



## Histology of the Human Dura Mater: A review article

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**T**HE dura mater is the outermost soft tissue covering the brain. Dura mater can be involved in many pathologies such as intracranial haemorrhage, meningitis, tumours, congenital anomalies and cerebrospinal fluid leak. It is not just a fibrous cover of the central nervous system, rather it is a complex, highly vascularized, and well-innervated tissue. Studying the normal structure of the dura mater is fundamental to neurosurgeons, radiologists, anesthesiologists, and pathologists. The Dura mater is a tough and inextensible sheath that lies directly inner to both the skull and vertebral column. It is classified anatomically into the cranial dura which covers the brain, and the dural sac which forms a tube surrounding the spinal cord. Both dural parts differ histologically. The dura mater is mainly composed of collagen fibers, entrapping in between elongated fibroblasts. In addition, elastic fibers share in their formation along with collagen fibers to offer some flexibility. Many recent anatomical updates were described in the research articles such as the presence of the telocytes in dural tissue, and the presence of lumbosacral dural venous sinuses. Understanding the normal histology of the dura mater is the first step toward diagnosing and treating various dural pathologies. In this review, we have presented a light and electron microscopic description of the dura mater and its related structures after reviewing original articles and textbooks on neuroanatomy. In addition, we have added new illustrations of the histology of the cranial and spinal dura mater.

**Keywords:** Histology, Cranial dura, Spinal dura, Nerve root cuff.

### Introduction

#### Background

Dura mater can be involved in many pathologies such as intracranial hemorrhage, meningitis, tumours, congenital anomalies, cerebrospinal fluid (CSF) leak, and even headaches [1-3]. It is not just the physical fibrous cover of the central nervous system (CNS). But it is a complex, highly vascularized, and well-innervated tissue [4]. Furthermore, studying the microanatomy of the dura mater is fundamental for neurosurgeons to perform duraplasty, either by direct closure or by applying a variety of dural substitutes or as glue. This reconstructive surgical procedure is performed to treat CSF leak, substitute dural loss resulting from trauma or tumours, or repair myelomeningocele [5-8].

The term “meninges”, singular “meninx”; is a Greek term that means membranes. They are usually grouped into two major classes; outer pachymeninx (patchy; thick) and inner leptomeninx (leptós; thin). The latter is further subdivided into arachnoid and pia mater [9]. While the term “mater” is derived from an ancient description from an anonymous Muslim scientist. He described the meninges as the mother of the brain “om al-dimagh”[10].

The meninges develop from cells derived from both the neural crest (ectoderm) and mesenchyme (mesoderm), these cells initially form a cellular network around the CNS called the meninx primitiva. The latter is further divided into two layers: the endomeninx which differentiates into the leptomeninx, and the ectomeninx which

forms the dura. Many studies suggest that the cells derived from the neural crest form the leptomeninges, while the mesenchymal cells form the dura mater. At any given point during development, both dura and arachnoid remain attached. Thus, there is no anatomic preformed subdural space [3, 6, 10, 11].

#### *Histology of the dura mater*

Dura mater is a tough and inextensible sheath that lies directly inner to the skull and the vertebral column. It is classified anatomically into cranial dura which covers the brain, and dural sac which forms a tube surrounding the spinal cord. Surprisingly, both of the dural parts differ histologically [12, 13].

Generally, the dura mater is mainly composed of collagen fibers, entrapping in between them elongated fibroblasts. These cells lie parallel to the axis of the underlying neural parenchyma [10, 14].

#### *Cranial dura mater (Fig.1)*

The thickness of the cranial dura mater in humans is  $564 \pm 50$   $\mu\text{m}$  and it is composed of three continuous layers; the outer periosteal layer, middle meningeal layer, and inner dural border cell (DBC) layer [14].

