Meningitis & Encephalitis

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CNS Infection

- **Meningitis:** Inflammation of the meninges (Pia/Arachnoid/Dura)
- **Aseptic meningitis:** Inflammation of the meniges w/ -ve culture
- **Encephalitis:** Inflammation of the brain parenchyma itself
  (frequently encephalitis presents w/ meningitis → Meningoencephalitis)
- **Myelitis :** Inflammation of the spinal cord

- **Meningitis:**
  - Inflammation of the meninges
  - CSF pleocytosis

* أطلب blood test الـ WBC
إذا الـ WBC طبيعي ← مش Meningitis

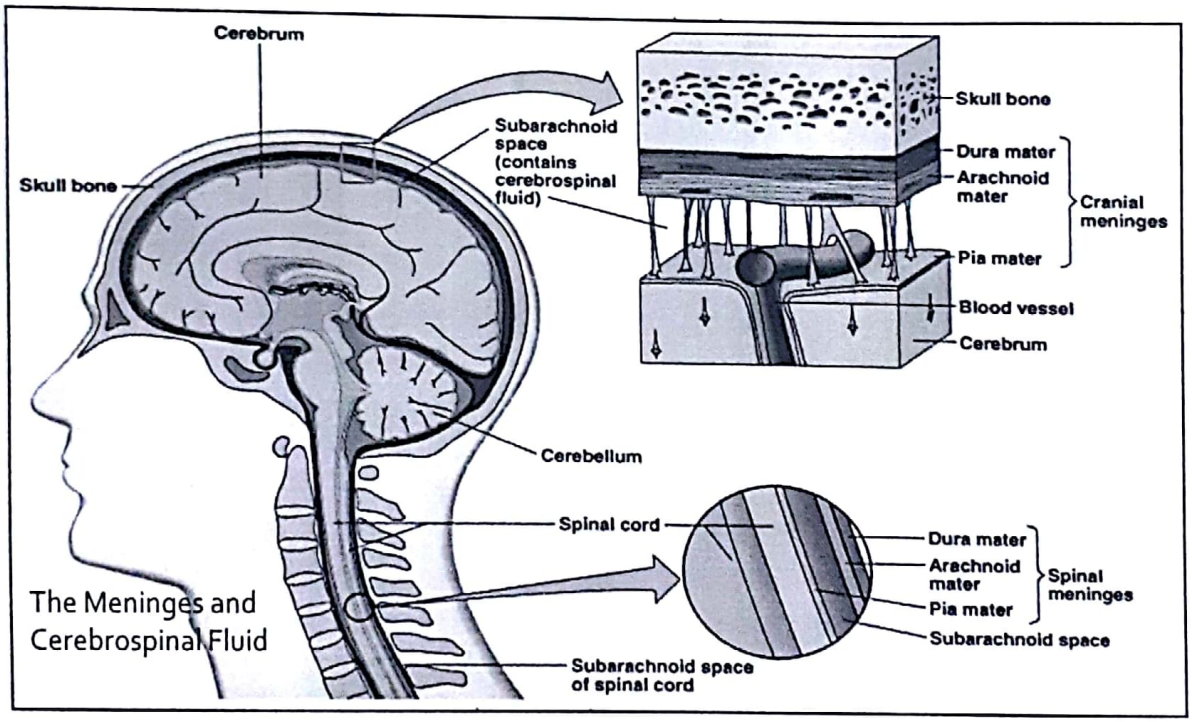
- **Aseptic meningitis:**
  - Meningeal inflammation with negative CSF bacterial cultures
  - No prior antibiotic usage
  - Infectious and noninfectious causes .

ex. Kawasaki disease

- **Encephalitis:**
  - Inflammation of the brain
  - Produces neurologic dysfunction:
    - Altered mental status
    - Behavior, or personality changes
    - Motor or sensory deficits
    - Speech or movement disorders
    - Hemiparesis
    - Paresthesias
    - Ataxia

- **Myelitis**
  - Inflammation of the spinal cord
  - Symptoms: (weakness يكون عندو)
    - flaccid paralysis and reduced or absent reflexes.

