ON THE

DEVELOPMENT

OF THE

BLOOD AND BLOOD-VESSELS,

BEING

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BY

JAMES DRUMMOND, M.D., EDINBURGH.

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In the following paper it is proposed to consider the structure and mode of formation of the blood and blood-vessels in the embryo of the different classes of vertebrate animals.

In the first section will be described—1st, The mode of development of the blood corpuscle; 2d, The origin of the colouring matter of the same; and 3d, The source of the serum and fibrin of the blood.

In the second section, the structure and mode of formation of the blood-vessels will be described.

SECTION I.—DEVELOPMENT OF THE BLOOD CORPUSCLES.

a Reptitia.—In this class, the frog, as being most easily procured, is the animal in which the development has been chiefly studied, although perhaps it is not so well adapted for this purpose as certain others of the same class.

In order to understand the development of the blood corpuscle, it will be necessary in the first place to describe the different structures which enter into the composition of the ovum of the frog. This, when newly deposited, presents the aspect of a small, dark, round mass enclosed in a jelly-like substance. When examined with a power of 250 diameters, it is found to consist of an external layer, of more or less round or angular cells, which are filled with granules of dark pigmentary matter, and are placed close together so as to constitute a single layer or membrane, within which is contained the vitellus. The latter is composed of the following structures: 1st, A number of granules varying in size from what appears like a mere point on the field of the microscope, up to the $\frac{1}{4000}$th or $\frac{1}{3000}$th of an inch in diameter. The smaller of these bodies are generally round and exhibit, as described by Prevost and Lebert, the phenomenon of molecular motion. The larger are more or less angular, and commonly present a flattened oblong form. In their angular shape as well as in their general character, they appear to be more or less analogous to crystals, and have been termed by Vogt and others stearine plates (fig. 1, *a*). They are colourless and

occur either free or included within a cell-wall. These particles are occasionally seen to contain a smaller body in their interior. They swell out on addition of acetic acid, assuming often an oval or round shape, and then gradually fade away. Carbonate of soda does not produce any very marked effect upon them. Turpentine was added to them. They did not, however, appear to be changed by it. 2d, Bodies measuring from the $\frac{1}{4000}$th to the $\frac{1}{2500}$th of an inch in diameter. These are generally round, rarely oval in shape (fig. 1, *b*), are clearer and apparently more delicate than the bodies above described. In some of them are seen a few very minute granules; in others there are larger granules, similar to those floating free, and situated towards one side of the cell; again, in others, we find stearine plates. Sometimes they appear to be half-filled with these. They frequently contain one or two minute, spherical particles. 3d, Masses of a round, irregular, or oval shape, formed merely of granules similar to those described No. 1 around the bodies No. 2, and without any distinct investing membrane or cell wall (fig. 1, *c*). 4th, Perfect cells, consisting of a transparent external membrane, enclosing a body similar to No. 2, which seems to hold the relation of a nucleus, and also a quantity of granular matter (fig, 1, *d*). The cells in question present a more or less dark grey appearance, and have some resemblance to the bodies occurring in organs during inflammation—the compound granular cell. When isolated, they commonly present a round or oval shape, but when aggregated together they appear to be more or less angular. The granular matter they contain is sometimes present in such quantity, as to obscure the nucleus, or conceal it entirely from view. They vary considerably in size. In many, the contained granules are nearly all large, and present the angular character already described; in others, they are smaller and round.

FIG. 1.—Corpuscles in the vitellus of frog's ovum. *a*, Round and oblong granules. *b*, Free nucleus. *c*, The same with granules aggregated around it. *d*, Perfect embryonic cell. 250 dia.

These bodies, which may be termed embryonic or primary cells, have been divided by Prevost and Lebert into two classes. The one is termed by them the vitelline globules, the other, the organo-plastic globules. The former, according to these observers, is spherical or oval; the spherical measure about 0·05 to 0·0875 of a millimetre in diameter; in those which are not spherical, the longitudinal diameter is about 0·125 of a millimetre, while their transverse diameter varies between 0·075 and 0·875. The granules with which they are filled belong chiefly to the larger oblong variety. The organo-plastic globules are perfectly spherical, measure from 0·02 to 0·03 of a millimetre in diameter, have a brownish-yellow colour, or brown colour, and contain a nucleus which resembles those in the vitelline globules, excepting that it is smaller, measur-

ing from 0·0125 to 0·0175 of a millimetre. They also contain granules and simple globules. The former term is applied by Prevost and Lebert to the smaller rounded granules already described, while the term *simple* globules is given by them to the larger angular granules, or so-called stearine plates.

The vitelline globules correspond, according to these authors, to the mucous or vegetative layer of the germinal membrane in the bird, while the organo-plastic correspond to the serous layer of the same. The former are destined to be developed into the tissues composing the organs of vegetative life, while the latter go to the formation of those which constitute the organs of animal life.

The distinction which has been made by these authors does not, however, appear to be very well founded. The cells which exist in the abdominal portion of the tadpole, and which appear to be destined for the formation of the organs of vegetative life, are certainly larger in general than the cells in those parts from which the organs of animal life are formed. It must be observed, however, that among the former there are cells as small as any of the so-called organo-plastic globules, and amongst these again there are cells present which have a diameter as great as that possessed by any of the vitelline globules. Moreover, the cells which go to the formation of the organs of animal life, and which, therefore, correspond to the organo-plastic globules of Prevost and Lebert, are not always spherical as these observers maintain, many of them being oval in shape. The other marks of distinction, as given by these authors, are in like manner not well characterised.

It seems, then, much better to employ the term embryonic or primary cells to designate these bodies without attempting to separate them into two distinct classes as Prevost and Lebert have done. The first blood corpuscles resemble the embryonic cells in every respect. They are round, do not possess any colouring matter like that which exists in the perfect blood corpuscle, and are filled with granules similar in every respect to those contained in the embryonic cells; when the blood corpuscles and embryonic cells are mingled together, it is impossible, for the first few days, to distinguish between them, and it is only by examining the former as they circulate in the vessels of the living animal that we are enabled to ascertain that they are blood corpuscles. By and by, however, the blood corpuscle may be distinguished from the embryonic cell by the circumstances of its presenting a slightly yellowish tinge.