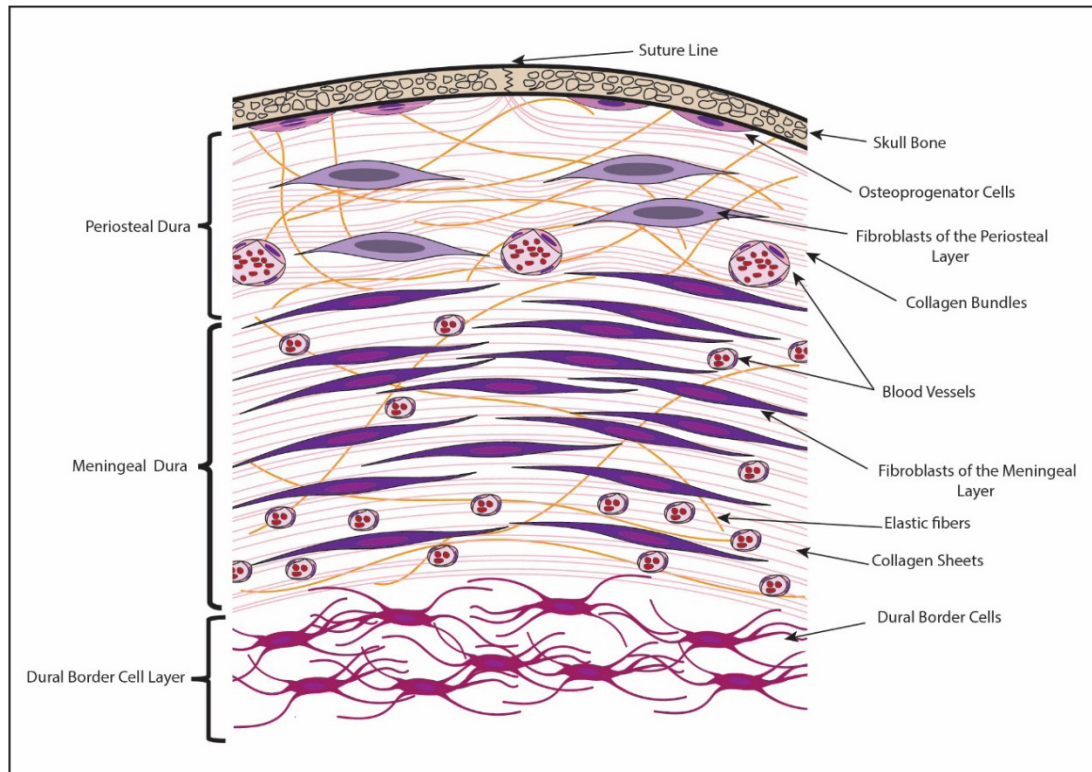
In routine Hematoxylin and Eosin-stained sections, cranial dura mater is formed of wavy collagen bundles which are arranged into two concentric layers. The outer represents the periosteal layer, while the inner represents the meningeal layer. Fibroblasts are entrapped between these collagen bundles, and they are arranged parallel to the fibers. Blood vessels are also interposed in between these fibers. In the periosteal layer, blood vessels are large and present almost exclusively in the inner part of this layer. While blood vessels of the meningeal layer are smaller, more abundant, and located at the border between the meningeal and border cell layer. Lastly, the DBC layer is formed of delicate long-processed cells inner to the meningeal layer. A network of randomly arranged elastic fibers can be visualized by orcein and Verhoeff-van Gieson stains, interposed between the collagen bundles. These elastic fibers are more abundant in the periosteal layer than in their meningeal counterpart [8, 14]. Morphometric quantification of the elastic fibers showed that the area occupied by them represents around 1.7% of the cranial dura mater [8].

