J. Physiol. (1956) 133, 202–212

THE FOETAL CIRCULATION AND ITS CHANGES AT BIRTH IN SOME SMALL LABORATORY ANIMALS

By J. J. HANDLER

From the Nuffield Institute for Medical Research, University of Oxford

(*Received* 17 *March* 1956)

The course of the foetal circulation has been studied by cineangiographic methods in the sheep (Barclay, Barcroft, Barron & Franklin, 1939), goat (Barclay, Franklin & Prichard, 1944) and man (Lind & Wegelius, 1954). The general conclusions as to the course of the foetal circulation in the sheep, and the changes which occur at birth, have been confirmed by measurements of the pressures and oxygen contents of blood in the great vessels, and by direct measurements of the changes in pulmonary blood flow on ventilation (Dawes, Mott, Widdicombe & Wyatt, 1953; Dawes, Mott & Widdicombe, 1954, 1955). However, little is known of these matters in smaller laboratory animals, some of which, such as the dog, rabbit and cat, are born in a relatively immature state. The introduction of the X-ray image amplifier and the use of condenser manometers has now made such investigations practicable.

The mechanism of closure of the ductus arteriosus is of particular interest. Strassmann (1894) supposed that there was a valve at the junction of the ductus arteriosus and aorta, which prevented blood from flowing from the aorta through the ductus. Strassmann reported the presence of this valve in man, dogs and cats. Woodbury, Hamilton & Woods (1935) and Hamilton, Woodbury & Woods (1937) confirmed its existence in rabbits and dogs, but Harman & Herbertson (1938) and Kennedy & Clark (1941) did not find it in guinea-pigs. It certainly does not exist in sheep (Barclay *et al.* 1944; Born, Dawes, Mott & Rennick, 1956). It therefore seemed desirable to study its anatomy once more in dogs and rabbits, and to determine whether it was competent to prevent blood flow from the aorta into the ductus arteriosus.

METHODS

Cineangiography in foetal dogs. Six pregnant dogs (10·6–17·9 kg) of about 58 days gestation (full-term 58–63 days) were anaesthetized with sodium pentobarbitone in a dose of 30 mg/kg intravenously. The maternal carotid pressure was recorded with a mercury manometer. The

foetuses (nineteen in number) were delivered by Caesarean section, with precautions against any undue tension on the umbilical cord, which was protected with gauze moistened in warm saline. Breathing was prevented by pulling a rubber bag filled with amniotic fluid or warm saline over the head. The foetus was kept warm and was placed, usually in a lateral position, on a Philips X-ray image intensifier, level with or just below the placenta. Indirect cineradiographs were taken at 25 frames/sec, using a 35 mm camera (Ardran & Wyatt, 1954). As contrast medium thorium dioxide (Thorotrast; Heyden Chemical Co.) was used in a volume of 0·15–1·0 ml. (usually 0·25 ml. or less). It was injected either into a catheter passed down an external jugular vein into the superior vena cava, or directly into the umbilical vein. When both superior and inferior vena caval blood flows were depicted in the same foetus, the umbilical injections was given *after* the jugular, as bleeding from the umbilical vein on withdrawal of the needle could not be controlled. Injections into the aortic arch were made through a catheter introduced into the left carotid artery. All films were examined both on projection and as stills.

In ten foetuses carotid arterial blood samples were obtained on an average 5 min before the injection of thorotrast, by direct arterial puncture or after cannulation with a polythene catheter. The samples were mixed with a small quantity of heparin (20%) and sodium fluoride (4%) and were kept at 0° C. They were analysed for their oxygen contents and capacity by the method described by Born, Dawes & Mott (1955) using 0·2 ml. samples and 0·3 ml. of buffer solution.

Positive pressure ventilation of the rabbit, dog and cat foetus. Thirteen rabbit, six dog and three cat foetuses were used. The rabbits were at 28–31 days gestation. Five of the puppies were at 55–60 days, while one was at a much earlier gestational age, judging by its weight, crown-rump length and general appearance. The kittens were all at 55–60 days gestation. The maternal rabbits and dogs were anaesthetized with sodium pentobarbitone, 30–40 mg/kg intravenously, followed where necessary by a little ether. The cats were anaesthetized with chloralose, 60 mg/kg, after ethyl chloride induction. The maternal carotid blood pressure was recorded with a mercury manometer.

