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Localised coarctation of the aorta
An age dependent spectrum

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SUMMARY Localised coarctation of the aorta was studied histologically in 45 cases. The age range of the patients, from 2 weeks to 40 years, enabled us to make a comparison between early and late findings.

The basic histological architecture of all coarctations was identical. The ridge consisted mainly of thickening plus some infolding of the aortic wall. Ductal tissue formed the inner part of the ridge for more than half of its total circumference. In older cases masses of secondary intimal proliferation were present, which narrowed the residual lumen of the coarctation.

The coarctation was located preductally in most young patients and postductally in the majority of older patients.

It is concluded that ductal tissue is invariably present in the ridge and that all coarctations develop in a preductal position. Secondary changes include a gradual shift of the ridge from a preductal to a postductal position, and progressive narrowing of the residual lumen by intimal proliferation.

There is still controversy in the published reports concerning the aetiology of aortic coarctation, and the possible relation between coarctation and the ductus arteriosus. The fact that a coarctation of the aorta in its most typical form is located near the entrance of the ductus arteriosus into the aorta has led several investigators to study the possible relation between the two. Reports concerning the role of the ductus arteriosus in the aetiology of coarctation have been conflicting. Some authors[1-3] have given pathophysiological explanations for the development of a coarctation, suggesting it resulted from fetal flow abnormalities through the ductus arteriosus. Another hypothesis explaining the development of a coarctation is based on the presence of ductal tissue in the aorta, leading to narrowing of the aorta during the closing process of the ductus.[4] In histological studies ductal tissue was indeed found in the ridge of the coarctation by some investigators,[5 6] but whether ductal tissue plays an active part in the narrowing process has been questioned, since a coarctation can be present in combination with a widely patent ductus.[5] Some investigators[1 7 8] denied the presence of ductal tissue in the coarctation because they could not trace it in their histological studies.

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Bonnet[9] introduced the terms infantile and adult type of aortic coarctation to describe a long narrow segment and a sharp localised constriction, respectively. This classification does not account for the frequent finding of an adult type of coarctation in a newborn baby. We have chosen to use the terminology of Edwards *et al.*[7] and to refer to the long narrow segment as "tubular hypoplasia", and reserve the term "coarctation" for a sharp localised constriction (ridge or shelf). In the present study, which is confined to localised coarctation, special attention was paid to the following.

(1) The histology of the coarctation and the ductus arteriosus, and their possible relation.
(2) The level of the coarctation in the aorta and the site of entrance of the ductus arteriosus.

In contrast to several previous investigations,[1 5 6] we chose our material from a very wide age range, allowing comparison of young and old cases.

Subjects and methods

Forty-five specimens with aortic coarctation, most of them obtained at operation, were studied. The age range of the patients was from 2 weeks to 40 years (Table 1). Some of the specimens studied had been described earlier by Wielenga.[5] None of the patients

Table 1 *Coarctations*

Case No.	*Age*	*Site of coarctation in relation to ductus arteriosus*	*Patency of ductus arteriosus*	*Intimal proliferation*
1	2 w	Pre	+*	−
2	2 w	Para‡	−	+
3	2 w	Pre	−	−
4	4 w	Pre	−	−
5	5 w	Pre	−	−
6	5 w	Pre	−	−
7	6 w	Pre	−	−
8	2 mth	Pre	−	−
9	4 mth	Pre	+†	−
10	5 mth	Pre	−	+
11	9 mth	Post	−	++
12	2 y	Pre	−	+
13	3 y	Pre	−	+
14	3 y	Para	−	−
15	4 y	Para	−	+
16	4 y	Pre	+†	+
17	4 y	Para	−	+
18	4 y	Para	+†	+
19	5 y	Post	−	++
20	6 y	Post	−	+
21	6 y	Para	−	++
22	6 y	Para	−	+
23	7 y	Pre	−	+
24	8 y	Para	−	++
25	8 y	Para	+†	++
26	10 y	Para	−	++
27	12 y	Para	−	++
28	12 y	Pre	+†	+
29	12 y	Para	−	++
30	15 y	Para	−	+++
31	19 y	Post	−	+++
32	19 y	Post	−	+++
33	20 y	Post	−	+++
34	20 y	Para	−	++
35	21 y	Pre	−	++
36	21 y	Post	−	+++
37	21 y	Para	−	+++
38	23 y	Post	−	+++
39	26 y	Para	+†	++
40	26 y	Post	−	++
41	26 y	Post	+†	+++
42	29 y	Post	+†	+
43	34 y	Post	−	+++
44	38 y	Post	−	+++
45	42 y	Post	−	+++

