CONCERNING THE POSTNATAL OBLITERATION OF THE UMBILICAL VEIN AND ARTERIES, THE VITELLINE VEIN AND ARTERY, AND THE DUCTUS ARTERIOSUS IN THE GUINEA PIG

by

JAMES EGLY HERBERTSON

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INTRODUCTION

It is a well known fact that there are modifications of action and function which take place at birth or soon thereafter. The functional modifications of the circulatory system are among the most extensive of these postnatal changes.

The purpose of this investigation is to determine the rate and type of obliteration which take place in the umbilical vein and arteries, the vitelline vein and artery, and the ductus arteriosus in the guinea pig after birth.

REVIEW OF LITERATURE

Many investigations have been made concerning the stages at which the postnatal obliteration of the fetal blood passages occur in man. According to Scammon and Norris (1918), many of our current concepts of these changes can probably be traced to the early investigations of the French clinician, Billard (1828). This investigator collected data on the obliteration of the ductus venosus, the ductus arteriosus, and the foramen ovale in a series of 128 children who died in the first eight days of life. Billard's observations were confirmed by Bernutz (1865) who found variation in the stages of closure of the ductus arteriosus

in a series of 59 children who died between the tenth and the 60th days of life. Elasasser (1852) in a series of nearly 300 observations upon children of the first month, found obliteration of the ductus arteriosus in about two per cent, and of the foramen ovale in about three per cent of his cases. Alvarenga (1869) found practically no instances of obliteration of the ductus arteriosus nor the foramen ovale before 60 days of life. The findings of later observers, Alexeieff (1900), Therenin (1887-1895), Kucheff (1901), and others agree essentially with those of Elasasser and Alvarenga although they have noted some instances of earlier obliteration of these passages. Considerable data have been compiled by Scammon and Norris (1918) concerning the postnatal obliteration of the ductus arteriosus, the ductus venosus, and the foramen ovale.

A review of the available literature indicates that (1) most of the work concerning the postnatal obliteration of the fetal blood passages has been done on man; (2) very little work, of this nature, has been done with other animals; (3) the investigations have dealt, for the most part, with the ductus arteriosus, the ductus venosus, and the foramen ovale. Many of our text books do not mention the time of the postnatal changes in the circulatory system while others merely state that these changes take place at birth or a

few days later. Bryce (1908), however, in discussing the postnatal changes of the fetal blood passages in man states that this obliteration commences at birth, and is perceptible after a few respirations have occurred. It makes rapid progress in the first and second days, and by the third or fourth day the passage through the umbilical arteries is usually completely interrupted. The ductus arteriosus is rarely found open after the eighth or the tenth day, and by three weeks it has in almost all instances become completely impervious.

The process of closure of the veins is slower; but they remain empty of blood and collapsed, and by the sixth or seventh day they are generally closed.

Although there has been little investigation concerning the obliteration of these fetal blood passages, their development in a number of animals has been given. The development and fate of the aortic arches in the cat has been given by Coulter (1909), in the rabbit by Bremer (1912), in the guinea pig by Fedorow (1911), and in other mammals by Huntington (1919) and Reagan (1912). The development of the vascular system of the liver has been described by Mall (1906), Davis (1910), and Ingalls (1908). "The Course of the Blood through the Fetal Mammalian Heart" by Pohlman (1908) and "A Case of a Patent Ductus Arteriosus in an Adult" by Arnold

(1919) have been of considerable aid in the investigation of the ductus arteriosus in the guinea pig.

MATERIALS AND METHODS

Most of the guinea pigs used in this investigation were offspring from adults obtained from the Department of Animal Husbandry, Kansas State College. A total of 98 guinea pigs were used; 73 were offspring of the previously mentioned adults and were between the ages of one day and three weeks; ten were adults and 15 were young born dead in the pens of the Department of Animal Husbandry.

The females were kept in a large pen with a male and when one appeared to be within a week of parturition she was put in a separate cage from the rest of the colony. These cages were examined for newly born young at least twice daily, thus all young were found within 12 hours after birth. The color, sex, length, and weight of the young were recorded and complete records for the adult females with their respective litters were kept. The young were killed at ages varying from one day to three weeks, after which the adult female was returned to the large pen containing the male.

The colony and the isolated females were fed a normal diet consisting of a prepared oats mixture, alfalfa hay, and an abundance of green feed in the form of carrot tops, let-

tuce, and fresh alfalfa. Other miscellaneous greens were obtained from a restaurant. A sufficient amount of fresh water was available at all times.

