The Circulation of Mixed Blood in the Embryo Mammal and Bird, and in the Adult Reptile, Amphibian and Fish.

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Our conception of the course of the blood through the heart of the lower vertebrates appears to be based almost entirely on the conditions found in the adult of the warm-blooded forms (birds and mammals). It is well known that the adult bird and mammal possess a double circulation, i. e., a cycle in which venous blood is propelled from the heart to be returned oxygenated (pulmonary circulation), and one in which arterial blood is expelled to be returned venous (systemic circulation). The afferent and efferent vessels are in no way connected save through a capillary system, and for this reason the heart may be divided into a right or venous and a left or arterial heart. While the greater part of the seventeenth century was occupied with the Harvey doctrine, the eighteenth century found men equally engaged with the course of the blood through the fetal heart. Three distinct theories were suggested before the beginning of the nineteenth century—one based on alleged physiological necessity, a second on the anatomical relations found in the fetal mammalian heart, and a third on the logical deductions from the differences between the fetal and adult circulatory conditions. The differences between the fetal and adult heart in mammals are, briefly, the right auricle receives the precavals (venous) and the post-caval vein (V. cava inf.), which is arterial; a communication between the right and left auricle is present (foramen ovale), and a connection is found between the heart efferents (pulmonary artery and aorta) in the ductus arteriosus.

The theory based on physiological necessity (von Haller-Sabatier) was this: if the left heart in the adult is arterial, then the chances are it must also be arterial in the fetus; hence the oxygenated blood in the post-caval vein must pass through the foramen ovale into the left heart. It was further inferred that because the ductus arteriosus short-cut the venous blood from the pulmonary artery into the descending aorta, the vessels arising from the aortic arch would convey a better quality of blood.

The net result of this scheme was that not only did the head and upper extremities receive a better quality of blood, but a right venous and a left arterial heart was maintained and a function was suggested for the Eustachian valve in the right auricle. Unfortunately this doctrine has been antagonized since 1835 with little effect on the described circulation in the mammalian fetus, and with no consideration of its evident defects in the latest text-book (3) on chick embryology. At the last meeting of the Academy I labeled the scheme "morphologically inaccurate, developmentally unnecessary and physically impossible." The second theory (Wolff) was based on excellent anatomical observation but does not fulfil the physical requirements of the proposition. The third theory (Harvey), a mixing of the blood in the right auricle, was quite definitely demonstrated to occur in the living fetal pig. I found by injection experiments that the blood passing into the heart from the right precaval and the postcaval veins found its way into both ventricles. Interpreted in a physiological manner, the result is that all the arteries in the mammalian embryo contain a mixed blood. The point raised, while of no practical importance in itself, is interesting because it was first suggested by Harvey in 1628; because it may lead to a more perfect understanding of the anatomical changes from the fetal to the adult circulation; and lastly because of its morphological significance. It is the latter point that I would bring out in greater detail.

It is well known that the double circulation is found only in the warm-blooded adult vertebrates (bird and mammal); animals in other words, where the body temperature demands a greater degree of oxygenation and in which the oxygenation is entirely confined to the lungs. In the lower vertebrates this condition does not obtain, reptiles excepted. The amphibian has other means of obtaining oxygen than through the lungs, and the fish, other paths than through the gills. The relatively low body temperature does not necessitate so rich a content of oxygen in the blood. If we examine this statement closely we see that the embryos of mammal and bird resemble the reptile and amphibian; they do not possess a distinct four-chambered heart, and while in the latter the element of warmth does not enter, in the former all of the warmth, practically speaking, is supplied by the maternal body through internal or external incubation. The metabolic processes of the mammal and bird are therefore insufficient to maintain the essential body temperature.

If we examine the phylogenetic relation of the mammal and bird we note that the higher mammals carry the offspring to term; the marsupials have a short period of gestation, and while the young are born in a very immature condition, they are brooded in a sac (marsupium); the monotreme's method does not differ essentially from that of the bird save perhaps in the mode of the incubation of the egg and the postembryonal care of the offspring. It would therefore be a logical inference to grant that the circulatory conditions in the fetal mammal and bird were about the same. Indeed the von Haller-Sabatier theory has been carried over directly to the bird, i. e., the right heart of the fetal bird is described as venous, the left as arterial.

I have stated that the latest text-book on chick embryology translates this blood segregation theory from mammal to bird with no comment on its defects. If the postcaval vein in the chick does carry the arterial blood richly laden with nourishment from the yolk to the left auricle through the foramen ovale, then the relations of the precaval to the postcaval openings must be vastly different from what they are in the mammal —but they are not. Further, if this is a developmental necessity, what is the character of the circulation in the anomalies where the right precaval opens with or into the postcaval? Is it possible for the described conditions to obtain in these cases or in Rhea americana, where, according to Gasch (2), the common opening of the right precaval and the post caval is the normal. I have no experimental evidence to bring up as yet for the mixing of the blood in the right auricle of the bird, but I believe there is sufficient ground for the claim that it occurs from the similarity to the mammal in heart structure, developmental requirements, and from the aberrant types such as I have mentioned.

