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Ectopic Origin of Coronary Arteries from the Aorta in Syrian Hamsters (*Mesocricetus auratus*)

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Sumary

An ectopic origin of the coronary artery from the aorta beyond the sinotubular junction, a condition commonly referred to as 'coronary artery high take-off', has been described in man and C57BL/6 mice. The present paper reports this congenital coronary artery anomaly in the Syrian hamster (Mesocricetus auratus). Hearts from 14 individuals, aged 53–350 days, were examined by means of a corrosion-cast technique, scanning electron microscopy or histological and immunohistochemical techniques. In 11 hamsters, the right coronary artery was the ectopic vessel. In the other three animals there was a solitary coronary ostium in the aorta. In all cases, the ectopic coronary artery originated at an acute angle and a valve-like ridge was in front of the coronary artery ostium. The ectopic arteries examined microscopically showed an intramural trajectory within the aortic wall. In the hearts with a solitary ostium in the aorta, the left main coronary artery coursed between the aorta and the pulmonary artery. In man, all of these anomalous conditions place the individual at risk of myocardial ischaemia and sudden death. However, none of the affected hamsters had clinical signs of disease. Intimal thickenings of increasing size with age were present in the intramural coronary artery segment of eight hamsters aged 106 days or older, examined histologically. The present findings fit with the notion that coronary arteries with acute angle take-off and an intramural course are subjected to unusual wear and tear, leading to tissue changes in the vessel wall.

Introduction

An ectopic origin of coronary arteries from the aorta beyond the sinotubular junction has been reported in man (Hackensellner, 1954, Alexander and Griffith, 1956, Ogden, 1970, Virmani et al., 1984, Virmani et al., 1989, Mahowald et al., 1986, Rao et al., 1994, Frescura et al., 1998, Piegger et al., 2001), in C57BL/6 mice (Fernández *et al.*,

2008) and in *iv/iv* (Icardo and Colvee, 2001) and *connexin43* (Li et al., 2002, Clauss et al., 2006) mutant mice, both developed on a C57BL/6 background (Fernández *et al.*, 2008). Controversy exists concerning the clinical significance of this congenital anomaly, which is commonly referred to as 'coronary artery high take-off'. The ectopic location of the coronary ostium in the aorta is not a pathological condition in itself (Roberts, 1987, Angelini et al., 1999); however, coronary artery high take-off often occurs in association with other defects such as acute angle take-off, slit-like ostium, valve-like ostium and intramural course of the first coronary artery segment, all of which have been incriminated as possible causes of myocardial ischaemia and even sudden death in man (Ogden, 1970, Allwork, 1979, Boucek et al., 1984, Íñiguez Romo et al., 1991, Steinberger et al., 1996, Frescura et al., 1998, Angelini et al., 1999, Houyel and Planché, 2002, García-Rinaldi et al., 2004).

Several studies have described a variety of congenital anomalies in the origin of the coronary anomalies in the Syrian hamster (*Mesocricetus auratus*), most of which are similar to those occurring in man (Sans-Coma et al., 1991, Sans-Coma et al., 1999, Fernández et al., 2000, Durán et al., 2007a, Durán et al., 2007b). However, none of these anomalies includes location of a coronary ostium outside of the aortic root.

In an investigation of congenital cardiac anomalies in Syrian hamsters, 14 specimens were found to have a coronary artery arising from the aorta beyond the cephalad border of the aortic valve sinuses or the sinotubular junction. The aims of the present study were (1) to describe the anatomical and histological features of the anomalously originating arteries, taking into account the condition of the aortic root and the proximal course of the anomalous vessels, and (2) to compare the present observations with analogous findings in man and mice.

Materials and Methods

Animals

Fourteen Syrian hamsters (five male, nine female), aged 53–350 days, were included in this study. They belonged to a group of 20 inbred families in our laboratory. The hamsters were handled in accordance with the Spanish Regulations for the Protection of Experimental Animals (R.D. 1201/2005; B.O.E. 21.10.2005). They were housed in polypropylene cages and kept in a well-ventilated room at 22–25°C. The light cycle was 14 h light and 10 h dark. Commercial food and water were given as required, starting at weaning. The animals were killed for examination and the hearts were exposed by means of a thoracotomy at the level of the fifth intercostal space and perfused through the ventricles with 0.1M buffered saline (pH 7.3).

