Blood Vascular Architecture of the Rat Cerebral Hypophysis and Hypothalamus. A Dissection/Scanning Electron Microscopy of Vascular Casts

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Summary. Complete casts of the hypophyseal and hypothalamic blood vascular beds of newborn, pubescent, adult and aged rats were produced by infusion of low viscosity methacrylate media, dissected under a binocular light microscope, and observed with a scanning electron microscope.

The primary capillary plexus projected capillary loops into the median eminence and infundibular stalk. These loops were composed of anastomosing capillaries, being numerous in the central area of the anterior lip of the median eminence. The well developed long loops received their proper afferent arterioles from the arterial terminals in the primary plexus, and emitted their proper efferent venules continuous with the long portal vessels. The loops in newborn rats were poorly developed, appearing as simple ball-like protrusions of the capillaries of the primary plexus.

Many branches of the anterior, middle and accessory midde hypophyseal arteries penetrated the primary plexus, and ascended as infundibular ascending arterioles in the median eminence and infundibular stalk. These infundibular ascending arterioles continued into the capillary bed of the hypothalamus, especially in its basilar and peri-ventricular areas. The subependymal capillary network was fairly independent, and located dorsal to the loops. This network received some of the infundibular ascending arterioles, and emitted infundibular descending venules continuous with the long portal vessels. The subependymal network also received the infundibular descending arterioles from the hypothalamic arteries, and emitted the infundibular ascending venules continuous with the hypothalamic veins. Thus, neither a feedback nor a retrograde portal route from the hypophyseal capillaries to the hypothalamic capillaries was noted.

The capillary bed of the pars tuberalis was observed only in the adult and aged rats; it was a very coarse network which was derived from the primary capillary plexus and connected to the secondary capillary plexus.

In order to observe with a scanning electron microscope the fine blood vascular architectures of the hypophysis and other organs, we improved the conventional high viscosity methacrylate media (TANIGUCHI et al., 1952, 1955; BATSON, 1955) by preparing some low viscosity methacrylate media which were widely useful for thorough castings of the entire blood vascular beds, including the capillaries and veins, of these organs (MURAKAMI, 1971, 1975a; MURAKAMI et al., 1973, 1984). Among these improved media, the monomeric methyl and hydroxypropyl methacrylate mixture has been proved to be very fluid and useful even for casting such fine vessels as liver bile.
canaliculi (MURAKAMI et al., 1984).

The casts prepared with these low viscosity methacrylate media, including the monomeric ones, are durable enough to sufficiently withstand tissue maceration with sodium or potassium hydroxide, cleaning by ultrasonation, air- or freeze-drying, conductive treatment by metal coating or osmium impregnation, and also electron bombardment during scanning electron microscopy (MURAKAMI et al., 1973, 1984). Furthermore, they are appropriately brittle to be suited for dissection with sharpened needles within and outside the scanning electron microscope (MURAKAMI et al., 1973, 1984).

The positioning of each vessel to the tissue elements cannot be examined in the casts since the tissue has been removed. In spite of this limitation, microdissection/scanning electron microscope observation has an advantage over the conventional light microscope observation of India ink-injected or other tissue samples in that it allows a clear, three-dimensional and long range viewing of the microvascular connections and distributions (MURAKAMI, 1971; MURAKAMI et al., 1973, 1983, 1984). Thus, the method has become one of the standard techniques for the morphological study of microcirculation (HODDE, 1981; MURAKAMI et al., 1983; LAMETSCHWANDTNER et al., 1984).

The conventional light microscope method has long established that in man and various animals, including the rat that the hypophyseal portal system originates in the primary capillary plexus in the median eminence, infundibulum and stalk, and terminates in the secondary capillary plexus in the pars distalis (for references, see: DANIEL, 1966; CHRIST, 1966; GREEN, 1966; WINGSTRAND, 1966; BERGLAND and PAGE, 1979). Scanning observation of the vascular casts has clearly confirmed in the monkey, dog, rat and some other animals this, or long portal system, as well as the so-called short portal system connecting the infundibular process and pars distalis (MURAKAMI, 1975a, b; PAGE et al., 1976, 1978; PAGE and BERGLAND, 1977; LAMETSCHWANDTNER et al., 1977; BERGLAND and PAGE, 1978, 1979; OHTANI et al., 1983; KIKUTA et al., 1984; MURAKAMI et al., 1985). Another short or intraadenohypophyseal portal system between the pars intermedia and pars distalis has been further documented in the rat (MURAKAMI, 1975a; MURAKAMI et al., 1985).

Light microscope methods have also long shown that in man and various animals, including the rat, the primary capillary plexus of the hypophyseal portal system has many communications with the hypothalamic vessels (for reference, see: DANIEL, 1966; GREEN, 1966; WINGSTRAND, 1966; BERGLAND and PAGE, 1979). However, these communications have been a subject of controversy. Some authors have claimed that the communications originate in the capillaries of the primary plexus, and thus regard them as a possible feed-back portal route from the hypophysis to the hypothalamus (BASIR, 1932; TÖRÖK, 1960, 1964; BERGLAND and PAGE, 1979), others have maintained that they arise directly from the arterial branches in the primary plexus to supply the hypothalamic capillaries (DUVERNOY, 1972). Our previous studies by dissection/scanning electron microscopy of the methacrylate vascular casts of the monkey, dog and rat have supported the latter view of the arterial origin (MURAKAMI, 1975a, b; KIKUTA et al., 1984; MURAKAMI et al., 1985).

The present paper reinvestigates the blood vascular beds of the rat hypophysis and hypothalamus by the dissection/scanning electron microscope method, and clarifies the intricate organization of the long, short and intra-adenohypophyseal portal systems as well as their relation to the hypothalamic capillary beds, including the subependymal network.
Fig. 1. A scanning electron micrograph of the methacrylate-reproduced hypophyseal, hypothalamic and other arteries (adult male rat, ventral view, partial infusion through the ascending aorta). Note in Inset A (a closer view of the left anterior and middle hypophyseal arteries, HA and HM) that these arteries show marked constrictions at their origins (thick arrowheads). Note in Inset B (a closer view of the left posterior hypophyseal artery, HP) that this artery has less marked original constriction (thin arrowhead). Abbreviations: see also Table 1. ×20, Inset A: ×150, B: ×200
Fig. 2. A scanning electron micrograph of the methacrylate-reproduced hypophyseal, hypothalamic and other veins (adult male rat, postero-dorsal view, partial infusion through the superior vena cava). Caudal parts of the pars distalis (PD) and infundibular process (IP) injected by this venous infusion. Note that the capillary bed of the pars distalis (PD) has two efferent routes, ventral and dorsal adenohypophyseal veins (VV and DV), which continue into the basi-occipital sinus (BS) and neurohypophyseal vein (NV), respectively. Inset A shows a light micro-
MATERIALS AND METHODS

Newborn, pubescent, adult and aged rats of both sexes, weighing 20–30, 100–250, 300–400, and 600–700g, were used. The hypophyseal and hypothalamic blood vascular beds of these animals were entirely reproduced by the thorough infusion of the laboratory-prepared low viscosity methacrylate casting media (1.2–2.5 centipoise), including the monomeric methyl and hydroxypropyl methacrylate mixture, under a moderate infusion pressure (40–60 mmHg) into the ascending aorta (about 5, 25, 40 and 50 ml for each animal group), after ligation of the thoracic aorta and perfusion with saline through the ascending aorta (technical details, see: MURAKAMI et al., 1973, 1975a, 1984). For additional castings, the arteries or veins of the blood vascular beds were reproduced simply by partial infusion of a small amount of a commercially available casting medium (Mercox 2B or 2R containing 1.0–1.5% MA catalyst, Oken Shoji Co. Ltd.) into the ascending aorta or superior vena cava (about 1, 3, 5 and 7 ml for each animal group). In some instances of thorough reproduction, a diluted Mercox (2B) containing 30–50% monomeric methyl methacrylate and 2.0–2.5% benzoyl peroxide (Katayama Chemicals, Co. Ltd.) was used as a substitute for the laboratory-prepared low viscosity media.

