Chapter 1
Definition of Conotruncal Anomalies

Richard Van Praagh

Abstract Conotruncal anomalies are malformations of the infundibulum (conus arteriosus) and great arteries (truncus arteriosus) that have abnormal ventriculo-arterial alignments and connections: tetralogy of Fallot, truncus arteriosus, interrupted aortic arch type B, transposition of the great arteries, double-outlet right ventricle, double-outlet left ventricle, anatomically corrected malposition of the great arteries. Normally related great arteries have complete right-left (R-L) asymmetry in the development and anatomy of the subarterial conal free walls, with involution of the subaortic conal free wall musculature and good growth and expansion of the subpulmonary conal free wall musculature.

All conotruncal anomalies lack this type of complete R-L conal free wall asymmetry. Solitus normally related great arteries (SNRGA) result from involution of the right-sided subaortic conal free wall and from simultaneous good growth and expansion of the left-sided subpulmonary conal free wall. Briefly, $\mathrm{SNRGA} = \mathrm{OR} + 4\mathrm{L}$. The right-sided subaortic conal free wall muscular development is grade 0 (absent) and the left-sided subpulmonary conal free wall muscular development is grade 4 (normal). This is how the embryonic aortic switch is normally performed. The left-sided PA is carried superiorly, anteriorly, and rightward above the RV, away from the interventricular foramen, atop the developing subpulmonary conal free wall. Simultaneously, the right-sided Ao moves inferiorly, posteriorly, and leftward because the subaortic conal free wall is undergoing involution, thought to be due to apoptosis. Consequently, the aorta passes mostly through the interventricular foramen and normally comes into direct fibrous continuity with the developing mitral valve (MV), above the morphologically left ventricle (LV), thereby accomplishing the normal embryonic aortic switch. Eleven normal and abnormal developmental and anatomic conotruncal equations are presented in this chapter. From an evolutionary perspective, the conotruncal anomalies appear to represent physiologically unsuccessful attempts to perform the embryonic aortic switch. Conotruncal anomalies are infundibular malformations, causing the great arteries to be abnormally connected, abnormally aligned, and abnormally related in space.

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To summarize, the evolution of complete R-L asymmetry in the development of the subarterial conal free walls made possible the embryonic aortic switch. This in turn led to the development of solitus normally related great arteries: $\mathrm{SNRGA} = \mathrm{OR} + 4\mathrm{L}$. Its mirror-image isomer is: $\mathrm{INRGA} = 4\mathrm{R} + 0\mathrm{L}$. Any other pattern of conal development results in a conotruncal malformation.

Keywords Conotruncal anomalies, infundibulo-arterial malformations • Abnormal ventriculo-arterial alignments • Abnormal ventriculo-arterial connections • Tetralogy of Fallot • Truncus arteriosus • Interrupted aortic arch • Transposition of the great arteries • Double-outlet right ventricle • Double-outlet left ventricle • Anatomically corrected malposition of the great arteries • Great arterial equations • Infundibuloarterial situs concordance and discordance

What Really Are The Conotruncal Malformations?

To be a conotruncal malformation, there must be anatomic anomalies of both the infundibulum (conus arteriosus) and the great arteries (truncus arteriosus) compared with the normal human heart. *Infundibulum* means funnel (Latin), and *conus arteriosus* means arterial cone (Latin). Infundibulum describes the inside anatomic appearance of this structure as it leads from the right ventricle (RV) into the main pulmonary artery (MPA). This structure really does look like a funnel leading from the RV into the MPA. Looking at an embryonic reconstruction from the outside, this same structure looks like a hollow cone between the RV below and the MPA above. So, *infundibulum* (funnel) describes the inside anatomic appearance, while *conus* (cone) describes the outside embryonic appearance of the same structure. Hence these terms are used interchangeably.

What Are Normally Related Great Arteries and How Did they Get That Way?

Following looping of the straight heart tube to the right forming a dextral or D-loop, the developing great arteries are both above the developing RV (Fig. 1.1) [2]. The developing semilunar valves are approximately side-by-side, with **the aortic valve to the right** and **the pulmonary valve to the left** (Fig. 1.1), reminiscent of the Taussig-Bing malformation.

Then normally, the right-sided subaortic infundibular free wall undergoes involution, due to apoptosis (programmed cell death) and migration of cells out of this area. Simultaneously, the left-sided subpulmonary infundibular free wall undergoes strong growth and expansion, elevating the pulmonary valve superiorly above the RV, and getting the developing pulmonary valve out of the way, well above the interventricular foramen (the normal embryonic ventricular septal defect). Elevating

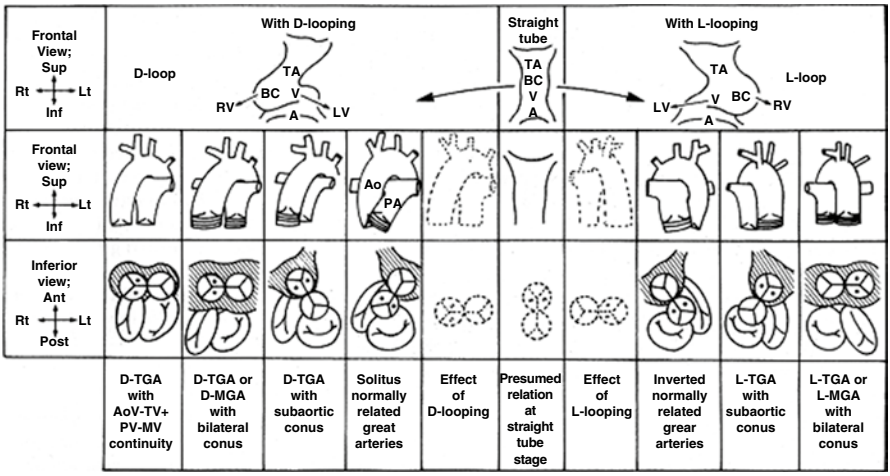


Fig. 1.1 Morphogenesis of normally and abnormally related great arteries, with ventricular D-loops and L-loops. Great arteries and infundibulum or conus arteriosus are shown from the front and from below. Subsemilunar conal musculature is indicated by cross hatching. Aortic valves are indicated by two coronary ostia, pulmonary valves by no coronary ostia. Mitral valves are bicuspid. Tricuspid valves have three leaflets. When great arteries and semilunar valves are depicted with broken lines, this means that these structures have not yet separated at straight tube or early D-loop or L-loop stages; they are so depicted for clarity of comprehension. For discussion, please see text. All of the diagrams in *row 3* showing the relationships between the semilunar and the atrioventricular valves are based on geometrically measured heart specimens; i.e., they are data-based, not hypothetical. **Abbreviations**: *A and Ant* anterior, *Ao* aorta, *AoV* aortic valve, *BC* bulbus cordis, *D-MGA* dextro-malposition of the great arteries, *D-TGA* dextro-transposition of the great arteries, *Inf* inferior, *Lt* left, *L-MGA* levo-malposition of the great arteries, *L-TGA* levo-transposition of the great arteries, *LV* morphologically left ventricle, *MV* mitral valve, *Post* posterior, *PA* main pulmonary artery, *PV* pulmonary valve, *Rt* right, *RV* morphologically right ventricle, *Sup* superior, *TA* truncus arteriosus, *TV* tricuspid valve, *V* ventricle (of the bulboventricular loop) (Reproduced from Van Praagh and Van Praagh [1] with permission of Elsevier)

the pulmonary valve and artery superiorly — above the interventricular foramen — facilitates the leftward movement of the aortic valve from above the RV to above the left ventricle (LV).

Strong growth of the left-sided subpulmonary conal free wall and involution of the right-sided subaortic conal free wall result in further dextral rotation of the developing great arteries. The aortic valve moves inferiorly, posteriorly and somewhat leftward, passing mostly through the interventricular foramen and coming into direct fibrous continuity with the developing mitral valve above the LV (Figs. 1.1 and 1.2) [2]. Simultaneously, the pulmonary valve moves reciprocally superiorly, anteriorly, and somewhat rightward above the RV (Figs. 1.1 and 1.2). This continuing dextral rotation goes from a side-by-side semilunar relationship, i.e., 90° rotation to the right relative to the sagittal plane, to the solitus normal semilunar interrelationship of approximately 150° dextrorotation relative to the sagittal plane (Figs. 1.1 and 1.2). The first 90° of dextrorotation of the developing semilunar valves appears to be due to D-loop formation of the heart tube.