Two of the 14 specimens with anomalously originating coronary arteries were detected in a survey of a database consisting of 1,202 internal casts of the heart, great arterial vessels and coronary arteries. The other 12 were found among 2,770 hearts, in which the condition of the aortic valve and coronary arteries was assessed by means of a stereomicroscope. In two of these 12 cases, the aortic valve and the first portion of the ventral aorta were removed and processed for scanning electron microscopy

(SEM) in order to obtain accurate images of the ectopically located coronary artery ostium. In the remaining 10 cases, the heart and proximal aorta were studied by means of histological and immunohistochemical techniques.

Corrosion-cast Technique

Vinyl resin (Rhodopas$^{@}$ AX85/15; Rhone-Poulenc, Courbevoie, France) in a 20% ketone solution was injected via a cannula placed in the ventral aorta through the apex of the left ventricle. Internal casts of the left ventricle, aorta and coronary arteries were obtained by macerating the specimens in a 20% hydrochloric acid bath. They were examined by means of a Leica MZ10F stereomicroscope (Wetzlar, Germany) and photographed with a Nikon DXM1200 camera (Tokyo, Japan).

Scanning Electron Microscopy

The aortic valve, together with the first segment of the ventral aorta, was removed and fixed by immersion in 1% paraformaldehyde and 2% glutaraldehyde in 0.05 Msodium cacodylate buffer (pH 7.3) with osmolarity adjusted to 330 milliosmol/l for 3 h (ratio of fixative: tissue volume, 80:1). Thereafter, the specimen was dehydrated in increasing concentrations of ethanol, dried by the critical point method and gold sputter coated. Observations were made using a Jeol JSM-840 scanning electron microscope (Jeol, Tokyo, Japan), operated at 10 kV.

Histology and Immunohistochemistry

Hearts were removed, transferred to 0.1M buffered saline (pH 7.3), and dissected under a stereomicroscope to assess the condition of the aortic valve and the anatomical origin of the coronary arteries. The specimens were then fixed by immersion in 4% paraformaldehyde (ratio of fixative: tissue volume, 80:1), embedded in Histosec (Merck KGaA, Darmstadt, Germany) and sectioned serially (10 μm) in transverse orientation. Sections were stained with Delafield's haematoxylin and eosin (HE) for a general assessment of the microscopical features of the specimen or with resorcin-fuchsin or Weigerte-van Gieson stains for the detection of elastin. In addition, monoclonal anti-smooth muscle α-actin (clone 1A4, Sigma Chemical Co, Poole, UK) was used for the detection of smooth muscle. For immunohistochemistry (IHC) the sections were dewaxed in xylene, hydrated in an ethanol series and washed in Tris-phosphate buffered saline (TPBS pH 7.8). Endogenous peroxidase activity was quenched by incubation with H_2O_2 3% in TPBS for 10 min. After washing with TPBS, non-specific binding sites were saturated for 1 h with 10% sheep serum and 1% bovine serum albumin in TPBS plus 0.5% Triton X-100 (SBT). Endogenous biotin was blocked with the avidin-biotin blocking kit (Vector, Burlingame, California, USA). Sections were washed with TPBS and then incubated overnight in the primary antibody diluted in SBT. Control slides were incubated in SBT only. After overnight incubation, the sections were washed in TPBS (3 x 5 min) and incubated for 1.5 h at room temperature with biotin-conjugated anti-mouse immunoglobulin (Ig) G (Sigma) diluted 1 in 100 in

TPBS, washed again and incubated for 1 h in ExtrAvidin® conjugate (Sigma) diluted 1 in 150 in TPBS. Peroxidase activity was developed with Sigma Fast 3, 3'-diaminobenzidine tablets, according to the manufacturer's instructions. In some cases, the sections were counterstained with haematoxylin. Observations were made with a Leica DMSL microscope, equipped with a Nikon DXM1200 camera.

Nomenclature

The nomenclature used in this study is that suggested by Sans-Coma et al. (1993) and Durán et al. (2007b) for coronary arteries and Sans-Coma et al. (1996) for components of normal and anomalous aortic valves in the Syrian hamster. The classification established by Durán et al. (2005) was used to describe the course of the anomalous coronary arteries detected by means of internal casts.

Results

The normal aortic valve of the Syrian hamster is tricuspid; it has three aortic sinuses, right, left and dorsal, each supporting its own leaflet (cusp), and three commissures located in the right-left, right-dorsal and left-dorsal positions (Sans-Coma et al., 1996, Fernández et al., 2009). The normal coronary artery pattern is characterized by the presence of two coronary arteries, right and left, which become intramyocardial shortly after their origin from their respective ostia located in the walls of the right and left aortic sinuses (Fig. 1a). The right coronary artery runs parallel to the atrioventricular sulcus and gives off a dorsal interventricular artery that corresponds to the subsinuosal interventricular artery of veterinary anatomists and to the posterior descending artery of human cardiologists. The left coronary artery consists of a left main coronary artery trunk, which divides into two major components, namely, the left circumflex and the obtuse marginal arteries (Fig. 1b). Physiologically, this latter vessel is equivalent to the paraconal interventricular artery of non-human mammals with subepicardial coronary arteries and to the left anterior descending artery of man (Durán et al., 2009). The interventricular septum is basically supplied by a septal artery (Fig. 1b) that arises from the right coronary artery in 70%of hamsters. In 25%of cases, it originates from the right coronary artery, whereas in the remaining 5%, the vessel has its own ostium, placed in the right or in the left aortic sinus (Dur_an et al., 1992, 2007a; Sans-Coma et al., 1993).

