THE DEVELOPMENT OF THE AZYGOS VEINS IN THE ALBINO RAT

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Recorded accounts of the development of the azygos veins of the albino rat (*Mus norvegicus albinus*) are scanty and difficult to interpret owing to confusion in the terminology applied to embryonic veins. Reagan (1927) described the development of capillary vascular arches between the proximal parts of the dorsal aortic rami and their accompanying segmental veins. Longitudinal anastomoses between these arches form the azygos veins. According to Schneider (1938) the left azygos vein, from its junction with the left superior vena cava to the point of entry of the inferior hemi-azygos vein at the 10th or 11th intercostal space, is developed from the left postcardinal vein. The remainder of the left azygos vein and the inferior hemi-azygos vein are developed from the supracardinal plexus. This plexus was first described in the rat by Butler (1927). Thus the development followed a pattern similar to that described by Hochstetter (1893). This pattern has since been shown to be incorrect for man (Seib, 1934), pig (Sabin, 1915; Reagan, 1919) and cat (Huntington & McClure, 1907).

TERMINOLOGY

Huntington & McClure (1907) defined the supracardinal veins as bilaterally symmetrical venous channels developed from longitudinal anastomoses between the segmental veins, and situated dorso-medial to the postcardinal veins. Cranially they join the postcardinal veins near their termination, and caudally at the point of entry of the hind limb-bud veins. Each vein is divided into a thoracic and a lumbar portion. The terminal arch of the adult azygos vein develops from the cranial end of the postcardinal vein and the remainder from the thoracic supracardinal veins. The final development of this bilaterally symmetrical azygos venous system varies from species to species. With the exception of the rat and the golden hamster the right lumbar supracardinal vein becomes the pre-renal inferior cava, i.e. the portion of the adult inferior vena cava between the common iliac veins and the renal veins. The left lumbar supracardinal vein disappears entirely.

Huntington & McClure (1907, 1920) do not state the position of the supracardinal vein relative to the sympathetic trunk, but Reagan (1919) states that they placed this vein on the medial side of the sympathetic trunk. Reagan (1927) pointed out that the azygos vein lies medial to the sympathetic trunk and its peri-aortic branches, whereas the pre-renal inferior vena cava lies lateral to these nerves. Thus the supracardinal portion of the azygos vein could not be regarded as being homologous with the pre-renal inferior vena cava. He regarded the main part of the azygos vein as developing from the medial sympathetic venous lines which have the following characteristics:

(1) They lie ventro-medially to the sympathetic trunk and its peri-aortic branches.

(2) Their segmental tributaries drain dorso-medially with reference to the sympathetic trunks.

(3) They lie ventro-laterally to the dorsal aortic rami.

Reagan & Tribe (1927) and Reagan & Robinson (1927) described the lateral aortic plexus as a venous line extending from the mid-thoracic to the mid-sacral region and lying lateral to the aorta and to the sympathetic trunk and its peri-aortic branches. It is divided into:

(1) A cranial thoraco-lumbar portion which acts as a functional substitute for the segmental tributaries of the degenerating postcardinal veins until the medial sympathetic venous line is fully developed. It then disappears completely, but for a time it exists side by side with the medial sympathetic venous line in the caudal portion of the thorax but separated by the sympathetic trunk.

(2) A caudal portion called the para-ureteric vein. On the right side this vein becomes the pre-renal inferior vena cava, on the left side it normally disappears.

The relationship of these embryonic veins and their adult derivatives may be summarized thus:

(1) The right and left medial sympathetic venous lines are the same as the thoracic supracardinal veins and form most of the azygos veins.

(2) The thoraco-lumbar venous line is not represented by any part of the supracardinal veins. It is functional only for a short time in the embryo and then disappears completely.

(3) The para-ureteric vein is the same as the lumbar supracardinal vein, and on the right side it becomes the pre-renal inferior vena cava. The left vein normally disappears.

