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The Relationship of Epidural Anesthesia to Neural Membranes and Arachnoid Villi

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DESPITE THE SIMPLICITY of administering epidural anesthesia, the precise location of the neural blockade is not well understood. The gross anatomy of the epidural space has been described by Cheng.[1] However, the anatomic relationship of the membranes of the spinal cord, spinal nerve roots, and peripheral nerve with regard to the spread of solution within the epidural space is not generally appreciated. Both Bromage[2, 3] and Usubiaga *et al.*[4] believe that the relationship of these membranes to specific neural structures is intimately related to the mechanism of spread and the locus of action of epidurally-injected local-anesthetic solutions. They contend that there are multiple sites of epidural local anesthetic action.

The recent studies of Shantha and Bourne,[5] describing in detail the micro- and macroscopic characteristics of the neural membranes, provide a new basis for re-evaluating the primary mechanism of spread and locus of action of epidural anesthesia.

Epidural Anesthesia Related to Anatomy

Membranes and anatomic spaces surrounding the spinal cord, spinal nerve roots, and trunk are considered in the following sections:

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DURA MATER (FIGS. 1–10)

This is the outermost membrane covering the brain (cranial dura), spinal cord (spinal dura), and dorsal and ventral spinal roots (root dura). The cranial dura has two layers: an external layer, which forms the innermost layer of the periosteum of the cranial bones, and an internal layer. The external layer is firmly attached to the foramen magnum, whereas the internal layer continues as the spinal-cord dura, as well as dorsal and ventral root dura. The spinal and root dura are not firmly tethered to the vertebral periosteum like the cranial dura, but are continuous with the peripheral nerve as epineural and perineural connective tissue. Structurally, the dura is composed of thick collagen bundles mixed with elastic fibers and fibroblasts, running obliquely and longitudinally. It contains an abundant amount of mucopolysaccharides. The thickness of the spinal dura is greatest cephalad and becomes progressively thinner in the caudad direction.[1] The root dura is thin compared with the spinal dura, and becomes progressively much thinner towards intervertebral foramen and continues as epi- and perineural connective tissue of peripheral nerves.

EPIDURAL SPACE (FIGS. 1–10)

Normally, there is no epidural space in the cranial cavity because of the firm attachment of the external layer of dura to the cranial bones. Further, the spinal epidural space does not communicate with the cranium because of the attachment of the external layer of cranial dura to the bony margins of the foramen magnum. The epidural space in the spinal column is the space found between the in-

FIG. 1. Sacral spinal cord of the rabbit 24 hours after introduction of India ink into the subarachnoid space. Note the spread of the ink from the subarachnoid space to the proximal part of the nerve roots. ×4.

ternal periosteum of vertebrae and the spinal and root dura. Spinal epidural space contains fat, loose areolar tissue, blood vessels, venous plexuses, and lymphatics. The gross anatomic boundaries of the epidural space are: cephalad, the foramen magnum; caudad, the periosteum of the sacrococcygeal canal, including the sacrococcygeal membrane; anteriorly, the posterior longitudinal ligament; posteriorly, the ligamentum flavum attached to the periosteum of the vertebral lamina; laterally, the periosteum of the pedicles of the vertebrae. Laterally, the epidural space communicates with the paravertebral space through the intervertebral foramen. With advancing age, this communication appears to be blocked (fig. 11) due to an increase in connective-tissue elements.

The epidural space can be subdivided into: 1) anterior or ventral, which is between the posterior longitudinal ligament and the ventral spinal roots and ventral surface of the spinal cord; 2) posterior or dorsal, situated between the ligamentum flavum and lamina and the dorsal roots and the dorsal part of the spinal cord; 3) right and left inter-root or lateral, situated between the ventral and dorsal roots. These spaces are indistinct below the sacral 2 vertebral level. The importance of these subdivisions of the epidural space in epidural anesthesia is well described by Usubiaga *et al.*[6] These subdivisions of the epidural space communicate with one another in the majority of cases.

The dorsal epidural space is the usual site of epidural entry for the deposition of local anesthetic agents. According to Cheng,[1] there is little or no dorsal epidural space from the foramen magnum down to the cervical 3 vertebra, and it is extremely narrow down to the cervical 5 vertebra. It gradually increases in size below the midthoracic region. This space is largest between lumbar vertebrae 2 and 3 (6 mm anteroposteriorly in adults), again becoming narrow at the lumbosacral junction. The sacral canal below the sacral 2 vertebra is occupied by dura-clad nerve roots (cauda equina) and the filum terminale.

PERIDURAL SPACE (FIGS. 1–7)

In anatomic terms, this name indicates the space found in the immediate vicinity of the outermost part of the spinal and root dura. When we say "peridural anesthesia," strictly speaking, we imply that the anesthetic enters only this space, which is not properly descriptive. The term "epidural anesthesia" is more appropriate, since it includes all the space outside the dura mater, where, in fact, the local anesthetic agent is more diffusely placed.

SUBDURAL SPACE (FIGS. 3–10)

The subdural space refers to that space found between the arachnoid and the dura mater. It can be divided into spinal (surrounding spinal cord) and root (surrounding dorsal and ventral spinal roots) subdural spaces. It contains small amounts of tissue fluid, some of which may be derived from the seeping of cerebrospinal fluid (CSF) through the arachnoid villi protruding into the root subdural space (figs. 3–10). The importance of this space in the production of a sub-

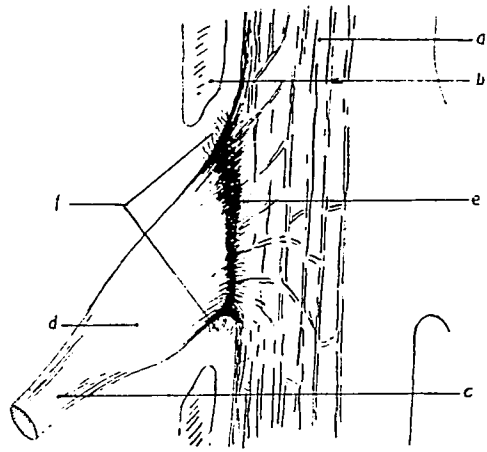


FIG. 2. Diagram showing ink cuff of upper sacral nerve roots in the rabbit. *a*, dura mater; *b*, pedicle of vertebra; *c*, spinal nerve; *d*, dorsal root ganglia; *e*, ink cuff; *f*, fine black lines arising from ink cuff.[8]

dural block (a third mode of vertebral anesthesia) will be discussed.