By electron microscope, the periosteal dura mater contains two types of cells: the osteoprogenitor cells and large elongated fibroblasts. The collagen fibers of this layer are organized bundles that are loosely attached to the inner surface of the skull, except at the suture lines and at the base of the skull, where the attachment is firm. With advancing age, the cranial dura becomes thicker, tougher, and more adherent to the skull [10]. Due to this attachment, there is no anatomical epidural space in the cranial vault rather than it is a potential space that is created during hemorrhage. In this case, blood dissects the periosteal dura from the skull except at suture lines. So, epidural hematoma appears lenticular in shape in radiological images; short and wide [15].

On the other hand, the meningeal dura mater is the middle layer. It has smaller blood vessels. Meningeal dura has more cellular and less fibrous components than its periosteal counterpart. In addition, its fibroblasts are smaller, darker, and more elongated. Moreover, its collagen fibers are arranged in the form of sheets rather than bundles [14].

The two previously described layers are usually fused with no distinct border between them, except at sites of dural infoldings where they are separated by endothelium-lined dural venous sinuses [16]. Opposite the systemic veins, dural venous sinuses have evident internal elastic lamina. In addition, they have no tunica media, tunica adventitia, or valves [10].

The third innermost layer is the dural border cell layer. Many authors refer to this layer as (the inner dural cell layer), (subdural cell layer), (subdural compartment), or (dural limiting layer). It is composed of loosely arranged, three to eight layers of flattened fibroblasts exhibiting long processes. These processes are occasionally attached by a few desmosomes and gap junctions. Surprisingly, collagen fibers are absent in this layer. Instead, there is a copious amount of extracellular proteoglycan present in the extracellular spaces which vary in size and shape [14]. When the dural border cells were early visualized, they were mistakenly classified as mesothelial cells, hence the name (mesothelial layer), (neurothelium) [10]. DBC layer is a plane of structural weakness at the dura-arachnoid interface. Its loose arrangement, wide extracellular spaces, and absence of collagen fibrils, allow this layer to become easily disrupted during bleeding in pathological processes. In such conditions, bleeding dissects this plane freely and



**Fig. 1. A diagrammatic presentation of the histological structure of the cranial dura mater.**

creates a pathological subdural space with is not normally present in a healthy subject. Moreover, the hematoma in these cases has a classical long and thin crescent on imaging [17].

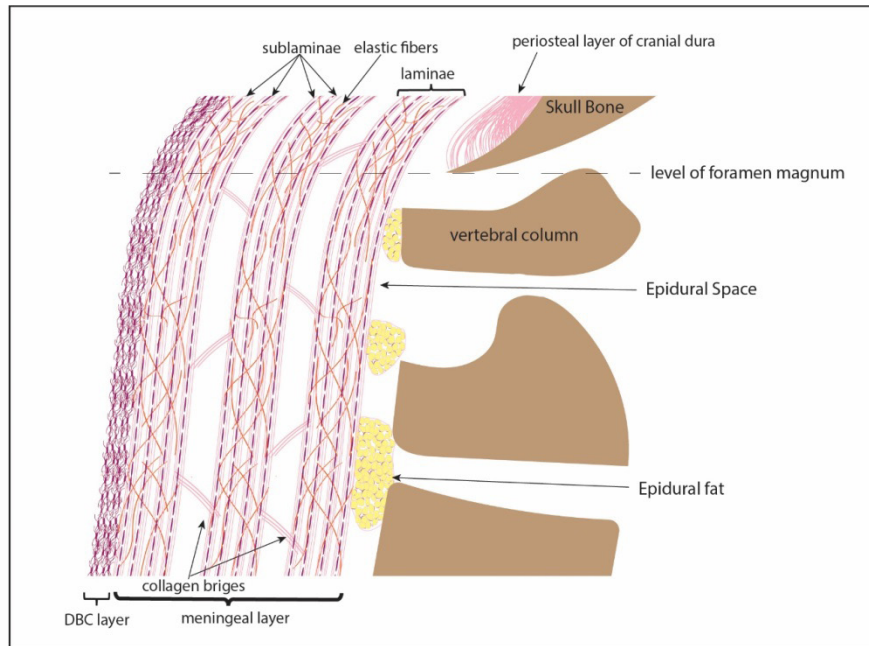
#### *Spinal dura mater* (Fig. 2)