Dorsal to the aorta and medial to the dorsal aortic rami is a pair of longitudinal venous lines described by Strong (1927), and called the dorsal aortic plexus. Reagan & Robinson (1927) called these the subcentral venous lines. They are connected to each other and to the medial sympathetic venous lines by cross anastomoses. These cross anastomoses form the retro-aortic connexions between the right and left azygos veins. The caudal portions of these longitudinal venous lines form the medial azygos root of Seib (1934).

Two further venous lines have been described but, as yet, little is known about them. Gladstone (1929) figured in an 11 mm. (6th week) human embryo the pre-costal or lumbo-costal venous line which lies immediately ventral to the transverse processes of the vertebrae and dorsal to the thoraco-lumbar line. Seib (1934) postulated a lumbo-costal venous line as a result of the study of anomalies of the adult human azygos veins. It lies between the postcardinal vein and the thoraco-lumbar venous line and becomes the ascending lumbar vein.

In the following descriptions the term supracardinal vein will not be used and wherever possible the terminology introduced by later writers will be employed.

MATERIAL AND METHODS

Twenty-six rat embryos ranging from the 14th to the 20th day were used. The post-copulation age was estimated as follows. The oestrous cycle of isolated virgin albino rats was charted by daily examination of vaginal smears (Long & Evans, 1926).

A buck was introduced when a pro-oestrous smear was found and frequent vaginal smears were made until spermatozoa were found. The midpoint between the time of the last sperm-free pro-oestrous smear and the oestrous smear containing spermatozoa was taken as the approximate time of copulation.

Some embryos were fixed in Bouin's fluid, embedded in wax and sectioned serially at 8–15μ according to their size. Sections were stained with haematoxylin and erythrosin.

Other embryos were injected with indian ink according to the method described by Popoff (1894). In most cases the anterior cardinal vein close to the ear was used for the injection. In small embryos the injection was sometimes made directly into the heart or liver. When the injection was completed the embryo was immediately fixed in Carnoy's fluid, embedded in celloidin and sectioned serially at 60–150μ. Some were bulk-stained in Grenacher's carmine prior to sectioning and others were cut and mounted unstained. Details of age and length of the embryos is given in Table 1. The C.R. length was measured after fixation.

Table 1

				Serial sections (thickness in μ)		
				Uninjected		
Group 1	Age (days hr.)	Serial no.	C.R. length (mm.)	Transverse	Sagittal	Injected transverse
1	13 9	30	7	—	—	60
	—	30.1	—	—	—	60
2	13 10	20	7	8	—	—
		20.1	—	—	8	—
		20.2	—	—	—	75
		20.3	—	—	—	75
		20.4	—	—	—	100
		20.5	—	8	—	—
3	14 15	28	10	12	—	—
		28.1	—	—	—	100
		28.2	—	—	—	100
		28.3	—	—	—	100
		28.4	—	12	—	—
		28.5	—	—	15	—
4	15 9	27	11	12	—	—
		27.1	—	—	—	100
		27.2	—	—	—	100
		27.3	—	—	—	100
		27.4	—	—	—	100
5	17 9	33	15	15	—	—
		33.1	—	15	—	—
		33.2	—	—	—	100
		33.3	—	—	—	100
		33.4	—	—	—	150
		33.5	—	—	—	150
6	19 9	35	16	15	—	—

OBSERVATIONS

(1) *Embryos of groups* 1 (13 *days* 9 *hr.*) *and* 2 (13 *days* 10 *hr.*)

The postcardinal veins are almost fully developed and the right vein has a slightly smaller diameter than the left. At this age the segmental veins are mainly concerned with draining the relatively large spinal cord (Evans, 1912). The 9th segmental vein, which will become the first intercostal vein, drains into the anterior cardinal vein and

all the segmental veins caudal to this drain into the postcardinal vein. The segmental veins pass ventro-lateral to the sympathetic cord before they join the cardinal veins. The junction of the anterior and posterior cardinal veins is at the level of the 10th segment on both sides. The iliac anastomosis is a plexiform capillary connexion between the caudal extremities of the postcardinal veins.

