

Lecture:



Peripheral Nerves Disease

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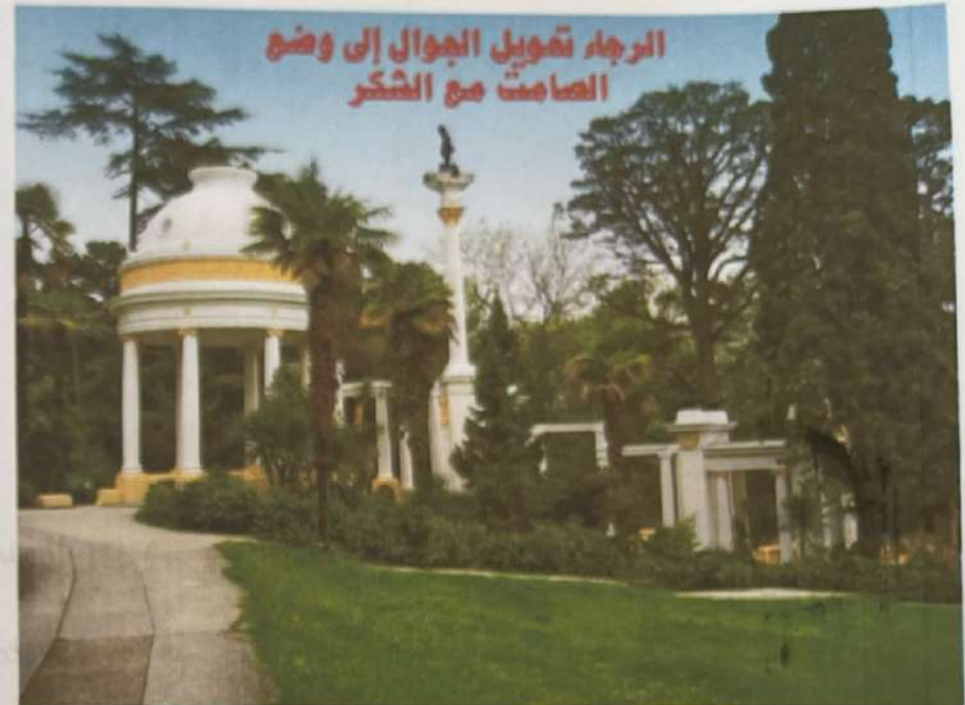
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Case # 1

A 52-year-old man complained of "numbness and stiffness" in his legs for the past 4 months. His gait has gradually deteriorated because of unsteadiness.

On examination the patient appeared older than his stated age. His hair was nearly completely gray. His tongue was red and depilated.

His gait was broad based, and he was unable to walk a straight line. He was able to stand with his feet together with his eyes open, but he nearly fell when his eyes were closed. He had normal arm coordination but was ataxic on the heel-knee-shin maneuver. Both knee reflexes were 3+, and absent at the ankles. Both plantar responses were extensor. There was a stocking decrease in sensation and a marked decrease in vibration and joint position sense in the toes and ankles. Cranial nerves were normal, and there were mild problems with memory and calculation with urine incontinence.



Case # 1

- ◆ What is the most likely diagnosis?
- ◆ What is the next diagnostic step?
- ◆ What is the next step in therapy?

Case ٥: مرضها الأول

♂ 35y , weak in 4 limbs for one day on admission

had common cold 2 weeks before admission

weakness become severe and lead to tetraplegia

on 3 day , Swallowing difficult , numbness

no difficult in urination or defecation

سحب sphincter عند النظر

spinal cord lesions

on exam: quadriplegia more distal , m. hypotonia ,

↓ elevation of Palatal , gag reflex disappear.

anorexia , Babinski ⊕ , Stocking-glove type pain
and Paresthesia

(GBS) , Left Lip

Case # 1

Blood test:

- anemia + raised MCV (105)
- Low vitamin B12 levels

The Peripheral Nervous System

- The peripheral nervous system consists of cranial and spinal nerves and their associated ganglia.
- Its function is to carry impulses to and from the CNS.
- There are 12 pairs of cranial nerves, which leave the brain and pass through foramina in the skull.
- There are 31 pairs of spinal nerves, which leave the spinal cord and pass through intervertebral foramina in the vertebral column.
- All of the spinal nerves are mixed nerves contain motor, sensory and autonomic fibers

x

Case # 1

MRI of the spine showed a hyperintense signal along the posterior column of the spinal cord.

NCS/EMG: axonal polyneuropathy affecting lower extremities

The Nerve Fibers

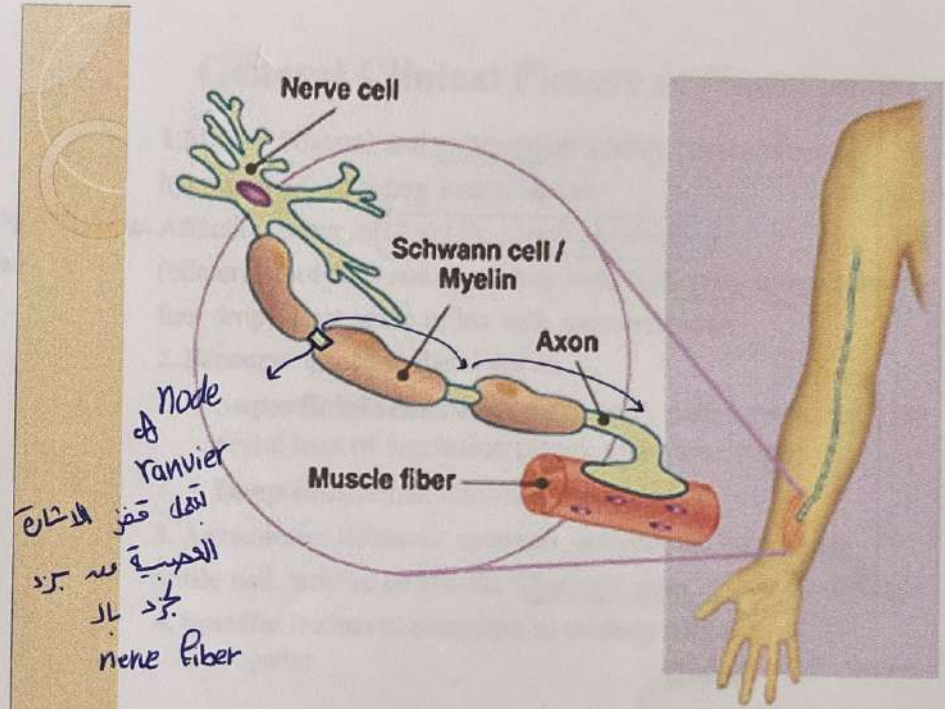
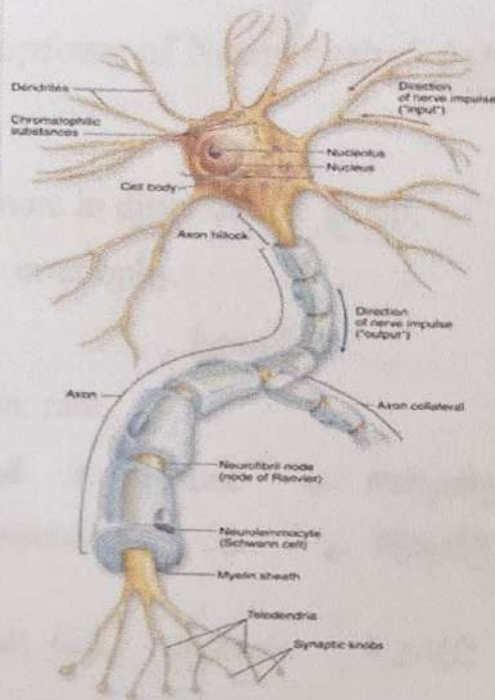
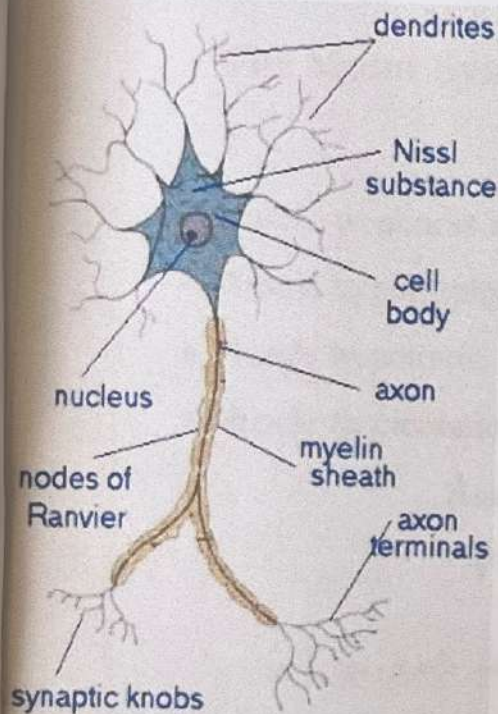
Definition: it is an axon or a dendrite of a nerve cell.