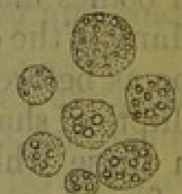


FIG. 2.—The blood corpuscles of a tadpole two lines and a half long. 250 diam.

In tadpoles measuring about three lines in length, the branchiæ are already pretty well developed, and the circulation in them established. In these, therefore, we have an opportunity of examining the corpuscles as they circulate in the vessels, and in this way are certain that the bodies we are examining are really blood corpuscles.

They are spherical, possess a delicate membrane or cell wall, and contain a number of round and oblong granules like those already described. In many these exist in such number as completely to fill them, in others they are fewer in number. Besides these granules the blood corpuscles contain a fluid which possesses considerable viscidity. Sometimes when the blood corpuscles are treated with water, a hernia-like protrusion may be seen projecting from the side of one or more of them, formed apparently by this fluid.

In each of the branchial tufts there are two vessels, in one of which the corpuscles run in the direction of the periphery, in the other they are directed inwards towards the heart; the two vessels become continuous at the extremity of the branchial tuft forming a vascular loop. They admit the blood corpuscles only in single file. The latter do not for the most part present any approach to the oval or elliptical form which they have in the full-grown tadpole or in the perfect frog. The nucleus is not always very distinctly seen.

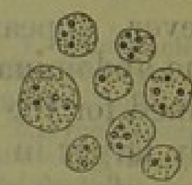


FIG. 3.—The blood corpuscles of a tadpole further developed, showing the gradual disappearance of the granular matter. 250 diam.

As regards their behaviour with reagents, acetic acid dissolves the cell wall or at least renders it invisible. Citric and tartaric acids produce the same effect upon them as acetic acid.

In tadpoles somewhat older there are still seen many corpuscles presenting the same characters as those above described. In most of them, however, the contained granules are of smaller size and fewer in number than those contained in the corpuscles of younger animals. The blood corpuscles vary considerably in size, some being nearly twice as large as the others; the largest measure about $\frac{1}{1000}$th of an inch in breadth and about $\frac{1}{800}$th of an inch in length. The smaller measure about the $\frac{1}{2000}$th of an inch in their long diameter. In many, a round or oval finely granular nucleus is distinctly visible even without addition of reagents, and sometimes two such bodies may be seen in a single corpuscle.

Many of the corpuscles present the same spherical shape as before. Others have a more or less oval or elliptical shape. The latter are generally smaller than those which present the spherical form, and are often more or less pointed at their extremities. They contain several small granules similar to those in the spherical corpuscles. The oval or elliptical corpuscles approach in character those of the fully formed tadpole. All the corpuscles present a more or less yellowish hue, deeper in some than in others. In the oval or elliptical corpuscles, the colouring matter is more abundant than in the varied ones. Besides the bodies thus described, there are sometimes observed corpuscles which in their character resemble, more or less, the white blood corpuscles which

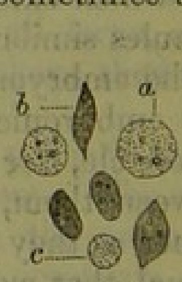


FIG. 4.—The blood corpuscles of the tadpole still further developed; *a*, Primary blood corpuscles; *b*, Corpuscles belonging to the second set; *c*, White or colourless blood corpuscles. 250 diam.

are seen more distinctly in the blood of tadpoles farther advanced.

In tadpoles, measuring about six lines in length, the tail has become much more transparent, so that the circulation can now be observed in it, as well as in the branchiæ. The blood corpuscles, which have been described as presenting an oval or elliptical shape, are now much more numerous than those belonging to the round or spherical variety. In many of them there are one or two granules, like those contained in the corpuscles of the previous animal. Such of the corpuscles as present a spherical shape also contain more or less granular matter. The elliptical or oval corpuscles have the same colour as those in the perfect animal.

If we watch the circulation, as it goes on in the branchiæ or tail of the animal at this period, we observe much more distinctly than before the presence of bodies analogous to the white or colourless corpuscle of the perfect frog. They are round for the most part, colourless, faintly granular, and have a diameter of about $\frac{1}{2800}$th of an inch, some of them, however, being considerably larger, while others again are smaller. They contain a distinct, round, or oval nucleus. Sometimes these bodies may be seen to have a somewhat oval shape, and appear slightly coloured.

In tadpoles farther advanced than the above, the chief change which is found to have taken place, is the more or less complete disappearance of the original round or spherical corpuscles. The blood corpuscles are now almost all elliptical or oval, and few of them contain any of the granules described as existing in those of young embryos. There are also present white or colourless corpuscles, like those already described. Occasionally some of these bodies appear of a more or less oval shape, and have a slight yellow tinge. They are probably transition forms, between the coloured and colourless corpuscle.

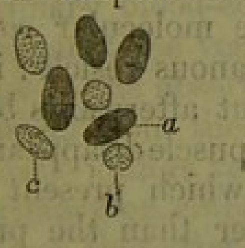


FIG. 5.—The blood corpuscles nearly fully formed in the tadpole; *a*, Coloured blood corpuscle; *b*, Colourless corpuscle; *c*, Intermediate stage between coloured and colourless corpuscles. 250 diam.

In yet older animals, in which the extremities have appeared, the elliptical blood corpuscles seem to be less pointed at their extremities than before, and present more the perfectly oval character of those in the fully formed frog. The relation between the coloured and colourless corpuscles is also much the same as in the perfect animal.

From what has been stated, it appears that, during the development of the frog, the blood corpuscles present at least two distinct phases.

1*st*, The corpuscles which first appear are spherical, granular, and colourless, agreeing in their characters with the embryonic cells. The granular matter at first contained in these gradually disappears, while, at the same time, colouring matter is formed so that at length they present the aspect of more or less smooth, round, coloured cells.

During the clearing up of these cells it is the larger granules—the so-called stearine plates—which disappear first.

2d, Succeeding these we have a series of corpuscles formed, which present a distinctly elliptical shape and yellow colour, and contain few or no granules.

It remains to inquire, in what relation the blood corpuscles of the second set stand to those of the first set. Are they merely the former, altered in shape and other characters, and in this way derived directly from these? Or are they new structures, which have been developed, independently of those of the first set?

