Serious Pediatric Infections

objectives:

- Learn special concepts related to children ID.
- Outline a framework 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 therapeutic and preventive measures

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Special thanks to team 437 & Faisal alsaif

Notes

Important

Book

Pediatric Infectious Diseases

Special consideration:

- Most common problem you will encounter in pediatrics
- They are exposed to the causative agent for first time
- Immature immune system: more infection in mucosal surfaces i.e. more gastroenteritis.
    - o IgM starts forming in utero and reaches adult number by the first year of life.
    - o IgG rise gradually till 3-4 years.
    - o IgA by 10-14 years.
- URTI are common
- LRTI is also more common because they have smaller airway; get blocked by secretions more easily, weak cough impulse because they can't expel secretions leading to atelectasis.
- Non-specific signs/symptoms: commonest presentation of infections in children and adults is fever, whereas in neonates it is irritability and crying and they can be either afebrile or hypothermic, not specific.
- Age-dependent etiology
- One agent and different syndromes: EBV can present as infectious mononucleosis, hepatitis, splenomegaly, fever of unknown origin or malignancy.
- Several agents and one syndrome: CMV, toxoplasmosis or EBV can cause Infectious mononucleosis. Can't differentiate these agents except with investigations

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- Fever:>38.2
- How accurate are different types of thermometer readings?
  1- Ear/oral: very accurate take the reading as it is
  2- Axilla: add 0.5
  3- Rectal: subtract 0.5

Pediatric Infectious Diseases

Principle for studying infectious diseases

- Etiology
- Pathogenesis
- Clinical manifestations/course:
  - o Immunocompetent
  - o Immunocompromised
- Epidemiology
- Mode of transmission
- Incubation period
- Reservoir: where it is present in the environment.
- Period of communicability
- Susceptible individuals
- Diagnosis
- Complications: are classified as early and late
- Management
  - o Treatment
  - o Prevention
  - o Infection control

Serious pediatric infections

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

- We have to consider four imp, parameter when we think of pediatric infections:

1- Age
2-Etiology
3-Host (immunocompromised vs competent)
4-Environment (community acquired vs hospital)

Meningitis

- is an inflammation of the leptomeninges, can be caused by bacteria, viruses, or, rarely, fungi.
- The term **aseptic meningitis** refers principally to viral meningitis
- **Partially treated meningitis** refers to bacterial meningitis complicated by oral antibiotic treatment before the lumbar puncture, which may result in negative CSF cultures, although other CSF findings suggestive of bacterial infection persist.

Etiology:

Determined by age:

- **Neonate - 3 months** : Group B strep, E-coli (others coliforms), listeria monocytogenes[1]
- **3 months – 6 years**: strep. pneumoniae , N. meningitidis , Haemophilus influenzae[2]
- **>6 years**: strep. pneumoniae , N. meningitidis

Special risk factors

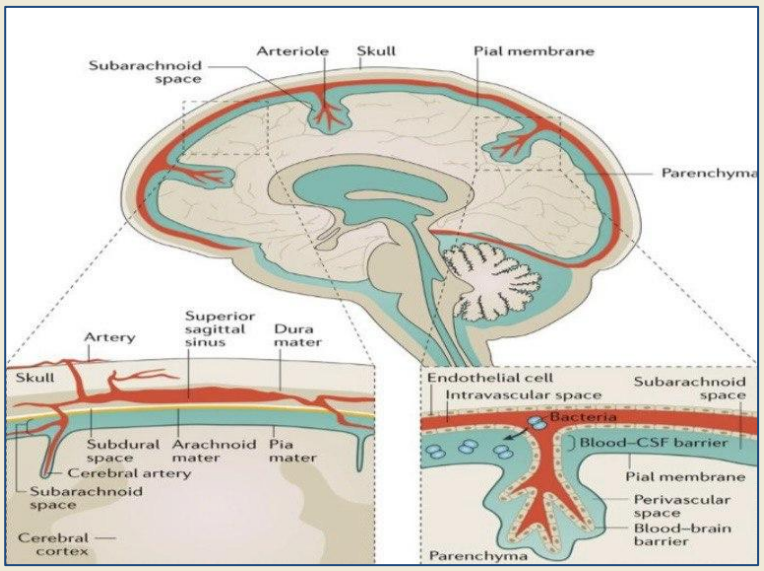
1. Post-traumatic: Basal skull fractures: consider risk of strep. pneumoniae[3].
2. Post neurosurgical: staph and gram negatives.
3. Ventricular (VP) shunts: staph epidermidis (coagulase negative).
4. Immunocompromised: include fungal
5. Asplenia and SCD: Salmonella and encapsulated organisms.
   - look for sinus tract from skin to subarachnoid space (careful exam of the back)

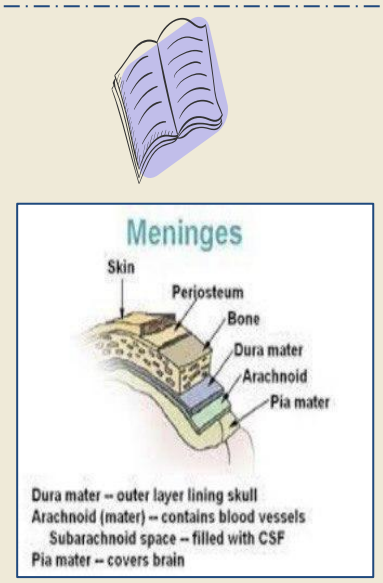
1- Source: unpasteurized milk & milk product
2- Type B: less due to vaccine, which makes other types more common
3- Ascending infection through the cribriform plate

Pathogenesis

- Mucosal colonization > local invasion > bacteremia > Meningeal invasion > bacterial replication > subarachnoid space inflammation.
- Colonization occurs in nasopharynx
- Replication leads to autolysis, which leads to the release of cell wall component (endotoxin in gram –ve and teichoic acid in gram +ve) resulting in the release of inflammatory mediators > activating leukocytes causing cytotoxic edema >increase ICP >endothelial injury and thrombosis causing further increase in ICP> resulting in decreased cerebral blood flow.

