less serrated. Under these conditions, their original form may be restored by adding to the specimen a liquid of about the density of the serum. When they have been completely dried, as in blood spilled upon clothing or on a floor, they can be made to assume their characteristic form by carefully moistening them with an appropriate liquid. This property is taken advantage of in examinations of old spots supposed to be blood; and if the manipulations be carefully conducted, the corpuscles may be recognized without difficulty by means of the microscope.

If pure water be added to a specimen of blood under the microscope, the corpuscles swell up, become spherical and are finally dissolved. The same effect follows almost instantaneously on the addition of acetic acid.

Structure.—The blood-corpuscles are perfectly homogeneous, presenting, in their normal condition, no nuclei or granules, and are not provided with an investing membrane. The appearances presented upon the addition of iodine to blood previously treated with water, which have been supposed to indicate the presence of shreds of ruptured vesicles, are not sufficiently distinct to demonstrate the existence of a membrane. The great elasticity of the corpuscles, the persistence with which they preserve their biconcave form, and their general appearance, rather favor the idea that they are homogeneous bodies of a definite shape, than that they have a cell-wall with semi-fluid contents; especially as the existence of a membrane has been only inferred and not positively demonstrated.

Development of the Blood-Corpuscles.—Very early in the development of the ovum, the blood-vessels appear, constituting what is called the area vasculosa. At about the same time, the blood-corpuscles are developed, it may be before, or it may be just after the appearance of the vessels, for this point is undetermined. The blood becomes red when the embryon is about one-tenth of an inch (2·5 mm.) in length. From this time until the end of the sixth or eighth week, they are thirty to one hundred per cent. larger than in the adult. Most of them are circular, but some are ovoid and a few are globular. At this time, nearly all of them are provided with a nucleus; but from the first, there are some in which this is wanting. The nucleus is $\frac{1}{8000}$ to $\frac{1}{7000}$ of an inch (3·1 μ to 3·6 μ) in diameter, globular, granular and insoluble in water and acetic acid. As development advances, these nucleated corpuscles are gradually lost; but even at the fourth month, a few remain. After this time, they do not differ anatomically from the blood-corpuscles in the adult.

In many works on physiology and general anatomy, accounts are given of the development of the red corpuscles from the colorless corpuscles, or leucocytes, which are supposed to become disintegrated, their particles becoming developed into red corpuscles; but there seems to be no positive evidence that such a process takes place. The red corpuscles appear before the leucocytes are formed; and it is mainly the fact that the two varieties co-exist in the blood-vessels which has given rise to such a theory. It is most reasonable to consider that the first red corpuscles are formed in the area vasculosa in the same way that other anatomical elements make their appearance at that time, the exact process not being understood. In the later periods of devel-

opment of the fœtus and in the adult, it is probable that the red marrow of the bones and, perhaps, to a certain extent, the spleen have important uses in connection with the development of the red blood-corpuscles. The observations of Neumann, of Königsburg, and of Bizzozero, of Turin, about the year 1868, have been extended and confirmed by others, and show that there is a generation of red corpuscles in the red marrow of the bones, which is now regarded as the most important of the so-called corpuscle-forming organs. In the fœtus and in the young infant, the marrow of nearly all the bones is red, or of the kind called lymphoid. In the adult, the marrow of the long bones is yellow, or fatty, the red marrow being confined to the cancellated structure of the short and the flat bones. Although the researches with regard to the spleen are less positive and definite in their results, it is probable that this organ also contributes to the development of the red blood-corpuscles.

The exact mode of development of the red corpuscles in the marrow and in the spleen has not been very satisfactorily described and is still a question concerning which there is much difference of opinion among histologists. A full discussion of this question would be out of place in this work, which is intended to embrace only those points in histology that have been definitely settled.

It is probable that the red corpuscles are, in certain number, destroyed in the passage of the blood through the liver and perhaps, also, in the spleen, the coloring matter contributing to the formation of the biliary and the urinary pigmentary matters. If this view be accepted, the spleen is concerned in both the formation and the disintegration of blood-corpuscles.

