

Aberrant Subclavian Artery (Arteria lusoria): Sex Differences in the Prevalence of Various Forms of the Malformation

Evaluation of 1378 Observations

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Summary. 43 original and 1335 previously published observations of aberrant subclavian artery (A. lusoria) were analyzed. The sex distribution varied for different types of the malformation: females predominated over males in instances of *right* aberrant subclavian artery and if pre-stenotic A. lusoria was combined with coarctation of the aorta. Male predominance was found in cases of combination of post-stenotic A. lusoria with coarctation and of aberrant *left* subclavian artery. An equal sex distribution was observed for A. lusoria combined with interruption of the aortic arch. Clinical, pathological and embryological aspects of the condition are discussed.

Key words: A. lusoria dextra — Coarctation — Aortic arch interruption — A. lusoria sinistra — Sex distribution.

Introduction

The term “Arteria lusoria”, suggested by Arkin (1926) is used to designate an anomaly of the right subclavian artery characterized topographically as follows: the artery originates below the left subclavian artery as the fourth main branch of the aortic arch and turns to the right behind the oesophagus and in front of the vertebral column.

The A. lusoria has been considered a variant, originating as a chance phenomenon during the development of the aortic arch. Recent investigative results suggest a female predominance of the anomaly and justify the supposition that the aberrant vessel is not a variant but a true developmental error (Molz, 1976).

Usually the aberrant vessel represents a single anomaly of the aortic arch; it may, however, be combined with coarctation, complete interruption of the aortic arch or with a right-sided aortic arch. The possibility of a female predominance in the combined forms of the malformation is presently being analyzed.

Material and Methods

1335 observations from 311 publications (716 clinical and 662 autopsy cases) were reviewed and 43 original cases were added; 35 from a total of 1432 autopsies in the paediatric age group and 8 from 375 children with clinically diagnosed congenital heart disease.

Group 1 comprises instances of isolated right subclavian artery (IRASA).

Group 2 is composed of instances of combination of right aberrant subclavian artery (RASA) with coarctation:

Subgroup 2.1 represents pre-stenotic origin of RASA.

Subgroup 2.2 represents post-stenotic origin of RASA.

Group 3 includes instances of RASA with complete interruption of the aortic arch.

Group 4 includes the combination of aberrant subclavian artery with a right-sided aortic arch. Since this combination involves the *left sided subclavian artery*, the combination is designated as left aberrant subclavian artery (LASA).

The authors' own cases were, in addition, evaluated with regard to the occurrence of multiple births, birth-order, maturity and chronological age, blood-groups of child and/or mother, maternal age and the presence of additional malformations.

Results

Group 1: Isolated Right Aberrant Subclavian Artery (Fig. 1)

With 1110 observations this group represents 80% of the total investigated. 738 cases could be classified according to sex, 426 (58%) being females, and 312 (42%) being males. The female predominance is statistically significant at the 5% level.

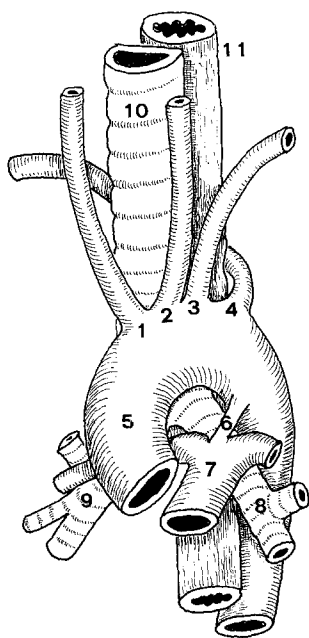


Fig. 1. Isolated right aberrant subclavian artery (IRASA). (1) Right common carotid artery. (2) Left common carotid artery. (3) Left subclavian artery. (4) Right subclavian artery. (5) Ascending aorta. (6) Ductus arteriosus. (7) Pulmonary trunk. (8) Left main bronchus. (9) Middle lobe bronchus. (10) Trachea. (11) Oesophagus