The guinea pigs used in this investigation were killed with chloroform and pinned upon a dissecting board, (Fig. 1). An incision was made along the mid-ventral line of the neck; the skin reflected and the flesh teased away to expose the carotid artery. For the purpose of general dissection and observation of the gross morphology, the left carotid artery was injected with a mass composed of lead chromate, corn starch, and distilled water. The femoral artery was exposed on the ventral surface of the right thigh in order to determine the extent of penetration of the injection mass. For the corrosive and masceration examinations an injection mass of celloidin in acetone was used. The injection fluid was colored differently depending upon the blood vessels to be injected. Lead chromate was used in the mass for all the arteries and the injections were made through the carotid artery. Aniline blue was added to the mass to inject the portal vein and the umbilical vein. In these injections the mass filled both veins equally well, whether the fluid was introduced into the portal vein or into the umbilical vein. Carmine was added to the mass used in injecting the

inferior vena cava. The purpose of using these differently colored masses was to show any relations which may exist between the portal vein, the umbilical vein, and the inferior vena cava within the liver tissue. The injected animal was then soaked in water for 20 minutes in order to harden the injection mass, after which the abdominal viscera were removed from the animal and mascerated under water. The mesenteries and other tissue were easily separated from the injected blood vessels.

In order to determine the presence or absence of a lumen and its extent in the vitelline blood vessels, the vessels were injected with black India ink by means of a fine glass injection tube. The ability of these vessels to convey blood was determined by forcing the blood contained in them along the lumen of the vessel. When no blood was present the injection fluid was used. This procedure was also employed when investigating the lumen of the umbilical arteries and vein.

In several investigations of the ductus arteriosus an injection fluid of celloidin in acetone, colored with lead chromate was used to inject the carotid arteries. Aniline blue was substituted for the lead chromate when the external jugular vein was injected. In other investigations of the

ductus arteriosus, the hearts with their accompanying blood vessels were removed from guinea pigs of various ages. The pulmonary artery and aorta were cut at the point of emergence from their respective ventricles. The carotid arteries and the left subclavian artery were cut leaving approximately one-eighth inch stumps connected with the aorta; about one inch, more or less, of the aorta posterior to the union of the ductus arteriosus was removed. The blood vessels were fixed in Bouin's fluid, imbedded, and sectioned serially. The sections mounted included the ductus arteriosus from the branching of the pulmonary artery to the union of the ductus arteriosus with the aorta.

All measurements of the blood vessels were made with a pair of dividers and a millimeter scale. The drawings were made with the aid of a projection camera and a tracing table.

OBSERVATIONS

The blood vessels examined were the vitelline vein, the vitelline artery, the umbilical vein, the umbilical arteries, the portal vein, the inferior vena cava, and the ductus arteriosus. The umbilical vessels are considered together in the order named; the portal vein, the umbilical vein, and the inverior vena cava and their relations to one another

are considered as a unit, and finally the ductus arteriosus is discussed.

The Umbilical Blood Vessels

At birth the cut portion of the umbilical vessels appear as a blood clotted stump on the outer abdominal surface of the skin. An area, of the external surface of the body wall directly around the umbilical cord, approximately 15 mm. in diameter, is clearly hemorrhagic. This condition begins to disappear during the second day after birth and is lost on the fourth day. The skin of the animal is continuous with the umbilical cord until the sixth day when there is complete separation. The beginning of this separation is first noticed on the second day and after that until the sixth day there is a gradual thinning of the connection which may easily be broken in reflecting the skin away from the body wall.

In the following examinations, the blood vessels were all observed within the body cavity. At birth the vitelline vein has little evidence of a lumen while the vitelline artery has a lumen partially filled with blood. The vitelline vein extends for a distance of 20 mm. from the umbilicus into the mesenteries of the small intestine where it joins

with the portal vein (Fig. 3). The vitelline artery which is two millimeters shorter than the vitelline vein, enters the mesenteries of the small intestine caudal and dorsal to the vitelline vein. The umbilical arteries have a lumen partially filled with blood, and extend for a distance of 27.5 mm. from the iliac arteries along each lateral surface of the urinary bladder to the umbilicus. In the injected specimens the injection fluid filled the lumina of the vessels for a distance of 18 to 20 mm. from the right and left iliac arteries toward the umbilicus. The lumen of the umbilical vein is much larger than any of the other vessels examined and has a much thinner wall. The umbilical vein is distended with blood for the entire length from the umbilicus to the liver.

