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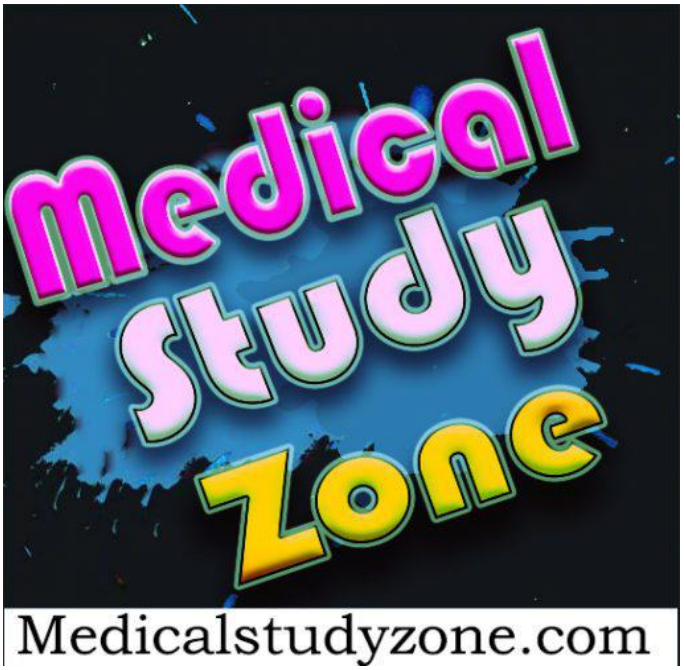


GROWTH

GROWTH CHARTS:

→ GROWTH → increase in **physical size**

EMBRYO	1st 8 weeks
FETUS	Rest of IUL (from 9 weeks)
NEONATE	1st 28 days of life
INFANT	1st year of life
TODDLER	1-3 years
PRE SCHOOL	3-6 years
ADOLESCENT	10-19 years

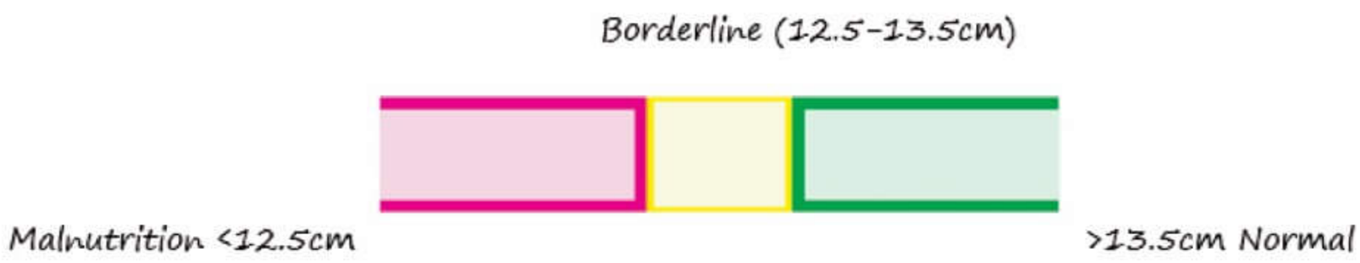
GROWTH ASSESSMENT:

Growth is assessed by **ANTHROPOMETRIC PARAMETERS** like

1. Weight
2. Height
3. Head circumference
4. Mid arm circumference
5. Skin fold thickness
6. Chest circumference
7. Body Mass Index (BMI)

MID ARM CIRCUMFERENCE:

→ Device used by health workers to measure MAC → **SHAKIR'S TAPE**



SKIN FOLD THICKNESS:

→ Device used to measure → **HARPENDEN CALLIPERS** (Gives an idea of the amount of subcutaneous fat)

→ **Areas to be measured:**

- Supra scapular
- Subscapular
- Biceps
- Triceps

→ **Tanner's charts** used previously

- **WHO charts** are used now

CHEST CIRCUMFERENCE (CC):

AT **birth** → **Head Circumference > Chest Circumference**

By **9 months – 1 year → HC = CC**

> 1 year → CC > HC

Note: If any of the above parameters differ, it indicates **MALNUTRITION**

BODY MASS INDEX (BMI):

$$\text{BODY MASS INDEX (BMI)} = \frac{Weight\ (Kg)}{Height\ (m)2}$$

GROWTH CHARTS:

→ Graphical representation of the anthropometric parameters

→ NCHS GROWTH CHARTS (1977)

→ CDC GROWTH CHARTS (2000)

→ WHO GROWTH CHARTS (2006)

NCHS → National Center For Health Statistics

CDC → Center For Disease Control & Prevention

WHO GROWTH CHARTS:

→ Preferred growth charts for under-5 children all over the world

→ Based on MGRS (Multicenter Growth Reference Study)

- Conducted in 6 countries across the world including India
- Countries (**BONGUI**)

Brazil	**G**hana
Oman	**U**S
Norway	**I**ndia [New Delhi]

→ **Enrolled those babies who are exclusively breast-fed children in 1st few months of life**

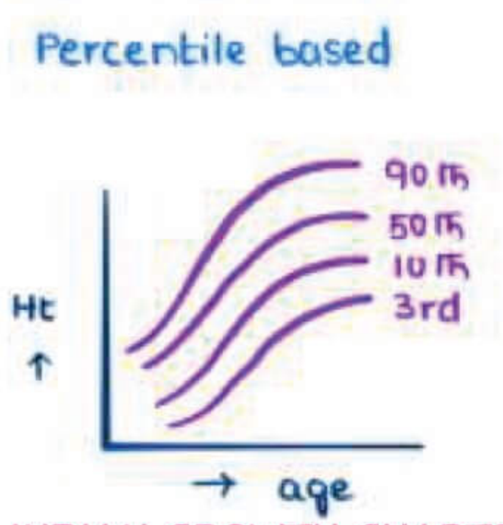
→ **Excluded factors like Maternal smoking & Alcohol**

