones in 1871. In October, 1875, William Pepper[1] described changes in the medulla of the sternum and radius from a case of pernicious anæmia, consisting, first, of a paleness as compared with health, and, second, in being made up for the most part of pale granular cells with single nuclei. Just a year later, Cohnheim[2] described changes in the medulla, characterized by the absence of fat-cells, by the presence of colorless cells of epithelial habitus and of various sizes very closely resembling lymph-cells, and containing one and two nuclei, a few multinuclear giant cells, and a very few blood-corpuscles holding marrow-cells. There was about an equal proportion of colored elements, among which the biconcave red discs were in a decided minority. More numerous were the spherical non-nucleated corpuscles of different sizes, while most numerous were the red nucleated cells.

In 1877 Pepper and the writer published a note in Virchow's Archiv[3] containing the results of the study by the latter of the marrow from the shaft of a femur from a case of pernicious anæmia. This marrow resembled a fresh blood-clot in appearance, but on examination was found to be made up of about equal proportions of red blood-discs and of granular cells of epithelioid character, for the most part larger than white blood-cells, but otherwise similar. The largest were one one-thousandth of an inch (.0254 millimetre) in diameter, the smallest one three-thousandth of an inch (.0084 millimetre). Most of these contained a single comparatively large nucleus. A few contained two nuclei. Some contained granular fat particles, while others were completely filled with granular fat (compound granule-cells), but there were no true adipose vesicles.

About the same time I also examined the medulla from a clavicle and radius sent from Montreal by William Osler. The mass was dark red and diffluent, being slightly decomposed. There was a relatively small number of red corpuscles, but a very large number of granular cells resembling colorless blood-corpuscles, but of larger average size, ranging from $\frac{1}{3000}$ inch (.0084 millimetre) to $\frac{1}{1500}$ inch (.016 millimetre). While many of them were nucleated and epithelioid, containing one, two, and rarely even more nuclei, in many no nuclei could be brought out even by aid of acetic acid. In addition to these two sets of cells were a number of nucleated colored cells, usually $\frac{1}{1500}$ inch (.016 millimetre) in diameter and oval in shape, containing from two to five nuclei. These were presumably the red nucleated cells described by Cohnheim. Finally there were found free oil-globules, compound granular cells, fat crystals doubtless from decomposition, and undetermined granular matter probably from the same source.

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[1] Progressive Pernicious Anæmia, American Journal of the Medical Sciences, October, 1875.

[2] Virchow's Archiv, October, 1876.

[3] Die Betheiligung des Knockenmarkes bei Perniciöser Anæmia, Virchow's Archiv, 1877, lxxi. 118–126.

These reports do not differ essentially, and, although the appearances described are not identical, they are sufficiently constant to justify their association as more than accidental. Summed up they amount to this: marrow dark-red, consistence less soft, fat-vesicles absent, specific cellular elements increased, numerous nucleated red corpuscles present.

The deposition of iron in the liver-cells has already been alluded to. It is found in the outer and middle zones of the lobules, and in two specimens examined by Osler was so distributed as to outline the bile capillaries. The iron is in like manner sometimes increased in the kidney, but not in the spleen, but these organs are not otherwise essentially changed.

The heart-muscle is fatty, while the other muscles are unusually red. Other morbid changes are described, but they cannot be regarded as essential. Such are changes in the ganglion-cells of the sympathetic, and sclerosis of the posterior columns of the cord. Osler and Henry describe a complete atrophy of the secreting tubules of the stomach in one case. But I should not regard this as a case of pernicious anæmia, but rather one of anæmia secondary to the atrophy of the gastric tubules, whereby the preparation of a suitable blood-making material is interfered with.

Diagnosis.—The diagnosis of pernicious anæmia may be uncertain at first, but its true nature soon declares itself. The intense anæmia, extreme weakness, digestive derangements, and cardio-vascular symptoms, in connection with a blood-count of two million or below, with a corresponding hæmoglobinæmia, and an admixture of megalocytes, microcytes, and poikilocytes, point to a condition scarcely mistakable.

Prognosis.—The prognosis is to-day regarded as less unfavorable than a few years ago, since recent experience has developed the fact that temporary improvement is not uncommon, and it is said that recovery sometimes takes place. Still, Addison's original prognosis, of a termination sooner or later fatal, is not often a wrong one.

Treatment.—Treatment of this form of anæmia is, however, not fruitless. The same measures which are almost a specific for chlorosis are not without effect in pernicious anæmia. Accordingly arsenic, to a less degree iron, good food, and favorable hygienic surroundings are to be adopted. The arsenic treatment has been followed by results which justify the words "temporary cure," and it is said that permanent cure has followed. Such temporary cures have covered a period of three years. The best preparation appears to be Fowler's solution in gradually increasing doses, until twenty and even thirty minims are reached, and this three times a day. The drug thus administered is wonderfully well borne, nausea and vomiting being rare. Rest in bed is indispensable, but may be supplemented with massage. Food should be in easily assimilable shape, such as beef-juice, beef-peptonoids, and peptonized milk.