The foetuses were delivered by Caesarean section, and the trachea was cannulated. Foetal blood pressure was recorded from a carotid artery by a no. 20 or 21 Luer needle attached to the gauge-head of a condenser manometer. Heparin was injected into the gauge-head to mitigate clotting. The damped natural frequency of the needle and gauge-head was about 50 c/s. The pressure record was displayed on a cathode-ray tube (which was photographed at intervals), and also on meters reading directly in mm Hg (mean pressure). The photographic records were measured with a travelling microscope and are estimated to have a possible absolute error of ± 2 mm Hg and a probable absolute error of ± 1 mm Hg.

After allowing the preparation to become stable, the fluid present in the upper air passage was sucked out and positive pressure ventilation was begun, using a Palmer Miniature Ideal respiration pump (total capacity, 25 ml.) at a frequency of 38–40 strokes/min. The stroke volume varied from 2 to 8 ml. according to the size of the foetus.

RESULTS

Cineangiographic observations on foetal puppies

In ten foetal puppies the carotid O_2 saturation ranged from 19 to 68%, and in seven of them it exceeded 50% (Table 1). The majority of these puppies were therefore in satisfactory condition. Barcroft, Barron, Cowie & Forsham (1940) recorded a value of $49{\cdot}1 \pm 9{\cdot}7$% for seven lambs over 130 days of gestation, while that of Dawes *et al.* (1954), $62{\cdot}3 \pm 5{\cdot}3$%, is rather higher. The low figure of 19% recorded in one foetal puppy confirmed the poor state of the umbilical cord which was observed at that time; this particular sample was, however, taken about 15 min *after* injection of Thorotrast.

External jugular vein injection. The contrast medium, entering the heart from the anterior (superior) vena cava, passed through the right side of the heart, leaving it along the ductus arteriosus and pulmonary arteries, and producing a picture (Pl. 1, fig. 1) in twelve out of thirteen instances which is similar to that shown by Barclay *et al.* (1944) in the lamb. In the thirteenth injection, the antero-posterior position of the foetus precluded observation of the usual appearance, but even here it was seen that flow proceeded through the right ventricle. Pl. 1, fig. 1, also confirms the conclusion of Franklin (1948), based on post-mortem dissection, that the anterior vena caval flow in the dog foetus proceeds directly to the right atrio-ventricular orifice, without any reflected component. Flow through the pulmonary arteries was only seen after nine jugular injections, because of the small calibre of the vessels and the limit to the amount of contrast medium which could be injected without producing undesirable pressure changes.

TABLE 1. Carotid O_2 saturation of foetal puppies from three litters

Foetus	Carotid arterial % O_2 saturation	Foetus	Carotid arterial % O_2 saturation
A1	55	B4	66
A2	55·5	B6	59
A3	19*	B7	55
A4	40·6	C1	68
B1	53	C3	31

* Umbilical cord in poor condition.

Retrograde flow past the crista interveniens (tubercle of Lower) and down the thoracic inferior vena cava (Pl. 1, fig. 2) occurred after eight of the thirteen injections, and resulted in the appearance of Thorotrast in the left heart, as indicated by opacification of the arch of the aorta, in five instances. However, this flow through the aortic arch could not account for the descending aortic shadow seen *almost immediately* after entry of the contrast medium into the right ventricle. These records also showed that in the dog, unlike the sheep, there is an appreciable space between the aortic arch and ductus arteriosus on lateral or oblique projection. The descending aorta and the umbilical arteries were often shown and it was obvious that the umbilical (not the iliac) arteries are the true terminations of the aorta in the foetus.

Umbilical vein injection. In all five puppies Thorotrast passed up the umbilical vein to the liver and thereafter entered the thoracic inferior vena cava both directly by way of the ductus venosus, and indirectly, after traversing part of the liver, by the hepatic veins. Pooling of the contrast medium was always seen at a point just distal to where it entered the thoracic vena cava, corresponding to the anatomical sinus present at this level (Barclay *et al.* 1944, p. 170). The part of the liver vessels outlined by the umbilical venous flow corresponded with the arrangement which Barclay *et al.* (1944)

described in lambs (Pl. 1, fig. 3). The ductus venosus, on lateral projection, appeared as a straight line rather than the angled structure seen in fig. 34*c* of Barclay *et al.* (1944). The Thorotrast usually proceeded to the far end of the portal sinus (sinus intermedius). It is unfortunate that the small size of the puppies prevented mesenteric venous injections from being made, in order to depict the portal venous distribution.

