Coarctation, tubular hypoplasia, and the ductus arteriosus
Histological study of 35 specimens[1]

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SUMMARY A histological study has been made in an attempt to study further the relation between the ductus arteriosus, coarctation, and tubular hypoplasia of the aortic arch. Thirty-five aortic arch systems were studied using serial sectioning techniques. Twelve were from patients with coarctation and/or tubular hypoplasia. The other 23 hearts were from patients without aortic obstructive lesions, 7 from anatomically normal hearts, and the others from malformed hearts with anomalies elsewhere from the aortic arch. The anatomical study of the hearts with obstructive aortic lesions emphasised the necessity of distinguishing 'coarctation' from 'tubular hypoplasia', since the curtain lesion of coarctation was found to coexist with tubular hypoplasia in some cases. The histological study showed that the ductus was easily distinguished from the walls of the aorta or pulmonary artery. In all these cases with coarctation or tubular hypoplasia a sling of ductal tissue was located around the aortic isthmal orifice. In 6 hearts a diaphragm of ductal tissue was seen to form the coarctation lesion.

'Coarctation' is derived from the Latin word 'coarctatio' which means (a drawing together to make tight). When applied to the aortic arch, this term refers to an abrupt constriction situated in the aortic isthmus between the origin of the left subclavian artery proximally and the aorta-ductus arteriosus junction distally. This isthmic coarctation involves an obliterative or obstructive curtain lesion, the aetiology of which is still in dispute (Krediet, 1965; Balis *et al.*, 1967; Wielenga and Dankmeijer, 1968; Hutchins, 1971; Bruins, 1973; Rosenberg, 1973).

Another lesion which produces restriction of aortic flow in this region is tubular or isthmal hypoplasia. This lesion may or may not accompany a curtain lesion. Indeed, Sinha *et al.* (1969) proposed a radiographic definition of tubular hypoplasia as distinct from coarctation. Bremer (1948) considered this lesion to be the persistence of the fetal configuration of the aortic isthmus. Though a gradual narrowing of the aortic isthmus is a normal finding in the first 3 months of life (Evans, 1964), persistence of this stricture in later life is pathological.

Although the coarctation lesion is generally located in the region of the isthmus, there is much contention in its classification. Indeed, one of the first attempts at classification was that by Bonnet in 1903 which has become a classical reference. Since then many workers have found the simple classification into infantile and adult types inadequate (Evans, 1933; Bramwell, 1947; Edwards *et al.*, 1948; Johnson *et al.*, 1951; Clagett *et al.*, 1954; Lemmon and Bailey, 1958; Rudolph *et al.*, 1972). Becker *et al.* (1970) generalised that coarctation occupied the area of junction between the arch and descending aorta. The lesion could be proximal to, opposite to, or distal to the ductus arteriosus. Rudolph *et al.* (1972) introduced the term 'juxtaductal' coarctation and this term has since been used by other workers (Shinebourne and Elseed, 1974; Elseed *et al.*, 1974).

In the present study we have studied the anatomy of coarctation and attempted to define its relation to tubular hypoplasia and the ductus arteriosus.

Materials and methods

Thirty-five specimens were obtained from the cardiopathological collection of the Brompton Hospital, London, and the Wilhelmina Gasthuis, University of Amsterdam. Segments of aortic

Table *Morphology of 12 hearts with tubular hypoplasia and/or coarctation of aortic arch*

Diagnoses Situs—AV connection—VA connection	Aortic stenosis or obstruction	Associated anomalies	External localised aortic stricture	Obstructive coarctation lesion
Solitus—AV concordance—VA concordance	+	Mitral atresia, hypoplastic LV, VSD, muscular subaortic stenosis, PDA	−	−
Solitus—AV concordance—VA concordance	+	Mitral stenosis, aortic atresia, hypoplastic LV, PDA	−	−
Solitus—AV concordance—VA concordance	+	Mitral stenosis, aortic atresia, hypoplastic LV, PDA	−	−
Solitus—AV concordance—VA concordance	+	Mitral stenosis, fibromuscular subaortic stenosis, bicuspid aortic valve, hypoplastic LV, PDA	−	+
Solitus—AV concordance—VA concordance	+	ASD, membranous subaortic stenosis, VSD, PDA	+	+
Solitus—absent right AV connection—VA concordance	+	Univentricular heart, LV type with OC, PDA	−	−
Solitus—absent right AV connection—VA discordance	+	Univentricular heart, LV type with OC, PDA	−	−
Solitus—absent left AV connection—VA discordance	+	Univentricular heart, LV type with OC, PDA	−	+
Solitus—AV concordance—DORV	+	ASD, VSD, PDA	−	+
Solitus—AV concordance—VA discordance	+	VSD	+	+
Solitus—AV concordance—VA discordance	+	VSD (AV canal type), PDA	−	+
Solitus—AV concordance—VA concordance	+	Anomalous pulmonary venous return, common atrium, PDA	−	−

