بسم الله الرحمن الرحيم

تتقدم **لجنة الطب والجراحة** لكم بهذه الدوسية الخاصة **بمادة الأطفال** / جامعة مؤتة ..

و التي تحتوي على مادة **السنة الخامسة كاملة** ، والتي ساهم بإعدادها الطالبة :

مارلين معن حجازين

وأشرف على طباعتها وتنسيقها الطالب :

طارق نظمي أبولبدة

نسأل الله أن يكتب فيها النفع والفائدة ، ونرجو منكم تقديم التغذية الراجعة بملاحظاتكم الرامية لتحسين جودة هذه الدوسية ..

حبُّ السلامةِ يثني عَزْمَ صاحبِهِ // عن المعالي ويغري المرء بالكسلِ

أعلِّلُ النفس بالآمال أرقُبها // ما أضيقَ العيشَ لولا فُسحةُ الأملِ

فهرس المواضيع

Pediatric GIT Bleeding

- **Epidemiology :**
  Gastrointestinal bleeding in infants & children is a fairly common problem , accounting for 10% - 20% of referrals to pediatric gastroenterologists .
- **Pathophysiology of GI bleed**

1- Consequence of blood loss .

2- Risk of hemorrhagic shock .

3- Compensatory mechanism .

1- Consequence of blood loss

Loss of fluid (blood) → ↓extracellular fluid → dehydration shock→ ↓ glomerulofiltration rate → anuria

→ Small volume concentrated urine with high specific gravity → Pre-renal A.R.F (↑bun and nitrogen)

2- Risk of hemorrhagic shock

- Age dependent vital sign → inaccurate interpretation of early sign .

- High ratio surface area to body mass → limited thermoregulation → hypothermia → venous constriction → hypoxemia & acidosis .

- Smaller total body volume .

3- Sequence of compensatory mechanism

Loss of less than 15% of BV is compensated by:

- Contraction of the venous system .

- Fluid shift ECFC → IVFC .

- Preferential direction of blood to the brain and the heart → No hemodynamic changes .

Compensated shock

(1) Loss 15%-30% BV :

- Sympathetic stimulation .
- Secretion of aldosterone, ADH, prostaglandins .
- Release of catecholamine .
- Release of ACTH and corticosteroids.
  →→ Hemodynamic instability

- Tachycardia, O2 consumption, tissue hypoxia
  →→ Maintain blood volume

Decompensated shock

(2) Loss of more than 30% :

- Hypotension (Shock), ↑ cardiac output → acidosis → tissue damage.
- Acute renal failure .
- Liver failure .
- Heart failure .

SYMPTOMS OF UPPER GI BLEED

Symptoms of upper gastrointestinal bleeding include :

- **Hematemesis** vomiting of blood which can be bright red blood or dark clots, or coffee ground-like material .
- **Melena** passing black, tar-like stool

SYMPTOMS OF LOWER GI BLEED

Symptoms of lower gastrointestinal bleeding include :

- **Hematochezia** passing pure blood ,Blood clots mixed with or in between stool .
- Acute **bloody diarrhea** should be considered a medical emergency in preterm and infant (NEC , Volvulus and intussusception) .

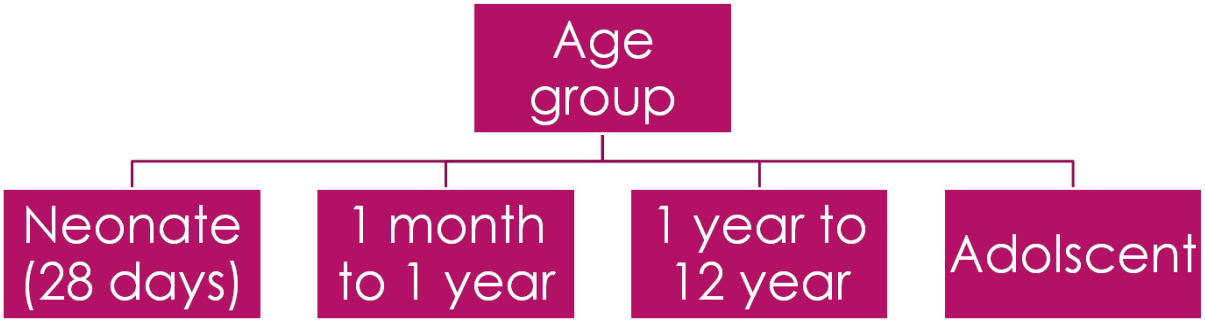
☒ Hematemesis : 50% of upper gastrointestinal bleeding cases . Hematochezia : 80% of all gastrointestinal bleeding.

☒ Melena :

- 70% of upper gastrointestinal bleeding .
- 33% of lower gastrointestinal bleeding .
- To form black, tarry stools (melena), there must be 150-200 cc of blood and the blood must be in the gastrointestinal tract to turn black .

CAUSES

The causes were divided according to the age group :



Causes of GI bleed in neonates :

Upper GI bleeding	Lower GI bleeding
swallowed maternal blood	swallowed maternal blood
stress ulcers, gastritis	dietary protein intolerance
vascular malformations	infectious colitis/enteritis
HDN	necrotizing enterocolitis
hemophilia	Hirschsprung's enterocolitis
maternal ITP	Coagulopathy
maternal NSAID use	vascular malformations

Neonatal causes of upper GIT bleeding

1- Maternal blood ingestion - The most common cause of upper GI bleeding in neonates is due to maternal blood ingestion. This can also present as lower GI bleeding. This occurs when blood is swallowed during birth or from breast feeding. The Apt tests differentiates between maternal and fetal hemoglobin.

2- Stress gastritis is found mainly in neonates who are in the neonatal intensive care unit and it is highly correlated with prematurity, neonatal distress, and mechanical ventilation. Diagnosis is made by upper endoscopy in order to determine signs of erythema, diffuse bleeding, erosions or ulcerations of the gastric mucosa.

3- Hemorrhagic disease of the newborn resulting from a deficiency in vitamin K–dependent coagulation factors. levels of clotting factors II, VII, IX, and X decline rapidly after birth, reaching their nadir at 48-72 hours of life. In 0.25%-0.5% of neonates, severe hemorrhage may result..

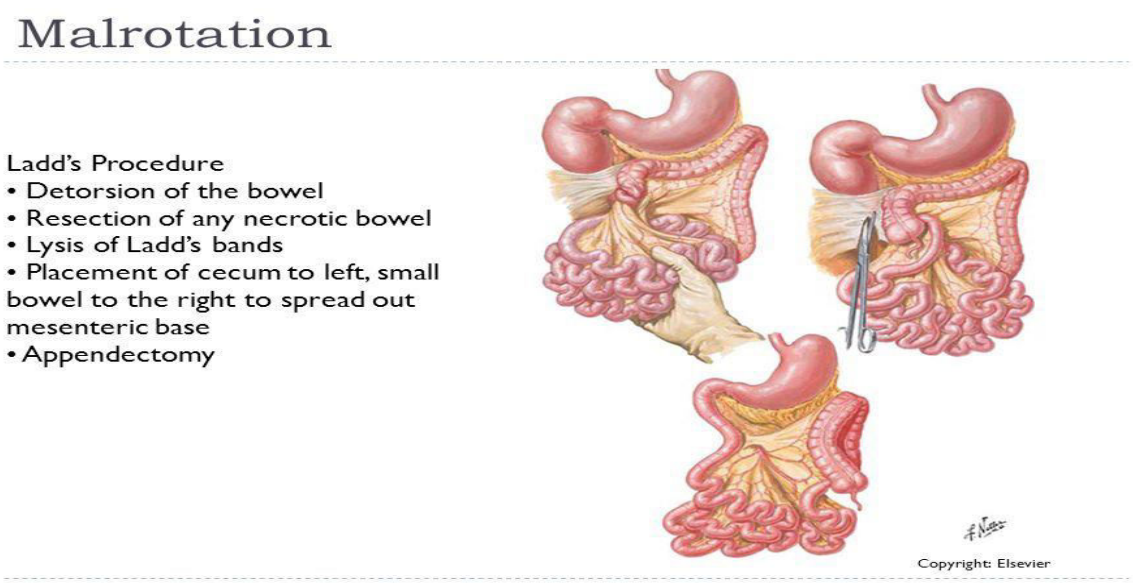
Neonatal causes of lower GIT bleeding

1- Anorectal Fissures are among the most common causes of lower GI bleeding in neonates. Stooling is often painful and in infants is characterized by straining, grunting and arching while passing a bowel movement. They produce bright red blood that streaks the stool or causes spots of blood in the diaper that is caused by a tear at the mucocutaneous line most commonly located dorsally in the midline.

2- Necrotizing enterocolitis (NEC) usually develops within 10 to 16 days after birth most commonly in premature infants, though can present in 13% of term infants. Although the pathophysiology is currently unclear. the underlying mechanism is believed to involve a combination of poor blood flow and infection of the intestines. Symptoms of this condition include abdominal distension, poor feeding, vomiting, diarrhea, frank or occult bloody stools, lethargy and apneas.

3-Malrotation with midgut volvulus is diagnosed with the sudden onset of melena in combination with bilious emesis and abdominal distention in a previously healthy neonate. Immediate upper GI contrast study should be performed to confirm diagnosis of malrotation with midgut volvulus. Immediate laparotomy reveals the anomaly and allows derotation of the bowel, assessment of intestinal viability, possible bowel resection, and performance of a Ladd procedure.

Ladd's procedure:



Causes of GI bleed in infants :

Hematemesis, melena	Hematochezia
Esophagitis	Anal fissures
Gastritis	Intussusception
Duodenitis	Infectious colitis/enteritis
Coagulopathy	Dietary protein intolerance
	Meckel's diverticulum
	Vascular malformation
	Coagulopathy

Common causes of bleeding in children (1 Month to 1 Year)

Upper GI tract bleeding :

1- Esophagitis (Peptic esophagitis) is the most common cause of bleeding in children aged 1 month to 1 year. This condition is caused by gastroesophageal reflux and is present in infants with regurgitation, dysphasia, odynophagia and failure to thrive.

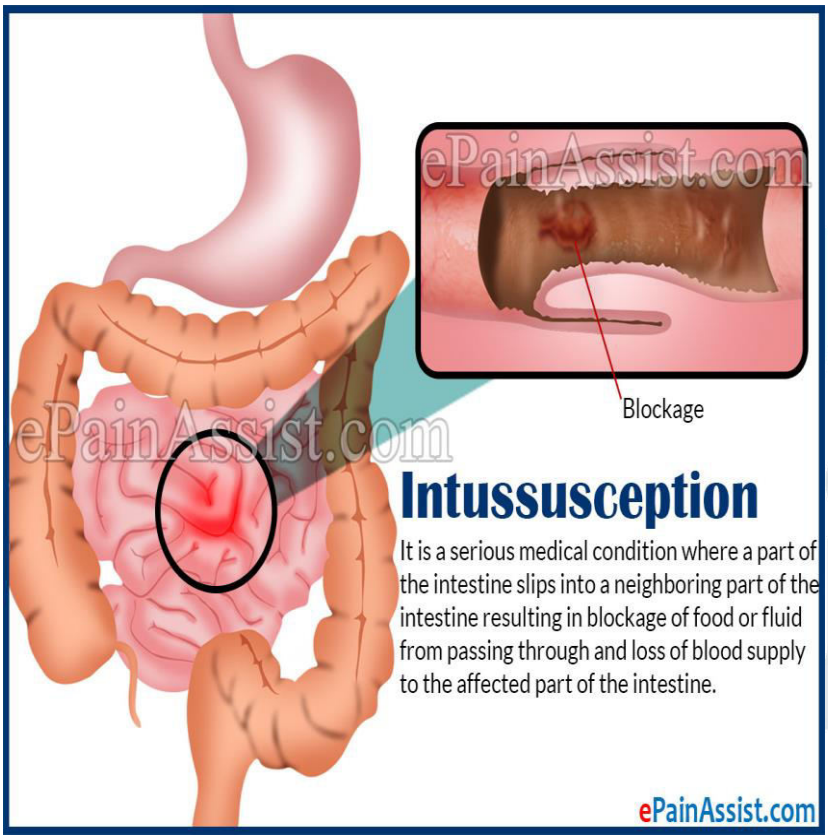
2- Gastritis can be distinguished as primary or secondary in etiology. Primary gastritis is correlated with Helicobacter pylori infection and is the most common cause of gastritis in children. Other causes of gastritis are non steroidal anti- inflammatory drug use, Zollinger-Ellison syndrome, and Crohn disease.

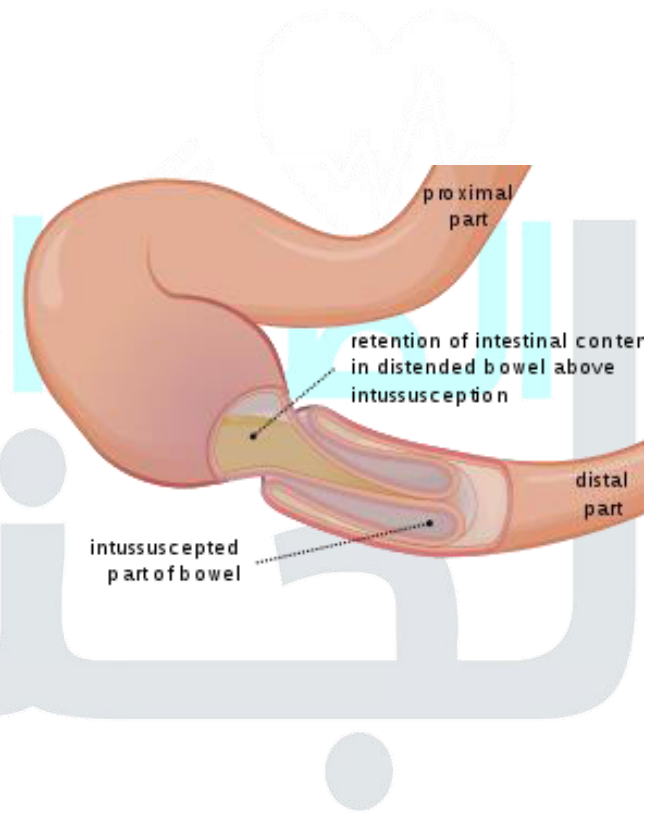
Lower Gastrointestinal tract bleeding :

1- Anal fissures produce bright red blood that streaks the stool or causes spots of blood in the diaper that is caused by a tear at the mucocutaneous line. Anal fissures can be diagnosed with an anal examination

2- Intussusception is the most common cause of lower GI bleeding in infants ranging from 6-18 months of age. Symptoms include cramping, abdominal pain, vomiting, a palpable sausage shaped mass, and currant jelly stools are common in patients with intussusception .

Intussusception :





3- Gangrenous bowel is the second most common cause of lower GI bleeding of this age group. Causes include malrotation with volvulus, omphalomesenteric remnant with volvulus, internal hernia with strangulation, segmental small-bowel volvulus, and on rarely, sigmoid volvulus.

4- Milk protein allergy causes a colitis that may be correlated with occult or gross lower GI bleeding. It is caused by an adverse immune reaction to cow's milk and have additional symptoms that can include diarrhea, weight loss, vomiting, and irritability.

Causes of GI Bleed in Children 1 - 2 yrs

Upper GI bleeding	Lower GI bleeding
Esophagitis	Anal fissures
Gastritis	Infectious colitis
Peptic ulcer disease	Polyps
Mallory-Weiss tears	Lymphoid nodular hyperplasia
Esophageal varices	IBD
Pill ulcers	HSP
Swallowed epistaxis	Intussusception
Foreign body	Meckel's diverticulum
Coagulopathy	HUS
	Sexual abuse
	Coagulopathy

Common causes of bleeding in children (1 to 2 years)

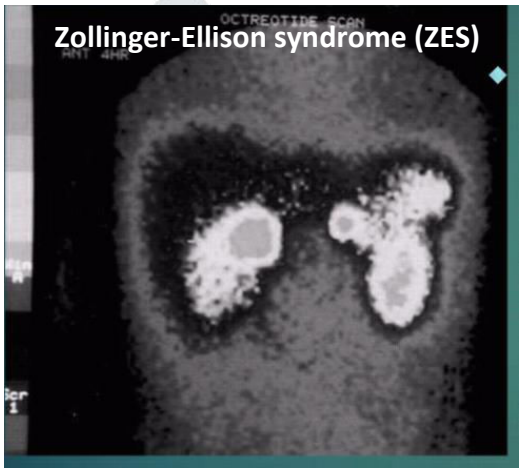
Upper GI tract bleeding:

1- Peptic ulcer disease is most common in children greater than 1 year old and is the most common cause of hematemesis. Peptic ulcer disease occurs when the protective mucus layer wears away allowing damage to occur from the natural acids of the stomach.

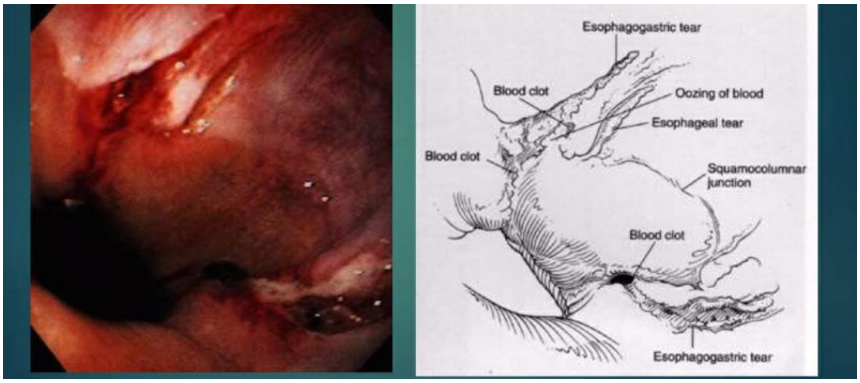
Most of the peptic ulcers occurring in children of this age range are secondary to other systemic diseases, such as burns (Curling ulcer), head trauma (Cushing ulcer), malignancy, or sepsis.

2-Gastritis can be distinguished as primary or secondary in etiology. Primary gastritis is correlated with Helicobacter pylori infection and is the most common cause of gastritis in children. Other causes of gastritis are non steroidal anti- inflammatory drug use, Zollinger-Ellison syndrome, and Crohn disease.

Zollinger-Ellison syndrome (ZES) is a rare condition characterized by peptic ulcers that are refractory to conventional medical therapy. Gastrin-producing tumors or gastrinomas cause excessive gastric acid secretion, leading to these ulcers of the upper gastrointestinal (GI) tract, as well as diarrhea and severe abdominal pain



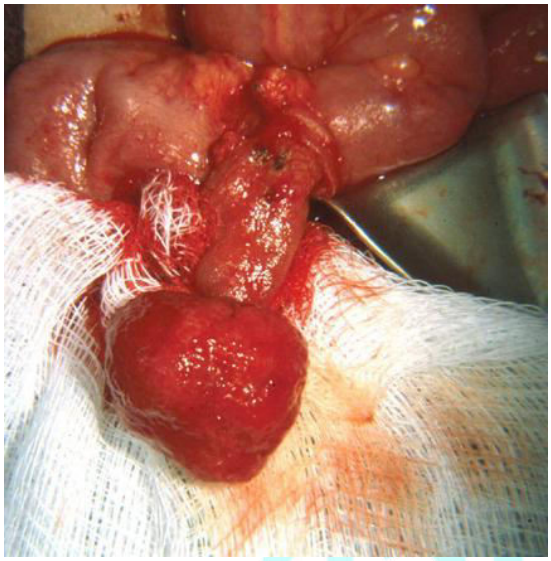
Mallory-Weiss Tear :



Lower GI tract bleeding:

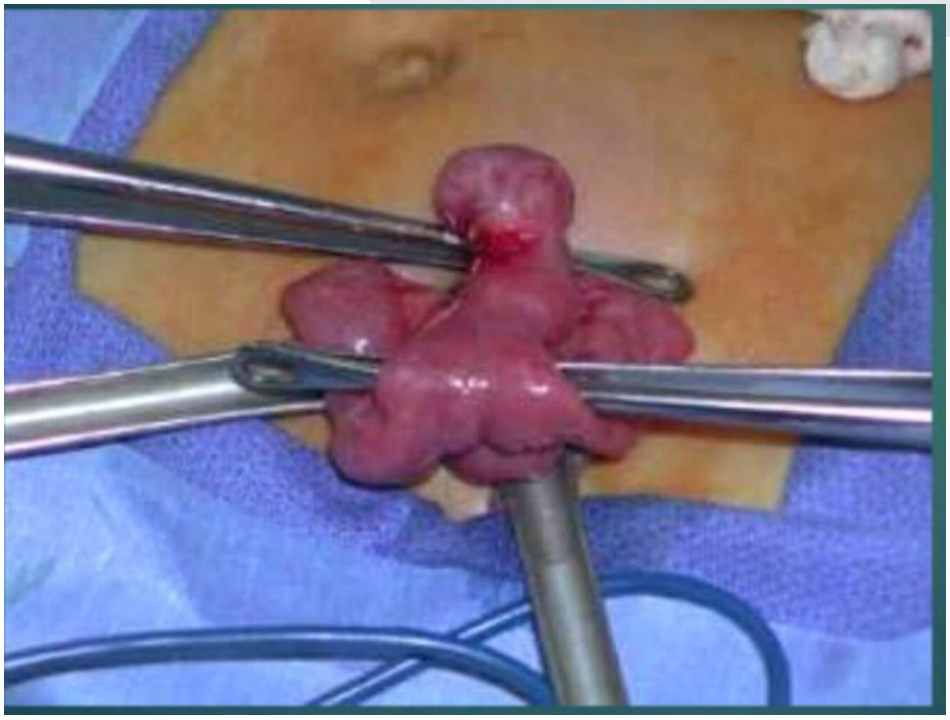
1- Polyps are mainly found in the juvenile type of this age group and are located throughout the colon. These are benign hamartomas and usually require no treatment because they autoamputate. Children present with painless bleeding per rectum, which often streaks the stool with fresh blood.

Intraoperative view of a bleeding juvenile polyp:



2- Meckel's diverticulum consists of a small pouch that is a remnant of tissue from prenatal development in the wall of the intestine located close to the junction of the small and large intestines. The remnant tissue produces acid similar to the tissue of the stomach which can lead to ulcers unless treated. If remained untreated, the ulcer can rupture, causing waste products from the intestine to leak into the abdominal cavity. Peritonitis can result in a serious abdominal infection and can ultimately lead to a blocked intestine which inhibits the passage of digested food resulting in intestinal obstruction.

Intraoperative view of the bleeding Meckel's diverticulum.



Common causes of bleeding in children (2 years and above)

-Upper Gastrointestinal tract bleeding:

Esophageal and gastric varices :

Esophageal varices : are caused by portal hypertension which occurs when there is increased resistance to blood flow through the portal system that is due to prehepatic, intrahepatic, and suprahepatic obstruction, but the most common causes of portal hypertension in children are portal vein thrombosis & biliary atresia .

Gastric varices : are most commonly found in the fundus and are characterized as dilated blood vessels.

-Lower GI tract bleeding :

Polyps are the most common cause of lower GI bleeding in children older that 2 years. They are located throughout the colon and are characterized as benign hamartomas and usually require no treatment because they autoamputate. Children present with painless bleeding per rectum, which often streaks the stool with fresh blood. Colonoscopy is the diagnostic evaluation of choice because it allows examination of the entire colon and potential excision of bleeding polyps when they are identified.

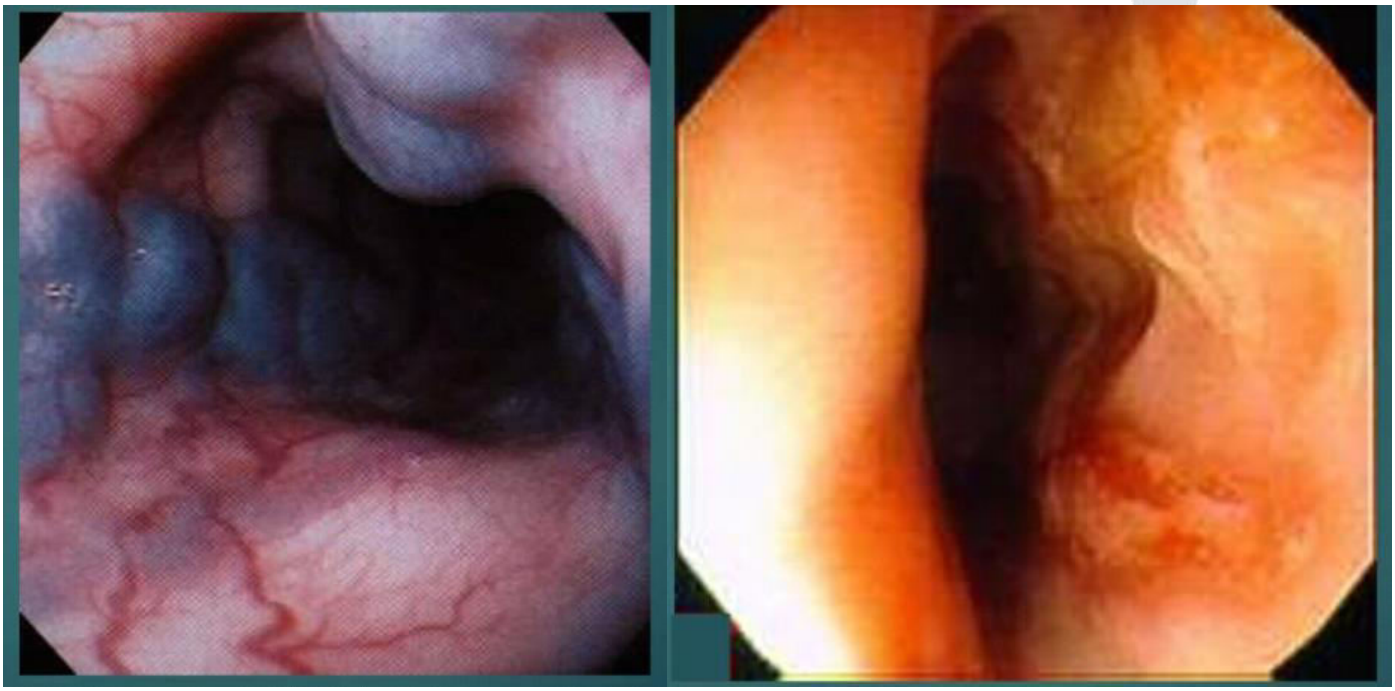
Inflammatory bowel disease refers to ulcerative colitis and crohn's disease, which are chronic diseases that result in inflammation of the intestines. Although bleeding may be less common in individuals diagnosed with crohn's disease compared to ulcerative colitis, both may consist of bloody diarrhea which can lead to acute or persistent bleeding resulting in anemia.

