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REVIEW ARTICLE

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Brain cooling in humans – anatomical considerations

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Abstract Vascular arrangements allowing a bulky transfer of venous blood from the skin of the head and from nasal and paranasal mucous membranes to the dura mater provide an excellent anatomical basis for the convection process of cooling, caused by evaporation of sweat or mucus. The dura mater, with its extraordinarily high vascularization controlled by a potent vasomotor apparatus, may transmit temperature changes to the cerebrospinal fluid (CSF) compartment. Temperature gradients of the CSF may in turn influence the temperature of brain parenchyma (1) directly, along the extensive contact area between the cerebrocortical surface and the CSF-compartment, or (2) indirectly, via brain arteries that extend over long distances and arborize within the subarachnoid space before entering the pial vascular network and brain parenchyma. Numerous subarachnoid and pial arterial branches exposed to the CSF have diameters in the range of the vessels of the retia mirabilia of animals in which selective brain cooling has been clearly established experimentally. It is also shown that the arrangements of venous plexuses within the vertebral canal provide anatomical preconditions for a cooling of the spinal cord via the CSF. The possibility of spinal cord and spinal ganglia cooling by temperature convection via venous blood – cooled in the venous networks of the skin of the back – flowing through numerous anastomoses to the external and internal vertebral plexuses and, finally, into the vascular bed of the spinal dura is discussed on the basis of anatomical facts.

Key words Brain cooling · Meninges · Meningeal vessels · Brain vessels · Cerebrospinal fluid · Dural nerves

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Introduction

Selective brain cooling (SBC) is understood as a natural mechanism that enables mammals to maintain their brain temperature below the temperature of the rest of the body during states of hyperthermia (Baker 1979). In many species this mechanism has been associated with arterial retia mirabilia in certain head regions. These retia are immersed in venous sinuses or pass through dense venous plexuses, receiving blood from cooler mucosal or cutaneous areas (Simoens et al. 1987). Therefore, during hyperthermia caused by high environmental temperature or by muscular exercise and increased neuronal activity, heat transfer from the warm arterial to the cooler venous blood is possible before the blood reaches the central nervous system (CNS), thus protecting the brain from overheating. The fundamental ideas about the role of arteries in carrying cool blood to the brain and of veins in cooling retia mirabilia and draining warm blood from the brain are discussed extensively in the studies of Hayward and Baker (1969) and Baker (1979). For a review, see Baker (1982). Physiological data about thermal signals controlling SBC can be found in a recent study of Kuhnen and Jessen (1994). These authors conclude that the onset and degree of brain cooling in rete-mirabile species depend on internal body temperature and are predominantly determined by temperature signals generated in the hypothalamus. However, there are also indications of temperature sensors in other regions of the brain and in the trunk.

Selective brain cooling in humans?

The question whether SBC also operates in humans, who lack cranial retia mirabilia, has led to an interesting controversy. For some authors (Brengelmann 1987) the copious and constant arterial blood flow to the brain appears sufficient to cool the brain under all conditions. Others (Cabanac 1993) concede that this concept may be correct for the conditions at normothermia, but they propose that

an additional brain-directed cooling mechanism becomes effective during hyperthermia. These authors draw attention to vascular arrangements in humans, which permit effects comparable to SBC in "rete species". Cabanac (1993) points to several sites of intimate thermal contact between the arterial and the cooler venous blood, e.g., the internal carotid in the carotid canal, where the artery is tightly surrounded by the venous plexus caroticus and thereafter immersed in the cavernous sinus, and the vertebral arteries surrounded by a plexus of veins where they course through the transverse foramina (see our Fig. 14). Furthermore, Cabanac refers to the high cooling capacity of the skin of the head (particularly rich in sweat glands), whence venous blood, cooled by sweat evaporation, flows via emissary veins towards the brain in hyperthermic situations (Caputa et al. 1978; Cabanac and Brinnel 1985; Deklunder et al. 1991; Hiroshita et al. 1991). An additional loss of heat occurs in the upper airways (Cabanac 1993), including the paranasal sinuses. A direct conductive skin-brain heat exchange has also been considered.

Can anatomy contribute to an understanding of man's extraordinary adaptability to extreme temperature conditions?

There is no question that humans are capable of considerable mental and physical performances even in the hottest tropical regions. Convincing evidence for the existence or nonexistence of SBC in humans – practically very difficult to obtain (Jessen and Kuhnen 1992) – can only be provided by physiologists. However, detailed analysis of certain anatomical evidence may contribute to a better assessment of the different standpoints in the present controversy.

In this paper, in particular, we shall direct attention to: (1) the outstanding anatomical preconditions for bulk transfer of blood between extra- and intracranial venous plexus, and (2) the possible role of cerebrospinal fluid (CSF) in the thermoregulation of the CNS.

Anatomical considerations in the human

The vascular elements

Vascular arrangements in human meninges

Meninges must not be regarded simply as a sequence of three separate membranes. In fact, they constitute a distinct organ with various functions relating to the CNS: mechanical protection, metabolic and immunological functions and – last but not least – involvement in the thermoregulation of the brain and spinal cord. In the following, the anatomical facts relevant to an understanding of the last-mentioned function will be analysed.

A striking characteristic of the dura mater is its extraordinarily dense vascularization (Kerbler and Newton 1973; Roland et al. 1987), which cannot be explained exclusively by the periosteal function of the cranial dura; practically the same density of vessels is found in the spinal dura (Fig. 1), which does not serve any periosteal function. As the proper dural connective tissue, containing an abundant amount of collagen fibers, must be regarded as a bradytroph tissue with a low metabolic rate, the rich dural vascularization obviously meets particular functional needs, e.g. reabsorption of CSF (Zenker et al. 1994), and it also seems to be the clue to an understanding of the involvement of the meninges in thermoregulative mechanisms of the brain parenchyma.

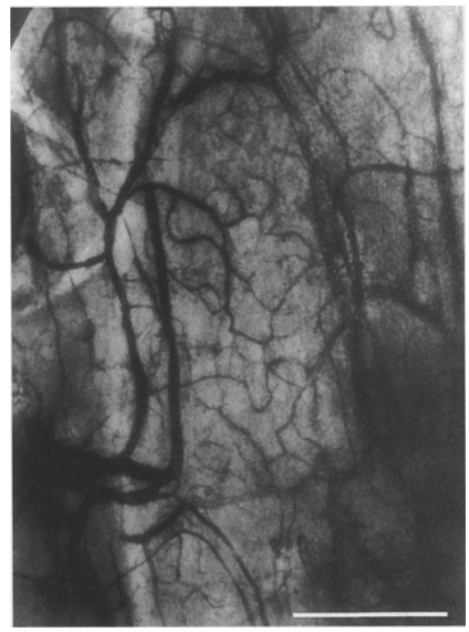

Fig. 1 Whole mount preparation of human spinal dura mater, 9-month-old male; focus directed on a net of naturally filled venules; capillaries only partly filled. *Bar* 1 mm

The arterial supply of the cranial dura mater

Three arterial systems participate in the supply of the cranial dura: the external and internal carotid arteries and the vertebro-basilar system. The dominant role is played by the external carotid arteries. All dural branches arising from these arteries show internal diameters between 400 and 800 μm and are interconnected by many intradural anastomoses that are found on the outer (periostal) surface of the dura (Kerber and Newton 1973; Roland et al. 1987). These "primary anastomotic arteries" with more or less constant diameters of 100–300 μm, give rise to (1) numerous smaller arteries (40–80 μm i.d.) supplying the skull bones, many of them reaching the scalp and the skin of the head via tiny canals in the bones or along emissary veins; (2) small arteries and arterioles penetrating the dural tissue obliquely, to end in an extremely rich capillary network in the inner part of the dura where the latter is connected with the arachnoid membrane.