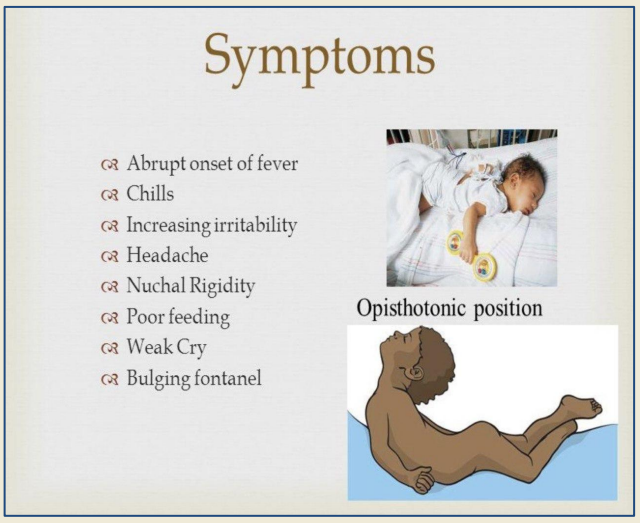
Mid-sagittal view of the brain showing the meninges: the dura mater,
the subarachnoid mater and the pia mater.
Bacteria can reach the meninges through the blood–CSF barrier.





Assessment & investigation of meningitis

- History
- Physical exam (Signs associated with neck stiffness) Neck stiffness (not always present in infants, Due to the open fontanelle.). Bulging fontanelle in infants Opisthotonus (arching of back)



Assessment & investigation of meningitis/encephalitis

History
Fever – Abrupt onset
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

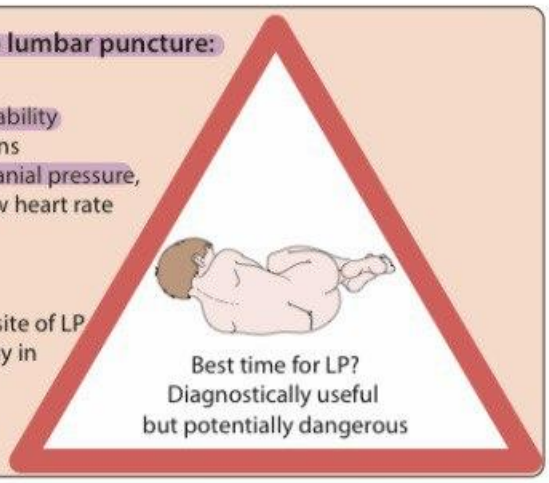
Signs associated with neck stiffness

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:

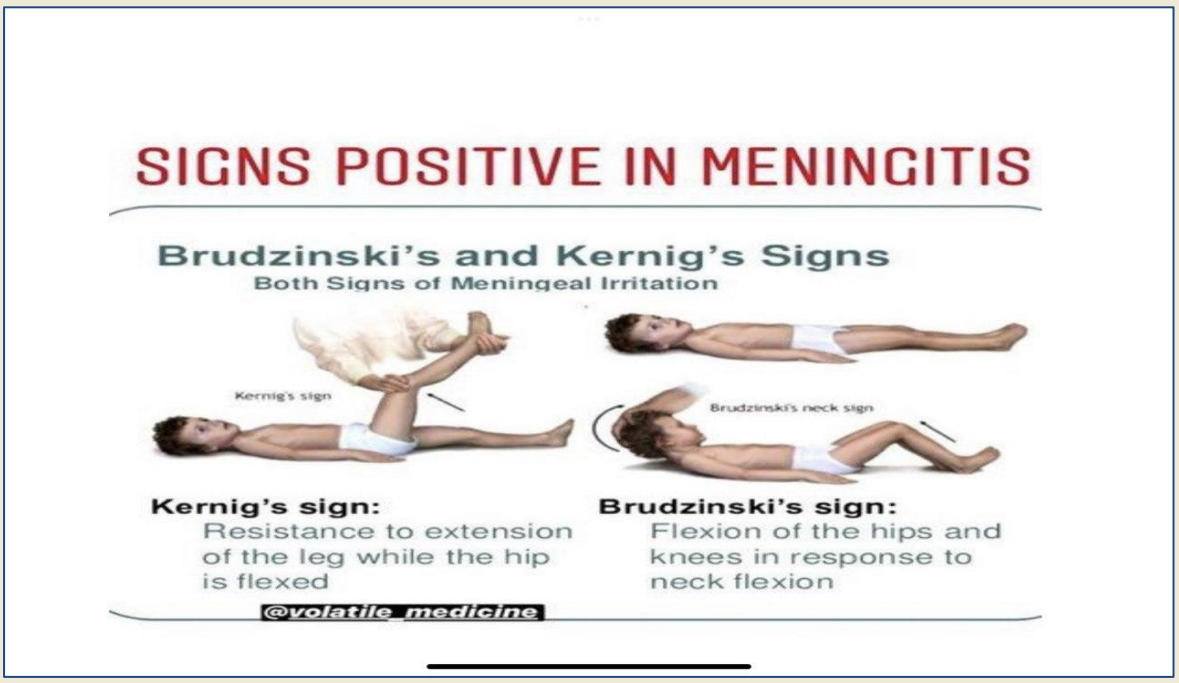
- Cardiorespiratory instability
- Focal neurological signs
- Signs of raised intracranial pressure, e.g. coma, high BP, low heart rate or papilloedema
- Coagulopathy
- Thrombocytopenia
- Local infection at the site of LP
- If it causes undue delay in starting antibiotics



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.