Meningitis



The Meninges and Cerebrospinal Fluid

In General (regardless of age)
- * Most Common etiology of Meningitis is Viral
- * Most Common bacterial etiology is Strep pneumonia

* However each age has it's own organisms:

Etiology oF Bacterial Meningitis by age group

Newborn Period → GBS أول اشي في new born بطفل infx أي *
E.coli و

More than 2/3 are caused by:

↳ ≡ Streptococcus agalactiae

- Group B streptococcus (GBS) → from the birth canal
- Gram-negative enteric bacilli
  - E. coli, Salmonella, Enterobacter
- Listeria monocytogenes

Etiology of Bacterial Meningitis by age group

Children 1-23 months

↳ Gram +ve diplococci

- *• **Streptococcus pneumoniae** → The most common, The most fatal, The most likely to cause side effects
- • *Neisseria meningitidis*
- *• Group B streptococcus
- *• *E. coli*
- • *Haemophilus influenza type B* المطعوم هاد ← vaccine بطلنا نشوف فيها بسبب دخل العالم أول التسعينات

↳ Vaccine type is "Conjugated" → PCV (Pneumococcal Conjugated Vaccine)

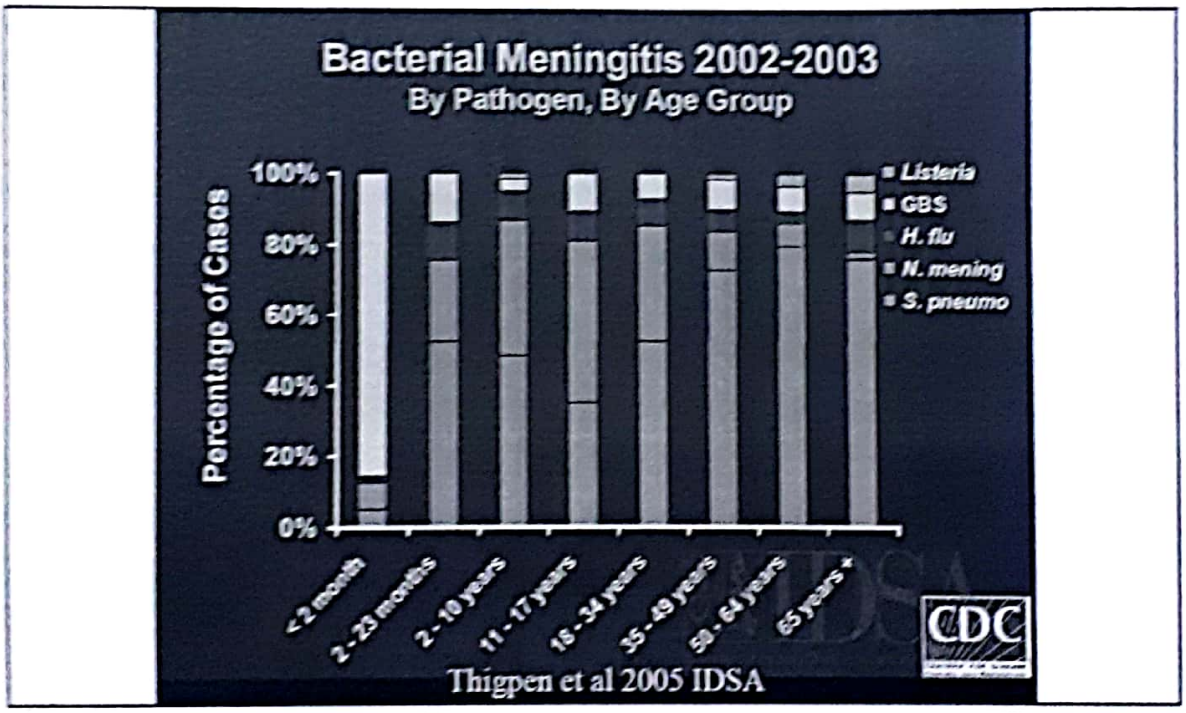
* The vaccine only works for H. influenzae type B only

↳ Pneumonia is caused by nontypable H. influenzae (also otitis + sinusitus) (so the vaccine doesn't prevent this)

Etiology of Bacterial Meningitis by age group

Children ≥ 2 years

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*



Bacterial Meningitis

Bacterium	Percentage of Cases	Fatality Rate
Streptococcus pneumoniae	30–50	19–46
Neisseria meningitidis	15–40	3–17
Haemophilus influenzae	2–7*	3–11

Other bacteria causing meningitis account for 6–8% of cases.

**Before introduction of Hib vaccine, H. influenzae accounted for about 45% of cases of bacterial meningitis; about 70% of these cases occurred in children under age 5.*
SOURCE: Adapted from E.J. Phillips and A.E. Simor, "Bacterial Meningitis in Children and Adults," Postgraduate Medicine 103 (3):104 (1998).