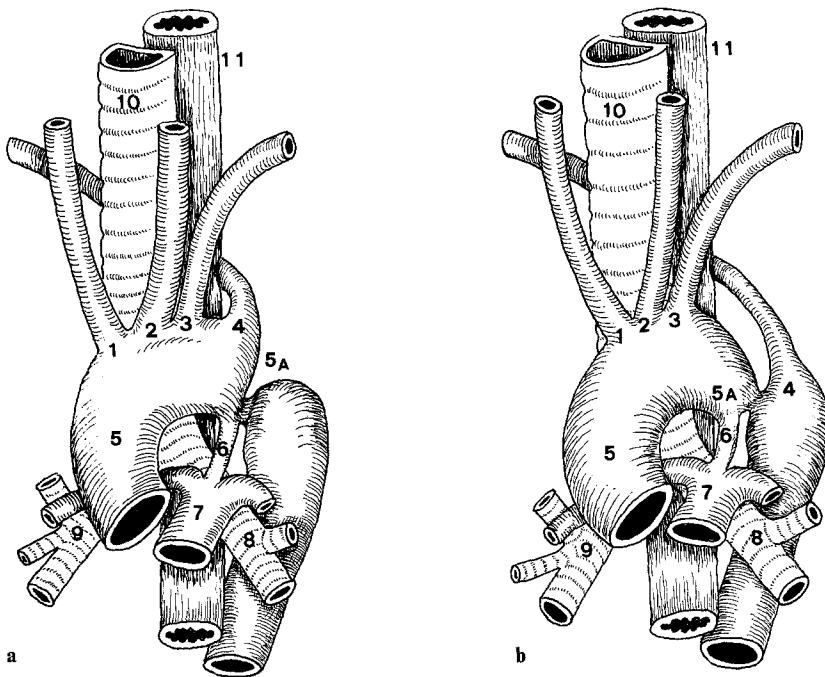


Fig. 2. **a** RASA combined with coarctation and pre-stenotic origin of *A. lusoria*. **b** RASA combined with coarctation and post-stenotic origin of *A. lusoria*. (1) Right common carotid artery. (2) Left common carotid artery. (3) Left subclavian artery. (4) Right subclavian artery. (5) Ascending aorta. (5 A) Coarctation. (6) Ductus arteriosus. (7) Pulmonary trunc. (8) Left main bronchus. (9) Middle lobe bronchus. (10) Trachea. (11) Oesophagus

Group 2: Combination of Right Subclavian Artery With Coarctation

The combination of RASA with coarctation is rare. Abbott (1928) observed it twice among 300 cases of coarctation and Brodén (1952) found it three times among 150 cases of coarctation; Richter (1966) observed it in 5 of 137 cases of coarctation. RASA may originate *proximal* (Fig. 2 a) or *distal* (Fig. 2 b) to the coarctation. Pre-stenotic origin is by far less common than post-stenotic: among 53 subjects the former occurred 17 times, the latter 32 times; no data regarding the location of the artery were available for 4 observations.

24 of the 53 patients were males and 19 were females, suggesting equal propensity of the sexes to develop the anomaly. Broken down according to location, however, sex distribution differs from that of the total: *pre-stenotic* origin is more common in females (9 of 12), whereas *post-stenotic* origin is seen more often in males (19 of 28).

Group 3: Combination of Right Aberrant Subclavian Artery With Complete Interruption of the Aortic Arch (Fig. 3)

Complete interruption of the aortic arch (IAA) has three sites of predilection. Accordingly, Celoria (1959) has suggested the following classification: *Type*