In regard to this question, Prevost and Lebert believe that the first blood corpuscles are derived from that portion of the embryonic cells to which they give the name of organo-plastic globules: that these become gradually coloured, their granular contents disappearing, while, at the same time, they assume an oval or elliptical shape. In this way the second set of blood corpuscles are, according to these authors, derived immediately from the first set.

Vogt, on the other hand, maintains that the perfect blood corpuscles, corresponding to what has been above described as the second set of corpuscles, are not derived directly from the embryonic cells, but are their nuclei. At first, according to Vogt, the blood corpuscles cannot be distinguished from the cells, of which the different organs are composed. They are round, and have molecular contents. The nucleus is at first seen as a clear diaphanous vesicle: its contents are at first hyaline and perfectly fluid, but afterwards become granular. The cell wall of the primary blood corpuscle disappears, and now we find in the blood only spherical cells, which present a feebly yellowish colour, and are considerably smaller than the primary blood corpuscles, and contain more or less granular matter. In proportion as the embryo advances the granular matter disappears, and they become quite transparent. At this period a fine shadow begins to appear in the interior of the blood corpuscle. This corresponds to the first stage in the formation of the nucleus. The blood corpuscle itself is round, more or less flattened, and presents a pale yellow colour. According to Vogt, the blood corpuscles only assume the elliptical form towards the termination of embryonic life. In support of the view, that perfect blood corpuscles are the nuclei of the original embryonic cells, he states, that the size of the nucleus of the embryonic cell corresponds with that of the perfect blood globule in the tadpole. Again, according to him, the nucleus of the first blood corpuscle is when it is first observed, very distinct: afterwards the blood corpuscles are seen to be smaller, and contain only a nutritive fluid, no nucleus being seen in them. If, then, the perfect blood corpuscles be formed by a contraction and alteration in form of the embryonic cells or primary blood corpuscles, we ought, according to Vogt, to observe the nucleus in them throughout.

In regard to Vogt's observation, Prevost and Lebert state, that they have been able to trace the primary embryonic cell (organo-

plastic globule) in all its stages, into the perfect blood corpuscle of the tadpole. They have never, on the other hand, observed anything in the development of the blood corpuscle in the tadpole which indicates the disappearance of the original cell wall, and the liberation of the nucleus, or the formation of another body within the latter, such as Vogt's view implies must be the case.

As regards the smaller size of the perfectly formed blood corpuscle, as compared with that of the primary cell, Prevost and Lebert say, that the difference in this respect is very inconsiderable. According to their measurements, the primary blood cells measure 0·02 to 0·03 of a millimetre in diameter; their nuclei vary from 0·0125 to 0·0175. Afterwards when the granular matter was nearly absorbed, the blood corpuscles presented a diameter of 0·0175 to 0·0225. In those which presented an oval shape, the length was 0·0225 to 0·0275, the breadth 0·0150 to 0·0125. The animal in which these measurements were made was but little developed. In embryos, after the appearance of the limbs, and in which the circulation was complete, and the blood globules perfectly formed, they found that the latter measured 0·02 to 0·225 in length, and 0·0125 to 0·150 in breadth. Their nuclei measured 0·0075 to 0·01. From these measurements, the difference in point of size between the primary blood-cell and that which is perfectly developed does not appear to be very great, and may, according to those observers, be due to the absorption of the contents of the former. It would also appear from these measurements, that the perfectly developed corpuscle differs very much in point of size from the nucleus of the primary or embryonic corpuscle. In regard to the observation of Vogt, that after the disappearance of the membrane of the original embryonic cell, no nucleus is observed in the blood corpuscle, and that at a farther stage the nucleus again appears in them, they remark that they have been able to distinguish the nucleus throughout all the stages of the development of the blood corpuscle.

The difference in point of size between the primary and secondary blood corpuscles, appears to be certainly greater than the measurements of Prevost and Lebert suppose. We do not, so far as I can remember, find that any cell structure, while being developed into higher tissue, becomes smaller than before, the tendency being, on the other hand, always to growth—to become larger, at the same time that it becomes altered in shape. The oval blood corpuscle in the tadpole, on the other hand, appears, as has been just stated, to be considerably smaller than the original embryonic corpuscle. And this, therefore, is opposed to the view that the one is immediately derived from the other. Those of the first set, however, often pass so insensibly into those of the second, that it is very possible some of the latter may be derived from the former. In regard to Vogt's view, that they are the nuclei of the primary blood cells, it is in accordance to a certain extent at least with what is known in regard to the development of the blood in the higher animals. Moreover,

it is quite true that the nuclei are not always very distinctly seen in the blood corpuscles of the young frog. The difference, however, between the nucleus of the primary or embryonic cells and the blood corpuscles as regards size as well as other characters, are such as to render it improbable that the one is formed from the other. The different stages of the transition from the one to the other, such as Vogt describes, cannot be seen.

We have already seen that so soon as the perfect oval corpuscles appear in the blood, there also appear at the same time a number of round pale granular bodies corresponding in shape, size, etc., to the white blood corpuscles of the perfect animal. These also present, in general, corpuscles which appear to be intermediate between the coloured and colourless corpuscle, and which, therefore, may be regarded as transition stages from the one to the other. The most probable view, then, in regard to the origin of the second set of corpuscles in the frog is, that while a portion of them may be formed by a direct transformation of those of the first set, by far the greater number of them are derived from the white or colourless corpuscles. This view of the formation of the perfect or second set of blood corpuscles in the tadpole accords with what must take place in the perfect frog.

b. Aves.—At a very early period in the development of the chick, even before the forty-eighth hour of incubation, we find blood corpuscles formed, which differ but little from perfect blood corpuscles. Mingled with these, however, are cells which evidently point to a stage when the blood corpuscles, as yet consisted only of embryonic cells similar in their nature to the first set of blood corpuscles in the tadpole. In blood from the vessels of the area varculosa in the chick on the third day of incubation, we find the following structures:—1st, Round or spherical cells, measuring from the $\frac{1}{2000}$th to the $\frac{1}{1500}$th of an inch in diameter. They possess a delicate, transparent cell wall, and contain a number of spherical particles, which refract the light strongly, and are evidently of a fatty nature (fig. 6, *a*). In many of these cells, the nucleus is not very distinct. Many of them are colourless, others present a slightly yellowish tinge. 2d, Bodies similar to the above in shape and size, but which contain few or none of the refracting particles, and are more distinctly coloured (fig. 6, *b*). 3d, Bodies measuring from the $\frac{1}{3000}$th to the $\frac{1}{2500}$th of an inch in diameter, generally round and colourless, and containing more or less granular matter, the particles, however, being in genera[l] finer than those occurring in the cells first described. They resembl[e]