Phylogenetically the connecting link between bird and reptile is particularly strong; ontogenetically the requirements for development differ only in body temperature (viviparous forms excluded), and we would therefore expect little difference in the character of blood circulation, although the heart structure is quite different. Taking the turtle as the type, the described circulation is about as follows: the right auricle is venous, the left auricle arterial—both open into the incompletely divided ventricle by separate openings. The blood from these two sources is segregated in corresponding parts of the ventricle, and when the ventricle contracts, the incomplete septum touches the ventricular wall, isolating a part of the venous blood in a sort of right chamber of the ventricle. The venous blood is expelled through the pulmonary artery, mixed blood is sent out through the right aorta, while the left aorta is purely arterial. This is again the same scheme as we found in the mammal and results in the head receiving a better quality of blood.

Experiments were performed on three species of turtles to ascertain if this condition prevailed. The plastron removed and the heart laid bare, a double ligature was passed through the transverse pericardial sinus and arranged to tie one at the distal, the other at the proximal edge of the sinus. Next cornstarch granules suspended in nórmal salt solution were introduced into the auricles during diastole; the auricle allowed to contract, giving time to have the distal ligature ready to tie off; the distal ligature was tightened during ventricular systole and immediately the proximal one—isolating three columns of blood in the three vessels. These were bled separately into watch glasses containing dilute acetic acid and examined for the granules. It was found that granules injected into the right and left, and in both auricles simultaneously, were always recovered from all three efferent vessels. It must also be remembered that in the turtle the fetal circulation is not unlike that found in the fetal bird—the postcaval vein conveys the oxygenated blood, and if this segregation of blood occurred as described in the adult, the head would receive only venous blood. This objection also holds good in the Crocodilia, where, according to Wiedersheim (6), the condition is as follows: "The blood from the right ventricle passes into the pulmonary artery as well as into the left aortic arch and, according as the septum ventriculorum is complete or incomplete, is either entirely venous (Crocodilia) or mixed (other reptiles). A complete septum ventriculorum thus appears for the first time in crocodiles, in which, consequently, the right ventricle contains unmixed venous blood and the left ventricle unmixed oxygenated blood, although, as will be seen presently, an admixture takes place in the systemic arteries." Again, according to this scheme, the head will receive a better quality of blood because the carotids arise from the left aortic arch, but again the objection as to the manner of transformation from the fetal crocodile to the adult crocodile heart would arise. This form certainly needs careful investigation. The purely venous blood would far exceed the purely arterial, and the mixture at the foramen of Panizza might be very complete.

The amphibian circulation is naturally described on the basis of the segregation of blood and must therefore fall into two classes, the anural and the urodele. The description of the anural circulation is delightfully exact and comprehensive and is as follows: "It will be perceived that the blood poured into the right auricle is mostly impure or venous, that poured into the left fully aerated or arterial. When the auricles contract, which they do simultaneously, each passes its blood into the corresponding part of the ventricle, which then *instantly* contracts before the venous and arterial bloods *have time to mix*. Since the conus arteriosus springs from the right side of the ventricle, it will at first receive only venous blood, which, on contraction of the conus, might pass either into the bulbus aortae or into the aperture of the pulmo-cutaneous trunks. But the carotid and systemic trunks are connected with a much more extensive capillary system than the pulmo-cutaneous, and the pressure in them is proportionately great, so that it is easier for the blood to enter the pulmo-cutaneous trunks than to force aside the valves between the conus and bulbus. A fraction of a second is, however, enough to get up the pressure in the pulmonary and cutaneous arteries, and in the meantime the pressure in the arteries of the head, trunk, etc., is constantly diminishing owing to the continual flow of the blood toward the capillaries (sic). *Very soon*, therefore, the blood forces the valves aside and makes its way into the bulbus aortae. Here again the course taken is that of least resistance; owing to the presence of the carotid gland the passage of blood into the carotid trunks is less free than into the wide elastic systemic trunks. These will therefore receive the next portion of blood, which, the venous blood having mostly been driven to the lungs, will be a mixture of venous and arterial. Finally, as the pressure rises in the systemic trunks, the last portion of blood from the ventricle, which, coming from the left side, is arterial, will pass into the carotids and so supply the head."

