

## Editorial

# Asplenia and polysplenia syndromes: time of successful treatment and updated terminology



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## ARTICLE INFO

## Article history:

Received 22 May 2018

Accepted 18 June 2018

Available online 21 June 2018

## 1. Nosography and embryology

A single Center observational study on right and left isomerisms, also known with the names of asplenia and polysplenia syndromes respectively, is published in this issue (Baban et al. in press), reporting the experience of the largest Paediatric Cardiology and Cardiac Surgery Department in Italy.

In the past, these types of malformations were regarded as “teratologic” conditions with prohibitive surgical treatment. The authors report impressive surgical results with long-term survival, despite quite severe defects.

This is particularly astonishing in cases with right isomerism where there is a concomitant presence of total anomalous pulmonary venous drainage, unbalanced complete atrioventricular septal defect with univentricular heart and cono-truncal malformations with pulmonary outflow tract obstruction, even pulmonary artery atresia. Also extra cardiac anomalies may be associated with involvement of genito-urinary, gastrointestinal, skeletal and nervous systems, complicating the clinical presentation.

These syndromes are characterized by a symmetrical development of normally asymmetrical organs like liver, lungs, bronchial tree and atria. In other words, there is a mistake of laterality organogenesis.

The spleen is the only mesenchymal, unilateral left organ since its origin at Streeter Horizon XIII, appearing in the embryo at the 4th–5th week of gestation as a thickening of the left layer of the dorsal mesogastrium. Its agenesis implies the absence of left morphology in the plan of visceral symmetry with the development of right isomerism.

Development of the atria with bilateral right appendages (right isomerism) implies that the lungs are unable to connect the pulmonary veins with the heart, since they do not find a morphologically left atrium like a “plug for electricity”, so that the pulmonary venous circulation remains intrinsic part of the systemic venous circulation (Fig. 1, left). Moreover, the development of two atria with both appendages of right morphology entails the development of bilateral superior vena cava with two cristae terminalis, two sinus nodes and two pacemakers, with the frequent ECG recording of two P waves with different morphology [1].

On the opposite, the development of multiple spleens implies a bilateral left morphology with both atria able to connect with the pulmonary veins (Fig. 1, right). With the development of two atria with bilateral left morphology (left isomerism) and absence of a morphologically right atrium, the inferior vena cava is unable to connect directly with the atrial platform and reaches the heart through the superior vena cava via azygous vein (azygous continuation of the inferior vena cava). With the development of atria with bilateral left appendages, there is neither crista terminalis nor sinus node and the pacemaker function is taken over by the atrioventricular node (nodal rhythm), with a not so rare need of artificial pacemaker, as reported in Baban et al. It is noteworthy that the development of the spleen is contemporary to the development of the heart and the association with multiple cardiac malformations is not incidental.

The bilateral morphology does not involve the ventricles and the arterial pole. In isomerism of the atrial appendages, there are neither bilateral morphologic right or left ventricles nor two aortae or pulmonary trunks. There is no evidence of ventricular or arterial isomerism.

Somebody believes that transposition of the great arteries is a localized defect of lateralization [2], but this remains a controversial issue.