The resin-infused animals were placed in a hot water bath (60°C), immersed in Plank-Rychlo’s solution for decalcification, corroded in a hot 10–20% sodium hydroxide bath (60°C), incubated in a hot neutral detergent bath (60°C), and washed in water. The corrosion casts thus prepared were freeze-cut with razor blades into appropriate blocks, air dried, stained with vaporized osmium tetroxide and hydrazine hydrate or coated with gold in a vacuum evaporator, dissected with sharpened forceps and needles under a stereo-binocular light microscope, again coated with gold, and then observed with a scanning electron microscope (JSM U-3, JEOL, or HHS-2R, Hitachi) at an acceleration voltage of 5 kV (technical details, see: MURAKAMI, 1971, 1975a; MURAKAMI et al., 1973, 1982, 1983, 1984). This series of dissection and scanning electron microscopy was repeated until the intricate connections and distributions of a vessel or vessels of interest were thoroughly elucidated. The dissection included freeze-cutting with razor blades or sharpened knives under the stereo-binocular light microscope. The osmium and hydrazine treated samples were sometimes microdissected with electron-etched tungsten probes within the scanning electron microscope equipped with a micromanipulator (HS-M2, Hitachi, or M-12-1, MFG) (MURAKAMI et al., 1973, 1984).

Inset A: ×30, Inset B: ×10

Inset B shows a scanning electron micrograph of the sagittally freeze-cut and dissected form of the specimen in Inset A. Note in Inset B how a constriction (arrowhead) separates the basi-occipital sinus (BS) from the cavernous sinus (CS). Abbreviations: see also Table 1.
Table 1. Abbreviations in Figure 1-22

| Arteries connective with the hypophyseal and hypothalamic arteries |
|---------------------------------------------------------------|
| AC anterior cerebral artery, BA basilar artery, CA anterior cerebellar artery, CO posterior cerebellar artery, IC internal carotid artery, LA labyrinthine artery, MA mamillary artery, MC middle cerebral artery, OA optic artery, PC posterior cerebral artery, TA trigeminal artery, ad peri-hypophyseal dural artery |

| Veins connective with the hypophyseal and hypothalamic veins |
|-------------------------------------------------------------|
| AB and ab Anterior basal vein and its branch, AE anastomosis of the right and left cavernous sinuses, AS anastomosis of the anterior and posterior basal veins, AV anastomosis of the apical and anterior basal veins, BS basi-occipital sinus, BV and bv apical basal vein and its branch, CA cavernous sinus, EC emissary vein of the cavernous sinus, EJ external jugular vein, FV facial vein, IM internal maxillary vein, MB mamillary vein, PB and pb posterior basal vein and its branch, TV temporal vein, VM vertebral vein, vd peri-hypophyseal dural vein |

| Hypophyseal and hypothalamic arteries, and their branches |
|----------------------------------------------------------|
| HA and ha Anterior hypophyseal artery and its branch, HM and km middle or accessory middle hypophyseal artery and its branch, HP and hp posterior hypophyseal artery and its branch, ah hypothalamic branch (artery) of the anterior hypophyseal artery, ia infundibular ascending arteriole, mh hypothalamic branch (artery) of the middle or accessory middle hypophyseal artery, pa peri-infundibular ascending artery, pp hypothalamic branch (artery) of the posterior hypophyseal artery |

| Hypophyseal and hypothalamic veins, and their branches |
|-------------------------------------------------------|
| AV and av Anterior hypothalamic vein and its branch, CV and cv apical hypothalamic vein and its branch, DV and dv dorsal adenohypophyseal vein and its branch, MV and mv middle hypothalamic vein and its branch, NV and nv neurohypophyseal vein and its branch, PV and pv posterior hypothalamic vein and its branch, VV and vv ventral adenohypophyseal vein and its branch, ci posterior long portal vessel, cs posterior short portal vessel, li lateral intra-adenohypophyseal portal vessel, lp lateral long portal vessel, ls lateral (dorsal) short portal vessel, ri anterior intra-adenohypophyseal portal vessel, rp anterior long portal vessel, rs anterior short portal vessel, vh infundibular descending venule, vp infundibular descending venule |

| Capillary beds of the hypophyseal, hypothalamic and other tissue components |
|-----------------------------------------------------------------------------|
| AM capillary bed of the median eminence, BC capillary bed of the basi-sphenoid bone, CH and ch capillary network and its capillary of the hypophyseal capsule, CL and cl deep capillary plexus and its long loop in the median eminence and infundibular stalk, CM capillary bed of the mamillary body, DS capillary bed of the infundibular stalk (dorsal part), HS postero-basilar and peri-ventricular part of the hypothalamic capillary bed, HL latero-basilar and peri-ventricular part of the hypothalamic capillary bed, HP capillary bed of the hypothalamus, HR antero-basilar and peri-ventricular part of the hypothalamic capillary bed, IP capillary bed of the infundibular process, IS capillary bed of the infundibular stalk, OC capillary bed of the optic chiasma, PD capillary bed of the pars distalis, PI capillary bed of the pars intermedia, PM capillary bed of the median eminence (posterior lip), PN capillary bed of the paraventricular nucleus, PT capillary bed of the pars distalis, SB and sb subependymal network and its capillary, TC capillary bed of the trigeminal nerve, VS capillary bed of the infundibular stalk (ventral part) |

| Others |
|--------|
| LR leaked resin mass or macerated remnant of tissue element, PL hypophyseal cleft, VC third ventricle |
RESULTS

Infusion of the low viscosity methacrylate or diluted Mercox into the ascending aorta could completely reproduce the entire blood vascular beds of the cephalic organs, including the hypophysis and hypothalamus, in newborn, pubescent, adult and aged rats (Fig. 3-7). Discontinuities in the casts of the vessels, including the capillaries and veins, could be avoided, while leakage of the casting media was occasionally noted as globular or coagulant bodies (Fig. 11, 19). The casts, after complete elimination of tissue, displayed detailed configurations of the hypophysis, hypothalamus and other related organs (Fig. 3, 5-7).

The osmium-impregnated or gold-coated casts gave a good contrast under the stereo-light microscope and facilitated dissection under this microscope. Successive scanning electron microscopy allowed a clear visualization of the dissected forms of the casts. Thus, repeated dissection and scanning electron microscopy allowed a detailed analysis of the complicated vascular networks of the hypophysis as well as their connections or relation to the adjacent blood vascular beds, including the subependymal and hypothalamic capillary plexuses (Fig. 3-21). Direct dissection within the scanning electron microscope was of special use in demonstration of the efferent and afferent vessels of such compactly conglomerated networks as those of the capillary loops in the median eminence and the infundibular stalk (Fig. 13-Inset A, B). Partial infusion of a non-diluted Mercox medium in the ascending aorta or superior vena cava abrogated the repeated microdissection and scanning of the arteries or veins (Fig. 1, 2).

This dissection/scanning electron microscopy of vascular casts showed that the basic blood vascular architecture of the hypophysis and hypothalamus was similar throughout the newborn, pubescent adult and aged rats, though some age-related differences occurred in the median eminence, pars distalis and pars intermedia. No sex-related differences were noted in animals of any age. The detailed findings are described below and schematically illustrated in Figures 21 and 22.

Hypophyseal and hypothalamic arteries, and their origins and terminations

The blood vascular beds of the hypophysis and hypothalamus were supplied by the anterior, middle and posterior hypophyseal arteries which arose from the internal carotid, internal carotid and superior cerebellar (or labyrinthine) arteries, respectively (Fig. 1, 3, 4). The middle hypophyseal arteries were usually accompanied by the accessory middle hypophyseal arteries arising from the posterior cerebral arteries (Fig. 1, 4). The anterior, middle and accessory middle hypophyseal arteries showed marked circular constrictions at their origins (Fig. 1-Inset A). Such marked original constrictions were not noted in the posterior hypophyseal arteries (Fig. 1-Inset B).