It will be seen on critical examination of this scheme that several points are open to argument even if we grant the segregation of bloods in the spongy ventricle: 1. the element of time; 2. the mechanics; 3. the comparative anatomy; and 4th, the experimental evidence. 1. The frog's heart under normal conditions beats about 60 to the minute with a ventricular systolic phase of about 0.2 sec. Now if one reads the description, bearing in mind that the whole process is completed in one-fifth of a second, and that all this is inferred in order that the head shall receive a better blood supply, one is tempted to hold one's breath. The time is short and much must be accomplished. If the blood in the systemic arteries is being forced toward the capillaries, what is holding it back in the pulmo-cutaneous and carotid trunks? Again the regulation of the valves and resistance to the flow of blood must indeed be very minutely adjusted to separate the venous from a mixed and a mixed from an arterial blood issuing from the same opening with say, one-fifteenth of a second to accomplish each phase. 2. Further the tracings made by Gompertz show that the blood reaches the pulmo-cutaneous and aortic trunks at the same time and under the same pressure. Still further the inspiration in the frog increases, not decreases, the intrathoracic pressure and would retard the pulmo-cutaneous system, and it has not been demonstrated satisfactorily to my knowledge that the capillary system of the pulmo-cutaneous vessels is actually less developed than in the systemic area. 3. The comparison of the various types of amphibian circulation is of interest. Bruner (1), for example, makes the following statement: "The fact that the septum atriorum disappears with the lungs indicates clearly that in the salamanders with lungs the septum performs a certain function which becomes superfluous or impossible after the loss of these organs. This function is the separation of the venous blood of the right auricle from the aerated blood of the left auricle. But what is the significance of this separation if the two sorts of blood are afterward mixed during the passage through the ventricle and conus? Or is there, after all, in salamanders with lungs a partial separation of the aerated and the venous blood in its entire course through the heart? Such a separation occurs, as is well known, in the heart of Rana. Now as regards the atrium and ventricle, we find essentially the same structure in Salamandra as in Rana. It is true that the septum atriorum in the salamander is perforated, while in the frog it is not. But during the brief stay of the blood in the auricles the small perforations which have been described would permit little mixing of the blood. There would be much better opportunity for this to occur in the ventricle, but here we have the same spongy condition in Salamandra and Rana. So far then, Rana does not seem to have a decided advantage over the salamander in respect to the separation of venous and arterial blood in the heart. We may therefore conclude that in the salamander, as in Rana, the first blood passing from the ventricle into the conus during the ventricular systole is chiefly venous. In Rana this is directed into the pulmonary artery. In the salamander, however, the structure of the conus does not indicate that it could influence the direction of the blood current. We must turn, then, to the bulbus arteriosus and the great arterial vessels for further light on our problem." "The spiral valve of the salamanders can have no control over the direction of blood which passes through the conus." Preceding this Bruner states: "The conus of the Salamandrina shows the same general structure as that we found in the conus of the Salamandra. A spiral valve is distinctly recognizable in the lungless form." (Salamandra has lungs; Salamandrina has none.)

This point in the comparative anatomy of the amphibian circulation I hold to be an excellent objection to the described course of the blood through the frog heart.

4. Experimental evidence on the amphibian circulation leaves much still to be done. Mayer found that if the tip of the ventricle was cut off the blood issued in two distinct streams. This, in addition to the coloration in the beating frog heart, seems to hold for a segregation of the venous and arterial blood in the spongy ventricle. But Gompertz's experiments also seem to indicate that even if this be true a mixing must occur in the vessels.

The step from the amphibian to the class of Dipnoi is not a very great one, and still we find something which may throw light on the character of blood circulating in the fish. According to Wiedersheim "in Ceratodus the conus arteriosus is provided with eight rows of valves and begins to be divided into two chambers. In Protopterus this division is complete, so that two currents of blood, mainly arterial and mainly venous respectively, pass out from the heart side by side. The former comes from the pulmonary vein, from which it passes into the left atrium, thence into the left portion of the ventricle, and thence to the two anterior branchial arteries. The venous current, on the other hand, passes from the right portion of the ventricle into the third and fourth afferent branchial arteries and thence to the corresponding gills, where it becomes purified; it reaches the aortic roots by means of the efferent branchial arteries. The paired pulmonary artery, like the corresponding vessel in the crossopterygians, arises from the fourth efferent branchial in Ceratodus, and from the aortic root in Protopterus and Lepidosiren."

There appears to be a physiological flaw in this description unless the fish blood behaves quite differently from that in other animals. Under the assumption that the blood in the fish becomes fully oxygenated in its passage through the gills, the blood carried to the lungs from the efferent branchial artery would already be charged with oxygen, and in this case the lungs would only be functional when the fish is hibernating in the dried mud. Under the assumption that the fish blood is not fully oxygenated in its passage through the gills, the lungs would be accessory to the gill function. In neither case would there be any physiological reason for the separation of the blood issuing from the conus. If the gills in the fish do not entirely oxygenate the blood, and in some fish the fins apparently assist in oxygenation, then the fish blood really corresponds to our notion of "the mixed blood" (not fully oxygenated) in the higher forms. Here again is a problem upon which no definite information may be given.

In conclusion, my position on the quality of blood circulating in the arteries of the vertebrates is that it is what may be termed "mixed" in all forms from the embryo mammal and bird to the fish, and if there have been advanced various theories on the mechanics of the passage of the blood through the heart of a given form they have been based on the alleged physiological necessity for a better quality of blood circulation in the head. In other words the systemic arteries convey arterial blood only in the mammal and bird after birth. I believe if one eliminates the idea that the head must receive a better quality of blood (Sabatier scheme) the whole doctrine of the character of the circulation in all forms of vertebrates is not only simplified but placed upon a sound physiological and developmental basis.

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