Infectious diarrhea is suspected when lower GI bleeding occurs in association with profuse diarrhea. Recent antibiotic use raises suspicion for antibiotic associated colitis and clostridium difficile colitis.

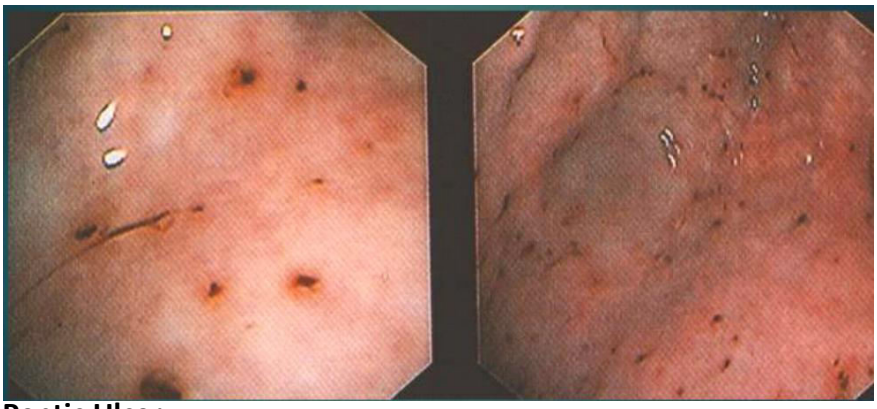
Vascular lesions consist of a variety of malformations that include hemangiomas , arteriovenous malformations, and vasculitis. Lesions located in the colon can be diagnosed with colonoscopy. However, bleeding can cause this to be challenging making localizing the bleeding practically impossible.

Esophageal varices:

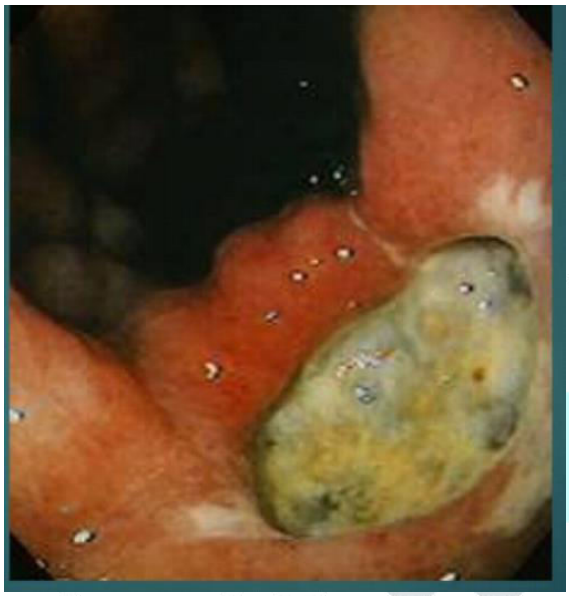
Erosive esophagitis :



NSAID induced ulcers



Peptic Ulcer



Common Causes of GIT Bleeding

Age Group	Upper Gastrointestinal Bleeding	Lower Gastrointestinal Bleeding
Neonates	Swallowed maternal blood Hemorrhagic disease of the newborn Coagulopathy Esophagitis Stress Gastritis Gastroduodenal ulcers Duplication cyst	Swallowed maternal blood Anorectal fissures Necrotizing enterocolitis Malrotation with midgut volvulus Coagulopathy Hirschsprung's disease
1 month to 2 years	Esophagitis Gastritis Gastroduodenal ulcer NSAID-induced ulcer Foreign body ingestion	Anorectal fissures Allergic colitis (cow's milk protein allergy) Intussusception Meckel's diverticulum Gastrointestinal duplication Polyps Ischemic bowel secondary to volvulus
2 years and older	Esophageal varices Gastric varices Mallory Weiss tears	Infectious diarrhea Juvenile Polyps Inflammatory bowel disease Vascular lesions Hemolytic uremic syndrome (HUS) Henoch Schlonlein Purpura (HSP)

HISTORY

GENERAL QUESTIONS

- **Age**
- Acute or chronic bleeding
- Color & quantity of the blood in stools or vomitus
- Emesis & Antecedent symptoms
- History of straining
- Abdominal pain
- Trauma
- History of foods consumed or drugs

NEONATE :

- Milk or soy protein enteritis
- NSAIDs, heparin, tolazoline
- Indomethacin
- Maternal medications e.g. Aspirin , cephalothin & Phenobarbital
- Stress gastritis e.g. prematurity, neonatal distress, and mechanical ventilation

Children aged 1 month to 1 year

- Episodic abdominal pain that is cramping in nature, vomiting, and currant jelly stools (intussusception)
- Fussiness and increased frequency of bowel movements in addition to lower GI bleed (milk protein allergy)

Children aged 1-2 years

* Upper GI Bleed

- systemic diseases, such as burns (Curling ulcer), head trauma (Cushing ulcer), malignancy, or sepsis
- NSAID

* Lower GI Bleed

- Polyps :- painless fresh streaks of blood in stools

Children older than 2 years

- lower GI bleeding occurs in association with profuse diarrhea :- Infectious Diarrhea
- Recent antibiotic use : antibiotic-associated colitis and Clostridium difficile colitis
- A history of vomiting, diarrhea, fever, ill contacts, or travel → infectious etiology .
- Sudden onset of melena in combination with bilious emesis in a previously healthy, nondistended baby → intestinal malrotation .
- Bloody diarrhea and signs of obstruction → volvulus intussusception or necrotizing enterocolitis , particularly in premature infants
- Recurrent or forceful vomiting → Mallory-Weiss tears
- Familial history or NSAID use → ulcer disease

- Ingested substances, such as NSAIDs, tetracycline's, steroids, caustics, and foreign bodies, can irritate the gastric mucosa enough to cause blood to be mixed with the vomitus
- Recent jaundice, easy bruising, and changes in stool color → liver disease
- Evidence of coagulation abnormalities elicited from the history → disorders of the kidney or reticuloendothelial system

PHYSICAL EXAMINATION

- Signs of shock
  Airway, breathing, and circulation should be assessed to evaluate hemodynamic stability
- Vital signs, tachycardia, tachypnea, hypotension, orthostatic hypotension,
  General presentation should be noted, including confusion, irritability, and respiratory distress.
- Skin: pallor, jaundice, ecchymoses, abnormal blood vessels, hydration, cap refill
- Abdomen:
  - organomegaly, tenderness (right upper quadrant tenderness, or other signs or sequelae of chronic liver disease, ascites, caput medusa
  - Abdominal Surgical scars, Hyperactive bowel sounds (upper GIT bleeding)
  - Abdominal tenderness, with or without a mass(intussusception or ischemic Bowel disease)
- Perineum: fissure, fistula, trauma
- Digital Rectum Examination: polyps, mass, occult blood, evidence of child abuse

FURTHER ASSESSMENT

- Nasogastric aspiration and lavage
  - Clear lavage makes bleeding proximal to ligament of Treitz unlikely
  - Coffee grounds that clear suggest bleeding stopped
  - Coffee grounds and fresh blood mean an active upper GI tract source

- Is it really blood (haemoccult test
- Apt-Downey test in neonates
  - Used to differentiate between maternal and baby blood. blood placed in test tube → add sterile water (to hemolye the RBCs yielding free Hb) → mix with 1% sodium hydroxide if solution turns yellow or brown maternal blood

Table 126-12 Evaluation of Gastrointestinal Bleeding

LABORATORY INVESTIGATION	Sigmoidoscopy or colonoscopy
All Patients	Meckel scan
CBC and platelet count	Mesenteric arteriogram
Coagulation tests: prothrombin time, partial thromboplastin time	Video capsule endoscopy
Tests of liver dysfunction: AST, ALT, GGT, bilirubin	INITIAL RADIOLOGIC EVALUATION
Occult blood test of stool or vomitus	*All Patients*
Blood type and crossmatch	Abdominal x-ray series
Evaluation of Bloody Diarrhea	*Evaluation of Hematemesis*
Stool culture, *Clostridium difficile* toxin	Barium upper GI series if endoscopy not available
Sigmoidoscopy or colonoscopy	*Evaluation of Bleeding with Pain and Vomiting (Bowel Obstruction)*
CT with contrast	Abdominal x-ray series
Evaluation of Rectal Bleeding with Formed Stools	Pneumatic or contrast enema
External and digital rectal examination	Upper GI series

ALT, Alanine aminotransferase; *AST*, aspartate aminotransferase; *CBC*, complete blood count; *CT*, computed tomography; *GGT*, γ-glutamyltransferase; *GI*, gastrointestinal.

Laboratory studies

- CBC in all cases
hemoglobin, hematocrit, platelet count, wbc (Leukocytosis→ infectious etiology)
(Normal hematocrit → hypovolemia and hemoconcentration)

-prothrombin and partial thromboplastin times

-blood urea nitrogen , creatinine

(blood urea nitrogen—to–creatinine ratio >30 may be helpful to))distinguish UGIB from LGIB (specificity, 98%; sensitivity, 69%)

-liver enzymes (eg, aspartate transaminase and alanine aminotransferase),

- bilirubin
- *Albumin, total protein
- *type and crossmatch
- *ESR in all cases
- Stool to evaluate the presence of heme using hemoccult testing also for culture
- Plain abdominal X-ray (NEC in neonates)

Endoscopy

Urgent endoscopy, which is performed <12 hours after admission, is indicated for bleeding that requires transfusion or for hemodynamic instability; otherwise, endoscopy can be performed within the first 24 hours of admission. The reported efficacy of endoscopy for controlling UGIB is approximately 90%

- Identifies site of upper GI bleed in 90 % cases
- FORREST classification:

I – Active hemorrhage

Ia :- bright red bleeding

Ib :- slow bleeding

II – Recent hemorrhages

IIa :- non bleeding visible vessel

IIb :- adherent clot on base of lesion

IIc :- flat pigmented spot

III – No evidence of bleeding

- Colonoscopy

- Identifies site of lower GI bleed in 80 % cases
- Polyps, hemangiomas, vascular malformations, ulceration, biopsy

- Barium contrast studies
  -GER, FB, esophagitis, IBD, Polyps, malrotation, volvulus

- Doppler USG (Intussusception)

- Barium enema (IBD, polyps, intussusception)

- H.pylori stool antigen, IgG levels, rapid urease test or mucosal biopsy

- Ultrasound abdomen (intussusception)

- Arteriography (helpful when endoscopy has failed)

- Treatment of GI bleeding should begin with an initial assessment, rapid stabilization, and a logical sequence of diagnostic tests.
- When a treatable cause is identified, specific therapy should be started.
- In many cases, the amount of blood is small, and no resuscitation is required.
- For children with large-volume bleeds, the **ABCs of resuscitation (airway, breathing, circulation)** should be addressed first.
- Oxygen should be administered and the airway protected with an endotracheal tube if massive hematemesis is present
- cardiopulmonary and urine output monitoring

INITIAL MANAGEMENT

The initial approach to all patients with significant GI bleed is :

- to establish adequate oxygen delivery.
- to place intravenous line.
- to initiate fluid and blood resuscitation
- to correct any underlying coagulopathies.

Therapy

Supportive care : begin promptly

- Bowel Rest and NG decompression (esp. in NEC)
- IV fluids
- Blood products (FFPs, RCC)

Specific care :

- H2 receptor antagonists (cimetidine, ranitidine, etc.)
- Proton pump inhibitors (omeprazole, lansoprazole)
- Vasoconstrictors (somatostatine analogue[Octreotide], vasopressin, Beta Blockers)
- -Inj Vitamin K (HDN)
- Stool Softeners (Anal Fissure)
- Antibiotics (for enteritis, Cl. Difficile ass. Colitis)

- H.pylori Eradication (triple therapy)

- Endoscopic treatments include the application of clips, coagulation, banding, injection, sclerotherapy, and the use of tissue adhesives
- angiography is indicated when endoscopic therapy is unsuccessful.

Surgical options

If all medical measures fail

- Laprotomy

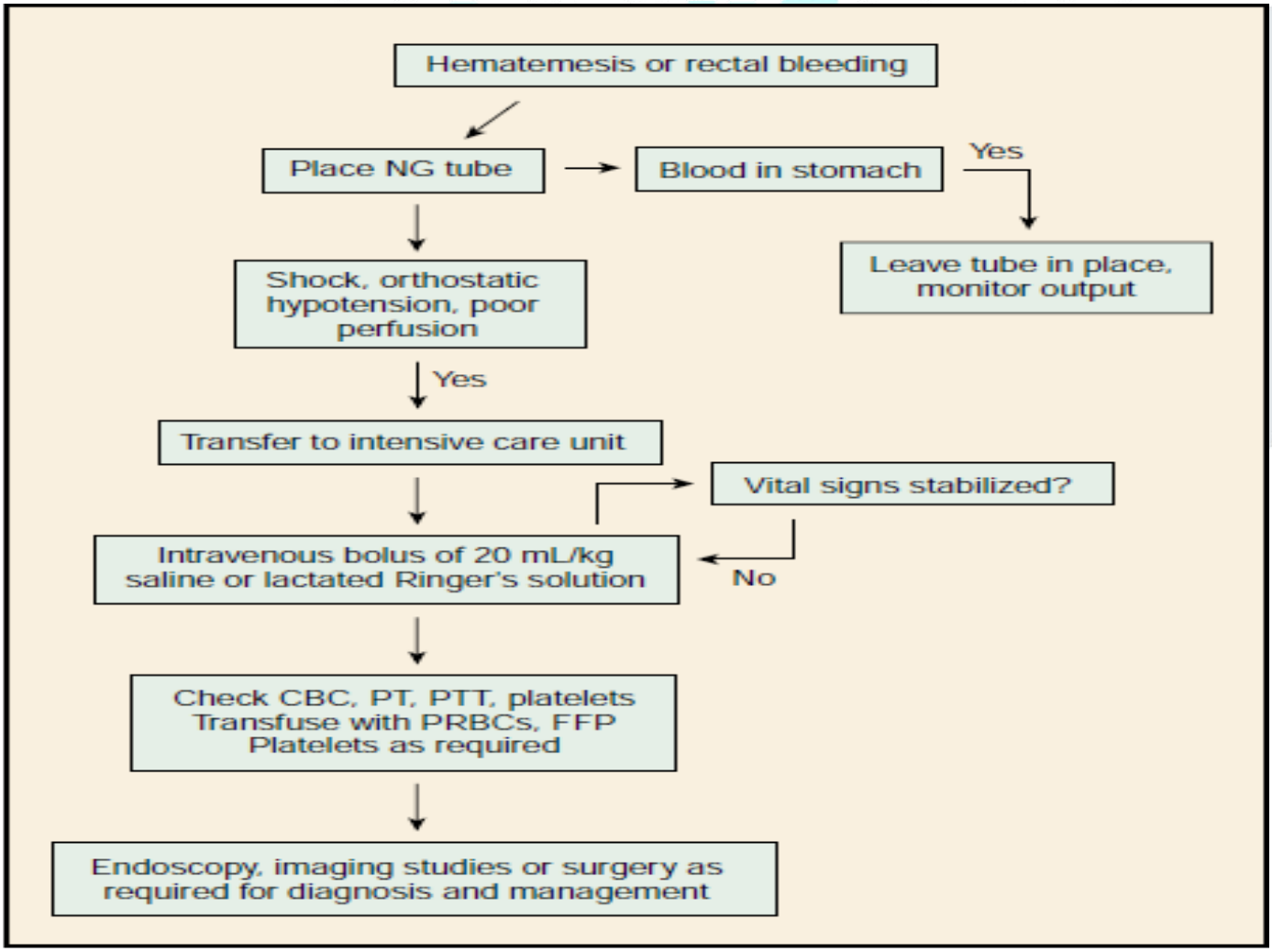
- Laproscopy

- Vagotomy

- Pyloroplasty

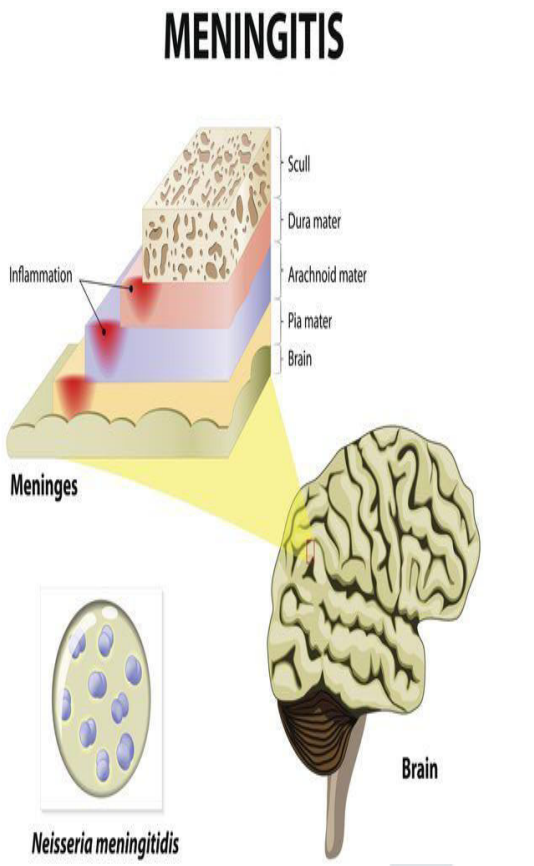
- Fissurotomy, fistulectomy

- Diverticulectomy



Meningitis

- **Introduction :**
  - Meningitis : is inflammation of the leptomeninges .
  - One of the most common CNS infections .
  - It may involve both the meninges and brain parenchyma (meningoencephalitis).



► **Acute bacterial meningitis .**

► **Aseptic meningites .**

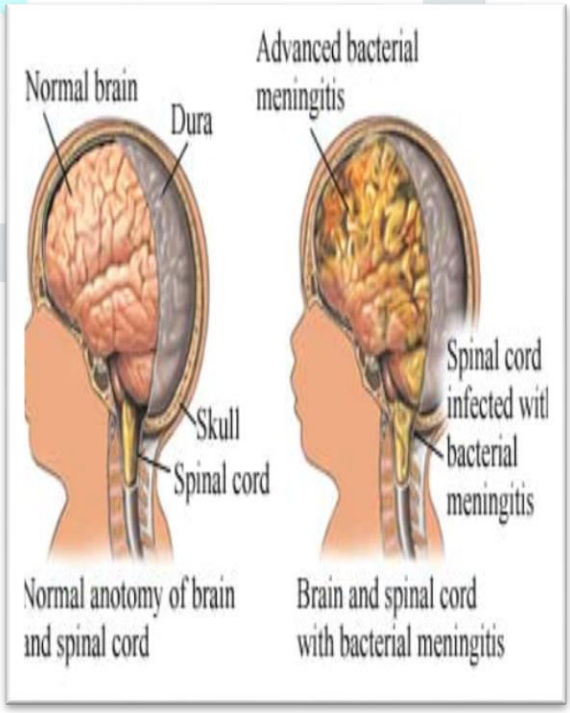
- **Acute Bacterial Meningitis:**
  - **NEONATAL MENINGITIS**
  - **POST-NEONATAL MENINGITIS .**

Neonatal Meningitis

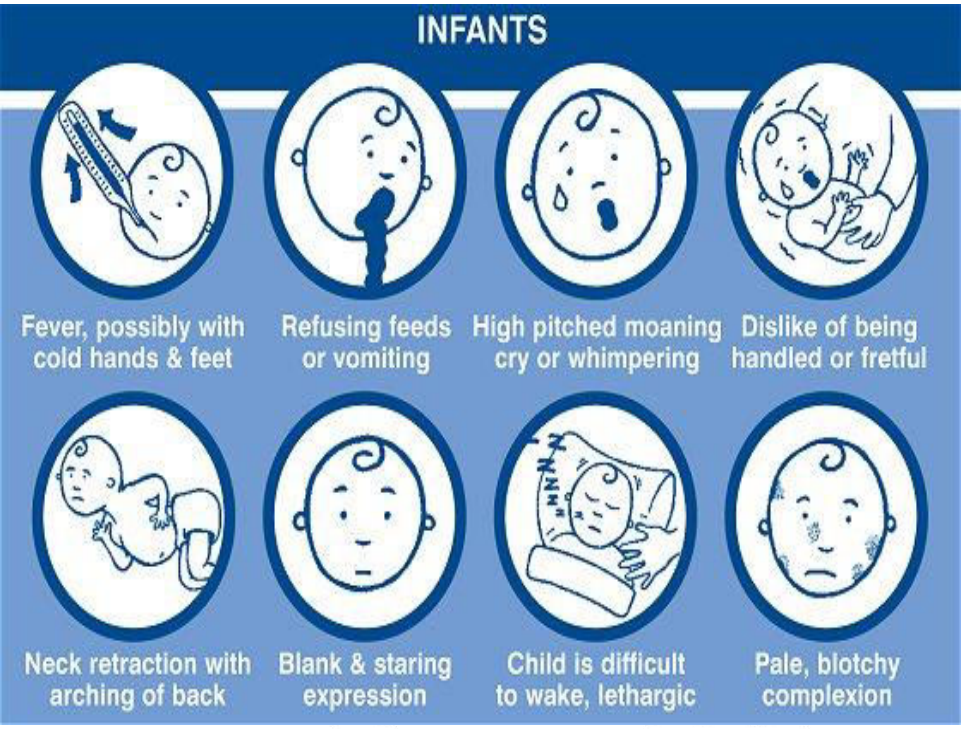
☒ **Definition:** It's inflammation of meninges due to bacterial invasion in the first 90 days of life .

☒ **Etiology :**

- GBS (predominantly type 3)
- E.coli (predominantly those containing the K1 polysaccharide) .
- Listeria Monocytogenes .
- These 3 categories constitute about 75% of the causes .
- The 25 % (peusomonas ,proteus ,klibsella ….)
- Neonatal meningitis most frequently results from the bacteremia that occurs with neonatal sepsis .
- Meningitis can also result from scalp lesions , particularly when developmental defects lead to communcation between the skin surface and the subarachnoid space , which predisposes to thrombophlibitis of the diploic veins .
- Less commonly , meningitis can result from direct extension to the CNS from a contagious otic focus (otits media) .

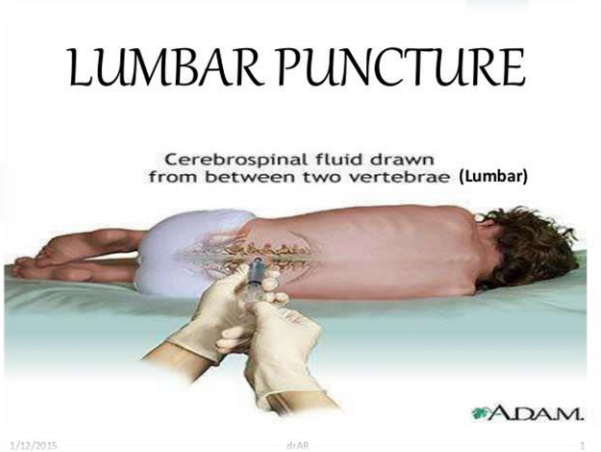


- **The most important symptom is :**
  Poor feeding , Its always indication of admission



- **Neonatal Meningitis (S & S) :**
  - Usually , manifestations are those associated with neonatal sepsis : temperature instability, respiratory distress, jaundice, apnea .
  - CNS signs : lethargy , seizures (particularly focal) , vomiting and irritability more specifically suggest meningitis .
  - A bulging or full fontanelle occurs in about 25% and nuchal rigidity in only 15% .
  - Cranial nerve abnormalities (especially the 3rd , 6th and 7th) may also be present .

- **Diagnosis**
  - Definitive Diagnosis is made by CSF examination via LP , which should be performed in any neonate suspected of having sepsis or meningitis .



- **Lumbar puncture:**
  - Put the patient in left lateral position with neck flexion and knee in full extension (fetal position) .
  - Determine L3 –L4 OR L4 –L5 depend on post. iliac crest .
  - Sterile the area in circular manner .
  - Inject local anesthesia under the skin .
  - By spinal needle enter to subarachnoid space

- However, LP can be difficult to perform in a neonate , and there is some risk for hypoxia.
- Poor clinical condition (resoiratory distress, shock , thrombocytopenia) makes LP risky .
- If LP is delayed , the neonate should be treated as though meningitis is present .
- We have to take 5 tubes of CSF FOR :
  - Cytology . Chemistry. Gram stain . Antiginicity . Culture .

- **Laboratory Values :**

	WBCs (/microL)	Protein (mg/dL)	Glucose (mg/dL)
Normal	0 - 5 (Lymphocytes)	20 – 40	50 – 100 ½ - 2/3 blood glcouse
ABM	100 - 10,000 (PMNs)	> 100	> 25

Normal RBC = 0 , If there is blood with CSF :

- Trauma
  1- Clear with time .
  2- Do centrifugation and see RBC-WBC ratio.

- Subarachnoid hmg

- **Gram stain result (Need 10 min)**

E coli	gram – bacilli
Listeria	Gram + bacilli
H.Infulenza	Gram - cocobacilli
N.Meningitidis	Gram – diplococi
GBS	Gram + coci
Strep pneumonia	Gram + dipolccoi

- **Don't forget :**
  - ❑ Blood glucose
  - ❑ Blood culture

- **When I have to repeat LP ?**
  - LP should be repeated at 24 - 48 hr if clinical response is questionable and at 72 hr when gram-negative organisms are involved (to ensure sterilization) .
  - Some experts believe that a repeat LP at 24 hr in neonates with GBS meningitis has prognostic value .
  - LP should not be repeated at the end of therapy if the neonate is doing well .

☒ **Prognosis:**

- Without treatment , the mortality rate from neonatal meningitis approaches 100% .
- With treatment , prognosis is determined by birth weight, organism and clinical severity .
- Mortality rate for gram-negative neonatal meningitis is 20 - 30% .
- Mortality rate for gram-positive neonatal meningitis (e.g. GBS) is 10 - 20% .
- For organisms that produce vasculitis , meningitis and brain abscess (necrotizing meningitis) , the mortality rate may approach 75% .
- Neurological sequelae (hydrocephalus , hearing loss, mental retardation) develop in 20 - 50% of infants who survive , with a poorer prognosis when gram-negative enteric bacilli are the cause .

☒ **Treatment:**

- Empiric treatment is begun with : ampicillin plus cefotaxime .
- Drug should be :
  - Cross BBB .
  - I V .
  - Broad spectrum .
  - Bactericidal .

- **Treatment duration :** Parenteral therapy for gram-positive meningitis is given for a minimum of 14 days, and for complicated gram-positive or gram-negative meningitis , a minimum of 21 days .

- Patients should be closely followed for neurological complications during the first 2 years of life :
  - Head circumference .
  - Hearing assessment .
  - Developmental assessment .

