Brit. Heart J., 1968, **30**, 269.

Juxtaposition of the Atrial Appendages*

A Sign of Severe Cyanotic Congenital Heart Disease

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Juxtaposition of the atrial appendages is an apparently rare congenital cardiac anomaly in which the atrial appendages lie side by side, both to the left or to the right of the great arteries, known as left or right juxtaposition of the atrial appendages, respectively (Dixon, 1954).

This abnormality now may readily be diagnosed by angiocardiography (Ellis and Jameson, 1963), and it is widely regarded as an ominous sign of severe cyanotic congenital heart disease. Beyond this general impression, however, the specific types of cardiac malformation likely to be associated with juxtaposition of the atrial appendages, and the relative frequencies of each, remain far from clear. This is not surprising since only 21 post-mortem cases have been published, to our knowledge, almost all as isolated case reports (see Table III). This paper represents an attempt to clarify the picture.

Material, Methods, and Terminology

This study is based upon 21 necropsied cases of juxtaposition of the atrial appendages from two centres: the Congenital Heart Disease Research and Training Center, Chicago, Illinois, U.S.A., 15 cases; and the Hospital for Sick Children, Toronto, Ontario, Canada, six cases.

The heart specimens were measured by the method of Lev, Rowlatt, and Rimoldi (1961) in order to permit quantitative statements concerning chamber mass and volume, and they were measured geometrically by the method of Van Praagh, Ongley, and Swan (1964a) in order to assess relationships accurately. When these methods could not be employed, this is indicated (Tables I and VI).

Received May 6, 1966 (revised May 2, 1967).

* This study was supported by grants from the National Heart Institute, Bethesda, Maryland, U.S.A.

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The previously published 21 post-mortem cases of juxtaposition of the atrial appendages were carefully reassessed (Table III).

In view of the high incidence of transposition of the great arteries (92%) in these 42 cases of juxtaposition of the atrial appendages (Tables I–IV), they were compared with a control group of 100 post-mortem cases of transposition of the great arteries that were randomly selected, except that juxtaposition of the atrial appendages was not present (Table V) (from Paul, Van Praagh, and Van Praagh, 1968). This control study was undertaken in an effort to discover the difference between transposition with and without juxtaposed atrial appendages.

Sections of human embryos from Horizons 2 to 23 (Streeter, 1942, 1945, 1948) were studied histologically (by R.VP.) at the Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland, U.S.A., and models of the heart reconstructions were studied and photographed, in an effort to understand better the morphogenesis of juxtaposition of the atrial appendages.

An abbreviated segmental method is used in Tables I, III, and IV, the three major cardiac segments (the basic parts of the heart) being (1) the viscero-atrial situs (locations of viscera and atria), (2) the ventricular loop (relative ventricular locations), and (3) the conotruncus (infundibulum and great arteries) (Van Praagh *et al.*, 1964b). The following *segmental abbreviations* are used:

Types of viscero-atrial situs: solitus = S, inversus = I, and asplenia = A.

Types of ventricular loop: *d*-loop (morphologically right ventricle right-sided) = D, and *l*-loop (morphologically right ventricle left-sided) = L.

Types of relation between the great arteries at the semilunar valves: solitus (usual) normal = N; *d*-transposition (aortic valve to the right of the pulmonary) = D; *l*-transposition (aortic valve to the left of the pulmonary) = L; and the inverted (mirror-image) normal relation = I.

These segmental symbols (abbreviations) are used in a veno-arterial sequence: *situs-loop-semilunar valves.*

Types of conus (infundibulum) are given in Tables I,

TABLE

ANATOMICAL FINDINGS AT NECROPSY IN 21 CASES

Case No., sex, and age at death	Heart position	Cardiac segments	Atrial septum	Morph. R atrium	Morph. L atrium	R. A-V valve	L. A-V valve	Morph. R vent.	Morph. L vent.
Left Juxtaposition of Atrial Appendages									
1 F 4 ½ yr.	L	S-D-D	PFO	H and E	H and E	N	N	H s̄ E	H and E
2 F 5 mth.	L	S-D-D	ASD II	H and E	H and E	N	N	H and E	H and E
3 M 9 wk.	L	S-D-D	PFO	N	H and E	N	N	H and E	H and E
4 M 9 mth.	L	S-D-D	ASD II	H and E	H and E	N	N	TW.SC	H and E
5 F 2½ yr.	L	S-D-D	PFO	H and E	N	N	N	TW.SC	Hypoplasia
6 F 9 mth.	L	S-D-D	ASD II	H and E	N	N	N	H and E	N
7 NK NK	L	S-D-D	ASD II	H and E*	H and E*	N	N	TW.SC*	H and E*
8 NK NK	L	S-D-D	ASD II	H and E*	H and E*	N	N	TW.SC*	H and E*
9 M 17 mth.	L	S-D-D	ASD II	H and E	N	N	N	H s̄ E	N
10 M 3½ yr.	L	S-D-D	ASD II	H and E	H and E	N	N	H s̄ E	H and E
11 M 10 mth.	L	S-D-D	PFO	H and E	H and E	TS	N	TW.SC	H and E
12 NK NK	L	S-D-D	ASD II	H and E*	H and E*	TAt	N	TW.SC*	H and E*
13 M 4 dy.	L	S-D-D	ASD II	H and E	H and E	TAt	N	Hypoplastic	H and E
14 M 2 mth.	L	S-D-D	ASD II	H and E	N	TAt	N	Absent sinus	N
15 F 5 wk.	D	S-D-D	ASD II + ASD I (small)	H and E*	H and E*	TAt	N	Hypoplastic*	H and E*
16 F 7 mth.	D	S-D-L	ASD II	H and E	H and E	TAt	N	Hypoplastic*	H and E*
17 F 2 yr. 20 dy.	D	S-D-L	ASD II	H and E	H and E	TAt	N	TW.SC	H and E
18 F 4 wk. 3 dy.	L	S-D-L	ASD II	H and E	H and E	N	N	Hypoplastic	H and E
19 F 4½ mth.	L	S-D-D	ASD II	H and E	Slight hypoplasia	N	N	H and E	Slight hypoplasia
Right Juxtaposition of Atrial Appendages									
20 M 2 hr.	D	S-L-L	ASD II	H s̄ E	Hypoplasia	N MV (R)	Hypoplasia TV (L)	Hypoplasia (L)	N (R)
21 F 3 dy.	M	S-L-N	ASD II	H and E*	N*	N MV (R)	TAt (L)	Absent sinus (L)	H and E (R)*

0 = absent; + = present; s̄ = without; H = hypertrophy; E = enlargement; N = normal for age; NK = not known.
Heart position: L = laevocardia; D = dextrocardia; M = mesocardia.
Cardiac segments: See segmental terminology and abbreviations, in text.
Atrial septum: PFO = patent foramen ovale, valve competent; ASD II = secundum type of atrial septal defect; ASD I = primum type of atrial septal defect.
Chambers: Morph. = morphologically; TW.SC = thick-walled and small-chambered; * = qualitative estimation, not measured by method of Lev *et al.* (1961).
A-V valves: TV = tricuspid valve; MV = mitral valve; TS = tricuspid stenosis; TAt = tricuspid atresia; (R) = right-sided; (L) left-sided.
Ventricular septum: VSD = ventricular septal defect.

III, IV, and V. There are four main anatomical types (Van Praagh and Van Praagh, 1965, 1966, 1967).

(1) *Subpulmonary*, with no subaortic, permitting aortic-mitral fibrous continuity, and occurring with normally related great arteries (both solitus and inversus normals).

(2) *Subaortic*, with no subpulmonary, permitting pulmonary-mitral fibrous continuity, and occurring with typical transposition of the great arteries (both *d*- and *l*-).