Table 1 summarizes the main findings in the 14 cases included in this study.

Scanning Electron Microscopy and Internal Cast Findings

In one of the two hearts examined by SEM, the aortic valve was tricuspid (normal) and the left coronary artery originated from the left aortic sinus. The right coronary artery arose from a slit-like ostium located in the aorta beyond the sinotubular junction (Fig. 2a; compare with Fig. 1a). In the other heart, the aortic valve was bicuspid; two aortic sinuses, dorsal and ventral, were present, each supporting its own leaflet (Fig. 2b). A

large, elliptical solitary coronary ostium in the aorta was located at the cephalad border of the ventral aortic sinus.

In one of the two hearts studied by means of the corrosion-cast technique, the aortic valve was tricuspid (Fig. 2c). In the other heart, the valve was bicuspid (Fig. 2d). In both cases a solitary coronary ostium was present in the aorta, beyond the sinotubular junction (compare Fig. 2c, d with Fig. 1a). The ostium was aligned with the right aortic sinus in the heart with a tricuspid aortic valve (Fig. 2c) and with the ventral aortic sinus in the heart with a bicuspid aortic valve (Fig. 2d). A single coronary artery trunk arose at an acute angle from the solitary ostium (Fig. 2c, d). The single trunk divided in a fan-like fashion into right coronary artery, septal artery and left main coronary artery trunk. The left main coronary artery coursed to the left side of the heart between the aorta and the pulmonary artery, crossing the infundibular septum (compare Fig. 2c, d with Fig. 1b). Having reached the obtuse margin of the heart, the vessel divided into left circumflex artery and obtuse marginal artery (Fig. 2c, d).

Histological and Immunohistochemical

Findings Dissection of the heart under a stereomicroscope revealed that nine of the 10 specimens examined later by means of histological and immunohistochemical techniques had a tricuspid aortic valve. In the remaining heart, the valvewas bicuspid. In all specimens there was a normal left main coronary artery that arose from the left aortic sinus when the aortic valve was tricuspid and from the left side of the ventral aortic sinus when the valve was bicuspid. The right coronary artery originated from a slit-like ostium located in the aortic wall, at a variable distance fromthe sinotubular junction. In six cases, the ectopic ostiumwas placed just ahead of the cephalad border of the aortic sinus. In the heart with a bicuspid aortic valve, the ostium was aligned with the left side of the ventral aortic sinus. In the hearts having a tricuspid aortic valve, itwas alignedwith the right aortic sinus and occupied a variable position with regard to the right-dorsal and right-left commissures.

In contrast to coronary arteries originating normally from their aortic sinuses (Fig. 3a), the ectopic right coronary artery of the present specimens had an acute angle take-off (Fig. 3b). A valve-like ridge was in front of the ostium (Fig. 3b). After its origin from the aorta, the vessel showed an aortic intramural trajectory. Its tunica media was totally fused with that of the aorta (Fig. 3c). In nine cases, the right coronary artery coursed obliquely from its origin at the aortic wall until the point where the vessel penetrated the right ventricular myocardium. In the remaining case, the coronary artery ran parallel to the aorta until reaching this latter point.

Two hamsters, 83 and 99 days old, examined histologically, showed no tissue changes at the origin or along the intramural course of the ectopic coronary artery (Table 1). In a further four hamsters, aged 106e136 days, small, focal thickenings of the intima occurred at different sites of the intramural coronary artery segment (Table 1). The location of the foci varied between individuals. However, in all four cases there

was a more or less patent focus at the origin of the coronary artery, where the vessel bended in an acute angle with regard to the aortic wall.

