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The routes of intracranial infections

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THE ROUTES OF INTRACRANIAL INFECTIONS

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E. Lloyd Wilbur

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PREFACE

This thesis is written to discuss the anatomy of the skull and its contained structures in regard to intracranial complications due to preexisting routes. There is no attempt to discuss clinical medicine other than in a direct connection with these preexisting routes. In this way the dangerous potentialities of certain common infectious and pyogenic conditions may be more clearly understood and carefully watched for. To thoroughly comprehend these dangerous potentialities a knowledge of the anatomy of the skull and its contents is essential. This thesis is written to make this anatomy a basis of an understanding of certain types of intracranial pathology especially those arising as complications of previous pyogenic infectious processes.
THE ROUTES OF INTRACRANIAL INFECTIONS

It seems probable that much of the damage done by intracranial infections could be prevented or lessened by watching for them when a situation occurs which has potentialities of intracranial complications. A thorough understanding of the anatomy of the skull and blood supply of the cranial cavity would enable one to possibly prevent or at least make an earlier diagnosis and thus institute earlier treatment of an intracranial complication when it does arise. The anatomy in regard to potential routes of infection will be discussed.

Anatomical Considerations

The Meninges.—The brain and spinal cord are enveloped by three membranes. From the outside inward these are; the dura mater, the arachnoid and the pia mater.

Dura Mater.—The dura mater or primitive pachymeninx arises from perimeningeal mesenchyme relatively late in embryonic life. The dura is a thick dense fibrous membrane composed of two layers. The outer serves as the internal periosteum of the skull and is probably derived from the endosteal or enchondrial tissue, and by Kapper's opinion should not be considered as a dural lamellae. The dura serves several functions; a lining for the cranial cavity, a mechanical support for the brain, and forms the great dural sinuses which are needed to remove the venous blood from the brain.

The relative simplicity of the dura may be accounted for by the concept that the skull with its lining dura forms an articulation as to other bones. In this case not with another bone but with soft tissues, the brain and pia arachnoid,
the cavity of this articulation being the subdural side of
which, as demonstrated by Maximow, is composed of fibroblastic
tissue as lines other bony articulations. 3

The dura is adherent to the inner surface of the cranium. The degree of adhesion varies, being greatest at
the suture lines and about the base, it is most adherent over
the projecting portions of the base such as the petrous por-
tions of the temporal bones. The firm adherence to the base
is augmented by the dural sheathes which follow the cranial
nerves through various foramina of the skull. Extracranially
these prolongations of dura blend with the nerve sheathes and
also become connected with the external periosteum of the
skull. Along the vault the dura is less adherent to the cran-
ium. It is fastened to the skull by many fine fibrous processes
and blood vessels which pass between it and the bone. Between
these processes are small lymph spaces (epidural spaces) here
the outer surface of the membrane is covered by endothelial
cells.

At certain places along the inner surface of the dura
strong fibrous partitions arise. These project into the cranial
cavity and divide it into several freely communicating compart-
ments. These septa are; the falx cerebri, tentorium cerebelli,
falx cerebelli, and the diaphragma sellae.

The falx cerebri projects into the sagittal fissure
dividing the cerebral hemispheres. It is attached superiorly
to the dura of the cranial vault in the midline. The anterior
inferior portion is attached to the ethmoid bone at the crista
galli. The midportion, about two-thirds of its length, is un-
attached, while the posterior third is attached to the superior surface of the tentorium cerebelli in the midline.

The tentorium cerebelli is a crescent shaped septum forming the roof of the posterior cranial fossa. It is closely applied to the superior surface of the cerebellum intervening between the cerebrum and cerebellum. The tentorium is attached posteriorly and laterally to the cranial wall, antero-laterally it is attached to the superior border of the petrous bone. The anterior border is concave in shape and is unattached. This concave free border helps to form the opening for the mesencephalon.

The falx cerebelli is a small partition inferior to the tentorium in the midline projecting between the cerebellar hemispheres. On approaching the foramen magnum it bifurcates forming two divergent ridges which fade out as they follow around opposite sides of the foramen magnum.

The diaphragma sellae is a small fold forming the roof of the sella turcica. This fold is perforated by an opening for the stalk of hypophysis.

The Subdural Space.--This is a relatively potential space lying between the dura mater and the arachnoid. The subdural space is lined by two different membranes. Externally is the dura which is permeable to infection and injection materials, and organizes and removes blood from the subdural space, also it has a standard capillary circulation. Injury to the dura without injury to the arachnoid does not produce adhesions.
The arachnoid membrane is relatively impermeable to those things to which the dura is permeable, this will be further considered under the discussion of the pia-arachnoid. In studies of response to injury it appears that the dura is held in check from forming adhesions to the arachnoid in the normal body only by the integrity and resistance of the cells covering the arachnoid, for if these are injured adhesions are promptly formed.

This sharp distinction between the dura and the pia-arachnoid indicates that the subdural space does not correspond to the description of other serous cavities such as the peritoneal or pleural cavities. Part of this difference may be explained in the origin of the lining membranes. The dura, as previously stated, has a mesenchymal origin, while the pia-arachnoid is ectodermal in origin. As previously explained it would probably be better to consider the subdural space and its lining as an articulation rather than as a serous cavity.3

The subdural space is carried outward for a very short distance on the cranial nerves, however on the optic nerve it is carried the full length of the nerve. The space in no way is in free communication with the subarachnoid space. It does, however, communicate with the perineural spaces as shown by Key, Retzius, and later by Cuneo. These men demonstrated that material injected into the subdural space could be found in the perineural spaces. By similar injections into the subdural space it was also demonstrated that there was a free communication with the extracranial lymphatics especially those of the nose. Key and Retzius also found that the true lymphatics did not
communicate with the perineural spaces. The subdural space has another communication that is unusual and will be described when discussing the middle ear. This is a continuation through a patent subarcuate fossa and in some cases the dura actually lined the antrum.

The Arachnoid.—This is a thin non-vascular membrane. It lines the inner surface of the subdural space and is loosely attached to the pia mater and forms the external limiting membrane of the subarachnoid space. The arachnoid does not follow the minor contours of the brain. It does not dip into the sulci except the longitudinal cerebral fissure, but is loosely attached over the crests of adjacent gyri.

The Pia Mater.—The pia mater, a thin membrane, lies everywhere in intimate contact with the external surface of the brain, and penetrates into the depths of the cerebral sulci.

The Pia-Arachnoid and Subarachnoid Space.—The pia-arachnoid or leptomeninx is ectodermal in origin arising from cells in the neural crest. Harvey and Burr have shown that they fail to develop in the absence of the neural crests.

These tissues form a relatively impermeable sac enclosing the cerebrospinal fluid after it leaves the brain. The impermeability of the pia-arachnoid is shown by experimental evidence. It is completely permeable to alcohol alone of the foreign substances injected to test its permeability. It is only partially permeable to methenamine, chloroform and ethyl carbonate. To toxins and antitoxins its permeability is slight or absent. Zylberblast-Zand has shown that this barrier action which protects the central nervous system is a function of the
pia-arachnoid and not the choroid plexus. Zylberblast-Zand has observed that after removal of an area of the pia mater from the brain, trypan blue injected intravenously accumulated in this denuded area and the rest of the central nervous system was entirely free from the dye. This barrier action will be discussed in greater detail.