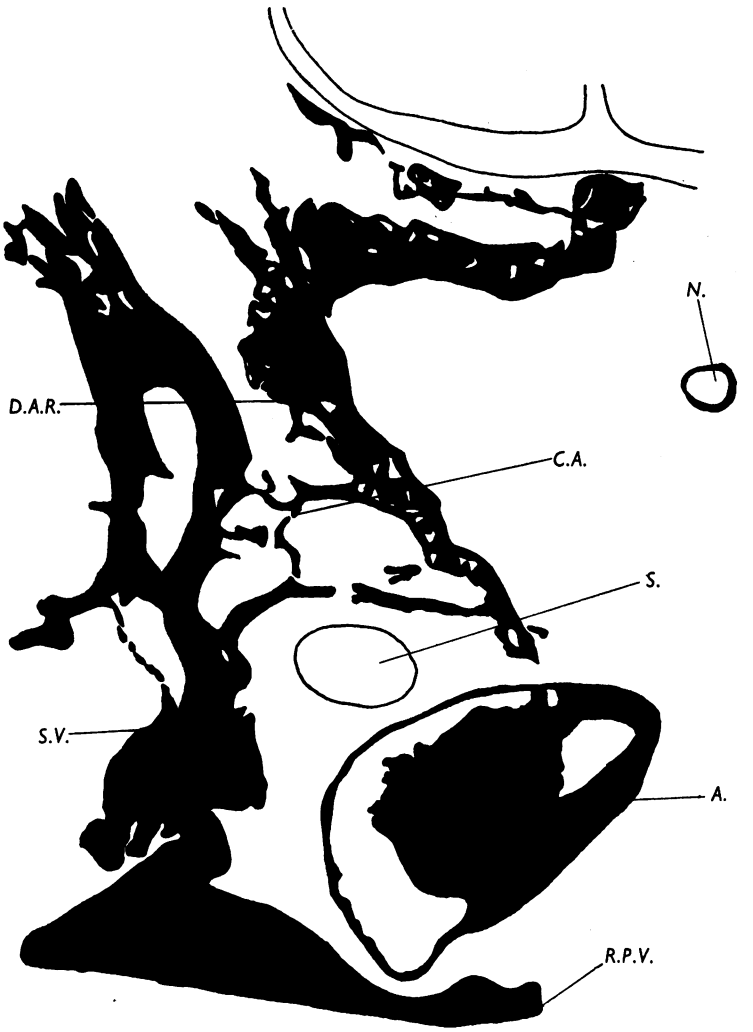

Fig. 1. Camera lucida drawing of a transverse section of embryo 30.1. Age 13 days 9 hr. C.R. length, 7 mm. Vessels injected. ×200 (owing to reduction).

A new capillary plexus, more dorsally situated, develops at this stage. It commences as a series of vascular arches between the segmental veins and the accompanying dorsal aortic rami. The sympathetic cord lies within a triangle bounded by the stem of the dorsal aortic ramus, the stem of the segmental vein and the dorso-lateral aspect of the dorsal aorta (Fig. 1). Immediately dorsal to the sympathetic cord the artery and vein are in close proximity and it is here that the capillary arch

is formed. At first the arch is single, but it rapidly becomes plexiform and surrounds the sympathetic cord. Medial outgrowths from this perisympathetic plexus spread towards the mid-line dorsal to the aorta and form cross anastomoses. At this stage the perisympathetic plexuses are confined to the neighbourhood of the segmental vessels and there are no longitudinal anastomoses between them. The plexuses are first formed in the cervical region and their development proceeds caudally as far as the lumbar region.

The subcardinal veins are well developed and a plexiform intersubcardinal anastomosis is present. The connexion between the right subcardinal vein and the hepatic vein which will form the hepatic segment of the inferior vena cava is present as a capillary plexus.

Embryos of group 3 (14 *days* 15 *hr.*)

The inferior vena cava is well developed and consists of hepatic, subcardinal and postcardinal segments. The left subcardinal vein is still large. The iliac anastomosis is now a large channel. The body wall is well developed and the ribs are visible. The segmental veins are more concerned with the drainage of the body wall and so the segmental veins 9 to 21 may now be called intercostal veins 1–13. Portions of the postcardinal veins are beginning to disappear and certain intercostal veins have acquired new channels of drainage. The disappearance of the postcardinal veins commences at the level of the caudal postcardinal-subcardinal anastomosis and progresses in a cranial direction. It is more advanced on the left side than on the right.