When it reached the heart the stream of contrast medium was split into two by the crista dividens (Pl. 1, fig. 4). The further course of the right-hand stream through the right atrium and ventricle was impossible to follow, because the small volume of medium traversing this route cast such a faint shadow. The left-hand stream passed from the inferior vena cava through the foramen ovale, into the left heart, round the aortic arch and down the descending aorta.

Changes on ventilation

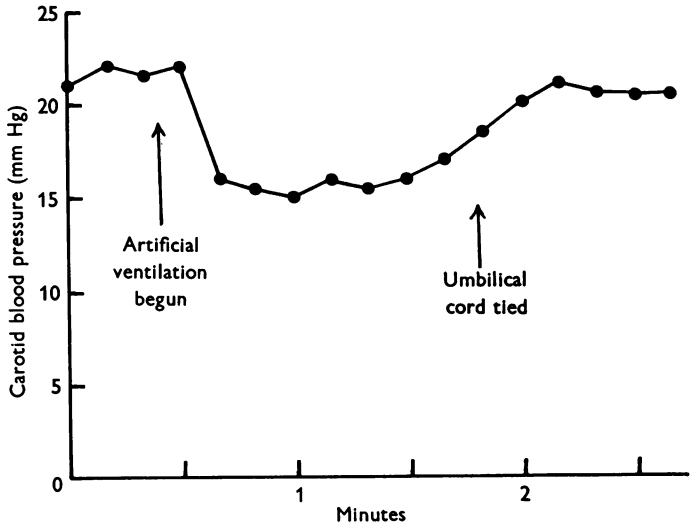
Blood pressure. The stroke of the respiration pump was adjusted so that the chest was gently expanded. Ventilation was adequate, as shown by the carotid arterial O_2 saturation, which exceeded 85% in three out of four rabbits, 10 min after tying the cord and beginning ventilation. Post-mortem examination showed no evidence of over-distension of the lungs.

The carotid arterial blood pressure in mature foetal rabbits is about 20 mm Hg, and in ten out of fourteen rabbits there was an immediate fall on ventilation (Table 2, Text-fig. 1). In one other rabbit no record was taken, but the pressure was also seen to fall. In five mature foetal puppies and three kittens there was also a fall in blood pressure on ventilation. This fall is attributable to an increase in pulmonary vascular conductance, such as has been demonstrated directly in the lamb (Dawes *et al.* 1953). All these foetuses were pink and in good condition.

By contrast, in four rabbits, in which umbilical flow had almost ceased, ventilation caused a rise of blood pressure. These were the four rabbits with the lowest heart rates. When the umbilical circulation is impaired the heart slows and the blood pressure begins to fall, but only very gradually. These rabbits were partly asphyxiated, and the rise of blood pressure is a measure of the recovery of their heart and circulation.

In general, tying the umbilical cord some minutes after ventilation had begun caused an immediate small rise of blood pressure, such as would be expected from interruption of blood flow through any large fraction of the peripheral vascular bed.

In one puppy the thorax was opened 33 min after beginning ventilation. The aortic and pulmonary arterial pressures were recorded simultaneously by needles plunged through the vessel wall. They were 35 and 21 mm Hg respectively. A similar large pressure difference between the two vessels was observed in four other puppies which had breathed spontaneously after natural



Text-fig. 1. Mature rabbit foetus, delivered by Caesarean section 14 min. Positive pressure ventilation caused a fall in systemic blood pressure.

TABLE 2. Changes in mean blood pressure on ventilation of foetuses for the first time

	Heart rate* (beats/min)	Blood pressure (mm Hg) Initial	After ventilation	Change (%)
Rabbit	248	17	12	-29·4
	186	18·5	10	-47
	222	22	15	-32
	60	8·5	26	+206
	108	24	32	+33
	108	19·5	25	+28
	114	19	15	-21
	300	21	13	-38
	192	19	16	-15·8
	192	18	15	-16·7
	234	22·5	18	-20
	66	20	34	+70
Dog	186	35	28·5	-18·5
	126	48	30·5	-36·5
	198	29	18·5	-36
	108	31·5	29	-8
	186	46	36	-22
Cat	120	18	13·5	-25
	228	26·5	20·5	-23
	264	31·5	26·5	-15·9

* Heart rate denotes the level recorded just before beginning ventilation.

delivery 17–26 hr previously. In one of the latter, and in one other puppy, a murmur was heard on auscultation over the ductus.

