CENTRAL NERVOUS SYSTEM

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- ● Sheet
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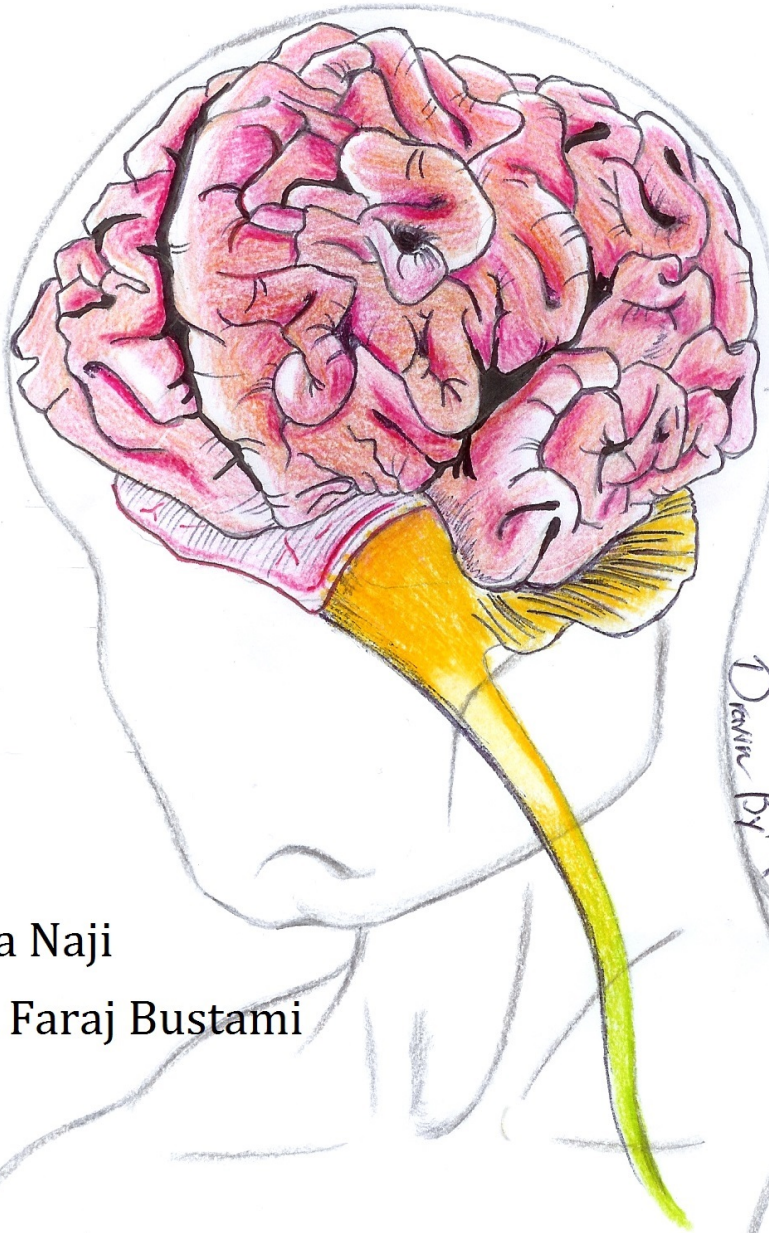
- ● Anatomy
- ○ Physiology
- ○ Pathology
- ○ Biochemistry
- ○ Microbiology
- ○ Pharmacology
- ○ PBL