The termination of the right intercostal veins in embryo no. 28.4 is:

(1) Intercostal vein 1 joins the anterior cardinal vein.

(2) Intercostal veins 2–5 join the right postcardinal vein passing ventro-lateral to the sympathetic cord.

(3) Intercostal veins 6–11 still join the postcardinal veins, but now have a second route of drainage into the perisympathetic plexus by a vessel passing dorsal to the sympathetic cord. This vessel corresponds to the dorsal basal anastomosis described by Reagan & Robinson (1927).

(4) Caudal to intercostal vein 11 the postcardinal vein has disappeared and the last two intercostal veins join the posterior aspect of the subcardinal segment of the inferior vena cava. They also drain into the perisympathetic plexus by dorsal basal anastomoses.

Between intercostal veins 6–12 there are indications of the formation of longitudinal anastomoses between the segmental perisympathetic plexuses. They are best developed caudally between intercostal veins 11 and 12. They lie on the dorsomedial aspect of the dorsal aortic rami in the position of the dorsal aortic plexus (Strong, 1927), or subcentral venous line (Reagan & Robinson, 1927) (Fig. 2).

The greater part of the left postcardinal vein has disappeared and has been replaced by a new longitudinal vein formed from longitudinal anastomoses between the segmental perisympathetic plexuses. The left intercostal veins terminate as follows:

(1) Intercostal veins 1 and 2 join the left anterior cardinal.

(2) Intercostal veins 3, 4 and 5 join the remaining part of the left postcardinal, passing ventral and lateral to the sympathetic cord.

(3) Intercostal veins 6–12 join the new longitudinal vein passing dorsal to the sympathetic cord via the dorsal basal anastomosis. The new longitudinal vein joins the remnant of the left postcardinal vein just caudal to intercostal vein 5, and terminates caudally by joining the cross anastomosis between the 12th pair of intercostal veins. It lies medial to the sympathetic cord and, except for its most caudal segment, it lies ventral and lateral to the dorsal aortic rami. Thus it is the medial sympathetic venous line (Reagan, 1927). The most caudal segment lies dorsal and medial to the dorsal aortic rami in the subcentral venous line. Examination of other embryos of this age and older shows that the new longitudinal vein on the left lies mainly in the medial sympathetic venous line, but occasional segments are in the subcentral venous line.