Structures of the nerve cell and axon:

- ✓ 1. Cell body
- ✓ 2. Nucleus
- ✓ 3. Schwann cell (formation of the myelin sheath)
- ✓ 4. Myelin sheath (a protein-lipid complex)
- ✓ 5. Node of Ranvier

gib. →
myelin

↓
↓ → Passive transmission of nerve impulse



نقطة قفص لا شارة
العصبية فيه برد
جود بال
nerve fiber

Mechanism of Peripheral Nerves Damage

- **Demyelination:** when Schwann cells and myelin sheath are damaged. This occurs in Guillain-Barre syndrome, postdiphtheritic and hereditary sensori-motor neuropathies.
- **Axonal degeneration:** affects the axon. Axonal degeneration occurs typical in toxic neuropathies.
- **Wallerian degeneration:** axon and distal myelin sheath degeneration over weeks in diabetic polyneuropathy.
- **Compression:** focal demyelination at the point of compression occurs in entrapment neuropathies (carpal tunnel syndrome).
- **Ischemic:** occurs in vasculitis and atherosclerosis of peripheral arteries.
- **Infiltration:** infiltration by inflammatory cells in sarcoidosis or malignant cells.

→ Paraneoplastic neuropathy

(Nerves) Toxin هتدمر (malignant cell) بتطلع

The Sensory Symptoms of Neuropathy

Negative phenomena: في المراحل المتقدمة من المرض بتغير

loss of sensation (anaesthesia or hypoaesthesia), stocking-glove type
لغيبة ألم
كم زيم لاسب جراب وكفانات

↑ sensation **Positive phenomena:** يعني الاحساس زايه عند المرضي

Paraesthesia: a "pins and needles" sensation. لفر خاصة تدعي

- **Hyperaesthesia:** increased sensitivity to any stimulus.
- **Hyperalgesia:** increased sensitivity to a painful stimulus.
- **Hyperpathia:** increased sensitivity with increasing threshold to repetitive stimulation.
- **Causalgia:** severe sympathetic pain.
- **Phantom pain** post amputation pain

بعد فترة من البتر ايجي شعور من ايم بقدره ا كيف ومن اشارة، العصب لما موجود
نلو حارة irritation لنهاية العصب هتدمر مركزه بالمخ فبعد ايم ايجي قده مثله

The Motor Symptoms of Neuropathy LMNL

- Muscle weakness more in distal muscle group.
- Muscle hypotrophy or atrophy.
- Muscle hypotonia. , hyporeflexia
- Muscle fasciculation: rare.

distal weak ← neuropathy *
proximal " " ← myopathy *

Myokemia * رجفة العضل تبصر مع التوتر ...

Investigation of Neuropathy

- CBC, ESR.
- Blood chemistry. — هم على يكون مريض سكري ، إلخ
- Vit. B12 serum level. هذه complication وهو من
- TSH. عارف أضيق انه مرض DM
- ANA. to exclude SIE
- **Special investigation:**
 - Nerve conduction studies. (NCS)
 - Electromyography.
 - Nerve biopsy (multiple mononeuropathies in vasculitis, amyloidosis, sarcoidosis etc).
 - Genetic study.

General Clinical Picture of Neuropathy

1. Motor: bilateral and symmetrical LMNL (hypotonia and hyporeflexia) affecting longer nerves.

← Affection occur in LLs > ULs, distal > proximal
(bilateral foot drop and wrist drop with high steppage gait due to foot drop). Lost ankle reflex with preserved knee.

2. Sensory: affecting distal nerves

- **Superficial sensation:** early pain, paresthesia and later distal loss of sensation (stock and glove type).
- **Deep sensation:** later sensitive ataxia.

3. Autonomic: coldness, cyanosis, anhidrosis, loss of hair, brittle nail, trophic ulcers and Charcot's joint. painless deformity joint

4. Specific features: according to etiology and type of neuropathy.

← يشونه إل diabetic

Neuropathy

Mononeuropathy

احبة صحن واحد

Polyneuropathy

Mononeuritis multiplex

صحن آخره بين clinical ، صحن NCS

لو طلع severe loss conduction velocity

- Axonal
- Demyelinating

لانه هو الجول عن Demylin

nerve transmission.

