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Origin of the adenohypophyseal vessels in the rat

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INTRODUCTION

It has been a generally accepted premise that the developmentally different parts of the pituitary gland would receive their primitive blood supply separately according to their site of origin, i.e. the *anlage* of the neurohypophysis from the diencephalon and that of the adenohypophysis (Rathke's pouch: Rathke, 1838) from the roof of the primitive pharyngeal wall. Then, at a later developmental stage, the adenohypophysis would lose its primitive blood supply from the pharynx and new vascular channels, the portal vessels, would connect its vascular structure with the hypothalamus (Glydon, 1957). Earlier we also accepted this theory (Szabó & Csányi, 1981*a*, *b*, 1986) since vessels around the pharyngeal stalk of Rathke's pouch, connecting its vascular network with that of the subepithelial layer of the stomatodeal roof, suggested the pharyngeal origin of the adenohypophyseal vessels. In continuation of our previous study on the developmental sequence of the hypothalamo-adenohypophyseal complex (Szabó & Csányi, 1982), it was the aim of the present investigation to establish the origin of the portal circulation and its outflow. Special attention was paid to the primitive pharyngeal wall and the early formation of Rathke's pouch.

MATERIALS AND METHODS

Twenty two pregnant albino rats (Sprague–Dawley) were anaesthetised by an intraperitoneal injection of sodium pentobarbitone. The onset of pregnancy was determined by daily vaginal smears, the day on which spermatozoa were found in the smear being called Day 0. The vascular system of the fetuses at the 11th (6 animals of 3–4 mm), 12th (31 animals of 4–5 mm) and 13th (13 animals of 5–7 mm) fetal day were perfused with India ink via the umbilical vein as described in our previous paper (Szabó & Csányi, 1981*a*). Serial sections (50–90 μm thick) were cut of celloidin embedded embryos in frontal, horizontal and sagittal planes. Sections were cleared and lightly stained with haematoxylin.

RESULTS

At gestational Day 11 Rathke's pouch is a wide shallow impression of the stomatodeal wall which contacts the diencephalon vesicle and its infundibular process in the midline along a narrow strip without intervening mesenchyme. This contact zone is demarcated by the surface capillary network of the diencephalon, which is mainly supplied by the primitive maxillary arteries originating at the lateral walls of Rathke's

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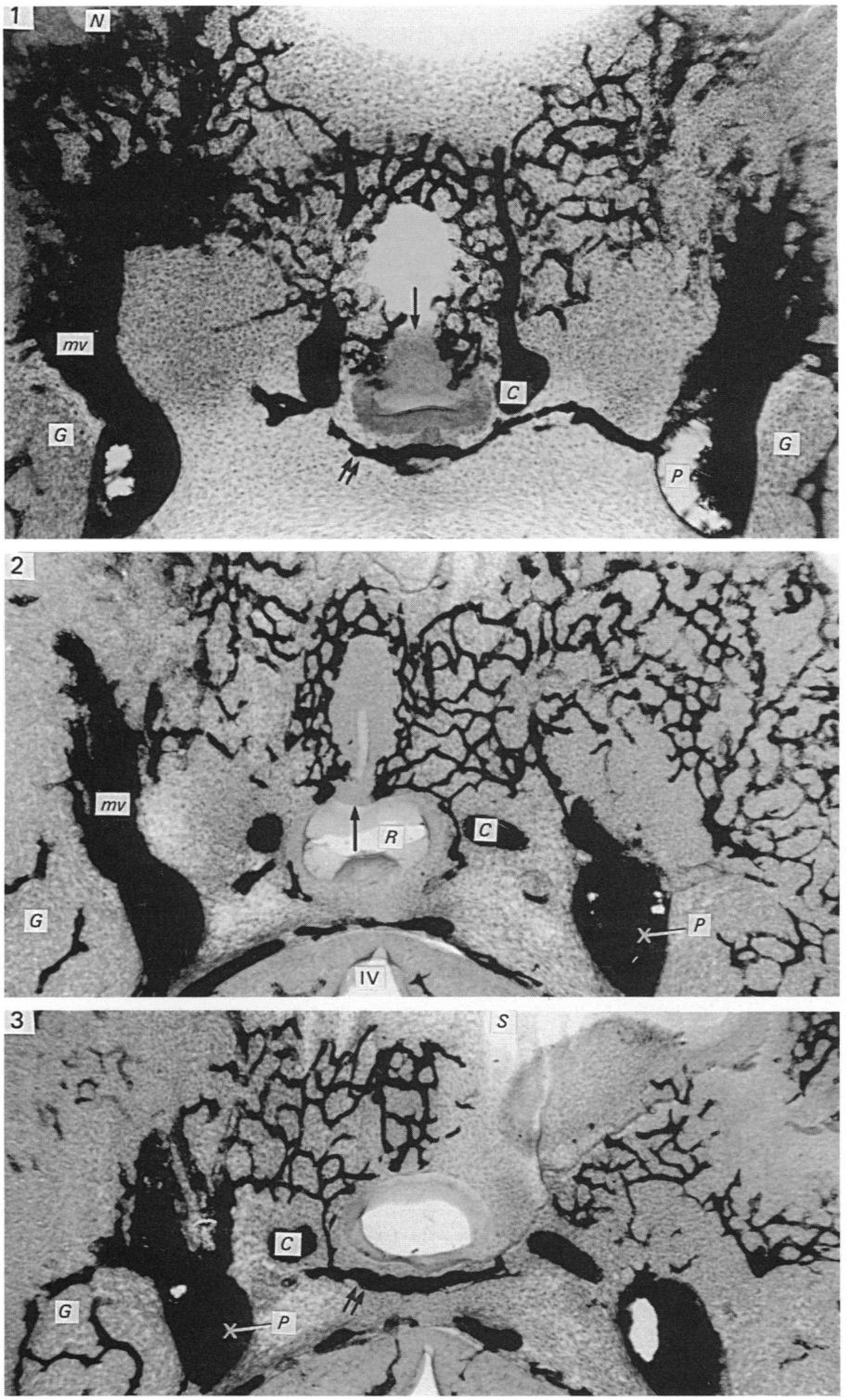
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pouch from the internal carotid arteries. The primitive pharyngeal wall does not contain vessels. In the developing maxillary processes near the surface, there is a short prominent tributary of the primary head vein, the primitive maxillary vein.