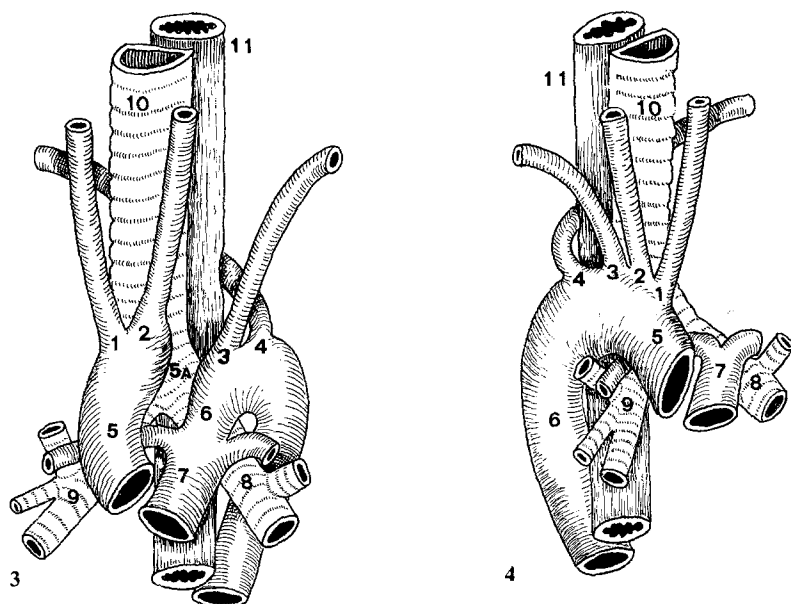


Fig. 3 RASA combined with complete interruption of the aortic arch. (1) Right common carotid artery. (2) Left common carotid artery. (3) Left subclavian artery. (4) Right subclavian artery. (5) Ascending aorta. (5A) Interruption of the aortic arch: Type B. (6) Ductus arteriosus. (7) Pulmonary trunc. (8) Left main bronchus. (9) Middle lobe bronchus. (10) Trachea. (11) Oesophagus

Fig. 4. Left subclavian artery (LASA). (1) Left common carotid artery. (2) Right common carotid artery. (3) Right subclavian artery. (4) Left subclavian artery. (5) Ascending aorta. (6) Descending aorta. (7) Pulmonary trunc. (8) Left main bronchus. (9) Middle lobe bronchus. (10) Trachea. (11). Oesophagus

A: Interruption distal to the origin of the left subclavian artery (42–44%). *Type B:* Interruption between the origin of the left subclavian artery and that of the left common carotid artery (51–53%). *Type C:* Interruption between the origin of the left carotid artery and that of the innominate artery (4–5%). Although IAA is rare, the combination of this developmental error with RASA is surprisingly common. Both, Van Praagh (1970) and Fishman (1976) observed the change twice among 13 cases and Jaffe (1975) found twice among 21 cases of IAA. The present authors observed the combination once among their 3 cases of IAA. Altogether 38 cases of the combination were found among 153 subjects with IAA (24%). A lusoria occurs practically only in association with Type B of IAA (37 of 38 cases).

Among the 38 subjects there were 18 males and 18 females; in 2 reports no data on sex were given.

Group 4 : Left Aberrant Subclavian Artery LASA (Fig. 4)

This group constitutes the second most common anomaly; 177 cases (12%). For 92 observations data on sex distribution were available either in the original

reports or through follow-up inquiries (Felson, 1969, 1977). 62 were males and 30 were females. The male predominance (66% versus 34%) is significant at the 5% level. 66 observations have no data on sex distribution and no information could be obtained from subsequent inquiries (Stewart, 1964, 1977). The origin of LASA is usually located at the transition of the aortic arch to the descending aorta. Both, the bifurcation and the proximal portion of the aberrant artery are often somewhat dilated.

Additional Personal Observations (Table 1)

Multiple Births. The material includes one partner of two pairs of twins (both twins B) and one partner of a set of triplets (triplet C); the sibs of the affected infants were clinically not remarkable. *Sibs.* A younger and deceased brother of case No 6 (Table 1) reportedly had no malformations, an older sister of case No 32 (Table 1) had died with an advanced coarctation of the aorta.

Order of Birth. Among the total of 43 cases of *A. lusoria* there were 10 first-born (23%), 18 second-born (42%), 6 third, 5 fourth-born as well as one fifth, sixth and seventh child each (32%); for one child the order of birth was not given.