At the level of the foramen magnum, the dura mater forms a tubal sac that is formed by the meningeal layer and the dural border cell only. The term “dural sac” refers to the dural part that covers the spinal cord. It extends down to the second segment of the sacrum, and it is attached to the coccyx by the filum terminale externum “the coccygeal ligament”. The dural sac lacks the periosteal layer, which allows it to become separated from the vertebrae by an anatomical “spinal epidural space”. This space contains adipose tissue grouped in packs. This fatty tissue has a role in the neuraxial analgesia techniques, in which the lipophilicity of the drug and the body mass index must be taken into consideration [18, 19].

On routine H&E examination, the dural sac is composed of concentric branching lamellae of collagen. These lamellae enclose clefts filled with ground substance [20]. Ultrastructurally, the meningeal layer of the dural sac is formed of around

80 concentric collagen lamellae, each lamella is around five micrometers and it is formed of 8-12 sublamellae. Along with a ground substance, collagen bridges connect the large lamellae. Thicker elastic fibers (one to two micrometers each) are also present between the collagen fibers in a lesser proportion. These elastic fibers allow considerable flexibility when subjected to the stretching forces during postural changes, in addition to the tensile strength of collagen fibers that protect the spinal cord. Moreover, adipose tissue of the spinal epidural space cushions the cord through these positional changes [20-27]. Like their cranial counterpart, fibroblasts of this layer are elongated with flattened dense nuclei. They also show a variable number of organelles and pinocytotic vesicles [28, 29].

Dural sac thickness is 250-400  $\mu\text{m}$  [29, 30]. Thickness differs among the various segments of the spinal cord; in which the thoracic segment is the thickest, while the lumbar region is its thinnest part. Moreover, many studies show the difference between ventral and dorsal parts of the dural sac, in which the central part is the thickest along with all the segments. This intra-individual thickness variation, along with the inter-individual variation should be carefully taken into consideration



**Fig. 2.** A diagrammatic presentation of the histological structure of the spinal dura mater (the dural sac) - sagittal view.

during the management of the different dural lesions [12, 31].

Opposite the cranial dura, the dural sac has no dural infoldings nor venous sinuses. Although, some investigators have described the presence of endothelium-lined lumbosacral dural venous sinuses in the posterior region of the dural sac between the level of L5 to S1 in 14 adult cadaveric specimens [32-34]. This novel anatomical fact needs to be extensively studied.