POST-NEONATAL MENINGITIS

☒ **Etiology**

In post-neonatal period , the most common organisms causing meningitis are :

- Neisseria meningitidis (meningococci).
- Streptococcus pneumoniae (pneumococci).
- Hemophilus influenza type b .
- Meningococci exist in the nasopharynx of about 5% of people and spread by respiratory droplets and close contact . Only a small fraction of carriers develop meningitis; what makes them susceptible is unknown .
- Children between 6 mo and 3 yr (peak = 1st year) are mostly affected , it also tends to occur in epidemics among closed populations (e.g. boarding schools ,military barracks and college dormitories)
- ***Pneumococci*** are the most common cause of meningitis in older children and adults .
- Especially at risk are patients with chronic otitis , sinusitis , mastoiditis , CSF leaks , recurrent meningitis , pneumococcal pneumonia , sickle cell disease or asplenia .
- Incidence of pneumococcal meningitis is decreasing because of routine vaccination (ideally!!!) .

- Bacteria typically reaches the meninges by hematogenous spread from sites of colonization in the nasopharynx or other foci of infection (e.g. pneumonia) .
- Bacteria can also enter CSF by direct extension from nearby infections (sinusitis, mastoiditis) or through exterior openings in normally closed CSF pathways (e.g. due to meningocele , spinal dermal sinus , penetrating injuries and neurosurgical procedures)

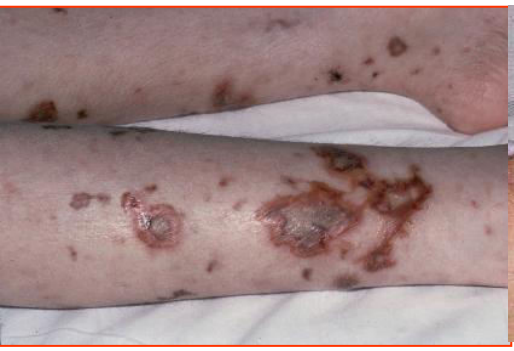
☒ **Signs & symptoms :**

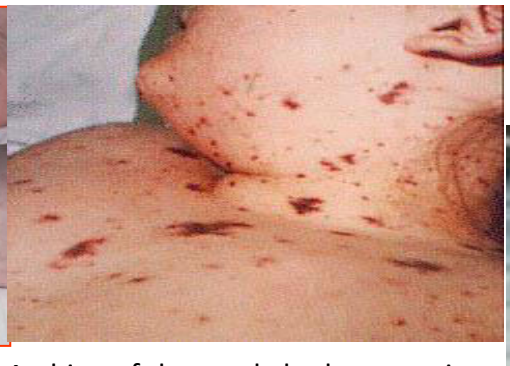
- A respiratory illness or sore throat often precedes the more characteristic symptoms of fever, headache, stiff neck and vomiting.
- Brudzinski's and Kernig's signs are present in ½ of patients .
- Neck stiffness and Brudzinski's and Kernig's signs are termed meningeal signs or meningismus ; they occur because tension on nerve roots passing through inflammed meninges causes irritation .

- **Brudzinski's Sign :** Attempts at neck flexion induce flexion of the hip or knee .
- **Kernig's Sign :** Resistance to passive extension of the knee while the hip is flexed.

- Adults may become desperately ill within 24 hr , and children even sooner .
- Seizures occur in about 30% of patients .
- Cranial nerve abnormalities (e.g. 3rd or 7th cranial nerve palsy ; occasionally deafness) and other focal deficits occur in 10 - 20% .
- In patients > 2 yr , changes in consciousness progress through irritability , confusion , drowsiness , stupor and coma .
- Opisthotonos posturing may occur .
- Dehydration is common , and vascular collapse produces shock .
- A maculopapular or hemorrhagic petechial rash often appears soon after disease onset .
- Fulminant meningococcemia syndromes include Waterhouse-Friderichsen syndrome (septicemia, profound shock, cutaneous purpura and adrenal hemorrhage), sepsis with multiple-organ failure , shock and DIC .

- **Meningococcal Rash:**

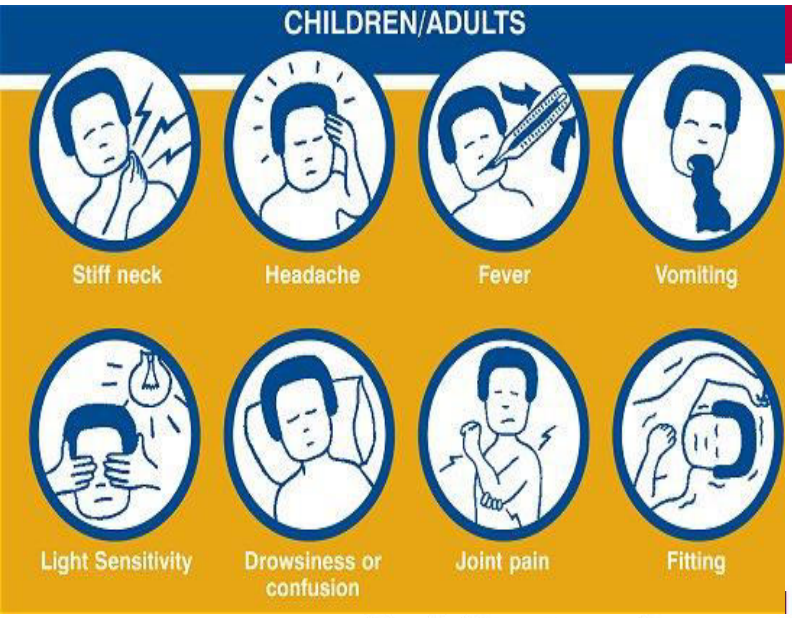




- **Opisthotonos Position:** Arching of the trunk, bad prognosis :

☒ Complications

- Systemic complications include hyponatremia due to SIADH , DIC and septic shock .



☒ Diagnosis

- Because acute bacterial meningitis , especially meningococcal , can be lethal within hours , it must be diagnosed and treated rapidly .
- Prompt LP is required but it should not delay immediate treatment with antibiotics and corticosteroids

- Gram stain shows organisms in CSF in 80% of patients
- CSF neutrophil count usually exceeds 2000/microL .
- Glucose is usually < 40 mg/dL because of impaired - CNS glucose transport and glucose consumption by neutrophils and bacteria .
- Protein is typically > 100 mg/dL (up to 14% of patients may have a CSF protein level < 100 mg/dL on the initial LP) .
- Cultures are positive in 90% of patients ; they may be falsely negative in patients who are partially treated .

- Peripheral blood tests include blood cultures (positive in 80 %).
- cell count with differential , electrolytes , glucose , renal function and coagulation tests .
- Serum Na is monitored for evidence of SIADH , and coagulation results are monitored for evidence of DIC .
- Urine and any nasopharyngeal or respiratory secretions and skin lesions are cultured .
- ***Waterhouse-Friderichsen*** syndrome should be suspected in any febrile patient who remains in shock despite adequate volume replacement and who has rapidly evolving purpura and evidence of DIC .

- Serum cortisol level is measured , and CT , MRI , or USS of the adrenal gland is done .

☒ **Prognosis**

- Early antibiotics and supportive care have reduced the mortality rate of ABM to < 10% .
- However , if meningitis is treated late or occurs in neonates or immunocompromised patients, death is common .
- A poor outcome is predicted by persistent leukopenia or development of Waterhouse-Friderichsen syndrome .
- Survivors occasionally have deafness , other cranial nerve deficits , cerebral infarction , recurrent seizures or mental retardation .

☒ **Treatment**

- If meningitis is suspected, antibiotics and corticosteroids are given as soon as blood cultures are drawn or even before.
- **Dexamethasone** (0.15 mg/kg IV q 6 hrs.) should be given 15 min before the 1st dose of antibiotics and continued for 4 days .
- It may prevent hearing loss and other neurologic sequelae , possibly by inhibiting release of proinflammatory cytokines triggered by antibiotic-induced bacterial lysis.
- Dexamethasone should not be given to patients with immunodeficiency because it may impair host defenses against non-bacterial meningitis.

  A- 3 generation cephalosporin
  (Cefotaxime or ceftriaxone)
  B- vancomycin

- ***Treatment Duration***

  Generally :

. If N .MENINGITIDS : 5 -7 DAYS .
. IF H.INFLUENZA : 7- 10 DAYS .
. PNEUMPCOCUS : 10 – 14 DAYS .

- Drug doses are not reduced when clinical improvement occurs because drug penetration commonly decreases as meningeal inflammation decreases .

☒ **Prevention**

- A conjugated pneumococcal vaccine effective against 7 serotypes , including > 80% of organisms that cause meningitis is recommended for all children .
- It is recommended for children aged 2 - 23 mo.
- Prevnar , peumovax ….
- Routine vaccination for H.influenza type b is highly effective and begins at age of 2 months .
- a quadrivalent meningococcal vaccine is given to children > 2 years with immunodeficiency or functional asplenia .

- **Aseptic meningitis**

- **All non-bacterial causes of meningitis**
- **Most common cause is viral**
- **Typically less ill appearing than bacterial meningitis**

☒ **Definition**

- A syndrome characterised by acute onset of meningeal symptoms and fever, with pleocytosis of the cerebrospinal fluid and no growth on routine bacterial

- Viral meningitis is common and often goes unreported.
- In the absence of a LP, viral and bacterial meningitis cannot be differentiated with certainty, and all suspected cases should therefore be referred.
- LP & analysis of cerebrospinal fluid may be done primarily to exclude bacterial meningitis, but identification of the specific viral cause is itself beneficial.

☒ **Viral diagnosis:**

1- informs prognosis
2-enhances care of the patient
3-reduces the use of antibiotics
4-decreases length of stay in hospital
5- help to prevent further spread of infection.

- **How common is viral meningitis?**
  Viral meningitis can occur at any age but is most common in young children. Usually affected children under 5 years of age

☒ **The most common cause of viral meningitis:**

- Mump & measles viruses
- Enteroviruses
- herpes virus
- HIV

☒ **What is the initial approach to the patient?**

- Viral meningitis and bacterial meningitis are both characterized by acute onset of fever, headache, photophobia, and neck stiffness, often accompanied by nausea and vomiting.
- Untreated patients with bacterial meningitis show progressive deterioration in mental status, whereas spontaneous recovery is usual in viral cases.
- Particular caution is warranted with young children, in whom meningitis is manifest as fever and irritability, without, as a rule, evidence of meningeal irritation.

- Assessment should include evaluation for possible encephalitis, suggested by seizures, reduced Glasgow coma score, or focal neurological signs.
- **Suspected encephalitis warrants empirical antiviral treatment with intravenous aciclovir.**
- CSF needs to be processed promptly to avoid depletion of cell counts during transport or storage.
- Although characteristically associated with a mononuclear pleocytosis, neutrophils may predominate initially in viral meningitis

- **CSF finding**

	Cell Count (WBC cells/microL)	**Protein** (mg/dL)	**Glucose** (mg/dL)
Normal	0-5 cells/microL	< 40 mg/dL	40 - 70 mg/dL
Bacterial	↑ PMNs	↑	↓
Viral	↑ Lymphocytes	↑ /normal	normal

- The usual initial approach to viral diagnosis is to test the CSF for enteroviruses, HSV, varicella zoster virus by using polymerase chain reaction technology, estimated to be threefold to 1000-fold more sensitive than routine viral culture.
- identification of a viral cause has been shown to be beneficial, facilitating reduced administration of antibiotics and decreased length of stay in hospital.

☒ **Treatement**

- Supporative exept for HSV?

Juvenile idiopathic arthritis

"juvenile rheumatoid arthritis"

- **Commonest** type of arthritis in children and adolcents (chronic).
- In children < 16 yrs for more than 6 months
- Autoimmune non infective , inflammatory
- Age group →two peaks (1-3 years) and (8-12) but can happen at any age in childhood period.
- Females > males → more with digoarticular type.
- Etiology is unknown but pathophysiology :
  - common maifestaion is chronic synovitis → thick synovium + hyperscular with lymphocyte infiltration → release of tissue protease and collagenase
- If left untreated → tissue distruction (articular cartilage) and bone strucre.

- It can be devided into several subtypes according to :
  1- number of joints involved (5 joints more or less)
  2- presence of sacroiliac involvement
  3- presence of systemic features

Common features :

1- slow onset
2- actual joint swelling noticed by the child or parent (can be confused with trauma even of tho traumatic effusions are rare in children)
3- pain
4- stiffness and limitation of movement (refuses to use the joint)
5- moving stiffness
- Red eyes + limping + arthritis + knees pain + extremities pain

By examination:

1- Signs of inflammation on affected joint (tenderness, effusion, erythema)
2- Limitation of joint movement (due to pain, swelling, contracture)
3- In children, they have active growth plate so:
   - it may be possible to find bone abnormalities.
   - You may also find length discrepancy if it's asymmetrical.

- These patients are at high risk of for iridocyclitis and uveitis, so if +ve ANA → the child is at high risk for chronic uveitis, but not all types of JIA have the same risk .

- Oligoarthritis + female + +ve ANA → 80% risk

- it may be asymptomatic until visual loss → but it's treatable, so it's crucial to do regular ophthalmology visits and slit-lamp examination to anterior chamber → every 3-4 months

Types of JIA :

1- **Oligoathritis 55%**
2- **Polyarthritis 40%**
3- **Systemic onset arthritis**
4- **Psoriatic arthritis**
5- **Enthestitis arthritis**

► **oligoarthritis** : pauciarticular

- most common type , often mild , less than 5 joints →medium to large joints , common knee →ankle→ wrist
- rarely small joints (toes or fingers) بس ممكن تصير بحالات نادرة
- girls > boys
- the patient may be well without systemic inflammation or lab evidence of systemic inflammation (↑wbc, ↑ ESR, ..)
  all tests normal except ANA it's +ve in 60%.
- The subset later develop polyarticular disease (extended oligoarthritis)
- Most likely type to cause anterior uveitis , and carries excellent outcome (90% will have complete remission)

► **Polyarthritis**

- 2nd most common type
- Onset: sudden or steadily more joints over months.
- It can present at any age but peak in early childhood, other peak in adolescence but differ by :
  1-+ve anti-CCP antibodies, +ve rheumatoid factor, +ve ANA
  2- it represent with true adult RA →same course and prognosis
  * 50% complete remission but carry some risk for disability
- Clinically :
  1- Symmetrical arthritis
  2- Affect any joint but more in small joints of hands
  3- Malaise, low grade fever, growth retardation
- Long term complications:
  1- Sublaxation and fusion of cervical spine with loss of lordosis and limit extension
  2- Associated with erosions and deformity (bouonnieve finger) → PIP flexion, DIP hyperextention

► **Systemic onset JIA** (still's disease)

- Usually > 5 joint
- The patient presentation will be systemic inflammation then arthritis.
- Definitive Dx → wait until the development of arthritis .
- Systemic inflammation →→6 weeks – 6 months →→ arthritis (extensive polyarticular) and resistant to tt (in small joints) .

- Clinically :
  1- Spiking fever *39 c) once or 2 times daily
  2- Hepatospleenomegaly
  3- Generalized lymphadenopathy
  4- Serositisl (pluritis, pericarditis)
  5- Malaise, FTT, myalgia
  6- Salmon-pink macules (vary in size)

- Migrate to different sites every hour (trunk, proximal extremities or pressure areas)
- Female = male
- DX: -ve RF and –ve ANA
  ↑ (ESR, CRP, Ferritin), on CBC (neutrophilia, ↑platelet, anemia "in chronic", ↑wbc)

- Outcome variable depends on arthritis extention

► **Psoriatric arthritis:**
- Psoriatric rash + arthritis
- If no rash, at least 2 of the following :
  1- Clactylitis (sausage-like fingers)
  2- Nail pitting
  3- Psoriatric in 1st relatives
  4- Oncholysis (painless separation of nail from nail bed)

- Age : 11-12 yrs but boys may have it older than 12 and girls less than 11
- Plaques : typically on extensor side of joints, perineum, umbilicus, haired skin.

► **Enthesitis related arthritis**
- On <u>tendon insertion</u> (common in Achilles tendon)
- Boys > 6 years
- Has relation to inflammatory bowel and ankylosing spondylitis.
- -ve RF, -ve ANA, +ve HLA B27 (in 80%)
- Asymmetric in lower extremitis.
- Dx by Hx and examination, labs may be normal and not diagnostic.
  - we use lab testing for follow-up → CBC, ANA, RF, CRP, ESR, HLA B27, CCP, synovial fluid analysis.
  - CBC → degree of inflammation by WBC, platelets, anemia , lymphocytosis + thrombocytopenia→ high possibility of ALL.
  - ESR, CRP → usually high in systemic type and polyarthritis, and within normal range in oligo type, when it's high → do inflammatory markers → monitor activity of the disease.
  - ANA→ in oligoarthritis with high uveitis risk specially in less than 6 yrs in onset.
  - RF → in polyarticular in 10% of pts , titer doesn't correlate with the activity of the disease .

- Radiology :early changes (1st 6 months) like :
  1- Soft tissue swelling
  2- Periarticular osteopenia and new bone formation periosteal around affected joints.

- If disease continued > 6 months :
  1- Subchondral erosions and loss of cartilage.
  2- Many degrees of bone distruction then fusion.

- Diagnostic criteria :
  1- Age > 16 years
  2- Arthritis in one or more joints
  3- Duration > 6 months
  4- Exclude other forms of arthritis and connective tissue diseases.

- Complications :
  1- If uveitis untrated → visual loss or blindness
  2- Loss of function at affected joints due to contractures, loss of joint space.
- Long term comlications :
  1- Permanent joint damage
  2- Disproportionate limbs
  3- ↓Growth
  4- Anemia

Macrophage activation syndrome :

- One of the most serious complications → multisystemic organ failure with 8% mortality despite early detection and treatment.
- ↑Fever, liver dysfunction, lymphadenopathy, hepatospleenomegaly.
- Lab results :
  - Pancytopenia, highly elevated (ferritin, trigleceride, transaminase)
  - Evidence of DIC (↑D-dimer,↓ fibrinogen, abnormal blood smear)

- Treatment:

- 1st choice → NSAIDs → naproxen, indomethacin, sulindac, ibuprofen.
- 2nd line→ hydoxychloroquuinine, sulphasalazine.
- Methotrexate → tt of choice for polyarticular and systemic
- Should do regular monitoring because of one marrow suppression and hepatotoxicity.

IV fluids

IV fluids therapy:

- If the child was younger → high amount of fluids, so:
  infant > neonate > child 1 y > 2 y ..
- Male > female
- Premature > mature body , premature has high surface area and high water content → more loss
- Fluid loss :
  - Sensible 1- urine 2- stool
  - Insensible 1- skin 2- Breathing (surface area) : most common site of fluid loss

What is maintenance?

The amount of water that you need every day to excrete sodium salt to maintain a normal sodium osmolarity.

. Urine output plays a major rule in detecting the maintenance.
. Osmolarity : ADH (very narrow correction) \ water
. What triggers aldosterone production is renin.
. Volume → aldosterone, renin, sodium
  -Dehydration or low kidney perfusion

. Effective circulatory volume: assessment of hydration status volume
  volume of fluids that perfuse the tissue with O2.

. If the fluid is interstitial and not in circulation, it's not effective circulatory volume.
. Polyuria → directly with ASH

- The best way to know how much the baby loss of fluid is to know his weight previously and now, and measure the difference → the lost fluid.
  - 1Kg → 1 L
  - but it's not applicable, so we know the signs and symptoms of dehydration and the lost depends on the signs . (Vital signs changes & objective signs)

- Depressed anterior fontanelle → up to 18 months

- **Capillary refill:**
  - mild → maybe normal
  - moderate → up to 3 sec
  - sever → up to 5 sec
  * in neonates and small babies in big toe or heal , older age → fingers

- **Tachycardia** →>140 B\min "significant"
  > 160 severe tachycardia

- **Oliguria** → less than 1ml\Kg\Hr
  *less than 2 yrs or 10 Kg :
  - mild : 5% moderate : 10% severe : 15%
  * above :
  - mild : 3% moderate : 6% severe : 9%
- **Low urine output** → pre-renal due to low kidney perfusion
- **Low BP** → shock
- **Hyponatremia** → cerebral edema
  rapid correction → pontine myelinolysis
- **In non-dehydrated** pts : sodium 135-145 normal
  in dehydrated pts : 130-150 normal
- **GI losses** → hypokalemia
- **Renal impairment** → hyperkalemia

- Serum bicarbonate usually if low causes normal anion gap , if wide it's severe.
- In dehydrated pts the sodium in urine is low and high urine osmolarity.
- Repletion or deficit: not commonly used in normal conditions, used in diarrhea, dehydration, or any fluid loss.
- Maintenance: daily requirement
  give it orally, but if he can't tolerate oral intake give IV .

- Emergency → we only use isotonic saline 20ml\kg
  bolus 15-30 min, only repeat 3 times.

- 1st sign that changes with therapy is **PULSE**.
  Assessing of dehydration by urine output.

- **Water deficit** = % of dehydration x 10 x wt
- **Na deficit** = fluid deficit (L) x 80 meq
- **K deficit** = 20 meq \ 1L \ day , or in hypokalemia 30-40 meq\day

❖ Don't use oral rehydration in severe dehydration, we use it only in mild to moderate .

- Sodium correction 10-12 meq\day

- In hypo or hyperthermia :
- Maintenance :
  - Na 2-3 meq\Kg\day
  - K 1-2 meq\Kg\day

Water 1st 10 Kg x 1 , 2nd 10 x 5 , rest x1
give 1\2 in the first 8 hrs and the rest at the rest.

Hypernatremia causes : 1- irrigation with normal saline 2- misuses of oral rehydration T.

-If it was **isonatremia** always use **1\2 normal saline**
glucose 5 يعني برا الخداج بحسب بس كم بده سوائل وبستخدم 1\2 نورمال سالاين وبرضه بستخدم

-In **NICU** → use glucose 10
correct to 130 →Na→ regardless the pt hydration status.

-**Hyponatremia** <120 → rapid IV infusion of hypertonic saline

-If we need large amount of sodium which equals also large amount of fluid → use hypertonic solution "high concentration low water""

CASE :

In ER, high grade fever 40 c, vomiting + diarrhea 2 days, 20 Kg, sunken eyes, dry lips, pulse 175, BP 90\50 :

Examination → weak pulse, delay capillary refill

DDx : 1- severe dehydration 2- sepsis 3- DKa 4- HF (acquired cardiomyopathy) , infection

1- Resuscitate :
- fluids : colloid blood, plasma, albumin, crystalloid normal saline
we usually use bolus normal saline : 20 ml \Kg = 400 ml immediately for 15-30 min

2- Take sample for KFT and LFT

3- Maintenance → 1500 ml water, Na 2-3\kg = 40-60 meq
K= 1-2 → 20-40 meq

- deficit: water 9x20x10 = 1800 (above 10 so it's 3,6,9)
- since it's isonetremia use glucose 5 normal saline

- total volume = fluid 1800 + 1500 = 3300\14 hrs
1\2 in 1st 8 hrs , other 1\2 over 16 hrs.

- If the patient Na 120, the correction will be for 125 so 5xwt (20) x .6 →

الناتج بزيده ع الصوديوم لل maintenance
لو الخسارة أكبر بزيد الفرق بالنورمال سالاين 24 hrs

لو الصوديوم 170 بعطي ال maintenanceعلى يومين أو 3

1- Detect degree of dehydration → :-

- mild : no fluid , just observation
- Moderate to severe:

- resuscitation:

20mg\kg IV bolus (15-30 min) up to 3 times.

Continue deficit: water = 10x wt x degree of dehydration

Na = fluid x 80

K = 20 x fluid (per L), if hypokalemia up to 30-40\L

give 1\2 the amount in the 1st 8 hrs and the other 1\2 in the rest 16 hrs .

- maintenance :

fluid = 1st 10 kg x 100

2nd x 50

3rd and more x 20

Fluid usually use 1\2 normal saline , the safest one.

Na = 2 – 3x kg

k = 1 – 2x kg

☒ slow correction :

hypernatremia → brain edema

hyponatremia → pontine demyelination

Deficit: 8 لو اعطاني نسبة الصوديوم بدي اضرب النسبة ب140 حتى اطلع رقم قريب من

Rheumatic fever

- Caused by group A bata hemolytic strep.
- It's very common → causing (impetigo, pyoderma in skin) and upper respiratory tract infection (pharyngitis)
- Rarely or less common :
  1- vaginitis 2- perianal cellulitis 3- septicemia
  4- pneumonia 5- endocarditis 6- pericarditis 7- osteomylelitis and arthritis
- May also cause :
  1- scarlet fever 2- strept. Toxic shock syndrome 3- necrotizing fasciitis
- Non-suppurative complication → acute GN rheumatic fever.
- Most ignificant complication of acute RF → rheumatic heart disease.
- 2\3 of pts has Hx of upper RTI several weeks before.
- Only (1, 3, 5, 6, 12, 29) serotypes cause RF.
- Age 5-15 yrs for initial infection and recurrence.
- Rheumatic heart D. is the most common acquired heart disease in all age groups.
- There is antibodies formation against M.protien when there is URTIs.
  M.protein also present in heart + smooth muscle (brain) which cause cytokine release and destruction.
- No pathognomonic lab finding but there are 5 major and 4 minor criteria that indicates recent GAS infection.

When to Dx the recurrence or even the 1st attack ?

When pt fulfills :

a- 2 majors b- 1 major with (2 minors or evidence of GAS recently)

Major criteria : J♡NES →

J → joint polyarthritis migratory

♡ → carditis

N → ndule subcutaneous

E → erythema magrinatum

S →sydenham chorea

Minor criteria :

- clinical : arthralgia, fever
- lab results: ↑ ESR, CRP + Prolonged P-R interval.

. Also we should have +ve throat culture or +ve antigen test
  ↑strept. Antibodies titer.

Migratory polyarthritis (75%) :

- Large joints (knee, ankle, wrist, elbow)
- By Hx → very painful even when friction with clothes

- The affected joint becomes normal within 1-3 days without tt but 1 or more other joints become involved.
- IT'S NOT DESTRCTIVE ARTHRITIS
- Arthritis may correlate with peak of ASO titer
- Synovial fluid analysis :
  1- protein near 4g\dL
  2- normal glucose
  3- 10000 – 100000 WBC → predominant neutrophils.

→ There is inverse relation between arthritis severity and cardiac involvement.

Carditis :

- 50-60% and usually pericarditis.
- it's present as murmur + tachycardia
- it includes :
1- fatal exudative carditis
2- mitral valve disease (start as regurge and end up with stenosis)
3- or involve both mitral and aortic >
*mitral : high pitched apical holosystolic radiate to axilla.
*aortic: high pitched decrescendo diastolic at Lt sternal border.

