

Stage 15 Formation of Posterior Neuropore; Forelimb Bud

9 1/2 Days, 21–29 Somites, 1.8–3.3 mm

Horizon XII
21–29 somites,
homo = 3–4 mm

External Shape

During this phase, the condensation of the *forelimb bud* may become apparent for the first time. It is situated at the level of the 8th–12th somite (Fig. 116). A distinct condensation of the hind limb bud does not appear until the end of this period.

A prominent feature is the presence of 3 *branchial bars* compared to two in the preceding age group.

The *optic vesicle* is still spherical and has not yet begun to invaginate. In Figs. 115–116, the central light spot represents the wide open stalk of the optic vesicle and not the lens rudiment.

The *otic vesicle* is usually closed, in any case from the 24-somite stage onward.

The anterior *neuropore* is invariably closed, while the posterior one is open in all specimens examined. Compared to humans the closing of the posterior neuropore is thus retarded in mice and does not start before the next period.

Length. The extent of curvature of the embryo varies considerably, and therefore the length varies. In the fresh state, they range from 1.8 to 3.3 mm. After fixation in formalin, followed by storage in 70% alcohol, length is reduced by nearly one-third.

Sagittal Section (Fig. 121)

Figure 121 shows the relationships between some of the internal organs. Rathke's pouch is still open. The liver anlage is still covered by the heart.

Circulatory System

The *heart* consists of a convoluted tube, not yet divided into right and left parts. Through its transparent myocardial wall, the fine endocardial tube may be recognized (Fig. 118). The cardiac gelatinous coat (subendocardial jelly) contains only a few cells and is in the process of forming the atrio-ventricular cushions (Fig. 122).

The first *aortic arch* is of small caliber. The second and third are well developed (Fig. 122). They conduct the blood into the paired dorsal aortae and through the umbilical artery into the placenta. The vitelline artery (*A. omphalo-mesenterica*) develops a new origin from the dorsal aorta by way of a newly developed anastomosis [49] (Fig. 112).

The sinus venosus receives the same tributaries as in the previous stage (Fig. 110). However, it gradually separates from the atrium proper (atrium commune) by the development of a transverse ridge (Fig. 122).

Intestinal Tract

The intestinal tract is now undergoing important transformations, which are shown in Fig. 123.

The *lung rudiments* appear at the beginning of this period as epithelial thickenings which are now delimited posteriorly. The laryngo-tracheal groove deepens and begins to detach from the intestinal canal.

The *stomach primordium* is expanding rapidly. At the same time the omental bursa develops as a lateral peritoneal pocket (Fig. 124).

Within the *hepato-duodenal field*, columns of cells (hepatic epithelial cords) continue to invade the mesenchymal tissue of the septum transversum.

The *pancreas* develops from two separate areas of the duodenal epithelium. The anlage of the ventral pancreas is a small, circumscribed ventral evagination in the caudal part of the hepato-duodenal field. The dorsal pancreas, on the other hand, is a broad evagination in the dorsal half of the duodenal epithelium, which is not constricted until the end of this period (Fig. 123). It is not situated cranially to the ventral rudiment as in man. The reconstruction of the 10 1/2 day stage (Fig. 123) does not show the entire intestinal tract because of a lateral curvature of the embryo.

The *vitelline duct* is now closed, and its epithelium has disappeared.

Urogenital Tract

The nephric duct has grown far into the mesonephric region (Fig. 122). As an example, in specimen KT 997/5 (25 somites), it extends from the 11th to the 25th somite and parts of it have a distinct lumen. In specimen KT 939 (28 somites), the nephric duct has reached the vicinity of the cloaca (Fig. 126).

Figs. 115–120: Foreleg bud, 9 1/2 days, 22 and 24 somites, 1.8 and 2.9 mm length

FIG. 115. Embryo of 22 somites, formalin fixed, translucent.

Rb = rhombencephalon with fourth ventricle, *O* = ear vesicle, separating from epidermis. 36:1

FIG. 116. Same embryo, surface illumination.

Ab = eye vesicle, *Aa* = forelimb bud, 1 and 2 = first and second branchial bars. 36:1

FIG. 117. Same embryo, from left, translucent.

Hn = posterior neuropore. 30:1

FIG. 118. Embryo of 24 somites, formalin fixed, on a millimeter scale.