In the present state of knowledge, the following seem to be the most rational views with regard to the development and destination of the red blood-corpuscles.

1. At the time of their first appearance in the ovum, the blood-corpuscles are formed by no special organs, for no special organs then exist.

2. In the fœtus, after the development of the marrow of the bones and of the spleen, and in the adult, these parts have important uses in the formation of the red corpuscles, especially the red marrow of the bones.

3. It is probable that the red blood-corpuscles are constantly undergoing destruction, and that their coloring matter contributes to the formation of other pigmentary matters. As the corpuscles are thus destroyed, and as they are diminished in number in disease or by hæmorrhage, they are probably replaced by new corpuscles formed in greatest part in the red marrow of the bones.

4. Pathological observations seem to show that in certain cases of anæmia, when there is an abnormal destruction of red corpuscles, the activity of the corpuscle-forming office of the marrow is increased, compensating, to a certain extent, the conditions which involve the abnormal destruction of the corpuscles.

Uses of the Red Blood-Corpuscles.—Although the albuminoid constituents of the plasma of the blood are essential to nutrition, the red corpuscles are the parts most immediately necessary to life. It is well known that life may be restored to an animal in which the functions have been suspended by hæmorrhage, by the introduction of fresh blood; and while it is not necessary that this blood should contain the fibrin-factors, it has been shown by the experiments of Prévost and Dumas and others, that the introduction of serum, without the corpuscles, has no permanent restorative effect. When all the arteries leading to a part are tied, the tissues lose their properties of contractility, sensibility etc., which may be restored, however, by supplying it again with blood. It will be seen, in treating of respiration, that one great distinction between the corpuscular and fluid elements of the blood is the great capacity which the former have for absorbing gases. Direct observations have shown that blood will absorb ten to thirteen times as much oxygen as an equal bulk of water; and this is dependent almost entirely on the presence of the red corpuscles. As all the tissues are constantly absorbing oxygen and giving off carbon dioxide, a very important office of the corpuscles is to carry oxygen to all parts of the body. In the present state of knowledge, this is the only well defined use which can be attributed to the red corpuscles, and it undoubtedly is the principal one. They have an affinity, though not so great, for carbon dioxide which, after the blood has circulated in the capillaries of the system, takes the place of the oxygen. In a series of experiments on the effects of hæmorrhage and the seat of the "sense of want of air," it was demonstrated that one of the results of removal of blood from the system was a condition of asphyxia, dependent upon the absence of these respiratory elements (Flint, 1861).

Leucocytes, or White Corpuscles of the Blood.—In addition to the red corpuscles of the blood, this fluid always contains a number of colorless bodies, globular in form, in the substance of which are embedded a greater or less number of minute granules, forming a nucleus of irregular shape. These have been called by Robin, leucocytes. This name seems more appropriate than that of white or colorless blood-corpuscles, inasmuch as these bodies are not peculiar to the blood, but are found in the lymph, chyle, pus and various other fluids, in which they were formerly known by different names. The description which will be given of the white corpuscles of the blood, and the effects of reagents, will answer, in the main, for all the corpuscular bodies that are grouped together under the name of leucocytes.

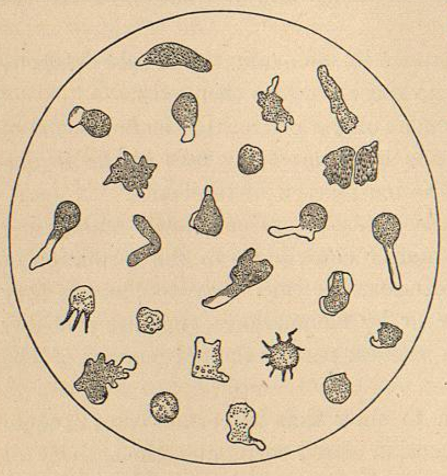

FIG. 6.—*Human leucocytes, showing amœboid movements* (Landois).

