operation will sometimes bring relief, but is not an infallible remedy.

The leucorrhœa in little children which is caused by worms is also one of the varieties which are often chronic and persistent, chiefly for the reason that the cause may fail to be discovered and removed. There is often very strong objection, on the part of parents, that their children should be subjected to the necessary examination and treatment, and it is frequently their fault that the condition remains obscure and uncured.

The leucorrhœa which occurs in aged women, technically known as *senile vaginitis*, is essentially a chronic disease. It sometimes proceeds from the vagina alone, and sometimes from the uterus as well. The discharge is usually a dirty, watery, acrid fluid which irritates the mucous membrane and skin, causing the most intense itching, and the rubbing and scratching to which it gives rise produce the most annoying and even painful results. The tissues become swollen and excoriated, and the patient is deprived of peace and comfort by day and by night. The general health is often as greatly deranged by this form of leucorrhœa as by any in the entire category. Nevertheless, I have seldom seen a case in which great relief could not be obtained by careful and persistent treatment. An examination must first be made, and if the source of trouble is found to be within the uterus, the endometrium must be thoroughly curetted. The uterus and vagina must be irrigated with an astringent solution (alum or tannic acid) and the vagina tamponed with cotton wool saturated with a mixture of subnitrate of bismuth and glycerin, enough of the former being added to the latter to make a rather thick paste. This paste must also be smeared over the swollen and inflamed external genitals. The treatment should be repeated every day or every second day until a cure has resulted. Many cases of this character have come under my observation and the treatment which has been alluded to has invariably brought relief.

The leucorrhœa which is an accompaniment of *malignant disease* of the uterus and vagina is susceptible only of palliative treatment. The discharge is profuse, watery, and very offensive. Curettage, irrigation with strong astringent solutions, and tamponade of the vagina will give a certain degree of relief, but the result will be uniform and uniformly fatal unless extirpation of the diseased organ is practised at a very early period.

We now come to the subject of leucorrhœa which occurs as a secondary phenomenon in the course of some constitutional or general disturbance. The list of diseases which may have this symptom is a long one, and the characteristics of the discharge are such as to make this the typical form of leucorrhœa as it is ordinarily considered. Foremost among these diseases may be mentioned those in which there is a chronic condition of malnutrition, the leucorrhœal discharge being one of the elements of its expression. The tissues are relaxed, the tension of the blood current is low, there are stasis of the venous circulation and transudation of serum and corpuscles in the vagina where the vessels are numerous and the resistance is slight. Diseases which at once suggest themselves as possessed of these conditions are tuberculosis, malaria, anæmia, chronic rheumatism, and the various forms of chronic, slowly progressing nervous disease. Those who suffer from excessive obesity, with its accompanying impairment of circulation, may also be placed in this category.

Another class of cases includes individuals who suffer with the infectious diseases, typhoid fever, scarlet fever, diphtheria, and measles. In such cases there is congestion of the genital organs, and the discharge sometimes continues long after all other symptoms of the disease have disappeared. Especially is this the case with children, and often, in addition to the leucorrhœa, an impression is produced upon the structure of the uterus—whether as the result of toxic influence or of interference with the circulation, is not known—which permanently affects its development and lays the foundation for future trouble which may prove of a serious nature.

Yet another class of cases includes those in which the causative influence is transient in character but may recur an indefinite number of times. Illustrations of such a cause are climatic variations, especially great heat and dampness, fatigue and emotion, particularly the extremes of emotion which are experienced by the hysterical and by those who are passing through the menopause. In all these varying forms of disease, if leucorrhœa is present as a symptom (and it frequently is present), there is one characteristic discharge which is usually observed, viz., the white watery variety, more or less abundant, more or less irritating, more or less persistent, and more or less pronounced in its debilitating and irritant effects.

The treatment for leucorrhœa in the three classes of cases last mentioned must consist primarily in the treatment of the cause. With such diseases as tuberculosis, syphilis, anæmia, etc., the local symptom is not usually removed by any form of local application or manipulation, however judicious or skilful, until the underlying cause is either removed or greatly ameliorated. If the discharge is due to an infectious general disease, such as one of the specific fevers, it will tend to self-limitation, but it may continue a long time after the fever has disappeared, and permanent lesions of the sexual organs, with leucorrhœa as one of their persistent accompaniments, are frequently attributable to such a cause. If the discharge is due to emotional causes, hysteria, etc., the removal of the cause is almost a hopeless task, for the changing of one's nature and characteristics is not a common occurrence. It is certainly proper in all these various cases to impress upon the patient's mind the necessity for the observance of a most careful personal hygiene, whether any medicinal or surgical treatment is employed or not. The constant use of the vulvar pad of absorbent cotton, the employment, morning and evening, of the vaginal douche with a hot astringent solution, and rigid attention to the skin, the bowels, the diet, the sleep, and the mode of occupation, may be more serviceable than any amount of professional attention.