Diagnosis

- **CBC**: leukocytosis or leukopenia (worst prognosis signifies meningococcal disease). Never discharge a patient with normal CBC and fitting clinical picture.
- **Blood culture 60-70% specific.**
- **CSF**: Appearance: clear, turbid, bloody
- **Cell count and differential.**
- **Chemistry:** Sugar & Proteins
- **Gram stain** is positive in 70-80% of the patients.
- **Culture**
- **molecular study** (PCR)

	Normal	Bacterial	Viral
WBCs/uL	<5	>100-5000+	5-1000
Cell predominance	None	Neutrophils	Lymphocytes
Protein	<0.5g/dl	Raised	Mildly raised
Glucose	2.6-4.5 mmoL	Very low	Low/normal – usually in bumps
CSF/plasma glucose	>0.66	Very low	Low/normal

Table 1: CSF findings in meningitis. *Adapted from: McGill et al (2016)*

Management

1. Supportive care is the most important. Careful monitoring of the patient.
2. Antibiotics
3. Dexamethasone modulates the release of inflammatory mediated factors, it should be given at the time of AB or just before first dose of antibiotic. It decreases deafness, which is a complication of meningitis.

Antibiotics

- **for kids >3 months:**

Ceftriaxone[1] + vancomycin[2]

- **Neonates:**

Cefotaxime[3] + ampicillin (Cover: listeria)
Gentamicin + ampicillin

1- Covers strep pneumo, meningococcus, type b haemophilus
2- Covers resistant strep pneumo
3- Covers group B strep, E. Coli, klebsiella

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 WBC, but cultures are usually negative.
- PCR are helpful
- Where the diagnosis is suspected clinically, a full course of I.V antibiotics should be given

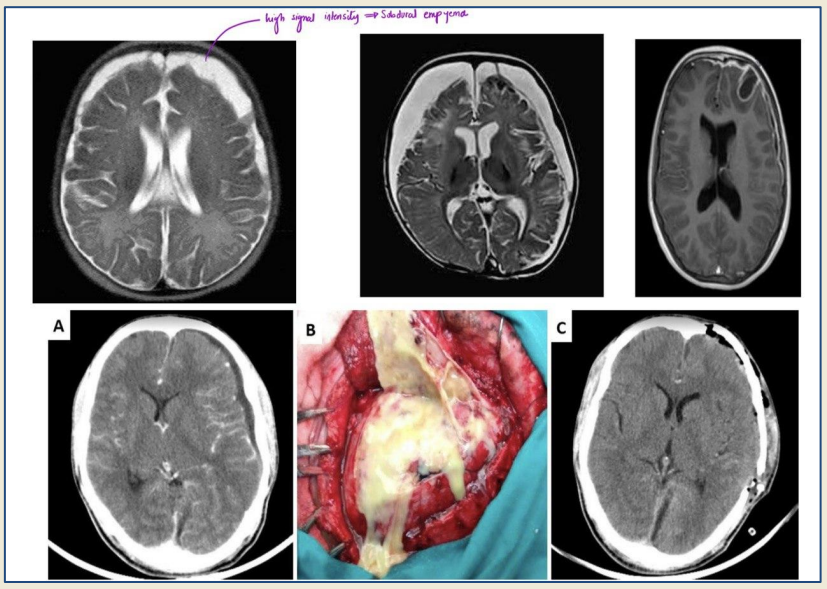
Complications

Early:

- **SIADH**: monitoring of urine output and fluid administration.
- **Subdural effusion:**[1] most effusions are sterile and asymptomatic, and they do not necessitate drainage unless associated with increased intracranial pressure or focal neurologic signs.
- **brain abscess**[2] is a rare complication of meningitis and is seen in a specific age group and bacterial organism.
- **Persistent fever** is common during treatment, but it also may be related to infective or immune complex–mediated pericardial or joint effusions, thrombophlebitis check iv site , drug fever, or nosocomial infection.

late:

- Deafness[3], seizures, learning disabilities, blindness, paresis or hydrocephalus[4] , Local vasculitis which may lead to cranial nerve palsies



1- Particularly with H. Influenza, we do CT or MRI to confirm the diagnosis
2- esp group -ve in young age group (< 3 month), which causes signs of space occupying lesion + deterioration. **Dx**: CT or MRI. **Rx**: drainage
3- Decrease risk if steroid started early. All children who have meningitis must have audiological assessment
4- Communicating or non-communicating. may require Ventricular shunt

Primary 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.
- Choices: rifampin, ciprofloxacin, (pregnancy: ceftriaxone)

Vaccination:

- HiB, meningococcal, and **some require pneumococcal vaccine** whom are at high risk of invasive disease:
  1- Patients with Sickle cell anemia 2- Elderly

Encephalitis

Inflammation of the brain parenchyma, although the meninges are often also affected. Onset can be insidious and includes behavioral change

- Most common pathogen is enteroviruses fortunately they are self-limiting.
- Most serious is HSV, which increases morbidity and mortality.
- Others: mumps, rabies, arboviruses, influenza, mycoplasma,..

Diagnosis: MRI/CT + EEG may be normal and it needs to be repeated again after few days