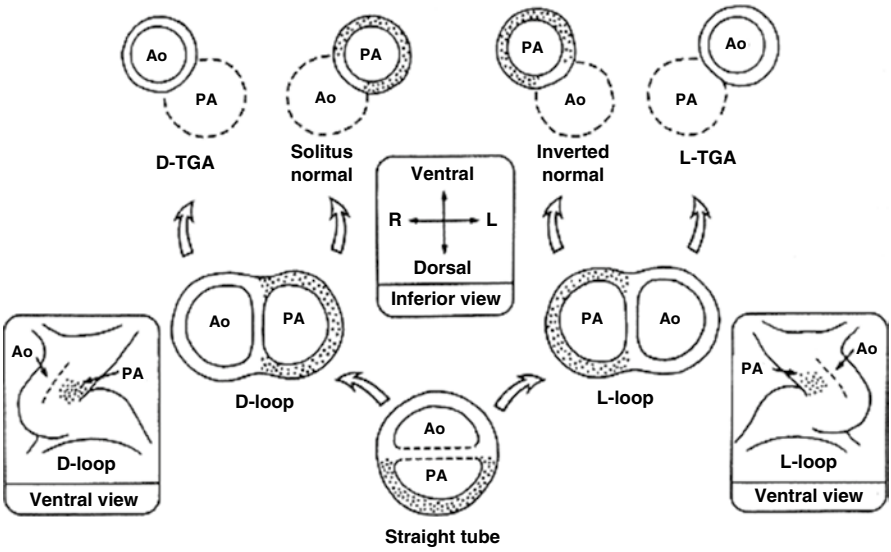


Fig. 1.2 Morphogenesis of normally related great arteries (solitus and inversus) is contrasted with that of transposition of the great arteries, D- and L-. Subpulmonary conal free wall is stippled. Subaortic conal free wall and conal septum are shown as clear (not stippled). Dashed circles indicate involution of subsemilunar conal free wall musculature. Arrows indicate progression of morphogenetic stages. Straight tube leading to D-loop ventricles and straight tube leading to L-loop ventricles are thought to be *different*, even though they are morphologically indistinguishable at this early stage. D-loop ventricles (solitus ventricles) and L-loop ventricles (inverted ventricles) do not arise from the same straight heart tube. Embryonic situs (solitus or inversus) is determined at, or shortly after fertilization. For discussion, please see text. *Abbreviations*: *Ao* aorta, *PA* main pulmonary artery, *D-TGA* dextro-transposition of the great arteries, *L-TGA* levo-transposition of the great arteries (Reproduced from Van Praagh [3] with permission of Elsevier)

The remaining 60° of normal dextrorotation of the semilunar valves appears to be due to complete right-left (R-L) asymmetry in the development of the subsemilunar conal free walls, which may be symbolized as follows: subaortic = grade 0 (0), and subpulmonary = grade 4 (4) (Figs. 1.1 and 1.2). The morphogenesis of solitus normally related great arteries (SNRGA) may be represented by the following equation: **SNRGA = 0R + 4L . In words, solitus normally related great arteries have complete R-L asymmetry in the development of the subarterial conal free walls. Normally, there is no right-sided subaortic conal free wall (0R) and (+) a well developed left-sided subpulmonary conal free wall (4L).**

This is the developmental and anatomic equation, or formula, or definition of solitus normally related great arteries. This is the *normal* conotruncal developmental and anatomic formula. This is the equation or formula of "Mother Nature's" normal aortic switch procedure. There is only one way to do it right (correctly), as above. There are many ways of doing it wrong (incorrectly), and they always result in a conotruncal malformation. A few examples follow.

In D-transposition of the great arteries (**D-TGA**), the development of the conal connector is the opposite of normal (Figs. 1.1 and 1.2): **the right-sided subaortic conal free wall develops well**, which may be symbolized as grade 4 (4), and **the left-sided subpulmonary infundibular free wall** typically undergoes complete involution, which may be symbolized as grade 0 (0).

So the conotruncal developmental and anatomic equation for typical **D-TGA is**:

$$\mathbf{D\text{-}TGA = 4R + 0L}$$

This equation has complete R-L asymmetry, but it is the opposite of the normal type of complete R-L asymmetry. So the wrong great artery gets switched. The right-sided aorta is elevated high above the RV, atop the developing subaortic conus; and the left-sided pulmonary artery is switched through the interventricular foramen and comes into direct fibrous continuity with the mitral valve above the left ventricle (LV), which is made possible by the involution (disappearance) of the left-sided subpulmonary infundibular free wall (Figs. 1.1 and 1.2).

Briefly, typical D-TGA has complete R-L conal free wall asymmetry that is the opposite of normal, so the wrong great artery, i.e., the pulmonary artery, gets switched embryologically. In other words, **D-TGA has subarterial conal free wall inversion** (**right-left reversal**) relative to what is normal in visceroatrial situs solitus.

The Taussig-Bing type of double-outlet right ventricle [4, 5] has a bilateral conus. Both the right-sided subaortic conal free wall and the left-sided subpulmonary conal free wall are well developed; neither has undergone involution (Fig. 1.1) [5]. Consequently both great arteries remain high above the RV, with no semilunar-atrioventricular valvar fibrous continuity, and with a subpulmonary ventricular septal defect (VSD) [4, 5].

The developmental and anatomic conotruncal equation for the Taussig-Bing malformation is:

$$\mathbf{Taussig\text{-}Bing\ DORV = 4R + 4L}$$

The Paul type of double-outlet left ventricle (**DOLV**) [6] has **no right-sided subaortic conal free wall** or septal musculature and **no left-sided subpulmonary conal free wall** or septal musculature, facilitating aortic-mitral and pulmonary-mitral direct fibrous continuity. The ventricular septum was intact [6]. The developmental and anatomic conotruncal equation for the Paul type of DOLV [6] is:

$$\mathbf{Paul\ type\ of\ DOLV = 0R + 0L}$$

Typical tetralogy of Fallot (**TOF**) **is**:

$$\mathbf{TOF = 0R + 1L, or}$$
$$\mathbf{= 0R + 2L, or}$$
$$\mathbf{= 0R + 3L.}$$

In TOF, the left-sided subpulmonary conus is underdeveloped in 3 dimensions and hence is obstructive. TOF is a subnormality. In TOF, the conal septum may be normal, underdeveloped, or absent. **1L means that a small amount of subpulmonary conus is present**, **but unexpanded**, **and hence pulmonary outflow tract atresia is present. 2L means severe stenosis of the pulmonary outflow tract. 3L means mild to moderate stenosis of the pulmonary outflow tract. 4L means normal development with no stenosis of the pulmonary outflow tract**.

Truncus arteriosus type A1 [7] is a TOF with pulmonary infundibular and valvar atresia, plus an aortopulmonary septal defect or AP window (APW).

Truncus arteriosus type A1 = 0R + 1L + APW

Type A means that a subtruncal ventricular septal defect (VSD) is present.

Truncus arteriosus type A2 [7, 8] is TOF with pulmonary infundibular and valvar atresia, with absence of the main pulmonary artery (MPA), and origin of the right pulmonary artery (RPA) and of the left pulmonary artery (LPA) from the ascending aorta (from the aortic sac) [8]. The equation for truncus arteriosus type A2 is:

Truncus Arteriosus type A2 = 0R + 1L − MPA

Because the MPA is absent, the RPA and the LPA remain in their site of origin — arising from the aortic sac, because there is no main pulmonary artery on to which they would normally migrate. This is also why there is no remnant of the aortopulmonary septum.

We think that the conventional understanding of truncus arteriosus is wrong [7, 8], i.e., that truncus is caused by a failure of downgrowth of the trunco-conal septum. Instead, truncus appears to be closely related to TOF. Truncus arteriosus type A1 is a common aortopulmonary trunk (i.e., a truncus arteriosus communis). But truncus arteriosus type A2 is a solitary aortic trunk (i.e., a truncus aorticus solitarius). This is why we refer to **truncus arteriosus**, but not to truncus arteriosus *communis*, because type A2 is a *solitary aortic* trunk, not a *common arterial* trunk.

In hearts with a ventricular L-loop, the developmental and anatomic conotruncal equations or formulas are inverted, or right-left reversed (Figs. 1.1 and 1.2).

Anatomically corrected malposition of the great arteries (**ACM**) is a rare type of conotruncal anomaly in which there is a malposition of the great arteries, but in which the great arteries nonetheless arise above the morphologically appropriate ventricles, aorta above the LV and pulmonary artery above the RV. In this sense, the malposition of the great arteries is "anatomically corrected." This is possible because *the abnormal conotruncus and the ventricles twist in opposite directions* [9]. In patients with visceroatrial situs solitus, there are two anatomic types: *ACM* {*S*,*D*,*L*} and *ACM* {*S*,*L*,*D*}.