Chorea (10-15%) :

- Acute, isolated, frequent subtle movement

1- Milk maid's grisp → irregular contraction and relaxation of muscles
2- Spooning and pronation of hands when arms are extended
3- Wormian darting of the tongue upon protrusion
4- Examine the handwriting to evaluate fine motor movement.

- He may have lability, incardination, poor school performance, facial grimacing and abnormal movement → increase by stress and decrease with sleep.
  → latent period may persist for months.

Erythema marginatim (1%) :

. Macular lesion, erythematous with pale center without itching.
. Found on trunk and extremities but not on face.
. ↑By warming the skin.

Subcutaneous nodule (1%) :

. Firm 1cm, found on extensor surface of tendon near bony prominences
. There is correlation between nodules and rheumatic heart disease.
. If the patient has carditis → you can't count prolonged P-R as a criteria
  If the patient has carditis → then developed polyarthritis → not minor criteria

- 1\3 of acute rheumatic fever don't have Hx of pharyngitis.
  evidence of GAS infection by ↑ serum ASO titer. (+ve in 85%)
  if he has the 3 types of antibodies (ASO, anti-DNAse B, antihyaluronidase) , that's in 95%100% of cases.

DDx : 1- JIA 2-Sickle cell disease 3- Reactive arthritis 4- Malignancy 5- SLE 6- Pyogenic arthritis
7- Post strep. Reactive arthritis.

Management :

- All pts should have bed rest and monitor for carditis.
- According to criteria one DX is established regardless the throat culture.
- Start oral penicillin x10 days.
  or single dose of benzathine penicillin IM :
  - wt > 60 Ib → 1.2 million IU
  - wt < 60 → 600000 IU
  or amoxicillin for 10 days orally.
  to ensure eradication of GAS.

- If the patient is allergic to penicillin → 10 days erythromycin, 5 days azithromycin or clindamycin.
- We may give long-term prophylaxis antibiotics.
- We may use acetaminophen to control pain and fever but don't use ibuprofen; it masks the symptoms.
- If he has typical migratory polyarthritis + carditis without complication (CHF or cardiomegaly) , start aspirin orally.
- If he has carditis with noticed cardiomegaly or CHF → corticosteroid.
- If the pt has moderate to severe carditis → digoxin, fluid + salt restriction, O2, diuretics.
- If he has chorea (in early course) :
  drugs of choice : phenobarbital, chlorpromazine, haloperidol.

Prognosis
depends on :

1- Presentation : clinically at time of Dx
2- Severity of initial episode
3- Presence of recurrences.
4- 50-70% of pts with carditis in initial episodes → no residual HD.
   if more severe initially → high risk of residual and recurrence about 50% of reinfection URT otr pharyngitis.

- Risk of recurrence is highest in in 1st 5 yrs of iitial episode, then with time.
- Prevention of initial or recurrent attack depends on controlling GAS in respiratory infections.

Duration of prophylaxis?
- without carditis or with carditis → 5 yrs or 21 yrs أيهما أول
- persistent valvular disease → lifelong
- with carditis + residual HD → 10 yrs or 40 ys أيهما أول

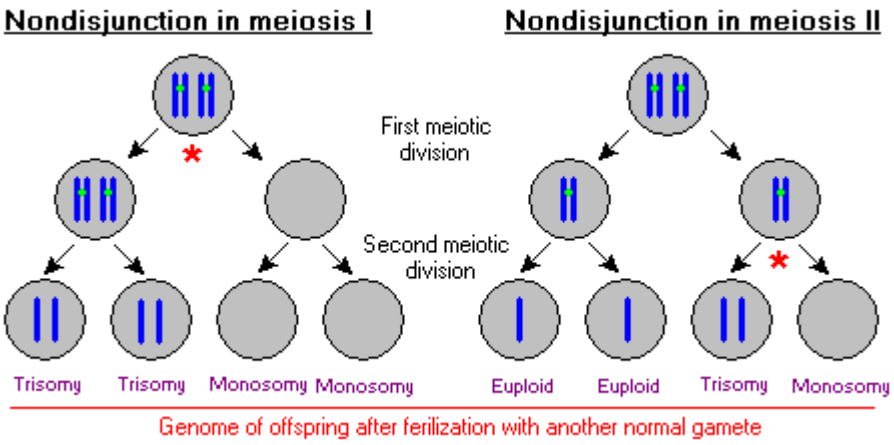
Chromosomal and genetic abnormalities

Chromosomal abnormalities :

- in structure - in number (Down 21)

How it happens ?

1- **During meiosis** :
defect in cell division so one will have 24 chromosomes and other has 22 لو كانت بالمرحلة الاولى



Trisomy → Klein felter xxy, down (21)
monosomy → turner xo

Down syndrome:

- trisomy 21
- Commonest abnormality → presence of part oor all of 3rd copy of chromosome 21
- Commonest genetic cause for mental retardation
- Risk factors :
  1- Advanced maternal age ≥ 35 y
  2- Hx of previous down hild (high risk for next pregnancy)
  3- Parents who are carriers for genetic down translaocation.

- Regarding the age of the mother:
  25 yrs → 1\300 at 35 yrs → 1\365 at 45→ 1\30

- Etiology :
  95% → trisomy 21
  2% → mosaicism
  3% robertsonism translocation (inherited

- The occurrence is about 88% coming from mother non-disjunction, and only 8% from father.

Rebertosinan :

- Mostly, translocation of long arms of 2 of acrocentric chromosomes 13, 14, 15, 21, 22
  - part of all parts of extra chromosome 21 is fused with another one
  بالعادة بتصير أو بتخليك تشك لما يكون عمر الام صغير وعندها أكثر من طفلdown syndrome .

- Trisomy → when the non-dijunction happen before conception. (all cell body are 47)
  if happened after → it's called mosacism →(46. Xx \ 47, xx +21)
- Life expectancy 55 yrs

- Clinical features :
  1- Flat facial profile
  2- Upward slant eyes
  3- Short neck and small neck
  4- Abnormal shaped ears
  5- Brush field spots → white spots on iris
  6- Single deep transverse crease on palm of the hand
  7- Hand: short 5th finger that curves inward and wide hard.
  8- Widely separated 1st and 2nd toes an increase skin creases.
  9- Flattened nose and face
  10- Tall forehead with narrow temples
  11- Hypertelorism → wide spaced eyes
  12- Swollen edematous dorsum of hands and feet
  13- Nuchal skin
  14- Oval-shaped, low set, posteriorly rotated ears with thick helix excess.
  15- Downward slant of palpebral fissure and epicanthal folds.
  16- Short, broad nose with depresses root and full tip.
  17- Deeply grooved

Later on :

  1- Failure to grow and mentally retarded
  2- Uni or bilateral absence of ine rib.
  3- Pyloric stenosis and umbilical hernia, duodenal atresia, GERD, celiac
  4- Dental abnormality
  5- Enlarged colon
  6- Congenital heart disease (combined ASD eith USD)
  7- Cancer (teticular, ALL, AMKL)

- They may have infantile spasm and epileptic sizures also Alzheimer's, strabismus, cataract, keratoconus and glaucoma
- Endocrine epicanthal 50% hypothyroidism and type 1 DM
- Recurrence depends in cytogenetic finding and which parents is carrier

- Cytogenetic finding: recurrence 1% added to the risk of mother's age until 40 yrs, after 40 the age itself is a risk factor.

- If the child has robertsonisian translocation you sould do chromosomal analysis for both parents.
  35% has balanced translocation>
  65% the analysis is normal.

- Which parent is carrier :
  if the mother is carrier 10-15%
  if the father 2-5%

Edward's syndrome :

- trisomy 18
- 47, xx, +18 or 47, xy, +18 →2nd most common trisomy
- Clinical features :
  - hypertonia, small for gestational age
  - Head: prominent occiput, micrognathia, low-set and malformed ears, hypertelorism , upturned nose.
  - Limbs: rocker-bottom, club feet, hypoplastic nails, clenching of fists.
    2nd and 5th digits overlap the 3rd and 4th.
  - Heart: VSD, ASD, PDA
  - Chest : small nipple, short sternum
- Prognosis: usually they sponanuosly aboted but less than 10% kive for 1 yr.
- Risk: vary with maternal age.

Patau syndrome:

- trisomy 13
- 47, xx +13 \ 47, xy, + 13
- Clinical features:
  - General: microcephalic, small for gestational age.
  - Face: 1- small and malformed ear 2- sloped forehead 3- microphthalmia and anophthalmia
    4- midline facial defect : single nostril, cyclopia (single orbit), cleft lip and palate .
  - Limbs: post axial polydactyly and club foot or rocker-bottom feet.
  - Genitalia:
    -in girls: hypoplasia of labia minora
    -in boys: hypospadias and cryptorchidism
  - Cvs: most of them have congenital disease, VSD and PDA.
  - Pathognomonic: aplasia cutis congenital.
    in conjuction with polydactyly + some or all facial finding.

- Usually they die in the 1st year but 9% survive beyond it.

Sex chromosome disorders:

Klinefelter syndrome:

- They are males with one extra x chromosome → xxy
- Most mmon sex chromosome disorder (1:500)
- Affects physical and cognitive development.
- The most common disorder with hypogonadism and infertitllity.
- It's not inherited → non-disjunction in reproductive cell, even the mosaic type (after conception) → 46, xy \ 47, xxy in early fetal development
- Presentation : Common symptoms (hypogonadism, gynecomastia, infertility)

Hx :

1- Taller than peers
2- Erectile dysfunction
3- Delay or incomplete pubertal development
4- Spared facial, body and sexual hair.
5- Osteoporosis
6- Behavioral problems (substance abuse)
7- Chronic inflammatory disease like (SLE) and breast cancer
8- Learning disabilities (low verbal IQ the performance IQ)
9- Poor self-esteem (anxiety and depression)
10- Poor muscular tone
11- Small testis and infertility

By Ex:

Babies:
- poor muscle tone and strength
- hypospadias \ undescended testes
- impaired gross and fine motor skills and coordination.

Childhood:
- learning disabilities
- less muscle coordination and control
- synkinetics movement and tremor
- expressive language, understand constructions, oral language production
- memory deficit and lower social skills

Puberty (delayed)
- gynecomatia
- failure to produce viable sperms
- ↓ testosterone from testes → failure of 2ndry character → libido, facial hair and deepening of voice.

Adulthood:
- infertility, psteoprosis, osteopenia

Lab studies :

Prenatal:
1-Fetal cytogenic analysis (amniocyte or chorionic villi)
2- Non-invasive tests → fetal cells in maternal blood

Post-natal :
1- clinically (age-related)
2- karyotype analysis

Treatment and management:

1- Androgen replacement : most important line, start at puberty and increased overtime.
2- Speech and behavioral therapy.
3- Physical and occupational therapy (hypotonia)
4- Infertility tt :
   - testicular biopsy → isolate viable sperm → IVF or intracytoplasmic injection
   - all children born to these men wehad normal chromosomes

Turner syndrome: xo

- Usually the other x chromosome is missing or altered structurally.
- 1- Developmental delay 2- Short stature 3-infertility 4- coarcitation of aorta
- The only monosomic condition which survive to term.
- 99% spontaneously aborted (13% in the 1st trimester loss)

Pathophysiology:

1- no x chromosome in all cells 50%
2- No x in some cells 30_40% (mosaic)
3- Defect x in all cells 10-20%

Signs and symptoms:

1- Face: low set ears, triangular face, webbed neck (skin folds around neck), flat nasal bridge maybe associated with cystic hygroma.
2- Horseshoe kidney >50%
3- Short stature
4- Hypothyroidism
5- Gonadal dysgenesis (only 10% will be normal)
6- Buffiness of hand and feet
7- Shield like chest

8- Cardiac: commonest → bicuspid aortic valve then coarcitaion, post stenotic aortic dilatation and aneurysm.
9- Hyperconvex nails → u shaped.

Diagnosis:

Prenatal:
- U\S → chronic villous sampling or amniocentesis.
How? Nuchal cystic hydroma, horse shoe kidney, Lt side cardiac anomaly

Karyotype:
- 45, xo or cell line with deletion of short arm of x.
- regardless of karyotype if he's male exclude your Dx.

Labs:

1- TFT → obtain it at Dx then repeat every 1-2 yrs.
2- Gonadotropin → LH and FSH are high if untreated and > 4 yrs .
then they are normal or near-normal up to 10 yrs
then start to rise to menopausal level.
3- ECHO at Dx and\or MRI for heart + aorta
4- BP in 4 limbs → for coarcitaion

How to DX ?

Usually:
newborn → by heart disease or features
child → short stature
adolescence → failure to develop 2ndry sexual character.

Management :

1- Growth hormone (for short stature)
2- Sex hormones replacement therapy
- estrogen at age 12-15 yrs
- infertility won't be corrected by estrogen.

Hepatitis

- **Inflammation of the liver parenchyma.**
  1- Viral
  2- metabolic : Wilson
  3- autoimmune: SLE, hepatotropic viruses (A, B, C, D, E) or non-hepatotrophic (CMV, EBV, adenovirus)
  4- ischemic hepatitis : shock, CHF
  5- drugs and toxin induced acetaminophen, alcohol, mushroom.

- Commonest cause worldwide is viral hepatitis due to hepatotropic viruses.
- Notes:
  1- All of them are RNA except hepatitis B virus is DNA.
  2- Types A & E transmitted fecoorally but others by sexual, perinatal and parenteral.
  3- All of them are chronic infection except A & E.

Pathogenesis:

- infection of hepatocytes → activate the innate and adaptive immunity → inflammatory response → cellular damage and response

- the strength of immunity determine the type of cell involved and the ability to evade body defense which can
lead to clearance (acute) or persistent (chronic) .

- Acute response → direct cytopathic and immune mediated
- chronic (HBV, HCV) → multiple inflammation, injury then healing → scaring\fibrosis → HCC
- in recovery → normal morphology within 3 months.

Hepatitis A : (7-14 days)

- RNA virus, transmitted fecoorally, host → human and other primates.
- Fecal excretion starts late and reaches the peak just before onset of symptoms and resolves within 2 weeks after onset of jaundice.
- Symptomatic in children (acute abrupt anorexia, fever, vomiting, jaundice, malaise, hepatomegaly, splenomegaly, regional lymph nodes, GI ulcers, nephritis, myocarditis, acute pancreatitis, arthritis → due to circulating immune complex)

- Diagnosis →
  1- IGM (in 1t 4-6 months)
  2- viral particles in feaces
  3- igG in 1st 8 weks.
  → in all hepatitis forms there is a rise in transaminase, phosphate, bilirubin.

Complications: most have full recovery.
1- Acute liver failure → rare, in immunocompromised and who have liver disorders.

- 2- Prolonged cholestatic syndrome → persistent: a. hyperbilirubin b. pruritis c. constitutional symptoms last for 12-16 weeks in absence of biliary obstruction on sonography.

Hepatitis B (60-180 days) :

- DNA, acute and chronic course \ most common to cause complications
- Common cause in children due to HBsAG from +ve mother (perinatal) then 1- sexual 2- parenteral 3- horizontal

- Clinical presentation:
  1- jaundice 2- anorexia 3- malaise 4- N & V 5- polyarthritis nodosa 6- glomerulonephritis 7- gianotti crash syndrome 8- aplastic anemia

- Investigations:
- active replication → HBeAg
- current infection → HBsAg
- viral load → HBV DNA
- resolved infection or immunized → anti-HBs
- low risk of transmission → anti-HBe

- Complications:
  1- cirrhosis 2- HCC 3- death 4- fulmintal hepatitis

- +ve HBsAg → <10% of infants infected
  +ve HBsAg + HBeAg in abscent of PEP → 70-90% infected
- Trans-placental viral infection is uncommon, associated with acute HBV in 3rd trimester

Notes:

1- after birth → breastfeeding not associated with transmission
2- time of delivery → infected vertically by peripartum exposure.

How to minimize the transmission risk ?

1- Post exposure prophylaxis to infant (PEP)
2- antiviral to suppress HBV in mother (↓ vertical transmission)

Hepatitis C (30-60 days) :

- RNA , direct cytotoxic effect cause liver injury.
- Transmission : perinatal, transfusion, parenteral
  perinatal is the commonest, also during delivery (مستحيل و هي حامل)
- Safe to breastfeed the baby but if there is a nipple crack or bleeding stop feeding until it heals.
- Chronic carriers 50%, and 50% are chronic active or persistent.

- Diagnoses:
  1- ELISA → +ve of HCV enzyme linked to it + 2- RIBA immunoblot → which detect HCU antigens.

  By PCR → detect the RNA which is sensitive for active infection.
  ببين بعد 3 أيام .

Hepatitis D:

- It's RNA with HBsAg coat

Delta agent:

لازم يكون معه HBV لحتى يشتغل يا إما co-infection أو super-infection بمريض عنده اصلا HBV أو carrier

- Dx by antibodies or it's RNA in PCR.
- Fulminant hepatitis: after both types but more with co-infection.

Hepatitis E (35-60 days) :

- RNA, fecooral, no chrnic infection or risk of HCC.

- Clinically: for 1 week
  headache, anorexia, N&V, abd. Discomfort, precedes the disease
  → in young children → maybe asymptomatic.
  or jaundice and tender large live →icteric phase

- DDx of hepatitis:
  1- bacterial → E.coli sepsis
  2- viral → HSV, varecilla
  3- cholicystitis and cholilithiasis
  4- drugs → phenytoin, isoniazide, carbamezopine
  5- metabolic disorders: galactosemia, tyrosinemia, α-1 antitrypsin.

- Prevention: Especially who will travel.
  - HAV less than 12 months → immunoglobulin + vaccine
  - HBV → to all babies at 2, 4, 6 months, check serology after 12 months.
    if the mother is +ve HBV you should give

- Treatment :
  - *Supportive*:
    1- fat soluble vitamins (bcs they need bile and it doesn't exist)
    2- hydration
    3- prevent the spread by disposal of diaper and needles.
    4- Avoid hepatotoxic drugs or elective surgeries.

- *Indication of admission:*
  1- hydration + severe vomiting
  2- prolonged PTT
  3- hepatic encephalopathy → with cirrhosis, which may include coma.

- HAV → immunoglobulin without antiviral
  HEV → self-limiting or Ribavirin
  HBV :
  acute → supportive + monitor
  chronic :
    - interferon α
    - transplant + antiviral + immunoglobulin
    - nucleotide\nucleosides analog → Lamivudine
      Tenovir\Entecavir

Hepatitis C:

1- Old agents → interferon α + oral ribavirin, but it has low efficacy, long regimen + side effects
2- Liver transplant → only if the liver is cirrhosed
   + antiviral
3- New agent → sustained response 99% but expensive.

Common problems in neonates

Meconium aspiration:

- It's viscous, dark green substance, wich compsed of 90% of water and 10-15% of solid materials (GI secretions like bile, protein, lipid, ..)
- It's sterile → don't have bacteria and it's PH is 5.5 to 7, it should pass normally within 24-48 Hrs.
- Many factors causes passage of meconium in amniotic fluid but hypoxic stress and fetal maturity are the two main majors.
  others include:
  1- infection 2- acidosis 3- maternal drug abuse (tobacco, cocaine) 4- preeclampsia 5- oligohydromnious 6- placental insufficiency 7- maternal HTN

Its effect ?

1- Antibacterial activity
2- Irritation of fetal skin
3- Aspiration of meconium-stained fluids
   It's effect :
   - airway obstruction → atelectasis
   - Surfactant dysfunction
   - Chemical pneumonitis
   - Pulmonary HTN

Airway obstruction:

Ball-valve effect → it's partial obstruction so there is good inflow during inspiration but it orevents outflow in expiration → trapping + hyperdestination → pneumothorax, pneumopericardium, pneumomediastinum.

Surfactant dysfunction: by preventing spread over alveoli, ↓ surfactant proteins (SP-A, B)
it depends on surfactant concentration and meconium.
↑ Surfactant → limited meconium effect
↓ surfactant → even very high diluted meconium has an effect.
- It will lead to respiratory distress.

Chemical pneumonitis:
By activation of immune system and cytokines release → tissue damage
happen with 72 hrs after birth → gross ventilation perfusion mismatch, V\Q mismatch.

Persistent pulmonary HTN :

It's frequently with meconium aspiration due to chronic in-utero stress or thickening of pulmonary vessles + Rt to Lt shunt (PDA, foramen ovale)

It's one of the leading causes of death.

Presentation: may develop shortly after delivery
1- cyanosis 2- tachycardia 3- end-expiratory grunting 4- nasal flaring 5- retractions 6- rales and rhonchi 7- barrel chest 8- green stained skin, cord, finger nails.

Investigations:

1- Pulse oxymeter and ABG
   hypoxia + hypercapnia, metabolic acidosis due to perinatal stress complicated by respiratoy acidosis.
   → continuous monitor is necessary

2- Serum electrolytes:
   sodium, potassium, calcium, at 24 hrs of life.
   bcs SIADH and AKI are common complications of perinatal stress.

3- CBC → polycythemia
4- ECHO → ensure cardiac structure \ severity of PPHTN and Rt to Lt shunt.
5- CXR → patchy infiltration, coarse streaking of both lung fields
   anterio-posterior diameter and diaphragm flattening, air trapping, hyper-expansion, acute atelectasis.

How to manage? According to APGAR score

- if he's vigorous → normal RR, tone, HR >100 → 1. Don't intube 2. Clean moth and now by bulb syringe or large bore suction catheter.
- Not vigorous : use direct laryngioscopy, intubate and suction immiedetly → suction up to 5 sec → re-evaluate :
  - if no meconium → don't repeat
  - if still but no bradycardia, HR<100 → reintubate + suction
- If there's meconium + low HR → give the pressure ventilation + suction again later

Then continue the care in NICU by :

1- Continuous O2 by +ve pressure to maintain arterial oxygenation
2- We may use vasopressors (dopamine) in maintaining systemic BP greater than pulmonary to ↓ shunting through PDA.
3- Hb at least 13 g\Dl to ensure adequate oxygen carrying capacity
4- Minimal handling → these infants are easily agitated, which ↑ pulmonary HTN, shunting → hypoxia + acidosis, so we may need sedation to ↓ agitation.
5- Mechanical ventilation
6- Surfactant when needed
7- If we suspect pneumonia give → prophylactic antibiotics
8- Inhaled nitric oxide for PPHN.

Prevention → by rapid identification of distress and suction before 1st breathe if not vigorous.
→ intra-partum nasopharyngeal suction of meconium stained infants don't decrease the risk.

Complications:
1- PPHN 2- chronic lung disease 3- recurrent infections on 1st year of life

Prognosis:

1- May have residual lung problem → cough, hyperinflation for 5-10 yrs.
2- Ultimate prognosis depends on CNS asphyxia and pulmonary HTN

Transient tachycardia:
self-limiting, happens in term and near term babies with CS.
it's due to slow resorption of lung fluids → ↓ compliance, fetal volume, dead space.

How the fetus clears fluids?

1- 35% clear few days prior to birth → by change in epithelial Na channel
2- 30% during active labor → trans-pulmonary force, catecholamine surge
3- 35%postnatally by crying and breathing
→ it results in fluid in alveoli → ↓gas exchange

Risk factors:
1- male 2- born CS without labor trial 3- age <39 weeks 4- infant of DM mother 5- low APGAR score
6- prolonged rupture of membrane 7- excessive maternal sedation 8- perinatal aspiration
9- maternal asthma and smoking

Symptoms:
1- tachycapnea RR>60 2- grunting and flaring 3- retardation 4- cyanosis 5- clear lung fluids or crackles.

By examination:
immediately or within 6 hrs the baby will develop early onset tachypnea with grunting, retractions, flaring, on extreme cases severe hypoxia and cyanosis (but rarely).
Chest is clear without added sounds except rarely you can find crackles
→ usually there is no sign of acute distress → quiet tachypnea persists 12-24 hrs maximum up to 72 then resolves.

Diagnosis: by exclusion
rabid recovery, no radiological findings, no ROS or oter disorders.

DDx:
1- congenital HD 2- diaphragmatic hernia 3- congenital lung defect 4- pneumothorax 5- meconium aspiration 6- RDS 7- PPHN 8- neonatal paneumonia

Work up:

1- ABG, pulse oximetry → no O2 retention.
2- ECHO → rule out cardiac cause or pulmonary HTN
diagnostic standard → CXR
fluid in the fissure, small plural effusion, hyperinflation and flat diaphragm and prominent perihilar streaks (sunburst) and complete cleaning by 48-72 hrs.

Management : supportive
IV Fluid, O2 supplement, correct any metabolic disorders, regulate temperature.

Birth injuries:

- Structural destruction or functional deterioration of the body due to trauma at birth.
  ** You can avoid them by appropriate care in delivery.
- **Birth trauma**→ from mechanical forces during birth process
- **Birth defect** → congenital disorder, present at birth regardless the cause.
  * Large babies (wt > 4500 g) are at high risk.

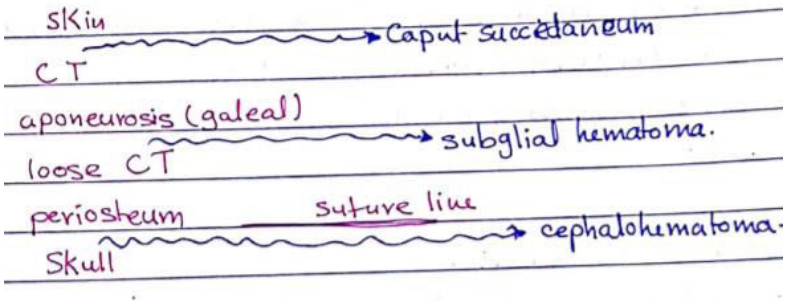
Maternal :
1- primi gravida 2- pelvic abnormality 3- oligohydromnious 4- small maternal stature 5- cephalopelvic disproportion

Fetal:
1- very low BW. 2- Extreme prematurity 3- large baby 4- fetal anomalies. 5- breech presentation

Delivery:
1- prolonged or rapid labour 2- instrument use 3- version + extraction 4- deep, transverse, arrested descend.

Types of injury:
1- soft tissue 2- bone injury 3- intra-abdominal injury 4- neurological→ descend laryngeal nerve, brachial plexus, cranial nerves, spinal cord.

Soft tissue injury:



Cephalohematoma:
blood beneath the periosteum due to ruptured vessels between skull and periosteum, maybe uni or bilateral. Commonly over parietal bone and don't cross the suture lines.

. By examination → palpable edge at the margin of thelesion.
usually it will enlarge in 1st few days then slowly resolve in weeks or months.

- Significant bleeding or jaundice → 2ndry infection or calcify.
- X-ray not routinely done except if it's associated with fractures.
  → usually linear and don't need Mx except if there's neurological findings.
- Mx by observation, if there is anemia or hypovolemia → resuscitation → transfusion may be needed
- May be confused with encephalocele.