The prognosis for this condition depends upon many factors. It is frequently entirely curable, recurring if the original cause is repeated, or it may be of a character which will preclude radically successful treatment, as in the case of malignant diseases. Its importance is sufficiently great to warrant careful study on the part of every physician who may be called upon to treat the disorders of the female sexual apparatus. *Andrew F. Currier.*

LEUKÆMIAS, THE.—(Synonym: Leucocythæmia.)

Definition.—The leukæmias are diseases of unknown causation (possibly varieties of the same disease), characterized anatomically by overgrowth of hæmatopoietic tissue, myeloid or lymphatic, infiltrations in the various organs of the corresponding leucocytes, myelocytes, or lymphocytes, and, when unmodified by treatment or intercurrent disease, accompanied by a great, usually an extreme increase of the circulating white cells of the same type.

Historical Account.—This unusual and most interesting malady was first recognized and described in October, 1845, by Hughes Bennett and independently a few weeks later by Virchow. The former published the account of an autopsy upon the body of a man who died, with a much enlarged spleen and liver, and whose blood was filled with corpuscles which Dr. Bennett described as exactly resembling pus. In his discussion of the case he laid stress upon the absence of phlebitis and of the evidence of local suppuration in the body, which separated the condition clearly from pyæmia, or pus absorption, and he reached the conclusion that he was dealing with a new and distinct pathological process, in which pus corpuscles in great number originated within the blood itself. How far the hypertrophy of the liver and spleen was concerned with the change in the blood he was unwilling to say. Virchow, in his original publication, not only described independently a similar case, but came to the conclusion, which has been substantiated by all subsequent investigation, that the corpuscles in question

were not pus, but the white cells of the blood, present in many times their normal number. He also inclined to the view that there was some direct relation between the splenic enlargement and the diseased condition of the blood. Reviewing an older case of Rokitansky's, which had been diagnosticated "general pyæmia," he correlated it with his own and proposed the name leukæmia, or white blood, for the disease. Upon this followed a prolonged controversy with Bennett—who now adopted the name leucocythæmia (white cell blood)—for the honor of priority in discovery and concerning the true nature of the newly recognized pathological condition. A few older cases, all included under pyæmia, were brought to light, and now that the attention of physicians everywhere was directed to the disease, reports of new cases were soon forthcoming. With this increasing material Virchow continued to elaborate his theories as to the real nature of the process, and in a series of articles made great additions to our knowledge of the leukæmias. He early described a case which differed from all preceding ones in presenting marked enlargement of the lymphatic glands throughout the body, accompanied by an increase in the small and not the large white cells of the blood. This he named lymphatic leukæmia, calling the previously described disease splenic.

Since the pioneer work of Virchow the study of leukæmia has been of marked interest to pathologists, and its true nature forms, even yet, a part of that great debatable territory of medicine into which theory and speculation press eagerly, while exact knowledge, by the slow acquisition of one fact after another, makes but gradual encroachment on its borders. The nature of the leukæmias is of course so intimately associated with the still unsolved problem of the physiology of the blood-making organs, of the normal mode of formation of blood, and especially of the white cells in the adult, that of late years it has been studied mostly by those who have devoted themselves to hæmatology. In this period of many theories and much valuable work it is hard to choose the most important, but Ehrlich's studies in staining and the introduction of his methods in the investigation of the blood during life, the recognition of acute leukæmia by Ebstein and the study of its blood changes by Fränkel, and Neumann's work on the rôle of the bone marrow in the pathology of leukæmia, have been perhaps the most notable. Of the various theories which have played so large a part in the history of our knowledge of the disease, we shall treat later.