The anterior, middle and accessory middle hypophyseal arteries divided on the ventral surfaces of the hypothalamus and reached the median eminence (Fig. 3, 4). On their way to the median eminence, they gave off many hypothalamic arteries and peri-infundibular ascending arterioles to the hypothalamus (Fig. 3, 4, 6-Inset B, 15-2, 17-Inset B). The peri-infundibular ascending arterioles arose at the upper margins of the median eminence. The anterior hypophyseal arteries sometimes gave off a few twigs to the dural capillary plexus around or near the hypophysis (Fig. 3-Inset A).
Fig. 3. A scanning electron micrograph of the thoroughly methacrylate-reproduced blood vascular beds of the hypophysis and hypothalamus (newborn male rat, seven days after birth, ventral view). **Inset A** shows an aberrant dural branch (arrowhead) of...
posterior hypophyseal arteries divided near the posterior end of the hypophysis and reached the infundibular process (Fig. 1, 9, 9-Inset B, 10, 11). The posterior hypophyseal arteries gave off neither hypothalamic arteries nor peri-infundibular ascending arterioles, though they sent off some twigs to the capsular capillary network of the hypophysis (Fig. 9-Inset B).

After giving off the hypothalamic arteries and peri-infundibular ascending arterioles, the anterior, middle and accessory middle hypophyseal arteries descended on the external surfaces of the median eminence and infundibular stalk and supplied the capillary beds of these components (primary capillary plexus of the hypophyseal portal system) (Fig. 3, 4, 8). These arteries gave off many infundibular ascending arterioles on the external surfaces of the median eminence and infundibular stalk. These then penetrated the primary capillary plexus and ascended up the median eminence and infundibular stalk to supply either the subependymal capillary network or hypothalamic capillary plexus or both (Fig. 8-Inset A, 14-1, 14-2-Inset A, B, 18, 19-Inset A, 20) (see below). Furthermore, at the upper margins of the median eminence, the anterior, middle and accessory middle hypophyseal arteries gave off some fine twigs which descended along the external surface of the median eminence and anastomosed into the long portal vessels (Fig. 7-Inset) or sinusoidal vessels of the pars tuberalis (Fig. 8) (see below).

Main or thick branches of the middle and accessory hypophyseal arteries descended over the infundibular stalk and supplied the upper one third of the infundibular process and pars intermedia (Fig. 9-11). The posterior hypophyseal arteries ascended along the infundibular process and supplied the lower two thirds of the infundibular process and pars intermedia (Fig. 9). Regardless of their origins, the arterial branches to the infundibular process and pars intermedia could be classified into the ventral (trabecular) and dorsal types; the ventral branches ran along the ventral surface or in the ventro-superficial layer of the infundibular process and supplied this process and pars intermedia from the ventral and dorsal aspects, respectively (Fig. 10, 11), while the dorsal branches ran along the dorsal surface or in the dorso-superficial layer of the infundibular process and supplied this process from the dorsal aspect (Fig. 9).

The hypothalamic arteries (see above) ascended into the hypothalamus and formed the capillary bed of the hypothalamus (Fig. 3, 4, 17) (see below). The peri-infundibular ascending arterioles were small, short vessels which also ascended into the hypothalamus to supply the hypothalamic capillary bed, especially its basilar and peri-ventricular areas (Fig. 16-Inset B, 15-b, 15-b-Inset A, 17-Inset B) (see below). Some terminal twigs of the hypothalamic arteries, and peri-infundibular ascending arterioles entered or descended into the median eminence and connected, as the infundibular descending arterioles, with the subependymal capillary network (Fig. 14-b, 15-b, 17-Inset B) or primary capillary plexus of the hypophyseal portal system (Fig. 15-a, 17) (see below).

The pars distalis received neither an arterial branch nor an arterial capillary.

the anterior hypophyseal artery (HA) (newborn male rat, ventral view). Inset B shows an aberrant venous branch (arrowhead) which arises from the capillary bed of the median eminence anterior lip (AM) and continues into a branch (av) of the anterior hypothalamic vein (adult female rat, ventral view). Abbreviations: see also Table 1. ×30, Inset A : ×30, B : ×40
Fig. 4. A dissected form of the thoroughly reproduced blood vascular beds of the hypophysis and hypothalamus (pubescent female rat, ventral view). Capillary beds of the hypophysis—except that of the median eminence posterior lip (PM) have been removed. Some parts of the cavernous sinuses (CS), internal carotid arteries (IC) and other vessels have also been pinched off by dissection. Note that the subependymal capillary network (SB) receives the arterial twigs (infundibular descending arterioles) (thin arrowheads) from the anterior hypophyseal artery (HA) and emits venous twigs (infundibular ascending venules) (thick arrowhead) continuous with the middle hypothalamic vein (MV). Abbreviations: see also Table 1. ×30
Fig. 5. Thoroughly reproduced and sagittally freeze-cut blood vascular beds of the hypophysis, hypothalamus and adjacent tissues (adult male rat). Note that the capillary bed of the pars intermedia (PI) is inserted between the capillary beds of the pars distalis (PD) and infundibular process (IP), and that the vascular beds of the mamillary body (CM) and paraventricular nucleus (PN) are somewhat denser than that of the hypothalamus (HP). Inset A shows the thoroughly reproduced and sagittally freeze-cut blood vascular beds of the hypophysis and hypothalamus of a newborn male rat (two weeks after birth). Note in this inset that no vessel is observed between the pars distalis (PD) and infundibular process (IP). Abbreviations: see also Table 1. ×30, Inset A: ×50
Fig. 6. Horizontally freeze-cut blood vascular beds of the basilar and peri-ventricular areas (HC, HL, HR) of the hypothalamus (adult female rat, dorsal view). Note that the subependymal capillary network (SB) is located dorsal to the capillary bed of the median eminence (AM, PM). Inset A shows the frontally freeze-cut blood vascular beds of the median eminence anterior lip (AM), subependyma (SB), and latero-basilar and periventricular hypothalamus (HL). Inset B shows a dissected form of the...
Hypophyseal and hypothalamic veins, and their origins and drainage

The hypophysis emitted the ventral adenohypophyseal, dorsal adenohypophyseal and neurohypophyseal veins. The neurohypophyseal veins arose deep in the infundibular process, left the infundibular process from the postero-dorsal aspect and continued into the cavernous or basi-occipital sinuses (Fig. 2, 4, 9, 10-Inset A) (see below). The ventral and dorsal adenohypophyseal veins originated in the caudal end of the pars distalis (Fig. 2). The ventral adenohypophyseal veins left the pars distalis from the ventro-posterior aspect and continued into the basi-occipital sinuses (Fig. 2) (see below). The dorsal adenohypophyseal veins, quite thin, left the pars distalis from the postero-lateral aspect and continued into the cavernous or basi-occipital sinuses either directly or via the neurohypophyseal veins (Fig. 2, 12). The neurohypophyseal veins were well developed, and larger than the ventral adenohypophyseal veins (Fig. 2).

The hypothalamus emitted apical, anterior, middle and posterior hypothalamic veins (Fig. 2-4). The apical hypothalamic veins originated in the anterior areas of the hypothalamus and continued near the optic chiasma into the anterior or apical basal veins. The anterior hypothalamic veins originated in the antero-lateral areas of the hypothalamus and continued near the origins of the middle cerebral arteries into the anterior basal veins. The middle hypothalamic veins originated in the postero-lateral areas of the hypothalamus and continued near the origins of the posterior cerebral arteries into the anterior basal veins or cavernous sinuses. The posterior hypothalamic veins originated in the posterior area of the hypothalamus and entered close to the distal ends of the posterior communicating arteries into the cavernous sinuses either directly or via the mamillary veins.

The apical basal veins passed through the palatine fissures and continued into the distal portions of the internal maxillary veins. The anterior basal veins descended along the anterior cerebral arteries and continued into the cavernous sinuses, though they sent off a few anastomosing branches to the apical basal veins (Fig. 2-Inset B). The posterior basal veins descended along the posterior cerebral arteries and continued into the cavernous sinuses from the postero-dorsal aspects. Before entering into the cavernous sinuses, the anterior and posterior basal veins were adjoined by a well developed anastomosing branch (Fig. 2-Inset B).