Maturity. There were: one fetus (18. week of gestation), 3 immature infants, 7 pre-term, 24 term children, 4 "small for dates" and 4 infants of unknown maturity. *Chronological age:* There were 3 stillborns, 21 newborns (1.-28. days), 13 infants 2.-12. months, 4 infants 13.-24. months and 2 children 2 years 9 months and 11 years respectively. *Blood groups: Children:* Among 20 observations available there were 6 group A, 3 group B, and 11 group O. *Mothers:* Among 40 observations there were 20 group A, 5 group B, one group AB and 14 group O. *Maternal age:* mean age of the mothers of first- and second-born children was 28 years, of the mothers of third-born it was 30.5 years and for the mothers of the fourth-born it was 35 years.

Additional Malformations with IRASA

Multiple cardiac and vascular malformations were observed; there were 12 intracardial defects, 4 extracardial vascular malformations, 5 combined intra- and extra-cardial defects. 18 of these 21 children also had additional visceral malformations, two thirds of which were functionally significant (Table 1).

Additional Malformations Associated with A. lusoria of Groups 2, 3 and 4

5 of the 6 children had additional cardiac malformations, one of these and the sixth child had functionally significant visceral defects.

Table 1. Summary of data collected by authors

Case No	Necropsy No	Birth Order	Maturity	Age	Bloodgroups		Mothers Age	Additional Malformations		
					Child	Mother		Cardiac	Vascular	Non-cardiac defects
Group 1: IRASA										
Males										
1	1329/64	7 ^e	T ^a	21 ds	A rh	A rh	28	—	—	Preauricular appendage rt, ear
2	2274/67	2	T	1 mo	A Rh	O Rh	28	—	—	—
3	1209/64	1	T	2 mo	O Rh	A Rh	27	—	—	—
4	8/74	2	T	6 mo		A Rh	24	—	—	Ectopic thymus
5	750/66	2	—	15 mo	Ø rh	—	30	—	—	—
6	10/73	1	Im ^c	5 min	—	O Rh	23	—	—	Oesophag. atresia. Tracheo-oesoph. fistula
7	2395/68	2	T	44 h	B Rh	B Rh	26	Pulm.-sten.	—	Annular pancreas
8	430/64	3	S f d ^d	9 ds	O Rh	O Rh	42	Ao.-sten. VSD	—	Meckels' diverticulum
9	13/67	6	T	13 ds	—	O Rh	35	VSD	—	Agen. philtrum of upper lip
10	1952/67	5	T	7 wk	O Rh	A Rh	42	ASD	—	Agen. olfact. tract
11	2101/69	1	T	12 mo	O Rh	O Rh	28	ASD	Pers. lt. Sup. V. Cava	Incompl. lobes both lungs
12	1226/68	2	—	+2 y 9 mo	—	O Rh	32	ASD VSD	—	Mongolism. Duod. stenosis. Annular pancreas. Microcephaly. 2-lob. rt. lung

