AMYLOID DEGENERATION OF THE SPLEEN.—This disease consists in the deposits of the amyloid matter, either in the form of small patches, forming the well-known "sago-spleen," or in a general diffusion of the material through the whole organ. In the former the patches may be very numerous and almost unite, but there still remains normal spleen-tissue between them. In the latter form the texture of the spleen is firm and tough, but easily divided with the knife, although not readily broken up into a pulp, and it has a brownish or yellowish-brown color, and no part remains untouched by the new deposit—the pulp, the trabeculæ, the Malpighian bodies, the vessels, all are changed in structure and physical properties by the amyloid matter. The test for this matter is iodine—Lugol's solution—which when brushed over colors the tissues yellowish, but the amyloid matter red or reddish brown: now, on the addition of sulphuric acid, while the yellowish parts remain yellow, the amyloid becomes a dark violet. The amyloid, or lardaceous, or waxy degeneration of the spleen occurs, simultaneously with the same form of degeneration in the liver and intestinal canal, and hence the symptomatology is rather that of the disturbance in the function of the other organs. These symptoms have been detailed in the remarks on amyloid liver. The only contribution made to the symptomatology by the alterations in the spleen are, the increased area of splenic dullness and a greater degree of anæmia and pseudo-leukemia. The great cause of amyloid degeneration of the spleen as of other organs is suppuration, especially protracted suppuration in connection with bone. Next to this are the syphilitic cachexia and inherited syphilis. Chronic alcoholism and chronic malarial poisoning are supposed to have some influence in its production, but it is extremely doubtful whether they have any real influence.

ECHINOCOCCUS OF THE SPLEEN.—The embryo of the tænia echinococcus is deposited in the spleen as in other organs, and more frequently in the spleen than in any, except probably the liver. The liver is reached readily by the portal vein, and the spleen directly, as the two organs come into contact. When established in its home, growth begins, chiefly by the development of daughter-vesicles in the mother-sac. The symptoms produced are due to the size to which the sac attains, the pressure on neighboring organs, and the interference with the circulation in the great vessels of the abdomen. The slowness of the growth, the absence of constitutional disturbance, the freedom from pain, and the absence of symptoms except those due to the size of the tumor, separate the echinococcus from other tumors of the spleen. The sense of fluctuation, and especially the purring tremor, serves to distinguish this from hypertrophy of the spleen. The employment of the aspirator-needle will contribute to certainty of diagnosis, but the presence of hooklets and the absence of albumen can not always be depended on, for the hooklets may be absent, and albumen may be present in echinococcus tumors of the spleen. For further details the reader is referred to the subject of echinococcus of the liver.

DISEASES OF THE BLOOD-FORMING ORGANS.

THE BLOOD.

It will facilitate the comprehension of the maladies treated of in this section, to precede the account of the several morbid states with some observations on the nature and composition of the blood.

Composition.—The ultimate chemical composition of the blood is as follows: *

Reaction	alkaline
Specific gravity, from	1,045 to 1,075
Water	781·6
Globules	135·
Albumen	70·
Fibrin	2·5
Fats	1·5
Extractive matters	2·4
Salts	6·5
Iron	·5

The results of chemists vary according to the method of analysis employed. The most considerable departure from the ordinary method is that of Flint, who tries to measure the several constituents in their natural state; that is, with their water of composition and the inorganic salts so closely associated with them as to be separated only by incineration.† There is much to be said in favor of this method. Without engaging in this discussion, the several constituents of the blood will be briefly considered, with reference to the changes induced by disease.

In general terms, the blood may be considered as made up of certain morphotic or formed constituents—the corpuscles, red and white—floating in a complex fluid, containing, dissolved in it, albumen, fibrin, fats, and salts. The red corpuscle consists of two parts: the matrix, or stroma, which seems only to serve the purpose of a vehicle for its

* Becquerel et Rodier, "Traité de Chimie Pathologique Appliquée à la Médecine Pratique," etc.