Varieties.—The older writers distinguished two forms of leukæmia on the basis of their gross anatomical features: the splenic type, in which the spleen is enormously enlarged, and the lymphatic, with a somewhat enlarged spleen but with general enlargement of the lymphatic glands. Later, when Neumann had demonstrated the constant presence of a characteristic change in the bone marrow in the splenic cases, these were called splenic-myelogenous—the term still most frequently employed. Since that time marrow changes of equal importance, but of a different type, have been found in lymphatic leukæmia and they probably exist in all cases, and very interesting cases of leukæmia without any anatomical changes outside of the bone marrow have been reported. The investigation and classification of the leucocytes, since the pioneer work of Ehrlich, have led to many changes in the theories held as to their derivation. The part which the spleen is known to play in their origin has been narrowed to insignificant dimensions. The bone marrow and the lymphoid tissues have been proved to be the great centres of leucocyte proliferation, and the distribution of lymphoid tissue has been found to be far wider than previously supposed, areas of it existing even in the bone marrow itself. Whether we follow Uskoff, Löwit, and Gulland in regarding all forms of leucocytes as merely different stages in the development of a single cell, or believe with Ehrlich and Ribbert that they are so many distinct cell types, it is clear that a nomenclature which is based upon gross anatomical changes is misleading from the pathological standpoint, and, since the spleen is enlarged in lymphatic leukæmia and the lymph nodes may be in the splenic variety, it is unsatisfactory clinically as well.

The subdivision made by Ehrlich and Lazarus fulfils all practical and theoretical requirements in the light of our present knowledge and will be adopted here. It distinguishes two forms. "1. Myelogenous leukæmia—leukæmic processes with growth of myeloid tissue; 2. Lymphatic leukæmia—leukæmic processes with growth of lymphoid tissue."

Under lymphatic leukæmia we may well consider acute leukæmia as a clinically distinct type; whether from theoretical considerations it should be regarded as a different process from chronic lymphæmia is perhaps an open question.

Myelogenous Leukæmia.

(Synonyms: Splenic-myelogenous, splenic, myelocytic and leucocytic leukæmia; myelæmia.)

Occurrence.—This, by far the most usual form of leukæmia, is still to the average practitioner a very rare disease. Bramwell, in the analysis of 141,777 consecutive medical cases, found only 5 of leukæmia. It would appear to be more prevalent in the United States than in England and is quite frequently met with in Russian Poland. In this country the highest percentage has been reported by Dock from the University Hospital, Ann Arbor, viz., 11.3 cases of leukæmia in 10,000 admissions.

Predisposing Conditions.—In a disease so infrequent, statistics are not to be relied upon. Men are said to be more commonly affected than women, and adults to show a larger preponderance of the myelogenous form over the lymphatic than children. It has been attempted to show that an antecedent malaria predisposes to the development of leukæmia. Injuries over the spleen have been followed by the disease; in one case which I have seen, only a short interval elapsed; but whether there was a direct connection between the two must be pure conjecture.

Onset, Course, and Termination.—The onset in the great majority of cases is gradual. The patient's attention will first be called to the slow failure of health, to the change in color, to the fulness and distress caused by the enlarged spleen, or to pain in the splenic region. In some cases a rise of temperature daily is an early symptom. Priapism occasionally is among the first complaints. The course of myelogenous leukæmia is essentially chronic. In most cases there are periods, sometimes of considerable length, when the disease remains stationary or even recedes. Some cases are more subacute, with fever and progressive anæmia. Rarely, sudden hemorrhage may be the initial symptom.

The termination is invariably fatal. That genuine leukæmia is ever recovered from must be doubted, for cases in which recovery has been recorded were probably of extreme leucocytosis, the report of the blood findings in older cases not sufficing to differentiate the two conditions. Bramwell reports a case of apparently acute myelogenous leukæmia with recovery under quinine; but here again the blood was examined only in the fresh state.

General Clinical Description.—During the early stages of the disease there is nothing in the appearance of the patients to suggest the existence of so grave a malady, and as a rule they do not seek medical advice until it has been established for some time. Before the custom of making examinations of the blood for diagnostic purposes was thought of, many cases were undoubtedly overlooked, either throughout their whole course or until a late stage. The apparent anæmia is usually but slight; there is some loss of weight and of strength; but apart from the examination of a stained blood specimen nothing may arouse the physician's suspicion until the enlargement of the spleen becomes prominent.

As the disease progresses this splenic tumor is usually the most conspicuous feature. It is associated with some and often considerable enlargement of the liver, so that the abdomen becomes quite prominent, in contrast with

the emaciated condition of the thorax and extremities. In a well-marked case there is generally some pallor of the skin and mucous membranes, or a muddy color; but some patients are not visibly anæmic, and the apparent anæmia is always less than in any other condition with the same reduction in hæmoglobin, this being due without doubt to the marked increase in the opacity of the blood from its excess of white corpuscles and to the abnormal fulness of the vessels which ordinarily exists. In fact, even a leukæmic plethora has been described.