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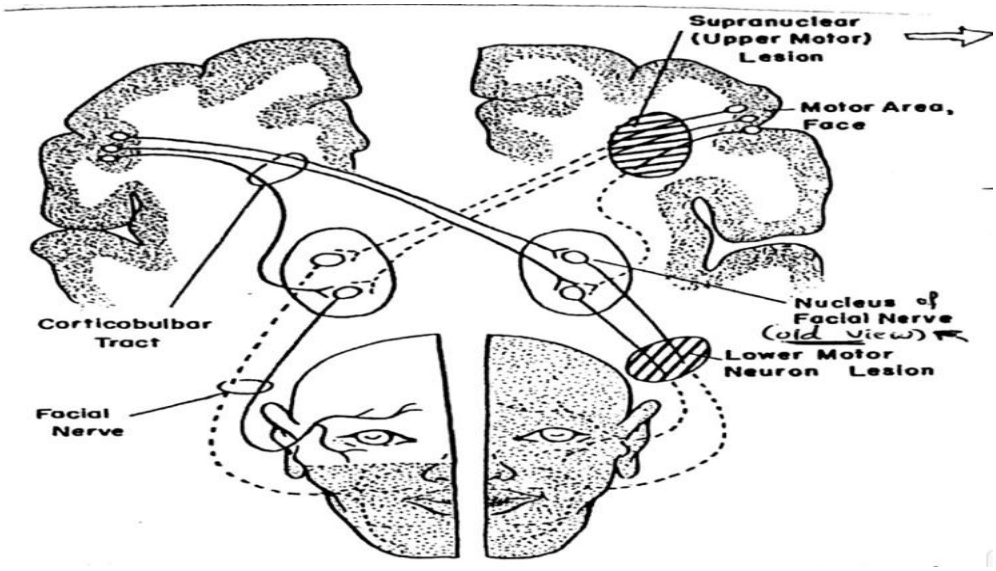
Facial nerve (cont'd)

The figure below is a little bit deceiving as there are 2 concepts with regard to the motor nucleus of facial nerve; The OLD concept and the NEW concept.



The new concept:

The **upper** part of motor nucleus of facial nerve, which is found in the Pons, sends its nerve fibers to control the **upper** facial muscles, whereas fibers descending from the **lower** part of motor nucleus of facial nerve control the **lower** facial muscles.

The old concept:

stated the opposite; nerve fibers descending from the **upper** motor nucleus of facial nerve control muscles of the **lower** face, and those from the **lower** motor nucleus descend to control muscles of the **upper** face.

However, it is not that important to know which concept is more accurate than the other because what really matters is that the part of the motor nucleus of facial nerve that supplies the lower facial muscles receives ONLY contralateral corticobulbar fibers.

So according the **OLD** concept (which is still mentioned in many clinical books), the lower motor nucleus of facial nerve receives both contralateral and ipsilateral corticobulbar fibers, while the upper one receives only from the contralateral side. This means that lesions affecting the corticobulbar fibers on one side would affect the upper motor nucleus (which supplies the lower facial muscles) more than the lower motor nucleus since the latter receives bilateral corticobulbar fibers, so that it can compensate for the damage.

In the case of a stroke (Upper Motor Neuron Lesion/UMNL) affecting the left side of internal capsule, what would happen?

-Right spastic hemiplegia,

-Contralateral weakness in the lower part of the face,

-Deviation of the angle of the mouth **to the side of the lesion** (in this example it will be deviated to the left).

What is the difference between a lesion to the facial nerve or facial nucleus (facial palsy >> LMNL) and a supranuclear lesion (stroke >> UMNL, i.e. before reaching the nucleus, such as corticospinal and corticobulbar fibers)? <<IMPORTANT>>

- **Supranuclear lesion (UMNL)**>> results in a contralateral weakness of the lower face and deviation of the angle of the mouth to the side of the lesion.

- **Lesion to the facial nerve or facial nucleus (LMNL)**>> leads to ipsilateral paralysis in the lower AND upper facial muscles because the nerve will be distributed to all muscles of the upper and lower face.

In the advanced cases of facial palsy (**LMNL**) where the facial nerve becomes compressed (especially when it leaves the stylomastoid foramen since it is a narrow opening), the following signs can be observed:

1- Weakness in the upper and lower facial muscles,
2- Inability to close the eye on the affected side,
3- Deviation of the angle of the mouth to the **healthy side**. (You can observe this sign by asking the patient to smile or to show you their teeth)
4- Absence of transverse creases,

Note: there is a muscle called occipitofrontalis, which is innervated by the facial nerve and inserted into the skin (actually all facial muscles have their insertion in the skin). The frontal belly of occipitofrontalis muscle draws the scalp back which raises the eyebrows and wrinkles the forehead giving the appearance of transverse creases/folds. So in the case of facial palsy, where the facial nerve is damaged, this muscle cannot perform its action and therefore the creases disappear.

5- Absence of naso-labial folds, giving rise to a masked/ironed face.

