Note are aded by **Afnan AlMalki**

Serious Pediatric Infections

Important= ★

Not mentioned by doctor ✕

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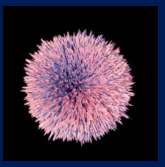


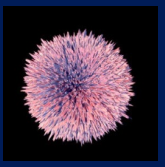
Serious Pediatric Infections

During this lecture we will talk mostly about CNS infection

Objectives

By the end of this session you will:

- Learn special concepts pertinent to children ID
- Outline a frame work for study of infectious diseases
- Enumerate examples of serious infections
- Classify episodes of bacteremia based on the clinical pattern
- Describe how the child age and other risk factors determine etiology of certain infections in pediatrics
- Appreciate utilization of knowledge of pathogenesis of diseases in the therapeutic and preventive measures



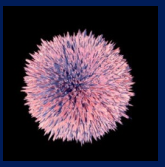
Pediatric Infections Diseases

*SPECIAL CONSIDERATIONS

- **First exposure**
  most children will encounter the organism for the first time, whereas elderly will have had previous exposure with same or similar organism, which will cross react and form AB with less intense symptoms than pediatrics.

- **Immature Immune System**
  more infection in mucosal surfaces i.e. more gastroenteritis.
  IgM starts forming in utero and reaches adult number by the first year of life.
  IgG is not formed until 3-4 years.
  IgA by 10-14 years.

- **URTI are common because of narrower, shorter, horizontal, easily plugged and more fluid accumulation impairs eustechian tube function. This increases the risk of children easily acquiring these infections (otitis media).**
  LRTI is also more common because they have narrow tract and weak cough



Pediatric Infections Diseases

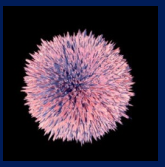
*SPECIAL CONSIDERATIONS

- **Limited Reserve**
  they have smaller airway; therefore, they get blocked by secretions more easily and have higher risk of URTI.

- **Non-specific signs/symptoms**
  commonest presentation of infections in children and adults is fever, whereas in neonates it is irritability and crying and usually they are either afebrile or hypothermic but it is not specific

- **Age-dependent Etiology**

- **One agent and different syndrome**
  EBV can present as hepatitis, spleenomegaly, pyrexia of unknown origin, malignancy, or infectious mononucleosis.
  Several agents and one syndrome: CMV, toxoplasmosis or EBV can cause Infectious mononucleosis. Can't differentiate these agents except with investigations.



Guidelines for study of Infectious Disease

- Etiology
- Pathogenesis
- Clinical Manifestations/course
  - Immunocompetent
  - Immunocompromized

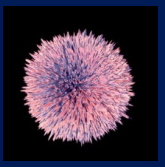
- Epidemiology
  - Mode of transmission
  - Incubation period

Serious Pediatric Infections

1. Bacteremias
2. Meningitis and encephalitis
3. Neonatal jaundice
4. Neonatal sepsis
5. Epiglotitis
6. Osteomyelitis
7. Septic arthritis
8. Endocarditis
9. Tuberculosis…. Etc.

1- Bacteremias:

- The same in pediatric as adult, what happened? The bacteria will be there in the blood and it will cause s/s including fever, patient will looking very sick and usually the bacteria will be either gram - or gram +. The tx is Abx and it will depend on the bacterial.
- It is very common entity to have Bacteremias, so whenever you have child with fever with no focus (for example I examine ENT and there is no OM no phyringitis ..) to explain this fever after hx and PE and there is nothing!! So you have to think of Bacteremias (**fever without explanation)**
- **You have to order blood cultures as it is the gold stander for dx.**



Guidelines for study of Infectious Disease

- **DIAGNOSIS**
- **COMPLICATIONS**
- **MANAGEMENT**
  - **TREATMENT**
  - **PREVENTION**
  - **INFECTION CONTROL MEASURES**

BACTERIAL

MENINGITIS

- Etiology
- Pathogenesis
- Molecular pathophysiology
- Clinical Manifestations
- Diagnosis
- Therapy
- Complications
- Prevention
  - Chemoprophylaxis
  - Vaccination

As Pediatrician the age is the most important because the Etiology will really depend on the age.

- Age: neonate = infant = newborn = baby (all of them <1 month) but in some textbook you can found it up to 3 month so don't be surprised if someone call a 3 month as neonate or baby ما بنزعل من بعض عشان هذي النقطة
  - Neonates (< 3 months): Q: from where the baby have this bacteria? From the mother (birth canal)
    - 1- Group B strep: the most common, from birth canal
    - 2- > E-coli (and other gram negatives): from birth canal
    - 3- > listeria: in utero تروح الام حفلة وتأكل جبنة ويحطون لها شوية مقبلات والجبنة تحتوي على هذي البكتيريا فتصيب الجنين من خلال المشيمة، الأم بيصير عندها باكتيريما و الطفل بيولد وعنده بكتريميا فخلال ٢٤ ساعة ممكن تجيه حرارة !
  - 3 months – 5 years:
    - 1- strep. pneumoniae: same as adult the most common cause
    - 2- > N. meningitides: in certain circumstances, whenever you have any crowdedness remember AlHaj session, university camp...
    - 3 > HiB: particular for < 5 years.
  - >5 years: No HiB even in non-vaccinated children because of vaccination. So it will be either strep. pneumoniae or N.meningitides.
- نقطة مهمة لازم تعرفونها لما مثلا تقول لك طفل عمره 4 سنوات في موسم الحج وبعدين تسأل ايش اكثر اورقانزم ممكن تسبب لا تنطون على نيسيريا صح هي تجي مع الزحمة لكن الأكثر منها في هذا السن هي الستريبت

BACTERIAL MENINGITIS

ETIOLOGY

Determined by:

(I) AGE

- Neonates (< 3 months) : Group B strep > E-coli (and other gram negatives)> listeria.
- 3 months – 5 years: strep. pneumoniae > N. meningitides > HiB.
- >5 years: No HiB even in non-vaccinated children because of vaccination.

Or < 1 month this is definitely the definition

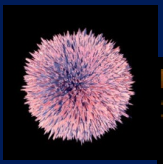
In our textbook it is up to 6 year

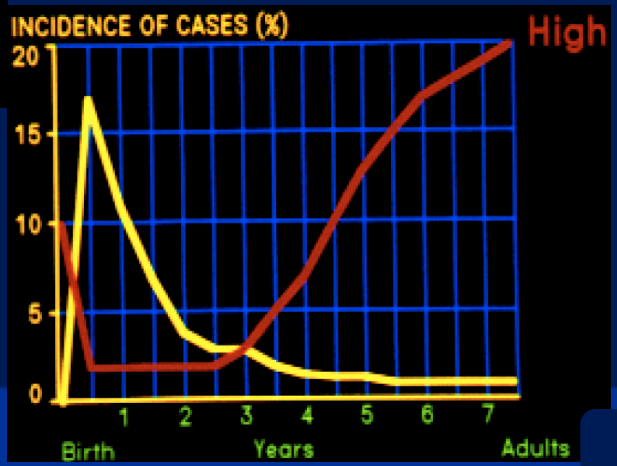
(II) SPECIAL RISK FACTORS:

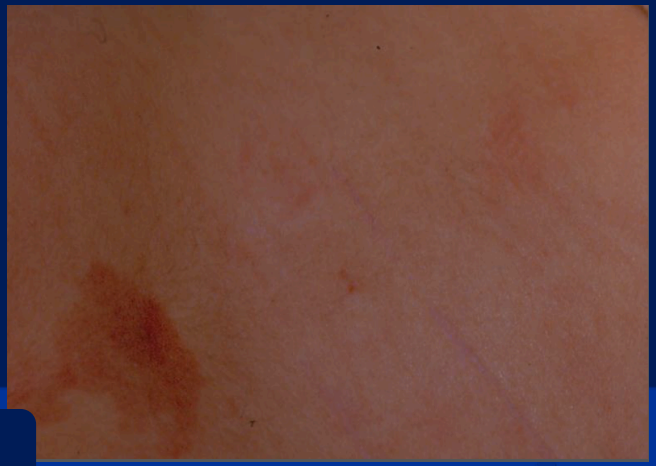
- Post-traumatic: Basal skull fractures: 80% are strep. pneumoniae.
- Post neurosurgical: staph and gram negatives.
- Ventricular shunts: staph epidermidis (coagulase negative).
- Immunocompromised: depends on the organism.
- Asplenia and SCD: Salmonella and encapsulated organisms.

