Developmental & Growth milestones
According to Nelsons' pediatrics textbook
Done By: Diaa Imran©

Developmental milestones

Gross motor

Head lag	
Head lag	3m
No head lag	4m

Ventral suspension	
Head below body	1m
Head within level of body	2m
Head above body	3m

Sitting	
With truncal support	6m
With pelvic support	7m
Alone with rounded back	8m
Alone with straight back	9m

Standing & Walking	
Creeps	8m
Crawls & Pulls to stand	9m
Cruise	10m
Stands alone	12m
Walks alone	15m
Runs + Up\downstairs (one leg)	2y
Upstairs alternating	2.5y
Downstairs alternating	3y
Tricycle	3y
Hops	4y
Skips & rope jumping	5y

Any other thing would be 5-8 months

Fine motor

General	
Hands closed	<3m
Hands open	3m
Hands midway open	5m
Mouthing	5m
Transfer objects from hand to hand	6m
Pincer grasp	9-12m
Release objects on command & drinks from cup	12m
Eats with spoon and misses	1.5y
Eats with spoon without missing	2y
Ties the shoes	5y

Drawing	
Vertical lines	15m
Horizontal lines	2y
Circle	3y
Square & cross	4y
Triangle	5y

Language

Coos	**3m**
Babbles	**6m**
Mama, Dada (non-specific)	**9m**
Mama, Dada (specific) + 3 other words	**12m**
6 words (responds to name)	**15m**
10 words (tells body parts)	**18m**
20 words	**20m**
2-3 word sentences	2y
Knows age & sex	3y
Counts to 4	**4y**
Names 4 colors & tell a 10 word sentence	5y

Social

Prefer human face & light source	1m
Smile to anyone	2m
Smile to know ones	3m
Laughs	4m
Prefers mother	7m
Separation anxiety	8m
Plays pee-ka-boo	9m
Waves bye-bye	10m
Hugs parents	15m
Kisses parents & complains when wet	1.5y
Plays with others	3y
Goes to the toilet alone	4y
Understands rules	5y

Growth milestones

Weight	
6m	Birth weight × 2
1y	Birth weight × 3
2y	Birth weight × 4
3y	Birth weight × 5
5y	Birth weight × 6
7y	Birth weight × 7
10y	Birth weight × 10
N.B: birth weight will decrease 10% in the 1st 4 days, then returns to normal at the 10th day	

Length\height	
Birth	50cm
3m	60cm
1y	75cm
2y	90cm
4-5y	100cm
5-10y	100 + 5cm/year
>10y	125 + 9cm/year

Head circumference	
0-3 months	1cm/1 month
3-12 months	1cm/1.5 months
1-3 years	1cm/ 6 months
3-6 years	1cm/ year
N.B: at birth, the HC is 35 cm ± 2 | at 6y the HC is alike of the HC of an adult	

Immunization

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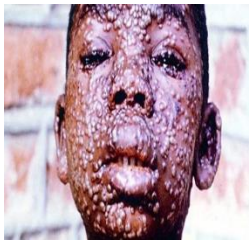
Vaccination: the act of giving a vaccine (antigen)

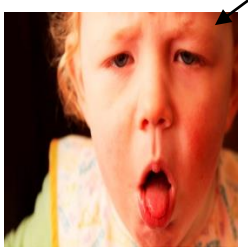
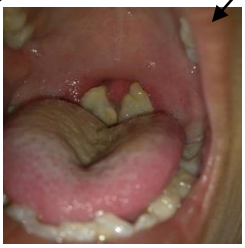
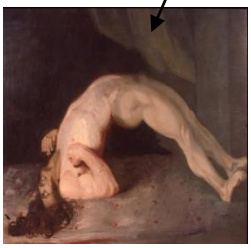
Immunization: the induction of an immune response following exposure to an antigen

Active VS Passive immunity:

	Active	**Passive**
Nature	Antigen is given then the body forms its own protective antibodies	Ready-made immune globulin (antibodies) from human or animal sources are given to the body
Duration of protection	Long	Shorter
Examples	Natural: Infection Artificial: Vaccination	Natural: Mother's Ig to infant Artificial: Administration of antibodies (HB IG)

N.B: diseases eradicated by vaccines: smallpox, poliomyelitis, whooping cough, diphtheria & tetanus



Complications of whooping cough: syncope, sleep disturbance, incontinence, rib fractures, pneumonia, conjunctival bleeding, hernia, hypoxia, seizures & death

Complications of diphtheria: airway obstruction, myocarditis with heart block & cranial neuropathies

Live attenuated VS killed vaccines:

Live attenuated	**Killed vaccines**
Can produce antigens	Can't
One shot is enough	Booster shots needed
Induce humoral & cellular immunity	Only humoral immunity
Risk of actual infection	No risk
Contra indicated in immune-compromised	Safe
BCG, MMR, OPV, Rota, Varicella, typhoid & nasal influenza virus vaccine	Tdap, DTP, IPV, Hib, HAV, Meningococcal & Pneumococcal

Recombinant vaccines: are made by inserting viral genes that code for important antigens into common baker's yeast. The yeast then produces the antigens, which are collected and purified for use in the vaccine.

Pure polysaccharide vaccines: induce a T-cell INDEPENDENT immune response, (humoral immunity only); this causes them to have weaknesses

- How was this problem solved? By joining the polysaccharide molecule to a protein molecule and making conjugated polysaccharide vaccines. This way the polysaccharide vaccine will stimulate a T-cell DEPENDENT immune response

Routs of administration:

Intradermal: BCG (for TB) | Intranasal: Nasal influenza

Subcutaneous: Varicella, IPV & MMR (measles, mumps & rubella)

Oral: OPV, Rota

- Any other vaccine is given IM "lateral thigh or deltoid"

Side effects of all vaccines: local reaction, fever, syncope & anaphylaxis

DTP side effects	
Mild	fever, redness, swelling, tiredness, poor appetite & vomiting
Moderate	seizure, ≥3 hrs non-stop crying & high fever
Severe	serious allergic reaction, long-term seizures & permanent brain damage

MMR side effects: measles-like rash & thrombocytopenia (measles component)

Orchitis (mumps component)

Arthralgia (rubella component)

Febrile seizures

The followings are NOT contraindications to vaccine administration: mild illness with\without fever, breast feeding, penicillin allergy, antibiotics use & family history of seizure or controlled seizures

Jordanian National Vaccination Program:

Time	Vaccine
ASAP after birth	BCG
2 months	DTap, IPV, Hib, HepB & Rota
3 months	DTap, IPV, Hib, HepB & Rota + OPV
4 months	DTap, OPV, Hib, HepB & Rota ± IPV
9 months	Measles & OPV
12 months	MMR & HepA
18 months	MMR & HepA + OPV & DTP
6 years	OPV & Td
10 years	Td

Vaccines non in JNVP: pneumococcal, meningococcal, influenza & varicella

N.B: BCG vaccine can cause abscess formation with regional lymphadenitis
Complications\CIs of Rota: intussusceptions & immune-deficiency

Rotateq VS Rotarix: VERY IMPORTANT!

	Rotateq	Rotarix
Doses	3	2
Minimum age	6 weeks	6 weeks
Max age for 1st dose	12 weeks	20 weeks
Max age for any dose	32 weeks	24 weeks

Contraindications of vaccines in general: immunosupression & previous dose anaphylaxis

Prematurity

Done by: Diaa Imran©

Stillbirth: infant expelled from birth canal at or after 24weeks of pregnancy, but shows no signs of life and has no heart beat. **N.B**: Miscarriage: early pregnancy loss "previable "<24weeks"".

Gestational age: is the time from the 1st day of the last menstrual period to the date of birth.

Term delivery: is delivery between 37-41+6 weeks.

Preterm: delivery before 37weeks.

- **Complication of preterm delivery**: birth asphyxia\pulmonary diseases, thermal instability, jaundice, PDA, infections, NEC, glycemic problems, renal disorders, hematologic disorders & retinopathy of prematurity.

Post-term: delivery after 42weeks.

Low birth weight: any infant weighs 1.5-2.5kg. **N.B**: normal birth weight is 2.5-4kg.

Very low birth weight: any infant weighs 1-1.5kg.

Extremely low birth weight: any infant weighs <1kg.

- **Small for gestational age**: weight below than the 10th percentile or >2 standard deviation below the mean birth weight.

Causes of LBW: prematurity, IUGR, smoking, TORCH infections, placental problems & constitutional

Complications of LBW: disabilities, mental retardation, learning problems, cerebral palsy, vision\hearing loss & death.

Management of IUGR: treat the cause "HTN, placental hypopefusion…etc"

Complications of prematurity

NEC

Done by: Diaa Imran©

NEC: is an idiopathic, acquired inflammatory disease of the premature; it is the most common newborn surgical emergency.

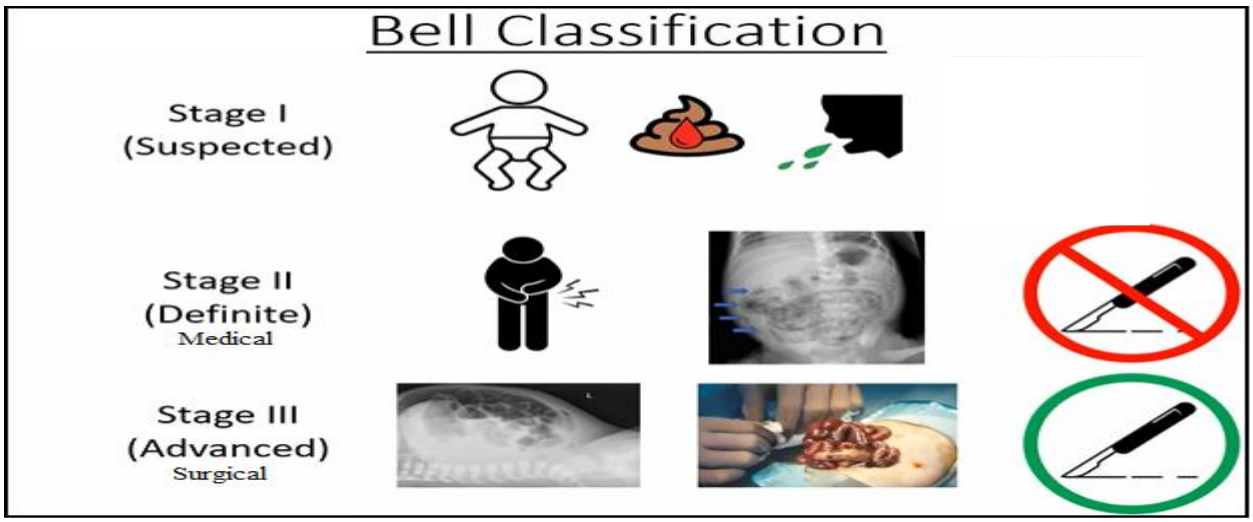
RFs: prematurity & low birth weight.

Pathophysiology: the onset of disease occurs after the 1st feed, with unknown cause, but it is thought to be due to immature gut, that when exposed to food, an inflammatory process occurs leading to the S & Sx of NEC, when injury to the gut occurs, the bacteria in the gut translocates to the blood stream via injured gut, leading to septicemia.

S & Sx: abdominal distension, bloody stool or occult blood in stool, feeding intolerance, vomiting, lethargy, bradycardia, hypo\hyperthermia & ± episodes of apnea

Dx: Labs: neutropenia, lymphocytopenia & low pH

Gold standard Dx is X-ray: pneumatosis intestinalis (stage II) or pneumoperitoneum (stage III)



Treatment: bowl rest (NPO, TPN & NGT decompression)

Empirical ABx for suspected septicemia

Serial imaging to determine if surgery is required

Surgery (resection & anastomosis if perforation occurs)

Prematurity apnea

Done by: Diaa Imran©

Apneic spell: is a cessation of breathing for ≥ 20 sec OR shorter pause if accompanied by pallor, cyanosis or bradycardia.

Causes: central, obstructive or mixed

RFs: prematurity (100% <28 weeks & 85% of 30 weeks babies will have apnea)

In 37 weeks CGA, 92% will stop having these spells, & 98% in 40 CGA.

Consequences: retinopathy of prematurity*****, neuro-developmental disabilities, altered growth & CVS problems.

*ROP is believed to occur because of an increase in angiogenic factors caused after a preterm infant is no longer in supplemental oxygen and the avascular retina becomes hypoxic

N.B: apnea itself is NOT associated with increased risk of SIDS, however, prematurity DOES

Prevention: prevent hyperflexion\extension of the neck

Maintain patent airway, maintain stable thermal environment, limit nasal suction, and use humidified air to maintain nasal patency instead & maintain SPO_2 88-94%

Treatment:

Caffeine citrate: blocks adenosine receptors → improve diaphragmatic contractility; improve CO_2 sensitivity & decreases hypoxic depression.

N.B: stop caffeine after 5-7 days apnea free or at 33-34 CGA, whichever comes first.

SE: tachycardia, seizures, feeding intolerance & increase metabolic demand

CPAP

Blood transfusion: increases respiration due to increased O2 binding capacity & tissue oxygenation

N.B: apneas where shown to more occur in patients with low hematocrit

Retinopathy of prematurity

Done by: Diaa Imran©

ROP: abnormal blood vessels to growth in the retina, which can lead to blindness; due to retinal detachment.

RFs: prematurity, apnea (any hypoxia causing event) & low birth weight

ROP stages:

Stage 1	Demarcation line separates avascular from vascularized retina
Stage 2	Ridge arising in the region of demarcation line
Stage 3	Ridge with extraretinal fibrovascular proliferation (neovascularization)
Stage 4	Partial retinal detachment
	4a: Extrafoveal
	4b: foveal
Stage 5	Total retinal detachment

Or: **stage I**: mild abnormal vascularization | **stage II**: moderate | **stage III**: severe

N.B: stages I & II needs to treatment

Treatment: laser and\or anti-VEGF

Resources: NICU essentials & NCBI

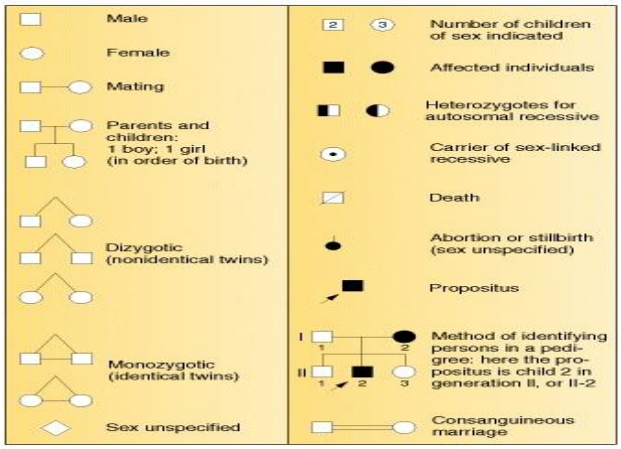
Chromosomal abnormalities

Done by: Diaa Imran©

Aneuploidy: having an abnormal number of chromosomes, it is the most common and clinically significant type of human chromosomal abnormalities.

The most common cause of aneuploidy is "**nondisjunction**": the failure of chromosomes to disjoin normally during meiosis I or II or during mitosis.

Types of inheritance:



1. **Autosomal dominant**: one abnormal gene is sufficient to cause the disease.

It has vertical transmission, "does not skip generations", with equal M:F ratio

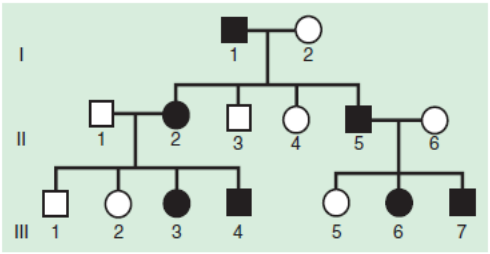


Figure 75-5 Autosomal dominant pedigree. Pedigree showing typical inheritance of a form of achondroplasia *(FGFR3)* inherited as an autosomal dominant trait. *Black*, affected patients.

Mnemonic for Autosomal Dominant disorders:

Very Powerful DOMINANT Humans

- Von willebrand disease / Von hippel-lindau
- Pseudo-hypoparathyroidism
- Dystrophia myotonica
- Osteogenesis imperfecta / Osler-weber-rendu
- Marfan syndrome
- Intermittent porphyria
- Neurofibromatosis
- Achondroplasia / Adult polycystic kidney disease
- Noonan syndrome
- Tuberous sclerosis
- Hypercholesterolemia
- Huntington's disease
- Hypertrophic obstructive cardiomyopathy
- Hereditary spherocytosis
- Hereditary non polyposis coli
- Hereditary hemorrhagic telangiectasia

2. **Autosomal recessive**: mutations in both copies of a gene is needed to cause the disease

It has horizontal transmission "may skip generations", with equal M:F ratio

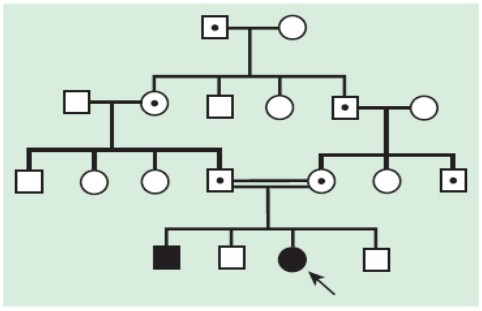


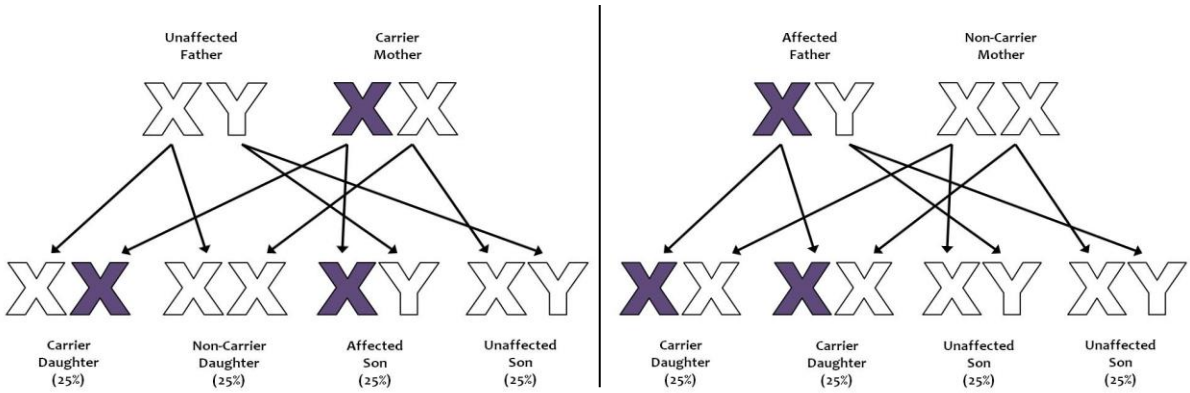
Figure 75-7 Autosomal recessive pedigree with parental consanguinity. *Central dot,* carriers; *black,* affected patients.

AUTOSOMAL RECESSIVE

- CF
- PKU
- GALACTOSEMIA
- HOMOCYSTINURIA
- LYSOSOMAL STORAGE
- A-1 ANTITRYPSIN
- WILSON DISEASE
- HEMOCHROMATOSIS
- GLYCOGEN STORAGE DISEASES

Hgb S
THALASSEMIAS
CONG. ADRENAL HYPERPLASIA
EHLERS-DANLOS (some)
ALKAPTONURIA
NEUROGENIC MUSC. ATROPHIES
FRIEDREICH ATAXIA
SPINAL MUSCULAR ATROPHY

3. **X-linked**: the disease is transmitted on the sex chromosome "X", so the males are more prone to be affected; as they have only one X chromosome, while female have 2 copies, thus they could be only carriers. (e.g: G6PD)



Risk factors for chromosomal abnormalities: advanced maternal age, multiple abnormalities on fetal ultrasound, multiple congenital anomalies, unexplained growth retardation mental retardation, primary amenorrhea or infertility & 1st-degree relative affected

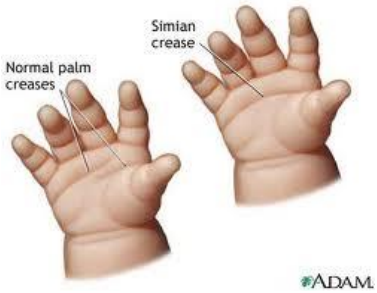
- **Non-sexual chromosomal abnormalities**:

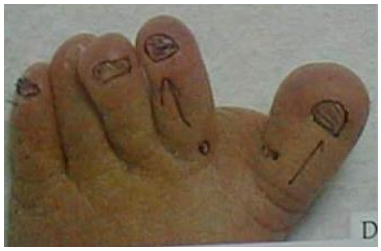
Trisomy: is characterized by the presence of 3 chromosomes, instead of the normal 2, of any particular chromosome. Risk of trisomies increases with advanced maternal age

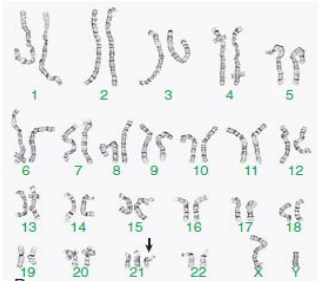
A. **Trisomy 21** "**Down syndrome**": the most common trisomy and the most common genetic cause of moderate mental retardation. With a life expectancy up to 55 years.

Featrures:

Morphology	CNS	CVS	GI	Others
-Epicanthal folds -3 fontanels -Wide space between 1st two toes -Pelvic dysplasia -Micocephaly -Flat nasal bridge -Small ears -Simian crease -Large protruded tongue	-Hypotonia -Poor motor reflexes -Delayed development	-ASD -VSD -PDA -PHTN -**Endocardial cushion defect**	-Duodenal atresia -Hisrchsprung -Imperforated anus	-Leukemias -DM -Infertility -Thyroid abnormalities







Screening for Down syndrome: in their 2nd trimester by quad screen: β-hCG, unconjugated estriol, inhibin-A & α-FP".

N.B: 60% of cancers affecting Down syndrome patients are Leukemias.