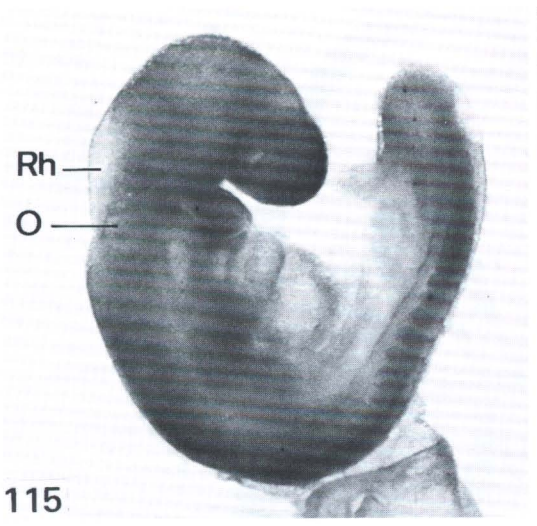
O = ear vesicle, separating from epidermis; *Aa* = forelimb-bud; *N* = suture line of neural folds; *E* = endocardium within bulbus arteriosus; 1, 2, 3 = branchial bars 1–3. 21:1

FIG. 119. Cross section of uterus with embryo of 22 somites.

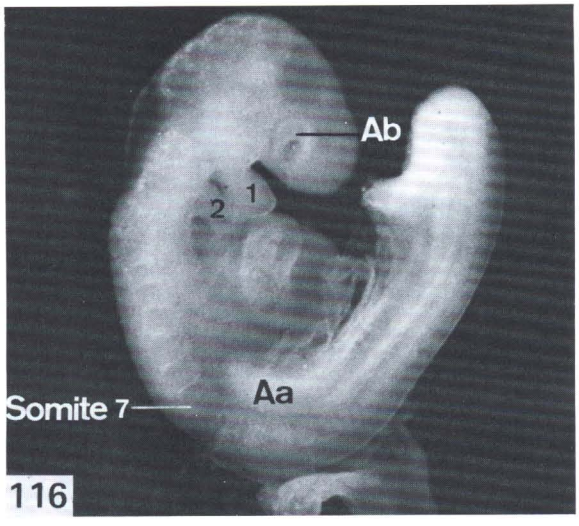
Aa = forelimb bud, *Ri* = olfactory placode, *D* = yolk sac, visceral layer. 16:1

FIG. 120. Detail of Fig. 119.