Emaciation becomes considerable with the advance of the process. There is digestive disturbance. The patients are troubled, on exertion, with dyspnœa, palpitation of the heart, and faintness. General lassitude and disinclination to exertion are marked. Tenderness of the bones is present in some cases. A slight or moderate febrile movement, most often attaining its maximum in the afternoon, is not uncommon.

In all these features there is the widest variation in different cases, and in any individual there may be remissions in any or nearly all of the symptoms for considerable lengths of time, with or without treatment. Late in the disease a tendency to hemorrhage becomes prominent and this may be the direct cause of death, especially when the hemorrhage is in the brain. Other causes of a fatal issue are intercurrent infections, such as pneumonia, suppurations, and ulcerative processes in the mouth or throat. Nephritis occurs in some cases as a terminal event and patients die extremely emaciated and dropsical after weeks of suffering, worn out with the disease itself.

The duration ranges from six months to several years, the general average being from one to three years. The longest case which I have seen lasted four years.

There are exceptional cases of myelogenous leukæmia which deserve special notice. One of the rarest forms, but one of the most interesting, for an understanding of the real process, is that in which there is no enlargement of the spleen, liver, or lymphatic glands, the bone marrow alone showing the characteristic changes. This form is sometimes called pure myelogenous leukæmia, in contrast to the ordinary splenic-myelogenous type; but, as the blood picture is the same in both forms, and as they are both alike in all other respects, it seems better to speak only of myelogenous leukæmia.

Contrasted with these are cases in which enlargements of the lymphatic glands occur, without increase of the lymphocytes of the blood. These have been erroneously considered a mixed form of the disease, but when they present only the myelogenous blood type it does not seem right to class them as such. The nature of the enlargements will be explained later. Another interesting and very rare condition is the so-called "dermal leukæmia."

Special Pathological Anatomy and Physiology.—The Blood. The blood changes of leukæmia are best studied during life and constitute the most reliable diagnostic evidence of its existence. The gross appearance of the drop obtained by puncture may be normal, but usually it is somewhat paler and of a more opaque and muddy hue. It may resemble a mixture of blood and pus. The older writers described especially the peculiar white or creamy color and friable nature of the clots found in the heart and vessels after death. In blood that has been kept for a time Charcot-Leyden crystals can usually be found. Fibrin formation is not more rapid than in health.

Leukæmic blood is difficult to spread in a thin layer, and the preparations for staining must be made with especial care. For its accurate study the examination of stained films is absolutely essential, and methods which show the granulations of the leucocytes must be used. Formerly the distinction between leukæmia and leucocytosis was held to be a quantitative one; in other words, a purely arbitrary line was drawn to separate the two blood states. Now we know that the most far-reaching qualitative differences exist, in every way equivalent to deep-seated anatomical changes in other tissues.

Quantitative changes.—With the exception of cases under treatment or suffering from intercurrent disease, which will be considered later, the blood in myelogenous leukæmia shows a diminution in the number of red cells and a great, usually enormous, increase in white cells. Accompanying the decrease in red cells is a reduction in the content of hæmoglobin in the blood; but the quantitative estimation of this by the colorimetric methods, Gowers', von Fleischl's, etc., is not accurate, the changed color of the blood rendering a satisfactory comparison with the scale impossible. The oligocythæmia is in most cases moderate, the red cells averaging about 3,000,000 per cubic millimetre, but in the later stages, and especially if severe or repeated hemorrhages occur, it may be extreme. I have seen one case of two years' duration in which the red cells shortly before death were only 800,000. The increase in white cells, on the other hand, is generally so great as to justify the older clinicians in having considered it pathognomonic; but some reported cases, especially those under arsenic treatment, have shown no increase whatever. As a rule the number of leucocytes exceeds 100,000 per cubic millimetre and it may pass 1,000,000.

Qualitative changes.—It is in the study of these that we find the essential features of the blood in myelogenous leukæmia. The word which best expresses the picture which a stained specimen presents is "polymorphous." In no other condition is so great a variety of cell types present. Ehrlich and Lazarus sum up under four heads the changes which are now generally regarded as constituting the specific characters of the blood:—

1st. That, in addition to the polymorphonuclear cells, their antecedents, the mononuclear granulated leucocytes (myelocytes, marrow cells), also circulate in the blood.