B. **Trisomy 18** "**Edwards syndrome**": it is the 2nd most common trisomy

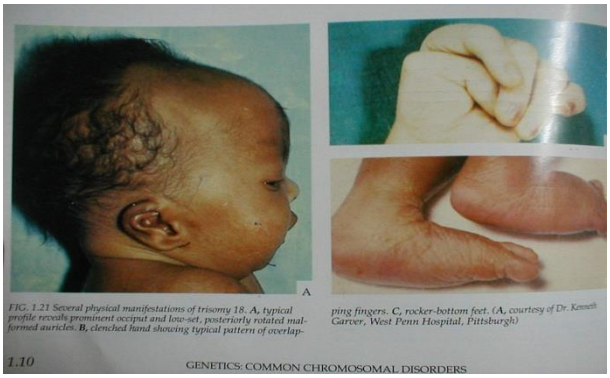
Feartures: Mnemonic "MR. EDoARD":

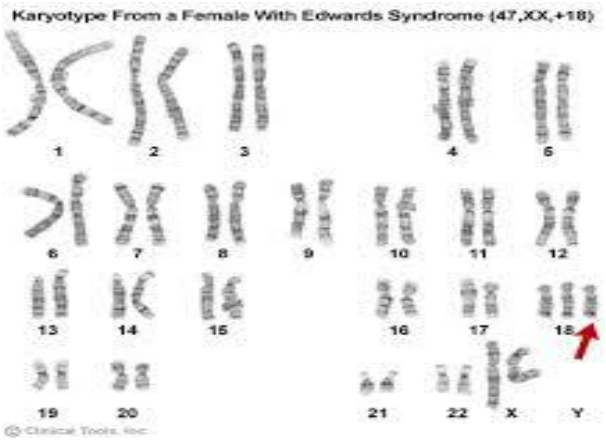
M: Micrognathia | **A**: Absent mental development

R: Renal abnormalities "horse-shoe kidney" | **R**: Rocker-bottom feet

E: Eighteen trisomy | **D**: Diseased heart

Do: Digits Overlapping "due to hypertonia"





N.B: only 5% lives >1 year

Screening: by quad test: Edward = Everything decreased

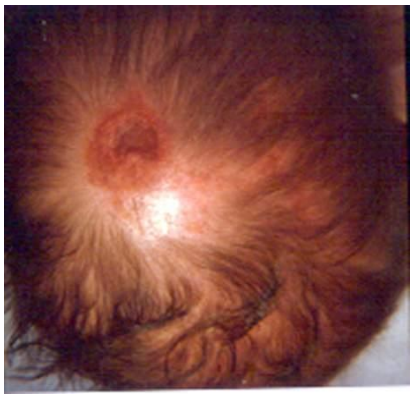
C. **Trisomy 13** "**Patau syndrome**": is the 3rd most common trisomy

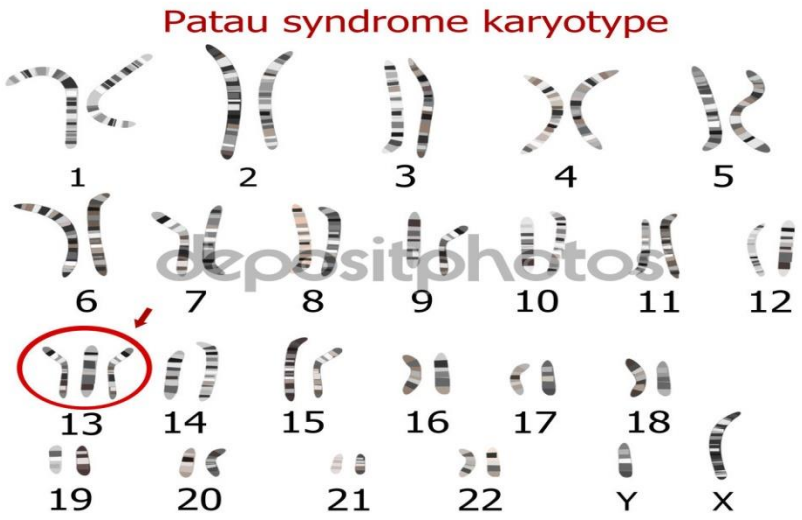
Featrures: Mnemonic "<u>CRAMP</u>"

C: Cleft palat\lip | **M**: Mental retardation

R: Renal abnormalities "horse-shoe kidney" | **P**: Polydactaly

A: Aplastic cutis





N.B: only 5% lives >6 months

Screening: quad test → decreased β-hCG

- **Sexual chromosomal abnormalities**:

1. **Turners' syndrome** "**45Xo**": caused by the lack of one X chromosome, in which 75% of patients, the lost sex chromosome is of paternal origin. Mental retardation is seen in 6%

Features & symptoms:

Table 76-15 SIGNS ASSOCIATED WITH TURNER SYNDROME

- Short stature
- Congenital lymphedema
- Horseshoe kidneys
- Patella dislocation
- Increased carrying angle of elbow (cubitus valgus)
- Madelung deformity (chondrodysplasia of distal radial epiphysis)
- Congenital hip dislocation
- Scoliosis
- Widespread nipples
- Shield chest
- Redundant nuchal skin (in utero cystic hygroma)
- Low posterior hairline
- Coarctation of aorta
- Bicuspid aortic valve
- Cardiac conduction abnormalities
- Hypoplastic left heart syndrome and other left heart abnormalities
- Gonadal dysgenesis (infertility, primary amenorrhea)
- Gonadoblastoma (increased risk if Y chromosome material is present)
- Learning disabilities (nonverbal perceptual motor and visuospatial skills) (in 70%)
- Developmental delay (in 10%)
- Social awkwardness
- Hypothyroidism (acquired in 15-30%)
- Type 2 diabetes mellitus (insulin resistance)
- Strabismus
- Cataracts
- Red-green colorblindness (as in males)
- Recurrent otitis media
- Sensorineural hearing loss
- Inflammatory bowel disease
- Celiac disease (increased incidence)

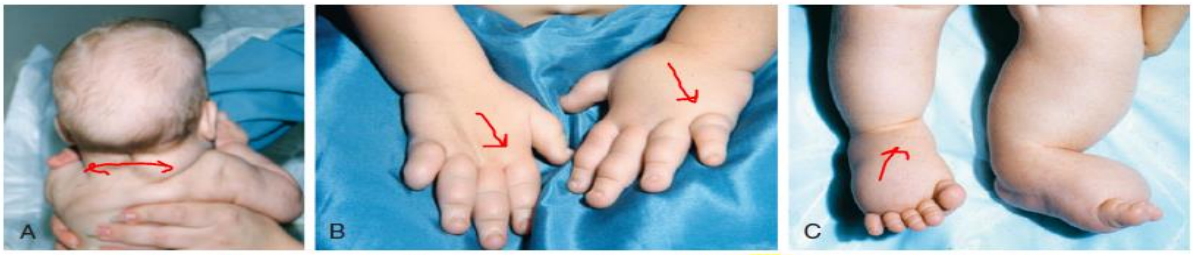
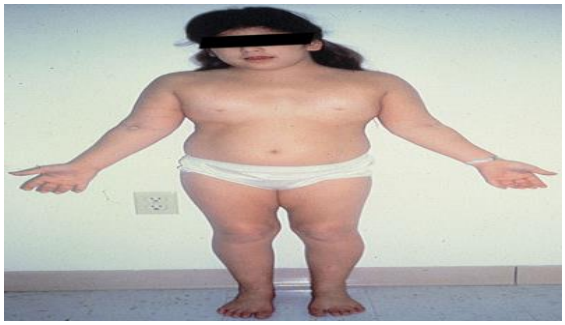


Figure 76-17 Redundant nuchal skin *(A)* and puffiness of the hands *(B)* and feet *(C)* in Turner syndrome. (From Sybert VP, McCauley E: Turner's syndrome, *N Engl J Med* 351:1227–1238, 2004. Copyright © 2004 Massachusetts Medical Society. All rights reserved.)



There is a 15-30% risk of developing gonadoblastoma, if the Y chromosome is present, use FISH analysis to look for Y-chromosome mosaicism in all 45 X patients. If Y chromosome material is identified, laparoscopic gonadectomy is recommended.

N.B: **Noonan syndrome**: features similar to Turner syndrome, but with different pattern of congenital heart disease typically involving right-sided lesions.

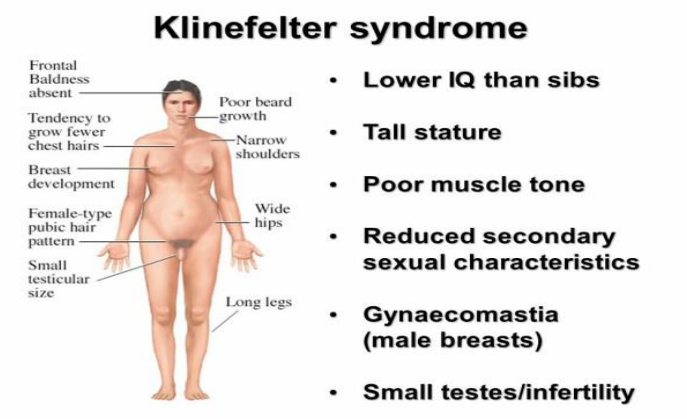
2. **Klinefelter Syndrome** "**47 XXY**": is the most common cause of hypogonadism and infertility in males

80% of Klinefelter syndrome have a male karyotype with an extra X chromosome "47,XXY", remaining 20% have multiple sex chromosome aneuploidies "48,XXXY; 48,XXYY; 49,XXXXY".

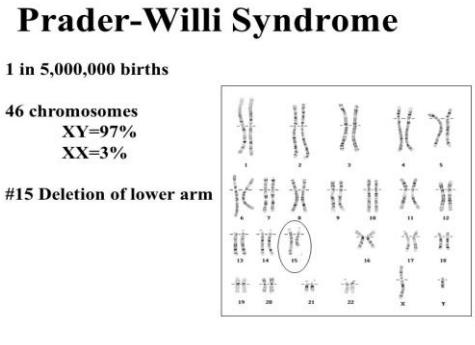
N.B: each additional X chromosome reduces the IQ by 10-15 points

Puberty occurs at the normal age, but the testes remain small, presentation usually in adulthood as infertility.

Features:



3. **Prader Willi Syndrome**:



Featrues: obesity, short stature, mental retardation, short hands\feet & hypogonadism

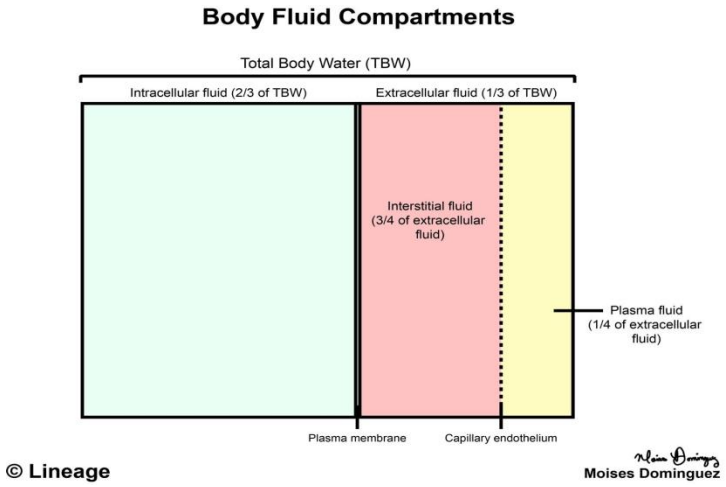
Diagnosis: FISH

Maintenance fluid therapy in pediatrics

Done by: Diaa Imran©

60% of total body weight is water, the younger the person, the more water he have in his body, reaching 80% in neonates.

Distribution of body fluids:



Major body electrolytes:

	Intracellular	**Extracellular**
Na^{+}	10	140
K^{+}	160	4
Ca^{+2}	2.5	2.5

Common fluids used to rehydrate a patient:

D5W: contains 5g glucose in each 100ml water. **N.B**: D10W

Normal saline: contains 154 mEqNa in each 1L water. **N.B**: 0.5 NS & 0.3 NS

Maintenance fluids: the amount of fluid needed to compensate the ongoing losses under normal physiological circumstances "due to metabolism, sweating, urinating… etc".

- **Calculation of maintenance fluids**:

Holliday-Segar method:

100cc\kg for the 1st 10 kg

50cc\kg for the 2nd 10 kg

20cc\kg for the rest of the body weight

e.g: calculate the maintenance fluid needed for a 7kg & a 25kg patients using H-S method:

100 X 7 = 700cc | (100 X 10) + (50 X 10) + (20 X 5) = 1600cc

- **N.B**: we need to give 3mEqNa\100cc & 2mEqK\100cc
- **N.B**: if the baby is NPO, he should be given the maintenance via IV, if NPO persists for >5 days, the patient should also have amino-acids & lipids; to avoid body wasting.

Volume depletion "**deficit**": occurs when the patient looses more fluid than he consume, in cases such as: vomiting, diarrhea, poly-urea, burn… etc

When this happens: ECF decreases → hypo-perfusion → hypoxia → death

We need to know the amount of fluid lost & the type of fluid, in order to correct the deficit.

Calculation of deficit: pre-illness weight – illness weight ÷ pre-illness weight **OR** according to Sx.

	Mild loss "3-5%"	**Moderate loss "6-10%"**	**Severe loss ">10%"**
Systemic signs	Thirst	Irritable	Lethargic
Urine output	Normal	<1ml\kg\hr	Anuria
HR	Normal	Increased	Marked increase
RR	Normal	Deep	Deep & fast
BP	Normal	Low normal	Decreased
Fontanels	Normal	Sunken	Markedly sunken
Capillary refill	Normal	Delayed	Marked delay
• Deficit = percentage lost X body weight X 1000 | 50% over 8 hrs & other 50% over 16			

Types of fluid loss: Isonatremic dehydration: loss of equal amounts of H_2O & Na^+

Hyponatremic dehydration: more Na^+ loss

Hypernatremic dehydration: more H_2O loss

Isonatremic dehydration	Hyponatremic dehydration	Hypernatremic dehydration
Maintenance fluid & electrolytes	Maintenance fluid & electrolytes	Maintenance fluid & electrolytes
Deficit fluid & electrolytes	Deficit fluid & electrolytes	Deficit fluid & electrolytes
-	Additional Na deficit, desired Na is 130mEq (0.6 * wt * 130-current Na^+)	Additional water deficit, 4ml\kg per each additional Na above 145 Don't decrease Na^+ >10-12\day
Total over 24 hrs	Total over 48 hrs	Total over 48 hrs

- **N.B**: in severe situations "shock" in the ER, we give ONLY bolus normal saline "20cc\kg over 30 mins", then wehen stable; give the normal maintenance & deficit.

Oral vs IV rehydration: if the patient can tolerate oral intake, give the fluids orally.

Mild: 50cc\kg every 4 hrs

Moderate: 100cc\kg every 4hrs

N.B: Each defecation\vomiting, give additional 10cc\kg

Once stable, 100cc\kg\day

N.B: ORS cantaions: "90 Na, 20 K", "110 glucose", "80 Cl^- & 30 bicarbonate"

e.g: a 5.5kg pre-illness weight baby, came to the ER for dehydration "shock", his current weight is 5kg, his Na: 120, what do you do?

Assess dehydration: (5.5-5)\5.5= 9% "moderate"

Give bolus NS: 20 * 5.5 = 110cc | it has 17 Na

Deficit: 9% * 5.5 * 1000 = 495cc | "add 8.4 Na\100= 42"

Maintenance: 100 * 5.5= 550cc "subtract bolus: 550-110= 440cc" | "add 3 Na\100cc= 16"

Na^+ deficit: 0.6 * 5.5 * (130-120) = 33mEq Na

- Total fluid: 550+495-110= 935cc ≈ 1000
- Total Na: 42+16+33-17= 74
- Give 0.5 NS as 1000cc of it contains 77 Na

N.B: **Maintenance fluid has**: 3 Na & 2 K\100cc | **Deficit fluid has**: 8.4 Na & 6 K\100cc

Asthma

Done by: Diaa Imran©

Asthma: the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. >2y

The most common presentation of asthma in children is: cough, wheezing, dyspnea & nocturnal awakenings. **N.B**: NO fever, except if the patient had the asthmatic attack as a response of an infection.

There are 3 types of wheezing according to the child's age:

Transient: present at age of 3, but absent at age of 6. **Caused by**: impaired lung function & maternal smoking.

Persistent: present at both 3 & 6 years. **Caused by**: atopy, elevated IgE, maternal smoking & male gender

Late: absent at age of 3, but present at age of 6. **Caused by**: atopy & male gender

For a wheeze to be diagnosed as asthma it should be: recurrent, other wheezing conditions^ have been excluded, child responds to anti asthma therapy & child have risk factors.

Risk factors of pediatric asthma: atopy, viral infections, male gender, family history & smoking.

N.B: viral infections are both risk factor for developing asthma & a trigger for an asthma flare up.

Asthma Predictive Index "API": used in children younger than 3y to predict the likelihood of developing asthma.

API is positive when: 3 Episodes of wheezing + either 1 major or 2 minor criteria.

Major criteria: family history, atopy & positive sensitization to environmental allergen.

Minor criteria: allergic rhitinits & eosinophils >4% in peripheral blood.

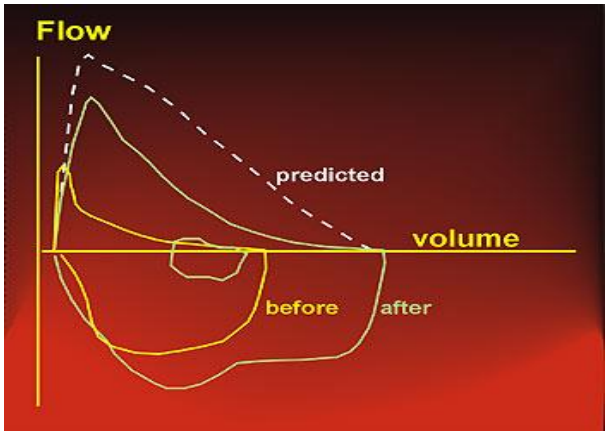
^DDx of wheezing: Bronchiolitis "<2y", cystic fibrosis, HF, foreign body inhalation, GERD… etc

Diagnosis: physical exam: decreased air entry bilateral, prolonged forced expiration, use of accessory muscles & hyperexpansion of the chest. However examination of the chest may be normal.

Spirometry: an increase in FEV_1 of 12% post-bronchodilator is suggestive of asthma*****, but spirometry is difficult in children <4 yrs

Assessing airway function: sputum eosinophils, exhaled NO, allergy testing & infant lung testing

Remember: asthma is a COPD, meaning that FEV_1\FVC is <80%



*****

GINA assessment of asthma control in children ≤5 years: In the past 4 weeks

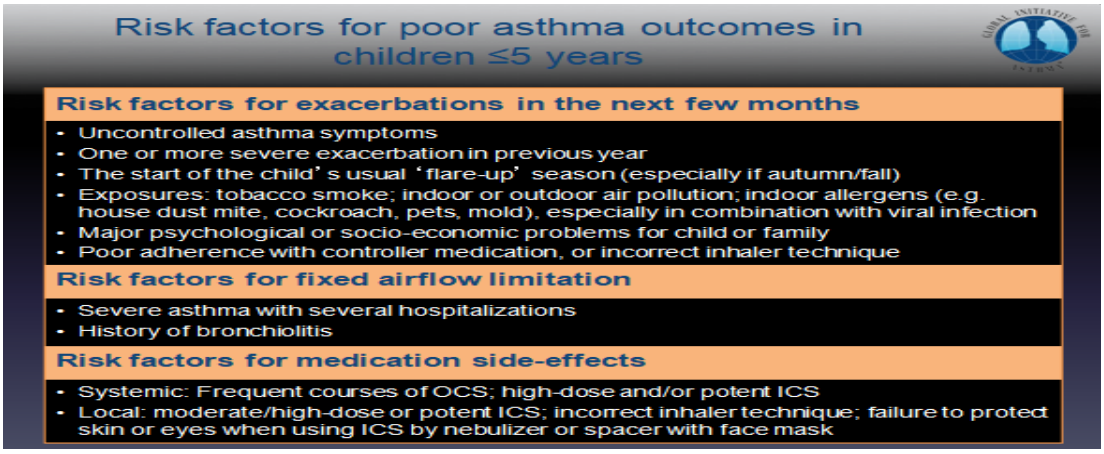
Daytime asthma symptoms for more than few minutes, more than once per week?

Activity limitation due to asthma?

Reliever needed more than once a week?

Night awaking or night coughing due to asthma?

1-2 of the above = partial control | 3-4 of the above = poor control



Treatment:

	<=5 years	**6-11** years
Stage I: <2/month & no nigh Sx	As needed SABA	As needed low dose ICS + SABA
Stage II: >2/month & 1 night Sx/month	Low dose ICS	Low dose ICS
Stage III: common/month & >1/week night Sx	Double low dose ICS	Low dose ICS & LABA
Stage IV: severe	Continue as stage III with specialist refer	Medium dose ICS & LABA
Stage V: very severe		High dose ICS & LABA

Management according to slides: SAβA, inhaled steroids*****, anti-cholenergic, LAβA, anti-leukotriens & oral steroids

***Side effects**: Hypothalamic-pituitary-axis suppression, oral thrush, decrease in height & effect of oral steroids in high doses

Note: treatment of asthma has many guidelines; the slides were not specific to determine the treatment, so I included what was possible to collect from the slides, in addition to the "management according to 4th year family medicine "the table above""

Respiratory tract infections

Done by: Diaa Imran©

Bronchiolitis: is the infection of bronchioles, with resultant inflammation, edema & increased mucus secretion, mainly before the age of 2-3 years. **N.B**: asthma mostly diagnosed after the age of 2-3yrs

High risk patients: prematurity, crowding\sick contact, congenital heart diseases, cystic fibrosis or chronic lung disease

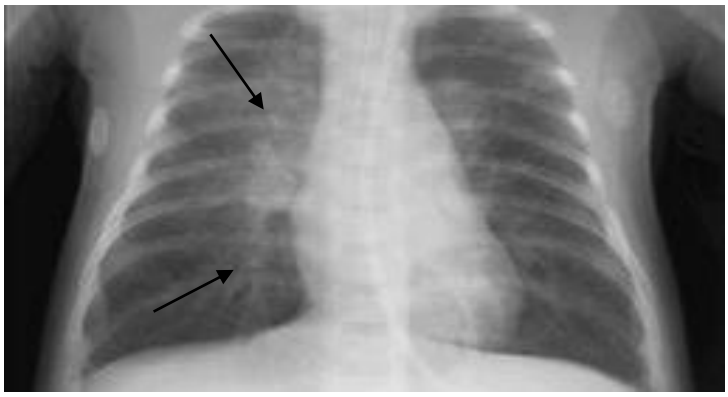
Causative organisms: RSV, Metapneumvirus & Rhinovirus

Symptoms: FEVER, cough, wheezing, dyspnea & uncommonly cyanosis. Asthma has NO fever

Diagnosis: mostly is a clinical diagnosis. Physical exam: crackles, retractions & cyanosis

Viral swab: not indicated for uncomplicated cases.

CXR: Hyperinflation, perihilar infiltrates & atelectasis. **N.B**: X-ray is not always\routinely indicated



N.B: Clinical course is worsening first 48-72h, then a plateau for 2-3 days followed by improvement, symptoms can last 3 weeks. But about 25-50% of patients with Bronchiolitis develop recurrent wheezing

Treatment: supportive | For severe disease: IV fluid if unable to take PO, CPAP & intubation

Steroids are not recommended, but Bronchodilators "Albuterol & epinephrine" may help

N.B: prophylactic Palivisumab, monoclononal RSV antibody, has decreased admission by 50% in high risk infants

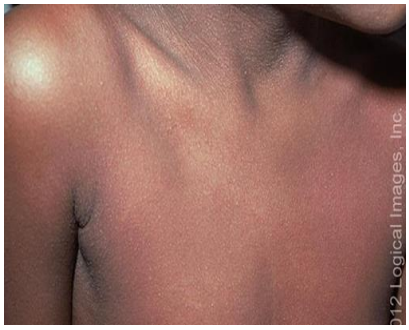
Pharyngitis: inflammations of the pharynx, mostly of a viral cause "Adeno\Rhino viruses". But group-A strep, is associated with the disease in older children.

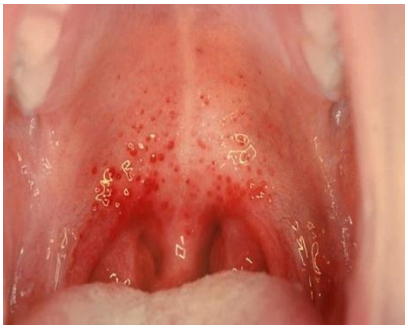
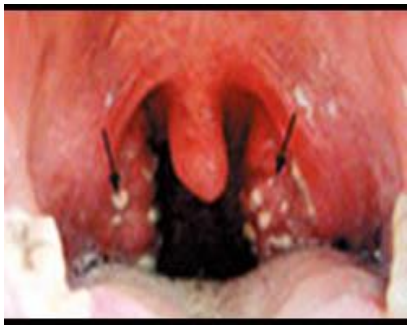
Symptoms: Sore throat, fever, coughs & lymph nodes enlargement

- **Tonsillitis**: form of pharyngitis, with involvement of the tonsils

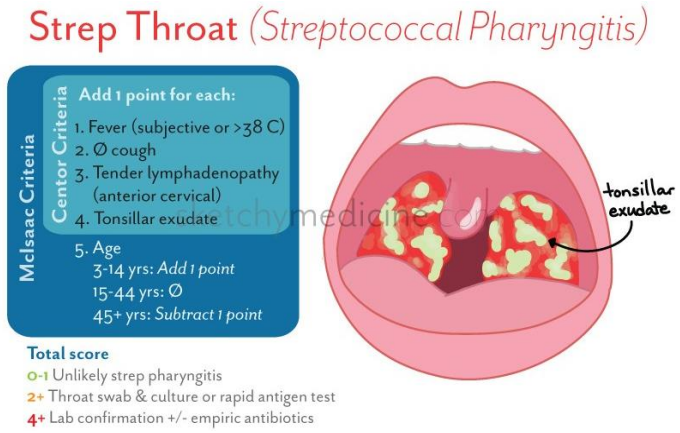
Causative organisms: GAS & EBV

Streptococcal tonsillitis symptoms: erythema, swelling of the tonsils, exudate, petechia on the palate, tender anterior cervical lymph nodes & can be associated with <u>sandpaper rash</u>.



Diagnosed: clinically, Rapid Antigen Detection Test & throat culture



Treatment: penicillin or erythromycin. **N.B**: <u>treatment does not prevent post-strept nephritis</u>

Complications: rheumatic fever, nephritis, bacteremia, chorea & peritonsillar abscess

Croup: is Laryngotracheobronchitis, Parainfluenza virus is the most common organism, but also RSV, Rhinovirus & influenza may contribute to cause the disease.

Symptoms: preceded by upper respiratory tract infection, Harsh barking cough, worse at night, tachypnea, stridor & tired appearing. **N.B**: steeple sign on X-ray

Severity assessment: Westleys' score

The Westley Score: Classification of croup severity[5][6]

Feature	Number of points assigned for this feature					
	0	1	2	3	4	5
Chest wall retraction	None	Mild	Moderate	Severe		
Stridor	None	With agitation	At rest			
Cyanosis	None				With agitation	At rest
Level of consciousness	Normal					Disoriented
Air entry	Normal	Decreased	Markedly decreased			

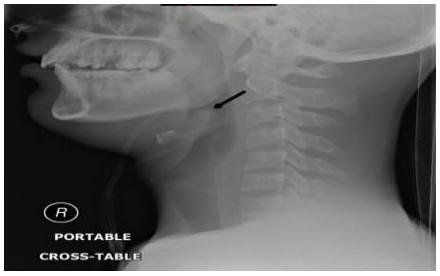
Mild: 0-2 | Moderate: 3-7 | Severe: 8-11 | Respiratory failure: >11

Treatment: Mild: Dexamethasone

Moderate & severe: Dexamethazone & Racemic epinephrine

Epiglottitis: inflammation of the epiglottis, mostly by the Hemophilus influenza B "Hib vaccination"

Symptoms: fever, anxious, drooling, tripod position & "thumb sign on X-ray"



If suspected do NOT examine. If severe obstruction send to OR for intubation

Treatment: IV antibiotics after airway has been secured

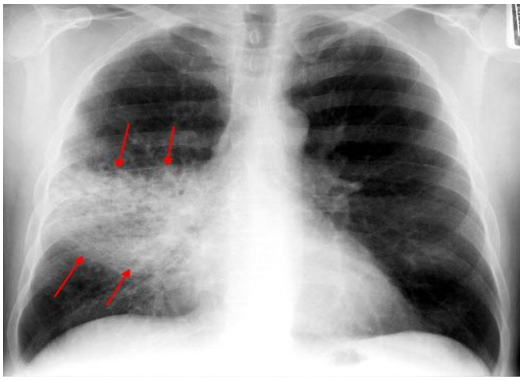
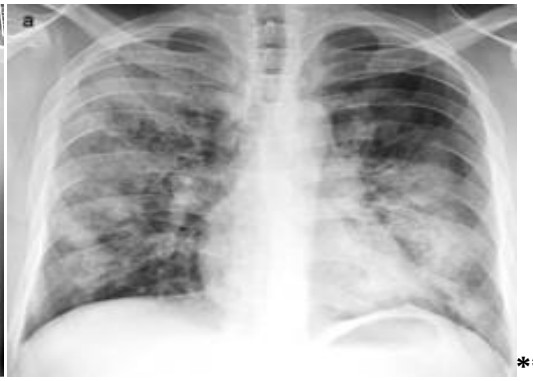
Pneumonia: is infection of the lung parenchyma

It could be:

Lobar: affecting a whole\partial lobe of the lung. Mainly bacterial in cause*****

Bronchopneumonia: affecting almost the whole lung "sometimes bilateral". Mainly viral in cause******

Interstitial: affecting the tissue that surrounds and separates the tiny air sacs of the lungs

*   **

Most common causative organisms according to age: Impt exam Q!