In order to determine the side of the lesion in the case of facial palsy, you should follow the side on which the eye cannot be closed. For example, if the lesion is on the left side, the patient will not be able to close their left eye; however, the angle of the mouth will be deviated to the RIGHT.

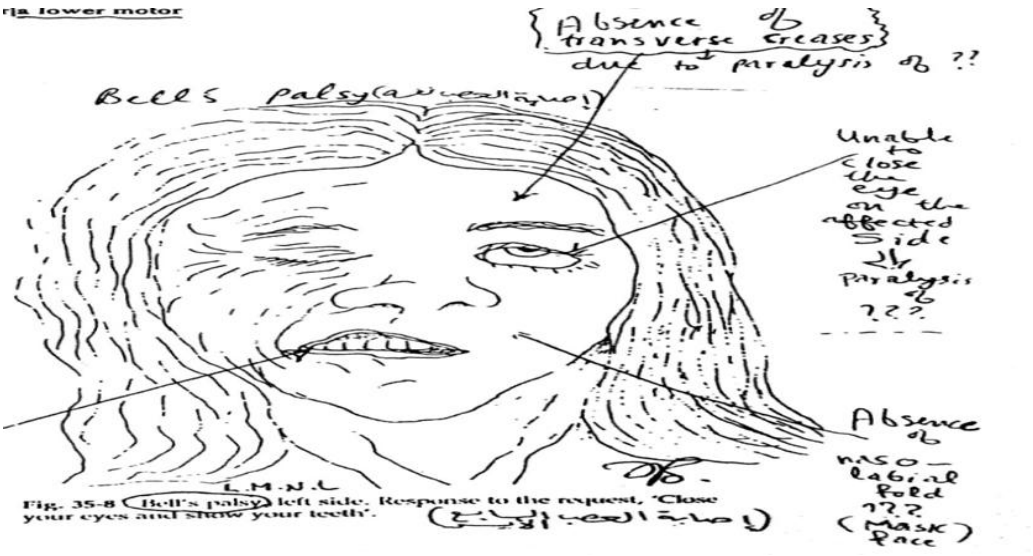


Fig. 35-8 Bell's palsy left side. Response to the request, 'Close your eyes and show your teeth'.

Most cases of facial palsy, aka Bell's palsy, are commonly seen in diabetic patients. 70-80 % of the cases recover spontaneously even without treatment.

Unfortunately, it has become a trend to prescribe B complex (B1, B6, & B12) injections by a lot of general practitioners, and what is even much worse is that some of them give the Bell's palsy patient a high dose of cortisone. Even though cortisone relieves the swelling (edema) of facial nerve and speeds up the recovery, it has many side effects especially if the patient is at the prediabetic stage (borderline diabetes) because the high dose of cortisone would transform him/her into a diabetic patient.

<u>In a nutshell:</u> there is no need to prescribe cortisone or B complex injections to a patient diagnosed with Bell's palsy since in the majority of cases the symptoms subside on their own.

In the **early** cases of facial palsy, signs and symptoms might not be very obvious. Therefore, if you suspect that the patient is having Bell's palsy, ask them to close their eyes. Upon attempting to open the eyelid on the healthy side, it will be difficult; however, you will find it much easier to open the eyelid on the affected (*weak*) side. Also, if you want to further confirm your diagnosis, ask the patient to show you their teeth and then look for any deviation in the angle of the mouth.

On the other hand, in the **advanced** cases, the signs are more pronounced; the patient is unable to close his/her eye on the affected side (the affected eye may appear to be tearing excessively). If the palpebral part of orbicularis oculi muscle (which is responsible for blinking) is paralyzed, the patient will not be able to blink. The importance of blinking lies in its ability to spread tears over the cornea, so if the blinking mechanism is absent or disrupted, there will be dryness in the cornea, which is considered one of the most serious complications of facial palsy. In order to avoid corneal dryness in this case, we give the patient lubricating eye drops to keep the eye moist. For nighttime protection, we ask them to use eye patches so that the eye can be taped closed while sleeping. It is very important to manage this point because dryness could damage the cornea.

Writer's note:

For many Bell's palsy patients, although the lacrimal gland produces tears, without a blink the tears cannot coat the eye. As the doctor said, the eye may appear to be tearing excessively, it actually only seems that way because the tears are not being spread over the eye, but instead are collecting in the limp lower lid or running out of the eye. That's why the eye dries up.