Definitions

- **Neuropathy**: a pathological process affecting a peripheral nerve or nerves.
- **Mononeuropathy**: a process affecting a single nerve.
- **Mononeuritis multiplex**: (multiple mononeuropathy, or multifocal neuropathy) affects several or multiple nerves (asymmetrical).
- **Polyneuropathy**: diffuse, symmetrical disease, usually beginning distally. The course is either:
- Acute, subacute, chronic.
 - Static, progressive, relapsing.
 - Motor, sensory, autonomic and mixed.
 - Demyelinating or axonal types.
- **Plexopathy**: disease affecting multiple nerves in plexus.
- **Radiculopathy**: disease affecting nerve roots.
- Handwritten notes and diagrams:
- Arabic notes: "لغني بصير لزا", "عصب نكن", "asymm", "لغني", "R+", "Radial", "Ulnar", "نكن", "R+", "Ulnar", "نكن", "R+", "Ulnar".
 - Diagram of a line graph showing a wave pattern with labels: "static", "progressive", "relapse", "remission".
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Nerve Compression and Entrapment

- **Carpal tunnel syndrome:** median nerve compression in the carpal tunnel (at the wrist).
wrist drop *عصب میانی*
- **Cubital tunnel syndrome:** ulnar nerve compression in the cubital tunnel (at the elbow).
- **Radial neuropathy:** radial nerve compression in spiral groove of humerus.
عصب رادیال
- **Meralgia paraesthetica:** lateral femoral cutaneous nerve compression in inguinal ligament. *ant. lat. surface of thigh*
- **Common peroneal neuropathy:** common peroneal nerve compression at the neck of fibula. *→ drop foot*
- **Tarsal tunnel syndrome:** tibial nerve compression in the tarsal tunnel (at flexor retinaculum).

Classification of Neuropathies

آقل سے شعر

1. **Acute neuropathies**- a few days -4 weeks: Postinfectious, Guillain-Barre syndrome, postdiphtheritic.
2. **Subacute neuropathies**- develop over weeks "4-8 weeks": Drug induced, alcoholic, deficiency vit. B complex.
3. **Chronic neuropathies**- develop over 8 weeks:
Paraneoplastic, connective tissue disorder (SLE, rheumatoid arthritis etc), amyloid disease, metabolic (hypothyroidism, diabetes, uremia), chronic inflammatory demyelinating polyneuropathy (CIDP), hereditary sensorimotor neuropathies (Charcot-Marie-Tooth disease).

Carpal Tunnel Syndrome



- Carpal tunnel syndrome – median nerve entrapment secondary to excessive use of the wrist, local inflammation, arthritis, hypothyroidism, diabetes mellitus, pregnancy , S/E
 - Nocturnal paresthesia of the thumb, index and middle fingers

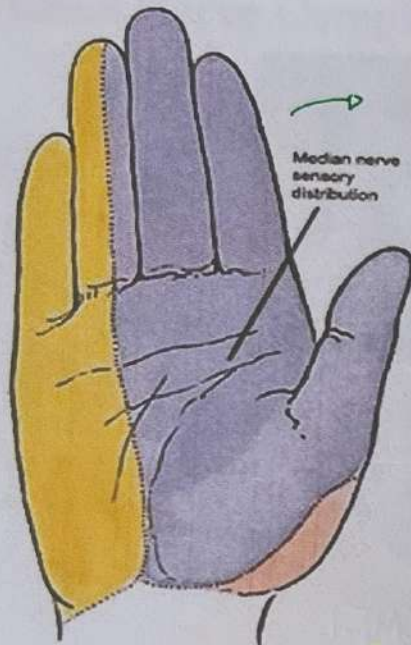
فندلاہ ہاؤس سراجہ

← meralgia هذا ال lat. lemon art. بمره قن

inguinal ligament ، بنفند عليه أكثر عند الناس

ال Obese ، بامسوا اولي فنيقه

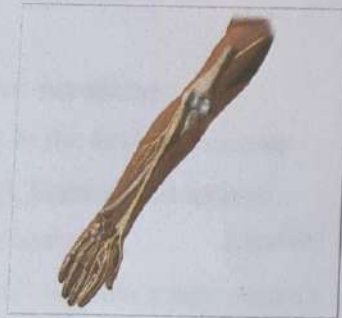
نقنوا في Flexion Position نقنقوا لاص



Median nerve sensory distribution

✓ هنا فزالان
بأول ٣ أصابع
ورف

Radial Neuropathy



- Radial Neuropathy – most common site of compression is in the humeral groove (**Saturday night palsy**)

◦ Wrist palsy

لانه يوم السبت بيترجوا ليمول كثير
ورجوا drop wrist

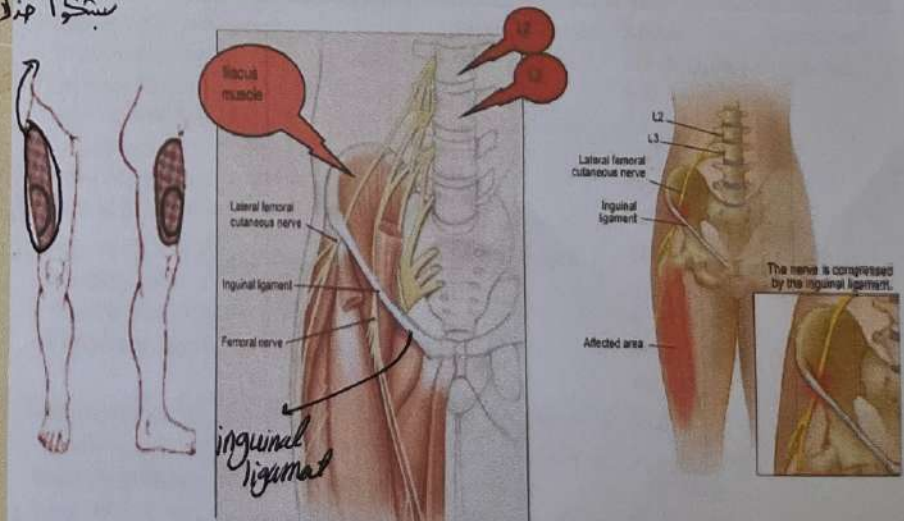
Ulnar Neuropathy



- Trauma, compression, entrapment
 - Ulnar Neuropathy – most common site of compression is in its superficial site in the elbow "the cubital tunnel syndrome"

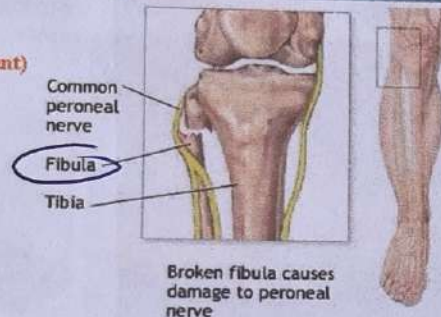
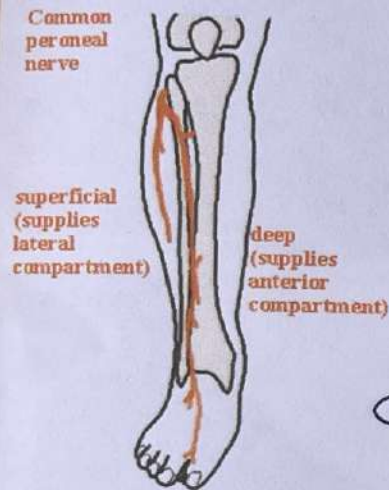
Meralgia Paraesthetica

سببوا فزالان هنا



- Lateral femoral cutaneous nerve entrapment – meralgia paresthetica (pain and paresthesia over lateral thigh).