#### *Histology of the nerve root cuffs (Fig. 3)*

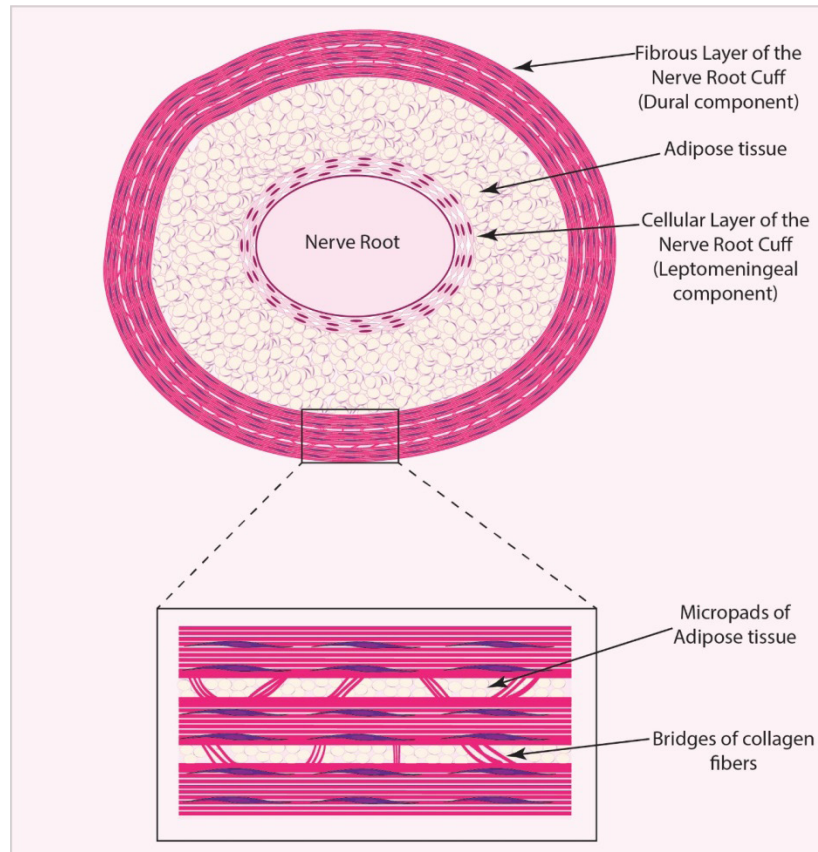
The dural sac also differs from the continuous cranial dura in which it is pierced by the peripheral nerves and blood vessels, through a cuff of the dura that is continuous with their epineuria and adventitia respectively [10, 23, 28]. Spinal nerve root cuffs are lateral extensions of both dural and leptomeninges. These extensions cover the nerve roots in their course towards the vertebral foramina to enter the nerve root sheath. They were formally known as “dural sleeves”, which is an inaccurate description due to the contribution of the leptomeninges in their formation. When examined by different visualization techniques, nerve root cuffs show mainly two layers: fibrous and cellular. The fibrous layer corresponds to the dural component of the nerve root cuff. As seen in the dural sac, this layer is also composed of concentric lamellae which are formed of collagen

fibers and a very scanty number of elastic fibers. But unlike its counterparts of the dural sac, this fibrous layer is thinner (around 150 microns thick) and its dural lamellae are often separated from each other by micro-pads of adipocytes, in addition to the collagen bridges. While the cellular layer corresponds to the leptomeningeal components. Its thickness ranges from five to eight microns and it is formed of around 14 cellular strata. Cells of these strata are flattened, elongated, and parallel to the long axis of their covered nerve root. Cells of each stratum are joined together by desmosomes and tight junctions to serve as a barrier. The innermost stratum of these cells is in direct contact with the nerve fibers. Unlike the dural sac, the fibrous layer is partially or separated from its corresponding nerve roots by a sleeve of adipose tissue. Its density differs among the different nerve root cuffs. Epidural fat is also present to cushion these cuffs from the surrounding vertebrae [35, 36].

#### *Telocytes (Fig. 4&5)*

Telocytes are recently identified interstitial cells present in many mammalian organs. These are special stromal cells that have been discovered in 2005 by Hinescu and Popescu, they first called them “cardiac interstitial Cajal-like cells”, they demonstrated their presence of them by using the conventional transmission electron microscope from human atrial ultra-





**Fig. 3. Diagrammatic picture of a transverse section of the nerve root cuff.**

thin sections, followed by image reconstructions from serial photomicrographs [43]. Afterwards, many studies have visualized the telocytes either by transmission electron microscope (TEM) or by immunohistochemical techniques throughout the body [45-47]. They have a heterochromatic nucleus and small spindle-shaped cell bodies with high nucleocytoplasmic ratio, and extremely thin 2-5 prolongations called telopodes, their length could range from ten to hundreds of micrometers, and 0.1-0.5  $\mu\text{m}$  thick. Such telopodes consist of multiple dilatations (podoms) which are linked by thin segments, termed (podomeres). These alternating patterns of podoms and podomeres resemble a string of beads, which is described with the Latin-derived term (moniliform) [44, 48, 49]. Because of these minute dimensions, telocytes can't be seen by the routine hematoxylin and eosin technique (H&E) [50]. Telocytes also have unorganized bundles of filaments, lipid droplets, dense bodies (primordial Z-lines), desmosome-like structures (primordial intercalated discs), large mitochondria, numerous caveolae, and a thin basal lamina. Telopodes surround the