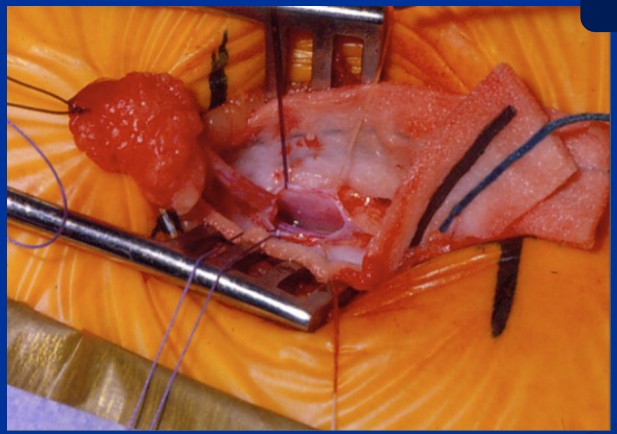
This is some specific organisms for each scenario but still the common is common so first age then what is the most common organisms in each age then look for the scenario to add this organism to your differential

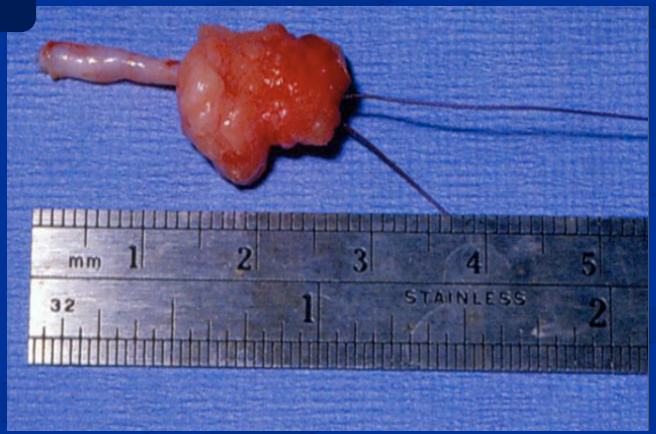
احنا في منطقتنا الطفل عندنا لغاية ١٢ او ١٣ سنة لكن فيه دول ثانية الطفل عندهم لغاية ١٨ سنة فهنا يختلف نعامله معاملة البالغين ونقول ايش اكثر مسبب لهم ؟ هي الستريبت نومونيا
So more than 5 years up to 18 and also more than 18 the most common causative organism is ? Strep.pneumoniae




INCIDENCE OF CASES (%)
High
20
15
10
5
0
1
2
3
4
5
6
7
Birth
Years
Adults






mm
1
2
3
4
5
32
1
STAINLESS
2

PATHOGENESIS

Mucosal Colonization

↓

Local Invasion

↓

Bacteremia

↓

Meningeal Invasion

↓

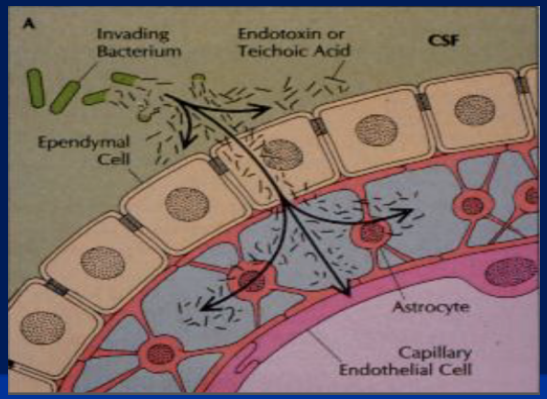
Bacterial Replication

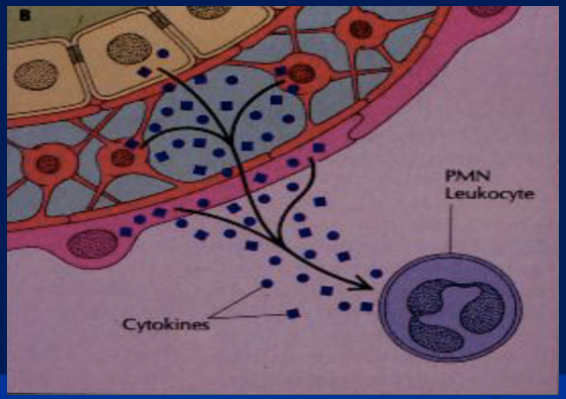
↓

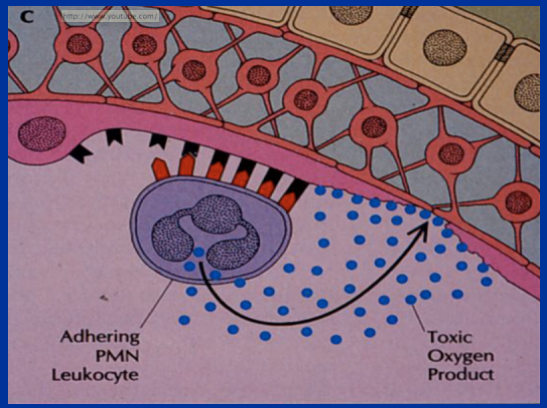
Sub-arachnoid space Inflammation

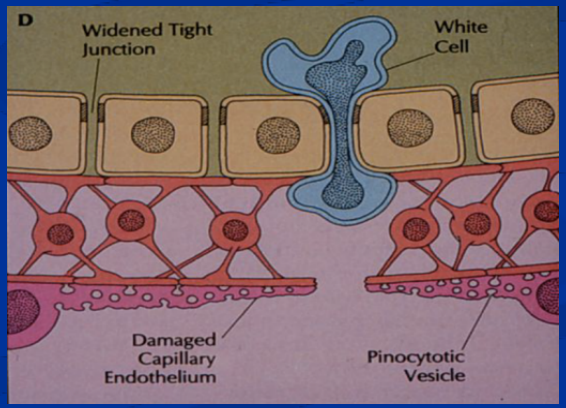
غالبا بتجيك الأم الاسعاف بتقول يا دكتورة ولدي كان كويس بس قبل كم يوم زكم راح المدرسة وشكله لقطها من واحد من العيال والحين الحرارة مره مو راضية تنخفض حتى مع المسكن وطول الوقت يقول مصدع مصدع (طبعا الصداع يقوله ابو ٤ او ٥ سنين لكن لو اصغر ممكن يقول بطني يعورني او بيجلس يبكي طول الوقت ولا يقدر ينام ولا ياكل)

الدكتورة ماعجبتها هذي السلايد ولا اللي بعدها لكن قالت بشرحها لكم باختصار لانها مستوى رزدنت

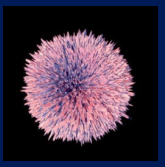








Once you have bacterial infection there will be a-lot of mediator will be producing causing the fever and other manifestation, like TNF,IL .. > then there will be activation of leukocyte , endothelial injury then cytotoxic interstitial edema and all of these will lead to BBB permeability and vasogenic edema leading to increased in ICP causing this headache and vomiting



MOLECULAR PATHOPHYSIOLOGY OF BACTERIAL MENINGITIS

Read

BACTERIAL PRODUCTS (ENDOTOXIN, TEICHOIC ACID)

MEDIATORS

TNF, IL-1, ARACHNOID ACID METABOLITES PLATELET-ACTIVITING FACTORS, OTHER INTERLEUKINS, ETC

ACTIVATION OF LEUKOCYTES

ENDOTHELIAL INJURY

THROMBOSIS

CYTOTOXIC AND INTERSTITAL EDEMA

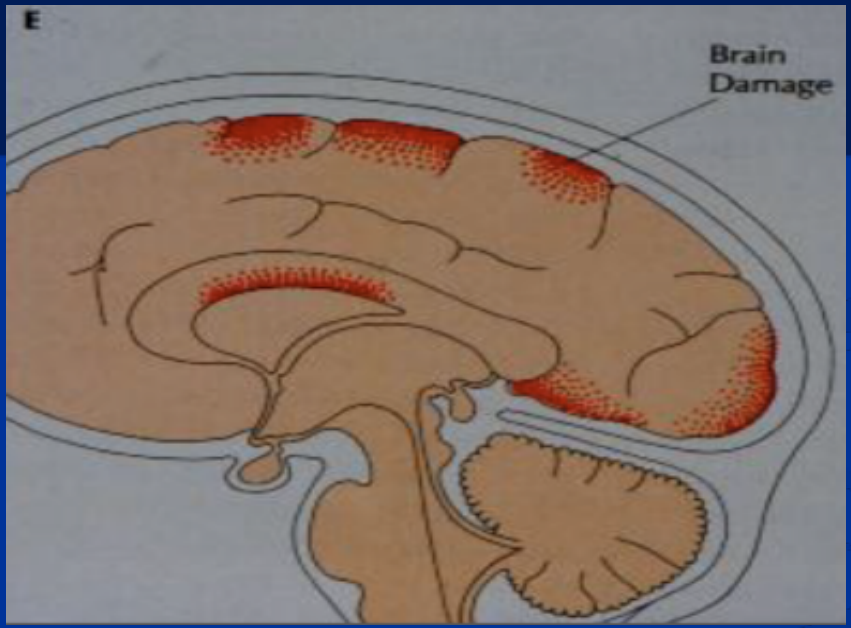
BBB PERMEABILITY

VASOGENIC EDEMA

ICP

CBF

What is meningitis? Inflammation of meningeal layers
What is meningeal layers? What is the content of it? the three membranes (the dura mater, arachnoid, and pia mater) that line the skull and vertebral canal and enclose the brain and spinal cord.



CLINICAL PRESENTATION

IN NEONATE

- **Excessive crying** and **irritability** مو على بعضه
- refuse eating (breastfeeding or milk formula)
- **no sleep or sleep less than 12** h or excessive sleep (الطفل الطبيعي كم ينام؟ كل اليوم تقريبا ما يصحى الا يرضع وكمان لما انتي تصحينه عشان يرضع هذا يعتبر نوم اكثر من اللازم فتشكين في الوضع لما يكون الطفل تعبان تلقينه صاحي طول الوقت ويبكي او نايم طول الوقت حتى ما يقوم يرضع)
- **Fever**: but baby (1 month or less) can have hypothermia and this is even worse

IN OLDER CHILDREN

Older children 1 years or more the mother came and said he have ..... what is the symptoms that will make you worried about meningitis and you go as fast as you can to call the team?