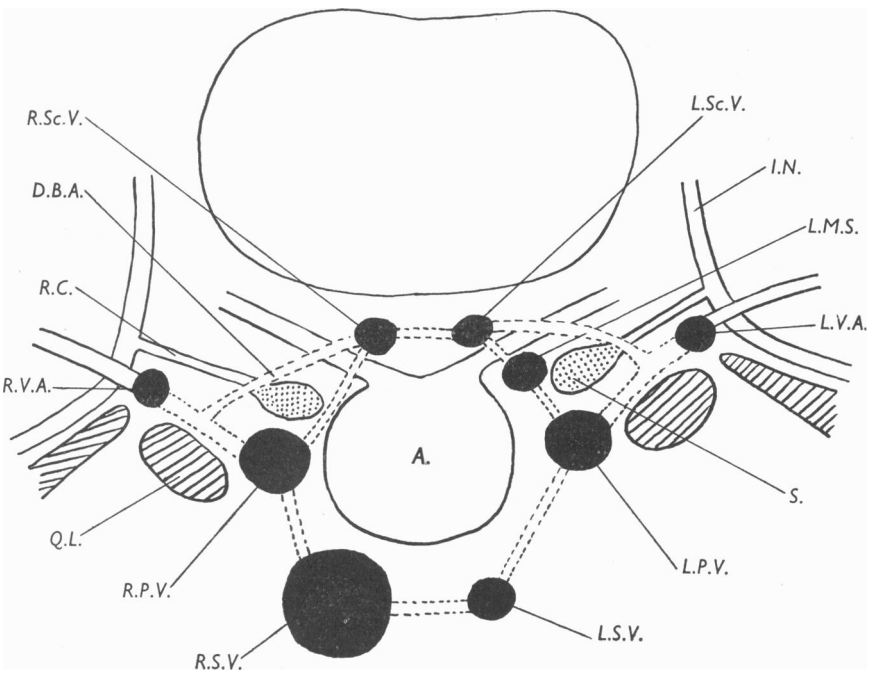

Fig. 2. Diagram to show the relationships of the longitudinal venous lines to the sympathetic cords and aorta.

(4) Intercostal vein 13 drains mainly into the posterior aspect of the left subcardinal vein and partly into the perisympathetic plexus (Fig. 3).

Litter-mates of this embryo showed a similar pattern with slight variations in the number of veins joining the subcardinal veins and in the extent of the new longitudinal veins.

(3) *Embryos of group* 4 (15 *days* 9 *hr.*)

The features of this stage are:

(1) Further disappearance of the right postcardinal veins.

(2) Extension of the longitudinal anastomoses in the right subcentral venous line.

(3) Disappearance of the intercostal drainage into the subcardinal veins.

The first right intercostal vein joins the right anterior cardinal vein. The right posterior cardinal vein extends from its junction with the anterior cardinal vein to the point of entry of intercostal vein 6. It receives intercostal veins 2–6. The remaining right intercostal veins pass dorsal to the right sympathetic cord and the aorta to join the new longitudinal vein developed in the left medial sympathetic venous line. The new portion of these veins which runs dorsal to the sympathetic cord and

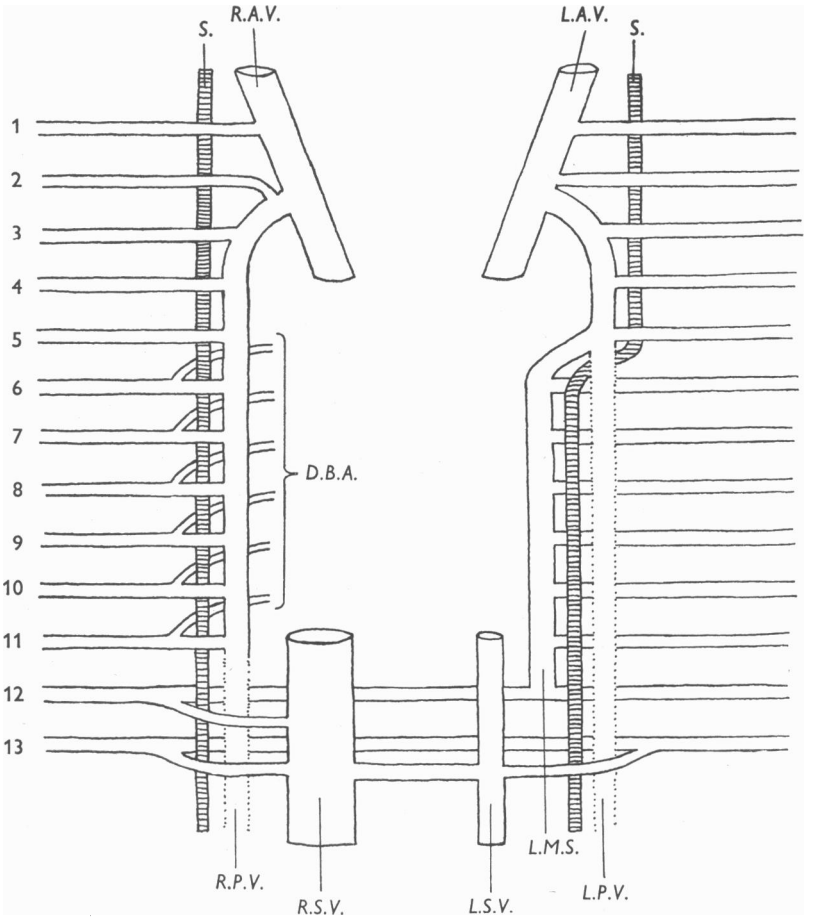

Fig. 3. Diagram of the venous lines in embryos of group 3. C.R. length, 10 mm.

aorta has developed from the perisympathetic plexus. Intercostal veins 6–13 are linked by a longitudinal anastomosis developed in the right subcentral venous line. This anastomosis is best developed in the caudal half of the thorax. The last two intercostal veins no longer join the right subcardinal vein.