Intimal proliferation: − not present, + minimal, ++ pronounced, +++ excessive.
* Normal ductal wall structure.
† Persistent type of ductal wall.
‡ Second stenosis in aortic arch, see text.

had complex intracardiac lesions, though in some of them a ventricular septal defect or a bicuspid aortic valve was present. Ten normal aortic arches were used as control material. Three of these specimens were derived from patients with a grossly normal aortic arch but with an intracardiac lesion. The remaining specimens were from patients who died of non-cardiac diseases (Table 2).

All specimens were fixed in formaldehyde 4% solution immediately in the operating room. They were completely serially sectioned and mounted on glass slides. The slides were stained alternately with haematoxylin and eosin, azan, and an elastic tissue stain. Special attention was paid to the possibility of ductal tissue being present in the aortic arch, and to the spatial relation between ductus and coarctation. In order to clarify this relation, graphic reconstructions were made of some of the specimens using the technique described by Tinkelenberg.[10]

Table 2 *Normal subjects*

Case No.	*Age*	*Intracardiac lesions*
1*	< 1 w	No
2*	< 1 w	No
3*	< 1 w	No
4	< 1 w	No
5	1 w	No
6	2 mth	Tetralogy of Fallot
7	3 y	No
8	1 y	VSD
9	1 y	VSD
10	13 y	No

* Prematures, gestational age 32 to 36 wk.
VSD, ventricular septal defect.

Results

NORMAL SUBJECTS: HISTOLOGY

In the first few months after birth the difference between the aortic and ductal wall was easily visualised, especially in the elastic tissue stains. In the aortic media ± 40 concentric elastic lamellae could be distinguished, with smooth muscle cells in between. The aortic intima was thin; only a few cellular layers were found underneath the endothelium. The ductus arteriosus was built as a muscular artery. Its media consisted principally of smooth muscle cells and was very poor in elastic tissue. The internal elastic lamina formed the borderline between media and intima. In the normal mature ductus arteriosus the intimal thickness varied from only a few cellular layers in some areas to distinct intimal cushions in other areas. These cushions contained more elastic material than the media. The elastic material was present as fine elastic fibres, very different from the elastic lamellae of the aorta.

In older specimens the aortic wall was thicker, with an increasing number of elastic lamellae in the media. There was a thickening of the subendothelial layer of the intima as well, which merged gradually with the media. Anatomical closure of the ductus arteriosus was complete and a ligamentum arteriosum formed, consisting principally of fibrous tissue, relatively poor in elastic tissue. This made the ligament easily discernible from aortic wall tissue.

In a transverse section of a normal aorta at the level of the ductus arteriosus or ligamentum arteriosum, ductal tissue was found to border a small part of the aortic lumen. At the site of the junction of ductal and aortic wall the inner third of the aortic lamellae merged into the internal elastic lamina of the ductus, whereas the outer two thirds merged into the adventitia of the ductus. This resulted in a typical fish tail appearance of the elastic tissue of the aorta bordering the ductus (Fig. 1, 2).

The percentage of aortic wall occupied by ductal tissue was limited. Up to 30% of the total circumference of the aorta could contain ductal tissue. In the specimens of the older patients relatively less ductal tissue was present (Fig. 1, 2).