Between the arachnoid and the pia project numerous delicate trabeculae connecting these two membranes and thus forming a delicate mesh. The arachnoid, pia, and trabeculae lining and occupying the subarachnoid space are covered by flattened polygonal mesothelial cells. The meshes vary in size, increasing from the very fine reticular spaces over the cerebral hemispheres to wider more open spaces in the cerebral sulci and about the spinal cord, reaching their maximum in the cisternal dilatations about the cerebello pontine angle.

The mesothelial lining cells are also of importance because of their changing morphology under varying physiological conditions. These cells will phagocytose carbon granules introduced in the subarachnoid space, and when phagocytic these cells increase in size. It was shown by Essick that the presence of foreign material caused these cells to become enlarged, vacuolated, phagocytic and finally detached to form free macrophages in the cerebrospinal fluid.

The subarachnoid space is formed by the separation of the pia and arachnoid membranes. The width of the space varies in different areas. It is smallest over the cerebral gyri. Being larger in the sulci and the cisterns.
Greatest of these cisterns is the cisterna cerebello-medullaris. This is formed by the arachnoid bridging over the wide interval between the posterior part of the inferior surface of the cerebellum and the medulla oblongata. It is continuous with the posterior part of the wide subarachnoid space of the spinal medulla.

On the floor of the cranium lies the cisterna pontis and it is a continuation upwards of the anterior part of the subarachnoid space of the spinal medulla. In the region of the medulla oblongata it is continuous behind with the cisterna cerebellomedullaris thus entirely surrounding this section of the brain with a wide subarachnoid space.

In front of the pons the arachnoid bridges between the temporal lobes thus covering a deep hollow in this area, and forming the cisterna interpeduncularis which contains the circle of Willis. Leading out from this cistern are certain wide subarachnoid channels. Two of these are prolonged into the lateral fissures and accommodate the middle cerebral arteries. Anteriorly it passes into a space in front of the optic chiasm, the cisterna chiasmatis, from here it is prolonged in the longitudinal fissure above the corpus callosum. The anterior cerebral arteries course through this subarachnoid space.

The most intimate contact between the dura and the arachnoid is made by the arachnoid granulations. These are small, fleshy appearing excrescences, purplish-red in color. These may be found in any place on the dura but mostly along the great dural sinuses especially along the superior sagittal. The arachnoid granulations are prolongations of the arachnoid membrane so that
the arachnoidal mesothelial cells come into direct contact with vascular endothelium of the great dural venous sinuses. These villi are covered by typical arachnoid cells usually of a single layer but often forming whorls and presenting double layered coverings. The core of such a villus may be a strand like network reduplicating the subarachnoid space or a myxomatous groundwork simulating the perimedullary mesenchyme.7

All structures, blood vessels and nerves traversing the subarachnoid space are covered by the mesothelial elements lining the space. About each of the blood vessels perforating the brain substance is a distinct fluid space. This is a continuation of the subarachnoid space, these are called the perivascular channels or spaces. The cells of the pia mater turn inward to form the outer cuff of a perivascular channel, while the cells of the arachnoid as they cover vessels traversing the subarachnoid space are continued inward to form the inner cuff. Thus each blood vessel penetrating the central nervous system is surrounded by a cell enclosed, fluid filled, perivascular channel space which communicates directly with the subarachnoid space.

This perivascular channel when the mesothelial cell cuff ceases, continues inward directly connecting with the perineuronal spaces surrounding the nerve cells. These ultimate spaces are potential in normal conditions but under certain circumstances become readily recognizable microscopically. Although these were originally termed lymphatic in character they have no connection with the lymphatic system. They do represent, however, an important accessory fluid system of the neuraxis, affording a direct pathway uninterrupted by cell membranes between
The Cerebrospinal Fluid.—The cerebrospinal fluid is entirely enclosed within the brain and the subarachnoid space, at no point does it have uninterrupted contact with other body tissues or fluids. The fluid has much the same constituents as lymph. Normally it differs from blood in its constituent parts mostly in having a high chloride and a low protein.

Complete enclosure of the cerebrospinal fluid is accomplished by the unbroken mesothelial covering of the subarachnoid space and the ependyma. The ependyma is the epithelium of the central nervous system and lines all of its cavities. It has no normal breaks in continuity. This epithelium has two limiting membranes. The outer separates it from the pia mater, the inner is formed by the cuticle of the cells. The cells of the ependyma normally vary from flattened to columnar in different areas.

In the circulation of the cerebrospinal fluid several factors should be considered: These are the source, the area involved and the flow, also the point of exit or absorption. The source or origin has been rather well established as the choroid plexus. Whether this is by secretion or by dialysis is a controversial point. The anatomy of the choroid gives some basis to both theories.

The choroid plexuses are found attached to the walls of the ventricles. They are formed by masses of blood vessels in folds of pia mater bulging into the ventricles. The choroidal tela and the choroid plexus are composed of a highly vascular pial membrane which is separated from the lumen of the ventricle.
by a cerebral epithelial membrane. The pial tissue resembles formless connective tissue but comprises only the smaller portion of the structure. In this tissue the collagen fibers form a loose network which is condensed immediately under the epithelium as well as at the bases of the villi. The bulk of the subepithelial portion of the plexus, however, is formed of blood vessels. Characteristic of these vessels is the presence of large venous sinuses as well as the dilated capillaries which lie in each villus. The sinuses are composed of caverns of variable width which extend to the epithelial cells. The cavern walls are much thinner than those of the vein, they do not contain any muscle fibers but do contain elastic fibers. In the villi themselves sinuous dilated capillaries appear and these also border directly on the epithelial cells.°

That the choroid plexus is the main source of the cerebrospinal fluid was shown by Dandy when he experimentally produced an unilateral internal hydrocephalus by blocking one foramen of Monro and later preventing the development of an unilateral internal hydrocephalus by extirpating the corresponding choroid plexus. Weed also has produced anatomical evidence to indicate that the perivascular spaces pour some fluid into the subarachnoid space. The ependymal cell lining may also contribute even in the adult a minimal addition to the fluid.

The circulation of the fluid is from the lateral ventricles through the foramina of Monroe into the third ventricle and through the aqueduct of Sylvius into the fourth ventricle. From here it enters the subarachnoid space through the
foramina of Magendie and Luscka. After spreading through the
subarachnoid space it is absorbed by the arachnoid granulations. The control of the circulation is probably dependent upon differences in pressure. The pressure in the capillaries of the choroid plexus is probably 60 to 80 mm. of mercury. That of the fluid is from 110 to 130 mm. of Ringer's solution. Then it comes in contact with the dural venous sinuses where the pressure is lower that that of the cerebrospinal fluid as determined by punctures in the superior sagittal sinus and the cisterna magna. The rate of production and circulation may be altered by changing the blood osmotic tension, by the injection into the blood stream of hypotonic or hypertonic solutions.