ASD, atrial septal defect; AV, atrioventricular; DORV, double outlet right ventricle; LV, left ventricle; OC, outlet chamber; PDA, persistent ductus arteriosus; VA, ventriculoarterial; VSD, ventricular septal defect.

arches which included the ductus arteriosus and portions of the pulmonary artery were resected and studied histologically. Measurements were made of all the specimens and each one was drawn to scale. Seven of the arches were from anatomically normal hearts, and 28 from congenitally malformed hearts of which 12 were associated with coarctation and/or tubular hypoplasia.

Twenty-one specimens were sectioned in a plane parallel to the longitudinal axis of the arch, 5 in the sagittal plane of the ductus, and 9 transversely. The ribbons of serial sections were collected on cardboard trays. Initially, every twenty-fifth section was mounted and stained with the modified Masson's trichrome technique (Smith *et al.*, 1977). Where necessary, additional sections were later stained in haematoxylin and eosin or Verhoeff's van Gieson.

Results

(i) NORMALS
(This includes the 'normal-looking' arches from congenitally malformed hearts. The term 'normal-looking' is used in this study to refer to those arches

without distinctly perceptible external strictures. Right sided aortic arches and discordant ventriculo-arterial connections may also be covered by this term.)

The 7 specimens from anatomically normal hearts were newborn (3 specimens), 1 day old (2 specimens), 3 days old (1 specimen), and 6 days old (1 specimen). The ductus arteriosus was probe patent in all cases except for the 3-day-old specimen. The isthmal region in each case was slightly narrower than either the ascending or descending aorta but no plication was observed (Fig. 1).

The other 16 normal-looking arches were from congenitally malformed hearts. Five of those were associated with non-patent ductus and the age range was 3 days to 2¼ years. The rest ranged from 1 day to 6 months old. From an histological standpoint, the aorta, being one of the great arteries, had the characteristic appearance of regularly spaced elastic lamellae in the media. The isthmus had a similar histological structure to the rest of the aorta though the elastic lamellae were more condensed, giving it a slightly thinner wall. As in the great arteries, the ductal wall was made up of three layers—the intima,
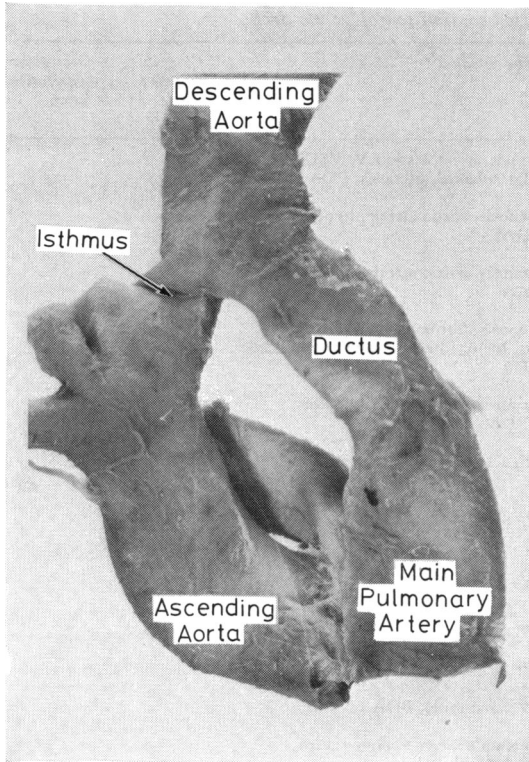
Fig. 1 *Normal aortic arch from a newborn infant. The isthmus is slightly narrower than either the ascending or descending aorta.*
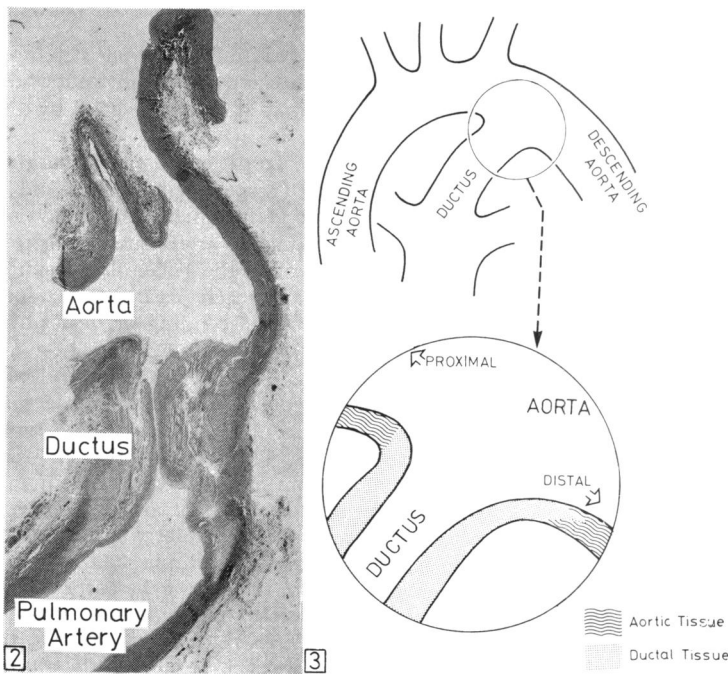