The remaining four hamsters, 148e350 days old, showed several, conspicuous focal intimal thickenings along the intramural coronary artery (Table 1). At these intimal proliferative zones, the inner elastic lamina was slightly folded, but not disrupted (Fig. 3d). The elastic fibres of the tunica media shared by the intramural coronary artery segment and the aorta were somewhat disarranged (Fig. 3d). Staining with HE revealed leucocytic infiltration at this site of the common media (Fig. 3e). Immunolabelling with anti-smooth muscle α-actin indicated an absence of smooth muscle cells in the intimal proliferation (Fig. 3f). The intimal changes were particularly expanded at the ectopic anatomical origin of the coronary artery, where a valve like ridge existed in front of the ostium. At this site there were conspicuous focal intimal thickenings. The inner elastic lamina was wrinkled, but intact, and the elastic fibres of the common media were disarranged (Fig. 3g). In addition, the medial tissue showed leucocytic infiltration (Fig. 3h).

Discussion

This paper is the first to describe the occurrence of coronary arteries arising ectopically from the aorta, beyond the sinotubular junction, in the Syrian hamster. Overall, 14 animals had a coronary artery ostium placed just ahead of the cephalad boundary of the aortic sinuses or at a certain distance from this boundary. The sample examined is too limited to speculate on the nature of the aetiological factor/s involved in the formation of the anomaly, a process that apparently entails a distortion in the normal development of the coronary artery main stems, which takes place by the ingrowth of the embryonic coronary plexus into the walls of the right and left aortic sinuses (Bogers et al., 1989; Bernanke and Velkey, 2002; Fernández, 2005). The aetiology of coronary artery high take-off is also unknown in man, where this condition is regarded as very rare (Angelini et al., 1999). In C57BL/6 mice and mutant mice developed on a C57BL/6 background, coronary artery high take-off has been suggested to be influenced by genes (Fernández et al., 2008) and might be integrated in the C57BL/6 genotype.

In man (Boucek et al., 1984; Petit and Reig, 1993) and C57BL/6 mice (Icardo and Colvee, 2001; Fernández et al., 2008), coronary artery high takeoff involves predominantly the right coronary artery. This is also the case in the Syrian hamster. Indeed, in 11 of the 14 affected animals examined, the ectopic coronary artery was the right one; the left coronary artery had a normal origin. The reason for this difference is undetermined.

In the remaining three hamsters there was a solitary coronary artery ostium located ectopically in the aortic wall. The existence of a sole coronary opening is a congenital abnormality that has been studied in detail in the Syrian hamster (Durán et al., 2005), but no case with ectopic location of the ostium beyond the aortic sinus limit has been reported previously. The two hamsters with a solitary ostium examined by means of

internal casts had a coronary artery distribution pattern that corresponded to the type 2A1 described by Durán et al. (2005) and is equivalent to the categories IIB2 and IIB3 established by Shirani and Roberts (1993) inman. The pattern is characterized by the aberrant course of the left main coronary artery trunk between the aorta and the pulmonary artery. Occurrence of a sole coronary ostium in the aorta, beyond the sinotubular junction, was reported in C57BL/6 mice (Fernández et al., 2008). However, no description of the coronary artery distribution pattern associated with the presence of the ectopic solitary ostium was given in this paper.

In three hamsters with an ectopically located coronary ostium, the aortic valve was bicuspid (Table 1). It is well known that in the Syrian hamster, several congenital anomalies in the origin of the coronary arteries are significantly associated with the bicuspid condition of the aortic valve (Fernández et al., 2000). Therefore, concurrence of an ectopic coronary ostium in the aorta and a bicuspid aortic valve in an individual might be regarded as the product of this morphogenetic association. However, more data are needed to verify this notion.

In man, the ectopic origin of a coronary artery from the aorta is commonly seen as a benign cardiac abnormality (Roberts, 1987; Angelini et al., 1999). However, the ectopic take-off of the vessel is often associated with other anomalous conditions of clinical relevance. The ectopic artery very often leaves the aorta at an acute angle from a slit-like opening, a condition that results in a flap-like mechanism at the coronary ostium. Expansion of the aorta during exercise may cause ostial stenosis by the flap, thereby leading to myocardial ischaemia and even sudden death (Cheitlin et al., 1974; Mahowald et al., 1986; Steinberger et al., 1996; Frescura et al., 1998; Basso et al., 2001). Ostial valve-like ridges created by the aortic and coronary artery walls, as they meet to form the ectopic coronary opening, may account for sudden death if the surface area of the ridge exceeds 50% of the coronary ostial luminal area (Virmani et al., 1984, 1989; Frescura et al., 1998). Sometimes, the first segment of the ectopically originating coronary artery runs intramurally within the aortic wall (Houyel and Planché, 2002). This condition has been suggested to be a potential cause of myocardial ischaemia during effort (Frescura et al., 1998; Basso et al., 2001). Acute angle take-off from a slitlike opening, together with an intramural course, may cause acute obstruction of the proximal coronary artery segment when the ascending aorta becomes dilated during left ventricular systole, a complication that can lead to sudden death (Iñiguez Romo et al., 1991; Frescura et al., 1998; Pijoan Rotgé et al., 1999; Piegger et al., 2001; García-Rinaldi et al., 2004).