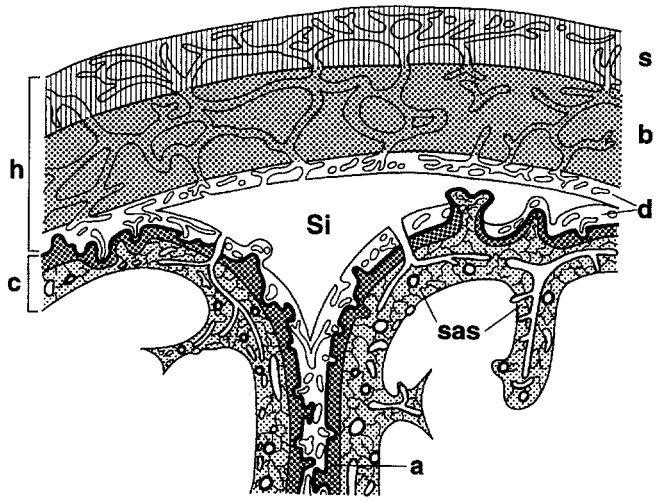

Fig. 2 Diagram showing communications between skin and dural venous systems. *a* Arachnoid membrane with projections of arachnoid villi into dura mater and into the wall of superior sagittal sinus (*Si*); *b* bony calvaria; *c* CSF compartment comprising arachnoid membrane and subarachnoid space (*sas*); *d* dura mater; *h* haemal compartment, comprising dura, calvaria, scalp and skin (*s*)

Dural veins

The dural veins and venules form a dense network of multiply anastomosing vessels (Fig. 1). The lumina of both the large and the small veins are separated from the dural tissue only by an endothelium (Roland et al. 1987). Fenestrated postcapillary venules and capillaries are found in dural layers near the arachnoid membrane (Nabeshima et al. 1975; Krisch et al. 1983; Andres et al. 1987; Zenker et al. 1994). Contrary to the principles governing the arterial system, where the dural supply is independent of cerebral arteries, there is a common drainage of cerebral, cerebellar *and* meningeal veins into the internal jugular veins via dural sinuses. Additionally, there are many interconnections with the external jugular veins and the vertebral venous plexuses. In particular, veins drain (1) into cranial sinuses and their plexiform extensions; (2) into "satellite" veins accompanying the main meningeal arteries, thus communicating with venous plexuses of the infratemporal region as well as with veins of the orbita, which in turn anastomose with facial veins; (3) into diploic veins of the skull and via this system into extracranial veins (veins of the scalp and adjoining subcutaneous venous plexuses).

The system of communication between meningeal and extracranial veins

The diploe of the bones of the calvaria contains a number of larger veins (3–5 mm i.d.) anastomosing with each other and with a network of microscopically small venous channels (Fig. 2). All diploic veins are lined merely by an endothelium and are devoid of valves. They communicate with dural sinuses and pachymeningeal veins on the one hand (Fig. 3) and with pericranial veins on the other (Fig. 2). Apart from the well-known "emissary

Fig. 3 Corrosion cast of cranial blood vessels in an adult human, demonstrating the distribution of both meningeal and cerebral vessels (preparation by A. Lang; *c* cerebral vessels reaching cortical tissue from the intergyral compartment of the SAS, *dv* dural vessels, *ma* middle meningeal artery accompanied by two satellite veins, *arrows* vessels from the dural vascular bed entering head bones, *p* pial vascular rete with many tiny vessels entering brain parenchyma) *Bar* 1 cm

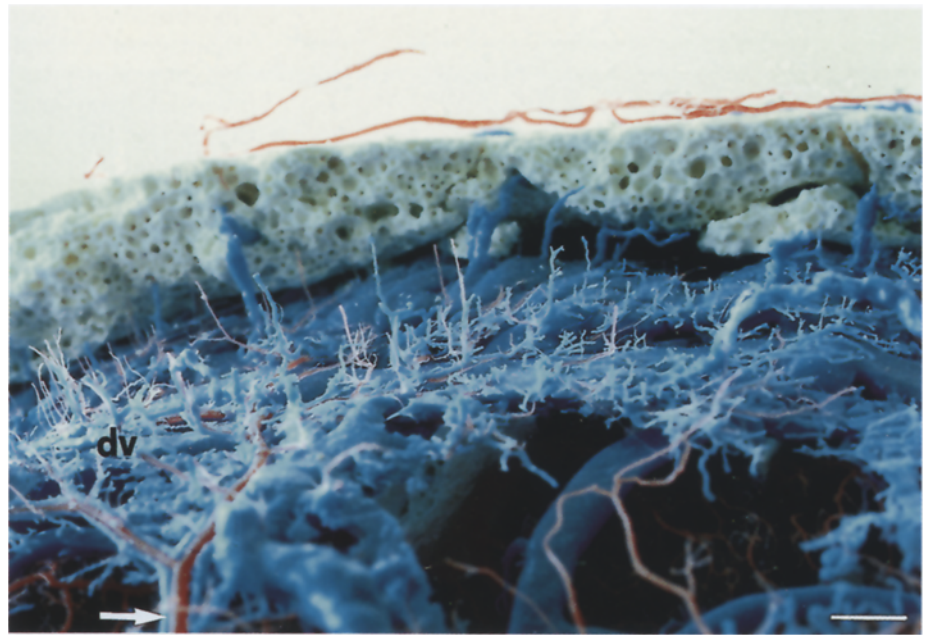

Fig. 4 Corrosion cast of cranial blood vessels. Parietal bone preserved. Note vessels arising from the dural vascular rete, entering the bone (*dv* dural vessels, *arrow* branch of middle meningeal artery) *Bar* 2 mm

Fig. 5 The external aspect of the calvaria (adult human). Note the density of vessels emerging from the parietal bone. *Bar* 6 mm

veins", there are innumerable connections to the systems of extracranial veins (Figs. 2, 4, 5). The term "emissary veins" is in fact misleading, because the blood often flows from outside to inside. Moreover, in many cases valves – sometimes well developed, sometimes rudimentary – can be found. Gisel (1958) has already suggested to call them "perforating veins". A similar wealth of connections can be found between the dura of the skull base and underlying extracranial venous plexuses: plexus maxillaris, plexus vertebralis, veins and venous plexuses of nasal and oral mucosa, pharyngeal plexus. In Fig. 6 we present a synopsis of the interconnections of venous systems, which are relevant for an understanding of the possible functional interactions via veins in heat transfer between the skin or mucosal membranes and the brain.

