

Anatomy of the hypothalamus and pituitary gland

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Some knowledge of the anatomy of the hypothalamus and pituitary and of the neurovascular pathways connecting them is essential for understanding the endocrine and other dysfunctions that result from any lesion involving either the hypothalamus or the pituitary or which damages their connecting pathways. When the pituitary gland is removed or is deprived of stimuli from the hypothalamus 'hypopituitarism' results. In hypopituitarism the endocrine organs show the most striking changes, but all the tissues of the body are affected to a greater or lesser extent (Sheehan, 1937; Sheehan and Summers, 1949; Daniel and Prichard, 1975).

The anterior lobe (pars distalis) of the pituitary gland develops as an upgrowth of epithelial tissue from the primitive pharynx (Rathke's pouch) which

meets a downgrowth from the base of the brain, the latter being destined to form not only the infundibular process (posterior, or neural, lobe) of the pituitary but also the neural part of the pituitary stalk. The early arrangements in the human have been illustrated by Daniel (1966a). The parts of the adult human pituitary gland and of the pituitary stalk are shown in Fig. 1. The nomenclature of these structures is confusing and some of the names which have been applied to certain parts of the pituitary complex and the hypothalamus in animals should not be transferred uncritically to man. Daniel and Prichard (1975) have explained the names of the various parts of these structures.

Hypothalamus

The hypothalamus lies at the base of the brain, around the third ventricle, extending from a plane immediately anterior to the optic chiasma to one immediately posterior to the mammillary bodies. Laterally its borders, somewhat ill-defined, are roughly the optic tract, the internal capsule, pes pedunculi, globus pallidus, and ansa penduncularis at various anteroposterior planes, while superiorly it does not extend above the level of the anterior commissure. Its weight in the adult human is less than 2.5 g. Lévêque (1974) thinks that the hypothalamus should be given the status of an endocrine organ, while Stumpf (1975) suggests that the whole brain should be regarded as an endocrine gland.

NERVE CELLS OF THE HYPOTHALAMUS

The small mass of cerebral tissue which comprises the hypothalamus contains some extremely well-defined nuclei but also others whose outline cannot be so easily determined. Some of the latter stand out more clearly in the fetus than in the adult (Clark, 1938). The general arrangements of the more readily identifiable nuclei are shown in Figs. 2 and 3. The most striking of all are the supraoptic, composed almost wholly of large nerve cells, and the paraventricular nuclei, composed mainly of large nerve

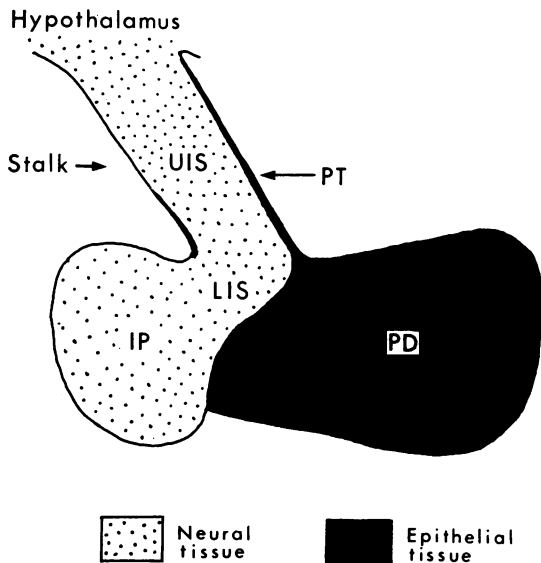


Fig. 1 Diagram of human pituitary gland in sagittal section. 'Neural tissue' indicates the neurohypophysis; 'epithelial tissue' the adenohypophysis. IP = infundibular process (posterior lobe). LIS = lower infundibular stem. PD = pars distalis (anterior lobe). PT = pars tuberalis. UIS = upper infundibular stem.