(3) *Bilateral* (combined)—both subaortic and subpulmonary, permitting no semilunar-atrioventricular

TABLE II

ADDITIONAL ANATOMICAL FINDINGS IN THE PRESENT SERIES OF JUXTAPOSITION OF THE ATRIAL APPENDAGES

Case No.	
1	Bicuspid pulmonary valve
3	Small right atrial appendage, compressed by pulmonary artery
8	Persistent left superior vena cava to coronary sinus to right atrium
10	Intra-aortic band; bicuspid pulmonary valve; persistent left superior vena cava to coronary sinus to right atrium
11	Minute right coronary ostium; bicuspid pulmonary valve
16	Absent left coronary ostium; biscuspid pulmonary valve
17	Bicuspid pulmonary valve
19	Bicuspid pulmonary valve; double-outlet right ventricle
20	Polysplenia; left diaphragmatic eventration; bicuspid pulmonary valve; persistent left superior vena cava to coronary sinus to right atrium; total anomalous pulmonary venous connexion to right atrium
21	Polysplenia; left subclavian artery from descending thoracic aorta

I

OF JUXTAPOSITION OF THE ATRIAL APPENDAGES

Vent. septum	Type of conus	SL valve-A-V valve continuity	Outflow tract obstruction	Aortic arch	Pre-ductile coarct.	Patent ductus arteriosus	AS∠ (H) N≈30°L	VS∠ (H) N≈40°L	VS∠ (F) N≈0°	Rot SLVs (H) N≈±150°
VSD	B	0	0	L	0	0	30°L	5°R	40°R	+50°
Intact	B	0	PS inf.	L	0	0	80°L	35°L	0°	+30°
VSD	B	0	0	L	0	0	30°L	0°	20°R	+15°
VSD	B	0	AS inf.	L	+	+	60°L	70°R	15°R	+65°
Intact	B	0	0	L	0	0	90°L	35°L	20°R	+50°
VSD	B	0	PAt	L	0	0	50°L	50°L	0°	+50°
Minute VSD	A	PV–MV	0	L	0	0	45°L	40°L	40°R	+30°
VSD	B	0	0	R	0	0	70°L	70°R	5°L	+75°
Closed VSD	A	PV–MV	PS inf.	L	0	0	30°L	5°R	NK	+50°
VSD	A	PV–MV	PS inf. +v	L	0	+	20°L	15°R	40°R	+50°
VSD	B	0	PS inf. +v	L	0	0	75°L	50°R	10°L	+60°
VSD	B	0	0	L	+	0	75°L	30°R	0°	+20°
VSD	A	PV–MV	AS inf.	R	+	+	30°L	80°R	NK	+45°
VSD (2)	B	0	PAt	R	0	+	80°L	0°	20°R	+20°
VSD	B	0	AS inf.	L	+	+	90°L	60°R	NK	+45°
VSD	B	0	PS inf. +v	R	0	0	55°L	100°R	NK	−30°
VSD	B	0	PS inf. +v	R	0	0	60°L	60°R	0°	−20°
VSD	B	0	PAt	R	0	+	60°L	10°L	30°R	−10°
VSD (muscular)	B	0	PS inf. +v	L	0	0	NK	25°R	NK	+40°
VSD (2)	B	0	PS inf. +v	NK	NK	NK	NK	70°R	NK	−50°
VSD	P	AoV–MV	AS inf.	L	Arch atresia	+	0°	NK	NK	+70°

Type of conus: See segmental terminlogy and abbreviations, in text; B = bilateral; A = subaortic; P = subpulmonary.
Semilunar valve—AV valve continuity: PV–MV = pulmonary valve-mitral valve; AoV–MV = aortic valve-mitral valve.
Outflow tract obstruction: PS = pulmonary stenosis; AS = aortic stenosis; PAt = pulmonary atresia; inf. = infundibular; v = valvar.
Cardiac geometry: AS∠ = atrial septal angle; VS∠ = ventricular septal angle; Rot SLVs = rotation at the semilunar valves; (H) = horizontal plane; (F) frontal plane; septal angles measured relative to the Z axis (horizontal plane) and the Y axis (frontal plane); +° = *d*-rotation, and −° = *l*-rotation (see Van Praagh *et al.*, 1964a).
Cases 17 and 18 have recently been published separately (Van Praagh and Van Praagh, 1967).

fibrous continuity, and occurring with atypical transposition of the great arteries (both *d*- and *l*-).

(4) *Absence of the distal conus*—neither subaortic nor subpulmonary, permitting aortic-mitral fibrous continuity, as occurs, for example, with truncus arteriosus communis.

Observations

For brevity and completeness, the anatomical findings are presented in Tables and photographs. Tables I and II summarize the anatomical data of the present 21 cases. Table III presents the findings of the previously published 21 necropsied cases, each of which was carefully considered. Table IV summarizes the salient anatomical findings in these 42 cases. Table V compares the 42 cases of juxtaposed appendages with 100 transpositions without juxtaposition. Table VI lists five factors which appear relevant to the morphogenesis of juxtaposition of the atrial appendages, and the incidence of each in our 21 cases. A spectrum of the anatomical findings associated with this anomaly is shown in Fig. 1 to 4. Models of the cardiac lumina of two early human embryos from the Carnegie Collection are presented in Fig. 5 and 6, relative to the morphogenesis of juxtaposition of the atrial appendages.

Discussion

Anatomy. Left juxtaposition is much more frequent than right, occurring in 39 of the 42 cases (93%) (Tables I and III). This seems related to the fact that *d*-loops (non-inverted ventricles) are much more frequent than *l*-loops (inverted ventricles). Left juxtaposition occurs almost exclusively with *d*-loops, in 37/39 cases (95%), while right juxtaposition is known only with *l*-loops, in 3/3 cases (Tables I and III).

Both transposition and non-transposition of the great arteries have been observed with left and with right juxtaposition, but transposition is virtually the rule, in 36/39 cases (92%) (Table IV). *D*-transposition is almost four times as common as *l*- (3·75/1). Fig. 1 and 2 show fairly typical cases of left juxtaposition with complete *d*-transposition.

Fig. 4, however, shows a rare case of right juxtaposition with isolated ventricular inversion. The

TABLE

ANATOMICAL FINDINGS IN THE PREVIOUSLY REPORTED 21 POST-

Case No., sex, and age at death	Heart position	Cardiac segments	Double-outlet R vent.	Atrial septum	A-V valves	Morph. R vent.	Morph. L vent.	Vent. septum
Left Juxtaposition of Atrial Appendages								
22 F 20 yr.	D	S-D-L	+	ASD II	N	Large	Large	VSD
23 F 10¼ yr.	D	S-D-D	+	PFO	TV hypopl.	Small	Large	VSD's
24 NK 10 wk.	L	S-D-D	0	ASD II	TS	Small	Large	VSD
25 M 5½ mth.	NK	S-D-N	0	ASD II	TAt	Small	Large	VSD
26 M 15 mth.	L	S-D-D	+	ASD II	TAt	Small	Large	VSD
27 F 3 mth. 10 dy.	D	S-D-D	0	ASD II	TV hypopl.	Small	Large	VSD
28 F 5¾ mth.	L	S-D-D	0	PFO	TV hypopl.	Small	Large	VSD
29 M 1 yr.	L	S-D-D	0	ASD II	N	TW.SC	Large	VSD
30 F 25 yr.	D	I-L-L (or A-L-L)	0	Common atrium	Common A-V valve	Sinus absent	Large	VSD
31 F 11 mth.	L	S-D-D	0	ASD II	MV hypopl.	Large	Large	Intact
32 M 12 yr.	L	S-D-D	0	ASD II	TAt	Small	Large	VSD
33 F 7½ yr.	L	S-D-L	+	ASD II	N	TW.SC	Large	VSD's
34 F 7½ yr.	L	S-D-D	0	ASD II	N	TW.SC	Large	VSD
35 F 7 mth.	L	S-D-D	0	PFO	N	Small	Large	VSD
36 M 20 dy.	D	S-D-D	0	ASD II	TAt	Small	Large	VSD
37 F 14 mth. 1 wk.	L	S-D-L	0	ASD II	TAt	Small	Large	VSD
38 F 53 hr.	L	S-L-N	0	ASD II	MAt (R)	Large (L)	Small (R)	Intact
39 M 6 wk.	L	S-D-D	NK	NK	TS	NK	NK	VSD
40 M 3 mth.	L	S-D-D	0	NK	TAt	Small	Large	VSD
41 NK NK	L	S-D-D	0	NK	TAt	Small	Large	VSD
Right Juxtaposition of Atrial Appendages								
42 F 3 wk.	L	S-L-D	+	Common atrium	MV hypopl. (L)	Large (L)	Small (R)	VSD

ventricles are inverted, due to *l*-looping. But the great arteries are not transposed relative to the atrioventricular canal (aortic-mitral fibrous continuity is present) or to the ventricles (the aorta is normally related to the morphologically left ventricle, and the pulmonary artery is normally related to the morphologically right ventricle). A normal type of conus is present—subpulmonary. However, the spatial semilunar relationship is very abnormal: aortic valve anterior and to the right, pulmonary valve posterior and to the left. This abnormal semilunar relation is related to the very abnormal locations of the ventricles from which these great arteries originate. Ventricular inversion is present, but the apex points far to the left instead of well to the right, as is usual with ventricular inversion (e.g. in mirror-image dextrocardia). When the ventricular apex was pointed rightward to correct for the abnormal ventricular locations, the semilunar relation then appeared normal (non-transposed).