## 2. History and terminology

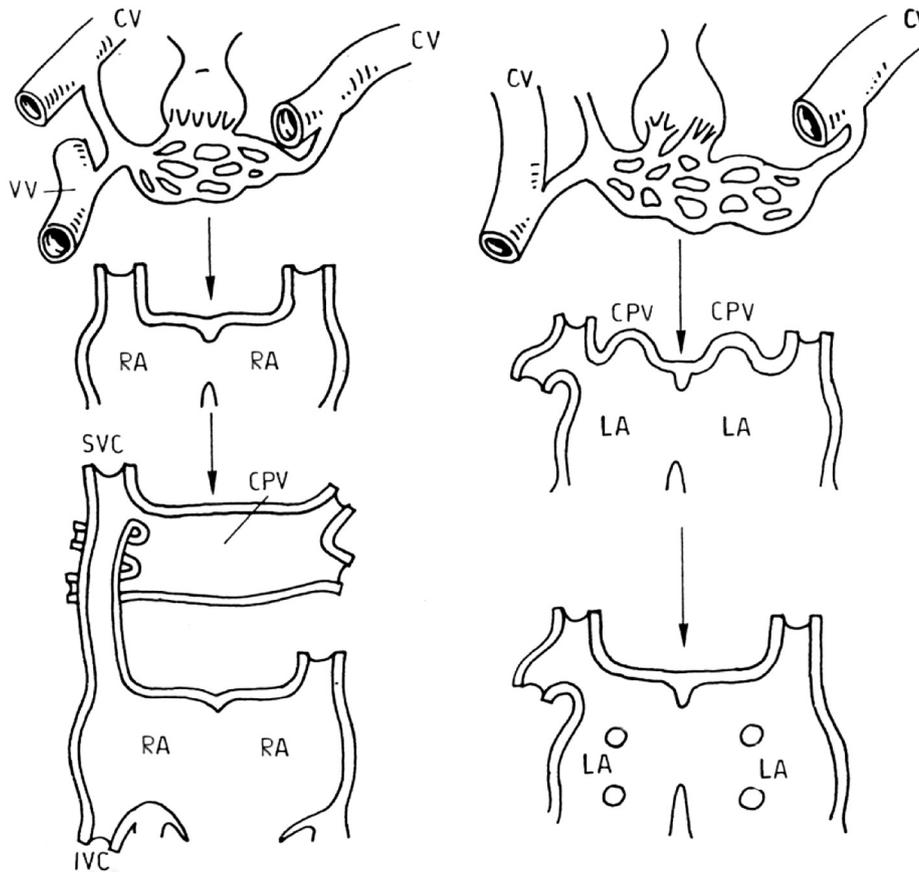
In 1826 Martin [3] and Breschet [4] first described the association of congenital malformations of the heart and agenesis of the spleen. In 1952 Polhemus and Schafer [5] outlined the syndromic character of these cases and considered the so called “ostium atrio-ventriculare commune” as a specific denominator without drawing the attention to atrial morphology.

Ivemark in 1955 reported the data of 69 cases with agenesis of the spleen, focusing the attention on cardiac malformations, morphology

DOI of original article: <https://doi.org/10.1016/j.ijcard.2018.02.050>.

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**Fig. 1.** Development of venous drainages in isomerism of right and left atrial appendages. In the presence of right atrial isomerism, the pulmonary veins are unable to connect with the atria, both of right morphology, and the result is a total anomalous pulmonary venous drainage (left side of the figure). In hearts with left atrial isomerism (right side of the figure), the inferior vena cava is unable to connect with the atria which are both of left morphology and interrupted of inferior vena cava with azygos continuation is present in these cases, whereas pulmonary veins connect with both atria. CPV: common pulmonary vein; CV: cardinal vein; IVC: inferior vena cava; LA: left atrium; RA: right atrium; SVC: superior vena cava; VV: vitelline vein.

of the lungs and abnormal position of the abdominal viscera, anticipating the concept of visceral symmetry:

*“the association of cardiac malformation and agenesis of the spleen had a varied picture of malformations that has a common pattern with a tendency towards visceral symmetry”* [6].

Ivemark described also cases with hypoplastic spleen or multiple spleens with similar cardiac malformations. He reported also the high incidence of infections (bronchopneumonia, meningitis....) as cause of death, a finding interpreted as a poor immunological defense of the body because of the absence of the spleen.

Nowadays the term Ivemark syndrome has fallen in disuse, but for long time the absence of the spleen (asplenia or asplenia syndrome) or the presence of multiple spleens (polysplenia or polysplenia syndrome) were frequently employed as nomenclature.

Van Mierop and Winglesworth in 1962 [7] demonstrated the isomerism of the cardiac atria and the presence of bilateral sinoatrial nodes in the asplenia syndrome.

Moller et al. in 1967 [8] discovered that a symmetrical arrangement of morphologically left-sided structures was present in patients with polysplenia.

With the introduction of the segmental approach for classification of Congenital Heart Disease [9], Van Praagh stressed that the starting point for analysis of cardiac chambers sequence was the determination of the atrial platform: situs solitus, situs inversus and situs ambiguus. For long time, situs ambiguus was referred to the presence of bilateral atria of right or left morphology. Anderson et al. proposed to remove the term situs ambiguus, focusing on the presence of right or left isomerism [10].

In general, patients with asplenia show isomerism of the right atrial appendages and patients with polysplenia present isomerism of the left atrial appendages.

Some authors popularized the use of the terms heterotaxy or heterotaxy syndrome as a synonymous of asplenia or polysplenia syndromes or situs ambiguus to emphasize the failure to establishing a normal asymmetry during embryonic development and this terminology is still used in Baban et al. In this setting, bilateral structures show symmetrical development, i.e. *isomerism*, thus the terminology “right or left isomerism” should be preferred.

#### Funding sources

This work was supported by the Registry of Cardio-Cerebro-Vascular Pathology, Grant 2018, Veneto Region, Venice, Italy.

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