Cineangiographic observations on ventilated puppies. After ventilation the pulmonary vessels filled more rapidly and more completely, though the Thorotrast could not be seen in the smaller branches (compare Pl. 1, figs. 1 and 5). This is in accord with the observations of Barclay, Barcroft, Barron, Franklin & Prichard (1942) and of Reynolds, Ardran & Prichard (1954) in sheep.

TABLE 3. Cineangiographic observations on blood flow through the ductus arteriosus in new-born puppies after ventilation

Site of injection	Foetus	Time after ventilation (min)	Flow seen through ductus arteriosus
Jugular vein	1	10	Yes
	2	15	Yes
	3	15	Yes
	4	18	Yes
	5	25	Yes
	6	230*	Yes
	7	10	No
	8	20	No
	9	285*	No
	9	285*	No
Carotid artery	8	28	Yes
	10	30	Yes
	10	40	Yes
	5	45	Yes
	6	256*	Yes
	9	290*	Yes

* Spontaneous breathing.

Apart from changes in the lungs, the principal interest in the course of the circulation in the new-born puppy centres round the flow of blood through the ductus arteriosus. Table 3 shows that after six out of ten jugular injections contrast medium was seen to pass through the ductus arteriosus and into the descending aorta between 10 and 230 min after ventilation. In the remaining four puppies there was no evidence of the passage of contrast medium through the ductus, and in two of these a 'stub' was seen at the point where the ductus springs from the pulmonary trunk, similar to that observed by Barclay *et al.* (1944) in lambs. In one or two instances Thorotrast passed from the right ventricle into the descending aorta through the ductus arteriosus, and then travelled some little distance up the arch of the aorta. This finding tends to support the statement of Burchell, Swan & Wood (1953) that, in human beings with a patent ductus arteriosus and pulmonary hypertension, there may be cyanosis of the left arm.

After all six carotid injections, Thorotrast was seen to pass from the aorta along the ductus arteriosus towards the pulmonary arteries, but in only two

puppies were the latter seen (Pl. 1, fig. 6). This was perhaps because of dilution of Thorotrast with non-opaque blood from the right ventricle.

Hamilton *et al.* (1937) suggested that there was a valve at the aortic end of the ductus arteriosus which prevented blood passing from the aorta to the lungs, in new-born puppies and rabbits. In the present experiments, saline, indian ink or air injected into the descending aorta passed with equal facility along both the aortic arch and the ductus arteriosus. After injection of indian ink a heavy deposit of pigment was seen in the lungs. In some animals the ductus arteriosus had constricted. This constriction was always at a point proximal to the junction between ductus and aorta, and the indian ink or saline travelled along the ductus as far as the point of constriction. Examination of the junction afterwards showed no evidence that excessive force had torn a valve.

Specimens of this area were examined from fifty-eight foetal or new-born rabbits and thirty foetal dogs. The union between ductus arteriosus and aorta resulted in the formation of a ridge (the crista reuniens) which had a well-defined, rather blunt, crescentic margin, with the concavity of the crescent directed distally (Pl. 2). This is very different from the 'flap-like structure' described by Hamilton *et al.* (1937). In fact, the ridge is merely the distal edge of the party wall at the point where the ductus arteriosus and the aortic arch meet to form the descending aorta. In Pl. 2 it can be seen that the ductus is constricted at a point which is an appreciable distance proximal to the crista reuniens. There is no evidence that the crista reuniens can act as a valve, and it must therefore be the muscular wall of the ductus arteriosus which causes constriction, as in the lamb (Barclay *et al.* 1944; Barcroft, 1946; Born *et al.* 1956).