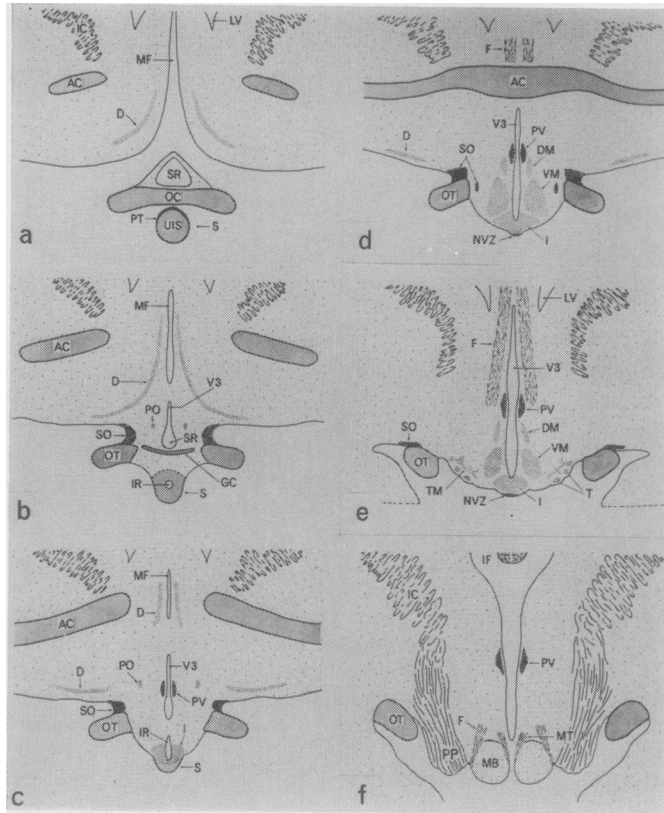


Fig. 2 Human hypothalamus and adjacent parts in coronal planes. Sequence of diagrams showing main landmarks and structures in anteroposterior sections (a to f) based on study of serial sections of many normal human cases (see also Fig. 3) AC = anterior commissure. D = nucleus of diagonal band of Broca. DM = dorsomedial nucleus. F = anterior column of fornix. GC = Gudden's commissure. I = infundibular nucleus. IC = internal capsule. IF = intraventricular foramen. IR = infundibular recess of third ventricle. LV = lateral ventricle. MB = mamillary body. MF = midline fissure separating the two hemispheres. MI = massa intermedia and part of thalamus. MT = mamillo-thalamic tract. NVZ = neurovascular zone. OC = optic chiasma. ON = optic nerve. OT = optic tract. PO = preoptic nucleus. PP = pes pedunculi. PT = pars tuberalis. PV = paraventricular nucleus. S = pituitary stalk. SO = supraoptic nucleus. SR = supraoptic recess of third ventricle. T = lateral tuberal nucleus. TM = tubero-mamillary cells. UIS = upper infundibular stem (neural tissue of pituitary stalk). VM = ventromedial nucleus. V₃ = third ventricle.

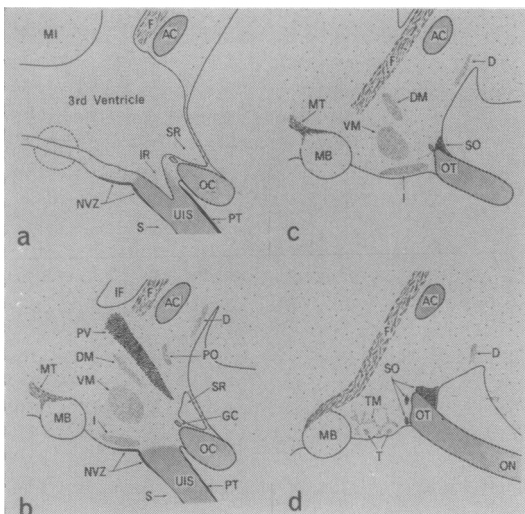


Fig. 3 Human hypothalamus and adjacent parts in sagittal planes traced from median plane laterally (a to d; anterior to right). For key to lettering see Fig. 2.

cells but also with a number of smaller cells. The large cells of these nuclei synthesise vasopressin and oxytocin and also a binding protein, neurophysin, which is rich in cystine (Hope, 1975; Watkins, 1975; Zimmerman *et al.*, 1975).

This complex of substances, but probably mainly the neurophysin, can be stained by Gomori's chrome-alum-haematoxylin method. Since this complex passes down the axons of the cells into the hypothalamo-neurohypophysial tract on its way to end by entering the capillaries of the infundibular process the course of the axons, both in the hypothalamus and the tract, may be traced by this means. The classical studies on neurosecretion by the Scharrer and by Bargmann are reviewed by Stutinsky (1974), as is more recent work.