Transfusion of blood and of milk, which seemed at one time to give promise of favorable results, have been discontinued.

III.—LEUKÆMIA.

The third of the essential anæmias is *leucocythæmia*, or *leukæmia*, the former of these words meaning white-cell blood, the latter simply white blood. From the etymological and histological stand-point, leucocythæmia, suggested by Hughes-Bennett, is the more accurate term, but, as the German mind leads the medical thought of the day, Virchow's term leukæmia has become the more usual one.

The extremely rapid course of certain cases of leukæmia justifies its division into an acute and a chronic form. An instance of the former was a fatal case reported by Ebstein, in which the whole course of the disease, including a prodromal stage, was but six weeks. Similar cases are reported. The duration of the chronic form may extend over years. Leukæmic women have had multiple pregnancies and have borne children at term.[1]

Etiology.—Nothing definite is known of the cause of leukæmia. It occurs in all countries, in both sexes, and at all ages, although more common in middle life and more frequent in males. The eighth week and seventieth year have found cases. It is sometimes hereditary. Malaria has been assigned as a cause, and certainly its association with this disease has been seemingly more than accidentally frequent. To a less degree this is true of syphilis. It is said to have followed a blow or injury, and to have been found in the lower animals.

Morbid Anatomy.—Leukæmia has a definite morbid anatomy, consisting in alterations in the blood and in the hæmogenic apparatus, including the spleen, the lympathic glands, and the marrow of bones, and it is called accordingly splenic, lymphatic, myelogenic, while a compound word, as splenic-myelogenous, is used when two of these agents are at fault.

The splenic changes exhibit three stages in their development. In the first the spleen is simply hyperæmic, soft, and swollen even to the extent of rupture. The Malpighian bodies share in the hyperæmia and may be slightly enlarged, but are overshadowed by the swollen pulp. In the second stage hyperplastic changes make their appearance in the Malpighian bodies, and as these grow the pulp is intruded upon. They may reach such size as to be recognized by the naked eye as spherical gray nodules one to three lines in diameter, or they may be elongated, or forked, following the course of the blood-vessels. The third stage furnishes the granitic spleen, in which white dots are separated by dark streaks representing the destroyed pulp, pigmented by the disintegrated blood. The spleen is now hard and is cut with resistance. Its size may be enormous and the organ weigh from two to eighteen pounds.

The lymphatic enlargement is a true hyperplasia. Not only do the glands enlarge, but new foci of lymphatic tissue appear in various organs,

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[1] See cases reported by J. Chalmers Cameron and Saenger, Sajous' Annual for 1891, E.

as the liver and kidneys. These are also said to be simple extravasations of leukæmic blood from the capillaries. All the more prominent groups may share in the enlargement,—the cervical, axillary, inguinal, and perineal glands. The individual glands remain, however, soft. The lymphatic follicles in the tonsils and in the tongue, pharynx, and mouth may enlarge. This is also occasionally the case with the solitary glands of the intestine and the agminated glands of Peyer.

In myelogenic leukæmia the marrow-changes may be described in a word as reversion to the embryonal type of medullary tissue. The fat of the adult marrow has disappeared, and a mass of lymph-cells mingled with nucleated red corpuscles in all stages of development takes its place. The lymph-cells include numerous large mononuclear cells in the act of division by karyokinesis, multinuclear leucocytes, and a few mononuclear cells. There are also numerous marrow cells, including both eosinophiles and myelocytes like those found in the blood.

The liver is often enlarged, and, according to Von Jaksch,[1] *pari passu* with the spleen, and it has this further peculiarity, that its edges are rounded, while in what he describes as *pseudoleukæmia infantum* the edges are sharp and the enlargement does not go hand in hand with that of the spleen. The liver is also at times infiltrated with leukæmic patches and nodules not unlike miliary tubercles. The same is occasionlly true of the kidney.

The thymus gland has been found enlarged in some cases of acute lymphatic leukæmia, and even the skin, stomach, and gastro-splenic omentum have been the seat of growths presumably lymphatic. In fact there is no situation in which such growths may not make their appearance. The possibility of their being blood extravasations, white in consequence of the large proportion of white cells, is always to be remembered.

The lungs and heart alone seem free from encroachment by the lymphatic tissue. The heart may, however, be dislocated by a large spleen.

The alterations in the blood constitute really a part of the morbid anatomy of leukæmia, but are commonly treated under the head of symptomatology, where I, too, will consider them.

