

Excluding for the present, all consideration of the products of disassimilation, there remain the various constituents of the blood that are more or less directly concerned in nutrition.

Physiological chemists recognize certain chemical constituents of the organism, which may be elementary substances, but which are more frequently compounds. Sodium chloride is spoken of as a constituent of the blood, because, as sodium chloride, it gives to the blood certain properties. The chemical elements, chlorine and sodium, are not regarded as constituents of the blood, because they do not exist uncombined in the blood. Still, a chemical constituent may be a chemical element, as in the case of oxygen, which, as oxygen, has certain important uses in the economy; although even oxygen probably is loosely combined in the body with other matters.

A chemical constituent of the blood or of any of the animal tissues or fluids may be defined as a substance extracted from the body, which can not be subdivided without chemical decomposition and loss of certain characteristic properties. This definition will apply to all classes of chemical constituents of the body, organic as well as inorganic. The chemical elements of which the constituents are composed are properly the ingredients of the body.

The constituents of the blood, and, indeed, of the entire organism, may be classified as follows:

1. *Inorganic Constituents*.—This class is of inorganic origin, definite chemical composition and crystallizable. The substances included in this class are all introduced from without and are all discharged from the body in the same form in which they entered. They never exist alone, but are always combined with the organic constituents, and form a part of the organized fluids or solids. This union is so intimate that they are taken up with the organic matters, as the latter are worn out and become effete, and are discharged from the body, although themselves unchanged. To supply the place of the constituents thus thrown off, a fresh quantity is deposited in the process of nutrition. They give to the various organs important properties; and although identical with substances in the inorganic world, in the interior of the body they behave as organic substances. They require no special preparation for absorption, but are soluble and taken in unchanged. They are received into the body in about the same proportion at all periods of life, but their discharge is notably diminished in old age, giving rise to calcareous incrustations and deposits and a considerable increase in the calcareous matter entering into the composition of the tissues. Water, sodium chloride, the carbonates, sulphates, phosphates and other inorganic salts may be cited as examples of this class of constituents.

The uses of water in the blood are sufficiently evident. It acts as a solvent for the inorganic salts, the organic salts and the excrementitious matters. In conjunction with the nitrogenized matters, it constitutes a medium in which the corpuscles are suspended without solution.

The various salts enumerated in the table exist in solution in water and are

more or less intimately combined with the coagulable organic matters. Of these, the sodium chloride is the most abundant. It undoubtedly has an important use in giving density to the plasma and in regulating the processes of endosmosis and exosmosis. In connection with the organic salts and crystallizable excrementitious matters, it may be stated, in general terms, that the blood contains 14 to 16 parts per 1,000 of matters in actual solution, of which 6 to 8 parts consist of inorganic salts. The presence of these substances in solution, with the organic coagulable matters, prevents the solution of the corpuscular elements of the blood. The presence of the chlorides and the alkaline sulphates assists in dissolving the sulphates, carbonates and the calcareous phosphates. The carbonates and phosphates are in part decomposed in the system and furnish bases for certain of the organic salts, such as the lactates, urates etc.

2. *Organic Saline Constituents*.—These substances are in greatest part formed in the organism and they exist in the blood in very small quantity. The lactates are probably produced by decomposition of a portion of the bicarbonates and the union of the bases with lactic acid, the lactic acid resulting, possibly, from a change of a portion of the saccharine matter in the blood. The physiological relations of these substances are little understood. The salts formed by the union of fatty acids with bases are probably produced by decomposition of fatty matters, a great part of which is derived from the food.

3. *Organic Non-nitrogenized Constituents*.—These usually exist in the blood in small quantity and are derived mainly from the food. Lecithine, although it contains nitrogen, is included in this class because it presents many of the properties of the fats. It exists in the blood, bile, nervous substance and the yolk of egg. Its chemical properties and physiological relations are not well understood. The saccharine matters and glycogen are derived in part from the food and in part from the liver, where glycogen is formed. They are of organic origin, definite chemical composition and crystallizable. The fats and sugars are distinguished from other organic substances by the fact that they are composed of carbon, hydrogen and oxygen. In the sugars, the hydrogen and oxygen exist in the proportion to form water, which fact has given them the name of carbohydrates. The constituents of this class play an important part in development and nutrition. One of them, sugar, appears very early in foetal life, formed first in the placenta and afterward in the liver, its formation by the latter organ continuing during life. Fat is a necessary constituent of food and is also formed in the interior of the body. The exact influence which these substances have on development and nutrition is not known; but experiments and observation have shown that this influence is important. They will be considered more fully in connection with the physiology of nutrition.