The nervous elements

Dural nerves – a potent vasomotor apparatus

In the light of the rich vascularization of the dura mater and its potential relevance for thermoregulative processes, it seems worthwhile to summarize the state of our present knowledge concerning the nerves of the dura mater and their vasomotor function.

Figure 7a, a whole-mount preparation stained for acetylcholinesterase activity, gives an idea of the density of nerves in the dura mater in man. There is now clear evidence (Stöhr 1928; Andres et al. 1987; Keller and Marfurt 1991) that various sources participate in the innervation of the cranial dura mater: all three divisions of the trigeminal nerve, the first three spinal nerves, vagal sensory fibres, the superior cervical ganglion of the sympathetic trunk (sympathetic fibres) and the pterygopalatine and otic ganglia (parasympathetic fibres). A considerable

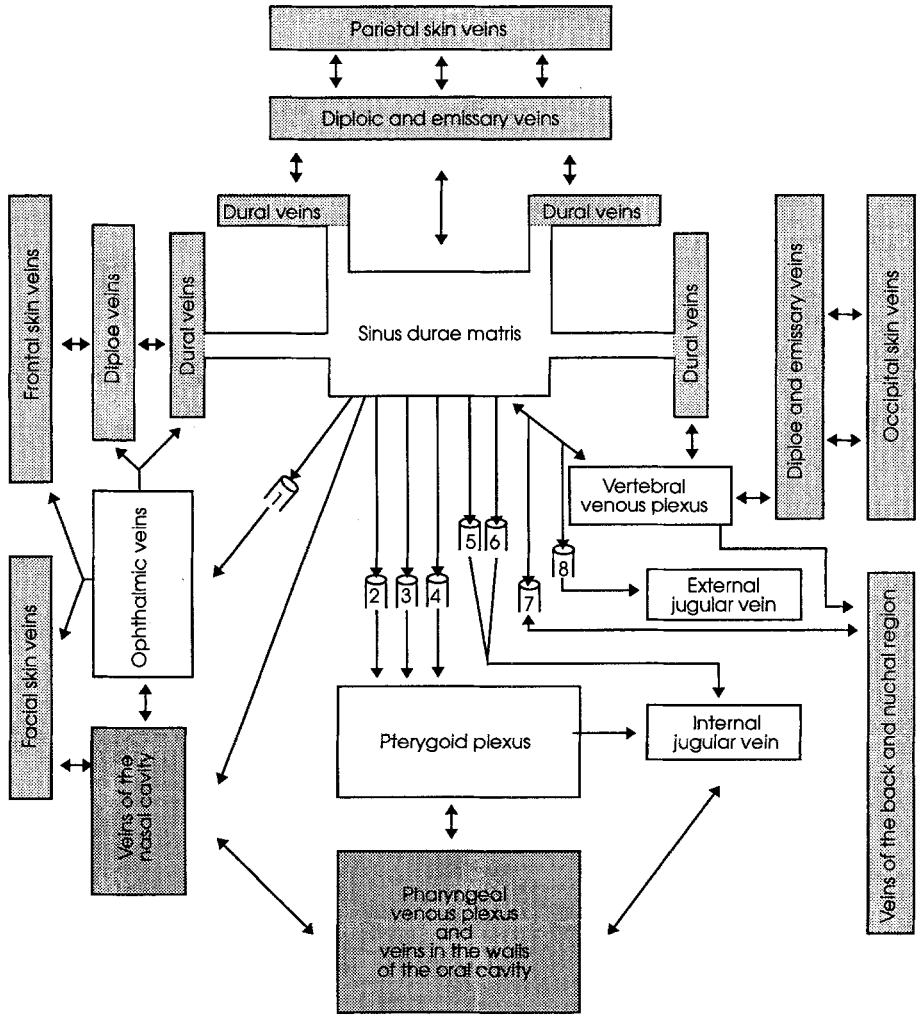

Fig. 6 Diagram showing the complexity of venous communications between vessels of skin and mucosal membranes on the one hand and dural veins and deep venous plexus of the head on the other. The pathways of drainage into the jugular veins and vertebral venous plexus are indicated (*light grey ground* veins under influence of sweat evaporation, *dark gray ground* veins under influence of evaporation of mucosal secretions, *1* superior orbital fissure, *2* venous plexus of foramen ovale, *3* venous plexus of foramen spinosum, *4* veins traversing the foramen lacerum, *5* venous plexus of hypoglossal canal, *6* venous plexus of carotid canal, *7* posterior condylar emissary vein, *8* petro squamous sinus)

diversity of neurotransmitters and neuropeptides has been revealed in dural nerve fibres: acetylcholine, serotonin, substance P (SP), calcitonin gene-related peptide (CGRP), neurokinin A, neuropeptide Y, and vasoactive intestinal peptide (Amenta et al. 1980; Edvinsson and Uddman 1981; Edvinsson et al. 1983, 1988; Furness et al. 1982; Mayberg et al. 1984; Suzuki et al. 1988, 1989; Silverman and Kruger 1989; Düring et al. 1990; Keller and Marfurt 1991; B. Csillik, E. Csillik-Knyihar, W. Zenker, unpublished observations). A high proportion of fibres course perivascularly along meningeal arteries and arterioles, veins and venules as well as near dural sinuses. However, many fibres take their course all over the dura mater, ending freely in the connective tissue (Andres et al. 1987). Accumulated sensory nerve terminals were found within the arachnoid granulations and in dura-associated lymphatic tissue. Ultrastructural studies revealed many afferent endings obviously serving mechanoreceptive and nociceptive functions (Andres et al. 1987). However, the extensive sensory innervation of the dura mater does not seem to be involved exclusively in the transmission of sensory modalities. Most probably, they also participate in vasomotor functions; the close association of fine afferent peptide-containing fibres (Fig. 7b) with microvessels in the entire dura mater can be linked to antidromic activation of sensory neurons inducing vasodilatation and extravasation (Faraci et al. 1989). Knyihar-Csillik et al. (1994) demonstrated structural alterations of CGRP-immunoreactive perivascular sensory nerve terminals in the rat cerebral dura after stimulation of the Gasserian ganglion. The alterations suggest an increased release of CGRP following sensory nerve stimulation. It has been shown that infusion of SP and serotonin increased blood flow to the dura mater two- to three-fold (Faraci et al. 1989). The occurrence of many mast cells near dural nerve fibres and vessels, combined with the evidence for mast cell degranulation following trigeminal sensory nerve fibre stimulation, indicates indirect neurogenic effects (Dimitriadou et al. 1991). Local factors also seem to participate in regulating meningeal blood flow, e.g. adenosine was shown to produce vasodilatation in the dura mater (Faraci et al. 1989). Adenosine is a product of 5′-nucleotidase, which has been shown to be localized all over the arachnoid membrane and on the surface of dural vessels (Zenker et al. 1992). Thus, a highly complex vasomotoric apparatus is available in the dura mater for precise adjustment of the blood perfusion. This, in turn, cannot fail to influ-