Symptoms.—The early symptoms of leukæmia are precisely those of the other anæmias, insidious onset, pallor, rapid breathing amounting to dyspnœa on exertion, weakness and faintness, headache, loss of appetite, and indigestion. The last two symptoms may precede all others. Moderate fever with rapid pulse is also present in the majority of cases, the temperature sometimes reaching 103° F. Headache more or less continuous is also a symptom. Swelling of the abdomen from an enlarged spleen may be the first noted, lymphatic glandular enlargements more rarely. In a case recently under my advice the first intimation of the presence of a large spleen was an attack of circumscribed peritonitis, favored, doubtless, by the presence of the splenic

[1] Sajous' Annual for 1890, vol. ii., E. p. 12.

tumor and excited by exposure to cool air while perspiring. Hemorrhages from the nose and stomach are common, and dropsical swelling towards the close. Very recently Thomas Oliver reported a case terminating fatally by sudden post-peritoneal hemorrhage.[1] Hæmatemesis may be an early, an almost initiatory, and fatal symptom. Osler has recorded two striking cases terminating thus. Purpura hæmorrhagica sometimes presents itself as a manifestation of the same tendency, as may also cerebral hemorrhage, producing coma. Priapism is sometimes a symptom, and in a case of Edes was the first noted.

The urine often contains a little albumen, is high-colored and scanty, and deposits a copious sediment of uric acid.

Blood Changes.—The blood exhibits a most marked and diagnostic change, consisting in an enormous leucocytosis. Normal blood contains about six thousand colorless corpuscles to the cubic millimetre, which, with the red discs at four and a half million, makes the proportion one to seven hundred and fifty; or with the eruthrytes at five million, one to eight hundred and thirty-three. There is a physiological leucocytosis which after a full meal may reach one to one hundred and fifty, and even one to one hundred. In leukæmia, however, there may be one to fifty, to twenty-five, to ten, to three, to two, or the leucocytes may equal and in rare cases even exceed the red discs. A case at this time under my observation has one to six. The maximum proportion of colorless corpuscles impresses decidedly the color of the blood *en masse*, making it pink, or even the color of chocolate and milk, while aggregations of leucocytes may produce white streaks, and well justify the notion of the older pathologists that there was pus in the blood,—a suppuration of the blood, as they called it.

There is also a reduction in the total number of blood-cells, including white and colored, the quantity per cubic millimetre being sometimes reduced to between two and three millions. This reduction may be even more positive, as in a case reported by Suchannek,[2] in which there were three hundred and one thousand six hundred red discs and three hundred and six thousand one hundred colorless corpuscles.

Numerous nucleated red discs are sometimes present, and occasionally also poikilocytes. The hæmoglobin falls below the normal proportion, so that the value of each disc is lowered. The blood-plaques may be slightly increased.

An early discovery in the study of leukæmia was certain transparent octahedral crystals, known as Charcot's crystals, which form in blood which has been kept for some time on slides. Neumann referred these crystals to the bone-marrow, but Von Jaksch says they are the same as those sometimes found in the expectoration and in fæces and seminal fluid. There is reason to believe they are decomposition products, and that they hold no essential relation to leukæmia. That the alkalinity of the blood is some-

[1] American Journal of the Medical Sciences, November, 1892.

[2] Sajous' Annual for 1891, vol. ii., E.

times diminished is true; that it is ever replaced by acidity is not true, although this was at one time held.

The further minute study of the blood in leukæmia requires a review of the histological characters of the colorless corpuscles in normal blood. These, through the studies of Ehrlich and others, have assumed a much greater complexity than heretofore. It occurred to Ehrlich that important differences in white corpuscles could be differentiated by staining-fluids, and, putting into practice this conception, he was enabled to discover five different varieties, as follows:

1. Lymphogenous elements arising in lymphatic glands. (*a*) Small lymphocytes. (*b*) Large lymphocytes.

2. Myelogenous elements arising in marrow, including eosinophile cells.

3. Undetermined elements arising in spleen and marrow, or in marrow only. (*a*) Large mononuclear cells. (*b*) Transitional forms. (*c*) Polynuclear cells.

I. (*a*) The small lymphocytes are somewhat smaller than the red blood-corpuscle (Fig. 1), and contain a large, round, deeply-staining nucleus, surrounded by a very scanty and almost invisible layer of homogeneous protoplasm. (Fig. 2.)

(*b*) The large lymphocytes are a further development of the first, and differ from them only in possessing a larger and easily recognizable rim of protoplasm. (Fig. 3.)

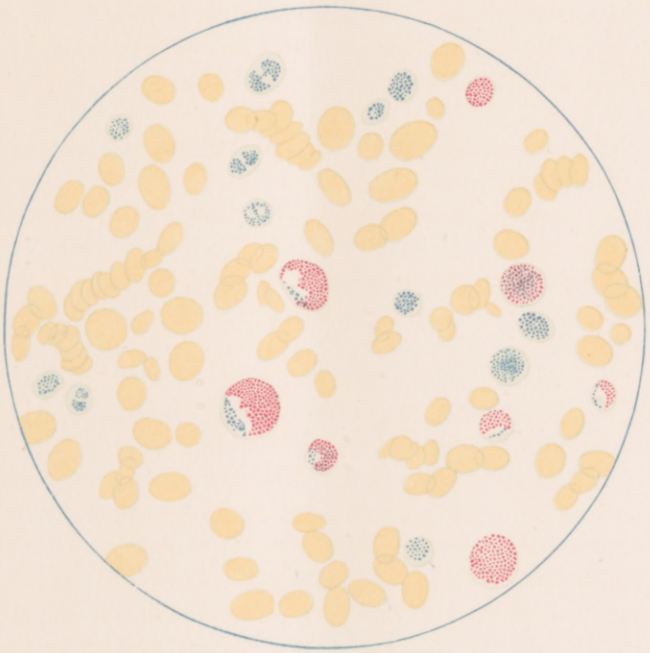
II. The eosinophile cells, originating in the bone-marrow and only rarely seen in normal blood, are colorless corpuscles, characterized by coarse granulation, containing one, two, and more rarely three nuclei. They take the *a*- or eosinophile granulation stain described below. (See plate, Fig. 8.)