Eye vesicle with emigrating cells of the ophthalmic neural crest (*Op*). 200:1



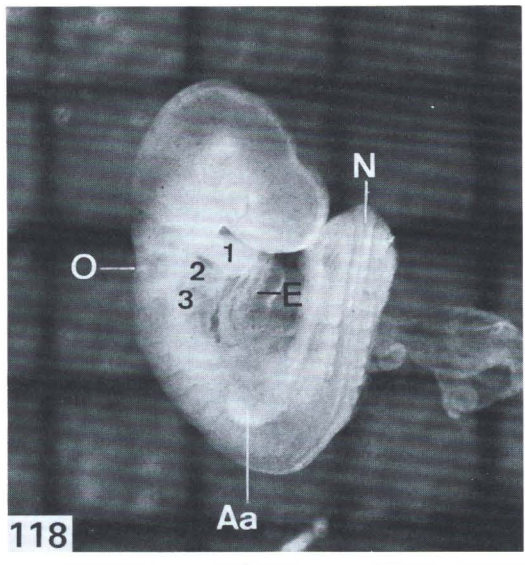
115



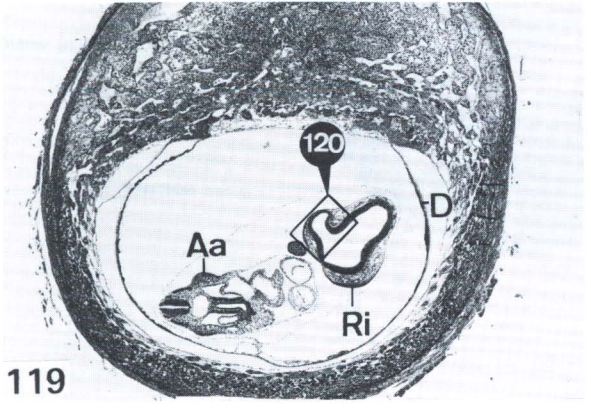
116



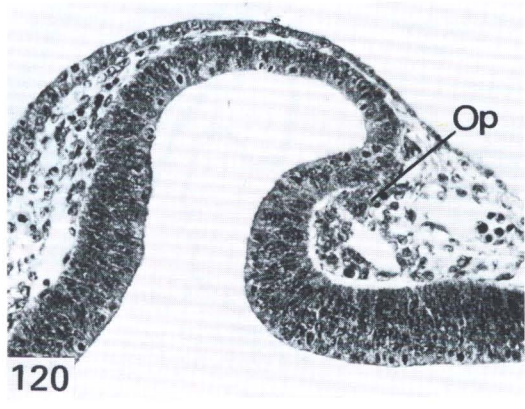
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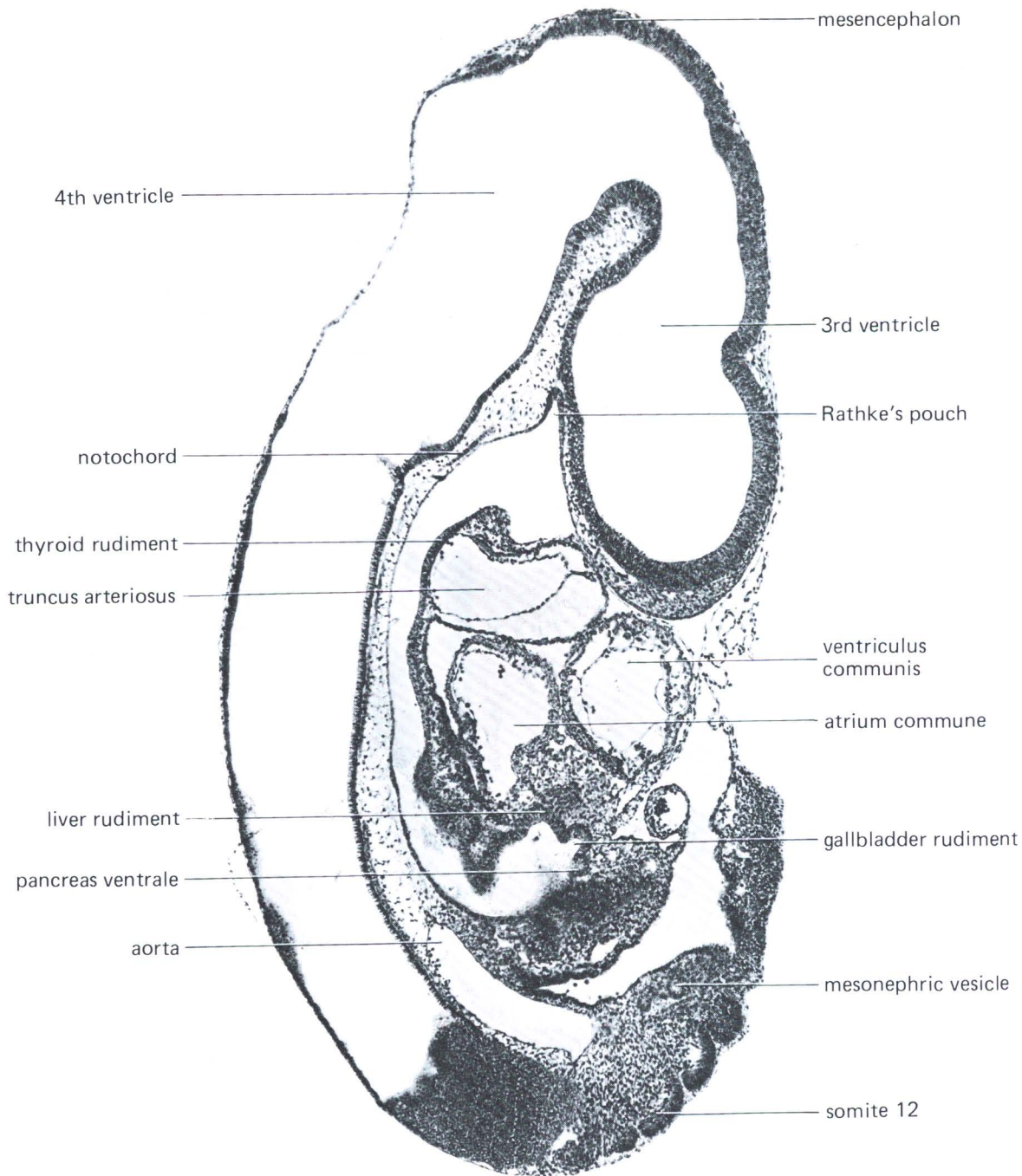


