The Cardiac Malpositions

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Dextrocardia was known in the 17th century and was 1 of the first congenital malformations of the heart to be recognized. Fifty years elapsed before Matthew Baillie published his account of complete transposition in a human of the thoracic and abdominal viscera to the opposite side from what is natural. In 1858, Thomas Peacock stated that "the heart may be congenitally misplaced in various ways, occupying either an unusual position within the thorax, or being situated external to that cavity." In 1915, Maude Abbott described ectopia cordis, and Richard Paltauf's remarkable illustrations distinguished the various types of dextrocardia. In 1928, the first useful classification of the cardiac malpositions was proposed, and in 1966, Elliott et al's radiologic classification set the stage for clinical recognition. The first section of this review deals with the 3 basic cardiac malpositions in the presence of bilateral asymmetry. The second section deals with cardiac malpositions in the presence of bilateral left-sidedness or right-sidedness. Previous publications on cardiac malpositions are replete with an arcane vocabulary that confounds rather than clarifies. Even if the terms themselves are understood, inherent complexity weighs against clarity. This review was designed as a guided tour of an unfamiliar subject. **(Am J Cardiol 2011;108:1352–1361)**

Dextrocardia was 1 of the first congenital malformations of the heart to be recognized. The malposition was mentioned by Hieronymus Frabricius in 1606 and by Aurelio Severino in 1643. A century and a half then elapsed before Matthew Baillie[1] published his account of "complete transposition in the human subject, of the thoracic and abdominal viscera to the opposite side from what is natural." In 1858, Thomas Peacock[2] wrote, "The heart may be congenitally misplaced in various ways, occupying either an unusual position within the thorax, or being situated external to that cavity." In 1915, Maude Abbott described ectopia cordis. Richard Paltauf's[3] remarkable illustrations, also in 1915, distinguished the various types of dextrocardia, and in 1928, Mandelstam and Reinberg[4] proposed the first useful classification of cardiac malpositions. Estimated prevalence is 0.10 per 1,000 live births.

In 1931, Maria de la Cruz, 1 of the world's foremost cardiac embryologists, began to shed light on the embryologic basis of the malpositions,[5] and the landmark observations of Van Praagh[6] appeared in 1977. Campbell's practical diagrams[7,8] and Elliott et al's[9] radiologic classification in 1966 set the stage for the clinical recognition of the malpositions.

The first section of this review deals with the 3 basic cardiac malpositions in the presence of bilateral asymmetry. The second section deals with malpositions in the presence of bilateral left-sidedness or bilateral right-sidedness. The bronchi and lungs are bilateral but asymmetric. The liver is unilateral but transverse. The atria are asymmetric, but their appendages are symmetric.

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The published research on cardiac malpositions is replete with an arcane vocabulary that confounds rather than clarifies. Even if the terms themselves are understood, inherent complexity weighs against clarity. So let me begin with definitions that may at least make the terms accessible.

Cardiac position: The intrathoracic position of the heart as left sided, right sided, or midline (i.e., levocardia, dextrocardia, or mesocardia).

Cardiac malposition: An abnormal intrathoracic position of the heart.

Situs: Site or position.

Solitus: Normal or usual.

Situs solitus: Normal position (Figure 1).

Situs inversus: Mirror image (Figure 2).

Displacement: An abnormal cardiac position secondary to eventration of a hemidiaphragm, agenesis of a lung, or congenital complete absence of the pericardium.

Ectopia cordis: Location of the heart outside the thoracic cavity (Figure 3).

Chamber designations: Right and left, as in right and left atrium and right and left ventricle.

Great arterial designations: The ascending aorta and pulmonary trunk defined by their ventricle of origin and by their morphology.

Heterotaxy: From the Greek "heteros," different, and "taxis," arrangement. Loosely and poorly translated as "another arrangement" or "a different arrangement." The internal thoracic organs and the abdominal organs exhibit abnormal left-right relations. The concept of bilateral right- and left-sidedness as it applies to the heart is a good

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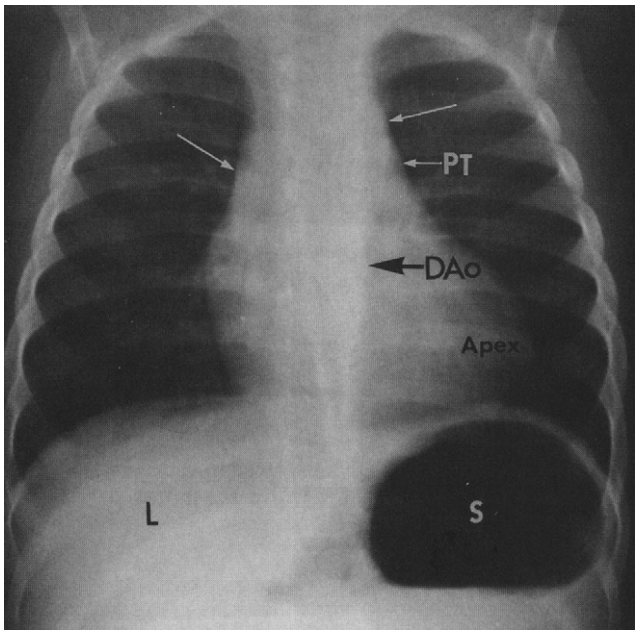

Figure 1. Normal heart and abdominal viscera in situs solitus. The stomach (S) is on the left, the liver (L) is on the right, the heart is left sided, the base-to-apex axis points to the left, and the left hemidiaphragm is lower than the right hemidiaphragm. The ascending aorta, the aortic knuckle *(unmarked white arrows)*, and the pulmonary trunk (PT) are in normal positions. The descending aorta (DAo) is concordant on the left. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

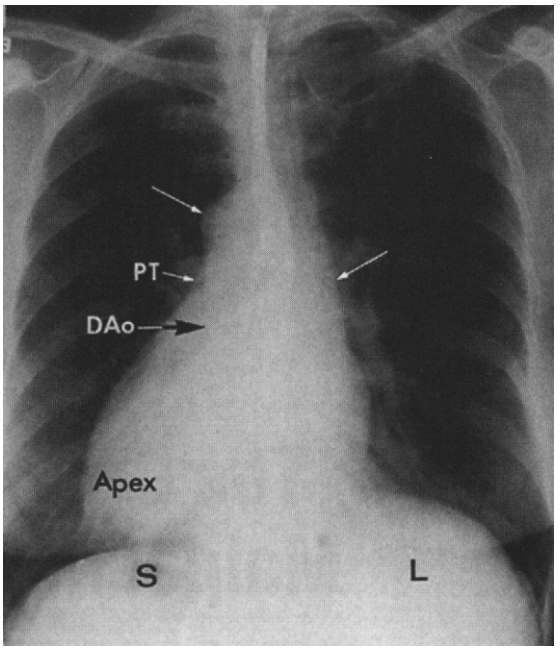

Figure 2. The heart and viscera in a 65-year-old woman with complete situs inversus. The stomach (S) is on the right, the liver (L) is on the left, the heart is on the right, and the hemidiaphragm is lower on the side of the right cardiac apex. The ascending aorta, aortic knuckle *(unmarked white arrows)*, and pulmonary trunk (PT) are in mirror-image positions. The descending aorta (DAo) is concordant on the right. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

mnemonic but is not supported by developmental or embryologic observations.