Haemophilus influenzae Meningitis

- Occurs mostly in children (6 months to 4 years)
- Gram-negative aerobic bacteria, normal throat microbiota
- Capsule antigen type b
- Prevented by Hib vaccine (PCV)
  - ↳ Helped ↓ in the rate of meningitis, ~~pneumonia~~, and epiglottitis... etc

Haemophilus influenzae Meningitis

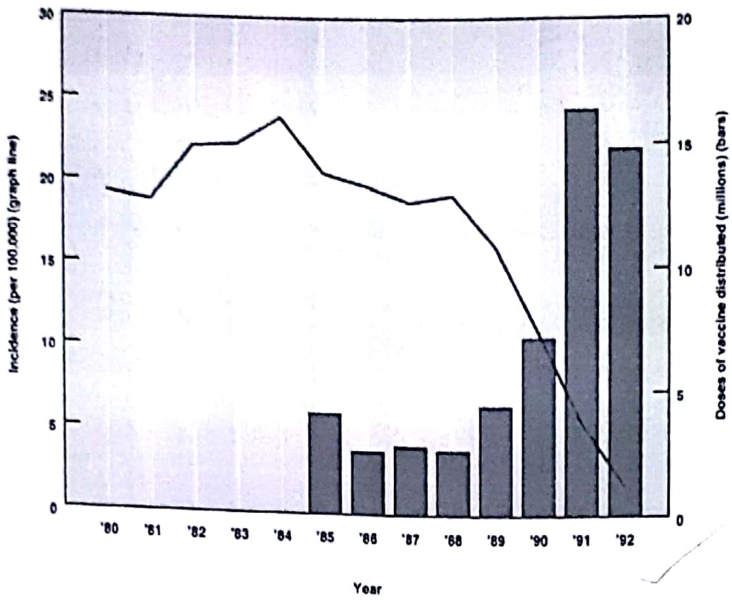
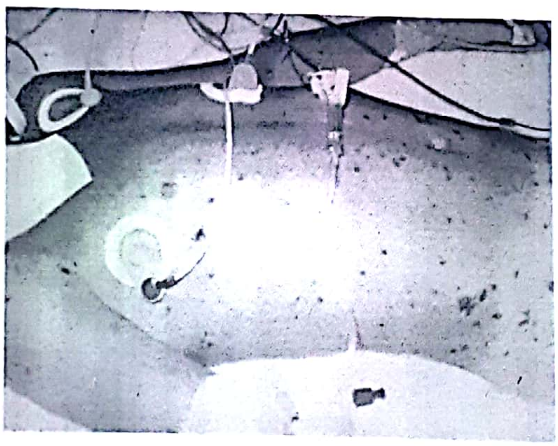


Figure 22.3



Petechial Rash → Indicative of Neisseria Meningitidis

← ما يروح لما تضغط عليها
(نزيف تحت الجلد)

Neisseria Meningitis

(Meningococcal Meningitis)

- *N. meningitidis*
- Gram-negative aerobic cocci, capsule
- 10% of people are healthy nasopharyngeal carriers
- Begins as throat infection, rash
- Serotype B is most common in the U.S.

* بهينا إذا gram +ve or -ve لأنه أول اشي بنعمل الـ gram stain ← فبعطيني فكرة شو ممكن الـ organism يكون

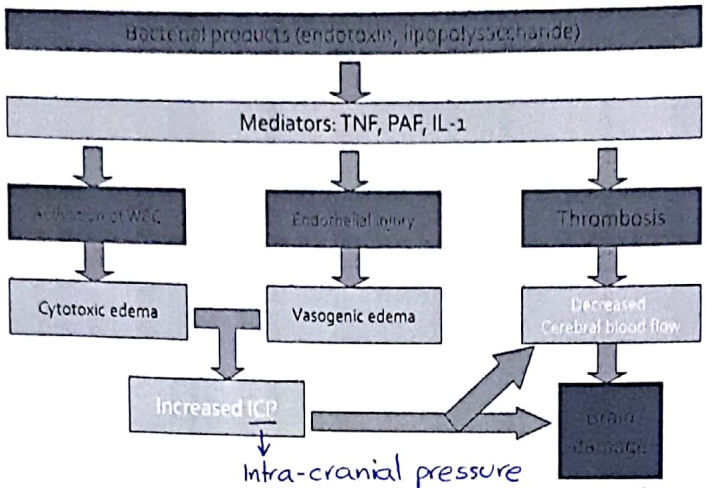
Streptococcus pneumoniae Meningitis

- Gram-positive diplococci
- 70% of people are healthy nasopharyngeal carriers
- Most common in children (1 month to 4 years)
- Mortality: 30% in children, 80% in elderly
- Prevented by vaccination (Pneumococcal Conjugated Vaccine, PCV)