There are still many puzzling features about neurosecretion. For example, in the normal adult human hypothalamus and hypothalamo-neurohypophysial tract few cells or nerve fibres take the stain for neurosecretory material, although in children and in cases of hypophysectomy or section of the pituitary stalk the picture is different (Daniel and Prichard, 1975). Knowles and Vollrath (1974) review neurosecretion.

The nuclei in the basal part of the hypothalamus, especially those in the tuber cinereum (around the

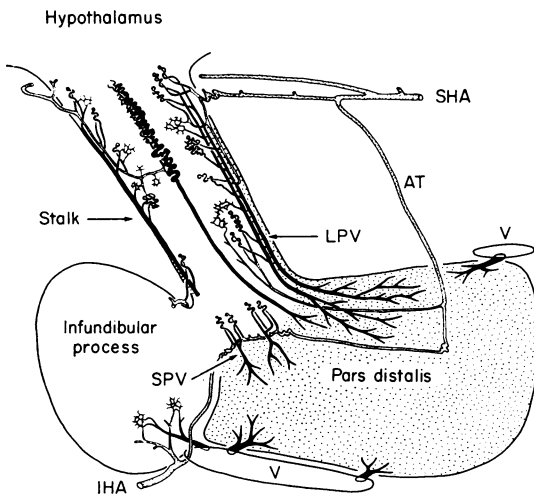


Fig. 4 Human pituitary gland. Diagram in sagittal section showing main features of blood supply. Note sinusoids of the pars distalis are supplied by two groups of portal vessels: long portal vessels (LPV) draining characteristic capillary loops in the upper infundibular stem (neural tissue of stalk) and short portal vessels (SPV) draining similar capillary loops in lower infundibular stem. AT = artery of the trabecula. IHA = inferior hypophysial artery. SHA = superior hypophysial artery. V = venous sinus.

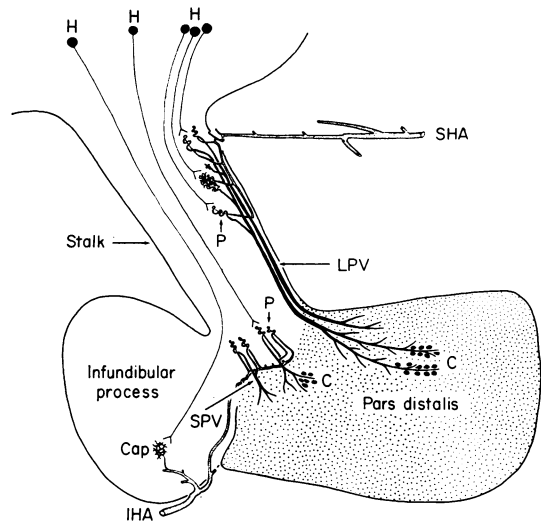


Fig. 5 Diagram of human pituitary gland in sagittal plane showing neurovascular pathways by which nerve cells in certain hypothalamic nuclei (H) control output of anterior and posterior pituitary hormones. Axon on left ending on the capillary bed (Cap) in the infundibular process represents the tract from the large nerve cells of the supraoptic and paraventricular nuclei, which are concerned with posterior pituitary function. The other axons have their origin in nerve cells in the so-called hypophysiotrophic area of the hypothalamus and end on the primary capillary bed (P) feeding the portal vessels which supply the pars distalis. Here their neurohormones are transmitted into the blood stream and are then carried through the long and the short portal vessels (LPV, SPV) to the epithelial cells (C) in a given area of the pars distalis to control the output of hormones from these cells.

infundibular recess) and in the adjacent parts (Figs. 2, 3) are concerned mainly with the production of the releasing and inhibiting factors (neurohormones) which control the activities of the pars distalis, the anterior lobe. This region has been called the 'hypophysiotrophic area' and information on its activities has been derived almost entirely from animal work (Szentágothai *et al.*, 1968; Halász *et al.*, 1975). However, Okon and Koch (1976) have recently localised gonadotropin-releasing hormones in this area of the human brain. Halász *et al.* (1975) describe some of the afferent connections of this area. The efferent nerve fibres from the nuclei of the hypophysiotrophic area are non-myelinated and join the fibres of the hypothalamo-neurohypophysial tract to end on the coiled capillaries which form the primary capillary bed of the long and short portal vessels (Figs. 4, 5).