In ACM {**S**,**D**,**L**}, as the segmental anatomy indicates, there is visceroatrial situs solitus, concordant D-loop ventricles, and L-malposition of the great arteries. The malposed aorta is anterior and to the left above the LV, and the malposed pulmonary

artery is posterior and to the right above the RV. So, ACM {S,D,L} is corrected both anatomically and physiologically. Surgically, ACM {S,D,L} may just require VSD closure.

In ACM {S,L,D}, as the segmental anatomy indicates, there are discordant L-loop ventricles associated with D-malposed great arteries. Although the great arteries are *anatomically* corrected, they are *physiologically* uncorrected. Surgically, ACM {S,L,D} may benefit from an atrial switch operation.

In ACM, there is ventriculoarterial concordance, but the great arteries are *not* normally related. In ACM, the conus is either bilateral (subaortic and subpulmonary), or subaortic only with pulmonary-atrioventricular valvar fibrous continuity [9]. Thus, **ventriculoarterial concordance** does not always mean normally related great arteries (solitus or inversus) because anatomically corrected malposition of the great arteries also has VA concordance. For more information on ACM, please see Chap. 33.

Interrupted aortic arch (IAA) may be regarded as "anti-tetralogy" — the opposite of tetralogy of Fallot [10]. In TOF, the conal septum is displaced anteriorly, superiorly, and leftward, with narrowing of the pulmonary outflow tract and typically with a large subaortic VSD. In IAA type B (distal to the left common carotid artery), the conal septum is displaced inferiorly and posteriorly, too close to the mitral valve, resulting in a narrowed subaortic outflow tract and a large subpulmonary VSD. IAA may have excessive dextral rotation at the semilunar valve level, accounting for the conal septal malalignment, whereas TOF has deficient dextral rotation at the semilunar valves, which also accounts for the conal septal malalignment in typical TOF.

The etiology of the conotruncal anomalies is now undergoing intensive investigation. Molecular genetic evidence suggests that malformations of right-left development may be caused by one or more mutations in the Nodal cascade [2], the anterior heart field [10], the neural crest cells [10], the Pax 3 gene [10], and Pit x2c [11]. Rapid dextral rotation at the conotruncal junction between Carnegie stages 15 and 19 has been observed in normal mice, but fails to occur in mouse models of DORV, truncus, and TGA [12].

The conotruncal equations or formulas are presented here in print for the first time. They help to provide a quantitative approach to the definition and understanding of the many different anatomic types of conotruncal malformation.

Spiral Versus Straight Great Arteries

In TGA, why are the great arteries straight, or parallel, or uncrossed, whereas with normally related great arteries, the great arteries are spiral, or twisted about each other? It used to be thought (Quain, 1844 [13]) that TGA results from straight downgrowth of the truncoconal septum that separates the great arteries and the ventricular outflow tracts; whereas with normally related great arteries, the truncoconal septum grows down from the aortic arch 4/6 junction in a spiral or twisted fashion.

We now think that it's a matter of simple developmental and anatomic geometry: i.e., the difference between the highly variable semilunar spatial relationship proximally, and the fixed aorticopulmonary relationship distally between the aortic arch and the pulmonary arterial bifurcation. As long as it is present (i.e., not absent), the aorta is always anterior (ventral) and superior (cephalad) relative to the pulmonary arterial bifurcation, because this is the fixed relationship between embryonic aortic arches 4 and pulmonary arterial arches 6. This is why the aorta always arches over the pulmonary artery bifurcation.

So, the aorto-pulmonary relationship distally is a *constant*: aorta anterior and superior, pulmonary artery posterior and inferior. But, the semilunar valvar interrelationship proximally is a *variable* (Fig. 1.1).

Looping of the heart tube to the right usually carries the developing aortic valve to the right of the developing pulmonary valve, in an approximately side-by-side relationship (Fig. 1.1). Then this side-by-side semilunar relationship may be modified in various ways by development (growth or involution) of the subsemilunar conal free walls. With solitus normally related great arteries, the right-sided subaortic conal free wall involutes (disappears), and consequently the aortic valve moves inferiorly, posteriorly and leftward (Fig. 1.1). The left-sided subpulmonary conal free wall grows well, and consequently the pulmonary valve is carried superiorly, anteriorly, and rightward (Fig. 1.1).

In D-TGA, the aortic valve moves superiorly and anteriorly, while the pulmonary valve moves inferiorly and posteriorly, because of reversed right-left development (inversion) of the subsemilunar conal free walls (Fig. 1.1). In this diagram (Fig. 1.1), the D-transposed aortic valve is only 30° to the right of the sagittal (antero-posterior) plane. In contrast, the normally related aortic valve is 150° to the right of the sagittal plane (Fig. 1.1).

Thus, normally related great arteries (Fig. 1.1) have much more untwisting to do than do transposed great arteries. In this case (Fig. 1.1): 150° − 30° = 120° difference. This is why normally related great arteries look as though they are twisting about each other; in fact, they are **untwisting** about each other. Normally related great arteries have approximately 150° of dextral rotation to undo. This is also why transposed great arteries look parallel, or straight, or uncrossed — because they have so little rightward twisting to undo between the semilunar valves below, and the aortic arch and pulmonary bifurcation above — compared with the untwisting done by normally related great arteries (Fig. 1.1): only 30° compared with 150°. Thus, in this heart specimen with D-TGA, the great arteries have only 20 % as much untwisting to do as do normally related great arteries (30°/150° × 100). 80 % of the untwisting has been abnormally accomplished by the R-L reversed (inverted) development of the subarterial conal free walls.

An equation for magnitude of the untwisting of the great arteries is as follows: **Untwisting of Ao and PA** $= \mathbf{R_v - R_{Ao\ \&\ PA}}$ [1]

[1] Ao, aorta; PA, main pulmonary artery; R_v, rotation of semilunar valves (V) relative to the antero-posterior (AP) plane; $R_{Ao\ \&\ PA}$ rotation of the aortic arch and pulmonary bifurcation relative to the AP plane; measurements in degrees (°).

The morphogenesis of normally related great arteries and transposition of the great arteries is contrasted in Fig. 1.2. The "engines" controlling semilunar morphogenesis are thought to be (Figs. 1.1 and 1.2): (1) ventricular loop formation (the first approximately 90° relative to the sagittal plane); and (2) subsemilunar conal free wall development (variations from a side-by-side relationship). When the subsemilunar conal free walls are equally developed bilaterally (equally well developed as in the Taussig-Bing malformation [4, 5], or equally deficient as in the Paul type of double-outlet left ventricle) [6], the semilunar relationship is approximately side-by-side, aortic valve to the right and pulmonary valve to the left, when D-loop ventricles are present.

In the so-called conotruncal malformations, **the great arteries *per se* are almost always normally developed. The only exception is truncus arteriosus**. The so-called conotruncal malformations, from a developmental viewpoint, are almost all infundibular or conal malformations only (Fig. 1.1 and 1.2). The anatomic anomalies of the great arteries are secondary to the primary developmental anomalies of the **conal connector**. This is why these normally formed great arteries are abnormally connected with the underlying ventricles and atrioventricular canal, resulting in abnormal ventriculo-arterial *alignments*. This is also why abnormally connected and therefore abnormally aligned great arteries are also abnormally related great arteries, i.e., abnormally related relative to external spatial coordinates (right-left, anterior-posterior, and superior-inferior). The designation *conotruncus* serves as a helpful reminder that the conus arteriosus belongs with the great arteries, i.e., that the conus is not an intrinsic part of either ventricle, or of both ventricles. The conus arteriosus is the great arteries' connecting segment. That is why abnormally, the subarterial conus can override the ventricular septum to any degree, from mostly or entirely above the RV, to mostly or entirely above the LV — because the conus is really an intrinsic part of neither ventricle.

The great arteries do not *connect* with the ventricles directly, tissue to tissue, because of the interposition of the conus. [Note the active voice of the verb *connect*.]

Instead, the great arteries *are connected* with the ventricles (ventricular sinuses or inflow tracts) in many different ways by the conal connector. [Note the passive voice of the verb *are connected*.] This distinction is made in the interests of anatomic accuracy.

Consequently, we talk and write about ventriculoarterial *alignments* (not ventriculoarterial *connections*) because, accurately speaking, the ventricles do not connect with the great arteries, because of the interposition of the conus. Only the VA alignments can be described as concordant, or discordant, or double-outlet, etc. The conal connections cannot be so described.

This anatomically based distinction between *alignments* and *connections* is not a semantic quibble. This distinction has nothing to do with verbal preferences. **An accurate understanding of the normal and abnormal anatomy of the conus arteriosus is the key to an accurate understanding of the conotruncal anomalies**. The conus is not "just part of the RV." The conus is much more interesting than that (Tables 1.1 and 1.2).