4. *Excrementitious Constituents*.—A full consideration of these substances, which are all formed by the process of disassimilation of the tissues and are taken up by the blood to be eliminated by the proper organs, be-

longs to the physiology of excretion. The relations of carbon dioxide to the system will be fully considered in connection with the physiology of respiration.

5. *Organic Nitrogenized Constituents*.—This class of constituents is of organic origin, indefinite chemical composition and non-crystallizable. The constituents included in this class are apparently the only matters that are endowed with so-called vital properties, taking materials for their regeneration from the nutritive fluids and appropriating them to form part of their own substance. Considered from this point of view, they are different from any substances met with out of the living body. They are all, in the body, in a state of continual change, wearing out and becoming effete, when they are transformed into excrementitious substances. The process of repair in this instance is not the same as in inorganic substances, which enter and are discharged from the body without undergoing any change. The analogous substances which exist in food undergo elaborate preparation by digestion, before they can even be absorbed by the blood-vessels; and still another change takes place when they are appropriated by the various tissues. They exist in all the solids, semi-solids and fluids of the body, never alone, but always combined with inorganic substances. As a peculiarity of chemical constitution, they all contain nitrogen, which has given them the name of nitrogenized or azotized matters.

Of the different classes of constituents of the blood, it is at once apparent that the organic nitrogenized matters are more complex in their constitution, properties and uses than the other classes. These substances, as they exist in the blood, possess certain peculiar and characteristic properties.

Plasmine, Fibrin, Metalbumin, Serine.—The name plasmine was given by Denis to a substance which he extracted from the blood by the following process: The blood drawn directly from an artery or vein is received into a vessel containing one-seventh part of its volume of a concentrated solution of sodium sulphate, which prevents coagulation; in a short time the corpuscles gravitate to the bottom of the vessel, and the plasma may be separated by decantation; to the plasma is added an excess of pulverized sodium chloride, when a soft, pulpy substance is precipitated, which is plasmine. This substance, after desiccation, bears a proportion of about twenty-five parts per thousand of blood. It is soluble in ten to twenty parts of water, when a portion of it coagulates and may be removed by stirring with twigs or a bundle of broom-corn, in the way in which fibrin is separated from the blood. The fibrin thus separated is called by Denis concrete fibrin, and the substance which remains in solution, dissolved fibrin. By most writers of the present day, the dissolved fibrin of Denis is called metalbumin.

According to Denis, plasmine is a proper constituent of the blood, and after extraction by the process just described, it is decomposed into concrete fibrin and dissolved fibrin, or metalbumin. Having removed the concrete fibrin from the solution of plasmine, the metalbumin is coagulated by the addition of magnesium sulphate, which does not coagulate ordinary albumin. The proportion of dried metalbumin in the blood is about twenty-two parts

per thousand. The proportion of dried fibrin is about three parts per thousand.

After the extraction of plasmine from the blood, another coagulable substance remains, which is called serine. This is coagulated by heat, the strong mineral acids or absolute alcohol, but is not coagulated by ether, which coagulates egg-albumen. Serine bears a close resemblance to ordinary albumin but is much more osmotic. Its proportion, desiccated, in the blood is about fifty-three parts per thousand.

Peptones etc.—A certain quantity of nitrogenized matter, distinct from the constituents just described, has been extracted from the blood, which is analogous to peptone. This is separated by coagulating the serum of the blood with hot acetic acid and filtering, when the peptones pass through in the filtrate. These substances are probably derived from the food. Their proportion in the plasma is about four parts, dried, per thousand, or twenty-eight parts before desiccation.

A small quantity of coloring matter exists in the plasma. If the corpuscles be separated as completely as possible, the clear liquid still has a reddish-amber color. This coloring matter has never been isolated and studied. It is analogous to the coloring matter of the red corpuscles, the bile and the urine.

