Clinical implications of epidural fat in the spinal canal.  
A scanning electron microscopic study

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Abstract: Background and objectives: This review of articles summarizes recent developments in relation to fat located in the epidural space and also in dural sleeves of spinal nerve roots in order to improve our understanding of the clinical effects of the epidural blockade.  
Method: Medline search was carried cross-matching of the following words: “epidural fat”, “epidural space”, “adipose tissue” and “fat cells” from 1966 to 2008 in which articles referring to different pathologies that alter the epidural fat were also reviewed. Techniques used by different authors included the use of samples from dissections, cryomicrotome sections, as well as light and electron microscopy.  
Results: Fat in the epidural space has a metameric distribution along the spinal canal that can be altered in some pathological conditions. Epidural fat is not evenly distributed. At cervical level fat is absent while in the lumbar region, fat in the anterior and posterior aspects of the epidural space forms two unconnected structures. Fat cells are found also in the thickness of dural sleeves enveloping spinal nerve roots but not in the region of the dural sac. Epidural lipomatosis is characterized by an increase in epidural fat content. When a patient has a combination of kyphosis and scoliosis of the spine, the epidural fat distributes asymmetrically. Spinal stenosis is frequently accompanied by a reduction in the amount of epidural fat around the stenotic area.  
Conclusions: The epidural space contains abundant epidural fat that distributes along the spinal canal in a predictable pattern. Fat cells are also abundant in the dura that forms the sleeves around spinal nerve roots but they are not embedded within the laminas that form the dura mater of the dural sac. Drugs stored in fat, inside dural sleeves, could have a greater impact on nerve roots than drugs stored in epidural fat, given that the concentration of fat is proportionally higher inside nerve root sleeves than in the epidural space, and that the distance between nerves and fat is shorter. Similarly, changes in fat content and distribution caused by different pathologies may alter the absorption and distribution of drugs injected in the epidural space.  
Key words: Epidural fat; epidural space; dural sac; dural sleeves.
Methods for the study of epidural fat

Anatomical dissection is the initial method used to identify epidural fat (7-8). However, soon after death, cellular degeneration leads to a reduction of cerebrospinal fluid pressure and epidural venous vessels tend to dilate due to changes in the epidural space. This method is therefore limited by these changes; fat falls apart and the epidural space may appear bigger. Treating cadavers for conservation leads to tissue alteration. Other techniques used are, injection of resins prior to dissection (9-10), contrasts (11-12) or air and saline injection for epiduroscopy of the epidural and subarachnoid spaces (13-14). Any injection of a substance into the epidural space alters its real shape. Keeping cadavers at very low temperatures preserves the structures from damage, avoiding alterations of their morphology, size and relations between compartments and tissues (2-4). CT scan and MRI confirmed minimal differences in measurements of less than 2% between both techniques (2-5). MRI show the distribution of epidural fat due to increased signal in T1-weighted images and reduced signal in T2. Turbospin echo sequences in T1-weighted image render anatomical information (3). Ligaments and bone have a very low density, vertebral discs and cerebrospinal fluid have a moderately low density and epidural fat has a high density. Turbospin echo sequences in T2-weighted image are essential to evaluate pathological changes (4). For “in vitro” study of fat contained in the epidural space and in the dural sleeves of spinal nerve roots, examination techniques involve the use of light and scanning electron microscopy (15-16).

Characteristics of epidural fat in adults

Fat is the main component of the epidural space (Fig. 1). Fat cells are unilocular and their colour varies from white to yellow according to the amount of carotenes in the diet (17-19). These large cells (diameter of up to 120 µm) are shaped spherically and acquire a more polyhedral shape when large amounts of cells join together to become fat tissue (17-19) (Fig. 2). Every fat cell has a single large lipid vacuole in the centre and a peripheral oval nucleus. Fat tissue is held together in packs inside the epidural space by pedicles containing vessels. Under the microscope collagen fibres are frequently observed protruding out of the inferior aspect of fat tissue packs, although seldom from its superior surface. Fat cells contained in packs of fat tissue can be sometimes compartmented by these collagen fibres (20-23). The epidural fat is usually described as a semifluid tissue (24). Such description may lead to confusion. Although the fat that fills the posterior

Fig. 1. — Posterior human epidural fat seen in spinal surgery, with packs of fat cells inferior and above the dural sac. Epidural fat is partially lost during surgical manipulation (with permission, ref. #1).