The cavernous sinuses occupied a position lateral to the hypophysis (pars distalis) and the internal carotid arteries (Fig. 3, 4) and emitted cavernous emissary veins which passed through basisphenoid canals and continued into the proximal portions of the internal maxillary veins (Fig. 2-Inset B). A well developed anastomosis traversed the corpus of the basisphenoid bone and connected with the cavernous emissary veins on both sides (Fig. 2-Inset A, B). The cavernous sinuses were continuous with the basis-occipital sinuses which were located bilaterally on the basis-occipital bone (Fig. 2, 2-Inset A, B). A marked constriction was observed between the cavernous and basis-occipital sinuses (Fig. 2-Inset B). The basis-occipital sinuses, therefore, generally continued into the internal jugular and vertebral veins (Fig. 2-Inset A). The internal antero-lateral upper margin of the median eminence anterior lip (AM) (dorsal view) (hypothalamic capillaries were removed). Note in Inset B the capillary bed of the median eminence (AM) (thick arrowheads), and that these branches give off, at the upper margin of the median eminence, the peri-infundibular ascending arterioles (thin arrowheads), then supply the hypothalamic capillary bed. Abbreviations: see also Table 1. ×70, Inset A: ×50, B: ×100.
Fig. 7. Legend on the opposite page.
maxillary veins continued, together with the facial, external maxillary and temporal veins, into the external jugular veins.

The median eminence occasionally emitted one or two aberrant venous twigs. These aberrant twigs originated in the apical portions of the anterior lip of the median eminence and continued into the anterior or apical hypothalamic veins (Fig. 3-Inset B).

**Capsular capillary network of the hypophysis**

The whole external surface of the hypophysis was surrounded by a very thin and coarse capillary network (Fig. 9-Inset B) which was continuous with the dural capillary networks near the hypophysis (Fig. 3-Inset A). The capsular network of the hypophysis mainly received its arterial twigs from the internal carotid and posterior hypophyseal arteries (Fig. 1, 9-Inset B), and emitted its venous twigs to drain into the neurohypophyseal, dorsal adenohypophyseal and ventral adenohypophyseal veins (Fig. 9-Inset B). The capsular network also received some additional arterial twigs from the optic, trigeminal and other arteries, including the superior hypophyseal arteries (see above), and emitted some additional venous twigs which drained into dural veins near the hypophysis or around the hypothalamus (Fig. 2-Inset B). These dural veins finally continued into the cavernous or basi-occipital sinuses (Fig. 2-Inset B) (see above).

**Hypothalamic capillary bed and its arterial supply and venous drainage**

The hypothalamic arteries (see above) formed the hypothalamic capillary plexus which was continuous with those of mamillary bodies, paraventricular nuclei, and supraoptic nuclei (Fig. 5-7). The anterior, middle and accessory middle, and posterior hypothalamic arteries supplied the anterior, lateral, and posterior areas of the hypothalamic capillary plexus, respectively. However, no area of the hypothalamic capillary plexus was separately identified, even though its basilar and peri-ventricular parts—including the areas of arcuate nuclei—surrounding the lower margins of the third ventricle received peri-infundibular ascending arterioles and some of the infundibular ascending arterioles.

The capillary plexuses of the mamillary bodies were somewhat denser than the hypothalamic capillary bed (Fig. 5). They mainly received their arterial branches (mamillary arteries) from the posterior communicating arteries (Fig. 1), and emitted mamillary veins continuous with the cavernous sinuses (Fig. 4) (see above). The capillary plexuses of the paraventricular and supraoptic nuclei were also somewhat denser than the hypothalamic capillary bed (Fig. 5). They were supplied by the branches of middle cerebral arteries, and continued into the anterior veins.

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**Fig. 7.** Sagittaly freeze-cut blood vascular beds of the infundibular stalk (IS) and median eminence (AM,PM) (adult male rat). Inset A shows a dissected form of a part of the median eminence anterior lip (AM). Note in this inset that a long portal vessel (pp) receives a terminal branch (ha) of the anterior hypophyseal artery (thick arrowhead), and that the subependymal capillary network (SB) anastomoses into the capillary bed or loops (CL) of the median eminence (AM) (thin arrowheads). Abbreviations: see also Table 1. ×100, Inset A : ×100
Fig. 8. Dissected form of the hypophyseal capillary beds (aged male rat, ventral view). A part of the capillary bed of the median eminence anterior lip AM has been removed to expose the subependymal capillary bed (SB) and the dorsal part (DS) of the capillary bed of the infundibular stalk. Note that some sinusoidal capillaries (thin arrowheads) arise from the capillary bed of the median eminence (AM) and descend
Capillary beds of the median eminence and infundibular stalk and their portal drainage into the capillary bed of the pars distalis

The capillary bed of the median eminence consisted of anastomosing capillaries with a mesh-like structure. It had a large anterior extension (anterior lip) and a small posterior extension (posterior lip), and formed the primary capillary plexus of the hypophyseal portal system together with that of the infundibular stalk of a similar mesh-like structure (Fig. 3-9, 13-20). This primary capillary plexus received at its upper margins and also on its external surfaces the arterial terminals from the anterior, middle and accessory middle hypophyseal arteries, and emitted from its external surfaces the long portal vessels descending into the pars distalis. The long portal vessels could be classified into anterior, lateral and posterior types; the anterior, lateral and posterior long portal vessels originated in the anterior, lateral and posterior areas of the plexus, and ran into the pars distalis from the antero-ventral, antero-lateral and antero-dorsal aspects, respectively (Fig. 3, 8, 9, 12). These long portal vessels divided in the pars distalis and formed the sinusoidal capillary bed of the pars distalis (secondary plexus of the hypophyseal portal system) (Fig. 3, 5, 7, 8, 9, 12). Although intercommunicating by many fine transverse capillaries (Fig. 12-Inset A), the sinusoidal capillaries descended parallel to each other in the pars distalis (Fig. 12). Thus, it could be said that the anterior, lateral and posterior long portal vessels supplied the central, lateral and dorsal areas of the pars distalis, respectively (Fig. 22).

Capillary beds of the infundibular process, pars tuberalis and pars intermedia, and their portal drainage into the capillary bed of the pars distalis

The capillary bed of the infundibular process was dense and continuous with the primary capillary plexus (Fig. 5, 7, 9). It gave off its proper systemic efferent veins, the neurohypophyseal veins (see above). In addition to these, the capillary bed of the infundibular process sent off the short portal vessels which could be classified into anterior, lateral and posterior types; these anterior, lateral and posterior short portal vessels originated in the antero-ventral, dorso-lateral and postero-ventral areas of the process, and ran into the pars distalis from the antero-dorsal, dorso-medial and postero-dorsal aspects, respectively (Fig. 9, 9-Inset A).

The capillary bed of the pars intermedia was not noted in the newborn and pubescent rats, but was only observed in the adult and aged rats. The capillary bed of the pars intermedia was rather coarse and sent off anterior, lateral and posterior intra-adenohypophyseal portal vessels which ran into the pars distalis from the antero-ventral surface of the median eminence to continue into the capillary bed of the pars distalis (PD). Also note that these sinusoidal capillaries supplying the pars tuberalis receive thin arterial capillaries or arterioles (thick arrowhead) from the branches of the anterior hypophyseal artery (ha). Inset A shows a dissected form of the vascular loop indicated by a thin arrow. Note in this inset that the loop, (thin arrowhead) is penetrated by an arterial twig (infundibular ascending arteriole) which arises from a branch of the middle hypophyseal artery (hm) and continues into the subependymal network. Inset B shows a dissected form of the tree-like vascular loop indicated by the thick arrow. Note in this inset that the loop (thick arrow) receives its proper afferent arteriole from a branch of the middle hypophyseal artery (hm) and emits its proper efferent venule continuous with an anterior short portal vessel (cp). Abbreviations : see also Table 1. ×60, Inset A : ×90, B : ×100
Fig. 9. Blood vascular bed of the infundibular process (newborn male rat, ten days after birth, dorsal view). Note that the capillary bed of the infundibular process (IP) has additionally given off lateral (dorsal) and posterior short portal vessels (ls and cs) which continue into the capillary bed of the pars distalis (PD) from the medio-dorsal and postero-dorsal aspects, respectively. **Inset A** shows an anterior short portal vessel (rs) connecting the capillary beds of the infundibular process (IP) and pars
dorsal, dorso-medial and postero-dorsal aspects, respectively (Fig. 10, 11). In addition
to these, the capillary bed of the pars intermedia had many capillaries communicating
with that of the infundibular process (intercommunicating capillaries between the pars
intermedia and infundibular process) (Fig. 11-Inset B). These communications were
observed throughout the junctional areas of the pars intermedia and infundibular
process.