ARACHNOID MATER (FIGS. 3–10)

Arachnoid mater is the membrane covering the brain, the spinal cord, and the dorsal and ventral spinal roots, and is found between the pia mater and the dura mater. It is made up of several layers of flat squamous cells laid one on top of the other with potential space (interarachnoid spaces) between the layers and a delicate network of collagen, elastic fibers, and blood vessels within.[5] Laterally in the spinal cord, this membrane is attached to the dura by denticulate ligaments. The latter are strands of arachnoid tissue extending between the pia and arachnoid, standing in the fashion of pillars in the subarachnoid space, called the "arachnoid trabeculae." The cranial arachnoid mater extends down into sulci and fissures of the brain surface, a phenomenon which is not observed in the spinal arachnoid.

PIA MATER (FIGS. 3–5 AND 8–10)

The pia mater is a single squamous-cell layer applied directly to the brain, spinal cord, and dorsal and ventral spinal roots. Blood vessels which enter the brain and spinal cord carry this membrane for some distance into the neural substances. This structure is histologically identical to the arachnoid mater.[5] There are 21 pairs of pial bands called "denticulate ligaments" extending from the foramen magnum to the conus medullaris and attached to the dura mater at regular intervals. These bands are found between the dorsal and ventral roots in the subarachnoid space.

PERINEURAL EPITHELIUM (PE) (FIGS. 3 AND 8–10)

The perineural epithelium is a continuation of the pia arachnoid membranes of the spinal nerve root with the peripheral nerves as their principal covering.[5] This multicellular layer continues with the entire somatic and autonomic nervous system, including most of the sensory and motor end-organs.[5, 25] This is quite contrary to the previous description of arachnoid fusing with the epineurium and pia mater continuing with the epineurium of the peripheral nerves.[7]

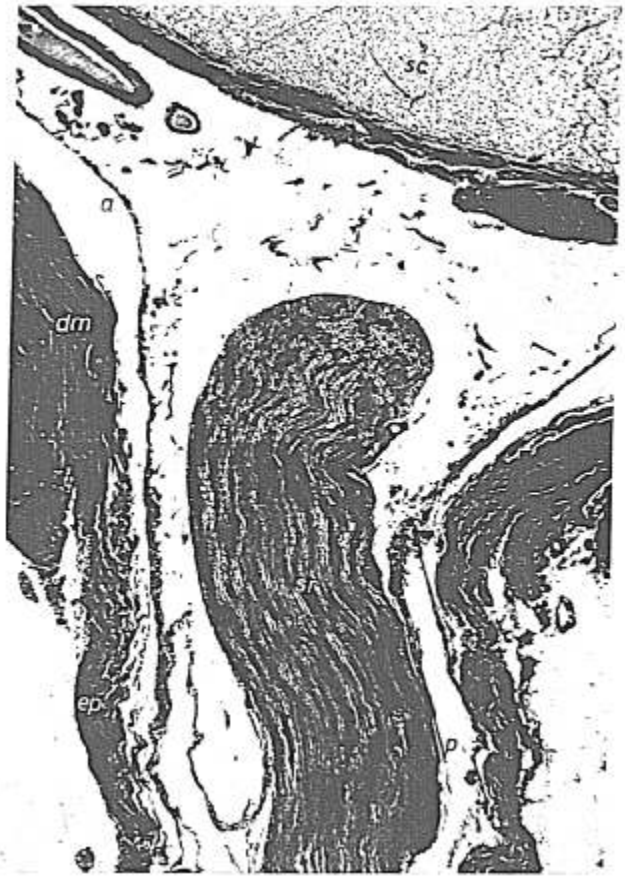


FIG. 3. A section through the spinal cord (*sc*) and spinal root (*sr*) of the horse. Stained by van Gieson's stain, demonstrating that the arachnoid mater (*a*) continues as the perineural epithelium (*p*) of the nerve root, whereas the dura mater (*dm*) of the spinal cord continues as epineurium (*ep*). Note the disappearance of the subarachnoid space as the arachnoid comes into contact with the pial covering of the nerve root. After the arachnoid mater joins the pial covering on this nerve root, both these membranes continue on the peripheral nerve as perineural epithelium. Compare this with the diagram (fig. 8) based on this photograph.

SUBARACHNOID SPACE (SAS) (FIGS. 3–10)

The subarachnoid space is located between the arachnoid membranes and the pia mater. Its three divisions are cranial (surrounding the brain), spinal (surrounding the spinal cord), and root (surrounding the proximal parts of dorsal and ventral spinal roots). All these subdivisions communicate freely with each other and contain the cerebrospinal fluid.