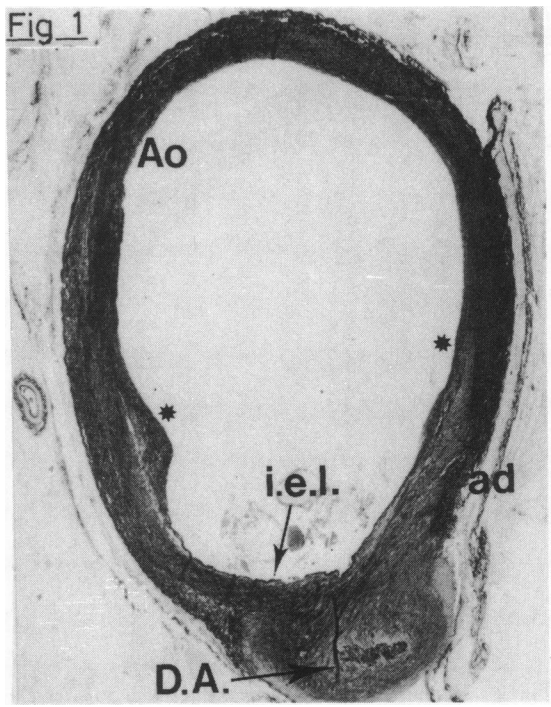

Fig. 1 *Transverse section of a normal aorta of a newborn (case 5) at the level of the ductus arteriosus (D.A.). Ductal tissue stains lighter than aortic tissue because it is relatively poor in elastin. The inner third of the elastic lamellae of the aorta (Ao) merges into the internal elastic lamina (i.e.l.) of the ductus whereas the outer two thirds merge into the adventitia (ad), resulting in a fish tail (*) like connection of the walls of the two vessels (more clearly visible on the right side of the figure than on the left). Ductal tissue does not extend beyond one third of the total circumference of the aorta. (Elastic tissue stain; original magnification × 10.)*

PATIENTS WITH COARCTATION: HISTOLOGY

All 45 coarctations consisted mainly of a thickening, with some degree of infolding of the aortic media. At the site of the coarctation the number of elastic lamellae was the same as in the normal aortic wall. The thickening appeared to be related to an increase in the distance between the elastic lamellae. The infolding of aortic wall was very pronounced in some specimens and hardly visible in others.

The junction between aortic and ductal tissue did not resemble a fish tail, as it did in the normal subjects. Instead, all elastic lamellae of the aortic media formed the outer part of the coarctation and eventually merged into the adventitia of the ductus (Fig. 3).

Ductal tissue was invariably present in the ridge. In a transverse section of the aorta at the level of the coarctation, ductal tissue bordered the aortic lumen for more than half of the total aortic circumference in all cases. In some cases ductal tissue encircled the lumen completely (Fig. 3). Both medial and intimal tissue of the ductus were present in the coarctation, but an extension of intimal cushions into the ridge was found in only two very young specimens (Fig. 3).

In sagittal sections of coarctation specimens, ductal tissue was located predominantly at the side of the ridge which faced the descending aorta in all except one case (No. 2 in Table 1.)

This case was a 2 week old infant who died in con-

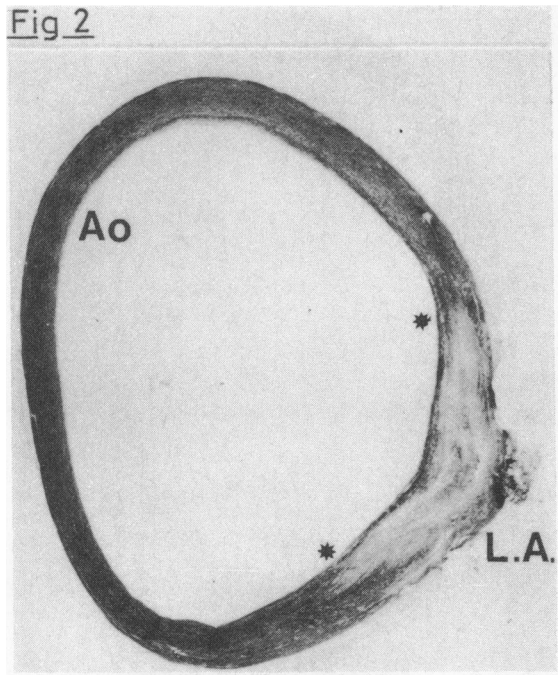

Fig. 2 *Transverse section of a normal adult aorta at the level of the ligamentum arteriosum (L.A.) (case 10). Note the similarity with Fig. 1. Ligamentous ductal tissue is poor in elastin and stains light. The fish tail like connection (*) is clearly visible on both sides. The total extension of ligamentous tissue is less than the ductal extension in Fig. 1. (Elastic tissue stain; original magnification × 6.)*