The pars tuberalis of the newborn and pubescent rats was not provided with its
proper vessels. In the adult and aged rats, however, some sinusoidal vessels, with a few
anastomoses among them were seen in the pars tuberalis, or ventral to the anterior and
lateral long portal vessels (Fig. 8). These sinusoidal capillaries, though, received a few
arterial terminals from the hypophyseal arteries, especially anterior ones (see above); they arose from the primary capillary plexus and continued to the capillary bed of the
pars distalis from the antero-ventral aspect (Fig. 8).

Capillary loops of the primary plexus

The primary capillary plexus consisted of the mesh-like capillary beds of the median
eminence and infundibular stalk (see above). This plexus projected the capillary loops
into the median eminence and infundibular stalk.

The capillary loops in the newborn rats were small with a simple ball-like
appearance, though some of them were somewhat developed to contain a few
anastomosing capillaries (Fig. 13-Inset C). The loops in the pubescent and more aged
rats were higher, larger and more complicated than those in the newborn rats, and
contained more anastomosing capillaries (Fig. 13). These developed loops were usually
columnar, though occasionally fungiform or circumvallate (Fig. 8, 13).

The developed loops could be classified into short and long types: the long loops
reached the subependymal layer of the median eminence or infundibular stalk (long
loops), while the short ones terminated within the superficial or middle layer of the
median eminence or infundibular stalk (Fig. 13). The short loops arose within and
terminated in the capillary network of the primary plexus. In contrast, the long loops
contained core arterioles which arose from the arterial terminals in the primary plexus
(Fig. 13-Inset A). The long loops also contained core venules directly continuous with
the anterior, lateral or posterior long portal vessels (Fig. 13-Inset B). As aberrant
forms, some short and long loops were penetrated by the infundibular ascending
arteries (Fig. 8-Inset A, 14-2-Insets A, B, 18, 19-Inset B, 20) or the infundibular
descending venules (Fig. 15-1, -2, 18) (see below). In such cases, the loops always had
some communication with the penetrating arterioles or venules (Fig. 20-Inset B, C). At rare times, the loops were supplied by the infundibular descending arterioles (Fig.
15-1, -2, 17).

The loops were distributed most densely in the central areas of the anterior lip of
the median eminence, where numerous short and long loops bristled very closely (Fig.
13). Few short and long loops were observed in the posterior lip of the median eminence
or in the peripheral areas of the anterior lip of the median eminence (Fig. 14-1, 14-2,
Fig. 10. Isolated blood vascular beds of the infundibular process (IP) and pars intermedia (PI) (adult male rat). The blood vascular bed of the pars intermedia has been disrupted during the isolation. Note that the arterial branches (arrowheads) run along the ventral surface or in the ventro-superficial layer of the infundibular process (IP), to supply the capillary beds of the infundibular process (IP) and pars intermedia (PI). Inset A shows a dissected form of the capillary bed of the infundibular process (IP) (adult male rat). Note in this inset that the original branches (nv) of the neurohypophyseal vein (NV) arise deep in the infundibular process (IP). Abbreviations: see also Table 1. ×50, Inset A: ×30
15-2). However, the infundibular stalk, especially its dorsal network, protruded a small number of the long loops, some of which were fully developed and characterized by their circumvallate or tree-like structures (Fig. 8).

**Subependymal capillary network**

The median eminence and infundibular stalk was provided with another set of deep capillary network, subependymal network, either dorsal to the loops or beneath the ependyma of the lower floor of the third ventricle (Fig. 4-9, 13-16, 18). This network was rather coarse and consisted of anastomosing capillaries with sinusoidal appearances.

The subependymal network received some of the infundibular ascending arterioles (see above) and emitted some venous twigs (infundibular descending venules) which ran down, penetrated the primary capillary plexus, and connected into the anterior, lateral or posterior long portal vessels (Fig. 14-1, 14-2-Inset C, 15-2, 18). The subependymal network also received some arterial twigs or capillaries (infundibular descending arterioles, see above) from the hypothalamic arteries or peri-infundibular ascending arterioles, see above) (Fig. 4, 14-1, 15-1, -2) and emitted some venous twigs (infundibular ascending venules) which continued into the hypothalamic veins (Fig. 14-1, 14-2, 16, 16-Inset A). The latter venous drainage into the hypothalamic veins was usually well developed to receive most capillaries of the subependymal network (Fig. 14-2, 16). In addition to these, the subependymal network gave off a few capillaries which continued into the capillary loops or meshworks of the primary plexus (Fig. 7-Inset A).

**DISCUSSION**

The present paper clearly shows that our low viscosity methacrylate media are useful for completely casting all the blood vascular beds of the hypophysis and hypothalamus (MURAKAMI, 1975a, b; MURAKAMI et al., 1984, 1985). Our preliminary experiments in this study have shown that the commercially available Mercox media or Batson's plastic are so viscous that they are not always suited for complete infusion into such complicated capillary networks as those of the hypophysis and hypothalamus. For the complete casting of the blood vascular beds of these organs, the Mercox media or Batson's plastic should be diluted with monomeric methylmethacrylate or other monomeric media prior to use (OHTANI and MURAKAMI, 1978; NOPANITAYA et al., 1979). The diluted Mercox media were sometimes infused in this study, which is otherwise characterized by the use of benzoyl peroxide as a catalyst. The use of benzoyl peroxide prolongs the hardening of the diluted Mercox media, and here facilitated complete infusion of the diluted media into the hypophyseal capillary beds as well as the capillary bed of the hypothalamus.

The arterial and venous patterns of the hypothalamus and hypophysis as here observed in the rat are principally similar to those previously reported in the rat by the light microscopic observation of India ink-injected and transilluminated specimens (LANDSMEER, 1957). In fact the only difference may be our separate description of the basi-occipital sinuses which receive the ventral adenohypophyseal veins. More exactly, LANDSMEER (1957) described our basi-occipital sinuses as the posterior segments of the cavernous sinuses, thus including them among the cavernous sinuses. HODDE (1981) and PAGE and BERGLAND (1977), who used the vascular casting/
Fig. 11. A typical posterior intra-adenohypophyseal portal vessel (ci) connecting the capillary beds of the pars intermedia (PI) and pars distalis (PD) (adult male rat). Inset A shows an arteriole (arrowhead) which arises from a branch (hm) of the accessory middle hypophyseal artery and continues into the capillary bed of the pars intermedia (PI) (adult male rat). Inset B shows a rostral portion of the capillary bed of the pars intermedia (PI) (adult female rat). Note in this inset that the capillary bed of the pars intermedia (PI) receives the arterioles or arteriolar capillaries (thick
Fig. 12. Dissected blood vascular bed of the pars distalis (PD) (adult female rat, dorsal view). Note that the main or sinusoidal capillaries of the pars distalis (PD) descend in parallel fashion to converge into branches (dv, vv) of the dorsal and ventral adenohypophyseal veins. Note in Inset A that the sinusoidal capillaries in the pars distalis (PD) are intercommunicated by fine transverse capillaries (arrowheads). ×30, Inset A: ×100

...arrowheads) from the branch (hn) of the middle hypophyseal artery and also the capillaries (intercommunicating capillaries between the pars intermedia and infundibular process) (arrow and thin arrowhead) from the capillary bed of the infundibular process (IP). Inset C shows a typical anterior intra-adenohypophyseal portal vessel (ri) connecting the capillary beds of the pars intermedia (PI) and pars distalis (PD) from the ventro-anterior aspect. Abbreviations: see also Table 1. ×150, Inset A: ×150, B: ×90, C: ×80
Fig. 13. Legend on the opposite page.
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...electron microscope method, also included our basi-occipital sinuses with the cavernous sinuses. However, our basi-occipital sinuses should rightly be described as independent venous units, since they are clearly isolated by the marked constrictions from the cavernous sinuses and also provided with proper efferent routes to the internal jugular and vertebral veins.