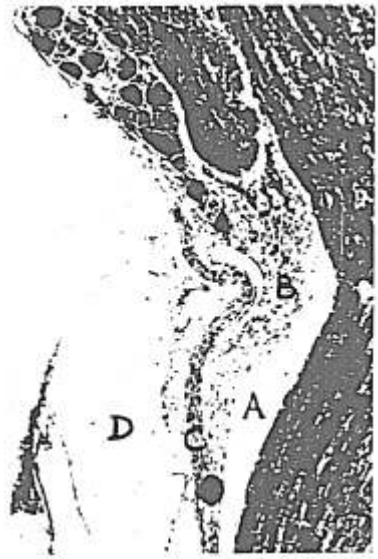


FIG. 4. Longitudinal section through a nerve root and proximal root ganglion of the rabbit. *A*, subarachnoid cul-de-sac; *B*, arachnoid proliferation, which is described as a reduplication of arachnoid mater; *C*, dura; *D*, epidural connective tissue. Note the thinness of the dura mater (*C*) as it approaches the dorsal root ganglion and its permeation by arachnoid villi at that area. ×95, reduced from ×125.[22]

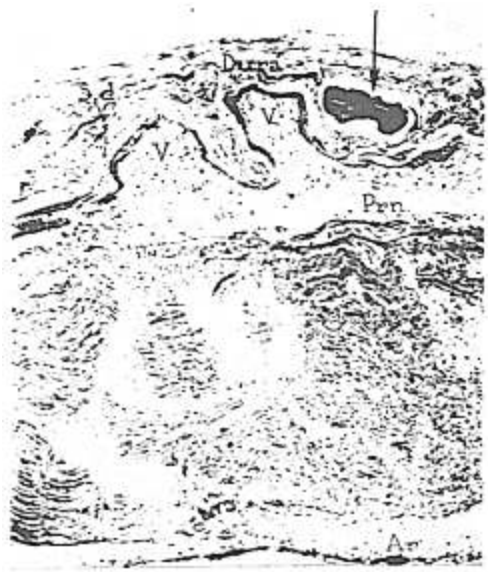


FIG. 5. Dorsal spinal root section from man; stained by hematoxylin–eosin. The dura is invaded by villi (*vv*) causing reduction in dural thickness. *sd*, subdural space; *Prn*, subarachnoid space; *Ar*, arachnoid. The dark body within the empty space to the right (arrow) is a section of the villus (its dark summit). ×80.[20]

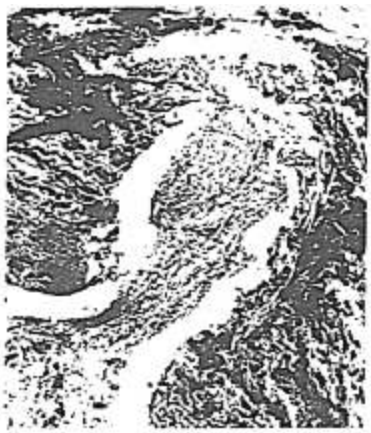


FIG. 6. Section through the human spinal root, showing the arachnoid proliferation in the form of a villus penetrating the dura. Note that the thick dura is almost breached by these villi. ×65, reduced from ×74.[22]

INK CUFF SPACE (ROOT SUBARACHNOID SPACE) (FIGS. 1–4 AND 8–10)

This term refers to the root subarachnoid space surrounding the dorsal and ventral roots of the spinal cord. When India ink is injected into the subarachnoid space, it accumulates in this root subarachnoid space.[8] Concentrations of ink particles are most pronounced in the cul-de-sac where pia and arachnoid come into opposition to obliterate the root subarachnoid space (figs. 1–4, 8 and 10). The termination of the root subarachnoid space is at the level of the proximal portion of the dorsal root ganglion.

SUBPIAL AND SUBPERINEURAL SPACE (FIGS. 3–5 AND 8–10)

This is a potential space found beneath the layers of pia mater, perineural epithelial cells in the spinal cord, nerve roots, dorsal root ganglion, and nerve trunks. The subperineural space of the peripheral nerves is in direct continuity with the subpial space of the nerve roots, spinal cord, and brain. Thus, at the area of dorsal-root entry into the spinal cord, the substantia gelatinosa comes almost in direct continuity with these spaces (figs. 9 and 10). This is in marked contrast to the situation of the ventral root, where the anterior horn cells are not on the surface of the cord (see below).

Relationship of Meninges and Spaces to the Spinal-Cord Nerve Roots and Trunk

SPINAL CORD

The spinal cord in adult man starts approximately at the level of the foramen magnum and ends at the level of the lumbar 2 vertebra. A cross-section of the spinal cord at any level shows that the substantia gelatinosa (where the dorsal sensory root enters the spinal cord) lies very close to the surface of the spinal cord, separated from the cerebrospinal fluid only by a layer of pial cells and the tract of Lissauer (fig. 9). By contrast, the cell bodies or origin in the motor axons of the ventral motor root are deep in the spinal cord, separated from cerebrospinal fluid by the pial covering and a thick layer of heavily myelinated descending and ascending nerve tracts of the spinal cord (fig. 10). Because of this anatomic peculiarity, the substantia gelatinosa is more exposed to the effects of local anesthetic agents in the spinal CSF and subpial space.

NERVE ROOTS WITHIN THE SPINAL SUBARACHNOID SPACE (FIGS. 1–3 AND 8–10)

The dorsal and ventral nerve roots leave the spinal cord separately, covered by pia mater and surrounded by spinal CSF in the subarachnoid space which is contained by the spinal arachnoid mater, which is, in turn, surrounded by spinal dura mater.

NERVE ROOTS WITHIN THE SPINAL ROOT SUBARACHNOID SPACE (FIGS. 1–10)

The dorsal and ventral spinal roots pass beyond the spinal dura, carrying with them all three meningeal coverings as they pass through the epidural space. These roots are surrounded individually by pia, arachnoid, and dura mater and have distinct epidural, subdural, subarachnoid and subpial spaces. This