Females

13	9/71	2	18.wk	Stillb.	O Rh	28	—	—	—	—
14	1081/69	2	Im	3 ds	A Rh	25	—	—	—	—
15	911/70	2	Im	6 ds	O Rh	31	—	—	—	Cleft uvula
16	10/71	2	Pt	Stillb.	AB rh	35	—	—	—	—
17	729/70	2	Pt	8 h	—	24	—	—	—	—
18	1963/66	1	Pt	5 min	A Rh	20	—	—	—	—
19	612/69	1	T	Stillb.	A Rh	25	—	—	—	—
20	94/68	1	T	4 mo	A Rh	38	—	—	—	—
21	1614/67	1	T	13 mo	A Rh	22	—	—	—	—
22	958/64	3	T	24 mo	O Rh	28	—	—	—	—
23	631/68	4	T	3 min	A Rh	36	Pat. form. ov.	Aortic origin lt. vertebr. art.	—	—
24	1350/68	1 ill	T	32 h	O Rh	25	Pat. form. ov.	—	—	—
25	1643/66	3	T	9 ds	A Rh	28	Pat. for. ov.	—	—	—
26	59/69	2	T	11 mo	—	36	VSD	—	Asplenia. Inverted stomach	—
27	419/70	1	T	8 mo	—	34	Perist. av.- ventr. canal	—	Mongolism. Large tongue	—
28	1624/68	2	S f d	4 ds	—	25	Pulm.-sten. VSD	Agcn. rt. umb. art.	Extra 18. chromosome lt. hare lip. Incompl. intestine rotat. Cleft uvula	—
29	723/64	4	T	7 mo	O Rh	38	Pulm.-sten.	Aortic origin rt. vertebr. art.	Agcn. gall-bladder Mobile caecum	—
30	857/70	—	—	11 y	—	—	Tetral. Fallot	—	—	—
31	1959/65	4	T	10 ds	B Rh	40	Ao.-atresia	Perst. lt. sup. v. cava.	Accessory adrenal tissue in broad ligament	—
32	1878/68	2	Pt	2 h	O Rh	27	Single atr. VSD	—	Polycyst. horseshoekidney. Agcn. of bladder and urethra	—

^a Term ^b Preterm ^c Immature ^d Small for date ^e Triplet C ^f Twin B

Table 1 (continued)

Case No	Necropsy No	Birth Order	Maturity	Age	Bloodgroups		Mothers Age	Additional Malformations		
					Child	Mother		Cardiac	Vascular	Non-cardiac defects
33	MK 776	4	Pt	4 ds	O Rh	A Rh	28	Tr. art. Single ventr.	—	Mobile caecum Non-lob. lungs
34	2094/67	2 ^f	Pt/S f d	2 mo	A Rh	A rh	22	—	Pat. duct. art.	Anal atresia. Recto- vaginal fistula. Double uterus and vagina
35	903/67	3 ^f	Pt	12 h	—	A Rh	30	—	Agen. lt. umb. art.	Accessory spleen
36	14/71	3	S f d	32 min	—	A Rh	24	—	Agen. lt. umb. art.	Ectromelia both arms. Diaphragm hernia lt.
37	1472/64	1	T	3 mo	O Rh	B Rh	24	—	Agen. lt. umb. art.	Sacr. Spina bif. Bilat. bifid. ureters
Group 2: RASA combined with coarctation										
38	1435/65	1, m	—	10 ds	B Rh	B Rh	42	—	—	Mongolism. Agangl. megacolon
39	3348/75	2, f	T	Alive	O Rh	O rh	32	—	—	—
Group 3: RASA combined with interruption of the aortic arch										
40	30/70	2, m	S f d	3 ds	—	A Rh	25	VSD	—	Agen. lt. kidney Hydroureter rt. 2-lob. rt., non-lob. lt. lung
Group 4: LASA										
41	759/70	2, m	T	14 ds	O Rh	O rh	26	Tr. art.	—	Hammer-toes
42	1222/64	2, m	T	5 mo	B Rh	B Rh	27	Pulm.-sten. VSD	—	Bilat. four finger line
43	1685/69	3, f	T	6 mo	A Rh	O rh	31	Tr. art.	—	—

Discussion

Historical Data. The first communication dealing with A. lusoria was published by Hunauld in 1735. In 1794 Bayford used the term "Dysphagia lusoria", believing that in his patient the dysphagia and her death from marasmus were attributable to the vascular anomaly which he found at the autopsy. In the following years the clinical significance of the lesion became the subject of controversy. In 1871, Hamburger designated dysphagia lusoria as the "result of imagination rather than a discover" and suggested, to change the term from A. "lusoria" to "illusoria". During the past century, Bayford's view was confirmed. It became apparent, however, that dysphagia is not a regular symptom of the anomaly. In 1926, Arkin therefore, suggested the term "Art. lusoria".