Absorption of the fluid is normally by way of the arachnoid granulations. However, under influence of the increased salt content of the blood as produced by strongly hypertonic salt solutions, absorption also takes place by way of the perivascular channels and the ependymal lining into the capillaries of the central nervous system. In the normal process filtration is probably the chief factor, but in great differences of osmotic tension, osmosis and diffusion apparently play the greatest roles. The arachnoid membrane is imperforate around the nerve roots and any fluid that passes into the perineural spaces must do so by extravasation.

The Hematoencephalic Barrier.—The term hematoencephalic barrier refers to a phenomenon which shows itself as a selective permeability of the membranes separating the blood stream from the cerebrospinal fluid. One of the outstanding characteristics of this phenomenon is that the select-
ive permeability acts from the blood stream to the cerebrospinal fluid, while from cerebrospinal fluid to bloodstream the permeability appears to be complete.\(^6\)

The main anatomical constituents of this barrier probably are; the choroid plexus, ependyma, neuroglia, cerebrospinal vessels, and leptomeninges.

Part of the selective permeability was shown by Kafka when he demonstrated that uranine injected into the blood stream accumulates mainly in the choroid plexuses, only traces were found in the ependyma. Goldman has shown the dyes such as trypan blue, methylene blue, and osamine blue injected intravenously accumulated in the choroid plexuses and no other part of the nervous system showed any of the dye.

The work of Zylberblast-Zand on the barrier action of the pia mater in relation to intravenous injections of trypan blue has already been described.

L. Stern advocates the idea that in normal conditions the passage of crystalloids is mainly controlled by the choroid plexuses and the ependyma, while the passage of colloids is regulated chiefly by the walls of the vessels.\(^6\)

So far as is known there is no substance in the cerebrospinal fluid as it comes from the choroid plexus which is not already present in the plasma. Some substances with large molecules are completely excluded from the cerebrospinal fluid, namely fibrin, lipoids, most ferments and immunological substances such as antibodies, complement and lysins.\(^11\)

Certain pathological conditions alter the permeability of the barrier. The best measure of the permeability of
the barrier is by the bromide test designed by Walter. So far a relationship between the permeability quotient and age, sex or menstruation has not been demonstrated. The permeability quotients show little variations for the same individuals on repeated examinations.\textsuperscript{12} Histologic studies of cases of paresis in persons whose permeability index was determined shortly before death showed that there was a definite relationship between the index and the amount of iron in the cerebral vessel walls.

The fluctuations of the index generally preceded the corresponding changes in the clinical picture of the patients with paresis.\textsuperscript{13} The permeability may also be increased by active tuberculosis, cerebral arteriosclerosis, acute infection and the reactions to typhoid inoculations.\textsuperscript{14}

The Intracranial Circulation and Vascular Communications.--The intracranial arterial blood is brought into the cranial cavity by the carotid and vertebral arteries. The final return circulation is predominantly carried out by the internal jugular veins.

Close to the skull between the inner and outer layers of the dura are the dural sinuses forming the larger intracranial veins. These sinuses are grouped as the paired and unpaired. The unpaired are the superior sagittal and inferior sagittal, the straight, the anterior and posterior intercavernous and the basilar.

There are six paired sinuses, the transverse, the occipital, the cavernous, the superior petrosal, the inferior petrosal and the spheno-parietal.
As potential routes of infection these sinuses are important chiefly through their extracranial communications.

The superior sagittal sinus communicates at its anterior end through the foramen caecum by a vein connecting it with the nasal cavity or the angular vein. Near the vertex it has venous communications with the exterior of the skull, through the parietal foramina. At its posterior extremity in the confluent sinus there is an emissary vein passing to the external side of the occipital bone where there is a communication with the occipital vein and an occipital diploic vein.

The transverse sinuses pass along the inner surface of the mastoid bone. Here it communicates with the exterior of the skull through an emissary vein especially the mastoid emissary vein which will be discussed with the mastoid bone.

Small veins draining the tegmen tympani, tegmen antri and the middle ear mucosa pass through the petrosquamous suture connecting these structures with the superior petrosal sinus.

The inferior petrosal sinus is connected with the inner ear by the internal auditory veins. These veins sometimes drain into the transverse sinus.

The cavernous sinus has many extracranial communications. It receives blood from:

1. The dura mater through the spheno-parietal sinus.
2. From the cerebrum and meninges through the inferior and anterior cerebral and meningeal veins.
3. From the mucous membrane of the sphenoid air cavity through small veins penetrating the bony wall of this nasal accessory sinus.
4. From the forehead, supraorbital region, nose, eye and other parts of the upper face, through the main venous supply, the superior and inferior ophthalmic veins and their communications.

The frontal and supraorbital veins unite at the root of the nose to form the angular vein. The angular vein courses downward and at the lower margin of the orbit becomes the facial vein. A small tributary called the nasal frontal, branches from the angular and communicates with the superior ophthalmic. As the superior ophthalmic continues toward the cavernous sinus it receives: At the margin of the orbit, a tributary from the frontal diploe; within the orbit the anterior and posterior ethmoid veins from the ethmoid and sphenoid air sinuses and the intranasal tissues; also the ciliary veins from the tissues of the orbit. Finally it enters the anterior portion of the cavernous sinus at the sphenoid fissure. A network of veins on the inner portion of the floor of the orbit gives rise to the inferior ophthalmic vein. This plexus communicates with the facial veins and passes toward the fundus of the orbit, receiving tributaries from the various eye muscles. It may open directly into the cavernous sinus or into the superior ophthalmic vein just before it enters the cavernous sinus. An important branch of the inferior ophthalmic vein communicates with the pterygoid plexus through the sphenomaxillary fissure.

The branches leading blood from the cavernous sinus are:
1. Small veins that pass from its under surface through the foramen ovale, the foramen rotundum to communicate with the pterygoid plexus. Through these branches there is an indirect relationship between the cavernous sinus, the soft palate, the faucæ, alveolar processes and pharynx, the veins from these areas enter the pharyngeal and pterygoid plexuses which communicate with each other.

2. A number of fine veins which accompany and surround the internal carotid artery while it passes through the carotid canal and thus they reach the jugular bulb.

3. The superior and inferior petrosal sinuses which pass from the posterior extremity of the cavernous sinus and carry blood to the transverse sinus.

There are also intercommunicating passages between the cavernous sinuses, these are:

1. The coronary or circular sinus which consists of a double cross anastomoses between the cavernous sinuses, it lies in front and behind the infundibulum of the pituitary body.

2. The transverse occipital or basilar sinus at the caudal end of the cavernous sinus serves as an intercommunication between the two.

The major portion of the blood entering the angular
vein is carried off by the facial vein only a small part enters the superior ophthalmic. There is also an important branch of the facial, the deep facial or anterior internal maxillary vein, originating in the pterygoid plexus and entering the facial vein beneath the zygomatic muscles.

The pterygoid plexus with its many communications lies in the pterygoid fossa. By the deep facial it communicates with the facial vein; with the pharyngeal plexus by anastomotic branches; with the cavernous sinus through small veins traversing the foramina ovale, lacerum medium, rotundum, and Vesali; and by a small branch through the sphenomaxillary fissure with inferior ophthalmic. Most of the blood of the pterygoid plexus drains into temporomaxillary vein which combines with the posterior auricular to form the external jugular.