Isomerism: From the Greek "isos," equal, and "meros," part. The similarity of bilateral structures that are normally dissimilar, such as right and left bronchi and right and left lungs. Isomerism is not an erroneous concept, Van Praagh[6] notwithstanding.

Right isomerism: Bilateral structures with morphologic right characteristics, such as bilateral morphologic right bronchi and bilateral trilobed lungs.

Left isomerism: Bilateral structures with morphologic left characteristics, such as bilateral morphologic left bronchi and bilateral bilobed lungs.

Asplenia: Congenital absence of the spleen.

Polysplenia: Multiple spleens, each of which is appreciably smaller than a normal-sized spleen.

Ventricular loop: The straight heart tube of the embryo forms the left ventricle of the definitive heart. Looping is the consequence of the addition of new material at the arterial pole of the developing heart.

D-loop: Rightward (d = "dextro") bend.

L-loop: Leftward (l = "levo") bend.

Concordant: From the Latin "concordare," to agree. A loop that agrees with the visceroatrial situs.

Atrioventricular concordance: Connection of a morphologic right atrium to a morphologic right ventricle and a morphologic left atrium to a morphologic left ventricle.

Ventriculoarterial concordance: Connection of a morphologic right ventricle to a pulmonary trunk and a morphologic left ventricle to an aorta.

Discordant: From the Latin "dis," apart. Inappropriate.

Transposition of the great arteries: Each great artery arises from an anatomically discordant ventricle, the aorta from a morphologic right ventricle, and the pulmonary trunk from a morphologic left ventricle.

Malposition of the great arteries: Abnormal spatial relations of the aorta and pulmonary trunk to each other. Each of the abnormally related great arteries arises above the anatomically correct ventricle. The definition applies more accurately to anatomically corrected malposition, because the great arteries are also malposed in double-outlet left or right ventricle, but they do not arise from concordant ventricles.

Inversion: Mirror imagery.

Atrioventricular discordance: A morphologic right atrium connects to a morphologic left ventricle, and a morphologic left atrium connects to a morphologic right ventricle.

Ventriculoarterial discordance: A morphologic right ventricle gives rise to the aorta, and a morphologic left ventricle gives rise to the pulmonary trunk.

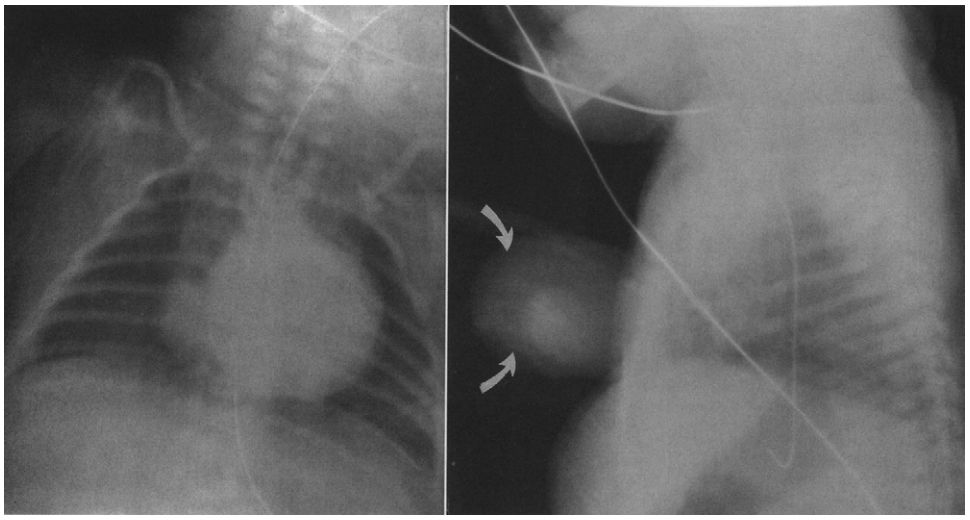

Figure 3. X-rays from a 2-day-old male infant with ectopia cordis. The external position of the heart is obvious in the lateral projection *(right, arrows)* but not in the frontal plain *(left)*. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

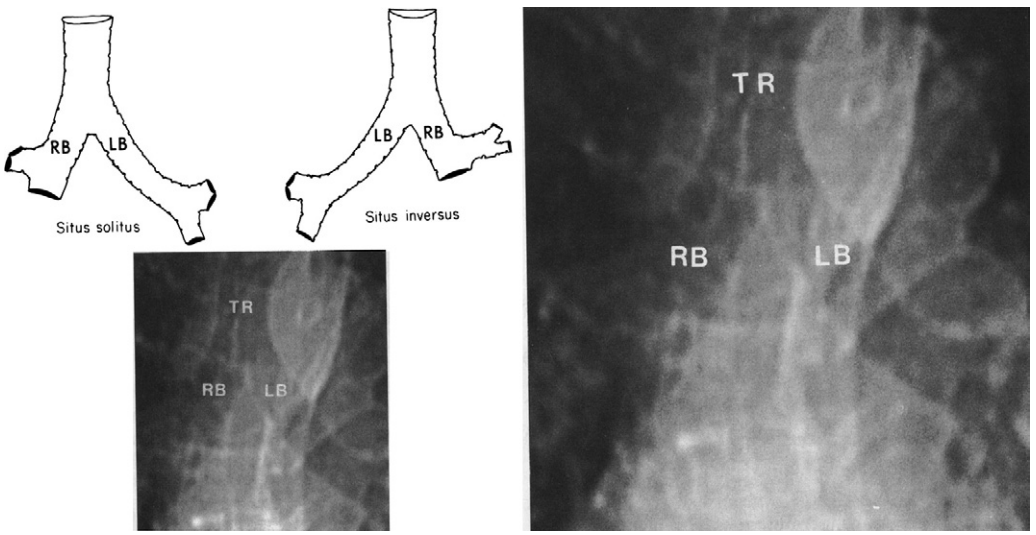

Figure 4. In situs solitus, the morphologic right bronchus (RB) is short, wide, and straight, and the morphologic left bronchus (LB) is long, thin, and curved *(upper left)*. In situs inversus *(upper right)*, the morphologic right bronchus is left sided, and the morphologic left bronchus is right sided. Tomograms *(lower and right images)* show the morphologic RB and morphologic LB in situs solitus. TR = trachea. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

Double discordance: Atrioventricular discordance together with ventriculoarterial discordance. The result is physiologically correct circulatory flow.