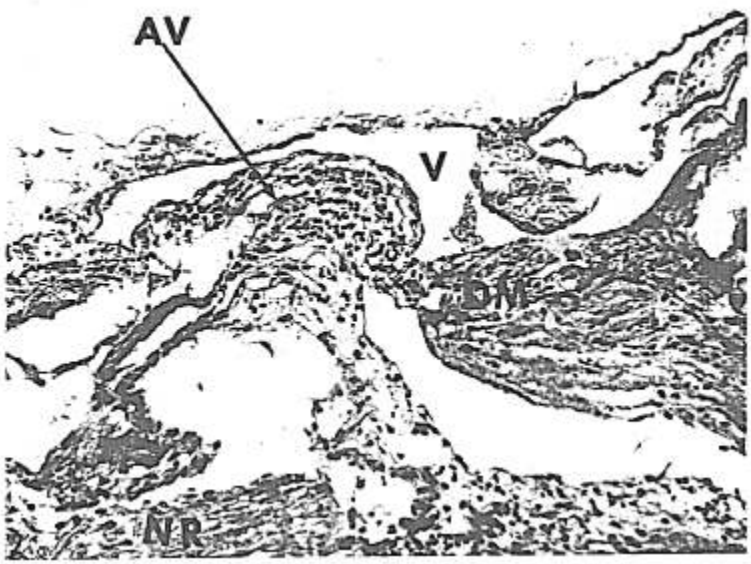


FIG. 7. Longitudinal section through spinal nerve roots from the monkey, showing a typical arachnoid villi (*AV*) protruding into a vein (*V*) outside the dura. Note that the dura (*DM*) is completely breached by this protrusion. *NR*, nerve root. ×264, reduced from ×280.[12]

region has a number of important anatomic features not observed elsewhere and is probably the most important region with regard to epidural anesthesia. At dissection, as well as in histologic section, it is evident that the junction of the root dura and the spinal dura is the narrow portion of the root dura (figs. 3 and 8–10). This "dural collar," or constriction, is particularly striking around the dorsal nerve roots.

As we trace the dura further out towards the vertebral foramen, it becomes much thinner than the spinal dura (figs. 3–10). The subarachnoid space extends separately along both the dorsal and ventral roots to the portion at the level of the dorsal root ganglion. The arachnoid covering of the ink cuff space (root arachnoid) has an important and remarkable histologic feature. Proliferations of arachnoid cells forming villus structures have been consistently demonstrated in dogs,[9] humans,[10, 11] rats,[12] and primates.[13] In humans and primates, arachnoid proliferations and villi have been demonstrated along both dorsal and ventral roots [11] (figs. 5–7). These proliferations were found in greater number and more extensively with advancing age, as observed in the sagittal sinus. Various types of arachnoid proliferations, or villi, are described by Shanthaveerappa and Bourne,[14] who found similar villus structures in the optic nerves of man and monkey. From their detailed studies, they established the following anatomic classification to include all arachnoid proliferations, *i.e.*, villi. There is no major anatomic difference between the arachnoid villus structures of the spinal nerve root, the sagittal sinus, and the optic nerve.

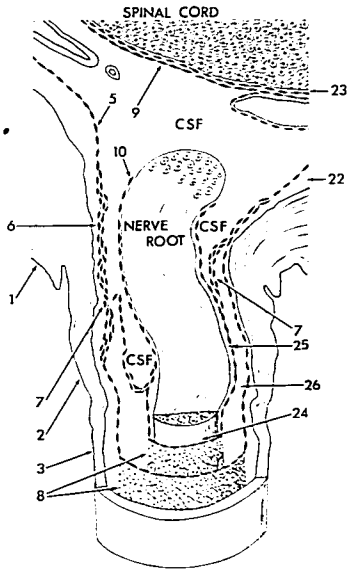


FIG. 8. Drawing from figure 3, showing the relationship of the spinal cord and nerve root meninges to membranes of the peripheral nerve. This illustration also shows the relationship of spinal-cord subpial, subarachnoid, subdural, and epidural spaces to spinal-root subpial, subarachnoid, subdural, and epidural spaces. Note that the subperineural space of peripheral nerve continues with spinal-root and spinal-cord subpial spaces. Interperineural spaces (potential space) continue with spinal-root and spinal-cord interarachnoid spaces (potential space). The spinal dura reduces in thickness as it becomes spinal-root dura.

Types of Arachnoid Villi [14]

Type I. Simple arachnoid proliferations, consisting of several layers of arachnoid epithelial cells, are found along the root arachnoid. They are consistently found where the pia and arachnoid come together to obliterate the subarachnoid space (figs. 3 and 4). These proliferations are of many shapes and sizes and may protrude into adjacent subdural spaces.

Type II. Arachnoid villi partially protruding into the dural sheath without breaching the dural continuity but, at the same time, reducing the thickness of the dura at that site (fig. 5).

Explanation of Arrows in Figures 8, 9 and 10

1. Spinal-cord dura mater
2. Spinal-root dura mater
3. Perineurium and epineurium of peripheral nerve
4. Dural collar
5. Spinal-cord arachnoid mater
6. Spinal-root arachnoid mater
7. Spinal-root pia and arachnoid coming together, with obliteration of the subarachnoid space; note the arachnoid proliferation at this point (circled)
8. Perineural epithelium, a continuation of pia arachnoid membrane on to the peripheral nerve
9. Spinal-cord pia mater
10. Spinal-root pia mater
11. Arachnoid proliferations (Type I) protruding into spinal-root subdural space
12. Arachnoid villi (Type II) partially penetrating the spinal-root dura
13. Arachnoid villi (Type III) completely penetrating the spinal-root dura and then exposing itself to the epidural space
14. Arachnoid villi (Type IV) protruding out of the spinal-root dura into the epidural space
15. Arachnoid villi (Type V) protruding into a vein in the epidural space after emerging out of the spinal-root dura
16. Epidural vein
17. Intervertebral foramina
18. Dorsal root ganglion
19. Dorsal spinal root
20. Substantia gelatinosa
21. Ventral spinal root
22. Spinal-cord subdural space
23. Spinal-cord subpial space
24. Peripheral nerve subperineural space (a continuation of the root subpial space [25])
25. Spinal-root subpial space
26. Spinal-root subdural space
27. Inter-root or lateral epidural space (between dorsal and ventral spinal roots)

CSF Cerebrospinal fluid in the spinal cord and spinal-root subarachnoid spaces

Type III. Villi which completely breach the dura but do not protrude beyond it (fig. 6).