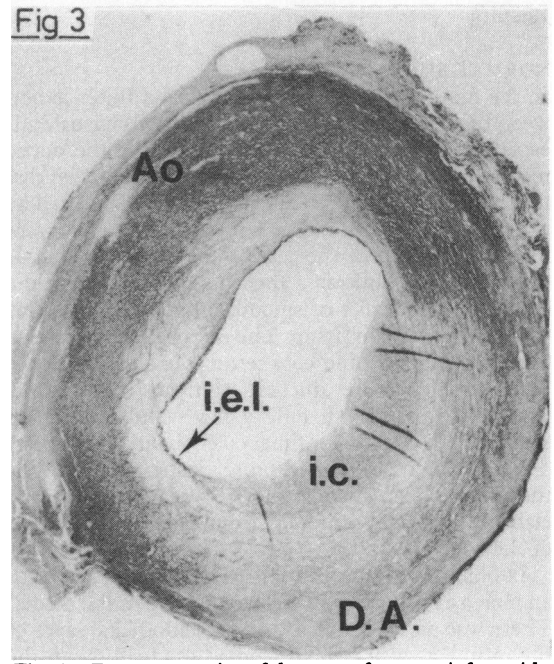

Fig. 3 *Transverse section of the aorta of a young infant with preductal coarctation (case 1) at the level of the ductus arteriosus. The lightly stained tissue of the ductus is clearly seen to encircle the lumen of the aorta. A small intimal cushion (i.c.) is present in this specimen. Compare with Fig. 1 and 2. (Elastic tissue stain; original magnification × 10.)*

gestive heart failure. Necropsy showed two muscular ventricular septal defects, a bicuspid aortic valve, and two sites of localised narrowing in the aorta. One narrowing was located in between the left carotid and left subclavian artery. At histological examination it was found to consist exclusively of an infolding of the aortic wall. The second narrowing was located just opposite the site of entrance of the ductus arteriosus. On histological examination this ridge consisted of an infolding and thickening of the aortic media with ductal tissue on top of the ridge, both at the distal and the proximal side. (This case has been reported by Bruins[2].)

The basic histological picture, as described above, was identical in all coarctation specimens. No difference was found between young and old cases. In older specimens though, on top of the original coarctation and directly distal to it large masses of intimal proliferation were present (Fig. 5). This intimal proliferation narrowed the residual lumen of the coarctation, and was present whether or not ductal tissue or aortic wall tissue bordered the original lumen. A distinct histological difference was noted between intimal proliferation and intimal cushions of the ductus (Fig. 3, 5). The intimal proliferation consisted principally of loose fibrous tissue, with some scattered smooth muscle cells. Elastic material was present only in the intimal proliferations of some of the older specimens, where it presented as thick, irregularly distributed elastic lamellae. The elastic material in the intimal cushions of the ductus, as mentioned before, was more abundant, with regularly distributed fine elastic fibres (Fig. 3 and 5).

In nine specimens with coarctation a persistent ductus arteriosus was present (Table 1). In eight of these cases an abnormal structure typical for a persistent ductus arteriosus (Fig. 4) was found.[11] One, a 2 week old infant, had a normal ductal wall. There was no difference in histological architecture of the coarctation between specimens with a patent and those with a closed ductus arteriosus.

PATIENTS WITH COARCTATIONS: SPATIAL AND TEMPORAL RELATION

The level of the coarctation, compared with the site of entrance of the ductus arteriosus, varied considerably.

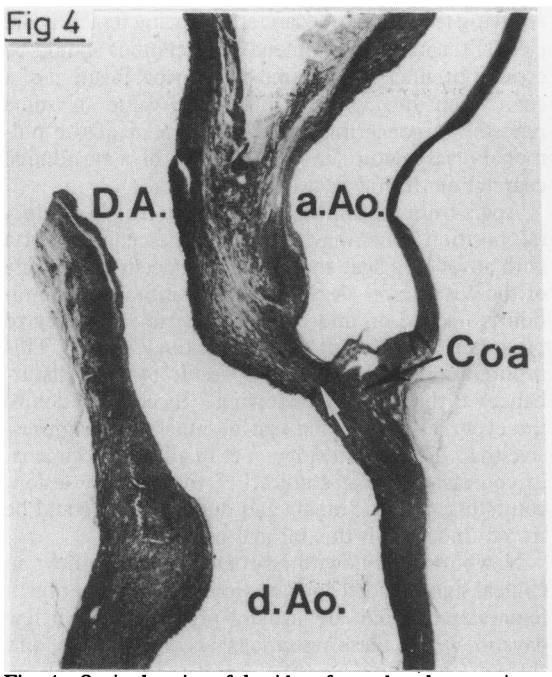

Fig. 4 *Sagittal section of the ridge of a preductal coarctation with persistent ductus arteriosus (case 16). The ridge (Coa) lies proximal to the entrance of the ductus into the descending aorta (d.Ao.). a.Ao., aortic arch. The structure of the ductus arteriosus is of a persistent type, showing aortification, with increase in elastic material.*[11] *Ductal tissue is still distinguishable from aortic tissue, though it stains darker than a normal ductus. Ductal tissue extends into the ridge (top of white arrow). (Elastic tissue stain; original magnification* × *10.)*