TABLE IV

SUMMARY OF ANATOMICAL FINDINGS IN 42 POST-MORTEM CASES OF JUXTAPOSITION OF ATRIAL APPENDAGES

Sex	Heart position	Cardiac segments	Double outlet RV	Atrial septum	A-V valves
M = 15 F = 22 NK = 5	L = 31 D = 9 M = 1 NK = 1	S-D-D = 30 S-D-L = 6 S-D-N = 1 S-L-L = 1 S-L-D = 1 S-L-N = 2 I-L-L = 1	7	PFO = 7 ASD II = 30 ASD I = 1 Common at. = 2 NK = 3	TV hypopl. = 4 TS = 3 TAt = 14 MtV hypopl. = 2 MtAt = 1 Common AVV = 1
Morph. R vent	**Morph. L vent**	**Vent. septum**	**Type of conus**	**Outflow tract obstruction**	**Aortic arch**
Large = 11 Small = 30 NK = 1	Large = 33 Normal = 4 Small = 4 NK = 1	VSD = 37 Intact = 5	Bilateral = 30 Subaortic = 6 Subpulmonary = 3 NK = 3	PS = 16 PAt = 6 AS = 6 AoAt = 2 Preduct. coarc. = 8	L = 30 R = 8 NK = 4

Abbreviations: as before.

III

MORTEM CASES OF JUXTAPOSITION OF ATRIAL APPENDAGES

Type of conus	Outflow tract obstruction	Aortic arch	Additional anatomical data
B	PS, inf. +v	R	L SVC to coronary sinus to RA
B	PS, inf. +v	L	L SVC to coronary sinus to RA
B	0	L	Coronary artery from all 3 aortic sinuses of Valsalva
P	PS	L	AoV–MV fibrous continuity
B	PS, inf. +v	L	R SVC absent, but R SA node present; L SVC to coronary sinus to RA; common pulm. vein to LA; 2-chambered RV
B	0	R	Absent L coronary ostium
B	PAt	L	
B	PAt	L	Absent L coronary ostium
B	PS	L	Hepatic part of IVC absent; L pulm. veins to RA (L-sided); spleen not described (? asplenia)
A	0	L	
B	PS, inf. +v	L	
B	PS, inf. +v	L	Common pulm. vein to LA
B	0	NK	L SVC to coronary sinus to RA
B	Preduct coarct.	L	
A	AoAt	L	
B	PAt	L	Anatomically corrected transposition
P	AoAt	NK	Isolated ventricular inversion
NK	PS	L	
NK	AS, inf. + predcut. coarct. mild	L	
NK	0	NK	
B	As, inf. + preduct. coarct.	L	Absent hepatic IVC; prominent R venous valve; common pulm. vein to L of common atrium

Abbreviations: same as Table I.

Cases: 22 = Birmingham, 1893: 23 = Wenner, 1909; 24 = Dünner, 1914; 25 = Huebschmann, 1921; 26 = Kettler, 1933; 27 = Ngai, 1935; 28 = Bredt, 1936; 29 = Harris and Farber, 1939; 30 = Taussig, 1947; 31 = Miskall and Fraser, 1948; 32 = Rogers, Cordes, and Edwards, 1950; 33 and 42 = Dixon, 1954; 34 = Edwards *et al.*, 1954; 35 = Smyth, 1955; 36 = Polanco and Powell, 1955; 37 = Stewart and Wynn-Williams, 1956; 38 = Fragoyannis and Nickerson, 1960; 39 and 40 = Sherman, 1963; 41 = Edwards *et al.*, 1965.

An anterior, non-transposed aorta, as in this case (Fig. 4), is rare, but serves to illustrate that transposition of the great arteries basically is not a question of the type of semilunar relation relative to fixed *external* co-ordinates (e.g., anterior-posterior), but rather that the critical relations are the *internal*

TABLE V

COMPARISON OF JUXTAPOSITION OF ATRIAL APPENDAGES WITH TRANSPOSITION CONTROL SERIES

	Juxtaposition of appendages	Transposition control series
Number of cases	42	100
Male/female	0·7/1	1·9/1
Median age at death (mth.)	8	2
Situs solitus of viscera and atria	41 (98)	91
Situs inversus of viscera and atria	1 (2)	5
Asplenia	0 (0)	4
Dextrocardia	9 (22)	12
Double outlet right ventricle	7 (17)	7
Anatomically corrected transposition	4 (9·5)	0
Patent foramen ovale, valve competent	7 (17)	61
Atrial septal defect, secundum type	30 (71)	23
Common atrium	2 (5)	6
Tricuspid atresia and severe stenosis	17 (40)	4
Mitral atresia and severe stenosis	1 (2)	2
Common atrioventricular canal	1 (2)	12
Ventricular septal defect	37 (88)	57
Small or absent right ventricular sinus (inflow)	30 (71)	20
Small left ventricle	4 (10)	8
Bilateral conus (infundibulum)	30 (77)	25
Subaortic conus	6 (15)	75
Subpulmonary conus (no transposition)	3 (8)	0
Pulmonary outflow obstruction	22 (52)	19
Aortic outflow obstruction	16 (38)	8
Right aortic arch	8 (21)	10

Percentages are given in parentheses.