The only change on the left side is that the last intercostal vein drains entirely into the perisympathetic plexus and has lost its connexion with the left subcardinal vein.

(4) *Embryos of group* 5 (17 *days* 9 *hr.*)

Caudal to intercostal vein 11, on both sides, the left medial sympathetic venous line and the right subcentral venous line become abruptly reduced in diameter. This is related to the formation of a new and more laterally situated longitudinal anastomotic vein between intercostal veins 11, 12 and 13. This new vein is situated:

(1) Along the lateral border of the quadratus lumborum muscle. The sympathetic cord lies along the medial border of this muscle.

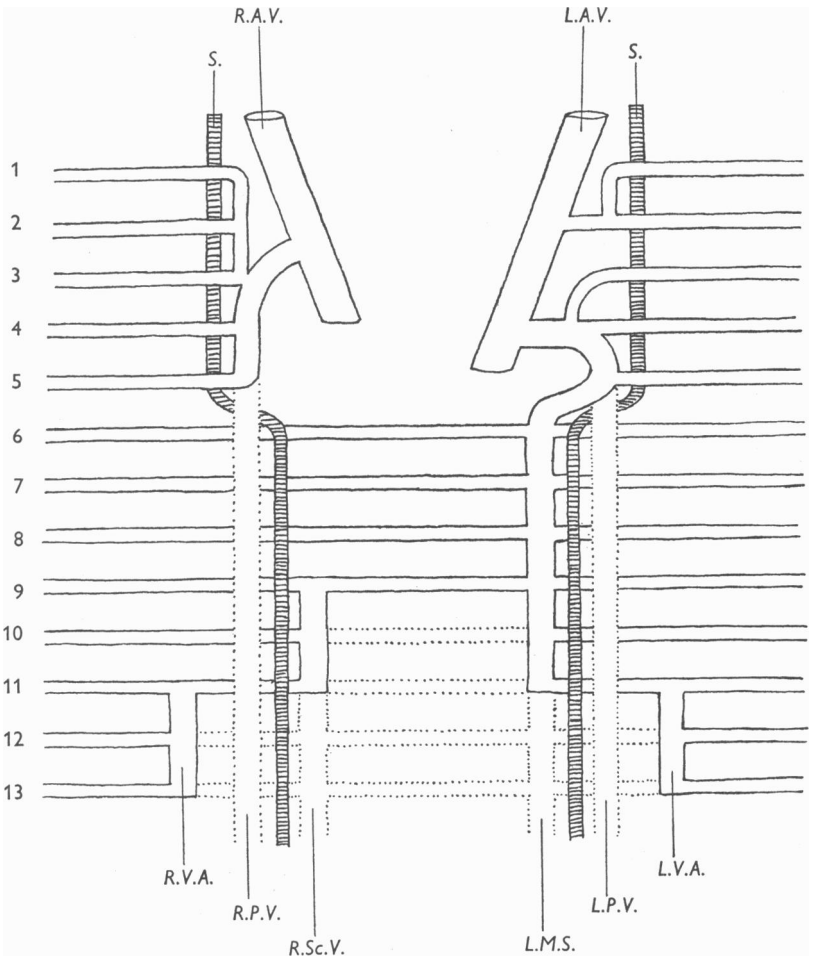

Fig. 4. Diagram of the venous lines in embryos of group 6. C.R. length, 16 mm.

(2) Ventral and lateral to the ramus communicans in the angle between the ramus communicans and the intercostal nerve.

(3) Either dorsal or ventral to the dorsal aortic ramus.