III. Undetermined elements originating in spleen and marrow or marrow only. (*a*) The large mononuclear cells are about three times the size of a red blood-corpuscle, and contain a large round or ovoid nucleus and a large ring of protoplasm. (Fig. 5.) (*b*) The mononuclear transition form differs from these only in that the nucleus is no longer round or ovoid, but indented. (Fig. 6.) (*c*) The polynuclear elements (Fig. 7) are somewhat smaller, but still larger than the red corpuscles, and their nuclei exhibit further differentiation in that they are polymorphous. These are the more usual white blood-corpuscles, which have long been recognized. Except in the lymphocytes the protoplasm of these cells is granular, but the granulations possess different properties, which have also been investigated by Ehrlich, who makes five different varieties of granulation, which he distinguishes by letters of the Greek alphabet from α to ε, as follows:

The *α-granulation*, or *eosinophile* granulation, is characterized by large granules, highly refracting or oil-globule-like, and stainable by all acid aniline staining fluids. They are found in the myelogenous elements, very rare in normal blood, but strongly increased in leukæmic processes, and called *eosinophilic* by Ehrlich because of their strong affinity for eosin. (See plate.)

PLATE II.

FIG. 8.



BLOOD FROM CASE OF LEUKÆMIA, SHOWING EOSINOPHILOUS CELLS.—Ocular, Zentmeyer A, Objective, Zeiss $\frac{1}{12}$, oil immersion.

FIG. 1.

Red corpuscle.

FIG. 2.

Small lymphocyte.

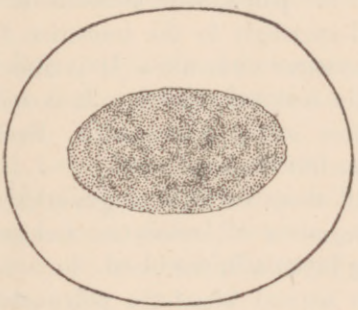
FIG. 3.

Large lymphocyte.

FIG. 4.

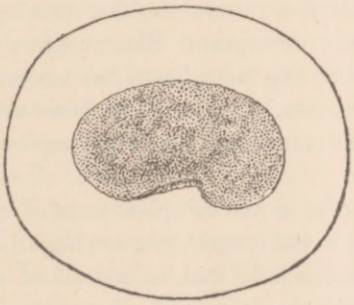
Myelogenous cell-element, including the α-granulation, or eosinophile granulation. Seldom found in normal blood, but greatly increased in leukæmic processes. Granules stainable in acid staining fluids.

FIG. 5.



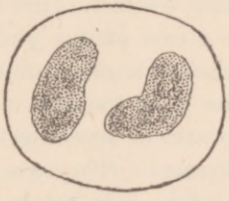
Large, mononuclear cell. δ-granulation, or basophilic granulation. In leukæmia are found large cells like these, but presenting the "neutrophilic" granulation. Also myelogenic.

FIG. 6.



Transition form.

FIG. 7.



Polynuclear cell. ε-granulation, or neutrophilic granulation. Very delicate, neutral colors.

Figs. 1 to 7 are diagrammatic, intended to show the relative sizes of the various cells compared with the red corpuscle. After a drawing by my colleague Prof. Guiteras.

The *β-granulation*, or *amphophilic* granulation, is found especially in the cells of the medulla of bones, but also in blood, often in the leucocytes of rabbits and guinea-pigs, and is stained by acid and basic or similar fluids, hence called *amphophilic*.

The *γ-granulation*, or *basophilic* or "mastzellen granulation,"[1] is stainable by basic aniline colors, as are bacteria: The granules are coarse and refract light but slightly. This granulation is almost altogether wanting in healthy human blood, but is increased in leukæmic processes. These granules are also found in the blood of some animals in health, as the white rat.

The *δ-granulation*, also basophilic, is finer, stainable in basic aniline colors like bacteria, and is found in the large mononuclear leucocytes.

The *ε-granulation*, or *neutrophilic granulation*, is very delicate, and pervades the polynuclear elements of normal human blood very densely, is found sparingly in the transition forms of cells, and very seldom in the mononuclear elements. It is also characteristic of the *myelocyte* found only in leukæmic blood. It is stained by neutral coloring-matters, and therefore called *neutrophilic*. Such is the granulation of the common polynuclear leucocyte.