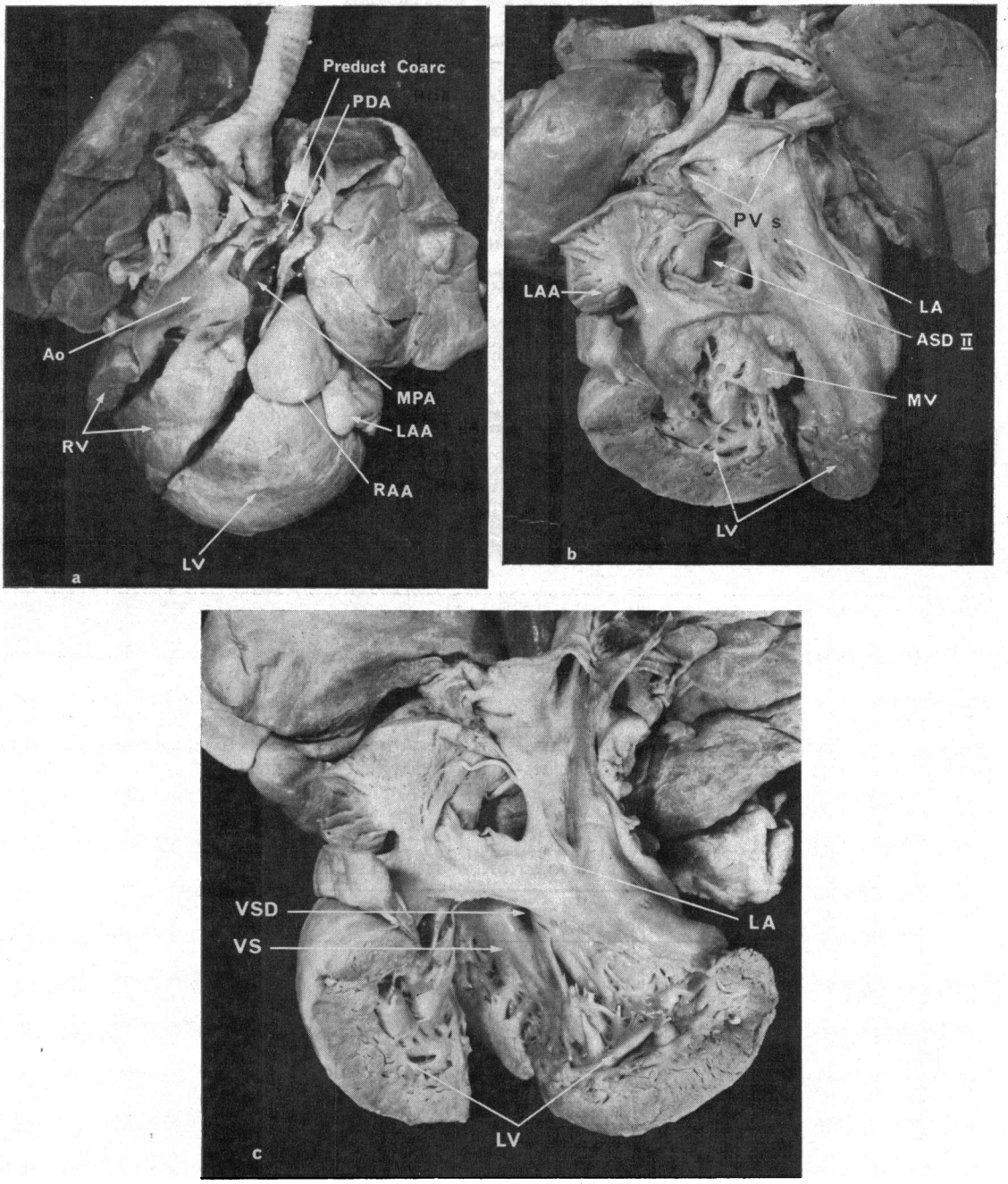


FIG. 1.—Fairly typical case of left juxtaposition of the atrial appendages (Case 4, Table I), with complete *d*-transposition (a). Combined conus, small right ventricle (a), high ventricular septal defect (VSD) (c), and large secundum atrial septal defect (b, c). Less typical features include muscular subaortic stenosis, preductile coarctation (a), and patent ductus arteriosus (PDA) (a). Removal of the mitral valve (c) attempts to show the 130° angulation between the atrial and ventricular septa (Table I), but this angulation is artefactually reduced by opening and positioning for photography. Although the ventricular septum and apex pointed rightward, i.e. 70° to the right (Table I), dextrocardia (right-sided heart) was not present in the postero-anterior chest film, apparently because of the smallness of right ventricle and the largeness of left ventricle. Thus, rightward orientation of the ventricular apex and right-sided heart (dextrocardia) are not necessarily synonymous.
[Photographs of heart specimens by Frederick Sharp.]

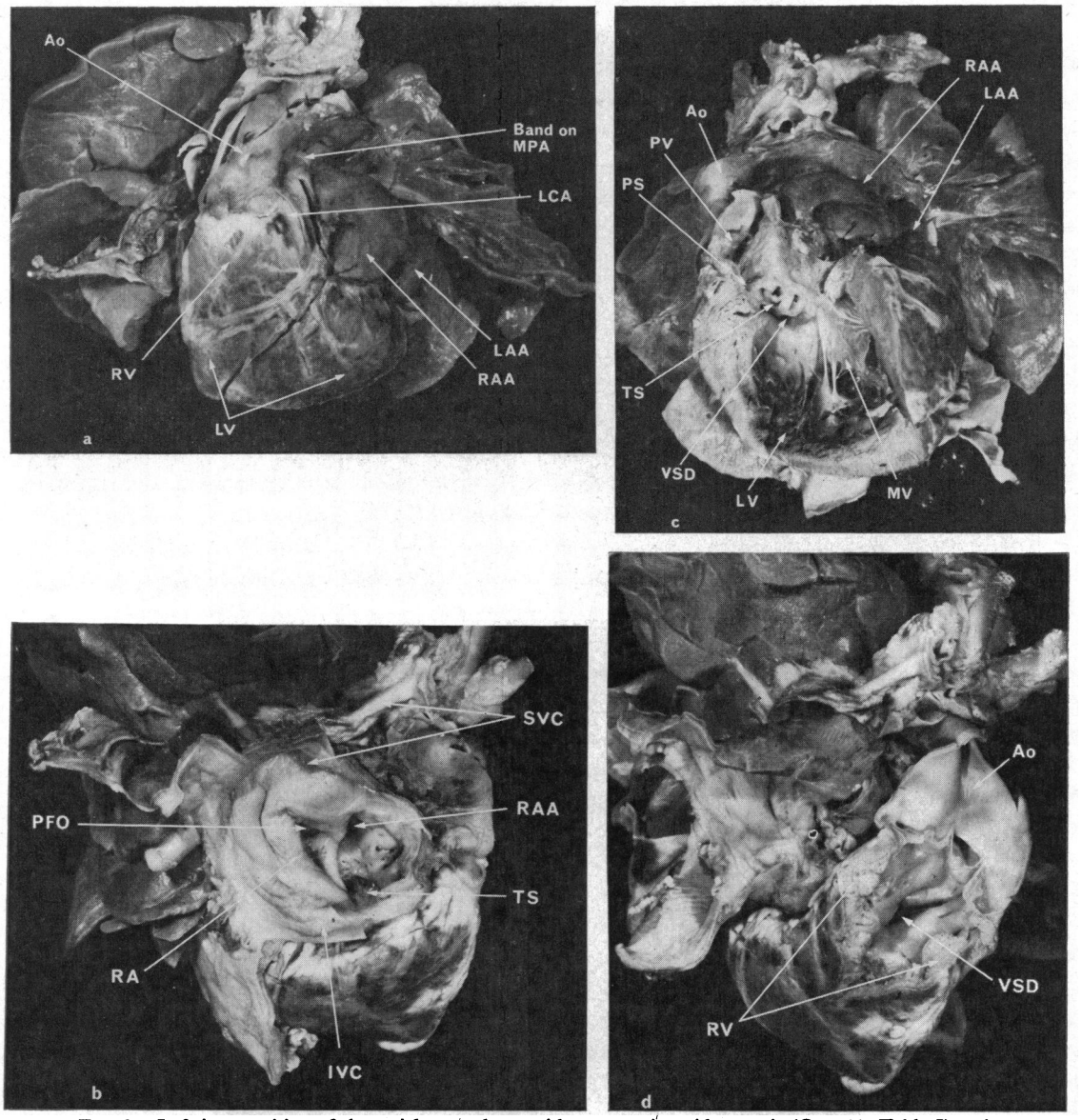


FIG. 2.—Left juxtaposition of the atrial appendages with severe tricuspid stenosis (Case 11, Table I). A very abnormal *d*-bulboventricular loop is present. Note: *d*-transposition (a); combined conus, with a relatively well-developed subaortic component (d); and a comparatively poorly developed subpulmonary component (c); with subpulmonary stenosis (c); the underdeveloped right ventricle (d) and the well-developed left ventricle (c); the marked malalignment between the ventricular and the atrial septa of 125° (Table I); severe tricuspid stenosis (b), opening into the left ventricle immediately above the ventricular septal defect, as in Dünner's case (1914); and the abnormally leftward lie of the atria, atrial septal angle = 75° left, horizontal plane projection (Table I).

ones—within the heart itself (semilunar–mitral, and semilunar–ventricular). The conclusion that aortic–mitral fibrous continuity indicates non-transposition of the great arteries was also reached by Keith (1909) and by Grant (1962).