- **High grade fever**: not respond to anything or respond for few hours then comes back again. اسال الام كيف لما نزلت الحرارة هل لاحظتيه تحسن ورجع يلعب ولا نفس وضعه وما رجع لطبيعته ؟ لان في التهاب السحايا بيكون حرارة عالية وما يرجع لطبيعته حتى مع نزولها
- **Vomiting :** indicates high ICP
- **Photophobia**
- **Irritability**
- Confusion: when there is element of encephalitis
- LOC: can be in severe cases need ICU admissions
- **Headache**: بعض الاطفال وبالذات الصغار اللي مايقدرون يعبرون تلقونهم يضربون روسهم او ممكن يقول بطني يعورني وهو بطنه مايعوره بالاساس بس مو عارف يعبر

How to differentiate between meningitis and encephalitis?

- Encephalitis is brain inflammation بتقول لك الام الولد مو علي بعضه أكلمه مايرد عليه دايخ
  - Brain and CN involvements
  - level of conscious affected , confusion, delirium (even after the fever down)
  - can not answer you
  - Can present with coma or low GCS
- Meningitis is meninges layer inflammation بتقولك الام صداع وحرارة
  - Aware level of conscious is good , he can talk to you but look irritable and sick
  - The patient can have the encephalitis presentation once he have both **meningoencephalitis** (it rare but it can happen especially in **herpes virus**)
- احنا في البيديا ناخذ الطفل اول مايجيبوه أهله بيكون نايم او مستلقي اقول لامه وقفيه او انا اوقفه اشوف لو انتبه لي واستغرب انا مين هذا طفل كويس بفكر باشياء اقل خطر لكن لو مهما سوينا مافي استجابة او كان بس يبكي ومشوش الطفل هنا فكروا بالاخطر

In pediatric when the patient have high grade fever and you examine the TM and notice redness don't assume it is OM because high grade fever will cause redness

- First thing you should put it in your mind if you suspect this child have meningitis even 1% you should take it seriously and **call your senior**. As if you miss the dx the child will die or have mental retardation.
- Hx is very important

DIAGNOSIS

- **CBC** - leucocytosis (Neutrophils) or leucopenia (worst prognosis signifies meningococcal disease). Never discharge a patient with normal CBC and fitting clinical picture.

- **BLOOD CULTURE** - 60-70% specific.

Don't do LP unless you have clear CT scan

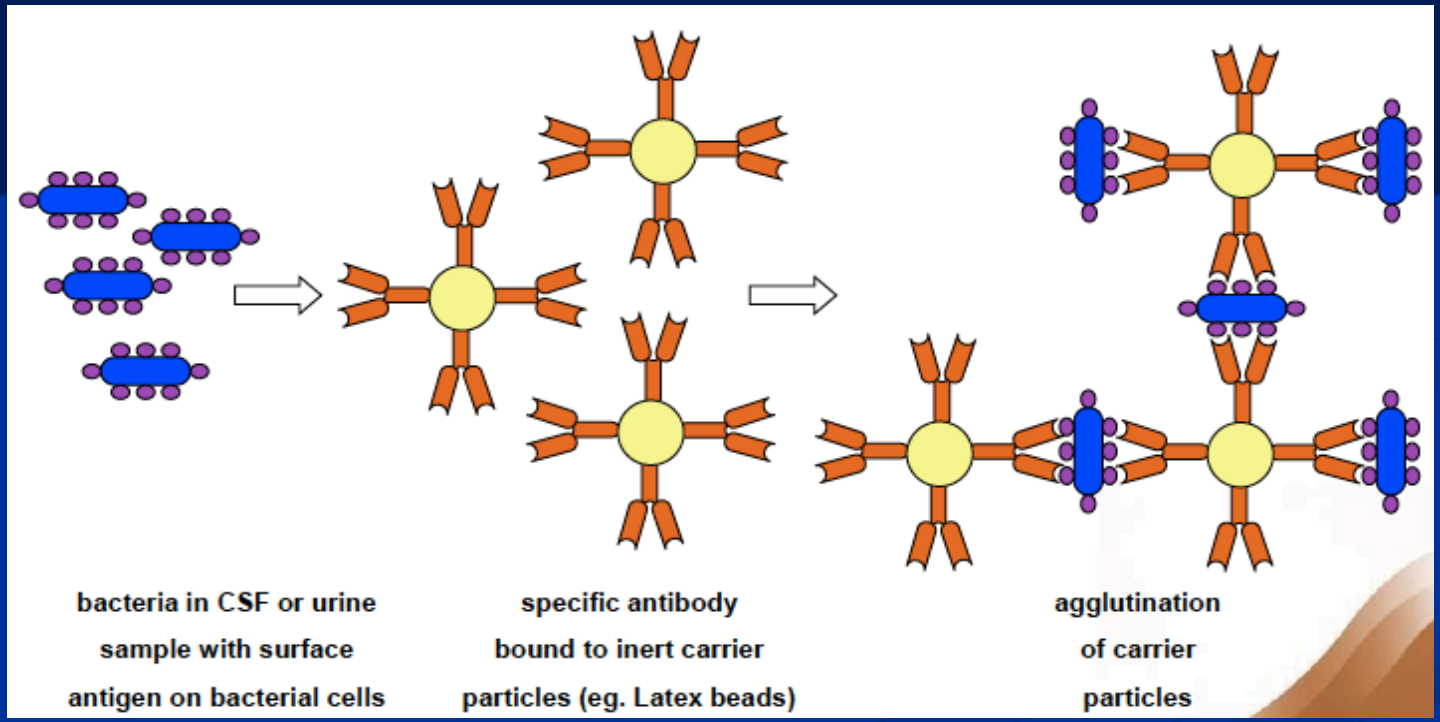
- **CSF** (Must be done) - there are three components in the CSF we should look at- WBC, glucose, and protein
  - For bacterial meningitis, the WBC is mainly polymorphic and the glucose is less that 50% of serum glucose (normal is 2/3 of serum glucose). If it was partially treated bacterial meningitis the lymphocyte predominates.
  - For Viral or TB, the WBC is mainly lymphocytic. Sugar is normal.
  - For fungal and TB meningitis, the glucose is less than 50% the serum glucose. The protein is raised in all, but might be normal in viral.

- Color — Normal is transparent (but don't surprise if this becomes infected with high WBC) , **turbid color** abnormal high suspensions
- Cell count and differential. — Normal cell count (pus) is **zero** so anything things more than zero is abnormal, **Neonate (1 month) up to 30-40 is normal**
  - differential: neutrophils (bacteria) , lymphocytes (virus)
- Chemistry: Sugar & Proteins — If less than 2/3 of that in the blood then it is meningitis
- Gram stain is positive in 70-80% of the patients.
  - Gram + diplococci = Streptococcus Pneumoniae
  - Gram - diplococci = N.meningitdies
  - Gram - bacilli = h.influenza Or any enterobacteries such as E.coli and klabsella (especially newborn)
- Latex agglutination or co-agglutination is used to detect the antigen instead of culture because the culture takes 24 hours. □ not accurate if the pt on Abx
- Culture is the gold standard

اعرفوها اذا صرتوا رزدنت بس بالمختصر يجيبون ميديا ويكون فيها ضد انواع البكتيريا المشهورة اللي تسبب منينجايتيس ويحطون عليها العينة وتطلع بوستيف لو حصل تفاعل

LATEX AGGLUTINATION OR CO-AGGLUTINATION

The latex agglutination test is a laboratory method to check for certain antibodies or antigens in a variety of body fluids including saliva, urine, cerebrospinal fluid, or blood.
The sample is sent to a lab, where it is mixed with latex beads coated with a specific antibody or antigen. If the suspected substance is present, the latex beads will clump together (agglutinate).
Latex agglutination results take about 15 minutes to an hour.



MANAGEMENT

First call your senior then Supportive care call ICU and don't admit the patient in ward unless he is stable

- **Supportive care** -is the most important. Careful monitoring of the patient, by checking the blood pressure for hypertension and the respiration for the RR, and pH.

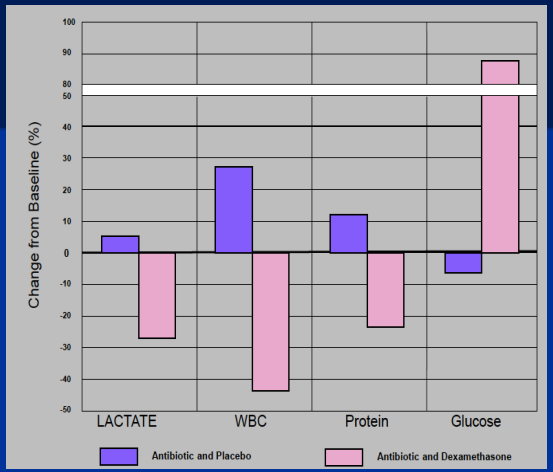
- **Antibiotics**
  - Which one?
  - How much?
  - For how long?

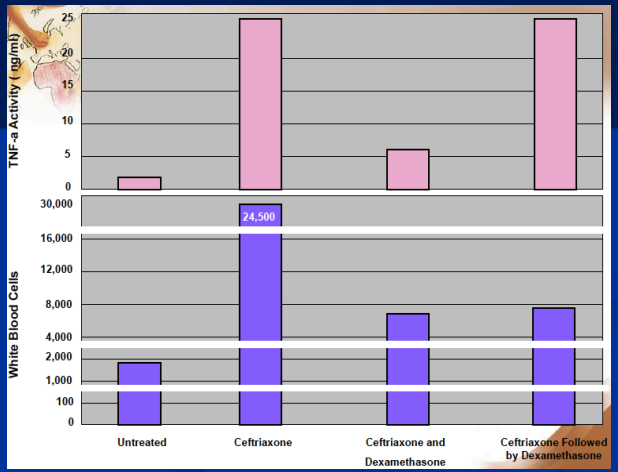
  - Empirical Broad spectrum Abx: **ceftriaxone** (3rd generation) + vancomycin (because there is high resistance to Streptococcus Pneumonia) + Acyclovir (once you suspect haptic encephalitis) + dexamethasone
  - But in newborn (less than 3 months) give **cefotaxime** (3rd generation) not cause any biliary sludge

- *doctor: I never give it !!*
  Dexamethasone - modulates the release of inflammatory mediated factors.