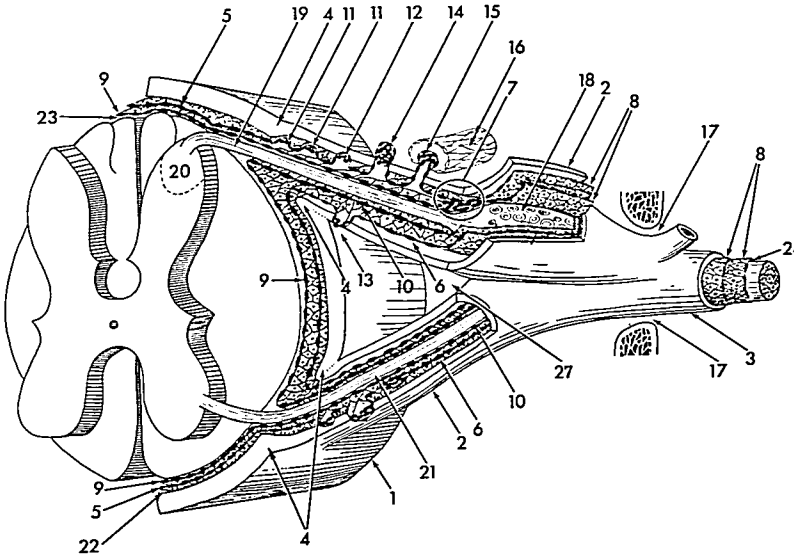
Type IV. Villi protruding out of the dura lying in the epidural space (figs. 5 and 7).

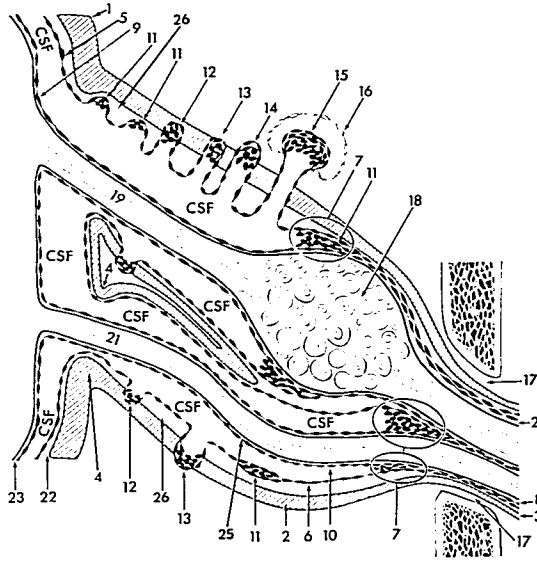
Type V. Villi protruding beyond the dura in proximity to epidural veins and partially protruding into the veins, as commonly observed in the sagittal sinus (fig. 7).

These studies indicate that villi belonging to Types I, II and III are commonly found, while Types IV and V are less frequent (figs. 9 and 10).

NERVE ROOTS AND TRUNKS BEYOND THE SPINAL ROOT SUBARACHNOID SPACE

Beyond the spinal-root subarachnoid space, the dorsal and ventral roots and dorsal root





FIGS. 9 (*above*) and 10 (*right*). Drawings of the spinal cord, dorsal and ventral roots, dorsal-root ganglion, and common nerve trunk. These diagrams show the relationship of spinal and root meninges to membranes of the peripheral nerve. Note the continuation of spinal epidural, subdural, and subarachnoid spaces with dorsal and ventral spinal roots for some distance. The pia arachnoid membrane (6, 10) of the spinal roots continues as perineural epithelium of peripheral nerves (8). Spinal-cord and spinal-root subpial space and subperineural epithelial spaces are only potential spaces and are continuous with each other (23, 24, 25). Interperineural epithelial space continues with interarachnoid spaces (only potential spaces) (6, 24). Various types of arachnoid villi given off from the root arachnoid mater are also illustrated (11, 12, 13, 14, 15). The location of the dural collar (4) as the nerve roots emerge from the spinal subarachnoid space has also been shown. Figure 9 shows the anterior (anterior to ventral spinal-root), lateral (arrow 27), and posterior (posterior to dorsal spinal-root) epidural spaces.

ganglion continue for a short distance and unite to form a common nerve trunk. After passing through the intervertebral foramen, the trunk again divides into posterior and anterior portions, forming the paravertebral nerve trunks. The pia and arachnoid come close together (at which point there are arachnoid proliferations, figs. 3 and 4) and continue as perineural epithelium throughout the entire peripheral somatic and autonomic nervous system [5] (figs. 3, 4 and 8–10). The dura mater becomes progressively thinner (figs. 3, 4 and 7–10) and continues as epineural and perineural connective tissue.

Anatomic Basis for Epidural Anesthetic Spread

Usubiaga and co-workers,[4] in their careful quantitative studies, demonstrated that the transfer of procaine from the epidural to the subarachnoid space appeared to occur by diffusion. Isolated postmortem spinal dura was shown by Bertocchi [15] to be quite impermeable to local anesthetics; since Bromage *et al.*[16] demonstrated only very little radioactive lidocaine in the spinal dura itself, another site for the diffusion process had to be found. The most likely area for diffusion is the "ink cuff" area of the root subarachnoid space. Rather than postulate diffusion through the whole dura, we suggest that local anesthetic agents pass from the epidural to the subarachnoid space and to spinal roots through the arachnoid villus tissue (which penetrates the root dura) herein described.

Meyer *et al.*[17] suggested that the endothelial lining of the arachnoid villi may be a mosaic of lipid and pores, the latter occupying a larger part of the surface than do the blood–CSF barriers. Lipid-soluble substances would penetrate both lipid and pores, whereas water-soluble substances would escape and pass through the pores. The presence of intercellular pores has been demonstrated by various workers, including Shanthaveerappa and Bourne.[14] Simmonds [18] has shown that these pores are large enough to allow passage of erythrocytes 6–7 microns in size in addition to CSF.