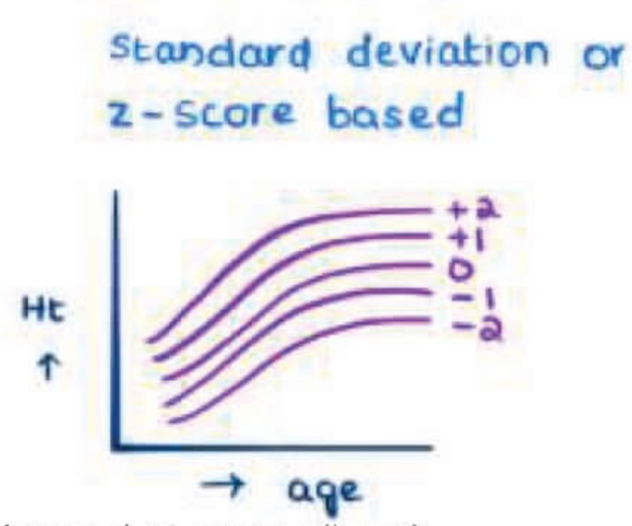
→ WHO growth charts available for

1. Weight for age
2. Weight for height
3. Height for age
4. Head circumference for age
5. Mid Arm Circumference for age
6. Skin fold thickness for Age
7. BMI for age
8. Major motor milestones

→ Separate charts for boys & girls

→ 2 types of growth charts are available





INDIAN GROWTH CHARTS: (Preferred beyond 5 years of age)

1. IAP (Indian Academy of Pediatrics) charts

2. K.N. AGARWAL CHARTS

3. KHADILKAR CHARTS

NORMAL ANTHROPOMETRIC PARAMETERS:

WEIGHT:

Birth weight of an average Indian baby ~ 2.8 – 2.9 kg

Birth weight	→ W
At 5 months	→ 2 w
At 1 year	→ 3 w
At 2 years	→ 4 w
At 3 years	→ 5 w
At 5 years	→ 6 w
At 7 years	→ 7 w
At 10 years	→ 10 w

➔ Birth weight doubles at 5 months

➔ Birth weight triples at 1 year

EXPECTED WEIGHT OF CHILD:

< 1 year	→ $\frac{x+9}{2}$	x – age in months
1-6 year	→ 2x + 8	x – age in years
7 – 12 years	→ $\frac{7x-5}{2}$	x – age in years

HEIGHT:

→ Length → 1st 2 years of life

- Device used to measure length → INFANTOMETER

→ Height → > 2 years of life

- Device used to measure height → STADIOMETER

Infantometer

LENGTH/ HEIGHT OF CHILD:

At birth	50 cm
By 3 months	60 cm
By 9 months	70 cm
By 1 year	75 cm
At 2 years	90 cm
At 4 – 4 ½ years	100 cm

→ Maximum growth takes place during → 1st year > Puberty

→ Length of the child ↑ ses by 50% in → 1st year

→ Height of a child doubles itself or increases by 100% → 4 – 4 ½ years

→ Expected height of a child = (6x + 77) cm; x → age in years

UPPER SEGMENT: LOWER SEGMENT RATIO:

→ Upper segment – Part of the body above symphysis pubis

→ Lower segment – part of the body below symphysis pubis

AGE	US:LS ratio
At Birth	1.7 – 1.9 : 1
At 3 years	1.3 : 1
At 7-10 years	1:1

HEAD CIRCUMFERENCE/ OCCIPITO FRONTAL CIRCUMFERENCE (OFC):

→ Measured using **Non stretchable measuring tape** with 'mm' marking

→ At Birth, HC → 33 – 35 cm

AGE	RATE OF INCREASE IN HEAD CIRCUMFERENCE
1st 3 months	2 cm/ month
Next 6 months	1 cm/ month
NEXT 6 months	0.5 cm/ month
next 2 years	0.2 cm/ month

Q. If Head Circumference at birth is 35 cm. When it will become 43 cm?

A. At birth → 35 cm

1m → 37 cm

2 m → 39 cm

3 m → 41 cm

4 m → 42 cm ; [5m → 43 cm]

BRAIN DEVELOPMENT:

SIZE OF BRAIN

At 1 month → 36% of adult size

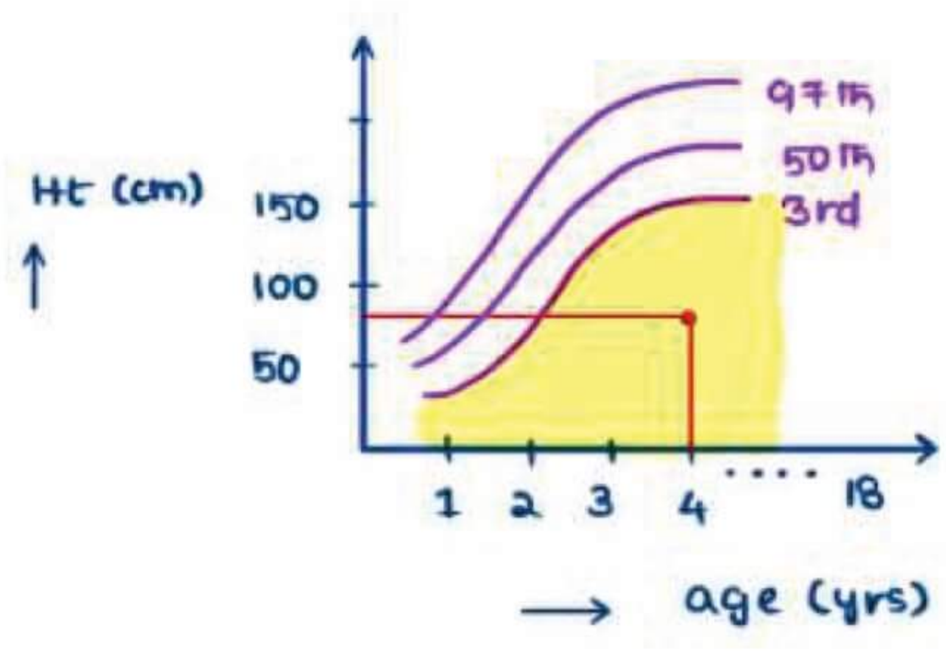
At 1 year of age → 72% of adult size

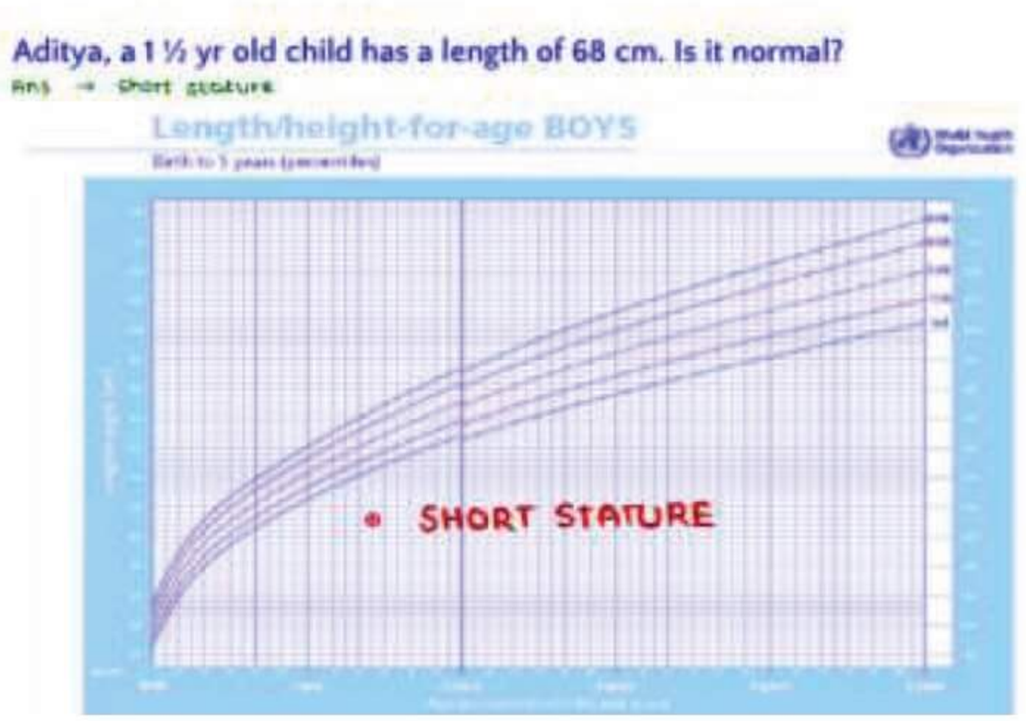
At 2 years of age → 85% of adult size

➔ Maximum growth is in 1st & 2nd years of life

SHORT STATURE:

DEFINITION → Height of child < **3rd percentile** (or) < **-2 SD of expected**, according to age & sex of child





CLASSIFICATION:

PROPORTIONATE SHORT STATURE → US:LS ratio unchanged

DISPROPORTIONATE SHORT STATURE → US:LS ratio changes

IMPORTANT CAUSES OF PROPORTIONATE SHORT STATURE:

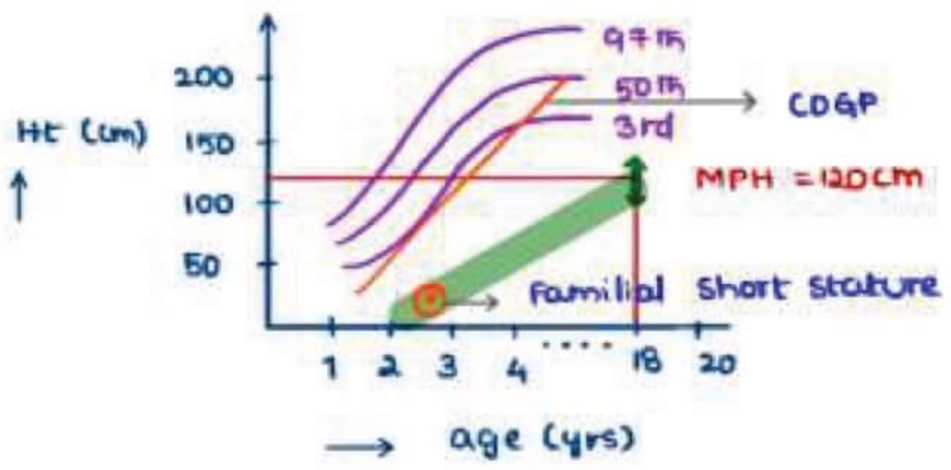
1. NORMAL VARIANTS
2. INTRA-UTERINE CAUSES
3. POST-NATAL/ ACQUIRED CAUSES

I) **NORMAL VARIANTS:**

1. Familial Short Stature

2. CDGP (constitutional Delay in Growth & Puberty)

CDGP



FAMILIAL SHORT STATURE	CDGP
1. Child's height is < 3rd percentile of expected, according to age & sex, but it is normal as per his target height.	1. Child's height is less than expected during childhood, but Final adult height attained is normal
2. Child has normal puberty	2. child has delayed puberty
3. Family H/O short stature ⊕	3. H/O delayed puberty in parents
4. Bone age = chronological age	4. Bone Age < chronological age

MID PARENTAL HEIGHT (MPH):

Boys → $\frac{FH+MH+13}{2}$ cm
Girls → $\frac{FH+MH-13}{2}$ cm

BONE AGE: Preferred X rays for its estimation-

In neonates → X-ray Knees

Infants → X-ray shoulder

1 – 13 years → X-ray hand & wrist

BONE AGE < CHRONOLOGICAL AGE

1. CDGP (Mc cause of short stature during childhood)
2. Congenital hypothyroidism
3. GH deficiency
4. Severe Malnutrition

ii) **INTRA UTERINE CAUSES**

1. IUGR
2. Intra Uterine Infections (TORCH)
3. Genetic syndromes:
   - Turner syndrome
   - Down syndrome
   - Seckel syndrome (Bird headed dwarfism)

iii) **POST NATAL/ ACQUIRED CAUSES**

1. SEVERE LONG-STANDING MALNUTRITION
2. ANY CHRONIC SYSTEMIC DISEASE (chronic kidney disease)
3. ANY MALABSORPTION (celiac disease)
4. ENDOCRINE DISORDERS: GH deficiency, Cushing syndrome (Mc cause is Iatrogenic)
5. PSYCHO SOCIAL DWARFISM (maternal deprivation)

GH DEFICIENCY:

→ US : LS Ratio is normal

→ Bone age < Chronological age

→ **GH STIMULATION TEST:**

- Dynamic test
- Done by using any one of
  - Clonidine
  - Insulin
  - Arginine

→ Rx → Recombinant GH therapy (S/E → Pseudo tumor cerebri)

IMPORTANT CAUSES OF DISPROPORTIONATE SHORT STATURE:

Short trunk dwarfism (US: LS ratio → Decreases)	**Short limb Dwarfism** (US: LS Ratio → increases)
1.Short → Spondyloepiphyseal dysplasia	1. Rickets
2. Man → Mucopolysaccharidosis	2. Achondroplasia
3. May → Muco-lipidosis	3. Osteogenesis imperfecta
4. Climb → Caries spine (pot'ts disease)	4. Congenital hypothyroidism
5. High → Hemivertebra/ Butterfly vertebra	5. Chondroectodermal dysplasia

ALAGILLE SYNDROME COMPONENTS:

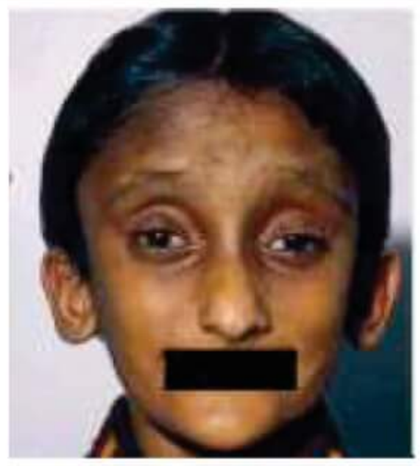
→ Neonatal cholestasis

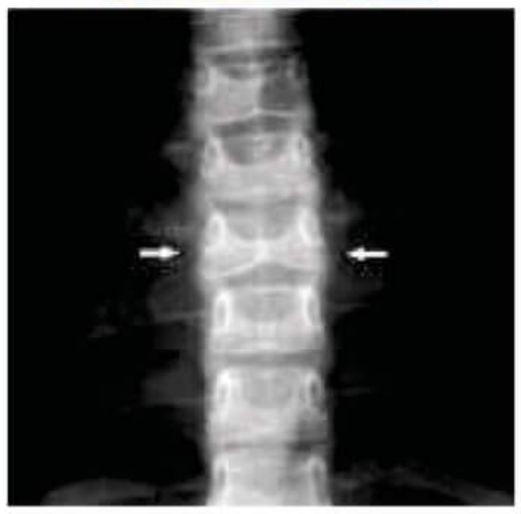
→ Triangular facies

→ Pulmonary stenosis

→ Hemi vertebra

TRIANGULAR FACIES → Also seen in **RUSSEL SILVER SYNDROME**





ACHONDROPLASIA:

→ **A**utosomal dominant inheritance — **A**

→ **C**hampagne glass pelvis on x ray — **C**

→ **H**and abnormality (TRIDENT HAND) — **H**

→ **O**besity — **O**

→ **N**eurological problems — **N**

→ **D**elayed motor milestones — **D**

→ **R**ecognized at birth — **R**

→ B**O**wing of legs — **O**

→ **P**roximal limb shortening — **P**

→ **LA**rge head — **LA**

→ **S**hort stature — **S**

→ **I**nter-pedicular distance b/w vertebra decreases — **I**

→ Gene involved → **FGFR 3 gene** [Fibroblast Growth Factor Receptor 3 Gene]

OSTEOGENESIS IMPERFECTA/ BRITTLE BONE DISEASE/ DENTIGEROUS IMPERFECTA:

→ **TRIAD:**

- Recurrent fractures / Body deformity
- Blue sclera
- Deafness

→ Type-I collagen Defect

→ **Rx**: by Bisphosphonates [PAMIDRONATE]

ABNORMALITIES OF HEAD SIZE & SHAPE:

MICROCEPHALY/ SMALL HEAD

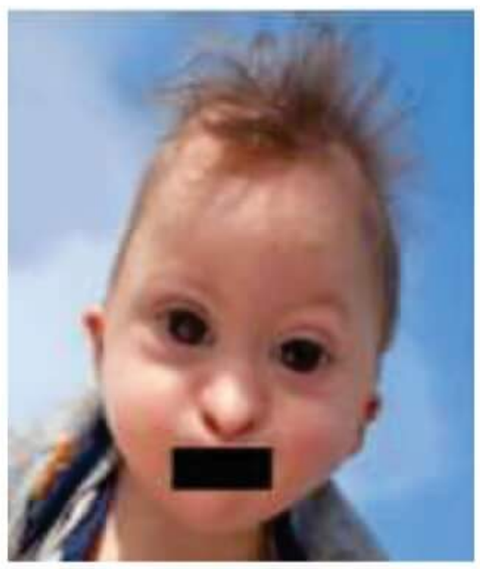
DEFINITION → HC of a child < - 3 SD or Z score of expected according to age & sex of child

IMPORTANT CAUSES:

PRIMARY/ GENETIC CAUSES:

1. CRI-DU-CHAT SYNDROME ($5P^-$)	Can not
2. SMITH LEMLI OPITZ SYNDROME	See
3. PATAU SYNDROME (TRISOMY 13)	P
4. EDWARD SYNDROME (TRISOMY 18)	E
5. FAMILIAL	F
6. RUBINSTEIN TAYBI SYNDROME	R in
7. CORNELIA DE LANGE SYNDROME	Child

SECONDARY CAUSES:

MATERNAL CAUSES	OTHER CAUSES
1. INFECTIONS (TORCH) 2. SMOKING 3. ALCOHOL INTAKE (FETAL ALCOHOL SYNDROME) 4. RADIATION EXPOSURE 5. PHENYLKETONURIA 6. PHENYTOIN INTAKE	1. SEVERE MALNUTRITION in baby 2. CNS INFECTIONS DURING INFANCY (MENINGO ENCEPHALITIS) 3. ACQUIRED MICROCEPHALY → RETT SYNDROME (X-LINKED DOMINANT) → ANGELMAN SYNDROME → SECKEL SYNDROME 

ABNORMALITIES OF HEAD SHAPE:

- ➔ It is due to premature fusion of cranial sutures → called as **CRANIOSYNOSTOSIS**
- ➔ **DOLICHOCEPHALY:**
  - Elongated head → due to premature fusion of sagittal suture
  - Most common type of craniosynostosis
- ➔ **TRIGONOCEPHALY:**
  - Premature fusion of metopic suture
- ➔ **TURRICEPHALY:**
  - Premature fusion of coronal, spheno-frontal, fronto-ethmoid sutures

SYNDROMES ASSOCIATED WITH CRANIOSYNOSTOSIS:

- ➔ Carpenter syndrome
- ➔ Apert syndrome
- ➔ Pfeiffer syndrome
- ➔ **Crouzon syndrome:**
  - It is due to premature fusion of coronal suture
  - **Features of Crouzon syndrome:**
    - Brachycephaly
    - Bulging eyes
    - Mid-face hypoplasia
    - Prognathism → protruding jaw

NORMAL & ABNORMAL DENTITION:

NORMAL DENTITION:

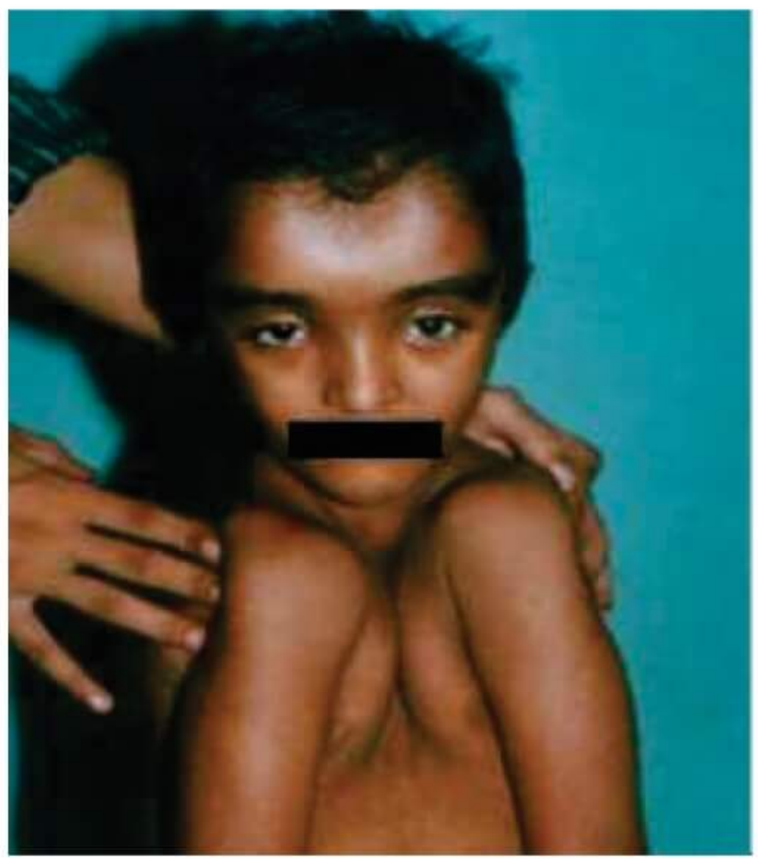
	PRIMARY DENTITION MILK/ TEMPORARY TEETH	SECONDARY DENTITION / PERMANENT TEETH
Begin at	6 – 7 months	6 years
1st tooth to erupt	Lower central incisor	1st molar
Last tooth	Second molar	3rd molar (or) wisdom tooth
Completes at	2 and half – 3 years	12 years (except the 3rd molar) 3rd molar (18-25 years)
Total no. of teeth	20	28-32

ABNORMALITIES OF DENTITION:

DELAYED DENTITION:

Definition → When no tooth erupts by the age of **13 months**

IMPORTANT CAUSES [Mnemonic → "**FRIED CHOP**"]

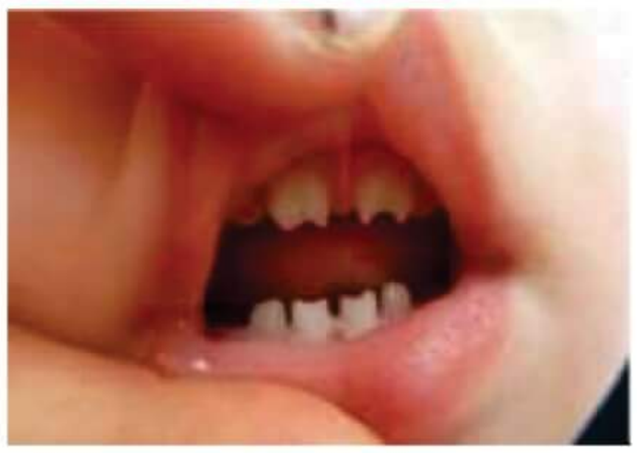


1. **F**amilial
2. **R**ickets
3. **I**diopathic
4. **E**ndocrine
   - → Hypopituitarism
   - → Hypothyroidism
   - → Hypoparathyroidism
5. **D**own syndrome
6. **C**leidocranial dysostosis:
   - Absent clavicles
   - Large anterior fontanelle
   - Delayed closure of anterior fontanelle
   - Supernumerary teeth (also found in Gardner syndrome → precancerous condition of carcinoma of colon)

NATAL TEETH:

1. Pierre Robin sequence
2. Ellis van creveld syndrome
3. Epidermolysis bullosa (lethal acantholytic variety)
4. Soto's syndrome