At Day 12 Rathke's pouch is still open but the area of the contact zone is reduced. Three or more branches of the primitive maxillary arteries and some from the internal carotid arteries supply the network of the hypothalamic *anlage* (Figs. 1, 5). The terminal arborisation of the primitive maxillary arteries continues into the network covering the lamina terminalis. Branches from the hypothalamic capillary network demarcating the contact zone (Figs. 1, 2, 4, 5) start to grow over the lateral walls of Rathke's pouch, and these may be considered as the forerunners of the primary portal vessels (Figs. 2, 3). At this stage the adjacent primitive pharyngeal wall still does not contain any vessels (Figs. 1, 2, 3, 4).

The primitive maxillary vein elongates to a wide and flat vessel passing ventral to the optic stalk, then at the medial aspect of the trigeminal ganglion opens into the primary head vein (Figs. 1, 2, 3). It collects veins from the maxillary arch, the olfactory *anlage*, the ventral division of the telencephalon, the lamina terminalis and the *anlage* of the hypothalamus.

Transversely running vessels around the posterior surface of the pituitary *anlage* connect the primitive maxillary veins at the medial aspects of the trigeminal ganglia. This is the *anlage* of the intercavernous sinus and receives blood from the pituitary gland (Figs. 1, 3, 4).

On Day 13 the anterior wall of Rathke's pouch is separated from the diencephalic vesicle and it also starts to separate from the stomatodeal epithelium (ductus craniopharyngeus). The contact zone is restricted to the *anlage* of the neurohypophysis. The entire surface of Rathke's pouch and that of the canalis craniopharyngeus is overgrown by hypothalamic vessels and the primary portal veins are clearly distinguishable (Fig. 6).

The primitive maxillary artery diminishes in size, and at Day 14 (about 9 mm) only its proximal part can be recognised running to the tuberal vessels.

The primitive maxillary vein does not change its shape substantially.