Peroneal Nerve Compression



Charcot-Marie-Tooth Disease (CMT) (Hereditary Sensorimotor Neuropathies)

Definition: hereditary polyneuropathy with gradual onset occurring in the first and second decades of life also called *مرض داري*

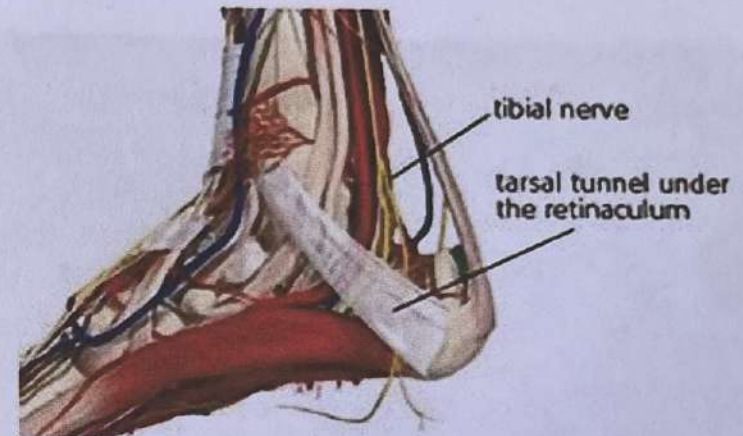
"Peroneal Muscular Atrophy". *بقول atrophy* *ليؤثر على الاغصان الحركية*

Clinical picture: *Peroneal م. بار* *المستة*

- Motor:** weakness and wasting in LLs (in peronii muscle), then the anterior tibial group, then involve of the lower 1/3 of the thigh resulting in "Inverted Champagne Bottles", later ULs may be affected. *ليكون عضلات thigh ذرية لك leg رضية*

- Sensory:** stock and gloves hypoesthesia, with affection of vibration sense. *فشيحوما*
- Skeletal deformities:** pes cavus, talipes equinus and kyphoscoliosis. *نمارة الشبيهة المتقلبة*

Tarsal Tunnel Syndrome



- Tarsal Tunnel syndrome- tibial nerve entrapment in the posterior area of the medial malleolus due to fractures of the ankle, posttraumatic fibrosis, cysts, arthritis
- Pain and numbness in the ankle and sole of the foot

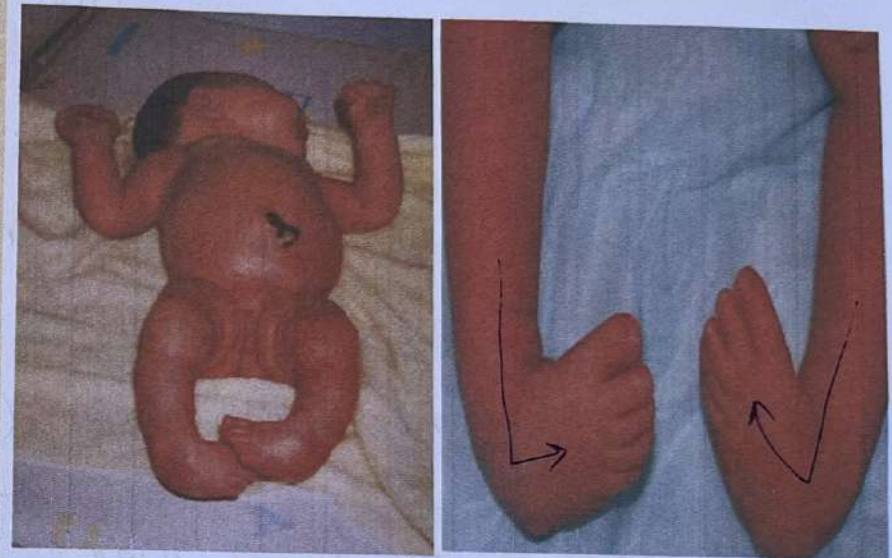
Types of Charcot-Marie-Tooth Disease (CMT)

Type	Clinical feature	Pathology	Neuro-physiology	Inheritance
CMT-I < 30y	- Age of onset <30 years - Wasting and weakness of intrinsic foot muscle, peroneal and tibial groups, distal UL involvement - Peripheral nerves palpable - Foot deformities in 75% - Ataxia and tremor in 10%	Demyelination with thickened areas of remyelination	Motor conduction velocities < 38 m/sec in common peroneal nerve	Autosomal dominant
CMT-II	- Age of onset >30 years - Wasting and weakness as type I - Absent foot deformities - Peripheral nerves not palpable	Axonal loss	Motor conduction normal or marginally slowed	Autosomal dominant
CMT-III Dejerine-Sottas disease	- Age of onset childhood - Wasting and weakness of distal muscles groups, proximal muscles may be involvement - Peripheral nerves palpable - Foot deformities - CSF protein elevated	Demyelination with thickened areas of remyelination	Motor conduction velocities 5-10 m/sec	Autosomal recessive

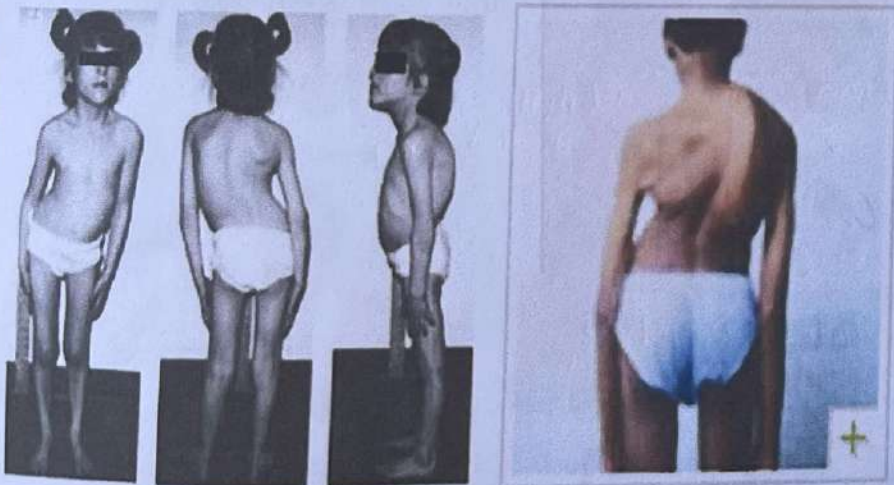
Pes Cavus



Talipes Equinus



Kyphoscoliosis



Diabetic Polyneuropathy

- About 60-70% of people with diabetes have mild to severe forms of nervous system damage, including:
 - ✓ ♦ Impaired sensation or pain in the feet or hands.
 - ✓ ♦ Carpal tunnel syndrome.
 - ✓ ♦ Distal muscle hypotrophy.
 - ✓ ♦ Trophic changes.
- More than 60% of nontraumatic lower-limb amputations in the US occur among people with diabetes.