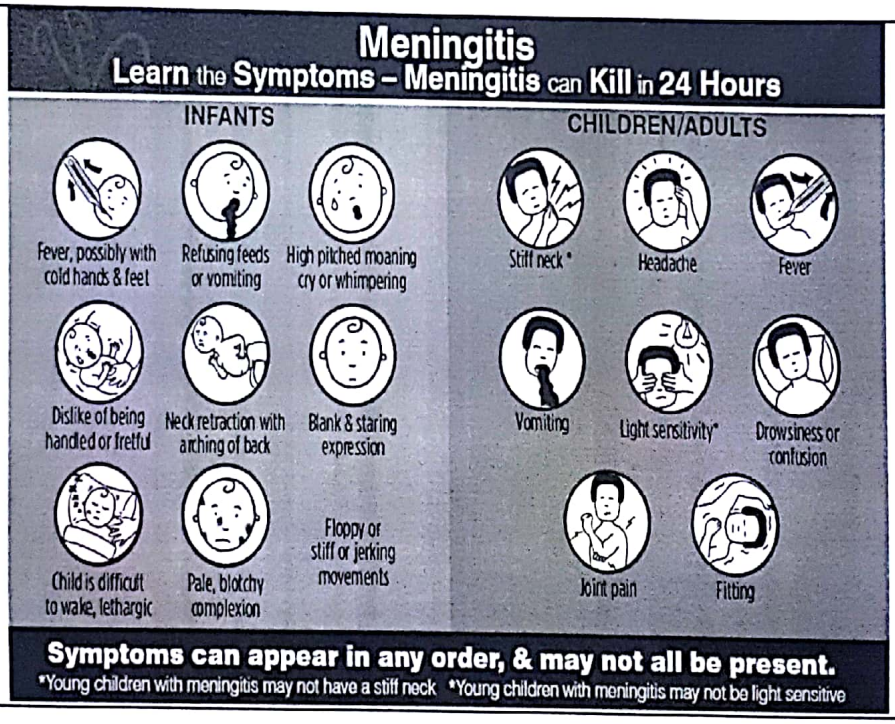
بس ما بعطوا عنا إلا إذا شو بيته لحالك و شوي غالي

* Most common complication is hearing loss (⅓ of pts develop hearing loss)

Pathogenesis



Intra-cranial pressure
(causes headache / neck stiffness ...)



Clinical Manifestations of Bacterial Meningitis

- Young infants
  - Proceeded by URTI بكون موسّخ قبل أسبوع زمن.
  - Irritability
  - Somnolence نعس
  - Fever
  - bulging fontanelle and diastasis of sutures in the infant.

Note: Anterior fontanelle closes b/w 1-1½ yrs (9-18 mths)

Clinical Manifestations of Bacterial Meningitis

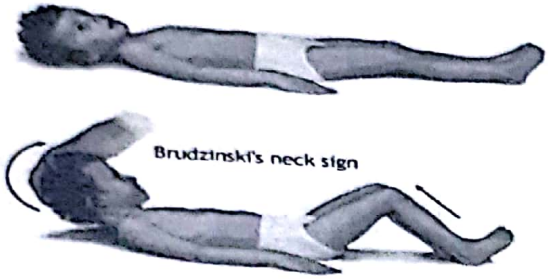
- Older Children:
  - Increased intracranial pressure is the rule:
    - Vomiting, irritability, anorexia, headache, confusion, photophobia and nuchal rigidity
    - Nuchal rigidity, positive Kernig and Brudzinski signs

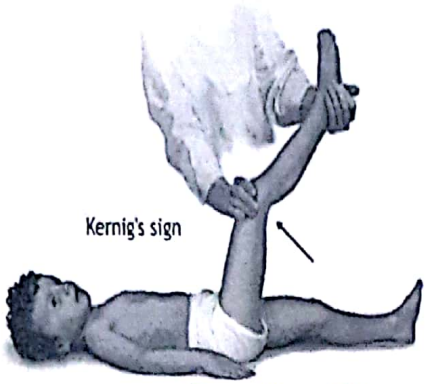
مهمين و بيجي أسئلة كتير عنهم (Meningeal signs)

Physical Examination

Brudzinski's Sign

- A Positive Brudzinski's sign occurs when flexion of the Neck causes involuntary flexion of the Knee and Hip Joints.