FIG. 121. Sagittal section through embryo of 10 days, 26 somites.
KT 939. 62:1

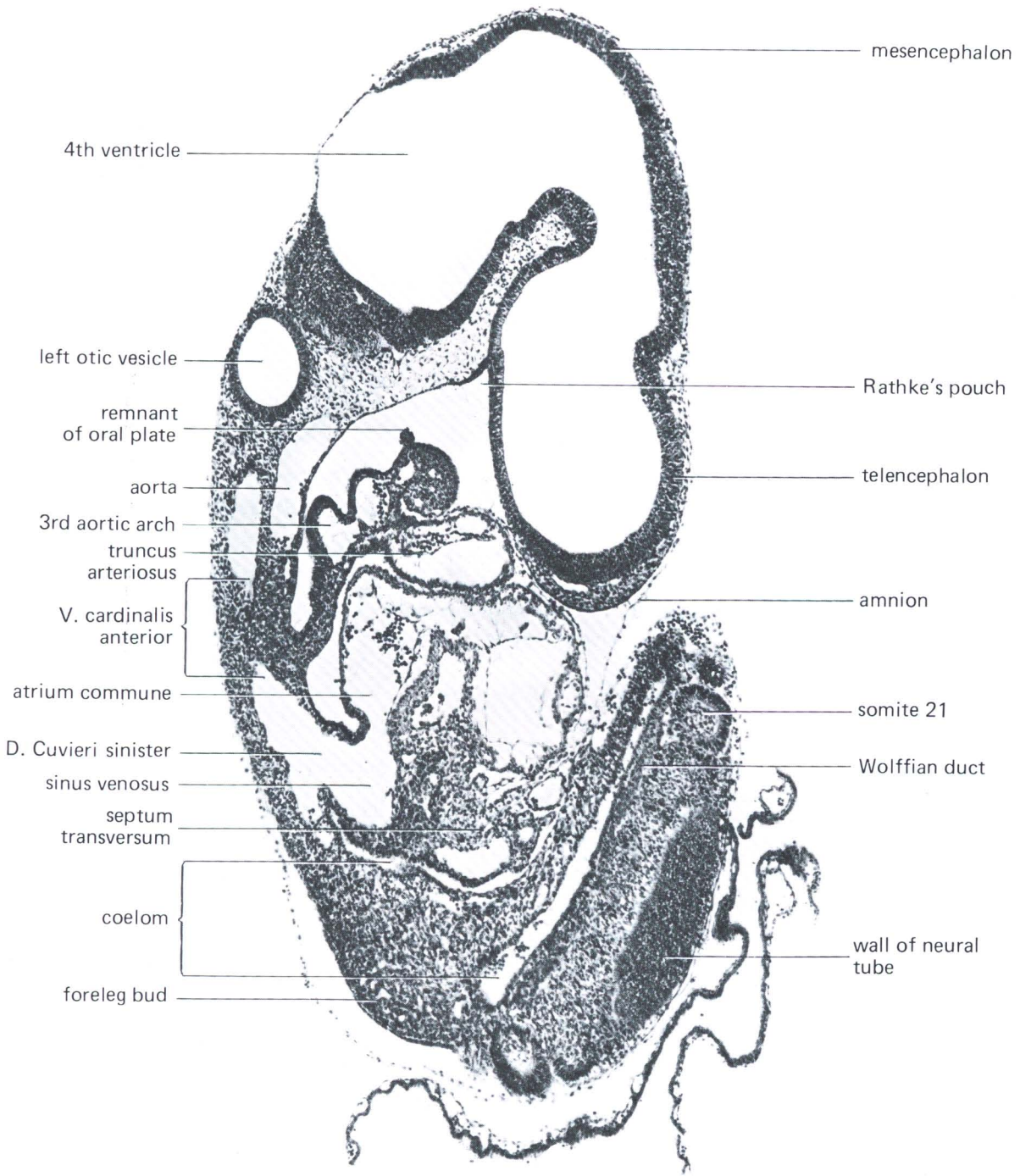


FIG. 122. Development of the circulatory system. Parasagittal section through mouse embryo of 9 days 3 h.