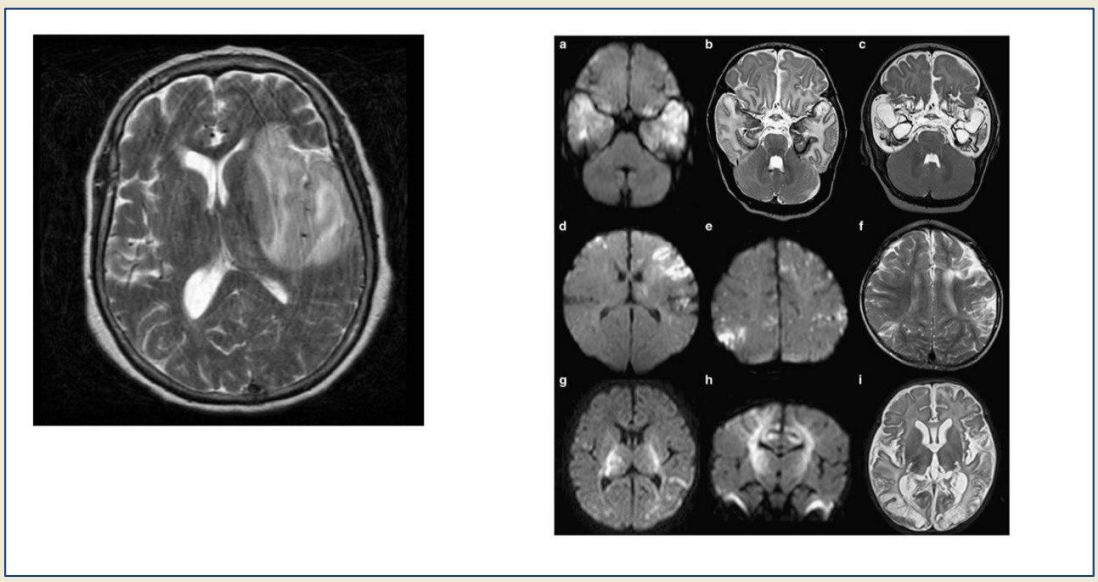
- CSF
- PCR
- MRI
- Brain biopsy rarely needed
- EEG

Treatment:

- If HSV encephalitis is suspected, start acyclovir early. Only clinically, don't wait for pcr or mri results

HSV encephalitis

Usually infects temporal lobe unilaterally or bilaterally



Bacteremia

Definition

- Bacteria in the blood, but doesn't indicate the severity of the disease. It can be:

1. Transient: will be cleared by the reticuloendothelial system; however, can lead to complications in a group of high risk patients including those with certain types of cong. heart disease. Therefore, prophylactic antibiotics are indicated for those before dental procedures due to risk of endocarditis.

2. Occult: Not expected to be bacteremic on presentation but has a positive blood culture.
NB : Some can progress to severe infection and other might settle to be local infection in any part of the body, however majority resolve

3. Serious
- Fulminant with shock: common with E-coli and pseudomonas and other gram negative bacteria
- +/- focal infection.

Meningococcal infection

Meningococcal infection is a serious disease , can kill previously healthy children within hours

However, of the three main causes of bacterial meningitis, meningococcal has the lowest risk of long-term neurological sequelae, with most survivors recovering fully.

The septicemia is usually accompanied by a purpuric rash which may start anywhere on the body and then spread.
The rash may or may not be present with meningococcal meningitis.

Characteristic lesions

non-blanching on palpation, irregular in size and outline and have a necrotic center

★ Any **febrile child** who develops a **purpuric rash** should be treated immediately, with systemic antibiotics such as penicillin before urgent admission to hospital[1]

Prevention Meningococcal conjugate vaccine (MCV4: A,C,Y,W135), Meningococcal serogroup B vaccine

1- IM- benzylpenicillin or IV- third generation Cephalosporin before urgent admission

Meningococcal infection

Case history 15.1

Meningococcal septicaemia

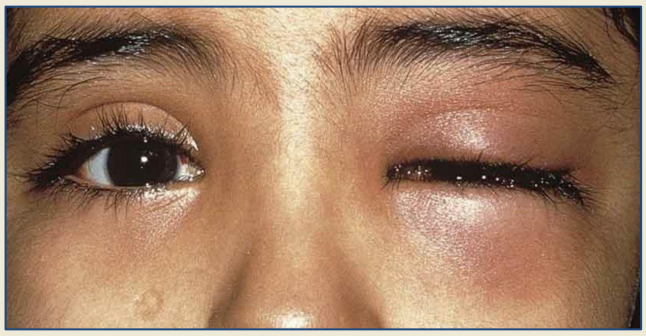
This 7-month-old boy presented with a 12-hour history of lethargy and a spreading purpuric rash. In hospital, he required immediate resuscitation and transfer to a paediatric intensive care unit for multiorgan failure (Fig. 15.7a). The gross oedema is from leak of capillary fluid into the tissues. He required colloid and inotropic support and peritoneal dialysis for renal failure. He made a full recovery (Fig. 15.7b).

Meningococcal septicaemia can kill children in hours. Optimal outcome requires immediate recognition, prompt resuscitation and antibiotics

(a) (b)

Figure 15.7 (a) A boy with meningococcal septicaemia receiving intensive care. (b) After full recovery. (Courtesy of Dr Parviz Habibi.)

Orbital Cellulitis



Affects the optic nerve and it is an **emergency.**

Periorbital Cellulitis

Is usually an extension from the sinuses[1].

- It is almost always unilateral. In young, unimmunized children it may also be caused by Haemophilus influenzae type b which may also be accompanied by infection at other sites, e.g. meningitis
- Periorbital cellulitis should be treated promptly with **intravenous antibiotics** to prevent posterior spread of the infection to become an orbital cellulitis.
- In orbital cellulitis, there is proptosis, painful or limited ocular movement and reduced visual acuity. It may be complicated by abscess formation, meningitis or cavernous sinus thrombosis.
- Where orbital cellulitis is suspected, a CT scan should be performed to assess the posterior spread of infection.

1- Entry point: skin or paranasal sinuses (commonly ethmoidal sinuses)

Necrotizing fasciitis/cellulitis

ID emergency

This is a severe subcutaneous infection, often involving tissue planes from the skin down to fascia and muscle.