Etiology

AGE GROUP	FREQUENT PATHOGENS (IN ORDER OF FREQUENCY)
Neonates (<3 wk)	Group B streptococcus, Escherichia coli, other gram-negative bacilli, Streptococcus pneumoniae, Haemophilus influenzae (type b,* nontypable)
3 wk-3 mo	Respiratory syncytial virus, other respiratory viruses (parainfluenza viruses, influenza viruses, adenovirus), S. pneumoniae, H. influenzae (type b,* nontypable); if patient is afebrile, consider Chlamydia trachomatis
4 mo-4 yr	Respiratory syncytial virus, other respiratory viruses (parainfluenza viruses, influenza viruses, adenovirus), S. pneumoniae, H. influenzae (type b,* nontypable), Mycoplasma pneumoniae, group A streptococcus
≥5 yr	M. pneumoniae, S. pneumoniae, Chlamydophila pneumoniae, H. influenzae (type b,* nontypable), influenza viruses, adenovirus, other respiratory viruses, Legionella pneumophila

Symptoms: fever, cough, tachypnea, grunting, retractions, decreases air entry & crackles

Diagnosis: mainly clinically & CXR

CBC: elevated WBCs. **N.B**: Atypical lymphocytes may be seen in viral infections

Blood culture only in hospitalized patients

Treatment for bacterial pneumonia: Oxygen, IV fluids if unable to do PO feeds & Antibiotics

For newborns: ampicillin, gentamicin or ceftazidime

Older children: ampicillin clavulanate. In severe cases third generation cephalosporins

If older than 5 and mycoplasma suspected: macrolides can be used

If patient is toxic looking add vancomycin

Treatment for viral pneumonia: Zanamivir. Second line is oseltamivir plus rimanitidine

Complication: Necrosis, Abscess formation, Pneumatocele, Effusions, Sepsis & toxic shock syndrome

Sinusitis notes: Physical findings: nasal discharge, post nasal drip, facial tenderness

- **Causative rganisms**: S.pneumonia, S.aureus, non typable Hemophilus influenza, moraxella catarralis

Diagnostic criteria "AAP guidelines 2014":

URI Symptoms of 10 days duration

Or worsening URI symptoms after initial improvement

Or Sever onset of purulent to discharge and high grade fever of 3 days duration

N.B: frontal sinuses do not appear until the 7^{th} to 8^{th} year of life and are not completely developed until adolescense

Pertussis: aka. Whooping cough, **caused by**: Bordetella pertussis bacteria

Symptoms: 3 stages:

Catarrhal: URI like symptoms

Paroxysmal: paroxysms of intense cough

Convalescent: chronic cough

Prevention: DTap for patients <6yrs & Tdap for patients >6yrs

Diagnosis: clinically, PCR, nasopharyngeal culture,

N.B: PCR and culture can be negative after the first few weeks of symptoms

Treatment: Antibiotics "macrolides"

Complications: pneumonia, hypoxic encephalopathy, otitis media, hernia, seizures & cerebral hemorrhage

Mycobacterial infections

Done by: Diaa Imran©

Mycobacteria: is an acid-fast positive, non motile, gram positive bacteria.

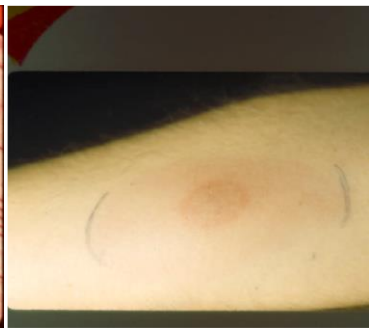
Risk factors: high prevalence countries, healthcare workers, family history of TB, IV drug use & contact with HIV patients\inmates of prisons.

Stages of mycobacterial infection:

Exposure: via air-born route, children <5 years should be treated with INH; because they may develop disease rapidly, while older children and adults often not treated

Infection "latent": you have the bacteria, with NO symptoms. Only positive skin test.

- **N.B**: Tuberculin Skin Test "TST" takes 3 weeks to 3 months to turn positive after infection has occurred.



TST

- **Risk factors for infection to become disease**: extremes of age, recent "<3 years" infection, immune suppression & certain diseases "silicosis & DM"

Disease: clinical and\or radiographic manifestations of progressive tuberculosis infection

- **N.B**: infection can NOT be spread from children to adults; as children cannot produce sputum, or cough to produce air droplets properly, however the opposite can occur.

Types of TB: Miliary "systemic" & Meningeal: the most fatal

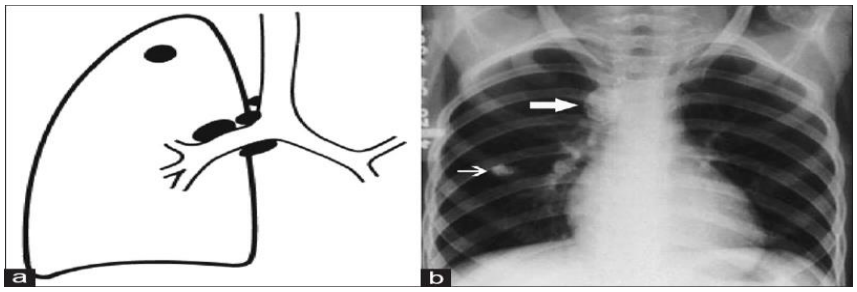
Pulmonary TB

Lymph node TB

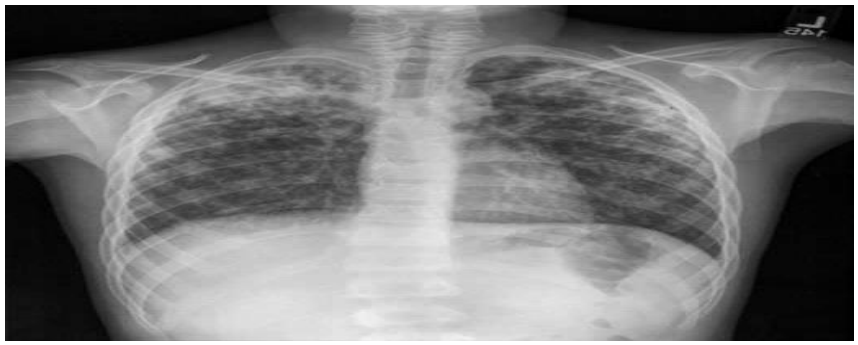
Skeletal TB

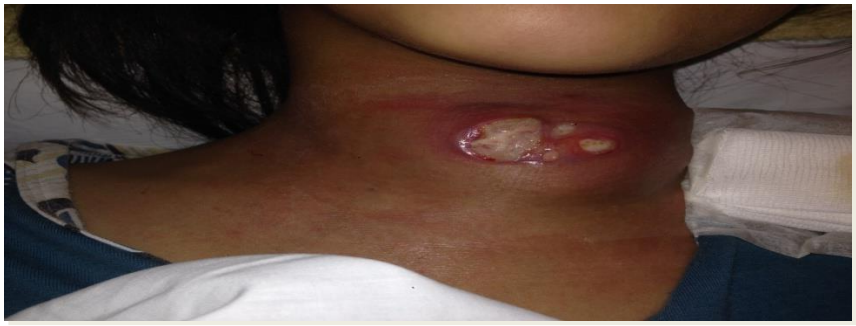
Renal TB

When the bacteria is introduced to the body and go to the lung, the immune system attacks them and are eaten by the lymphatic macrophages, making granulomas, called "**Ghons' foci**", which are viable bacteria, but only surrounded by granuloma, and can be reactivated whenever the immune system weakens. If these foci underwent calcification, they are called "**Ranke complex**". These two findings are characteristic on the CXR, alongside with **hilar\madiastinal adenopathy**.



Ghon focus & adenopathy


Miliary TB


TB adenitis

- **N.B**: when TB adenitis is suspected, perform excesional biopsy, which is both diagnostic & curative; do NOT do incesion and drainage; not to cause sinus formation & recurrence.

Symptoms: fever, night sweats, weight loss, malaise & cough progresses from dry cough to purulent sputum. Hemoptysis suggests advanced TB.

Diagnosis: clinically, gram stain, acid-fast, culture "sputum & bronchi", PCR & CXR

Treatment: RIPE "Rifampin, Isoniazid, Pyrazinamide & Ethambutol" for disease stage

Isonizid "INH" for latent infection

BCG vaccine: used in all but 2 countries USA and Netherland, and is given in first month of life in Jordan. Does not prevent infection; used for preventing life-threatening forms of TB "military & meningeal".

- **N.B**: Does BCG vaccine have an effect on positive TST? very minimal "up to 2 years"

Tuberculin Skin Test VS Interferon-gamma Release Assays:

	TST	**IF-γRA**
Visits required	2	1
Distinguish between infection & disease	No	No
Antigens studied	PPD "purified protein derivative"	CFP-10 & TB7.7
Cross-reactivity with BCG	Yes	No

TST erythema is considered positive in:

If >5 mm: immune compromise, recent contact to TB & suspected disease

If >10 mm: drug users, <4 years & high prevalence country (Jordan)

If >15 mm: if no risk factors

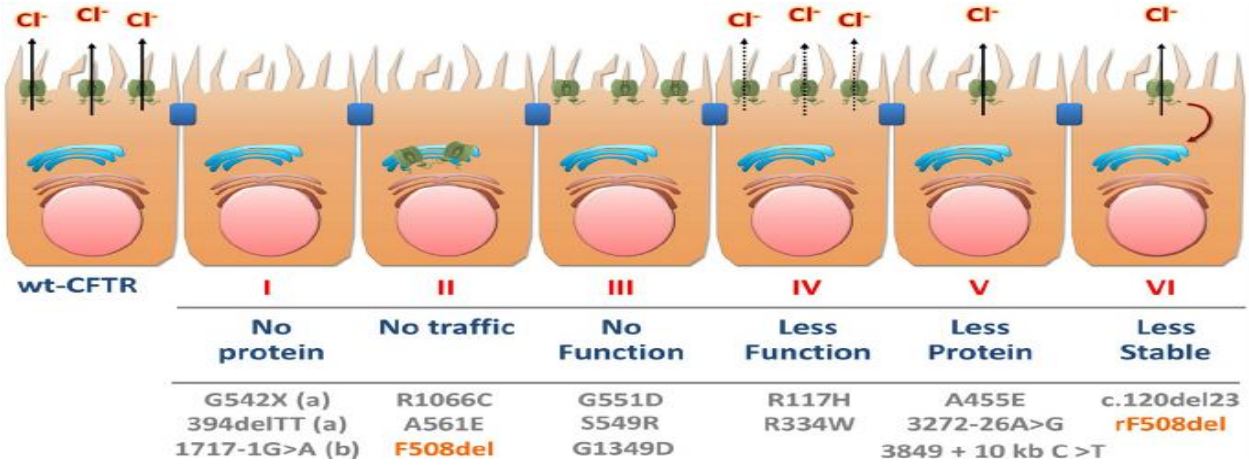
Cystic fibrosis

Done by: Diaa Imran©

It is a chronic, progressive obstructive lung disease, occurs due to mutation in the chromosome 7q31.2, which codes for the cystic fibrosis trans-membrane conductance regulator (CFTR) protein.

This protein moves the Cl^- out of the cells, when absent, the cell will maintain more negative charge, thus Na^+ will compensate by entering the cell, the water follows, keeping any secretions of the body with very low content of water, rendering it very viscid.

A mutation may lead to 1 of 6 classes:



N.B: Classes 1-3: are associated with early onset of disease, and pancreatic insufficiency

Classes 4-5: are associated with later onset lung disease, and pancreatic sufficiency

N.B: Most common mutation is called delta 508

When secretions are viscid, they lead to many **manifestations**:

Lungs: Mucus plugging → inflammation, chronic infection, small airway obstruction & bronchiectasis

Exocrine pancreas, intestines & liver: viscid secretions → pancreatic insufficiency, intestinal obstruction & cholestasis.

Other systems: pansinusitis, nasal polyps and infertility, increased salt excretion in the sweat

N.B: triad of CF: recurrent lung infections, steatorrhea & failure to thrive

Diagnosis: The gold standard for diagnosis of CF remains the pilocarpine iontophoresis sweat test

Infants age 0–6 months:

0–29: CF is unlikely | 30–59: Intermediate | 60: Indicative of CF

Infants age >6 months, children, & adults:

0–29: CF is unlikely | 40–59: Intermediate | 60: Indicative of CF

Diagnostic criteria: The presence of 1 or more phenotypic symptoms of CF, mentioned above

OR positive family history of CF in a sibling OR positive newborn screen

False positive results of the sweat test: eczema, malnutrition, CAH & hypothyroidism

False negative results of the sweat test: Dilution, edema & inadequate sweat

Management: 1. Maintain optimal lung function: antibiotics*****, lung clearance****** & anti inflammatory drugs

*****against S.aureus & P.auregonosa "most common infections in CF"

******by percussion, postural drainage, active cycle breathing, positive expiratory pressure, high frequency chest wall oscillation & mucus alternating agents like "DNase"

2. Pancreatic enzyme replacement therapy: must be taken with every meal and snack & AKED vitamins. May require insulin late in the course
3. CF liver disease: ursodeoxycholic acid
4. Ivacaftor: is an oral pharmacologic potentiator, activates defective CFTR in patients with class 3 mutation G511D
5. Lung transplant

Respiratory distress diseases of the new born

Done by: Diaa Imran©

Introduction:

Symptoms & signs of all RD causing diseases: tachypnea, nasal flaring, grunting, retractions, acidosis & cyanosis

Causes:

Pulmonary: RDS, pneumonia, lung hypoplasia, TTN, lung hemorrhage & MSS

Systematic: infections, temperature, anemia, CHD & PHTN

Obstruction

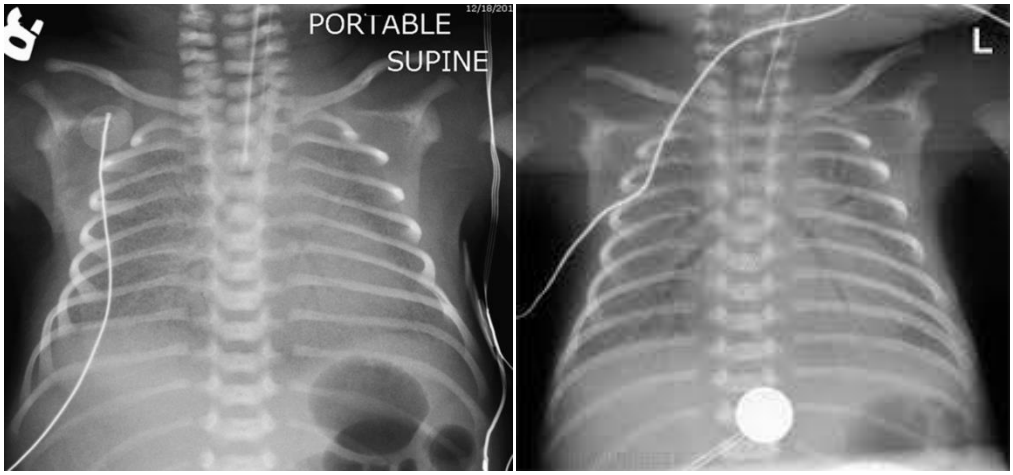
	Term baby	**Pre-term baby**
<6hrs old	TTN, MAS & asphyxia	RDS, pneumonia & lung anomaly
>6hrs old	Pneumonia & CHD	Pneumonia, CHD & lung hemorrhage

Respiratory Distress Syndrome: most frequent cause of respiratory distress in premature infants "due to surfactant deficiency" leading to atelectasis "lung collapse"

Risk factors: prematurity, DM mother, male baby, hypoxia, familial & acidosis

Symptoms: same as introduction & swollen extremities

Diagnosis: clinically & CXR: ground-glass appearance and air bronchograms "visible air in bronchi"



Complications: pneumothorax, PDA & infections

Treatment: Surfactant

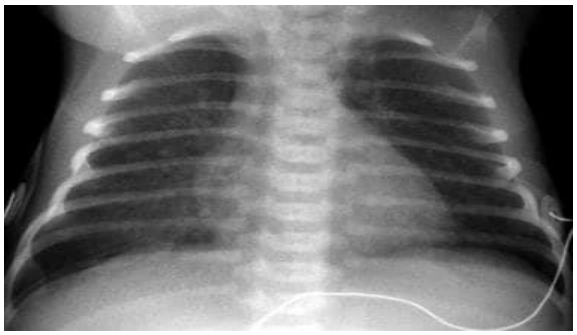
Supportive: thermal, fluid\nutrition & oxygen | Mechanical ventilation

Meconium Aspiration Syndrome: is aspiration of the meconium, with risk of lung collapse & infection

Symptoms: same as introduction & visible meconium

Prevention: Avoid vasoconstriction: acidosis, hypoxia & metabolic disturbances

Diagnosis: clinically: meconium-containing amniotic fluid and symptoms & CXR: hyperinflation with variable areas of atelectasis and flattening of the diaphragm

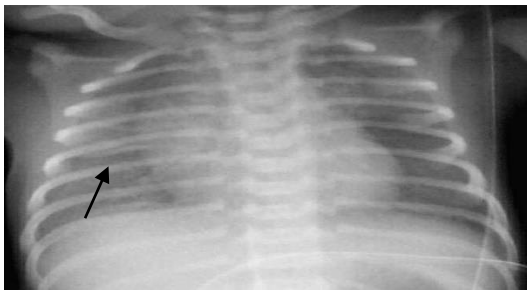


Transient Tachypnea of Newborn: is the most common cause of respiratory distress, due to residual fluid in fetal lung tissues.

Risk factors: maternal asthma, C-S, male sex, macrosomia & maternal DM

Symptoms: Tachypnea immediately after birth or within two hours, with other predictable signs of respiratory distress. Symptoms can last few hours to two days, and resolves spontaneously

Diagnosis: clinically & CXR: diffuse parenchymal infiltrates, a "wet silhouette" around heart, or intralobar fluid accumulation & fluid in the fissure. | **Treatment**: conservative



Fluid in the fissure

Acute rheumatic fever & infective endocarditis

Done by: Diaa Imran©

Acute rheumatic fever: is a diseases follows inappropriate treatment of GAS pharyngitis, in which the host immune system tries to attack the bacterial antigen "M-protein", it cross reacts with a host protein that is similar to the bacterial antigen, leading to autoimmune disease.

Symptoms: strep throat, fever, carditis, arthritis, erythema marginatum, subcutaneous nodules & chorea

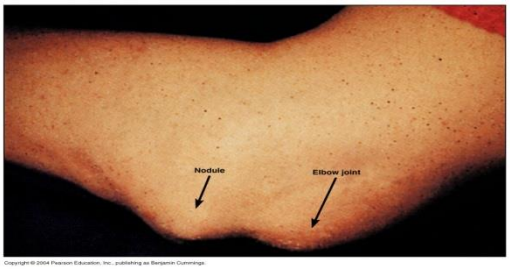
Diagnosis: Jones' criteria 2 major or 1 major and 2 minor criteria + evidence of preceding GAS infection

Major criteria	Minor criteria
Migratory polyarthritis	Arthralgia
Carditis	Fever
Erythema marginatum	First degree heart block
Syndenham chorea	Elevated inflammatory markers (ESR, CRP)
Subcutaneous nodules	

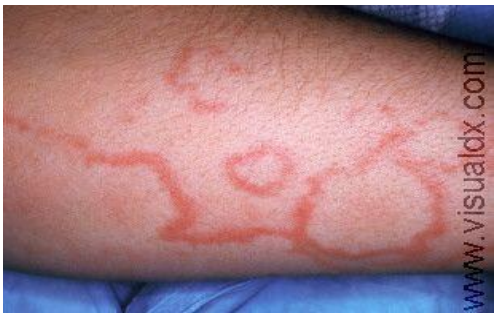
Migratory polyarthritis: migratory, non deforming arthritis of larger joints. Response to salicylates is characteristic. It is the earliest sign of the disease.

Chorea: random-appearing, continuous, involuntary movements.

Subcutaneous nodules:



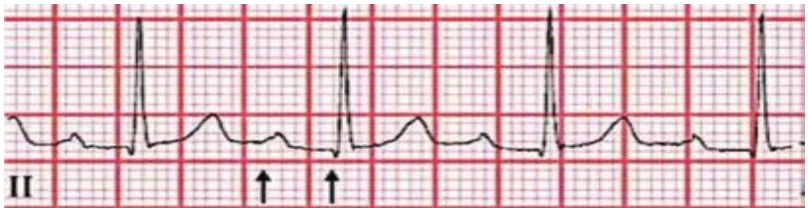
Erythema marginatum:



Minor criteria: Arhtralgia "used if arthritis is not used as a major criterion"

Fever> 38.0°c, elevated ESR

Prolonged P-R interval on ECG "unless carditis is a major criterion"



Prolonged P-R interval

DDx of carditis: Kawasaki disease, endocarditis & pericarditis

DDx of arthritis: JRA, SLE & sickle cell

DDx of chorea: Wilsons' disease & SLE

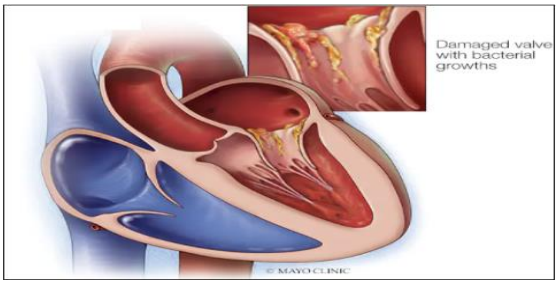
Treatment: bed rest, ABx & anti-inflammatory "NSAIDS\steroids"

- **N.B**: salicylates for arthritis, steroids for carditis & phenobarbital for chorea

Infective endocarditis: is inflammation of the endocardium of the heart. Always suspect endocarditis in a patient with a new heart murmur and unexplained fever or bacteremia.

Pathogenesis: areas such as valves of the heart have turbulent blood flow, which leads to endothelial damage; this damage leads to platelets aggregation, which favors a good media for the bacteria to settle in, leading to vegetations. These vegetations "bacterial growth" may dislodge leading to many manifestations will be later mentioned.

Causative organisms: Strep > Staph > HACEK > -ve culture "fingi… etc"

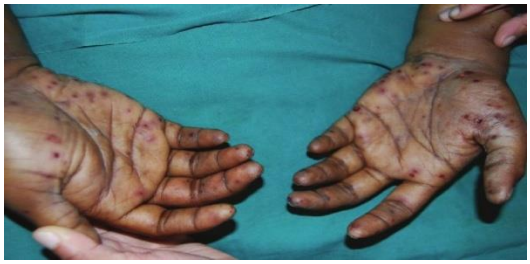


Vegetations

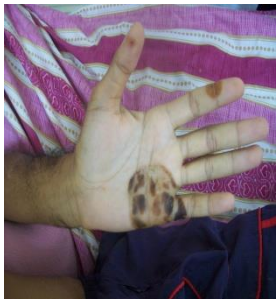
Risk factors: prosthetic heart valve, illegal drugs, immunosuppression & dialysis

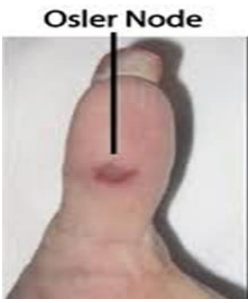
Symptoms:

Symptom	Average (%)	Physical Finding	Average (%)
Fever	90	Splenomegaly	55
Malaise	55	Petechiae	33
Anorexia/weight loss	31	Embolic phenomena	28
Heart failure	30	New or change in heart murmur	24
Arthralgia	24	Clubbing	14
Neurologic findings	18	Osler nodes	7
Gastrointestinal findings	16	Roth spots	5
Chest pain	9	Janeway lesion	5
		Splinter hemorrhages	5

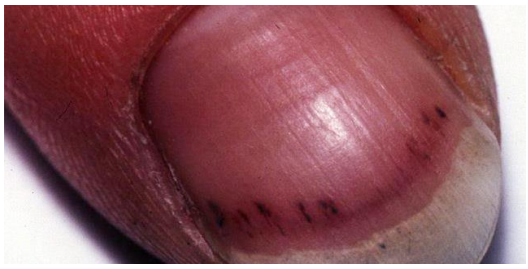


Janeway lesions, painless small, hemorrhagic lesions

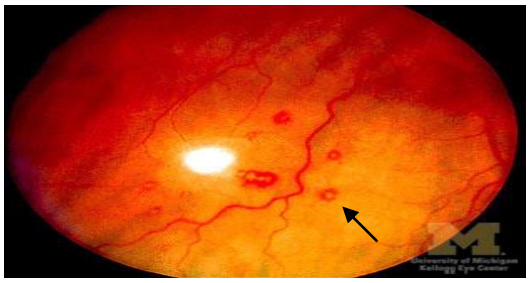




Osler nodes "painful"



Splinter hemorrhage



Roth spots

All these changes are caused by dislodgment of a vegetation leading to septic embolus which may lodge anywhere in the body leading to many manifestations, of which, the mentioned above.