Leucocytes are normally found in the blood, lymph, chyle, semen, colostrum and vitreous humor. Pathologically, they are found in the secretion of mucous membranes, following irritation, and in inflammatory products, when they are called pus-corpuscles. They are globular, with a smooth surface, somewhat opaque from the presence of more or less granular matter, white, and larger than the red corpuscles. In examining the circulation under the microscope, the adhesive character of the leucocytes as compared with the red corpuscles is readily noted. The latter circulate with great rapidity in the centre of the vessels, while the leucocytes have a tendency to adhere to the sides, moving along slowly, and occasionally remaining stationary for a time, until they are swept along by a change in the direction or force of the current.

The size of the leucocytes varies somewhat, even in any one fluid, such as the blood. Their average diameter may be stated as $\frac{1}{2500}$ of an inch (10 μ). It is in pus, where they exist in greatest abundance, that their microscopical characters may be studied with most advantage. In this fluid, after it is discharged, the corpuscles sometimes present remarkable changes in form. They become polygonal in shape, and sometimes ovoid, occasionally presenting projections from their surface, which give them a stellate appearance. These alterations, however, are only temporary; and after twelve to twenty-four hours, they resume their globular shape. On the addition of acetic acid they swell up, become transparent, with a delicate outline, and present in their interior one, two, three or even four rounded, nuclear bodies, generally collected in a mass. This appearance is produced, though more slowly, by the addition of water. In some corpuscles a nucleus may be seen without the addition of any reagent.

Leucocytes vary considerably in their external characters in different situations. Sometimes they are very pale and almost without granulations, and sometimes they are filled with fatty granules and are not rendered clear by acetic acid. As a rule, they increase in size and become granular when confined in the tissues. In colostrum, where they are called colostrum-corpuscles, they generally undergo this change. As the result of inflammatory action, when they are sometimes called inflammatory or exudation-corpuscles, leucocytes frequently become much hypertrophied and are filled with fatty granules.

The deformation of the leucocytes to which allusion has already been made is sometimes so rapid and changeable as to produce creeping movements, due to the projection and retraction of portions of their substance. These movements are of the kind called amœboid and are supposed to be important in the process of migration of the corpuscles.

The relative number of leucocytes, can only be given approximately. It has been estimated by counting under the microscope the red corpuscles and leucocytes contained in a certain space. The average proportion in man is probably 1 to 750 or 1000. It has been found by Hirt, whose observations have been confirmed by others, that the relative quantity of leucocytes is much increased during digestion. He found, in one individual, a proportion of 1 to 1800 before breakfast; an hour after breakfast, which was taken at 8 o'clock, 1 to 700; between 11 and 1 o'clock, 1 to 1500; after dining, at 1 o'clock, 1 to 400; two hours after, 1 to 1475; after supper, at 8 P. M., 1 to 550; at $11\frac{1}{2}$ P. M., 1 to 1200. The leucocytes are much lighter than the red corpuscles, and when the blood coagulates slowly, they are frequently found, with a certain quantity of colorless fibrin, forming a whitish layer on the surface of the clot. Their specific gravity is about 1070.

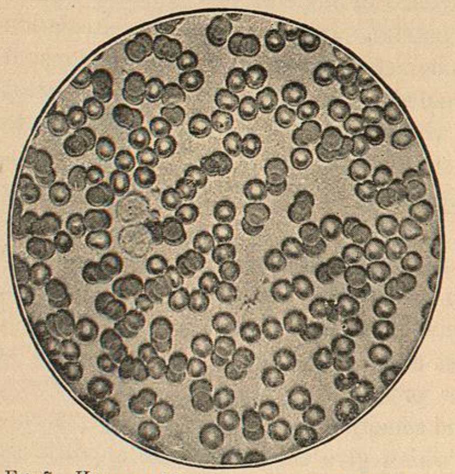

FIG. 7.—*Human red blood-corpuscles and two leucocytes* (Sternberg).