DISCUSSION

The course of the circulation through the principal vessels of the dog foetus near term, as seen on cineangiography, corresponds closely with that previously described in the sheep and the goat foetus (Barclay *et al.* 1943). These findings are, however, at variance with the inferences drawn by Everett & Johnson (1950) who injected a radioactive phosphorus solution into the umbilical or external jugular vein of puppies near term. Simultaneous blood samples were taken from the ventricles. From measurements of the radioactivity of these samples, it was concluded that superior vena caval flow proceeded directly both to the right ventricle and, through the foramen ovale, to the left ventricle in the proportion of 3·4:1. They did not, however, consider the influence of an appreciable pulmonary circulation on these results. Thus, blood flow through the lungs after superior caval injection might account for recovery of material from the left ventricle. It is also apparent from the cineangiographic records that when a solution is injected too rapidly into the superior vena cava, some

of the material may flow past the tubercle of Lower into the thoracic inferior vena cava, and so reach the left side of the heart.

We may conclude that, under normal circumstances; (i) superior vena caval blood flows only to the right side of the heart and does not pass through the foramen ovale, (ii) the output of the right ventricle travels mainly through the ductus arteriosus and also in part through the lungs, (iii) the umbilical arteries are large and are the true terminal branches of the aorta in the foetus, (iv) the inferior vena caval flow divides, on the crista dividens, into a major left and a minor right terminal stream, and (v) blood leaving the left ventricle proceeds round the aortic arch and down the descending aorta as well as to the heart, the head and the fore-quarters.

The fall in systemic arterial blood pressure, seen in the normal mature rabbit, dog and cat foetus on beginning ventilation of the lungs, is probably due to an increase in pulmonary blood flow as in the sheep (Dawes *et al.* 1953). Woodbury *et al.* (1935) and Hamilton *et al.* (1937) stated that right ventricular pressure fell on ventilating dog and rabbit foetuses. However, both Abel & Windle (1939) and Smith & Kaplan (1942) pointed out that their records showed that both pressures *rose*, though the right rose less than the left. In four rabbit foetuses in the present paper, ventilation did indeed cause a *rise* in systemic arterial pressure. But these were the foetuses with the lowest heart rates, and there is good reason to believe that they had a low umbilical flow and were severely asphyxiated. Woodbury *et al.* (1935) also observed that there was no change in blood pressure when the umbilical cord was tied in their experiments, and thence inferred that umbilical flow must have been much reduced. Therefore, while adequate ventilation of the lungs causes a fall of blood pressure in dogs or rabbits which are in good condition, it may cause a rise when they are asphyxiated. This is probably attributable to an increase in cardiac output as asphyxia is relieved. These observations do not necessarily imply that there is a fall in pulmonary arterial and systemic blood pressures when breathing begins in *unanaesthetized* subjects of all species. In lambs which breathe spontaneously there is usually an asphyxial rise of blood pressure after the umbilical cord is tied (Barcroft, 1938; Born *et al.* 1956). When asphyxia is prevented by adequate ventilation, the fall of pressure due to increased pulmonary flow is seen. Asphyxia does not cause a rise of blood pressure in rabbits (Bauer, 1939; Handler, unpublished) although it does in cats (Clark, 1932). No reliable data exist for the dog foetus at term. The response of each species may vary.

It is evident that for some time after birth the ductus arteriosus is patent in the puppy. The cineangiographic observations, which were made while the chest was intact, suggested that blood might flow in either direction according to the site of injection of the contrast medium. The limitations of cineangiography were discussed by Dawes *et al.* (1955), and they suggested that the

volume of contrast medium injected might sometimes disturb the pressure relations across the ductus arteriosus. Certainly, when the chest was opened some time after delivery the pressure in the pulmonary trunk was less than that in the aorta. So long as the ductus arteriosus is wide open, any change of pressure in the pulmonary artery will be communicated to the aorta. The fact that, within a short time of beginning breathing, the pressures differ so greatly in the new-born puppy, suggests that the ductus rapidly constricts or shuts. Woodbury *et al.* (1935) and Hamilton *et al.* (1937) attributed closure of the ductus to the action of a valve at its aortic end, consequent on the fall of pulmonary arterial pressure. No such valve exists. Although the crista reuniens may sometimes look like a valve, contrast medium, saline or indian ink readily passes through the ductus from aorta to the lungs. The mechanism of closure of the ductus has not been studied systematically in puppies, kittens or rabbits, but is probably due to the muscular contraction of the vessel wall.