At one day of age the vitelline vein has become a fibrous cord with no trace of a lumen. The vitelline artery now contains but a trace of blood which may be forced to flow along the length of the vessel, showing that a lumen is still present. The umbilical arteries contain less blood than at birth and the injection fluid penetrates for approximately half their length. The umbilical vein contains a large amount of blood but does not seem distended as much as in the newly born guinea pigs.

In the two day old guinea pigs the vitelline vein has

become a solid cord and has lost some of its fibrous condition. The vitelline artery contains a trace of blood which may be forced through only a portion of the proximal end of the vessel. The umbilical arteries contain a lesser amount of blood than the one day old guinea pigs but the injection mass still penetrates about half their lengths. The umbilical vein is filled with approximately the same amount of blood as it contained in the one day old guinea pigs. The lumen is sufficiently large to permit rather easy injections.

In the three day old guinea pigs the vitelline artery has no blood in it and only a trace of the lumen is present. The umbilical arteries contain scattered amounts of blood within the proximal half of their lengths. The injection mass penetrates nearly one-third their lengths, a distance of ten to 11 mm. There is no visible difference in the umbilical vein from the preceding stage of obliteration.

During the fourth day the lumen of the vitelline artery is completely obliterated and has much the same appearance as the vitelline vein in the two day old guinea pigs. The umbilical arteries have only a trace of the lumen in the proximal half of each vessel. The umbilical vein contains a lesser amount of blood than it does in the three day stage and shows signs of fibration at the proximal end which enters the liver.

During the fifth day the umbilical arteries show signs of obliteration and have the appearance of a fibrous cord. The umbilical vein contains only a trace of blood and can still be injected along the entire length.

During the sixth day the umbilical arteries appear as solid fibrous cords, one on each side of the urinary bladder. The umbilical vein has only a trace of a lumen and successful injections are difficult. The final obliteration of the umbilical vein is a gradual process and does not reach its complete consumation until the 12th to the 14th day, when it appears as a flat fibrous band extending along the inner surface of the body wall.

The vitelline artery and vein as well as the umbilical arteries become comparatively cylindrical fibrous cords when their lumina have completely obliterated. Their obliteration begins at the umbilicus and progresses toward the mesenteries and toward the iliac arteries respectively. The umbilical vein, however, begins its obliteration at the proximal end near the liver and progresses toward the umbilicus.

The Relations of the Umbilical Vein, the Portal Vein, and the Inferior Vena Cava within the Liver

During the examinations of the umbilical vein and dur-

ing the injections of this vein with India ink it was observed that the injection fluid appeared in the venules of the portal system. Further investigation showed a direct connection existing between the umbilical vein and the portal vein. This direct connection persists until the fourth day after birth when the umbilical vein shows signs of fibration near the proximal end where it enters the liver. There was no direct connection persisting after birth between the portal vein and the inferior vena cava nor between the umbilical vein and the inferior vena cava. The above relations were shown by the masceration method as mentioned previously and the results were equally good when the portal vein was injected instead of the umbilical vein.

The Ductus Arteriosus

The obliteration of the ductus arteriosus is accomplished in two stages. The first stage is a rapid functional closure effective on the third day after birth. The progressive external changes of the ductus arteriosus are shown on Plate IV, figure 5, a, b, and c. This first functional closure is accomplished by two methods. The first is a constriction of the entire ductus arteriosus and the second is the laying down of a loosely packed mass of connective tissue from the walls of the ductus arteriosus. The pro-

gressive stages in this internal fibration of the lumen are shown on Plate IV, figure 6, a, b, c, d, and e. The constriction of the ductus arteriosus is evident on the first day after birth and becomes more pronounced until the third day when the size of the ductus arteriosus has been reduced to one-half of its original size at birth. The final anatomical obliteration of the lumen is accomplished in gradual progressive stages until the second or third week when it has the appearance of a solid cord. This is the condition persisting in the adult animals. The lumen of the ductus arteriosus was completely obliterated in most of the animals examined by the fourth day. The exceptions to this condition are: One animal out of 12 examined at five days, one out of nine examined at six days, and two out of seven animals examined at seven days. In these animals a small lumen was present in the ductus arteriosus.