Systematic analysis: Sequential attention to the atria, atrioventricular valves, atrioventricular connections, ventricles, ventriculoarterial connections, great arteries, and position or malposition of the heart and abdominal viscera.

I shall first deal with normal cardiac and abdominal visceral positions, then with the 3 major cardiac malpositions.

The embryonic straight heart tube initially bends to the right (d-loop), then moves to the left until the ventricular portion occupies a normal left thoracic position. Situs solitus can be inferred from the physical examination by percussing a left-sided heart, a left-sided stomach, and a right-sided liver. Chest x-ray confirms these positions (Figure 1) and identifies concordant bronchial morphology (Figure 4). Chest x-ray also establishes a leftward base-to-apex axis, which is appropriate for situs solitus (Figure 1).

The relative levels of the 2 hemidiaphragms are determined by the location of the cardiac apex, not by the location of the liver.[10] In situs solitus, the left hemidiaphragm is lower than the right hemidiaphragm and vice versa. The ascending aorta is convex at the left basal aspect of the heart, and the descending thoracic aorta runs a course parallel to the left border of the vertebral column (Figure 1). Situs inversus with a structurally normal right thoracic heart is usually a chance discovery on a routine chest x-ray that had been read as normal because the film was reversed.

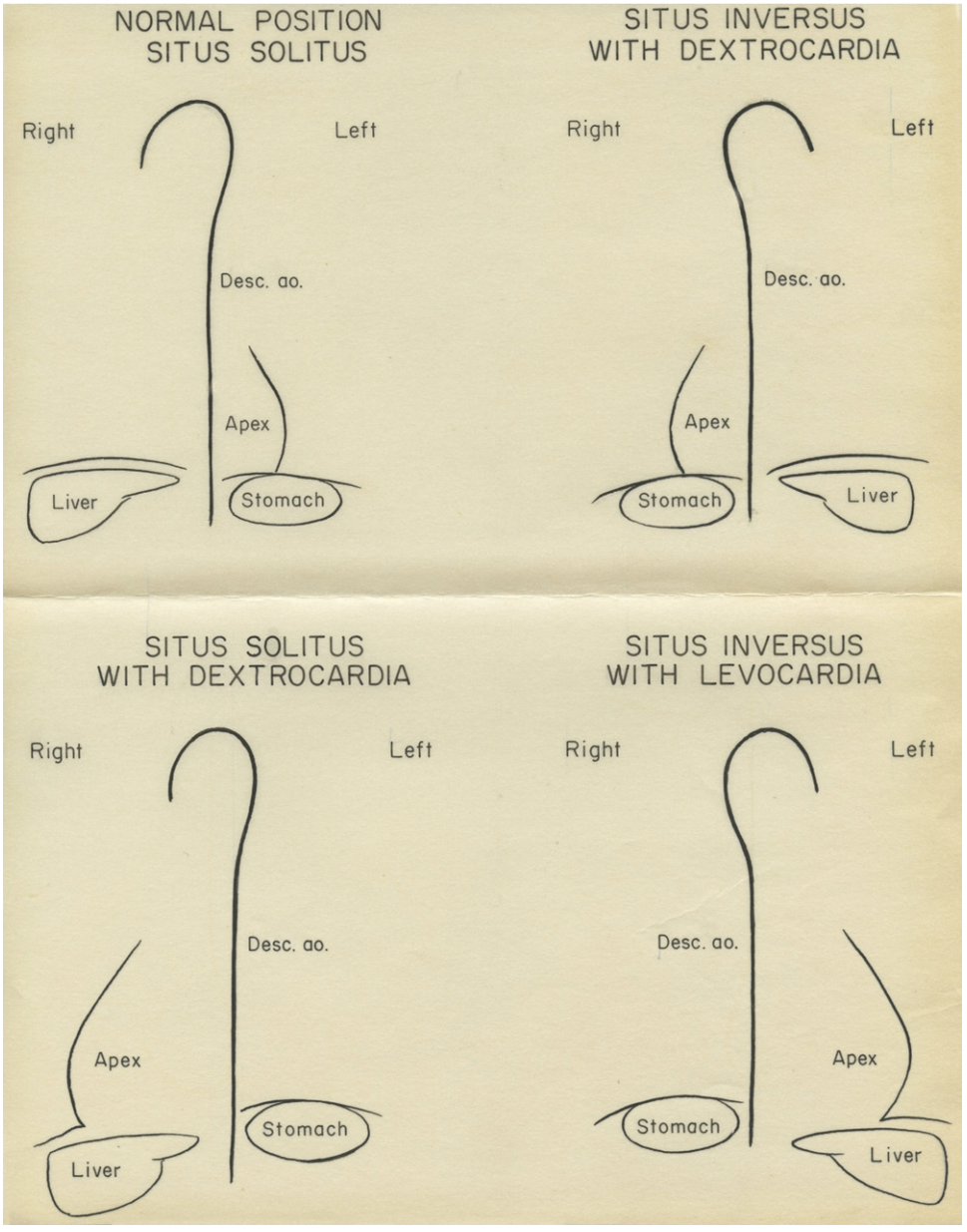

Figure 5. Schematic illustrations of the 4 basic cardiac positions (normal and 3 malpositions) and the relations of the descending aorta (Desc. ao.), cardiac apex, stomach, and liver as viewed on a frontal plain chest x-ray. In situs solitus, the descending aorta, cardiac apex, and stomach are on the left. In situs inversus with a right thoracic heart, the descending aorta, cardiac apex, and stomach are on the right. In situs solitus with a right thoracic heart, the descending aorta and stomach are on the left, and the cardiac apex is on the right. In situs inversus with a left thoracic heart, the descending aorta and stomach are on the right, but the cardiac apex is on the left. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

There are 4 basic cardiac positions, normal and 3 malpositions (Figure 5): (1) situs solitus with a right thoracic heart, (2) situs inversus with a right thoracic heart, and (3) situs inversus with a left thoracic heart. A midline heart (mesocardia) is sometimes regarded as a fourth malposition.

In the general population, the incidence of situs inversus with a right thoracic heart is about 1 in 8,000. The thoracic and abdominal viscera are mirror images of normal, a morphologic right bronchus is concordant with the morphologic right atrium and a trilobed lung, and a morphologic left bronchus is concordant with the morphologic left atrium and a bilobed lung (Figure 4). The heart is right sided; the right hemidiaphragm is lower than the left hemidiaphragm (Figure 2); the ascending aorta, aortic knuckle, and pulmonary trunk; are in mirror image positions; and the aorta descends on the right.