Caput succedaneum:

non-pitting edema in skull soft tissue, usually over the presenting part and use of vacuum in labor (prolonged).

- It has ill-defined margin, no need for X-ray and will resolve in days.
- Significant bleeding is rare; but jaundice can worsen if blood is reabsorbed.
- Not associated with fractures but may have skin ecchymosis.
- No Mx needed.

Subgaleal hematoma:

between periosteum and scalp aponurosis.

- DX→ clinically → it presents as firm, fluctuant swelling over scalp (petting edema)
  it may extend posterior to neck and\or displacing the ears laterally.
- Due to vacuum use, then it develops gradually 12-72 hrs or in severe cases it may develop immediately
- It's highly associated with head trauma → fractures or intracranial hemorrhage, or it may be the 1st presentation of hemophilia.
- May cause significant bleeding → then hypotension, shock, coagulopathy, jaundice.
- Lab investigation → hematocrit, coagulation study.
- Mx→ observation and treat when needed.
  If no shock or intracranial injury → good prognosis.

Abrasion and laceration (could be deep) :

Partial thickness wound, skin damage (friction).

- may be superficial or deep → with minimal bleeding.
- Happens in CS or due to instrumental use.
- The pt may develop infection but most cases heal uneventfully.
- Mx → cleaning, antibiotic ointment + observation\laceration needs suturing.

Subcutaneous fat necrosis:

- Not usually detected at birth.
- Irregular hard subcutaneous plaque with overlying dusky red-purple discoloration on extremities, face, trunk, buttocks → caused y pressure on delivery.
- In 1st week of birth.
- It's a form of panniculitis.
- Risk factors include:
  1- Fetal distress during labor 2- Large birth wt 3- CS 4- low O2 5- cold tempreture 6- infection
- Commonest complication →hypercalcemia → in blood testing in 1st few mhours.

- Can cause: irritability, constipation, poor wt gain, rarely rhythm disturbance.
- Also may have thrombocytopenia and hyperlipidemia.
- Management → is Mx of hypercalcemia by ↑ fluid, fusemide (↓ calcium milk) it usually subsides without Mx.

Brachial plexus injury → peripheral nerve damage due to:
1- large baby 2- breech delivery 3- shoulder dystocia

Evb's palsy (c5-c6) → commonest

- Lack of shoulder motion.
- It involves extremities → adducted, prone, and internally rotated.
- Moro, biceps and radial reflexes are absent on affected side, but grasp reflex is present.

Klumke's paralysis (c7-8, T1) → rare, presentation is claw hand

- Hand intrinsic muscles are weak with no grasp reflex.
- 1st thoracic spine is affected so horner syndrome is present.

Horner syndrome

- (meiosis, ptosis, ipsilateral anhydrosis)
- Congenital or from lesion involving sympathetic in spine (cervical) or brain stem.
- Cranial nerve and spinal cord due traction, hyperextension, overstretching, causes neuropraxia or complete nerve or cord transection.
- Unilateral branch of facial and vagus (recurrent laryngeal) commonly involved
  - temporary or permanent paralysis.
  1- Asymmetrical face while crying
  2- Deep wrinchles on normal side
  3- Mouth toward normal side
  4- No evidence of trauma

Laryngeal nerve (vocal cord paralysis) →

- affects swallowing (superior branch) and breathing \ intrauterine the baby is rotated and flexed
- If unilateral → hoarse cry, stridors \ bilateral → respiratory distress and asphyxia.

Spinal cord injury → during delivery by traction and rotation.

- Hemorrhage (epidural, intraspinal edema)
- Typical presentation → still birth or neonatal death with fracture to establish of respuartory function especially if the injury in brain stem or cervical or neuromuscular disorder or transient hypoxic attack.
- Dx by MRI or CT myelography.

Bone injury: following breech, shoulder dystocia or with high wt baby.

Skull fractures results from:

1- forceps 2- maternal symphysis pubis 3- ischial spine 4- Sacral promintary

Fractures:

Skull :

Types:
1-linear: commonest
- no symptoms
- no tt needed

2- depressed
- plung-pong ball
- due to foreceps use or fetal compression

Sites:
1- occipital:
- in breech
- common cause of fetal hemorrhage : disruption of vascular sinuses.
2- base: intracranial hemorrhage
3- vault fracture:
- frontal or partial bone
- linear or depressed
no tt needed unless there is intracranial hemorrhage.

Clavicles :

- Commonest type
- its unpredictable unavoidable
- due to
1- birth wt 2- shoulder dystocia 3- forceps use

- Present with pseudoparalysis
- by examination:
1- crepitus
2- palpable irregular one
3- sternoclidomastiod spasm

- confirm Dx by radiology

Diabetes mellitus

- Common chronic metabolic disorder hyperglycemia is cardinal feature.

Type 1:
- due to pancreatic β-cell damage
- causes insulin secretion deficiency.

Type 2:
- due to insulin resistance at level or skeletal, liver and adipose tissue.
- With variant degree of β-cell impairment.

Secondary DM →
1- exocrine pancreatic disease (cystic fibrosis)
2- Cushing syndrome.

Impaired glucose tolerance → Between DM and normal glucose level.

- Diagnostic criteria of impaired tolerance and DM:
  - Impaired glucose:
    fasting glucose 100-125 mg\dL or 5.6 – 7 mmol\L
    OR 2 hrs plasma glucose in OGTT ≥ 140 mg\dL but <200 (11.1 mmol\L)
  - Diabetes:
    - symptoms of diabetes + random or casual glucose ≥ 200 mg\dL (11.1 mmol\L)
    OR fasing (at least 8 hrs) ≥ 126 (7 mmol\L)
    OR 2 hrs plasma glucose in OGTT ≥ 200
    OR HbA1c ≥ 6.5%

- Diagnostic criteria of genetic defects of β-cell function: (maturity-onset DM)
  1- DM in at least 3 generations with AD inheritance.
  2- Dx before 25 yrs in at least one affected subject.

Type 1 DM:

- Insulin dependent DM or juvenile diabetes.
- Onset → at any age with median age 7-15 yrs.
- Females = males
- 10% of DM pts are type 1.
- → IMP: peak of presentation → 5-7 yrs and at time of pubery
- Genetics:
  - There is clear familial clustering with prevelance ≈ 6%
  - Risk increases when the parents has DM (mother 3-4%, father 6%)
  - In dizygotic 6-10 but monozygotic 30-65%.

- Environmental:
  1- diet 2- psychological stress 3- viral infection (mumps, congenital rubella, enterovirus) + hygiene

- Natural Hx of type 1 DM involves some or all of the following stages:
  1- Initiation of autoimmunity
  2- Preclinical stage with progressive loss of β-cell function.
     then
  3- Onset of clinical disease
  4- Transient remission
  5- Established disease
  6- Development of complications.

- Genetic susceptibility:

- Exposure to unknown trigger\changes → autoimmunity (if no apparent β-cell loss = no diabetes) → progressive β-cell loss → clinical DM → clinical remission (honeymoon period) OR complication

- No triggers or changes → no autoimmunity → no diabetes

- When an insult to pancreas leads to β-cell antigens release (GAD 65) → taken up by
  1- antigen presenting cells (APCs)
  2- epitopes presented to CD4 cells.

- Type and stage of APC activation + cytotoxic environment in which CD4 take place → dictate the auto-reactive differentiation toward diabetogenic T-helper type 1 and 2 or antigen specific regulator T-cell.

- Predominant T-helper type 1 response results in recruitment and differentiation of cytotoxic CD8 cells → attack pancreatic β-cell → massive release of β-cell antigens, epitope spreading → destruction to pancreatic islets → type 1 DM

- β-cell destruction more rapid and complete in younger children.
  in older and adults → surviving β-cells are greater (10-20%) and some β-cells may survive up to 30 yrs after the onset.

- Clinical presentation:
  1- Polyuria, hyperphagia, polydipsia
  2- Weight loss
  3- The first presentation may be DKa (20-40%) :
     a. Abdominal pain or discomfort b. nausea & vomiting c. dehydration d. fruity breath odor (acetone) e. ↓ neurocognitive function or even coma. F. kussmaul breathe (rapid, non-labored, deep, heavy breath)

- Dx :
  - if random blood sugar > 200 ml\dL with typical symptoms with or without ketonurea
  - If the child is obese → excluse type 2.
  - If the pt has transient hyperglycemia with stress → monitor again for persistent hyperglycemia.
  - Once you confirm hyperglycemia in DK apt → look for ketones + electrolytes even if the pt has minimal dehydration
  - We need to have baseline HbA1c as a confirmatory way and allow us to compare the effectiveness of therapy later on.

- -False low HbA1c in :
  1- hemolytic anemia
  2- pure cell aplasia
  3- blood transfusions
  4- hemolytic anemia with hemorrhage, cirrhosis, myeloplasia, renal disease tt with erythropoietin.

- Other autoimmune disease with type 1 DM: celiac and thyroiditis

- Main aim of treatment:
  1- tight control of hyperglycemia
  2- eliminate symptoms
  3- avoid hyperglycemia
  4- normal growth and development
  5- minimal effect on lifestyle

- **Insulin therapy:**
  - prepubertal dose in DKa .75 – 1 unit\Kg\day
    if non diabetic ketosis → .25 - .5 unit\Kg\day
  - Pubertal in DKa → 1-1.2 unit\Kg\day
    if non diabetic → .5 -.75
  - Post-pubertal in DKa → .8–1
    in non-diabetic → .25-.5

سلايد 19 من سلايد الدكتور عبد الرحمن

Types: .
1- rapid acting → lispro, aspart and insulin
2- short acting → regular insulin
3- intermediate acting → lente insulin, neutral protamine hagedorn (NPH)
4- long acting → glargine
(سلايد 21و 22 مهم للميني اوسكي)

How to calculate insulin doses?

- SC insulin dose = .5-1 unit\Kg\day → total daily dose
- Basal dose → 1\2 dose
- Carbohydrate coverage = 450 I total daily dose
- Correction factor = 1800 for Lispro \ 1500 regular insulin
- Insulin pumps → rapid or short acting insulin 24 hr\day through catheter under skin and doses are separated into:
  1- basal rate 2- bolus doses to cover carbohydrate meals 3- correction or supplement dose.
- Site rotation: placed on body where you inject insulin
  insulin shots work faster in abdomen → بس مل بعطيه بنفس المكان كل مرة بخليه يحقنها حوالين المنطقة → if at same site every time → hard lumps or extra-fatty deposits may develop

Nutritional management → 55% carbohydrate, 30% fat, 15% protein

- 70% of carbohydrate → starch
- You should count carbohydrates for education and Mx of DM pts.
- High fibers diet improves glycemic control.
- Total calorie intake can be increased in exercise, puberty and low wt.

Monitoring → pts should monitor blood glucose at least 4 times\day before breakfast, lunch, supper and at bedtime

- Normally 80mg\dL (fasting) – 140 (after meal) up to 200.
- Glycosylated Hb → long-term control (2-3 months)
  recommended to do 3-4 times\year
  used to predict complication → if ↓ level →↓ risk for retinopathy and neuropathy and if good control → you may avoid complications

Exercise→ no forbidden forms of exercise but should be aware of hypoglycemia during or within hrs after it but regular exercise improve glucoregulation by ↑ insulin receptors.
- be aware, if the pt has poor control → it may induce ketoacidosis bcs it increases counter-regulatory hormones.

Hypoglycemic reactions → not predictable
caused by: exercise, delayed meals or snacks and wide swing in glucose level.
Especially → infants and toddler لانه وجباته والحركة تاعتهم ما بنقدر نتحكم فيها
and they are unable to recognize early signs of hypoglycemia.

<u>Hypoglycemic symptoms</u>:
pallor, hunger, tremor, tachycardia, sweating, apprehension, drowsiness, personality changes, behavioral changes, seizures, coma.

<u>Prolonged severe hypoglycemia</u> → depresses sensorium or stroke like motor deficits
hypoglycemiaال بتضل لحد ما اعدل

Mx of hypoglycemia : should have emergency source of glucose
1- should always document hypoglycemia.
2- Don't give too much glucose → 5-10g as juice, candy, sugar containing carbonated beverage.
Re-check 15-20 min.

- Should train pt, parents, teacher how to give glucose if he can't take oral.
- Should have injection kit in school and home.
- 5mg IM → if wt 20 kg and 1mg > 20 kg
  if hospitalized and experienced hypoglycemia give 4ml\Kg , Dextrose water 10 IV.

Early morning hyperglycemia:

Dawn phenomenon: overnight growth H secretion ↑ insulin clearance.
but type 1 DM can't compensate.
it's recurrent and usually morning readings are high.

Somogyi phenomenon: rebound hyperglycemia from late-night or early morning hypoglycemia due to exaggerated counter-regulatory response caused by ↑ dose oat night.

How to differentiate between them?
Measure blood glucose at 2-3 am, if:
1- low at that time → could be somogyi
2- if normal or high → dawn

- Long term complication depends on glycemic control.

Complications:

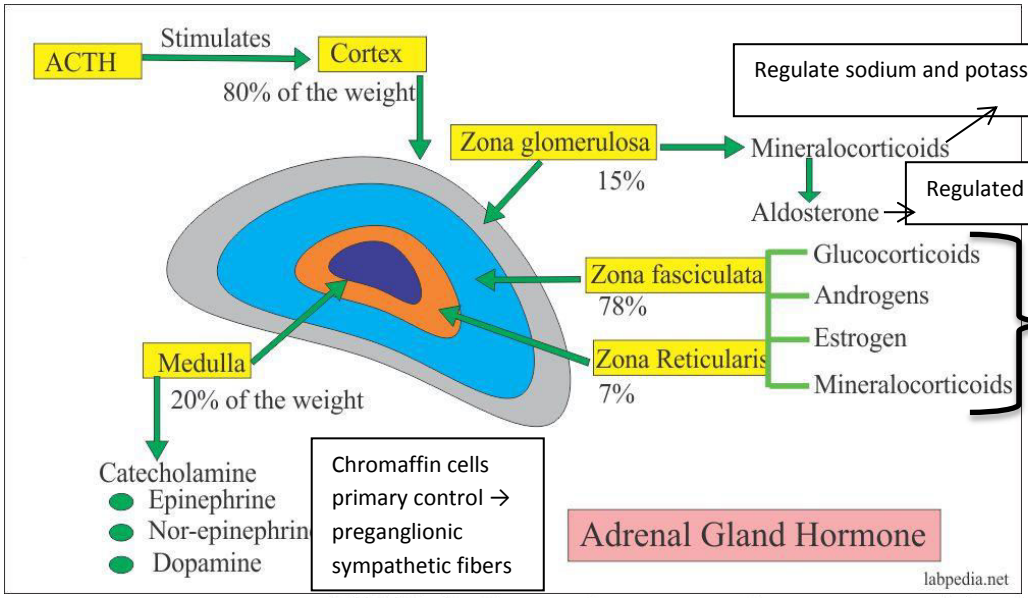
Complication	Start of screening	frequency	Method of screening	intervention
Retinopathy	After 5 yrs قبل البلوغ a yrs post	1-2 yrs	- fundal photography (Best) - mydiatric ophlamascope	1- Sugar control 2- laser therapy
Neurovascular disease	After 2 yrs	Every 5 yrs	1-lipid screening (best) 2- BP	1-statin 2-Bp control
Nephropathy	5 yrs pre 2 yrs post pubertal	yearly	1-spot urine sample for albumin, creatinine (best) 2-24 hrs excretion of albumin creatinine ratio	1-Sugar and BP control 2-ACE inhibitors
Neuropathy	In peds unclear in adults : - type 1 after 5 yes - type 2 at time of Dx	unclear	1-physical exam (best) 2-pupilometry, NCS, VCR	Sugar control

Thyroid	At Dx	2-3 yrs	1-TSHH (best) 2- peroxidase Ab	Thyroxin
Celiac	At Dx	2-3 yrs	1-anti TTG (best) + endomyceal 2- antiglidin	Gluten-free diet

- Life span of age 10 yrs shorter than the non-diabetic population.
  Usually they eventually have normal range height but less than the genetic potential, but puberty may be delayed.

Congenital adrenal hyperplasia

- Corticol diff. , aldosterone diff., androgen ↑ or ↓.



- It's autosomal recessive disorder → affect each enzyme (deficiency) which is involved in cortisol or aldosterone or both.

- Common cause is 21 hydroxylase deficiency → > 90% of cases, due to mutation or deletion in CYP 21A.
  - You need 2 mutated genes to happen.

- **Clinically**:
  - 70% classic salt wishing
  - 30% classic simple virilizing
  - .1% non-classic.

  ارجعوا للسلايد 6

- **Pathophysiology** → depends on the degree of cortisol or aldosterone deficiency.
  Some cases the manifestation reflects precursor accumulation (adrenocortical hormone)

Supra-physiological concentration

- Virilization: excess androgen production
- Sodium retention + HTN: due to minerocorticoid properties.

- Phenotype depends on degree or type of gene and the deficiency of sterogenic enzyme.

- **It varies:**
  1- Unapparent disease (occult or cryptic)
  2- Mild → in aldosterone or adulthood (non-classic)
  3- Severe → adrenal insufficiency (classic type) in infancy +\- virilization and salt wasting.

- **Race** → in all races
  and both sexes are affected equally.

- **Age** :
  - classic CAH → at birth or early childhood (ambigius genitalia , salt wasting, early virilization)
  - non-classic → at or after puberty (oligomenorrhea or virilizing signs in female)

- **Clinical presentation** depends on nature and severity of enzyme deficiency.
  Presentation varies according to sex by chromosomes.

by examination. فما بقدر احدد ambiguous genetalia لانه بكون عندهم

Females :

- Mild 21 hydroxylase → present in late childhood with precocious pubic hair, and\or clitoromegaly, often with accelerated growth and maturation (simple virilizing A.H)

- Severe 21-hydroxylase or 11-b hydroxylase or 3-B hydroxysteroid hydrogenase → present at birth with ambiguous genetalia with genital anomalies varies from complete fusion of labioscrotal folds and phallic urethra or partial fusion of both +\- clitoromegaly. (Classic virilizing A.H)
  - if it was milder (moderate) → may present in adolescence or adulthood with oligomenorrhea, Hirsutism +\- infertility. (Non-classic A.H)

- If 17-hydroxylase (may have HTN) was deficient → it's female at birth but don't develop breasts or menstruation in adolescence.
- 21 hydroxylase deficiency :
  1- deficient activity result in ↓ in conversion of 17 α–hydroxyprogesterone to II-deoxycortisol.
  2- Conversion of progesterone to deoxycorticosterone.

In males:

21 hydroxylase:
- normal genetalia
- moderate: late in childhood with early pubic hair development and\or phallic enlargement with accelerated linear growth and skeletal maturation (simple virilizing A.H)

*the moderate in males is the same as the mild in females .
بكون بالأول سريع بس بصير early fusion → بصير طوله قليل مقارنة بأقرانه
- severe (salt wasting)

-neonate at age 1-4 weeks present with FTT, dehydration, hypotension, recurrent vomiting, hypernatremia, hyperkalemia shock (classic salt wasting A.H)

1- Male in chromosomes + female genetalia or ambiguous
2- Or female who seeks medical care due to HTN or no breast development.
   It's steriogenic acute regulatory deficiency classic:
   1. 3 β-hydroxysteroid dehydrogenase
   2. 17-hydroxylase deficiency.

- Infants may have un-noticed signs → poor feeding, vomiting, dehydration, ↓BP, hyponatremia and hyperkalemia.
- In stressful conditions → hyponatremia, hyperkalemia, +\- hypoglycemia
  look for adrenal insufficiency.
- If pt has hyperpigmentation especially in areolae and genetalia, look for enzymatic deficiency of cortisol synthesis.
- Male or female pt, in 2nd or 3rd week of life → salt losing crisis development and later on he\she developed hypertension and\or hyperkalemia alkalosis, your Dx ?!
  - 11-hydroxylase deficiency.

في حال كان الطفل انثى اعضاءها الداخلية طبيعية المشكلة بس بالgenetalia

- 21-hydroxylase CAH → hypotension
- 11-hydroxylase and 17-hydroxylase → hypertension, why?
  - These result in accumulation of supraphysiologic concentration of deoxycorticosterone.

Diagnosis: inadequate production of cortisol +\- aldosterone + precursor hormone accumulation

1- <u>21-hydroxylase:</u>
   - serum 17-hydroxyprogesterone > 1000 ng\dL
   - urine pregnanetriol +ve with symptoms → metabolite of hydroxyprogesterone.
   - 24 hrs collection of urine → elevated 17-ketosteroid level.

2- <u>β-hydroxylase</u>
   - ↑serum II-deoxycortisol
   - ↑ serum deoxycorticosterone
   - high ratio of 24 hrs urine tetrahydrocompound S, II-deoxycortisol : tetra hydrocompound F, cortisol metabolite.
   - ↑24 hr urine 17-ketosteroid.

3- <u>3-β hydroxysteroid dehydrogenase:</u>
   - abnormal ratio of:
   1. 17-hydroxypregnenolone : 17 hydroxyprogesterone
   2. Dehydropiandrosterone : androstenedione

- **Other tests:**
  - in case of salt losing CAH (21-hydroxylase): hyponatremia, hyperkalemia,↓ aldosterone in serum, high plasma renin activity (hypovolemia).
- 2 other forms ← hypertensive forms → hypokalemia and low plasma renin activity.
- In non-classical forms: synthetic corticotrophin stimulation test → accumulation of precursors of steroid.
- Be aware: in mild forms salt-wasting may not be apparent until an illness or stress happen.

- **Imaging studies:**
  1- CT of adrenal gland: if the pt presented with acute adrenal failure without ambiguous genetalia or other clues of adrenal hyperplasia.
  - for bilateral adrenal hemorrhage.
  2- Pelvic U\S : if pt is infant with ambiguous genitalia (renal anomalies لو في رحم او لا عشان احدد جنسه لو في)
  - for mixed gonadal dysgenesis (they have ambiguous genitalia) , & Denys-drash syndrome.
  3- Urogenitography : identify the anatomy of internal genitalia.
  4- Bone age study: for advanced skeletal maturation, how would I know ?
  - Child in childhood age with precocious pubic hair, clitoromegaly and accelerated linear growth.

-In ambiguous genitalia → karyotype study to establish sex.

-Screening of 21-hydroxylaase → especially for males.
salt-wasting crisis لانو ما ببين عليهم اشي لحد ما يصير

- **Genetic testing** → for prenatal Dx and counseling

<u>Management</u> :
1- if ambiguous genitalia present → close observation for salt-wasting crisis
لحد ما اتاكد من التشخيص
2- electrolyte from few day up to 3 weeks
لأنه بتوخذ لحد 3 اسابيع حتى يصير التغييرات

☒ Should seek psychiatric consultation due to genital abnormality, infertility or even short stature.

Emergencies:

1- <u>Salt wasting crisis:</u>
- dehydrated, hyponatremia, hyperkalemia
- iv bolus of isotonic NaCl (20ml\Kg) over 1st hour then re-evaluate BP? If low repeat then IV infusion continuous, no potassium given.

2- <u>Hypoglycemia</u>: 2-4 ml of dextrose 10% in water then continuous infusion of 5% dextrose in water.
- If not hypoglycemic you should give 5% dextrose to prevent hypoglycemia.

- If the cause is II-hydroxylase or 17-hydroxylase → we give potassium but I should measure it in the blood first.

- Obtain samples for:
  1- electrolytes 2- blood sugar 3- hormonal profile

☒ ملاحظة مهمة: أول ما أشك بعالج ما بستنى أتاكد من التشخيص
treat with glucocorticoid or\and aldosterone replacement.
لو كان في حالة stress ممكن ازيد الدوز لحد 3 اضعاف متى ؟
temperature < 38 x2 , temperature >38 x3

Hydrocortisone 50-100 mg\m2 or 1-2 mg\kg IV as initiated dose.
. خصوصا لو عندي salt-wastingلانو باقي الانواع بتزيد الحالة سوء
Followed by 50-100 mg\m2\d IV.
IM or IV بكمل vomiting بقسم الكمية ع 4 مرات باليوم جرعة كل 6 ساعات, لو في
: ممكن استخدمsalt-wasting لو ما عندي
IM or IV methyl prednisolone 10-20 mg\m2 or 1-2 mg\m2 dexamethasone.
minerocorticoid effect ما بستخدمهم لانه الهم"

☒ لو جرعة steroid اقل ما رح الاقي تحسن بالأعراض ولو أعلى رح الاقي hyperglycemia, cushioned features, HTN, growth failure .

Chronic management:
goal :
1- achieve normal linear growth and normal bone age
2- prevent virilization.

- General average dose 10-25 mg\m2\d hydrocortisone orally divided into 2-3 doses, we change the dose depending on the pt.

: سهل أعدل الجرعة للمريض بس البدائل كالآتي low potency ولأنه 20 ,10 ,5 موجود بعيارات hydrocortisone أفضل اشي

1- Prednisone → suspension of 1mg\mL
1 mg = 4 mg of hydrocortisone.

2- Prednisolone → solution of 5 or 15 mg\5mL
1 mg = 5 mg of hydrocortisone

3- Dexamethasone → 1 mg = 50 mg hydrocortisone

☒ متى بستخدم البدائل ؟ لما اليكون المريض مش compliant عشان جرعات كثيرة غير هيك ببعد عنهم لانو بأثرو ع النمو وهمه high potency

- In mineralocorticoid → give oral flurocortisone .05-.2 mg\d)
- you can give NaCl 22-5 g\d to infant to counteract salt-wasting.
- Older children may lose their salt-wasting tendency with maturity.

Follow up:

1- Hormonal profile → 17 hydroxyprogeterone, should be 200-500 ng\dL
2- ACTH for adjustment of steroid dose بس مش كثير
3- Monitor growth
4- Monitor electrolytes, plasma renin activity, BP.
5- Clinical evaluation.

☒ لو عملت follow up ولقيت المريض ضغطه عالي و PRA قليل ؟ بقلل جرعة ال flurocortisone

- Surgical approach: only if ambiguous genitalia → clitoral recession then vaginoplasty post-puberty.
غير هيك بعطي أدوية تقلل ال virilization بس ما بعمل جراحة.

- If the patient developed precocious puberty 2ndry to advanced growth due to androgen exposure → treat with GnRH.
- Sometimes adrenal missed as gonadal tumors and causes pain
- In adulthood follow up → vaginal adequacy test because some of them present with dysparunia due to stenosis (if she got pregnant she'll probably deliver CS).
- If the Dx confirmed prenatal, give dexamethasone 20mg\Kg\d to mother into 3 doses to suppress fetal ACTH and prevent female fetus virilization.

<u>متى أوقفه ؟</u>
1- villus sample at 8-12 weeks or amniocentesis 18-20 week :
لو كان unaffected fetus لانو ال virilization بصير أول 12 اسبوع لو طلع البيبي سليم معناها خلص .