† The "Physiology of Man," vol. i, p. 133.

active constituent, the *hæmoglobin*, the other part. The most important function of hæmoglobin is its power to form compounds with gases of a very unstable nature, the chief being the combination with oxygen, *oxy-hæmoglobin*, or *oxide-hæmoglobin*. The oxygen is readily taken up and as readily parted with, this process constituting the so-called ozonizing or respiratory function of the blood. The arterial blood contains 16·9 per cent. in volume of oxygen ; whereas the venous blood only has 5·96 per cent. Now, as this process of oxidation and deoxidation of the hæmoglobin goes on incessantly, the importance of the function is obvious. Hæmoglobin is soluble in water, and crystallizes from its solution in fine crystals, called "blood-crystals."

The white corpuscles, leucocytes, contain a good deal of protoplasm, and are closely allied to lymph and pus-corpuscles. They are derived from the lymphatic glands and lymph, and have a power of motion, which is called amœboid, in virtue of which they may migrate from the vessels into the surrounding textures.

The relative proportion of red and white corpuscles varies considerably within physiological limits. The average of the red corpuscles is in the proportion of five millions in a cubic millimetre of blood, and the white bears the proportion to the red of one to 800, and after a meal of one to 300 or 400. These figures must be regarded as merely approximative. The red corpuscles "constitute about one third of the weight of the blood, and contain about 43 per cent. of solids, and 39 per cent. of hæmoglobin" (Burdon-Sanderson).

The fluid in which the corpuscles are suspended is the *plasma*. Serum is the plasma which has lost its plasmin by coagulation. When blood is allowed to stand under suitable conditions, it separates into corpuscles and plasma. At ordinary temperature, plasma coagulates, and a clot forms, composed of fibrin, with the corpuscles entangled in its meshes. This fibrin-clot when in its dissolved state is *plasmin*. The coagulation of blood consists in the solidification in delicate filaments of the plasmin, which when it assumes this form becomes fibrin. Besides plasmin, which is an albuminous substance, there are two albumens in plasma—ordinary albumen, and a small quantity of alkali-albumen. The serum, and coagulable liquids generally, contain *paraglobulin* and *fibrinogen*, but the action of a third substance is necessary to coagulation. This is a *ferment*, now supposed to be produced by the white corpuscles. When these substances are present, spontaneous coagulation will take place.

Blood plasma contains, also, 0·5 per cent. of the solid salts of the blood, consisting, for the most part, of sodic chloride, sodic phosphate, and sodic carbonates (chloride, phosphate, and carbonate of. sodium).

Examination of the Blood.—Apply a suitable ligature to the finger, make a puncture with a lancet, and receive a drop of blood on a perfectly clean glass slide warmed to 100° Fahr. ; cover at once with thin

glass, which has been moistened by breathing on, and gently press it down until there is a stratum of blood so thin as hardly to appear red. It can now, and as quickly as possible, be examined with a quarter-inch objective. The red globules are particularly well seen with the binocular of Beck. The condition of the red corpuscles, of the white, and their relative numbers, should be noted. The action of a reagent may be watched by bringing it to the margin of the cover-glass, when it will gradually diffuse into the blood. Besides the ordinary constituents of the blood, there may be seen, under peculiar circumstances, certain parasites, pigment granules and cells, crystals of uric acid, etc.

The Hæmacytometer.—This instrument, as its name indicates, is intended to ascertain the number of blood-corpuscles. Devised in a crude form by Vierordt, afterward improved by Melassez and Hayem, the most convenient arrangement has been perfected by Gowers, and made by Hawksley, of London. The process of counting the corpuscles by means of the hæmacytometer consists essentially in dilution of the blood to a definite degree, and numbering the corpuscles contained in a cell of given depth on a slide marked with ruled lines which indicate the lateral dimensions of the dilution. In this way quite a close approximation to the true number of cells in a given measure of blood can be made. The morbid conditions of the blood to the diagnosis of which this method is applicable will be considered further on.