In addition to the organic nitrogenized constituents which have just been described, some physiological chemists recognize a substance called paraglobuline, or fibrinoplastic matter, and fibrinogenic matter. These are supposed to be factors of fibrin, which come together in the coagulation of the blood. They will be considered in connection with the theories of coagulation. The so-called sodium and potassium albuminates have not been positively established as normal constituents of the blood.

COAGULATION OF THE BLOOD.

The blood retains its fluidity while it remains in the vessels and circulation is not interfered with, and is then composed of a clear plasma holding corpuscles in suspension. Soon after the circulation is interrupted or after blood is drawn from the vessels, it coagulates or "sets" into a jelly-like mass. In a few hours, contraction will have taken place, and a clear, straw-colored fluid expressed, the blood thus separating into a solid portion, the crassamentum, or clot, and a liquid which is called serum. The serum contains all the constituents of the blood except the corpuscles and fibrin-factors, which together form the clot. Coagulation takes place in the blood of all animals, beginning a variable time after its removal from the vessels. In the human subject, when the blood is received into a moderately deep, smooth vessel, the phenomena of coagulation present themselves in the following order:

First, a gelatinous pellicle forms on the surface, which occurs in one minute and forty-five seconds to six minutes; in two to seven minutes, a gelatinous layer has formed on the sides of the vessel; and the whole mass becomes of a jelly-like consistence, in seven to sixteen minutes. Contraction

then begins, and little drops of clear serum make their appearance on the surface of the clot. This fluid increases in quantity, and in ten or twelve hours separation is complete (Nasse). The clot, which is heavier, sinks to the bottom of the vessel, unless it contain bubbles of gas or the surface be very concave. In most of the warm-blooded animals, the blood coagulates more rapidly than in man. Coagulation is particularly rapid in blood taken from birds, and sometimes it takes place almost instantaneously. Coagulation is more rapid in arterial than in venous blood. In the former, the proportion of fibrin formed is notably greater and the characters of the fibrin are somewhat different. A solution of sodium chloride dissolves the fibrin of venous blood, but does not dissolve the fibrin of an arterial clot.

The relative proportions of the serum and clot are very variable, unless that portion of the serum which is retained between the meshes of the coagulated mass be included in the estimate. As the clot is composed of corpuscles and fibrin, and as these in their moist state represent, in general terms, about one-half of the blood, it may be stated that after coagulation, the actual proportions of the clot and serum are about equal. Simply taking the serum which separates spontaneously, there is a large quantity when the clot is densely contracted, and a very small quantity, when it is loose and soft. Usually the clot retains about one-fifth of the serum.

On removing the clot, after the separation of the serum is complete, it presents a gelatinous consistence, and is more or less firm according to the degree of contraction which has taken place. As a general rule, when coagulation has been rapid, the clot is soft and but slightly contracted. When, on the other hand, coagulation has been slow, the clot contracts for a long time and is much denser. When coagulation is slow, the clot frequently presents what is known as the cupped appearance, having a concave surface, a phenomenon which depends merely on the degree of its contraction. It also presents a marked difference in color at its upper portion. The blood having remained fluid for some time, the red corpuscles settle, by reason of their greater weight, leaving a colorless layer on the top. This is the buffy-coat spoken of by some authors. Examined microscopically, the buffy-coat presents fibrils of coagulated fibrin with some of the white corpuscles of the blood. On removing a clot of venous blood from the serum, the upper surface is florid from contact with the air, while the rest of it is dark; and on making a section, if coagulation have not been too rapid, the gravitation of the red corpuscles is apparent. If the clot be cut into small pieces, it will undergo farther contraction and express a part of the contained serum. If the clot be washed under a stream of water, at the same time kneading it with the fingers, nearly all the red corpuscles may be removed, leaving the meshes of fibrin.

After coagulation, if the serum be carefully removed, it is found to be a fluid of a color varying between a light amber and a clear red. This color depends upon a peculiar coloring matter which has never been isolated. The specific gravity of the serum is about 1028, somewhat less than that of the entire mass of blood. It presents all the constituents of the plasma, or liquor sanguinis, with the exception of the fibrin-factors. It can hardly

be called a physiological fluid, as it is formed only after coagulation of the blood.

Coagulation of the blood is due to the formation of fibrin. Coagulation of this substance first causes the whole mass of blood to assume a gelatinous consistence; and by reason of its contractile properties, it soon expresses the serum, while the red corpuscles are retained. One of the causes which operate to retain the corpuscles in the clot is the adhesive matter which covers their surface after they escape from the vessels.