There is either an absence or total incompetency of the valves of the facial, angular and ophthalmic veins. Furthermore the intracranial veins, those of the pterygoid plexus, and the small veins joining it with the cavernous sinus are free from valves. This absence of valves permits the blood to flow unimpeded in either direction.

The direction of blood flow in the emissary and intracranial channels is frequently changed due to such conditions as changes in gravity, muscular exertion, the relative pressure inside and outside of the cranium and respiratory cycle.

Inspiration tends to rapidly drain the blood from the skull. The opposite effect is produced by expiration and muscular exertion or strain. The blood may flow between the cavernous and petrosal sinuses out into the ophthalmic at times of
severe muscular exertion may flow up the facial and emissary veins of the cavernous sinus from the pterygoid plexus, depending on the relative difference in forces exerted in different parts of the respiratory cycle. 15

Another set of important venous channels are the diploic veins. The diploe of the cranial bones of the adult contain numerous tortuous channels. These are lined more or less completely by a layer of compact tissue. These veins are large, their walls are thin being formed only of endothelium resting on an elastic tissue layer. At irregular intervals there are pouch like dilatations or culdesacs which serve as reservoirs for blood. These diploic veins are confined to their particular bones as along as the bones are distinct and separate, when the sutures unite they intercommunicate and increase in size. Some of the small veins of the mucous membrane of the nasal accessory sinuses communicate with the diploic veins. There are also anastomoses between the veins of the diploe and the veins of the skull dura. 16

The Nasal Accessory Sinuses - Nasal Mucosa.-- In relationship to intracranial pathology the most important of the sinuses are the frontal, ethmoids and sphénoid. 17

The frontal sinus is lined with a mucous membrane that is continuous with that of the rest of the upper respiratory tract. Some of the veins of this mucous membrane communicate with the diploic veins. 17 The frontal sinuses come into relationship with the brain cortex in the region of the frontal pole. The amount of potential brain exposure is in proportion to the areal of the frontal sinus. 4 When perforations occur
in disease of the frontal sinus they are found in:

1. The anterior wall or outer table of the skull.
2. The floor or the orbital wall, and if the orbital periosteum is perforated, into the orbit.
3. The posterior and into the intracranial cavity.\(^{17}\)

The ethmoidal sinuses lie in close relationship to the basal brain cortex near the gyrus rectus and for some distance lateral to it.\(^4\) They are separated from the orbit by a very thin bony wall. There is also a close relationship to the filaments of the olfactory nerve. There is frequently a vein draining the mucous membrane of this area which passes through the cribiform plate and into the anterior end of the superior sagittal sinus. The lymphatics of this region are not well worked out, though Key and Retzius and Cuneo have shown that they in some way probably connect with the subdural space.\(^4\)

Perforations occurring in disease of these sinuses are found to enter:

1. The orbit.
2. The nasal cavity.
3. The intracranial cavity.\(^{17}\)

The sphenoidal sinus is in close relationship to the base of the brain and the basal cisterns. It is separated from these only by a thin bony wall. This sinus is also very close to the cavernous sinus only a thin bony partition forming the barrier.\(^4\) There is free venous communication between the sinus and the venous sinuses of the dura, the cavernous and petrosal sinuses and the basilar and carotid plexuses, as well as with the arachnoid vessels within the bulbar cistern. Through these communications emboli which have formed in the veins of the
sphenoid may reach any part of the return circulation of the head.\textsuperscript{18}

There exists a potential connection which sometimes under pathological conditions becomes an actual connection of the optic nerve. H. Herzog of Innsbruck, Austria demonstrated that there are often extensive marrow spaces of the bone between the sphenoid sinus and the optic canal. These are intimately connected with the submucosa of the sinus and the dural sheath of the optic nerve by means of cellular processes running from the dura into the spaces where they blended with cellular elements derived from the submucosa of the sphenoid sinus extending into the same spaces.\textsuperscript{19}

Perforations occurring in sphenoidal sinus disease appear through:

1. The roof into the intracranial cavity.
2. The floor or anterior wall into the pharynx.\textsuperscript{17}

In relation to intracranial pathology the portion of the nasal mucosa about the olfactory epithelium is probably the most important.

That there exists a direct connection between this area and the central nervous system is well established. In specimens prepared from animals, W. E. Clark found that a solution of potassium ferrocyanide and iron ammonium citrate, which had simply been dropped into the nasal cavities, was very rapidly absorbed by the nasal mucous membrane and within an hour had reached the surface of the brain. The intermingling of the prussian blue granules with the cells of the olfactory epithelium
is evidence that the solution had penetrated throughout the thickness of the epithelium.

In a few cases minute capillaries which run among the fibers of a olfactory nerve bundle and passed through the cribiform plate were found to contain prussian blue granules. Occasionally a larger vessel presumably a small vein also passing through the cribiform plate but along the side of a nerve bundle was found.

Blood vessels which pass through the cribiform plate lie in the sheaths of the nerves which they accompany, that is among the meshes of the trabecular tissue which is an extension of the pia-arachnoid through the cribiform plate and into the nose.

The nasal mucosa is connected directly with the substance of the brain by the axis cylinders of the olfactory nerves and the trigeminal nerves thus connecting the mucous membrane with the olfactory bulb and the medulla.

Evidence that there is a connection between the nasal mucosa and substance of the brain in man is presented by a case quoted from Hayen by Logan Turner. "A man had an attack of epistaxis and sought the aid of a pharmaceutical chemist who plugged his nose with a tampon soaked in perchloride of iron. A few days later the man died from meningitis. At the necropsy it was found that the olfactory bulbs were stained brown and gave the prussian blue reaction."

The direct connection between the nasal olfactory epithelium and the brain is by the olfactory nerves. The olfactory cells are bipolar and extend through the entire thickness of thickness of the neuroepithelium. The peripheral pro-
cesses are short and extend to the surface of the mucosa. The central processes become grouped in twenty to twenty-five bundles and pass through the cribiform plate to the olfactory bulb. The olfactory bulb is brought into connection with the brain by fibers passing through the olfactory peduncle.

Connections of the olfactory bulb within the central nervous system are important if the passage of a neurotropic virus is considered. One of these tracts is the basal olfactory bundle of Wallenberg which terminates in the hypothalamic region in or near the mamillary body partly in the interpeduncular region and partly in the lower areas of the brain stem. By another tract the bundle of Vicq d'Azyr, the tract to the mamillary body connects with the anterior nucleus of the thalamus, and with the dorsal tegmental nucleus of Gudden in the central gray matter of the midbrain. This is an important olfactory relay point. Thus there are tracts and connections to all parts of the central nervous system either direct or by connections through the thalamus.

The Orbit and Optic Nerve.--The orbit is structurally weakly walled on three surfaces:

1. On the roof between the frontal sinus and the brain.

2. In median wall next to the ethmoid sinuses.

3. On the floor over the maxillary sinus.

On these surfaces the bones are thin and weak being easily perforated by suppurative processes.

The most important structures of the orbit in regard to potential paths of infection are, the inferior and superior ophthalmic veins and the optic nerve.
A discussion of the veins has already been given, therefore only the optic nerve will be described.