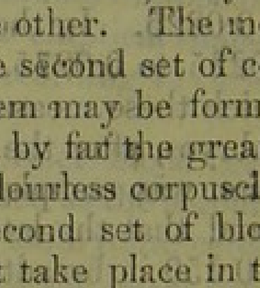


FIG. 6.—Blood from the area vasculosa of the chick, forty-eight hours after incubation; *a*, Large colourless cell; *b*, Large coloured cell, both belonging to the primary set of blood corpuscles; *c*, Coloured oval corpuscle, belonging to the second set of blood corpuscles; *d*, White or colourless blood corpuscle; *e*, Coloured granule with central spot. 250 diam.

the white or colourless cells of the blood (fig. 6, *d*). A few of them present a more or less oval form, and contain fewer granules than the others. 4th, Oval blood corpuscles, presenting a distinct yellow colour, flattened, and containing small oval nuclei (fig. 6, *c*). The latter appear when seen within the corpuscles, as a dark shadow. When the blood corpuscles are seen upon their edge, the nucleus is observed as a small projection on either side of the corpuscle. Addition of acetic acid dissolves the cell wall, setting free the nuclei, when these appear as small oval finely granular bodies. The greater portion of the blood corpuscles just described agree in their general characters with those in the perfect animal. In a few of them we find two or three bright refracting particles, of spherical form, similar to those contained in the cells, No. 3. Lastly, There are almost always present in the blood of the chick more or fewer free granules of various sizes from a mere point up to about the $\frac{1}{7000}$th of an inch in diameter. Some of these are slightly coloured, and present a small dark point in their interior (fig. 6, *e*).

Between the colouring matter contained in the blood corpuscles and that of the yolk there is a very great resemblance.

Occasionally in some of the corpuscles we find, after addition of dilute acetic acid, two nuclei similar to what Fahrner and Köllike have described as occurring in the blood corpuscles of the fœtal mammal.

From this period onwards the only changes which take place are the gradual disappearance of the large cells above described, and the increase in the number of the oval coloured cells. Almost all the changes which take place in the development of the blood in the chick are so rapid that it is difficult to trace them. In general, most of the changes which take place before the appearance of the oval blood corpuscles seem to be completed before the 36th hour of incubation.

FIG. 7.—The same, fifteen days after incubation; *a*, Blood corpuscle of second set; *b*, Colourless corpuscle; *c*, Oval, granular colourless corpuscle, a transition stage between the two former bodies; *d*, Granule with central spot. 250 diam.

In blood from the chick on the 15th day of incubation, there are very few, sometimes none, of the large cells described 1 and 2 present. It consists almost entirely of the corpuscles 3 and 4, with a number of free granules similar to those already described. There are, however, not unfrequently present bodies which have the same oval shape as the blood corpuscles, but are either colourless, or very slightly coloured. They do not, moreover, present the distinct, flattened appearance of the blood corpuscles. They also contain an oval granular nucleus, and sometimes a few granules (fig. 7).

Some of the oval coloured blood corpuscles contain a granule or two of a bright refracting appearance.

During the development of the blood in the chick, it seems prob-

able that there are two sets of corpuscles just as in the frog; the one set corresponding to the large cells described 1 and 2, derived from the embryonic corpuscles; the other formed partly from these, partly probably in the liver, but chiefly from the white or colourless blood corpuscles.

c. Mammalia.—In blood taken from the umbilical vein of an embryo calf about $1\frac{1}{2}$ or 2 inches in length, the following structures were found:—1st, Bodies presenting a more or less spherical shape, measuring from the $\frac{1}{2500}$th to the $\frac{1}{2000}$th of an inch in diameter, and perfectly colourless. They contained one, sometimes two nuclei, besides finely granular matter. The nuclei measured from the $\frac{1}{4000}$th to the $\frac{1}{3500}$th of an inch in diameter, were generally round, and finely granular. 2d, Bodies agreeing in size and shape with the above, but differing from in presenting a smooth surface, and in being more or less coloured. These also contained one, and sometimes two nuclei. 3d, Corpuscles presenting the same characters as the blood corpuscle in the animal after birth, but smaller and more spherical than discoid in shape. 4th, Bodies presenting the characters of the nuclei described as contained in the corpuscles 1 and 2 (fig. 8).

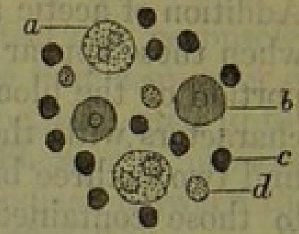


Fig. 8.—Blood from the umbilical vein of an embryo calf, two inches long; *a*, Large colourless cell; *b*, Large cell coloured—both corpuscles of the first set; *c*, Coloured corpuscle of second set; *d*, Free nucleus. 250 diam.

Between the large colourless and coloured cells 1 and 2 there are corpuscles present which seem to be transition stages from the one to the other; so also between the free nuclei and coloured blood corpuscles 3.

In blood taken from the umbilical vein of an embryo sheep about 3 inches in length structures similar to those above described were found.

In blood from the umbilical vein of an embryo calf 12 inches long the large coloured corpuscles, as well as the corresponding pale ones, were very few in number. The blood corpuscles consisted entirely almost of the bodies 3, and of white blood corpuscles. The latter were present apparently in much greater numbers than in the adult animal. They often adhered together in clumps.

Blood from the heart presented the same characters.

The younger the embryo the more numerous are the bodies 1 and 2. They appear to be analogous to the primary set of corpuscles in the frog and bird, etc. Those containing two nuclei are evidently identical with the bodies which have been described by Kölliker and Fahrner.

The bodies 3 correspond to the second set of corpuscles or perfect fœtal blood corpuscles.