2d. That the three types of granulated leucocytes—the neutrophilic, eosinophilic, and basophilic (mast cell)—all participate in the increase in the number of the white cells.

3d. That atypical cell forms, dwarf forms of the various white cells, and cells showing karyokinesis, appear.

4th. That nucleated red cells are constantly present, often in great number.

These changes are all demonstrable in every case of myelogenous leukæmia unmodified by treatment or intercurrent disease, but in varying combination. In some the neutrophilic myelocytes are the most noticeable abnormal feature; in others the great numbers of eosinophilic cells, and in still others the mast cells. The extent to which atypical cell forms and nucleated red cells appear differs widely in individual cases. The typical picture, once seen, cannot be mistaken for anything else. The distinguishing feature is to be found, not in the presence of the mononuclear neutrophilic cell, the ordinary myelocyte, but rather in that of mononuclear cells of all three types of granulation, with atypical forms and nucleated red cells. Ehrlich previously laid great stress on the increase in eosinophiles as pathognomonic. Certainly no other condition shows them so uniformly exceeding their normal absolute number per cubic millimetre, though their relative number may not be greatly changed. Dwarf forms of leucocytes are often conspicuous. Karyokinetic figures occur, but they are of great rarity and of no value for diagnosis. The nucleated red cells present are almost always normoblasts, but occasionally megaloblasts and intermediate forms appear.

Other changes which should be mentioned are the presence of slight poikilocytosis and polychromatophilic changes in the red cells, the amount depending on the severity of the anæmia; also the occurrence of white cells which, in their staining reactions, show degeneration. These are so marked in some cases as to be classed as an essential feature.

An intercurrent inflammatory process, which is ordinarily accompanied by a polymorphonuclear leucocytosis, may have a profound influence upon the blood picture. A great reduction in the total leucocyte count usually occurs and with this a qualitative change, the myelocytic character of the blood becoming less and less conspicuous, until in some cases the polymorphonuclear cells attain the proportions of an ordinary leucocytosis, even to ninety per cent. of the total white cells. Mononuclear granulated cells are not entirely absent, however, nor are nucleated red cells. Another interesting feature is the persistence of some eosinophiles, which, under similar conditions in the non-leukæmic, entirely disappear from the circulation. Sometimes a severe infection will cause a veritable leucopenia.

Continued dosage with arsenic in certain patients produces a similar reduction in the number of the white cells, which may be extreme and may result in a condition closely resembling primary pernicious anæmia. Usually the qualitative changes are less marked than the quantitative, and even with a normal leucocyte count the diagnosis would be evident from the cell types present; but cases have been reported in which there were present both a permanent normal count of white cells and an absence of the leukæmic characters so nearly complete that a diagnosis from the blood was impossible; yet the leukæmic process continued to a fatal issue. Two most interesting cases of this kind are reported by A. E. Taylor, from the Pepper Laboratory of Clinical Medicine of the University of Pennsylvania. In all cases the effect of arsenic upon the oligocythæmia and the nucleated red cells seems to have been slight. This is in marked contrast to the remissions of pernicious anæmia so commonly seen under this treatment, during which the number of red cells rises rapidly;—remissions which are also observed independently of this treatment.

The Bone Marrow. Though constant and marked changes are here present, in only a portion of the cases do they give rise during life to symptoms, such as tenderness of the sternum, tibiæ, etc. The characteristic lesion is the so-called "pyoid" transformation first described by Neumann. This occurs even in bones which ordinarily have no blood-making function, and consists in an overgrowth of the true myeloid tissue, which replaces the fatty marrow and usually encroaches on the shaft of the bone, causing rarefaction and an actual enlargement of the medullary cavity. The proliferated tissue is yellowish-gray in color and often shows areas of softening and hemorrhage. There may also be some increase in the red erythrocytic portion of the marrow, as is seen in severe anæmias.

Microscopically, this "pyoid" marrow shows a multiplication of the true myelogenous elements, the mononuclear and polymorphonuclear neutrophilic and eosinophilic cells, the mast cells, and the macrophages, with evidence of rapid division. There is a marked disturbance of the mechanical circulatory conditions by the hypertrophied tissue, and infiltrations may be found in the walls of the blood-vessels. Areas of excessive pigment accumulation and of necrosis are also seen.