Always remember that most cases of facial palsy are seen in diabetic patients, and even if a patient came to your clinic having facial palsy and is not diabetic, there is a high probability that s/he might develop diabetes after 1 or 2 years. So keep in your mind that facial palsy is closely linked to DIABETES.

In cases of **stroke** (**UMNL**), never ignore testing the cranial nerves. You should not only test the power, tone, and reflexes on the affected side. Indeed, many physicians miss the proper examination of cranial nerves (by the word "proper" I mean that some physicians only remember the fact that all cranial nuclei receive bilateral corticobulbar fibers but they forget the most important exception, that I have mentioned at the beginning of the sheet, which is that the motor nucleus of facial nerve supplying the lower facial muscles receives corticobulbar fibers from the contralateral side only).

So, you should also include the facial nerve in your examination whenever you suspect a stroke. This nerve can be tested by talking to the patient or asking them to smile and you will immediately notice a weakness in the lower face that is contralateral to the side of the lesion. This weakness is considered part of the stroke.

Note: The stroke could be emotionally involved. How?
The motor nucleus of facial nerve receives corticobulbar fibers from the *limbic cortex* (cingulate gyrus, hippocampus, parahippocampal gyrus), and this connection usually passes through the ***basal ganglia***. Why?
Because it is suggested that patients with basal ganglia diseases lose the motor expression of emotions. So it turned out that the basal ganglia play a role in cases of stroke.

Now, suppose the stroke was emotionally involved (related to the limbic system), if the physician was such a funny creature with a great sense of humor "Nahfeh" (which is kind of rare to find nowadays) and he made the patient laugh so hard by telling him a joke for e.g., the deviation in the angle of the mouth would disappear, i.e. The palsy goes away. So you guys should master telling jokes

Input (afferent) Connections of the Motor Nucleus of Facial Nerve

(1) **Corticobulbar Fibers,** which work on the alpha and gamma motoneurons that supply muscles of mastication, pharynx, and larynx. (Remember that corticospinal fibers work on the alpha and gamma motoneurons supplying the upper and lower limbs).
All cranial nuclei receive bilateral corticobulbar fibers except the part of the motor nucleus of facial nerve supplying muscles of the lower face which receives only *contralateral* corticobulbar fibers. [I must've repeated it a THOUSAND TIMES.. To tell you how much important.. Understanding the story of facial nerve is ..Hopefully it will never.. Confuse you anymore.. Ooh anymore.. Inta7rat Adele]. Therefore, in lesions affecting one hemisphere, the other side cannot compensate for the damage and there will be weakness in the lower facial muscles contralateral to the lesion, while the other cranial nuclei will not be affected too much.
>>this leads to hemiplegia and hemiface. Always keep it in your mind.

(2) **Basal Ganglia,** through which the input from the limbic cortex passes to the motor nucleus of facial nerve. What is the evidence?
Parkinson's patients have abnormally functioning basal ganglia, thus they lose the motor expression of emotions. This is the only hint confirming the fact that the motor nucleus of facial nerve receives an input from the basal ganglia.

(3) **Superior Olive,** which is an important station in the auditory pathway. As we go from the superior olive rostrally, the pathway becomes bilateral, i.e. it brings information from both ears, but more from the *contralateral* ear.

The superior olive sends impulses to the motor nucleus of facial nerve.
What is the evidence?
When your facial muscles grimace in response to loud sounds (e.g. scraping a chalkboard with the fingernails which generates a sound that is extremely irritating).

(4) **Trigeminal System,** which has a relation with the motor nucleus of facial nerve as this system is sensory to the cornea as well as to the motor facial nucleus. Again, what is the evidence?

Touching the cornea with a cotton wisp elicits a bilateral blink response. Another example is when dust gets into your eye and reaches the cornea, you blink both eyes reflexively. This corneal reflex is protective and **has NOTHING to do with the oculomotor nerve** since this reflex receives its sensory innervation from the **trigeminal nerve**, particularly the ophthalmic branch. (Very important)

As mentioned in previous lectures, every reflex has both afferent and efferent limbs. In corneal reflex, the **afferent** limb is the **ophthalmic** nerve (to be more specific, its nasociliary branch which innervates the cornea), while the **efferent** limb is the **facial** nerve.