Development of Leucocytes.—These corpuscles appear in the blood-vessels very early in fœtal life, before the lymphatics can be demonstrated. They appear in lymphatics before these vessels pass through the lymphatic glands, in the fœtus anterior to the development of the spleen, and also on the surface of mucous membranes; so that they can not be considered as produced exclusively by the lymphatic glands, as has been supposed. Although they frequently appear as a result of inflammation, this process is by no means necessary for their production. Robin has observed the phenomena of their development in recent wounds. The first exudation consists of clear fluid, with a few red corpuscles. There appears afterward, a finely granular blastema. In a quarter of an hour to an hour, pale, transparent globules, $\frac{1}{8000}$ to $\frac{1}{6000}$ of an inch (3 μ to 4 μ) in diameter, make their appearance, which soon become finely granular and present the ordinary appearance of leucocytes.

Histological researches show that in the adult, the number of leucocytes in the lymph is increased during the passage of this fluid through the lymphatic glands. The blood, also, in passing through the spleen has been shown to gain largely in these corpuscles. These facts are important in connection with the pathology of leucocythæmia. This disease, which is characterized by an excess of leucocytes in the blood, is now generally regarded as having a close relation to certain changes in the spleen, the lymphatic glands and the marrow of the bones. There is, indeed, a variety of the disease, known as lymphatico-splenic leucocythæmia, in which the spleen and certain of the lymphatic glands are enlarged, and another form, called medullo-lymphatic leucocythæmia, in which changes have been noted in the lymphatic glands and in the marrow. The anatomical changes which have been observed in the spleen, lymphatic glands and marrow, in leucocythæmia, are largely hyperplastic; that is, the normal structure of these parts is increased in extent. On the other hand, a disease called pseudo-leucocythæmia, presenting the anatomical characters and general symptoms of leucocythæmia, without an increase in the leucocytes of the blood, has been accurately described. Pathological observations, therefore, are not entirely

in accord with the theory that the spleen, lymphatic glands and the bone-marrow are always directly concerned in the production of leucocytes.

Taking into consideration the histological and pathological observations bearing on the question, the following seems to be the most reasonable view with regard to the mode of development of leucocytes:

1. In early fœtal life the leucocytes of the blood are developed without the intervention of any special organs, and perhaps, also, these bodies are multiplied by division.

2. In adult life the same processes of development probably occur in the blood and lymph and in other situations.

3. It is probable, though by no means certain, that the spleen, lymphatic glands and the red marrow of the bones are more or less actively concerned in the production of leucocytes, both under physiological and pathological conditions; but it is certain that these organs and parts are not the exclusive seat of development of the so-called white blood-corpuscles and lymph-corpuscles.

Uses of the Leucocytes.—It is impossible, in the present state of physiological knowledge, to assign any definite use to the leucocytes of the blood and lymph. These bodies may be concerned to some extent in the development of the red blood-corpuscles, but this view, which is held by many physiologists, has no absolutely positive basis in fact. All that can be said is that the office of the leucocytes has not been ascertained. Their action, however, is important in the process of coagulation of the blood, lymph and chyle.

Blood-Plaques.—The so-called blood-plaques, described quite elaborately by Bizzozero and others, have been long known to histologists, under a variety of names, such as globulins, elementary corpuscles, granular *débris*, granule masses, hæmatoblasts etc. Until within a few years these bodies have not been thought to be of much importance, and even now little is known of their physiological and pathological relations.

The blood-plaques in human blood may be easily observed, preparing the blood by the following method (Osler):

"Upon the thoroughly cleansed finger-pad a single drop of the solution is placed, and with a sharp needle, or pricker, the skin is pierced through the drop, so that the blood passes at once into the fluid, which is then received upon a slide and covered. The withdrawal of the corpuscles into the solution prevents the plaques from aggregating, and they remain as isolated and distinct elements. The amount of blood allowed to flow into the drop must not be large, and should be quickly mixed. In many respects the most suitable medium is osmic acid, one-half to one per cent., which has the advantage that by its use permanent preparations can be obtained."

