

# PATENT DUCTUS ARTERIOSUS WITH PULMONARY HYPERTENSION

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In most cases of patent ductus arteriosus the diagnosis is readily made on recognition of the typical murmur. In some, however, the continuous murmur is lacking, and a systolic murmur only, of variable loudness, is heard at the pulmonary area. This is not uncommon in infants and young children, who may later develop the characteristic murmur (Gilchrist, 1945). Occasionally the continuous murmur is absent in adults in whom patency of the ductus is found subsequently at autopsy: in such cases the state of the pulmonary arteries and the presence of right ventricular hypertrophy may indicate that the pulmonary arterial pressure was much raised in life (Holman, 1925; Keys and Shapiro, 1943 (Case 3); Chapman, 1944; Douglas *et al.*, 1947; Ulrich, 1947). As a result, the pressure gradient between the aorta and the pulmonary artery may be so diminished that the blood flow along the ductus is insufficient to set up a continuous murmur. In extreme examples the pressure in the pulmonary artery may exceed that in the aorta, causing a reversal of the usual left to right shunt (Johnson *et al.*, 1950; Campbell and Hudson, 1951; Dammann *et al.*, 1953).

Three cases of patent ductus arteriosus complicated by severe pulmonary hypertension are presented here. The diagnosis was made in each on cardiac catheterization. In two, pulmonary hypertension caused reversal of the shunt; in the third the shunt was not reversed, but there was, in addition, coarctation of the aorta.

*Case 1.* A woman, aged 27, had dyspnoea on effort for many years. At the age of 5 she had had chorea, but no cardiac abnormality was ever noted in childhood. In the past two years dyspnoea had become worse, and she developed slight cyanosis. On examination no colour difference was seen between the hands and feet, and there was no clubbing of the fingers or toes. The apex beat was not displaced; the second sound was accentuated and closely split at the pulmonary area, where a faint systolic murmur was also heard. Radioscopy showed enlargement of the right atrium and ventricle, and the main and right pulmonary arteries were enlarged and pulsating. The electrocardiogram showed marked right ventricular hypertrophy.

On cardiac catheterization the tip of the catheter passed readily from the pulmonary artery into the aorta in the position typical of passage through a ductus arteriosus (Bouchard *et al.*, 1951). Pressures (capacitance manometer) and blood oxygen content and capacity (Haldane) were as follows:

	Pressure mm./Hg	Oxygen content ml./l.	Oxygen satn. percentage
Superior vena cava .. .. .	—	126	58
Inferior vena cava .. .. .	—	104	48
Right atrium (2 positions) .. .	7	115	53
Right ventricle (2 positions) .. .	150/5	115	53
Right pulmonary artery .. .. .	150/88	115	53
Descending aorta .. .. .	130/92	163	75
Descending aorta (after breathing O <sub>2</sub> for 5 min.) .. .. .	130/92	173	79
Left radial artery } 5 days .. .. .	—	201	92
Right femoral artery } later .. .. .	140/94	163	75

Blood oxygen capacity: 218 ml./l.    Oxygen consumption: 228 ml./min.  
Pulmonary blood flow: 2.65 l./min.    Total pulmonary resistance: 3300 dynes. sec. cm<sup>-5</sup>.

There was, therefore, a shunt from the pulmonary artery into the aorta, for pulmonary arterial pressure exceeded that in the aorta, and a reduced oxygen saturation was found in the descending aorta and femoral artery, and was not fully corrected by breathing oxygen.

*Case 2.* A girl, aged 9, had always had some dyspnoea on effort. She was able to lead a normal life, although strenuous effort caused considerable dyspnoea and cyanosis. At rest in bed, cyanosis was visible in the feet but not in the hands, and there was clubbing of the toes but not of the fingers. The apex beat was not displaced; the second sound was loud and closely split at the pulmonary area, and a moderately loud systolic murmur was heard all over the præcordium. Radioscopy showed enlargement of the right atrium and ventricle, and of the pulmonary arteries, with pulsation of the main branches. The cardiogram showed right ventricular hypertrophy.

On cardiac catheterization the tip of the catheter passed from the pulmonary artery into the aorta in the position typical of passage through a ductus arteriosus. The pressure in the right ventricle was 120/6, in the left pulmonary artery 120/70, and in the aorta 120/84 to 130/90 mm./Hg.

On another occasion, under nitrous oxide and oxygen anaesthesia, blood samples were withdrawn simultaneously from the carotid and femoral arteries. Oxygen content was estimated by van Slyke's method, the results being uninfluenced by the presence in the blood of nitrous oxide. The O<sub>2</sub> saturation in the carotid artery was 68 per cent and in the femoral artery 52 per cent.