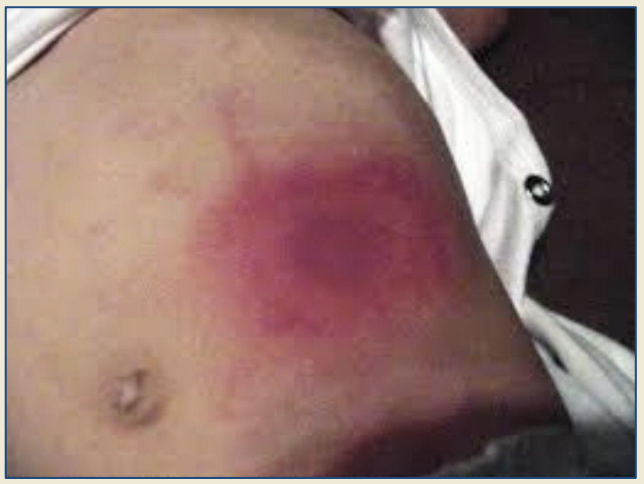
The area involved may enlarge rapidly[1], leaving poorly perfused necrotic areas of tissue, usually at the center.

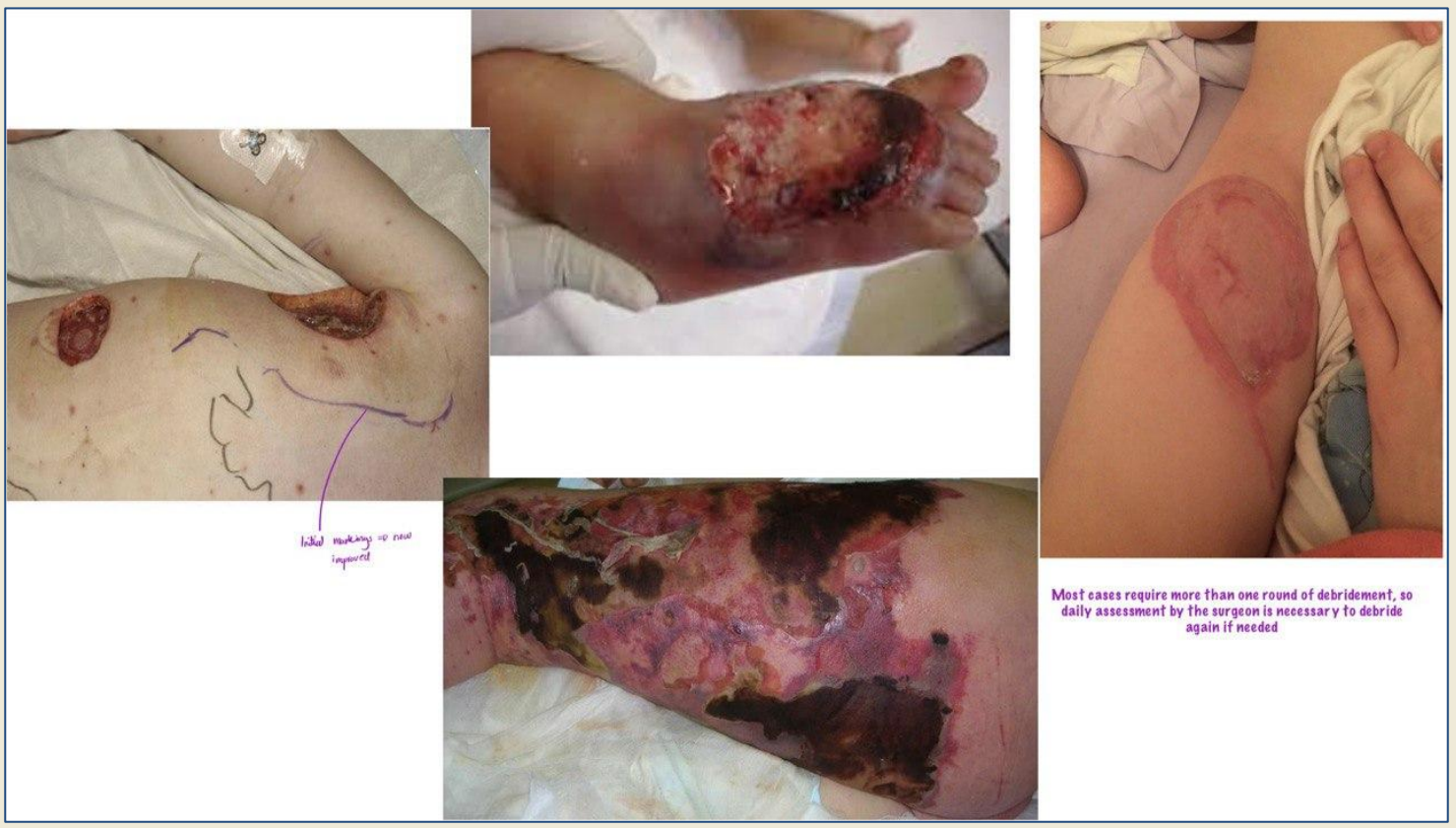
There is severe pain and systemic illness, which may require intensive care. The invading organism may be Staphylococcus aureus or a group A streptococcus, +/- anaerobic organism.

Intravenous antibiotic therapy alone is not sufficient to treat. Without surgical intervention and debridement of necrotic tissue, the infection will continue to spread. Clinical suspicion of necrotizing fasciitis warrants urgent surgical consultation and intervention.

Treatment:

- penicillin or cloxacillin +clindamycin
- Intravenous immunoglobulin (IVIG) may also be given





1- Within hours while cellulitis usually slow

Toxic shock syndrome

- Toxin-producing Staphylococcus aureus and group A streptococci can cause this syndrome.
- The toxin can be released from infection at any site, including small abrasions or burns, which may look minor.
- The toxin acts as a superantigen and, in addition to the features above, causes organ dysfunction.

characterized by:

- Fever >39°C
- Hypotension
- Diffuse erythematous, macular rash
- Mucositis :conjunctivae, oral mucosa, genital mucosa
- Gastrointestinal: vomiting/diarrhea
- Renal impairment
- Liver impairment
- Clotting abnormalities and thrombocytopenia
- Central nervous system: altered consciousness

Figure 14.6 A child with toxic shock syndrome receiving intensive care, including artificial ventilation via a nasotracheal tube. The lips are red and the eyelids are oedematous from capillary leak. (Courtesy of Professor Mike Levin.)