DISCUSSION

The arterial supply of the *anlage* of the hypothalamus in the early stages (Days 11 and 12) is derived from the primitive maxillary arteries as described by Padget (1948) in man and Moffat (1961) in rats, and by some small branches of the internal carotid arteries. The network covering the hypothalamic *anlage* demarcates the contact zone between diencephalon and Rathke's pouch. Later (Day 13) the primitive maxillary

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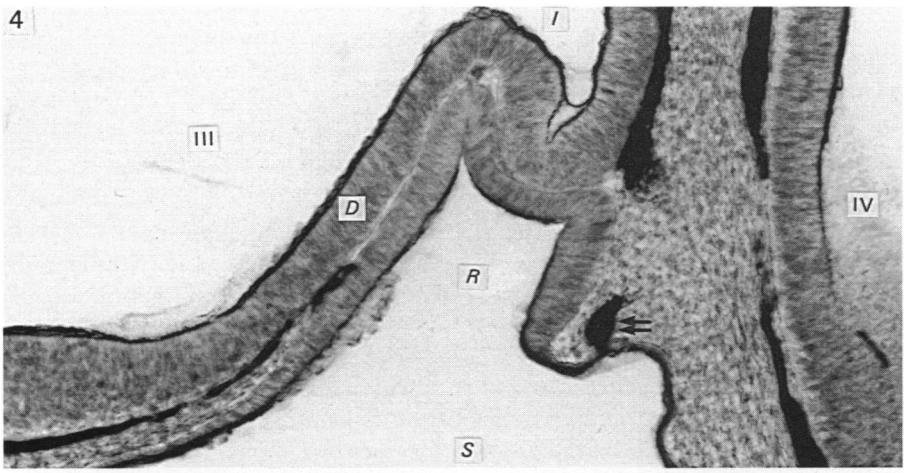
Fig. 1. Day 12. The vascular bed at the level of the hypothalamo-adenohypophyseal *anlage*. Horizontal plane. The primitive maxillary arteries originate from the carotid arteries and supply branches to the hypothalamic network of the diencephalon which demarcates the avascular contact zone (arrow). The primitive maxillary vein runs ventral to the optic stalk into the primary head vein. It drains blood from the maxillary process, olfactory *anlage*, telencephalon, lamina terminalis and hypothalamic *anlage*. The double arrow indicates the *anlage* of the intercavernous sinus at the posterior surface of the pituitary *anlage* passing into the primary head vein. *C*, internal carotid artery; *P*, primary head vein; *mv*, primitive maxillary vein; *N*, olfactory anlage; *G*, trigeminal ganglion. × 70.