Note: Studies were done giving antibodies alone, which showed worse outcome by increasing the inflammatory markers (TNF is higher with AB due to autolysis). On the other hand, dexamethasone with AB gave promising results with values approaching the normal. There is still a need for more data to indicate the need for dexamethasone in every case. Dexamethasone should be given at the time of AB and not after and in some cases it can be given just before (don't give dexamethasone if it's late presentation). Long-term dexamethasone decreases deafness, which is a complication of meningitis.

Steroids are important because they decrease the level of inflammatory mediators, which are the cause of complications.

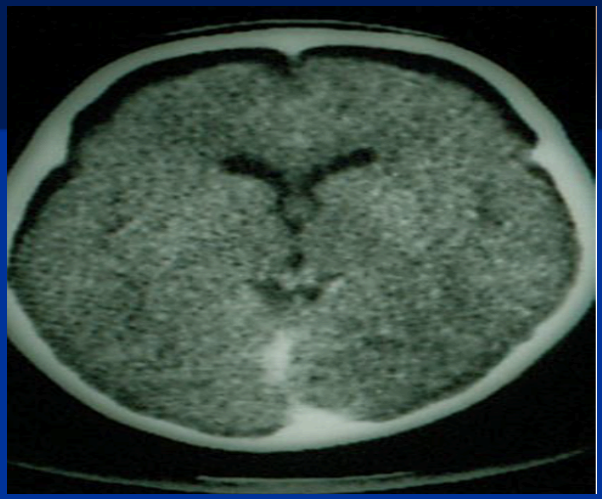

Change from Baseline (%)
100
90
80
50
40
30
20
10
0
-10
-20
-30
-40
-50
LACTATE
WBC
Protein
Glucose
Antibiotic and Placebo
Antibiotic and Dexamethasone

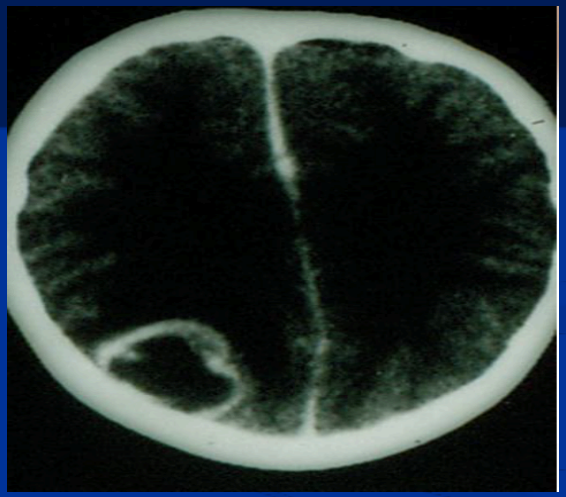

TNF-a Activity (ng/ml)
25
20
15
10
5
0
White Blood Cells
30,000
24,500
16,000
12,000
8,000
4,000
2,000
1,000
100
0
Untreated
Ceftriaxone
Ceftriaxone and Dexamethasone
Ceftriaxone Followed by Dexamethasone

COMPLICATIONS

- **EARLY** - subdural effusion with fever resolves alone when the patient is on antibiotics. It rarely needs drainage.

- **LATE** - brain abscess is a rare complication of meningitis and is seen in a specific age group and bacterial organism.





PREVENTION

- CHEMOPROPHYLAXIS
  - Rationale - If one person is infected with meningococcal meningitis, it increases the risk by an 800 to 1000 fold of the community being affected; therefore, we treat the entire family.
  - Protocol
- VACCINATION - HiB, meningococcal, and some require pneumococcal vaccine.

PATHOGENESIS

Mucosal Colonization

↓

Local Invasion ← *Chemoprophylaxis*

↓

Bacteremia ← *Vaccination*

↓

Meningeal Invasion ← *Antibiotic Therapy*

↓

Bacterial Replication

↓

Sub-arachnoid space Inflammation

ENCEPHALITIS

Encephalitis:

- can cause by bacteria but most of the time by virus such as **HSV 1 , enterovirus** (كذا تجين بعد المطر تلاقين ثلاثة بالفصل عندهم التهاب سحايا ونسميها aseptic menegitits) , **influenza** virus (causing severe meningitis) and **varicella** (after Chickenpox)
- Dx not by culture instead we use PCR (**HSV PCR**) or if I suspect enterovirus I send for viral multiplex (بتاع كلو) why ? Because we don't have treatment for viruse except for HSV and maybe varicella we use **acyclovir**. So it is treatable and if you missed it حيروح في ستين داهية
- They will present with seizure as early and late manifestation بجانب الاشياء اللي تكلمنا عنها قبل

General:

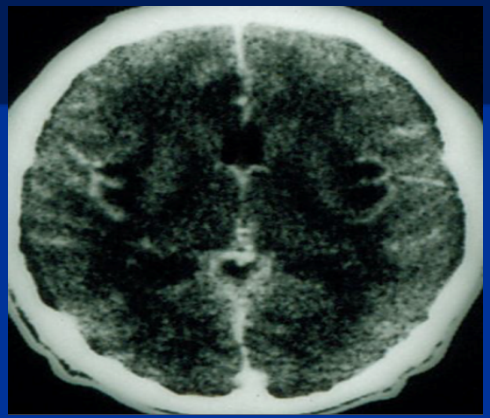
Most common pathogen in pediatrics is entero-viruses fortunately they are self-limiting, and the most serious is HSV, which increases morbidity and mortality.

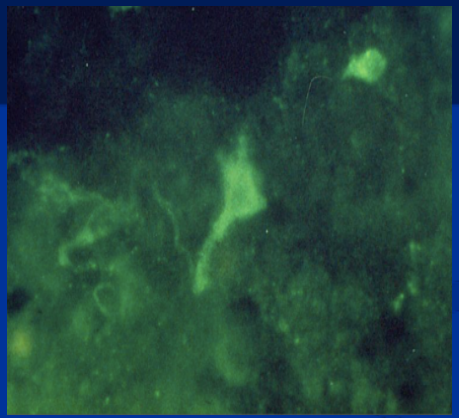
Diagnosis:

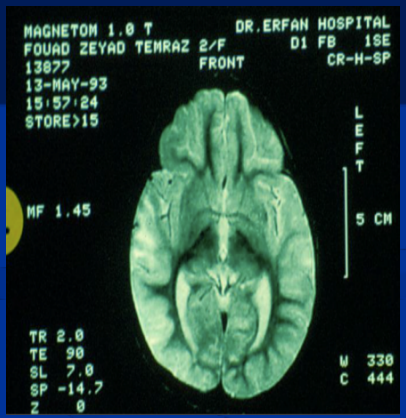
Previously by brain biopsy but nowadays PCR is the diagnostic tool.
MRI shows the effects early.

Treatment:

If HSV encephalitis is *suspected*, start acyclovir immediately even if the diagnosis was not yet confirmed because this type is very serious.



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OSTEOARTICULAR INFECTIONS

Osteomyelitis or septics arthritis

- lower limb: If walking the mother said he doesn't want to walk and if walk there is Limping
  - Crying whenever the mother change the diaper > hip involvement
- Upper limb: no movement of limb

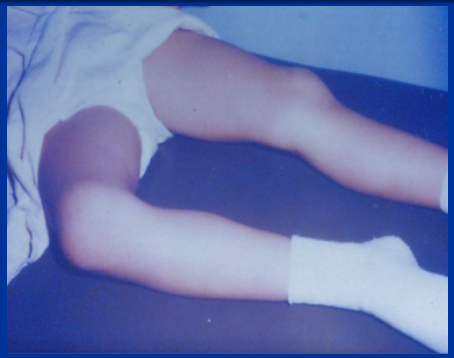
Presentation: the commonest presentation.

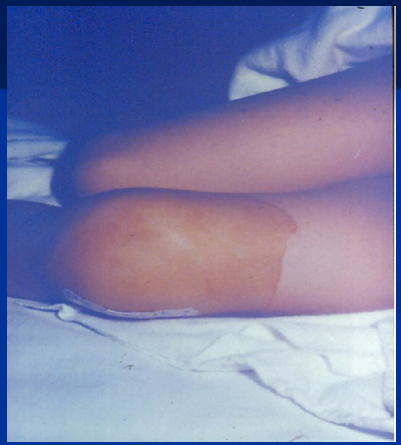
1. Pain.
2. Limping.
3. Swelling.

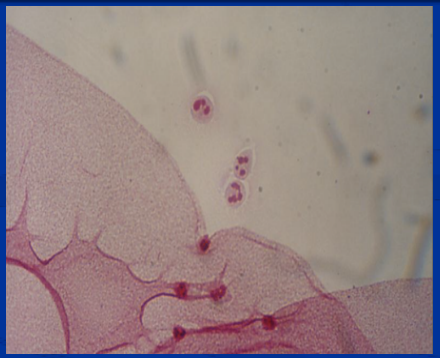
Note: Septic arthritis of the hip is very dangerous because it is a deep-seated infection and doesn't cause any swelling. It can lead to vascular necrosis because the blood supply is from the acetabulum and goes around the joint, if there is pus it will press on the vessels therefore ER drainage is important.