In the living subject the first roentgenological demonstration was reported by Kommerell in 1936 and the first angiography is study in 1949 by Apley. The first surgical intervention was attempted by Girard in 1913 in order to relieve the associated dyspnoea, however, he did not resect the vessel. The first successful correction of an aberrant subclavian artery was carried out by Gross in 1945.

Clinical Aspects. The anomaly is often latent and innocuous; yet the location of the vessel may cause considerable dysphagia or dyspnoea which may necessitate therapeutic intervention.

Pathological Complications. *Aneurysms* have been observed in cases of IRASA as well as of the the combined forms of A. lusoria. Of the 19 cases of aneurysm in IRASA, 14 were men and 5 were woman (Stoney, 1975; Wagner, 1976). There were 2 aneurysms, each associated with coarctation (Candardjis, 1961; Sakurai, 1973) and with LASA (Dévé, 1925; Dikman, 1974). The former were successfully resected, the latter ruptured with exsanguination. The presence of A. lusoria may become a serious or even fatal complication during correction of a dissecting aneurysm of the descending aorta. Two patients bled to death from a ruptured A. lusoria, (DeBakey, 1955; Weinberger, 1977). In the third case (Weinberger, 1977) the presence of the vessel was not suspected and death occurred from cerebral anoxia following clamping of both subclavian arteries. *Erosion* of the anomalous vessel may develop as a result of tracheal (Merchant, 1977) or oesophageal (Dotzauer, 1966) intubation with the development of an erosive ulcer. *Thrombotic occlusion:* Stockmann (1975) reported a successful thrombectomy in a 45 years old patient who had developed gangrene of the fourth finger of the right hand. The lesion regressed following thrombectomy. *Papilloedema* has been observed in combination with coarctation and post-stenotic origin of A. lusoria, following surgical treatment the oedema disappeared (D'Abreu, 1960/61). *Diagnostic misinterpretation of clinical symptoms:* Sanger (1967) discussed 9 patients compleining of dysphagia, who were misdiagnosed as neurotics and were treated unsuccessfully for periods up to 3 years. The radiological examination of one patient disclosed the correct diagnosis which was then made in the remaining 8 patients.

Table 2. Aberrant subclavian arteries: Clinical and autoptic prevalences

Anomaly type	Total No of patients examined	ASA		Diagnosis Radiol. Surg.		Total number of autopsies	ASA	
		No	%				No	%
IRASA	22, 201	517	2.3	395	122	68, 049	593	0.7
RASA	1, 032	45	4.3	26	19	26, 787	8	0.2
+ Coarctation								
RASA	296	24	8	12	12	20, 885	14	0.06
+ IAA								
LASA	1, 594	130	8	97	33	11, 870	47	0.4

Prevalence (Table 2)

Group 1. Cairney (1925) gives a figure of 0.9%, Goldbloom (1922) one of 1.5% and Hyrtl (1859) one of 2% in the general population. Obviously results of clinical and pathologic surveys differ. In clinical material which is selected on the basis of clinical signs the prevalence amounts to 2.3%; in autopsy material, which is not selected, the prevalence is a mere 0.7%.

Group 2. The prevalence in clinical material is reported as 4.3%, in an autopsy population as 0.03%.

Group 3 Clinical material discloses a prevalence of 8%, the autoptic material one of 0.06%.

Group 4. The clinical prevalence amounts to 8%, that in the autopsy population to 0.4%.

Sex Distribution. Sex distribution varies according to the type of A.lusoria. The percentage of affected females (75%) is particularly high in instances of group 1 (IRASA). The female predominance has been discussed repeatedly: Autenrieth in 1807 stressed the finding of 5 cases of A.lusoria in women and 2 men. Felson (1950) had no explanation for the occurrence of A.lusoria in 9 women and none in men; similarly Klinkhamer (1962) failed to explain the phenomenon, although he observed A.lusoria in 25 women and 12 men. The first statistically significant sex difference was demonstrated by Zschoch (1959) on the basis of 104 cases of A.lusoria in a total of 68 women and 36 men. Beabout (1964) did not draw any conclusions from the findings of A.lusoria in 76 females and 30 males.