When an epidural injection is made, the fluid pressure in the epidural space rises above CSF pressure momentarily.[19] It is at this point that the direction of flow through the arachnoid villi could be reversed and part of the epidurally-injected local anesthetic could enter the root subarachnoid space. This fact is further substantiated by the finding of Usubiaga *et al.*[19] that the level of the epidural block is directly proportional to the residual epidural pressure following injection. High residual epidural pressure increases penetration of the local anesthetic through villi. Higher levels of local anesthetic in the root and spinal CSF then result in higher dermatome levels of analgesia. Most of the spinal-root arachnoid villi penetrating the root dura are anchored on lateral sides to the dura mater. Therefore, they are not vulnerable to collapse, which might result in obstruction to flow with increasing fluid pressure, a phenomenon observed in villi protruding into the sagittal venous sinus.[20] Even without a fluid differential pressure, a concentration gradient across the arachnoid villi could produce diffusion of local anesthetic agent into the CSF of root subarachnoid space. Thus, a conduction block of dorsal and ventral roots would be produced.

Dogliotti,[21] Bromage,[2] Usubiaga *et al.*,[4] and other early investigators felt that epidural anesthesia was a multiple paravertebral block produced by leakage of the epidural local anesthetic through the neural foramina into the paravertebral tissue, where dura no longer covers the spinal nerve. In the young patient, epidural injections of local anesthetic and aqueous radiopaque contrast solutions certainly extend through the neural foramina around the spinal nerves, and could partly explain the mechanism of epidural anesthesia (fig. 12). However, in the aged, this mechanism is not operative, since the neural foramina are occluded by fibrous tissue (fig. 11). Fig. 11 illustrates the lack of paravertebral spread in an aged arteriosclerotic patient given epidural anesthesia with the same radiopaque–local anesthetic mixture.

In the aged, arachnoid villi increase in number and size and penetrate farther into the root dura.[10] This will result in a decrease in the thickness of the root dura, increasing the area of permeability and penetration into the spinal roots. Lack of paravertebral escape, along

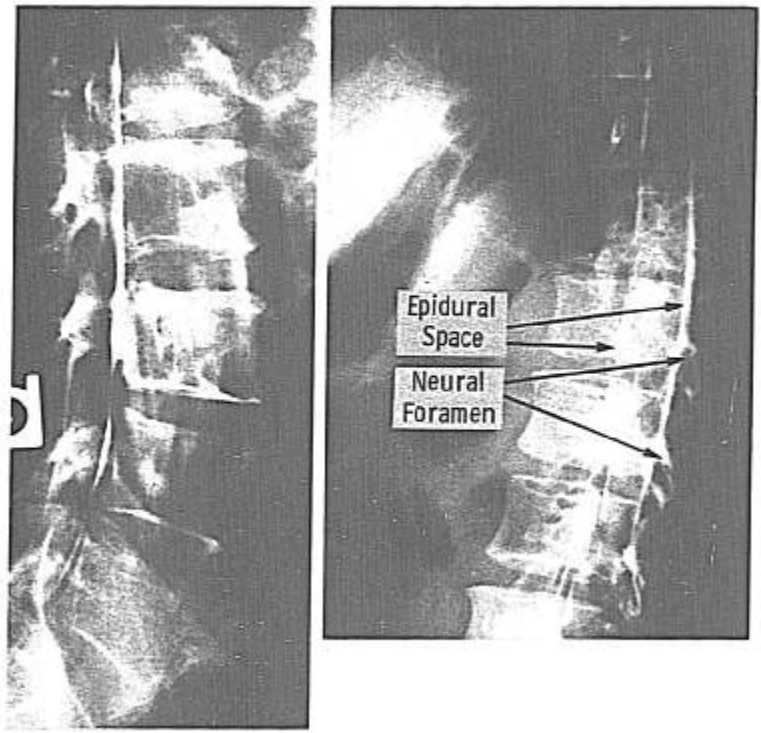


FIG. 11 (*left*). Radiograph of lumbar vertebral area of an elderly arteriosclerotic patient, taken after epidural injection of local anesthetic along with radiopaque material. Note that the only spread of this material is longitudinal, without any paravertebral spread due to closure of the intervertebral foramina.

FIG. 12 (*right*). Radiograph of lumbar vertebral area of a young healthy adult taken after epidural injection of local anesthetic in combination with radiopaque material. Note that both longitudinal and paravertebral spread of the material (arrows) through the intervertebral neural foramina. Compare with figure 11, noting the remarkable difference between spreads of epidural solutions in old and young.

with the increased permeable area in the aged, is probably responsible for the faster onset and higher dermatome levels of analgesia, even with smaller doses of local anesthetic. With little or no leakage into the paravertebral space through the intervertebral foramina, the result is a sharper rise in epidural pressure during epidural injection, facilitating increased penetration of local anesthetic agent into the root subarachnoid space. Thus, multiple paravertebral block need not play a major role in epidural anesthetic spread.

This is probably one of the reasons why the development of spinal headache after lumbar puncture in advanced age groups, compared with younger ages, is rare. In the aged, the

FIG. 13. Routes of dispersion of epidurally-injected solutions. The bold arrows and the underlined block letters indicate main routes of spread.

CSF continues to leak into the epidural space, but cannot escape into paravertebral spaces through the intervertebral foramina because these neural foramina are occluded. With the lapse of time, CSF leaking into the epidural space builds up enough fluid pressure to result in partial or complete blockade of further CSF leaking. In younger age groups, owing to the patent intervertebral foramina, when the CSF continues to escape from the subarachnoid space to the epidural space and to paravertebral spaces, the result is low subarachnoid CSF pressure and its sequela (spinal headache). There is dramatic relief of spinal headache if the leaking point in the dura is closed by autologous blood or if epidural hydrostatic pressure is kept high by continuous epidural infusion of Ringer's lactate solution. These data support the contention that the spinal headache is due to continuous leakage of CSF through the lumbar puncture site in the arachnoid and dura mater into the epidural and paravertebral spaces.