Table 1.1 Normally and abnormally related great arteries correlated with right-left conal free wall development: grades 0–4

Relation between great arteries	Right-sided conal free wall	Left-sided conal free wall
D-loop ventricles	*AoV right-sided*	*PV left-sided*
Normal	0	4
Tetralogy	0	1/2/3
Truncus	0	1
D-TGA	4	0
DORV	4	4
DOLV	0	0/1/2
L-loop ventricles	*PV right-sided*	*AoV left-sided*
Inverted normal	4	0
Inverted TOF	1/2/3	0
L-TGA	0	4
Inverted DORV	4	4

Abbreviations: *D-loop* heart tube that has folded or looped in a rightward or dextral direction, *DOLV* double-outlet left ventricle, *DORV* double-outlet right ventricle, *D-TGA* dextro-transposition of the great arteries, *L-TGA* levo-transposition of the great arteries, *L-loop* heart tube that has looped in a levo or leftward direction. Grades of subarterial conal free wall development: *0* absent, *1* present but atretic, *2* severe stenosis, *3* mild stenosis, *4* normally well developed & not stenotic, *TOF* tetralogy of Fallot; other abbreviations as previously

Table 1.1 correlates normally and abnormally related great arteries with right-left subarterial conal free wall development, with D-loop ventricles and with L-loop ventricles.

Table 1.2 presents 11 conotruncal or infundibuloarteiral equations, with ventricular D-loops and with ventricular L-loops. It should be understood that there are many more than 11 equations; these are just examples. The equation concerning an individual case should precisely reflect the subarterial conal free wall anatomy of that patient, and such anatomy is highly variable.

The anatomic and developmental equations presented in Table 1.2 may be used as **quantitative indices of the size of the subarterial conal free walls** as follows: A quantitative index of the size of the conal free wall = the distance between the semilunar valve (SLV) above and the atrioventricular valve (AVV) below (in mm or cm). These are measurements of the "height" of the conal musculature that separates (or does not separate) the semilunar valves above from the atrioventricular valves below.

Why is inverted truncus arteriosus not included in Table 1.2? Because we have never seen truncus arteriosus in situs inversus totalis. Table 1.2 is data-based (not "conceptual"). There are many more anatomic variations than are represented by these 11 equations (Table 1.2); these equations are examples of some of the more common anatomic data.

Anatomic types of human heart are presented diagrammatically in Fig. 1.3 **in terms of segmental sets**, **AV and VA alignments**, **and conal connections**.

Conotruncal (**infundibuloarterial**) **malformations** are shown in rows 5–8 inclusive (Fig. 1.3): TGA, row 5; ACM, i.e., anatomically corrected malposition of the great arteries, row 6; DORV, row 7; and DOLV, row 8.

Table 1.2 Normal and abnormal infundibuloarterial equations

With D-loop ventricles, Ao Rt & PA Lt
1. Solitus NRGA = 0R + 4L
2. TOF = 0R + 1L, or
= 0R + 2L, or
= 0R + 3L
3. Truncus Arteriosus
Type A1 = 0R + 1L + APW
Type A2 = 0R + 1L – MPA
4. D-TGA = 4R + 0L
5. TGA {S, D, L} = 2R + 4L[a]
6. DORV, Taussig-Bing type = 4R + 4L
7. DOLV, Paul type = 0R + 0L
With L-loop ventricles, PA Rt & Ao Lt
8. Inverted NRGA = 4R + 0L
9. Inverted TOF = 1R + 0L, or
= 2R + 0R, or
= 3R + 0L
10. L-TGA = 0R + 4L
11. Inverted DORV = 4R + 4L

Abbreviations: *Ao* aorta, *DOLV* double-outlet left ventricle, *DORV* double-outlet right ventricle, *APW* aortopulmonary window, *D-TGA* dextro-transposition of the great arteries, *Lt* left-sided, *L-TGA* levo-transposition of the great arteries, *MPA* main pulmonary artery, *NRGA* normally related great arteries, *PA* main pulmonary artery, *Rt* right-sided, *TOF* tetralogy of Fallot, +, and, –, without. TOF = 0R + *1L* means TOF with pulmonary outflow tract atresia. TOF = 0R + *2L* means TOF with severe pulmonary outflow tract stenosis. TOF = 0R + *3L* means TOF with mild to moderate pulmonary outflow tract stenosis

[a]In TGA {S, D, **L**}, as the segmental anatomic diagnosis indicates, the subaortic conal freewall is left-sided, and the subpulmonary conal free wall is right-sided

Figure 1.3 depicts some, but by no means all, of the anatomic types of human heart.

So, what really are conotruncal or infundibuloarterial malformations?

From the anatomic standpoint, as the name *conotruncal* or *infundibuloarterial* indicates, such malformations have anomalies both of the infundibulum (conus) and of the great arteries (truncus arteriosus) that may be expressed verbally, or diagrammatically (Figs. 1.1, 1.2 and 1.3), or symbolically with infundibuloarterial equations (Table 1.2).

Isolated semilunar valvar anomalies — such as congenital pulmonary stenosis or congenital aortic regurgitation — are *not* regarded as conotruncal anomalies because neither the conus, nor the truncus is malformed.

One may harbor some doubts regarding the accuracy of excluding isolated semilunar valvar anomalies because the aortic and the pulmonary valves are located right at the cono-truncal or infundibulo-arterial junction. Nonetheless, it is difficult to