Diagnosis: Dukes' criteria: Two major criteria, one major and three minor criteria, or five minor criteria are required to diagnose

TABLE 1-3 Duke Criteria

Major	Minor
• **Sustained bacteremia** by an organism known to cause endocarditis • **Endocardial involvement** documented by either echocardiogram (vegetation, abscess, valve perforation, prosthetic dehiscence) or clearly established **new valvular regurgitation**	• **Predisposing condition** (abnormal valve or abnormal risk of bacteremia) • **Fever** • **Vascular phenomena:** Septic arterial or pulmonary emboli, mycotic aneurysms, intracranial hemorrhage, Janeway lesions[a] • **Immune phenomena:** Glomerulonephritis, Osler nodes,[b] Roth spots,[c] rheumatoid factor • **Positive blood cultures** not meeting major criteria • **Positive echocardiogram** not meeting major criteria

Risk factors of complications: prosthetic valve, left-sided IE, S.aureus\fungal IE, cyanotic CHD & poor clinical response to ABx

Prevention: oral hygiene & antibiotics for dental procedures in those with:

- Prosthetic valve
- History of previous IE

Treatment: selective ABx

Acyanotic Congenital Heart Diseases

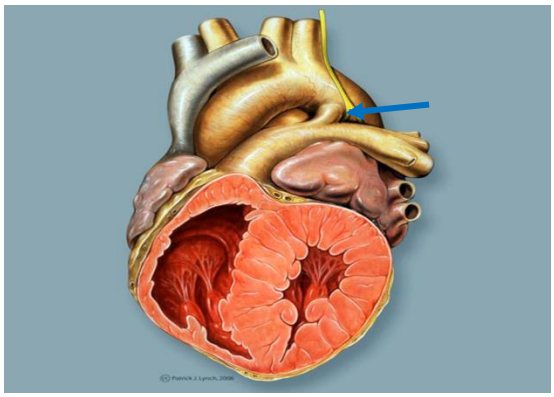
Done by: Diaa Imran©

This summary includes only the most important topics of ACHD, for more information, get back to slides

Patent Ductus Arteriosus: is a communication between the pulmonary artery and the aorta, distal to left subclavian.

- **N.B**: DA is kept patent by the effect of PGs

Risk factors: maternal Rubella infection, maternal amphetamine use & prematurity



During fetal life, the ductus arteriosus is a normal structure that allows most of the blood leaving the right ventricle to bypass the pulmonary circulation and pass into the descending aorta; as there is no need for the lung, so more blood can feed the body. At birth, the placenta is removed, eliminating a major source of prostaglandin production & the lungs expand, activating the organ in which most prostaglandins are metabolized; DA closes.

Symptoms & Findings: irritable, poor feeding, FTT, excessive sweat, increased respiratory effort & recurrent upper respiratory infections and pneumonia

Systolic murmur, paradoxically split S2, <u>continuous thrill</u> & wide pulse pressure

In the presence of significant pulmonary hypertension, there may be evidence of right ventricular hypertrophy

- <u>DOPPLER ECHO is the gold standard for diagnosing PDA</u>

Complications: HF, Eisenmenger "opposite shunting" & calcification of the ductus

Treatment: NSAIDs & surgical closure of the DA "coiling or patching"

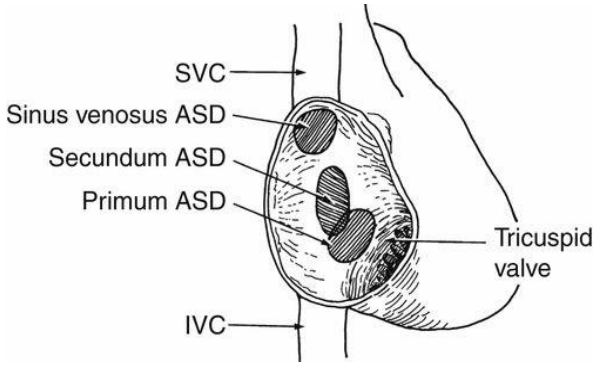
Atrial Septal Defect: is an acyanotic CHD characterized by defect in the interatrial septum causing a left to right flow between the atria.

Risk factors: Down syndrome & environmental factors

Types of ASD: Secundum: located in the region of the fossa ovalis. Associated with: partial anomalous venous return, pulmonic stenosis & mitral valve prolapse

Primum: occur in the lower portion of the atrial septum. Often associated with: cleft mitral valve

Sinus venosus defects: located near the orifice of the superior vena cava. Often associated with: anomalous pulmonary venous return



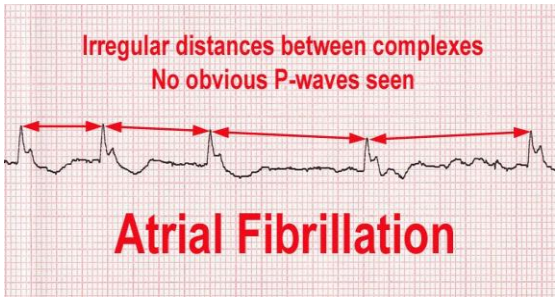
Left to right shunting makes the right work more, which may lead to right sided failure, overtime, the excessive blood moving to the lungs, causes vascular damage, narrowing to the arteries leading to pulmonary HTN

N.B: CVA can result from paradoxical embolization through an ASD. A-fib\flutter can also occur

Symptoms & Findings: easy fatigability, FTT & recurrent pulmonary infections

Mid systolic ejection murmur & fixed splitting of S2

ECG: tall P-waves & A-fib



Treatment: mostly closes spontaneously

Cyanotic Congenital Heart Diseases

Done by: Diaa Imran©

Cyanosis: bluish discoloration of the skin, nail beds & mucus membranes appears when tissues are deprived of adequate amount of O_2. Visible when 5 gm/dl hemoglobin circulates unbound to O_2 and the measured O_2 saturation drops below 85%.

Cyanosis occurs due to either one of these causes:

Decreased pulmonary blood flow & pumping deoxygenated blood to the body.

Consequences of cyanosis: polycythemia, endocarditis, CNS injury & clotting abnormalities

Findings in CCHD: tachypnea without retractions, no crackles, no increase in PO_2 with oxygen mask, cardiac changes in CXR & $\pm$ heart murmurs.

Causes of CCHDs: mnemonic 5Ts:

Tetralogy of fallot "TOF"

Transposition of great vessels "TGV"

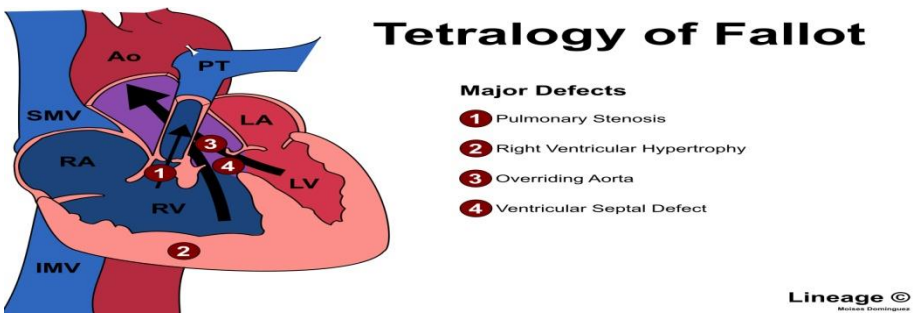
Tricuspid atresia

Truncus arteriosus

Total anomalous pulmonary venous drainage

1. **Tetralogy of Fallot**: the most common cyanotic heart disease.

The name tetralogy came from the fact of 4 defects in the heart: VSD, pulmonary stenosis, RVH & overriding aorta.



N.B: severity of TOF, depends on the degree of the pulmonary stenosis

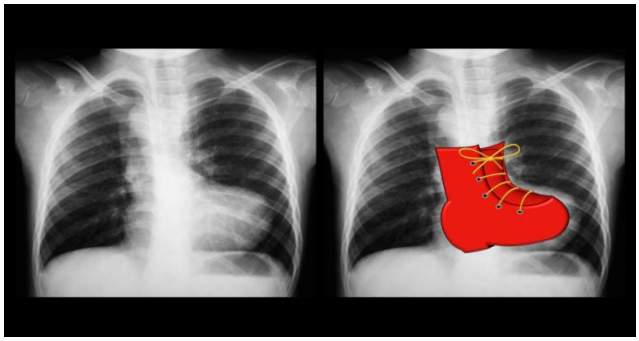
Symptoms & Findings: dyspnea, failure to thrive, finger clubbing & cyanotic spells*****

***Cyanotic spells**: are paroxysmal cyanotic\hypoxic events in a child "1st 2 years"; due to decreased pulmonary blood flow "acidosis" and right to left shunting, occurs after exercise\crying

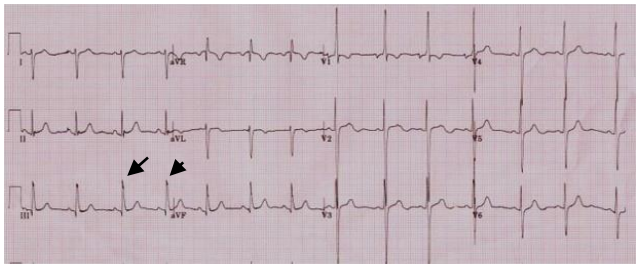
Management: knee-chest position, IV fluid, bicarbonate, ketamine, propranolol & Morphine

Long systolic ejection murmur; due to pulmonary stenosis

CXR: boot-shaped heart, large aorta & oligemic lungs



ECG: right axis deviation & peaked\bifid P waves



Complications of TOF: mnemonic 3Bs & C

Brain thrombosis "due to polycythemia"

Brain abscess, Bacterial endocarditis & Congestive heart failure

Treatment: surgical repair of the VSD & pulmonary stenosis "elective at 4-6 months"

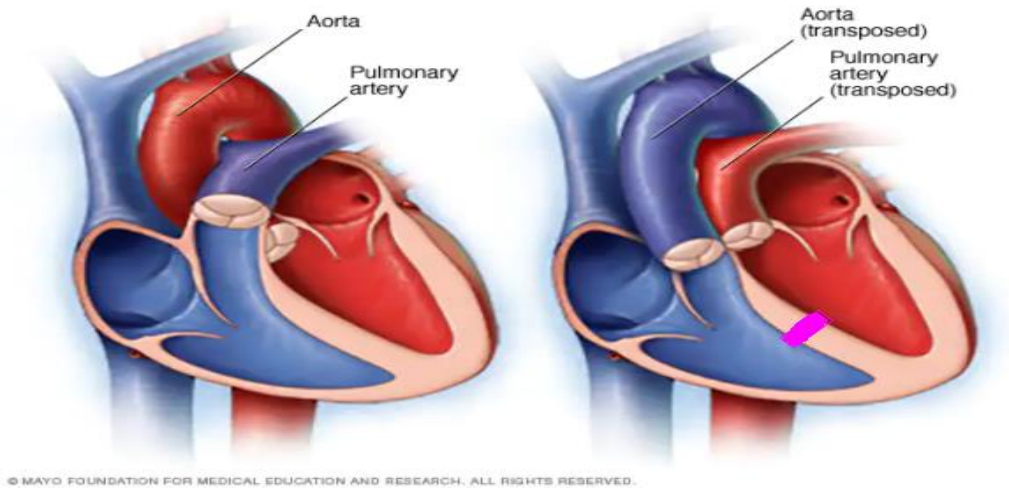
Urgent surgery is needed in: worsening O_2 levels, severe cyanotic spells & dependence on PGE_1*****

***PGE_1**: keeps PDA as a source of pulmonary blood flow until surgery, in severe pulmonary stenosis.

2. **Transposition of the great arteries**: it is the 2nd most common CCHD, as the name suggests, here, there is a transposition of the aorta and the pulmonary artery, where the LV pumps oxygenated blood to the pulmonary artery, and the RV pumps deoxygenated blood to the aorta!

The patient will surly die with this TOW PARALLEL CIRCUITS, thus a VSD or a PDA are also present, so some blood mixes, so the patient is living.

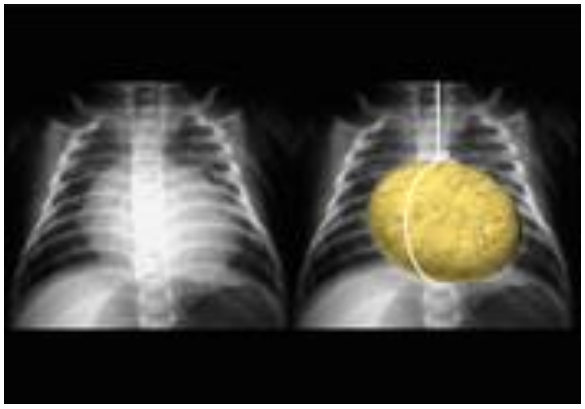
N.B: it is the most common cyanotic defect presents with cyanosis at neonatal period.



Symptoms & Findings: cyanosis SINCE BIRTH, dyspnea & feeding problems

Severe arterial hypoxemia. Hypoglycemia and hypocalcemia are occasional findings

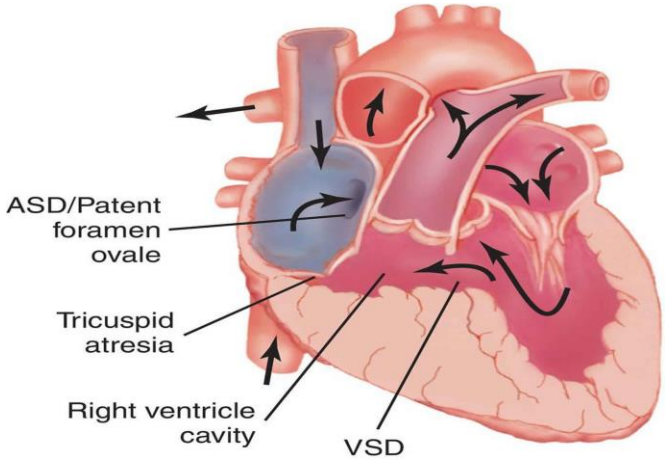
CXR: egg on a string



Management: PGE_1 until surgery "arterial switch procedure"

3. **Tricuspid atresia**: the 3rd most common cyanotic cardiac condition, in this disease, there is atresia of the tricuspid valve, with absence\non-functioning RV → one cardiac ventricle.

Therefore an ASD is present, thus the LV pumps blood to both aorta and pulmonary artery



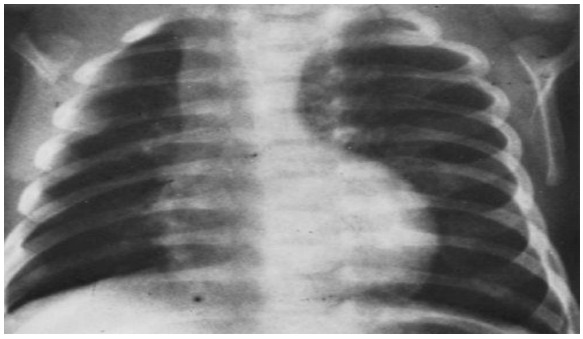
Symptoms & Findings: cyanosis FROM BIRTH, tachypnea, poor feeding & ± clubbing

Hepatomegaly may indicates inadequate interatrial communication

Single S2 sound "due to one functioning ventricle"

ECG: Superior QRS axis "S-wave had greater amplitude than the R-wave in all inferior leads"

CXR: decreased pulmonary vasculature & very rarely boot-shaped heart



Management: PGE_1 "as pulmonary stenosis may be present" until surgery "Fontans' procedure*****"

*****Performed by anastomosing the right atrium or atrial appendage directly to the pulmonary artery, and now is performed by anastomosing IVC to the pulmonary artery

4. **Total Anomalous Pulmonary Venous Return**: occurs when the pulmonary veins drains into the RA instead of LA, it is accompanied with ASD, otherwise death occurs.

Since RV works double its job, TAPVR is also accompanied with RVH & small LV due to less work

Types of TAPVR:

Supra-cardiac: pulmonary veins drains into the right SVC, "50% of cases"

Cardiac: pulmonary veins drains into the RA, "20% of cases"

Infra-cardiac: pulmonary veins drains into the IVC or hepatic vein, "20% of cases"

Mixed: mix of any of the above types, "10% of cases"

- **N.B**: supra & infra cardiac cases are accompanied with pulmonary HTN
- **N.B**: pulmonary HTN\edema may occur due overloaded RV

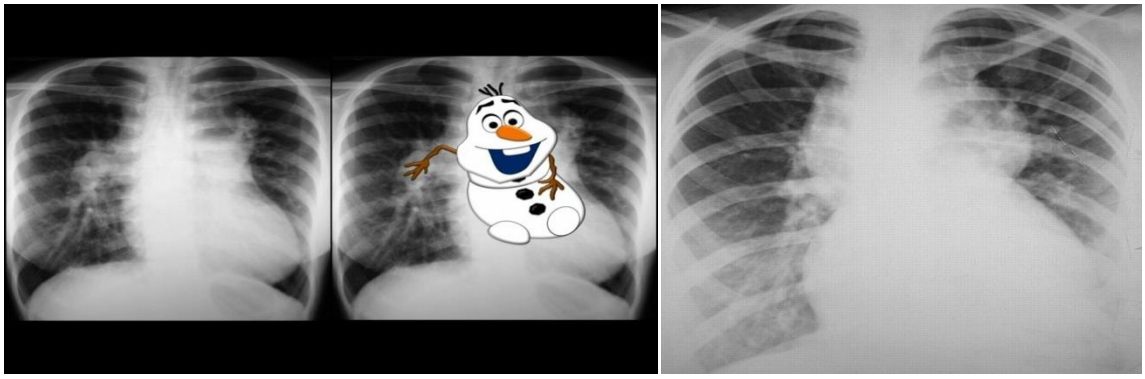
Symptom & Findings: mild to moderate cyanosis & undernourishment

Widely split and fixed S2 & systolic ejection murmur

ECG: RVH in the form of tall R waves in the right precordial leads

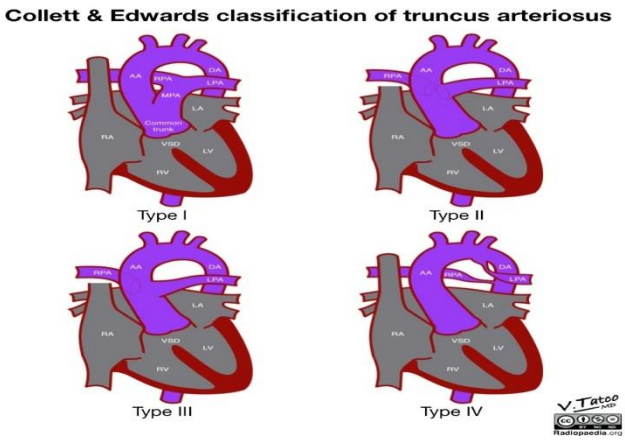
CXR: moderate to marked cardiomegaly involving the RA & RV is present with increased pulmonary vascular markings.

"Snowman" or figure-of-8 signs may be seen in the supracardiac type, but rarely before 4 months of age



Management: O_2, diuretics, bicarbonates & surgery

5. **Truncus arteriosus**: failure of truncus arteriosus to develop properly, so the aorta & pulmonary artery are adjoined.

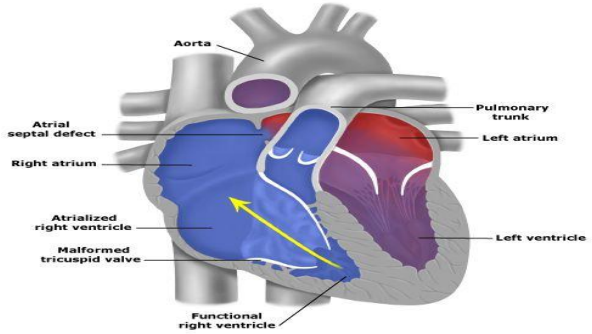


Symptoms & Findings: cyanosis FROM BIRTH, failure to thrive & recurrent lung infections

CXR: cardiomegaly, with increased pulmonary vascularity

Management: surgery

- **Ebstein anomaly**: downward displacement of the tricuspid valve into the RV, so that a portion of the RV is incorporated into the RA "atrialized RV" and functional hypoplasia of the RV results. WPW syndrome is frequently associated with the anomaly.



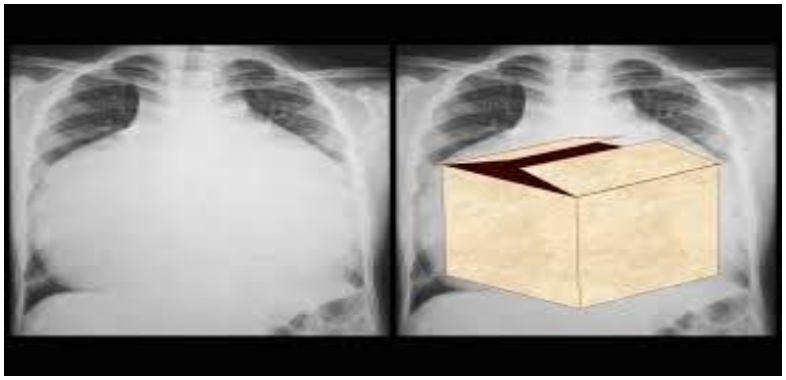
Symptoms & findings: cyanosis and CHF develop during the first few days of life, dyspnea, fatigue, & palpitation on exertion

SVT may occur.

Hepatomegaly is usually present.

ECG: characteristic RBBB and RA dilatation are present in most patients with this condition, first-degree AV block is frequent and occurring in 40% of patients & WPW syndrome is present in 20% of patients with occasional episodes of SVT

CXR: balloon\box-shaped heart and decreased pulmonary vascular markings



Management: PGE_1 until surgery

- **N.B**: this disease is more frequent in maternal use of Lithium

Biliary disorders

Done by: Diaa Imran©

1. **Disorders of bile conjugation**:

Crigler-Najjar syndrome I: is an autosomal recessive disease, which leads to Glucuronyl transferase deficiency, an enzyme involved in bile conjugation. Leading to severe unconjugated hyperbilirubinemia develops in the first 3 days of life.

Symptoms & signs: Kernicterus "brain damage" & pale stools

Diagnosis: Decreased bilirubin in the bile

Liver biopsy showing low hepatic glucuronyl transferase activity

DNA diagnosis

Treatment: keep serum unconjugated bilirubin <20 mg/dL

Exchange transfusions and phototherapy.

Liver transplantation cures the disease

N.B: Crigler-Najjar syndrome II is the other type with partial enzyme deficiency, normal stool color & no kernicterus. It has a significant response to phenobarbital

2. **Cholestasis disorders**:

Biliary atresia: an idiopathic, progressive, fibro-obliterative disease of the extrahepatic biliary tree, and is the most common indication for liver transplantation in children

It has 3 types:

I: Obstruction of the CBD, **II**: obstruction of the CHD, **III**: obstruction of most of the extra-hepatic tree

Symptoms: jaundice, tee-dark urine, pale stool, prutitis "Sx of biliary obstruction" & abdominal distention

Diagnosis: US "gallbladder is either absent or irregular in shape"

Hepatobiliary scintigraphy "failure of tracer excretion"

Liver biopsy

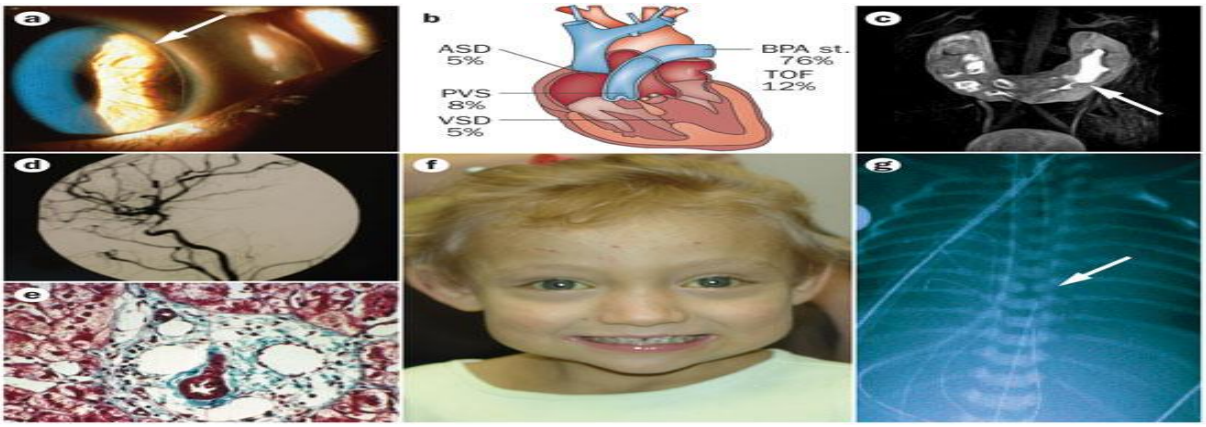
Treatment: Kasai procedure

Transplantation

Alagille syndrome: is an autosomal dominant disease caused by mutation in the JAG1 gene, leading to decreased number of bile ducts in the liver with a resultant cholestasis; due to decreased bile movement out of the liver.