Direct connection between the eye and the brain is formed by the optic nerve, the coverings of which are also continuous with those of the brain.

The outer covering is continuous posteriorly with the dura and anteriorly with the outer layers of the sclera. It joins the optic nerve in the optic canal and at its anterior exit it splits into two layers, the outer going to form the peri orbita, while the inner continues forward as the external covering of the nerve.

The subdural space of the optic nerve is potential being crossed by trabeculae, it is in direct continuity with the subdural space surrounding the brain.

The arachnoid sheath of the brain is extended along the optic nerve forming the middle sheath and inserting anteriorly into the sclera. From the chiasm to the optic canal it is loosely attached to the nerve, in the orbital portion of the nerve it is closer to the dura than the pia. The subarachnoid space of the optic nerve is fluid filled and is a direct continuation of the subarachnoid space which envelopes the brain.

Closely surrounding the optic nerve is the pia. It is continuous with the pia of the brain and inserts anteriorly into the inner layer of the sclera and the chorioid.

Key and Retzius were able to inject the subdural and subarachnoid spaces from the corresponding spaces of the brain.
The Temporal Bone and Middle Ear.--The middle ear is a narrow cleft-like space in the temporal bone. Anteriorly it communicates with the nasopharynx by the Eustachian tube. Posteriorly the attic communicates by the aditus with the antrum and through it with the mastoid cells. There are also communications with cells of the petrous pyramid. The middle ear is developed by an upward and backward growth into the temporal by a hollow bud of mucosa from the nasopharynx. Other parts of the temporal bone to be dealt with in this section are: The inner ear, the mastoid process and the petrous pyramid.

The inner ear is contained in a hard compact bony capsule, this houses the labyrinth and is composed of three layers. The innermost or endosteal layer arises from the connective tissue endosteum which lines the entire perilymphatic space. The intermediate or endochondrial layer is developed from cartilage and throughout life it retains islands and strands of cartilage. These two layers are compact bone and have reached their full size at birth. The outer or periosteal layer is a connective tissue bone derived from the periosteum. The portion which forms the inner tympanic wall comes in contact with the tympanic mucosa, and in its developmental stage may be subject to that tissue's pneumatizing power. Therefore the periosteal layer often shows definite tracts of pneumatic spaces which surrounds the other layers. There are no reports of pneumatization ever occurring in the inner two layers. Thus the inner ear is protected from invasion at all points except the natural openings, the oval and round window, the endolymphatic
and cochlear aqueduct, the internal auditory meatus and the blood vessels.

Veins of the inner ear drain into the superior and inferior petrosal sinuses and the jugular bulb. The lymph drainage is divided into two parts. The endolymph system ends in the saccus endolymphaticus which lies between the layers of the dura. The perilymph system communicates directly with the subarachnoid space of the posterior cranial fossa by means of the narrow cochlear aqueduct. The oval and round windows are exposed to the middle ear cavity.

The mastoid process of the temporal bone generally is a porous structure containing many air cells, only about 20% of the mastoids are acellular.

This porous structure with its air cells is the result of pneumatization. This pneumatization is carried out by the mucosa derived from the nasopharynx. Thus the lining epithelium of the middle ear and mastoid cells arises primarily from the Eustachian tube. In the front part of the middle ear cavity and in the tube the epithelium is ciliated, toward the mastoid antrum the cells become more flattened. A full developed mastoid cell is usually lined by a single layer of flattened epithelial cells.

The cellular structure of the mastoid is varied, usually there are three types of cells, any one of which may predominate. The marrow spaces large and small apparently inter-communicate throughout. These cells have no lining membrane. In addition to the marrow spaces there are small spaces which are not cells, in the sense of their being air containing, but
are filled with a loose, sparsely cellular areolar tissue in which there are one or more blood vessels of varying size.

A layer of surface epithelium and tunica propria composes the lining of the pneumatic cells. This tunica propria consists of a rather loose areolar ground work in which are found many young connective tissue cells, some plasma cells and a few monocytes; but of greatest importance a veritable network of small thin walled capillaries. Some show evidence of containing blood, some others appear empty and are probably lymph vessels. This tunica propria is in contact with the bone and is a continuous system from the Eustachian tube to the smallest mastoid cell. This does not extend into the marrow spaces but only to the openings. As a result these are closed off from the air containing cavities of adjacent cells, though capillaries are seen to pass into the marrow spaces, and red and white cells from the marrow spaces cluster about the capillaries in the tunica propria of adjacent cells, thus a close communication is established between the mastoid cells and the marrow spaces. ²⁶

There are two other structures to be considered in relation to the mastoid process, these are the subarcuate fossa and the mastoid emissary vein.

The subarcuate fossa should be gradually obliterated during childhood. During this period, however, a depression or canal may be found which contains sometimes a vein and artery surrounded by a process of the meninges, and communicates with the mastoid cells. D. Wolff has noted five cases, the oldest of which was 48 years, in which the subarcuate
fossa communicated with the mastoid antrum, the dura actually serving as a lining for the antrum.

The mastoid emissary vein may be absent but is usually present, generally single and small but may vary in size. It originates on the outer edge of the lateral sinus groove just below the bend, and has a short course in the substance of the bone in an upward and backward direction. This vein opens on the surface just behind the upper posterior edge of the base of the mastoid process and drains into the occipital or posterior auricular vein. The vein varies in size from thread-like to three-eights of an inch in diameter. In two of fifteen hundred skulls examined, the mastoid emissary vein took the place of the lower part of the lateral sinus. The mastoid cells may extend up to it above, outside and below, but never medial to the vein. Some of the diploic veins may open into this emissary.\(^2^8\) The vein may drain into the occipital vein which is usually associated with a definite plexus, the ramifications of which are prone to anastomose through its many vessels with any or all of the veins of the neck either superficial or deep.\(^2^9\)

The petrous portion of the temporal bone, exclusive of the otic capsule, is normally a spongy bone containing marrow spaces. However if it is subjected to the pneumatizing influence of the tympanic mucosa, it may be converted into a bone consisting of air containing spaces.\(^2^4\)

There must be a contiguity of tissue as far as the epithelial tissue of the petrous pyramid is concerned. Developmental steps take place in the pneumatized petrosal pyramid, the
same as take place in the mastoid process. The same histological structure is found in both bones. The cellular type of the petrous apex may be either pneumatic or diploetic. It is through the thin capillary walls that an intimate anastomoses is said to exist between the pneumatic and marrow containing spaces, however direct communications are often found.

The osseous lamina forming the walls of the petrous pyramid are exceedingly thin, and bony defects or dehiscences are not infrequent. These are most frequent in the roof and under the Gasserian ganglion, also in the middle fossa and the carotid canal. Along the posterior border where the bony cortex is thicker, dehiscences were not found. Even where dehiscences were not found under the Gasserian ganglion, the cortex was so thin that the pneumatized and marrow spaces were in intimate contact with the ganglion.

In some sections the distal extremity of the apex, near the posterior inferior border, appears fused with the sphenoid bone. This fusion may also take place with the basilar part of the occipital bone.