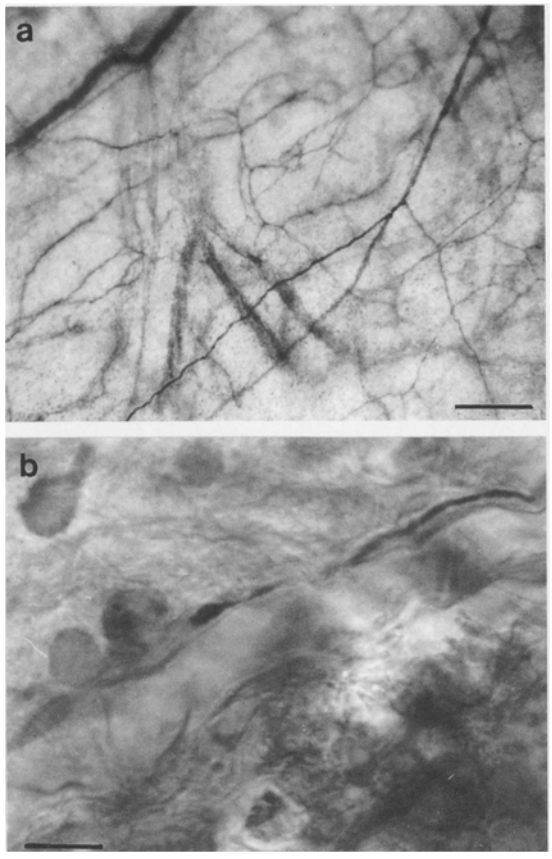

Fig. 7 **a** Whole mount preparation of spinal dura mater of a 9-month-old human. Staining for AChE activity, demonstrating the density of dural nerve fibre net. **b** Dural capillary in close relation to a calcitonin gene-related peptide-immunoreactive perivascular sensory nerve terminal. Whole mount preparation of rat dura mater. *Bars* **a** 0,1 mm, **b** 7 μm

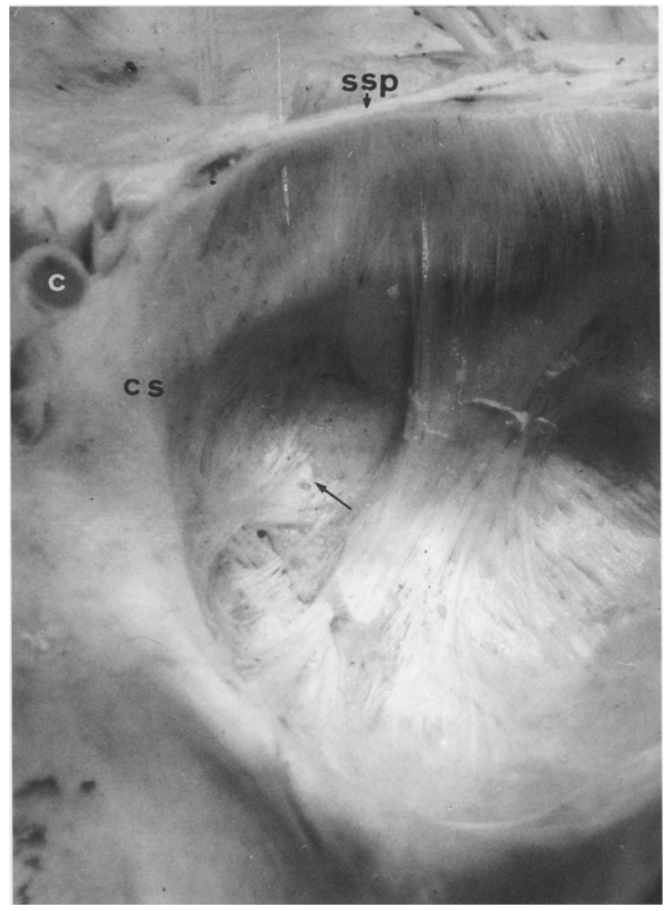

Fig. 8 Dura mater of middle cranial fossa. *sc* Cavernous sinus; *ssp* sphenoparietal sinus (at the lesser wing of sphenoid bone). To either side of the *arrow tip* throughs for arachnoid villi. At this site, the inner surface of the dura is characterized by numerous ridges, which, in intact preparations, emerge into arachnoid tissue

ence the temperature of the CSF in the subarachnoid space.

The cerebrospinal fluid

The possible role of the external CSF compartment (leptomeninges and subarachnoid space) in heat exchange between the brain and environment

The highly vascularized dura mater (haemal compartment) is directly adjacent to the compartment of the CSF, which forms a fluid coat surrounding the entire CNS. An epithelium-like tissue, called neurothelium, separates the dura from the arachnoid membrane. It consists of flat cells, interconnected by desmosomes, gap and tight junctions. The following layers of the arachnoid membrane, by contrast, are variable in structure; mostly they show a reticular arrangement of cells with fluid-filled intercellular lacunae in between, often containing macrophages or collagen fibrils. CSF has access to this spongy part of the arachnoid tissue via intercellular gaps and fenestrae in the cell layer lining the subarachnoid space (Cloyd and Low 1974; Zenker et al. 1994). Thus, it is the delicate neurothelium which represents the proper "barrier" between the arachnoidal CSF compartment and the haemal compartment of the dura mater (Andres 1967; Klika 1967; Schachenmayr and Friede 1978; Alcolado et al. 1987; Krisch 1988; Haines 1991; Haines and Frederickson 1991; Orlin et al. 1991). It is noteworthy that, in the vicinity of dural venous sinuses as well as in certain areas of the calvarial floor (Fig. 8) and at the sites where cranial nerves leave the cranial cavity or spinal nerves the vertebral canal, the interface between dura and arachnoid is considerably increased by the occurrence of numerous arachnoid villi (Krisch 1988) that intrude deeply into the dura mater, while at the same time vascularized projections of the dura mater protrude into the arachnoid tissue (Figs. 2, 8, 9). Arachnoid villi are generally considered as the preferential sites where CSF is returned to the venous blood from the subarachnoid space. They are