All these varieties of granules may become free in the blood by the disintegration of leucocytes, and are among the sources of error in recognizing bacteria in the blood.

In normal blood the polynuclear cells form sixty-five to eighty per cent. of the colorless corpuscles, the lymphocytes fifteen to thirty per cent., the mononuclear and transition forms about six per cent., and the eosinophiles two to four per cent.

Diagnosis.—The diagnosis of leukæmia requires the microscope, but with it becomes easy. A refinement of diagnosis, thus aided, attempts with more or less success to separate the different varieties, which are known as simple or complex, according as one or more of the cytogenous organs are implicated. Thus, of the simple forms there would be the splenic, lymphatic, and myelogenous. In his recent monograph Rieder says that, so far as he knows, pure splenic and pure myelogenous forms have never been observed, while the pure lymphatic form has.[2] The latter is, however, rare, while a case of the pure myelogenous variety is, however, reported by Fraenkel, in a girl of fourteen.[3]

The most frequent of all the varieties is the complex form of *splenic myelogenous* or lieno-myelogenous. In it the *lymphocytes* are slightly if at all increased. They are relatively diminished; that is, instead of representing fifteen to thirty per cent. of all the leucocytes, they represent a smaller proportion. The *eosinophiles*, on the other hand, which are very

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[1] This word is retained because there seems to be no corresponding word in English.

[2] Beiträge zur Kenntniss der Leukcytosis. Von Dr. Hermann Rieder, 1892, S. 36.

[3] Deutsche medizinische Zeitung. Berlin, 1890. Sajous' Ann., vol. ii., E. 19.

rare in normal blood, are increased and conspicuously handsome in a stained preparation by their bright red granules. The polynuclear neutrophiles are either normal, sixty-five to eighty per cent., or relatively diminished, particularly towards the close. But the most characteristic feature of this variety is the presence of cells not found in normal blood, the *myelocytes* of Ehrlich, so called because of their supposed origin from the marrow of bone. They are mononuclear, as large as, and even larger than, the large mononuclear leucocytes, which they resemble also, but from which they differ in the fact that the protoplasm is "neutrophilic," while the mononuclear cells are "basophilic." To these forms Müller[1] has recently added another large mononuclear cell which exhibits karyokinetic figures. It is found in leukæmic blood and in the marrow, and is apparently the marrow-cell originally described by Cornil, and which is said not to occur in normal blood.

If relatively large leucocytes prevail, we may infer the presence of the splenic form with a relatively small involvement of the lymphatic glands and of the bone-marrow.

If there are numerous transitional forms between the white and red blood-cells, if there are nucleated red blood-corpuscles, but especially large polynuclear leucocytes, containing large eosinophilic granules, we may infer marked alterations in the bone-marrow; in a word that myelogenous leukæmia predominates.

In pure lymphatic leukæmia the colorless cells are never so numerous, scarcely ever exceeding one in ten, while the lymphocytes only are increased, all the other forms being greatly diminished, and myelocytes are altogether absent. In a case reported by Uthemann, ninety-three per cent. of all the leucocytes were lymphocytes, as compared with fifteen to thirty per cent. in normal blood.

In acute leucocytosis the ε-granulation or neutrophilic cells, both mono- and polynuclear forms, are increased, while the α-granulation or eosinophilic cells are apparently diminished. The reverse obtains in incipient leukæmias, where the eosinophilic and basophilic cells are increased.

Too much stress must not, however, be laid upon the diagnostic value of these cells, until observations multiply. Thus Von Jaksch found eosinophile-cells in the blood of an adult in health, of a boy with tuberculosis, in a case of pneumonia, and in all forms of anæmia. Dolega and Aldehoff have recently found numerous eosinophiles in the blood of malaria in three cases. Müller and Rieder have made similar observations, and Fink found numerous leucocytes of the eosinophilic-granulation type in the blood of asthmatics. So also Von Jaksch found the karyokinetic forms described by Müller in the blood of a case of sarcomatosis, as did also Weiss.[2]

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[1] Archiv f. Klin. Med., 48, 51, 1891.

[2] For references to all the above see Von Jaksch, Klinische Diagnostik, third edit., 1892, p. 31. All are within the dates 1890–91.

Caution should be observed, too, in basing the presence of a leukæmia solely on a leucocytosis, as some remarkable instances of this condition have been reported wherein leukæmia did not supervene. Thus Von Jaksch, in his studies of the anæmia of children, found such proportions as one white to twelve red corpuscles, one to seventeen, and one to twenty; and in the case of an adult one to eight, and still no leukæmia followed.[1] The association of lymphatic or splenic or myelogenous change with the leucocytosis is essential to a diagnosis. And especially valuable as diagnostic of leukæmia is a large number of eosinophiles, and, according to Von Jaksch, Klein, and others, in the beginning of leukæmia this increase in the eosinophiles is the only change. Rieder is also inclined to regard the cases of so-called acute leukæmia as really acute inflammatory leucocytosis rather than leukæmia.