4. In neonates, it is not obvious because they can't complain but it is noticed when the mother changes the diaper and the baby cries. The neonates usually maintain their hip in lateral rotation and flexion to have more space in the joint and thus relieving the pressure.

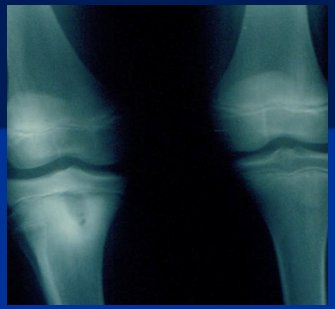
Inflammatory symptom

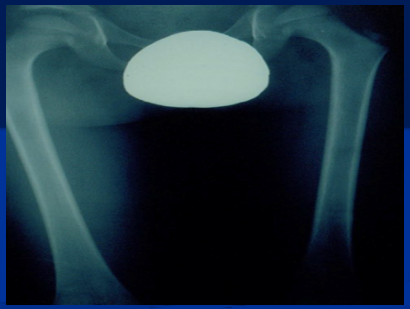


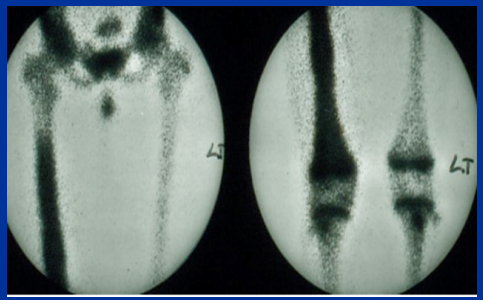


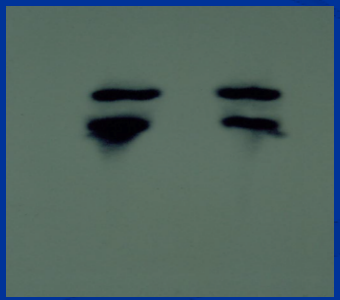


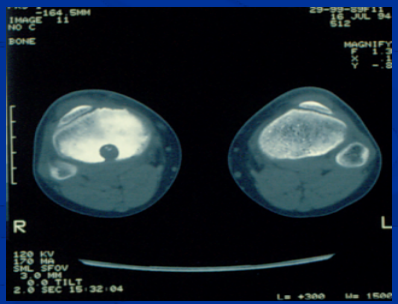
- Dx same as adult clinically + Image
  - When you do Xray immediately it will not show anything but when you do it late it will show **periosteal reaction**
  - You can do
    - X-ray
    - Neuclear
    - CT
    - **MRI the best**











Imaging

•Bone change (such as avascular necrosis or periosteal reaction) is not seen on X-ray until the 10th day, but it can be detect it earlier by nuclear scan.

•The radionuclear scan will show increased uptake **sequestrum** by the osteoclasts and periosteal reaction, which indicates chronic infection.

•If there is any radiolucency, suspect malignancy.

* MRI *

Complications **For Septic arthritis** Tx for septic arthritis: **Abx** depends on suspected organisms 2-3 week

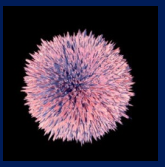
1. Avascular necrosis.
2. Joint destruction.

Treatment Tx for osteomyelitis Abx 2-4 week

3. **Debridement** and removal of sequestrum to prevent recurrence along with
4. Long-term antibiotics. Antibiotics use in acute osteomyelitis is 4-6 weeks, and 4-6 months in chronic.

Case: 10 year old limping for two months

CONGENITAL INFECTIONS (TORCHS)



TORCHS and others no longer limited to TORCHS.
Certain presentation common to all

1.Hydrocephlus

2.Cerebral Calcifications (seen in toxoplasmosis and CMV)

3.Blue muffin syndrome seen in all

4.Owl eye in urine in CMV مهمه

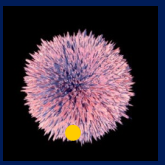
Tetanus in neonates

- Prevented by vaccination of the mother.
- Two doses if mother is not vaccinated or the doses can't be determined.
- The vaccine is safe during pregnancy but better given before.

Same as adult

- **causative organism**: Mycobacterium tuberculosis Or Mycobacterium bovis (vaccine in immunocompromised patients because of that they change BCG vaccines time to 6 month instead of at birth)
- s/s and dx same as adult
  - Progressive cough, fever, loss weight
  - **Contact hx (dx for TB in pediatric by Hx**) is the most important in pediatric because محد يجيه السل من الهواء
  - **Extra Pulmonary TB more common in pediatric than pulmonary**

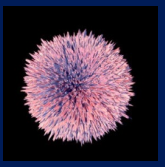
Childhood Tuberculosis



- **Tuberculosis** is a chronic infectious disease caused by *Mycobacterium tuberculosis* characterized by vague constitutional symptoms and a protracted course of illness with remissions and exacerbations

- **Tuberculosis** is the reaction of tissues of the human host to the presence and multiplication of *Mycobacterium tuberculosis*

- The clinical states arising from TB infection are the outcome between the capacity of the host to contain and eliminate the organism versus the capacity of the organism to multiply and proliferate

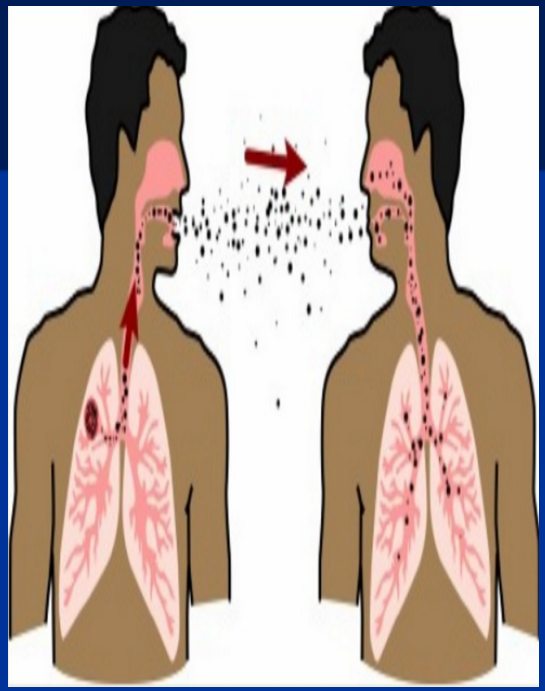


TB Diagnosis in Children

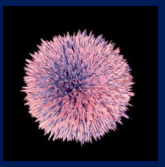
- Bacteriologic confirmation is achieved in only about 30-40% of cases
- Therefore, diagnosis often based on presence of a combination of the following characteristics:

- History of close contact with adult with TB (especially if smear positive)
- Triad of :
  - Signs and symptoms compatible with TB disease
  - A positive tuberculin skin test (TST)
  - Suggestive lab results or radiographic findings

How TB is Transmitted?



- Person-to-person
  - Through the air by a person with pulmonary TB disease of the lungs when he or she coughs, sneezes, or speaks
- Less frequently transmitted by ingestion of Mycobacterium bovis
  - Found in unpasteurized milk products
- Other modes of transmission
  - Vertical transmission (rare) – congenital TB
  - Contaminated bodily fluids (very rare)

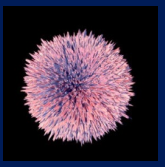


TB: Adults vs Children

Compared to adults, children:

- Tend to develop primary active TB more often afer initial infection (0-4 years)
- Are more likely to have extra-pulmonary disease, especially TB meningitis (0-4 years)
- Are more likely to have extra
- Are less contagious
- Are more difficult to diagnose Week cough impulse so there is difficulties to obtain sputum so they insert NG aspirate for acid fast bacilli for 3 day
- A child with active TB is an indicator of unidentified contagious adult/adolescent with TB
- A child suspected of having active TB may not yield any positive cultures/smears
- Need the adult contact's culture results for drug sensitivities and to determine treatment regimen for the child