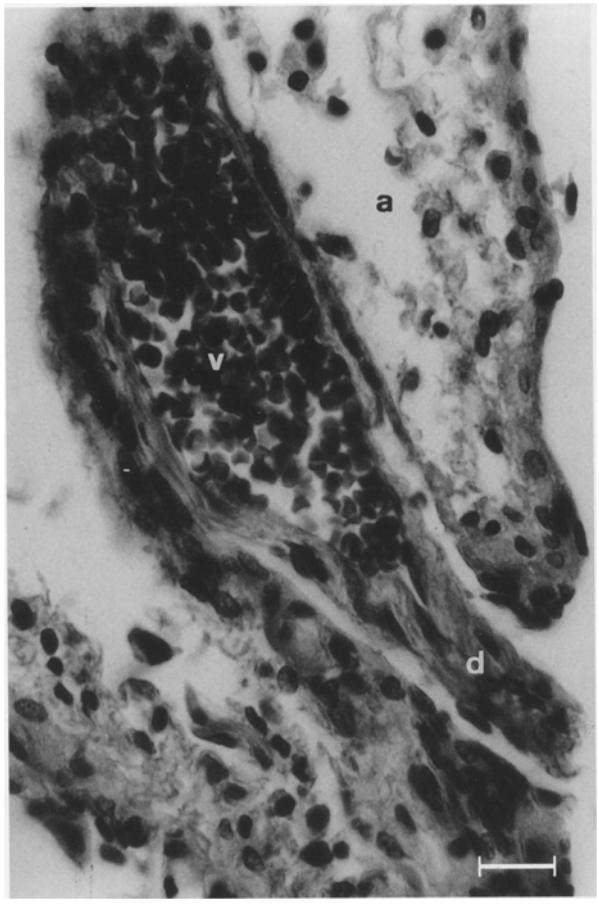

Fig. 9 Section (8 µm) through a specialized contact zone between dura (*d*) and arachnoid (*a*). A dural ridge projecting into arachnoid tissue contains a vessel (*v*). Haematoxylin-eosin staining. *Bar* 20 µm

most numerous in humans. They occur either as microscopic protrusions of the arachnoid and subarachnoid space into the adjacent dura mater or dural walls of major venous sinuses, coming here in close relation with the dural vascular bed, or as macroscopically visible complex transdural evaginations into the lumen of dural sinuses. Altogether, these structures contribute to a considerable increase of contact area between the CSF compartment and the venous system, and play a major role in the drainage of CSF into the venous blood. Following the demonstration of compliance-mediated volume compensations during fluctuations of hydrostatic pressure (Butler et al. 1983), an additional function for arachnoid villi as "volume buffer" came to be discussed (Krisch 1988). It cannot be excluded that such function-associated increases of the contact zone between arachnoid villi and the venous compartment may also play a role in heat transfer.

All brain vessels coursing through the subarachnoid space are ensheathed by a coat of meningeal tissue (e.g. Alcolado et al. 1987; Krisch 1988; Zenker et al. 1992). This coat is delicate and displays a microstructure similar to that of the arachnoid membrane. Therefore, close relations exist between the walls of brain vessels and the CSF and a mutal thermal influence can be assumed. The same applies for the dense network of vessels – mostly arterioles and venules – harboured by the pia mater (Fig. 13). The latter forms a slender membrane with flat cells forming the inner lining of the subarachnoid space and with reticularly arranged meningeal cells and collagenous fibrils underneath. At the sites where brain vessels enter the pial vascular rete, the pial lining cells reflect onto the cells lining the outer surface of subarachnoid vessels. The vascular branches entering the brain parenchyma are surrounded by pial connective tissue, formerly called Virchow-Robin spaces (Krahn 1982; Krisch et al. 1984).

For our considerations it is of great significance that the surface area of the telencephalon and cerebellum, covered by pia mater and thus in close contact with the subarachnoid space, is extraordinarily large. Extensions of the subarachnoid space intrude deeply into the sulci between cerebral gyri or cerebellar laminae and, importantly, the leptomeningeal tissue is part of the tela choroidea. In adult humans, the cerebrocortical surface area alone was calculated by Elias and Schwartz (1971) to be about 2300 cm^2. This extended surface area is exposed to and washed around by CSF. Thermal influences interacting between CSF and the CNS must be inferred from these extensive anatomical relations.

CSF – a temperature buffer for the CNS

In addition to many other functions, the CSF compartment plays an important role as a temperature buffer for the brain and spinal cord. The temperature of CSF in humans is about 37° C, with circadian variations between 36.5 and 37.5° C (Dijk et al. 1994). A recent study (Landolt et al. 1995) presents the first direct measurements of the time course of the intracranial temperature of the CSF in humans. The data are based on recordings by multipolar electrodes (allowing for simultaneous temperature and EEG measurements) implanted bilaterally through the foramina ovalia, their tips positioned at the caudal ends of the ambient cisterns (close to the parahippocampal gyri). Measurements were performed in unanaesthetized subjects. For most of the time, the patients were lying in bed and their intracranial temperature was recorded continuously for several days. A clear 24-h rhythm became apparent, with a crest at 20–21 h (37° C) and a decline setting in when the light was switched off, attaining its lowest value (36.5° C) in the early morning; thereafter it increased during the day until he maximum was reached in the second half of the waking episode. The phase relationship of intracranial temperature and sleep was shown to be similar to that of body temperature.

It has to be emphasized that these data reflect the situation of normothermia at a constant room temperature of 20–22° C. It would be of great interest to measure the values in states of hyperthermia, during brain and high muscular activity or in a hot environment.

From the anatomical point of view, the temperature of the CSF must depend on the blood temperature in the choroid plexus where the main portion of the fluid is produced, and on influences from all contact areas lining the CSF compartment, from the inner (ventricular) and external surface of the brain as well as from the meninges. The latter, in turn, are influenced by direct and indirect (vascular-mediated) cooling from outer layers of the head wall and from the skull base respectively. Cabanac (1993) emphasized the particularly high sweating capacity of the skin of the head in humans and the cooling effect of sweat evaporation through the calvaria upon the brain. Using direct recordings of intracranial temperatures in patients, the dural temperature was shown to be 1° C lower than the blood temperature. Also, intracranial temperature was more influenced by face-fanning than were oesophageal and tympanic temperatures (Brinnel et al. 1987). Moreover, brain temperatures measured at a distance of 2 cm below the surface of the brain were found to be 0.4° C lower than those at a distance of 4 cm (Whitby and Dunkin 1971). In the rhesus monkey, Hayward and Baker (1969) showed that the centres of the hemispheres (basal ganglia, capsula interna, midbrain reticular formation) were the hottest parts of the brain. These authors, however, assume that the temperature level of a certain brain site depends upon the distance of the site from the arterial blood, entering from the circle of Willis or from the arterial net on the hemispheres.

The mechanism of temperature transfer

Cooling transmission from the skin to the brain via CSF compartment

It is well established in physiology that the transfer of heat from an organ in which it is being generated to the body surface generally can take place in two ways: by conduction or by convection.