The present paper clearly demonstrates that the hypophyseal portal system in the rat mainly consists of: 1) the capillary beds of the median eminence and infundibular stalk (primary capillary plexus) supplied by the anterior, middle and accessory middle hypophyseal arteries; 2) the capillary bed of the pars distalis (secondary capillary plexus) draining into the adeno-hypophyseal veins continuous with the cavernous and basi-occipital sinuses; and 3) the long portal vessels arising from the primary capillary plexus and continuing into the secondary plexus.

It is difficult to say who first described the hypophyseal portal system in any animal and by what method. DANDY and GOETSCH (1911) observed carmine gelatin-injected and sectioned or transilluminated specimens of the dog with a light microscope, and described how the pars distalis was supplied by the arterial branches from the Willis circle. POPA and FIELDING (1930, 1933) observed by light microscope the India ink-injected and sectioned or transilluminated specimens from humans and described the portal vessels which arose from the capillary bed of the pars distalis, and continued into the capillary beds of the median eminence and infundibular stalk. Although these descriptions by DANDY and GOETSCH (1911) and POPA and FIELDING (1930, 1933) were subjects of dispute (BASIR, 1932; ESPINASSE, 1933; MORATO, 1939), WISLOCKI and KING (1936), WISLOCKI (1937, 1938), HARRIS (1947 a, b), OFUJI (1947), Xuereb et al. (1954) and many other authors demonstrated, in their light microscope observations of India ink-injected and sectioned specimens or living tissues of the monkey, cat, rat, mouse and other animals, that the portal vessels originate in the capillary beds of the median eminence and infundibular stalk and terminate in the capillary bed of the pars distalis, and also that the blood flow in these portal vessels is directed principally toward the pars distalis. Owing to these findings and also the concomitant discovery of exertion of the portal vessels in the hypothalamic control over the pars distalis (HARRIS, 1948; HARRIS and JACOBSOHN, 1952; GUILLEMIN and ROSENBERG, 1955; McCANN and TALEISNIK, 1960; GUILLEMIN et al., 1962), the blood supply of the hypophysis and hypothalamus has drawn great interest among endocrinologists, neurologists as well as angiologists (for references see DANIEL, 1966; GREEN, 1966; WINGSTRAND, 1966; DUVERNOY, 1972; SATHYANESAN, 1972; LAMETSCHWANDTNER et al., 1977; BERGLAND and PAGE, 1979; PAINO et al., 1981; LAMETSCHWANDTNER, 1982). The results obtained by these authors, who mainly used

Fig. 13. Sagittally freeze-cut capillary bed of the median eminence anterior lip (central area) (AM) (aged male rat). Note that the capillary bed of the median eminence (AM) projects numerous loops (CL) consisting of anastomosing capillaries, and that some of the loops are sufficiently long (cl) to reach the subependymal capillary network (SB). Insets A and B show dissected forms of the long loops (adult male rat), where the proper afferent arteriole (thin arrowheads) and efferent venule (thick arrowhead) of the long loop (cl) are clearly observed. Inset C shows the capillary bed of the central area of the median eminence anterior lip (AM) of a newborn rat (three days after birth, dorsal view). Note in this inset that the capillary loops of the newborn rat are small and simple (arrows). Abbreviations: see also Table 1. ×360, Inset A: ×320, B: ×360, C: ×300
light microscope methods (light microscopy of India ink-or other dye-injected and sectioned or transilluminated specimens, vital light microscopy of living tissues, and light microscopy of latex-injected and corroded samples), have confirmed that the hypophyseal portal system occurs throughout the vertebrates, though this system becomes increasingly more complicated with the evolutionary order of the species (Green, 1951, 1966; Hasegawa, 1960; Cummings and Habel, 1965; Daniel, 1966; Wingstrand, 1966). Similar findings have been obtained by modern workers who generally using the vascular casting/scanning electron microscope method (Murakami, 1975a, b; Page et al., 1976, 1978; Page and Berland, 1977; Lametschwandtner et al., 1977; Bergland and Page, 1979; Hodde, 1981; Paine et al., 1981; Lametschwandtner, 1982; Ohtani et al., 1983; Kikuta et al., 1984; Murakami et al., 1985). It has been also confirmed by the vascular casting/scanning electron microscope method that, in animals with a long hypophyseal stalk (e.g., monkey and rat), the portal (or long portal) vessels are thick, though their rate of occurrence is rather limited, while in animals with a short hypophyseal stalk (e.g., dog and guinea pig), the long portal vessels are thin and numerous (Murakami, 1975a, b; Page et al., 1976; Bergland and Page, 1979). It is interesting that the primary capillary plexus of the hypophyseal portal system, as demonstrated in Figure 3-Inset B, emits a few systemic venous twigs directly continuous with the hypothalamic veins. These previously unknown venous twigs—except in the dog (Murakami, 1975b)—are aberrant and small, so that even when they occur, the blood in the primary capillary plexus will primarily flow into the secondary capillary plexus via the long portal vessels.

Since the description by Adams et al. (1964), the portal vessels connecting the primary and secondary capillary plexuses have been called the "long" portal vessels. The present paper, employing this terminology, also shows that the long portal vessels in the rat can be classified into anterior, lateral and posterior ones, according to their origins and terminations; the anterior, lateral and posterior long portal vessels originate in the anterior, lateral and posterior areas of the median eminence and infundibular stalk and terminate in the central, lateral and dorsal areas of the pars distalis, as schematically diagramed in Figure 22. Thus, the present paper supports the "point to point" theory of hypophyseal portal circulation, principally obtained or introduced by transection experiments of the hypophyseal stalk, in which the blood in the anterior, lateral and posterior areas of the median eminence flows into the central, lateral and dorsal areas of the pars distalis, respectively (Donovan and Harris, 1954; Daniel et al., 1958; Adams et al., 1964). The fine transverse anastomoses here observed among the sinusoidal capillaries in the pars distalis may act as buffer channels to homogenize the blood flow within the pars distalis.

In addition to the long portal vessels, previous light microscopic studies of India ink-injected and sectioned or transilluminated samples of various animals—including the rat—have shown that the "short" portal vessels run in the dorsal (lateral) transitional zones and connect the capillary bed of the infundibular process to that of the pars distalis from the dorsal (lateral) aspect (Green, 1951; Daniel and Prichard, 1957; Adams et al., 1964; Smith-Agreda, 1966). These short portal vessels were clearly demonstrated in the present study and referred to as the lateral short portal vessels, judging from their positioning. In addition to these lateral short portal vessels, the present study elucidated other short portal vessels connecting the infundibular process and the pars distalis from the anterior and posterior aspects. For clear differentiation from the lateral short portal vessels, they are called the anterior
Fig. 14.1. Subependymal capillary network (SB) and its connecting vessels (pubescent female rat, dorsal view). Note that the subependymal capillary network (SB) receives its afferent vessels (thin arrows: infundibular ascending arterioles, thick arrow: infundibular descending arteriole) from the branches (ha, hm, mh) of the hypophyseal and hypothalamic arteries, and emits its efferent venules (thin arrowhead: infundibular descending venule, thick arrowhead: infundibular ascending venule) continuous with the long portal vessel (rp) and hypothalamic vein branch (av). Abbreviations: see also Table 1. ×90
Fig. 14-2. Legend on the opposite page.
Fig. 14-2. Another example of the subependymal capillary network (SB) and its connecting vessels (aged male rat, dorsal view). Note that this subependymal capillary network (SB) is derived from the peri-infundibular ascending arterioles (pa) and infundibular ascending arterioles (a, b) (see Insets A and B) and connected via the infundibular ascending venules (vh) into the branches (av, mv) of the hypothalamic veins (thick arrowheads) and also via the infundibular descending venule (arrow VP) (see Inset C) into the long portal vein. Also note that this network receives an arteriolar capillary (thin arrowheads, infundibular descending arteriole or arterial capillary) from a branch of the middle hypophyseal artery (hm). Insets A, B and C show the dissected forms of the a, b and vp vessels. These dissections clearly confirm that the a and b vessels are, though closely associated with the loops (cl1, cl2), the infundibular ascending arterioles (ia) arising from the branches of the anterior hypophyseal arteries (ha), and that the vp vessel is an infundibular descending venule continuous with a long portal vessel (rp). Abbreviations: see also Table 1. ×120, Inset A : ×200, B : ×180, C : ×180