*we flex the hip and extend the knee

فالطفل بصير يحكي انه ظهره بوجعه
و ممكن يحرك رجله الثانية عشان
يخفف الضغط

Seizures in Bacterial Meningitis

- 20% of patients have seizures prior to admission
- 32% of patients have seizures prior to or during 1st 48 hours of hospitalization
- Early, generalized or multifocal seizures of short duration and minimal frequency are related to "toxic encephalopathy" → chemical causes/change associated with bacterial toxins, hypoperfusion and metabolic derangements; EEG usually not helpful. Usually controlled easily and have no prognostic implications

Seizures in Bacterial Meningitis

- Seizures which are difficult to control, which persist beyond the 3rd hospital day or which develop initially after the 3rd hospital day may be associated with permanent sequelae.

- Persistent focal seizures or recurrent seizures of varying focality imply: Structural Damage:
  - * venous or arterial thrombosis
  - * infarction
  - * subdural effusion. or empyema

Clinical Manifestations of Bacterial Meningitis

- Papilledema is an uncommon finding in acute meningitis.
- When papilledema is observed:
  - venous sinus occlusion
  - subdural empyema
  - brain abscess

Papilledema → منتفخ بالfundoscope و مشوف

الoptic disc → المفروض يكون الـ sharp margins

أما إذا كانوا blurred → هاي papilledema

و بال meningitidis بتكون bilateral

*If papilledema is present → LP is Contraindicated

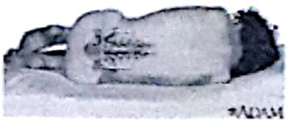
خارجي *In optic neuritis papilledema is unilateral

EVALUATION

- Hx
- Physical examination
- Investigation
  - CBC, KEF, ELECTROLYTES → most importantly Na^+ and glucose
  - CRP, ESR (Acute phase reactants) ← منحب ال CRP أحسن
  - Blood Culture. → for bacteremia
  - Lumber puncture and CSF analysis
  - Imaging study (brain CT)

* We compare b/w the sugar in the blood and the sugar in the CSF

إذا السكر بال CSF أقل من اللي هاد يعني بكتيريا



* The only way to diagnose meningitis is via LP and CSF analysis

CSF analysis (3 tubes) and 1 more
- ↳ One tube goes to the microbiology lab for gram stain and culture
- ↳ One tube goes to the hematology lab for WBC and differential / RBC
- ↳ One tube to the chemestry lab for protein ~~and glucose~~

*رابع تيوب للإحتياط إذا بدي اطلع اشي بال PCR → for viruses like enteroviruses or herpes

Lumbar Puncture or Spinal Tap

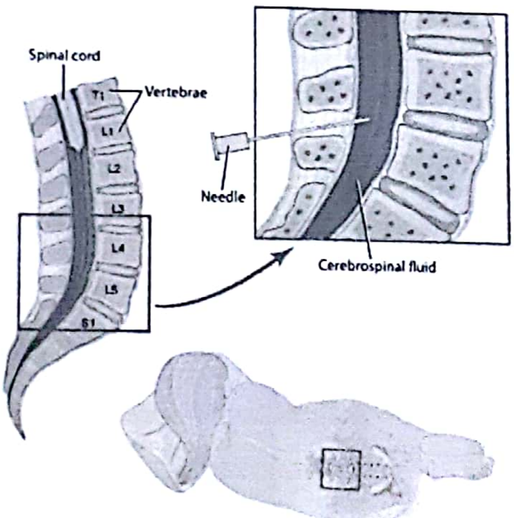


Figure 5. Spinal tap procedure.

✱ IMPORTANT

Suspicion for bacterial meningitis

↓ Yes

Immunocompromised, papilledema, or selected focal neurologic deficits; → Ex. focal seizure / Ataxic
history of selected CNS diseases → Ex. pt w/ VP shunt

هاي الأشياء اذا موجودة بتمنعني أعمل LP

No ↙

Blood cultures and lumbar puncture STAT

↓

± Dexamethasone[a] + empiric antimicrobial therapy[b]

↓

CSF findings c/w bacterial meningitis

↓ Yes

Continue therapy

Yes ↘

Blood cultures STAT

↓

± Dexamethasone[a] + empiric antimicrobial therapy[b]

↓

Negative CT scan of the head

↓

Perform lumbar puncture → (to: CSF findings c/w bacterial meningitis)

IDSA Guidelines *Clin Infect Dis* 2004

→ A poor prognostic factor in meningitis is delayed antibiotic administration

عشان هيك كل ما أسرعنا بال Abx كل ما كان أحسن

Neuroimaging(CT brain)

- Indications for imaging before LP in children with suspected bacterial meningitis include
  - Coma
  - Papilledema
  - Focal neurologic deficit
  - The presence of a CSF shunt
  - History of hydrocephalus
  - Recent history of CNS trauma or neurosurgery

Contraindication for LP

- Suspected brain abscess or subdural empyema (20% herniation)
- Bleeding disorders
- Skin infection at site of LP
- Papilledema? (1-6% herniation after LP)