SUMMARY

1. The course of the foetal circulation in mature foetal dogs, delivered by Caesarean section, was similar to that previously described in sheep, as shown by cineangiography.

2. Positive pressure ventilation of the lungs in mature foetal dogs, cats and rabbits usually caused a fall of blood pressure, which was attributed to an increase of pulmonary vascular conductance. In rabbits which were asphyxiated, because umbilical blood flow was impaired, ventilation caused a rise of blood pressure.

3. After ventilation the pulmonary vessels filled more rapidly and more completely in new-born dogs. Contrast medium passed in either direction through the ductus arteriosus according to the site of injection, although the pulmonary arterial pressure was less than that in the descending aorta. There was no functional valve at the aortic end of the ductus arteriosus in dogs or rabbits.

I wish to acknowledge the constant encouragement and help afforded by Dr G. S. Dawes. I am also grateful to Dr G. M. Ardran for advice on cineradiographic technique and to Dr D. G. Wyatt for instruction in the use of condenser manometers. For technical assistance, I am particularly indebted to Messrs T. G. Denton and G. K. Smith.

REFERENCES

ABEL, S. & WINDLE, W. F. (1939). Relation of the volume of pulmonary circulation to respiration at birth. *Anat. Rec.* **75**, 451–464.

ARDRAN, G. M. & WYATT, D. G. (1954). 35 mm ciné camera incorporating a Philips X-ray image intensifier. *J. Physiol.* **126**, 1–2*P*.

BARCLAY, A. E., BARCROFT, J., BARRON, D. H. & FRANKLIN, K. J. (1939). A radiographic demonstration of the circulation through the heart in the adult and in the foetus, and the identification of the ductus arteriosus. *Brit. J. Radiol.* **12**, 505–517.

BARCLAY, A. E., BARCROFT, J., BARRON, D. H., FRANKLIN, K. J. & PRICHARD, M. M. L. (1942). Pulmonary circulation times before and after functional closure of the ductus arteriosus. *J. Physiol.* **101**, 375–377.

BARCLAY, A. E., FRANKLIN, K. J. & PRICHARD, M. M. L. (1944). *The Foetal Circulation and Cardiovascular System, and the Changes that they Undergo at Birth.* Oxford: Blackwell Scientific Publications Ltd.

BARCROFT, J. (1938). *The Brain and its Environment.* New Haven: Yale University Press; London: Humphrey Milford, Oxford University Press.

BARCROFT, J. (1946). *Researches on Pre-natal Life.* Oxford: Blackwell Scientific Publications Ltd.

BARCROFT, J., BARRON, D. H., COWIE, A. T. & FORSHAM, P. H. (1940). The oxygen supply of the foetal brain of the sheep and the effect of asphyxia on foetal respiratory movement. *J. Physiol.* **97**, 338–346.

BAUER, D. J. (1939). Vagal reflexes appearing in asphyxia in rabbits at different ages. *J. Physiol.* **95**, 187–202.

BORN, G. V. R., DAWES, G. S. & MOTT, J. C. (1955). The viability of premature lambs. *J. Physiol.* **130**, 191–212.

BORN, G. V. R., DAWES, G. S., MOTT, J. C. & RENNICK, B. R. (1956). The constriction of the ductus arteriosus caused by oxygen and by asphyxia in the newborn lamb. *J. Physiol.* **132**, 304–342.

BURCHELL, H. B., SWAN, H. J. C. & WOOD, E. H. (1953). Demonstration of differential effects on pulmonary and systemic arterial pressure by variation in oxygen content of inspired air in patients with patent ductus arteriosus and pulmonary hypertension. *Circulation*, **8**, 681–694.

CLARK, G. A. (1932). Some foetal blood-pressure reactions. *J. Physiol.* **74**, 391–400.

DAWES, G. S., MOTT, J. C. & WIDDICOMBE, J. G. (1954). The foetal circulation in the lamb. *J. Physiol.* **126**, 563–587.

DAWES, G. S., MOTT, J. C. & WIDDICOMBE, J. G. (1955). The patency of the ductus arteriosus in newborn lambs and its physiological consequences. *J. Physiol.* **128**, 361–383.

DAWES, G. S., MOTT, J. C., WIDDICOMBE, J. G. & WYATT, D. G. (1953). Changes in the lungs of the new-born lamb. *J. Physiol.* **121**, 141–162.