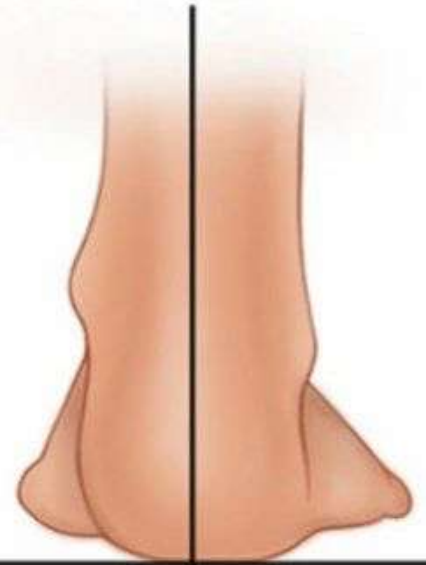
High arch feet (pes cavus)

Typical arch

Footprint



Ankle stability



High arch

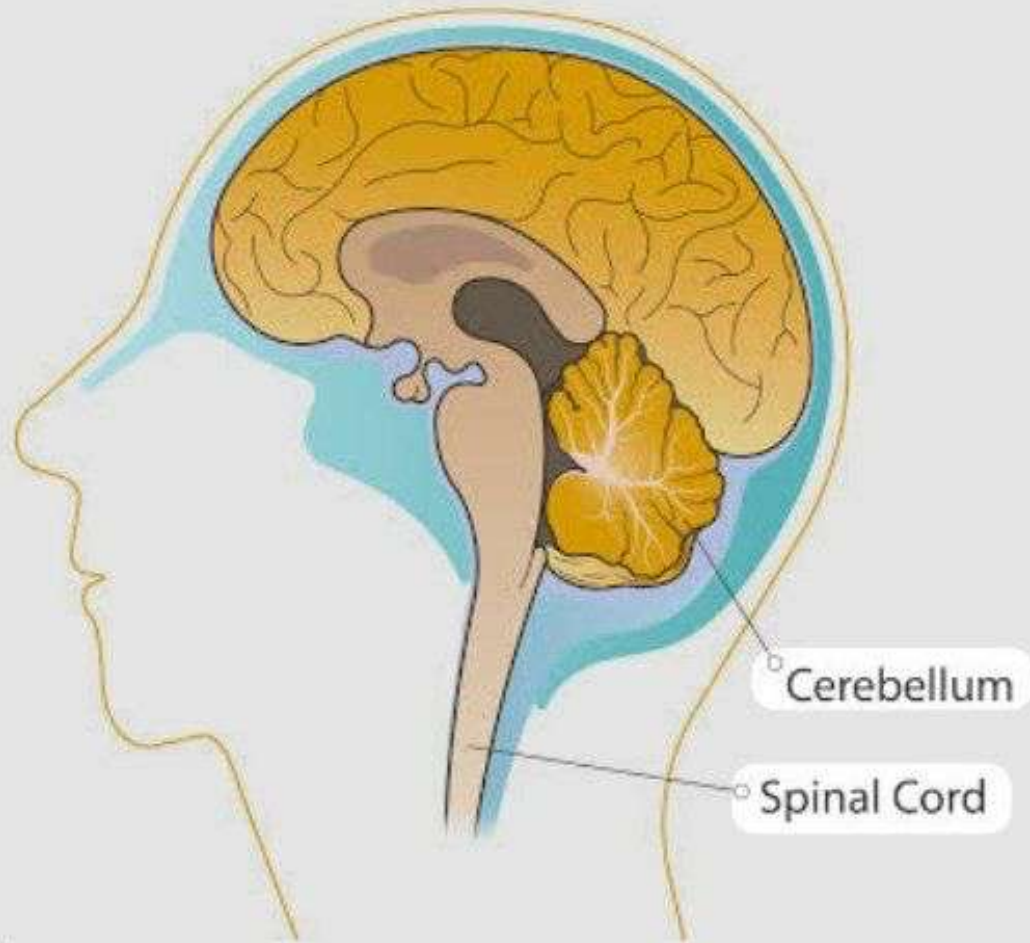
Footprint



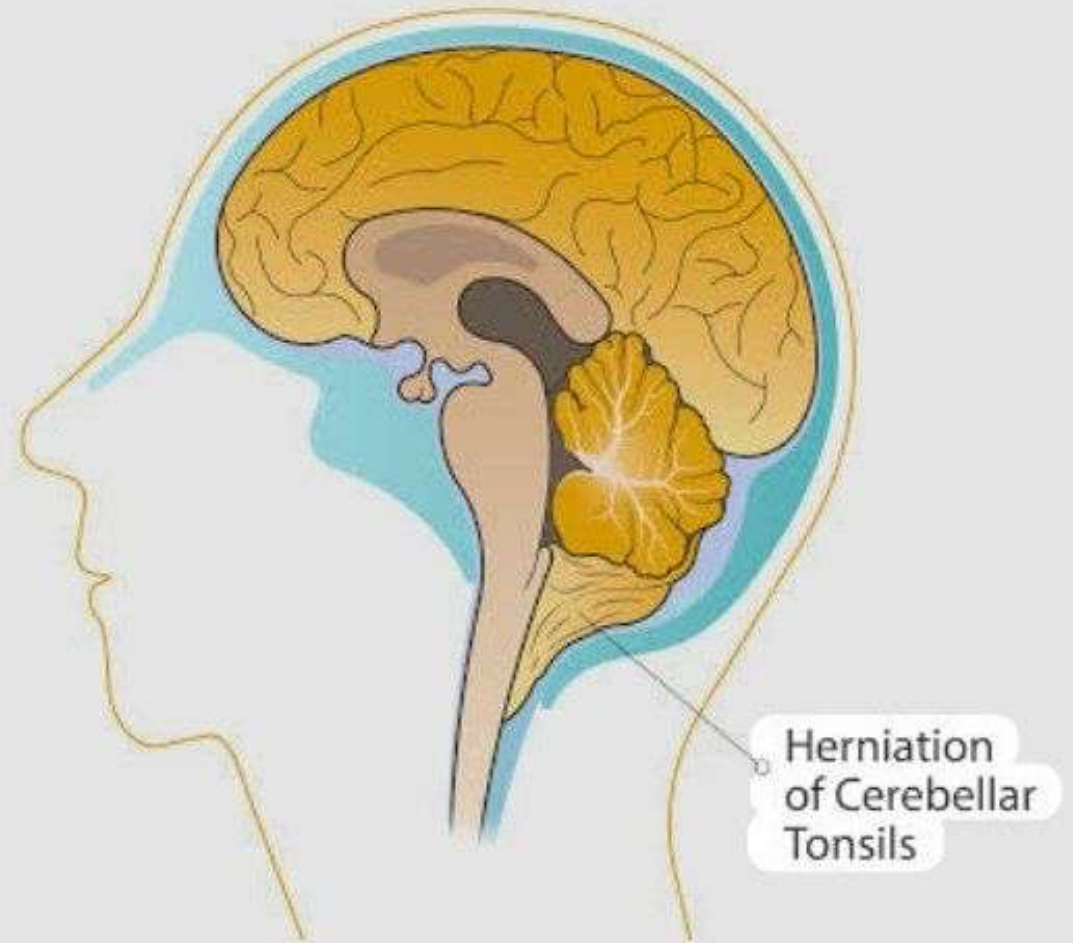
Ankle instability



Normal

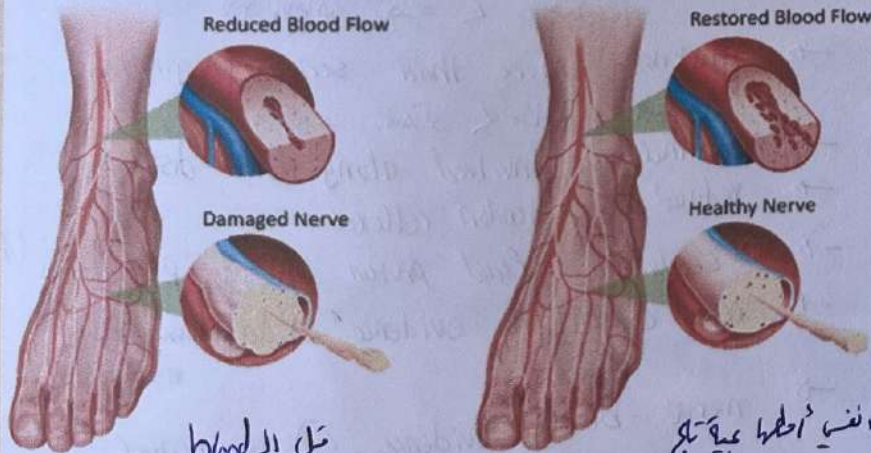


Chiari Malformation



Pathogenesis of Diabetic Neuropathy

- **Microangiopathy:** due to ischemia of vasa nervosa.
الشعيرات الدموية التي تلتقي بها peripheral N. ischemia
- **Macroangiopathy:** secondary to atherosclerosis. → ↓ nerve supply
- **Dyslipidemia.** ↑ Cholesterol, ↑ LDL, ↑ TG, ↓ HDL
- **High blood pressure.**
- **Hypovitaminosis:** polyuria wash water soluble B complex vitamins.
urine لا Vitamines group ب. لا يفقدوا
- **Toxic:** toxic effect of ketones bodies and sorbitol (transformation from glucose).
هناك P. neurop.



مثل الـ blood
الواصل للـ دماغ

(Cerebellar ataxia) سببها نقص الـ blood

↑ sensation, burning, hot sensation
↓ deep
لأنه عندهم
لقد قام بتفتت الـ blood

Diabetic Polyneuropathy- Risk Factors

- Glucose control. ✓
- Duration of diabetes. ✓
- Damage to blood vessels. ✓
- Mechanical injury to nerves. ✓
- Dyslipidemia. ✓
- Autoimmune factors. ✓ → عند RA مثلاً
- Genetic factors. ✓
- Lifestyle factors. ✓
 - Smoking ✓