How are both limbs connected?

Cornea receives peripheral processes (receptors) from sensory cells in the ganglion, similar to any other sensory pathway that starts at receptors. When a stimulus (dust for example) reaches the cornea, impulses run along the afferent limb (nasociliary nerve), and then the central process of the nerve goes to the **Spinal Trigeminal Nucleus,** where it synapses with interneurons. From the spinal trigeminal nucleus, many nerve fibers emerge which are eventually going to affect the facial motor fibers (efferent limb) innervating BOTH eyes. Meaning that if you stimulate the cornea of the right eye, both eyes will blink.

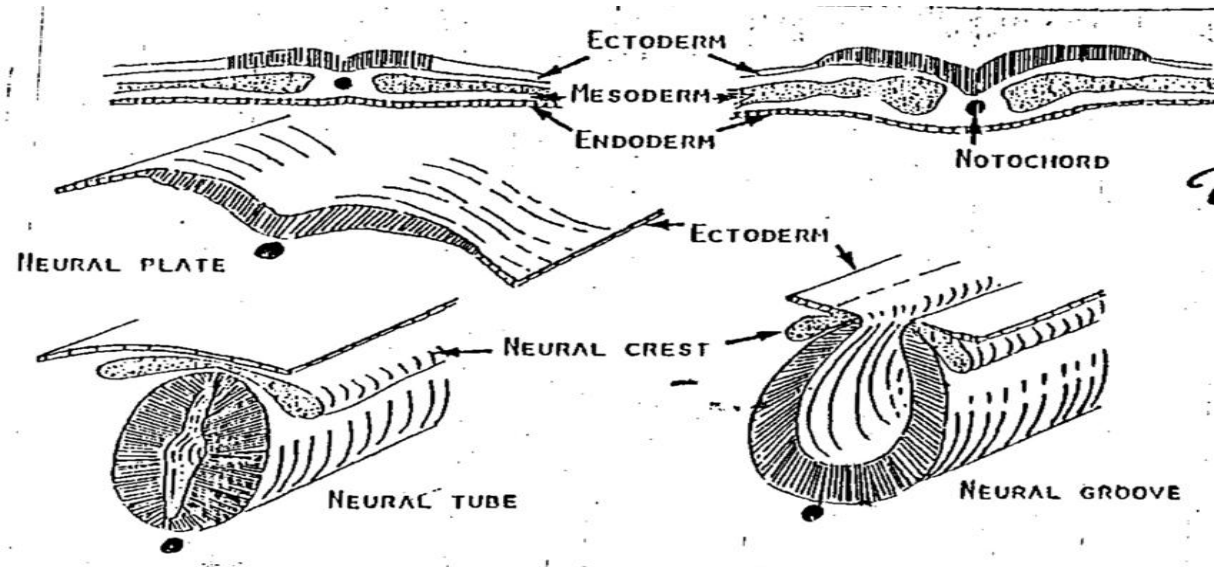
This is the basis of corneal reflex whose, once again, afferent limb is the 5th cranial nerve (trigeminal>> ophthalmic>> nasociliary), and efferent limb is the 7th cranial nerve (facial).

The 3rd cranial nerve (oculomotor) does NOT affect corneal reflex, but rather it is involved in the movement of extra-ocular muscles.
Damage to the oculomotor nerve leads to: *marked ptosis, diplopia (double vision), dilation of the pupil, and external squint.* Also, this should not be confused with the damage to the Medial Longitudinal Fasciculus/MLF. In MLF lesions, there is no paralysis in the oculomotor nerve, but rather the main connection (MLF) between para-abducens nucleus and oculomotor nucleus is cut.

Sometimes we call the para-abducens nucleus "**The Horizontal Gaze Center**" since it controls horizontal movements of the eye.

- End of cranial nerves -

Embryology Of The Nervous System



By the third week of development, the *embryonic disc*, as shown in the above figure, is trilaminar (formed of 3 layers: ectoderm, mesoderm, and endoderm) and in the middle is the *notochord*, which is a temporary axial skeleton that will be replaced by the vertebral column later on. So without the notochord, the nervous system will not be fully formed.

At the beginning of the **third week**, under the inductive influence of the notochord, the dorsal ectoderm thickens in the midline above the notochord forming the **Neural Plate**.