✡ Interpretation of CSF is important

* أول اشي بنطلع عليه بال CSF هو ال WBC

Cell count, differential and chemistry

	Normal newborn	Normal children	Bacterial meningitis	Viral meningitis	TB/fungal meningitis
WBC (mm^3)	0-30	0-6 in >3months 0-9 in 1-3 months	>1000	100-500	100-500
PMN (%)	**2-3**	**0**	>50*	<40	<50
Protein (mg/dl)	20-150	15-45	>100	50-100	100-1000
Glucose (mg/dl)	30-120	40-80	<30	normal	low-normal
CSF/blood glucose(%)	40-250	60-90	<40 (<60 for term infant)	normal	low-normal

*10% of bacterial meningitis presents with lymphocyte predominance.

Interpretation of CSF

- WBC:
  - WBC >6 cells is abnormal(>3 months)
  - WBC >9 cells is abnormal(1-3 months)

Interpretation of CSF

- The presence of a single neutrophil in the CSF is considered abnormal (except in newborns)
- Glucose: <40 mg/dL or ratio of the CSF to blood glucose concentration is usually depressed (<0.66)
  * If ratio of CSF to blood glucose is < 0.5 (50%) this indicates bacterial meningitis
- Traumatic LP: should be treated presumptively for meningitis pending results of CSF culture.

→ Why is it that in bacterial meningitis, CSF glucose is depressed (low)?
due to a transport problem (not consumption)

Gram's stain → جرام / سريع / وبساعدني

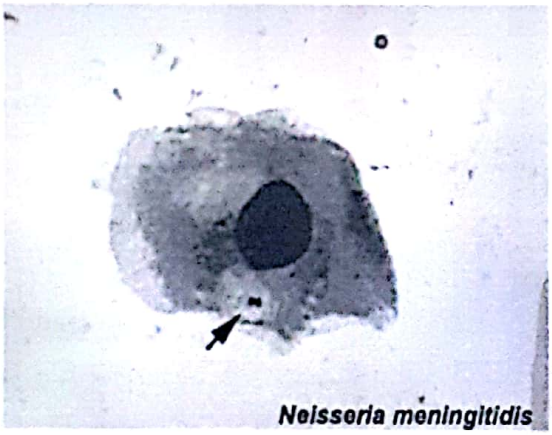
- Positive in 60-90% of untreated patients
- Positive in 97% of cases with organisms > 10^5 CFU/ml
- Positive in pneumococcus > H. influenzae > N. meningitidis >gram-neg bacilli > Listeria
- 90 % pneumococcal M , 80% meningococcal M , 50% G- bacillary M ,30% listeria M
- The yield is lower by 20% in those with prior antibiotic therapy.
- As sensitive as (or better than) antigen detection test.

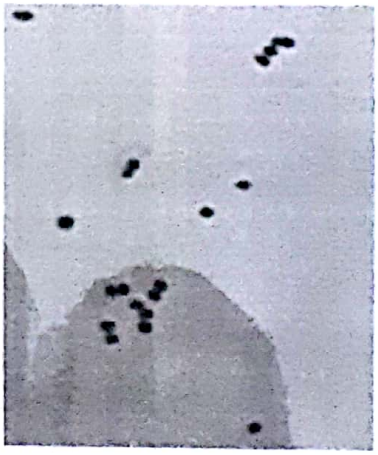
Bacterial culture

- Prompt culture to avoid loss of organisms such as *Neisseria meningitides*
- CSF cultures are positive in 85% of untreated patients

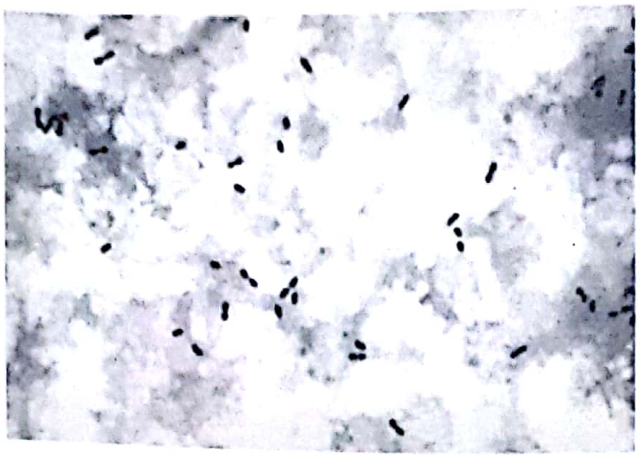
Latex agglutination → It is an antigen-antibody reaction