Fig. 2. — Posterior human epidural fat found at L5-S1. Immune-histochemical technique CD 34 (endothelial and interstitial fat cells colored brown) [× 125] (with permission, ref. #1).
aspect of the epidural space has a somewhat lesser density than subcutaneous fat, it does not “flow” into the dependent regions of the spinal canal (Fig. 1). Instead it remains in place within the epidural space as any other tissue does. Epidural fat contributes to the shape of the epidural space in the spinal canal. Lumbar epidural fat has a metameric and discontinuous topography (2-3) (Fig. 3A, 3B and 3C). It is mainly located in the posterior aspect of the epidural space. In the axial plane, the morphology of fat deposits is similar to a tetrahedron, with a blunt posterior apex in contact with the ligamentum flavum, an anterior base oriented towards the posterior surface of the dural sac, and lateral aspects determined by the vertebral arches. The distribution of the epidural fat in the spinal canal, especially in areas of higher mobility, suggests a protective function.

The epidural fat extends in the cranio-caudal direction from the lower aspect of one vertebral lamina to the upper portion of the lamina of the next caudal vertebra and in the lateral direction towards the point where articular facets and ligamentum flavum meets. It also fills the space between vertebral arches and intervertebral foramina, wrapping the dural sleeves of nerve roots. The epidural fat does not usually adhere to these structures, allowing mobility of the dura within the vertebral canal. However, small amounts of epidural fat covered by a thin connective membrane do adhere to the posterior midline by a vascular pedicle entering the epidural fat at the plane where the right and left portions of the ligamentum flavum meet.

The volume of the posterior epidural fat deposits increases caudally, from L₁₂ to L₅₆. The height of these deposits is approximately 21 mm (range 16-25 mm). Their width increases in the cranio-caudal direction from 6 to 13 mm (23).
Epidural fat in the posterior aspect of the epidural space is uniformly distributed while in the lateral areas fat is compartmented in groups of cells by a net of connective tissue that extends from the intervertebral foramen to the posterior longitudinal ligament. Adjacent to each vertebral disc, connective tissue fills the space left between the posterior longitudinal ligament and each vertebral disc. In the anterior aspect of the epidural space, epidural veins are often found with dura mater attaching to vertebral discs. Until recently, only fat present in the epidural space was examined. We examined other samples and found that fat cells are frequently and prominently present not only in the epidural space, but also within layers of the dura mater that forms the dural sleeves of spinal nerves (15-16), although fat cells were not identified inside the dura in the region of the dural sac (25-28). Dura mater that forms the dural sac contains approximately 80 laminae composed mostly of collagen fibres and a few elastic fibres (25-27). Its thickness varies between 270 to 350 microns (28). Characteristically no fat cells are found within the thickness of the dura mater that forms the dural sac (25-28) (Figs. 4A, 4B and 4C). However, in the dural sleeves (Figs. 5A, 5B and 5C), our electron microscope studies have demonstrated an abundant number of fat cells in between the layers of the dura that forms the dural sleeves of spinal nerves (Figs. 6A and 6B), dividing the dural laminae in groups of 3 to 5 concentric layers (15-16) (Fig. 7). Under scanning electron microscopy, fat cells appear empty, displaying a “honey comb” image (Figs. 8A and 8B) extending from the dural sac to the spinal nerve root ganglia (15-16) (Fig. 9).