The free nuclei seem to be structures in process of being converted into the corpuscles belonging to the 2d set or perfect blood corpuscle.

In blood from the umbilical vein of a calf $1\frac{1}{2}$ feet in length none of the bodies 1 or 2 were present.

The greater number of the blood corpuscles present the same characters as those in the adult animal, with this exception, that they are smaller, and appear less distinctly discoid in form. In the latter periods of embryonic life, the large cells described 1 and 2, gradually disappear, the round coloured corpuscles alone remaining. It is commonly stated that the blood corpuscles of the fœtus are distinguished from those of the adult by their greater size, as well as from the circumstance of their possessing nuclei. This, however, is true only of the first set of corpuscles, occurring in the very early periods of embryonic life. Those of the second set (Nos. 3 and 4), which form the great mass of the blood corpuscles during the greater portion of embryonic life are, as we have stated above, of smaller size than those in the adult, and do not contain any distinct nucleus. As has been shown by the researches of Harting, the different constituents of the fœtal organs are all of smaller size than the corresponding parts in the adult; the Harveian systems in the bones, for example, are much narrower; so also the elementary fibres of muscle are more than one-third finer than those in the perfect animal. Hence, then, it is only to be expected that the perfect fœtal blood corpuscle should also be of smaller size than those of the adult. According to Harting, the blood corpuscle grows very little during the last two-thirds of embryonic life. They grow very rapidly, however, shortly after an independent respiration has been established, and soon attain the size which they have permanently in the adult animal.

In regard to the development of the blood corpuscle in the different classes of vertebrate animals, different views, as may be supposed from what has been already stated, are entertained. They may be reduced to the following:—

1. The blood corpuscles are derived from the cells of the vitellus. These become gradually coloured and flattened, at the same time that they become altered in shape and lose their granular contents. Such is the view which is given by Schultz, from an examination of the development of the blood corpuscle in the frog. The same view has also been taken by Lebert and Prevost.

2. From the observations of Fahrner and Kölliker, the first blood corpuscles in the mammalian embryo also are formed in the manner above mentioned, from the cells of the mucous layer of the germinal membrane, but afterwards increase by a process of fissiparous generation.

3. Vogt, again, as has been already stated, while he believes that the first blood corpuscles are derived from the embryonic cells, maintains that the perfect blood corpuscles, those, namely, which we have described as the second set, are not those of the first set altered in shape and other characters, but are the nuclei of the same. The cell wall of the primary blood corpuscle disappears, its nucleus is set free,

and becomes developed into the perfect blood corpuscle. The nucleus which is seen in these is, according to Vogt's view, a secondary formation, a nucleolus, in short.

4. Another view in regard to the origin of the blood corpuscles, is that of Macleod and others, who hold that they arise from minute granules.

5. From the observations of Reichert and Kölliker, it appears that a portion at least of the blood corpuscles in the embryo are formed in the liver. According to Weber, when the vitellus is withdrawn into the cavity of the abdomen at the end of embryonic life, the fatty matter which it contains is absorbed by the blood-vessels and carried to the liver, where it is partly converted into bile and also in part into blood corpuscles.

There seems to be no doubt that the bodies which we have described as the first set of blood corpuscles are merely a portion of the embryonic cells, derived, according to most observers, from the mucous layer of the germinal membrane. On this point nearly all observers are agreed.

It is chiefly in regard to the origin of the second set of blood corpuscles that the differences of opinion exist—Schultz, Prevost, Lebert, and others, supposing that they are the first set of corpuscles altered in shape; Vogt, etc., believing them to be the nuclei of these. In addition to what has been already stated in regard to these two views, we will merely add that, granting the blood corpuscles of the first set are converted into those of the second in either of the two ways mentioned, the number of the corpuscles so formed must be very small indeed compared with the number actually existing in the blood. Moreover, the corpuscles of the second set increase greatly in number during the entire period of embryonic life, and long after the primary corpuscles have disappeared. Those, therefore, which are formed after the disappearance of the corpuscles belonging to the first set must have a different origin; they cannot be formed from these bodies, inasmuch as they no longer exist in the blood. From the observations of Kölliker and Fahrner, it is true the increase of the blood corpuscles in number might be ascribed to the fissiparous division of previously existing corpuscles. It must be observed, however, that it is chiefly or exclusively to the corpuscles of the first set that their observations apply.

We have already stated that, simultaneous with the appearance of the blood corpuscles of the second series, the white or colourless corpuscles also appear. Moreover, it is generally possible, in the blood of the chick and frog, to observe bodies which seem to be transition stages from the one to the other. Hence, then, although it seems probable that a portion of the coloured corpuscles of the second set are derived from those belonging to the first set, and are probably also formed in the liver, the great mass of these bodies seems to be derived from the colourless blood corpuscles. As regards the relation in which these two structures stand to each other, it seems to be

different in the higher and lower classes of vertebrate animals. In the latter the colourless corpuscle appears to be itself developed into the coloured, the nucleus of the former remaining as the nucleus of the latter. Such is the case in the frog, fish, and bird. In mammalia, again, it appears to be the nucleus only of the white or colourless corpuscle, which is converted into the coloured.

From all that has been stated in regard to the development of the blood corpuscle, it seems to follow :—

1. *That there are two sets of blood corpuscles in the fœtus of vertebrate animals.* Those belonging to the *first* set are round, granular, nucleated, and colourless. After a time they become more or less coloured, their granular matter at the same time disappearing to a great extent. Those of the *second* set differ from the corpuscles of the first set, in being coloured, in their smaller size, and in containing but little or no granular matter. In the lower vertebratæ, in addition to the marks of distinction above stated, they differ from those of the first set in being elliptical or oval, and in the mammal they differ from those of the first set in not containing any nucleus.

2. *That the former set of corpuscles are derived from the embryonic corpuscles, and probably increase by fissiparous division, others being also derived from the liver.*

3. *That the corpuscles belonging to the second set may in part be derived from those of the first set, as well as from the liver; the greater number of them, however, being formed from the white or colourless corpuscles.*

2. *Origin of colouring matter.*—The formation of the colouring matter of the blood corpuscle appears to be more a chemical, than a morphological process. Before therefore it can be determined from what source, or in what manner it is formed, it is necessary to ascertain accurately the various constituents of the blood, as well as the changes produced upon these when exposed to the influence of the different agents which may act upon them in the body. At present, however, such a knowledge is not possessed; it is not known with certainty whether the colouring matter is derived from those substances which pass into the blood for the nutrition of the different tissues, or whether it be formed from the effete matters derived from these. As little does it appear to be known in what part of the body it is formed.