EVERETT, N. B. & JOHNSON, R. J. (1950). Use of radioactive phosphorus in studies of fetal circulation. *Amer. J. Physiol.* **162**, 147–152.

FRANKLIN, K. J. (1948). *Cardiovascular Studies.* Oxford: Blackwell Scientific Publications Ltd.

HAMILTON, W. F., WOODBURY, R. A. & WOODS, E. B. (1937). The relation between systemic and pulmonary blood pressures in the fetus. *Amer. J. Physiol.* **119**, 206–212.

HARMAN, M. T. & HERBERTSON, J. E. (1938). Concerning the postnatal obliteration of the umbilical vein and arteries, the vitelline vein and artery, and the ductus arteriosus in the guinea pig. *Trans. Kans. Acad. Sci.* **41**, 369–377.

KENNEDY, J. A. & CLARK, S. L. (1941). Observations on the ductus arteriosus of the guinea pig in relation to its method of closure. *Anat. Rec.* **79**, 349–371.

LIND, J. & WEGELIUS, C. (1954). Human fetal circulation: changes in the cardiovascular system at birth and disturbances in the post-natal closure of the foramen ovale and ductus arteriosus. *Cold Spr. Harb. Symp. quant. Biol.* **19**, 109–125.

REYNOLDS, S. R. M., ARDRAN, G. M. & PRICHARD, M. M. L. (1954). Observations on regional circulation times in the lamb under fetal and neonatal conditions. *Contr. Embryol. Carneg. Instn*, **35**, 73–92.

SMITH, C. A. & KAPLAN, E. (1942). Adjustment of blood oxygen levels in neonatal life. *Amer. J Dis. Child.* **64**, 843–859.

STRASSMANN, P. (1894). Anatomische und physiologische Untersuchungen über den Blutkreislauf beim Neugeborenen. *Arch. Gynaek.* **45**, 393–445.

WOODBURY, R. A., HAMILTON, W. F. & WOODS, E. B. (1935). Respiratory changes in the right and left ventricular pressure before and after the adult circulation is established, with a note on the diastolic and systolic pressures of the white mouse. *Amer. J. Physiol.* **113**, 139 (Proc.)

EXPLANATION OF PLATES

PLATE 1

Fig. 1. Foetal puppy. Cineangiogram after injection of Thorotrast into an external jugular vein: to show flow through the right heart to the descending aorta.

Fig. 2. As fig. 1, to show retrograde flow from the superior vena cava past the tubercle of Lower into the inferior vena cava.

Fig. 3. Foetal puppy. Cineangiogram after injection of Thorotrast into the umbilical vein: to show flow through the liver.

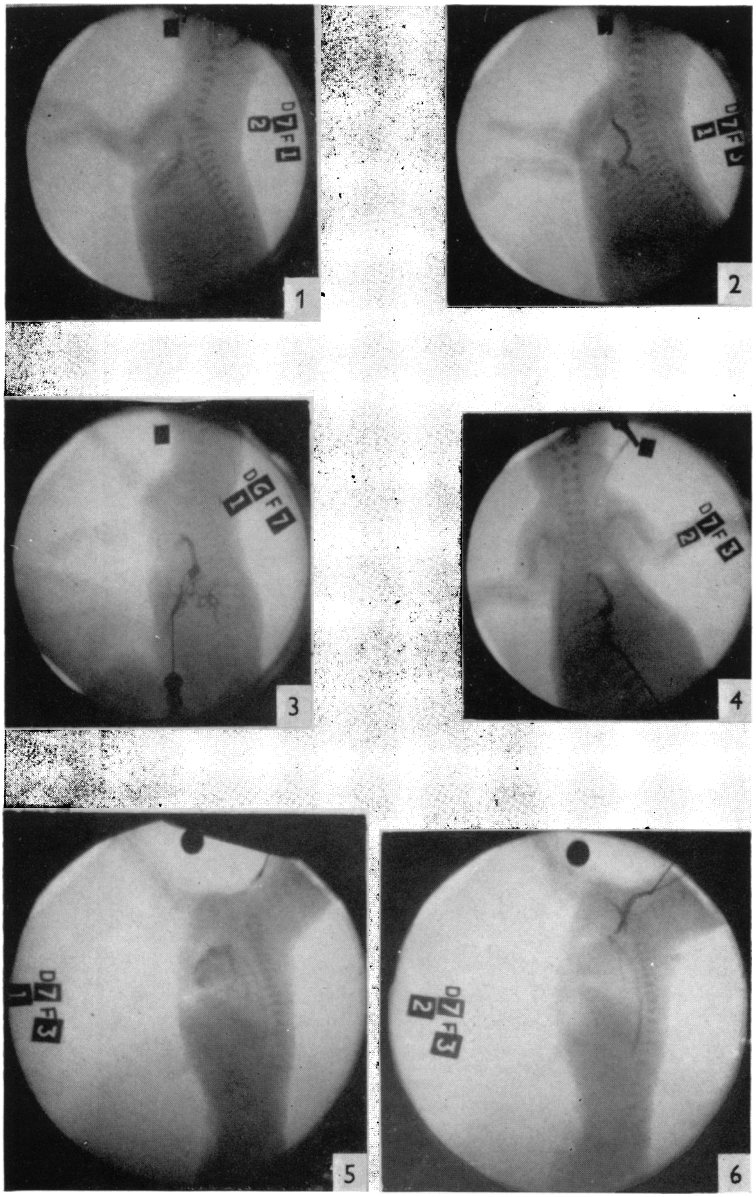
Fig. 4. As fig. 3, to show flow to either side of the crista dividens as the contrast medium enters the heart.