Distribution of epidural fat in adults

Epidural fat also has a different distribution in the cervical, thoracic, lumbar and sacral areas. This distribution remains constant at each vertebral level (1). At cervical level fat is absent or almost inexistent in the anterior and lateral aspects of the epidural space. In the posterior aspect a small deposit is sometimes seen. In the thoracic levels, the epidural fat forms a broad posterior band with “indentations”. It is thicker near the intervertebral disc and less prominent around the middle section of the vertebral bodies and close to the base of the spinous processes. In the upper to middle thoracic levels (T1-7), epidural fat is continuous and the indentations are more evident (Fig. 3B). In the lower thoracic region (T8-12), the distribution of epidural fat becomes patchy.

At lumbar levels, the epidural fat in the anterior and posterior aspects of the epidural space forms two unconnected structures (1). The posterior epidural fat acquires its greatest volume in the

Fig. 4. — Human dural sac. A) A sagital cut shows the entire thickness of the dural sac. Longitudinal lines correspond with 80 concentric laminae. To the right the arachnoid lamina and the subdural space are identified. Scanning electron microscopy [× 300] (with permission, ref. # 25). B) Two dural laminae observed at higher magnification [× 4000]. Each lamina is made by several concentric laminar subunits. Collagen fibers are distributed in different directions across the laminar plane. Fat cells are not found at this level. Scanning electron microscopy (with permission, ref. # 27). C) Entire wall of the dural sac, showing vessels within its thickness but fat is not present here (with permission, ref. # 56).
Average thickness of the epidural fat in adults, at the lower level of the lumbar spine is about 32% of the sagittal diameter of the spinal canal (5).

Epidural fat and gender

Computerized tomography scan images at the level of the third lumbar vertebra in 30 patients showed that, although men had more epidural fat at this level, the results were not statistically significant between genders when the amount of fat and vertebral sizes were compared (29). Wu et al. examined MRI from 111 patients and did not find significant differences in the amount of epidural fat in relation to gender (30). Younger studied the distribution of epidural fat in females and found that
although women seem to have more abundant epidural fat, posterior epidural and subcutaneous fat did not show significant differences (30).

Epidural Fat in Pathological Conditions

The distribution of epidural fat (5) can be altered under certain pathological conditions (31). The following is a brief description of conditions in which the characteristics of the fat of the epidural space are different from the most common arrangement.

a) Epidural fat and obesity

In 1959, Ramsey (20) stated that obese patients had more epidural fat than normal individuals and other authors supported the hypothesis that obese patients would therefore, be at higher risk of spinal canal stenosis (32-34). Wu et al. have challenged the idea that there is a correlation between obesity and increased deposits of epidural fat (30). They studied 66 men and 45 women. In this study, height was negatively correlated with posterior subcutaneous fat thickness, but had no significant correlation with epidural fat content. There was a correlation between the body mass index (BMI) and posterior subcutaneous fat, however, BMI did not correlate with either posterior or anterior epidural fat distribution. Moreover, the presence of obesity was associated with subcutaneous fat, but not with any specific or summed epidural fat measurement (30). Consequently, weight but not body habitus is associated with specific, usually posterior, patterns of epidural fat deposition. Overall obesity is unrelated to epidural fat (30, 35).

b) Epidural lipomatosis

Epidural lipomatosis is characterized by an increase in epidural fat content. Excessive fat deposits around the dural sac cause spinal cord or nerve root compression, leading to neurological symptoms. Epidural lipomatosis may be idiopathic, but it is also seen in patients on long term steroid therapy or conditions characterized by endogenous steroid hypersecretion (36-42). The observed increase in epidural fat can be up to 72% of the antero-posterior diameter of the spinal canal. MRI of the spinal canal demonstrate increased signal...
intensity where a high epidural fat content is found, predominantly in the posterior and postero-lateral aspects, displacing and compressing the spinal cord.