The 14 hamsters included in this study showed a combination of abnormal coronary artery features such as acute angle take-off, slit-like ostium, ostial valve-like ridge and intramural course of the first coronary segment inside of the aortic wall, each of which constitutes a more or less significant risk factor in itself. In addition, in two hamsters with an ectopic solitary coronary ostium, it was determined that the left main coronary artery trunk coursed between the aorta and the pulmonary artery. In man, this condition is considered to place an individual at risk of myocardial ischaemia and

even sudden death during or just after strenuous exercise (Cheitlin et al., 1974; Liberthson et al., 1979; Barth and Roberts, 1986; Basso et al., 2001). However, these coronary artery defects do not seem to cause any clinical abnormality in Syrians hamsters, at least under laboratory conditions. None of the present affected animals showed perceptible signs of disease before they were killed. Microscopical examination of the myocardium revealed no pathological changes. Further experiments involving endurance exercise would be required to gain more insight into this question.

Of note was the finding of multifocal intimal thickenings along the intramural coronary artery segment and, in particular, at the site where the vessel bends in an acute angle, just after its origin from the aortic wall. These tissue changes consisted of (1) proliferations of the intima, with no disruption of the intimal elastic lamina and no smooth muscle cells in the intimal thickenings, and (2) a more or less conspicuous disarrangement of the elastic fibres of the tunica media. The presence of leucocytic infiltration in the media pointed to a local inflammatory reaction. In man, coronary arteries with acute angle take-off and intramural course are predisposed to atherosclerosis, in particular at the ostium, because of rheological factors and unusual stress (Boucek et al., 1984; Angelini et al., 1999). The two younger hamsters examined histologically were devoid of any tissue change along the intramural course of their anomalous coronary artery (Table 1). In contrast, histological sections revealed that all of the eight hamsters aged 106 days or older had intimal thickenings of increasing size with age in both the ectopic coronary artery ostium and the intramural segment of the vessel. These findings fit with the notion that coronary arteries with acute angle take-off and intramural course are subjected to uncommon wear and tear that causes tissue changes in the vessel wall.

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Table 1. Details of 14 Syrian hamsters with ectopic coronary artery ostium in the aorta

No.	Age(days)	Sex	Techniques	Aortic valve	Ectopic ostium	Coronary course	Intimal thickenings
1	53	M	D, SEM	Tricuspid	RCA	NDA	NDA
2	179	F	SEM	Bicuspid	SCO	NDA	NDA
3	97	M	CCT	Tricuspid	SCO	NDA	NDA
4	54	F	CCT	Bicuspid	SCO	NDA	NDA
5	83	F	D, H	Tricuspid	RCA	Intramural, oblique	–
6	99	F	D, H, IHC	Bicuspid	RCA	Intramural, oblique	–
7	106	F	D, H	Tricuspid	RCA	Intramural, oblique	+
8	114	M	D, H	Tricuspid	RCA	Intramural, oblique	+
9	130	M	D, H, IHC,	Tricuspid	RCA	Intramural, oblique	+
10	136	M	D, H	Tricuspid	RCA	Intramural, oblique	+
11	148	F	D, H, IHC	Tricuspid	RCA	Intramural, oblique	++
12	187	F	D, H, IHC	Tricuspid	RCA	Intramural, oblique	++
13	227	F	D, H	Tricuspid	RCA	Intramural, oblique	++
14	350	F	D, H	Tricuspid	RCA	Intramural, oblique	++

M, male; F, female; CCT, corrosion-cast technique; D, dissection; H, histology; IHC, immunohistochemistry; NDA, no data available; RCA, right coronary artery; SCO, solitary coronary artery ostium in aorta; SEM, scanning electron microscopy; _, no thickenings; +, small focal thickenings; ++, conspicuous focal thickenings.

Fig. 1. Normal aortic valves and coronary arteries from Syrian hamsters. (a) Tricuspid (normal) aortic valve from an adult Syrian hamster opened through the dorsal aortic sinus to expose the ventral aspect of the valve. The ostia (arrows) of the normal right and left coronary arteries are located in the walls of the right (RS) and left (LS) aortic sinuses, respectively. The dotted line indicates the sinotubular junction. SEM. Bar, 200 μm. (b) Internal cast of the left ventricle (LV), aorta (Ao) and coronary arteries from an adult Syrian hamster. The aortic valve is tricuspid (normal). The right coronary artery (RC) arises from the right aortic sinus. The left main coronary artery trunk (LC) originates from the left aortic sinus, gives off the septal artery (SA) and divides into left circumflex artery (arrowheads) and obtuse marginal artery (arrow). The dotted line indicates the level of the sinotubular junction. Corrosion-cast technique. Bar, 1 mm.