The Spleen. Marked enlargement of the spleen is one of the most characteristic features of this form of leukæmia. The normal shape and the direction of its long axis are usually preserved, but occasionally the latter assumes a more transverse position. The lower border almost always reaches below the level of the umbilicus, often to the left iliac fossa, and I have seen a spleen which, besides increasing enormously in size, had become so twisted on its pedicle that it lay across the abdomen, almost filling this cavity, and resting with its previously external surface on the two iliac fossæ. The liver in this case was crowded posteriorly and the stomach and small intestines were pushed up under the ribs. Palpation will usually reveal one or more well-defined notches in the anterior border (a point of differentiation from tumor of the kidney), and often depressions at points on the surface. These depressions, which are found at autopsy, are due to scars of previous infarctions. Such infarcts at the time of their occurrence are accompanied by local inflammation of the overlying peritoneal coat (perisplenitis), causing rise of temperature for several days and local tenderness, with sharp pain on movement or respiration. Auscultation or palpation over such an area during respiration discloses a friction rub. The splenic tumor in itself is the cause of considerable discomfort. Its size may vary considerably from time to time, but tends to increase with the progress of the disease. There is no direct relation between its variations and those of the blood. Exceptionally, the spleen may shrink during the latter weeks of life. Post mortem the capsule is found much thickened, often adherent to surrounding organs, and showing the scars mentioned above. On section the consistency is found to be firmer than normal, the color is reddish or yellowish brown, and the Malpighian bodies are not visible or are less distinct than normal. There are pigment accumulations, hemorrhagic areas, and infarctions of various ages.

Histologically, there is seen a great infiltration of the splenic pulp and crowding of the splenic sinuses with the leukæmic white blood cells. Nucleated red cells and pigmented leucocytes are common and the macrophages seem increased. Karyokinetic figures are not frequent and hyperplasia of the Malpighian bodies or evidence of active cell production in them is not present. There is new connective tissue throughout, with fibroblasts. This evidence points to the splenic enlargement being the result of leukæmic infiltration and the production of fibrous tissue, and therefore a secondary change. The principal increase of function of the organ seems to be hæmolytic, in connection with the increased destruction of red blood cells.

The Lymphatic Glands. The connection of these with myelogenous leukæmia is a purely secondary one. They are usually to be found somewhat enlarged, but only in rare cases sufficiently so to be noticeable during life. There is not a hypertrophy of the true lymphoid tissue, but simply an infiltration with leucocytes, the same in kind as that described in the spleen, but less in degree. These leukæmic infiltrations are found in most of the organs of the body and are among the most characteristic lesions. In a few cases the lymph glands have been found to be much increased in size, but without blood changes of the lymphatic type. To call such cases lymphatic-myelogenous leukæmia is to magnify an anatomical peculiarity.

The Liver. The liver is increased in size, sometimes to a considerable degree. The enlargement is easily detected during life. Its normal shape is preserved, and the edge is thin. The surface is smooth and the consistency firm. Microscopical examination shows the presence of infiltrations throughout, especially in the portal spaces. The parenchyma cells show a marked fatty change.

The Circulatory System. The lesions here are all of a secondary nature. Infiltrations are found in the heart muscle and rarely in the walls of blood-vessels. The heart cavities may be dilated, petechial hemorrhages may be present in the peri- or endocardial surfaces, and the muscle is usually less firm than normal and pale or somewhat fatty, as in chronic anæmias. The disturbances of function are more striking. Weakness of the heart's action is a symptom which increases with the progress of the case, as evidenced by a frequent soft pulse, dyspnœa on exertion, and a tendency to dizziness or fainting attacks. Abnormal physical signs, if found, will be those common to anæmic states, a systolic murmur in the pulmonic area or at the aortic and mitral openings as well, and perhaps also over the carotids, with the venous hum. Œdema is present in the late stages.

Hemorrhages. The tendency to hemorrhages is so marked in many cases that it is one of the classical symptoms. The anatomical basis for it has not been satisfactorily elucidated, and we do not yet know whether it is to be found in leukæmic infiltration of the vessel wall or in some change of the kind which produces a similar tendency in other anæmic states. The commonest bleedings are from the nose and gums, then from the stomach and intestines: occasionally also hæmaturia is seen. The most dangerous form is cerebral hemorrhage and death from this is a termination to be borne in mind. Deafness from bleeding in the internal or middle ear is a rare accident. I have seen a case in which this occurred on both sides and was recovered from. The most easily studied vessel changes are in the retina, and these will be separately described.

Leukæmic Retinal Changes. The most common is the condition of great enlargement of the retinal veins, with arteries of normal size. The fundus is usually paler than