The Hæmoglobinometer.—The peculiar function of hæmoglobin is so essential to the work of the body that means for ascertaining its quantity are very desirable. The hæmoglobinometer is an instrument by which the proportion of hæmoglobin in the blood may be determined. Melassez and Hayem first demonstrated practicable methods, but the profession is here again indebted to the practical skill of Gowers for the perfection of an available apparatus. It consists, first, of a standardized solution of glycerin-jelly, colored to the tint of normal blood, and contained in a tube of given capacity ; second, of a tube of the same capacity as the first, for the diluted blood under examination. The degree of dilution necessary to make the blood-tint correspond in depth to the standard indicates the proportion of hæmoglobin. Less accurate but more ready methods for approximating to the proportion of the blood coloring-matter are given in the section on *hæmoglobinuria*.

Pathological Relations of the Blood.—Before entering on the subject of the special pathology of the blood, it will be useful to indicate in outline the modes in which the blood is changed. The several morphotic elements may be altered quantitatively and qualitatively, and the constituents of the plasma may be increased or diminished, or entirely removed.

The red corpuscles of the blood diminish in number, and that to an extreme degree, so that the normal proportion of red and white may

be reversed. Alterations in the shape of the corpuscles sometimes take place, but they have no precise signification, and have not thus far been studied with success. In the process of coagulation, the red corpuscles may not exhibit the normal behavior, and unite in *rouleaux*, but rather adhere in irregular masses. The significance of such a condition is not understood. New forms of corpuscles may appear, some of them transitional between the white and red.

The blood may assume the appearance known as "lake," and become transparent instead of opaque. Such a change as the term lake supposes, indicates disorganization of the red corpuscles, and the separation of the coloring matter, which dissolves in the plasma. Various changes of color may take place. The transformation of venous into arterial blood may not occur, and the whole mass of the blood continue of the venous hue. It may assume a chocolate tint, from the action of certain medicaments.

The plasma of the blood may be variously altered. The relative amount of water may be increased or diminished, or, as it should rather be stated, the proportion of solids is increased or diminished. This change may be effected by some medicaments, but is most pronounced in certain morbid states; for example, in the algid stage of cholera, when the loss of water from the blood, and its artificial replacement by intravenous injection, make a wonderful change in the condition of the subject. Variations in the proportion of albumens in the blood are caused by activity in the function of nutrition, and excess in the processes of waste and excretion. When albuminous foods are abundant, digestion active, and absorption prompt, the blood may contain relatively more albumen, but the excess above the needs of the organism will be deposited as fat, or excreted as uric acid and urea. Under some circumstances fibrin may be in greater than normal quantity, constituting the condition of *hyperinosis*, in which the coagulation of the blood is more prompt, and the clot firmer. Formerly the "buffy coat" was supposed to be indicative of hyperinosis, but this appearance is now known to be due rather to the condition of the red corpuscles, and their manner of settling in the process of coagulation.

The salts of the blood are subject to considerable variation under conditions not now understood. Salts of potassium base are contained in the corpuscles chiefly, while those of sodium base are to be found in the plasma. The normal reaction of the blood, which is alkaline, may be changed to neutral, even to acid, by chemical transformations in the salts.

The quantity of fat in the blood varies considerably within physiological limits. A diet rich in fat, the use of alcohol, obesity, tend to increase the proportion of fat in the plasma. The serum of the blood may, indeed, present a milky appearance in consequence of an excess in the number of fat-globules which have entered the vessels, and fat-

embolisms are caused by the admission of fat-cells into torn vessels in some cases of fracture of bones.

Urea and uric acid are found in the blood in small quantity quite constantly, but in certain morbid states in excessive amounts. Crystalline forms of urate of soda may, in some cases of gout, be detected in the serum. Leucin, tyrosin, acetone, and bile-pigment are also constituents of the blood, to be found during the existence of certain morbid states.