Figs. 2–3. Day 12. Forerunners of the primary portal vessels. Horizontal plane, serial sections. The arrow indicates the avascular contact zone. Branches of the hypothalamic capillary network overgrow Rathke's pouch and some of them run into the intercavernous sinus (double arrow in Fig. 3). *R*, Rathke's pouch; *C*, internal carotid artery; *P*, primary head vein; *mv*, primitive maxillary vein; *G*, trigeminal ganglion; *S*, stomatodeum; IV, fourth ventricle. × 73.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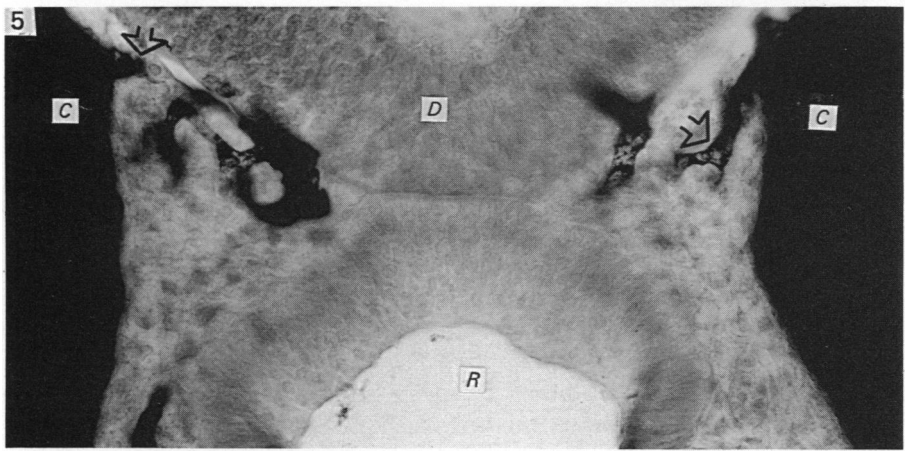
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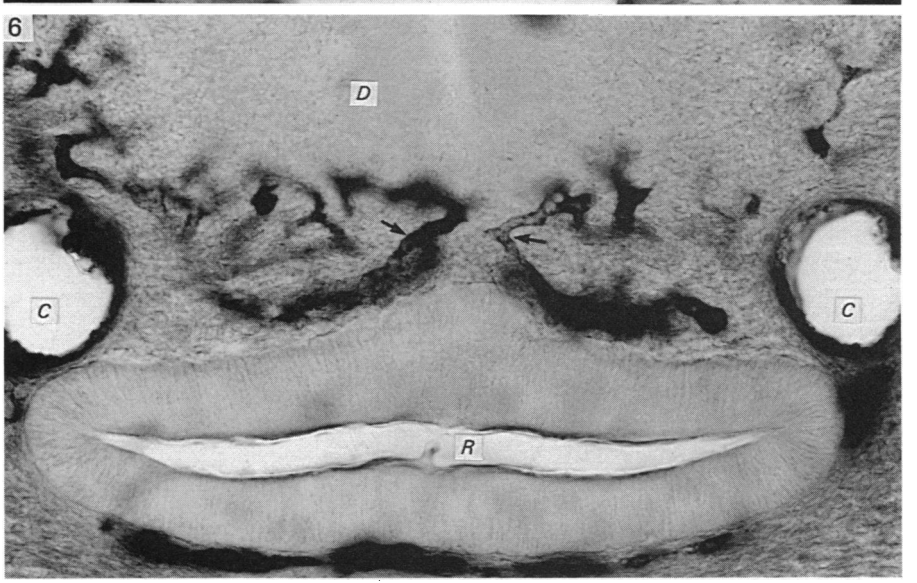
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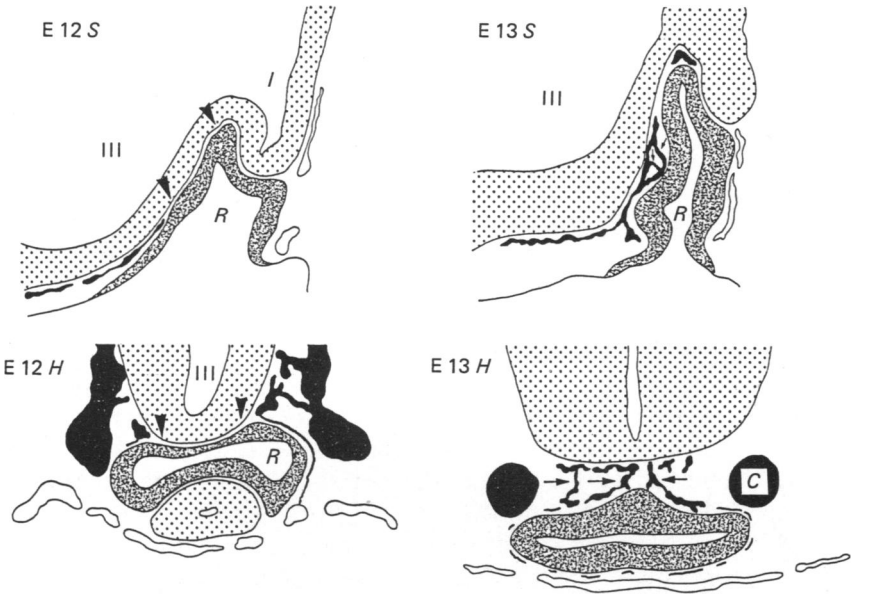

Fig. 7. Schematic drawing illustrating the origin of the adenohypophyseal portal vessels in the sagittal (*S*) and the horizontal (*H*) planes. At Day 12 (E 12) the anterior contact zone (between the arrowheads) is free of vessels. At Day 13 (E 13) the primary portal vessels (arrows indicate them) appear in the separated contact zone. The empty vessels represent the *anlage* of the intercavernous sinus which drain adenohypophyseal vessels into the primary head veins. *R*, Rathke's pouch; *I*, infundibular process; III, third ventricle; *C*, internal carotid artery.

artery diminishes in size and seems to be involved in the arterial supply of the hypophysis.