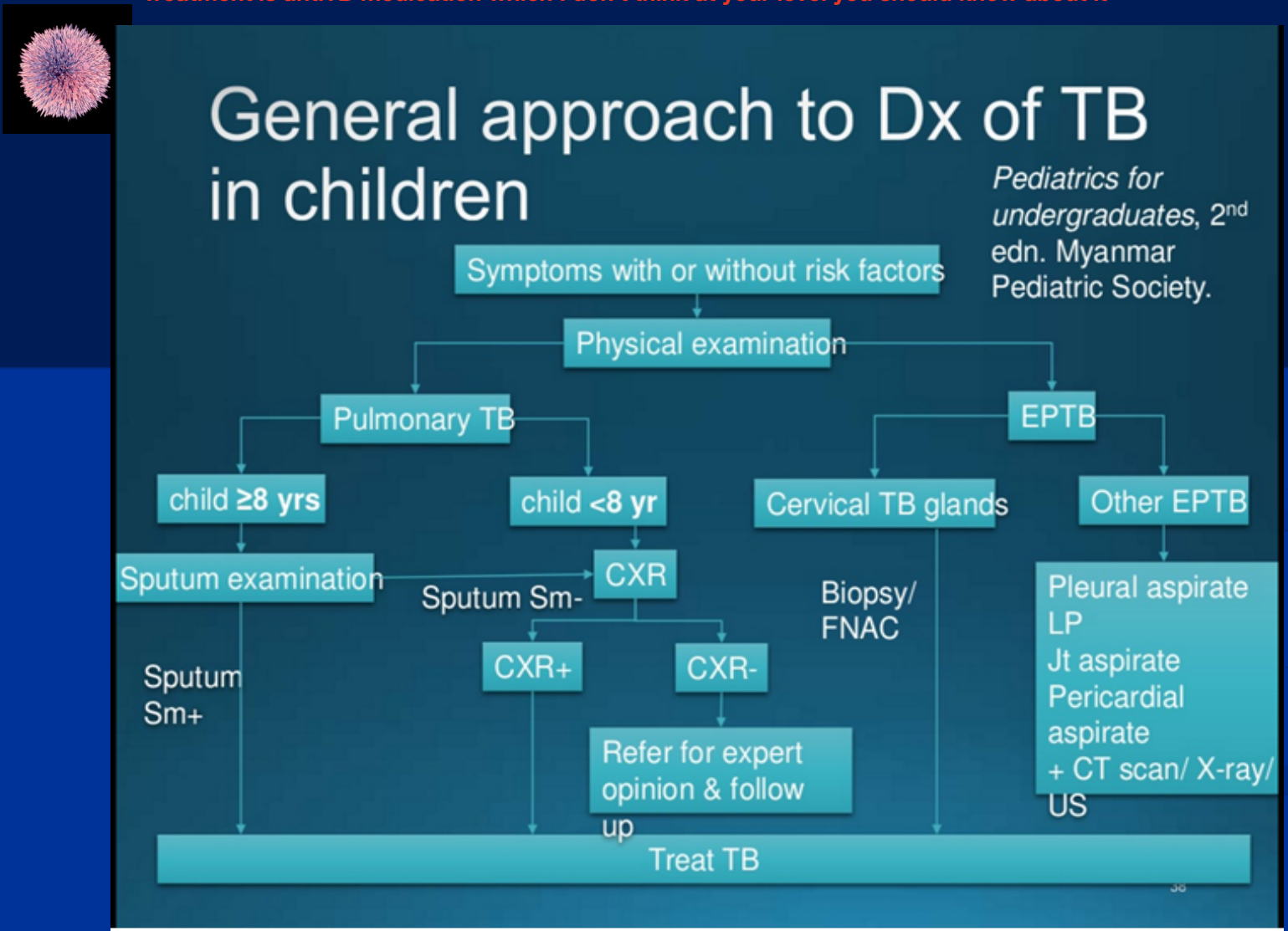
Abhjiit Mukherjee, et. al,



TB IN Children

- Points to remember:
  - Diagnosis may be difficult;
  - Sputum cannot often obtained;
  - Sputum often negative for AFB even on culture;
  - Symptoms are atypical
  - Diagnosis depends on clinical history, family contact history, X-ray examination and TST.

Treatment is antiTB medication which I don't think at your level you should know about it



Saudi Arabia

Tuberculosis profile

Population 2015 **32 million**

Estimates of TB burden*, 2015	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	0.66 (0.21–1.4)	2.1 (0.66–4.3)
Mortality (HIV+TB only)	0.018 (<0.01–0.09)	0.06 (0–0.28)
Incidence (includes HIV+TB)	3.8 (3.3–4.4)	12 (10–14)
Incidence (HIV+TB only)	0.14 (0.11–0.16)	0.43 (0.36–0.51)
Incidence (MDR/RR-TB)**	0.15 (0.12–0.18)	0.48 (0.38–0.57)

Estimated TB incidence by age and sex (thousands)*, 2015	0-14 years	> 14 years	Total
Females	0.17 (0.11–0.23)	1.1 (0.66–1.5)	1.3 (0.77–1.7)
Males	0.13 (0.087–0.17)	2.5 (1.9–3)	2.6 (2–3.2)
Total	0.3 (0.22–0.38)	3.5 (3.2–3.9)	3.8 (3.3–4.4)

TB case notifications, 2015	
Total cases notified	3 429
Total new and relapse	3 309
- % *tested with rapid diagnostics at time of diagnosis*	29%
- % *with known HIV status*	51%
- % *pulmonary*	75%
- % *bacteriologically confirmed among pulmonary*	88%

Universal health coverage and social protection	
TB treatment coverage (notified/estimated incidence), 2015	86% (75–100)
TB patients facing catastrophic total costs	
TB case fatality ratio (estimated mortality/estimated incidence), 2015	0.18 (0.06–0.37)

TB/HIV care in new and relapse TB patients, 2015	Number	(%)
Patients with known HIV-status who are HIV-positive	89	4%
- on antiretroviral therapy		

Drug-resistant TB care, 2015	New cases	Previously treated cases	Total number***
Estimated MDR/RR-TB cases among notified pulmonary TB cases			110 (89–120)
Estimated % of TB cases with MDR/RR-TB	2.6% (2–3.2)	20% (16–25)	
% notified tested for rifampicin resistance	34%	36%	1 186
MDR/RR-TB cases tested for resistance to second-line drugs			0
Laboratory-confirmed cases			MDR/RR-TB: 45, XDR-TB: 0
Patients started on treatment ****			MDR/RR-TB: 45, XDR-TB:

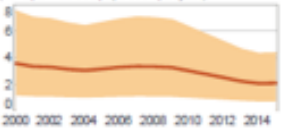
Treatment success rate and cohort size	Success	Cohort
New and relapse cases registered in 2014	62%	3 248
Previously treated cases, excluding relapse, registered in 2014	33%	88
HIV-positive TB cases, all types, registered in 2014	27%	63
MDR/RR-TB cases started on second-line treatment in 2013		
XDR-TB cases started on second-line treatment in 2013		

TB preventive treatment, 2015	
% of HIV-positive people (newly enrolled in care) on preventive treatment	0%
% of children (aged < 5) household contacts of bacteriologically-confirmed TB cases on preventive treatment	

TB financing, 2016
National TB budget (US$ millions)

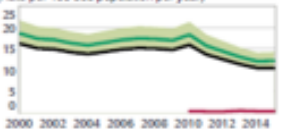
* *Ranges represent uncertainty intervals*
** *MDR is TB resistant to rifampicin and isoniazid; RR is TB resistant to rifampicin*
*** *Includes cases with unknown previous TB treatment history*
**** *Includes patients diagnosed before 2015 and patients who were not laboratory-confirmed*

(Rate per 100 000 population per year)



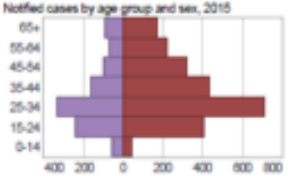
Mortality (excludes HIV+TB)

(Rate per 100 000 population per year)



Incidence
Notified (new and relapse)
Incidence (HIV+TB only)

Notified cases by age group and sex, 2015



Females Males

Treatment success rate (%)

New and relapse
Retreatment, excluding relapse
HIV-positive MDR/RR-TB XDR-TB

http://www.who.int/tb/country/data/profiles/en/

http://data.worldbank.org/indicator/SH.TBS.INCD?end=2015&locations=SA&start=2000

TB patient numbers and incidence rates/100,000 by age group in Saudi Arabia (1991-2010)

Year	1991		1995		2000		2005		2010		*P* value
Age	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	
<15	126	1.8	155	2.1	210	2.7	210	2.8	181	2	>0.05
15-44	1672	21.3	1763	19.9	2129	20.4	2233	18.6	2995	20.8	>0.05
>45	717	35.8	726	30.3	1005	37	985	30.4	1118	27.4	<0.01
Total	2514	15	2644	14.3	3344	16	3438	14.8	4294	15.8	>0.05

TB = Tuberculosis

Ann Thoracic Med. 2013 Jul-Sep: 8(3): 148 – 152.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3731856/

Suggested readings (TB)

- https://www.slideshare.net/oerafrica/childhood-tb-12277358
- http://gamapserver.who.int/gho/interactive_charts/tb/cases/atlas.html
- https://link.springer.com/book/10.1007/978-3-642-18937-1

Thank you

Textbook note

The febrile child

- Most febrile children have a brief, self-limiting viral infection. Mild localized infections, e.g. otitis media or tonsillitis, may be diagnosed clinically. The clinical problem lies in identifying the relatively small proportion of children with a serious infection which needs prompt treatment.
- A **fever** in children is a **temperature over 37.5° C**. In general, axillary temperatures underestimate body temperature by 0.5° C.
- **When assessing a febrile child**, consider the following
- **1- How is fever identified in children**?Parents usually know if their child has been febrile. In hospital, it is measured:
    - if less than 4 weeks of age, by an electronic thermometer in the axilla
    - if aged 4 weeks to 5 years, by an electronic or chemical dot thermometer in the axilla or infrared tympanic thermometer.
- **2- How old is the child?**
- **3- Are there risk factors for infection?**
- **4- How ill is the child?**
    - Red flag features suggesting serious illness and the need for urgent investigation and treatment are:
        - fever over 38° C if aged less than 3 months, or over 39° C if 3 months to 6 months of age
        - colour – pale, mottled, or cyanosed
        - level of consciousness is reduced, neck stiffness, bulging fontanelle, status epilepticus, focal neurological signs, or seizures
        - significant respiratory distress
        - bile-stained vomiting
        - severe dehydration or shock.
- **5- Is there a rash?**
- **6- Is there a focus for infection?**
- **Summary**
    - Upper respiratory tract infection is a very common cause.
    - Check for otitis media.
    - Serious bacterial infection must be considered if there is no focus of infection, especially urinary tract infection or septicaemia, or there are red flag features of potentially lifethreatening illness.
    - The younger the child, the lower the threshold for performing a septic screen and starting antibiotics.