Types of human heart: segmental sets and alignments

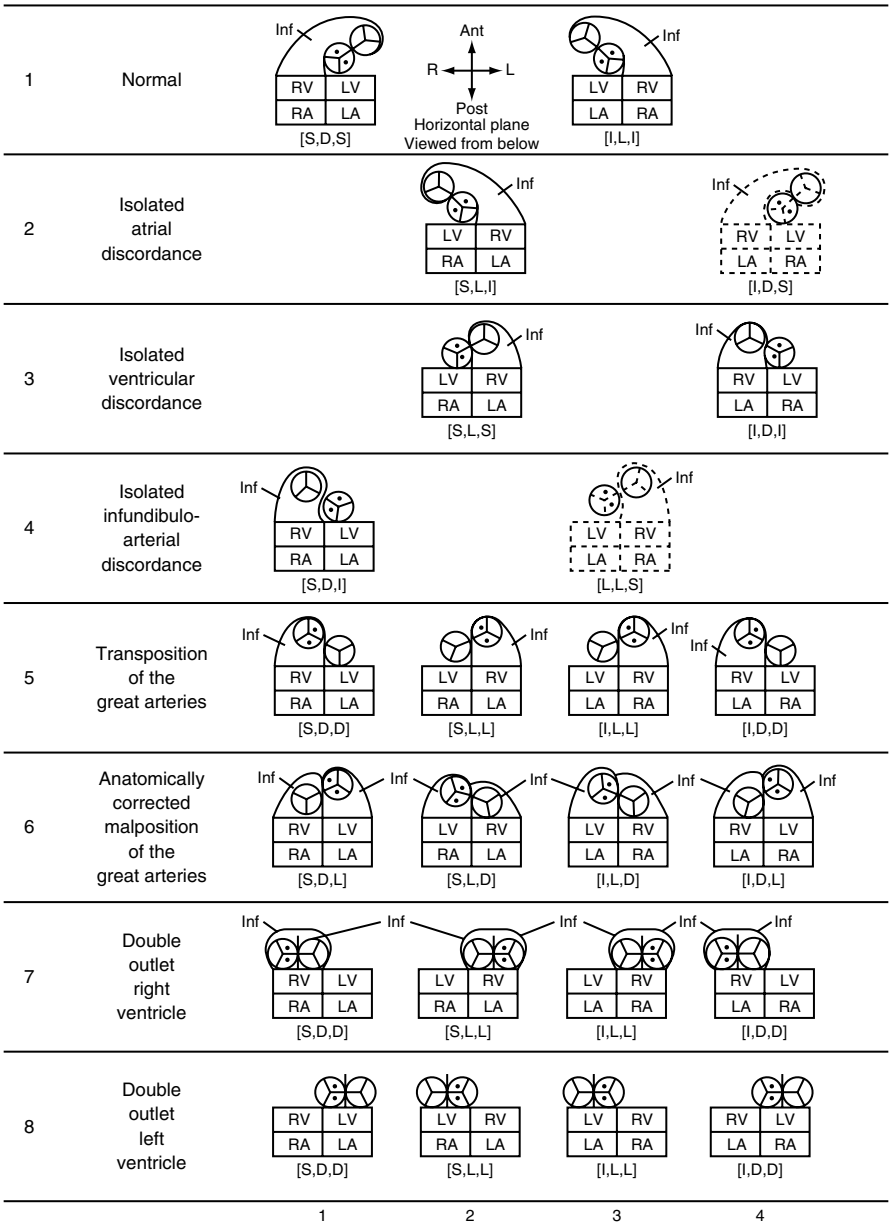


Fig. 1.3 Types of human heart in terms of segmental sets (combinations), AV and VA segmental alignments (what opens into what), and subarterial conal connections or infundibulum (*Inf*). All of the heart diagrams are shown as viewed from below, similar to a subxiphoid 2 D echocardiogram. Cardiotypes shown in broken lines had not been documented when this diagram was made. The aortic valve is indicated by the coronary ostia. The pulmonary valve is indicated by the absence of coronary ostia. Braces { } mean "the set of". Columns 1–4 are arranged in terms of **atrioventricular** (**AV**) **concordance and discordance. All of the heart diagrams in column 1 have AV concordance**. The morphologically right atrium (RA) opens into the morphologically right ventricle (RV), and the morphologically left atrium (LA) opens into the morphologically left ventricle (LV) because the viscera and atria are in situs solitus, i.e., {S,-,-} and a ventricular D-loop is present, i.e., {S,D,-}. Also important is that all 4 cardiac chambers are well developed. If the RV sinus (inflow) is absent, for example, then both atria can open into the LV, resulting in double-inlet single LV with an infundibular outlet chamber. **All of the hearts diagrammed in column 2 have AV discordance**, right-sided RA opening into right-sided LV and left-sided LA opening into left-sided RV, because the viscera and atria are in situs solitus, but a ventricular L-loop is present, i.e., {S,L,-}. **All of the hearts in column 3 have AV concordance** because the viscera and atria are in situs inversus, i.e., {I,-.-} and a ventricular L-loop is present, i.e., {I,L,-}. The left-sided RA opens into the left-sided RV and the right-sided LA opens into the right-sided LV. **All the hearts in column 4 have AV discordance** because the viscera and atria are in situs inversus, i.e., {I,-,-}, but D-loop ventricles are present, i.e., {I,D,-}. **The 8 rows are organized in terms of the type of ventriculo-arterial** (**VA**) **alignment that is present. Row 1** shows the solitus normal heart, i.e., {S,D,S} and the inverted normal heart, i.e., {I,L,I}. Both have AV and VA concordance, and a well developed subpulmonary infundibulum (Inf) and no subaortic infundibular free wall — permitting aortic-mitral fibrous continuity. **Rows 2**, **3**, **and 4** show solitus and inversus normally related great arteries with rare segmental sets: {S,L,I}, {S,L,S}, {I,D,I}, and {S,D,I}. **The conotruncal or infundibuloarterial anomalies are depicted in rows 5–8**. Some of the anatomic types of transposition of the great arteries are shown in *row 5*, anatomically corrected malposition of the great arteries in *row 6*, double-outlet right ventricle in *row 7*, and double-outlet left ventricle in *row 8*. **Visceroatrial situs ambiguus** with the heterotaxy syndromes of asplenia, polysplenia, and normally formed but right-sided spleen were intentionally omitted. Atrial situs ambiguus is not a third anatomic type of atrial situs; instead, atrial situs ambiguus, i.e., {A,-,-} means that the type of atrial situs is morphologically uncertain, or unknown. The atrioventricular valves are not depicted because they typically correspond to the ventricle of entry (not to the atrium of exit): tricuspid valve enters RV, and mitral valve enters LV. **The *segmental* method of diagnosis is *sequential***, i.e., it proceeds in a veno-arterial sequence, i.e., {atria, ventricles, great arteries}, as, for example, in TGA {S,D,D}. **VA concordance** does not always mean normally related great arteries. Anatomically corrected malposition of the great arteries (*row 6*) also has VA concordance. **Tetralogy of Fallot** has a subpulmonary conus, with absence of the subaortic conal free wall, like normally related great arteries {S,D,S} and {I,L,I} (*row 1*). However the subpulmonary conus is undeveloped, and hence is stenotic or atretic. **Truncus arteriosus** typically is tetralogy of Fallot with pulmonary outflow tract atresia, with additional malformations such as aortopulmonary septal defect (AP window) (type 1), or absence of the main pulmonary artery with origin of the right and left pulmonary artery branches from the ascending aorta (i.e., from the aortic sac) (type 2), or absence of a proximal portion of a pulmonary artery branch, with that lung being supplied by a ductus-like collateral artery (type 3), or interrupted aortic arch with a small ascending aortic component and a large main pulmonary artery component with a large patent ductus arteriosus supplying the descending thoracic aorta (type 4). Rarely, truncus arteriosus can arise above the RV, with a well developed subarterial conus arteriosus, preventing truncal-mitral or truncal-tricuspid fibrous continuity. It looks like a type 2 truncus with a subarterial muscular conus arteriosus arising above the RV. The general anatomic definition of truncus arteriosus is: one great artery arising from the base of the heart that gives rise to the coronary arteries (at least one), the pulmonary artery branches (at least one), and the brachiocephalic arteries. This definition permits the inclusion of multiple different anomalies. This is also true of most of the other conotruncal anomalies (rows 5–8, inclusive) (Reproduced from Foran et al. [14], with permission of Elsevier)

regard isolated aortic valvar and isolated pulmonary valvar anomalies as conotruncal or infundibuloarterial malformations when both the infundibulum (conus) and the great arteries (truncus) are normally formed anatomically.

Interrupted aortic arch (IAA) also merits explanation. **IAA type A** (the interruption being distal to the left subclavian artery) is *not* considered to be a conotruncal anomaly because the infundibulum typically is normally formed.

However, **IAA type B** is considered to be a conotruncal malformation because the infundibulum typically is malformed. The conal septum is malaligned posteroinferiorly — too close to the mitral valve — resulting in stenosis of the outflow tract from the LV to the ascending aorta, and also resulting in a large subpulmonary VSD. So IAA type A and IAA type B are very different malformations.

If this seems a little strange, it may be helpful to recall that cyanotic congenital heart disease has many different anatomic causes. IAA is a secondary malformation, not a primary one. In other words, IAA typically appears to be a secondary effect, not a primary cause. More specifically, IAA usually appears to be the result of reduced anterograde blood flow in the aortic arch. There are a variety of different anatomic malformations that can critically reduce anterograde aortic arch blood flow, predisposing to IAA, either type A or type B. IAA type C (distal to the right common carotid artery) is a rare form, that may have a different causation.

The so-called conotruncal or infundibuloarterial malformations are fascinating from a developmental (embryologic and genetic) viewpoint:

Almost all of the conotruncal malformations are conal or infundibular anomalies *only*. The great arteries (truncus arteriosus) are normally formed *per se*.

The only conotruncal anomaly in which the great arteries are abnormally formed is truncus arteriosus. In type 1, an aortopulmonary (AP) window is present [7]. In type 2, the main pulmonary artery appears to be absent.

Why then, do the great arteries look so abnormal anatomically, as for example, in TGA?

Because the conal connector is malformed. The subarterial infundibular free walls form the platforms on which the great arteries stand. If these subarterial platforms are malformed, then the great arteries are abnormally related (Figs. 1.1, 1.2 and 1.3), the ventriculo-arterial alignments are abnormal (Figs. 1.1 and 1.3), and the ventriculo-arterial connectors (the platforms) are abnormal (Fig. 1.2, Tables 1.1 and 1.2).

Abnormally related great arteries are abnormally connected great arteries.

The truncoconal malseptation hypothesis is wrong [13], i.e., spiral truncoconal septation results in normally related great arteries; whereas straight downgrowth of the truncoconal septum results in TGA, etc.

If ever you see an AP window in a conotruncal anomaly (apart from truncus), you should report it because AP windows are rare in non-truncus infundibuloarterial anomalies. If conotruncal anomalies were caused by truncoconal malseptation, definite anatomic evidence of such malseptation (like an AP window) should be common. But in fact, such anatomic evidence is vanishingly rare.

At the present time, most cardiologists and cardiac surgeons understand that tetralogy of Fallot is basically an infundibular anomaly. But at the present time, most informed observers do not understand that the same is true of TGA, ACM, DORV,

and DOLV, that the great arteries in all of these anomalies are normally formed *per se*, and that the malformation is at the infundibular or conal level. Since congenital heart disease is named, defined, and diagnosed *anatomically* (not physiologically, embryologically, or genetically), the term conotruncal anomalies is *anatomically* correct: the infundibulum is the site of the *primary* developmental and anatomic malformations, and the great arteries are the site of the *secondary* anatomic malformations.

Normal development of the infundibulum (conus arteriosus) is "Mother Nature's" way of performing the embryonic aortic switch procedure [2].

The infundibulum is basically a muscular structure, whereas the aortic and pulmonary valves are fibroelastic, similar to the great arteries. This may explain why it is possible for anomalies of the aortic and pulmonary valves to occur, without associated malformations either of the infundibulum or of the great arteries.