Fig. 15-1. Sagittally freeze-cut blood vascular bed of the median eminence anterior lip (AM). Note that the blood vascular beds of the hypothalamus (latero-basilar and periventricular area, HL) give off many vessels (a, b, c, d, e, f, g) which continue into the subependymal capillaries (sb1, sb2), median eminence capillary bed (arrowhead) and median eminence capillary loops (cl1, cl2). It is clear that the g vessel with its direct continuity with the median eminence capillary bed is an infundibular descending arteriole or arterial capillary since it arises from a hypothalamic branch (ah) of the anterior hypophyseal artery. Abbreviations: see also Table 1. ×140
Fig. 15-2. Dissected form of the specimen in Figure 15-1. Note that the a, b, c, d and f vessels arise from the peri-infundibular ascending arteries or arterioles (pα1, pα2, pα3). Also note that in Inset A that the e vessel arises from the peri-infundibular ascending arteriole (pα4) (thin arrowhead). Thus, the a, b, c, d, e and f vessels are all infundibular descending arterioles or arterial capillaries. The thick arrowhead indicates the broken edge of the g infundibular descending capillary in Figure 15-1. ×160, Inset A: ×150
Fig. 16. Typical infundibular ascending venules (vh) which arise from the subependymal capillary network (SB) or capillaries (sb) and continue into the hypothalamic vein branches (mv) (thick and thin arrowheads). Inset A shows a typical infundibular ascending venule (vh) which arises from the subependymal capillary network (SB) near the infundibular stalk and continues into a hypothalamic vein branch (mv) (thin arrow). An infundibular descending arteriole (thick arrow) is also seen in this inset. Abbreviations: see also Table 1. ×80, Inset A: ×50
Fig. 17. A typical infundibular descending arteriole (pd) which arises from a branch (ah) of the anterior hypophyseal artery (HA) and continues into a capillary loop (cl) of the median eminence anterior lip. The b vessel is also an infundibular descending arteriole which arises from the arterial branch (thick arrowhead) in the hypothalamus and continues into the loop (cl). An infundibular ascending arteriole penetrating the capillary bed of the median eminence posterior lip (PM) and continuing into the subependymal capillary network (SB) is observed at the lower part of this figure (thin arrowhead). Inset A shows a closer view of the pd and b
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Fig. 18. A typical infundibular descending venule (vp) which arises from the subependymal capillary network (SB), penetrates the capillary bed of the median eminence anterior lip (AM) and continues into an anterior long portal vessel (rp). A typical infundibular ascending arteriole (ia) is also seen, which penetrates the capillary bed of the median eminence anterior lip (AM) and continues into the subependymal capillary network (SB). Abbreviations: see also Table 1. X320

vessels and their connections to the loop (cl). Inset B shows a typical peri-infundibular ascending arteriole which continues into the hypothalamic capillaries (HL) (thin arrowheads) and subependymal capillary network (SB) (thick arrowhead). Abbreviations: see also Table 1. X80, Inset A : X280, B : X120
Fig. 19. A typical infundibular ascending arteriole (ia) which arises from a branch (ha) of the anterior hypophyseal artery (HA), penetrates the capillary bed of the median eminence anterior lip (AM) and continues into the hypothalamic capillaries (HL). Inset A shows an infundibular ascending arteriole (ia) which arises from a branch (hm) of the middle hypophyseal artery (HM), penetrates the capillary bed of the median eminence anterior lip (AM) and continues into the subependymal capillary network (SB). Abbreviations: see also Table 1. ×130, Inset A: ×290
and posterior short portal vessels, respectively. Our preliminary light microscopy of India ink-injected and sectioned samples has shown that the anterior and posterior short portal vessels pass through the anterior and posterior transitional zones, respectively. It is considered that the blood flow in the anterior, lateral and posterior short portal vessels is principally directed toward the pars distalis since these short portal vessels originate in the capillary bed of the infundibular process directly supplied by the middle, accessory middle and posterior hypophyseal arteries.

The present paper, together with our previous one (MURAKAMI et al., 1985), clearly demonstrates that, in the rat, the capillary bed of the pars intermedia fully develops after puberty and that this bed directly receives the arterial branches from the middle, accessory middle and posterior, or hypophyseal arteries. It then emits the anterior, lateral and posterior intra-adenohypophyseal portal vessels draining into the capillary bed of the pars distalis, though it has many fine capillary connections with the capillary bed of the infundibular process (intercommunicating capillaries between the pars intermedia and infundibular process) (see above). Our preliminary experiments in this study have shown that the anterior, lateral and posterior intra-adenohypophyseal portal vessels pass through the anterior, lateral and posterior transitional zones, respectively, and that the intercommunicating capillaries penetrate the membranous connective tissues between the pars intermedia and infundibular process. It is believed that the blood flow in the intra-adenohypophyseal vessels is principally directed toward the pars distalis since the capillary bed of the pars intermedia is directly derived from the arterial branches, and that the blood in the intercommunicating capillaries is principally directed toward the pars intermedia since the intercommunicating capillaries originate very close to the arterial capillaries in the pars distalis (MURAKAMI et al., 1985).

Some experimental studies in the rat, dog, monkey, and other animals have shown that the pars distalis can survive to a considerable degree even when the hypophyseal stalk is completely transected or interrupted (DONOVAN and HARRIS, 1954; DANIEL et al., 1958; ADAMS et al., 1964). It is thought that the anterior, dorsal and posterior short portal vessels and intercommunicating capillaries between the pars intermedia and infundibular process convey the blood in the capillary beds of the infundibular process and pars intermedia to the capillary bed of the pars distalis, there to survive the pars distalis after such stalk transection or interruption.

Certain authors have observed carmine gelatin-or India ink-injected and sectioned or transilluminated samples of the dog, rat, mouse and other animals with a light microscope, and described some ascending portal vessels which arose from the capillary bed of the infundibular process to continue on into the capillary bed of the hypothalamus (BASIR, 1932; OFUJI, 1949). Such ascending portal vessels were never noted in the present study. It is presumed that these authors misinterpreted the capsular capillaries of the hypophysis (more strictly, the fine venous twigs arising from the capsular capillaries and continuing into the perihypothalamic dural veins) as the ascending portal vessels. It has been reported in man, rat and other animals by the similar light microscope methods or scanning electron microscopy of vascular casts that the pars tuberalis is commonly supplied by the primary capillary plexus or by the long portal vessels (GREEN, 1966; PAGE et al., 1978). The present study, however, reveals that the pars tuberalis of the adult and aged rats is provided with its proper sinusoidal capillaries, which arise from the primary capillary plexus and descend into the capillary bed of the pars distalis. The present study also reveals that these sinusoidal vessels directly receive some arterial terminals or capillaries from the
Fig. 20. A typical infundibular ascending arteriole (ia or arrow) which arises from a branch (hm) of the accessory middle hypophyseal artery, penetrates the capillary loop (cl) of the capillary bed of the infundibular stalk (dorsal part, DS) and continues into the capillary bed of the hypothalamus (latero-basilar and peri-ventricular area, HL).
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anterior, middle and accessory middle hypophyseal arteries. Though not noted in the present study, some authors described some arterial terminals which arose from these arteries and directly continued into the capillary bed of the pars distalis (Wislocki and King, 1936; Negm, 1971). It is presumed that these authors misinterpreted those arterial terminals continuing into the tuberal vessels or the arterial vessels supplying the hypophyseal capsule as the direct arterial terminals to the pars distalis. The present study, moreover, gives evidence that the long portal vessels directly receive some arterial terminals from the anterior, middle and accessory middle hypophyseal arteries. As far as we know, no one has reported such direct arterial continuities into the long portal vessels.