In more advanced stages, the peripheral neural epithelial cells start to divide and enlarge. Therefore, due to the changes in the shape and size of neural cells and the changes in their connections with surrounding cells, the lateral margins of the neural plate become elevated to form the **Neural Folds.** The depression between the two folds is known as **Neural Groove.**

At about the 25th day of development, the neural folds approach each other and fuse to form the **Neural Tube.** The fusion begins in the cervical region and then progresses rostrally as well as caudally.

For a short time, the neural tube remains open at both upper and lower ends as the Rostral and Caudal Neuropores, respectively. The rostral (sometimes called Anterior) neuropore closes at about the 25th day, and two days later the caudal (or Posterior) neuropore closes (approximately on day 27).

Once the neural tube is formed by the fusion of neural folds, it detaches itself from the ectoderm and sinks into the underlying mesoderm. Before fusion of the neural folds, some cells at the margin of neural fold do not incorporate into the neural tube, and thus forming the **Neural Crest-** refer to the previous figure.

What are the derivatives of Neural Crest? (Very Important)

- **The ganglia**, whether spinal (dorsal root) ganglia or autonomic (sympathetic and parasympathetic) ganglia.
- **Adrenal medulla**, (the inner part of adrenal/suprarenal gland) which is basically a modified sympathetic ganglion. It secretes adrenaline and noradrenaline.
- **Melanocytes of the skin**.
- **Part of the skeleton of the face** (some of the skull bones). One would ask himself, how come that the neural crest (which is ectodermal) forms a bone (which is mesodermal, i.e. mesenchymal in origin)?!
  These ectodermal cells of neural crest are able to differentiate into mesenchyme.

- **Part of the aortopulmonary septum**. Recall from embryology of the cardiovascular system that a single artery known as truncus arteriosus arises from the heart. Later on, the aortopulmonary septum develops, dividing the truncus arteriosus into ascending aorta and pulmonary trunk. What is the significance of the aortopulmonary septum being derived from the Neural Crest?

If a baby was born with malformations in the face, this means that most probably he has malformations in the heart as well, *since some of the skull bones in addition to the septum that divides the truncus arteriosus are both derivatives of the neural crest.*

Defects In Closure Of The Neural Tube

In some cases, the neural tube does not fuse completely, and thus leading to many congenital neural tube anomalies, such as:

I. Rachischisis:

- A developmental birth defect that occurs when the neural tube for some reason fails to close in the spinal cord region (**posterior neuropore**). As a consequence, the vertebrae overlying the open portion of the spinal cord do not fully form and remain unfused and open. So because the neural tube does not close completely (after the fusion of neural folds), the spinal cord remains open/exposed >> very serious condition.
- It commonly accompanies Anencephaly, in which there is a massive deficiency of cranial structures.

II. Anencephaly:

(Anen means without / cephaly means brain)

- Failure of the cephalic part of the neural tube (**anterior neuropore**) to close.
- In most cases, the baby is delivered prematurely (in the 7^{th} month of gestation), and usually he dies before delivery (stillborn baby) or a few hours after birth.
- It is a common anomaly that occurs with an incidence of 1 per 1000 deliveries.
- More common in **Females** than males with a ratio of 4:1.

- At birth, the following signs appear :

-The vault of the skull is absent.
-The brain is largely represented by a mass of degenerative tissue exposed to the surface.
-The baby often shows signs of Rachischisis (open spinal cord) in the cervical region.
-The fetus lacks the central mechanism for swallowing. It is supposed that at some stage of pregnancy the fetus should be able to swallow the surrounding amniotic fluid and excrete it as urine. When the fetus is unable to swallow enough, too much amniotic fluid builds up around him. This causes **hydramnios, also referred to as polyhydramnios.**

The amount of amniotic fluid produced in normal deliveries is around 0.5 L, however, in the case of hydramnios it may reach up to 2 Liters!