Frequency. Much the most frequent type was left juxtaposition with an S–D–D segmental combination: situs solitus of the viscera and atria (S), *d*-loop (D), and *d*-transposition (D) in 30/42 cases (71%) (Table IV). This segmental combination

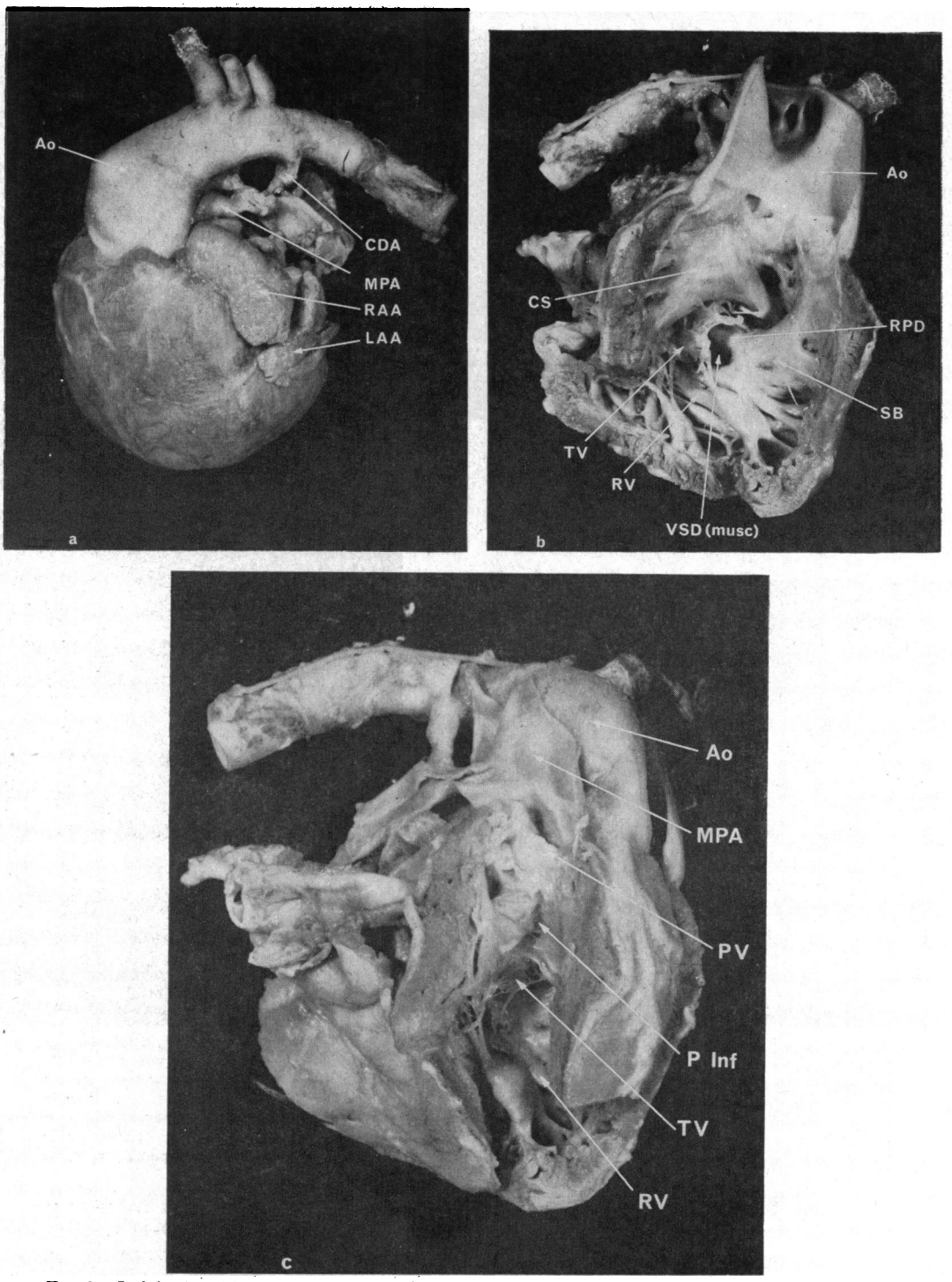
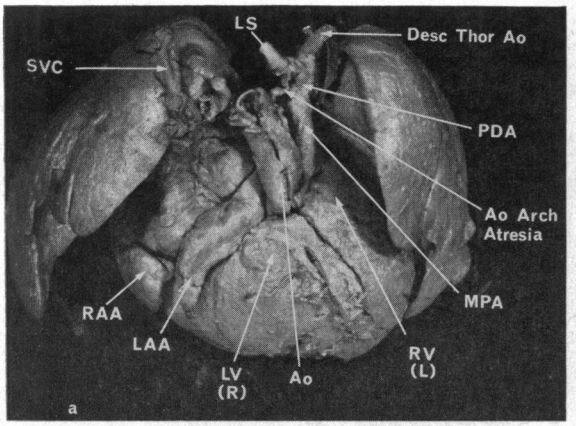
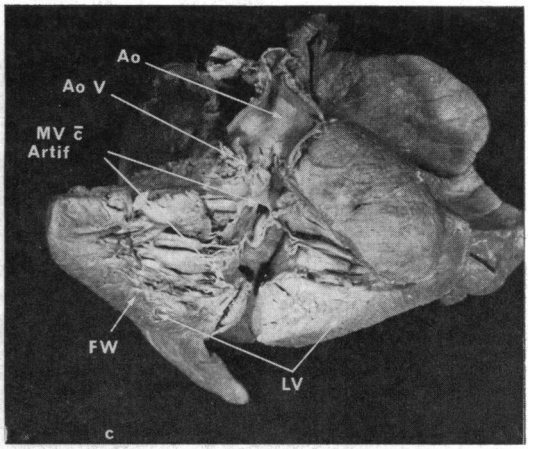
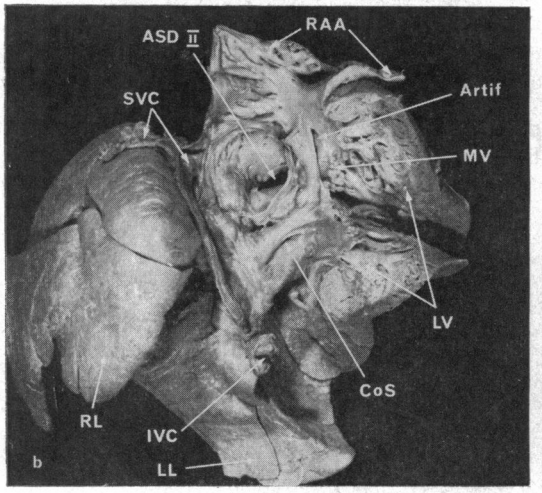
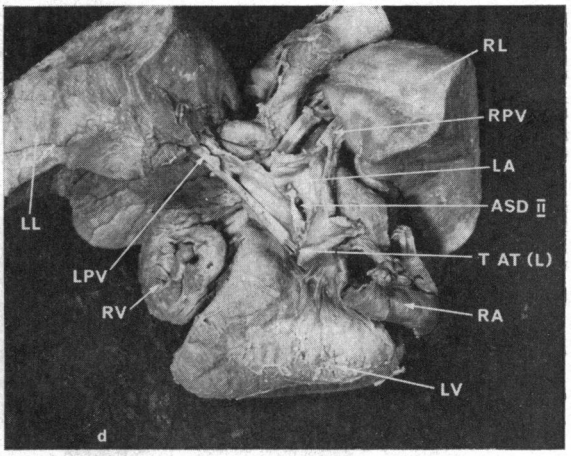


FIG. 3.—Left juxtaposition of the atrial appendages with double outlet right ventricle (Case 19, Table I). A very abnormal *d*-bulboventricular loop is present. Note: *d*-transposition (a); combined conus, subaortic (b) and subpulmonary (c); pulmonary stenosis, infundibular and valvar, apparently due to a poorly expanded pulmonary conal component (c); abnormally rightward ventricular septal angle, 25° right (Table I); muscular ventricular septal defect (VSD) beneath right posterior division (RPD) of septal band (SB), with no high VSD beneath conal septum (CS) (b).









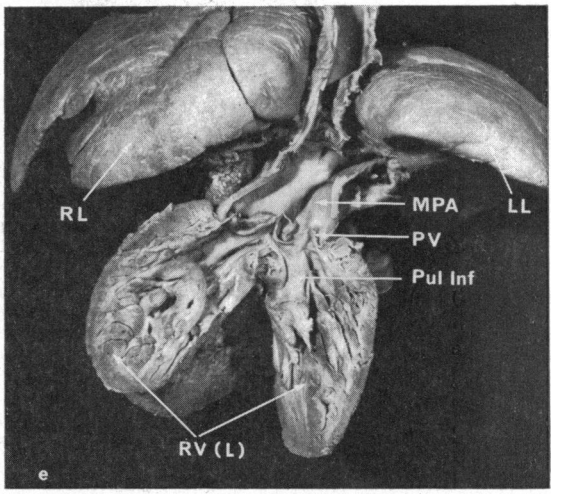


FIG. 4.—Right juxtaposition of atrial appendages with ventricular inversion and non-transposition of the great arteries, i.e. isolated ventricular inversion (Case 21, Table I). Note: mesocardia (a); situs solitus of viscera and atria (a); *l*-loop with small right ventricle left-sided (e), and large left ventricle right-sided (b, c); mitral-aortic (non-coronary) fibrous continuity (c); tricuspid atresia (left-sided) (d); subaortic stenosis (c) with aortic arch atresia, patent ductus arteriosus, and left subclavian artery from descending thoracic aorta (a); and well-developed pulmonary infundibulum (e). Aorta arises anteriorly and to right of pulmonary artery (a). See text.