 - Diet ✓

بجانب distal و LL

Clinical Feature of Diabetic Polyneuropathy

- **Features of DM:** polyuria, polydipsia, polyphagia.
- **Start as mononeuropathy or mononeuritis multiplex:**
 - P.N.: sciatic, femoral, ulnar, median.
 - Cranial nerves: II, III, IV, VI, VII and nerve deafness.
- **Polyneuropathy:**
 - **Mainly sensory:** early tenderness, distal paresthesia and burning sensation, later hypoesthesia (stock and glove).
 - **Lost deep sensation.**
 - **Motor:** muscle weakness with distal muscle hypotrophy and loss of deep reflexes. Diabetic myopathy.

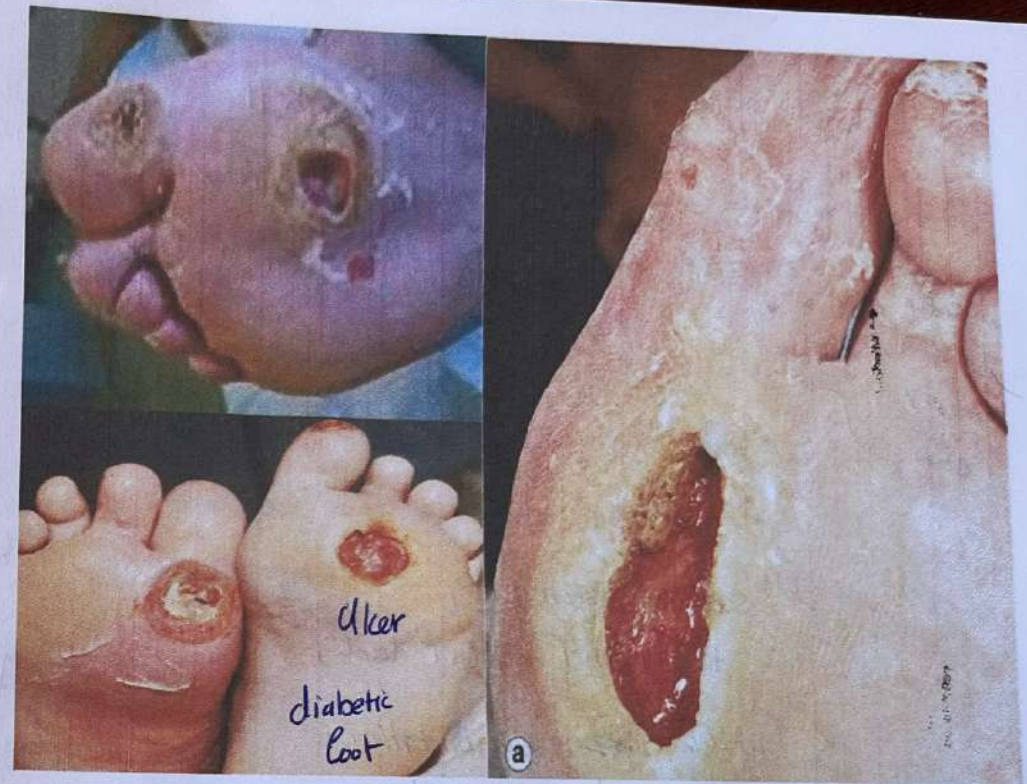
ببداية بالـ sensory
تلاها الكبير يتلاها
مما تارر انشط رجل
بالـ harm بالـ استاء
الـ في الـ علة

لأنه لا يتبعي شام عليه هتوف الـ atrophy
Thumb و الاصبع الثاني

Clinical Feature of Diabetic Polyneuropathy

- **Autonomic neuropathy:** → يمكن فيه خلل في القلب ولا داري
- **CVS:** postural hypotension, tachycardia, silent MI.
 - **Pupils:** mydriasis.
 - **Genito-urinary:** impotence, hypotonic dilated bladder.
 - **GIT:** gastroparesis, early nocturnal diarrhea, late constipation.
 - **Skin:** coldness and anhydrosis. or hotness
 - **Trophic changes:** ulcers, brittle nail, loss of hair, Charcot's neuropathic joint (painless deformed joint).