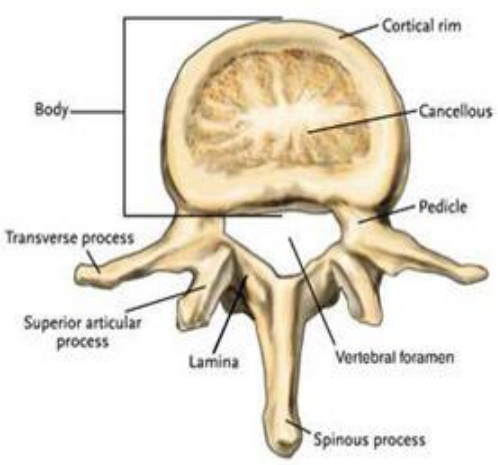
- How is this anomaly diagnosed?

By Ultrasound Scanning, which helps the gynecologist identify any problems with how the fetus is developing. Actually, the gynecologist can determine if there is anencephaly during the first two months of pregnancy. If the case is borderline, the findings are not very clear, and the gynecologist is uncertain if the fetus has anencephaly or not, this can be confirmed by injecting a needle into the wall of the womb to draw out a small sample of amniotic fluid (This is considered an invasive procedure though), then the gynecologist will test the sample and if s/he finds high levels of a protein called **"Alpha-Fetoprotein/AFP"** in the amniotic fluid, the elevated levels of AFP along with the ultrasound findings assure that the fetus has anencephaly. Forensic medicine permits abortion in this case since most anencephalic fetuses do not survive birth.

III. Spina Bifida:

- One of the most common anomalies that you are going to see in your career.
- Sometimes it is accompanied by changes in the location of spinal cord and meninges.

Note: This figure shows a typical vertebra. Notice the body and the transverse process.
The posterior part is composed of two laminae which unite to form the spine of the vertebra.
If for some reason the laminae fail to develop, the spine will not develop properly, giving rise to a split spine. (فقرة مشـقوقة)



There are 3 main types of Spina Bifida:

A. Spina Bifida Occulta:

- It is the mildest (most benign) form of Spina bifida that sometimes goes unnoticed for many years, maybe till the age of 50 or 60. Most people with this form do not know they have it until they get a back X-ray for another reason.
- *The spinal cord, cauda equina, and meninges remain in place*. So the arachnoid and dura mater layers are present but ONLY the <u>posterior</u> part of the vertebra isn't formed properly.
- The bony covering of one or more vertebrae is incomplete. The site of the defect is marked by a **tuft of hair.**

B. Meningocele:

- More severe than Spina Bifida Occulta.
- Dura mater is <u>absent</u> in the area of the defect and the <u>arachnoid layer bulges</u> prominently beneath the skin in the lower part of the back (lumbar region).
- *Spinal cord and cauda equina remain in place*. In this case, the cyst is prone to rupture which would allow infections to penetrate the subarachnoid membrane and spread to the CSF that is found behind it. So if the cyst ruptures, it would lead to many complications. However, neurologically, symptoms are mild since the spinal cord and nerve roots remain in place. (They are NOT displaced).

C. Myelomeningocele:

- Very severe condition. In this case the dura mater is absent, and a sac containing the arachnoid mater and CSF protrudes through a defect in the spinal cord.
- *Spinal cord and cauda equina form a bulge or are entirely displaced into the protruding subarachnoid space*. Because the spinal cord and nerve roots are **displaced** in this case, they will be compressed and damaged. So definitely there will be neurological symptoms.
- If the myelomeningocele is located in the lower part of the vertebral column (lumbosacral region), it may lead to paraplegia or disturbances in bladder functions. Keep in mind that bladder function is closely associated with cases of paralysis.

If a spinal X-ray has revealed that the patient has Spina Bifida, we cannot determine the severity of the case; it could be Spina Bifida Occulta/benign (without symptoms), or Spina Bifida Occulta with Meningocele, or it could be the worst of all, which is Spina Bifida Occulta with myelomeningocele (very severe).

All the aforementioned cases (in which there are **spinal defects**) cannot be well defined by simply taking a spinal X-ray. Only bony defects do appear on X-rays.

Note: In addition to the defects that affect bone formation around the spinal cord (such as Spina Bifida and Rachischisis), there are also defects affecting the *brain* region where bones of the skull are not formed (the cranium fails to close completely), leaving the brain exposed (the brain remains as an open neural tube).This case is called **Cranioschisis,** and it is incompatible with life.