Symptoms: jaundice, tee-dark urine, pale stool, pruritis, tetralogy of Fallot, facial features*****, thick cornea & butterfly vertebrae

*****broad forehead, widely sepereted eyes & pointed chin



Diagnosis: clinically, 3 out of the above 5 symptoms is sufficient for diagnosis. **N.B**: all bile obstruction Sx are counted as 1.

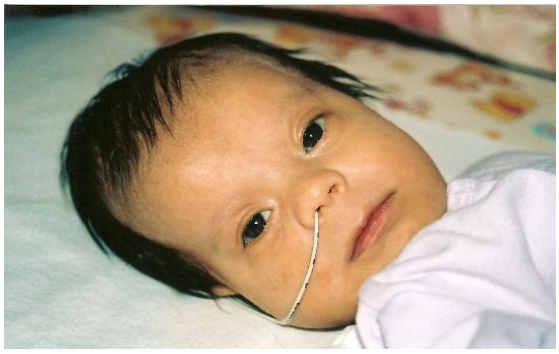
Liver biopsy & genetic study

Treatment: conservative, with minority requires transplant. **N.B**: patients are likely to have pruritus, xanthomas with markedly elevated serum cholesterol levels.

N.B: Tetralogy of Fallot: pulmonary stenosis, right ventricular hypertrophy, ventricular septal defect & overriding aorta

Zellweger "cerebro-hepato-renal" **syndrome**: autosomal recessive disorder marked by progressive degeneration of the liver and kidneys; due to absence of peroxisomes, which is usually fatal in 6-12 months.

Symptoms & signs: severe, generalized hypotonia, psychomotor retardation, abnormal head and facial features, hepatomegaly, renal cortical cysts, calcifications of the patellas and greater trochanter & ocular abnormalities.


High forehead, underdeveloped eyebrow ridges, wide-set eyes & neurological abnormalities such as mental retardation and seizures

Progressive familial intrahepatic cholestasis "PFIC": is a defect in the canalicuar membrane transporters, account for transporting bile from hepatocytes into bile ducts, leading of buildup of bile in the liver. It is of a 3 subtypes: **PFIC type I** "Byler disease"

PFIC type II "BSEP deficiency"

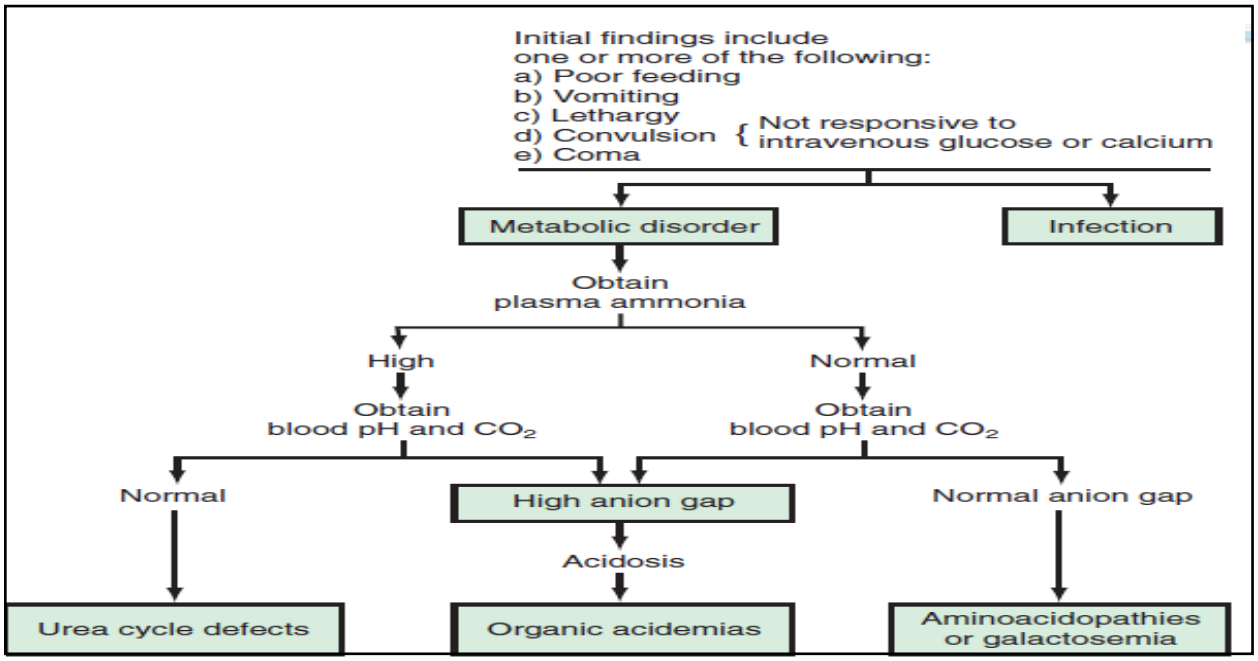
PFIC type III "MDR3 disease"

Symptoms: steatorrhea, pruritus, vitamin D-deficient rickets & gradually developing cirrhosis

3. **Metabolic liver disease**:

When should we consider of metabolic liver disease? In sick* neonate not responding to usual treatment

*vomiting, poor feeding, failure of thrive, seizures, dysmorphic features, metabolic acidosis & hepatomegally



Galactosemia: is the most common metabolic cause of liver disease, caused by deficiency of the galactose-1-phosphate uridyltransferase "GALT" enzyme, account for metabolize galactose.

Symptoms: poor feeding, vomiting, diarrhea, failure to thrive, hypoglycemia, jaundice, hepatomegaly, elevated transaminases, coagulopathy, ascites, liver failure, renal tubulopathy, lethargy, irritability, seizures, cataracts, and Escherichia coli neonatal sepsis

Diagnosis: elevated serum galactose & measuring GALT enzyme activity in erythrocytes

Treatment: Lactose-free formula should be started during the first 3 to 10 days of life. **N.B**: lactose after being absorbed will be converted into glucose & galactose by the enzyme lactase.

Tyrosinemia: is accumulation of tyrosine in the blood, due to deficiency of fumarylacetoacetate hydrolase

Diagnosis: Elevated tyrosine & methionine in plasma, elevated α-FP, confirme diagnosis by enzyme assay & molecular genetic testing. **Treatment**: Nitisinone & Low tyrosine diet

Hereditary Fructose Intolerance: occurs due to deficiency of fructose 1,6-biphosphate aldolase "aldolase B"

Symptoms: same as for metabolic liver disease

Diagnosis: enzymatically by measuring the aldolase B activity in liver tissue and molecularly by sequencing the ALDOB gene.

Management: sucrose, fructose & sorbitol free diet.

Brucellosis

Done by: Diaa Imran©

Brucellosis: is the infection with the aerobic, zoonotic, non-spore-forming, non motile & gram negative coccobacillary bacteria "Brucella".

There are 4 species of brucella that can infect humans:

B. abortus (cattle), B. melitensis (goat/sheep), B. suis (swine) & B. canis (dog)

Routs of infection: unpasteurized milk, skin cuts\abrasions, inhalation of infectious aerosols & ingestion of contaminated meat or dairy products.

Symptoms: begins 2-4 weeks after inoculation: fever, mold smelling sweat, malaise, fatigue, arthralgia, hepatosplenomegaly, abdominal pain, N\V & diarrhea.

Complications: bacteremia, meningitis & osteomyelitis

Diagnosis: history of exposure to animals or ingestion of unpasteurized milk

CBC: pancytopenia

- Definitive diagnosis is established by recovering the organisms: blood culture, bone marrow culture & Serology: serum agglutination test (SAT) "Measures total Abs"

False-positive results due to cross-reacting antibodies to other gram-negative organisms: Y. enterocolitica

Treatment:

<8 years: Rifampicin + TMP/SMX

>8 years: Rifampicin + Doxycyclin

- Add IV gentamycin for hospitalized patients.

Nephrotic syndrome

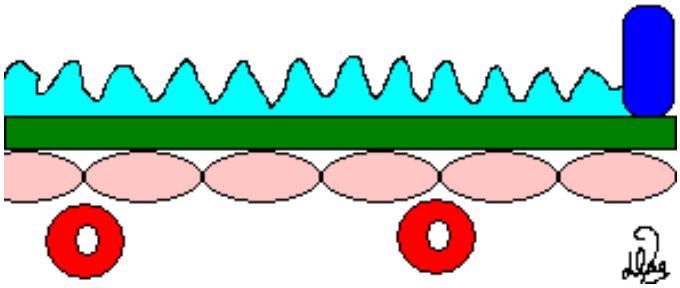
Done by: Diaa Imran©

The glomerular capillary wall is consisted of 3 layers:

Endothelial cells “pink cells”

Basement membrane “green rectangle”

Podocytes & their foot-processes “blue cell”



GCW is a barrier to the passage of plasma proteins from the capillary lumen to the urinary space.

Nephrotic syndrome: is a clinical entity of multiple causes characterized by a change in the GCW permeability, with resultant massive proteinuria. Can occur at any age, but peaks 2-6yrs,

Causes:

95% idiopathic: minimal change disease, FSGS, membranous nephropathy & MCGN

5% secondary: SLE, drugs, infections… etc

1. **Minimal change disease**: is the most common cause of nephrotic syndrome in children “M>F”. It is the result of idiopathically hypercytokinmeia. Usually disappears towards puberty, but 10-15% continue to have relapses as adults.

The nephrotic range of proteinuria is: 40mg/m^2/hr OR 50mg/kg/day

N.B: in urine dipstick:

+1 = 0.3gm/L | +2 = 1gm/L | +3 = 3gm/L | +4 = >4gm/L

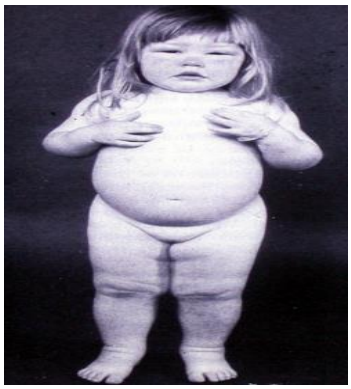
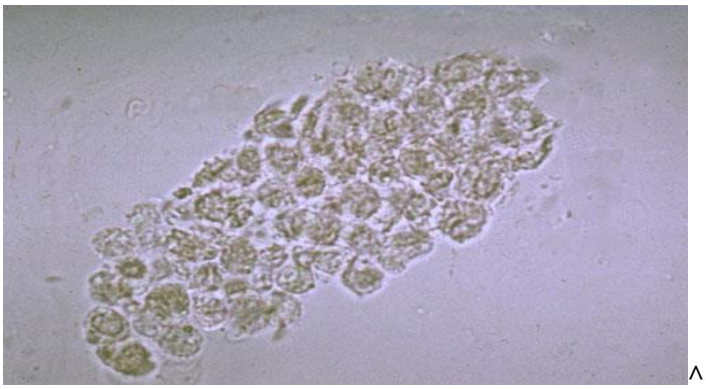
Minimal change disease is usually associated with:

Hodgkin lymphoma. **N.B**: reed-sterberg cells produce large amount of cytokines.

Atopy, asthma, hay fever & thymoma

When large amounts of proteins are lost in the urine, it leads to many **symptoms & complications**:

Defect	Result
Loss of **albumin** in the urine	Edema "mostly peri-ocularly
Loss of **gammaglobulines** in the urine	Infections
Loss of **proteins C, S & AT-III** in the urine	Hypercoagulation "thrombosis"
Loss of **transferrin** in the urine	Iron deficiency anemia
Loss of **cholicalciferol** in the urine	Vit-D deficiency
Loss of **element binding-protein** in the urine	Zinc & Copper deficiency
Hyperlipidemia	Atherosclerosis



^^

Diagnosis: Light microscopy: normal | Immune studies: normal

Electron microscopy: effacement of the podocytes

Serum & Urine albumin: low & high respectively

Urinalysis: may show RBCs & (protein casts^^)

Complement system: low C3 & C4

Serum lipids: hyperlipidema

For secondary disease: ANA, HBsAG & anti-dsDNA

Kidney biopsy*****: used for both diagnosis & staging

***Indications for biopsy**: secondary disease, frequent relapsing, steroid resistant, HTN & Low GFR

N.B: **Remission**: no edema, urine is protein free for 5 consecutive days.

Relapse: edema, or first morning urine sample contains >2+ protein for 7 consecutive days.

Frequent relapsing: ≥2 relapses within 6 months

Steroid resistant: failure to achieve remission with prednisolone given daily for 1 month

Management:

Admission, steroids, albumin, diuretics, anticoagulants, prophylactic antibiotics, ACEIs & ARBs

Steroid regimen: 2 mg/kg/day "divided", until urine is protein free for 5 days

Maintain Remission: Same dose, given as a single dose every 48 hours. Gradual tapering over about 2 months

For steroid dependent and frequent relapsers: maintain at a low dose "every 48 hours"

Steroids side effects: poor growth, osteoporosis, cushinoid features, adrenal suppression & HTN

Indications for other than steroids immunosuppressant "Cyclophosphamide & Calcineurin-inhibitors": steroid resistance, steroid dependence & frequent relapses.

Red urine

Done by: Diaa Imran©

Red urine can be caused by either:

1. **Hematuria**: the presence of >5 RBCs in the urine. Only small amount of blood may be necessary to produce discoloration "pink to red"

Fresh heavy bleeding, which is bright red in color, is mostly of a lower urinary tract origin
while the contact of blood with the acidic urine, gives it a brown color, rendering upper tract origin

Origin of hematuria: glomeruli, tubules, interstestium & urinary tract "collecting system, ureters, bladder & urethra"

Glomerular causes: IgA nephropathy, Alport syndrome, benign familial hematuria, post-strep GN, SLE, Rapidly progressive GN, HSP & Goodpasture's disease

Tubules & interstestium causes: pyelonephritis, TB & hematological "sickle cell & vWD"

Tract causes: infection, trauma, tumor & drugs

If the blood is glomerular in origin: RBC's casts & Proteinuria are present, and the clinical presentation is: edema, HTN & low urine output

If extra-glomerular: clots are mostly present

Detection of blood in urine: urinalysis, urine microscopy & dipstick*****

*****Dipstick for blood: blood is detected by the peroxidase-like action of hemoglobin

If positive with RBC's: hematuria

If positive with No RBC's: Hemo\myoglobinuria

Negative dipstick: foods, food dyes, urate, drugs…etc

Approach to hematuria:

Symptoms: Macroscopic hematuria: usually asymptomatic or seldom with dysuria, renal colic, loin pain

Microscopic hematuria: mostly asymptomatic and detected during screening test

Important history questions: Is the hematuria at the beginning or end of the stream "suggestive of a bladder or urethral cause"

Is the urine bright red "local cause" or tea/coca color "more likely to be glomerular"

Family history: deafness, Alport syndrome, PKD, sickle cell disease, CKD, kidney transplant

Investigations: Depstick, urine microscopy, culture\sensitivity, urine phase contrast microscopy: deformed red cells, renal US, KFT, electrolytes, albumin, CBC, 24hour urine: "Ca, oxalate, uric acid, creatinine, protein" & bopisy*****

***Children with persistent microscopic hematuria require biopsy when they have**: systemic illness, significant proteinuria, impaired renal function, HTN & FHx of hematuria

2. **Non-hematuria**: can be caused by:

Food "blueberries", hemo\myoglobinuria, drugs "rifampicin" & urate crystals

- **Rhabdomyolysis:** breakdown of the striated muscles resulting in the release of myoglobin, which is nephrotoxic "myoglobin precipitation in the kidneys" → AKI

Causes: massive muscle injury, strenuous exercise, prolonged seizures & myopathies

Symptoms & signs: myalgia, weakness, calf pain, muscle swelling, dark-red urine, positive dipstick for blood without RBCs & positive urine myoglobin

Treatment: IV fluids & monitor electrolytes if normal urine output

IV fluids + diuretics if low urine output "fluid challenge 10m/kg to know the output"

Dialysis: in severe electrolytes disturbances

- **N.B**: Cloudy urine May be secondary to: pyuria, calcium phosphate crystals & combination of calcium salts, uric acid, cysteine and struvite

Acute kidney failure\injury

Done by: Diaa Imran©

Acute kidney failure: a sudden, potentially reversible, inability of the kidney to maintain normal body chemistry & fluid balance.

AKI is defined as any of the following: Increase in serum Cr by >0.3 mg/dl within 48 hours

Increase in serum Cr to > 1.5 times baseline

Urine volume <0.5-1 ml/kg/h for 6 hours

RIFLE criteria: used for detection, classification & the correlation with clinical outcome of AKI.

Category	Criteria
Risk **(R)**	Increased serum creatinine level by 1.5 times or GFR decrease by >25%
Injury **(I)**	Increased serum creatinine level by 2.0 times or GFR decrease by >50%
Failure **(F)**	Increased serum creatinine level by 3.0 times, GFR decrease by >75% or serum creatinine level ≥354 µmol/L
Loss **(L)**	Persistent acute renal failure or complete loss of function for >4 weeks
End-stage kidney disease **(E)**	End-stage kidney disease for >3 months

GFR = glomerular filtration rate.

R= AKIN stage 1 | **I**= AKIN stage 2 | **F**= AKIN stage 3

Causes of AKI:

1. **Pre-renal**: is the most common cause, occurs due to hypovolemia and hypotension, but with structurally intact nephrons. Decreased perfusion = decreased GFR

Causes: bleeding, dehydration, GI losses, systematic vasodilatation, renal artery thrombosis… etc

2. **Renal**: insult to the kidney itself, with structural and functional damage.

Causes: GN, ATN, pyelonephritis, contrast media, heavy metals, vasculitis… etc

Structural injury in the kidney is the hallmark of intrinsic AKI. Where the most common form of intrinsic injury is Acute Tubular Necrosis

Acute Tubular Necrosis: occurs due to severe hypoperfusion, which leads to endothelial and tubular epithelial cell damage "mainly proximal tubules". **N.B**: brown casts in urinalysis

3. **Post-renal**: occurs due to obstruction of the urinary tract

Causes: PUV, stones, tumors, blocked catheter… etc

Symptoms of AKI: nonspecific "unwell patient with edema & abnormal breathing patterns"

Diagnosis: when suspected, try to find the cause

History: diarrhea, vomiting, urinary symptoms, pain, drug history, radiology… etc

Full physical exam

CBC, KFT, ABGs, CXR, urinalysis, & renal US… etc

$FeNa^+$: <1%: suggests pre-renal AKI | >2.5 % suggests established ATN "Renal cause"

	Pre-renal			**Renal cause**	
	Children	**Neonate**		**Children**	**Neonate**
Urine Na^+	<10	<20		>50	>40
$FeNa^+$	<1%	<2.5%		>1%	>2.5%
Urine osm.	>500	>400		<300	<400

Management:

Rule-out life-threatening conditions of AKI: hyperkalemia, hyper\hyponatremia, acidosis, pulmonary edema, shock & HTN

Resuscitation & conservative treatment

Treat the underlying cause

RRT "dialysis": in severe AKI

- RRT= Renal Replacement Therapy

Indications of RRT: BUN exceeding 100mg/dl

CHF with oligo\anuria unresponsive to diuretics

Hypertensive encephalopathy

Hyperkalemia, Hypo\hypernatremia

Severe acidosis & severe anemia

N.B: Nephrotoxic drugs: NSAIDs, ACEIs, ARBs, Vancomycin, methotrexate…etc

Congenital Adrenal Hyperplasia

Done by: Diaa Imran©

EMBRYOLOGY & BIOCHEMESTRY parts are NOT included and are mostly NOT important

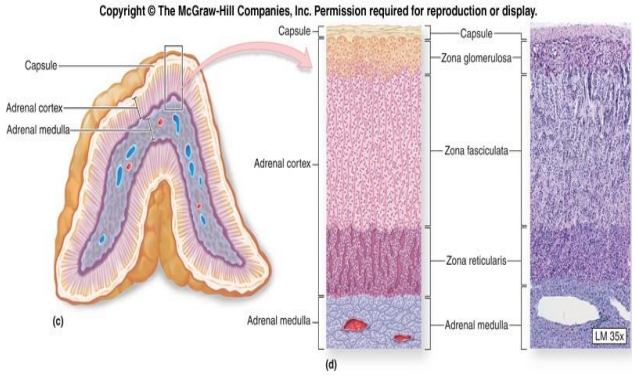
The adrenal gland is composed of a cortex and a medulla.

The cortex in turn is divided into 3 layers, in which each layer is responsible for the secretion of certain hormone.

The outer zone "**zona glomerulosa**": secretes aldosterone

The middle zone "**zona fasciculata**": secretes cortisol

The inner zone "**zona reticularis**": secretes sex hormones "androgens"



Congenital Adrenal Hyperplasia "CAH": is the benign enlargement of the adrenal gland.

Cause: autosomal recessive disorder in which there is impaired cortisol synthesis; due to 21-hydroxylase deficiency "90%", or 11-hydroxylase deficiency "10%".

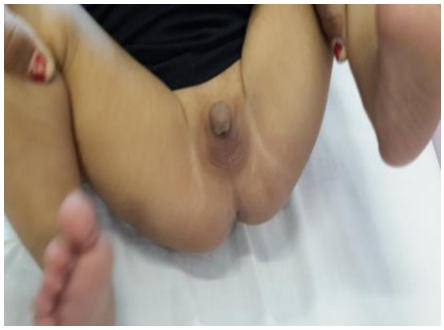
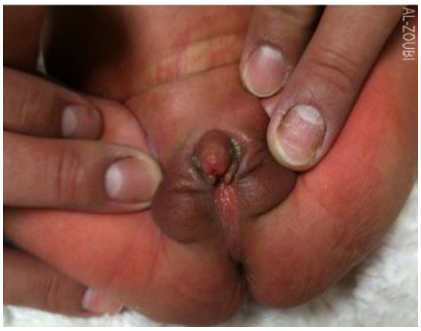
These hormones are essential for the synthesis of cortisol and aldosterone, when absent, no cortisol will be secreted, and thus no negative feedback to the pituitary occurs, so ACTH remains elevated. Since no cortisol can be made all ACTH will be used to make sex hormones "which are independent of 21-hydroxylase", hence huge amounts of sex hormone are made, leading to virilization.

Classification: 1. **Classical**: includes: a. virilization & b. salt wasting

2. **Non-classical**: milder form

Symptoms:

1. **Increased androgens**: dark scrotum, ambiguous genitalia, reduced fertility, premature closure of the epiphyseal plate & virilization
2. **Decreased cortisol**: loss of appetite, nausea, vomiting, abdominal pain, weight loss, hypoglycemia & production of ACTH and related proteins resulting in increased pigmentation of skin and mucous membranes.
3. **Decreased aldosterone**: hypornatremia, hyperkalemia, hypotension & metabolic acidosis.



Ambiguous genitalia "female"

Diagnosis: clinically

Labs: glucose, 17-hydroxyprogesterone, cortisol, ACTH, aldosterone

Synacthen test: synthetic ACTH given as IV bolus in a dose of 0.125-0.25 mg with measuring 17-hydroxyprogesterone before and 30 or 60 min after that.

Treatment: Classical CAH: Hydrocortisone replacement. **N.B**: do NOT use dexamethasone.

Non-classic CAH: asymptomatic patients do not require treatment with glucocorticoids "even in stress, in most cases". Treatment should be reserved for children and adolescents who are found to have significantly advanced skeletal maturation, which is predicted to negatively impact their adult height.

N.B: For severe stress & major surgery, administration of hydrocortisone "100 mg/m2 per day", divided in 3-4 IV doses for at least 24 hours peri- & postoperatively, before tapering over several days to a maintenance dose.

Monitoring & notes: Regular assessment of height, weight. Laboratory evaluation of 17-OHP, testosterone & androstenedione. Annual bone age

The height is usually 1.5 SD below the mean. Affected females may require surgical reconstruction

If prenatal suspicion, dexamethasone should be started before the seventh week of gestation to suppress the fetal pituitary adrenal axis before virilization occurs to prevent the female genitalia virilization.

Determine the sex of the fatus can be done by: Chorionic Villous Sampling at 10-12 weeks gestation

If the fetus is male: dexamethasone is discontinued

If the fetus is female: genetic testing is performed to determine if she has 21OHD, if the fetus is affected, maternal dexamethasone administration is continued to term.

N.B: In males genitalia usually are unaffected by the excess adrenal androgens, however, the penis, scrotum & prostate may become enlarged in affected boys.

Thyroid disorders

Done by: Diaa Imran©

Congenital hypothyroidism: it is mostly a permanent low thyroid function, but sometimes it could be transient, with a F:M = 2:1.