Fig. 2 *Longitudinal section of a normal obliterating ductus. Histologically, the ductus lacks the regularly spaced elastic lamellae of either the aorta or pulmonary artery. (Trichrome. × 8.)*

Fig. 3 *Diagram of aortic arch and ductus with inset to show the ductus-aorta junction.*
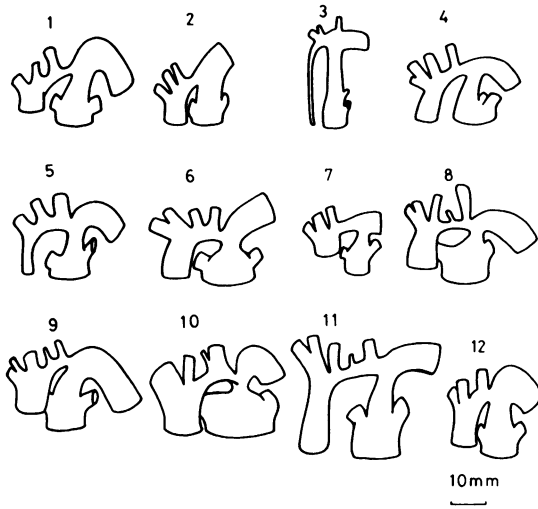
Fig. 4 *Scale diagram of the 12 coarctation and/or tubular hypoplasia specimens sectioned.*

media, and adventitia. However, in contrast to the aorta, the ductus lacked the regularly spaced elastic lamellae of the great arteries, being essentially a muscular artery (Fig. 2). The adventitia of the ductus was a poorly defined layer of fibrous connective tissue in continuity with that of the aorta. The media was mainly composed of loosely arranged smooth muscle fibres in a connective tissue matrix. Very fine, wavy elastic fibres could be seen in the matrix. An internal elastic membrane separated the media from the intima. Nearly all the patent ductus showed a tendency towards obliteration. The intima was thin and usually one-cell thick whereas the

inner portion of the media was much thickened and intercellular vacuoles numerous in most cases.

At the ductal-aortic junction, an abrupt proximal junction was observed with a more gradual junction distally (Fig. 3). The elastic lamellae of the isthmus stopped short at the junction. On the other hand, the ductal tissue attenuated slightly into the media of the descending aorta. Elastic tissue from the ductus continued into the distal aorta in some specimens, but in no specimens was there a 'sling' of ductal tissue encircling the aorta.

Histologically the 16 'normal-looking' aortic arches were similar to the other normal arches as was their relation to the ductus except for one case with ventriculoarterial discordance. This particular case showed a comparatively large extension of ductal tissue into the lateral aortic wall.