Fig. 5. New-born puppy, breathing spontaneously, about 4 hr old. Cineangiogram after injection of Thorotrast into a jugular vein: to show good pulmonary blood flow and passage of contrast medium from the pulmonary trunk down the descending aorta.

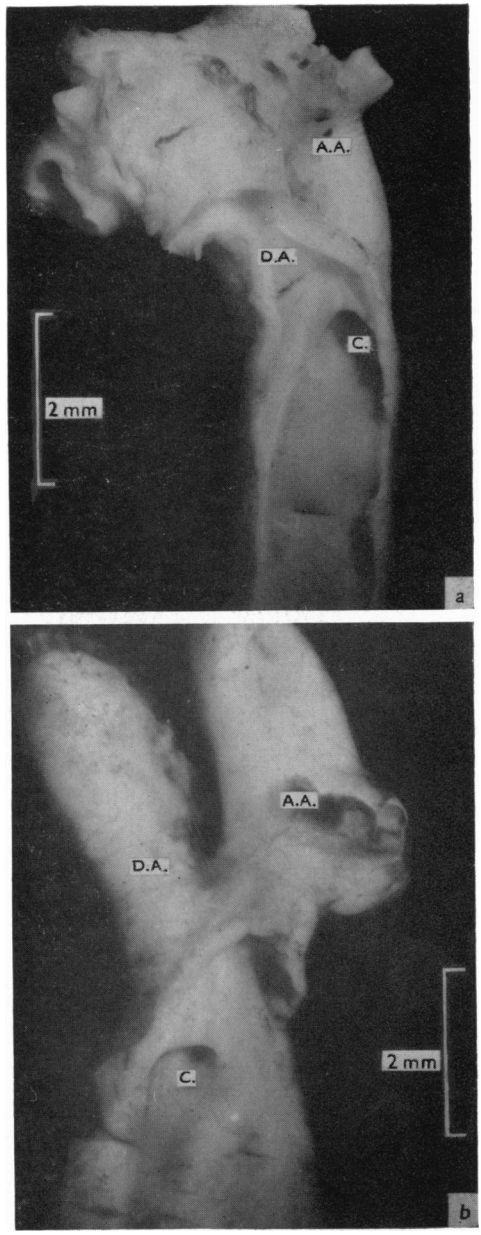
Fig. 6. As fig. 5, some minutes later. Cineangiogram after injection of Thorotrast into the aortic arch: to show passage of contrast medium down the descending aorta and simultaneously into a pulmonary artery.

PLATE 2

Photographs of the crista reuniens (C) in two mature foetal rabbits. In *a* the ductus arteriosus (D.A.) has been slit open; the ductus is partially constricted. In *b* the aortic arch (A.A.) has been opened to show the crista reuniens from the other side.



(*Facing p.* 212)


A.A.
D.A.
C.
2 mm
a
A.A.
D.A.
2 mm
C.
b