Infundibuloarterial or conotruncal equations, published here for the first time (Table 1.2), are a step in the direction of a more quantitative understanding of the development and the anatomy of normally and abnormally related great arteries.

Attention is focused on the subarterial infundibular *free walls* (rather than on truncoconal septation). It is important for current embryologic and genetic investigators to understand where the problem is located [12].

The infundibulum or conus arteriosus is an independent variable. The infundibulum can be located above either, or both ventricles, and the infundibulum can be beneath either, or both great arteries.

It is important to understand that the infundibulum is not "just part of the right ventricle." Instead, it is an independent connecting cardiac segment of the great arteries that is of major developmental and anatomic importance [2].

What About TGA {S,D,L}? [15]

In this form of TGA, as the segmental diagnsosis indicates, there is visceroatrial situs solitus, D-loop ventricles, and L-TGA, with AV concordance and VA discordance. The transposed aortic valve lies anteriorly and to the *left* relative to the transposed pulmonary valve that lies posteriorly and to the *right*. The right-sided RV ejected into the left-sided and anterior transposed Ao, and the left-sided LV ejected into the right-sided and posterior transposed PA.

Where Is the Subaortic Conal free Wall? And Where Is the Subpulmonary Conal Free Wall?

Ask the semilunar valves, because the subarterial conal free walls lie immediately beneath the semilunar valves. So, the subaortic conal free wall is anterior and to the left (beneath the aortic valve), and the subpulmonary conal free wall is posterior and to the right (beneath the pulmonary valve).

As the segmental anatomic diagnosis (TGA {S,D,L}) indicates, the ventricles looped to the right, but the conotruncus twisted to the left, like a backwards S (Ƨ). So, there is malrotation of the bulboventricular loop.

Usually, the bulboventricular loop is like the letter C: both the ventricles and the conotruncus twist in the same direction, to the right, as in TGA {S,**D**,**D**}.

Similarly, when the bulboventricular loop is inverted, as in TGA {S,**L**,**L**}, the ventricles and the conotruncus both twist in the same direction, to the left, like a backwards C (Ↄ).

But, TGA {S,**D**,**L**} is uncommon because the ventricles and the conotruncus have twisted in opposite directions — ventricles to the right, and infundibulum and great arteries to the left.

The segmental anatomic diagnosis indicates how this conotruncal equation should be written: $\mathrm{TGA}\{\mathrm{S,D,L}\} = 2\mathrm{R} + 4\mathrm{L}$ (Table 1.2, Eq. 8). The segmental anatomic diagnosis — TGA {S,D,**L**} indicates that the well developed subaortic conal free wall is left-sided, i.e., 4L. The subpulmonary conal free wall is right-sided and is often present, but underdeveloped and hence stenotic, i.e., 2R. Hence, the infundibuloarterial equation for TGA {S,D,L} often equals 2R + 4L [15].

Great Arterial Switch Procedures

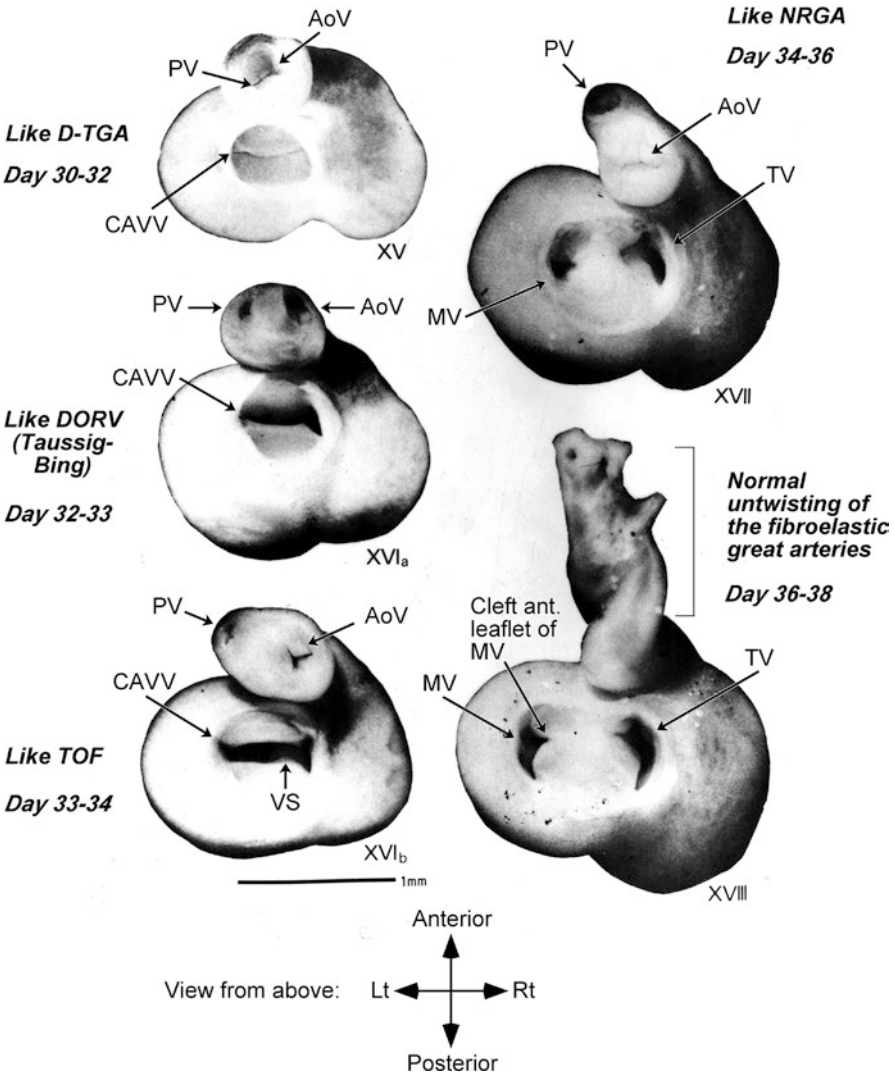
Normally, in "Mother Nature's" embryonic arterial switch procedure, only *one* great artery — the aorta — gets switched from the RV to the LV (Fig. 1.4). Even abnormally, as in TGA, only one great artery gets switched — the pulmonary artery.

Fig. 1.4 Dissected embryonic human hearts, great arteries removed above the semilunar valve level to expose the morphogenetic movements of the developing aortic valve (*AoV*) and pulmonary valve (*PV*). The atrial free walls have been removed to expose the division of the common atrioventricular valve (*CAVV*) into the mitral valve (*MV*) and the tricuspid valve (*TV*). View of the hearts from behind and above. The anterior (ventral) surface is towards the top of the page. The posterior (dorsal) surface is towards the bottom of the page. The right (*Rt*) surface is towards the viewer's right hand. The left (*Lt*) surface is towards the viewer's left hand. The Roman numerals indicate Streeter's horizons (stages). Horizon XV corresponds to an embryonic age (age since fertilization) of 30–32 days. Take Streeter's horizon (*XV*) and double it (30 days); that is when the horizon starts. Each horizon is 2 days long. Therefore, Streeter's horizon 15 corresponds to a stage that begins at 30 days of age and ends at the end of 32 days. Horizon XV1a indicates the first half of this horizon, i.e., day 32. Horizon XV1b means the last half of this horizon, i.e., day 33. (*ant*. anterior, *DORV* double-outlet right ventricle, *NRGA* normally related great arteries, *TOF* tetralogy of Fallot. NRGA undergo approximately 150° of dextrorotation relative to the sagittal plane at the semilunar valves. In contrast, abnormally connected great arteries with conotruncal malformations undergo much less dextrorotation at the level of the semilunar valves, i.e., much less than 150° dextrorotation. NRGA untwist through approximately 150° levorotation as they go from the semilunar valves below to the aortic arch and pulmonary arterial bifurcation above. Abnormally related great arteries have much less untwisting (i.e., levorotation) to do than do normally related great arteries — because abnormally related great arteries have undergone far less dextrorotation at the semilunar valve level and consequently have far less untwisting to do than do normally related great arteries. This is why the great arteries in TGA appear parallel, or straight, or uncrossed when compared with normally related great arteries, because normally related great arteries have much more leftward untwisting to do. Note also that the common AV valve normally starts to undergo septation into the mitral and tricuspid valves when the human embryo is 34–36 days of age (Modified from Asami [16], with permission of Wiley)

Only human cardiac surgeons routinely switch *both* great arteries for patients with TGA. Rarely, Mother Nature does do an embryonic double great arterial switch, as in DOLV (Table 1.2).

Morphogenetic Movement of the Great Arteries

Thus far, I have emphasized the importance of the pathologic anatomy and the pathologic development of the subarterial conal free walls (Tables 1.1 and 1.2), because this is what appears to cause abnormally related great arteries (Figs. 1.1, 1.2 and 1.3).