Charcot's Joint



Treatment of Diabetic Polyneuropathy

- **Strict control of DM:** diet, oral hypoglycemic, better insulin.
- **Antiplatelets:** aspirin and dipyridamol.
- **Vitamins and antioxidants:** B1, B6, B12 and **alpha lipoic acid**.
- **Peripheral microcirculation:** pentoxifylline (trental).
- **Control of dyslipidemia:** atorvastatine or bezafibrate.
- **Analgesics:** carbamazepine, gabapentine and amitriptyline. anti depressant antiepileptic
- **Physiotherapy**

Diphtheritic Polyneuropathy

Aetiology: exotoxin of corynebacterium diphtheria (Gram positive). Occuring 2-8 weeks after appearance of diphtheria.

Clinical picture:

- **Localized type:** III, VII, IX and X nerve affecting.
- **Generalized type:** paraesthesia and paralysis.

Prophylactic:

- Early treatment with antitoxin therapy of diphtheria.

Vitamin-deficiency neuropathies

Beri-Beri disease: deficiency of vit B1 (Thiamine).

Clinical picture:

Edema, cardiac failure and polyneuropathy mainly sensory.

Wernicke's-Korsakoff syndrome (encephalopathy):

- **Eye signs:** nystagmus, ophthalmoplegia with fixed pupils.
- **Ataxia:** broad-based gait, cerebellar and sensory ataxia.
- **Cognitive changes:** amnesia.
- **Hypothermia and hypotension:** due to hypothalamic involvement.

Treatment: vit B1, in heart failure diuretics and digitalis.

Toxic Polyneuropathy

Alcoholic: polyneuropathy, mainly in the lower limbs, occurs with chronic excess alcohol and associated with Korsakow's Syndrome.

Treatment: stop alcohol and thiamine (Vit B₁).

Drugs Toxins: phenytoin, chloramphenicol, metronidazole, isoniazide, nitrofurantoin, amiodarone.

Industrial Toxins: lead, plastics, arsenic, thallium.

Vitamin-deficiency neuropathies

Pellagra: multiple deficiency disease due to lack of vit B complex especially nicotinic acid.

Clinical picture: "Three Ds":

- **Sin- "Dermatitis":** deficiency of vit B2, B6 and nicotinic acid, bilateral symmetrical, in sun exposed areas with hyperkeratosis.
- **GIT- "Diarrhea":** deficiency of vit B12 and nicotinic acid, diarrhea, stomatitis, dyspepsia and hepatosplenomegaly.
- **CNS- "Dementia":** deficiency of vit B1, B6 and nicotinic acid, dementia, paraplegia, quadriplegia (pellagra lateral sclerosis), and peripheral neuritis mainly sensory.

Treatment:

- Treat the cause of vitamin deficiency (parasites, gastroenteritis).
- Diet rich in protein and vitamins.
- Vit B complex, nicotinamide.

Subacute Combined Degeneration

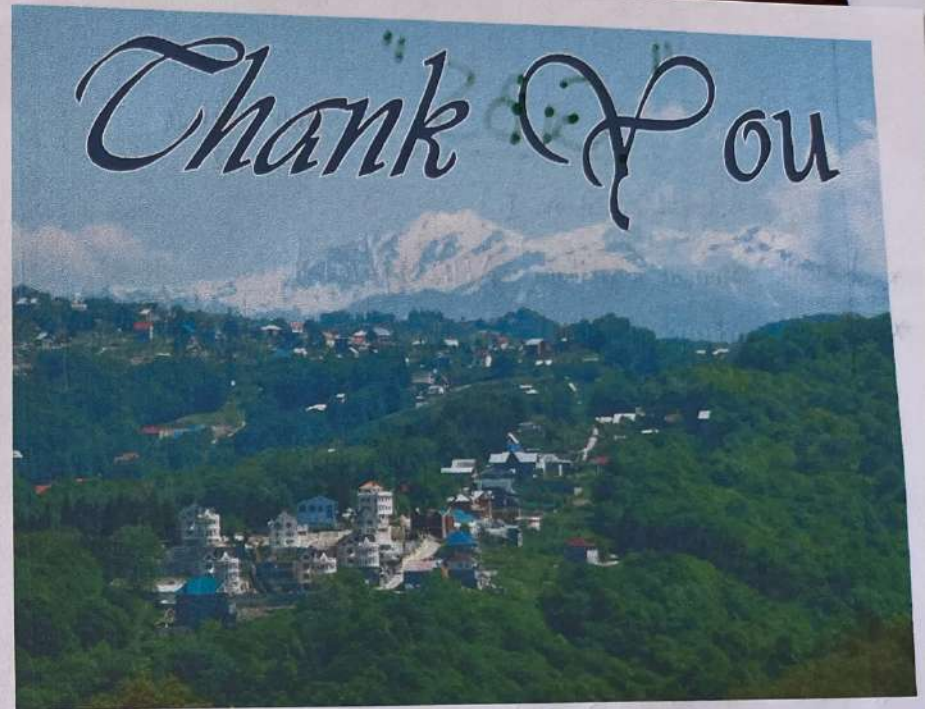
Etiology: vit B12 deficiency

Clinical Picture:

- **Blood:** megaloblastic anemia (Not all patients with neurologic abnormalities will have anemia)
- **GIT:** stomatitis, dyspepsia, diarrhea
- **Neurological manifestation:** a slowly progressive sensory ataxia, spastic paraplegia, polyneuropathy (combined degeneration of posterior, lateral column and peripheral nerves), dementia, urine and stool incontinence.

Investigation: CBC, blood film, serum vit B12 level, gastroscopy and dorsal spinal cord MRI

Treatment: vit B12



✓ فشل كل علاج عنه نقص vitB12 عنه انيميا

Neurologic symptoms
سبقت
hematologic manifestation

Subacute Combined

أولاً من حالة يتبع

من شو لشعره

✓ lat. Column & s. cord

✓ Perip - nerves

✓ Cortex

✓ Post. Column

يبدأ بكذا مكان

7 week

* العلاج حقنة vitB12 كل يوم بالحقن على 7 ايام ثم كل اسبوع حقنة

ثم كل شهر حقنة

* راجع عندي :-

↓ deep sensation , sensory ataxia (1)
loss joint sensation
damage Post. column

hyperreflexia, LL spasticity (2)
knee jerk

(lat. ext) lat. column

✓ راجع ينس ، وما يتبع بالبول

hyperintense signal spinal MRI

Post. part جاي

↓ s. cord .