- Not better than gram's stain
- High false-positive.
- Maybe most useful in pretreated patients → زي الناس اللي بكونوا ماخدين antibiotics





Gram -ve cocci



Streptococcus pneumoniae

Gram +ve diplococci

Listeria monocytogenes

Gram +ve bacilli

Bacterial Meningitis
Normal Child Greater than One Month Old

Expected Organisms:

Streptococcus pneumoniae (most common)
Neisseria meningitidis
Haemophilus influenzae **type b**

Empiric therapy*:

↳ 3'rd generation cephalosporins to cover strep pneumonia assuming it is resistant to Ampicillin

Ceftriaxone or Cefotaxime + Vancomycin

(Ampicillin + Gentamicin for newborns) ↳ In case of resistance we give vancomycin

(for E.coli)

* وزمان كانت الـ strep pneumonia حساسة و بشتغل عليها الـ Ampicillin بس من كتر ما بعطوا Abx عالطالعة و النازلة بطل يزبط زي أول.

Management of Pneumococcal Meningitis

Repeat lumbar puncture

- No improvement after 36-48 h
- penicillin resistant strep pneumoniae meningitis PRSP
  - (Isolate with MIC > 2 to cefotaxime/ceftriaxone)

*Penetration of vancomycin to the CSF isn't very good

مع انه الـ strep.pneumonia كتير إلها حساسة

Follow-up for sequelae (25-30%)

- Hearing test (most common complication of meningitis) → especially strep. pneumonia.
- Neurodevelopmental evaluation

Dexamethasone for Bacterial Meningitis

- Dexamethasone may be beneficial for treatment of infants and children :
  - with Hib meningitis:
    - to diminish the risk of neurologic sequelae including hearing loss
    - if given before or concurrently with the first dose of antimicrobial agent(s)
    - There probably is no benefit if dexamethasone is given more than 1 hour after antimicrobial agent(s).

- Red Book

* Steroids aren't routinely given
However if Hib is suspected we do give it

* Steroids lowers Vancomycin penetration to the CSF even further ☹

Management of Pneumococcal Meningitis

- Initial regimen for children > 1 mo with possible bacterial meningitis regardless of pneumococcal vaccination:

  Vancomycin 60 mg/kg/day
  +
  ceftriaxone 100 mg/kg/day
  (or cefotaxime 300 mg/kg/day)

  منعطيهم بالطوارئ ، بعد ما تطلع النتيجة لل culture منعمل adjustment لل ttt فمثلاً إذا كانت sensitive لل ceftriaxone ← بخليه و بشيل ال vancomycin

- Dexamethasone is controversial
- Treatment duration is 10-14 days

إذا ceftriaxone بشيل ال resistant و بخلي ال vancomycin و هكذا

Duration of treatment Bacterial Meningitis

Depended on causative organism and the clinical course:

- S. pneumoniae: 10-14 days → since it's most common فعادة العلاج بكون ١٠ أيام
- N. meningitidis: 5-7 days
- Hib: 7-10 days
- * *L. monocytogenes* – 14 to 21 days
- *S. aureus* – at least 2 weeks
- * Gram –ve: 3 weeks

هدول التنين علاجهم بطول أكثر من غيرهم.

لو عندك مريض سحايا و بتعالج فيه ، مر ٣ أيام و هو لسا ما بتحسن ... ليش ؟

Causes of Prolonged or Recurrent Fever in children with Bacterial Meningitis

- Inadequate Treatment
- Nosocomial Infection
- Phlebitis
- Immune mediated arthritis
- Drug Fever (rare)
- Unknown
- * Suppurative complication: Pericarditis, Pneumonia, Pyogenic arthritis, Subdural empyema
- Discontinuation of Dexametahsone

* The bacteria may be resistant
* Wrong choice of antibiotic
* Wrong dose

* Presence of a 2° infx, ex.-gastroenteritis
- Thrombophlebitis → IV line مكان الـ

Indications for Repeat Lumbar Puncture

- Patient not responding clinically after 48 h of appropriate therapy.
- Pneumococcal isolate resistant (MIC >2 μg/ml) to cefotaxime/ceftriaxone
- Neonate with Gram-negative meningitis

Indications for Neuroimaging of Head in Bacterial meningitis

- Persistent focal neurologic findings
- Persistently positive CSF cultures despite appropriate therapy
- Persistent elevation in CSF PMN % after >10 days of therapy
- Recurrent meningitis

Neuroimaging

- Cerebral edema
- Transient ventricular dilatation/hydrocephalus
- Ventriculitis
- Subdural effusion/empyema
- Cerebral infarct
- Brain abscess
- Venous sinus thrombosis
- Hemorrhagic stroke
- Spinal cord infarction