Conditions which modify Coagulation.—Blood flowing slowly from a small orifice is more rapidly coagulated than when it is discharged in a full stream from a large orifice. If it be received into a shallow vessel, it coagulates much more rapidly than when received into a deep vessel. If the vessel be rough, coagulation is more rapid than if it be smooth and polished. If the blood, as it flows, be received on a cloth or a bundle of twigs, it coagulates almost instantaneously. In short, it appears that all conditions which favor exposure of the blood to the air hasten its coagulation. The blood will coagulate more rapidly in a vacuum than in the air.

Coagulation of the blood is prevented by rapid freezing, but it takes place afterward when the fluid is carefully thawed. Between 32° and 140° Fahr. (zero and 60° C.), elevation of temperature increases the rapidity of coagulation. Agitation of the blood in closed vessels retards, and in open vessels, hastens coagulation.

Various chemical substances retard or prevent coagulation. Among them may be mentioned the following: solutions of potassium or of sodium hydrate; sodium carbonate; ammonium carbonate; potassium carbonate; ammonia; sodium sulphate. In the menstrual flow, the blood is kept fluid by mixture with the abundant secretions of the vaginal mucous membrane.

Coagulation of the Blood in the Organism.—The blood coagulates in the vessels after death, though less rapidly than when removed from the body. As a general proposition, it may be stated that this takes place between twelve and twenty-four hours after circulation has ceased. Under these conditions, the blood is found chiefly in the venous system, as the arteries are usually emptied by post-mortem contraction of their muscular coat; but in the veins, coagulation is slow and imperfect. Coagula are found, however, in the left side of the heart and in the aorta, but they are much smaller than those in the right side of the heart and in the large veins. These coagula present the general characters already described. They are frequently covered by a soft, whitish film and are dark in their interior.

It was supposed by John Hunter that coagulation of the blood did not take place in animals killed by lightning, or by prolonged muscular exertion, as when hunted to death; but it appears from the observations of others that this view is not correct. J. Davy reported a case of death by lightning, in which a loose coagulum was found in the heart twenty-four hours after. In this case decomposition was very far advanced, and it is probable that the

coagulum had become less firm from that cause. His observations also show that coagulation occurs after poisoning by hydrocyanic acid and in animals hunted to death.

Coagulation in different parts of the vascular system is by no means unusual during life. In the heart, coagula which bear evidence of having existed for some time before death are sometimes found. These were called polypi by some of the older writers and are often formed of fibrin almost free from red corpuscles. They generally occur when death is very gradual and when the circulation continues for some time with greatly diminished activity. It is probable that a small coagulum is first formed, from which the corpuscles are washed away by the current of blood; and that this becomes larger by farther depositions, until large, vermicular masses of fibrin are found attached, in some instances, to the chordæ tendineæ. Bodies projecting into the caliber of a blood-vessel soon become coated with a layer of fibrin. Rough concretions about the orifices of the heart frequently lead to the deposition of little masses of fibrin, which sometimes become detached and are carried to various parts of the circulatory system, as the lungs or brain, plugging up one or more of the smaller vessels. Blood generally coagulates when effused into the areolar tissue or into any of the cavities of the body; although, effused into the serous cavities, the tunica vaginalis for example, it has been known to remain fluid for days and even weeks, and coagulate when let out by an incision. Coagulation thus takes place in the vessels as the result of stasis or of very great retardation of the circulation, and in the tissues or cavities of the body, whenever it is accidentally effused. In the latter case, it is generally removed in the course of time by absorption.

The property of the blood under consideration has an important office in the arrest of hæmorrhage. The effect of an absence or great diminution of the coagulability of the circulating fluid is exemplified in instances of what is called the hæmorrhagic diathesis, or hæmophilia; a condition in which slight wounds are likely to be followed by alarming, and it may be fatal hæmorrhage. This condition of the blood is not characterized by any peculiar symptoms except the obstinate flow of blood from slight wounds; and it may continue for years.