Thus, on cardiac catheterization, the aortic and pulmonary arterial pressures were approximately equal, but at other times the colour of the limbs and analysis of arterial blood samples showed that blood flowed from the pulmonary artery into the aorta.

*Case 3.* A man, aged 25, was noted to have a heart murmur at the age of 10, but had no symptoms until he developed dyspnoea on effort at the age of 14. A year later he began to have cramp-like pains in the thigh muscles on effort. Systemic hypertension was found at the age of 23, when a diagnosis of coarctation of the aorta was made. On examination no cyanosis or clubbing of the fingers was seen, but his hæmoglobin level was 130 per cent. There was an asymmetrical shallow depression of the sternum and adjoining ribs on the right side. The apex beat was in the fifth intercostal space one inch beyond the mid-clavicular line. The pulmonary second sound was accentuated but not widely split; there was a moderately loud systolic murmur at the apex, and a high pitched early diastolic murmur at the left sternal border. The femoral pulses were palpable but poor compared with the brachial pulses; blood pressure in the arm, by sphygmomanometer, was 180/90, and in the leg systolic pressure was 120 mm./Hg.

Radioscopy showed considerable cardiac enlargement, involving both ventricles; the pulmonary artery was greatly enlarged, and it and its main branches were pulsating. A radiogram showed calcification in the wall of the main pulmonary artery; there was no rib notching (Fig. 1). The cardiogram showed right ventricular hypertrophy and incomplete right bundle branch block (Fig. 3).

On cardiac catheterization the catheter was passed along a patent ductus arteriosus into the aorta (Fig. 2), and the findings were as follows:

	Pressure mm./Hg	Oxygen content ml./l.	Oxygen satn. percentage
Right atrium .. .. .	10/0	134	59
Right ventricle (high) .. .. .	160/5	160	71
Pulmonary artery .. .. .	160/70	160	71
" Pulmonary capillary " .. .. .	12	—	—
Aorta, descending .. .. .	120/90	217	96
Left femoral artery .. .. .	120/85	217	96
Right brachial artery .. .. .	160/80	216	95

Blood oxygen capacity: 227 ml./l. Oxygen consumption: 394 ml./min.

Pulmonary blood flow: 6.9 l./min. Systemic blood flow: 4.7 l./min.

Pulmonary arteriolar resistance 1135 dynes. sec. cm.<sup>-5</sup> and total pulmonary resistance 1275 dynes. sec. cm.<sup>-5</sup>

As the catheter tip was withdrawn from the aorta back into the pulmonary artery the recorded pressure rose suddenly. Although the pulmonary arterial pressure clearly exceeded that in the descending aorta there was no evidence of a shunt from the pulmonary artery into the aorta. From this it was inferred that the ductus entered the aorta at or proximal to the site of coarctation, i.e. it entered that part of the aorta where the pressure was high. There evidently was a shunt from the aorta into the pulmonary artery, for the pulmonary arterial blood was richer in oxygen than that from the right atrium. The right ventricular blood sample, which was withdrawn from a point in the outflow tract, was similarly enriched as compared with right atrial blood, suggesting that the pulmonary valve was incompetent. The coarctation was

obviously not severe, for the catheter had passed through it into the descending aorta, and this explained the absence of rib notching.

At thoracotomy (Mr. R. Belsey) a greatly dilated and tense pulmonary artery was found, with a patent ductus arteriosus about 3 cm. in length and 0.5 cm. in external diameter, entering the aorta at the site of coarctation. Direct pressure records from the aorta and pulmonary artery gave results similar to those obtained at cardiac catheterization, though all were now somewhat lower. Temporary occlusion of the

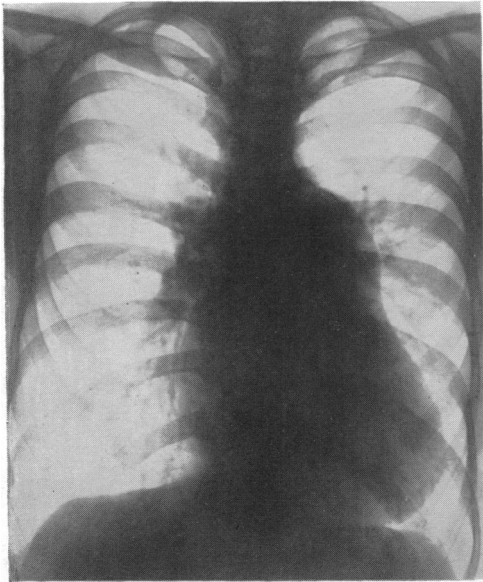


FIG. 1.—Case 3. Patent ductus, coarctation of aorta, and pulmonary hypertension. Tele-radiogram showing generalized cardiac enlargement. A line of calcification is seen in the wall of the main pulmonary artery; this and the right pulmonary artery are much dilated, and were seen to pulsate on radioscopy. The aortic knuckle is small and there is no rib notching.