The identifiable nuclei of the hypothalamus lie among numerous small nerve cells, which are not grouped into recognisable nuclei, and among fine nerve fibres which, in the main, are non-myelinated. A few tracts composed of myelinated fibres, such as the fornix and the mamillo-thalamic tract (Figs. 2, 3), pass through the hypothalamus, in which they originate or end.

There has recently been renewed interest in the function of some of the specialised cells of the ependyma of the third ventricle. Certain of these cells pass their secretions into the cerebrospinal fluid and others appear to send processes which end on coiled capillaries, and perhaps on other capillaries, into which they probably pass their secretions. Rodríguez (1976) gives a valuable review of the subject, while Kumar and Kumar (1975) report interesting findings about the so-called 'tanyocyte ependyma'.

AFFERENT AND EFFERENT NEURAL PATHWAYS OF THE HYPOTHALAMUS

The major afferent tracts tend to lie in the lateral parts of the hypothalamus while the efferent tracts lie nearer to the midline, although large numbers of both afferent and efferent non-myelinated nerve fibres connect the hypothalamic nerve cells with the various parts of the cerebral hemispheres, brain stem, and elsewhere and form a sort of capsule of nerve fibres around the hypothalamus. Relatively few of the neural pathways in the human hypothalamus are known in detail, and much of our knowledge of hypothalamic connections has had to be gained from animal experimental work (Raisman, 1966). Much remains to be learned from careful morphological studies of the human hypothalamus, especially from brains in which lesions have occurred which might be termed 'experiments of nature' (Daniel and Treip, 1977). There are various single studies on human material and Clark (1948) has reviewed some of the connections of the hypothalamus with the frontal lobes of the brain.

A massive tract of myelinated fibres, the fornix brings impulses from each temporal lobe to the ipsilateral mamillary body. One major efferent tract, more medially situated, is the mamillothalamic tract. It is composed of myelinated fibres and connects each mamillary body with the ipsilateral anterior nucleus of the thalamus, from which impulses are relayed to the frontal lobes. That there are efferent hypothalamo-autonomic tracts passing down the spinal cord directly to the preganglionic nuclei of the sympathetic and parasympathetic systems has recently been confirmed by Saper *et al.* (1976).

Another major efferent tract, composed almost

entirely of non-myelinated nerve fibres, is the hypothalamo-neurohypophysial tract formed by the axons of neurosecretory nerve cells in the supraoptic and paraventricular nuclei which carry neurohormones to the neural lobe (infundibular process) of the pituitary. This important neuroendocrine tract carries vasopressin and oxytocin, the hormones which are destined to be released into the blood stream in the neural lobe or infundibular process (Figs. 4, 5). The hypothalamo-neurohypophysial tract is joined by fibres of the tubero-infundibular tract arising from nerve cells situated in the hypothysiotrophic areas, which are destined to end on coiled capillaries (Fig. 5).

BLOOD SUPPLY OF THE HYPOTHALAMUS

The arterial supply is derived from the perforating vessels which spring from the various parts of the circle of Willis and pass through the anterior and posterior perforated substances. In addition to these small arteries two vessels, the superior hypophysial arteries, which arise from the internal carotid arteries, form an arterial ring around the tuber cinereum. Branches from this ring supply the optic chiasma and the adjacent parts of the hypothalamus. Many small arterial twigs from the ring pass into the pituitary stalk (Figs. 4, 6). The venous drainage enters into fairly large veins running in the basal cisterns (Duvernoy, 1975). Daniel (1963, 1966a, b) gives further details of the blood supply.

Pituitary Gland

The general arrangements of the pituitary gland are shown diagrammatically in Fig. 1. The epithelial cells forming the anterior lobe of the gland, or pars distalis, secrete their hormones directly into the blood flowing through the sinusoids that run between the cells (Figs. 5, 7). The granules within these cells identify the various types of cell. These granules however, are difficult to study in human glands since it is not easy to obtain fresh specimens. Conklin (1966, 1968) gives useful descriptions of these cells in the human (see also Doniach, 1977). The literature on the cells of the pars distalis in animals is vast, though relatively little work has been done on human material. The cells of the infundibular process have been rather neglected in recent years, but Daniel and Prichard (1975) give some data on their reactions.