In situs solitus with a right thoracic heart (Figure 5), the lungs and abdominal viscera are normally positioned, the ascending aorta and aortic knuckle are normally located, the descending aorta runs its normal course along the left side of the vertebral column, but the major cardiac shadow lies to the right of midline. The base-to-apex axis points to the right, so the right hemidiaphragm is lower than the left hemidiaphragm. In situs solitus with a right thoracic heart,

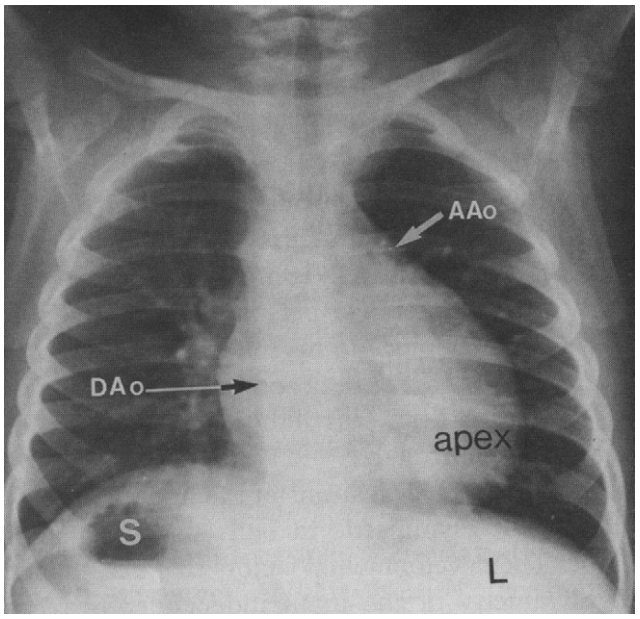

Figure 6. X-ray from a 2-year-old female infant in situs inversus with a left thoracic heart. The stomach (S) is on the right, the liver (L) is on the left, the heart is on the left, and the left hemidiaphragm is lower than the right hemidiaphragm. The descending thoracic aorta (DAo) is on the right, but the ascending aorta (AAo) is discordant. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

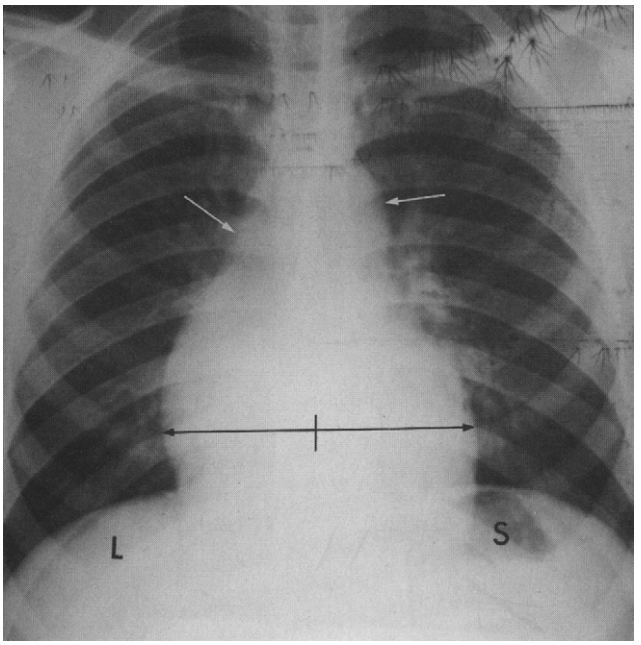

Figure 7. X-ray from a 16-year-old male patient in situs solitus with a midline heart and no congenital heart disease. The cardiac silhouette extends equally to the right and left *(black arrows)*. The stomach (S) is on the left, and the liver (L) is on the right. The ascending aorta and aortic knuckle *(unmarked white arrows)* are normally positioned. The hump-shaped appearance of the lower right silhouette is due to superimposition of the right atrium and right ventricle. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

the embryonic straight heart tube initially bends rightward (d-loop) but fails to move into the left chest. In situs inversus with a left thoracic heart (Figure 6), the lungs and abdominal viscera are mirror images of normal. The left hemidiaphragm is lower than the right hemidiaphragm; the bronchi, atria, and lungs are inverted; the stomach is on the right; and the liver is on the left.

A midline heart (mesocardia) extends equally to the right and left and occurs with both situs solitus and situs inversus. Mesocardia with a d-bulboventricular loop in situs solitus (Figure 7) is a variation of normal.

Once the malposition has been identified, assessment turns to the presence and type of accompanying congenital heart disease. Situs inversus with a right thoracic heart usually occurs with a structurally normal heart. Situs inversus with a left thoracic heart is associated with complex congenital heart disease.

The structurally and functionally asymmetric brain has become a focus of lively interest in patients with cardiac malpositions.[11] However, developmental factors that determine anatomic cerebral asymmetry differ from those that determine visceral asymmetry and lateralization of language.[11]

In situs inversus with a right thoracic heart, symptoms of acquired heart disease and of certain noncardiac diseases often lead to the discovery of the hitherto unsuspected cardiac malposition. The pain of angina pectoris is in the right anterior chest and radiates to the right shoulder and right arm.[12] The pain of appendicitis is in the left lower quadrant. Biliary colic is assigned to the left upper quadrant.

In 1933, Manes Kartagener,[13] a Swiss general physician, called attention to the association of sinusitis, bronchiectasis, and situs inversus, a combination subsequently referred to as the Kartagener syndrome or triad. The first English-language publication, in 1937, disclosed that as many as 1/5 of patients with situs inversus have bronchiectasis and sinusitis,[14] indicating that the association is not fortuitous. A blinded, controlled study of the ultrastructure of cilia in Kartagener syndrome revealed a widespread ciliary disorder that included the upper and lower respiratory tracts (bronchitis, bronchiectasis, sinusitis) and the testes[15] (immobile sperm with male infertility). Situs inversus is common in infertile men.[15] The syndrome is sometimes familial.[16] Six siblings included 2 patients with Kartagener syndrome and 2 with isolated bronchiectasis.[17]

Percussion and palpation are useful in the physical examination of cardiac malpositions (see earlier), because the malposition itself determines the thoracic location of cardiac dullness and the abdominal location of gastric tympany and hepatic dullness. If the stomach is not sufficiently air filled to generate a tympanitic percussion note, a carbonated beverage or deliberate aerophagia (an infant can suck an empty bottle) resolves the problem. Cardiac dullness is best determined with the patient supine but turned moderately to the left and then moderately to the right, because the heart decreases to the side of the base-to-apex axis. Situs solitus with a right thoracic heart can be suspected by percussing normal locations of gastric tympany and hepatic dullness, but cardiac dullness on the right. Situs inversus with a right thoracic heart can be suspected by percussing gastric tym-