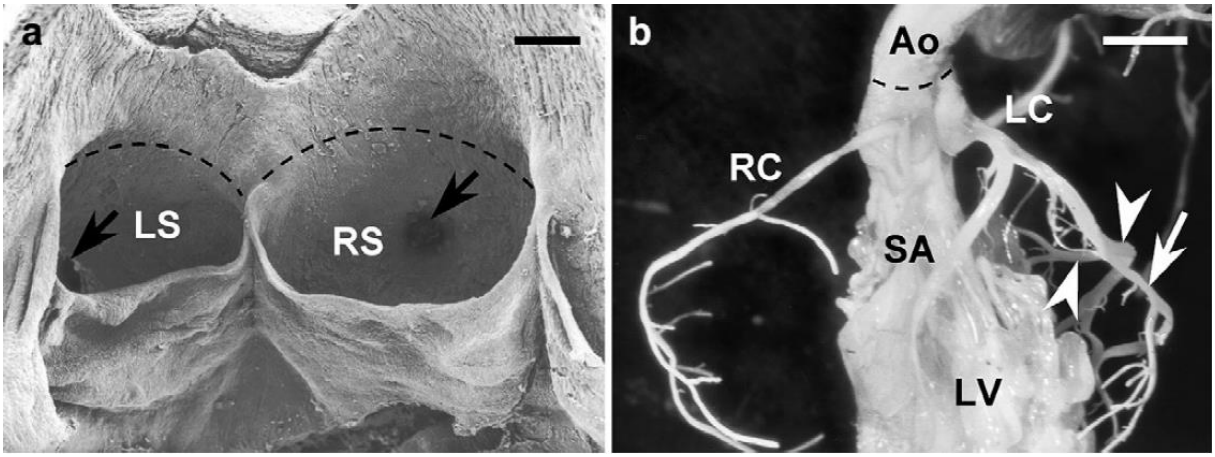


Fig. 2. Ectopic coronary artery ostia in Syrian hamsters. (a) Tricuspid aortic valve of Syrian hamster No. 1 (Table 1) opened through the dorsal aortic sinus (DS). The ostium (arrow) of the right coronary artery is located in the aortic wall beyond the sinotubular junction (compare with Fig. 1a). RS and LS indicate the right and left aortic sinuses, respectively. SEM. Bar, 200 μm. (b) Bicuspid aortic valve of Syrian hamster No. 2 (Table 1) opened through the dorsal aortic sinus (DS). A solitary coronary ostium (arrow) is placed at the cephalad border of the ventral aortic sinus (VS). SEM. Bar, 200 mm. (c) Internal cast of the left ventricle (LV), aorta (Ao) and coronary arteries of Syrian hamster No. 3 (Table 1). The aortic valve is tricuspid. A single coronary artery trunk (CT), arising beyond the sinotubular junction (compare with Fig. 1b), gives off the right (RC), left (LC) and septal (SA) coronary arteries. The arrowhead points to the left circumflex artery, the arrow to the obtuse marginal artery. Corrosion-cast technique. Bar, 1 mm. (d) Internal cast of the left ventricle (LV), aorta (Ao) and coronary arteries of Syrian hamster No. 4 (Table 1). The aortic valve is bicuspid. A single coronary artery trunk (CT) arises from the aorta, cephald with regard to the distal boundary of the ventral aortic sinus (asterisk). It gives off the right coronary artery, the septal artery (SA) and the left main coronary artery trunk (LC) that divides into left circumflex (arrowhead) and obtuse marginal (arrow) arteries. Corrosion-cast technique. Bar, 1 mm.