The plaques are thin, circular discs, homogeneous or very faintly granular and of a pale, grayish tint. They measure $\frac{1}{17000}$ to $\frac{1}{10000}$ (1·5 to 2·5 μ) in diameter, about one-sixth of the diameter of the red blood-corpuscles. They exist in the blood in the proportion of one to about eighteen or twenty red corpuscles.

In the circulating blood, the plaques are distinct; but when the blood is drawn from the vessels, they adhere together and are usually collected into masses. The plaques quickly undergo change out of the body, becoming

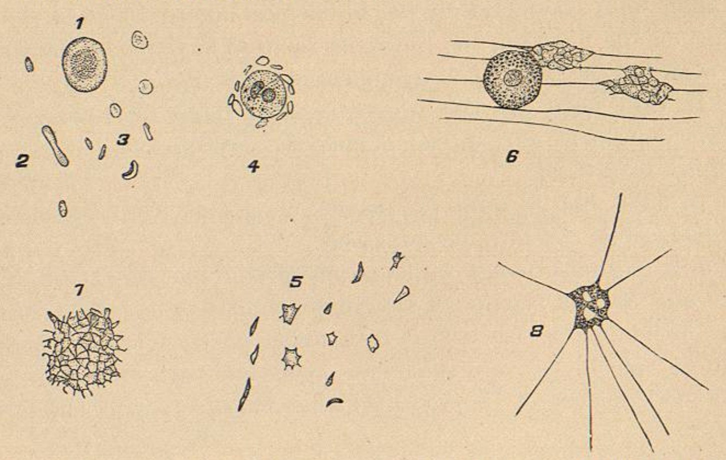

Fig. 8.—*Blood-plaques and their derivatives, partly after Bizzozero and Laker* (Landois).
1, red blood-corpuscles on the flat; 2, from the side; 3, unchanged blood-plaques; 4, a lymph-corpuscle surrounded with blood-plaques; 5, blood-plaques variously altered; 6, a lymph-corpuscle with two masses of fused blood-plaques and threads of fibrin; 7, group of blood-plaques fused or run together; 8, a similar small mass of partially dissolved blood-plaques with fibrils of fibrin.

ovoid, elongated or pointed. They sometimes send out processes which give them a stellate appearance.

Physiologists have no knowledge of the uses of the blood-plaques. The relations which have been supposed to exist between these bodies and the development of the other corpuscular elements of the blood, the phenomena of coagulation, etc., are as yet indefinite and uncertain.

Composition of the Blood-Corpuscles.

The red corpuscles of the blood contain an organic nitrogenized substance, called globuline, combined with inorganic salts and a coloring matter. The composition of the leucocytes has not been accurately determined, and nothing is known of the composition of the blood-plaques. The inorganic matters contained in the red corpuscles are in a condition of intimate union with the other constituents, and can be separated only by incineration. It may be stated, in general terms, that most, if not all of the various inorganic constituents of the plasma exist also in the corpuscles, which latter are particularly rich in the salts of potassium. Iron exists in the coloring matter of the corpuscles. In addition, the corpuscles contain cholesterine, lecethine, a certain quantity of fatty matter and probably some of the organic saline constituents of the blood.

Globuline.—Rollett, by alternately freezing and thawing blood several times in succession in a platinum vessel, has succeeded in separating the coloring matter from the red corpuscles. When the blood is afterward warmed and liquefied, the fluid is no longer opaque but is dark and transparent. Microscopical examination then reveals the corpuscles, entirely decolorized and floating in a red, semi-transparent serum. Denis extracted the organic

constituent of the corpuscles by adding to defibrinated blood about one-half its volume of a solution of sodium chloride containing one part in ten of water. Allowing this to stand for ten to fifteen hours, there appears a viscid mass, which is very carefully washed with water until all the coloring matter and the salt added have been removed. The whitish, translucid mass which remains is called globuline. Globuline is readily extracted from the blood of birds but is obtained with difficulty from the blood of the human subject.