Conditions which accelerate coagulation have a tendency to arrest hæmorrhage. It is well known that exposure of a bleeding surface to the air has this effect. The way in which the vessel is divided has an important influence. A clean cut will bleed more freely than a ragged laceration. In division of large vessels, this difference is sometimes very marked. Cases are on record in which the arm has been torn off at the shoulder-joint, and yet the hæmorrhage was, for a time, spontaneously arrested; while it is well known that division of an artery of comparatively small size, if it be cut across, would be fatal if left to itself. Under these conditions, the internal coat is torn in shreds which retract, their curled ends projecting into the caliber of the vessel and having the same effect on the coagulation of blood as a bundle of twigs. In laceration of such a large vessel as the axillary artery, the arrest can not be permanent, for as soon as the system recovers from the shock,

the contractions of the heart force out the coagulated blood which has closed the opening.

From the foregoing considerations, it is evident that coagulation of the blood has for its chief office the arrest of hæmorrhage. Coagulation never takes place in the organism unless the blood be in an abnormal condition with respect to circulation. Here its operations are mainly conservative; but as almost all conservative processes are sometimes perverted, clots in the body may be productive of injury, as in the instances of cerebral apoplexy, clots in the heart occurring before death, the detachment of emboli etc.

Cause of the Coagulation of the Blood.—Alex. Schmidt, in 1861, proposed a theory of coagulation, which involves the coming together of certain matters called fibrin-factors. This theory, which had been indicated by Buchanan, in 1845, has been adopted and more or less modified by Kühne, Virchow and others. If blood-plasma, rendered neutral with acetic acid, be diluted with ten times its volume of water at 32° Fahr. (zero C.), and then be treated with a current of carbon dioxide, a flocculent precipitate is formed, which has been called paraglobuline, or fibrinoplastic matter. This substance may be dissolved in water containing air or oxygen in solution. After this precipitate has been separated, if the clear liquid be diluted with about twice its volume of ice-cold water and be treated for two or three hours with a current of carbon dioxide, a viscid scum is produced, which has been called fibrinogen. More recently, a third principle, a ferment, has been described by Schmidt, which he considers necessary to the formation of fibrin. This ferment is produced in some way by the leucocytes of the blood, probably by partial decomposition of these bodies.

In view of the results of recent investigations with regard to the cause of the coagulation of the blood, which, unfortunately, are not as positive and definite as could be desired, some physiologists have adopted the following as a provisional theory of the mechanism of this process:

There exists, probably in small quantity in the circulating blood and in considerable quantity in blood drawn from the vessels or arrested in its circulation, a peculiar ferment which is produced in some way by changes in the leucocytes. This ferment may be concerned in the decomposition of plasmin. It is certainly thrown down with plasmin when plasmin is precipitated by the action of reagents. The action of this ferment either induces or hastens the separation of plasmin into the so-called fibrin-factors, paraglobuline and fibrinogen. Of these two substances, fibrinogen is the more important in the formation of fibrin, a small quantity of fibrin, only about three parts per thousand of blood, being formed. A large quantity of paraglobuline is not used in the formation of fibrin and remains in the serum. It is possible, indeed, that no part of the paraglobuline is concerned in coagulation. If the latter be true, paraglobuline may be regarded as identical with metalbumin, a view which was advanced by Robin many years ago and is now adopted by some physiologists.

Adopting these views, the mechanism of coagulation may be succinctly described as follows:

1. As a condition preliminary to coagulation, there is either an increase in the formation of fibrin-ferment or an appearance of ferment in the blood, due to changes in certain of the leucocytes. The red corpuscles are probably not directly concerned in coagulation, and there is nothing definite known of the action of the blood-plaques in this process.

2. The fibrin-ferment unites with fibrinogen and forms fibrin, which is the coagulating substance. Paraglobuline (or metalbumin) is little if at all concerned in this process.

3. The processes described as incident to the coagulation of blood take place also in the coagulation of lymph and chyle.

In accordance with the views stated in connection with the composition of blood-plasma, paraglobuline, or metalbumin, fibrinogen and, finally, fibrin are products of decomposition, are abnormal formations, and are not normal constituents of the blood.

It is possible that the statement just given of the mechanism of the coagulation of the blood may be modified in the future in accordance with the most recent views of Schmidt, who claims that all the so-called fibrin-factors result from decomposition of the leucocytes, a great number of which, it is said, are dissolved soon after blood is drawn from the vessels. There are, indeed, many experimental and pathological facts in support of this view; but it can not be adopted without reserve, until the experiments of Schmidt shall have been supplemented by more extended observations. Schmidt maintains that in certain classes of animals, dissolved red corpuscles are also concerned in the production of fibrin-factors.