Most patients do not develop spinal headache after lumbar puncture. This is probably because of the histologic character of the arachnoid membrane. The arachnoid mater is made up of numerous layers of squamous epithelial cells placed one on top of the other, separated by a few fine collagen fibers.[5] As the lumbar puncture needle is withdrawn, the arachnoid layers of cells overlap, thus partially or completely occluding the puncture site. This prevents the seepage of CSF; thus, headache does not occur. When a small spinal needle is used, there are more chances for complete occlusion of the punctured site, and there is less chance of spinal headache.

Elman [9] and Brierley,[22] using Prussian blue and India ink, showed that the most permeable part of the spinal root was the root dura. Bromage *et al.*,[16] in their autoradiographic studies of the distribution of epidurally-injected local anesthetic, found the largest accumulation in nerve roots and their pia arachnoid coverings. Subarachnoidally-injected India ink and blue plastic powder have also been shown all over the dorsal root ganglion and distant parts of mixed peripheral nerves.[22, 23] Because of anatomic continuity with the central and peripheral membranes,[5] once the local anesthetic enters the root subarachnoid space, it can spread centrifugally along these membranes, acting as a multiple paravertebral block, blocking both somatic and autonomic nerves.

Moore *et al.*,[7] using the monkey, have shown that methylene blue-colored Efocaine reached the spinal cord within 2–5 minutes of intraneural injection. Studies of the spread of rabies in mice have shown that within ten hours after injection of rabies virus into the right foot pad, the rabies virus can be isolated in the left sciatic nerve.[24] The development of transverse myelitis has been shown in rabbits after interneural injection of penicillin into the sciatic nerve.[25] All these studies demonstrate that subpial and sub- and interperineural epithelial spread from the periphery to the spinal cord does take place and, probably, occurs through these spaces. This explains the occurrence of subarachnoid and epidural types of block following peripheral nerve block. In addition, during sympathetic block procedures, spread of local anesthetic from the paravertebral area to produce epidural block demonstrates extraneural communications between the paravertebral space and the epidural space.[26] These communications are most likely to be through the neural membranes and the spaces surrounding them.

Frumin *et al.*[27, 28] and Rudin *et al.*[29] demonstrated in man and dog that epidurally-injected procaine produced sufficient local anesthetic concentrations in the subarachnoid space to account for sensory neural block. Sarnoff and Arrowood [30] and Arrowood and Sarnoff [31] have shown that the small nerve fibers [32] are easily blocked by diluted local anesthetic concentrations. Thus, even the low concentrations of local anesthetic in the subarachnoid space can block the dorsal root ganglia, substantia gelatinosa, and Lissauer's tract, which are involved in opening the gate for pain perception.[33] It appears from these anatomic findings that following epidural injection the greatest local anesthetic concentrations are found around the spinal roots, root subarachnoid space surrounding these roots, proximal part of the common nerve trunk, dorsal root ganglia, and meningeal coverings of the spinal roots. The concentration of local anes-

thetic found in the spinal-cord subarachnoid space, compared with the above-mentioned structures, is quite low.

The role played by the "dural collar" (see Anatomy section) is not known (figs. 3 and 8–10). It is known that in some cases a double-peak curve appears in spinal CSF about 30 minutes after epidural block. This phenomenon is said to be due to the re-entry of local anesthetic along the mixed nerves from the paravertebral area.[4] This is unlikely, because by 30 minutes most of it is absorbed by the rich lymphatics and blood vessels in the epidural space before it can find its way in sufficient concentration to enter the spinal subarachnoid space. The dural collar may play a role in producing this second peak. During epidural injection, the increase in epidural pressure may exert pressure on the dural collar, partially shutting off the spinal-root subarachnoid space from the spinal-cord subarachnoid space. As the epidural pressure falls, this dural collar may relax, allowing more local anesthetic to enter from the root CSF to the spinal CSF.

Woollam and Millen [12] suggested that epidural local anesthetic might be absorbed by the rich vascular supply of the epidural space and then transmitted directly to the nerve roots. Since these epidural veins are not part of the portal-redistribution system, and contact between these collecting veins and nerve roots is very limited, it is unlikely that significant local anesthetic could reach the neural structures by this route. It is possible that the small arteries which traverse the epidural space to supply the neural structures could absorb some local anesthetic agent and produce a block of the nerve structures they feed.

Figure 13 shows the various routes of dispersion of epidurally-injected solutions such as local anesthetics.

Subdural Anesthesia (Non-subarachnoid and Non-epidural)

The authors have observed that occasionally injection of 2–3-ml test dose of local anesthetic during epidural procedures results in a rapid onset of neuromuscular block to a very high dermatome level. We interpret this phenomenon as possibly representing misplacement of the local anesthetic solution into the subdural space. Because only arachnoid membrane and villi are present between the subarachnoid space and the subdural space, local anesthetic spread into the spinal and root CSF would occur very rapidly. This, in turn, acts on the spinal nerve roots and spinal cord, as seen in subarachnoid spinal block. During placement of these alleged subdural catheters, subarachnoid CSF is not aspirated. This block appears to be intermediate between an epidural block and a subarachnoid block in speed of onset and in local anesthetic drug dose needed to produce a block.