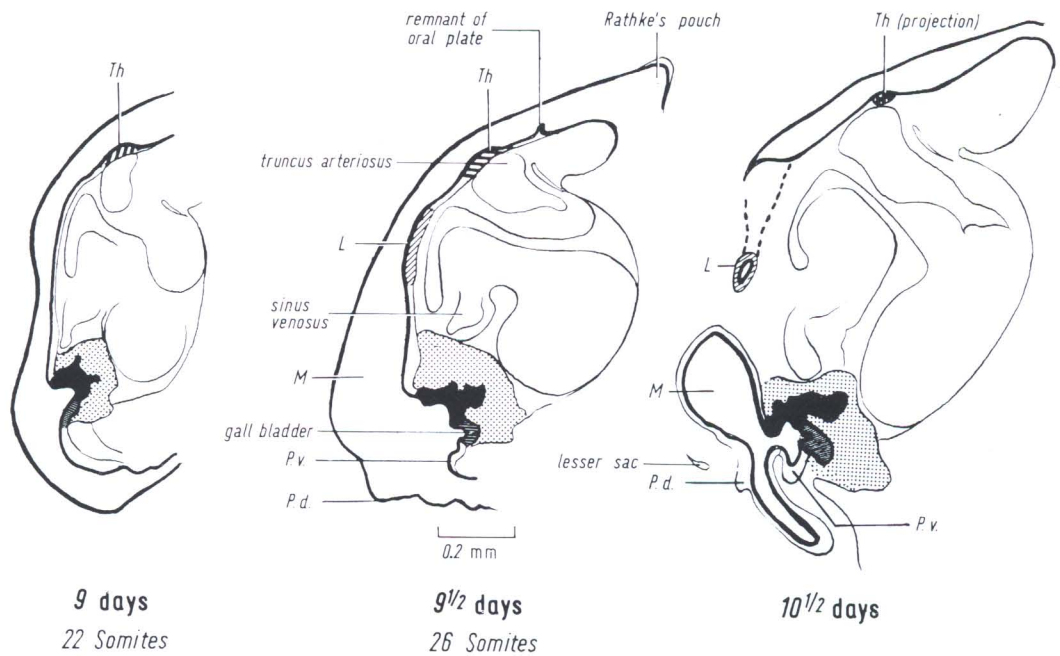


FIG. 123. Development of the intestinal tract, illustrated in 3 sagittal sections, 9–10 1/2 days, drawn to scale. *Th* = primordium of thyroid, *L* = primordium of lung, *M* = primordium of stomach, *Pd.*, *Pv.* = pancreas (dorsal, ventral); *stippled area* represents mesenchyme of septum transversum; *black area* represents liver anlage.

KT 936 9 days, KT 997 9 1/2 days, KT 999 10 1/2 days

Central Nervous System

The *posterior neuropore* begins to constrict but is still open in all embryos examined (Fig. 117), even in those with 26 or 28 somites (Fig. 126). Thus, the closure is definitely retarded in mice compared with human embryos of the same somite number. The completion of closure in mice has been observed as late as the 32-somite stage.

During this period the brain develops very rapidly. The *optic vesicles* have relatively large stalks. From the outer periphery of the vesicles, the cells of the *optic neural crest* spread into the surrounding mesenchyme (Fig. 120). They probably become pigment cells of the uvea. The other divisions of the cranial neural crest [161] have formed prior to this stage, when the anterior neuropore was still open.

The development of the cranial blood vessels parallels the extremely rapid growth of the brain. The central nervous system is being invested by an extensive vascular plexus.

The *lens placode* and the *olfactory placode* appear as distinct thickenings of the surface epithelium (Fig. 119).