(ii) COARCTATION AND/OR TUBULAR HYPOPLASIA

These 12 specimens ranged from 1 day to 10 months old in age. All the specimens had varying degrees and lengths of arch narrowing (Fig. 4). In one specimen the isthmus was imperforate. Only 2 specimens had distinct external strictures at the aortic wall in the region opposite the insertion of the ductus. In 4 specimens, the narrowing was limited to the isthmus, that is between the origin of the left subclavian artery and the ductal insertion. The narrowing extended into the aortic arch in 6 specimens affecting the region between the origin of the right brachiocephalic artery and the ductus. The remaining 2 specimens were associated with aortic atresia and gross aortic stenosis, respectively. All but one case were associated with grossly patent or probe patent ductus.
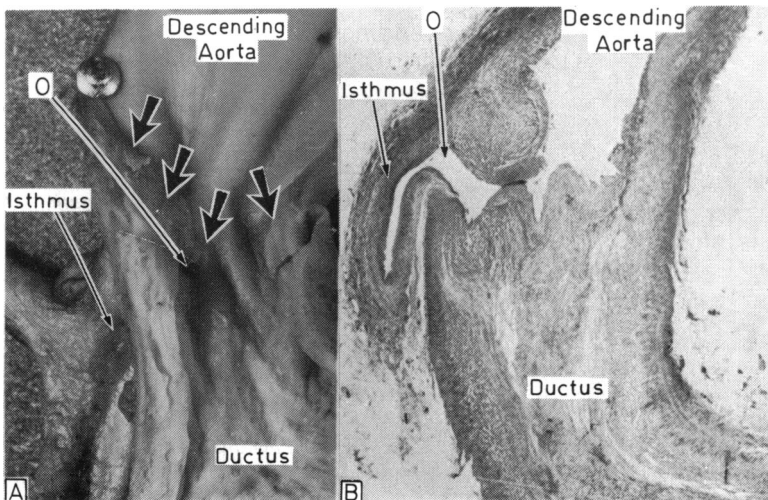

Fig. 5 (A) *Dissection of a specimen with tubular hypoplasia. The isthmus is narrow and its entrance to the ductus —descending aorta junction (O) is surrounded by ductal tissue. The extent of ductal tissue into the descending aorta is marked by the solid arrows. (B) Histological section of the same specimen shows the isthmal orifice (O) bound by ductal tissue. (Trichrome. × 13.)*

The morphology of the 12 cases is presented in the Table. All of them were affected by some form of obstruction or restriction to aortic blood flow. Two cases had aortic atresia, and in one of these the arch narrowed from the isthmus towards the heart (Fig. 4, case 3). In the other case the ascending aorta was wider than the isthmus (Fig. 4, case 2).

When the ductus-aorta junction was dissected longitudinally, the coarctation lesion could be seen as a tongue-like structure which suspended mainly from the superoposterior aortic wall and continued as a lesser lesion along the lateral and medial walls. Pulpy ductal tissue was identified in this area in two specimens of tubular hypoplasia. This tissue encircled the orifice of the isthmus (Fig. 5A).

When the junction was examined histologically, pale staining ductal tissue could be traced as a sling along the luminar surface of the aorta in 6 of the cases with tubular hypoplasia. This sling was usually as wide as the ductus and stretched from the ductal insertion along the superior, medial, and inferior walls of the aorta. The ductus were probe patent in all these cases though they all showed evidence towards closure.