This new longitudinal vein will be referred to as venous line *A* (Figs. 2, 4 and 5). It receives the 12th and 13th intercostal veins and anastomoses with the left medial sympathetic and right subcentral venous lines respectively.

The retro-aortic anastomoses caudal to intercostal vein 9 have disappeared, and the right intercostal veins 9–13 join the left medial sympathetic venous line by a single enlarged retro-aortic cross anastomosis.

(5) *Embryos of group* 6 (19 *days* 9 *hr.*)

The adult pattern (Fig. 4) is now fully developed and consists of:

(1) The right superior intercostal vein receiving the first five intercostal veins and joining the right superior vena cava at the level of T. 3, passing medial to the phrenic nerve and lateral to the vagus nerve.

(2) Right intercostal veins 6–8 passing separately across the mid-line to join the left azygos vein and passing dorsal to the right sympathetic cord and aorta. Intercostal veins 9 and 10 may do likewise.

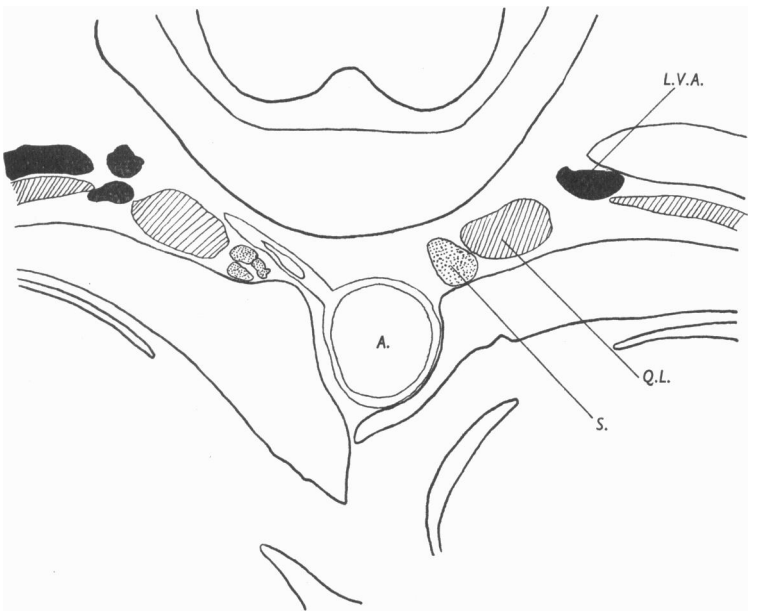

Fig. 5. Camera lucida drawing of a transverse section of embryo 33. Age 17 days 9 hr. C.R. length, 15 mm. Uninjected. × 55 (owing to reduction).

(3) The right azygos (inferior hemi-azygos) vein receiving the 9th to the 13th right intercostal veins and crossing the mid-line dorsal to the aorta and right sympathetic cord to join the left azygos vein.

(4) The left superior intercostal vein receiving the 1st and 2nd intercostal veins and then entering the left superior vena cava.

(5) The left azygos vein joining the left superior vena cava at the level of intercostal vein 4 and receiving left intercostal veins 3–13 and the inferior hemi-azygos vein. The terminal portion arches over the root of the left lung to join the left superior vena cava passing medial to the phrenic nerve and lateral to the vagus.

DISCUSSION

These observations show that only a small part of the azygos vein of the albino rat is derived from the postcardinal veins. The greater part of the azygos veins is developed from a more dorsally placed venous plexus which develops as the postcardinal veins disappear. The cranial end of the left azygos from its junction with the left superior vena cava to the point of entry of the 5th or 6th left intercostal vein is all that remains of the left postcardinal vein. The pattern of development is the same as that described for the pig (Reagan, 1919), and not as that described for all mammals by Hochstetter (1893) nor for the albino rat by Schneider (1938). Boyer's (1948) account of the development of the azygos vein of the golden hamster lacks sufficient detail for an accurate comparison but suggests that the pattern is similar.