About 1–2 weeks after the onset of the illness, there is desquamation of the palms, soles, fingers and toes.

Management

- Intensive care support is required to manage the shock.
- Areas of infection should be surgically debrided.
- Antibiotics often include a third-generation cephalosporin (such as **ceftriaxone**) together with **clindamycin**, which acts on the bacterial ribosome to switch off toxin production.
- IVIG may be given to neutralize circulating toxin.

Osteoarticular infections

Presentation:

1. **Pain.** Mother notices the baby cries upon diaper change
2. **Limping.** Unilateral, keeps the lower limb flexed (in hip infection)
3. **Swelling.**

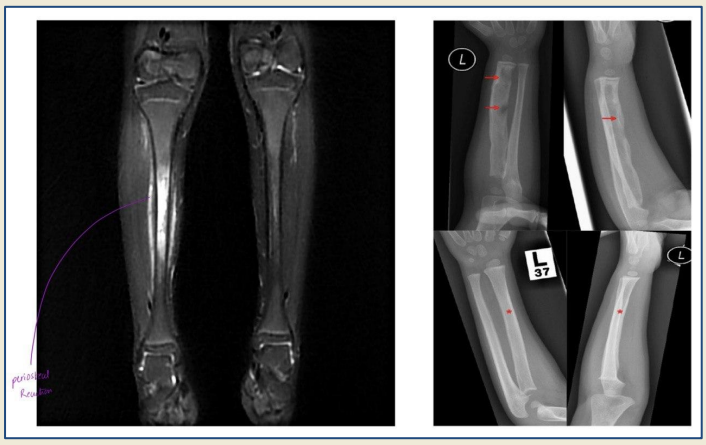
- Septic arthritis of the hip is serious because it is a deep-seated infection and doesn't cause any swelling. It can lead to avascular necrosis if there is pus, therefore drainage is important. In infants they usually maintain their hip in lateral rotation and flexion to have more space in the joint and thus relieving the pressure.

Etiology:

- Staphylococcus aureus, Streptococcus pneumoniae, Kingella kingae
- SCD: Salmonella
- Puncture wounds of the foot: Pseudomonas aeruginosa

Imaging:

- Bone change (such as periosteal reaction) is not seen on X-ray until the 10th day. So it will not help you for diagnosis, but helps you to rule out other Ddx (e.g. fractures)
- MRI Gold standard: very sensitive
- The radionuclide scan will show increased uptake



Complications

1. Avascular necrosis.
2. Joint destruction.

Treatment

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

Childhood Tuberculosis

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

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

1. **History of close contact with adult with TB** (especially if smear positive)
2. **Triad of :**
   - o Signs and symptoms compatible with TB disease
   - o A positive tuberculin skin test (TST)/IGRA essay Only for children 2 years or older, both can be false negative in immunocompromised patients (e.g. HIV co infection)
   - o Suggestive radiographic finding

How TB is Transmitted?

- Person-to-person: airborne from a person with open pulmonary TB

- Other modes of transmission in neonates: vertical transmission (rare) – congenital TB

TB: Adults vs Children

Compared to adults, children:

- Tend to develop primary active TB more often after initial infection (0-4 years)
- Are more likely to have extra-pulmonary disease, especially TB meningitis (0-4y)
- Are less contagious. Because they have lower bacterial load
- Are more difficult to diagnose
- 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

Needs the adult contact's culture results for **drug sensitivities** and to determine treatment regimen for the child

TB in Children

Points to remember:

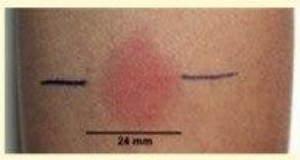
- Symptoms are atypical
- Diagnosis may be difficult
- Sputum cannot often obtained
- Sputum often negative for AFB even on culture
- Diagnosis depends on clinical history, family contact history, X-ray, examination and TST + IGRA (blood) Can be false +ve (eg. by BCG vaccine)
- All patients with TB should be tested for HIV, and vice versa

Clinical features of TB

Primary infection

Asymptomatic

Nearly half of infants and 90% of older children have minimal or no symptoms or signs of infection. A local inflammatory reaction limits the progression of infection. However, the disease remains latent and may therefore develop into active disease at a later time. Asymptomatic children with a positive tuberculin skin test (TST) (Fig 18.19a) or interferon-gamma release assay result (i.e. latent TB) should be given chemoprophylaxis to prevent future conversion to active TB.



a) Example of a positive TST (24-mm induration). A TST (2 units PPD, Purified Protein Derivative) is positive if the palpable induration is 5 mm or more in diameter irrespective of whether or not had BCG immunization (NICE guidelines, 2016). Only the induration should be measured (not the surrounding erythema).

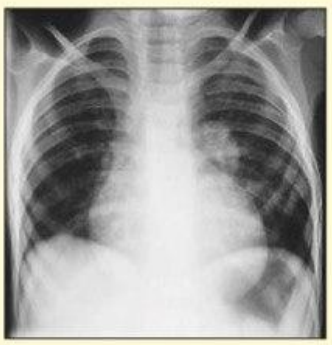
Symptomatic

In this case the local host response fails to contain inhaled *M. tuberculosis*, allowing spread via the lymphatic system to regional lymph nodes. The lung lesion plus the lymph node constitutes the 'Ghon (or primary) complex'. When the host's cellular immune system responds to the infection (3–6 weeks), mycobacterial replication diminishes but systemic symptoms develop:

- fever
- anorexia and weight loss
- cough
- chest X-ray changes (Fig. 18.19b).