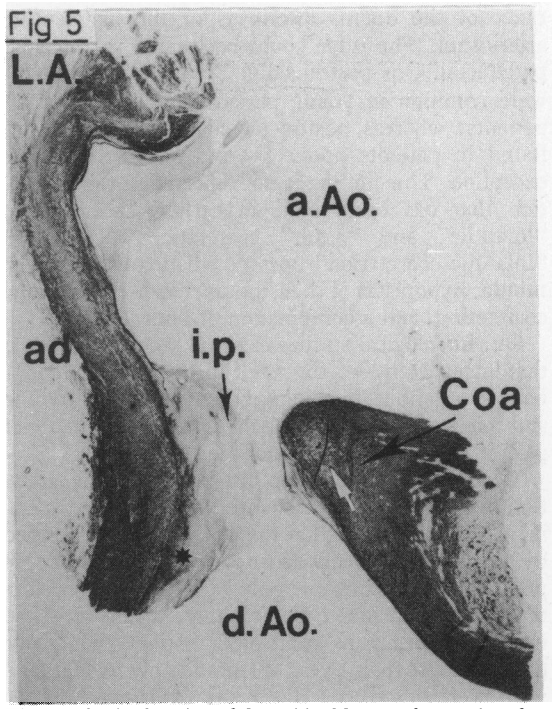

Fig. 5 *Sagittal section of the residual lumen of a postductal coarctation (case 44). Ligamentous ductal tissue extends into the coarctation and encircles the aortic lumen in this specimen, as can be seen from its presence on the right side of the picture (white arrow). On the left side of the picture (*) the connection between ductal and aortic tissue is clearly visible. All elastic lamellae of the aorta merge into the adventitia of the ligamentum. Compare with Fig. 1 and 2. Intimal proliferation (i.p.) almost closes the residual lumen of the coarctation. Note the difference in structure between intimal proliferation and the intimal cushion of the ductus in Fig. 3. (Elastic tissue stain; original magnification* × *7.)*

The ridge could be located just proximal to the entrance of the ductus, exactly opposite the ductal entrance, or below the ductus. We refer to the above mentioned positions as preductal, paraductal and postductal, respectively. Fig. 6 shows how the highest proportion of cases in these three positions moves smoothly with age, the highest proportion of the preductal being in infancy, of the paraductal in middle childhood, and of the postductal in adult life.

The basic histological architecture, as already mentioned, was identical in all specimens and independent of the position of the ridge. Even in distant postductal coarctations there was continuity between the ductal tissue in the ridge and the tissue of the ductus arteriosus.

Discussion

In our study coarctations were at different levels in the descending aorta compared with the site of ent-

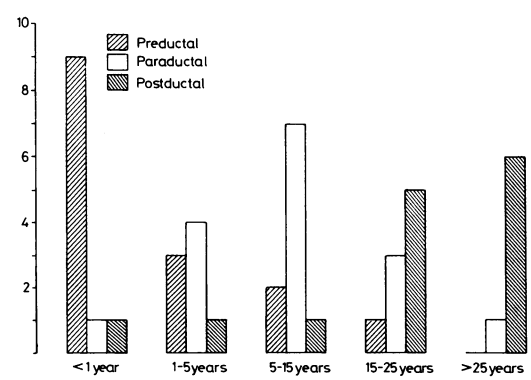

Fig. 6 *Age distribution of the three types of coarctation. Vertical axis: number of cases.*

rance of the ductus arteriosus or the ligamentum arteriosum. The ridge could be located preductally, paraductally, or postductally. Preductal coarctations were common in young patients and rare in older patients, whereas postductal coarctations were not found in patients under 5 years of age, with one exception. This finding is not reflected in the distinction that has been made in earlier days between "infantile" and "adult" coarctation.[9] The term "infantile coarctation" does not distinguish between tubular hypoplasia of the isthmus, localised preductal coarctation, and a combination of both.