The remainder of the left azygos vein, the inferior hemi-azygos vein and the retro-aortic portion of the 6th–8th right intercostal veins are developed from the peri-sympathetic plexuses. These plexuses begin as vascular arches between the dorsal aortic rami and the accompanying segmental veins in the embryos of groups 1 and 2 (7 mm. C.R. length). Subsequent developments of these capillary arches give rise to plexuses which surround the sympathetic cords and spread across the mid-line dorsal to the aorta. At this stage the rat embryo closely resembles the 13·5 mm. pig embryo described by Sabin (1915). Frazer (1931) described similar plexuses in the human embryo of about 8 mm. Longitudinal anastomoses grouped around the sympathetic cords and aorta link up the segmental perisympathetic plexuses (Fig. 2). Seib (1934) gives a full account of these longitudinal venous lines as seen in the human embryo. Only the right and left subcentral venous lines and the left medial sympathetic venous line can be recognized in the albino rat. The venous line *A* which develops in the embryos of group 5 (15 mm. C.R. length) does not correspond with any of the previously described venous lines. It is not necessary to give this a specific name and the left azygos vein caudal to intercostal vein 5 and the inferior hemi-azygos vein may be described as developing from the perisympathetic plexuses. The main feature of the perisympathetic plexus portion of these veins is that it lies medial to the sympathetic trunks. Their relation to the segmental arteries in the albino rat differs from that in man in that occasional segments of the left azygos vein pass dorsal to the intercostal arteries (Greene, 1935). The inferior hemi-azygos vein in the rat lies dorsal to the intercostal arteries whereas in man it lies ventral.

In the rabbit the intercostal veins drain temporarily into the thoraco-lumbar venous line since the postcardinal veins disappear before the medial sympathetic venous lines appear (Reagan & Tribe, 1927). The thoraco-lumbar venous line is derived from the perisympathetic plexus and has no adult derivative. It was not found in the albino rat. Auer (1946) failed to find this vein in a series of human embryos.

In man the azygos veins anastomose caudally with the subcardinal portion of the inferior vena cava (Seib, 1934). These connexions are developed from the perisympathetic plexuses and are not homologous with the temporary connexions between the lowest intercostal veins and the subcardinal veins found in embryos of group 3.

No attempt is made to give the venous line *A* a specific name; it is regarded as a part of the perisympathetic plexus. The extreme variability of the azygos venous

system, with the exception of the parts developed from the anterior portion of the postcardinal, is due to its development from a plexus of veins. Further attempts to analyse this plexus will only add to an already confusing terminology. Auer (1946) suggests the retention of the term supracardinal vein for that part of the perisympathetic plexus which lies medial to the sympathetic trunks. Even this is unnecessary if this venous plexus be regarded as consisting of a perisympathetic and a retro-aortic portion.

CONCLUSIONS

1. The major part of the left azygos vein, the inferior hemi-azygos vein and the retro-aortic portions of the 6th–10th right intercostal veins are developed from the perisympathetic plexuses.
2. The left postcardinal vein forms the left azygos vein from its junction with the left superior vena cava to the level of the 5th or 6th intercostal vein.
3. It is not necessary to give a special name to each longitudinal venous line developed from the perisympathetic venous plexus.

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ABBREVIATIONS

A.	Aorta	*N.*	Notochord
D.B.A.	Dorsal basal anastomosis	*Q.L.*	Quadratus lumborum
C.A.	Capillary arch	*R.A.V.*	Right anterior cardinal vein
D.A.R.	Dorsal aortic ramus	*R.C.*	Ramus communicans
I.N.	Intercostal nerve	*R.V.A.*	Right venous line *A*
L.A.V.	Left anterior cardinal vein	*R.P.V.*	Right postcardinal venous line
L.V.A.	Left venous line *A*	*R.S.V.*	Right subcardinal venous line
L.M.S.	Left medial sympathetic venous line	*R.Sc.V.*	Right subcentral venous line
L.P.V.	Left postcardinal venous line	*S.*	Sympathetic cord
L.S.V.	Left subcardinal venous line	*S.V.*	Segmental vein
L.Sc.V.	Left subcentral venous line		

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