The *otocyst* (ear vesicle) is completely detached from the surface at the 22–24 somite stage. It is one of the most reliable characteristics for determining the degree of development. For a while, the closing rim of the otocyst is stretched into a ductlike stalk by which the ear vesicle is attached to the surface (Fig. 125). Sometimes the process of detachment of the right and left otocyst is slightly asynchronous, but the differences observed are slight. The epithelium of the otocyst is highly specialized and is entirely different from the simple skin ectoderm. It consists of tall cells, and all mitoses are localized in the superficial layer bordering the lumen. In this respect, it resembles the wall of the neural tube.

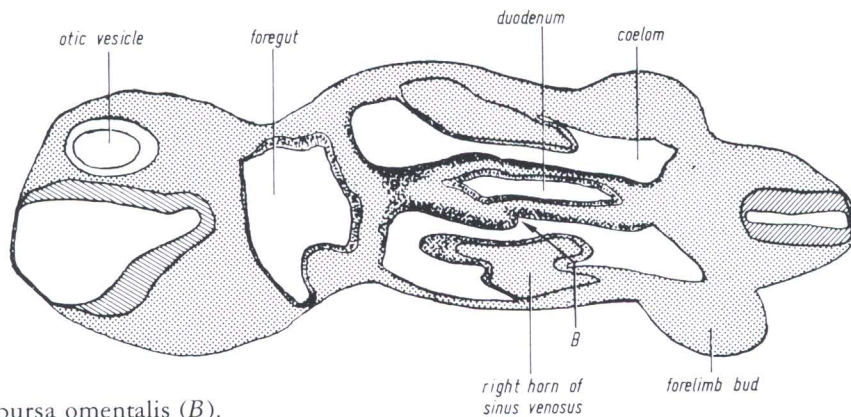


FIG. 124. Anlage of bursa omentalis (B).
KT 935/9, 9 days 3 h, 23 somites

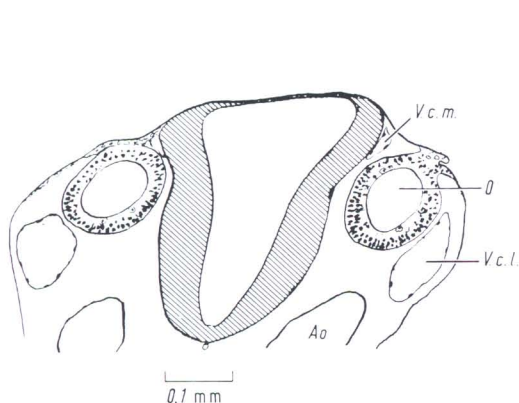


FIG. 125. Otic vesicle separating from epidermis, 9 days, 22 somites.
O = otic vesicle, Ao = aorta, V.c.l. = vena capitis lateralis, V.c.m. = vena capitis medialis.
KT 935

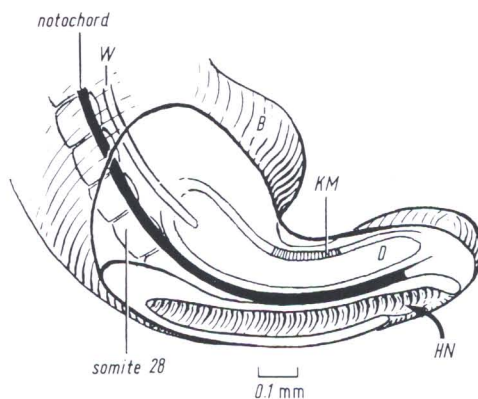


FIG. 126. Posterior part of the body. Graphic reconstruction.
10-day embryo, 28 somites; HN = posterior neuropore (arrow); W = Wolffian duct; KM = cloacal membrane; D = hindgut, extending into tail bud; B = hindleg bud.
KT 939/3

Material	Age	
KT 935-37	9 days 3 h	4 with 15-20 somites (mentioned before) 3 with 22 somites 1 with 23 somites 1 with 24 somites
KT 997-98	9 days 10 h	1 with 17 somites. Posterior neuropore open. 1 with 22 somites. Posterior neuropore open. 1 with 23 somites. Posterior neuropore open. 1 with 24 somites. Posterior neuropore open. 2 with 25 somites. Posterior neuropore open. 2 with 26 somites. Posterior neuropore open.
KT 648-49	9 days 23 h	7 with 22-23 somites. Posterior neuropore open. Two of them measured 3.2 and 3.5 mm (unfixed).
KT 938-40	10 days	9 with 25-34 somites, Five measured 3.2-3.9 mm (unfixed).