To an expert the examination of a drop of blood is a comparatively easy task. It is only rarely that such an examination is necessary, when the indispensable skill is available. There is reason to fear that the routine examination of the blood, now so much spoken of, is rather intended to impress the patient than increase the knowledge of the conditions present.

LEUCOCYTHEMIA—LEUCÆMIA.

Definition.—The terms leucæmia and leucocythemia were proposed by rival claimants for priority of discovery—Virchow and Hughes Bennett. The term leucocythemia, proposed by Bennett, seems to the author a more correct designation, meaning *white-cell blood*, than Virchow's leucæmia, which means *white blood*. The morbid change which has given the name to the disease is the enormous increase of the white corpuscles of the blood, accompanied by enlarged spleen and enlarged lymphatic glands, and by alterations in the marrow of bones. By Trousseau it is designated *adénie*, and by Griesinger *anæmia splenica*.

Causes.—The excessive production of leucocytes, which is the chief element in this disease, must necessarily be due to a functional and nutritive irritation of the blood-making organs. The evidence of this is afforded in the enlargement of the spleen and lymphatic glands. But the cause of this remains unknown, and hence the real nature of the malady continues an insoluble problem. Leucocythemia occurs at all ages and under every kind of social circumstance, but it attacks by preference the male sex, the most vigorous period of life—thirty to forty-five—and those who have been weakened by hardships and excesses. Menstrual irregularities have been supposed to have an influence in developing it, and, in twenty-one cases of this disease occurring in women, there were sixteen in whom some disorders of the uterus had existed (Mosler). It is probable that these sexual irregularities were rather coincident than causal. The cachexiæ of chronic malarial poisoning and of syphilitic infection have been invoked to account for its production, but no satisfactory data have as yet been published, although there are examples of accidental association. Regarded from the analogical point of view, leucocythemia may be classed with scrofula, cancer, tubercle, and other infectious diseases,

which, beginning at one point, or focus, diffuse thence over the body. The morbid alterations characteristic of this disease begin in the spleen, then attack the lymphatic glands, then the marrow of bones, and thus become general.

Morbid Anatomy.—The most constant lesion is in the spleen, which is increased in size, either uniformly, its form and shape being preserved, or some part of the organ undergoes the change. Not only the size but the firmness and density are increased. The color becomes a reddish blue; the pulp undergoes hypertrophy, but the normal relations of its elements are preserved; the trabeculæ may be more distinct, or may be obscured by the overgrown pulp; the Malpighian bodies are rather increased in number, very distinct, but less consistent than normal. The trabeculæ and pulp may be coated with a yellowish, fibrinous exudation; there may be seen white granules disseminated throughout the organ, and near the surface patches of indurated tissue, the remains of hemorrhagic infarctions. The change in the lymphatics consists in an initial hyperæmia, then hyperplasia of its constituent parts, first of the cellular elements, then of the stroma and vessels. They enlarge in proportion to the addition of new material, from a bird's egg to a goose-egg or larger. They have a smooth, rather glistening, appearance, and to the touch are soft, non-elastic, and sometimes fluctuating. All of the lymphatic glands in the body may be engaged, or the process may be confined to a few. Usually those situated about the hilus of the liver and spleen are enlarged. Similar changes take place in the lymphatics of the digestive tract, beginning in the follicles of the tongue and tonsils, of the stomach, and in the glands of Peyer. Corresponding changes occur in the marrow of long bones, and in the cancellated tissue of the ribs and sternum. The marrow is abundantly infiltrated with lymphoid cells, and the vascular network with its delicate connective tissue, which exists in the normal condition, disappears, and only the larger arterial branches remain. The result is that the marrow, instead of its rose-color, becomes yellowish or greenish yellow.* In somewhat more than one half of the cases the liver is enlarged and changed in structure by reason of the development of the new lymphadenoid tissue of the organ. It increases in size, sometimes immensely so, and weighs from four to eighteen pounds. This change is at first a mere proliferation of the lymph-cells; then occurs an infiltration of lymph new formations, or these are collected in masses or nodules, like tubercle. The cells penetrate the lobules from without inward, and by their numbers dispossess the hepatic cells, which atrophy and disappear, only spots of pigment remaining.† The most important change is that which gives the name to the disease, the increase of white cells in the blood.