The primary complex usually heals and may calcify. The inflammatory reaction may lead to local enlargement of peribronchial lymph nodes, which may cause bronchial obstruction, with collapse and consolidation of the affected lung. Pleural effusions may also be present. Further progression may be halted by the host's immunological response, or there may be local dissemination to other regions of the lung.

Although primary infection most commonly occurs in the lung, it may also involve other organs including lymph nodes, bones and joints, the genitourinary system, and the meninges.



b) Chest X-ray of pulmonary TB. There is marked left hilar lymphadenopathy

Dormancy and dissemination

Both asymptomatic and symptomatic infections may become dormant but subsequently reactivate and spread by lymphohaematological routes.

Reactivation

Post-primary TB

This may present as localized disease or may be widely disseminated (called miliary TB), to sites such as bones, joints, kidneys, pericardium, and CNS. Infants and young children are particularly prone to tuberculous meningitis. This was always fatal before antimicrobial therapy was available, and is still associated with significant morbidity and mortality if treatment is not initiated early.

Figure 15.19 Clinical features of tuberculosis.

Definitions of Positive Tuberculin Skin Test Results in Infants, Children, and Adolescents[a,b]

Induration ≥5 mm

Children in close contact with known or suspected contagious people with TB disease

Children suspected to have TB disease

- Findings on chest radiograph consistent with active or previous TB disease
- Clinical evidence of TB disease[c]

Children receiving immunosuppressive therapy[d] or with immunosuppressive conditions, including HIV infection

Induration ≥10 mm

Children with increased risk for disseminated TB disease

- Children younger than 4 years
- Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition (Box 155.2)
- Children born in high-prevalence regions of the world
- Children with significant travel to high-prevalence regions of the world[e]
- Children frequently exposed to adults who are living with HIV, experiencing homelessness, or incarcerated or to people who inject or use drugs or have alcohol use disorder

Induration ≥15 mm

Children without any risk factors

TB indicates tuberculosis; TST, tuberculin skin test.

[a] See **www.cdc.gov/tb/publications/guidelines/pdf/ciw778.pdf.**

[b] These definitions apply regardless of previous BCG immunization; erythema alone at the TST site does not indicate a positive test result. Tests should be read at 48–72 hours after placement.

[c] Evidence by physical examination or laboratory assessment that would include TB in the working differential diagnosis (eg, meningitis).

[d] Including immunosuppressive doses of corticosteroids or tumor necrosis factor-α antagonists or blockers or immunosuppressive drugs used in transplant recipients.

[e] Some experts define *significant travel* as travel or residence in a country with an elevated TB rate for at least 1 month.

Recommended Usual Treatment Regimens for Drug-Susceptible TB Infection and TB Disease in Infants, Children, and Adolescents

Infection or Disease Category	Regimen	Remarks
***Mycobacterium tuberculosis* infection** (positive TST or IGRA result, no disease)[a]		
• Isoniazid susceptible	12 weeks of isoniazid plus rifapentine, once a week	Most experts consider isoniazid-rifapentine to be the preferred regimen for treatment of TBI for children ≥2 years, and some experts prefer isoniazid-rifapentine therapy for TBI in children ≥2 years.
	OR , if isoniazid resistant	
	4 months of rifampin, once a day	Continuous daily therapy is required. Intermittent therapy even by DOT is not recommended.
	OR	
	3 months of isoniazid plus rifampin, once a day	To be considered if above 2 regimens are not feasible
	OR	
	6 or 9 months of isoniazid, once a day	If daily therapy is not possible, DOT twice a week can be used; medication doses differ with daily and twice-weekly regimens.
• Isoniazid resistant	4 months of rifampin, once a day	Continuous daily therapy is required. Intermittent therapy even by DOT is not recommended.
• Isoniazid-rifampin resistant	Consult a TB specialist.	Moxifloxacin or levofloxacin with or without ethambutol or pyrazinamide is most commonly given.
Pulmonary and extrapulmonary disease (except meningitis)[b]	2 months of RIPE daily or 3 times per week, followed by 4 months of isoniazid and rifampin[c] by DOT[d] for drug-susceptible *M tuberculosis*	Some experts recommend a 3-drug initial regimen (isoniazid, rifampin, and pyrazinamide) if the risk of drug resistance is low. DOT is highly desirable. If hilar adenopathy only and the risk of drug resistance is low, a 6-month course of isoniazid and rifampin is sufficient. DOT is required for intermittent regimens. Drugs can be given daily or 3 times per week; 2 times per week is acceptable if DOT resources are scarce.
	At least 9 months of isoniazid and rifampin for *Mycobacterium bovis* susceptible to these drugs	

(*continues*)

- Asymptomatic children who are Mantoux or IGRA positive and therefore latently infected should also be treated (e.g. with rifampicin and isoniazid for 3 months or isoniazid alone for 6 months) as this will decrease the risk of reactivation (i.e. conversion to active TB) later in life.

Table 155.1 (*continued*)

Infection or Disease Category	Regimen	Remarks
Meningitis Duration of treatment is extended to one year in TB meningitis and miliary TB	2 months of RIPE, if possible, or an aminoglycoside[e] or capreomycin, once a day[f,g]; followed by 4–10 months of isoniazid and rifampin, once a day or 3 times per week (9–12 months total) for drug-susceptible *M tuberculosis* At least 12 months of therapy without pyrazinamide for *M bovis* susceptible to isoniazid and rifampin	See text for information on corticosteroids.

DOT indicates directly observed therapy; RIPE, rifampin, isoniazid, pyrazinamide, and ethambutol; TB, tuberculosis; and TBI, TB infection.

[a] See text for comments and additional acceptable/alternative regimens.

[b] Duration of therapy may be longer for people living with HIV infection, and additional drugs and dosing intervals may be indicated.