The chief theories as to the source of the colouring matter or hæmatine are two in number. Neither of them, however, appears to be sufficiently supported by facts. The one is that it depends on the iron contained in the blood corpuscle, and this view seems to be strengthened by the generally admitted fact that the administration of iron in cases of chlorosis tends much to restore the blood to its normal condition. It appears, however, that certain other metallic tonics have much the same effect. Moreover, there is no reason to suppose that in the colourless corpuscle also iron does not exist. In

the solids of the lymph and chyle, indeed, the proportion of iron appears to be as great as it is in those of the blood. Again, iron is also present in the comparatively colourless blood of the invertebrata. If the colour of the blood corpuscle in the vertebrata depends on iron, the latter substance must, after it enters the blood, exist in a different state of combination from that in which it exists in the lymph and chyle. The researches of Simon and Scherer, however, show that the colour of hæmatine does not depend so much on the iron it contains, as upon its other constituents. According to these observers all the iron may, by means of concentrated sulphuric acid, be extracted, and yet the colour of the hæmatine remain.

The second theory in regard to the origin of the hæmatine is, that it arises from fatty principles.

The following facts would seem to indicate that the two are at least connected. In the young frog, as already mentioned, blood corpuscles of the first set contain much fatty matter. This exists in the shape of the round and angular granules which have been already described. In these bodies as soon as the colouring matter begins to be formed, the granules begin to disappear, and in the same proportion as the former increases, the latter decrease. So also in the corpuscles of the lympth and chyle, which on entering the blood constitute the white corpuscles, there are also more or less fatty granules present. In the conversion of these bodies into perfect blood corpuscles, their fatty granular matter gradually disappears, its place being taken up by colouring matter. The observations of Weber, already mentioned, that the coloured fatty matter of the yolk is, towards the termination of the embryonic life in the chick, carried to the liver and then goes to the formation of blood corpuscles, also show, if correct, the connection between the hæmatine and fatty matter. Between the colouring matter of the yolk and that of the young blood corpuscles, there certainly exists a great resemblance.

Most of the colouring principles in animals are at least associated with fatty matter. Thus the beautiful colouring matter in many insects, the red colouring principle in the shell of the crab and lobster, while insoluble in water, are perfectly soluble in all the media which dissolve fatty matters, such for example as alcohol or ether. The yellow colouring matter of the corpus luteum in the cow is also of the same nature.

Again, that the formation of the hæmatine is in some way or other connected with the respiration, is probable from the fact that in the frog it begins to be formed about the same time that the circulation in the branchiæ commences, and only after the respiration is fully established, does the colouring matter in the blood appear to be perfectly developed.

3d. Source of the Serum and Fibrine.—The embryonic corpuscles in the ova of all animals, are imbedded in a fluid which presents

much the same chemical constitution as the serum of the blood. It forms the blastema from which the cells of the ovum are developed, and from which they derive the material for their nourishment. It performs the same office to the cells of the ovum which the serum of the blood performs to the different tissues of the perfect animal. The serum of the blood in very young embryos appears to consist merely of a portion of this fluid, just as the embryonic corpuscles constitute the first blood corpuscles, so also the serum of the blood is at first formed of a portion of the fluid in which the embryonic corpuscles float. According to Prevost and Lebert, it is probable that the disappearance of the granules from the embryonic corpuscles is due to a liquefaction of the same, while the fluid so formed passes through the cell wall by a process of exosmosis, and constitutes the serum of the blood. It seems, however, more probable that the granules in question go to the formation of the hæmatine. In the mammal the serum must be chiefly derived from the maternal system by absorption through the medium of the placenta. As soon as the lymphatic system is formed, the serum of the blood must in the frog, at least, be chiefly derived from this source.

Zimmerman and others, regarding the fibrine as not intended to afford nourishment to the tissues, but as a product of their effete matter, have stated that the blood of the fœtus contains no fibrine. In the chick, however, on the third or fifth day of its development, I have sometimes removed from the heart a small mass of coagulated blood. In the mammalian fœtus pretty far advanced, I have also observed that when the blood taken from the umbilical vessels was allowed to stand for a short time a coagulum formed. This, however, is much looser and smaller compared with the quantity of blood than in the adult, and in the vessels and heart of the fœtus I have not observed firm coagula, such as occur after death in those of the perfect animal. The quantity of fibrine then in the blood of the fœtus appears to be much smaller than that in the blood of the adult, and in very young fœtuses it probably does not exist at all.

The presence of fibrine in the blood of the fœtus cannot be regarded as an objection to the views held by Zimmerman, Hughes Bennett, and others, in regard to the origin of this substance, inasmuch as we must expect that the process of disintegration goes on during embryonic life, in the same manner as in the growing animal, though perhaps in a less degree, and as a result of this process fibrine may be formed, though in smaller quantity than in the blood of the animal after birth.

SEC. II.—DEVELOPMENT AND STRUCTURE OF THE BLOOD-VESSELS.

In what follows on the development and structure of the fœtal blood-vessels, the same arrangement will be observed as in the preceding section. The mode of formation and structure of the greater

and smaller blood-vessels will be described, first in the lower, and, secondly, in the higher classes of vertebrate animals. For this purpose the frog has been selected as an example of the lower vertebrata, the embryo of the ox and sheep as examples of the higher.

a. Lower Vertebrata.—In the frog the development of the blood-vessels has been studied by several observers, chiefly by Vogt, Prevost and Lebert, and by Kölliker.

In the tadpole, before leaving the gelatinous-like material in which it is at first enclosed, the branchiæ are observed as two small swellings near the cephalic extremity of the body. When examined at this period, they are found to be entirely composed of the structures already described as forming the vitellus, and contain no distinct blood-vessels.