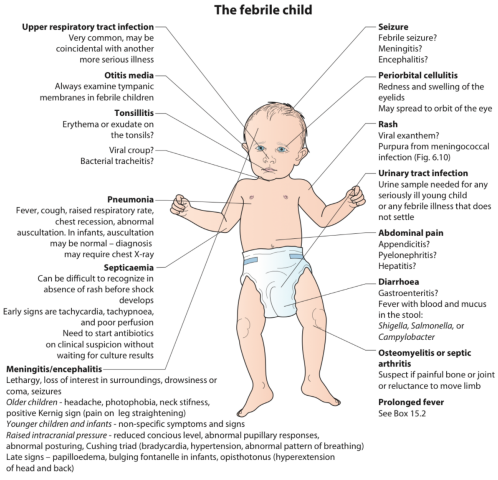


Figure 15.3 Diagnostic clues to evaluating the febrile child.

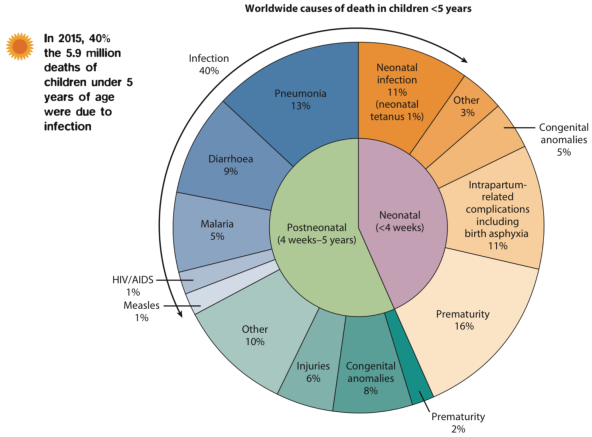


Figure 15.1 Globally, infection is responsible for 40% of the 5.9 million deaths in children under 5 years of age, 2015. (Data from http://www.who.int/gho/child_health/mortality/causes/en/, Accessed November 2016.)

Serious life-threatening infections

Meningitis

- Meningitis occurs when there is inflammation of the meninges covering the brain. (septics vs aseptic) aseptic= any cause except bacteria.

Table 15.1 Organisms causing bacterial meningitis according to age

Neonatal to 3 months	Group B streptococcus
	Escherichia coli and other coliforms
	Listeria monocytogenes
1 month to 6 years	*Neisseria meningitides*
	Streptococcus pneumoniae
	Haemophilus influenza
>6 years	*Neisseria meningitides*
	Streptococcus pneumoniae

- **Bacterial meningitis** may have severe consequences.
  - It is serious infection in children, with 5% to 10% mortality. Over 10% of survivors are left with long-term neurological impairment.
  - Presentation:
    - The clinical features are listed in Fig. 15.4 (last page). The early signs and symptoms of meningitis are nonspecific, especially in infants and young children.
    - Only children old enough to talk are likely to describe the classical meningitis symptoms of headache, neck stiffness, and photophobia. However, neck stiffness may also be seen in some children with tonsillitis and cervical lymphadenopathy.
    - As children with meningitis may also have sepsis, signs of shock, such as tachycardia, tachypnoea, prolonged capillary refill time and hypotension, should be sought. Purpura in a febrile child of any age should be assumed to be due to meningococcal sepsis, even if the child does not appear unduly ill at the time; meningitis may or may not be present in this situation.
  - Investigations: listed in Fig. 15.4 (last page)
    - Neutrophils is the predominant in bacterial infection exceptions can occur as lymphocytes can predominate in bacterial meningitis, e.g. in Lyme disease.
    - glucose levels can be low in viral meningitis, e.g. enterovirus meningitis
    - If any of the contraindications for performing a lumbar puncture are present, as listed in Fig. 15.4, it should not be performed, as under these circumstances, the procedure carries a risk of coning of the cerebellum through the foramen magnum. In these circumstances, a lumbar puncture can be postponed until the child's condition has stabilized. Even without a lumbar puncture, bacteriological diagnosis can be achieved in about half of the cases from the blood by culture or polymerase chain reaction (PCR), and rapid antigen screens can be performed on blood and urine samples.
    - Throat swabs should also be obtained for bacterial culture and viral PCRs. A serological diagnosis can be made on convalescent serum 4 weeks to 6 weeks after the presenting illness if necessary.
  - Management:
    - The choice of antibiotics will depend on the likely pathogen. A third-generation cephalosporin, e.g. ceftriaxone, is the preferred choice to cover the most common bacterial causes.
    - Beyond the neonatal period, there is some evidence suggesting that **dexamethasone** administered with the antibiotics reduces the risk of long-term complications such as deafness.
  - Complication:
    - hearing impairment, local vasculitis, local cerebral infarction, subdural effusion, hydrocephalus, cerebral abscess
  - Prophylaxis: with rifampicin or ciprofloxacin to eradicate nasopharyngeal carriage is given to all household contacts for meningococcal meningitis and Hib infection. It is not required for the patient if given a third-generation cephalosporin, as this will eradicate nasopharyngeal carriage.
  - Partially treated bacterial meningitis:
    - Children are frequently given oral antibiotics for a nonspecific febrile illness. If they have early meningitis, this partial treatment with antibiotics may cause diagnostic problems. CSF examination shows a markedly raised number of white cells, but cultures are usually negative. Rapid antigen screens and PCR are helpful in these circumstances. Where the diagnosis is suspected clinically, a full course of antibiotics should be given.
- **Viral infections** are the most common cause of meningitis, and most are self-resolving.
- **Tuberculous meningitis** is rare in countries with low TB prevalence. TB meningitis mainly affects children under 5 years of age.
- **Fungal and parasitic meningitis** are rare in children and predominately affect immunocompromised individuals.
- Causes of **noninfectious meningitis** include malignancy and autoimmune diseases.

- **Meningitis summary**
  - Predominantly a disease of infants and children.
  - Incidence has been reduced by immunization.
  - Clinical features: nonspecific in children under 12 months – fever, poor feeding, vomiting, irritability, lethargy, drowsiness, seizures, or reduced consciousness; late signs – bulging fontanelle, neck stiffness, and arched back (opisthotonos).
  - Septicaemia can kill in hours; good outcome requires prompt resuscitation and antibiotics.
  - Any febrile child with a purpuric rash should be given intramuscular benzylpenicillin immediately and transferred urgently to hospital.
  - The meningococcal vaccines now included in the infant and adolescent immunization schedule in the UK should further reduce the incidence of meningococcal sepsis and meningitis.

Encephalitis/encephalopathy

- It is inflammation of the brain substance, although the meninges are often also affected.
- Encephalitis may be caused by:
  - direct invasion of the brain by a neurotoxic virus (such as HSV)
  - delayed brain swelling following a dysregulated neuroimmunological response to an antigen, usually a virus (postinfectious encephalopathy), e.g. following chickenpox
  - a slow virus infection, such as HIV infection or subacute sclerosing panencephalitis (SSPE) following measles.
- In encephalopathy from a noninfectious cause, such as a metabolic abnormality, the clinical features may be similar to infectious encephalitis.
- The clinical features and investigation of encephalitis are described in Fig. 15.4.
- Most children present with fever, altered consciousness, and often seizures. Initially, it may not be possible to clinically differentiate encephalitis from meningitis, and treatment for both should be started.
- The underlying causative organism is only detected in fewer than half of the cases. In the UK, the most **common causes of encephalitis** are enteroviruses, respiratory viruses (influenza viruses), and herpesviruses [e.g. HSV, varicella zoster virus (VZV), and human herpesvirus 6 (HHV-6)].
- Worldwide, microorganisms causing encephalitis include Mycoplasma, B. burgdorferi (Lyme disease), Bartonella henselae (cat scratch disease), rickettsial infections (e.g. Rocky Mountain spotted fever), and arboviruses.
- All children with encephalitis should therefore be treated initially with high-dose intravenous aciclovir (acyclovir) until this diagnosis has been ruled out, because this is a very safe treatment.
- **PCR** is used in the majority of laboratories to detect HSV in CSF.
- Proven cases of HSV encephalitis or cases where there is a high index of suspicion should be treated with intravenous **acyclovir for 3 weeks**, as relapses may occur after shorter courses.

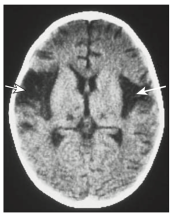


Figure 15.5 Herpes simplex encephalitis. The computed tomography scan shows gross atrophy from loss of neural tissue in the temporoparietal regions (arrows).

- As HSV encephalitis is a destructive infection, the electroencephalogram and CT/MRI scan may show focal changes, particularly within the **temporal** lobes either unilaterally or bilaterally (Fig. 15.5)
- **Summary Encephalitis**
  - Onset can be insidious and includes behavioural change.
  - Consider if HSV could be the cause.
  - Treat potential HSV with parenteral high-dose aciclovir until this diagnosis is excluded.