c) Angiolipoma

Spinal angiolipomas (42-47) are rare benign tumours containing adult fat cells and blood vessels. More than 90% of these tumours are found in the epidural space, representing about 0.1 - 0.5% of all spinal cord tumours in adults. These tumours have a yellowish appearance, a spongy consistence and frequent hemorrhagic spots. Microscopically angiolipomas are composed of lobules of adult adipose tissue and blood vessels. MRI of the spinal canal demonstrates areas of reduced signal intensity. Characteristics sequences of fat suppression helps to identify these tumours.

d) Kyphoscoliosis

When a patient has a combination of kyphosis and scoliosis of the spine, the epidural fat distributes asymmetrically along the concave portion of the curvature displacing the spinal canal and its contents in the opposite direction. Increasingly thinner vertebral bodies tend to collapse displacing the dura outwards. MRI demonstrates the increased amounts of epidural fat around the scoliosis areas (31).

e) Spinal stenosis

Spinal stenosis refers to a reduction in the cross-sectional area of the spinal canal leading to chronic pain and neurogenic functional deficits. Characteristically, the cervical and lumbar regions are more commonly affected. This condition is frequently accompanied by a reduction in the amount of epidural fat around the stenotic area, which helps in its identification during surgical exploration (Figs. 10A and 10B). The spinal cord may become compressed by bone or fat tissue, with or without involvement of spinal nerve roots (48-49).
f) Surgery and epidural fat

In degenerative illnesses, the stenotic area of the spinal canal lacks epidural fat and the neighbouring portion of dura mater becomes thinner. During surgical laminectomy it is not infrequent to observe epidural fat distributed above and below the margins of the stenotic site. Benign intradural tumours lead to a slow and progressive compression, displacing epidural fat away from the tumour. An important aspect of epidural fat considered by neurosurgeons is its protective function over the dural sac and spinal nerve roots.

DISCUSSION

a) Role of the epidural fat in the kinetics of drugs injected in the epidural space

A fraction of drugs injected in the epidural space is absorbed and stored in the epidural fat. The amount of drugs absorbed by epidural fat depends on the lipid solubility of the drug. As such, the epidural fat acts as a drug depot, especially for lipophilic drugs, which upon their release can move onto neighbouring structures such as the dural sac, nerve roots and nerve root dural sleeves. Redistribution of these drugs is in turn affected by tissue permeability, local blood supply and the surface area involved. Drugs that are more lipids soluble will be released more slowly, potentially leading to prolonged pharmacological effects. For example storage of highly lipid soluble alfentanil and fentanyl in epidural fat tissue is 20 to 30 times higher than that of the more hydro soluble morphine. It is very likely that the distance between fat and neighbouring tissues affects the redistribution of lipophilic drugs released from epidural fat following epidural injection. During the initial absorption phase of a drug, epidural fat competes with other tissues, such as nerve root axons, spinal cord and blood vessels.

The epidural space has areas where bone and ligamentum flavum are so close to the dural sac that the space is almost non-existent. There are other areas where the epidural space is larger, and completely filled with fat. Significant variations in epidural fat distribution along the spinal canal may affect the absorption of substances in the epidural space at different levels. The fact that epidural fat is more abundant around nerve root sleeves (15-16) may determine local variations in terms of intensity and timing of nerve root blockade.

b) Fat in nerve root sleeves and its potential role in epidural anaesthesia

We have already mentioned that the amount of epidural fat can have a role in the kinetics of drugs injected in the epidural space, especially lipophilic drugs, by acting as a reservoir for such drugs. Our finding of fat embedded within the layers that compose the dura mater of spinal nerve sleeves could potentially have an even greater role (Fig. 11). Drugs injected in the epidural space eventually reach neural axons at two possible sites, either inside the dural sac in the epidural space itself, or inside the dural sleeve of nerve roots. Drugs “sequestered” by the fat in the dural sleeves could have a greater impact on nerve roots than drugs from the epidural fat, given that the concentration of