Let us look at these normal and abnormal relationships between the great arteries in greater detail. **During normal development**, **the morphogenetic movements of the developing semilunar valves and great arteries are very real and very important** (**Fig**. 1.4) [16].

By 30–32 days of age in utero, the semilunar interrelationship of the human embryo looks like D-TGA The developing aortic valve (AoV) is anterior and to the right relative to the developing pulmonary valve (PV) which is posterior and to the left (Fig. 1.4, top, left). The rotation of the semilunar valves relative to the sagittal plane is 50° to the right (50° dextrorotation).

By 32–33 days of age in utero, the semilunar valves are side-by-side, AoV to the right and PV to the left — reminiscent of the Taussig-Bing malformation (Fig. 1.4, left, middle). The aortic and pulmonary valves now display 90° dextrorotation relative to the sagittal plane.

By 33–34 days of age, the semilunar valves of the human embryo resemble that of tetralogy of Fallot (Fig. 1.4, left, bottom). The AoV is mildly posterior and right-sided, whereas the PV is mildly anterior and left-sided. The semilunar valves have now rotated 110° to the right relative to the sagittal plane (110° dextrorotation). The AoV is beginning to be switched into the LV.

By 34–36 days of age (Fig. 1.4, top, right), normally related great arteries appear to have been achieved. The AoV is posterior on the right and the PV is anterior on the left. The semilunar valves have undergone 155° rotation to the right relative to the sagittal plane (155° dextrorotation).

By 36–38 days of age in utero (Fig. 1.4, right, bottom), the normal human great arteries are seen to be untwisting, to undo the approximately 150° of dextrorotation that makes possible to normal human aortic switch from above the RV to above the LV.

This elegant study by Asami [16] also shows the normal fusion of the superior and inferior endocardial cushions of the common atrioventricular valve (CAVV) above the ventricular septum (VS) to form the mitral valve (MV) and the tricuspid valve (TV). The cleft in the anterior leaflet of the MV is still incompletely fused.

The Roman numerals indicate Streeter's horizons: XV, XV1a, XV1b, XV11, and XV111 (Fig. 1.4).

The fifth week of gestation, when the mother is just realizing that she is pregnant, is when the embryonic human aortic switch normally occurs (Fig. 1.4).

What is responsible for these morphogenetic movements of the Ao and the PA?

The development of the subarterial conal free walls (Figs. 1.1, 1.2 and 1.3). "Development" includes growth and expansion, as well as involution and disappearance.

Cardiovascular Evolution

When did life come ashore and what made it possible? [2, 11]. Our phylum Chordata goes back to ancient fish of the Ordovician and upper Devonian periods, 500 million to 345 million years ago. These fish had a single ventricle, from which our left ventricle (LV) is derived.

Amphibia evolved 345–325 million years ago during the Carboniferous period. They had lungs and so could breathe air, but they had no right ventricle.

Some amphibia evolved into fully terrestrial animals, the Amniota — animals with an amniotic sac in which the embryo and fetus could float and "swim", like our piscine ancestors. Amphibia have to return to the water to breed, but the amniotes were fully terrestrial.

Some amniotes evolved into reptiles. Others evolved into birds — feathered reptiles — like *archeopterix*. Still other reptiles evolved into mammals — furry or hairy reptiles. Mammals evolved during the Jurassic period, about 180 million years ago.

Although fish and amphibia do not have a right ventricle (RV), the higher reptiles (crocodiles and alligators), birds, and mammals normally all do. The comparatively recently evolved RV is only about 36 % as old as the LV: 180 million vs at least 500 million years old, respectively. The RV is the lung pump. Most permanent air-breathers have an RV.

The development of the RV sinus (body, or inflow tract) was the second, key, cardiovascular evolutionary adaptation that helped to make it possible for us to become permanent land-living and air breathing vertebrates.

The embryonic aortic switch was achieved by complete right-left asymmetry in the development of the subarterial conal free walls, with involution of the right-sided subaortic conal free wall, and good development of the left-sided subpulmonary conal free wall [2]. Following normal D-loop formation: $\mathrm{NRGA} = 0\mathrm{R} + 4\mathrm{L}$.

Any other development of the conal connector results in a conotruncal malformation [2].

The third evolutionary cardiovascular adaptation that facilitated permanent land-living and air-breathing was cardiovascular septation that separated the unoxygenated and the oxygenated blood streams.

To summarize, the evolution of complete R-L asymmetry in the development of the subarterial conal free walls made possible the embryonic aortic switch. This in turn led to the development of solitus normally related great arteries — one of the most important evolutionary cardiovascular adaptations that helped to make possible permanent land-living and air-breathing:

$$\mathrm{SNRGA} = \mathrm{OR} + 4\mathrm{L}.$$

It's mirror-image isomer is:

$$\mathrm{INRGA} = 4\mathrm{R} + 0\mathrm{L}.$$

Any other pattern of conal development results in a conotruncal malformation (Table 1.2).

Infundibulo-Arterial (IA) Situs Concordance and Discordance

The following are newly understood basic principles:

1. When the pattern of anatomic organization, or situs, of the subarterial infundibulum and of the great arteries are concordant (the same), the great arteries are normally related.
2. When the pattern of anatomic organization, or situs, of the subarterial infundibulum and of the great arteries are discordant (different), the great arteries are abnormally related.

Examples of these basic principles follow (Fig. 1.1 and Table 1.1):

$$\mathbf{SNRGA = 0R + 4L.} \tag{1.1}$$

In solitus normally related great arteries, the subarterial infundibular situs formula is 0R + 4L, as in the above equation. This is the normal solitus infundibular formula or "recipe". The great arteries also are in situs solitus. The aortic valve is to the right of the pulmonary valve. Hence, in SNRGA, **IA situs analysis is solitus-solitus**; i.e., IA situs concordance is present.

$$\mathbf{INRGA = 4R + 0L} \tag{1.2}$$

In inverted normally related great arteries (INRGA), the subarterial infundibular formula is 4R + 0L. This is the normal inverted infundibular formula. The great arteries also are in situs inversus; the aortic valve is to the left of the pulmonary valve. Thus, **IA situs analysis is inversus-inversus.** Hence, in INRGA, there is IA situs concordance, both inverted.

$$\mathbf{TGA\{S, D, D\} = 4R + 0L} \tag{1.3}$$

In typical transposition of the great arteries with solitus viscera and atria, D-loop (solitus) ventricles, and D-TGA, with atrioventricular (AV) alignment concordance and ventriculoarterial (VA) alignment discordance, the subarterial situs formula is 4R + 0L. This is the same formula as in INRGA; please compare with Eq. (1.2) above. But the D-transposed great arteries are in situs solitus; the aortic valve is to the right of the pulmonary valve.

So, **in typical D-TGA, IA situs analysis is inversus-solitus.** Hence, in typical D-TGA, there is IA situs discordance.

Note: There is an important difference between *situs* concordance or discordance, and *alignment* concordance or discordance – that some of our colleagues call *connection* concordance or discordance.

Situs concordance or discordance refers to the pattern of anatomic organization of adjacent cardiac segments, which may be *solitus* (normal), or *inversus* (a mirror-image of solitus). *Situs ambiguus* (uncertain or unknown pattern of anatomic organization) is not a specific type of situs; it means situs not diagnosed.

Alignment concordance or discordance indicates what opens into what, and whether it is anatomically normal or not. The morphologically right atrium (RA) opening into the morphologically right ventricle (RV) is a concordant (or appropriate) atrioventricular (AV) alignment; whereas RA opening into the morphologically left ventricle (LV) is a discordant (inappropriate, anatomically abnormal) AV alignment.

Thus, *situs* concordance/discordance and *alignment* concordance/discordance are different concepts.

$$\mathbf{TGA}\{\mathbf{S,L,L}\} = \mathbf{0R + 4L} \tag{1.4}$$

The classical form of congenital physiologically corrected transposition of the great arteries with solitus viscera and atria, L-loop (inverted) ventricles, and L-TGA, with AV alignment discordance and VA alignment discordance has an infundibular situs formula of the solitus normal type (compare with Eq. 1.1 above). But the great arteries in L-TGA are inverted; the aortic valve is to the left of the pulmonary valve. **In typical L-TGA, IA situs analysis is solitus-inversus, hence discordant.**

$$\mathbf{Taussig\text{-}Bing\ DORV}\{\mathbf{S,D,D}\} = \mathbf{4R + 4L} \tag{1.5}$$

In the Taussig-Bing type of double-outlet right ventricle [4, 5] with solitus viscera and atria, D-loop (solitus) ventricles, and D-malposition of the great arteries, the subarterialinfundibular situs formula is 4R + 4L, which is neither that of infundibular situs solitus, Eq. (1.1) above, nor that of infundibular situs inversus, Eq. (1.2) above. This infundibular situs formula (4R + 4L) is one type of infundibular situs ambiguus. The aortic valve is to the right of the pulmonary valve; hence the great arteries are in situs solitus. Hence, the **IA situs analysis is ambiguus − solitus, which is nonconcordant.**

$$\mathbf{Paul\ DOLV}\{\mathbf{S,D,D}\} = \mathbf{0R + 0L} \tag{1.6}$$

In the Paul type of DOLV [6], the infundibular situs formula (0R + 0L) is different from both the normal solitus infundibular formula (0R + 4L) of Eq. (1.1) above, and from the normal inverted infundibular formula (4R + 0L) of Eq. (1.2) above. Consequently, the infundibular situs formula of the Paul type of DOLV (0R + 0L) is a second anatomic type of infundibular situs ambiguus.