❖ A similar spectrum of anomalies is associated with **Cranial Defects,** Such as :

I. Meningocele:

- Is typically associated with a small defect in the skull through which a meningeal cyst protrudes. In this anomaly, the cyst is composed of arachnoid mater and CSF, while the dura mater is often absent. So the cyst is basically formed of meninges.

II. Meningoencephalocele:

- Characterized by sac-like protrusions of the brain tissue and the surrounding meninges through openings in the skull.

III. Meningohydroencephalocele:

- Refers to the protrusion of a cyst containing meninges, brain tissue, and part of the ventricular system. (Hydro=fluid/ CSF).

The previous 3 anomalies are relatively common. It is important to differentiate between them depending on the nature of the protruding tissue.

IV. Microcephaly:

- It is an uncommon condition characterized by underdevelopment of both the brain and the skull. Why is the brain underdeveloped?

Some scientists have attributed this underdevelopment to the early/premature closure of skull sutures (which are basically fibrous tissue). So if the skull sutures fuse very early during fetal life, the skull stops growing, and so does the brain. This is a simple explanation.

It is necessary to encourage the mother to take extra good care of her child especially during the first year of age by regularly visiting the Maternal And Child Health Center. What for?

In order to follow up the growth of the child by physically examining him and measuring his height, weight, head circumference, etc…

Actually, the most important test to be performed is the **Head Circumference** to check whether the head is growing normally or not. The importance of measuring the head circumference lies in the early detection of *Microcephaly*, where the brain does not develop properly resulting in a smaller than normal head. There is a high probability that the microcephalic child will suffer from mental retardation in the future.

Mental Retardation:

-It is one of the **functional** defects of the nervous system.

-Its etiology can be attributed to a mixture of both hereditary and environmental factors. So, if the mother has been exposed to radiation or viral infection, or if she has been taking certain drugs during the first two months of pregnancy (which are very critical), the child is more likely to be mentally retarded.

Now we discuss the myelination process:

Myelination In The Spinal Cord

The process of myelination starts in the **cervical** portion of the cord and then extends caudally. It begins at about the **4thmonth** of fetal life.

The myelin sheath is formed by a type of neuroglial cells known as Oligodendrocytes.

Again, the process of myelination in the spinal cord begins at about the 4th month, and the **sensory fibers** are myelinated first (i.e. Sensory pathways will have their nerve fibers myelinated before those of motor pathways). The baby is born and the motor fibers are not yet myelinated.

On the other hand, if you look at the myelination of the *roots of spinal nerves*, you will find that the fibers of the **ventral (motor) nerve roots** are myelinated BEFORE those of the dorsal (sensory) nerve roots.

So never forget that at birth the descending motor pathways (corticospinal, corticobulbar, corticoreticular, etc…) are not yet myelinated.

Myelination In The Brain

Begins at about the **6th month** of fetal life and is restricted to the fibers of the ***basal ganglia*** (It begins in the basal ganglia and then progresses to the other parts).Later, the sensory fibers get myelinated, and like the spinal cord, the sensory pathways are myelinated before the motor ones.

Because at birth most of the motor pathways (corticospinal and corticobulbar in particular) are not yet myelinated, the newborn cannot move his limbs nor can he walk. Their myelination starts at about **6 months** after birth, and the process is largely completed by the end of the **second year**; meaning that the child should be able to walk maximally by the end of the 2nd year.

It is believed that some nerve fibers in the brain and spinal cord do not complete their myelination until puberty.

Some children start walking at the age of 11 months for example; this indicates that the process of myelination in the corticospinal and corticobulbar fibers has been completed early. Some parents may start thinking of mental retardation if their child has reached the age of 18 months and still cannot walk. This is not true. The rate of myelination in the motor fibers (which does NOT begin before the age of 6 months postnatally) is variable since every child is different from the next. (Writer's note: i.e. the age of walking has nothing to do with the eventual intelligence or motor skills).

-THE END-

P.S. For those of you who study sheets along with the recordings, the part discussed in the last 12 minutes of this lecture is not written here because the doctor started with a new topic so I found it much better to be included in sheet #20.

-Your feedback would be highly appreciated.

Special Dedication to my favorite Virgos on earth: Aseil & Sophia.
**The embryology part particularly is dedicated to Zahraa Altamimi hahah <3

And Shout-out to the gorgeous Layan Attili ✌