A.lusoria combined with coarctation and pre-stenotic origin (*subgroup 2a*) is three times more common in females than in males, whereas post-stenotic origin (*subgroup 2b*) affects males twice as often as females. The proportion of males and females in cases of *group 3* is one to one. A.lusoria of *group*

4 is more common in males, the sex ratio being 2 to 1. Owing to the relatively small number of observed cases of groups 2a and 2b the sex differences described represent trends without statistical significance. Sex differences in groups 1 and 4 are statistically significant at the 5% level.

The variability of sex distribution suggests a relationship of *A. lusoria* with a particular type of cardiac malformation. It is well-known that some of congenital heart diseases have a typical sex distribution. Thus, aortic valve anomalies, transposition of the great vessels, coarctation and right-sided aortic arch are more common in males than in females (Abbott, 1928; Campbell, 1973; Moss, 1968), whereas inter-atrial and inter-ventricular septal defects and patent ductus arteriosus are found more frequently in females (Doerr, 1950; Zschoch, 1959). As regards their sex distribution, the different types of *A. lusoria* may be grouped with these cardiac defects: *A. lusoria sinistra* and coarctation combined with post-stenotic origin of *A. lusoria* follow the pattern of defects with male predominance; isolated *A. lusoria* and coarctation combined with pre-stenotic origin of *A. lusoria* imitate the pattern of the group with female predominance.

A. lusoria in Animals. Among 150 dogs Kitchell (1957) found 5 instances of IRASA and Tsukise (1972) described the anomaly in 2 among 160 dogs. Smollich (1959) stressed a female predominance, stating that 5 of the affected 6 dogs were females. Wilson (1949) found 64 rat fetuses with malformations after feeding the mother a vitamin A-deficient diet during pregnancy; 4 of the fetuses had an *A. lusoria* (sex not given).

Embryological Aspects. During normal development the fourth aortic arch forms the proximal part of the subclavian artery, whereas the distal part is formed by the right 7th dorsal intersegmental artery. The left subclavian artery is formed entirely from the left 7th dorsal intersegmental artery. Isolated *A. lusoria dextra* is supposed to arise after complete regression of the fourth aortic arch or in its absence. In this condition, the 8th and 9th segments of the right dorsal aortic root persist, forming the proximal part of the right subclavian artery (Barry, 1951). An alternative hypothesis of the role haemodynamic disturbances as aetiological factors may be questioned after the discovery of an *A. lusoria* in a 14.5 mm SSL embryo (Hackensellner, 1955/56). The developmental stages of the aortic arch are closely related in time sequence with the formation of cardiac septa, thus the association of septal defects and *A. lusoria* both with female predominance suggest a relationship between the two anomalies, mediated either by some mutual interaction or by a governing common denominator. The nature of the common denominator is obviously a subject of speculation, but the singular sex distribution of those forms of *A. lusoria* involving the right, left or the center of the aortic arch respectively suggest the presence of local regulatory influences.

In conclusion, the evaluation of 1110 observations of isolated *A. lusoria* and of 268 observations of *A. lusoria* combined with coarctation, interruption of the aortic arch or right-sided aortic arch discloses the following:

1. *Isolated A. lusoria* shows 58–75% female predominance while *A. lusoria sinistra* has a 66% male predominance.

2. *A. lusoria with coarctation and pre-stenotic origin* discloses female predominance, with *post-stenotic origin* a male predominance is evident, when combined with *interruption of the aortic arch* *A. lusoria* is equally common in men and women, the abnormal artery being present in 1 of 4 cases of interruption of the aortic arch and occurs only in association with Type B of interruption of the aortic arch. 3. Among the *complications* of *A. lusoria* aneurysms are of particular clinical significance and they are found mainly in males. On the basis of 43 personal observations the following additional results were obtained. 4. The frequency of the *A. lusoria* increases with increasing birth order, in half of the subjects with *A. lusoria* additional cardio-vascular anomalies are found and in one third additional visceral anomalies are present.

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