2- If the fetus is male.

- We may give growth hormone with GnRH to improve height.

مريض اجا بشتكي من اعراض testicular tumor فكر ب CAH لانه ال2 نفس ال embryologic anlage وممكن بسبب azoospermia , oligo أو حتى . Infertility

- But with adequate tt and Mx the prognosis is good.
- Be aware to give the stress dose of glucocorticoid in trauma, surgery or any illness to prevent early death.

Congenital immunodeficiencies

- **The commonest:** B-cell
- Impaired ability to produce normal immune response, and mostly genetic.
- Presented as recurrent infections, and affect adaptive or innate immunity.

- Innate is the first line defense then the adaptive.
  innate includes:
  1- soluble factors → chemokines, cytokines, acute phase proteins
  2- cellular components → neutrophils, monocytes, macrophages, natural killers

- Adaptive → T and B lymphocytes and their effector molecules.

- Frequency of certain infections in childhood:
  1- URTI maximum up to 8 times
  2- Otitis media up to 6
  3- Diarrhea up to 2

- Most of recurrent infections (90%) due to 2ndry cause not immune deficiency.
- **2ndry causes** of recurrent infections:
- **Viral**: HIV, measles, rubella, influenza
- **Metabolic**: DM, malnutrition, uremia, sickle cell disease, burns, zinc & vitamin deficiencies, multiple **carboxylase deficiency**.
- **Protein losing state**: nephrotic syndrome, protein losing enteropathy.
- **Other causes**:
  - prematurity, acquired asplenia, sarcoidosis, SLE and autoimmune d.
  - acquired neutropenia (autoimmune, viral infection, drug induced)
  - immunosuppressive agents(steroids, radiation, antimetabolites)
  - stem cell transplant\graft-hvs host
  - malignancy (leukemia, non-lymphoid, Hodgkin.

When to suspect immunodeficiency?
- frequency, severity, location of infection and pathogen + age of symptoms onset.

- **By Hx:**
  1- Recurrent sinopulmonary with encapsulated bacteria → B-cell
  2- FTT, diarrhea, malabsorption + opportunistic infection (fungi, candida, pneumocystic, carinii) → T-cell
  3- Viral infections → T-cell or natural killers
  4- Delay cord separation especially with omphalitis and →later on periodontal disease + poorely formed abscess → leukocyte adhesive
  5- Deep seated abscesses + recurrent skin infections with staph aureus, asperigillus, serratia marcescens → neutrophils function
  6- Severe and recurrent skin and respiratory infection → complement

- **Associated problems:**
  1- Atoxic telangiectasia
  2- Di George syndrome (chronic heart disease, hypocalcaemia)
  3- Atopic dermatitis (hyper IgE syndrome, omen syndrome)
  4- Easy bruising or bleeding disorders (Wiskott-aldrich syndrome)

- Family Hx of primary immunodeficiency or death in young children due to infections.

- **10 warning signs of primary immunodeficiency:**
  1- One or more ear infections in 1 yr
  2- 2 or more serious sinus infection
  3- 2 or more pneumonia in 1 yr
  4- 2 or more months on antibiotics with little effect
  5- Recurrent deep skin\organ abscesses
  6- Failure of infant to gain wt or row normally.
  7- 2 or more deep seated abscess.
  8- Need for IV antibiotics to clear infections
  9- Family Hx of immunodeficiency
  10- Persistent thrush in mouth or elsewhere in skin after age of 1 yr

By examination: recurrent infection in immunodeficiencies associated with pathology at infection site → morbidity like scaring of tympanic membrane → heaving loss

1- Height, wt, nutritional status and subcutaneous fat.
2- Oral thrush, purulent nasal or ear discharge, chronic rales
3- Absence of tissue (tonsils) → agammaglobinemia
4- Increased size of lymphoid tissue → CVID or HIV (common variable)
5- Eczema, petieches or bruises → wiskott-aldrich syndrome

B-cell immunodeficiencies:

1- IgA deficiency
2- IgG subclasses deficiency
3- Common variable immunodeficiency
4- X-linked agammaglobulinemia
5- Transient hypogammaglobulenemia of infancy

- Pluripotent stem cell (in bone marrow) → lymphoid precursor cell → PRO-B cell → PRE-B cell → immature B-cell → (then to spleen) → mature B-cell (native) → (blood and lymph) → plasma cells

X-linked agammaglobulinemia:

- Mutation in the gene encoding bruton tyrosine kinase (BtK) on Xq22 (and rarely may be AR), affect signaling of pro and pre cells. (pro or pre cells are present but no Ab)
- Usually present during 1st 6-12 months

- **findings**:
  1- profound deficiency in B-cells
  2- no lymphoid tissue (no tonsils but thymus normal)
  3- low immunoglobulin in blood (↓ antibodies)

- high risk for infections (strept. Pneumonia, H-influenza B, S- aureus)

ليش ببين بعد 6 اشهر وممكن سنوات ؟ لانه ال antibodiesالي من الام بتروح لانو ببلش يقلل الرضاعة الطبيعية والمخزون بروح
ما في ab ← يا zero or very low ← يشخص هيك او انو اعطي IVIG

- They have high risk of having giardiasis and entroviral infections ← chronic enteroviral meningeocephalitis and vaccine associated poliomyelitis (if it eas viral, life attenuated)

- **Treatments**:
  1- antibiotics
  2- lifelong infusion of immunoglobulin:
  - pooled from many individuals
  - gives passive immunity
  - boosted immune system

- **Common variable:** It's heterogeneous disorder

- **Presentation:**
  . Infancy and childhood (but mostly 20-30 yrs) as a first presentation, initial periods of normal immunity then ↓in immunoglobulin
  . With males and females equally

- **Labs:**
  1- Mature B-cell normal in number and morphology (or even low)
  2- But ↓in (B-lymphocyte) plasma cells (failure of B-cells to differentiate), defect in interaction between B & T, mostly causes by T-cell defect (variable T-cell number)
  3- low levels of most or all (Ig) classes
  4- Frequent bacterial infections

- **Pathogenesis :**
  . Defect in gene encoding ICOS (inducible C0-stimulator), CD19, 21, 81 and trans-membrane activator and Ca+2 modulating cyclophilin (TACI) → arrest in plasma cell differentiation
  . Serum IgG < 500 , IgA < 10, IgM low

- **Presentation:**
  1- In young children FTT
  2- Malignancies → B-cell lymphoma
  3- Recurrent respiratory infection → damaged bronchi → bronchiectasis
  4- Autoimmune disease 20% → RA, vitiligo, hemolytic anemia, GI diseases, neutropenia, thrombocytopenia, pyoderma gangrenosum.

- **DDx:**

1. X-linked agammaglobulinemia
2. X-linked lymphoproliferative hypogluboulinemia
3. Hyper IgM syndrome
4. Hypogammaglobulenemia as associated with thymoma 2ndry to medications or protein losing enteropathy

IgA deficiency:

- Common congenital type (autosomal inheritance) → dominant or resesive
- Common 1ry Ab deficiency ← selective IgA → < 10 mg\dL but other types or Ig is normal
- Dx at age of 7 trs → ما بقدر اشخص قبل
- Total IgA deficiency → undetectable IgA in serum or <5 mg\dL
- Partial IgA → ↓ levels more than 2 standard deviation below normal age-adjusted mean.
- Some congenital non-inherited cases associated with TORCH
- Administration of phenytoin, D-penicillamine, sulfasalazine, hydroxychloroquine increases the risk.
- Most of them are asymptomatic with:
  1- celiac 2- food allergy 3- autoimmune 4- recurrent sinopulmonary infections 5- recurrent diarrhea

انتبه: ممنوع تعطي دم عادي لانه ممكن يكون في IgA بالدم الي رح تعطيه وعنده AB ضدهم فيصير معه anaphylactic shock بالتالي بتعطي free IgA blood.

- Treatment: antibiotics → we don't give IVIg except in certain criteria

IgG subclasses:

- Total IgG levels are normal but one or more of the 4 subtypes is selectively decreased.
- الناس الطبيعيين ممكن يصير معهم قلة بنوع او اكثر عشا هيك مهم اسال عن recurrent infection Hx
- How to Dx? Inability to form AB against protein or polysaccharide antigen (the best) + Hx of recurrent infections and requiring therapy.

- IgG1 → protein antigen (anti-tetanus\diphtheria AB)
- IgG2 → polysaccharide antigen (antipneumococcal) + IgG4 (capsulated bacteria)
- IgG3 → respiratory viruses
- Complement fixation and activation: IgG3, 1, IgM and lesser degree IgG2.

- Transient hypogammaglobulenemia of infancy:
  Temporary condition → delay in Ig production.
- Etiology unknown but thought to be prolongation of physiological type
  → Ig levels remain low up to 1 yr then starts to increase (2-4 yrs) to normal levels (age-appropriate levels)

- **Dx:**
  1- Hx of recurrent sinopulmonary infections
  2- Normal levels of B-cell and I-cell
  3- Normal AB response to protein antigens (tetanus, diphtheria)
  4- Ig levels <200 mg\dL up to 1 yr, then starts to increase

T-cell disorders (combined ID):

- Profound ↓ or absence of T-cell (# or function). + B-cell dysfunction (due to absence of the gene itself or 2ndry to T-cell dysfunction.

DI George syndrome:

- Genetics: 22q11.2 deletion
- Appears in newborn and infancy.

- **CATCH 22 syndrome:**
  - **C**ardiac anomalies, **A**bnormal facies, **T**hymic hypoplasia (may be aplasia), **C**left palate, **H**ypocalcaemia.
  - **22**: gene.
- May have pyogenic infections, partial or complete T-cell dif.
- They have hypoplasia of 3rd and 4th pharyngeal pouches
- Associated with hypoparathyoridism → seizures or mental retardation (mild to severe)

- **Dx:**
  1- fluorescent in situ hybridization
  2- OCR + DNA probe to detect the deletion.

- **Due to hypoplasia in 3rd and 4th pharyngeal pouch:**
  1- Thymic hypoplasia
  2- Parathyroid hypoplasia (neouronal sizures)
  3- Bifid uvula
  4- Dysmorphic features
  5- Esophageal atresia
  6- CHD (ASD, VSD)
  7- Anomalies of great vessels (right aortic arch)

  . **Dysmorphic features:**
  1- Micrognathia
  2- Fish mouth
  3- low-set, large, dorsally rotated ears
  4- Hypetelorism
  5- Short philtrum
  6- Medial cleft → vertical indentation in middle upper lip.

  . **Cardiac anomalies:**
  1- Tetralogy of fallot (common)
  2- Transposition of great vessles
  3- Double utlet Rt ventricles
  4- VSD, ASD
  5- Interrupted aortic arch. (common)

Severe combined ID:

- No adaptive immunity and sometimes natural killers
- **Types**:
  1- X-linked:
  - the most common t50% of severe CID ,
  - only males affected, mutation in Xq13.1 for gamma chain
  - pts don't have T-cell or natural killers but normal # of B-cells
  - Ig are low or undetectable → no CD4 T-cell to stimulate B-cell

  2- Autosomal recessive:
  - defect in Janus kinase 3 (JAK3) which bind to gamma chain.
  - Similar phenotype like X-linked
  - T-cell with normal B-cell and natural killer number.

  3- Adenosine deaminase (ADA) 15%

  4- Purine nucleotide phosphorylase (PNP)

- **Clinical presentation:**
  1- First few months of life
  2- Opportunistic infection + viral (C.albicans, measles, varicella, CMV, EBV, parainfluenza 3)
  3- Severe enterovirus infection (severe diarrhea)
  4- Severe lymphopenia at birth
  5- Graft versus host D. from maternal immunocomplement T-cells crossing the placenta.
  6- Pneumonia, sepsis, otitis media, cutaneous infections.

  No Ig, no lymphoid tissue, small tonsils, small or no thymus

- **Tt** → true pediatric emergency → bone marrow transplant or death by 1 yr of age
  now → recently gene therapy

Ataxia-telangiectasia:

- Usually after 5 yrs not before.
- Autosomal recessive, 2-5 yrs
- High alpha fetoprotein as lab.

- **Characterized by**:
  1- progressive cerebellar ataxia → from beginning of walking, wheel chair at 10-12 yrs
  2- oculocutaneous telangiectasia → start at 3-6 yrs
  3- chronic sinopulmonary D. and bronchiectasis

- **Manifested** as recurrent meningitis, pneumonia, otitis media
- Neurological and endocrine problems especially DM.
- High incidence for malignancy, highly sensitive to ionizing radiation

- **By examination:**
  1- tics 2- drooling 3- irregular eye movement 4- mask-like faces

- ال characteristics و ال alpha fetoprotein
والعمر اكثر من ٥ هيك بقدر اشخص

- قبل ٥ سنوات بعتمد ال ataxia وال clinical

Wiskott-Aldrich syndrome:

- X-linked, in early infancy
- **Manifested** as classical triad:
  - eczema
  - thrombocytopenia
  - susceptibility to opportunistic and encapsulated bacteria.

- Defect in 53-KD protein
  - associated with: small platelets, cellular and humeral immune dysfunction

BE CAREFUL → in T-cell defects, fatal reactions may occur from life attenuated vaccines or BCG.

- **T cell defects:**
  - carry high incidence for malignancy
  - poor survival beyond infancy or early childhood

Complement system:

- Plasma and membrane proteins:
  - innate immune response
  - adaptive immunity

- They can kill pathogens without Abs by opsonization
- It can be activated by 3 pathways : classic, alternative, lectin
- It's disorders can be inherited deficiency or 2ndry to increase in consumption.

- **What indicates defects?**
  1- Recurrent Neisseria meningitis
  2- Angioedema
  3- Severe, recurrent skin and respiratory tract infection
  4- ↑ Incidence of autoimmune D.
  5- Recurrent bacterial infections with extracellular encapsulated organisms → S.pneumonia and H.influenza.

- Deficiencies in early components of classic pathway (C1. , 2, 4):
  Not severe infections, pts may have recurrent encapsulated bacteria and sinopulmonary infections + if young → ear infections

- C1, 2, 3, 4 → high incidence for autoimmune d. especially SLE.

C3 (complete absence):

- pyogenic infections with encapsulated bacteria (H.influenza, S.pneumonia)
- With time ABS are formed so infections become less severe and less frequent.

C5, 6, 7, 8, 9 (terminal complement def.):

- Forms membrane attack complex (foe Neisseria and gram –ve)
- Invasive pneumococcal or meningococcal disease.
- These pts should be immunized against encapsulated organisms.

Congenital C1 inhibitor def. → angioedema

- Recurrent, non-pruritic lasts for 48-72 hrs.
- Happens spontaneously or after minor trauma, anxiety, stress.
- With acute abdominal pain, edema of upper airway (laryngeal edema):
  life threatening and may lead to RS arrest so need emergency tracheostomy.
- May also have extremities swelling.

Childhood leukemia

Is a group of malignancies which include genetic abnormalities in hematobioteuc cells, which will produce uncontrolled clonal proliferation of immature blood cells, with different immune markers, age <15 yrs

- It's lethal in 6-12 months without treatment
- Etiology is unknown
- Malignancy of bone marrow cells
- Acute lymphocytic leukemia is the most common childhood type, M>F, white >black

1-Also it's one of the **most** common malignancies in childhood

2-then CNS tumor (neuroblastoma)

3-non Hodgkin lymphoma. Wilms

4-Hodgkin (near 13 yrs) , rhabdomyosarcoma

(muscles and soft tissue) > may present as a mass in anterior abdominal wall or mass in posterior orbit

Classification:

1. acute or chronic
2. lympoblastic or myelogenic

Main types :

1. ALL(77%)
2. acute myelogenic
3. chronic myelogenic
4. juvenile chronic myelogenic (JCML)

- ALL :M>F, age 2-6 years
- If uts part /ptis syndromic can present earlier

Genetic factors:

1. down, turner, klinefelter
2. blooms syndrome
3. fanconi, diamond blackfan
4. ataxia telegictasia
5. neurofibromatosis type 1

Environmental factors :

1. drugs, radiation
2. advanced maternal age, smoking
3. benzene, nitrosuria
4. alkylating agents
5. epipodo phyllotoxin

- There is association between EBU and B cell ALL

Note : all enlargement in ALL (lymph nodes, Hepatosplnomegaly, testicular enlargement) all are ***painless***

Clinical presentation :

1. bone marrow failure and infiltration
. Mucocutanous bleeding and epistaxis
. Pallor, purpura, pain, pyrexia, Hepatospelnomegaly and lymphadenopathy(large, painless, in advance stage :fixed) in 50%

2. nonspecific symptoms :
. Fatigue, low grade fever, bone pain, joints pain and limbing, irritable
. If unexplained persistence of any of these you should thinking of malignancies
. So on examination :temperature, bone tenderness

3. CNS : if there leukemic infiltrate
a. increase ICP (vomiting, headache)
b. cranial nerve palsies (6,4,3) 3:the eye will be directed laterally downward

4. respiratory distress :
. If there is mediastinal tumor (T-cell type)
. SOB due to external pressure on lungs

5. testicular involvement (first presentation or relapse)

- Mature B-cell ALL may be associated with extramedullary masses (abdomen, head neck, CNS) >> lymph nodes, spleen, CNS

- B-precursor ALL : bone pain, limbing, arthritis (MSS involvement)

- Testicular enlargement (relapse) or CNS carry bad prognosis and it is painless

Differential diagnosis :

1. infectious mononucleosis :lymphadenopathy, constitutional symptoms, fever, Hepatosplnomegaly
2. aplastic anemia : primary bone marrow failure, pancytopenia
3. one cell line affection : ITP,
   لازم اعمل biobsy لو أكثر من line
4. rheumatoid arthritis :fever, joint pain
5. other malignancies : neuroblastoma
6. AML

Physical examination :

1. may present with chest infection (URTI) not responding to antibiotics
2. very sick specially if he has respiratory distress
3. joints tenderness
4. purpura
5. lymph nodes enlargement
6. Hepatosplnomegaly
7. stridor if mediastinal involvement
8. CNS and cranial nerve palsy
9. vitals :
   - -low grade fever
   - -if increase ICP triad of : bradycardia, bradypnea, HTN ++rigidity, papilledema
10. examine the testis

Diagnosis :

1-Start with CBC and blood film (more accurate than CBC so used in screening)

- WBC :10*10^9/L + blast
- >50000*10^9 in 20% of cases
- In 20% of cases there is no blast in blood film, so??

If Highly suspected ALL we do :

1. bone marrow biobsy (ببين كل شي)
2. bone marrow aspirate (ببين بس الخلايا)

If WBC on upper border and there neutropenia
كيف بدي اتاكد لو هي السبب وعندو(neutropenia) ولا لا؟

- By absolute neutrophilic count (ANC)
- Neutrophils *WBC (number) *10
- If >1200 it is ideal normal value
- 500-1000 moderate
- <500 it is sever neutropnia
- On CBC : neutropnia, anemia, thrombocytopenia

2-bone marrow biobsy and aspirate :for all patients whit high suspicion
Cytogenic analysis, immune typing
immunohistochemistry, CD markers, HLA markersممكن من نفس العينه اعمل
جديد صارو يستخدموهم للتشخيص والعلاج

3-CXR for mediastinal masses

4-US for testicular enlargement

5-baseline echo, why?

For treatment > some chemotherapy have cardiotoxic activity (pleomycin)

Pleomycin >regimen for treatment of leukemia

6-lumbar puncture for CNS infiltration

But should be done by highly trained, expert doctor, why?

1. it may cause bleeding, and if there bleeding it may increase the grade so should be pure CSF
2. may give intrathecal treatment (steroid/methotrexate) in case of remission - induction

7-Metabolic abnormalities : uric acid, K, Po4, LDH, hypocalcemia, AKI

Tumor lysis syndrome : happens with proliferation ir after starting the treatment

بتكون كل ال (parameters) عاليه ما عدا الكالسيوم، ليش؟
Due to hyperohosphatemia which cause precepitation of calcium and decrease serum calcium

Top emergency:

Hypokalemia : cardiac effect

Management :

1. stop any K intake
2. calcium gluconate (protect heart)
3. glucose +insulin (shift to intracellular)
4. chelating by K oxalate (excretion or dialysis)

- Treat dehydration

Rx high uric acid by allopurinol or rasburicase (مهم اعملG6PD as it causes crisis)

Classifications:

1-morphology :(FAB classification) :
(Shape under microscope)

- L1:small, scanty cytoplasm, uniform
- L2:large, more cytoplasm, heterogeneous
- L3:large, abundant cytoplasm, similar to Burkett lymphoma

So they differ in cytoplasm, determine the grade depends on this

2-immunological markers :
There are monoclonal antibodies of leukomic cells
بشوفو شو الموجود وبحددو النوعB cells (85%)/T cells

-Pre B-ALL :75%

- immune :t9:22/t4:11/t1:19
- FAB :1or2

-T-cell ALL :15%

- Immune :14q11, 7q34
- FAB 1or2

-mature B(Burkett) :5%

- Immune :t8:14
- L3

***note :** high LDH indicate hemolysis seen in sickle cell, leukemia, anemia

Immunophenotyping :

1. T-cell :CD3
2. mature B cell
3. B cell ALL :CD 10,19,20,21,22,24, 79 (non CD 3)

Cytigenic study:

Good outcome :

- Hyperploidy (>50 chromosomes)
- Triple trisomy (4,10,17)
- t12:21,p13:q22

Bad outcome :

- Hypoploidy (<44 chromosomes)
- t4:11,q21:23
- Pheladelphia chromosome :t9:22,q34:q11

Prognosis according to number of WBC at diagnosis :

Good prognosis :

- Count :<10,000
- Female, white, 2-8 yrs
- No extramedullary, CNS, testicular involvement
- L1 FAB
- Trisomy :12:21,TEL:AML1
- Hyperploidy
- Time of remission <14 days

Bad prognosis :

- Count >200,000
- Male, black, age <1/>10yrs
- CNS, testicular, extramedullary involvement
- L2 FAB
- (MLL:AF4) (4:11)
- (ber:abl) (9:22)
- Hypoploidy
- Time of remission >28 days

How to treat?

1-remission - induction (4 weeks) : vincristine IV, oral steroid, thecal methotrexate

2-CNS (3 weeks)

3-maintainance (2-3 yrs) : oral methotrexate, oral steroid, IV vincristine, 6-mercaptopurine

Then supportive care :

1-Packed RBC and platelets, irradiated and leukocyte depleted, and should be CMV negative ??

لانو ممكن نحتاج transplant بلاش يصير عندو AB

2-any febrile child with low neutrophils >> empirical antimicrobial (aggressive) (pseudomonas) to prevent sepsis

When to do bone marrow transplant?

-If the patient treated with chemotherapy and presented with 2nd relapse
Long term survival :>5yrs in 80%

1. relapse 15-20% in bone marrow
2. CNS relapse
3. testicular relapse 1-2%

Acute myelogenous leukemia :

- No male:female difference
- Clinical presentation :

1. bone marrow failure
2. DIC
3. gingival infiltration
4. subcutaneous nodules

- May have proptosis due to vetro-occular chloroma
  Or on skin (abdomen)

- They will have leukopenia

بس بالعاده بقرا ال immature blast على انها WBC فبتطلع عاليه

- M3 : DIC
- M5 : gingival bleeding

DDx of gingival bleeding or hyperplasia

1. AML
2. Phenytoin
3. gingivitis or gingivostomatitis

- Prognosis same as ALL
- Minimal residual disease : good prognosis
- 5 yrs survival 60%

Complications :

1. emesis
2. GI erosion and bleeding
3. nasuea
4. malnutrition
5. alopecia
6. serous infection
7. thrombosis
8. CHF
9. growth delay, endocrine abnormalities (pituitary, Thyroid, parathyroid)
10. death

Chronic myeloid leukemia :

بتفرق عنهم بييجي المريض بsever crisis

-Very high WBC with Splenomegaly (chronic phase) 3-4 yrs

بعدها بييجي المريض بالاعراض هاي:

- Bone marrow >accelerate phase >may have tumor lysis syndrome
- Treat with chemotherapy, hydroxyurea, interferon

-Defentive cure : bone marrow transplantation

Congenital heart diseas

. **Commonest is VSD**

. **Intrauterine risk factors :**

1. drugs use (alcohol, lithium, Phenytoin, thalidomide)
2. maternal illnesses (DM, PKU)
3. infection (rubella)

. **CHD (depends on cyanosis) :**

- *Cyanotic (blue) :*
  1,2,3,4,5
  Right to left shunt (systemic)

1. truncus arteriosus (one (1) great vessel override ventricle)
2. transposition of great vessels
3. tricuspid (tri :3) atresia
4. tetralogy(tetra:4) of fallot
5. total anomalus pulmonary venous return
   (5 words)

- *Acyanotic (pink babies) :*

. 3Ds
. VSD
. ASD
. PDA
. Left to right shunt to pulmonary

1-VSD :

Common in :

1. apert's syndrome (cranial deformity and fusion of fingers and toes)
2. down syndrome
3. fetal alcohol syndrome
4. TORCH syndrome (toxoplasmosis, other agents, rubella, CMV, HSV)
5. chat syndrome
6. trisomy 13 (patau),trisomy 18 (Edward)

Clinical presentation :

1. *Small defect* are asymptomatic except murmur, harsh holosystolic murmur (left lower sternum)
2. *large defect* : FTT, dyspnea, frequent RS infection, CHF
   Softer holosystolic murmur with blowing
   - Can be accompanied by : 1-crackles 2-systolic thrill 3-narrow S1+high P1 4-midsystolic rumbling apical reflect increase in flow in mitral valve

Diagnosis : Defentive is echo

- ECG and CXR :

1. LVH in small defect
2. LVH+RVH in large defect

- Also in CXR > increase pulmonary vascular marking

Management :

Small : usually closed spontaneously, echo monitoring

Surgery :

1. <1yr with pulmonary HTN
2. Older children with large defect that haven't decrease in size over time
3. failure of medical treatment with Symptomatic patients

- Should treat CHF with inotrops, ACEI, diuretics

- Treat RS infection

2-ASD :

Associated syndromes:

a) fetal alcohol
b) down syndrome
c) holt oram syndrome (absent radius, ASD, first degree heart block)

ASD seccundu /foramen ovale : late, Commonest, symptoms depend on its size

ASD primum : early presentation, murmur, fatigue on exertion

Generally : RS infections, FTT, fatigue, but are frequently asymptomatic

1. right ventricle heave
2. may have mid diastolic rumble at left sternal border
3. wide fixed split S2 +systolic ejection murmur on upper sternal border, increase flow to pulmonary valve

Diagnosis :

By doppler with echo

1. blood flow
2. paradoxical wall motion
3. dilated right ventricle

ECG : right axis deviation (RVH), PR prolongation

CXR : increase pulmonary marking, cardiomegaly

Management :

Small : spontaneous closure

Surgery :

1. CHF
2. if ratio pulmonary :systemic flow more than 2:1

Early correction prevents the complications :

1. paradoxical embolism
2. right ventricle dysfunction
3. arrhythmia
4. esinmenger syndrome : shunt + pulmonary HTN, and shunt reversed and cause cyanosis
   Occur in any untreated cardiac defect

3-PDA :

- Failure to close in the first days of life
- From aorta to pulmonary

Risk factors :

1. female
2. prematurity
3. first trimester rubella infection

To close PDA give indomethacin

Clinical presentation :

- Asymptomatic
- If large defect : FTT, lower extremeties clubbing, CHF, lower RS infection

By examination :

1. bounding Peripheral pulses
2. continuous machinary murmur with wide pulse on second left intercostal space
3. loud S2

Diagnosis :

1. Color doppler (diagnostic) :blood flow from aorta to pulmonary
2. ECG : LVH
3. CXR :cardiomegaly if present
4. echo :in large PDA : left atrial + left Ventricular enlargement

Management :

- Give indomethacin unless it is needed for survival in tetralogy of fallot, hypoplastic left heart, transposition of great vessels

- If it is contraindicated (interventricular hemorrhage) don't give it, do surgery

Surgery :

- If indomethacin failed
- Or he is >6-8 months old

4- coarctation of aorta : narrowing

- Constriction of portion of aorta, increase flow proximal and decrease flow distal to it
- 98% below subclavian artery

Associated with :

1. turner syndrome
2. berry aneurysm
3. male

- Usually preductal, if postductal it is adult type
- 2/3 of patients have bicuspid aorta
- ***Differential cyanosis*** : Hand red (or less blue), feets are blue

Clinical presentation :

1. asymptomatic HTN
2. lower limb claudication
3. syncope
4. epistaxis
5. headache
6. radio-femoral delay : difference in the systolic BP between upper and lower extremeties
7. radio-radial delay :site of coarctation between right and left arm (right : preductal increased, left :postductal decreased)
8. weak femoral pusle
9. short systolic murmur in left axilla +forceful apical pulse

- Baby presents in first few weeks of life in shock like state?