Heat conduction depends on the distance between the site of heat generation and the skin on the one hand, and on the characteristics of the tissues lying in between on the other. The brain is separated from the skin by the meninges, including the CSF compartment, skull bones, the epicranial aponeurosis and, intimately connected to it, the subcutaneous tissue containing only a relatively thin layer of fat.

Heat loss from the skin takes place by radiation, conduction, convection and evaporation of water from the skin (perspiratio insensibilis and sensibilis). At room temperatures above 35° C evaporation is the main factor. Radiation, conduction and convection change direction at this temperature and the body has to take heat up from its environment; this heat can then be given off only by evaporation.

For the inner temperature transfer, conduction seems to play only a minor role. An interesting observation regarding the susceptibility of the brain to conductive heat exchange with the environment was reported by Hayward and Baker (1969): following sudden death and arrest of cerebral blood flow, an immediate cooling of subcutaneous scalp and frontal and parietal cortical and subcortical areas was observed, whereas in deep brain structures (hypothalamus, midbrain reticular formation, pons) the temperature was retained or even rose due to continued heat production in loco and cessation of heat removal by cerebral blood flow. This lasted for about 5–8 min, after which the deep brain sites also cooled down. At an air temperature of 45° C, however, this immediate cooling of superficial brain sites and scalp, and the later cooling of all cranial sites, is eliminated (as could be expected). The major factor for the heat transfer from the brain to the skin (and cooling in the opposite direction) is heat convection by the CSF and the blood stream in the vessels connecting the dural plexus with the deep cutaneous and the subpapillary vascular plexus of the skin.

Convective cooling via veins is possible when the blood in cutaneous and subcutaneous venous plexuses is cooled by evaporation during intense sweating from the skin of the head. The cooled blood is being transported through the numerous venous communications in the diploe of skull bones into the venous plexuses of the dura mater (Fig. 2). Using Doppler flow probes, it could be shown in humans that such movements of venous blood, obviously serving heat exchange, do indeed take place at great speed in the veins of emissaria mastoidea and parietalia (Cabanac and Brinnel 1985) as well as in ophthalmic and angularis oculi veins in states of hyperthermia (Caputa et al. 1978; Deklunder et al. 1991; Hirashita et al. 1992). Comparable movements of blood may also occur in veins connecting submucosal veins of oral, nasal and paranasal cavities via plexus maxillaris with the venous elements of the dura mater at the base of the skull (Fig. 6).

These changes of direction and extent of blood flow are associated with physiological reactions to various influences such as hyperthermia, and they are probably controlled by the nervous system. The extraordinary density and diversity of vascular and dural innervation shown above is in line with the possibility of finely graduated regulating effects by the nervous system.

As, for anatomical reasons (valve-like lamellae in the lumen of sinuses at the sites where cerebral venae enter the sinuses), a reflux of venous blood into the brain parenchyma can be excluded under normal conditions, any transmission of temperature from the dura mater to the surface of the brain can take place via the CSF only.

Temperature transfer from the CSF on the brain via brain arteries?

To date, there have been no direct data to show whether thermal influences are exerted on brain vessels by the CSF. If such influences occur, the degree of potential temperature transfer might, in addition to the temperature gradients between blood and the CNS, depend on the distances covered by a given vessel on its way

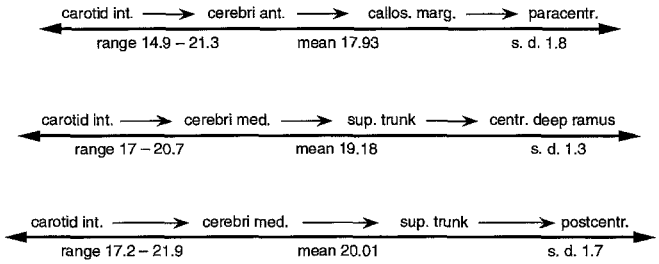

Fig. 10 Diagram indicating length in cms of the cerebral arteries and their cortical branches within the subarachnoid space. The unexpected lengths of these pathways provide vast surfaces for the exchange of temperature gradients

through the subarachnoid compartment, on its diameter, and on the thickness of its wall. We have therefore made appropriate measurements on 12 specimens from humans aged 45–65 years. The specimens were fixed according to Steinmann (1984). In 4 cases cerebral arteries had been injected with latex. Additional measurements were performed on two corrosion casts. To obtain the true length, tortuosities were evened out in dissected vessels. The results are given in Figs. 10 and 12. Two sets of branches arise from all cerebral arteries and from the circle of Willis – *central* and *cortical*. Central branches, after a short course, reach the inner core of the brain (basal ganglia, internal capsule, thalamus, hypothalamus). A thermal influence of CSF on these branches therefore cannot be expected. Cortical branches, on the other hand, extend over long distances (up to 20 cm) within the subarachnoid space (Figs. 10–13) before they reach the pial vascular rete, where arterioles and capillaries enter the brain tissue to supply cortex and adjacent white matter (estimated to comprise four-fifths of the total volume of the brain).

As shown in Fig. 10, the longest distances, measured from the point of entry of a main brain artery (internal carotid) into the subarachnoid space to the site where the longest sub-branches enter the pial rete, are about 18–20 cm in adults.

The diameters of the internal carotid artery, of the lateral and anterior cerebral arteries and of several of their branches are indicated in Fig. 12.

Taking into account the fact that all cortical arterial branches are thin-walled vessels with subdivisions showing diameters in the same range as branches of retia mirabilia in the head region of "rete species" (Simoens et al. 1987), it seems justified to assume reciprocal thermal influences between CSF and arterial blood flowing in long cortical vessels and their branches. The same applies to the pial vascular rete. These considerations could explain why superficial brain structures are cooler than the inner core of the brain, which is supplied by central branches.

Finally, it should be noted that choroidal arteries, before entering the choroid plexus, also course through the subarachnoid space over considerable distances. Therefore, a cooling effect of the CSF on vessels supplying the choroid plexus, the main organ of CSF production, can be expected.