Allusion has already been made to an anæmia described by Von Jaksch as *anæmia infantum pseudoleukæmica*, further studied by Loos and Luzet, which is not to be confounded with leukæmia. Its essential feature is an enormous falling off in the cellular elements of the blood, the red cells being as low as eight hundred and twenty thousand, and the white fifty-four thousand six hundred and sixty-six. The proportion of leucocytes is always increased, but never to the same degree as in leukæmia, nor is it so rapidly brought about. On the other hand, the leucocytes are characterized by their varied shape and unusual size. The red cells display a high degree of poikilocytosis, while white cells enclosing red cells and fragments of red cells are also found, together with occasional eosinophilic leucocytes and large multinuclear neutrophilic leucocytes and nucleated red cells. All of these modifications of the blood-corpuscles may occur in leukæmia, but in the latter disease there is not as marked a reduction either in the hæmoglobin or in the number of cellular elements. The difference in the form of the liver and splenic enlargement in the two conditions has been referred to.

Prognosis.—The prognosis of leukæmia is unfavorable, the best that can be expected from treatment being the deferring of the fatal end. Some rather remarkable fluctuations are noted, and cases of cure are even reported, especially of late by inhalations of oxygen. The lymphatic leukæmias are the more acute and more intractable.

Treatment.—The treatment has heretofore been mainly with iron, quinine, and arsenic, fresh air, and good food. Large doses of arsenic, as much as thirty drops of Fowler's solution, reached by gradual increment, have been especially recommended, and certainly should be tried.

Inhalations of oxygen, suggested in 1887, were used by Sticker and Pletzer with temporary benefit, and Da Costa and Hershey report the apparent cure of one case, a boy of thirteen, and such marked improvement in a man of thirty-five that he was thought for a time to be cured. This treatment deserves, therefore, to be tried along with that first named.

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[1] Op. citat., p. 29.

Thirty to one hundred litres (about four to twelve gallons) of oxygen are to be used daily.

IV.—LYMPHATIC ANÆMIA.

The fourth of the essential anæmias is *lymphatic anæmia*, also known as Hodgkin's disease, pseudoleukæmia, lymphadenosis, lymphadenoma, malignant lymphoma (Billroth), adénie and lymph-adénie. Hodgkin's paper, to which we are indebted for our first definite knowledge of the disease, appeared in 1832.

The disease consists essentially in an anæmia unassociated with an increase in the colorless corpuscles of the blood, accompanied by a fibro-adenic enlargement of the lymphatic glands, and the formation of lymphatic foci in the spleen, and occasionally in other glandular organs.

Etiology.—Its etiology is as undetermined as that of leukæmia. Depressing influences of all kinds are believed to favor it. Scrofulosis has sometimes preceded it. The presence of an irritating substance in the blood has been suggested, and the necessity of local irritation, associated with a lymphatic diathesis, has been insisted upon by Trousseau.

Morbid Anatomy.—Its morbid anatomy is, however, definite. There is both lymphatic and splenic involvement, the latter secondary to the former. The tonsils, intestinal lymphatic structures, and even the liver and kidneys, may be invaded. There is, moreover, a deposition of new foci of lymphatic tissue decidedly more marked than in leukæmia. The enlargement usually begins first in the more superficial groups, as those of the submaxillary region, neck, axilla, and groin, but the entire lymphatic system may be involved, including the retroperitoneal glands, resulting sometimes in marked abdominal enlargement. Occasionally the overgrowth is limited to the deep-seated glands. Of the abdominal, the retroperitoneal are most frequently involved, producing tumors which have been mistaken for myomata of the uterus. The bronchial glands may also be involved, and by their pressure produce dyspnœa.

The process is a hyperplastic one, shared by the cellular and trabecular tissue in varying degrees. When the former predominates the product is soft and exudes a milky juice on section; when the latter, it is firm and resisting. The individual glands are not disposed to fuse, nor to become adherent to adjacent tissue, differing in this respect greatly from glands enlarged by the tubercular process. The lymphatic enlargement exceeds also that in leukæmia, while the splenic involvement is more limited, the organ rarely exceeding ten inches in length, as contrasted with the colossal size of the leukæmic spleen.

The alteration in the spleen is hyperplastic, involving the pulp and Malpighian bodies jointly, or alone. The enlarged Malpighian bodies furnish the most characteristic feature. They form grayish-white masses, varying in size from that of a barley-grain to a walnut, a couple of millimetres to as many centimetres in diameter, and contrast strongly with the dark-red

parenchyma. The process in the Malpighian bodies is a true hypertrophy of the adenoid tissue, while in the pulp it is rather the trabecular tissue which is overgrown. The spleen, however, is not always involved. Thus, Gowers found splenic enlargement in seventy-five per cent. of the cases collected; the organ contained lymphoid growths in fifty-six of these.

There are, likewise, at times changes in the marrow of bones, which is converted into lymphoid tissue, sometimes pyoid in consistence.