Critical COA requires PDA for survival, presented due to closure of DA

- They may have cyanosis in left arm and both lower limbs

Diagnosis :

1-Echo with colored doppler (diagnostic)

2-CXR

- young children : cardiomegaly + pulmonary HTN
- older children :compensatory changes :
- LVH - 3 sign - rib notching

3 sign : pre and post dilitation of the aorta

Rib notching :collateral circulation by intercostal arteries

Management :

1. If sever : keep the DA open by prostaglandin E1 (alprostadil)
2. monitor for re-stenosis, aneurysm, dissection
3. surgery or balloon angioplasty (controversial)
4. give endocarditis prophylactic even if no abnormalities

5-TGA :

Commonest cyanosis H.D :
If it without PDA or septal defect : incompatible with life

Risk factors :

- Diabetic mother
- Rarely Digeorge syndrome

Digeorge syndrome : CATCH 22

- C:cardiac anomalies
- A:abnormal facies
- T:thymic aplasia
- C:clef palate
- H:hypocalcemia
- 22q11 deletion

Clinical presentation :

1. directly after birth :critical illness +cyanosis
2. reverse diffrential cyanosis if LV Outflow obstruction (coarctation, aortic stenosis)

By examination :

- Tachypnea, progressive hypoxia, cyanosis, no murmur if no VSD found
- May have sign of CHF, single loud S1
- **Note**: *reverse differential cyanosis* :the hand are blue and feet are red or less blue

Diagnosis :

1. echo
2. CXR :
   -narrow heart base
   -no main pulmonary artery segment (egg shape silhouette)
3. increase pulmonary vascular marking

Management :

- Start IV PGE1 to open or maintain PDA
- Do surgery within few days of life (atrial or arterial switch)

- If PDA can't be maintained by PG or surgery not feasible within few days > do balloon atrial septostomy (create or enlarge ASD)

6-TOF :

Note :

- TOF : common in childhood
- TGA : common in newborn
- TOF :PROVe

P: pulmonary stenosis **R:** RVH **O:** overriding aorta **V:** VSD

Risk factors :

1. digeorge syndrome
2. maternal PKU

- Early cyanosis due to left shunt due to VSD > right side pressure decrease after few weeks > shunt direction will reverse > cyanosis

- If pulmonary stenosis is sever the pressure may remains high and direction won't be reversed so the cyanosis may worsen with time

Clinical presentation :

1. in infancy or early childhood
2. dyspnea
3. fatiguability
4. no cyanosis at birth, they will have progressive cyanosis develops over the first tow years of life
5. FTT and change in mental status

They will have hypoxemic episodes

Infancy : asymptomatic up to 4-6 months, when CHF develops > fatigue on feeting (diaphoresis +tachypnea)

Children : tet spells
They often squat for relief during hypoxemic attacks

They will have systolic ejection murmur + right Ventricular heave + single s2 on left upper sternal border, due to right Ventricular Outflow obstruction

Diagnosis :

1. echo
2. catheterization
3. CXR : -boot shaped heart - decrease pulmonary marking
4. ECG :right axis deviation + RVH

Management :

- If the patient with severe stenosis or atresia > immediately PGE1 for PDA
- Surgery

If we can't perform surgery with specific time :

- Palliative management
- Artificial shunt (balloon atrial septostomy)

Surgery : blalock - taussing shunt

If the baby presented with tet spells?

1. put on O2
2. knee chest position
3. propranolol
4. phenylephrine
5. fluids +Morphine

Infants of diabetic mother

- The main cause of congenital anomalies in infants of DM mother is **hyperglycemia**
- Chronic DM causes small gestational and birth wt
- Gestational DM causes large gestational and birth wt
- MC complication is HIE

- M.C cardiac anomaly is septal hypertrophy
  - usually sub-valvular (cause murmur with wide splitting)
  - ductal dependent anomalies.

- Pathognomonic sign of these infants is sacral agenesis

- Factors risk of R.D in these neonates:
  1- HIE 2- TTN 3- INSULIN
  4- polycythemia (cause primary PHT) 5- congenital H.D

- High risk of sudden infant death syndrome → prevented by active sucking, prone position, sleep.

Management of hypoglycemia:

1) **Stable patient (no CVS manifestations, R.R < 50)**
   - Start feeding (70ml\Kg\day) divided into doses about 2 hrs in between
   - f.x: weight 4 kg → so need 280 ml, give 25 ml\2hrs

- Do random blood sugar after 30 min. of the meal.
- If still hypoglycemic: ↑ the volume of single meal (f.x: give 27 ml\2hrs)
- If still hypoglycemic →↑ volume, until you have 3 normal random blood sugar.

- But the upper limit of volume is up to 30 ml\2 hrs
- Start I.V fluid (70 ml\Kg\day) if you ↑ the volume up to 30 ml\24 hrs and the pt still hypoglycemic.

2) **Non-stable patient (R.R > 60 without seizures):**
- Start I.V fluid (70 ml\Kg\day)
- Avoid the bolus in this pt, due to the risk of rebound hypoglycemia.

3) **Non-stable patient (R.R > 60 with seizures):**
- Start with I.V bolus (4ml\Kg) of glucose water.
- Replace the bolus until the seizures resolve.
- Start with I.V fluid (70 ml\Kg\day) – (amount of bolus)

Which type & concentration of I.V fluid should be used?! Infusion rate ?!

- Normal glucose infusion rate is (4-6 mg\kg\min) but in any patient with hypoglycemia the rate is (6-8 mg\kg\min)
- Glucose water used in this case, but it's available with different concentrations, which one should we use?

Glucose = <u>infusion rate x weight x min of 1 day</u> (amount of glucose)
total volume to be given

f.x: weight = 4 kg → total volume 280 ml
infusion rate = 6
min = 1440\day

Glucose = 6 x 4 x 1440 \ 280
= 0.123 → 12.5% glucose water should be used.

❖ Any glucose water with calculation < 12.5 given I.V, but above it (12.5 & above) give the fluid through umbilical vein. (In adult through central line)

4) Patient still hypoglycemic after the I.V fluid
↑ the rate of infusion

5) Patient Still hypoglycemic after ↑ the rate of infusion:
↑ the rate of infusion, and calculate the new glucose fluid type.
- Upper limit of rate is 15 mg\Kg\min
- if the pt after that (infusion rate up to 15) still hypoglycemic, the medication therapy starts.

6) <u>Medication therapy</u>:
1. **Glucagon** → still hypoglycemic →
2. **Octreotide** → still hypoglycemic →
3. **Diazoxide** (anti-hypertensive so need BP monitoring) → still hypoglycemic →
4. **Corticosteroid** (consult the family for possible IQ defect) → still hypoglycemic → ???

7) <u>Surgical treatment:</u>
if still hypoglycemic despite the medication (CT then <u>pancreatectomy</u>).

7 Pediatric

Dr. Amjad Altamimi

Rudolph's Paedz.

INFANT OF THE DIABETIC MOTHER

Before the availability of insulin, the diabetic woman rarely became pregnant. Diabetes reduced her life expectancy and fertility. If she did become pregnant, the prognosis for mother and infant was poor. Before 1930, maternal mortality rates for diabetics ranged from 6 to 60%, and perinatal mortality from 25 to 73%. The availability of insulin dramatically improved the diabetic woman's life expectancy, fertility, and well-being during pregnancy. However, neonatal outcome was still poor until the establishment of a team approach by obstetricians, diabetologists, and neonatologists focused on achieving optimal maternal diabetes control to achieve a normal metabolic environment for the fetus. **With this effort, perinatal mortality rates of less than 2% have been achieved.**

The altered metabolic state of the pregnant diabetic is the critical factor responsible for the problems of the infant of the diabetic mother (IDM). **Maternal hyperglycemia causes fetal hyperglycemia,** subsequent fetal pancreatic β^2-cell stimulation, and **hyperinsulinism**. Hypertrophied β^2cells, seen at autopsy in IDMs, and elevated plasma insulin concentrations in newborn IDMs confirm the existence of the fetal hyperinsulinemic state.

Pregnancy in the insulin-dependent diabetic is commonly complicated by one or more of a wide variety of problems in the fetus and newborn. These include:

1. **Sudden fetal death late in the third trimester**
2. Premature birth from early induction of labor to avoid third-trimester fetal death
3. **Macrosomia**
4. **Birth trauma** as a result of macrosomia
5. **Intrapartum asphyxia**
6. **Cesarean section** delivery to avoid birth trauma and intrapartum asphyxia
7. Intrauterine growth restriction; **IUGR**
8. Neonatal respiratory distress; **RDS**
9. **Hypoglycemia**
10. **Hypocalcemia**
11. **Hyperbilirubinemia**
12. Hyperviscosity (polycythemia) syndrome
13. **Cardiomyopathy**
14. **Congenital anomalies, like sacral agenesis**
15. Increased risk of **obesity** and of **diabetes mellitus** in ***later life***

In general, **the risk of neonatal problems is GREATER when there is a history of POOR metabolic control of the mother.** Many of these complications coexist: **the combination of hypocalcemia, hypoglycemia, jaundice, and macrosomia is particularly COMMON.**

Gestational diabetes mellitus, the mildest form of maternal diabetes that has its onset during the pregnancy, also increases the risk of perinatal loss. Although improved maternal care has reduced the incidence of this complication, **infants of women with gestational diabetes remain at increased risk of all of the morbidities EXCEPT** for **congenital anomalies**, **subsequent obesity**, and **diabetes mellitus** late in life.

BODY SIZE

Macrosomia is a well-known characteristic of the offspring of diabetic women. Their large size increases their risk of birth trauma and the incidence of cesarean delivery. **The rate of delivery by cesarean section in diabetic women is four to five times greater than that in nondiabetic women. Much of the increased mass in macrosomic IDMs consists of fat.** Measurement of fat-cell size and skinfold thickness in IDMs, as well as postmortem analyses of IDMs who died during the neonatal period, suggest that **the IDM has almost twice as much fat as an infant of comparable gestational age born to a nondiabetic mother.** In addition, the IDM has an excessive amount of nonfatty tissue. **The liver and heart are often enlarged, and skeletal length is increased in proportion to weight.** The macrosomic IDM head may appear disproportionately small because

brain size is NOT increased relative to gestational age. Much of this excess tissue in IDMs is distributed in the shoulders and intrascapular area. This increases the risk of shoulder dystocia in IDMs compared with infants who are constitutionally large and have a more uniform distribution of tissue.
Because insulin is an anabolic hormone, the hyperinsulinemic state of the IDM fetus plays a major role in the development of macrosomia. The augmented insulin production by the fetus, plus excessive maternal glucose and amino acids, stimulates protein, lipid, and glycogen synthesis to cause macrosomia. Insulin-like growth factors also are increased in macrosomic IDMs and probably contribute to their large size. The excess fat in IDMs appears to accumulate during the third trimester, as IDMs who are delivered before 30 weeks of gestation are RARELY large for gestational age, and serial ultrasound measurements of the fetus show that the fetal IDM does not exceed normal growth limits until 28 to 30 weeks of gestation.
Metabolic fuels other than maternal glucose may also contribute to the macrosomia of IDMs. There is a positive correlation between the body size of the IDM and the concentration of amino acids and free fatty acids in maternal plasma when measured after an overnight fast.

Because fetal macrosomia increases the risk of birth trauma, asphyxia, and delivery by cesarean section, one major goal in caring for the pregnant diabetic is to reduce accelerated fetal growth by reducing fetal hyperinsulinemia. This usually can be achieved by frequent administration of short-acting insulin, to regulate maternal blood glucose concentration and by careful attention to diet and weight gain.
Despite intensive treatment, macrosomia develops in fetuses of 20 to 30% of insulin-dependent diabetic women. Women with gestational diabetes, the mildest form of carbohydrate intolerance, have an equally high incidence of macrosomia. These observations indicate that present insulin therapy cannot completely normalize metabolic fuel availability to the fetus. In the case of gestational diabetes, the present regimen of maternal diet regulation is not always successful because of poor compliance.

Some IDMs are small for gestational age; SGA. In general, the risk of IUGR is directly related to the severity of maternal diabetes. The most likely explanation for fetal growth restriction in the face of maternal diabetes is the presence of maternal vascular disease with resultant fetal deficiency of nutrients, including oxygen.

HYPOGLYCEMIA

Hypoglycemia in the neonate is usually defined as a blood glucose concentration less than 40 mg/dL. Hypoglycemia occurs in 25 to 50% of IDMs within the first 24 hours after birth. This is particularly likely in those who are macrosomic. The mechanism for development of hypoglycemia in the IDM includes both diminished production and increased clearance of glucose.

Most IDMs, unlike infants of normal women, have elevated plasma C-peptide or insulin concentrations. In addition, many IDMs have pancreatic β ²cells that respond to glucose challenge with a brisk outpouring of insulin, as compared with the sluggish response of the normal neonate. Maintaining maternal glucose concentrations within the normal range is, therefore, an important objective for reducing the risk of hypoglycemia. Several studies also suggest that the IDM fails to release glucagon or catecholamines in response to hypoglycemia. Thus, *because insulin clears glucose from the intravascular space*, and *glucagon and catecholamines normally stimulate glycogen breakdown and gluconeogenesis*, the IDM has BOTH increased glucose clearance and diminished glucose production, resulting in hypoglycemia.

Infants with hypoglycemia may present with lethargy, hypotonia, tremulousness, excessive sweating or cyanosis. They also may present with seizures. If the period of hypoglycemia is prolonged, myocardial contractility diminishes, and congestive heart failure may develop. IDMs are sometimes asymptomatic despite having blood glucose concentrations less than 30 mg/dL. Because hypoglycemia, even in the absence of symptoms, may cause brain damage and lead to long-term neurologic impairment, it is recommended that blood glucose concentrations be maintained above 40 mg/dL for all IDMs.

CARDIOMYOPATHY

IDMs have an increased incidence of cardiomyopathy, in which there is often **thickening of the interventricular septum and one or both ventricular walls**. This likely results from the fetal hyperinsulinemic state. *The majority of these infants are asymptomatic*, and the thickening is detected only by an electrocardiogram or echocardiogram. In some infants, an **ejection systolic murmur** is heard at the mid- to upper left sternal border. In a few with very marked septal thickening, left ventricular outflow obstruction may lead to left ventricular failure in the first few days after birth. The electrocardiographic and echocardiographic abnormalities generally regress over 3 to 6 months, and the condition appears to leave no permanent effects on the myocardium.

IDMs, especially those who experience **intrapartum asphyxia**, may present with **severe congestive heart failure soon after birth**. Respiratory distress and cardiomegaly may persist in such infants, and often they are hypoglycemic and hypocalcemic. If the left ventricle becomes dilated, a murmur of mitral valve insufficiency also may be heard. Such infants usually improved with application of assisted ventilation and correction of their metabolic abnormalities. They usually recover fully in a few days, although their hearts remain enlarged longer.

CONGENITAL ANOMALIES

Major congenital malformations occur **two to four times more frequently** in IDMs than in infants born to nondiabetic women. **Congenital heart defects, notably VSDs,** are especially common in IDMs. The incidence **of neural tube defects, gastrointestinal atresia, and urinary tract malformations** also is greater in IDMs than in infants born to nondiabetic women. **Spinal agenesis** associated with **caudal regression syndrome is a** malformation that occurs **almost EXCLUSIVELY in IDMs.**

A transient anomaly, unique to the IDM, is known as **neonatal small left colon syndrome,** or microcolon. This condition presents as gastrointestinal obstruction and may mimic congenital aganlionic megacolon or Hirshprung disease. Unlike infants with Hirschprung disease, however, these infants have normal innervation of the bowel and ultimately have normal intestinal function.

A considerable number of clinical observations **indicate that poor control of maternal diabetes during the first trimester, the key period for fetal organogenesis, is a major factor in causing congenital anomalies.** Alterations in the availability of numerous metabolic substances resulting from maternal diabetes have been suggested to cause these anomalies. Because the period of critical organogenesis is relatively long in the human, the day-to-day fluctuations in diabetes control may account for the frequent occurrence of multiple birth defects in a single infant and for the failure of the lesions to conform to one particular pattern. Assuring optimal metabolic control before conception and during the first trimester is an important clinical and cost-effective strategy to reduce the incidence of congenital anomalies.

OUTCOME

Infants of diabetic mothers, particularly those who are macrosomic at birth, **have an increased risk of obesity later in life.** Because childhood obesity of IDMs correlates with amniotic fluid insulin concentration during fetal life, insulin secretion from fetal pancreatic β^2 cells may be an important factor in the development of obesity.

Offspring of women with insulin-dependent diabetes have an **increased risk of acquiring diabetes in later** life. The mechanisms responsible for this are not understood. IDMs also are at risk for subsequent development of impaired insulin responsiveness during adolescence, as assessed by insulin secretion in response to a glucose challenge. A number of studies also suggest a unique gender risk. Offspring of fathers with insulin-dependent diabetes are at significantly greater risk of acquiring diabetes than offspring of insulin-dependent diabetic mothers.

In the past, IDMs were at great risk for brain damage, with **impaired motor** and **intellectual development.** This was attributed, at least in part, to **birth trauma, asphyxia, hypoglycemia,** and other neonatal morbidities. Careful medical and obstetric care of the mother and appropriate neonatal care greatly reduce the risk of these complications. Maintaining excellent treatment of maternal diabetes during pregnancy is equally important for long-term cognitive and psychomotor development. Poor maternal control during the second and third

HYPOCALCEMIA AND HYPOMAGNESEMIA

Hypocalcemia occurs in 10 to 20% of IDMs during the neonatal period. Hypocalcemia usually is associated with hyperphosphatemia and sometimes with hypomagnesemia. The mechanism responsible for hypocalcemia is unclear, although plasma parathormone concentrations in IDMs have been reported to be significantly LESS than in infants of normal mothers during the first 4 days after birth. This may result from hypomagnesemia, which limits parathormone secretion even in the presence of hypocalcemia. Maternal hypomagnesemia, *perhaps caused by increased renal losses with diabetes*, is believed responsible for the fetal and neonatal hypomagnesemia. Administering $MgSO_4$ to the IDM, however, does NOT prevent hypocalcemia. The active transport of calcium and magnesium by the placenta may be impaired in maternal diabetes. Birth asphyxia, which frequently occurs in IDMs, also may lead to hypocalcemia.

The clinical signs of hypocalcemia include tremulousness, twitching movements, or generalized convulsions. Arrhythmias also may occur, but the characteristic prolongation of the Q-T interval does not occur consistently in neonates with hypocalcemia.

Total or ionized plasma calcium concentrations should be measured 1 to 2 hours after birth and during the first several days in IDMs. Because birth asphyxia and RDS increase the risk of hypocalcemia, IDMs with these disorders should receive calcium gluconate with their daily parenteral fluids in the first postnatal days. Although in neonates the daily maintenance dose of elemental calcium is usually 75 to 100 mg per kilogram body weight, at least 100 to 200 mg/kg is needed daily, and many IDMs require two to three times that dose. Symptomatic hypocalcemia should be treated with an infusion of 10% calcium gluconate at 2 mL/kg body weight given over 5 minutes. This dose provides 18 mg/kg of elemental calcium. During infusion, continuous ECG monitoring of heart rate is important because a rapid intravenous infusion of concentrated calcium may cause arrhythmias. Daily maintenance of calcium should be initiated following this initial therapy. Infants who are hypocalcemic with associated hypomagnesemia will not become normocalcemic until their serum magnesium concentration is corrected. A 50% solution of magnesium at a dose of 0.25 mg/kg may be administered intramuscularly to correct hypomagnesemia.

HYPERBILIRUBINEMIA

Up to 30% of IDMs have jaundice with elevated indirect bilirubin concentrations within 3 days after birth. Their carbon monoxide production is increased, which is an indicator of hemoglobin catabolism and increased production of bilirubin. Hyperbilirubinemia in these infants may be related to their large size, which increases the risk of birth trauma. Resorption of blood from resulting hematomas or bruises causes hyperbilirubinemia. In addition, polycythemia frequently occurs in the IDM, and the normal rate of breakdown of the increased red cell mass results in a larger bilirubin load for the liver to conjugate than in normal infants. Therapy is the same as for neonatal jaundice from other causes.

HYPERVISCOSITY

Up to 20% of IDMs are polycythemic, which may account for their increased risk for the neonatal hyperviscosity syndrome. Several factors appear to contribute: the hematocrit of umbilical cord blood at birth tends to be elevated, probably because of increased erythropoiesis; IDMs often have enhanced placental transfusion at delivery; and elevated plasma fibrinogen concentration increases blood viscosity. The increased incidence of renal vein thrombosis reported in IDMs is probably related to hyperviscosity, although this disorder does occur in IDMs with normal hematocrits.

RESPIRATORY DISTRESS

The IDM is at risk for several forms of neonatal respiratory distress. The most important of these is hyaline membrane disease from insufficient pulmonary surfactant. The high risk of hyaline membrane disease is related to premature delivery as well as to retarded maturation of the pulmonary surfactant system. In cultured fetal lung tissue, insulin blocks the development of enzymes necessary for the synthesis of lecithin, a principal ingredient of surfactant. Even with the use of methods to detect maturation of surfactant by amniotic fluid analysis, there is a 10% incidence of hyaline membrane disease in IDMs.

trimesters, particularly alterations in ketone metabolism, can be directly correlated with abnormal neonatal behavior and with poor indices of infant development at age 2 years and of intelligence at age 4 years.

Reference:

Rudolph's Pediatrics, 21st Edition, Rudolph, Colin D.; Rudolph, Abraham M.; Hostetter, Margaret K.; Lister, George; Siegel, Norman J.

Designed by: Deya' Hwarat Abbady.

D. Hwarat©

عطاء تصوير جامعة مؤته
كلية الشريعة
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Pneumonia

المحاضرة + التبييض (اللي بمربعات)

- Community acquired
- Hospital
- Ventilator
- Co-infection 75% in infants (without viruses or bacteria)
- Inflammation of lung which will stimulate responses resulting in tissue damage. It's common in children and causes death yearly.

Introduction

- Pneumonia is defined as inflammation in the lung caused by an infectious agent that stimulates a response resulting in damage to lung tissue.
- Community-acquired pneumonia (CAP) is one of the most important health problems affecting children worldwide .
- (CAP) accounting for approximately **20%** of all deaths in children younger than 5 years.
- Viruses are, by far, the most common cause of CAP.
- The introduction of conjugate vaccines for **pneumococcus and *H. Influenzae*** in the past decade has reduced the burden of bacterial disease.
- Currently, *Streptococcus pneumoniae* and *Mycoplasma pneumonia* are the most prevalent bacterial agents among immunized populations, especially beyond the neonatal period.