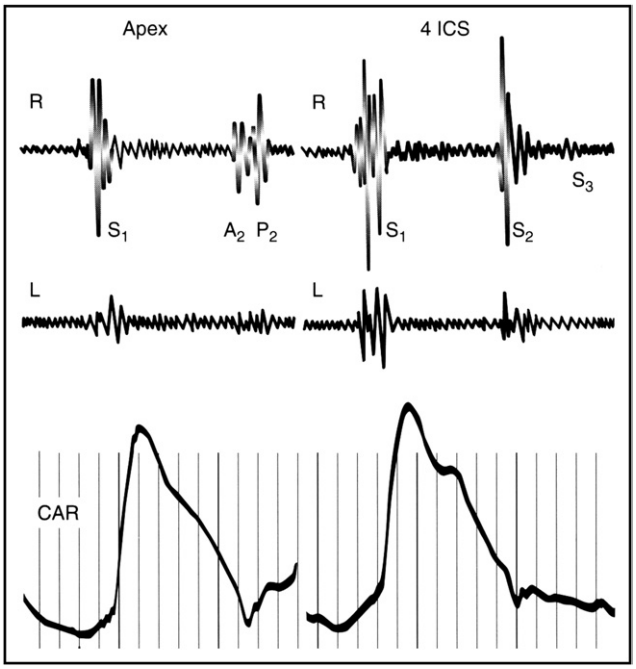

Figure 8. Phonocardiogram from a 7-year-old male patient in situs solitus with a right thoracic heart and an ostium secundum atrial septal defect. Heart sounds are louder on the right (R). The pulmonary component of the second sound (P_2) was recorded at the right cardiac apex, which was occupied by the right ventricle. CAR = carotid; 4 ICS = fourth left intercostal space. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

pany on the right, hepatic dullness on the left, and cardiac dullness on the right (Figure 2).

Palpation commences with the patient in the left lateral decubitus position and then in the right lateral decubitus position. In a normally positioned left thoracic heart in situs solitus (Figure 1), a morphologic left ventricle occupies the apex, and a morphologic right ventricle underlies the lower left sternal border. In situs solitus with a right thoracic heart, the apical right ventricle retracts, and the systemic morphologic left ventricle generates an outward systolic impulse adjacent to the lower right sternal border.

Auscultatory signs should be compared along the left and right sternal borders and at the cardiac apices, alternating from side to side to compare analogous right and left thoracic sites. In the presence of a right thoracic heart, splitting of the second sound is prominent in the second right intercostal space (Figure 8), and in situs inversus with a left thoracic heart, splitting is prominent in the second left interspace.

Long before the advent of clinical electrocardiography, it was postulated that ventricular potentials in situs inversus with a right thoracic heart should be diametrically opposite those in normally positioned hearts.[18] A mirror-image sinus node does in fact lie at the junction of a left superior vena cava and the left-sided morphologic right atrium, and the right and left bundle branches supply corresponding mirror image right and left ventricles. Interpretation is facilitated when the 12-lead electrocardiogram is intentionally "normalized" by reversing the arm leads and recording chest leads from right precordial sites that are the opposites of standard left precordial sites[19] (Figure 9). For situs solitus with a right thoracic heart, limb leads should remain unchanged, while chest leads are recorded from right precordial sites, a recommendation that is appropriate because atrial situs is normal, and the base-to-apex axis points to the right.

The direction of the P wave is determined by atrial situs unless the atrial pacemaker is ectopic.[20] In situs solitus with a left or right thoracic heart, atrial depolarization proceeds normally from a right sinus node, so the P-wave axis is normal.[20] Conversely, in situs inversus with either a right or left thoracic heart, atrial depolarization is initiated by a left sinus node, so P waves are inverted in leads 1 and aVL and upright in lead aVR. A left atrial ectopic rhythm is indicated by negative P waves in lead 1 and isoelectric or negative P waves in left precordial leads. The Valsalva maneuver transiently returns an ectopic atrial focus to the right sinus node. More distinctive but less common is a dome and dart P wave in lead V_1 or V_2[20] (Figure 10), a configuration associated with a left atrial ectopic focus irrespective of atrial situs.

Situs inversus with a right thoracic heart is accompanied by reversed ventricular activation and reversed repolarization, as predicted in 1889[18] (Figure 9). The major QRS deflection in lead 1 is negative, the T wave is inverted, lead aVR resembles aVL and vice versa, and the right precordial leads resemble leads from corresponding left precordial sites. Septal Q waves appear in right precordial leads because septal depolarization is from right to left. The electrocardiogram can be "corrected" by reversing the limb leads and recording chest leads from the right precordium (see earlier).

In situs solitus with a right thoracic heart, depolarization in the frontal plane is counterclockwise, so Q waves appear in leads 1 and aVL. Precordial leads exhibit prominent R waves in leads V_1 and V_2 and prominent RS complexes in most of the remaining right precordial leads. Normal left-to-right septal depolarization results in Q waves at standard left precordial sites.

Chest x-ray and echocardiography permit recognition of the cardiac malpositions[21] and are used herein because of their ready accessibility. High-technology contemporary imaging modalities are useful but not as readily accessible. The first necessity is to identify in the x-ray the orienting letters L (left) and R (right). From the radiologic point of view, that is all that is needed to recognize complete situs inversus (Figure 2), in which the stomach is on the right, the liver is on the left, and the major cardiac shadow is to the right of midline[22] (Figures 2 and 5). Situs inversus with a right thoracic heart is missed if the film is inadvertently reversed when read, because the x-ray then appears "correct."

Echocardiography with color flow imaging lends itself to segmental analysis of visceroatrial situs, atrioventricular connections, ventricular positions, and ventricular alignments of the great arteries.[23,24] Atrial situs can be established by identifying a right atrial appendage with its broad junction and a left atrial appendage with its narrow junction, best achieved with transesophageal echocardiography or with 3-dimensional capability. Atrial situs can also be in-

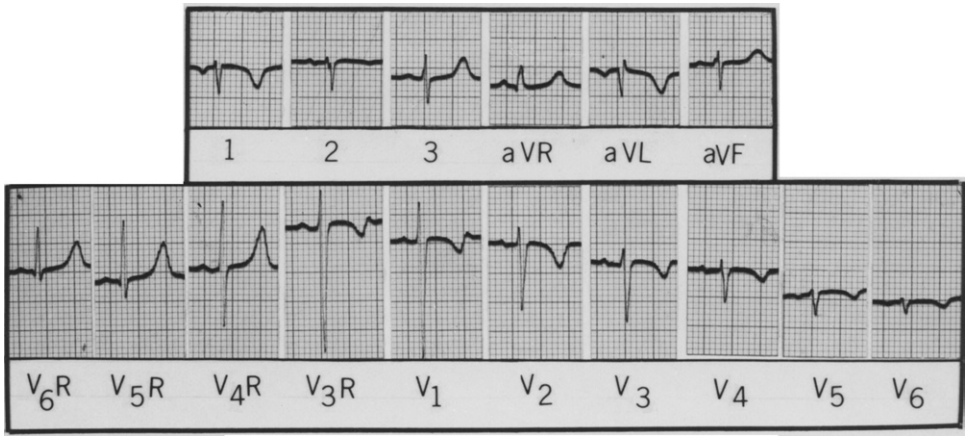

Figure 9. Electrocardiogram from an 11-year-old female patient in situs inversus with a right thoracic heart and no coexisting congenital heart disease. The P wave and T wave in lead 1 are inverted, and the major QRS deflection is negative. Leads aVR and aVL are mirror images of normal. Precordial leads V_2R through V_6R resemble leads from normal left precordial sites. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