Usually the petrous and mastoid tend to be similar in structure in the same individual. It is not unusual for the pneumatization to extend to the squamous, the zygomatic and even the occipital bones. There is an intercommunication between the system of cellular spaces in the mastoid and the petrous bones.

There are two great routes of pneumatization of the petrous pyramid:

1. The antrum epitympanic.
2. The hypotympanic.
Anatomically the cells can always be traced to one of these routes, embryologically they develop in this manner.

In the antrum epitympanic route the cells extend from the antrum and epitympanic space above the cochlea and above and behind the superior semicircular canal; then behind, above and in front of the internal auditory meatus and finally to the mass of cells under the tegmen of the anterior surface of the tip.

The hypotympanic route: The cells extend from the hypotympanic space below the cochlea; then below the internal auditory meatus and finally to the mass of cells under the tegmen of the posterior tip. The two groups meet immediately below the depression for the Gasserian ganglion. 32

Other routes of pneumatization noted are:
1. From the peritubal cells into the pyramidal tip.
2. From the peritubal cells directly into the carotid canal, or through dehiscences in the anterior tympanic wall into the carotid canal.
3. Along the perilabyrinth cells originating in the antrum. 30

All of this pneumatization arises from a common source, the mucosa of the nasopharynx which forms, first, the Eustachian tube, then the tympanic cavity and mastoid antrum, from here the pneumatization spreads especially to the mastoid and petrous bones.

The presence of dehiscenses in the carotid canal and close to cranial nerves are especially important due to the perivascular and perineural tissue spaces. The tissue spaces
of this region have been shown to be in communication with the lymphatics of the neck. Probably the most important demonstrated communication is the one shown by Papale. This is, that there is a direct communication of the pericarotid tissue spaces with those of the sixth nerve at the point where the nerve crosses the internal carotid in passing through the cavernous sinus.33
SECTION TWO

The Routes of Infection

The types of infection involving the intracranial contents are primarily of two varieties; one involves the nervous tissue, the other involves the meninges. Infection involving the nervous tissue may be walled off in one area as a brain abscess or may be relatively diffuse as encephalitis or acute anterior poliomyelitis. When the meninges are infected the process may be localized or general.

The anatomy of the meninges makes it evident that once infection has entered the leptomeninges and subarachnoid space it has potentialities of an uninterrupted spread to any part of the subarachnoid over any section of the brain or spinal cord.

Entrance of infection into the intracranial structures may be gained by three ways. These are: By direct extension, by blood stream and by nerve trunks, either through the axis cylinder or along the perineural spaces. These routes will be considered as the various sources of infection are studied.

Major potential sources of infection of the intracranial structures are:

1. The blood stream either arterial or venous.
2. The olfactory and nasal mucosa.
3. The nasal accessory sinuses.
4. The orbit and optic nerve.
5. The middle ear cavity and its extensions, the mastoid process and the petrous pyramid.
6. The cranial nerves.

The Blood Stream:--The arterial blood may bring infected emboli especially from a suppurative process in the lungs or a bacterial endocarditis. Another source of infection through the arterial blood is in case of a blood stream infection.

Chief factors in regard to entrance of infection by route of the venous blood is the absence of valves in these veins, as described, and frequent reversal of the direction of blood flow with various conditions.

These factors are very important when dealing with infections about the face and forehead which may gain access to the angular vein or its connections and thus by embolism or thrombophlebitis involve the cavernous sinus. Infections of the tonsil, palate, and pharynx may, through the pharyngeal and pterygoid plexuses, gain entrance to the cavernous sinus. There are other routes by which the cavernous sinus may be invaded. One of these is, from the sphenoidal sinus; some of its veins drain into the cavernous sinus. Also the superior and inferior ophthalmic veins drain the orbit into the cavernous sinus. There is a diploic vein from the frontal bone that drains into the superior ophthalmic vein. All of the intracranial blood is intimately connected with the cavernous sinus by the other dural sinuses.

The superior sagittal sinus is connected with the nasal mucosa by a vein passing through the cribiform plate. Thus infection in this region may pass into the superior sagittal sinus. There are emissary veins in the parietal and occipital regions
which connect the scalp with the superior sagittal sinus.

Of principle importance is the proximity of the transverse sinus to the mastoid process and its connection with the mastoid emissary vein. Thrombophlebitis of this sinus may occur either as a direct extension of infection of the mastoid or through the mastoid emissary vein. This mastoid emissary vein, through its connection with the occipital vein, may be invaded from the superficial head region and the deep and superficial areas of the neck through the occipital plexus.

Infection may enter the superior petrosal sinus by passing along the veins draining the tegmen tympani, the tegmen antri and the middle ear mucosa.

Drainage of the inner ear is by the internal auditory veins into the inferior petrosal and sometimes into the transverse sinus. Infection may thus enter the superior and inferior petrosal and the transverse sinuses from the middle and inner ear, either by emboli or by an extending thrombophlebitis.

Another important intracranial connection is that, the veins of the dura and the diploe intercommunicate and are valveless, thus offering free passage for infected material. A further connection in this regard is that, some of the veins of the mucosa of the paranasal sinuses and the mastoid process drain into the diploic veins. Thus a complete patent vascular channel connecting the paranasal sinuses and the mastoid processes with the dura mater is formed.

An important vascular channel is that between the sphenoidal sinus mucosa and the subarachnoidal vessels of the
basal cisterns. This gives a portal of entry for an early basilar meningitis and all the potentialities of further spreading. 18

The Olfactory and Nasal Mucosa.--As stated previously, W. E. Clark, Key, Retzius and Cuneo have demonstrated that there is a connection between the olfactory and nasal mucosa and the surface of the basilar portion of the brain. The absolute nature of this connection is not definitely established, it may be by minute capillaries or perineural spaces possibly due to an extension of the pia arachnoid along the olfactory nerves. However, though the exact mechanism is not established, the existence of this passageway is definitely proven.

The Nasal Accessory Sinuses.--As stated before, the most important of these are the frontal, the ethmoidal and the sphenoidal. Infection in these sinuses may extend to the inside of the cranium by either perforation or through the vascular channels, also by tissue continuity.

Perforation may occur from the sphenoidal sinus directly into the cranial cavity. An ethmoidal infection may cause a perforation into the cranial cavity or into the orbit. Perforations from the frontal sinus may be intracranial, or into the orbit. It is possible for a perforation from the maxillary sinus to enter the orbit.

By continuity of tissue an osteomyelitis of the skull may occur from the frontal sinus, thus involving the veins of the diploe and giving access to the dura. Also by continuity of tissue an infection may extend from the sphenoidal sinus to the sheath of the optic nerve which is an extension of the
coverings of the brain thus offering a potential route for the spread of meningitis.

By vascular spread, the veins of the diploe may invaded by some veins draining part of the mucosa of the sinuses into the veins of the diploe. This is especially true of the frontal sinus. However vascular intracranial connections of the mucosa of the sphenoidal sinus are even more direct, for here there are direct connections between the vessels of the subarachnoid space in basal cisterns and some of the veins draining the sphenoidal sinus mucosa.