HUTCHINSON'S TEETH

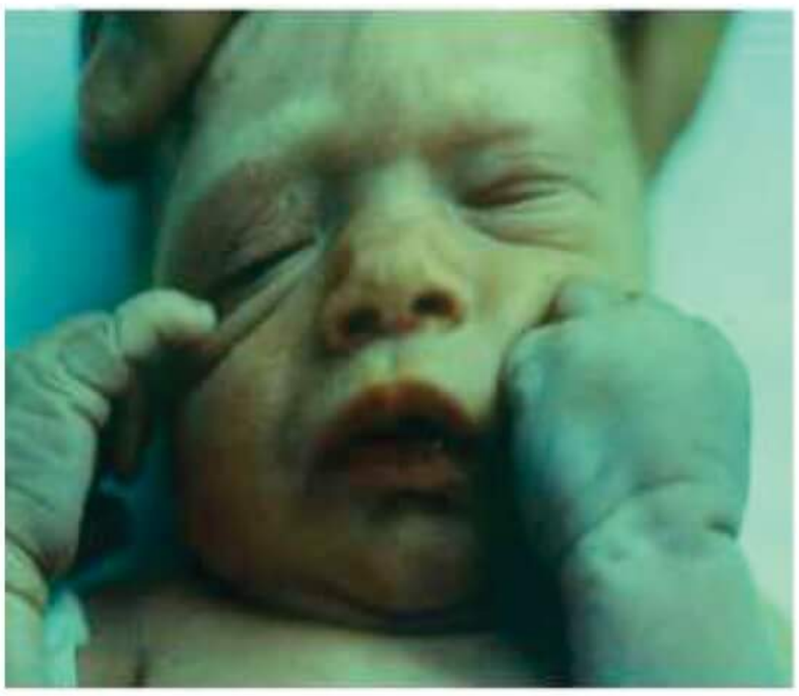


HUTCHINSON'S TEETH: → Notched incisors

→ Seen in congenital syphilis

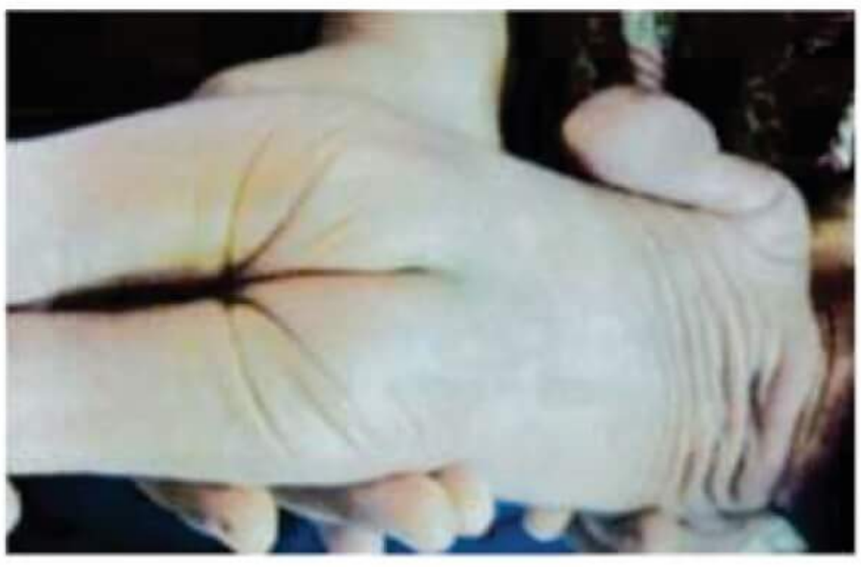
➔ Hutchinson's triad: Hutchinson's teeth, interstitial keratitis, SNHL

BAG & MASK VENTILATION

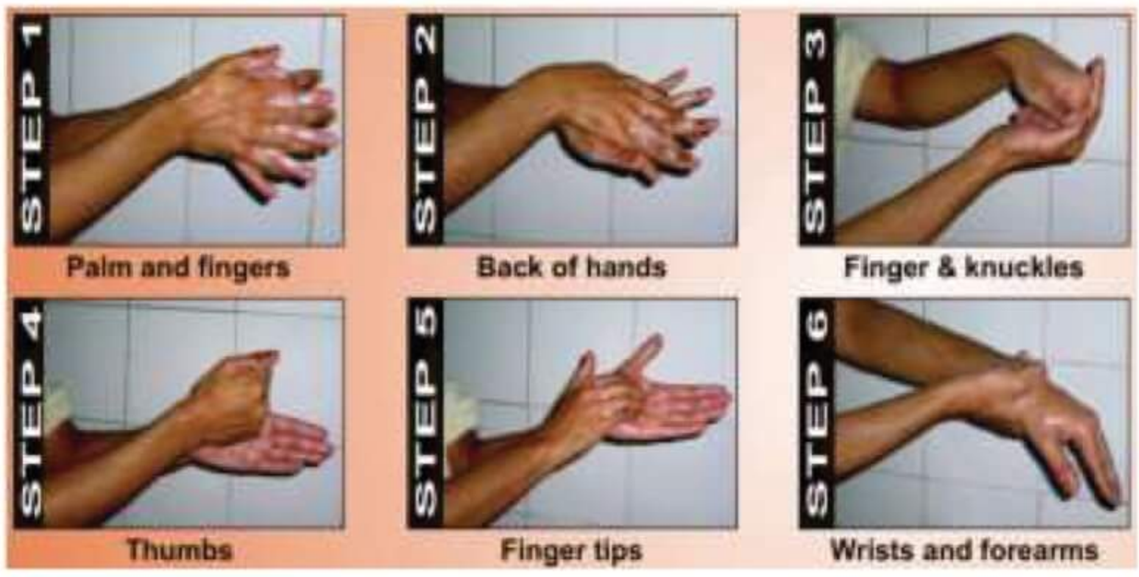


PERIPHERAL/ ACROCYANOSIS

Capillary refill time [Normal- <3sec]



IUGR



6 STEPS OF HAND-WASHING – Atleast 2 mins

4 months	Partial weight bearing when made to stand
5 months	Feet to mouth, complete neck control
6 months	-Supports his weight on extended arms in prone position -prone to supine -Sitting with support / sitting in tripod position
7 months	Supine to prone
8 months	Sitting without support; crawls
9 months	Standing with support
10 months	Creeping
10-11 months	Pivoting Cruising
1 year	• Stand without support • Walk with support • Walk with one hand held • Can walk on hands & feet like a bear
15 months	Creep upstairs Walks without support
18 months	• Goes upstairs & down stairs holding the side railing • pulls a toy • Runs
2 years	Goes upstairs & down stairs 2 feet per step Kicks a ball Walks backwards
3 years	Goes upstairs with alternating feet & down stairs 2 feet / sleep Rides a tricycle
4 years	Goes upstairs & down stairs with alternating feet Hopping
5 years	Skipping Can stand on 1 leg for > 10 sec

FINE MOTOR:

1 month	Hands kept closed Palmar grasp reflex present
3 months	Hands kept open Palmar grasp reflex lost Hold an object when placed in hand '**Hand regard**' appears (disappear at 20th week)
4 months	Tries to reach an object, but overshoots

5 months	Bidextrous grasp
6 months	Unidextrous or palmar grasp Can feed self a biscuit
7 months	Transfer objects from 1 hand to another
9 months	Immature/ assisted pincer grasp
12 months	Mature/ unassisted pincer grasp → 'CASTING'
15 months	Scribbles spontaneously Feeds self with a cup Tower of 2 cubes
18 months	Feeds self with a spoon Tower of 3 cubes Turn 2-3 pages at a time
2 years	Tower of 6 cubes Turns pages singly Undress self Copies a horizontal or vertical line Turns a door knob or unscrew a lid
3 years	Tower of 9 cubes Can dress/undress self except buttons Copies a circle Headedness get established
4 years	Can button & unbutton Copies a rectangle or a plus sign or cross Makes a bridge with cubes Catches a ball reliably
5 years	Can tie shoe laces Copies a triangle or multiplication sign or tilted cross makes a gate

SOCIAL & LANGUAGE MILESTONES:

SOCIAL:

1 month	Looks at the mother intently
2 months	Social smile
3 months	Recognizes mother
6 months	Mirror play appears
7 months	Stranger anxiety appears
8 months	Object permanence
9 months	Waves bye bye

10 months	Plays peek a boo
12 months	Kisses on request Plays a simple ball game
15 months	Points to object Indicates wet pants } 2 'P's
18 months	Domestic mimicry Dry during day time } 2 'D's
2 years	Parallel play
3 years	Joins in play Knows his name, age, gender Dry at night
4 years	Goes to toilet alone Asks questions
5 years	Starts helping in simple household tasks Distinguishes morning from evening compare 2 weights can follow 3 step commands