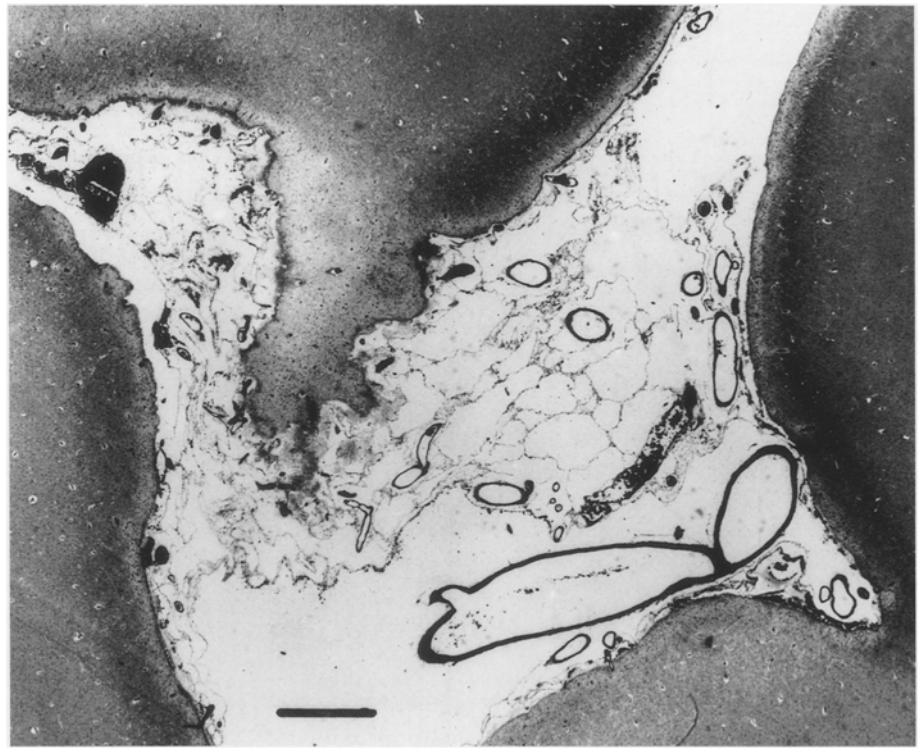

Fig. 11 An intergyral compartment of the subarachnoid space. Small arteries, veins, arterioles and venules, suspended in the net of arachnoid trabeculae, surrounded by CSF. Goldner staining. *Bar* 0.2 mm

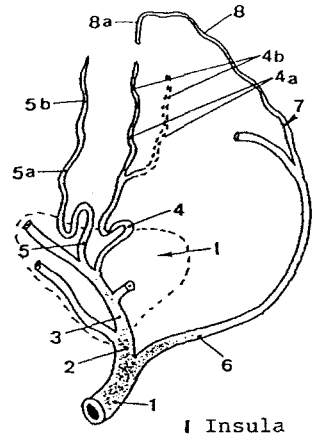

Fig. 12 Diameters of selected portions of cerebral arteries, determined in 12 adult specimens. *Left* Schematic drawing of the measured arteries. *Right* Table of values

Diameters in mm of several cerebral arteries

Artery	range	mean	s. d.
1 carotis int.	3.5 – 5	4.5	0.53
2 cerebri med.	3 – 4	3.44	0.49
3 superior trunk	1 – 2.5	1.9	0.46
4 sulci centr. stem	0.9 – 1.8	1.21	0.33
a. middle part	0.5 – 1	0.89	0.28
b. termin. part	0.2 – 0.5	0.3	0.11
5 sulci postcentr. stem	0.9 – 1.5	1.1	0.22
a. middle part	0.5 – 1	0.75	0.2
b. termin. part	0.2 – 0.5	0.35	0.12
6 cerebri ant.	1 – 3	1.99	0.53
7 callosomarg.	1 – 2.2	1.39	0.5
8 paracentr.	0.5 – 1	0.78	0.21
a. termin. part	0.1 – 0.5	0.29	0.14

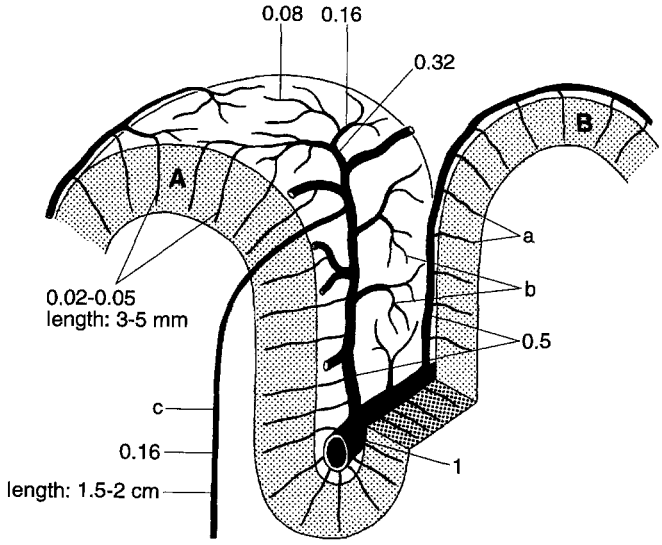

Fig. 13 Diagram showing terminal ramifications of cortical arteries prior to entering pial rete. Every gyrus is supplied from both sides. The mean diameters of branches, determined in 5 adult specimens, are indicated. Arteries with diameters of about 0.5 mm do not, or only marginally, change their calibres after having released side branches (*a* short cortical arteries, *b* pial plexus, *c* long cortical artery, *A* precentral gyrus, *B* postcentral gyrus)

Is there a countercurrent heat exchange between the main cerebral arteries (internal carotid and vertebral arteries) and the venous plexus surrounding them?

In the monkey and the rabbit, both species without a carotid rete, the temperature of blood in the circle of Willis is the same as the temperature of blood in the aortic arch; this contrasts with the situation in rete animals such as the cat, dog and sheep, where countercurrent heat exchange between rete and surrounding venous blood causes a decrease in the temperature in the circle of Willis. In humans, who lack a carotid rete, the situation seems to be comparable to that in monkeys. Yet, as arterial and venous flows come into intimate contact in the cavernous sinus, which collect venous blood from the skin of the face and from nose and mouth areas, several authors (Wenger 1987; Nielsen 1988; Numely and Nelson 1992), on the basis of theoretical calculations, have suggested a certain heat transfer from the arterial to the venous blood. In fact there are intimate anatomical contacts of internal carotid as well as vertebral arteries to the cavernous sinus and vertebral venous plexus respectively (Fig. 14). In our opinion, however, these contact zones are too short, the diameter of the arteries too large, their walls too thick, and the blood flow too fast to bring about an actual cooling effect.

Is there a comparable cooling mechanism for the spinal cord?

Undoubtedly, the spinal cord also produces heat. Here, motor impulses for all muscles of the trunk and the extremities, as well as autonomic impulses, are generated and the entire primary sensory input from the trunk and the extremities is being processed. Accordingly, a cooling mechanism should also be expected for the spinal cord. So far, no experimental data are known to the authors. A discussion of this problem must therefore be confined to comparing the anatomical situation of the spinal cord with that of the brain and to making functional deductions therefrom.