The Orbit and the Optic Nerve.--The chief importance of the orbit, as a route of infection, is its relationships to the paranasal sinuses, the optic nerve, and the superior and inferior ophthalmic veins. Perforations into the orbit have been discussed. Once the infection is established in the orbit it may spread intracranially by two routes. The first is vascular either by thrombophlebitis or embolism along the superior or inferior ophthalmic vein to the cavernous sinus. The other route is along the optic nerve especially by way of the sheath. The intimate association of the distal part of the optic nerve and its connections by way of the sheath of this nerve to the meninges, offers a dangerously direct and early accessible path for the development of intracranial infection.

The Middle Ear Cavity, the Mastoid Process and The Petrous Pyramid.--The most important factor in infections of these structures is the fact that the lining of the middle ear and the pneumatized cells of the mastoid and petrous portions are all developed from and continuous with the upper respira-
tory epithelium. This is important because of the frequency of upper respiratory infections. Another important factor bearing on this situation is that the tissue specificity of certain strains of bacteria would lead many to invade this region by the natural channel offered by the Eustachian tube. Continuity of tissue here is an important factor in the spread of infection through this area. The loose subepithelial tissue as described (lining the middle ear cavity and air cells) and its intimacy both directly and by capillaries with the diploic and marrow cells, gives an easy route by tissue continuity to all parts of this region. Once the infection is established in these structures intracranial spread may be by several routes. These are:

1. By direct extension through the mastoid cells to the lateral sinus.
2. By direct extension through the floor of the tympanic cavity to the jugular bulb. This may be by persistent vascular channels or by dehiscences.
3. By primary involvement of the mastoid emissary vein.
4. By thrombosis of the inferior petrosal sinus. This may be by extension of the disease to the labyrinth and resultant involvement of veins draining the labyrinth, or through necrosis of the cells of the petrous apex.
5. By primary involvement of the superior petrosal sinus. This results from involvement of the veins which pierce the tegmen tympani and tegmen antri.
These pass through the petro-squamous suture and join the veins draining the middle ear mucosa and empty into the superior petrosal sinus.

6. Through diverse or anomalous channels, such as the diploic veins or persistent vascular channels.15

Another route of spread is by preexisting channels either normal or anomalous. Two natural channels enter the inner ear, these are the oval and round windows. When the infection has invaded the inner ear it may enter the cranial cavity by certain other natural openings. These openings are the endolymphatic aqueduct which gives access to the dura, the cochlear aqueduct which enters the subarachnoid space in the basal cisterns, and internal auditory meatus. The anomalous opening most apt to be found is when the subarcuate fossa is not closed. This is especially dangerous when due to the failure of closure, the mastoid antrum is lined by the dura.

Direct extension and perforation is another means of infection entering the cranial cavity. Direct extension may occur anywhere in the mastoid process. In the petrous pyramid, however, there are certain routes of cells as have been discussed. These five main routes are:

1. The antrum epitympanic route.
2. The hypotympanic route.32
3. From the peritubal cells into the apex.
4. From the peritubal cells directly into the carotid canal or through dehiscences in the anterior tympanic wall into the carotid canal.
5. Along the perilabyrinth cells originating in the antrum.

There are certain portions of the petrous pyramid where an infection is more apt to become intracranial. At the apex along the roof and along the carotid canal the bone is very thin. Here dehiscences are most apt to occur and even though no dehiscences are present the bone is so thin that an infectious process might easily perforate it. The preexisting cell tracts make an easy natural path by which an infectious process may reach the tip and thus the potentially most dangerous part of the petrous pyramid. From here intracranial complications may arise easily.

The Cranial Nerves.—For any neurotropic virus as poliomyelitis, or rabies, or toxin such as that of tetanus, the cranial nerves offer a direct short pathway to the central nervous system.

It is well known that an infection of tetanus or rabies about the face is more quickly followed by symptoms than in similar wound about the extremities. The neurotropic factor here is well established and needs no discussion since this route of infection has been well established.

The route by which the virus of acute anterior poliomyelitis enters the central nervous system has not been definitely and unanimously agreed upon.

The work of Fairbrother and Hurst seems to establish the neurotropic character of the virus. The sequence of infection of the different regions of the central nervous system after intrasciatic inoculation shows a definite tendency to follow the nervous pathways. That sequence is as follows: The lumbar
cord, the motor area of the cortex, the cervical cord, and the arm area of the cortex. The motor cortex corresponding to the inoculated nerve is infected before that of the opposite side, this is indicative of a nerve pathway involvement. Also the thalamus corresponding to the inoculated limb is infected before the other.\textsuperscript{34}

Monkeys may be consistently infected by application of the virus to the uninjured nasal mucosa, by swabbing or drops. Although nasal application gives less uniform results than intracerebral inoculation, it is the only method by which experimental poliomyelitis may be produced without trauma and from a body surface.\textsuperscript{22}

This work indicates that the terminations of the olfactory nerves in the olfactory mucosa are an important portal of entry for the virus of acute anterior poliomyelitis.
SECTION THREE

Case Histories

Case 1. This case is quoted from Hayen By Logan Turner, and previously described in this thesis. "A man had an attack of epistaxis and sought the aid of a pharmaceutical chemist who plugged his nose with a tampon soaked in perchloride of iron. A few days later the man died from meningitis. At the necropsy it was found that the olfactory bulbs were stained brown and gave the prussian blue reaction".20

Comment.--This case seems to indicate that there is a clinical as well as experimental connection between the nasal mucosa and the basilar portion of the brain and involving the meninges. It therefore seems that this is a probable route of infection in meningitis.

Case 2. A girl aged two years had a furuncle on her forehead, this drained and the child felt quite well the following day. The child's left eyelids became swollen and her temperature went to 104°. Early the next day she began having convulsions. She then entered the hospital. Physical examination disclosed nothing other than the left eyelids were swollen so the eye was shut. Also the veins in this area were thrombosed. There was no neck rigidity. After admission her temperature rose progressively to 107.6°. The respirations became shallow and rapid and the child died.

Necropsy.--A thrombosis was found involving the left cavernous sinus, the circular sinuses and some of the right cavernous sinus. The inflammation had penetrated the dura and involved the meninges in this area.
Comment.—The route of intracranial involvement in this case was by extension along the veins about the orbit to the cavernous sinus with a resulting cavernous sinus thrombosis and meningitis. This illustrates one of the routes by which the cavernous sinus may be invaded by an infectious process.

Case 3. Boy aged two and one-half years. Three weeks before admission to the hospital the patient was kicked in the face by a horse and was unconscious for a short time. Two and one-half weeks later he developed a headache and earache and a temperature of 104°. He was taken to a doctor who found a fly in his ear and removed it. However his head continued to ache. The doctor examined him again and found his neck rigid. He then did a lumbar puncture and made his diagnosis of meningitis.

On admission to the hospital the patient was comatose, his neck extended, knees flexed and pupils contracted. The knee jerks were hyperactive and a positive Kernig was present. Examination of the spinal fluid revealed a type I Pneumococcic meningitis. The patient died seven days after admission.

Necropsy.—A greenish purulent material was found in the subarachnoid space. This followed many of the fissures especially on the lateral aspect of the brain. Similar material was found in the basilar system extending into the spinal canal. No basilar fracture was found. None of the sinuses were found to be thrombosed. The right mastoid was filled with a greenish-yellow exudate similar to that found in the sub-
This extended along through the petrous bone and a pool of pus was found beneath the Gasserian ganglion indicating the path of spread to the subarachnoid space.