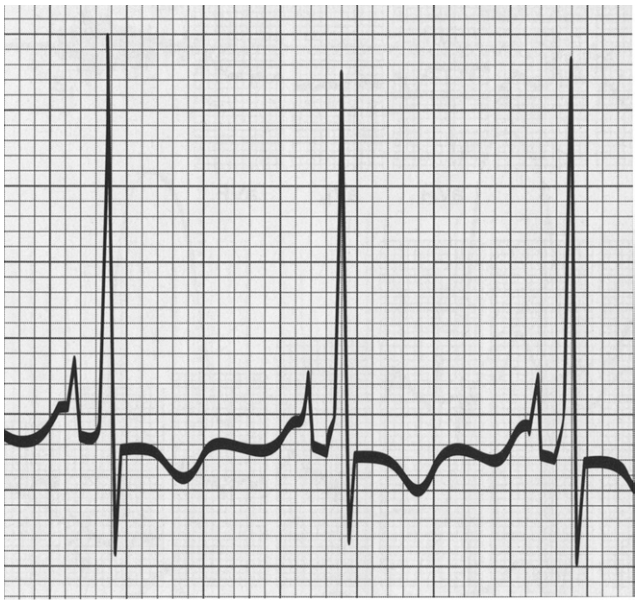

Figure 10. Dome and dart P wave in lead V_1 from a 5-year-old male patient in situs solitus with a right thoracic heart and a left atrial ectopic rhythm. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

ferred from the abdominal echocardiogram. With situs solitus and a left thoracic heart, the abdominal aorta lies to the left of the spinal column, and the inferior cava lies to the right. The morphologic right atrium is on the same side as the inferior vena cava, which can be distinguished from the pulsating aorta by color flow imaging. Situs inversus with a right thoracic heart is identified by the left atrium to the right of the aorta, the right atrium to the left of the aorta, the aorta to the right of the spinal column in the abdominal echocardiogram, and the inferior vena cava to the left of the spinal column.[23]

Once atrial situs is established, echocardiography focuses on the atrioventricular junction, ventricular location, and ventricular and great arterial connections.

Heterotaxy with right isomerism: Heterotaxy (from the Greek "heteros," different, and "taxis," arrangement) is loosely and poorly translated as "another arrangement" or "a different arrangement." Isomerism (from the Greek "isos," equal) refers to the similarity of bilateral structures that are normally morphologically asymmetric, such as right and left bronchi, right and left lungs, and right and left atrial appendages. There is strong concordance between a morphologic right bronchus, a trilobed right lung, and a morphologic right atrial appendage and an equally strong concordance between a morphologic left bronchus, a bilobed left lung, and a morphologic left atrial appendage. In right isomerism, the bronchi are symmetric morphologic right, the lungs are trilobed, and the atrial appendages exhibit right morphologic features.

A relation exists between right isomerism and asplenia. The spleen is the only organ that is left-sided from its inception, because it develops in the left side of the dorsal mesogastrium. In right isomerism, there is no left-sidedness, so there is no spleen. In about 5% of cases, however, a normal-sized spleen resides in the right upper quadrant.

A convenient clinical way of recognizing asplenia is by the presence of Howell-Jolly bodies in peripheral blood smears, although these formed element are occasionally found during the first week of life in normal infants.[25] Pitted red cells are also evidence of asplenia, but visualization requires wet preparations and a special optical system. Absence of a spleen can be diagnosed by ultrasound, even in the fetus. A wandering spleen can be mistaken for absence because the organ is located anywhere in the abdomen or pelvis and is hence overlooked.[26,27] There is a relatively consistent relation between the type of isomerism and the type of congenital heart disease.

Right isomerism with asplenia is characterized by a transverse liver, bilateral morphologic right bronchi, bilateral trilobed lungs, bilateral morphologic right atrial appendages,[28,29] bilateral superior vena cavae, bilateral sinus nodes,[28,29] and paired atrioventricular nodes. The

heart is likely to be to the left of midline.[30] Coexisting congenital cardiovascular malformations include common atrium, common atrioventricular valve, morphologic single ventricle,[30] functional single ventricle (hypoplastic right or left), pulmonary stenosis or atresia, absent coronary sinus, total anomalous pulmonary venous connection,[31] and bilateral ductus arteriosus.[32] Ventricular and great arterial connections are usually discordant. Noncardiac abnormalities are midline, such as tracheoesophageal fistula, meningomyelocele, encephalocele, cerebellar agenesis, cleft lip, cleft palate, and horseshoe kidney.[32] Gastrointestinal disorders include biliary atresia and intestinal malrotation.[33]

Infants with visceral heterotaxy and right isomerism are usually born at term at normal birth weights. Gender distribution is approximately equal, or with male predominance. Asplenia has been reported in siblings and families.[34] Neonatal cyanosis is invariable, conspicuous, and often evident in the first 24 hours.[34] Survival is determined largely by coexisting congenital heart disease, but noncardiac disorders (see earlier) weigh heavily in the balance. Most deaths occur within the first few months, with sporadic survivals after the first year[34] and a single remarkable survival of 21 years.[34] Asplenia is accompanied by serious recurrent infections because of the many immunologic functions of the spleen.[35]

In right isomerism, the atrioventricular conduction system is equipped with 2 nodes often but not always connected by a sling of tissue.[36,37] Supraventricular tachycardia is attributed to reentry between paired atrioventricular nodes.[38] The sinus nodes are paired because bilateral superior vena cavae are attached to bilateral morphologic right atria. The P-wave axis is normal because the right sinus node is usually the dominant atrial pacemaker.[37]

X-ray is especially useful when it includes the upper abdomen (Figure 11) that discloses a transverse liver. The bilateral symmetry of visceral heterotaxy is confirmed on the chest film by bilaterally symmetric bronchi. The next step is to determine whether the bronchi are symmetric right or symmetric left. An overpenetrated chest x-ray can make this distinction.

Thoracic echocardiography identifies morphologic right and left atrial appendages. Abdominal echocardiography discloses a transverse liver, an aorta that is anterior to or on the same side of the spine as the inferior vena cava, and hepatic veins that drain into the inferior cava as it joins a right-sided atrium. A spleen cannot be detected.

Heterotaxy with left isomerism: Heterotaxy with left isomerism is more prevalent in women[39] and is characterized by bilateral morphologic left bronchi, bilateral morphologic bilobed lungs, bilateral morphologic left atrial appendages, bilateral superior vena cavae attached to bilateral morphologic left atria, an absent or atretic sinoatrial node, common atrium, common atrioventricular valve, atrioventricular septal defect, and partial anomalous pulmonary venous connection. The pulmonary veins can be connected in a symmetric fashion, 2 to the right-sided atrium and 2 to the left-sided atrium, but it is questionable whether this should be considered partial anomalous drainage.