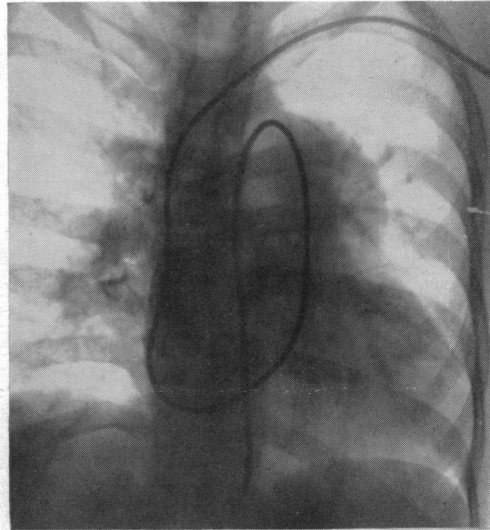


FIG. 2.—Case 3. The cardiac catheter has passed via the patent ductus through the coarctation into the descending aorta.

ductus caused a slight rise in pressure in the proximal aorta, but no significant fall in the pulmonary arterial pressure. Both the ductus and the coarctation were left *in situ*. Biopsy of the lung was performed, and microscopy showed great hypertrophy of the pulmonary arterial and arteriolar walls. In the arterial walls there was an increase in the muscle and elastic tissue in the media, with occasional small raised plaques of fibro-elastic tissue in the intima. The arteriolar walls showed hypertrophy of the media and thickening of the intima without plaque formation (Fig. 4).

#### DISCUSSION

Two main problems now arise. First, what is the connection, if any, between patency of the ductus arteriosus and pulmonary hypertension? and secondly, should the ductus be ligated?

Pulmonary arterial pressure is increased to a variable degree in the presence of a patent ductus. Usually this increase is small and appears to be due merely to the increased pulmonary blood flow, for in most cases of patent ductus arteriosus the pulmonary vascular resistance is normal or reduced (Dexter *et al.*, 1950; Wood, 1950; Wood, 1952). The patients described above were unusual in that their pulmonary arterial pressure and pulmonary vascular resistances were both greatly raised. There are few reports on the late effects of closure of the ductus upon pulmonary hypertension, but

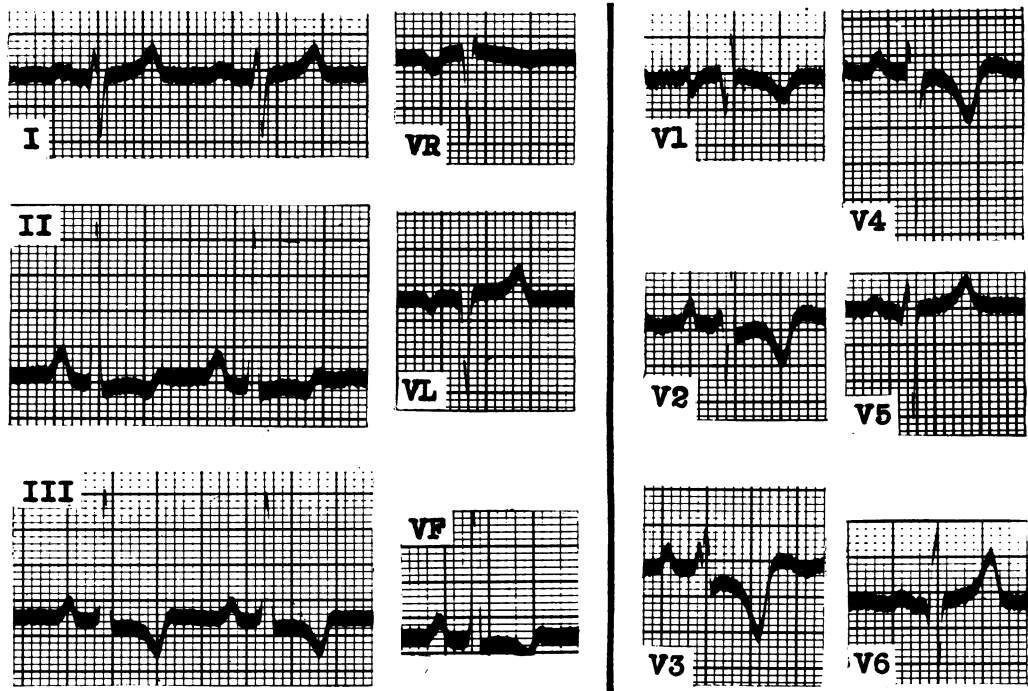


FIG. 3.—Case 3. Electrocardiogram showing right ventricular hypertrophy and incomplete right bundle branch block.