DISCUSSION

The obliteration of the fetal blood vessels is accomplished in two stages. The first of these stages, a functional closure, is brought about in the umbilical blood vessels by the severing of the umbilical cord. This severing of the umbilical cord separates the vessels from their blood supply or in the case of the umbilical arteries, it

interrupts the flow of blood from the iliac arteries to the placenta. The obliteration of the umbilical blood vessels is a gradual anatomical fibration as has been described in the observations. Although the fibration of the umbilical vein differs from that of the other umbilical blood vessels in that it starts its fibration at the proximal end and progresses toward the umbilicus while the other vessels begin their fibration at the umbilicus and progress toward their proximal ends. If, however, we take in consideration the direction of the flow of the blood in the respective vessels it is found that the fibration is similar in all the blood vessels in that it progresses from the postnatal terminal to the source of blood supply.

In their investigations of the vascular system of the liver Mall (1906), Davis (1910), and Ingalls (1908) show the presence of a direct connection of the umbilical vein, the portal vein, and the inferior vena cava by way of the ductus venosus. Scammon and Norris (1918) state in their conclusions that the ductus venosus is the first of the fetal blood passages to be obliterated after birth. In this investigation it was found that the obliteration of the ductus venosus was complete at birth as far as the connection of the umbilical vein and the portal vein with the inferior vena cava was concerned. The connection between

the portal vein and the umbilical vein persists until the fourth day after birth when the umbilical vein shows signs of fibration near the liver.

Before birth there is very little intrinsic circulatory activity in the pulmonary artery due to the inactivity of the lungs. The pressure, therefore, is nearly equal to that in the aorta. Pohlman (1909) states that "The capacity of the right and left fetal ventricles is equal and that the pressure exerted by the right and left fetal ventricles is equal." This condition of equalized pressure in the ductus arteriosus and in the aorta tends to keep the lumen of the ductus arteriosus open and functional. As soon as the lungs begin to function and require a greater supply of blood with freerer flow, the pressure is lessened in the ductus arteriosus. Mall (1906) states that "All vascular channels will disappear in which the rate of the blood stream falls below a certain maximum." Scammon and Norris (1918) conclude that the obliteration of the ductus arteriosus is not functional until after 60 days of life. Bryce (1908) states that "The ductus arteriosus is rarely found open after the eighth or the tenth day, and by three weeks it has in almost all instances become obliterated." In all but four of the guinea pigs examined after the

fourth day of life the ductus arteriosus was closed and non-functional. Arnold (1919) in describing the ductus arteriosus in man states that there is a "flap-valve-like structure" at the opening of the ductus arteriosus into the aorta. After birth this valve-like structure is supposed to affect the closure of the ductus arteriosus. No such structure was found in the guinea pigs examined. An explanation of the constriction of the ductus arteriosus after birth is given, according to Arnold (1919), by Abbott who says "The causes of patency of the ductus arteriosus are to be sought in the condition of its normal closure, and must thus depend upon the influences, mechanical or otherwise, of the changes in the circulation at birth, and on the action of the vessel wall, itself a fetal structure destined to involution." These changes in the circulatory system are so numerous and complicated that the process is consequently weak and the cases of the patent lumen existing in the ductus arteriosus after the fourth day in the four cases mentioned above is probably the exception to the normal rate of obliteration.

CONCLUSIONS

1. The process of obliteration of the umbilical blood vessels is a gradual fibration of the lumina of these vessels.

2. The vitelline vein is completely obliterated two days after birth; the vitelline artery by the fourth day; the umbilical arteries by the end of the sixth day; and the umbilical vein is not completely obliterated until the 12th to the 14th day.

3. There is a slight constriction of the ductus arteriosus on the second day after birth which marks the beginning of the occlusion of the lumen of that vessel. This constriction becomes more pronounced by the third day and is one of the important factors involved in the preliminary functional closure of the ductus arteriosus.

4. In most of the animals examined at four days and older the ductus arteriosus was functionally closed. In all the animals examined after seven days the ductus arteriosus was a fibrous cord.

5. The obliteration of the umbilical blood vessels, with the exception of the umbilical vein, begins with the umbilicus and progresses toward the proximal end of the vessels. The obliteration of the umbilical vein starts at the proximal end near the liver and progresses toward the umbilicus.