Comment.--The pathological findings in this case indicate the route of infection of the meninges and demonstrate that the cellular structure of the petrous bone offers a clinical route for intracranial infection.

Case 4. A child developed a coryza, a purplish rash, headache and vomiting. This was diagnosed as measles. Then all symptoms disappeared. A few days later there was a sudden rise in temperature and bilateral deafness without pain in the ears. There was a spontaneous rupture of one drum, the other drum was opened because it was reddened. After the opening of the drums there was profuse drainage from both ears. Slight tenderness was found over one mastoid. Then a double mastoidectomy was done, both mastoids were found to be hemorrhagic, the one without tenderness being the most involved. On the second post-operative day a positive blood culture was found. Following this the sigmoid sinus was explored but found to be uninvolved. The child then showed the symptoms of basilar meningitis but with no headache and soon died.

Necropsy.--A purulent basal cisternal meningitis was found. Also there was pus in the sphenoid sinus and an acute osteomyelitis of the sphenoidal roof.

Comment.--The suppurative sphenoidal sinusitis began during coryza. The initial headache and vomiting marked the beginning of the meningitis. Instead of measles the rash may have been toxic erythema. The patient's symptoms plus
the positive blood culture were indicative the suppurative sphenoidal sinusitis. This case indicates the potentialities of infection involving the sphenoidal sinus spreading to the cranial cavity.18

Case 5. A white male aged 18 entered the hospital with the history of an acute upper respiratory infection during the previous week. This was followed by the onset of severe headache, neck rigidity, and a positive Kernig on the day before admission. Spinal puncture showed this to be a case of Pneumococcic meningitis. The patient died three days after admission.

Necropsy.--A perforation was found in the bone and dura in the right anterior fossa beside the cribiform plate. This perforation was five by twelve millimeters in diameter and communicated with an ethmoid cell on that side. The edges were ragged but rounded as though present for some time. All the ethmoid cells were filled with a yellow purulent material. Another perforation was found in the anterior right portion of the middle fossa. This involved the dura and bone but ended blindly in the bone at a depth of one to one and one-half millimeters, no pus was found about this perforation. Other pathology found was a meningitis and a pressure cone on the cerebellum.

Comment.--The entrance of infection into the cranial cavity in this case was by the perforation from the ethmoid cell. This was a case of direct extension of infection from the ethmoid sinuses to the meninges.
Case 6. White male age 20 was in contact with a case of acute anterior poliomyelitis in the pre-paralytic stage undiagnosed at the time. This case complained of a backache and had his back massaged by the patient. He was on the patient's bed with his face in the patient's pillow. His back was rubbed with "Analgesic Balm" which was inhaled by the patient and caused a copious secretion of mucous from the nose. That night the patient slept in the same bed and on the same pillow. Two weeks later the patient developed a case of acute anterior poliomyelitis.

Comment.--It seems probable that the infection in this case gained entrance to the central nervous system by way of the nasal mucosa. This was further aided by the loss of mucous protecting the mucosa from the invasion of this virus. This case fits well with the conclusions and observations of Fairbrother and Hurst.
SECTION FOUR

Summary and Conclusion

In this paper various routes of infection on a pre-existing anatomical basis have been presented and discussed. Clinical factors have not been discussed except as they bear out the anatomical factors. These routes have been discussed mostly as originating from various foci.

These sources and routes by which infection may enter the cranial cavity are:

I. The blood stream:
   A. Arterial.
      1. Foci.
         (a) Lung.
         (b) Heart.
   B. Venous.
      1. Here the absence of valves and the frequent reversal of flow is an important factor.
      2. The cavernous sinus drains the area about the face, the pterygoid and pharyngeal plexuses, thereby having many portals for the entrance of infection.
      3. Venous connections between the sinuses and extracranial structures.
      4. By emissary veins connecting with the scalp to nasal mucosa, the middle and inner ear and the mastoid.
5. Venous connections with the diploe and thus with mucosa of the nasal accessory sinuses.

II. The nasal accessory sinuses:
   A. Perforation.
      1. Direct.
         (a) Into the cranial cavity.
      2. Indirect.
         (a) Into the orbit.
         (b) Into the sheath of the optic nerve
      3. By blood stream.
         (a) Extension through the bony structure.

III. The olfactory and nasal mucosa:
   A. By blood stream.
   B. By tissue spaces especially perineural.

IV. The middle ear cavity, the mastoid process and the petrous pyramid.
   A. By continuity of tissue, all these structures may be involved. Another factor being passage by preexisting cell tracts.
   B. Intracranial complication may arise by:
      2. Preexisting channels.
         (a) Patent subarcuate fossa.
         (b) Dehiscences.
         (c) Round window.
         (d) Oval window.
         (e) Endolymphatic aqueduct.
(f) Cochlear aqueduct.
(g) Internal auditory meatus.
3. Direct extension through the bone into the cranial cavity.

V. The orbit:
A. Blood stream.
   1. Superior ophthalmic vein.
   2. Inferior ophthalmic vein.
B. Optic nerve.

VI. By the cranial nerves:
A. These are important in connection with the neurotropic viruses.
   1. Rabies.
   2. Tetanus.
   3. Acute anterior poliomyelitis.

VII. The Hematoencephalic Barrier.
A. The exact anatomy and function of this phenomenon is not understood. In the role of being a factor in intracranial infection, probably the chief structure, is the choroid plexus. This structure is thought by some authorities to be of great importance in epidemic cerebrospinal meningitis. The correctness of the theory placing the choroid plexus in this important role depends on whether or not a choroiditis is the basis for the infection of the cerebrospinal fluid.
It is quite conceivable that there is some stagnation of blood in these plexuses. Such a stagnation would favor the development of a phlebitis in this structure and a chorioiditis. As to the barrier's action in preventing the entrance of toxic or infectious material into the cerebrospinal fluid, little is known. The best example of this action is shown by the fact that poliomyelitis convalescent serum injected intravenously in a normal person does not enter the cerebrospinal fluid. However if the barrier has been injured by the intraspinal injection of horse serum or some other simple irritant or by acute anterior poliomyelitis the serum is not prevented from entering the subarachnoid space.35

The sources and routes of intracranial infection come mainly under the supervision of the oto-rhino-laryngologist and the ophthalmologist. Although not usually having to deal with these situations in their advanced stages the general practitioner will see them in their early stages. It is in these early stages that the potentialities and dangers of these conditions should be recognized and if possible averted. If such complications do arise a knowledge of the various sources of such a complication is necessary. The source should be looked for and if found it should be removed and thus prevented from
continuing the damage. An example of the value of this is found in Case 5. At one point in this case the patient improved under treatment and if the primary source which was in the ethmoid cells had been known and removed and the improvement might have continued. However the primary source continued feeding infection into the cranial cavity.

Therefore a knowledge of the routes and sources of intracranial infections are important not only in the prevention of such complications but in their treatment after they arise. Especially in finding and removing a hidden causative agent.
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