Our histological studies of serial sections disclosed that, irrespective of the site, all coarctations had a basically identical histological architecture—infolding and thickening of the aortic media whereby the inner part of the ridge consisted of ductal tissue.

Wielenga[5] studied 27 specimens of aortic coarctation and found ductal tissue in the ridges of all specimens. He postulated that the coarctation was formed by traction of fibrously degenerated ductal tissue. No preductal coarctation and only a few paraductal coarctations were included in his study, which consisted mainly of specimens from older patients. Only one patient of less than 1 year of age and only two under 4 years were described. His theory explained how the coarctation could develop at the site where it was located, at the time the specimen was obtained (that is in most case postductally).

Ho and Anderson[6] reported 12 cases with coarctations, most of them in combination with tubular hypoplasia. A sling of ductal tissue, encircling the aortic isthmus, was present in all cases. The coarctations in their material were all located preductally, most probably because all their patients were under 10 months of age. Their hypothesis that the coarctation is caused by an abnormal connection of the embryological fourth and sixth left branchial arches (that is that the isthmus enters sideways into the ductus) and therefore develops preductally, seems attractive. Yet, as far as we could judge from their pictures, continuity between the elastic tissue of the isthmus and that of the descending aorta was present, just as in our material.

From our study and from other reports[6 12] it is evident that young infants with a localised coarctation almost always present with the preductal type. Our hypothesis is that the coarctation is formed preductally in all cases. With advancing age, and altered flow patterns after birth, the ridge can move gradually towards ductal level, and eventually pass the ductus, to become a postductal coarctation. Some authors[2 13] have already postulated from clinical observations that this movement took place, and our histological studies strongly support this.

Implications for pathophysiological experiments, studying the effects of coarctation during fetal life, are clear. Prenatally, experimental coarctations should be created preductally to mimic the normal position of a coarctation during fetal life. The value of some reports[14 15] concerning the development of the pulmonary vasculature in the presence of a postductal coarctation during fetal life is doubtful.

Apart from the shifting of the ridge from a preductal position downwards into the descending aorta with advancing age, another change occurs at the site of the coarctation. A thick layer of intimal proliferation is formed on and distal to the ridge, leading to progressive narrowing of the residual lumen. This proliferation probably is the result of flow disturbances at the place of narrowing.[7] Its contribution to the eventual obstruction can be much more impressive than the original ridge. Yet in all our specimens, in contrast to some studies,[1 7 8] the primary lesion, consisting of aortic media and ductal tissue, could be traced underneath this intimal proliferation.

Newborn infants with coarctation usually show no clinical signs of aortic obstruction. Directly after birth femoral pulsations are usually present. After a few days or weeks these pulsations become weaker, and signs of congestive heart failure may develop. Ductal tissue in the ridge of a preductal coarctation might contribute to aortic obstruction at the time of ductal closure, especially when ductal intimal cushions are present in the aorta. Intimal cushions in the aorta have been reported[6] but in our study they were found in only two cases. Talner *et al.*[16] postulated that flow from the aortic isthmus can easily bypass the coarctation as long as the aortic end of the ductus is patent. At the time of closure of the ductus at its aortic end, Talner *et al.*[16] suggest that an acute aortic obstruction is created. This theory only holds if the coarctation is located paraductally, which, in our experience is rare in a newborn infant. It therefore seems necessary to find another explanation for the role ductal closure plays in aggravating the clinical symptoms of a coarctation. The following theory might hold for several coarctations.

Most infants with aortic coarctation have pulmonary hypertension, sometimes up to systemic levels. As long as the ductus is patent, pulmonary, instead of aortic, pulsations can be felt in the femoral arteries. At the time of ductal closure these pulsations disappear. The obstruction to aortic flow, located preductally, is present at birth and may lead to some degree of left heart failure. The raised left atrial pressure gives rise to a left to right shunt through the foramen ovale, thus leading to right ventricular volume overload. As long as the ductus is patent a large pulmonary flow is well tolerated because part of it can escape through the ductus into the descending aorta. After closure of the ductus massive pulmonary vascular

engorgement and signs of right heart failure become apparent.