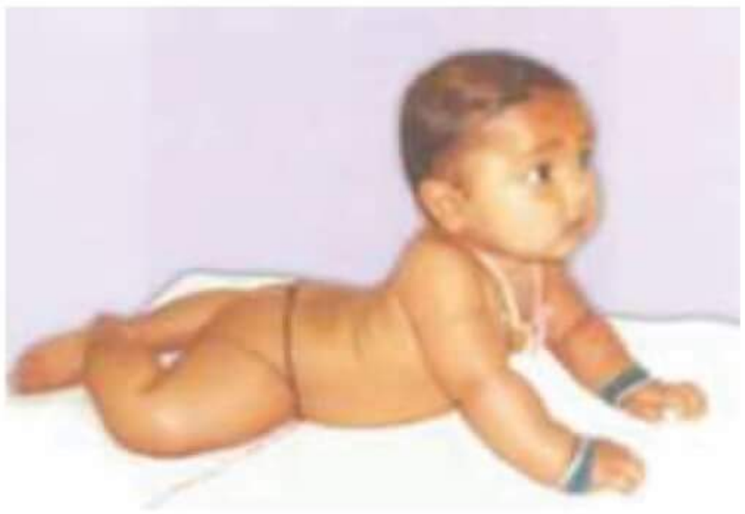
LANGUAGE:

1 months	Quietens when a bell is rung
2 months	Vocalizes
3 months	Cooing
4 months	Laughs aloud
5 months	Razzing
6 months	Speaks monosyllables like ma, ba, da (Babbling)
9 months	Speaks bi-syllables like mama, papa, without meaning Bi-syllable babbling
1 year	Speaks 2-3 words without meaning
15 months	Jargon speech
18 months	Knows 10 words with meaning
2 years	Speaks short sentences Uses pronounces like I, ME, YOU Vocabulary of 50-100 words
3 years	Uses pleural & past tense Repeats 3 digits, 3 words sentences
4 years	Tells a story/ poem, sings a song
5 years	Repeats 4 digits Names 4 colours

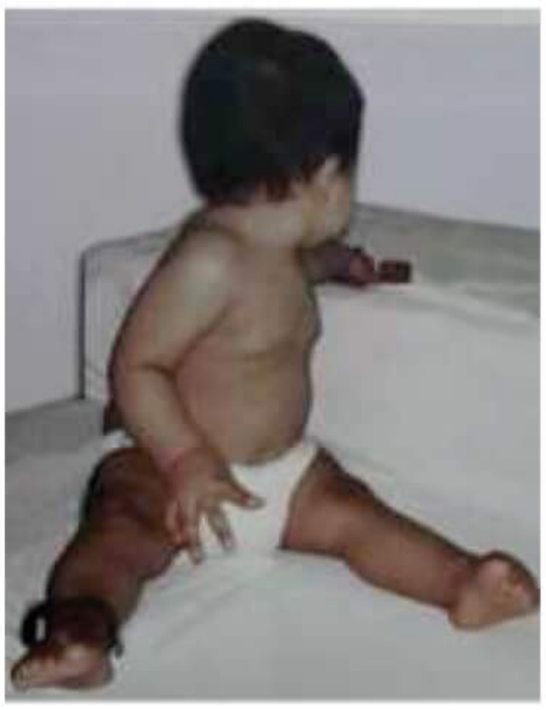
IMAGE BASED QUESTIONS:

CREEPING – 15 MONTHS

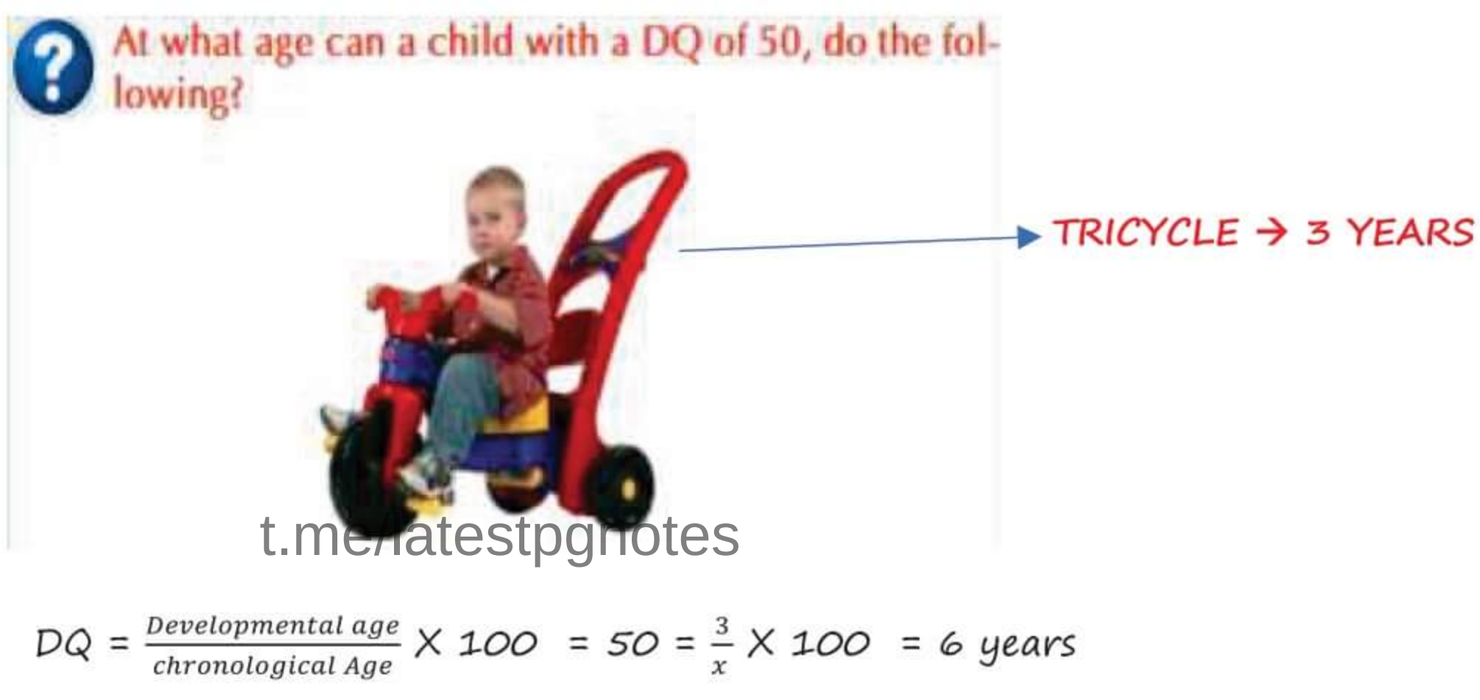
3 MONTHS



6 MONTHS



PIVOTTING -10-11M



$$DQ = \frac{Developmental\ age}{chronological\ Age} \times 100 = 50 = \frac{3}{x} \times 100 = 6\ years$$

\

HAND REGARD

PINCER GRASP-9 MONTHS

- Appears at 12 weeks
- Disappears at 20 weeks

What is the sequence in which the following milestones appear?