In animals about three lines in length, vessels are distinctly visible in the branchiæ with blood corpuscles circulating in their interior. It is difficult to ascertain exactly the mode in which these vessels are formed. According to Prevost and Lebert, the embryonic corpuscles become gradually diaphanous; the globules separate from one another towards either side, leaving between them a central space which is occupied by the vessel. They suppose it probable that there exists in the young frog a membranous expansion around the vitellus, beneath its outer envelope, to which they give the name "hemoplastic membrane," and from which they believe the blood vessels are formed. According to the observations of Kölliker, on the other hand, it would appear that the vessels in question must be formed by the transformation of cells in the manner stated by Schwann. As regards their structure, they appear at first as channels between the embryonic corpuscles: their margins are not straight and parallel to each other, but are more or less crenated from the projection inwards of the embryonic corpuscles, situated on either side. The vessels cannot however be regarded as mere intercellular spaces as some have stated, inasmuch as they have always a membranous wall distinct from that of the neighbouring cells.

In embryos measuring from five to six lines in length, the branchial vessels are much more distinct and the circulation within them more active. The vessels appear to be wider than before, and at the same time their margins are more straight and parallel to each other. The membrane of which their walls are formed is also much more distinct. It presents the aspect of a thin transparent homogeneous texture in which may occasionally be seen one or two more or less oval granular bodies presenting the character of nuclei. These give rise to a thickening in the wall of the vessel at the points where they occur. The existence of these nuclei would seem to indicate that the membrane constituting the wall of the vessel had been formed by the amalgamation of cells.

In the tail of animals about this period we can also observe the circulation partly established. It presents the following appearance: along the side of the chorda dorsalis we find one large vessel ex-

tending downwards from the cephalic extremity towards the end of the tail; here it becomes continuous with another large vascular trunk running parallel to it. In the former the current of the blood is from the head towards the tail, in the latter it is in the opposite direction. In the former also the rapidity with which the blood circulates is also seen to be greater than it is in the latter. The one of these vessels corresponds to the descending aorta, the other to the ascending cava. They are connected at different parts of their course by intermediate smaller vessels. The latter when traced from the artery are seen to pass outwards for a little distance towards the circumference of the tail; they then bend upon themselves, and again passing inwards towards the chorda dorsalis open into the vein. These intermediate vessels thus form a series of lateral vascular arcs along each side of the chorda dorsalis.

As regards the structure of the vessel, the two large vessels are so imbedded among pigment cells that it is difficult to observe clearly the elements of which they are composed; so far, however, as this can be done, they appear to consist of spindle-shaped corpuscles, some arranged longitudinally in the long axis of the vessel, others more or less transversely, and constituting several layers. Towards the point where the two become continuous, we find that they present the appearance of being composed of a homogeneous membrane. From what we know then of the relations of the larger to the smaller vessels in the perfect animal, it is probable that the homogeneous membrane in question constitutes the inner layer of the vessels throughout.

The smaller vessels which have been described as forming a series of intermediate vascular arcs between the two larger trunks, are at first only of sufficient calibre to admit the blood corpuscles in single file, so that in this respect they resemble capillary vessels. They are also similar to the latter in structure, consisting of a delicate homogeneous membrane with nuclei here and there imbedded in it. Like the vessels in the branchiæ, they cannot be regarded as mere intercellular spaces.

In several of them the margins run parallel to each other, so that the vessel is of equal breadth throughout. In others they are approximated towards one another more at one point than at another, so that the vessel presents a contracted and dilated portion. It is generally at this dilated portion that the nuclei already noticed exist. From this dilated portion of the vessel, there is also not unfrequently observed a process passing outwards for a short distance in the direction of the circumference of the tail.

In tadpoles farther advanced we find a second series of vascular arcs formed external to the first. The vessel of which each of these secondary arcs is formed, may be described as arising from one of the first series of arcs passing outwards towards the margin of the tail, and then bending upon itself again runs inwards and joins the next primary arc below that from which it arose. The vessels in

the second series of arcs resemble in structure those of the first. The latter, in animals about this period, are considerably wider and of much more uniform calibre than in younger embryos.

The changes which take place subsequently, consist merely in the formation of new vascular arcs, intermediate and external to those already formed, until at length they constitute a complete network which extends over the entire breadth of the tail of the animal.

In regard to the structures from which these vessels are formed, there can be little doubt that these are the embryonic cells. The tail of the young tadpole presents the following structure: Externally is a layer of dark pigment cells the same as those composing the vitelline membrane already described; along the middle line runs the chorda dorsalis, and on each side of it a number of more or less elongated embryonic cells in process of being developed into muscular fibre. The rest of the tail is entirely composed of oval and round embryonic corpuscles filled with granules, and presenting the same character as those already described. By degrees it becomes more transparent by the partial disappearance of the pigment from the cells forming the external layer, as well as by the separation of these from one another by the development of new cells between them which contain little or no pigmentary matter. At the same time, the granular matter contained in the embryonic corpuscles gradually decreases, and at the same time these latter send off two or three processes in different directions, so as to present the aspect of branching or caudate cells. The processes of neighbouring cells are often seen to be united (fig. 9). From these, then, according to the observations of Kölliker, the blood-vessels are formed—the nuclei which we have mentioned as seen in the walls of the latter, being the persistent nuclei of the former. The dilatation which we have described as occurring in the vessels when recently formed, corresponds to the cavity of the cell, while the constricted portions of the same correspond to its caudæ or processes. Of the same nature is the process which is seen passing off from one or more of the vascular arcs towards the margin of the tail.

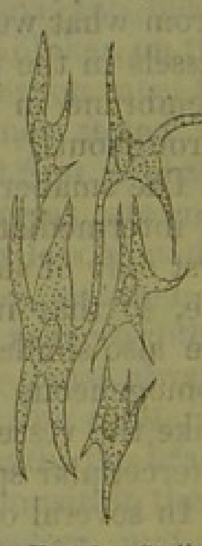


FIG. 9.—Stellate cells in the tail of the tadpole, developing into capillary vessels. 250 diam.

b. Mammalia.—1. Larger Vessels.—If a portion of any of the larger arteries, such as the hypogastric, carotid, or aorta in fœtal calves about an inch in length be examined, its walls will be found to be composed of embryonic corpuscles and spindle-shaped cells in different stages of development.

FIG. 10.—Inner layer of umbilical artery of calf 8 in. long. 250 diam.