Hæmaglobine.—This is the coloring matter of the red corpuscles. It has been called by different writers, hæmaglobuline or hæmatocrystalline; but the crystals called hæmatine and hæmatosine are derivatives of hæmaglobine and are not normal constituents of the blood. Hæmaglobine may be extracted from the red corpuscles by adding to them, when congealed, ether, drop by drop. A jelly-like mass is then formed, which is passed rapidly through a cloth, crystals soon appearing in the liquid, which may be separated by filtration (Gautier).

The crystals of hæmaglobine extracted from human blood are in the form either of four-sided prisms, elongated rhomboids or rectangular tablets, of a purplish-red color. They are composed of carbon, hydrogen, oxygen, nitrogen, sulphur and a small quantity of iron. They are soluble in water and in very dilute alkaline solutions, and the hæmaglobine is precipitated from these solutions by potassium ferrocyanide, mercuric nitrate, chlorine or acetic acid. The proportion of this coloring matter to the entire mass of blood is about one hundred and twenty-seven parts per thousand. It constitutes $\frac{9}{10}$ to $\frac{12}{13}$ of the dried corpuscles. A solution of hæmaglobine in one thousand parts, examined with the spectroscope, gives two dark bands between the letters D and E in Frauenhofer's scale.

Treated with oxygen or prepared in fluids in contact with the air, there occurs a union of oxygen with the coloring matter, forming what has been called oxyhæmaglobine. There can be no doubt that the oxygen enters into an intimate, though rather unstable combination with hæmaglobine, and this is an important point to be considered in connection with the absorption of oxygen by the blood in respiration. A solution of oxyhæmaglobine presents a different spectrum from that produced by a solution of pure hæmaglobine.

Composition of the Blood-Plasma.

Assuming that the blood furnishes matters for the nourishment of all the tissues and organs, there should be found entering into its composition all the constituents of the body which undergo no change in nutrition, like the inorganic salts, and organic matters capable of being converted into the organic constituents of every tissue. Farthermore, as the products of waste are all taken up by the blood before their final elimination, these also should enter into its composition.

Most of the constituents of the blood are found both in the corpuscles and plasma. It is difficult to determine all of the different constituents of these two parts of the blood. It has been shown, however, that the phosphorized fats are more abundant in the globules, while the fatty acids are more abundant in the plasma. The salts of potassium exist almost entirely in the corpuscles, and the sodium salts are four times more abundant in the plasma than in the corpuscles (Schmidt). In addition to the nutritive matters, the blood contains urea, cholesterine, sodium urate, creatine, creatinine, and other substances, the characters of which are not yet fully determined, belonging to the class of excrementitious matters. Their consideration comes more appropriately under the head of excretion.

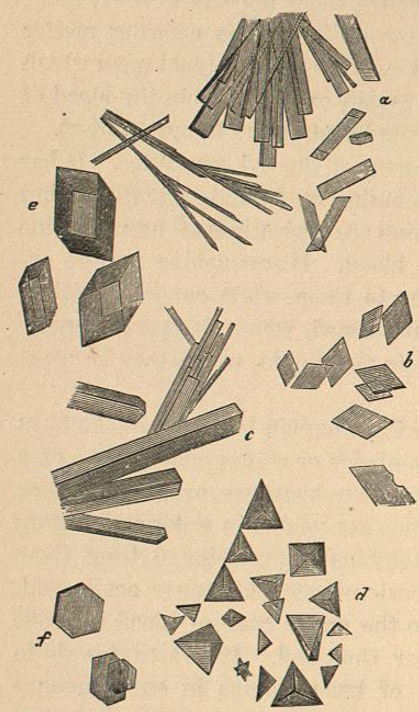

FIG. 9.—*Crystallized hæmaglobine* (Gautier). *a*, *b*, crystals from the venous blood of man; *c*, blood of the cat; *d*, blood of the Guinea pig; *e*, blood of the marmot; *f*, blood of the squirrel. (Gautier.)