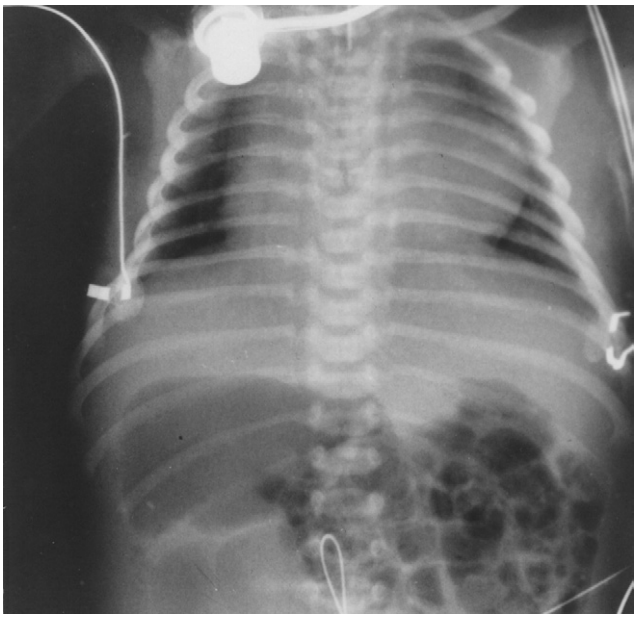

Figure 11. X-ray from an asplenic male neonate with right isomerism. The liver is transverse, the stomach is on the right, the heart is midline, but the base-to-apex axis points to the left. Reproduced with permission from Perloff JK. *The Clinical Recognition of Congenital Heart Disease*. 5th ed. Philadelphia, Pennsylvania: W.B. Saunders, 2003.

The most distinctive and therefore the most diagnostically useful clinical feature is inferior vena caval interruption with azygous continuation, in which the suprarenal segment of the inferior cava is absent, and the infrarenal segment continues as the azygos or hemiazygous vein.[40] Rarely, inferior caval interruption with azygos continuation occurs in isolation. Fetal complete heart block is presumptive evidence of in utero left isomerism.[37] Intrauterine loss for fetuses with left isomerism is greater than for those with right isomerism because of the association of complete heart block with left isomerism. Thoracic situs solitus with left isomerism (usual arrangement of the lungs and bronchial tree but with isomeric left appendages) is unique, with only 1 reported case.[41] Polysplenia, which is a feature of left isomerism, is characterized by a cluster of multiple splenules that collectively approximate the mass of 1 normal spleen.

In 1788, Matthew Baillie wrote, "There were three spleens, nearly of the size of a pullet's egg, found adhering to the larger spleen by short adhesions, besides two other still smaller spleens."[1] This arrangement occurs in about 10% of the general population.[40]

Morbidity and mortality are determined by coexisting cardiovascular malformations (see earlier) and by noncardiac anomalies, which are usually gastrointestinal,[42] including malrotation, biliary atresia, esophageal atresia, and congenital short pancreas.[43] Patients present as neonates with congestive heart failure or cyanosis, but an important minority come to attention because of the extracardiac malformations, especially biliary atresia.[42] Approximately 20% die as neonates; 50% do not survive adolescence.[44] Adult survival is uncommon but not unknown. There are reports of familial polysplenia and asplenia,[45] and attention has been called to sibling pairs

in which 1 twin was polysplenic and the other was asplenic.[46]

The normal sinus node is a right-sided structure located at the junction of a right superior vena cava and a morphologic right atrium (see earlier). In left isomerism, vena caval connections are necessarily to a morphologic left atrium, so the sinus node is absent or hypoplastic. The atrial pacemaker is therefore ectopic, and the P-wave axis is abnormal. The ectopic atrial pacemaker can shift from 1 site to another or may fire slowly (ectopic atrial bradycardia). Atrial fibrillation and atrial flutter are occasional. Complete atrioventricular block occurs in approximately 1 in 5 cases and has a significant impact on morbidity and mortality in the fetus and neonate.[46] Conduction is blocked at the level of the penetrating bundle, resulting in nodoventricular discontinuity and a narrow QRS interval. Intrauterine loss is greater for fetuses with left isomerism than for those with right isomerism because of the association with complete heart block.

When a transverse liver is accompanied by symmetric left bronchi, the diagnosis of left isomerism is secure. The heart is usually left sided. The stomach tends to be on the side opposite the descending aorta. Inferior vena caval interruption with azygous continuation is best identified on the frontal chest x-ray, because on the lateral projection, azygos continuation creates the erroneous impression of an uninterrupted inferior cava.[47] The aorta and inferior vena cava lie anterior to or on the same side of the spine. When there is inferior vena caval interruption with azygous continuation, hepatic veins connect directly to the atrium without joining the inferior cava.