The present study clearly demonstrated in the rat that many arterial twigs (infundibular ascending arterioles) penetrate the primary capillary plexus to supply the subependymal capillary network and hypothalamic capillary bed, and that many arterial branches or arteriolar capillaries in the hypothalamus (infundibular descending arterioles, see above) descend into the median eminence to supply the subependymal network and the primary capillary plexus. These findings primarily coincide with those of Duvernoy (1972) who studied the India ink-injected and sectioned samples of the monkey, dog and other animals. In accordance with Duvernoy (1972), neither a vessel originating in the capillaries of the median eminence and infundibular stalk and terminating in the hypothalamic capillaries, nor a vessel originating in the capillaries in the pars distalis, pars intermedia and infundibular process and terminating in the hypothalamic capillaries was noted. Thus, it is likely that Basir (1932), Török (1964), Holmes (1967), Negm (1971) and some other authors, who observed living dog tissues with a vital light microscope or India ink-injected and sectioned samples of the monkey, rat and mouse with a light microscope, misunderstood our infundibular ascending arterioles to be feedback portal vessels from the hypophysis or median eminence to the hypothalamus. Page and his associates observed vascular casts of the monkey, dog, rabbit, and rat with a scanning electron microscope, but failed to observe our infundibular ascending and descending arterioles and also infundibular ascending and descending venules. This is probably due to their omission of dissection or of their use of non-diluted Batson's plastic, which is highly viscous and not always suited for full infusion into the hypothalamic and hypophyseal capillary beds (see above) (Page et al., 1976, 1978; Page and Bergland, 1977; Bergland and Page, 1979). Page and his associates also described by their scanning electron microscopy of the vascular casts of the monkey, dog, rabbit and rat how numerous capillaries or fine vessels connect the capillary beds of the median eminence and infundibular stalk to the hypothalamic capillaries (Page et al., 1978; Bergland and Page, 1979). However, we could not observe such capillaries except for the infundibular ascending and descending arterioles and infundibular ascending and descending venules. That is to say, all the vessels herein observed in the hypothalamic-hypophyseal junctions were included in either of the infundibular ascending arterioles, infundibular descending arterioles, infundibular ascending venules or infundibular descending venules.

Inset A shows a dissected form of this infundibular ascending arteriole (arrow) prior to dissection. Insets B and C show further dissected forms of the loop (cl). Note in these insets that the loop (cl) has communication with the infundibular ascending arteriole (ia) (thin arrowhead) and also the capillary bed of the infundibular stalk (thick arrowhead). Abbreviations: see also Table 1. ×230, Inset A: ×110, B: ×360, C: ×470
Fig. 21. Schematic diagram showing the vascular arrangements of the rat hypophysis and hypothalamus. Abbreviations: see also Table 1
The present study, moreover, clearly demonstrated in the rat that the primary capillary plexus of the hypophyseal portal system protrudes numerous capillary loops into the anterior lip of the median eminence, and that the subependymal capillary network, located dorsally to the loops, receives the infundibular ascending and descending arterioles from the hypophyseal and hypothalamic arteries and emits the infundibular ascending and descending venules continuous with hypothalamic veins and long portal vessels. These loops may be especially importance for catching the hypothalamic hormones, especially thyrotropin and growth hormone releasing factors.

Fig. 22. Schematic diagram showing the distribution of the long portal vessels within the pars distalis. Abbreviations: see also Table 1
(FUXE et al., 1984). It is unknown whether or not the subependymal network catches the hypothalamic hormones. However, it may be natural to consider that the blood conveyed into the subependymal network via the infundibular ascending and descending arterioles flows into the capillary bed of the pars distalis via the infundibular descending venules and long portal vessels and also into the hypothalamic veins via the infundibular ascending venules. Many authors seem to include the subependymal capillary plexus in the loops (DUVERNOY, 1972; PAGE et al., 1978). However, this network should be described as an independent vascular unit, as it has only a few connections with the loops. Furthermore, it should be noted that the occurrence of the subependymal network is inconsistent among the species. For examples, the subependymal network poorly developed or absent in the monkey and dog (MURAKAMI, 1975b; KIKUTA et al., 1984), while it is well developed in the mouse (unpublished data).

As discussed above, it has generally been believed that the blood flow in the long, short and intra-adenohypophyseal portal vessels is directed toward the pars distalis, and that the blood flow in the intercommunicating capillaries between the pars intermedia and pars distalis is directed toward the pars intermedia. However, recent immunoassay studies of the rats have detected hypophyseal hormones, including MSH and oxytocin, in the blood in long portal vessels (OLIVER et al., 1977; GIBBS, 1984; HORN et al., 1985). These studies suggest that the blood in the long, short, intra-adenohypophyseal portal vessels and the intercommunicating capillaries can return in part to the median eminence, infundibular stalk and also infundibular process. PAGE and his associates investigated the monkey, dog, rat and other animals by the vascular casting/scanning electron microscope method, and showed limited potential for venous drainage of the pars distalis into the systemic veins, or the inflow of blood in the pars distalis into the median eminence, infundibular stalk and infundibular process (PAGE et al., 1978; BERGLAND and PAGE, 1979). The present study confirms that the efferent veins of the pars distalis (ventral and dorsal adenohypophyseal veins) are relatively thin in contrast to the thick efferent veins of the infundibular process (neurohypophyseal veins). It should be further noted that the anterior, middle and accessory middle hypophyseal arteries have marked original constrictions. These constrictions, probably representing endothelial cushions, may limit the inflow of blood into the median eminence, infundibular stalk and upper one third of the infundibular process as well as the hypothalamus, to keep the blood pressure in these components relatively low. Furthermore, it should be noted that the posterior hypophyseal arteries have no such marked original constrictions. This may mean that the blood pressure in the lower two thirds of the infundibular process is relatively high, in order to help the retrograde blood flow in the infundibular stalk and upper third of the infundibular process to the median eminence. The deep location of the original branches of the neurohypophyseal veins within the infundibular process may also be an important factor to allow such retrograde blood flow to the median eminence.

As discussed above, no feedback vascular route from the hypophysis to hypothalamus exists in the rat except for the possible countercurrent or switch vascular system between the hypophysis and median eminence. An interesting theory for a neural ultrashort feedback system has recently been proposed for the median eminence. FUXE et al. (1984) reported that, in the rat, the dopamine or catecholamine nerve terminals in the median eminence regulate the secretion of the respective hypothalamic hormones (hypophyseal hormone-releasing and hormone-release-inhibitory factors).
GLYDON (1957) studied India ink-injected and transilluminated specimens of the rat, offering evidence that the basic architecture of the hypophysis was established in the early fetal stage. Similar findings have also been obtained by TERNEBY (1972) who observed India ink-injected and sectioned samples of fetal, juvenile and adult rabbits. GALABOV and SCHIEBLER (1983) made supplementary studies of the sectioned samples of fetal and newborn rats with a transmission electron microscope, and described that the formation of the loops of the primary capillary plexus as being completed during the 18th fetal day and 10th day after birth. However, the present paper holds that the loops in this stage are simple, and that the capillary bed of the intermediate lobe develops much later (see above).

It is noteworthy that the paraventricular and supraoptic nuclei and mamillary bodies are provided with denser capillary beds than are adjacent ones of the hypothalamus. This may suggest that these nuclei and bodies have some increased metabolic activities (AKMAYEV, 1971).

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