Osteomyelitis

- It is infection of the metaphysis of long bones. The most common sites are the distal femur and proximal tibia, but any bone may be affected (Fig. 28.10). Haematogenous spread or direct spread from an infected wound.
- Presents with fever, a painful, immobile limb, swelling and extreme tenderness, especially on moving the limb. Beyond infancy, presentation may be with back pain in a vertebral infection or with a limp or groin pain in infection of the pelvis.
- **Blood cultures** are usually positive. Most infections are caused by Staphylococcus aureus, but other pathogens include Streptococcus and Haemophilus influenzae if not immunized. In sickle cell anaemia, there is an increased risk of staphylococcal and salmonella osteomyelitis.
- **X-rays** are initially normal, other than showing soft tissue swelling; it takes **7–10 days** for subperiosteal new bone formation and localized bone rarefaction to become visible.
- **Ultrasound** may show periosteal elevation at presentation. Magnetic resonance imaging (**MRI**) allows identification of infection in the bone (subperiosteal pus and purulent debris in the bone) and differentiation of bone from soft tissue infection. **Radionuclide** bone scan (Fig. 28.11) may be helpful if the site of infection is unclear. The X-ray changes of chronic osteomyelitis are shown in Fig. 28.12.
- Parenteral antibiotics must be given immediately and for several weeks followed by oral therapy for several weeks.
- Surgical **drainage** if unresponsive to antibiotic therapy. **Aspiration** or surgical decompression of the subperiosteal space may be performed if the presentation is atypical or in immunodeficient children.

Osteomyelitis

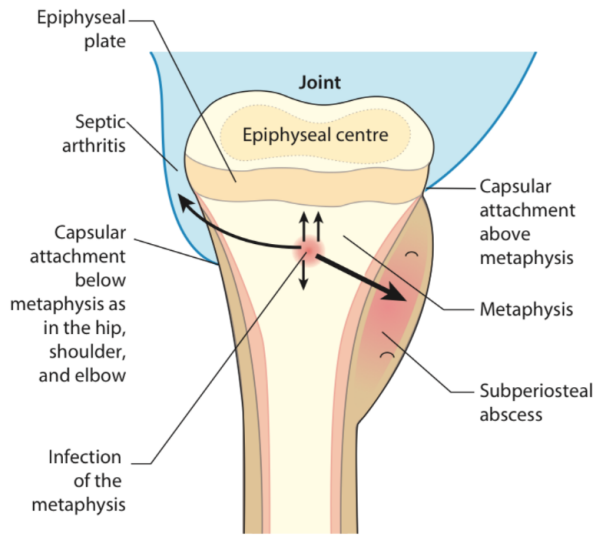


Figure 28.10 Possible spread of osteomyelitis. In children, the epiphyseal growth plate limits the spread of metaphyseal infection. In infants, before there has been maturation of the growth plate, infection can spread directly to cause joint destruction and arrested growth.

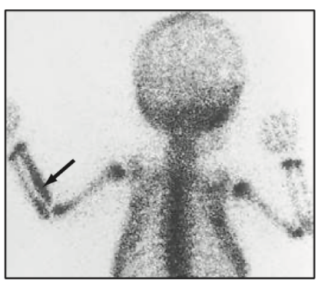


Figure 28.11 Bone scan of osteomyelitis with increased radionuclide uptake of the left radius. (Courtesy of H. Carty.)

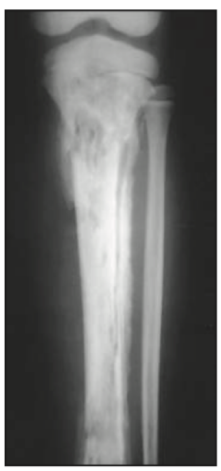


Figure 28.12 Chronic osteomyelitis, showing periosteal reaction along the lateral shaft of the tibia and multiple hypodense areas within the metaphyseal regions.

Septic arthritis

- This is a serious infection of the joint space, as it can lead to bone destruction. It is most common in **children less than 2 years old**. It usually results from haematogenous spread but may also occur following a puncture wound or infected skin lesions, e.g. chickenpox.
- In young children, it may result from spread from adjacent osteomyelitis into joints where the capsule inserts below the epiphyseal growth plate.
- Usually only **one joint** is affected, with the hip being a particular concern in infants and young children.
- Beyond the neonatal period, the most common organism is Staphylococcus aureus. H. influenzae was an important cause in young children prior to Hib immunization and often affected multiple sites.
- Presentation
  - erythematous, warm, acutely tender joint, with a reduced range of movement, in an acutely unwell, febrile child. Infants often hold the limb still (**pseudoparesis, pseudoparalysis**) and cry if it is moved. A joint effusion may be detectable in peripheral joints.
  - The **diagnosis** of septic arthritis of the hip can be particularly difficult in toddlers, as the joint is well covered by subcutaneous fat (Fig. 28.15). Initial presentation may be with a limp or pain referred to the knee.
- Investigation
  - There is an increased **white cell count** and acute-phase reactants.
  - **Blood cultures** must be taken.
  - **Ultrasound** of deep joints, such as the hip, is helpful to identify an effusion.
  - **X-rays** are used to exclude trauma and other bony lesions. However, in septic arthritis, the X-rays are initially normal, apart from widening of the joint space and soft tissue swelling.
  - **MRI** scanning or a radioisotope bone scan may be indicated if the site of infection is unclear.
  - **Aspiration** of the joint space under ultrasound guidance for organisms and culture is the **definitive investigation**. Ideally, this is performed immediately, unless this would cause a significant delay in giving antibiotics.
- Treatment
  - A **prolonged course of antibiotics** is required, initially intravenously.
  - Washing out of the joint or surgical drainage may be required if resolution does not occur rapidly or if the joint is deep-seated, such as the hip.
  - The joint is initially immobilizsed in a functional position, but subsequently must be mobilized to prevent permanent deformity.

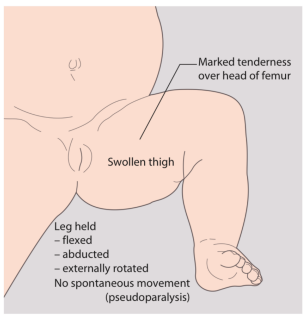


Figure 28.15 Septic arthritis of the hip in infants, showing the characteristic posture to reduce intracapsular pressure. Any leg movement is painful and is resisted.

Very important know it by heart

Assessment & investigation of meningitis/encephalitis

History
Fever
Headache
Photophobia
Lethargy
Poor feeding/vomiting
Irritability
Hypotonia
Drowsiness
Loss of consciousness
Seizures

Examination
Fever
Purpuric rash (meningococcal disease)
Neck stiffness (not always present in infants)
Bulging fontanelle in infants
Opisthotonus (arching of back)
Positive Brudzinski/Kernig signs
Signs of shock
Focal neurological signs
Altered conscious level
Papilloedema (rare)

Investigations
Full blood count and differential count
Blood glucose and blood gas (for acidosis)
Coagulation screen, C-reactive protein
Urea and electrolytes, liver function tests
Culture of blood, throat swab, urine, stool for bacteria
Rapid antigen test for meningitis organisms (can be done on blood, CSF, or urine)
Samples for viral PCRs (e.g. throat swab, nasopharyngeal aspirate, conjunctival swab, stool sample)
Lumbar puncture for CSF unless contraindicated (see below for tests on CSF)
Serum for comparison of convalescent titres
PCR of blood and CSF for possible organisms
If TB suspected: chest X-ray, Mantoux test and/or interferon-gamma release assay, gastric aspirates or sputum for microscopy and culture (and PCR if available)
Consider CT/MRI brain scan and EEG

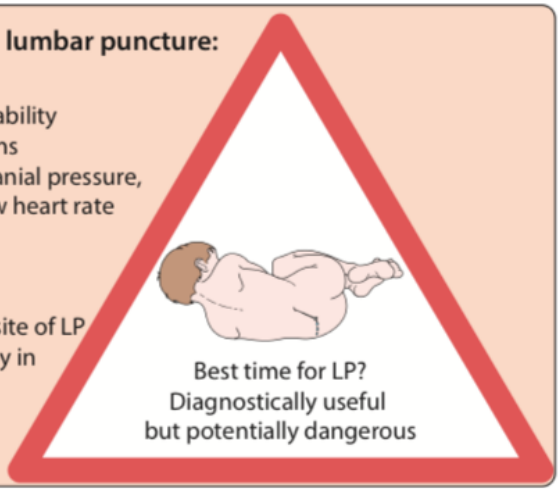
Signs associated with neck stiffness

Brudzinski sign – flexion of the neck with the child supine causes flexion of the knees and hips

Kernig sign – with the child lying supine and with the hips and knees flexed, there is back pain on extension of the knee

Contraindications to lumbar puncture:

- Cardiorespiratory instability
- Focal neurological signs
- Signs of raised intracranial pressure, e.g. coma, high BP, low heart rate or papilloedema
- Coagulopathy
- Thrombocytopenia
- Local infection at the site of LP
- If it causes undue delay in starting antibiotics



Typical changes in the CSF in meningitis or encephalitis, beyond the neonatal period

	Aetiology	Appearance	White blood cells	Protein	Glucose
Normal	—	Clear	0–5/mm^3	0.15–0.4 g/L	≥50% of blood
Meningitis	Bacterial	Turbid	Polymorphs:↑↑	↑↑	↓↓
	Viral	Clear	Lymphocytes:↑ (initially may be polymorphs)	Normal/↑	Normal/↓
	Tuberculosis	Turbid/clear/ viscous	Lymphocytes:↑	↑↑↑	↓↓↓
Encephalitis	Viral/unknown	Clear	Normal/↑ lymphocytes	Normal/↑	Normal/↓

Figure 15.4 Assessment and investigation of meningitis and encephalitis.