1. Baillie M. Of a remarkable transposition of the viscera. *Philos Trans R Soc Lond* 1788;16:1785–1790.
2. Peacock TB. On malformations of the human heart. In: Osler W, McCrae J, eds. Osler's Modern Medicine. Philadelphia, Pennsylvania: Lea & Febiger, 1927.
3. Paltauf R. Dextrocardie and Dextroversion cordis. *Wren Klin Wchnschr* 1901;14:1032–1036.
4. Mandelstam ME, Reinberg SA. Die Dextrokardie. *Ergeb Med Kinderheilkd* 1928;34:154–157.
5. de la Cruz MV, Anselmi G, Munos-Castellanos L, Nadal-Ginard B, Munoz-Armas S. Systematization and embryological and anatomical study of mirror-image dextrocardias, dextroversions, and laevoversions. *Br Heart J* 1971;33:841–853.
6. Van Praagh R. Terminology of congenital heart disease. *Circulation* 1977;56:139–143.
7. Campbell M, Deuchar DC. Dextrocardia and isolated levocardia. I Isolated levocardia. *Br Heart J* 1965;27:69–82.
8. Campbell M, Deuchar DC. Dextrocardia and isolated levocardia. II Situs inversus and isolated dextrocardia. *Br Heart J* 1966;28:472–487.
9. Elliott LP, Jue KL, Amplatz K. A roentgen classification of cardiac malpositions. *Invest Radiol* 1966;1:17–28.
10. Reddy V, Sharma S, Cobanoglu A. What dictates the position of the diaphragm—the heart or the liver? A review of sixty five cases. *J Thorac Cardiovasc Surg* 1994;108:687–691.
11. Kennedy DN, O'Craven KM, Ticho BS, Goldstein AM, Makris N, Hensen JW. Structural and functional brain asymmetries in human situs inversus totalis. *Neurology* 1999;53:1260–1265.
12. Hynes KM, Gau GT, Titus JL. Coronary heart disease in situs inversus totalis. *Am J Cardiol* 1973;31:666–669.
13. Kartagener M. Zur Pathogenese der Bronchiektasien; Bronchiektasien bei Situs Viscerum Inversus. *Beitr Klin Tuberk* 1933;83:489–501.
14. Katz M, Benzier EE, Nangeroni L, Sussman B. Kartagener's syndrome (situs inversus, bronchiectasis, and chronic sinusitis). *N Engl J Med* 1953;248:730–732.
15. Abu-Musa A, Hannoun A, Khabbaz A, Devroey P. Failure of fertilization after intracytoplasmic sperm injection in a patient with Kartagener's syndrome and totally immobile sperm. *Hum Reprod* 1999; 14:2517–2518.
16. Narayan D, Krishnan SN, Upender M, Ravikumar TS, Mahoney MJ, Dolan TF, Teebi AS, Haddad GG. Unusual inheritance of primary ciliary dyskinesia (Kartagener's syndrome). *J Med Genet* 1994;31: 493–496.
17. Bergstrom WH, Cook CD, Scannell J, Berenberg W. Situs inversus, bronchiectasis and sinusitis; report of family with 2 cases of Kartagener's triad and 2 additional cases of bronchiectasis among 6 siblings. *Pediatrics* 1950;6:573–580.
18. Waller AD. On the electromotive changes connected with the beat of mammalian heart and of the human heart in particular. *Philos Trans R Soc Lond* 1889;180:169–194.
19. Edenbrandt L, Rittner R. Recognition of lead reversals in pediatric electrocardiograms. *Am J Cardiol* 1998;82:1290–1292.
20. Blieden LC, Moller JH. Analysis of the P wave in congenital cardiac malformations associated with splenic anomalies. *Am Heart J* 1973; 85:439–444.
21. Van Mierop LHS, Eisen S, Schiebler GL. The radiographic appearance of the tracheobronchial tree as an indicator of visceral situs. *Am J Cardiol* 1970;26:432–437.
22. Partridge JB, Scott O, Deverall PB, Macartney FJ. Visualization and measurement of the main bronchi by tomography as an objective indicator of thoracic situs in congenital heart disease. *Circulation* 1975;51:188–196.
23. Huhta JC, Hagler DJ, Seward JB, Tajik AJ, Julsrud PR, Ritter DG. Two-dimensional echocardiographic assessment of dextrocardia: A segmental approach. *Am J Cardiol* 1982;50:1351–1360.
24. Huhta JC, Smallhorn JF, Macartney FJ. Two-dimensional echocardiographic diagnosis of situs. *Br Heart J* 1982;48:97–108.
25. Corazza G R, Ginaldi L, Zoli G, Frisoni M, Lalli G, Gasbarrini G, Quaglino D. Howell-Jolly body counting as a measure of splenic function. A reassessment. *Clin La Haemat* 1990;12:269–275.
26. Abell I. Wandering spleen with torsion of the pedicle. *Ann Surg* 1933;98:722–735.
27. Allen KB, Andrews G. Pediatric wandering spleen-the case for splenopexy: review of 35 reported cases. J Pediatr Surg 1989;24:432–435.
28. Macartney FJ, Zuberbuhler JR, Anderson RH. Morphological considerations pertaining to recognition of atrial isomerism. *Br Heart J* 1980;44:657–667.
29. Hashmi A, Abu-Sulaiman R, McCrindle BW, Smallhorn JF, Williams WG, Freedom RM. Management and outcomes of right atrial isomerism: a 26-year experience. *J Am Coll Cardiol* 1998;31:1120–1126.
30. Anderson C, Devine WA, Anderson RH, Debich DE, Zuberbuhler JR. Abnormalities of the spleen in relation to congenital malformations of the heart: a survey of necropsy findings in children. *Br Heart J* 1990;63:122–128.
31. Rose V, Izukawa I, Moses CAF. Syndromes of asplenia and polysplenia. A review of cardiac and non-cardiac malformations in 60 cases with special reference to diagnosis and prognosis. *Br Heart J* 1975; 37:840–852.
32. Formigari R, Vairo U, deZorzi A, Santoro G, Marino B. Prevalence of bilateral patent ductus arteriosus in patients with pulmonic valve atresia and asplenia syndrome. *Am J Cardiol* 1992;70:1219–1220.
33. Ticho BS, Goldstein AM, Van Praagh R. Extracardiac anomalies in the heterotaxy syndromes with focus on anomalies of midline-associated structures. *Am J Cardiol* 2000;85:729–734.
34. Wolfe MW, Vacek JL, Kinard RE, Bailey CG. Prolonged and functional survival with the asplenia syndrome. *Am J Med* 1986;81:1089–1091.
35. Sills RH. Splenic function: physiology and splenic hypofunction. *Crit Rev Oncol Hematol* 1987;7:1–36.
36. Ho SY, Fagg N, Anderson RH, Cook A, Allan L. Disposition of the atrioventricular conduction tissues in the heart with isomerism of the atrial appendages: its relation to congenital complete heart block. *J Am Coll Cardiol* 1992;20:904–910.
37. Wren C, Macartney FJ, Deanfield JE. Cardiac rhythm in atrial isomerism. *Am J Cardiol* 1987;59:1156–1158.

38. Wu M, Wang J, Lin J, Lai L, Lue H, Young M, Hsieh F. Supraventricular tachycardia in patients with right isomerism. *J Am Coll Cardiol* 1998;32:773–779.
39. Stanger P, Rudolph AM, Edwards JE. Cardiac malpositions. *Circulation* 1977;56:159–172.
40. Van Mierop LHS, Gessner IH, Schiebler GL. Asplenia and polysplenia syndromes. *Birth Defects* 1972;8:36–44.
41. Ratib O, Perloff JK, Child JS. Unique discordance. Thoracic situs solitus with left isomerism. *Circulation* 2004;109:2252–2253.
42. Nakada K, Kawaguchi F, Wakisaka M, Nakada M, Enami T, Yamate N. Digestive tract disorders associated with asplenia/polysplenia syndrome. *J Pediatr Surg* 1997;32:91–94.
43. Rodriguez-Recio FJ, Mainer A, Ochoa A, Ratia T, Aquise M. Polysplenia with congenital short pancreas without other associated malformations. *Eur J Med* 1993;2:443–453.
44. Herman TE. Left-isomerism (polysplenia) with congenital atrioventricular block and biliary atresia. *J Perinatal* 1999;19:155–158.
45. Peoples WM, Moller JH, Edwards JE. Polysplenia: a review of 146 cases. *Pediatr Cardiol* 1983;4:129–137.
46. Gilljam T, McCrindle BW, Smallhorn JF, Williams WG, Freedom RM. Outcomes of left atrial isomerism over a 28-year period at a single institution. *J Am Coll Cardiol* 2000;36:908–916.
47. Roguin N, Hammerman H, Korman S, Riss E. Angiography of azygous continuation of inferior vena cava in situs ambiguous with left isomerism (polysplenia syndrome). *Pediatr Radiol* 1984;14:109–112.