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Fat is proportionally higher inside nerve root sleeves than in the epidural space, and that the distance between nerves and fat is shorter. This effect could be compounded by the relatively low drug clearance from the dural sleeve due to the reduced number of blood vessels found in this area. Further research is needed to measure amounts of fat inside spinal nerve root cuffs, its distribution along the spinal canal and its relationships with its neighbouring root axons.

c) Implications in the epidural technique

In some areas of the epidural space the ligamentum flavum and periosteum are in direct contact with the dural sac. In other parts the epidural space is filled with epidural fat. Such a segmented distribution of fat inside the epidural space may affect epidural needle insertion and also placement of epidural catheters. Fat placed in the posterior aspect of the epidural space is attached to the midline by fibrous pedicles containing blood vessels. At this level the right and left portions of the ligamentum flavum join together (51). When the anaesthetist uses the midline approach, this point is precisely the target. If the tip of an epidural catheter hits the pedicle, it will probably deviate either to the right or left side (26-27). If the tip of the Tuohy needle hits the pedicle it may pierce a blood vessel. MRI show how posterior epidural fat is mainly distributed at intervertebral levels, just where the anaesthetist looks for the window area of needle insertion, at the level of intervertebral foramina in the lumbar region. Here a predominant portion of epidural fat can be found. The “loss-of-resistance” technique may not clearly detect the epidural space when the Tuohy needle meets the posterior epidural fat that is in direct contact with the ligamentum flavum.

d) Different pathologies and epidural fat

Pathological increases in epidural fat may alter the distribution of substances injected into the epidural space and alter the effects of the epidural blockade. Lang et al. (52) reported a patient with lipomatosis who experienced repeated failure of epidural blockade. MRI showed that epidural fat markedly increases at levels C₅₋₇ and T₃₋₉. The amount of epidural fat may have an influence on the intensity of the motor blockade and on the duration of sensory blockade (53). A pathological increase of epidural fat affects mainly the posterior aspect of the epidural space and may cause – in severe cases – dural sac and spinal nerve root compression, and rarely, the spinal cord may experience rotational deviation or even compression. In these patients, failure of an epidural blockade may be due to abnormal distribution of local anaesthetics leading to a patchy or non-symmetric sensory and motor blockade. Such patients could benefit from MRI to exclude a possible diagnosis of lipomatosis.

The amount and distribution of epidural fat may not only influence epidural effects of local anaesthetics, but could also alter cerebrospinal fluid distribution inside the dural sac and therefore, the dilution of anaesthetics injected into the subarachnoid space (54-55). In stenosis of the spinal canal, the volume of cerebrospinal fluid is reduced in the area of stenosis. If during subarachnoid injection, local anaesthetic is injected near the stenosis, lower amounts of cerebrospinal fluid would be available for dilution and relatively higher concentrations of local anaesthetic would have a more intense effect with a less predictable distribution of the spinal blockade (54-55). In scoliosis, deformity of the vertebral canal, epidural fat displacement and alterations in shape of the epidural space are, among others, changes that ought to be considered when a patient experiences repeated failures of epidural blockade.

Conclusions

Lumbar epidural fat has a metameric and discontinuous topography. The epidural fat does not usually adhere to these structures, allowing mobility of the dura within the vertebral canal. The distribution of the epidural fat changes along the spinal canal. Epidural lipomatosis is characterized by an increase in epidural fat content. When a patient has a combination of kyphosis and scoliosis of the spine, the epidural fat distributes asymmetrically. Spinal stenosis is frequently accompanied by a reduction in the amount of epidural fat around the stenotic area. Drugs absorbed by fat in the dural sleeves could have a greater impact on nerve roots than drugs stored in epidural fat, given that the concentration of fat is proportionally higher inside nerve root sleeves than in the epidural space, and that the distance between nerves and fat is shorter. The distribution of posterior epidural fat and its attaching pedicles may explain blood vessel puncture with needle or catheter, difficulties in the “loss of resistance” epidural technique and the deviation of epidural catheters from the midline. Pathological changes of posterior epidural fat may help explain repeated failures in epidural blockade.
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