Poor prognostic factors:

- ≥2 days of symptoms before admission. (delayed Abx administration)
- Etiology: Bacterial, especialy pneumococcal. (strep pneumonia)
- The number of organisms.
- CSF sugar < 20 mg / dl at admission.
- Delayed sterilization of CSF : > 24 hours
- Coma
- Seizure after 72 hrs of admission, prolonged, or difficult to control
- Malnutrition
- Focal neurologic deficits
- SIADH

(CNS complications of meningitis)

Neurologic Sequelae of Bacterial Meningitis

- mental retardation
  - language delay
  - learning disorders
- behavior disorders ex. ADHD
- delayed or abnormal motor development
- hemiparesis
- hearing handicap
- ataxia
- seizure disorder
- blindness
- hydrocephalus
- Hypothalamic dysfunction

* Hearing loss is the most common and it is irreversible because it's sensory-neuron

Sensorineural Hearing Loss in Bacterial Meningitis

- Unilateral or bilateral loss
  - *S. pneumoniae* 30%
  - *H. influenzae* type b 6-15%
  - *N. meningitidis* 5-10%
- Ataxia commonly associated with deafness
- Hearing loss appears to occur early (present at or near admission)

PREVENTION

- **Vaccines** (primary prevention).
- **Isolation :**
  - standard precautions + droplet precautions for 24 hours into treatment

for 1 day from the begining of ttt
بطل يعدي معدي بعد ما تعطي Abx لمدة ٢٤ ساعة

- **Chemoprophylaxis:**
  - Rifampicin to contacts of patients with meningococcal and Hib
- **Patient Education.**

Prognosis

ما حكا اني عن هاد السلايد

- Mortality: 5%in developed countries and 8 %in developing countries.
- Neurological sequele:15 % to 25 %
  - Deafness : 11 %
  - Mental retardation :4 %
  - Spasticity and/or paresis : 4 %
  - Seizures : 4%

Encephalitis in Children

Marwan Shalabi, MD

Definition of Encephalitis in Children

- Acute CNS dysfunction with radiographic or laboratory evidence of brain inflammation.
- CNS dysfunction:
  - Seizures
  - Focal neurologic findings
  - Alteration in mental status.

* Encephalitis is usually viral
  - Herpes virus family → mostly type 1
  - Entero virus family
  - Arbo virus family
* From these, the most common is Enterovirus.

How do they get there?

↳ Arthropod borne → أي عن طريق الحشرات

- Arboviruses: bloodstream infection → enter the CNS via endothelial cell infection
- HSV, rabies, and possibly poliovirus: retrograde transport in neurons.
- Amoeba *Naegleria fowleri*: through the olfactory mucosa.
  ↳ نادرة

Where do they stay there?

↳ bloody LP

- HSV : temporal lobe (herpes could cause high RBC in CSF)
- Rabies : pons, medulla, cerebellum, and hippocampus
- Japanese encephalitis virus: brainstem and basal ganglia.

Acute Viral Encephalitis

- Children, elderly & the immunocompromised most commonly affected
- More than 100 different viruses can cause encephalitis
- In the USA, the most frequently reported causes are:
  - Enteroviruses
  - HSV1 and HSV2
  - Arthropod-borne viruses (Arbo Viruses)
  - The majority of cases have an unknown cause. (idiopathic)

8/28/2019

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Virus	Treatment
Herpes simplex viruses 1 and 2	Acyclovir 10 mg/kg dose IV every 8 hours × 14 to 21 days
	Higher doses for neonatal encephalitis (20 mg/kg dose IV every 8 hours for 21 days)
	Oral acyclovir, famciclovir, valacyclovir for meningitis associated with primary genital herpes simplex virus
Varicella-zoster virus	Acyclovir 20 mg/kg dose IV every 8 hours
	?Famciclovir, valacyclovir
Cytomegalovirus	Ganciclovir
	Foscarnet
Epstein-Barr virus	Acyclovir (limited effectiveness)
Enterovirus	Pleconaril (compassionate release only)
	IV immunoglobulin (for hypogammaglobulinemic patients and neonates with sepsis syndrome)
La Crosse virus	? Ribavirin
Measles virus	Ribavirin
West Nile virus	Under study: IV immunoglobulin with high titer to West Nile virus, interferon, antisense nucleotides

IV = intravenous.

Management is mainly supportive

Antiviral Agents for viral CNS Diseases

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Thank you

* السلايدات اللي بعد Thank you ما جاب بسيرتها. *