The liver and kidney, and even the thymus gland and lungs, are sometimes the seat of lymphoid deposits; in fact, all organs and tissues may be invaded, including the nervous; and paraplegia has resulted from pressure on the cord of growths in the spinal canal. The posterior nares may be occluded by invasion of the tonsils and the numerous lymphoid follicles in the pharynx. In like manner the intestinal walls may be invaded, producing thickening, while even serous surfaces do not escape.

Symptoms.—The symptoms of Hodgkin's disease are again the pallor, weakness, dyspnœa, palpitation, and other signs of anæmia, concurrent, or even sometimes in advance of the glandular enlargement. There is quite often fever, very irregular and variable in degree, and cases have been observed by Murchison and De Renzi in which there was paroxysmal glandular enlargement, coinciding with fever, the enlargement subsiding with the decline of the fever, but not reaching the degree present prior to the enlargement. In a case of Laache's the glands diminished in size during the fever. In a case under my care in the wards of the Hospital of the University of Pennsylvania, in which the glandular enlargement was not conspicuous, there occurred an intermittent rise of temperature ascribed to a concurrent peritonitis, but the autopsy discovered this to be so limited that it is perhaps more reasonable to ascribe it to the feverish tendency characteristic of the disease.

The glandular enlargements themselves contribute further to the symptoms by their effects. Thus, in the case of the bronchial glands, dyspnœa from pressure on bronchi or trachea may occur, and is apt also to be intermittent. Pressure elsewhere may lead to pleuritic or abdominal effusions, while the entanglement of nerves in the growth may cause pain. Bronzing of the skin has been found associated with enlargement of the abdominal glands.

The external glandular growths are variously conspicuous; occasionally, however, they are wholly absent. There is no fixed order of involvement, although the submaxillary commonly enlarge first, and with the acme of their growth produce a striking picture. Extreme dyspnœa may arise from encroachment upon the trachea. The enlargement is not uniform, but at times remits and even ceases. It is said it may even disappear altogether for a time. The glands are usually soft, sometimes even to a sense of fluctuation. On the other hand, erosion of bone may result from pressure.

Macroscopically the blood appears thin and pale, and generally the red corpuscles are diminished in number, although not always. Minimum

counts make nine hundred and sixty thousand[1] to the cubic millimetre, while in a case reported by Henry,[2] that of a boy of five, with enormous enlargement of the right cervical glands, there were five million four hundred and sixty-two thousand to the cubic millimetre. Osler has never counted less than two million. Thus the diminution is less than in pernicious anæmia. The hæmoglobin is, however, reduced to at least sixty per cent., furnishing thus one of the conditions essential to anæmia.

There are few nucleated red corpuscles and poikilocytes, and especially microcytes. The leucocytes may be slightly increased, occasionally decidedly so, but this is rare, and there is no approximation to the leukæmic state of the blood, and the two states are distinct and separate. A combination of the two may be possible.

Diagnosis.—The diagnosis requires some care, as more than one condition is attended by similar glandular outgrowths. Chronic and even acute adenitis have been mistaken for the early manifestations of Hodgkin's disease, while the converse has obtained perhaps more frequently. Time is the arbiter of such uncertainty.

A group of tubercular glands resembles more closely the disease under consideration, but it is not usually difficult to distinguish the two. Tubercular glands are adherent to each other and adjacent tissues, while the lymphadenoid growths are loose and easily movable. Tuberculosis rarely involves more than one group of glands, is characterized by caseation and suppuration, while the lymphadenoid growths almost never suppurate. Yet the tubercular process is the slower. Tuberculosis is commonly found in young persons under twenty. Hodgkin's disease may occur at any age, and is more common in males. In Gowers' one hundred cases, seventy-five were males and fifty females; fifty were under thirty, and sixty-four under forty.

Simple lymphoma, affecting as it does a group of glands, resembles most closely lymphadenoma. But it is harder and slower-growing than the lymphatic growth of Hodgkin's disease, while it does not affect the system.

Sarcoma also involves groups of glands, and in the beginning the consistence of the glands is similar to that in Hodgkin's disease. But this disease rapidly invades surrounding tissues, fusing with them, and destructive ulceration soon makes its appearance.

Carcinoma of lymphatic glands should also be mentioned as producing a somewhat similar growth associated also with cachexia, but it is for the most part secondary to cancer somewhere else.

Finally all the conditions named as possible to be mistaken for Hodgkin's disease are limited to single groups, while the latter always extends, and the fact of such limitation is of itself sufficient to preclude the disease.

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[1] Case reported by Richard Geigel, quoted by Henry (Anæmia, Philadelphia, 1887), from Deutches Archiv für Klinische Med., 1885, Bd. 37, p. 59.

[2] Op. citat., p. 67.

From leucocythæmia the disease is easily distinguished by the leucocytosis characteristic of the former.

Prognosis.—While the prognosis is ultimately fatal, the course of the disease varies greatly, and death seldom results in less than a year. F. P. Henry puts the average duration of life at two years, but admits it is greatly modified by such circumstances as age and previous health of the patient.