The spinal cord, in a similar way to the brain, is surrounded by a coat of meninges and the CSF compartment. In general, the fine structure of the spinal meninges corresponds to that of the cranial meninges. Contrary to the cranial pachymeninx, the spinal dura has no periosteal function. It is separated from the inner wall of the vertebral canal by the epidural space, containing the internal vertebral venous plexus, which surrounds the spinal ganglia and the dural sac over its full length. The in-

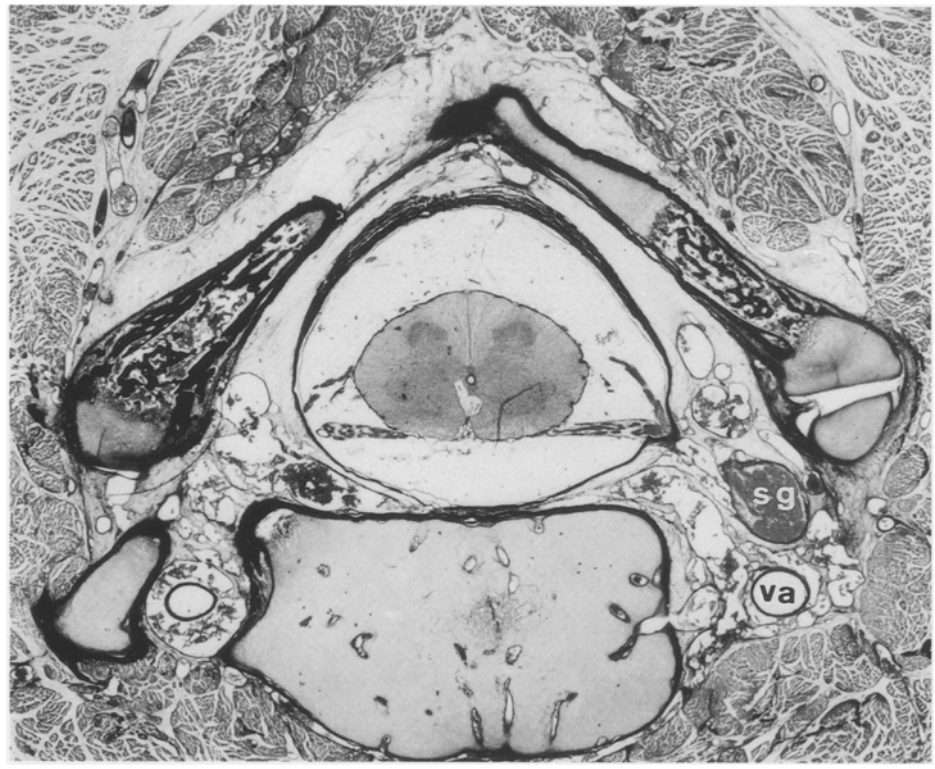

Fig. 14 Horizontal section (8 µm) through the neck of an 8-month-old male fetus. Goldner staining. Vertebral artery (*va*) and spinal ganglion (*sp*) surrounded by a dense net of communicating venous channels

ternal vertebral venous plexus can be considered as a topological equivalent of the cranial dural sinuses. The density of the vascular bed of the spinal dura is comparable to that of the cranial dura. It is connected by tiny veins with the internal vertebral plexus, which also receives tributaries from the bones, e.g. the basivertebral veins. Dural veins additionally drain to the intervertebral veins which, on the other hand, receive venous blood from the spinal cord. Several of the spinal cord veins drain to the dural vascular bed; these veins are equipped with valves at the sites where they enter the dura, thus preventing an inverse blood flow back to the spinal cord and protecting it from major pressure changes occurring in the intricate venous plexuses along the entire vertebral column. These plexuses, on the other hand, are devoid of valves and changes in the direction of blood flow within these vessels are therefore possible. The internal is connected with the external vertebral venous plexus by many segmental anastomoses that pass through and between the ligaments and the bones. Both plexuses communicate, via intervertebral veins, with vertebral, posterior intercostal, lumbar, sacral and pelvic veins. In all these veins and venous plexuses, blood flow can temporarily be reversed (Batson 1957). The external vertebral plexus is also interconnected with the veins of the skin of the back. These connections are represented by the segmental dorsal rami of intercostal veins and by various venous roots piercing the muscles of the back. Thus, anatomical preconditions exist for heat transfer by convection from the spinal cord via CSF, meninges and venous pathways to the vascular plexuses of the skin of the back; there, cooling of the blood can be caused by sweat evaporation. Up to now, nothing can be said about the efficiency of a mechanism operating in this way. Probably, cooling effects brought about by arterial perfusion of the spinal cord and by the extensive close contacts of spinal dura and spinal ganglia with the cooler blood of the internal vertebral venous plexus are of much greater importance.

A direct conductive temperature transfer from the spinal medulla to the skin cannot be assumed in view of the large tissue masses – the musculotendinous mass of the erector trunci external muscles of the back and neck, as well as connective tissue layers – lying between them.

Conclusions

These are summarized in Fig. 15.

It seems to be well established that in humans, who lack a rete mirabile, the general arterial blood temperature is the major determinant of changes in brain temperature. In this study we present a detailed analysis of vascular arrangements allowing a bulky transfer of venous blood from the skin of the head and from nasal and paranasal mucous membranes to the dura mater, providing an excellent anatomical basis for convection in cooling caused by evaporation of sweat or mucus. An unprecedented vascular bed, present in the dura mater, may transmit temperature changes to the CSF compartment. Temperature gradients of the CSF, in turn, may influence the temperature of the brain parenchyma (1) directly along the extensive contact area between the cerebrocortical surface and the CSF compartment or (b) indirectly

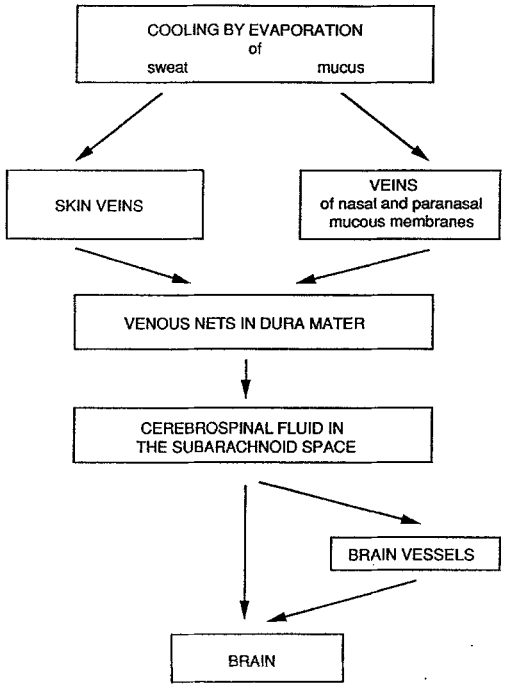

Fig. 15 Flow chart, summarizing our conclusions regarding brain cooling in humans by evaporation of sweat and mucus

via brain arteries which extend over long distances and arborize within the subarachnoid space before entering the pial vascular network and brain parenchyma.

These anatomical considerations about evaporation-induced cooling of CSF and its direct and indirect transmission to the CNS, leading possibly to a "selective" brain cooling in humans, are open to physiological verification or falsification. Exact measurements of CSF – as compared to trunk – temperature during normo- and hyperthermia in humans could be the next elucidative step.

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