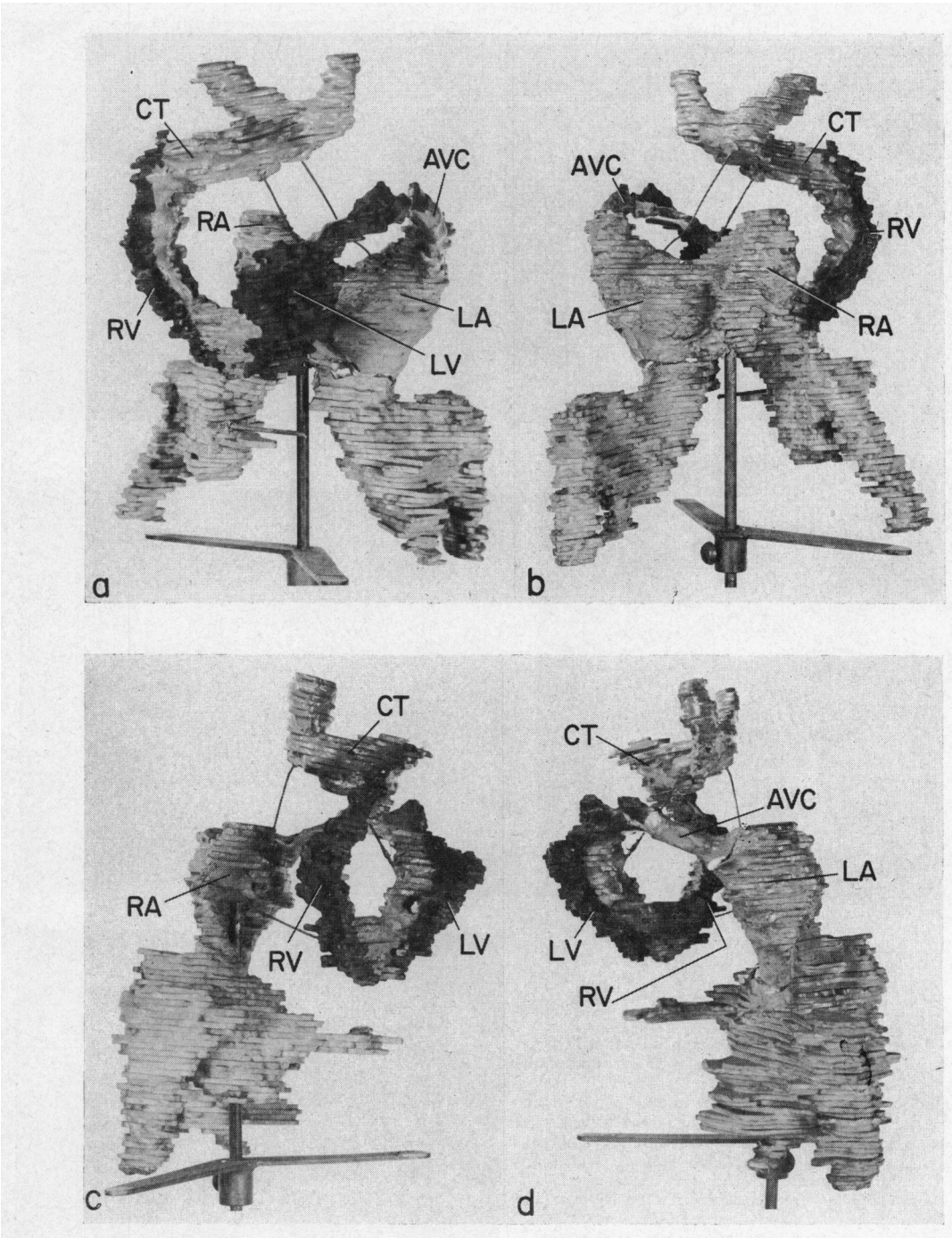


FIG. 5.—Model of the cardiac lumen of Carnegie human embryo 470, horizon 11, 17 somites, 4·3 mm., estimated ovulation age 23 days. The relations of left juxtaposition are present. (a) Ventral (anterior) view; (b) dorsal (posterior) view; (c) right lateral view; (d) left lateral view. RV, right ventricle; LV left ventricle; RA, right atrium; CT, conotruncus; AVC, atrioventricular canal.

[Fig. 5 and 6 by courtesy of the Carnegie Institution of Washington.]

[Photographs of heart models by Richard Grill.]

TABLE VI

DEVELOPMENTAL CONSIDERATIONS IN JUXTAPOSITION OF ATRIAL APPENDAGES (21 CASES)

Case No.	Bilateral conus	Failure of apical rotation (VS∠, H)	Small RV	Tilt of ventricles + great arteries (VS∠, F)	Abnormal atrial location (AS∠, H)
1	+	+	0	+	0
2	+	0	0	0	+
3	+	+	0	+	0
4	+	+	+	+	+
5	+	0	+	+	+
6	+	0	0	0	0
7	+	0	+	+	0
8	+	+	+	0	+
9	0	+	0	NK	0
10	0	+	0	+	0
11	+	+	+	0	+
12	+	+	+	0	+
13	0	+	+	NK	0
14	+	+	+	+	+
15	+	+	+	NK	+
16	+	+	+	NK	+
17	0	+	0	0	+
18	+	+	+	+	+
19	+	+	0	NK	NK
20	+	0	+	NK	NK
21	0	+	+	NK	+
Totals	+ =16 (76%) 0 = 5 NK= 0	+ =16 (76%) 0 = 5 NK= 0	+ =13 (62%) 0 = 8 NK= 0	+ = 8 (38%) 0 = 6 NK= 7	+ =12 (57%) 0 = 7 NK= 2

Abbreviations: as before.
Cardiac geometry: see footnote to Table I, and Van Praagh *et al.* (1964a).

resulted in complete *d*-transposition in 27 cases (64%), as in Fig. 1 and 2, and in double-outlet right ventricle with *d*-transposition in 3 cases (7%), as in Fig. 3.

Second in frequency was left juxtaposition with S–D–L: situs solitus of viscera and atria (S), *d*-loop (D), and *l*-transposition (L) in 6 cases (14%) (Table IV). This segmental combination resulted in double-outlet right ventricle in two (Cases 22 and 33) (Table III), and in anatomically corrected transposition in the other four (Harris and Farber, 1939) —transposed aorta from the morphologically left ventricle, transposed pulmonary artery from the morphologically right ventricle: Cases 16–18 (Table I) and Case 37 (Table III).

Five other segmental combinations ("types") have been observed in six cases (Table IV), but together they comprise only 14 per cent of the documented experience with this apparently rare anomaly. Juxtaposition probably is by no means as rare as the presently available anatomical data might suggest, since it has been possible to double the recorded anatomical experience with cases from only two centres.

The segmental symbols employed in this study merit mention because they have proved to be brief, convenient, and specific. They are not situs-related. Consequently, meanings do not vary with the type of situs (e.g. with complete and corrected transposition). They form convenient "thought packages", and facilitate use of the segmental approach to clinical and laboratory diagnosis, which is particularly helpful when one is confronted by a case of complex congenital heart disease. Essentially, one diagnoses the anatomical type of each cardiac segment, the relations among the three segments, and the associated anomalies within each segment and between them (Van Praagh *et al.*, 1964b, 1965; Van Praagh and Van Praagh, 1966). This approach makes it unnecessary to attempt to memorize classifications of complex congenital heart disease (e.g. of the transpositions, dextrocardias, laevocardias), when such classifications really are segmental combinations. This method is generally applicable to congenital heart disease as a whole, and it is useful at several levels—clinically, pathologically, and embryologically. Further, this symbolic segmental method of analysis is helpful in data processing (e.g. by computer).

Transposition Control Study (Table V). Statements of statistical significance and insignificance will be avoided because the degree of selection in each series is unknown.

Sex. The juxtapositions showed a female predominance, male/female = 0·7/1, contrasting sharply with the well-known male predominance in transposition as a whole; male/female = 1·9/1 in the control group.