Risk factors: trisomy 21, twin pregnancy, prematurity, old maternal age & asians

Causes: dysgenesis "aplasia, hypoplasia or ectopic". "permanent"

Passage of maternal thyrotropin receptor-blocking antibody. "transient"

Dyshormogenesis

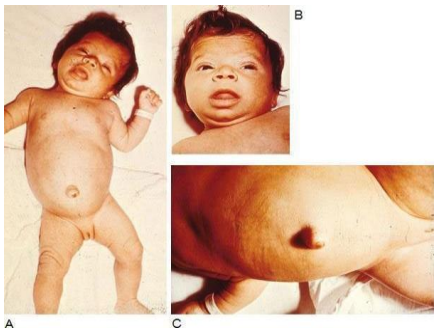
Central causes "low TSH\TRH"

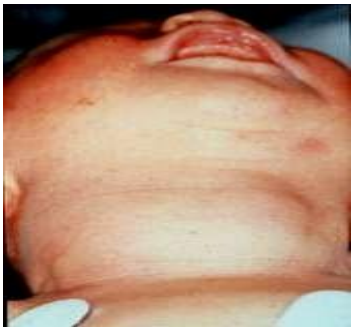
- **N.B**: Pendred syndrome: is a disorder typically associated with hearing loss and a thyroid dyfunction

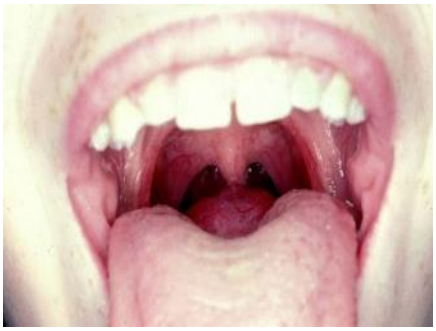
If transient it is attributed to: maternal medication, maternal blocking antibodies & low iodine

Symptoms: normal at birth, but later on, the baby develops the following:

Sleepiness, feeding difficulties, open mouth, protrude tongue, respiratory difficulties, prolonged jaundice, hoarse cry, goiter, umbilical hernia, dry skin, wide fontanels, constipation & cold intolerance





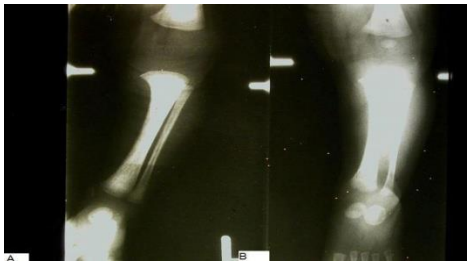


Lingual thyroid

Diagnosis: Serum TSH level is high, serum levels of T_4 or free T_4 are low, prolactin levels

Thyroid Isotope scan, Thyroid ultrasound, Hearing Test

Retardation of osseous development by 50%



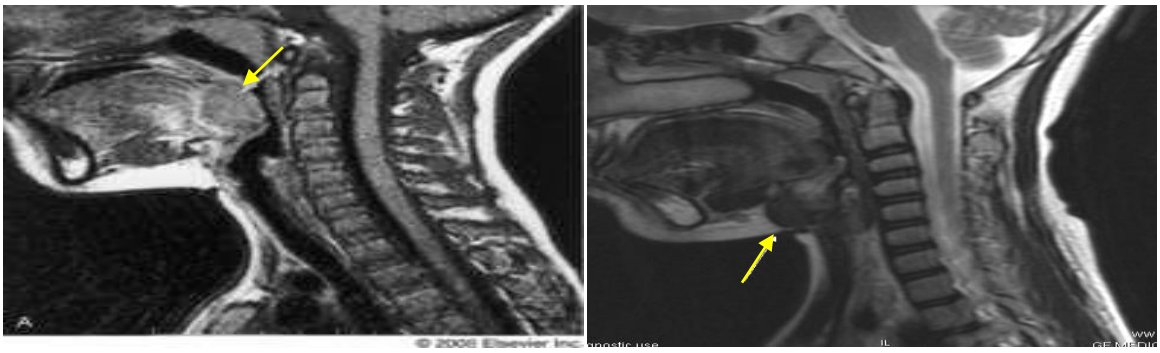
Absence of the distal femoral and proximal & tibial epiphyses

Treatment: Levothyroxine 10-15 mcg/kg/day. **N.B**: Soy milk formulas and iron medication can interfere with thyroxine absorption

Monitoring: T4, TSH and clinical evaluation

- 2 week after initial treatment is begun
- Every 1 month in the first 6 month.
- Every 2 months between 6-12 months.
- Every 4 months from 1-3 years.

Goal of therapy: maintain TSH at lower half of normal range and\or T4 in upper half of reference range.



Ectopic thyroid

Neonatal screening: measuring TSH alone will cause missing tertiary, while measuring T4 alone will cause missing the subclinical hypothyroidism. Thus the screening should involve both TSH & T4, at the age 2-4 days.

Developmental outcome: Growth rate and adult height are normal in children with congenital hypothyroidism in whom thyroid therapy is consistently maintained. The best outcome occurred with thyroid therapy started by 2 weeks of age

N.B: **congenital hypothyroidism is permanent if**: ectopic gland or absent thyroid tissue OR TSH above 10 mU/L after the first year of life. Otherwise it is transient*****

***Transient hypothyroidism may result from**: intrauterine exposure to maternal antithyroid drugs, maternal TRBAbs & iodine deficiency

In Transient hypothyroidism, normalize T4 within 2 weeks and "TSH within 1 month "between 0.5 and 2.0 mU/L during the first 3 years of life""

Hashimoto thyroiditis: is the most common cause of goiter and hypothroidism in older children and adolescent.

Causes: autoimmune, lymphocytic infiltration of thyroid due to the presence of antithyroperoxidase antibody.

N.B: it is usually associated with other autoimmune diseases "DM1, celiac, pernicious anemia… etc"

Symptoms: hypothyroid symptoms ± goiter. **N.B**: it is preceded by hyperthyroidism.

Diagnosis: TSH, T3, T4, antithyroperoxidase, Antithyroglobulin antibodies & thyroid US

N.B: biopsy is the definitive diagnosis, although it is not indicated

Treatment: levothyroxin

Hyperthyroidism: is increased in the function of the thyroid gland

Causes: toxic goiter, toxic adenoma, pituitary adenoma, drugs, McCune-Albright, lymphocytic thyroiditis & Graves' disease

- **Graves' disease**: is an autoimmune disease, causing hyperthyroidism, by Abs, working as TSH

Risk factors: other autoimmune diseases & trisomy 21

Symptoms: anxiety, irritability, deteriorating school performance and handwriting, weight loss despite increased appetite, palpitations, heat intolerance, insomnia & diarrhea.

Signs: exophalmos & peri-tibial myxedema

Diagnosis: elevated T4\T3 concentrations & with TSH suppression, TSH receptor antibodies positive, thyroid peroxidase antibodies positive, advanced bone age & thyroid isotope scan

Complications: thyroid storm: precipitated by surgery, infections, drug withdrawal/non-compliance & radioiodine treatment. The patient develops hyperthermia, severe tachycardia and restlessness and may become delirious, comatose or die

Treatment: PTU, radioiodine & surgery

Congenital hyperthyroidism "**congenital thyrotoxicosis**": is hyperthyroid state, caused by transplacental passage of TRSAb, characterized by early onset manifestations "at birth"

Fetal tachycardia and goiter allow prenatal diagnosis. Sometimes mothers have active or in remission Graves

Remits spontaneouslly within 6-12 weeks, but occasionally persists

Symptoms: goiter, restless, irritable, hyperactive, anxious, microcephaly & exophthalmic + other hyperthyroidism S&Sx

Diagnosis: TSH, T3, T4 & bone age

Treatment: carbimazole & propranolol

Diabetic KetoAcidosis

Done by: Diaa Imran©

DKA: is a medical emergency characterized by the presence of Hyperglycemia ">200mg", venous pH <7.3 or serum HCO_3 <15mmol/L & ketonemia or ketonuria.

Pathophysiology: DKA occurs in complete absence of insulin, in which glucose can no longer be transported into the cells leading to hyperglycemia, also, in the absence of insulin which normally acts as lipogenic, lipids starts to breakdown giving fatty acids, in which the liver convert them into keton bodies, that are acidic, leading to acidosis, thus decreased HCO_3. Polyurea & dehydration occur due to hyperglycemia

Severity of DKA:

	Mild	**Moderate**	**Severe**
pH	<7.3	<7.2	<7.1
HCO_3	<15	<10	<5
Dehydration	5%	7%	10%

Risk factors: children who omit insulin, poor metabolic control or previous episodes of DKA, gastroenteritis with persistent vomiting & children with psychiatric disorders.

Symptoms: nausea, vomiting, severe abdominal pain, acetone breath smell, kussmauls' breathing, dehydration, confusion, drowsiness & loss of consciousness.

Management: Immediate glucose measures, weigh the patient, assess the degree of dehydration, glasgow coma scale, give O_2 to patients with circulatory impairment

Cardiac monitor should be used for continuous ECG; to assess T-waves for evidence of hyper\hypokalemia.

Insert IV access for blood sampling and management, Obtain blood sample

Give bolus 0.9% saline 10ml/kg over 1 hour. **N.B**: "20ml\kg if in shock"

N.B: Deficit replacement should be with a solution that has a tonicity in the range 0.45%-0.9% saline, with added potassium chloride, potassium phosphate or potassium acetate.

Insulin therapy: for restore normal cellular metabolism, to suppress lipolysis and ketogenesis & to normalize blood glucose concentrations

Rehydration alone frequently causes a marked decrease in blood glucose concentration, however, Start insulin infusion at least 1 hour after starting fluid replacement therapy.

N.B: K^+ "4mmol/100ml" must be given with insulin; as insulin causes hypokalemia. Severe hypokalemia causes lethal arrhythmia.

Severe acidosis is reversible by fluid and insulin replacement; insulin stops further ketoacid production and allows ketoacids to be metabolized, which generates bicarbonate.

Complications of the therapy: hypoglycemia, hypokalemia, inadequate hydration, cerebral edema & hypercholremic acidosis.

- **Risk factors of cerebral edema**: younger age, new onset DM, severe acidosis at presentation, increased serum urea nitrogen at presentation & longer duration of symptoms
- **Signs & symptoms of cerebral edema**: onset of headache after beginning treatment, change in neurological status, Cushing's triad: "rising blood pressure, bradycardia & respiratory depression" & decreased O_2 saturation.
- **Treatment**: hyperosmolar agents "mannitol". **N.B**: Hypertonic saline may be used as an alternative or in addition to mannitol if there has been no response to mannitol within 15-30 minutes

Puberty

Done by: Diaa Imran©

Puberty: the sequence of physiological changes that include the development of secondary sexual characteristics associated with the pubertal growth spurt resulting in adult stature and reproductive capacity.

- **Onset of puberty**:

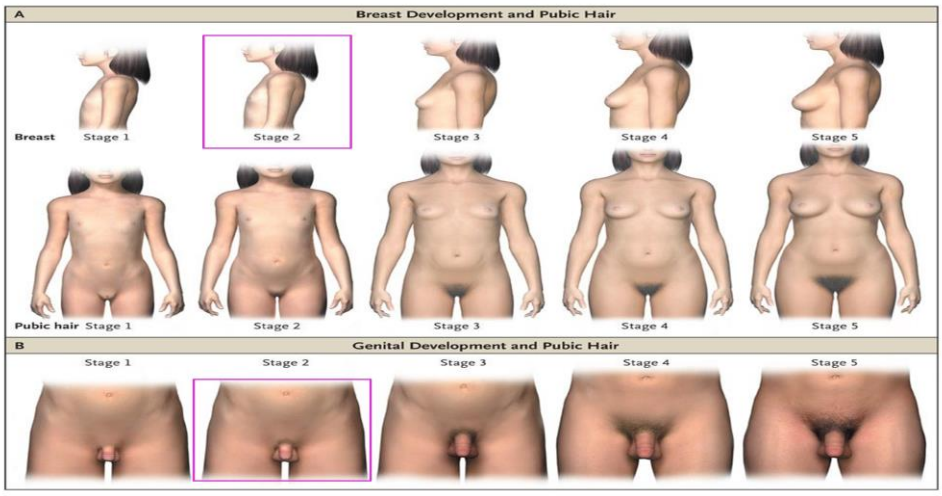
In males: LH stimulates the Leydig cells to produce testosterone which induces the features of secondary sexual development. FSH binds to receptors on the Sertoli cells, enhancing spermatogenesis.

In males, growth of the testes is the first sign of puberty.

In females: LH stimulates proliferation of follicular and theca cells, and during the follicular phase of the menstrual cycle induces androgen secretion by theca cells. FSH induces proliferation of granulosa cells; enhances aromatase activity so that androstenedione is converted to estradiol and increases progesterone production.

The breast bud is usually the first sign of puberty "10-11yrs", followed by the appearance of pubic hair 6-12m later. The interval to menarche is usually 2-2½ yrs.

- **Stages of puberty**:



Breast staging: **B1**: Prepubertal | **B2**: Breast budding

B3: Development of actual breast mound | **B4**: Areola projects at an angle to breast mound

B5: Adult configuration

Genital staging: **G1**: Prepubertal penis "unstretched length 2.5-6 cm", scrotum and testes "volume <3ml"

G2: Testes >4ml, but no penile enlargement | **G3&G4**: Penile lengthening and broadening, further development of the testes "volume 10-12ml"

G5: Adult genitalia, testes usually "15-25ml"

Pubic hair staging: **P1**: No pubic hair | **P2**: Fine hair over mons pubis and\or scrotum\labia

P3: adult type hair but distribution confined to pubis | **P4**: extension to near adult distribution | **P5**: adult

- **Precocious puberty**: the appearance of secondary sexual characteristics before the age of 9 years in boys or 8 years in girls

It could be:

1. **Central\true\Gonadotropin-Dependent**: resulting from activation of the hypothalamus, and following a normal sequence, but occurring abnormally early. More commonly in females and is mostly idiopathic.
2. **Peripheral\false\Gonadotropin-Independent**: caused by the abnormal secretion of sex steroids independent of hypothalamo-pituitary control.

The precocious puberty could be either: premature telarche, adrenarche or menarche.

Premature Menarche: is the early presence of the menstrual cycle.

Central causes: idiopathic, hypothalamic hamartomas, functional brain tumors, congenital subarachnoid cysts & congenital mid-line anomalies "hydrocephalus, meningomyelocele & optic nerve hypoplasia"

Peripheral causes: ovarian tumors, Leydig-cell tumors, hCG-secreting tumors "hepatoblastomas", McCune-Albright syndrome, adrenal hyperplasia & adrenal tumors

Diagnosis: FSH, LH, GnRH, estradiol, bone age "increased", pituitary MRI & pelvic US\MRI in females

Treatment:

Central PP: GnRH analogues "Triptorelin" | **Peripheral PP**: Medical: androgen receptor blocker "cyproterone acetate", 5 α-reductase inhibitors "finasteride", aromatase inhibitors "letrozole", estrogen receptor blocker "Tamoxifen" & Surgical

Object of treatment: to prevent early epiphyseal closure & to decrease psychological distress.

Anemias

Done by: Diaa Imran©

Anemia: is the reduction in hemoglobin, hematocrit, or number of red blood cells "two standard deviations below the mean".

Anemia can be classified according to the size of RBCs & MCV into:

Microcytic or low MCV: Iron deficiency anemia, Thalassemia, Sidroblastic anemia, Lead poisoning & Anemia of chronic disease

Normocytic or normal MCV: Autoimmune hemolytic anemia, Sickle cell anemia, Hereditary Spherocytosis, G6PD deficiency & Acute blood loss

Macrocytic or high MCV: Fanconi Anemia, Aplastic anemia, Trisomy 21, Hypothyroidism & B12/Folate Deficiency

1. **Macrocytic anemias**: is subdivided into:

    a. **Megaloblastic anemias**: B12 & folate deficiency

Both B12 & folate are mandatory for DNA synthesis and cell division, thus with their deficiency, the RBCs cannot be cleaved, thus maintain their large size, leading to megaloplastic anemia.

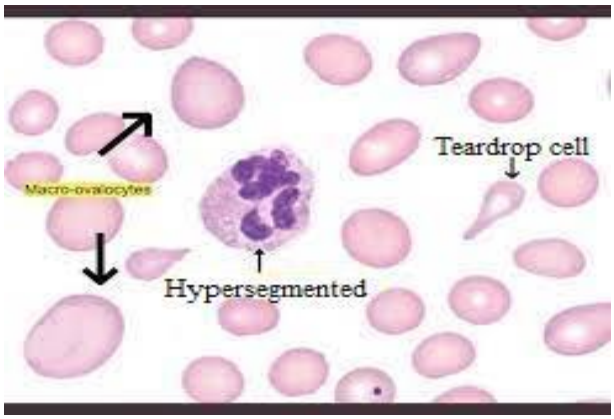
Causes of folate deficiency: Malnutrition, malabsorption, goat's milk consumption, methotrexate, phenytoin & trimethoprim/sulfa

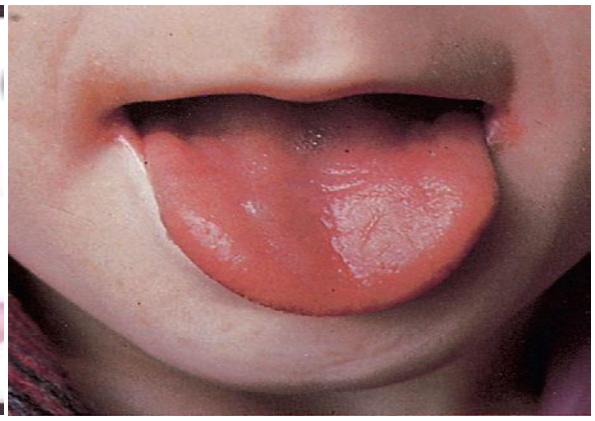
Causes of B12 deficiency: Pernicious anemia, ileal resection, strict vegetarian & congenital intrinsic factor deficiency

Symptoms: glossitis, symptoms of anemia "weakness, pallor, shortness of breath" & GI problems. B12 but NOT folate anemia can cause peripheral neuropathy, degeneration of the spinal cord, or demyelination of white matter of brain

Diagnosis: MCV is high on CBC; blood smear shows macrocytic cells with hypersegmented neutrophils & may show teardrop cells

Treatment: diet modification; treat underlying cause & replacement therapy

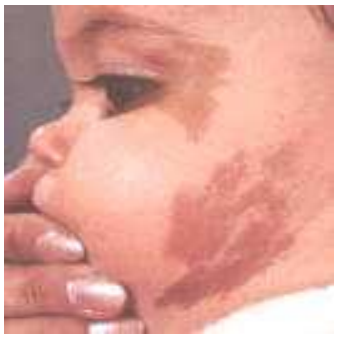


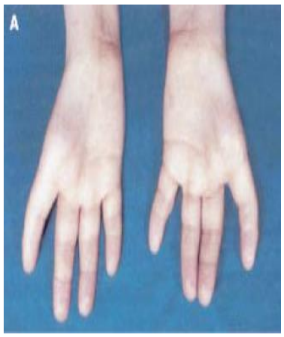


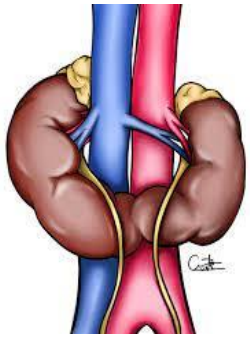
b. **Non-megaloblastic anemias**: Fanconi anemia, Diamond-Blackfan anemia, Aplastic anemia & Pearson syndrome

Fanconi anemia: autosomal recessive bone marrow failure. **N.B**: MCV is high in this type, due to the fact of failed bone marrow which leads to the production of numerous "nonfunctional" cells

Symptoms & signs: pancytopenia, Short stature, absence of or malformation in hands and arms, single kidney or of a horseshoe kidney & Café-au-lait spots







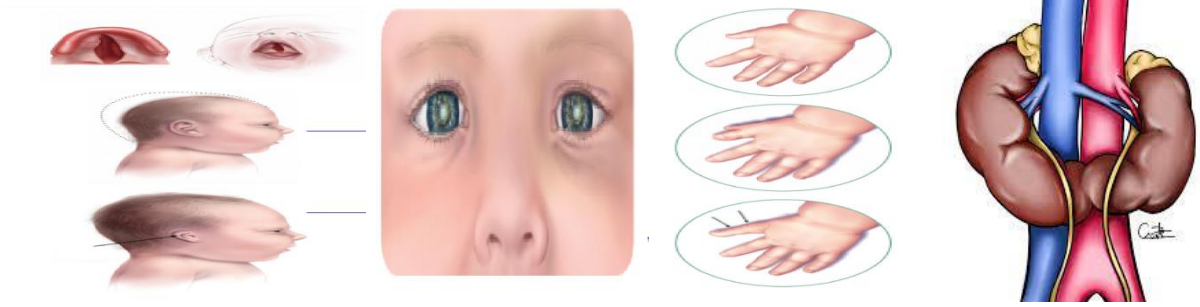
Complications: Myelogenous leukemia

Diagnosis: positive chromosome-breaking test effect to diepoxybutane or mitomycin C (MMC) test

Treatments: Bone marrow transplant, Hematopoietic growth factors, Androgens: stimulate the production of RBCs and platelets. & Future: gene therapy

Diamond-Blackfan anemia: autosomal dominant bone marrow failure.

It is associated with many malformations such as: cleft palate, microcephaly, small ears, ptosis, congenital cataract, strabismus, short webbed neck & single kidney\horseshoe kidney



Complications: AML, MDS & osteosarcoma.

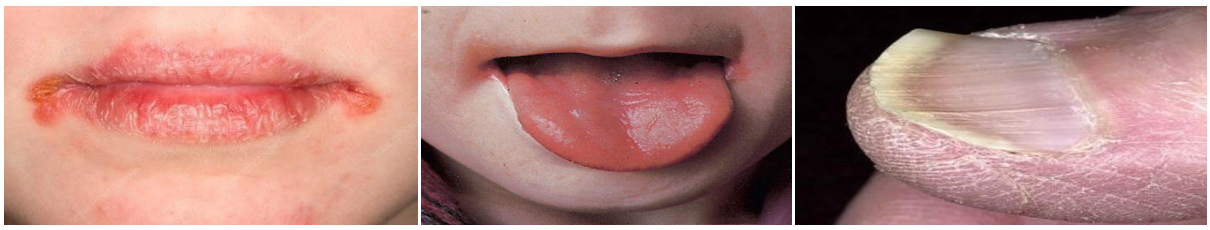
Treatment: Prednisone, chronic red cell transfusions & stem-cell transplant

2. **Microcytic anemias**:

Iron deficiency anemia: is the most common cause of anemia. **N.B**: iron is essential for DNA synthesis

Causes: Excessive Cow's Milk Intake, impaired absorption "celiac disease", poor meat intake, blood loss, menorrhagia & parasite\worm "1st cause of GI blood loss"

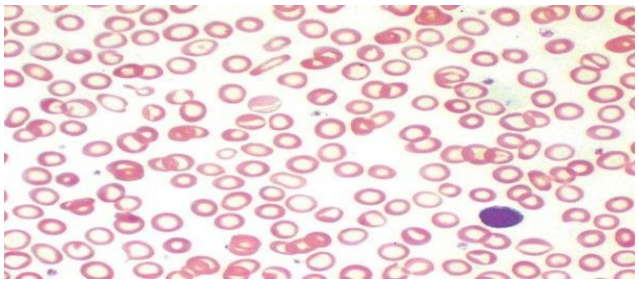
Symptoms: symptoms of anemia, neurocognitive effects "apathy, irritability & poor concentration, Pica, anorexia, poor weight gain & Epithelial changes: angular stomatitis, glossitis, finger nails koilonychias or spooning, dry skin & thin hair.



Diagnosis: CBC: low Hb, low MCV and MCH, high RDW & Low reticulocytes

Blood Film: hypochromic microcytic RBCs & anisopoikilocytosis "variable sizes and shapes"

Iron metabolism tests: low ferritin, low serum iron, low transferrin saturation & high total iron-binding capacity



Hypochromic microcytic & Anisopokilocytosis

Treatment: decrease milk intake, promote iron rich foods, control/evaluate for blood loss

Elemental iron 4-6 mg/kg per day & IV iron if malabsorption suspected

Thalassemias: a group of autosomal recessive hemoglobin disorders, in which the production of normal hemoglobin is partially or completely suppressed. Hypochromic microcytic anemia as a result of ineffective erythropoiesis and increased hemolysis

The disease is divided into: α-thalassemia & β-thalassemia

α-thalassemia: silent carrier "1 gene deletion", Trait "2 genes deletion", hemoglobin H disease "3 genes deletion" & major\ hemoglobin Bart's\ hydrops fetalis "4 genes deletions"

N.B: Alpha globin genes are coded on chromosome 16, while Beta globin genes are coded on chromosome 11

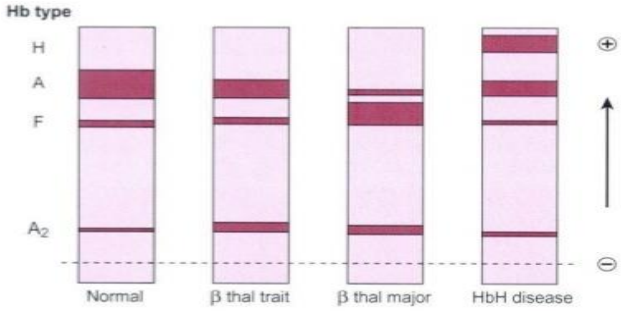
β-thalassemia: triat\minor, intermedia & major

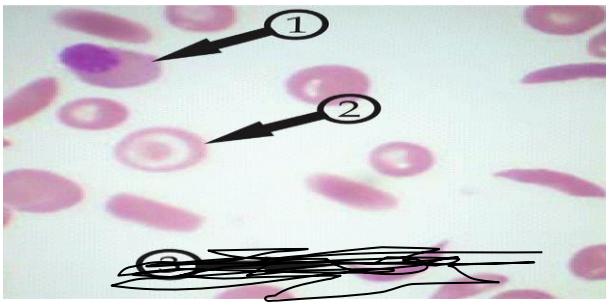
In intermedia & major types, there is moderate-severe anemia, in which all affected RBCs are degraded by the spleen, resulting in jaundice, the bone marrow will try to compensate thus becomes bigger, giving the appearance of hair on end & chipmunk, affected RBCs, shows target-sign appearance

Symptoms: severe anemia, pallor and jaundice, hepatosplenomegally, failure to thrive, cardiomyopathy & recurrent infections.