cardiomyocytes, forming networks around them [51]. They participate in tissue regeneration by guiding and nursing the myocardial precursors via exosomes (40-100 nm), ectosomes (100-1000 nm vesicles originate by direct budding from cytoplasmic membrane), and apoptotic bodies (vesicles formed by outward blebbing of cell membrane of apoptotic cells) [52-54].

Telocytes are first visualized in the cranial meninges of the rats by Popescu et al. in 2012 [37-41]. Three years later, Xu et al have visualized the telocytes in the spinal dura mater of beagles by the transmission electron microscope. In this study, Xu et al., reported that telocytes are usually adjacent to the meningeal blood capillaries [42]. Further studies are needed to visualize and study the role of the telocytes in meninges.

### **Conclusions**

Dura mater is a highly arranged tough tissue. Surprisingly, its cranial and spinal parts differ histologically. In addition, elastic fibers shares in their formation along with the collagen fibers

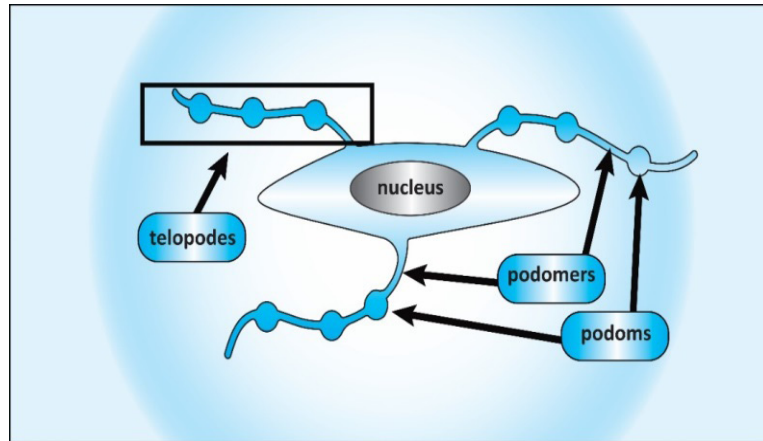


Fig. 4. A diagram illustrating the telocyte morphology.