It has been reported that prostaglandin E_1 can relieve heart failure and re-establish femoral pulsations in infants with coarctation, as long as the ductus is not anatomically closed and is able to reopen.[17 18] The explanation given in these reports for this beneficial effect of prostaglandin E_1, which is based on a paraductual position of the coarctation, is not in keeping with our findings, as has been argued before. From our present theory it is also evident that prostaglandin E_1 infusion, which dilates the ductus, will help infants with coarctation. The reason is the same as in infants with aortic arch interruption.[17] To evaluate further the true effect of prostaglandin E_1 in infants with coarctation, both differential pressures and differential oxygen saturations between the upper and lower part of the body will have to be measured before and after prostaglandin E_1 infusion.

It is very tempting to speculate about the exact aetiology of coarctation of the aorta. Our study, thus far, suggests that the explanation for the development of the coarctation must be sought with the coarctation in a preductal position. Abnormal fetal flow patterns and abnormal ductal tissue in the aortic arch must both be taken into consideration. The latter may be the result of the former, though a primary abnormality of ductal tissue still remains a possibility. Further studies of very young and fetal material will be necessary to answer this question.

References

1 Hutchins GM. Coarctation of the aorta explained as a branch-point of the ductus arteriosus. *Am J Pathol* 1971; **63**: 203–13.

2 Bruins C. Competition between aortic isthmus and ductus arteriosus; reciprocal influence of structure and flow. *Eur J Cardiol* 1978; **8**: 87–97.

3 Rudolph AM, Heymann MA, Spitznas U. Hemodynamic considerations in the development of narrowing of the aorta. *Am J Cardiol* 1972; **30**: 514–25.

4 Skoda J. Protokoll der Sektions-Sitzung für Physiologie und Pathologie, am 19. okt. *Zeitschrift der kaiserlich-königlichen Gesellschaft der Aerzte zu Wien* 1855: 710–22.

5 Wielenga G. De relatie tussen coarctatio aortae en ligamentum arteriosum. Leyden, 1959. Thesis.

6 Ho SY, Anderson RH. Coarctation of the aorta. In: Godman MJ, Marquis RM, eds. *Paediatric cardiology. vol. 2. Heart disease in the newborn*. Edinburgh, London: Churchill Livingstone, 1979: 173–86.

7 Edwards JE, Christensen NA. Clagett OT, McDonald JR. Pathologic considerations in coarctation of the aorta. *Proc Staff Meet Mayo Clin* 1948; **23**: 324–32.

8 Clagett OT, Kirklin JW, Edwards JE. Anatomic variations and pathologic changes in coarctation of the aorta. *Surg Gynecol Obstet* 1954; **98**: 103–14.

9 Bonnet LM. Sur la lésion dite sténose congénitale de l'aorte dans la région de l'isthme. *Rev Méd (Paris)* 1903; **23**: 108–26, 255–65, 335–53, 418–38, 481–502.

10 Tinkelenberg J. Graphic reconstruction and stereoscopy. *J Audiov Media Med* 1980; **3**: 68–71.

11 Gittenberger-de Groot AC. Persistent ductus arteriosus: most probably a primary congenital malformation. *Br Heart J* 1977; **39**: 610–8.

12 Becker AE, Becker MJ, Edwards JE. Anomalies associated with coarctation of aorta. Particular reference to infancy. *Circulation* 1970; **41**: 1067–75.

13 Hutchins GM. Two secondary lesions: coarctation of the aorta and idiopathic endocardial fibroelastosis. *Birth Defects* 1972; **8**: No. 5, 24–6.

14 Levin DL, Mills LJ, Parkey M. Morphologic development of the pulmonary vascular bed in experimental coarctation of the aorta. *Circulation* 1979; **60**: 349–54.

15 Burrington JD. Response to experimental coarctation of the aorta and pulmonic stenosis in the fetal lamb. *J Thorac Cardiovasc Surg* 1978; **75**: 819–26.

16 Talner NS, Berman MA. Postnatal development of obstruction in coarctation of the aorta: role of the ductus arteriosus. *Pediatrics* 1975; **56**: 562–9.

17 Heymann MA, Berman W Jr, Rudolph AM, Whitman V. Dilatation of the ductus arteriosus by prostaglandin E_1 in aortic arch abnormalities. *Circulation* 1979; **59**: 169–73.

18 Freed MD, Heymann MA, Lewis AB, Roehl SL, Kensey RC. Prostaglandin E_1 in infants with ductus arteriosus-dependent congenital heart disease. *Circulation* 1981; **64**: 899–905.

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