Diagnosis: hypochromic microcytic anemia, target cells & nucleated RBCs

Mentzer index "MCV/RBC" < 13, Leukopenia and thrombocytopenia & Hemoglobin electrophoresis "diagnostic": HbF raised; HbA2 increased





Treatment: Blood transfusion every 4-6 weeks, to <u>keep Hgb> 10g</u> with Iron chelating therapy, Splenectomy & Bone marrow transplant "the only curative treatment"

3. **Normocytic & hemolytic anemias**:

G6PD anemia, sickle cell disease, hereditary spherocytosis & others

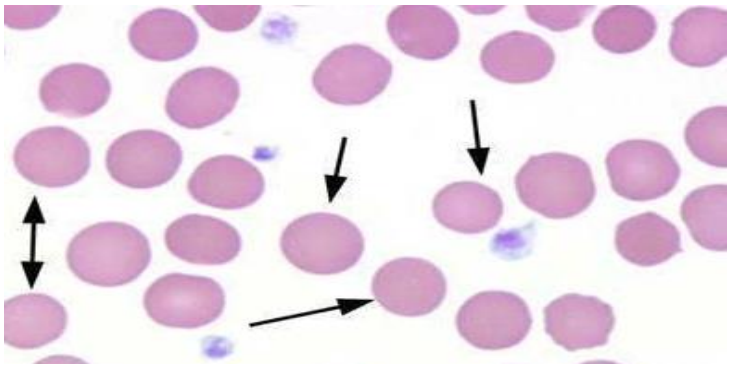
Hereditary spherocytosis: is an autosomal-dominant inherited disorder, caused by dysfunction or deficiency of a red cell skeletal proteins ankyrin and\or spectrin, that hold the RBCs into their unique biconcave shape, which without their function, the RBCs bulge to make a sphere, with resultant splenic degradation.

Symptoms: anemia, jaundice, splenomegaly & neonatal hyperbilirubinemia

Diagnosis: Blood film: microspherocytes, hyperdense cells & polychromasia

Negative DAT test & increased osmotic fragility

Complications: Hemolytic crisis, Erythroblastopenic crisis "dramatic fall in Hb level & reticulocyte count", folate deficiency, gallstones & rarely hemochromatosis

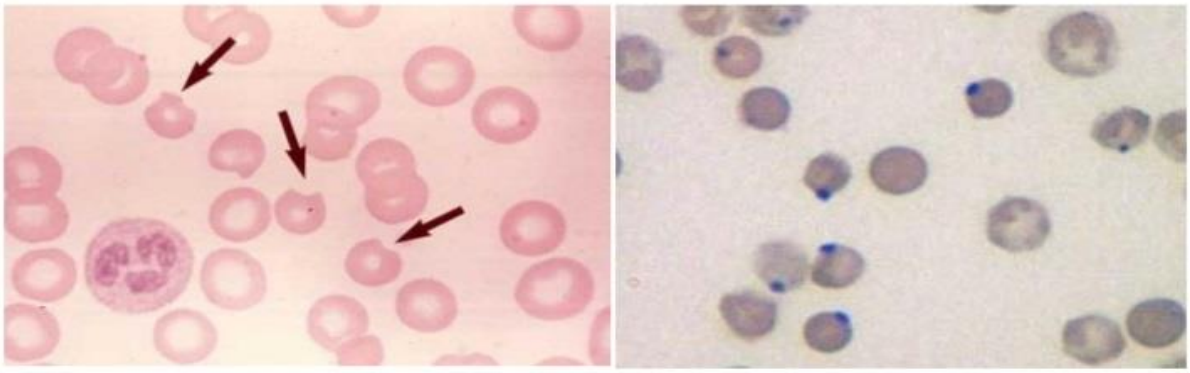


Treatment: Folic acid, packed red cell transfusion for severe erythroblastopenic crisis & splenectomy and cholecystectomy for moderate to severe cases

G6PD anemia: an X-linked recessive disease, also known as favism, it is the most common enzymopathy, G6PD increases NADH when the body is exposed to stressful oxidative conditions, NADH decreases ROS, thus decrease oxidation, and preventing damage to the RBCs, in the absence of this enzyme, non if this happens.

Oxidative agents: fava beans, sulfa drugs, methelyne blue dye & others

ROS makes the Hb to precipitate leading to Hienz-bodies, which removed by the spleen leading to bite cells on the blood film. Then hemolysis occurs leading to jaundice



Symptoms: normocytec normochromic anemia & jaundice

Treatment: avoidance & blood transfusion & Folic acid.

Please read sickle cell disease from slides

Hemostasis & Bleeding disorders

Done by: Diaa Imran©

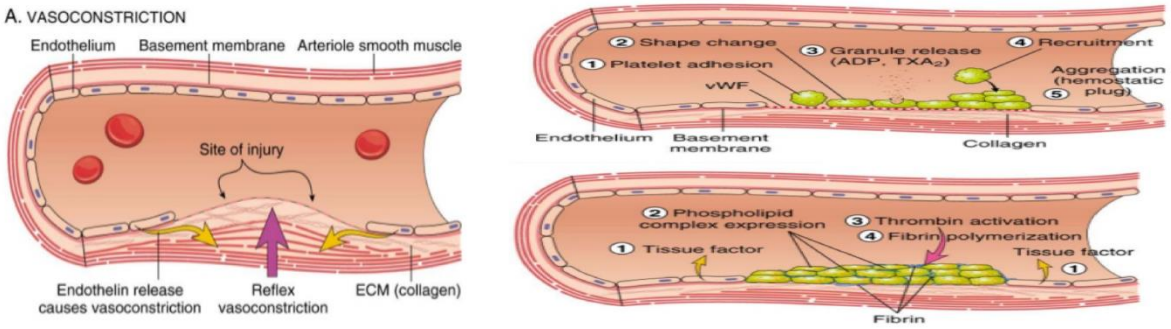
Main components of blood coagulation: platelets, vascular wall, procoagulant, anticoagulant proteins & fibrinolytic system.

Hemostasis stages after bleeding injury:

Vascular spasm "vasoconstriction"

Formation of a platelet plug; which stops bleeding within 3-7 minutes

Blood clotting or coagulation, which reinforces the platelet plug with fibrin mesh; that acts as a glue to hold the clot together. Once blood flow stops, tissue repair can begin.

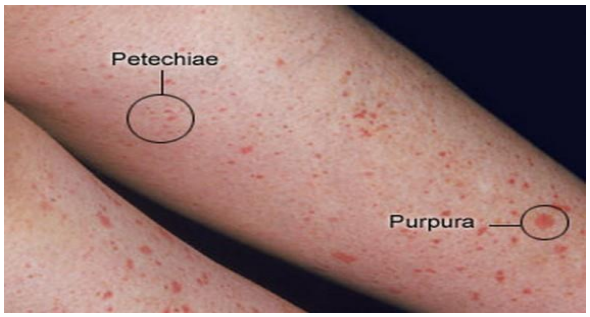


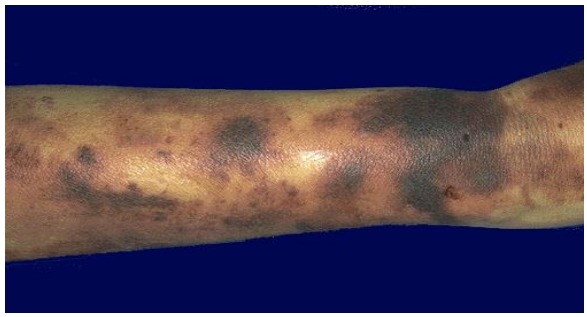
Terms: **Petechiae**: non-blanching lesion <2 mm.

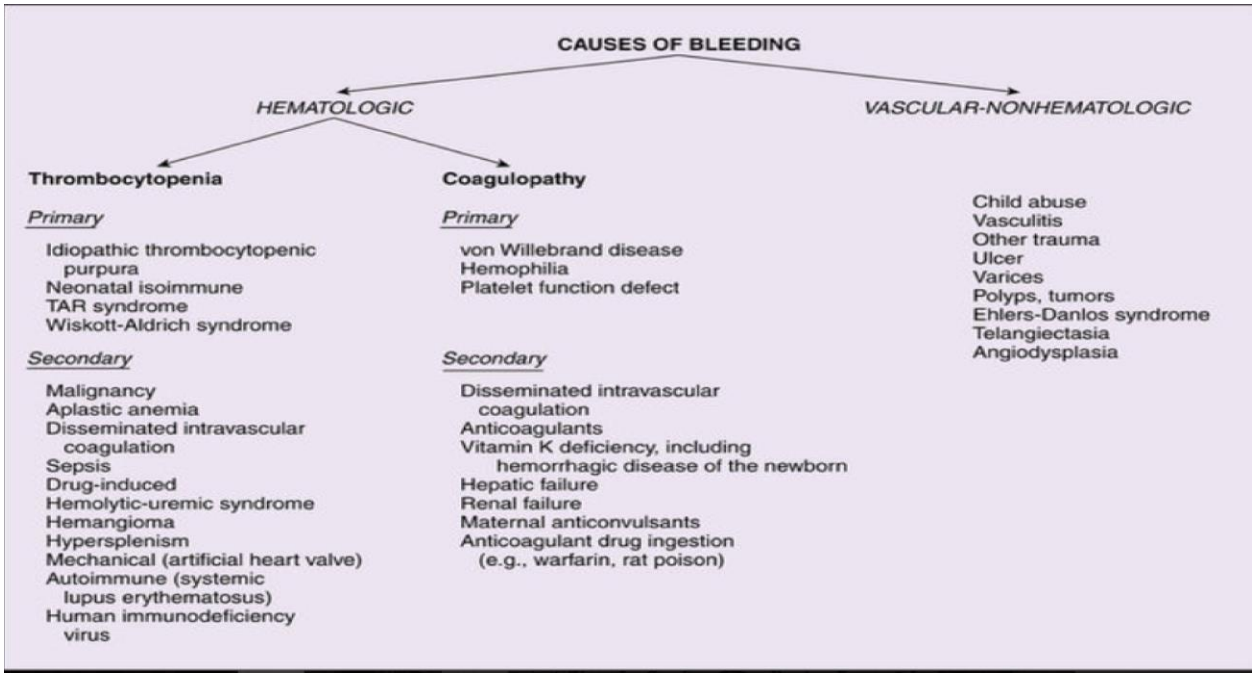
Purpura: is a group of adjoining petechiae,

Ecchymoses: are isolated lesions larger than petechiae

Hematomas: are raised, palpable ecchymoses







	Bleeding of platelets cause	**Bleeding of coagulation factors cause**
Bleeding after minor cut	Yes	Uncommon
Petechia	Common	Uncommon
Ecchymoses	Small & superficial	Large & deeper
Hematoma	Uncommon	Common in severe diseases
Bleeding after procedure	Develop immediately	May develop later

N.B: platelets causes might be: quantitative or qualitative, while factor causes might be inherited or acquired.

1. **Platelets disorders**:

a. **Disorders of platelets number**:

Thrombocytopenia: platelets < 150,000/mm^3, where mucocutaneous bleeding is the hallmark. Platelet counts < 20,000/mm^3 carries risk for spontaneous bleeding

Etiology: either decreased production, sequestration of the platelets or increased destruction of platelets.

Autoimmune thrombocytopenic purpura "aka ITP": is the most common cause of acute onset of thrombocytopenia, in children age 1-4.

Causes: the most common cause is post-viral infection, in which EBV & HIV were the most common viruses. In these infections, IgG or IgM binds to the platelet membrane, followed by splenic destruction of antibody-coated platelets leading to sever thrombocytopenia < 10.000

Symptoms: abrupt onset of petechiae, purpura & epistaxis. **N.B**: normal RBCs & WBCs

Complications: intracranial bleeding

Diagnosis: clinically

Treatment: Therapy is indicated only for moderate and severe clinical bleeding with severe thrombocytopenia $<10,000/mm^3$ by:

Prednisone 2-4 mg/kg/24 hours for 2 weeks | IVIG 1 g/kg/24 hours for 1 to 2 days

Splenectomy is indicated in acute ITP only for life-threatening bleeding.

N.B: treatments with IVIG, IV anti-D, or high-dose pulse steroids are effective in delaying the need for splenectomy

N.B: if the disease lasts for >6 months, it is chronic ITP, which is attributed to SLE & HIV, where splenectomy induces a remission in 70% to 80% of childhood chronic ITP cases

Other disorders of low platelets:

Wiskott-Aldrich syndrome: X-linked disorder characterized by: hypogammaglobinemia, eczema, and thrombocytopenia, where platelets are small

Treatment: Hematopoietic stem cell transplantation cures the immunodeficiency and thrombocytopenia

Thrombotic thrombocytopenic purpura: platelet consumption, due to a congenital or acquired deficiency of a metalloproteinase that cleaves von Willebrand factor which hold platelets together.

Treatment: plasmapharesis

DIC

b. **Disorders of platelets function**:

Bernard-Soulier syndrome: autosomal recessive platelet function disorder, is caused by absence or severe deficiency of the VWF receptor "GPIb complex" on the platelet membrane; thus the function of the VWF which adhere platelets together will not happen, with resultant diminished platelets function

N.B: characterized by thrombocytopenia!!, with giant platelets & prolonged bleeding time ">20min"

Diagnosis: flow cytometric analysis of the platelet glycoproteins

Glanzmann thrombasthenia: Is a congenital disorder associated with severe platelet aggregation dysfunction that yields prolonged bleeding time and a normal platelet count.

Platelets have normal size and morphologic features on the peripheral blood smear

Diagnosis: flow cytometric analysis of the platelet glycoproteins

2. **Disorders of coagulation factors**:

Hemophilia: is bleeding tendency, due to deficiency in factors 8 & 9, causing the more common hemophilia A & the less common hemophilia B respectively. **N.B**: type B is also called Christmas disease, and can NOT be clinically differentiated from type A

The severity of the disorder is determined by the degree of clotting factor deficiency:

Severe hemophilia: < 1% factor 8 or factor 9 is present

Moderate hemophilia: 1-5% factor 8 or factor 9 is present

Mild hemophilia: >5% factor 8 or factor 9 is present

Symptoms: easy bruising, intramuscular hematomas & hemarthroses begin when the child begins to cruise. **N.B**: 30% of male infants with hemophilia bleed with circumcision.

Diagnosis: prolonged aPTT, with normal other hemostatic mechanisms & assay for factors VIII and IX will confirm the diagnosis of hemophilia.

Treatment: replacement therapy. **N.B**: Desmopressin acetate increase factor 8 level in patient with mild or moderate hemophilia A.

Von-Willebrand disease: is the most common inherited bleeding disorder, characterized by deficiency of the VWF required for platelets aggregation. **N.B**: VWF is also a carrier protein for factor VIII. **N.B**: it has 3 types

Symptoms: Epistaxis, easy bruising & menorrhagia in women. **N.B**: women are more commonly diagnosed; due to their complaint of menorrhagia

Treatment: desmopressen for type I & some of type II | replacement therapy for types II & III

	Hemophilia A	**Hemophilia B**	**VWD**
Inheritance	X-linked	X-linked	Autosomal dominant
Factor defeciency	Factor VIII	Factor IX	VWF & factor VIII
aPTT	Prolonged	Prolonged	Prolonged or normal
Bleeding time	Normal	Normal	Normal
Bleeding sites	Joint, muscle & surgical	Joint, muscle & surgical	Mucus membranes, menses, surgical sites & skin
Treatment	Replacement	Replacement	DDAVP & replacement

N.B: deficiency of factors: II, V, VIII, IX, X & XI causes aPTT to be prolonged, and since VWF works as a carrier for factor VIII, its deficiency will lead to deficiency in factor VIII in the blood, hence prolonged aPTT

Neonatal sepsis

Done by: Diaa Imran©

Neonatal sepsis: a clinical syndrome of systemic illness accompanied by bacteremia, occurring in the first month of life. Mostly seen in premature & very low birth weight babies.

Normal birth weight: 2.5-4kg

Low birth weight: 1.5-2.5kg

Very low birth weight: 1-1.5kg

Extreme low birth weight: <1kg

Sepsis can be divided into:

1. **Early-onset sepses**: is sepsis that occurs within the first 5-7 days. Usually as a multi-system fulminant illness with prominent respiratory symptoms.

Typically, the infant has acquired the organism during the intrapartum period from the maternal genital tract.

With rupture of membranes, vaginal flora or various bacterial pathogens may ascend to reach the amniotic fluid and the fetus, causing "Chorioamnionitis", which leads to fetal colonization and infection. Aspiration of infected amniotic fluid by the fetus or neonate may play a role in resultant respiratory symptoms.

Primary sites of colonization: nasopharynx, oropharynx, conjunctiva & umbilical cord

2. **Late-onset sepsis**: is sepsis that occurs after the first 5-7 days. Usually present as meningitis in addition to sepsis

Typically, bacteria responsible for late-onset sepsis and meningitis are mostly acquired after birth from human contact or from contaminated equipment.

The late onset of the disease is due to the preference of the CNS, which shows its' symptoms late.

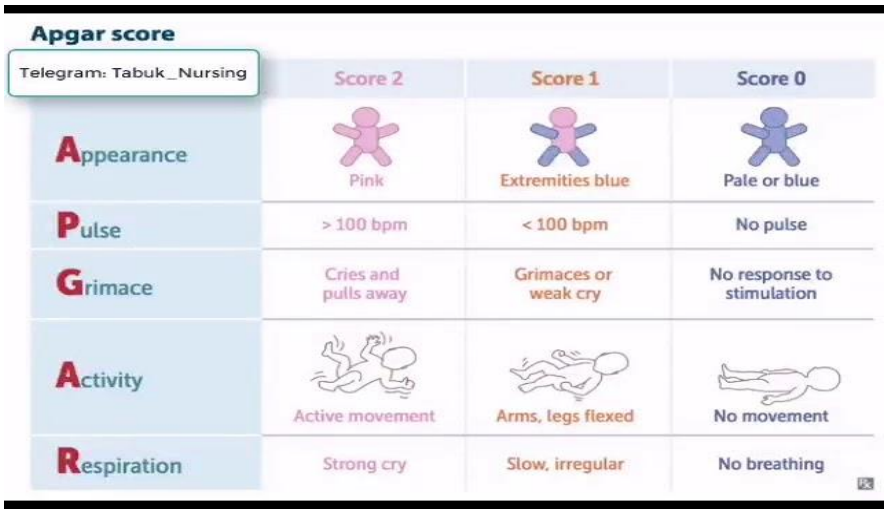
3. **Nosocomial sepsis**: mostly caused by staphylococci & gram-negative rods " P.auregonosa, Klebsiella, Serratia, & Proteus"

Sepsis causing bacteria: GBS, E.coli, L.monocytogenes, S.aureus & H.influenza

Risk factors:

Major RFs: PROM >24hrs, intra-partum maternal fever ">38°C", chorioamnionitis & sustained fetal tachycardia

Minor RFs: twins, intra-partum maternal fever ">37.5°C", low birth weight & low APGAR score*****



*****

Symptoms: **Cardiopulmonary:** respiratory distress symptoms & tachycardia, or hypotension, which tends to be late signs

Temperature irregularity. Hypo\hyperthermia

Change in behavior: Lethargy, irritability, or change in tone.

Skin: Poor peripheral perfusion, cyanosis, mottling, pallor, petechiae, rashes, sclerema, or jaundice

Feeding problems: Feeding intolerance, vomiting, diarrhea, or abdominal distention with or without visible bowel loops.

Metabolic: Hypo\hyperglycemia or metabolic acidosis.

Diagnosis: cultures "blood & other normally sterile body fluids". In many clinical situations, infants are treated for "presumed" sepsis despite negative cultures, with apparent clinical benefit; due to many false negative causing events "maternal antibiotics administered before birth & organisms that are difficult to grow and isolate"

Gram stain, WBCs count, platelets count, CRP, ESR, cytokines, lumbar puncture, X-ray & urinary US

DDx: RDS, metabolic disease, CNS disease, heart disease… etc

Treatment: GBS prophylactic "Ampicllin" & "3rd generation Cephalosporin". Vancomycin in suspected nosocomial infection.

Ensure adequate oxygenation & support BP and perfusion to prevent shock

Complications: shock, seizures & DIC*****

*****bleeding at puncture sites, increased PTT, decreased platelets & increased bleeding time → **treat with**: fresh-frozen plasma, vitamin K, platelet infusion & possible exchange transfusion

Connective tissue disorders

Done by: Diaa Imran©

Connective tissue: is the tissue that holds body structures together; mainly it is composed of collagen & elastin.

Disorders:

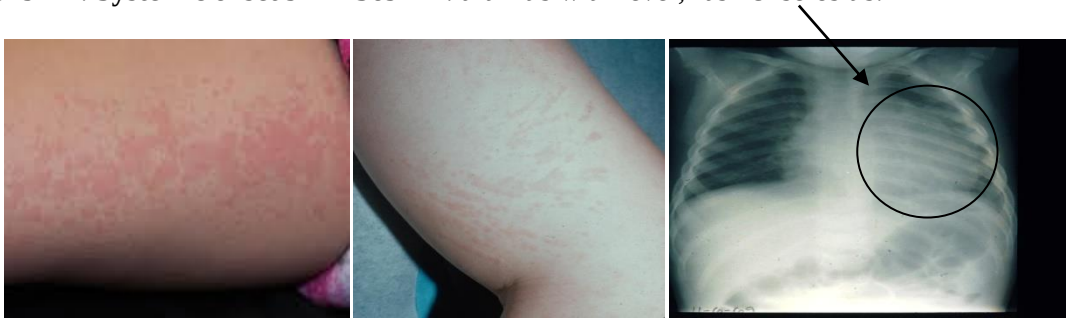
1. **Juvenile Rheumatic Arthritis**: a common, rheumatic disease of children and a major cause of chronic disability, characterized by a synovitis of the peripheral joints, swelling & effusion, FOR ≥ 6 WEEKS

To establish the diagnosis of arthritis in general, the patient must have: Swelling\effusion, or presence of two of the following:

- Limitation of range of motion
- Tenderness or pain of motion
- Increased heat in the joint

Causes: genetic autoimmune disease of unknown cause

Types of JRA: **Systemic onset JIA** "**SoJIA**": arthritis with fever, rash & serositis.



Oligoarthritis "extended VS persistant": ≤ 4 joints in the first 6 months of illness. Affects the joints of the lower extremities, such as the knees and ankles, the hip is almost never affected. It is associated with uveitis in 20% of cases.

Polyarthritis: > 4 joints in the first 6 months of illness. Characterized by involvement of both large and small joints, of both upper and lower extremities. It is associated with rheumatic nodules & micrognathia

- **N.B**: oligo & poly-arthritis types, have NO systemic manifistations

Symptoms: arthritis, morning stiffness, easy fatigability, limp, restriction of movement, eye symptoms & systemic manifestation

Diagnosis: arthritis for ≥ 6 weeks + information in the table.

	SoJRA	**Oligoarthritis**	**Polyarthritis**
Percentage	10%	50%	40%
F:M ratio	1	>1	>1
Joints affected	Any	Spares the hip	Spares the hip
Systemic symptoms	Fever & splenomegaly	No	No
Associated symptoms	-	Uveitis	Rheumatic nodules & micrognathia
Lab findings			
Leukocytosis	Yes	No	No
Anemia	Yes	No	No
ESR	Yes	Mild	Mild
ANA	No	Mild elevation	Mild elevation
Rheumatoid factor	Rare	No	Yes

DDx: trauma, infection & leukemia

Treatment: NSAIDs, steroids, TNF-α blockers & anti-rheumatoid drugs

- **N.B**: screen for uveitis

2. **Systemic Lupus Erythematosus** "**SLE**": is an idiopathic, chronic inflammatory multi-systemic autoimmune disease characterized by widespread inflammation.

Pathophysiology: when mass cell damage occurs, their nuclear proteins will be noticed as antigens, and autoantibodies attack them, the antigen-antibody complex deposit in the area leading to inflammation in that particular area, and since mass cell damage can occur all over the body, lupus symptoms are many, and occurs as flares, whenever mass cell damage occurs.