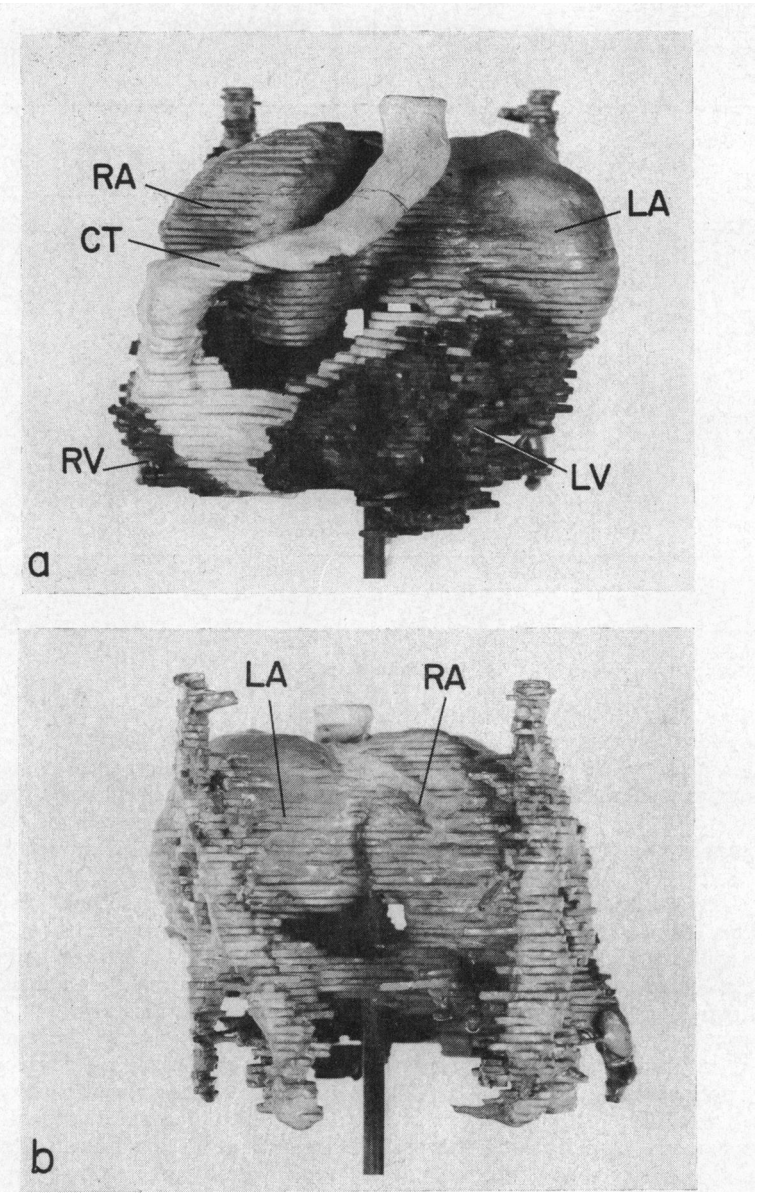
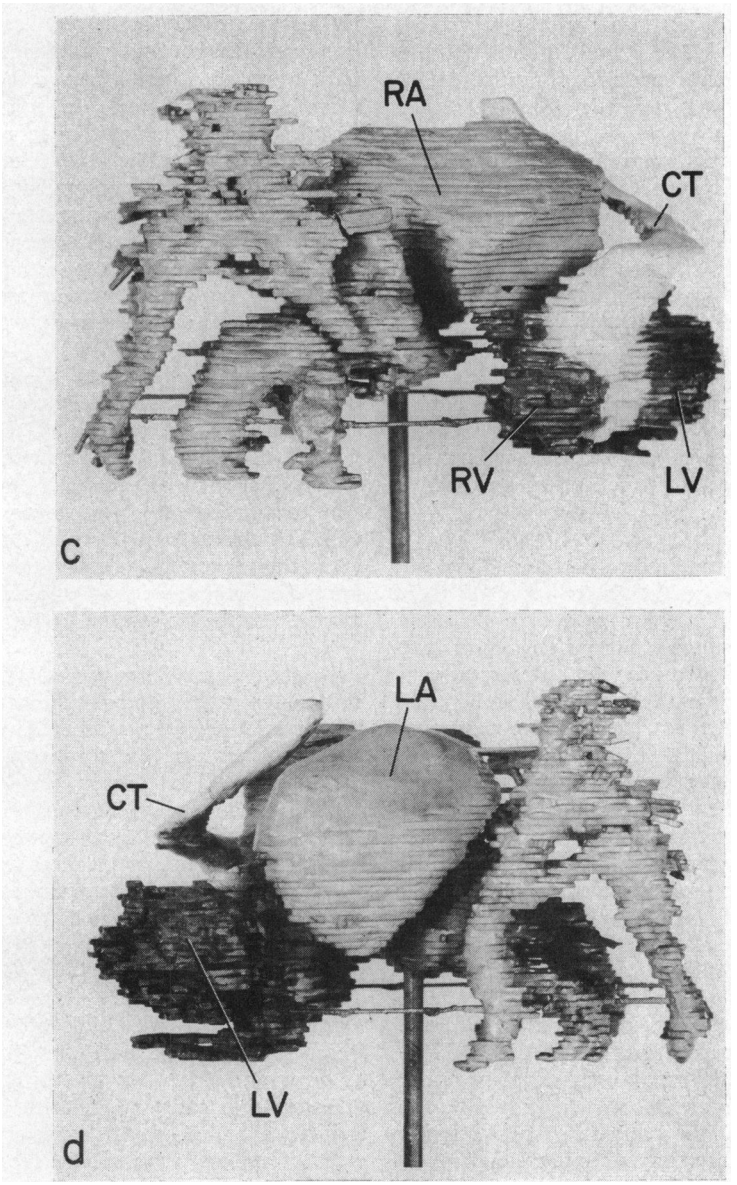


FIG. 6.—Model of the cardiac lumen of Carnegie human embryo 836, horizon 13, 4 mm., estimated ovulation age 27 days. The relations of left juxtaposition have largely disappeared. Orientation (a) to (d) and abbreviations as in Fig. 5.

Age at Death. The juxtapositions had a higher median age at death (8 months compared with 2 months), perhaps reflecting the higher incidence of pulmonary outflow tract obstruction with juxtaposition (52%) than without (19%).

Dextrocardia (right-sided heart). This was almost twice as common with juxtaposition (22%) as without (12%), apparently related to frequent failure of leftward rotation of the ventricular apex with non-inverted ventricles, indicated by the abnormally rightward ventricular septal angles in the horizontal plane (Tables I and VI).

Double-outlet Right Ventricle. This was more than twice as common with juxtaposition (17%) as



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without (7%). *Anatomically corrected transposition* occurred only with juxtaposition (9·5%) (Table V). Both of these cono-ventricular malalignments (between the conotruncus—infundibulum and great arteries—above, and the ventricles below) appeared related to the extraordinarily high incidence of bilateral (subaortic and subpulmonary) conus with juxtaposition (77%), compared with its relatively low incidence in transpositions without juxtaposition (25%). If the subpulmonary part of a bilateral conus is relatively well developed, it separates the pulmonary and mitral valves quite widely, transposing the pulmonary valve across the ventricular septum, thereby producing double-outlet right ventricle, as in Fig. 3c. A bilateral conus similarly appears essential to the morphogenesis of the cono-ventricular malalignment known as anatomically corrected transposition (Van Praagh and Van Praagh, 1967).

Atrial Septal Defects. Those of the secundum type, excluding valve competent patent foramen ovale, were far commoner with juxtaposition (82%) than without (29%), apparently for three main reasons. (1) The absence of the great arteries directly anterior to the interatrial fold appeared to permit septum secundum to protrude anteriorly to an abnormal degree. Normally, the great arteries in front of septum secundum serve as a constraining fulcrum, about which the atrial appendages expand anteriorly. (2) With juxtaposition, the atria themselves often are abnormally located, indicated by the abnormal atrial septal angles in the horizontal plane (Tables I and VI). The atrial septum may lie almost frontally, with the right atrium almost directly anterior (ventral) to the left. (3) Tricuspid atresia or severe stenosis was frequent with juxtaposition, also predisposing to secundum atrial septal defect (see below).