Leech-drawn blood remains fluid in the body of the animal. Richardson has observed, also, that the blood flowing from a leech-bite presents the same persistent fluidity, which explains the well-known fact that the insignificant wound gives rise to considerable hæmorrhage.

The existence of projections into the caliber of vessels, or the passage of

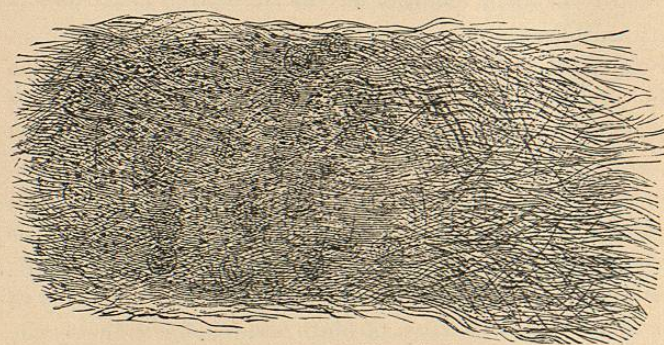


FIG. 10.—Coagulated fibrin (Robin).
Fibrinous clot, without red corpuscles, and containing leucocytes, thrown off in the form of a whitish pseudo-membrane in a case of ulceration of the neck of the uterus with hæmorrhage.

a fine thread through an artery or vein, will determine the formation of a small coagulum upon the foreign substance, while the circulation is neither interrupted nor retarded. In the present state of knowledge, explanation of these facts is difficult if not impossible. The process, under these conditions, can not be subjected to direct experiment as in the case of blood coagulating out of the body.

During coagulation, fibrin assumes a filamentous form, presenting, under the microscope, the appearance of rectilinear fibrillæ. These fibrillæ gradually increase in number, and as contraction of the clot occurs, they become irregularly crossed. They are always straight, however, and never assume the wavy appearance characteristic of true fibrous tissue.

The blood of the renal and hepatic veins, capillary blood and the blood which passes from the capillary system into the veins after death generally does not coagulate or coagulates very imperfectly; in other words, these varieties of blood do not readily form fibrin. The reason of this peculiarity is not known; but the fact affords a partial explanation of the normal fluidity of the blood; for this fluid, passing over the entire course of the circulation in about thirty seconds, seems to be constantly losing its coagulability in its passage through the liver, kidneys and the general capillary system, as fast as its coagulability is increased in the other parts. Taking into consideration the rapidity of the circulation, it is evident that coagulation can not take place while the normal circulation is maintained and while the blood is undergoing the constant changes incident to general nutrition.

CHAPTER II.

CIRCULATION OF THE BLOOD—ACTION OF THE HEART.

Discovery of the circulation—Physiological anatomy of the heart—Valves of the heart—Movements of the heart—Impulse of the heart—Succession of the movements of the heart—Force of the heart—Action of the valves—Sounds of the heart—Causes of the sounds of the heart—Frequency of the heart's action—Influence of age and sex—Influence of digestion—Influence of posture and muscular exertion—Influence of exercise etc.—Influence of temperature—Influence of respiration on the action of the heart—Cause of the rhythmical contractions of the heart—Accelerator nerves—Direct inhibition of the heart—Reflex inhibition of the heart—Summary of certain causes of arrest of the action of the heart.

HARVEY "set forth for the first time his discovery of the circulation," in his public lectures in 1616, and in 1628 published the "*Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*." This discovery, from the isolated facts bearing upon it which were observed by anatomists to its culmination in the experiments of Harvey, so fully illustrates the gradual development of most physiological truths, that it does not seem out of place to begin the study of the circulation with a brief sketch of its history.

The facts bearing upon the circulation developed before the time of Harvey were chiefly anatomical. The writings of Hippocrates are very indefinite upon all points connected with the circulatory system; and no clear and positive statements are to be found in ancient works before the time of Aristotle. The work of Aristotle most frequently quoted by physiologists is his "History of Animals;" and in this occurs a passage which seems to indicate that he thought that air passed from the lungs to the heart; but in his work, *De Partibus Animalium*, it is stated that there are