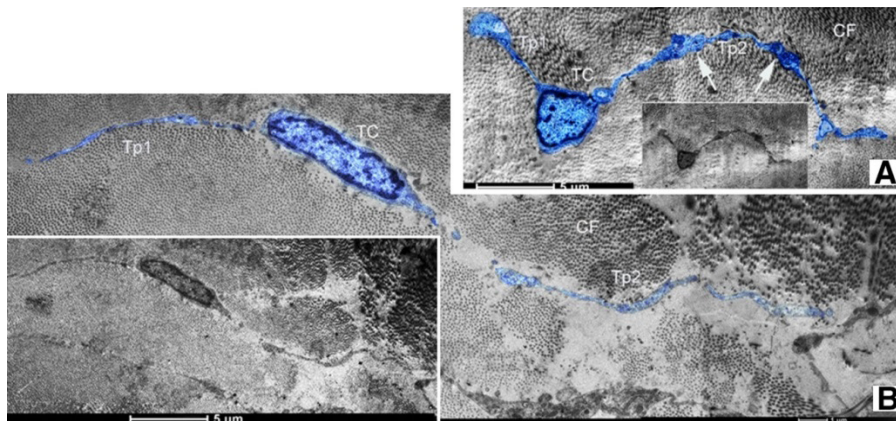


Fig. 5. “Transmission electron microscope (TEM) images of canine dura mater. (A) It shows a typical telocyte (TC) with two thin and long telopodes (Tps). The cell body of TC is round, which size is 6.56  $\mu\text{m}$  in length and 1.44  $\mu\text{m}$  in the average width. And the length of Tp1 and Tp2 is 8.34  $\mu\text{m}$  and 15.11  $\mu\text{m}$ , respectively. (B) Diameter of the TC oval cell body is 3.11  $\mu\text{m}$  approximately. The morphological feature of the telopodes with thin segments (podomers) and dilations (podoms, white arrows) is shown. Two typical Tps are 4.67  $\mu\text{m}$  (Tp1) and 15.33  $\mu\text{m}$  (Tp2) in length; CF-collagen fibre, bar =5  $\mu\text{m}$ .”[42]

to offer some flexibility. Moreover, many recent anatomical updates were described in the research articles such as the telocytes and the lumbosacral dural venous sinuses. understanding the normal histology of the dura mater is the first step toward diagnosing and treating various dural pathologies.

#### List of abbreviations

CNS: Central nervous system  
CSF: Cerebrospinal fluid  
DBC: Dural border cells

#### Declarations

Ethics approval and consent to participate  
Not applicable.

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#### Consent for publication

Not applicable

#### Availability of data and materials

Not applicable

#### Competing interests

Not applicable

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*Authors' contributions*

MHH conceived the review structure, wrote the manuscript, drew the scientific illustration, and revised the manuscript.

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## دراسة مرجعية عن التركيب النسيجي لطبقة الأم الجافية في الإنسان

مها حمدي حمدان

قسم الهستولوجي وبيولوجيا الخلية - كلية الطب - جامعة الاسكندرية - مصر.

طبقة الأم الجافية هي الطبقة الخارجية من أغشية المخ المكونة من أنسجة لينة. هذه الطبقة عرضة لمجموعة كبيرة من الأمراض الخلقية، والنزفية والمعدية والأورام الخبيثة. هذه الطبقة ليست مجرد غطاء ليفي للدماغ، وإنما تتكون من نسيج غني بالإمدادين الدموي والعصبي. تعتبر دراسة التركيب الهستولوجي الطبيعي لطبقة الأم الجافية في جسم الإنسان من المعرفة الطبية المهمة لأطباء الأشعة، وجراحي المخ وأطباء التخدير وأخصائيي علم الأمراض. تتميز طبقة الأم الجافية بكونها قوية وغير لينة بسبب تكونها من ألياف الكولاجين القوية، ومع ذلك يوجد بها كمية من الألياف المرنة. تنقسم طبقة الأم الجافية من حيث المكان تشريحياً إلى طبقة الأم الجافية الدماغية، وكيس الجافية الأنثوي الشكل والمحيط بالحبل الشوكي. تختلف هاتين الطبقتين نسيجياً عن بعضهما البعض. تصف بعض الدراسات تراكيب مكتشفة حديثاً متعلقة بطبقة الأم الجافية مثل الجيوب الوريدية الموجودة في المنطقة القطنية العجزية والخلايا ذات الامتدادات.

يعتبر الفهم المفصل والوافي لطبقة الأم الجافية خطوة أولى أساسية لتشخيص وعلاج الأمراض المتعلقة بها، بالإضافة إلى انه يساعد في فتح آفاق البحث العلمي.

في هذا البحث المرجعي قمنا باستعراض تركيب طبقة الأم الجافية تحت الميكروسكوب الضوئي والإلكتروني ، وذلك مع شرح التركيب الهستولوجي لبعض الأنسجة المتعلقة بها ، وذلك بعد مراجعة دقيقة للمقالات العلمية والمراجع في علم تشريح الأعصاب. بالإضافة إلى إلحاق بعض الرسومات التوضيحية الأصلية لأجزاء الأم الجافية في الدماغ وحول الحبل الشوكي.

**الكلمات الدالة:** علم الأنسجة، الأم الجافية الدماغية، الأم الجافية الشوكية، صفة جذر العصب.