Tricuspid Atresia or Severe Stenosis. This was ten times as common with juxtaposition (40%) as without (4%). This seemed related to the often gross malalignment between the ventricular loop and the atria, reflected by the very abnormal ventricular septal angles in the horizontal and frontal planes (Tables I and VI), and by the failure of apical rotation in the appropriate direction—to the left following *d*-looping and to the right following *l*-looping (Table VI). With tricuspid atresia, the expected site of the tricuspid orifice invariably overlay the posterior part of the muscular ventricular septum, also suggesting that tricuspid atresia results from ventriculo-atrial malalignment. Fig. 2 shows an unusual example of severe congenital tricuspid stenosis, similar to Dünner's case (1914).

Right Ventricular Underdevelopment or Absence. This was much commoner with juxtaposition (71%) than without (20%). Since normal development of the morphologically right ventricle may well be one of the factors causing the ventricular apex to swing in the appropriate direction, underdevelopment of this chamber may be important in the morphogenesis of malalignment between the ventricular loop and the atrioventricular canal.

When tricuspid atresia is present, underdevelopment of the right ventricle conventionally is regarded as secondary to the tricuspid atresia. However, the reverse may well be nearer the mark: tricuspid atresia secondary to right ventricular underdevelopment, such that the ventricular septum blocks the tricuspid orifice. When the right ventricle is exceedingly underdeveloped, as with *double-inlet left ventricle* (Mehrizi *et al.*, 1966), or virtually absent, as with *single left ventricle* (Van Praagh *et al.*, 1964a), the ventricular septum lies to the right of the tricuspid orifice. But with tricuspid atresia, the right ventricle often seems somewhat better developed, which appears to shift the ventricular septum leftward sufficiently to plug the tricuspid orifice. In this regard it is noteworthy that with juxtaposition, underdevelopment of the right ventricle was distinctly commoner (73%) than was tricuspid atresia or severe stenosis (40%). Hence it is suggested that an appropriate degree of right ventricular underdevelopment results in tricuspid atresia (rather than vice versa).

High Ventricular Septal Defects. These were commoner with juxtaposition (88%) than without (57%), apparently because of the frequently abnormal, malaligned, ventricular loops and the high incidence of bilateral conus (77%) with juxtaposition. The bilateral conus almost invariably is associated with a high ventricular septal defect at the conoventricular junction—between the usually abnormal infundibulum above and the often anomalously located ventricular septum below.

Outflow Tract Obstructions. These were much commoner with juxtaposition than without: pulmonary, 52 per cent compared with 19 per cent; and aortic, 38 per cent compared with 8 per cent, respectively. The higher incidence of outflow tract obstruction with juxtaposition appeared to be related to its more abnormal conal anatomy, as indicated by its higher incidence of bilateral conus, noted above. Underdevelopment, with consequently deficient expansion, of either part of the bilateral conus resulted in obstruction of the involved outflow tract.

Right Aortic Arch. This approached tetralogy frequency with juxtaposition (21%), being twice as common as without juxtaposition (10%).

Apart from comparisons with juxtaposition, the anatomical findings in this series of 100 post-mortem cases of transposition of the great arteries are of considerable interest *per se* (Table V).

Morphogenesis. The relationships of left juxtaposition normally are present early in embryonic life, shortly following the initiation of *d*-looping, as is shown in Fig. 5, which is a model of the cardiac lumen of a human embryo from the Carnegie Collection, with an estimated ovulation age of approximately 23 days (horizon 11) (Streeter, 1942, 1945, 1948). However, by about 27 days estimated ovulation age (horizon 13), the conotruncus lies largely between the expanding atrial appendages and is approaching its definitive normal location (Fig. 6).

This comparatively normal conotruncal-atrial relation is achieved before the bifid apex of the developing ventricles begins to swing leftward, this being accomplished soon thereafter—largely between the 28th and 38th days of estimated ovulation age (horizon 14 to 18).

The factors which appeared potentially important to the morphogenesis of juxtaposition of the atrial appendages, which may be viewed as a persistence of the normal approximately 23rd day (horizon 11) conotruncal-atrial relations, are summarized in Table VI. None of these five factors occurred in all 21 cases. Only three (Cases 4, 14, and 18) showed all five abnormalities. One (Case 6) had only one of the apparently important anomalies—a bilateral conus.

Thus, justaposition appeared not to have a single morphogenetic cause, nor a single group of causes; rather, it seemed to be a secondary effect, not a primary anomaly, which may result from one or several other cardiac malformations. An abnormal location of the atria never appeared to be the only significant anomaly (Table VI).

Diagnostic Applications. Do the anatomical findings associated with juxtaposition constitute an unrecognized syndrome? They may be so regarded. However, consideration of Tables IV, V, and VI has led us to the view that these findings are not as clear cut a syndrome as the findings associated with asplenia, for example (Ivemark, 1955). None the less, the angiocardiographic demonstration of juxtaposition certainly should suggest the coexistence of a number of other cardiac malformations. Based on all available anatomical data, the salient diagnostic probabilities appear to be as follows: with left juxtaposition, non-inverted ventricles, 95 per cent; with right juxtaposition, inverted ventricles, 100 per cent; with both types of juxtaposition, situs solitus of the viscera and atria, 98 per cent; transposition of the great arteries, 92 per cent; ventricular septal defect, 88 per cent; atrial septal defect, 78 per cent, nearly always secundum, 71 per cent; bilateral conus, 77 per cent; small or absent right ventricle, 71 per cent; tricuspid atresia or severe stenosis, 40 per cent; pulmonary outflow tract obstruction, 52 per cent; aortic outflow tract obstruction, 38 per cent; dextrocardia, 22 per cent; right aortic arch, 21 per cent; double-outlet right ventricle, 17 per cent; and anatomically corrected transposition, 10 per cent.

Summary

Twenty-one post-mortem cases of juxtaposition of the atrial appendages have been reported, and the previously published 21 necropsied cases have been reassessed. In view of the high incidence of transposition of the great arteries in these 42 cases with juxtaposition (92%), they were compared with a control series of 100 post-mortem cases of transposition of many types that were randomly selected, except that juxtaposition of the atrial appendages was not present.

Many differences were found. The cases with juxtaposition had a female predominance, in contrast to the male predominance in transposition as a whole. The juxtapositions also had higher incidences of dextrocardia, right aortic arch, bilateral conus (subaortic and subpulmonary), double-outlet right ventricle, anatomically corrected transposition, pulmonary and aortic outflow tract obstruction, ventricular septal defect, underdevelopment or absence of the right ventricle, tricuspid atresia or severe stenosis, and secundum atrial septal defect. Of the foregoing, perhaps the most striking differences displayed by the juxtapositions were the remarkably high incidences of bilateral conus (77%), small or absent right ventricle (71%), and tricuspid atresia or severe stenosis (40%).

From the standpoint of morphogenesis, juxtaposition of the atrial appendages appeared to be a secondary effect produced by one or more associated anomalies, not a primary cardiac malformation *per se*.

Diagnostically, the angiocardiographic demonstration of juxtaposition may be considered to indicate the presence of a very abnormal, often incompletely rotated, bulboventricular loop. The diagnostic probabilities concerning associated cardiac malformations were presented, based on all available anatomical data.

An abbreviated segmental approach to congenital heart disease, which is simple, specific, widely applicable, and designed to facilitate data processing, is presented.

The authors wish to thank Dr. John D. Keith and Dr. William Donohue of the Hospital for Sick Children, Toronto, Canada, for kindly permitting us to include six of their cases in the present series: Cases 9, 10, 15, 16, 19, and 21 (Table I). We are also indebted to Dr. James D. Ebert and Dr. Robert L. DeHaan of the Department of Embryology of the Carnegie Institution of Washington, Baltimore, U.S.A., for their co-operation in the embryological aspects of this study, and we wish to express our gratitude to Dr. Maurice Lev, Director of the Congenital Heart Disease Research and Training Center, Chicago, U.S.A., for unfailing encouragement.

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Addendum

Since submission of this paper for publication, an additional case report has appeared concerning left juxtaposition with an S–D–L segmental combination resulting in anatomically corrected transposition (Raghib, Anderson, and Edwards (1966).

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Raghib, G., Anderson, R. C., and Edwards, J. E. (1966). Isolated bulbar inversion in corrected transposition. *Amer. J. Cardiol.*, **17**, 407.