Neurovascular link between hypothalamus and pituitary gland

The pituitary stalk comprises mainly neural and vascular components, though an incomplete layer of

epithelial cells, the pars tuberalis, whose function is uncertain, covers its ventral aspect (Figs. 1, 5). The bulk of the stalk is made up of neural tissue in which lie the various coiled capillary vessels on which end the nerve fibres that are derived from cells in the hypophysiotrophic area. The neurohormones coming down these nerve fibres are transferred from the endings of the fibres into the blood passing through the coiled capillaries, and thus into the portal vessels. These portal vessels, as was first pointed out by Xuereb *et al.* (1954b), can be classified as long and short (Fig. 4). The origin of the vessels which supply them makes a distinction most important. The afferent arterioles to the coiled capillaries from which the *long portal vessels* are derived spring from the arterial ring supplied by the superior hypophysial arteries (arising from the internal carotid arteries

above the level of the diaphragma sellae), while those which supply the coiled capillaries that form the *short portal vessels* are derived from the inferior hypophysial arteries, which leave the internal carotid arteries within the cavernous sinus. The long portal vessels run down the pituitary stalk to supply the larger part of the pars distalis, while the short portal vessels supply a restricted part of the lobe adjacent to that part of the lower infundibular stem which is buried in the pars distalis (Fig. 4). Xuereb *et al.* (1954a, b) describe this system of vessels, and Daniel and Prichard (1975) also describe the system in other species. A portal system of vessels is found in all vertebrates, and a valuable recent study is of that in the horse (Vitums, 1975).

When the pituitary stalk is cut surgically, to try to produce regression of various forms of carcinoma

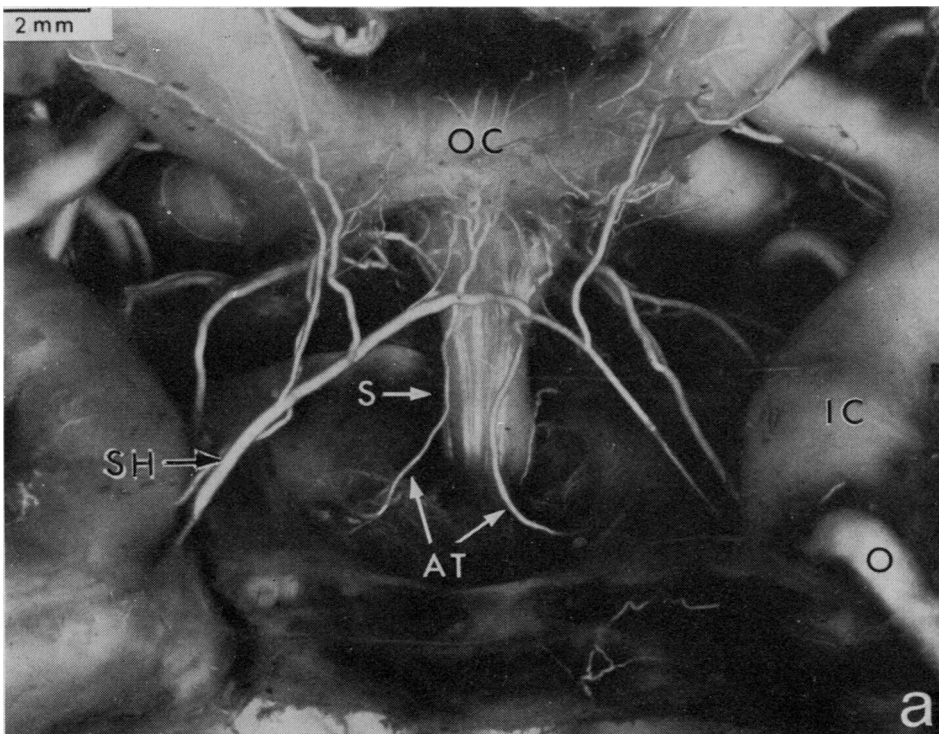


Fig. 6 *Injected, partially macerated preparation of human pituitary gland showing some of the main features of the vascular arrangements. Gland and neighbouring structures are viewed from the front. Note superior hypophysial artery (SH) springing from the internal carotid artery (IC) on each side, anastomosing in front of the pituitary stalk (S), and giving off branches to supply a primary capillary bed (not visible here) within the stalk. The long portal vessels which drain this bed and run down the stalk into the pars distalis are better seen in Fig. 7. The artery of the trabecula (AT), although plunging into the pars distalis, does not deliver blood directly to this lobe, which has a purely portal venous blood supply (see Fig. 4.) O = ophthalmic artery. OC = optic chiasma.*