* Mosler, *op. cit.*
† Rindfleisch, "Pathological Histology," pp. 183, 473, American edition.

The gross amount of blood is not lessened, but its specific gravity is reduced from 1055 to 1040, even to 1035.* The color is paler than normal, and purulent looking. The proportion of white corpuscles is relatively greatly increased; but the numbers vary from one to ten, to one to two; indeed, the white and the red may be equal in numbers; the white may even preponderate. The white corpuscles may differ from the normal in being larger; in splenic leucocythemia they contain one or several nuclei; sometimes the cells are smaller, and there is one large nucleus; and occasionally transitional forms are discovered between the white and red, such as are found in the cell-masses of the marrow.† The red corpuscles are both relatively and absolutely diminished in numbers, the water and fibrin are increased, the iron diminished, and certain abnormal ingredients are present, as formic, lactic, and acetic acids, hypoxanthin, uric acid, leucin, tyrosin; but, of these, lactic and formic acids and hypoxanthin only are constantly present (Mosler). According to the same authority, the reaction of the blood in this disease is not acid, but alkaline. The morbid processes of leucocythemia are not those of a merely splenic disease—a local malady. Hyperplasia of the spleen is, however, the first link in the chain; from this organ, immense numbers of leucocytes pour into the blood, and also, it is probable, some products of the splenic pulp, as lactic and formic acid, and hypoxanthin, etc.; the next step consists in the transplantation and subsequent development of heteroplastic materials in other organs, as the liver, etc.

Symptoms.—According to the preponderance of the leucæmic process in the spleen, lymphatics, or marrow of bones, the disease is entitled splenic leucocythemia, lymphatic leucocythemia, and myelogenic leucocythemia—for these organs seem equally to possess the power of producing white corpuscles and introducing them into the blood, and one may perform the office for the others. When the spleen is removed there are very few defined disturbances of the functions, as the lymphatics and the marrow of bone perform the necessary offices. It is the splenic form of the disease which is usually encountered, or the splenic-lymphatic, and the lymphatic very rarely, and the myelogenic never. The development of leucocythemia is so gradual that the beginning of symptoms usually passes unnoticed, unless preceded by syphilitic or other lesions, to which attention has been directed. There is usually a history of the gradual appearance of weakness and anæmia, inability for mental and especially for any physical exertion, headache, ringing in the ears, vertigo, palpitation. There are, as the anæmia gradually develops, alternations of an improved state with more decided decline, but the constant tendency is downward. These pro-

* Wagner, *op. cit.*, p. 546.
† Renaut, "Archives de Physiologie," September, 1881.