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PLATES

PLATE I

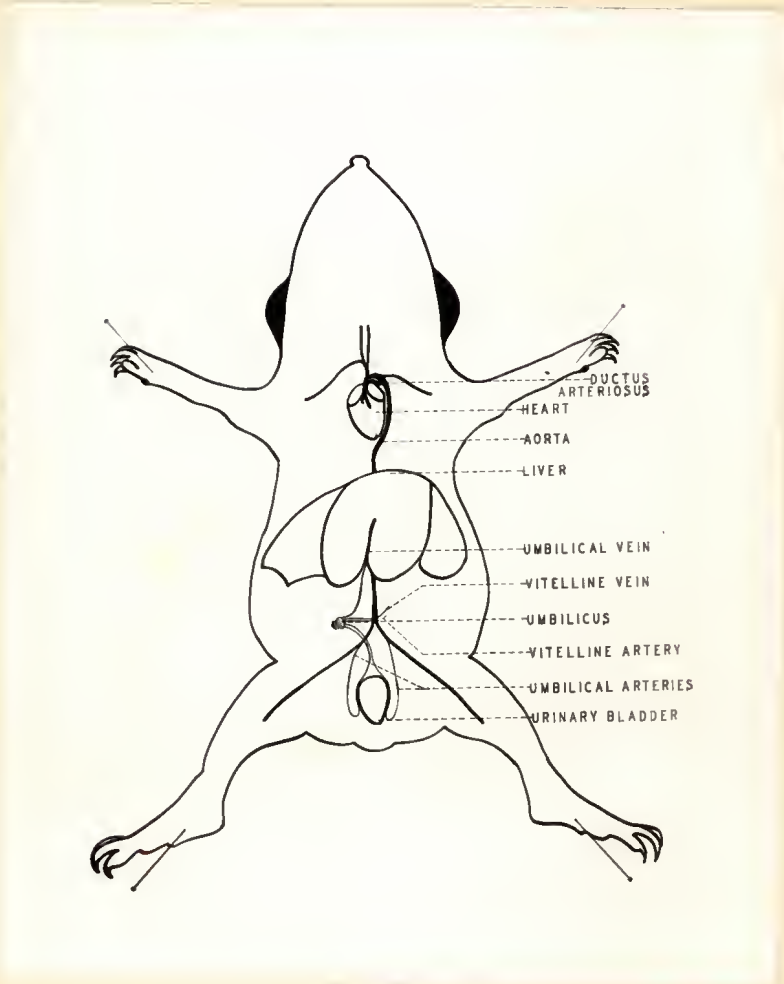

Fig. 1. Diagram showing the Umbilical Blood Vessels and the Ductus Arteriosus in the Guinea Pig.

PLATE II

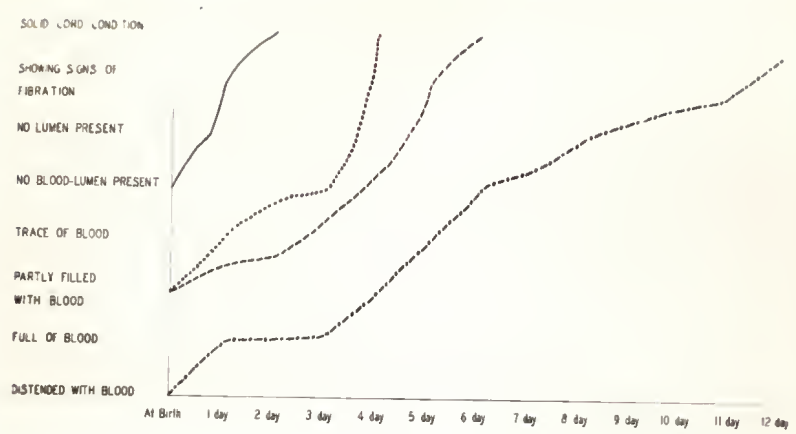

FIGURE 2

A GRAPH SHOWING THE RATES OF OBLITERATION OF THE UMBILICAL BLOOD VESSELS IN 88 GUINEA PIGS EXAMINED BETWEEN BIRTH AND 12 DAYS OF LIFE