The developmental origin of the portal vessels can be well explained if the formation of Rathke's pouch is surveyed along with the appearance of the pituitary placode (Schwind, 1928). The epithelium of the stomatodeum and the neuroepithelium of the prosencephalic vesicle maintain contact without interposition of mesoderm for a relatively long time. Romeis (1940) emphasised the major role played by this contact zone in the development of the pituitary gland. Since it is a narrow strip at the last stage before its separation (Day 12), thick sections of this region may include branches of the demarcating hypothalamic network (cf. Fig. 9 of Szabó & Csányi, 1982 and Fig. 7 of the present study). Branches of the hypothalamic vessels grow over the lateral walls of Rathke's pouch and some of them communicate with the *anlage* of the intercavernous sinus. The latter is represented by two or three branches, surrounding the posterior surface of the pituitary *anlage* and then passing by a single vessel on each side into the primitive maxillary veins.

By the time of the total separation of the contact zone (Day 13), the primary portal veins can easily be distinguished in the forming space (Fig. 7). The separation of

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Figs. 4–5. Day 12. The avascular contact zone of the *anlage* of the hypothalamo-adenohypophyseal system. The anterior wall of Rathke's pouch contacts the wall of the diencephalic vesicle without intervening mesenchyme. Open arrows indicate the branches of the internal carotid arteries supplying the hypothalamic plexus. *R*, Rathke's pouch; *I*, processus infundibularis; III, third ventricle; *S*, stomatodeum; *C*, internal carotid artery; *D*, diencephalon wall. Fig. 4, sagittal plane. × 185. Fig. 5, frontal plane. × 288.

Fig. 6. Day 13. Appearance of the portal veins. Horizontal plane. Arrows indicate the primary portal veins. *R*, Rathke's pouch; *C*, internal carotid artery; *D*, diencephalic wall. × 290.

Rathke's pouch from the stomatodeal epithelium (canalis craniopharyngeus) starts at the same stage. The latter, and the whole adenohypophyseal surface, is covered by a capillary network derived from the hypothalamus.

The vessels around the rudiment of the canalis craniopharyngeus remain for some time in secondary connection with the subepithelial vascular plexus of the stomatodeum. They lose their contact with the vessels around the adenohypophysis by the time ossification begins in the cranial base (Day 19: Szabó & Csányi, 1981*a*, 1982, 1984). It is probable that the presence of these vessels and the different developmental origin of the adeno- and neurohypophysis have supported the concept that Rathke's pouch receives its blood supply from the roof of the primitive pharyngeal wall, and that its vascular connection with the hypothalamus appears therefore to be the product of secondary development (Glydon, 1957). However, the main problem in our previous work was that we could not establish the process of merging of the two vascular systems. The present study shows that this concept is false and demonstrates that the adenohypophyseal vessels are derived only from the vascular network of the diencephalon, without any contribution from the pharyngeal vessels, and that the portal vascular bed develops as a single entity.

The venous drainage is very similar to the arterial supply in the early stages. The veins of the hypothalamus are collected by the primitive maxillary vein, a very important tributary of the primary head vein in the maxillary process. A similar vein is described by Padget (1957) in man. In contradistinction to the primitive maxillary artery, this vein is not a temporary branch. It forms the drainage of the venous system at the basal surface of the brain, some derivatives of the maxillary process and the orbit. The hypophyseal vessels are drained by the *anlage* of the intercavernous sinus. This developmental process will be the subject of a later paper.

SUMMARY

The origin of the portal vessels and the adjacent structures are described in rat embryos (gestational Days 11, 12 and 13) injected with India ink via the umbilical veins. Without the interposition of mesoderm Rathke's pouch comes into contact with the prosencephalic vesicle and its diverticulum, the processus infundibularis. Developmental changes in the shape of the prosencephalic vesicle influence the formation of Rathke's pouch. Before separation of the latter from the diencephalon and the processus infundibularis (Day 12), branches start growing around Rathke's pouch from the capillary network covering the prospective hypothalamus, and these vessels may be now considered as the forerunners of the primary portal vessels. After the separation of the anterior wall of Rathke's pouch from the diencephalon (Day 13) the primary portal veins are present and the hypothalamo-adenohypophyseal portal circulation is ready to function. The hypothalamic plexus is supplied by the primitive maxillary artery and by some small branches of the internal carotid arteries. The venous outflow leads into the intercavernous sinus and into the primitive maxillary veins. No arterial vessels in the primitive pharyngeal wall could be observed before the appearance of the primary portal vessels.

The present observations clearly demonstrate that the adenohypophyseal vessels are derived only from the vascular network of the diencephalon, without contribution from the pharyngeal vessels, and that the portal vascular bed develops as a single entity.

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