"GBS"

(Guillain-Barre S)

male : female
3 : 2

- * [acute immune-mediated polyneuropathy]
- * [acute monophasic paralyzing illness provoked by preceding infection]

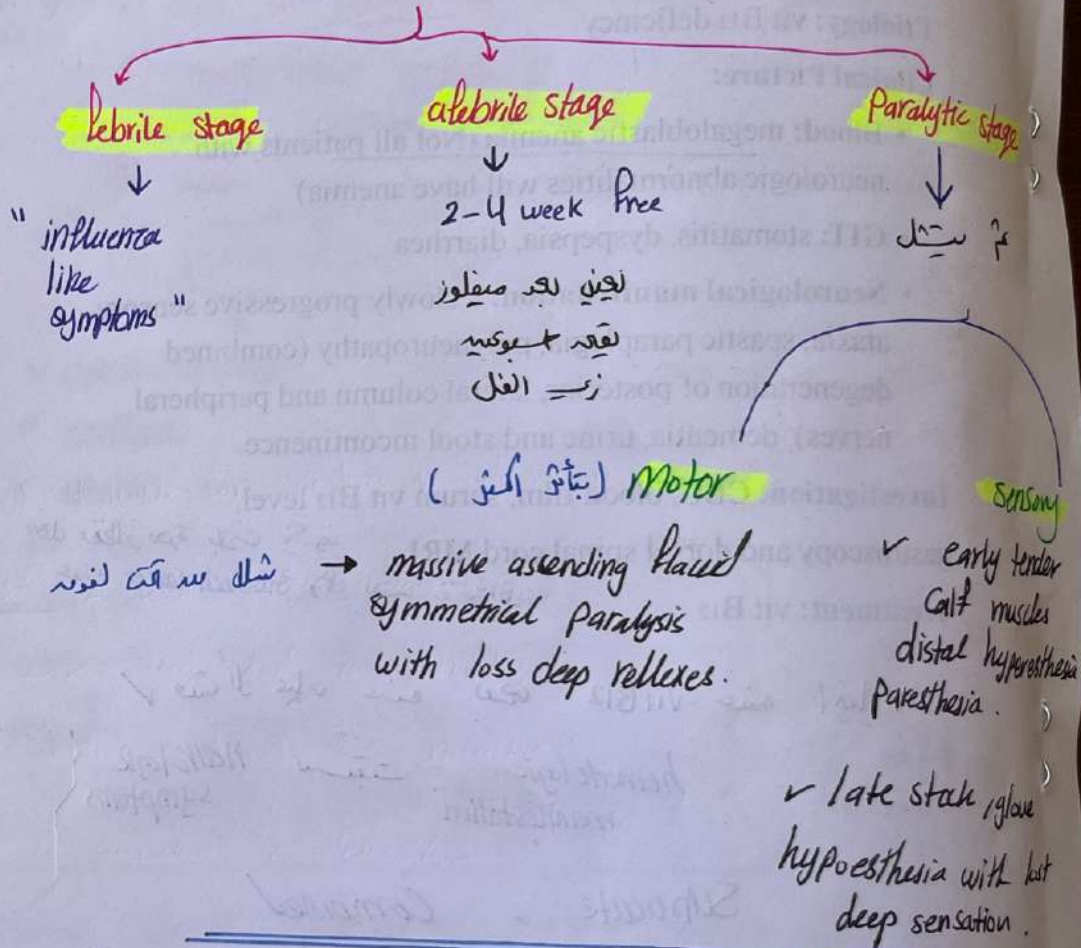
لأنه عند Common cold ثم السبوعين جال GBS مثل
✓ زمانه كله نوع واحد كل صار يغير Syndrome وليه
أنواع

- * rare in child < 2y
- * Peak in young adult, elderly

- Viral
 - Campylobacter
 - influenza vaccine
 - meningococcal "
- immune demyelination

السبب //

* clinical features 8



- * Facial + oropharyngeal weakness in > 50% of cases
 - * Oculomotor weakness occur in 15% of cases
 - * resp. + bulbar involvement in severe cases
 - * Tracheostomy / ventilation is required in 20% cases
- Paralysis resp. muscle
لأنه حركه

- * 79% neuropathic pain
- * 60% Paralysis LL
- * 51% autonomic dysfunction
- * 46% Cranial N. involvement
- * 24% Couldn't use their arms
- * 13% required mechanical ventilation.

* شو ال autonomic dysfunction لي هتوصل عندهم ؟

- ✓ Orthostatic hypotension
- ✓ Paralytic ileus
- ✓ Bladder dysfunction
- ✓ Transient or Persistent H/W
- ✓ abnormal sweating
- ✓ Cardiac dysrhythmia
 - ↳ Bradycardia
 - ↳ Persistent sinus tachycardia
 - ↳ atrial and Ventricular Tachyarrhythmia.

- * أنواع GBS
- ① acute inf. demyelinating polyneuropathy (AIDP)
 - ② acute motor axonal (AMAN)
 - ③ acute motor-sensory axonal (AMSAN)
 - ④ miller fisher

• Triad:

- ✓ ophthalmoplegia ازدواجية بالارضية
- ✓ areflexia وغيوبه عصبية
- ✓ ataxia زخ
- LL weakness لبدون

• دة سبب (AB against GQ1b) في 85-90% من المرضى

* اعرافه / GBS
(drop foot, atrophy muscles, loss hair in leg, distal m. hypotrophy)

investigation GBS II
1 CSF examination

بين نشيطة Clinically وينبأ علاج من اول يوم
لانه زي مشتات فيه الالتهاب لبد هيبوليد
في الاسبوع الثاني - ثالث
↑ Protein (> 45 mg/dL)
خللا في 20% ال Cell 50% (lymphocyte)
عكس تكون cell absent

2] nerve Conduction Studies

↓ Conductive Velocity

بيدانية لانه يكون لوزال

بعد هيبوليد خيلاني

* Treatment of GBS II

✓ قش نايه حيا ل Corticosteroid

• IV IGI → 400 mg/kg for 5 days → لو عنده مكنيه فيه

• Plasma exchange هذا اومش

وجود

صند

• anti coagulant for DVT prevention

• Symptomatic

✓ suction secretion ,
tracheostomy , NGT feed's

✓ medical ~~re~~ rehabilitation
and physiotherapy.

* Total dose = 2 g/kg

مثلا واحد وزنه 50 kg

$$50 \times 2 = 100 \text{ g}$$

له هوزها 5 ايام

بطلع كل يوم

20 g (يعني 400 mg/kg)

1g/kg daily
for 2 days

* الالتهاب ←