or halt the progress of diabetic retinopathy, all the blood coming down the stalk in the long portal vessels is cut off and a large infarct is formed in the pars distalis involving up to 90% of the lobe. The afferent blood supply to the short portal vessels, however, is spared so that they continue to transmit blood and the small part of the pars distalis which they supply remains viable (Daniel and Prichard, 1975).

In one interesting case of head injury, reported by Daniel *et al.* (1959), the pituitary stalk had been torn across *above* the level of the arterial ring derived from the superior hypophysial arteries (Fig. 4). Thus the afferent arterial supply to the coiled capillaries in the stalk, which gives origin to the long portal vessels, was preserved and an infarct had not developed in the pars distalis.

Although a small part of the pars distalis survives after transection of the pituitary stalk the surviving

cells do not secrete any appreciable quantity of hormones, since the nerve fibres bringing neurohormones down the stalk have been severed and the cells are thereby effectively 'denervated'—that is, the blood supplying them does not contain releasing or inhibiting factors (Daniel and Prichard, 1975). It should be noted that there is no appreciable *direct* arterial supply to the pars distalis.

Advances in knowledge of the pathological changes in the human hypothalamus and pituitary can be made only by experts in the field. Daniel and Prichard (1975) indicate the difficult and time consuming nature of the necessary investigations.

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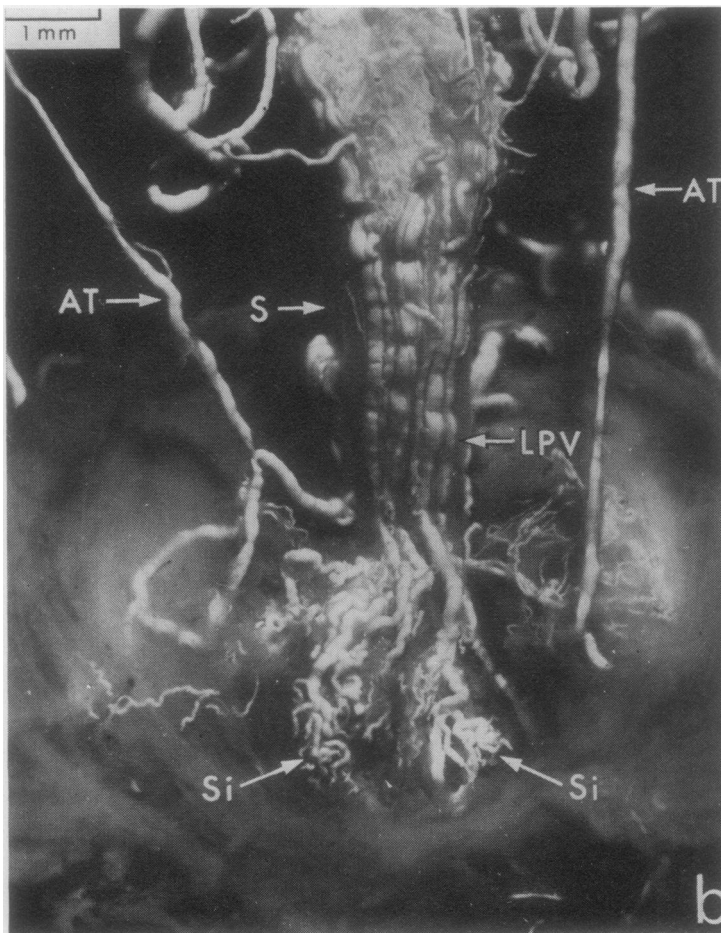


Fig. 7 *Injected, partially macerated preparation of human pituitary gland seen from the front showing some of the main features of the vascular arrangements. The long portal vessels (LPV) run down the stalk (S) and break up into the sinusoids (Si) of pars distalis. AT = artery of the trabecula.*

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