Symptoms: general Sx: fever, malaise & fatigue

Skin Sx: butterfly rash, oral ulcers & Raynaud's phenomenon

MSS: symmetrical polyarthlagia & arthritis | **HLS**: anemia & leucopenia

RS: pleuritis, pneumonitis & fibrosis | **CVS**: pericarditis, myocarditis & endocarditis

GU: GN, HTN, pyuria, protenuria & renal failure | **GI**: dysphagia, N/V, PUD

Diagnosis: the presence of 4 of the following 11 is sufficient for diagnosing lupus

Table 1. American College of Rheumatology Criteria for the Diagnosis of Systemic Lupus Erythematosus (SLE).*

Criterion	Definition
Malar rash	A rash on the cheeks and nose, often in the shape of a butterfly
Discoid rash	A rash that appears as red, raised, disk-shaped patches
Photosensitivity	A reaction to sunlight that causes a rash to appear or get worse
Oral ulcers	Sores in the mouth
Arthritis	Joint pain and swelling of two or more joints
Serositis	Inflammation of the lining around the lungs (pleuritis) or inflammation of the lining around the heart that causes chest pain, which is worse with deep breathing (pericarditis)
Kidney disorder	Persistent protein or cellular casts in the urine
Neurologic disorder	Seizures or psychosis
Blood disorder	Anemia (low red-cell count), leukopenia (low white-cell count), lymphopenia (low level of specific white cells), or thrombocytopenia (low platelet count)
Immunologic disorder	Positive test for anti–double-stranded DNA, anti-Sm, or antiphospholipid antibodies
Abnormal antinuclear antibodies	Positive antinuclear-antibody test

* Four of the 11 criteria are needed for the formal diagnosis of SLE.

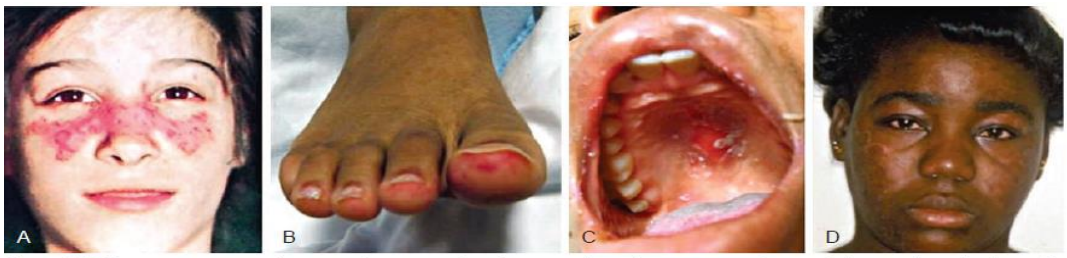


Figure 158-1 Mucocutaneous manifestations of SLE. **A,** Malar rash; **B,** vasculitic rash on toes; **C,** oral mucosal ulcers; **D,** discoid rash in malar distribution.

Anti-nuclear-antibodies in lupus: **ANA**, **Anti dsDNA** raised particularly in lupus nephritis

Anti-smith antibody: related to CNS involvement

Antiphospholipid antibodies: increase risk of thrombosis

Anticardiolipin antibodies: associated with episode of arterial and venous thrombosis

Treatment: Mild: NSAIDs | Moderate: steroids | Severe: cyclophosamide

- **N.B**: Neonatal lupus: is SLE affecting neonates, associated with maternal anti-Ro and anti-La antibodies

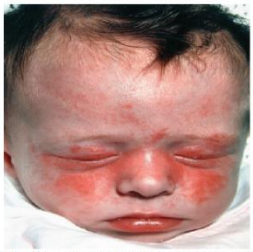


Figure 158-3 Neonatal lupus syndrome. Typical rash, often photosensitive with a malar distribution, appearing as annular plaques with erythema and scaling. *(Reproduced, with written parental permission, from Pain C, Beresford MW: Neonatal lupus syndrome, Paediatr Child Health 17:222–227, 2012.)*

Treatment: conservative & pace maker for congenital heart block

2. **Kawasaki disease**: is an acute febrile illness of childhood, characterized mainly by autoimmune attack of medium sized blood vessels "coronaries", in which 80% of patients are <5 years old.

Vasculitis leads to weakening of the vessel wall, leading to aneurysms.

Symptoms: persistent fever for ≥ 5 days

Hands & feet: erythema and edema of the extremities & peeling of fingers

Polymorphus exanthema "diffuse rash"

Conjuctival injection

Oral cavity: strawberry tongue, cracking lips, oral mucosa injection

- **N.B**: **CVS involvement**: Cardiac involvement is the most important manifestation, with tachycardia out of proportion to fever, with diminished left ventricular systolic function which rarely might lead to shock, pericarditis with pericardial effusion can occur & coronary artery aneurysm

In the absence of treatment:

- **Acute febrile phase(1-2 weeks):** Fever plus acute signs of the illness
- **Subacute phase(2-6 weeks):** thrombocytosis, coronary aneurysms & highest risk of sudden death if aneurysms developed
- **Convalescent phase(6-8 weeks):** begins when all clinical signs disappeared & continues until ESR is normal

All patients with Kawasaki have to have an echo, at diagnosis then after 2-3 weeks of illness

- **If normal**: repeat 6-8 weeks after onset of illness
- **If abnormal**: refer to pediatric cardiologist

Diagnosis: persistent fever + all 4 symptoms, or persistent fever + 3 symptoms + exclusion of other Dx

EPIDEMIOLOGIC CASE DEFINITION (CLASSIC CLINICAL CRITERIA)*
Fever persisting at least 5 days†
Presence of at least 4 principal features:
Changes in extremities:
Acute: Erythema of palms, soles; edema of hands, feet
Subacute: Periungual peeling of fingers, toes in weeks 2 and 3
Polymorphous exanthem
Bilateral bulbar conjunctival injection without exudate
Changes in lips and oral cavity: erythema, lip cracking, strawberry tongue, diffuse injection of oral and pharyngeal mucosa
Cervical lymphadenopathy (>1.5 cm diameter), usually unilateral
Exclusion of other diseases with similar findings‡

Treatment: IVIG & aspirin | Reyes syndrome: patient should receive annual influenza vaccine

Table 166-3 Treatment of Kawasaki Disease

ACUTE STAGE
• Intravenous immunoglobulin 2 g/kg over 10-12 hr *and*
• Aspirin 80-100 mg/kg/day divided every 6 hr orally until patient is afebrile for at least 48 hr
CONVALESCENT STAGE
• Aspirin 3-5 mg/kg once daily orally until 6-8 wk after illness onset if normal coronary findings throughout course
LONG-TERM THERAPY FOR PATIENTS WITH CORONARY ABNORMALITIES
• Aspirin 3-5 mg/kg once daily orally
• Clopidogrel 1 mg/kg/day (maximum: 75 mg/day)
• Most experts add warfarin or low-molecular-weight heparin for those patients at particularly high risk of thrombosis
ACUTE CORONARY THROMBOSIS
• Prompt fibrinolytic therapy with tissue plasminogen activator or other thrombolytic agent under supervision of a pediatric cardiologist

4. **Familial Mediterranean Fever** "**FMF**": autosomal recessive disease, characterized by self-limited episodes of fever and polyserositis

Cause: mutation on short arm of chromosome 16p13.3

N.B: many mutations were reported, however "M694V" mutation is the most common & carries the highest risk of complications "amyloidosis"

Symptoms: fever + 1 or more of the following: pleuritic chest pain, sterile peritonitis, arthritis & rash

Diagnosis: clinically & genetic testing. **N.B**: between flares the patient is symptom-free with persistent elevation of inflammatory markers.

Treatment: colchicine & "IL-1 inhibitor is good for cases not responding to colchicines"

- **N.B**: colchicine decrease development of amyloidosis, produce partial regression in amyloidosis, but GI side effects reduce the compliance
- **N.B**: Untreated amyloidosis will end in renal failure within 3-5 years

Juvenile dermatomyositis & Polymyositis are NOT included in this lecture

Osteomyelitis

Done by: Diaa Imran©

Osteomyelitis: is the inflammation of the bones, mostly long bones, mostly the metaphysis.

Most cases of osteomyelitis are acute hematogenous osteomyelitis, however, it could be of an exogenous rout "trauma, break skin… etc".

Causative organisms:

Neonates: S.aureus > E.coli

Infants: S.aureus > other gram negative

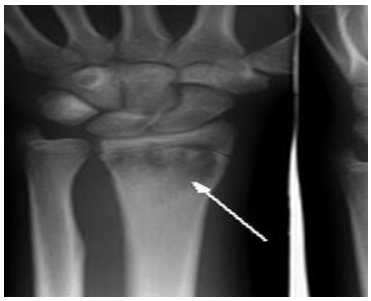
> 3 years: S.aureus > N.gonorrhoeae | Salmonella in sickle cell patients.

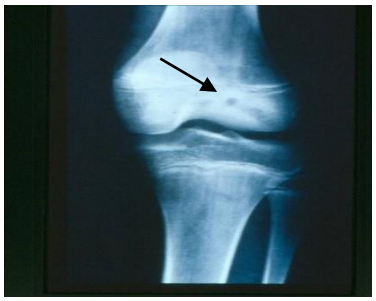
Symptoms: URT symptoms, fever, point tenderness, pseudo paralysis & ± systemic symptoms

N.B: fistula formation & sequestrum are signs of chronic disease

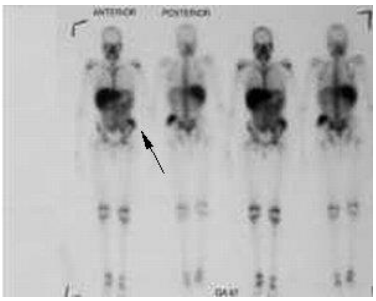
Diagnosis: Labs: CBC, CRP, ESR & culture

Imaging: MRI with contrast, X-ray "shows changes only late in the course" & bone scan





Acute disease



Bone scan

DDx: septic arthritis, trauma, Gaucher's disease & sickle disease crisis

Treatment: empirical treatment until culture has shown the organism & what drug suits it, when shown, treatment should take place for 4-6 weeks

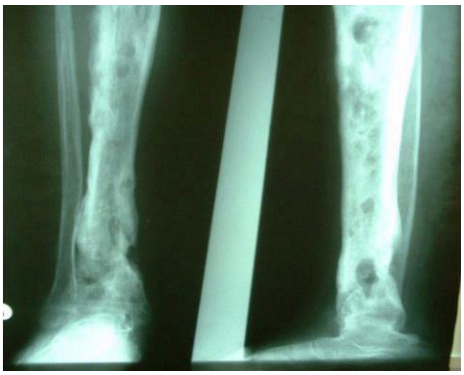
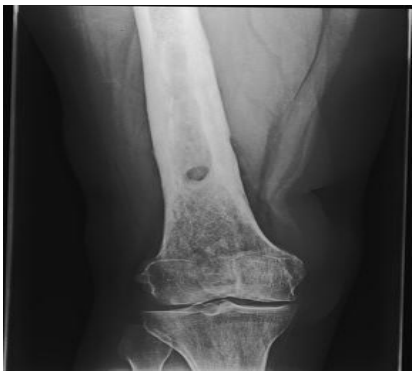
Empirical treatment: Neonate: Vancomycin + 3rd generation cephalosporin

≤ 3 years: Vancomycin + 3rd generation cephalosporin

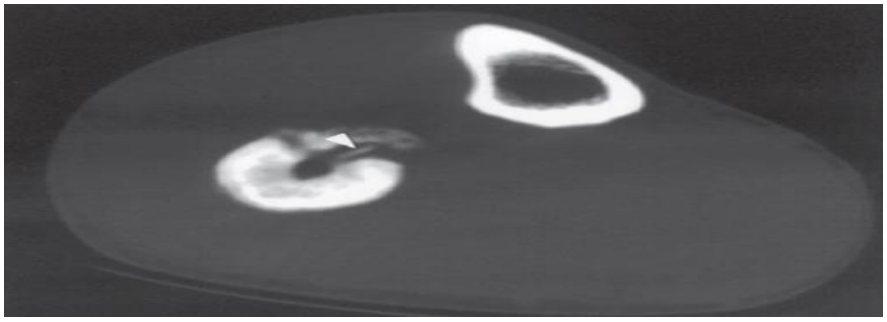
> 3 years: Vancomycin, nafcillin or clindamycin

Complications: chronic disease, septic arthritis, pathologic fracture & septicemia

Chronic osteomyelitis:

Sequestrum



Bone fistula

Complications: recurrence, Ca of the fistula & amyloid disease

Treatment: repeated debridement & antibiotics for 4-12 months

Criteria for changing to oral ABx: patient is improving, laboratory values are normalizing, oral antibiotic that has activity as the IV antibiotic & child can take large frequent doses of oral medicine

Hand, Foot & Mouth Disease

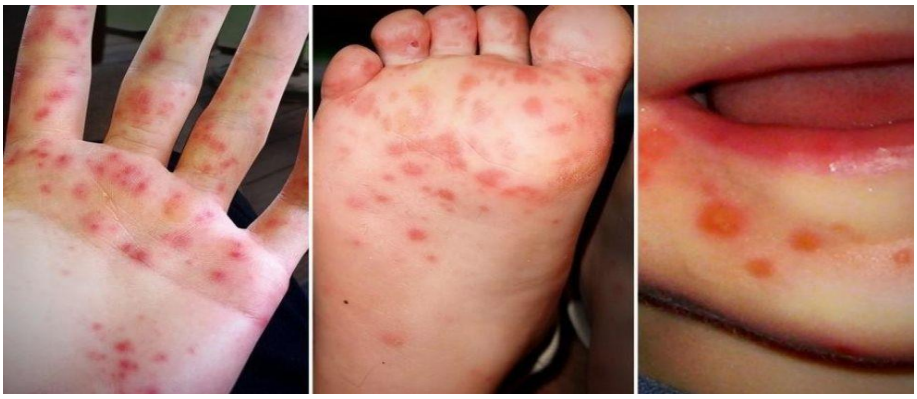
Done by: Diaa Imran©

HFMD: is a mild but highly contagious viral infection, usually affect patients <10 years.

Causative organism: Coxsackie-virus A16 & Entero-virus 17

Transmission: direct contact & air-droplets

Symptoms: after 3-6 days of incubation period, the patient will suffer from: Fever, sore throat, anorexia & painful ulcers in the hands, feet and mouth



Diagnosis: clinically & PCR

Complications: meningitis

Treatment: conservative "painkillers", the disease is self-limiting within 10-14 days

- **N.B**: patients should prevent salt, acidic, spicy food & soda, to make eating less painful

CNS infections

Done by: Diaa Imran©

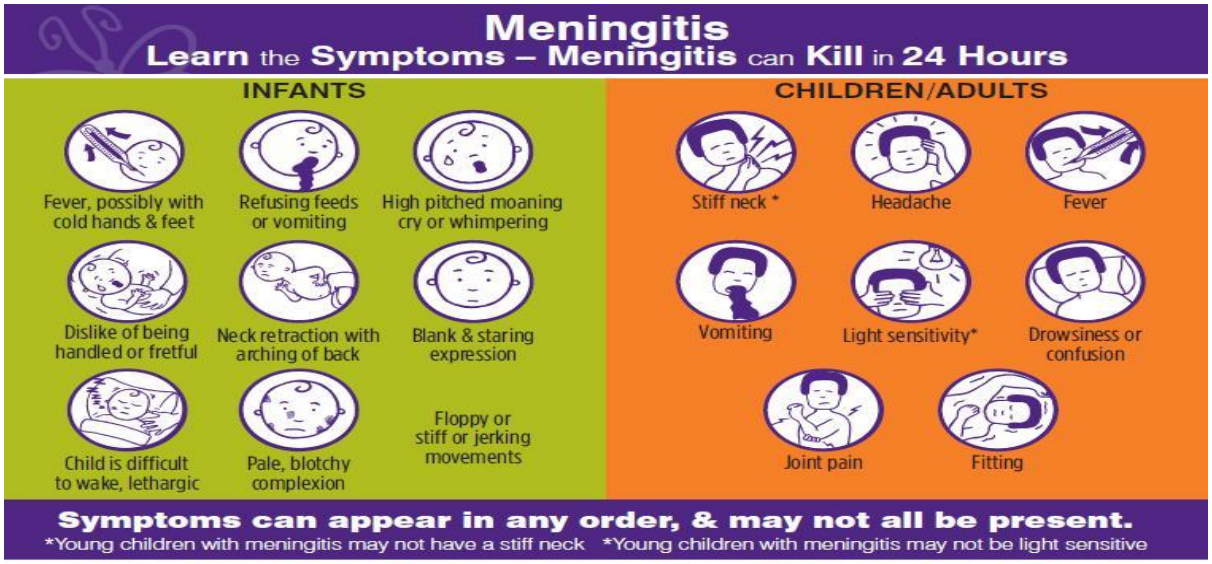
Meningitis: is the inflammation of the CNS layers, the meningies.

Causative organisms: <u>New born</u>: GBS & E.coli

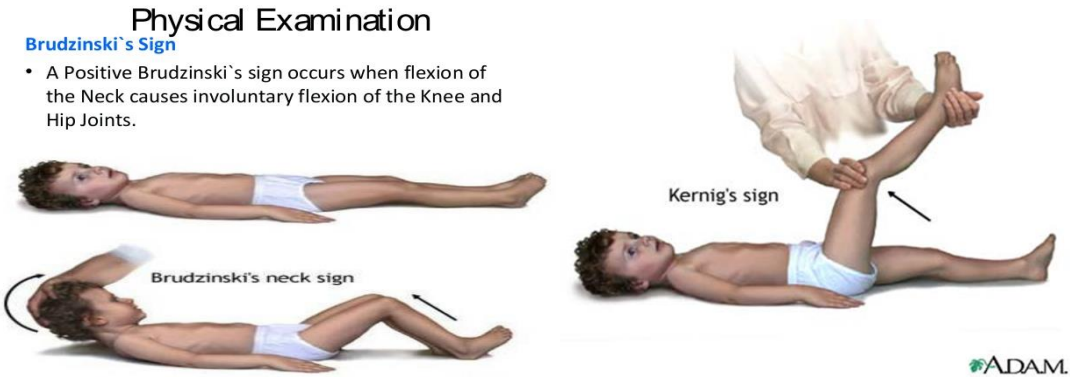
<u>>1 months</u>: S. pneumonia & N. meningetidis

- **N.B**: Hib was a cause of meningitis in patients up to 4 years, before the presence of its vaccine

Symptoms:



Signs: bulged fontanels, projectile vomiting, positive <u>Kernig & Brudzinski signs</u>



Seizures in bacterial meningitis: 20% of patients have seizures prior to admission & 32% of patients have seizures during 1st 48 hours of hospitalization. Seizures are related to "toxic encephalopathy" associated with bacterial toxins, hypoperfusion & metabolic derangements. Usually controlled easily and have no prognostic implications.

- **N.B**: Papilledema is an uncommon finding in acute meningitis.

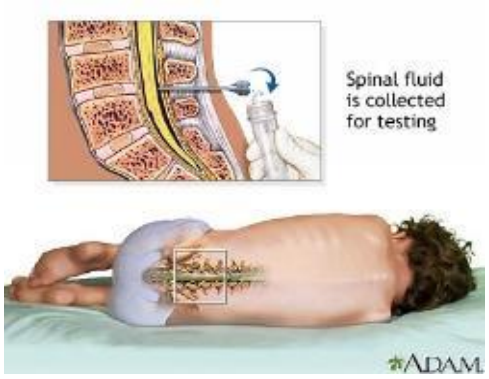
When papilledema is observed: venous sinus occlusion, subdural empyema & brain abscess

Diagnosis: clinically

CBC, electrolytes, CRP, ESR, Blood Culture, Imaging study "brain CT" & Lumbar puncture

- **Interpretation of LP**:

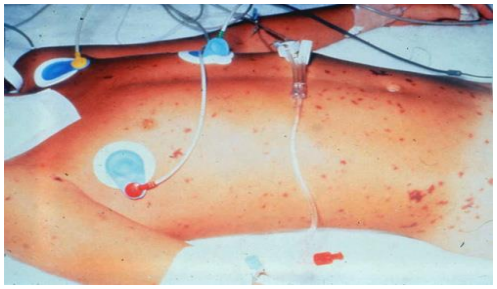
	Normal <1m	Normal >1m	Bacterial	Viral	TB
WBCs	0-30	Up to 9	>1000	Up to 500	Up to 500
PMNs	2-3	0	>50	<40	<50
Protein	20-150	15-45	>100	50-100	Up to 1000
Glucose	30-120	40-80	Low <30	Normal	Normal
Blood glucose	40-250	60-90	Low <50	Normal	Normal



Lumbar puncture

Contraindications of LP: skin infection, bleeding disorders, brain abscess & papilledema

Indications of CT: coma, papilledema, focal neurologic deficit, CSF shunts, history of hydrocephalus & recent history of CNS trauma.


Menengiococcal meningitis, by N.meningetidis

Management: Empiric therapy: Ceftriaxone + Vancomycin | Ampicillin + Gentamicin for newborns

Selective IV antibiotics after culture has shown the organism

- **N.B**: Dexamethasone may be beneficial for treatment of infants and children with Hib meningitis; to diminish the risk of neurologic sequelae including hearing loss

Cause of persistent fever after ABx: inadequate treatment, nosocomial infection, immune mediated arthritis, drug fever & suppurative complication: pericarditis, pneumonia & subdural empyema.

Indications for LP repetition: no improvement after 48hrs, gram –ve bacteria & ceftriaxone resistant pneumococcal.

Poor prognostic factors: coma, 2 days of symptoms before admission, pneumococcal, prolonged seizure >3 days, very low CFS glucose & neurologic deficits.

Neurologic deficits: deafness, seizures, paralysis & retardation

Encephalitis: is inflammation of the brain parenchyma, same S&S as for meningitis, mostly viral in origin; treating with anti-virals.

Convulsions

Done by: Diaa Imran©

This lecture contains about 60-75% only of the slides, perfect for OSCE & mini-OSCE only

Seizure: transient occurrence of signs and\or symptoms (change in LOC, motor activity… etc) resulting from abnormal excessive or synchronous neuronal activity in the brain.

Febrile convulsions: a seizure that is associated with febrile illness in the absence of CNS infection, or acute electrolyte imbalance in children between 6-60m. Its the most common form of seizures in children.

Types of febrile convulsions:

Simple: generalized, <15min & not recurring in 24h

Complex: any distortion of the above 3 conditions of simple, renders the FC as complex.

- If one FC occurs, there is 30% chance for recurrence, and 50% chance after the 2nd FC

Risk factors of recurrence: Age <12 m, FHx, height of temperature (the lowest the highest the risk), duration of fever (the shorter the higher the risk) & male gender

Treatment of FC: treat the acute illness, treat the convulsion (rectal diazepam) & educate the family

N.B: prophylactic diazepam treatment 3*1 is controversial.

Epilepsy: ≥2 unprovoked (without a cause) attacks, in a time frame >24 hrs.

Classification:

A. **According to semiology**:

Generalized: generalized loss of consciousness

Focal: aura, changes in LOC, brief motor seizures… etc

B. **According to etiology**:

Idiopathic: no identifiable cause

Symptomatic: a cause is known

C. **Syndromes**: there are many syndromes, according to age, here we will mention only:

Infantile spasms (**West syndrome**): peak onset 4-7m.

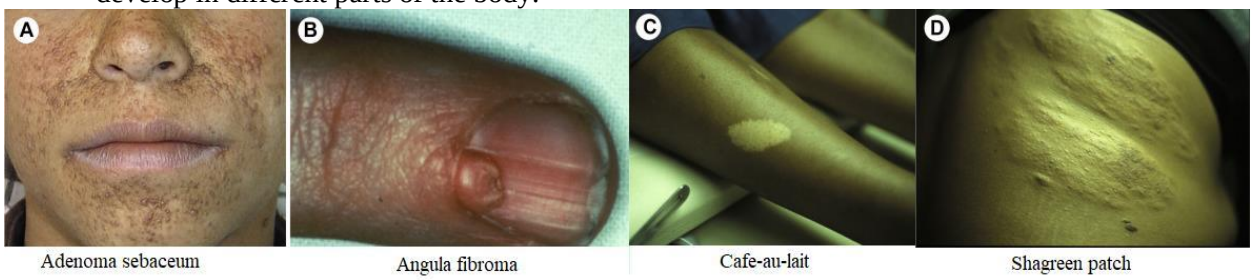
Causes: many, of which is (tuberous sclerosis*****).

Symptoms: spasms (flexion, extension, mixed), associated with variable encephalopathy

Treatment: ACTH and\or high dose oral corticosteroid

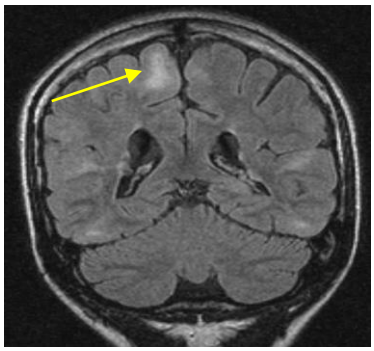
Prognosis strongly influenced by the underlying etiology, many will have seizures later in life & can evolve to Lennox Gastaut Syndrome.

- **Tuberous sclerosis**: a rare genetic condition that causes mainly benign tumors (tubers) to develop in different parts of the body.



Adenoma sebaceum | Angula fibroma | Cafe-au-lait | Shagreen patch

Tuberous Sclerosis



Cortical tubers

Status epilepticus: continuous, generalized or focal seizure ≥5 min, during which the patient remains unconscious.

Treatment: Medical: Phenobarbital, Valproic acic & Lamotrigine

Surgical: hemispherectomy

Others: Ketogenic diet