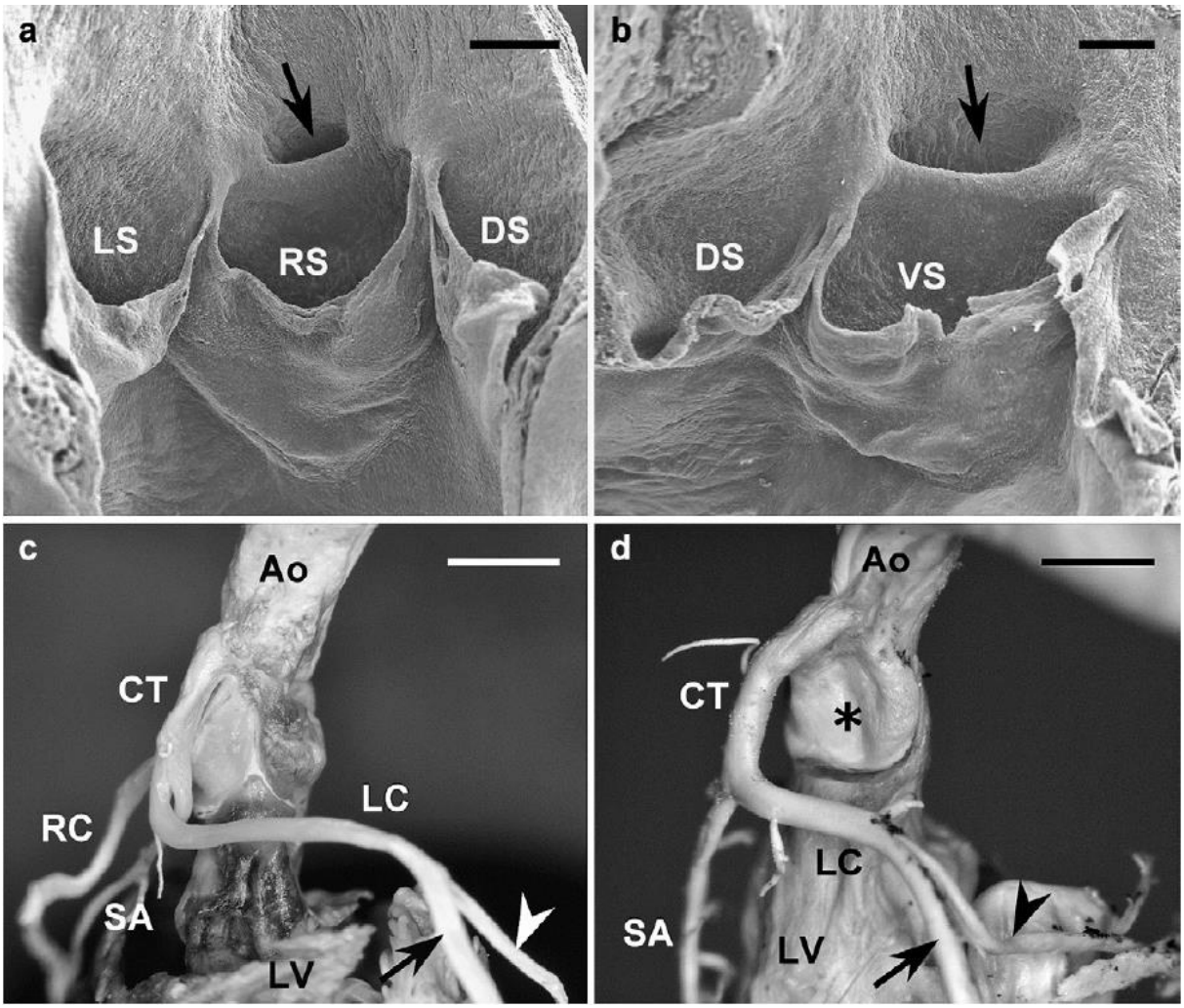
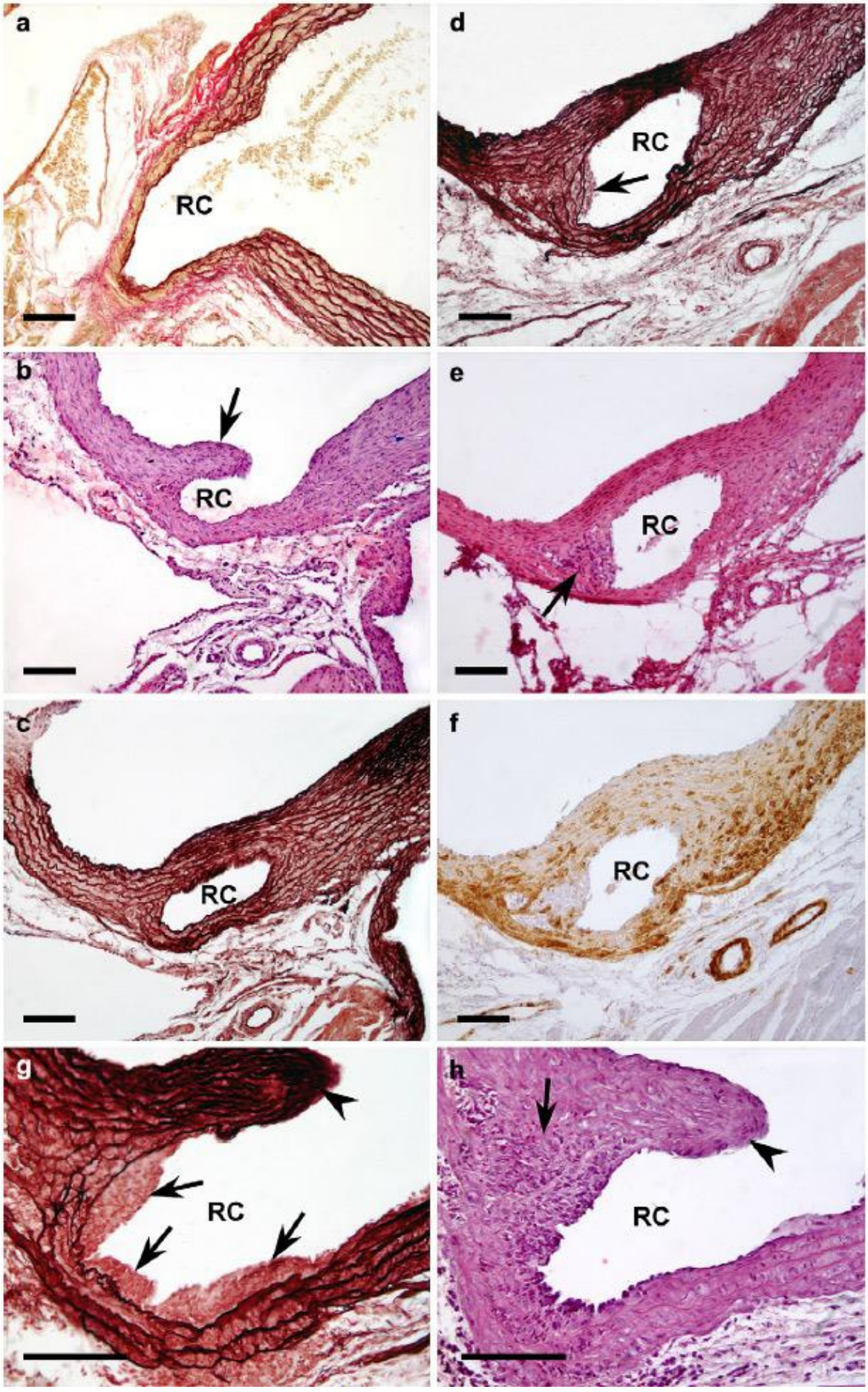