in two patients aged 3 and 6 years respectively (Cournand *et al.*, 1949; Voci *et al.*, 1951) pressure and resistance had fallen considerably some months after operation. This suggests that a sustained increase in pulmonary blood flow due to a patent ductus might cause in time an increase in pulmonary vascular resistance and a raised pulmonary arterial pressure. This is not the course of events, however, in typical cases of patent ductus arteriosus; only exceptionally has a patient with a classical continuous murmur been known to progress to severe pulmonary hypertension and loss of the murmur (Campbell and Hudson, 1952). It appears, rather, that those patients with severe pulmonary hypertension and a patent ductus arteriosus have always been atypical in that they have never been known to have a continuous murmur at an earlier stage. The relative frequency with which this combination occurs in children suggests that the pulmonary hypertension may be due to an inborn abnormality of function which resembles primary pulmonary hypertension, and is, perhaps, aggravated by the presence of the persistent ductus arteriosus.

The only conclusion that can be reached at present is that serious pulmonary hypertension is probably due to a separate abnormality, and is not merely secondary to persistence of the ductus arteriosus. There is some evidence, however, that pulmonary hypertension is made worse by the potency of the ductus, as it has on occasion been significantly relieved after closure of the ductus.

The second problem concerns the advisability of surgical closure of the ductus. In the presence of severe pulmonary hypertension operation carries an increased risk. Death has occurred at operation from tearing of a pulmonary artery (Johnson *et al.*, 1951) or in the period after the operation (Johnson *et al.*, 1950). Moreover, if the shunt through the ductus has been reversed by pulmonary hypertension, closure of the ductus will in theory increase the pulmonary arterial pressure still further. The patient reported by Swan *et al.* (1949) had a patent ductus and coarctation of the aorta, complicated by pulmonary hypertension causing reversal of the shunt. She died