In 4 cases with hypoplastic arches but without localised external strictures, the extensions of ductal tissue into the aorta were seen to be obstructive to aortic flow. In 3 cases, ductal tissue produced a raised diaphragmatic-like structure at the entrance of the isthmus to the descending aorta (Fig. 5B). This ridge was thickest on the superior wall of the aorta. On tracing this lesion across the aorta it was definitely found to be in continuity with the ductus at the ductal junction (Fig. 6). In the fourth case the aorta was imperforate at its junction with the ductus. A tongue-like obliterative curtain lesion was responsible for the lack of patency. The tip of the tongue was continuous with the medial ductal wall inferiorly and extended along the lateral sides of the aorta at the ductal junction. The front of the lesion was continuous with the outer ductal media while the back was in continuity with the inner ductal media (Fig. 7).
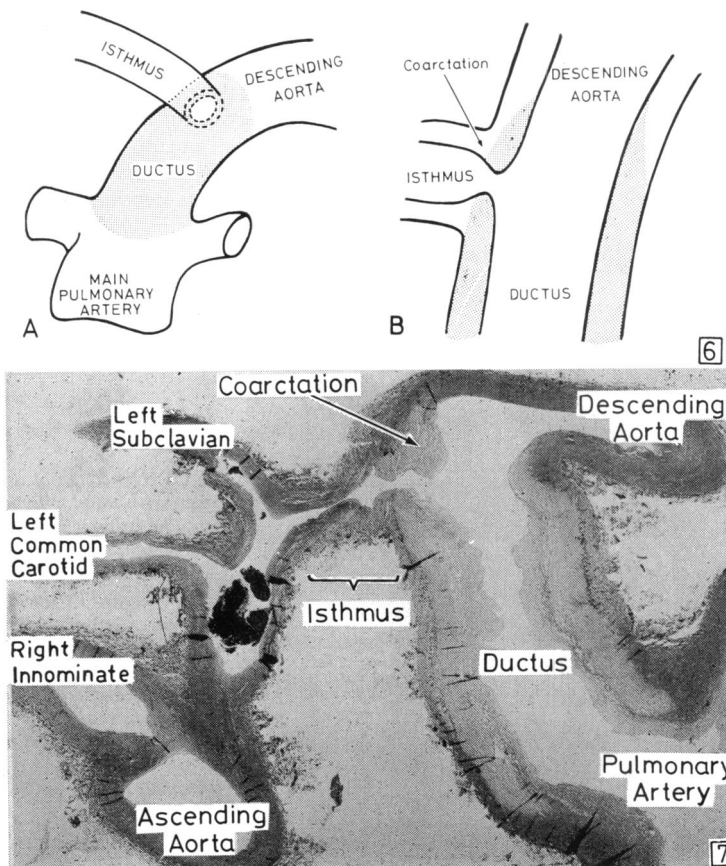

Fig. 6 (A) *Diagram to show the extension of ductal tissue (stippled) into the descending aorta.* (B) *A longitudinal section to show the diaphragmatic coarctation lesion. Ductal tissue is stippled.*

Fig. 7 *Longitudinal section of a specimen from an 8-day-old baby boy which clearly shows that pale staining ductal tissue constitutes the bulk of the coarctation lesion. The isthmus is hypoplastic in this case and there is no evidence of an external localised stricture. (Trichrome. × 8.)*
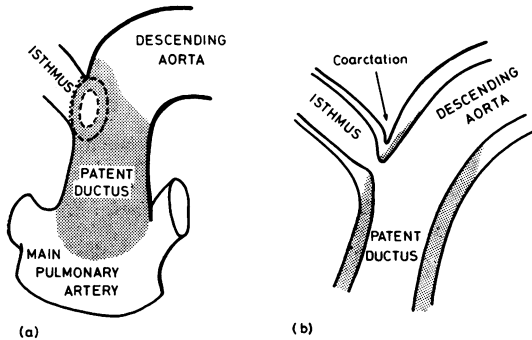
Fig. 8 *Diagram of a specimen with a distinct plication of the aortic wall. Ductal tissue (stippled) still constituted part of the coarctation lesion.*

In the remaining 2 cases the isthmal regions were narrowed in the presence of a curtain-like coarctation lesion. The ductus was closed in 1 case but supplied the descending aorta just distal to the plication of the aorta wall in the other. In each case, pale staining ductal tissue formed the bulk of the coarctation lesion and could be traced to the ductus (Fig. 8).

Discussion

The present investigation lends support to those who have criticised the classical approach of dividing coarctation into 'fetal' and 'adult' types (Calodney and Carson, 1950; Clagett *et al.*, 1954; Sinha *et al.*, 1969; Rudolph *et al.*, 1972; Rosenberg, 1973; Shinebourne and Elseed, 1974). The histological part of the study revealed that half the specimens had a combination of diffuse tubular narrowing and obstructive lesion; none was afflicted by the obstructive lesion alone. Moreover, though the specimens were mainly drawn from a collection of congenitally malformed hearts, the ages of manifestation of symptoms did not correlate with the anatomic types.