- Most common cause of CAP → viruses
- Bacterial in immunized pts →
- mycoplasma pneumonia
- In neonates → strept. Pneumoniae

Etiology

- Pneumonia can be caused by several different microorganisms:
- **viruses** →
- -the most prevalent cause of pneumonia throughout childhood, with the highest burden observed among infants.
- -Coinfection rates up to **75%** are commonly reported in infants
- **bacteria**
- **Fugual** Immunocompromised underlying pathology (dyskinesia and cystic fibosis
- **mycobacterium** Endemic areas
- **Parasites**

Table 400-2 | Causes of Infectious Pneumonia

BACTERIAL	
Common	
Streptococcus pneumoniae	Consolidation, empyema
Group B streptococci	Neonates
Group A streptococci	Empyema
*Mycoplasma pneumoniae**	Adolescents; summer-fall epidemics
*Chlamydophila pneumoniae**	Adolescents
Chlamydia trachomatis	Infants
Mixed anaerobes	Aspiration pneumonia
Gram-negative enterics	Nosocomial pneumonia
Uncommon	
Haemophilus influenzae type b	Unimmunized
Staphylococcus aureus	Pneumatoceles, empyema; infants
Moraxella catarrhalis	
Neisseria meningitidis	
Francisella tularensis	Animal, tick, fly contact; bioterrorism
Nocardia species	Immunosuppressed persons
*Chlamydophila psittaci**	Bird contact (especially parakeets)
Yersinia pestis	Plague; rat contact; bioterrorism
Legionella species*	Exposure to contaminated water; nosocomial
*Coxiella burnetii**	Q fever; animal (goat, sheep, cattle) exposure
VIRAL	
Common	
Respiratory syncytial virus	Bronchiolitis
Parainfluenza types 1-3	Croup
Influenzas A, B	High fever; winter months
Adenovirus	Can be severe; often occurs between January and April
Human metapneumovirus	Similar to respiratory syncytial virus
Uncommon	
Rhinovirus	Rhinorrhea
Enterovirus	Neonates
Herpes simplex	Neonates
Cytomegalovirus	Infants, immunosuppressed persons
Measles	Rash, coryza, conjunctivitis
Varicella	Adolescents or unimmunized
Hantavirus	Southwestern United States, rodents
Coronavirus (severe acute respiratory syndrome, Middle East respiratory syndrome [MERS])	Asia, Arabian peninsula
FUNGAL	
Histoplasma capsulatum	Ohio/Mississippi River valley; bird, bat contact
Blastomyces dermatitidis	Ohio/Mississippi River valley
Coccidioides immitis	Southwest United States
Cryptococcus neoformans	Bird contact
Aspergillus species	Immunosuppressed persons; nodular lung infection
Mucormycosis	Immunosuppressed persons
Pneumocystis jiroveci	Immunosuppressed, steroids
RICKETTSIAL	
Rickettsia rickettsiae	Tick bite
MYCOBACTERIAL	
Mycobacterium tuberculosis	Travel to endemic region; exposure to high-risk persons
Mycobacterium avium complex	Immunosuppressed persons
PARASITIC	
Various parasites (e.g., Ascaris, *Strongyloides* species)	Eosinophilic pneumonia

- Bacterial:
  - Strept. Pneumoniae → empyema, consolidation
  - Group A sterpt. → empyema
  - Mycoplasma → summer-fall
  - Gram –ve → nosocomial
  - Staph. Aureus → pneumatocele
  - Ligonella → contaminated water
  - Coxiella → fever, animals
- Viral:
  - Common RSV → broncholitis
  - Parainfluenza 1-3 → croup
  - Influenza → high grade fever in winter
  - Adenovirus → severe, from January to April

Table 25.1 Most Common Agents Causing Community-Acquired Pneumonia According to Age Group

bacteria

AGE				
Newborns	**1–6 Months**	**6–12 Months**	**1–5 Years**	**Older Than 5 Years**
Group B Streptococcus Enteric Gram-negative RSV	Viruses *Streptococcus pneumoniae* *Haemophilus influenzae* *Staphylococcus aureus* *Moraxella catarrhalis* *Chlamydia trachomatis* *Ureaplasma urealyticum* *Bordetella pertussis*	Viruses *Streptococcus pneumoniae* *Haemophilus influenza* *S. aureus* *Moraxella catarrhalis*	Viruses *M. pneumoniae* *S. pneumoniae* *C. pneumoniae*	Viruses *M. pneumoniae* *S. pneumoniae* *C. pneumoniae*

Commonly negative bacteria

Typical scenario:
URTI then start to have productive cough (or w\o)

Pathogenesis

- The upper airways are commensally colonized by a variety of organisms .
- Lower airways are not considered sterile any more
- URTI usually precede lower respiratory tract invasion by microorganisms, such as bacteria and viruses.
- Mechanisms of invasion :
    1- Contiguous spread and replication →viraus , atypical bacteria .
    2- Microaspiration →bacterial pneumonia.
    3- hematogenous spread : *S. aureus*
  - In children, significant aspiration may occur, due to swallowing dysfunction, gastroesophageal reflux, or congenital malformations.

In infection→
↑ airway resistance, atelectasis, necrosis, abnormal ventilation-perfusion ratio.

- In the lower airways, the infectious process begins with immune response leading to leukocyte infiltration, edema and consequent small airway obstruction; this is followed by loss of tissue compliance, increase in airway resistance, atelectasis, abnormalities in ventilation-perfusion ratios, and necrosis.
- Development of pneumonia depens on :
- **1- Microorganism Virulence factors**→ Invasion of tissue
  also facilitate the evasion of immune defenses, causing lung invasion and tissue destruction such as occurs with the protein NS1 from some influenza strains, and with surface proteins of *S. pneumoniae.*
- **2- host factors**
- Impairment of the epiglottic and cough reflexes, interruption of mucociliary clearance
- Both humoral and cellular immune responses are crucial to protect children against pneumonia

- Microorganism virulence → tissue invasion
- Host factors → immunity + impairment of reflexes interrupt with clearance

Clinical features depends on :

Below 3 months
fever ممكن بس

1. **Age :**
   Infants in the first 3 months of life may present with a cough and respiratory distress associated with low grade or no fever
2. **Immune system response**
3. **Virulence of the organisms**

يعني لو أجا مريض عنده بس fever & tachypnea
استثني انو asthmatic or bronchiolitis
عالج ع اساس pneumonia وانت مغمض

Gradual onset + general symptoms → mycoplasma
Insidious onset → Hib

SYMPTOMS

Common clinical findings include :

- **fever ➔ -the most sensitive sign**
  Children can have fever and pneumonia without over manifestations of respiratory disease(5.3%)
- productive cough : only 0.28% of the children has pneumonia without cough
- tachypnea
- abdominal pain and chest pain.
- retraction and grunting **➔most specific, associated with alveolar infiltrates found on a chest radiograph .**
- For Hib, the clinical picture is similar to other typical bacteria, although a more insidious onset is the rule.
- A more gradual clinical onset associated with a combination of symptoms, such as headache, malaise, nonproductive cough, and low-grade fever/no fever, is general associated with infection by atypical pathogens such as ***M. Pneumonia***

PHYSICAL FINDINGS

- Tachypnea :
  more sensitive and specific than crackles on auscultation, after the exclusion of a diagnosis of bronchiolitis or asthma.
- Chest retraction
- Cyanosis
- Dullness to percussion
- On auscution : crackles , bronchial breathing
  - Wheezing is most frequently associated with infection by viral agents, and *Mycoplasma* or *Chlamydia,* is an unlikely cause.

-Most sensitive is tachypnea
-Wheezes: mostly viral

LABORATORY TESTS

- of little clinical utility for an individual subject
- Higher white blood cell counts and concentrations of C-reactive protein, as well as procalcitonin, have been associated with bacterial pneumonia, but there is great overlap with pneumonia of viral etiology;

- Bacterial→ ↑ CBC, ↑ CRB, ↑ procalcitonin
but There is overlap with viral infection

1- CXR is standard in Dx pneumonia in hospitalized pts.
2- CXR don't affect the outcome of lower infection in pt > 2 months ما بعملها الهم

1. O2 sat.< 90 اي وحدة منهم
2. Central cyanosis
3. Severe respiratory distress
4. Altered conciseness or convulsions
5. Inability to eat or drink (vomit everything)

	Clinical signs
Severe pneumonia	Any one of: oxygen saturation <90%, central cyanosis, severe respiratory distress, inability to drink or breastfeed or vomiting everything, altered consciousness, and convulsions
Non-severe pneumonia	Lower chest wall indrawing or fast breathing (respiratory rate ≥50 breaths per min if aged 2–11 months; ≥40 breaths per min if aged 12–59 months), and without signs of severe pneumonia

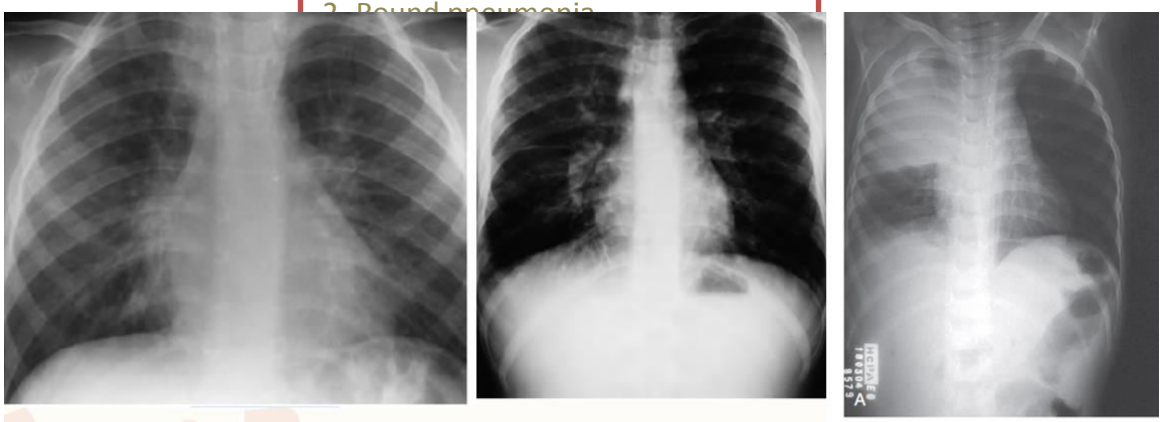
1) RR > 50 if 2-11 months
> 4 if 12-59 months
+ no signs of severity

radiological finding:

- مش بحاجة اضل اعيدها لل follow up
- بالبداية ممكن يكون عند المريض اعراض بس CXR Clear

- In general, chest radiographs are standard practice in hospitalized children for whom a diagnosis of pneumonia is being considered.
- Because chest radiographs do not change the outcome of LRTIs, guidelines do not recommend them for children older than 2 months of age who are cared for in an outpatient setting.
- In the early clinical stages of disease, patients with bacterial pneumonia may have normal chest radiographs.
- it is usually impossible to make an etiologic diagnosis based on a chest radiograph.
- No follow-up radiographs are needed to evaluate a CAP with good clinical response, except for cases of round pneumonias, lobar collapse, or whenever clinical deterioration may occur .

When to use CXR as follow up?
1- Clinical deterioration
2- Round pneumonia



Bronchopneumonia | Diffuse pattern of increased interstitial markings | Lobar pneumonia

Differential diagnosis

The differential diagnosis of CAP includes :

- viral bronchiolitis.
- Asthma.
- cardiogenic causes of tachypnea.
- interstitial lung diseases .
- chemical pneumonitis, especially those secondary to aspiration syndromes.

General Management

If the pt has mild symptoms → at home
are re-evaluate within 48 hrs.

- Infants and children with CAP without danger signs(mild) can be safely cared for at home.
- In this situation, the child usuall should be reexamined within 48 hours after beginning treatment.

indications for hospital admission for infants aged less than 2 months :

- SaO2 of 90%–92% or less,
- cyanosis, difficulty breathing, intermittent apnea ,grunting .
- a respiratory rate greater than 70 breaths per minute .
- an inability to feed .
- failure after oral therapy .
- severe malnutrition and other comorbidities
- a family incapable of providing appropriate care .

No need for physiotherapy

-Be careful when giving fluids SIADH will cause hyponatremia
بدي اشوف لو معهم ال NG tubeاو لا لانو بسكر الانف وممكن يزيد الdistress

In older children, the indicators are:

- a SaO2 of 92% or less .
- cyanosis, respiratory rate greater than 50 breaths per minute .
- grunting, difficulty breathing .
- signs of dehydration, or a family incapable of providing appropriate observation or supervision.

distress

General management for hospitalized children includes :

- oxygen delivery through a mask or nasal cannula to keep oxygen saturation above 92%,
- Antipyretics .
- IV fluids if the child is unable to drink.
- Fluid intake should be carefully monitored because pneumonia can be complicated by hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone secretion.
- The benefit of nasogastric tube feeding should be weighed against its potential for respirator distress due to the obstruction of a nostril, or by inducing gastroesophageal reflux.
- Respiratory failure, when present, should be managed appropriately and **noninvasive ventilation** may be used to avoid tracheal intubation.

- Children should be admitted to an intensive care facility with continuous cardiorespiratory monitoring capabilities when invasive ventilation is required, or pulse oximetry measurements are below 92% with the child o inspired oxygen concentrations of 50% or more.
- There is no evidence for the usefulness of chest physiotherapy in the management of CAP; therefore it is not currently indicated .

If respiratory failure present:
1- ICU admission 2- non-invasive ventilator
3- continuous cardiopulmonary monitoring if invasive ventilator required or if O2 sat. < 92%

Treatment With Antimicrobials:

- Don't give antibiotics directly since the common is viral
- Most tests don't differentiate viral from bacterial.
- When atypical infection → macrolide
- Guideline recommended oral amoxicillin (dose)
  if IV required → penicillin or ampicillin
- If the pt has resistance to pneumococcus + severely ill : give vancomycin or tiecoplanin
- Nenonate + CAP → IV ampicillin + gentamycin
- If there is evidence of S.aureus → methicillin or vancomycin
- Children from 3 weeks- 3 months + CXR changes of infiltration + it's not viral → macrolide (C.trachomatic, B.pertussis)

- All current guidelines recommend **oral amoxicillin(high dose) as the first choice, and penicillin or ampicillin if IV treatment is required .**
- Macrolid should be added when pneumonia due atypical bacteria is suspected .
- Vancomycin or teicoplanin should be reserved for severely ill patients, when coverage for highly resistant pneumococcus is desired .
- Neonates with CAP can be treated with a combination, such as IV ampicillin and gentamicin.
- Whenever there is a positive culture or a clinical picture suggestive of *S. aureus,* specific antibiotic coverage against this pathogen should be added (e.g., methicillin, oxacillin,clindamycin, or vancomycin in the case of MRSA strains).
- For symptomatic children between 3 weeks and 3 months of age with interstitial infiltrates visible on chest radiograph, if a viral etiology is not the most likely diagnosis, a macrolide should be used to cover for agents such as *C. trachomatis, B. pertussis,* and *U. urealyticum.*
- Children between 4 months and 5 years of age with CAP are most likely infected by pneumococcus, viral agents, or both, and amoxicillin, penicillin, or ampicillin are the drugs of choice .

- Strep → penicillin or dose amoxicillin or azithromycin, cefuroxime, cefotrixamine
- S.aureus → methicillin, oxicilin or vancomycin, tiecoplanin
- Moraxella → amoxicillin, clavulanate or cefuroxime.

Table 25.2 Choice of Antibiotic Treatment for Community-Acquired Pneumonia When Typical Bacteria Are Identified

Pathogen	First Choice	Other
Streptococcus pneumoniae, penicillin susceptible or intermediate	Penicillin, ampicillin, or high-dose amoxicillin	Cefuroxime, ceftriaxone, azithromycin
S. pneumoniae, penicillin resistant (MIC ≥ 4 µg/mL)	Second- or third-generation cephalosporins for sensitive strains; vancomycin	
Staphylococcus aureus	Methicillin/oxacillin	Vancomycin or teicoplanin (for MRSA)
Haemophilus influenzae	Amoxicillin	Amoxicillin/clavulanate, cefuroxime, ceftriaxone, other second- and third-generation cephalosporins
Moraxella catarrhalis	Amoxicillin/clavulanate	Cefuroxime

- Children 4 months – 5 years who are infected with pneumococcus or viral or both→ give amoxicillin, penicillin, ampicillin
- If H.influenza → amoxilcillin, 2nd and 3rd generation cephalosporin

Slowly Resolving Pneumonia:

the persistence of either clinical or radiological findings of pneumonia beyond the normal time course during which one would expect the infection to resolve (i.e., between 48 and 96 hours after empiric "adequate" antimicrobial treatment).

– However, radiologic resolution may take several weeks. Radiologi abnormalities are found 3–7 weeks after initial episode in a substantial proportion of patients.

- Slowly resolving persistence clinical or radiological finding beyond the normal time to resolve (48 to 96 hrs of empiric tt.

adequate بس بدي اتاكد انو

- Resolve of radiological findings need weeks, 3-7 weeks after initial episodes.

Causes:

- an inappropriate choice of drugs.
- The presence of empyema or an underlying lung abscess should be considered whenever there is persistence of fever with or without pleuritic pain (basal segment pneumonias may mimic acute abdominal pain).
- Inadequate host defenses or other coexisting diseases (e.g., ciliary dyskinesia, cystic fibrosis, HIV, or noninfectious causes) may also be associated with slowly responding or nonresponsive pneumonia.
- Tuberculosis
- persistent alveolar collapse or atelectasis, may be secondary to obstruction of the bronchial lumen, from either foreign body aspiration or lymph node enlargement.
- Congenital malformations, such as pulmonary sequestration, bronchogenic cysts, or other mediastinal masses, also may be causes for delayed radiologic improvement .
- Several differential diagnostic tests for such possible comorbidities may be considered including bronchoscopy with BAL, chest CT scan, or lung biopsy. Blood, pleural, and sputum cultures, as well as PCR, should be considered for the diagnosis of possible atypical microorganisms.

Causes of un-resolving pneumonia:

1- use of inappropriate drug.

2- empyema or abscess → persistence fever +\- pluritic pain

basal segmental pneumonia → mimic acute abdomen

3- inadequate host defense or co-exist disease (cystic fibrosis, ciliary dyskinesia, HIV, non-infectious causes)

4- TB

5- persistent collapse of alveoli or atelectasis → bronchial obstruction due to foreign body or lymph node enlargement.

6- congenital malformation → pulmonary sequestration, bronchogenic cyst, mediastinal mass.

7- co-morbidities (for atypical pneumonia) → should screen by : BAL, chest CT, kung biopsy, PCR, cuttures.

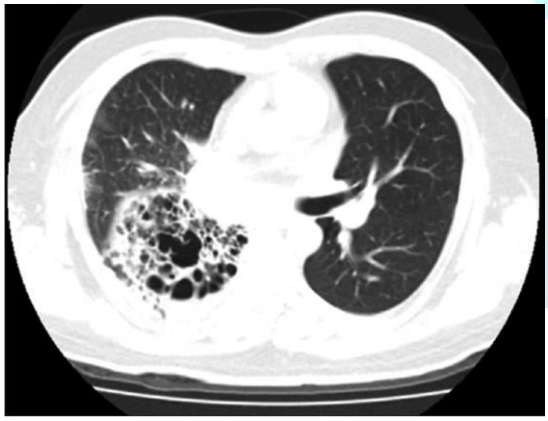
Major Clinical Complications:

NECROTIZING PNEUMONIA

- Happens 2ndry to pneumococcus, S.aureus and less common due to psudomonus.
- Mostly single but may be multiple
- CA-MRSA → associated with clinical presentation → production of panton-valentine leukocidin toxin.

- Necrotizing pneumonia is characterized by necrosis and liquefaction of consolidated lung tissue, which may be complicated by solitary, multiple, or multiloculated radiolucent foci, bronchopleural fistulas, and intrapulmonary abscesses.
- Most cases are confined to a single lobe, but sometimes there is multilobar involvement.
- Necrotizing pneumonia is usually secondary to pneumococcus, *S. aureus,* or, less commonly, *Pseudomonas aeruginosa* infections.
- CA-MRSA is often associated with this clinical presentation, since there is production of Panton-Valentine leukocidin, an exotoxin that causes tissue necrosis.
- In Europe, methicillin-sensitive *S. aureus* (MSSA), producing this same exotoxin, has been associated with necrotizing pneumonia

Necrotizing pneumonia → liquefaction and necrosis of lung consolidation.
Ay complicate by :
1- solitary, multiple or multiloculated radiolucent foci. 2- bronchoplural fistula. 3- intrapulmonary abscess

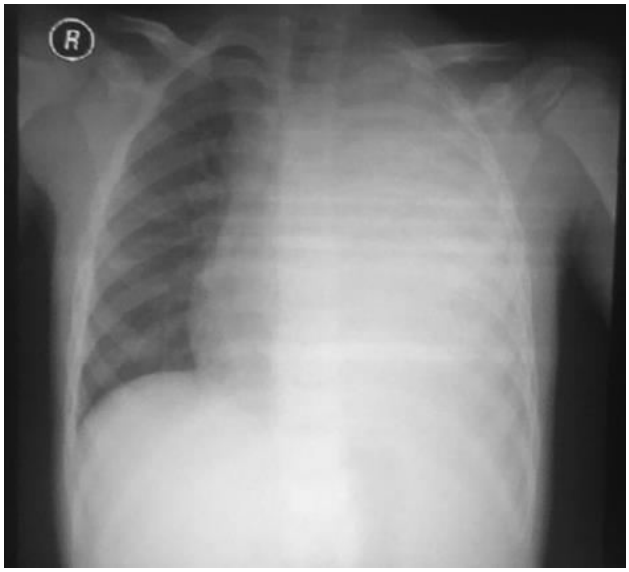


Clinical complications:
1- necrotizing pneumonia
2- recurrent pneumonia
3- lung abscess
4- pleural effusion and empyema

PLEURAL EFFUSION AND EMPYEMA

- Pleural effusion occurs when an inflammatory response to pneumonia causes an increase in permeability of the pleura with an accumulation of fluid in the pleural space. There is increased capillary permeability after parenchymal lung injury, favoring the migration of inflammatory cells into the pleural space.
- When bacteria enter the pleural space, pus appears, characterizing empyema.
- Either the child presents with typical, but usually more severe, signs of pneumonia or, after a few days of usual pneumonia symptoms, children deteriorate clinically, with persistent fever or respiratory distress.
- Pleuritic pain is common.
- On physical examination, there is reduced air entry and dullness to percussion over the affected area.
- the typical clinical outcome of children is good with full recovery

complete hemithorax opacification with mediastinal contralateral deviation:



- Increase in permeability of pleura with fluid in plural space.
- If bacteria enter pleura → pus → empyema
  - ❖ Presentation :

1- severe typical sign of pneumonia or
2- usual pneumonia symptoms then few days later child deteriorate clinically with distress and persistent fever, With pluritic chest pain.

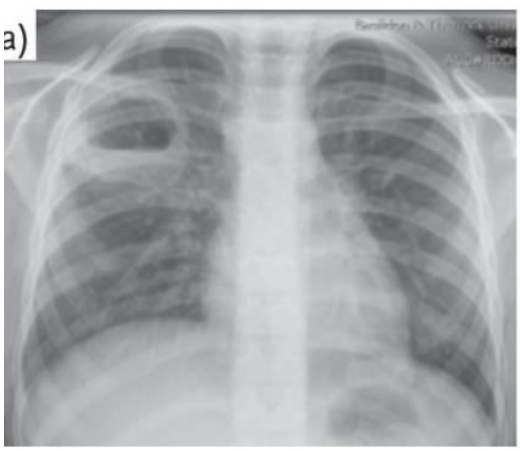
- ❖ By examination:

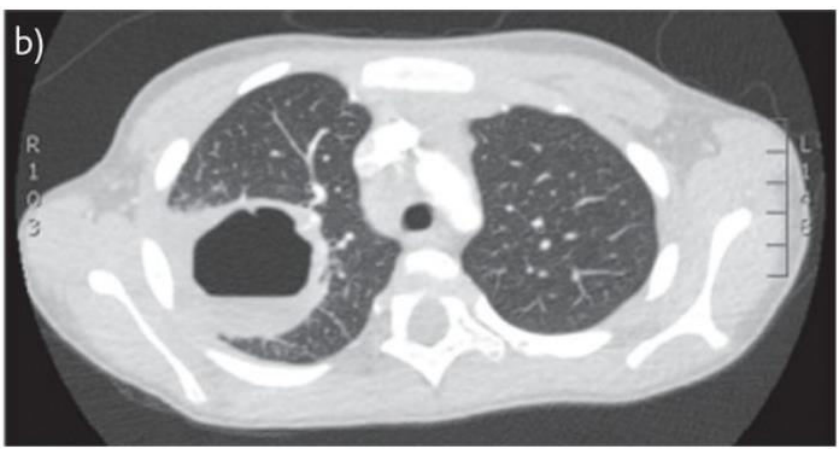
- ↓Air entry and dullness on percussion.
- Outcome is good with full recovery .

LUNG ABSCESS:

- Thick walled cavity with purulent fluid.
- If primary it's with infection due to gram +ve cocci, -ve, anaerobes.
- Presentation is like uncomplicated CAP with fever + cough, also dyspnea, chest pain, anorexia, nausea, vomiting, malaise and lethargy, (Main difference is progressive indolent)
- Tt is parenteral antibiotics for 4-6 weeks

- A pulmonary abscess is a thick-walled cavity that contains purulent liquid.
- Primary abscesses are associated with a pulmonary infection, especially due to gram-positive cocci *(S. pneumoniae, S. aureus, S. pyogenes)* and gram-negative bacteria (*P. aeruginosa* and *Klebsiella*). *S. pneumoniae, S. aureus, P. aeruginosa,* anaerobic bacteria.
- The initial clinical presentation of a lung abscess is like that of uncomplicated CAP, with fever and cough as the key features.
- Other common signs are dyspnea, chest pain, anorexia, nausea, vomiting, malaise, and lethargy.
- A main difference from usual CAP is that it progresses indolently.
- The mainstay of treatment is the use of a parenteral antibiotic for 4–6 weeks .





Recurrent pneumonia

2 or more episodes\ year or 3 or more ever
(with radiology clearance between attacks.

- is defined as 2 or more episodes in a single year or 3 or more episodes ever, with radiographic clearing between occurrences.

- Prevention:
1- hygiene
2- contact isolation with droplets precautions →↓ transmission
3- in children > 6 months and high risk groups annual influenza vaccine

Prevention

- Hygiene measures are universally helpful.
- In health care settings, contact isolation, together with droplet precautions, are additional measures that help reduce transmission:

. For influenza prevention, annual vaccination with inactivated vaccine is recommended in all children older than 6 months, especially in high-risk groups.

. Children at an elevated risk of influenza complications include those aged younger than 2 years, those on long-term aspirin therapy, and those with comorbidities (pulmonary, cardiovascular, hematologic, metabolic, neuromuscular, and immunosuppression).

Prognosis:

- Overall is complete recovery
- Younger age →↑ risk for admission and re-admission
- Viral more common than bacteria but bacteria causes death more.
- In both infections → malnutrition, chronic diseases, lack of vaccines → high risk for death.

Table 110-2	Differential Diagnosis of Recurrent Pneumonia
HEREDITARY DISORDERS	
Cystic fibrosis	
Sickle cell disease	
DISORDERS OF IMMUNITY	
AIDS	
Bruton agammaglobulinemia	
Selective IgG subclass deficiencies	
Common variable immunodeficiency syndrome	
Severe combined immunodeficiency syndrome	
DISORDERS OF LEUKOCYTES	
Chronic granulomatous disease	
Hyperimmunoglobulin E syndrome (Job syndrome)	
Leukocyte adhesion defect	
DISORDERS OF CILIA	
Immotile cilia syndrome	
Kartagener syndrome	
ANATOMIC DISORDERS	
Sequestration	
Lobar emphysema	
Esophageal reflux	
Foreign body	
Tracheoesophageal fistula (H type)	
Cystic adenomatoid malformation	
Gastroesophageal reflux	
Bronchiectasis	
Aspiration (oropharyngeal incoordination)	

- The overall prognosis of pneumonia in most children, especially those who were previously healthy, is complete recovery.
- A younger age is associated with an increased risk of admission and readmission.
- In high-income countries, death occurs in less than 1 per 1000 patients per year.
- In low- and middle-income countries, overall mortality can be as high as 65 per 1000 patients per year.
- Bacterial pneumonia, although less common than viral pneumonia, accounts for a high proportion of deaths.
- Chronic underlying disease, as well as severe malnutrition and lack of vaccination, are associated with an increased risk of death for both viral and bacterial infections.