Treatment.—Treatment, too, may avert the fatal termination for a long time. Extraordinary results in this respect have followed the administration of arsenic, and even recoveries have been reported. Large doses arrived at by gradual increment should be attained and kept up until some physiological effects are observed. Such doses are fifteen to twenty minims of Fowler's solution. Particularly happy results are claimed for the injection of arsenic into the lymphoid masses. Especially is this recommended when arsenic is not well borne by the stomach. From eight to thirty minims of Fowler's solution have been injected daily in divided doses. Inunctions of iodine and iodide of potassium are also recommended. Supporting treatment of all kinds, including quinine, cod-liver oil, and the best of food, is necessary.

Operative interference is sometimes necessary to avert danger to life threatened by the encroachment of enlarged glands on vital organs and functions, such as respiration. It has even been claimed that the removal of a group of primarily enlarged glands has cut short the spread of the disease, but while such an apparent result is rather an evidence of error in diagnosis, in view of the fact that at an early stage a diagnosis is impossible, the removal of a local group of glands should be recommended.

V.—SPLENIC ANÆMIA, OR SPLENIC PSEUDOLEUKÆMIA.

This term is applied to a condition in all respects analogous to Hodgkin's disease, where there is splenic enlargement only, and no involvement of the lymphatic glands. Attention was first called to it as a separate variety of pseudoleukæmia, by Horatio C. Wood,[1] in 1871, although reports of cases corresponding to it had been previously made by others. It has been more recently studied by Strümpell and Banti. It occurs alike in old and young without assignable cause.

Morbid Anatomy.—Its morbid anatomy consists in the splenic changes. The organ is greatly enlarged, approaching that of the leukæmic spleen rather than the spleen of Hodgkin's disease. It is three to four times its normal size, but retains its normal shape. It is indurated, and its incisures are deep. Its capsule is thickened and opaque in spots, and sometimes adherent to adjacent tissues, as is often true of any large spleen. The histology of the organ differs from that of the leukæmic enlargement and that of the enlarged spleen of Hodgkin's disease. There is no true overgrowth

[1] Relations of Leucocythæmia and Pseudoleukæmia, American Journal of the Medical Sciences, October, 1871.

of the lymphatic tissue in the Malpighian body, but rather a destruction, it being replaced by an overgrowth of the reticulum, producing a white body as large as a pea. In addition to this the organ is often traversed by bands of thickened reticulum, visible to the naked eye. The change corresponds rather with that in the harder lymphatic glands of Hodgkin's disease than that in the spleen. In a word, as well stated by Banti, the histological alterations of the spleen consist of an atrophy and sclerosis of the Malpighian corpuscles. Marrow changes like those described under pernicious anæmia are also sometimes present.

The blood exhibits the changes one would expect where there is destruction of the tissue devoted to its reproduction. It is anæmic. The red discs are notably diminished, from five million to as low as even one million. There are found also the other changes of the eruthrocytes characteristic of pernicious anæmia. There are poikilocytosis, megalocytosis, and microcytosis. Nucleated red blood-cells are also sometimes present. The leucocytes are sometimes slightly more numerous, at others they are in normal proportion, and are said to be generally mononuclear.

Symptoms.—As the blood-changes are analogous to those of pernicious anæmia, so are also the symptoms, which include pallor, weakness, dyspnœa, palpitation associated with the signs of enlarged spleen, evidence of which is sometimes shown by its weight and the pressure it exerts, before other symptoms show themselves. Finally, there results the cachectic state characterized by emaciation, a deeper yellow color of the skin and mucous membranes, a tendency to hemorrhage and pyrexia, œdema, serous effusions, extreme muscular prostration, and mental hebetude. There is also said to be at times, as in lymphatic pseudoleukæmia, an intermittent or *per saltem* course in the symptoms to the extent of apparent complete restoration to health in the intervals.

An increase in the urea of the urine has been noted by Strümpell, and is regarded as evidence of increased albuminoid metamorphosis.

All clinical facts go to show that the spleen is responsible in some way for a destruction of eruthrocytes and of their capacity for carrying oxygen.

The duration of the disease is from five or six months to three years.

Diagnosis.—The diagnosis of splenic leukæmia depends upon the presence of splenic enlargement associated with the phenomena of anæmia above described, and the absence of glandular enlargement so conspicuous in Hodgkin's disease. Anæmic symptoms attend the chronic malaria so often associated with enlarged spleen, but the history of malaria in such cases is invariably present, while the degree of anæmia is not so deep.

Prognosis.—The prognosis has been unfavorable, but may be modified by the results of splenectomy, which in the cases collected by Banti appears to have been successful in three out of four.

Treatment.—The treatment is that for the other anæmias, by iron and arsenic and nutritious food. The propriety of splenectomy must be determined on the merits of each case.

INTERNATIONAL MEDICAL MAGAZINE.

A MONTHLY

DEVOTED TO MEDICAL AND SURGICAL SCIENCE.

EDITED BY JUDSON DALAND, M.D.,

Instructor in Clinical Medicine, and Lecturer on Physical Diagnosis and Symptomatology in the University of Pennsylvania; Assistant Physician to the University Hospital.

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