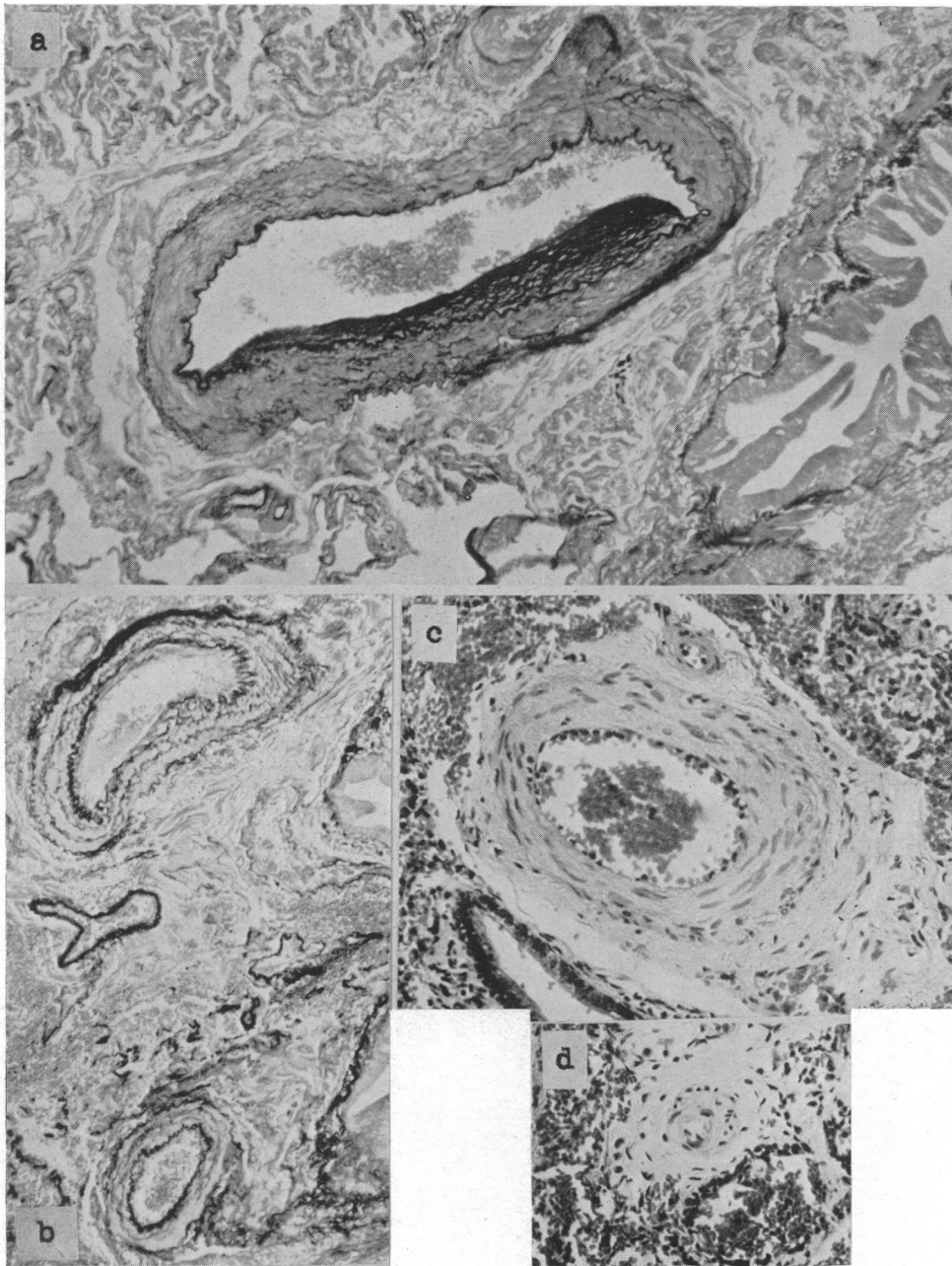


FIG. 4.—Case 3. Histology of pulmonary arteries. (a) and (b) ( $\times 100$ ): sections stained for elastic tissue show hypertrophy of the media and an increase in the elastic laminae with, in (a), a raised plaque of fibro-elastic tissue in the intima. (c) and (d) ( $\times 200$ ) show hypertrophy of the media and arteriosclerosis resembling that seen in systemic hypertension.

on the operating table shortly after ligation of the ductus, before resection of the coarctation could be attempted; autopsy showed an additional abnormality, an unsuspected congenital mitral stenosis. Another patient (d'Abreu, 1953), a woman of 26 with reversal of the shunt due to pulmonary hypertension, had the ductus ligated. She died on the following day with peripheral circulatory

failure and impalpable femoral pulses; there were no signs of congestive heart failure. On the other hand, successful operation and recovery have been reported in patients with pulmonary hypertension not severe enough to cause reversal of the shunt (Cournand *et al.*, 1949; Voci *et al.*, 1951; and Myers *et al.*, 1951).

It is dangerous, therefore, to ligate the ductus when pulmonary hypertension is severe enough to reverse the shunt, but while the shunt is still from the aorta into the pulmonary artery it is reasonable to ligate the ductus in the hope that pulmonary hypertension will later diminish.

The association of patent ductus with coarctation of the aorta is well known, and cases with pulmonary hypertension in addition are described by Edwards *et al.* (1949), Swan *et al.* (1949), Gotzsche *et al.* (1950), Taylor *et al.* (1950), and Johnson *et al.* (1951).

*Diagnosis.* The clinical recognition of the combination of patent ductus arteriosus with severe pulmonary hypertension is difficult. The symptoms are dyspnoea, possibly hæmoptysis, and cyanosis in the later stages. The signs are those of pulmonary hypertension with right ventricular hypertrophy: there is no continuous murmur, but there is a systolic murmur of variable intensity, generally maximal at the pulmonary area; the pulmonary second sound is accentuated but not widely split, and pulmonary valve incompetence may occur. The pathognomonic sign, of cyanosis greater in the lower limbs than in the upper, is only present when pulmonary hypertension is severe enough to reverse the shunt; this may occur intermittently, e.g. after effort. In the absence of this sign, confusion may occur with cases of atrial septal defect (although here there is usually right bundle branch block) and primary pulmonary hypertension. Confirmation may be sought by cardiac catheterization or angiocardiography. Even so, should the pulmonary arterial and aortic pressures be nearly equal the shunt may be so small that the diagnosis may be missed on cardiac catheterization if the catheter is not passed along the ductus into the aorta.

#### SUMMARY

Three patients are described in whom patency of the ductus arteriosus was accompanied by severe pulmonary hypertension. In two the shunt through the ductus was reversed, and in the third there was coarctation of the aorta. The diagnosis was made in all by passage of a catheter along the ductus into the aorta, and confirmed in one by thoracotomy. In none was the ductus ligated. The indications for operation and the relationship between patent ductus arteriosus and pulmonary hypertension are discussed.

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