[c] Medications should be administered daily for the first 2 weeks–2 months of treatment and can then be administered daily or 3 times per week by DOT; twice weekly is acceptable if resources for DOT are limited. Intermittent therapy is not recommended for people living with HIV infection.

[d] If initial chest radiograph shows pulmonary cavities and/or if sputum culture after 2 months of therapy remains positive, the continuation phase is extended to 7 months, for a total treatment duration of 9 months.

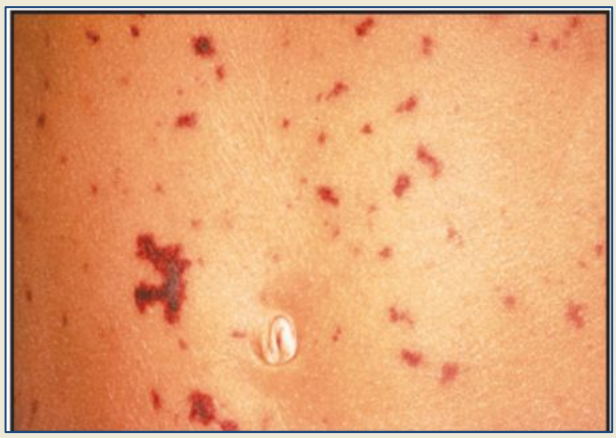
[e] Parenteral streptomycin, kanamycin, or amikacin.

[f] Many experts add a fluoroquinolone to this initial regimen.

[g] When susceptibility to first-line drugs is established, the ethionamide, aminoglycoside (or capreomycin), and/or fluoroquinolone can be discontinued.

Questions

1- Joseph, aged 3 years, has been unwell for 24 hours with irritability, vomiting and fever. He was seen by his general practitioner earlier in the day and started on amoxicillin. On examination his temperature is 38.5°C, pulse 140 beats/min and blood pressure 90/60 mmHg. He has a rash on his upper limbs and abdomen as shown\



What is the most likely diagnosis?
Select one answer only.
A. Henoch–Schönlein purpura
B. Immune thrombocytopenic purpura
C. Measles
D. Meningococcal sepsis
E. Pertussis

2- **What investigation is most likely to give a definitive diagnosis in Joseph's case?**
Select one answer only.
A. Blood culture
B. Lumbar puncture
C. Polymerase chain reaction (PCR)
D. Pernasal swab
E. Throat swab

3- Henry is 4 years old and has a 3 day history of fever. He presents to the Accident and Emergency department with a headache. A lumbar puncture is performed. You receive the following result from the laboratory:

- Cerebrospinal fluid (CSF) microscopy:
- 250 red blood cells/mm3
- 1200 neutrophils/mm3
- 250 lymphocytes/mm3
- CSF protein: 0.6 g/L
- CSF glucose: 2.1 mmol/L
- blood glucose: 7.2 mmol/L

What is the most likely diagnosis?
Select one answer only.
A. Bacterial meningitis
B. Blood-stained tap
C. Normal lumbar puncture result
D. Tuberculosis meningitis
E. Viral meningitis

Questions

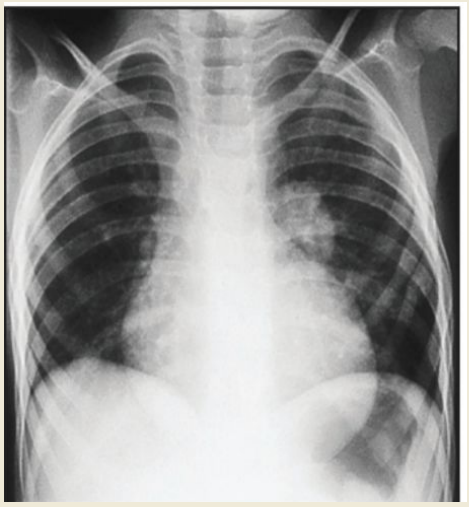
4- Graham is 5 years old and has had an intermittent fever for 4 weeks. He presents to the Emergency Department with a headache and neck stiffness. A CT scan is performed, which is normal. A lumbar puncture is performed. You receive the following result from the laboratory:

- cerebrospinal fluid (CSF) microscopy: 95 lymphocytes, 10 neutrophils and 0 RBC/mm3
- CSF protein: 2.2 g/L
- CSF glucose: 1.3 mmol/L
- blood glucose: 6.3 mmol/L

What is the most likely diagnosis?
Select one answer only.
A. Ascending polyneuritis (Guillain–Barré syndrome)
B. Bacterial meningitis
C. Blood-stained tap
D. Tuberculosis meningitis
E. Viral meningitis

5- Imran is a 3-year-old boy who moved to the UK from Bangladesh 4 months ago. He has not gained any weight for the last couple of months.
He has a cough. The general practitioner has requested a chest X-ray

What is the most likely diagnosis?
Select one answer only.
A. Asthma
B. Neuroblastoma
C. Pertussis infection
D. Pneumonia
E. Tuberculosis



Answers

1- **D.** Meningococcal sepsis
Correct. Meningococcal sepsis is most likely as the child has fever, malaise, and has the characteristic purpuric rash spreading across the abdomen.

2- **C.** Polymerase chain reaction
Correct. Meningococcal polymerase chain reaction is most likely to give definitive diagnosis. Treatment should not be delayed whilst awaiting results, which may take 2–3 days.

3-**A.** Bacterial meningitis
Correct. There is a markedly raised white cell count, mainly neutrophils. The CSF protein is raised, with a reduced ratio of CSF to blood glucose concentration.

4- **D.** Tuberculosis meningitis
Correct. The white cell count shows predominantly lymphocytes. This could also be seen in viral meningitis, but the very markedly raised protein and very low glucose in the CSF together with the clinical history are suggestive of tuberculosis.

5- **E.** Tuberculosis
Correct. Tuberculosis is the most likely diagnosis as he has marked left hilar lymphadenopathy on the chest X-ray, and it is endemic in Bangladesh.