VITELLINE VEIN ——— UMBILICAL VEIN -·-·-·-·-·-
VITELLINE ARTERY ····· UMBILICAL ARTERIES - - - - - -

PLATE III

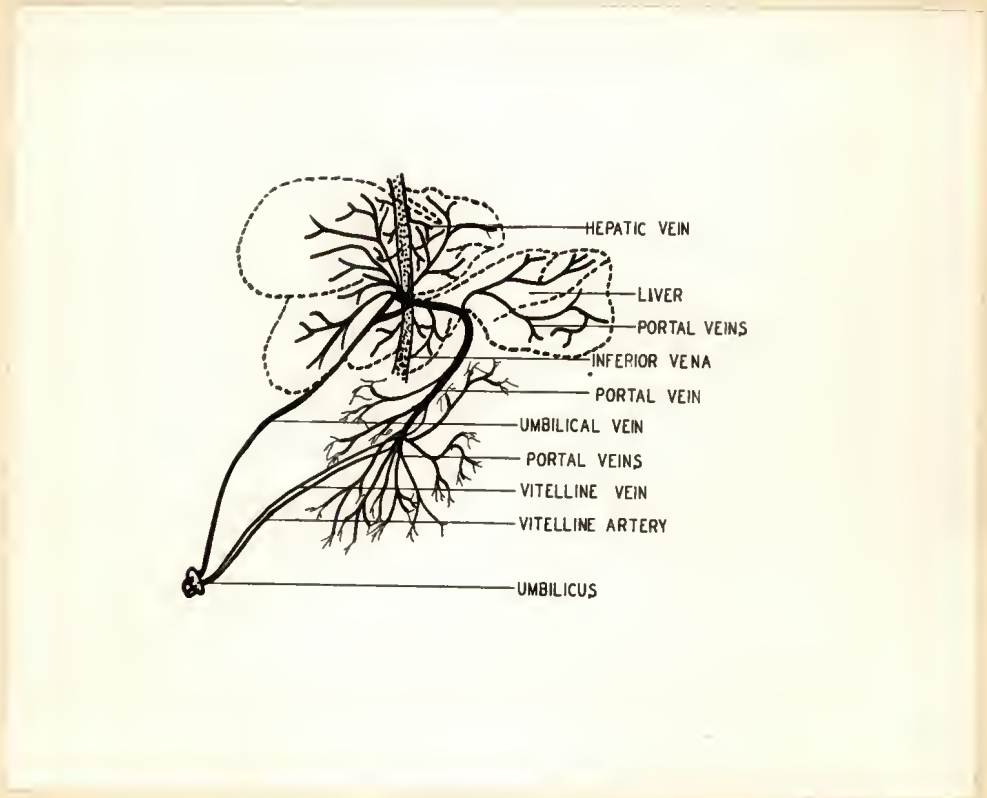

Fig. 3. Diagram showing the relations of the Umbilical Vein, the Portal Vein, and the Ductus Arteriosus within the Liver of the Guinea Pig.

EXPLANATION OF PLATE IV

Fig. 4. Diagram showing the Aorta and the Pulmonary Artery with the connecting Ductus Arteriosus in the Guinea Pig.

Fig. 5. Diagrams showing the progressive stages in the constriction of the Ductus Arteriosus in the Guinea Pig. a. 1 day; b. 2 day; c. 3 day.

Fig. 6. Diagrams showing the progressive stages in the obliteration of the lumen of the Ductus Arteriosus in the Guinea Pig. a. at birth; b. 1 day; c. 2 day; d. 3 day; e. 4 day.

PLATE IV

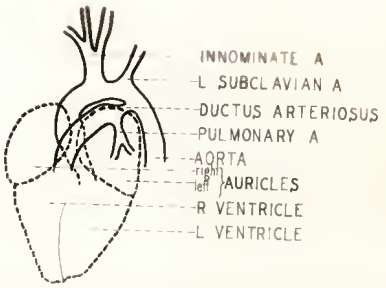

FIGURE 4 DIAGRAM OF HEART AND ADJACENT BLOOD VESSELS

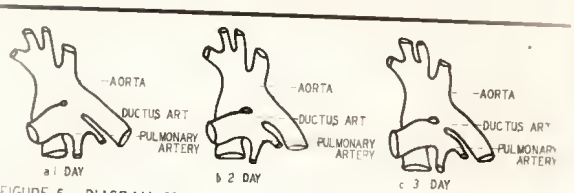

FIGURE 5 DIAGRAM OF THE DUCTUS ARTERIOSUS

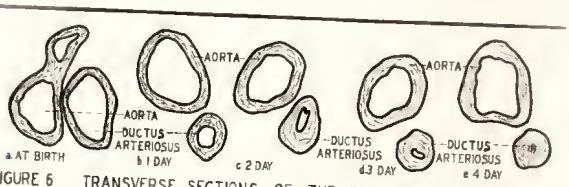

FIGURE 6 TRANSVERSE SECTIONS OF THE DUCTUS ARTERIOSUS

Date Due		