Towards the interior of the vessel, there are several layers of embryonic corpuscles imbedded in a more or less homogenous intercellular substance (fig. 10). Proceeding outwards towards the exterior of the vessel, we

find spindle-shaped corpuscles more or less perfectly formed. The more perfectly developed of these bodies are situated towards the exterior of the walls of them. These bodies present the same character as the bodies which we find in the walls of the vessels in the adult animal, and which have been described by Kölliker as organic muscular fibres. In the present case, however, I think, there can be little doubt, that they are merely transition stages in the formation of fibres (figs. 11, 12, and 13).

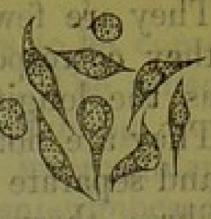
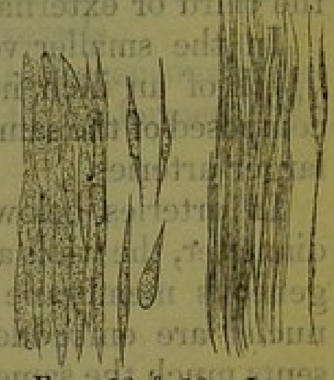


FIG. 11.—Succeeding layer in the same vessel, composed of spindle-shaped corpuscles. 250 diam.

There is as yet no distinction into inner, middle and external coats.

As regards the direction of these spindle-shaped corpuscles, most of them appear to be arranged in a direction more or less obliquely to the long axis of the vessel. Some are arranged more or less at right angles to these. The latter are not collected together, so as to constitute a single distinct layer or coat, but are found intermingled with the others throughout the entire thickness of the coats of the vessel.



FIGS. 12 & 13.—Layers more external in the same vessel, in different stages of development into fibres. 250 diam.

2. In fœtuses four inches long, the solid spindle-shaped corpuscles are increased in number, and towards the exterior of the vessel distinct fibres are seen formed by the union of two or more of these bodies. The layer of embryonic corpuscles with the homogeneous matrix, in which they are imbedded, presents the appearance of a more or less consistent membranous structure, lining the interior of the vessel.

3. In embryos pretty far advanced, as in those measuring about 18 inches in length, the arteries have the following structure. Lining the interior of the vessel is one or more layers of bodies resembling the primary or embryonic corpuscles. Proceeding outwards are found fibres presenting the following characters :—they are smooth, for the most part cylindrical, and measure from $\frac{1}{12,000}$th to $\frac{1}{10,000}$th of an inch in diameter. Many of them are branched and anastomose with neighbouring fibres. Mingled with these are considerable numbers of spindle-shaped corpuscles. Still further outwards the walls consist almost entirely of fibres, the spindle-shaped corpuscles either not existing, or being very few in number.

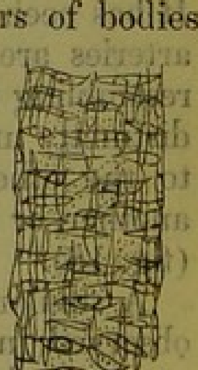


FIG. 14.—Common carotid artery of calf 2 in. in length, showing different directions of the fibre cells. 250 diam.

Besides the set of fibres above described which correspond to what is called a transverse coat in the artery of the full-grown animal, we find another set of fibres crossing the former at right angles. These consist of smooth, shining, cylindrical fibres, about the same breadth as those in the other set. They are not possessed of much

inherent elasticity, inasmuch as they break across very readily. They are few in number compared with the others. In direction they correspond to the fibres which have been described by Henle as the longitudinal coat in the artery of the animal after birth. They are not, however, collected together so as to form a distinct and separate coat, but are found intermingled with the other set of fibres, throughout almost the entire thickness of the walls of the vessel; both sets of fibres constituting but a single coat, composed, however, of many distinct layers (fig. 14.)

External to this we have a layer of white and yellow elastic tissue, the former predominating and forming a coat which corresponds to the third or external coat in the perfect artery.

In the smaller vessels down to about the $\frac{1}{100}$th of an inch in diameter, the walls are composed of the same structures as those of the larger arteries.

In arteries below the $\frac{1}{300}$th of an inch in diameter, the walls are composed only of homogeneous membrane in which round or oval nuclei are embedded. This membrane presents much the same aspect as that which lines the larger vessels.

Fig. 15.—Capillary vessels in different stages of formation, from stellate cells, in the eye of fœtal calf. 250 diam.

The capillaries appear to be chiefly formed from stellate or spindle-shaped cells in the same way as already described in the tadpole. The development of these vessels is best studied in the membranes of the fœtal eye, or in the gelatinous-like substance which is found on the chorion and in the umbilical cord (fig. 15.

There is a peculiarity in the arteries of the fœtus, which it may not be out of place here to mention. It has been already stated that the walls of the fœtal arteries are composed of many layers, each layer resembling the other in structure. These can be distinctly uncoiled continuously from one extremity to the other, the fibres either running into one another, or arranged in a more or less spiral manner (fig. 16).

Fig. 16.—Umbilical artery of fœtal calf 12 inches long, partially uncoiled, showing arrangement of its fibres in layers, and also probably their spiral direction.

A similar spiral arrangement may be frequently observed in the external coat of the fully-formed artery in the animal after birth.

From what has been stated, it seems to follow :—

1*st*, That the development and growth of the fœtal artery proceeds from the interior towards the exterior of the vessel.

2*d*, That all the structures occurring in the walls of the vessels are formed from the embryonic corpuscles.

3d, That at first there is no distinct demarcation into inner, middle, and external coats.

4th, That the perfectly-formed fœtal artery appears to be composed, as stated by the older anatomists, of three coats. The inner is formed of a number of round granular bodies resembling the embryonic corpuscles embedded in a homogeneous intercellular substance. The middle is composed of a number of superimposed layers, each layer consisting of two sets of fibres intermingled together. The external coat consists of white and yellow elastic tissue intermingled.

5th, That arteries whose calibre is below the $\frac{1}{300}$th of an inch, have their walls formed of homogeneous membrane, with nuclei embedded in it, similar to that lining the larger vessels.

6th, That the capillary vessels also consist of homogeneous membrane, with nuclei embedded in it, and appear to be formed from branching cells.

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