In the Paul type of DOLV, the great arteries are in situs solitus, with the aortic valve to the right of the pulmonary valve, as is indicated by the third element of the segmental situs anatomy: {S,D,**D**}.

In the Paul type of DOLV, IA analysis is ambiguus − solitus, which is nonconcordant.

In anatomically corrected malposition of the great arteries (ACM) (Fig. 1.3), the subarterial infundibulum can be subaortic only, or bilateral (subaortic and subpulmonary) [9].

$$\mathbf{ACM}\{\mathbf{S,D,L}\} = \mathbf{0R + 4L} \tag{1.7}$$

In this anatomic type of ACM, the infundibular situs formula is of the solitus normal type (0R + 4L), similar to Eq. (1.1). But the great arteries are inverted, with the aortic valve to the left of the pulmonary valve: {S,D,**L**}. Consequently, **IA analysis is solitus-inversus, i.e., discordant.**

If a bilateral conus (subaortic and subpulmonary) were present, IA analysis would be ambiguus–inversus, i.e., abnormal – even though in ACM, there is ventriculoarterial (VA) *alignment* concordance, by definition (Fig. 1.3). Thus, IA *situs* analysis indicates that an infundibuloarterial (or conotruncal) anomaly is present, whereas VA *alignment* analysis is concordant ("normal"). In ACM, the ventricles loop in one direction (say to the right) and the infundibular and the arterial segments (the conotruncus) twist in the opposite direction (say to the left), as in ACM {S,**D**,**L**}.

Both IA situs analysis and VA alignment analysis are accurate, but different.

In Eqs. (1.1) and (1.2) (Table 1.2), the subarterial infundibular situs and the great arterial situs are the same, typically resulting in normally related great arteries (solitus and inversus).

In Eqs. (1.3), (1.4), (1.5), (1.6), and (1.7) inclusive (Table 1.2), the infundibular situs and the great arterial situs are different, predictably resulting in abnormally related great arteries (D-TGA, L-TGA, DORV, DOLV, and ACM).

Is it possible to have infundibuloarterial (conotruncal) anomalies when the situs of the subarterial infundibulum and of the great arteries are the same?

Yes. Tetralogy of Fallot (TOF) and truncus arteriosus (TA) are familiar examples (Table 1.2)**.**

TOF {S,D,S} is characterized by variable underdevelopment of the normal or solitus type of subpulmonary infundibulum:

$$\mathbf{TOF\{S,D,S\} = 0R + 1L} \tag{1.8}$$

Grade 1 development of the left-sided subpulmonary infundibulum (0R + **1L**) indicates extreme underdevelopment and *atresia* of the left-sided subpulmonary infundibulum.

$$\mathbf{TOF\{S,D,S\} = 0R + 2L} \tag{1.9}$$

Grade 2 development of the left-sided subpulmonary infundibulum (0R + **2L**) indicates severe underdevelopment of the left-sided subpulmonary infundibulum with severe pulmonary outflow tract stenosis.

$$\mathbf{TOF\{S,D,S\} = 0R + 3L} \tag{1.10}$$

Grade 3 development of the left-sided subpulmonary infundibulum (0R + **3L**) indicates mild to moderate underdevelopment of the left-sided subpulmonary infundibulum, with mild to moderate pulmonary outflow tract stenosis.

In all three equations (1.8, 1.9, and 1.10, inclusive), the infundibular situs formulas are of the normal solitus type (0R + 4L), but with underdevelopment of the left-sided subpulmonary conus (infundibulum). The great arteries are of the solitus (normal) type, as the segmental anatomy indicates: TOF {S,D,**S**}.

Hence, in TOF, IA situs analysis is solitus-solitus, i.e., concordant.

Truncus arteriosus (TA) we think is TOF with pulmonary outflow tract atresia, with additional anomalies of the great arteries (Table 1.2) [7, 8].

$$\mathbf{TA\{S,D,S\} = 0R + 1L + APW} \tag{1.11}$$

This is what we call **TA type A1**. Type A indicates that a subtruncal ventricular septal defect (VSD) is present. Type 1 means that an aortopulmonary septal remnant is present, with an aortopulmonary septal defect or aortopulmonary window (APW).

$$\mathbf{TA\{S,D,S\} = 0R + 1L - MPA} \tag{1.12}$$

This is what we call truncus arteriosus type A2. Type A indicates that a subtruncal VSD is present. Type 2 means that there is no aortopulmonary (AP) septal remnant. We think that in TA type A2, the main pulmonary artery (MPA) is absent. This may explain why there is no AP septal remnant. The right pulmonary artery (RPA) and the left pulmonary artery (LPA) normally arise from the aortic sac on the dorsal aspect of the ascending aorta. Then, the LPA and the RPA normally migrate leftward on to the MPA. But in TA type A2, if the MPA is absent, the RPA and the LPA must remain in the aortic sac on the dorsal aspect of the ascending aorta. The RPA and the LPA have nowhere to migrate to.

This appearance in TA type A2 usually has been interpreted as a failure of the AP septum to develop.

However, it is helpful to remember that in TOF with pulmonary outflow tract atresia ("tet-atresia"), absence of the MPA does occur. And that the starting position of the RPA and the LPA is the aortic sac, on the dorsal aspect of the aorta. If the MPA is absent, the RPA and LPA have nowhere to migrate to.

We found that we could not tell "tet-atresia" from TA by examining the RV outflow tract. Both are very similar. Only when we allowed ourselves to look at the great arteries could we tell "tet atresia" (TOF) from TA. Consequently, we think that TOF and TA are very closely related, and that the classical concept of TA (absence of the AP and infundibular septa) is wrong. Also, we have never seen the classical four-leaflet truncal valve predicted by the classical hypothesis. Instead, the truncal valve looks like, and measures like, the aortic valve [7, 8].

In TA, IA situs analysis is solitus-solitus, i.e., concordant, like TOF.

Conclusions

The conotruncus or infundibuloarterial cardiovascular segment is a two-part system. The infundibulum (or conus arteriosus) and the great arteries (truncus arteriosus) are both critically important in determining the anatomic diagnosis. The development of normal and abnormal infundibuloarterial equations (Table 1.2) and infundibuloarterial (IA) situs analysis have been particularly helpful.

Understanding the anatomic type of conotruncus is a *systems* or *relationship* diagnosis between the conus (infundibulum) and the truncus (great arteries). It's not just one thing. Instead, it's the relationship between two different things. That's why the situs of the infundibulum and the situs of the great arteries are so important, as revealed by infundibulo-arterial (IA) situs analysis.

Do the infundibulum and the great arteries fit together normally?

Yes, if both have the same pattern of anatomic organization, the same situs, i.e., yes, if situs concordance is present.

No, if the patterns of anatomic organization, the situs[2] of the infundibulum and of the great arteries are different, i.e., no, if situs discordance, or nonconcordance is present.

Can an embryonic arterial switch procedure be performed from above the right ventricle to above the left ventricle, and if so, how?

When the usual ventricular D-loop is present, the following can occur (Figs. 1.1 and 1.2):

1. If the right-sided subaortic conal free wall involutes, the aorta is switched into the left ventricle and normally related great arteries result.
2. If the left-sided subpulmonary conal free wall involutes, the pulmonary artery is switched into the left ventricle, resulting in typical D-transposition of the great arteries.
3. If neither the right-sided subaortic conal free wall nor the left-sided subpulmonary conal free wall involutes, then neither the aorta nor the pulmonary artery is switched into left ventricle, resulting in double-outlet right ventricle.
4. If both the right-sided subaortic conal free wall and the left-sided subpulmonary conal free wall involute or fail to develop, then both the aorta and the pulmonary artery can be switched into the left ventricle, resulting in double-outlet left ventricle.

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[2] *Situs* is both singular and plural. *Situs, sitūs* is a fourth declension Latin masculine noun.

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