Summary

The anatomy of the membranes covering the spinal cord, spinal nerve roots and mixed nerve trunks and spaces surrounding these structures in relation to the membranes is described. The presence of various types of arachnoid villi on the dorsal and ventral roots and their relationship to the epidural, subdural, and subarachnoid spaces are defined. The possibility that these villi are main routes for the transmission of epidurally-injected local anesthetic to nerve roots is discussed. Routes such as paravertebral, direct spinal transdural, and vascular spread appear to be of secondary importance. Once the local anesthetic reaches sufficient concentration in the CSF, neural blockade is produced at numerous sites such as dorsal and ventral nerve roots, dorsal-root ganglia, autonomic nerves, mixed nerve trunks, Lissauer's tract, the substantia gelatinosa, and the surface of the spinal cord. The subdural block (non-subarachnoid and non-epidural) is described as a clinical possibility. The anatomic basis for this block is described.

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References

1. Cheng PA: The anatomical and clinical aspects of epidural analgesia. Anesth Analg (Cleve) 42:398–415, 1963

2. Bromage PR: Epidural Analgesia. Edinburgh, E. & S. Livingstone Ltd., 1954
3. Bromage PR: Physiology and pharmacology of epidural analgesia. ANESTHESIOLOGY 28: 592–622, 1967
4. Usubiaga JE, Wikinski J, Wikinski R, et al: Transfer of local anesthetics to the subarachnoid space and mechanisms of epidural block. ANESTHESIOLOGY 25:752–759, 1964
5. Shantha TR, Bourne GH: The Perineural Epithelium—A New Concept in the Structure and Function of the Nervous System. New York, Academic Press, 1968, pp 374–459
6. Usubiaga JE, Almiro DR, Usubiaga LE: Epidural misplacement of catheters and mechanism of unilateral blockade. ANESTHESIOLOGY 32:158–161, 1970
7. Moore DC, Hain RH, Ward A, et al: Importance of the perineural spaces in nerve blocking. JAMA 156:1050–1053, 1954
8. Brierley JB, Field EJ: The connexions of the spinal sub-arachnoid space with the lymphatic system. J Anat 82:153–166, 1948
9. Elman R: Spinal arachnoid granulations with especial reference to cerebrospinal fluids. Bull Johns Hopkins Hosp 34:99–104, 1923
10. Hassin GB: Villi (pacchionian bodies) of the spinal arachnoid. Arch Neurol Psychiatry 23:65–78, 1930
11. Rexed BA, Wennstrom KG: Arachnoidal proliferation and cystic formation in the spinal nerve-root pouches of man. J Neurosurg 19:73–84, 1959
12. Woollam DHM, Millen JW: Observations on the production and circulation of the cerebrospinal fluid, Ciba Foundation Symposium on the Cerebrospinal Fluid. Boston, Little Brown and Co., 1958, pp 125–146
13. Welch K, Pollay M: The spinal arachnoid villi of the monkey *Cercopithecus aethiops sabaeus* and *Macaca irus*. Anat Rec 145: 43–48, 1963
14. Shanthaveerappa TR, Bourne GH: Arachnoid villi in the optic nerve of man and monkey. Exp Eye Res 3:31–35, 1964
15. Bertocchi A: Rilievi sulla tecnica dell' anestesia peridurale. Boll Soc Piemonte Chir 2:163–176, 1932
16. Bromage PR, Joyal AC, Binney JC: Local anaesthetic drugs: Penetration from the spinal extradural space into the neuraxis. Science 140:392–394, 1963
17. Meyer SE, Maickel RP, Brodie BB: Disappearance of various drugs from the cerebrospinal fluid. J Pharmacol Exp Ther 128:41–43, 1960
18. Simmonds WJ: Observation of labelled erythrocytes from subarachnoid space in rabbits. Aust J Exp Biol Med Sci 31:77–83, 1953
19. Usubiaga JE, Wikinski JA, Usubiaga LE: Epidural pressure and its relation to the spread of anesthetic solutions in epidural space. Anesth Analg (Cleve) 46:440–446, 1967
20. Welch K, Friedman V: The cerebrospinal fluid valves. Brain 83:454–469, 1960
21. Dogliotti AM: Segmental peridural spinal anesthesia. Am J Surg 20:107–118, 1933
22. Brierley JB: The penetration of particulate matter from the cerebrospinal fluid into the spinal ganglia, peripheral nerves, and perivascular spaces of the central nervous system. J Neurol Neurosurg Psychiatry 13: 203–215, 1950
23. Steer JC, Horney FD: Evidence for passage of cerebrospinal fluid along spinal nerves. Can Med Assoc J 98:71–74, 1968
24. Baer GM, Shanthaveerappa TR, Bourne GH: Studies on the pathogenesis of fixed rabies virus in rats. Bull WHO 33:783–794, 1965
25. Tarlov IM, Perlmutter I, Berman AJ: Paralysis caused by penicillin injection. Mechanism of complication—a warning. J Neuropathol Exp Neurol 10:158–176, 1951
26. Evans JA, Dobben GD, Gay GR: Peridural effusion of drugs following sympathetic blockade. JAMA 200:573–578, 1967
27. Frumin MJ, Schwartz H, Burns JJ, et al: Sites of sensory blockade during segmental spinal and segmental peridural anesthesia in man. ANESTHESIOLOGY 14:576–583, 1953
28. Frumin MJ, Schwartz H, Burns JJ, et al: The appearance of procaine in the spinal fluid during peridural block in man. J Pharmacol Exp Ther 109:102–105, 1953
29. Rudin DO, Fremont-Smith K, Beecher HK: Permeability of dura mater to epidural procaine in dogs. J Appl Physiol 3:388–399, 1951
30. Sarnoff SJ, Arrowood JG: Differential spinal block. II. The reaction of sudomotor and vasomotor fibers. J Clin Invest 26:203–216, 1947
31. Arrowood JG, Sarnoff S: Differential spinal block. V. Use in the investigation of pain following amputation. ANESTHESIOLOGY 9: 614–621, 1948
32. Gasser HS, Erlanga J: Role of fiber size in establishment of nerve block by pressure or cocaine. Am J Physiol 88:581–591, 1929
33. Melzack R, Wall PD: Pain mechanisms; a new theory. Science 150:971–979, 1965