Fig. 3. Histological sections of aortic valves, aorta and coronary arteries from Syrian hamsters. (a) Transverse section of a tricuspid (normal) aortic valve from an adult Syrian hamster. The normal right coronary artery (RC) arises perpendicularly to the wall of the right aortic sinus. Weigert-Van Gieson's stain. Bar, 100 μm. (b) Transverse section of the aorta of Syrian hamster No. 6 (Table 1). The right coronary artery (RC) arises at an acute angle and obliquely with regard to the aorta. A valve-like ridge (arrow) resulting from the plicature of the aortic wall is present in front of the ostium. HE. Bar, 100 μm. (c) Transverse section of the aortic valve of Syrian hamster No. 6 (Table 1) at the level of the cephalad border of the aortic valve commissures. The right coronary artery (RC) shows an intramural course. Resorcin-fuchsin. Bar, 100 μm. (d-f) Consecutive, transverse sections of the intramural segment of the right coronary artery (RC) of Syrian hamster No. 11 (Table 1). In panel (d), the arrow indicates a small intimal thickening. At this site, the inner elastic lamina is intact, whereas the elastic fibres of the common media are somewhat disarranged (compare with Fig. 3a). Resorcin-fuchsin. Bar, 100 μm. In panel (e), the arrow points to a leucocytic infiltration in the common media, just in front of the intimal thickening. Resorcin-fuchsin. Bar, 100 μm. Panel (f) shows the distribution of smooth muscle tissue. Note the absence of smooth muscle cells in the intimal thickening. IHC (anti SMα-actin). Bar, 100 μm. (g, h) Consecutive, transverse sections of the aorta of Syrian hamster No. 13 (Table 1) at the level where the right coronary artery (RC) arises at an acute angle. In panel (g), the arrowhead points to a valve-like ridge. The arrows indicate intimal thickenings. The inner elastic lamina is intact and the elastic fibres of the common media are disarranged. Resorcin-fuchsin. Bar, 100 μm. In panel (h), the arrowhead points to a valve-like ridge. The arrow indicates a leucocytic infiltration. HE. Bar, 100 μm.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