It is desirable to consider diffuse tubular narrowing and localised narrowing which occurs in conjunction with an obstructive lesion as separate entities for a more precise evaluation as causes of congestive heart failure (Sinha *et al.*, 1969). It has been proposed that 'coarctation' be used solely to refer to the localised narrowing and its obstructive lesion (Edwards, 1953; Sinha *et al.*, 1969; Shinebourne and Elseed, 1974). Tubular hypoplasia as designated by Edwards (1953) refers to a zone of diffuse narrowing of the aortic arch. However, it does not preclude the occurrence of an obstructive lesion. As Rosenberg (1973) pointed out, histological

examination may be needed to identify the obstructive lesion in tubular hypoplasia. Be that as it may, the distinction between coarctation and tubular hypoplasia seems important, and in the subsequent discussion the term 'coarctation' will be restricted to the presence of an obstructive curtain lesion.

In the specimens we have studied coarctation was always associated with tubular hypoplasia though the converse was not always the case. Abbott (1928) observed that the sharply localised constriction usually occurs after some preliminary narrowing and Sinha *et al.* (1969) reported a 78 per cent association of the two arch anomalies. This finding is contrary to Rudolph and co-workers' statement (1972) that coarctation associated with isthmal narrowing is unusual. The external stricture of the aorta recognised as a prerequisite in distinguishing coarctation from tubular hypoplasia by many authors (Edwards *et al.*, 1948; Clagett *et al.*, 1954; Sinha *et al.*, 1969; Rudolph *et al.*, 1972; Rosenberg, 1973; Shinebourne and Elseed, 1974) is not always present even though an obstructive lesion is found anatomically.

Contrary to the beliefs of workers such as Rokitansky (1852) and Hutchins (1971), the normal ductus arteriosus has a different structure from its adjoining great arteries. When incised, the normal obliterating ductus of the human specimen has a pulpy appearance in contrast to the smooth inner wall of the aorta or pulmonary artery. Histologically, the difference is even more striking, as endorsed by many workers such as Langer (1857), Jager and Wollenman (1942), Everett and Johnson (1951), Noback *et al.* (1951).

The obstructive curtain lesion as described by Rudolph *et al.* (1972) is perhaps a misnomer as it is not merely a shelf which protrudes from the left and posterior aspects of the aortic wall immediately opposite the attachment of the ductus. Rather it encircles the aorta more like a diaphragm, originating from the ductal insertion. With regard to this, Claggett *et al.* (1954) and Rudolph *et al.* (1972) opined that ductal tissue was unlikely to have extended into the aortic wall because the curtain lesion was opposite the ductal attachment rather than in contiguity with it. The present findings in no way support this contention. Indeed, the histological study of 6 specimens with the coarctation lesion revealed that ductal tissue made up a substantial part of the lesion, and completely surrounded the aortic lumen. Histological study further confirmed the naked-eye observation of ductal tissue entirely surrounding the isthmal orifice like a diaphragm. This observation supports strongly the findings of Wielenga (1959), Brom (1965), and Rosenberg (1973). The other 6 specimens with only tubular hypoplasia also exhibited a ductal sling

around the aorta, albeit that the ductal tissue was mostly restricted to a thin layer lining the lumen.

Hypotheses on the pathogenesis of coarctation in relation to the ductus have mostly designated the ductal tissue in the aorta as 'ectopic', that is as an excessive spread of ductal tissue into the aorta (Craigie, 1841; Skoda, 1855; Bonnet, 1903; Krediet, 1965; Brom, 1965; Wielenga and Dankmeijer, 1968). The results of the present study suggest that the ductal tissue sling found in the aortic wall is not ectopic but rather represents the original distal wall of the sixth left arch as proposed by Rosenberg (1973). The ductus and descending aorta form a common channel of structural continuity and the isthmus enters this channel rather than the converse. Thus, though all the cases studied had evidence of lesions that would have reduced flow through the aorta, and to this extent support flow theories for coarctation (Rudolph *et al.*, 1972), they also paradoxically show that the ductus forms a sling which 'lassoes' the aorta. They therefore additionally support the 'Skodaic' hypothesis, which should not be dismissed as being without foundation (Shinebourne and Elseed, 1974).

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