dromal symptoms last from a few months to several years, the average being about eighteen months. As the cases progress, the condition of anæmia becomes more profound ; the lymphatics of the neck, or groin, or other superficial parts, are found to be somewhat enlarged, and now careful palpation discloses enlargement of the spleen. There are, then, extreme pallor, weakness and exhaustion, and breathlessness on the slightest exertion. The headache, vertigo, and tinnitus continue, and the mental state is depressed, hypochondriacal, and irritable, "due to the accumulation of white corpuscles in the capillary vessels of the brain."* The vision is obscure and amblyopic. There are now and then, without apparent cause, attacks of profuse sweating, and scaly and pustular eruptions. There is usually some feverishness toward evening, and the pulse is always accelerated. Œdema of the ankles, puffiness of the eyelids, and some effusion in the cavities are results of the hydræmia. The changed condition of the blood also induces the hæmorrhagic cachexia or diathesis, and bleeding occurs from the nose, mouth, and other mucous surfaces, and from slight wounds, so that the least abrasion or cut gives rise to severe hæmorrhage. The vessels remain unaffected except by capillary thromboses, due to the aggregation and adhesion of white cells, and such changes in their walls as are produced by imperfect nutrition. A soft-blowing murmur—anæmic murmur—is audible at the base of the heart. The appearance of the blood is very characteristic. A ready method of demonstrating its character has been mentioned by Sir William W. Gull †—that is, "puncture the finger of the patient, and receive the blood on to a piece of white linen, or a lawn handkerchief, and put by the side of it a similar stain of blood from a healthy subject. The full color of the latter contrasts strikingly with the stain of the former, which is hardly of a blood-color, and translucent." The relative proportion of blood-globules is best ascertained by counting, employing for this purpose the hæmacytometer as arranged by Gowers. In order to constitute leucocythemia, it has been attempted to fix arbitrary numbers, but, while the proportion of white to red corpuscles must be increased very largely above the normal, yet no definite number can be stated, and hence the diagnosis must rest rather on the concurrence of the splenic and lymphatic enlargements with increase of the white corpuscles. It may, however, be stated, as an approximation to the truth, that the relative proportion of white to red should be reduced to one to six, in order to constitute true leucocythemia. It has already been stated to what extent the disproportion may be carried in this disease when fully established. When the spleen has reached its maximum, the abdomen is greatly enlarged,

* Ollivier et Ranvier, "Nouvelles Observations pour servir à l'Histoire de la Leucocythémie ;" "Archives de Physiologie," vol. ii, 1869, p. 518.

† "Transactions of the Pathological Society," vol. xxix, 1878, p. 383.

and prominent, but in ordinary cases an increase of size, and usually of density, can be ascertained on palpation. The mesenteric glands can usually be felt through the abdominal walls, enlarged and firmer. The inguinal, cervical, and other lymphatic glands, are also enlarged. A capital illustration of these is given in the plate accompanying Surgeon-Major Porter's case,* as reported to the London Pathological Society.

The tumors of the tongue and tonsils interfere with mastication and the act of swallowing ; the gums become spongy and tender. The appetite may be keen ; it may be normal ; it may be wanting entirely. Constipation at first is present ; then diarrhœa alternates with constipation, and finally diarrhœa persists. The urine has a higher specific gravity than normal—from 1020 to 1030. The urea is greatly diminished, but the uric acid is increased, and hypoxanthin is present, in the cases of splenic leucocythemia.

Course, Duration, and Termination.—Leucocythemia is essentially a chronic malady. Its origin can not be often determined, because there is a slow development of uneasiness in the splenic region, fullness of the abdomen, breathlessness on exertion, and anæmia and pallor of the skin. The swelling of the spleen, until its size is considerable, escapes recognition ; when, however, the external lymphatic glands enlarge, attention is earlier directed to the nature of the case. Then an examination of the blood furnishes conclusive evidence. When the hæmorrhagic diathesis comes on, bleeding may be so severe as to exhaust the patient rapidly, or death may occur suddenly by cerebral hæmorrhage. The course and duration of cases are materially affected by the hæmorrhagic diathesis. When this does not exist, the progress is much slower and the duration more prolonged. The glandular and splenic enlargements may become enormous, and the patient die ultimately of exhaustion, death being preceded by cerebral symptoms—delirium, stupor, and insensibility. The case may be terminated by some intercurrent malady, as pericarditis, pleuritis, pneumonia, etc. The symptoms of the first stage, as already stated, continue for months, even years, the average being about eighteen months, and the second stage, or fully developed malady, lasting about one year. Probably the average duration of the whole disease is two years.

Diagnosis.—In the first stage of this malady a distinction is not possible from ordinary anæmia and chlorosis. When, however, the spleen enlarges, and the lymphatic glands also, and the anæmia becomes extreme, the picture of the disease is complete, and no one possessed of any knowledge could fail to recognize it. In the early stage, the persistence of the anæmia under appropriate treatment, the extreme degree of pallor, the breathlessness under slight exertion, the

* "Transactions of the Pathological Society," vol. xxix, p. 339, *op. cit.*