The following table gives approximately the quantities of the different constituents of the blood-plasma. These may be divided into the following classes: 1. Inorganic constituents; 2. Organic saline constituents; 3. Organic non-nitrogenized constituents; 4. Excrementitious constituents; 5. Organic nitrogenized constituents. This table will be taken as a guide for the study of the individual constituents of the blood-plasma. As regards gases, in addition to carbon dioxide, which is classed with the excrementitious constituents, the blood contains oxygen, nitrogen and hydrogen. The nitrogen and hydrogen are not important, and the relations of oxygen will be fully considered in connection with the physiology of respiration. Most of the coloring matter of the blood exists in the red corpuscles, which contain a peculiar substance that has already been considered in connection with the chemical constitution of these bodies.

In studying the composition of the blood, as well as the composition of food, the tissues, secreted fluids etc., it is convenient to divide its constituents into classes, and this has been done in the simplest manner possible.

It is evident, the blood receiving all the products of disassimilation as well as the nutritive matters resulting from digestion, that there should be a division of its constituents into nutritive and excrementitious. The excrementitious matters are the products of disassimilation of the organism, which are taken up by the blood or conveyed to the blood-vessels by the lymphatics, exist in the blood in small quantity, and are constantly being separated from the blood by the different excreting organs. Their constant removal from the blood is the explanation of the minute proportion in which they exist in this fluid.

CONSTITUENTS OF THE BLOOD-PLASMA.

Specific gravity, 1028.

Inorganic.	Water, 779 parts per 1,000 in the male; 791 parts per 1,000 in the female.	
	Sodium chloride, 3 to 4 parts per 1,000.	
	Potassium chloride, 0·359 parts per 1,000.	
	Ammonium chloride, proportion not determined.	
	Potassium sulphate, 0·288 parts per 1,000.	
	Sodium sulphate, proportion not determined.	
	Potassium carbonate, proportion not determined.	
	Sodium carbonate (with sodium bicarbonate), 1·200 parts per 1,000.	
	Magnesium carbonate, proportion not determined.	
	Calcium phosphate of the bones, and neutral phosphate,	1·500 parts per 1,000.
	Magnesium phosphate,	
	Potassium phosphate,	
	Ferric phosphate (probable),	
	Basic phosphates and neutral sodium phosphate,	
	Silica, copper, lead, and magnesia, traces occasionally.	
Organic saline.	Sodium lactate, proportion not determined.	
	Calcium lactate (probable), proportion not determined.	
	Sodium oleate,	1·475 parts per 1,000.
	" palmitate,	
	" stearate,	
	" valerate,	
	" butyrate,	
Organic non-nitrogenized.	Oleine,	
	Palmitine,	
	Stearine,	
	Lecethine, containing nitrogen and called phosphorized fatty matter, 0·400 parts per 1,000.	
	Glucose, 0·002 parts per 1,000.	
	Glycogen, proportion not determined.	
	Inosite, proportion not determined.	
Excrementitious.	Carbon dioxide in solution.	
	Urea, 0·177 parts per 1,000, in arterial blood; 0·088, in the blood of the renal vein.	
	Sodium urate, proportion not determined.	
	Potassium urate (probable), proportion not determined.	
	Calcium urate, " " " "	
	Magnesium urate, " " " "	
	Ammonium urate, " " " "	
	Sodium sudorates, etc., " " "	
	Inosates, " " "	
	Oxalates, " " "	
	Creatinine, " " "	
	Leucine, " " "	
	Hypoxanthine, " " "	
	Cholesterine, 0·455 to 0·751 parts per 1,000, in the entire blood.	
Organic nitrogenized.	Plasmine, 25 parts (dried) per 1,000.	Fibrin, 3 parts per 1,000. Metalbumin, 22 parts per 1,000.
	Serine, 53 parts (dried) per 1,000.	
	Peptones, 4 parts (dried) and 28 parts (moist) per 1,000.	
	Coloring matters of the plasma, proportion and characters not determined.	