A – mirror play → 6 m

B – Peek a boo → 10 m

C – Kisses on request → 12 m

D – Ways bye bye → 9 m

SEQUENCE → A, D, B, C

A – Ties shoes laces → 5 years

B – copies a circle → 3 years

C – Feed self with spoon → 18 months

D – buttons & Unbuttons → 4 years

SEQUENCES → C, B, D, A

DEVELOPMENTAL & BEHAVIOURAL DISORDERS

ABNORMALITIES OF DEVELOPMENT (3 'D' S):

DEVELOPMENTAL DELAY:

- When child's performance in 1 or more domains is significantly below average
- If developmental delay involves **2 or more domains** – **GLOBAL DEVELOPMENTAL DELAY**

DEVELOPMENTAL DISSOCIATION:

- **Substantial difference** in the rate of development between 2 or more domains
- **Example**– Isolated speech delay (remaining are normal)

DEVELOPMENTAL DEVIANCY:

- Developmental milestones occurring **out of sequence**
- **Example**–If Crawling comes before sitting

DEVELOPMENTAL RED FLAGS (upper limit):

GROSS MOTOR		FINE MOTOR	
Sitting with support	9 months	Pincer grasp	12 months
Standing with support	12 months	Scribbling	24 months
Walking with support	15 months		
LANGUAGE		**SOCIAL**	
Babbling	12 months	Social Smile	6 months
Single words	(15-16 months)	Waving bye-bye	12 months

- If these milestones are not attained by this time, then there may be some underlying abnormality of development

IMPORTANT CAUSES OF DEVELOPMENT DELAY ("CDGP PIC")

1. **C**hromosomal abnormalities (Trisomy **21**, **13**, **18**)
2. **D**evelopmental brain abnormalities (**lissencephaly** – brain appears smooth due to less gyri & sulci, **myelomeningocele**)
3. **G**enetic (**Fragile X** syndrome, **Red** syndrome, **Prader Willi** syndrome)
4. **P**erinatal factors→ **Asphyxia**, **HIE** (Hypoxic Ischemic Encephalopathy)
5. **P**ostnatal factors→ Trauma, infections, Hypothyroidism
6. **I**nborn errors of Metabolism→ **Maple Syrup Urine** Disease, **organic Acidemia**, **Tay sach** disease, **GM Gangliosidosis**, **Mucopolysaccharidosis**
7. **C**ongenital infections – TORCH (Toxoplasmosis, Other agents, Rubella, CMV, Herpes)

DEVELOPMENTAL ASSESSMENT [DQ]:

Eg: D.Q = Developmental age/Chronological age x 100

SCREENING TESTS FOR DEVELOPMENTAL ASSESSMENTS: (PART)

1. Phatak's Baroda Screening Tests
2. Ages & stages questionnaire
3. Revised Denver Developmental Screening Test
4. Trivandrum development screening chart

DEFINITIVE TESTS FOR INTELLECTUAL & DEVELOPMENTAL ASSESSMENT:

NAME OF TEST	AGE GROUP
Bayley scale for Infant development II	1 month-3.5 years
Wechsler Intelligence Scale for Children IV	6 years-17 years
Stanford Binet Intelligence scale, 5th ed	2 years-85 years
Vineland adaptive behavior scale II	Birth to 89 years

INTELLECTUAL DISABILITY (ID) / MENTAL RETARDATION (old name):

IQ = Mental age/ Chronological age x 100

DEGREE	IQ LEVEL
• MILD ID	51 – 70
• MODERATE ID	36 – 50
• SEVERE ID	21 – 35
• PROFOUND ID	0 – 20

• MORON	50 - 70
• IMBECILE	30 - 50
• IDIOT	< 30

BEHAVIOURAL DISORDERS IN CHILDREN:

NOCTURNAL ENURESIS:

DEFINITION – **Involuntary** passage of **urine** at night **beyond 5 yrs**. of age

EPIDEMIOLOGY:

- 60% are **boys**
- **Family history** is positive in 50%
  - if **1 parent had** Nocturnal Enuresis, each child has **44%** risk of Nocturnal Enuresis
  - If **both parents had** Nocturnal Enuresis, each child has **77%** risk of Nocturnal Enuresis

TYPES:

- **PRIMARY NOCTURNAL ENURESIS** → Never attained urinary continence at night **(MORE COMMON)**
- **SECONDARY NOCTURNAL ENURESIS→ previously normal** at night & now develops Nocturnal enuresis

MANAGEMENT:

1st Line : **Diet & Life style changes** □ **restrict** intake of caffeine, sugary substances/ much fluids after evening time
□ Give child **early dinner** & restrict intake of more fluids after dinner

+ motivational Therapy (STAR CHART)

- Maintain a dairy/calendar
  □ for every dry day that the child has dry day
  □ draw a star
  □ if the child has 7 consecutive stars, give gift for the child

2nd Line : **Bed alarm technique**

- There are **moisture sensing alarms** which are available
- As soon as the child passes urine in bed, the alarm would detect the moisture in undergarment of the child & it will ring
- Child wakes up, go to toilet & micturates
- Shown to produce excellent response

3rd Line: **Drugs** (used for refractory cases or short-term management)

- ORAL DESMOPRESSIN [nasal spray of desmopressin is no longer recommended d/t serious side effects]
- IMIPRAMINE
- OXYBUTININ

NOTE:

Combination of Drugs and Bed & alarm technique□ Lowest relapse rates

PICA:

□ **Persistent eating** of **non-nutritive**, non-food substances over a period of **at least 1 month**
□ **More common** in children with intellectual disability & autism spectrum disorders
□ **Treatment** by behavioral therapy

Pica

THUMB SUCKING:

□ Self-soothing behavior
□ Common in **infancy** & seen in 25% of children **aged 2 years**
□ Thumb sucking beyond 5 yrs., may be associated with SEQUALAE or complications like Paronychia, anterior open bite etc
□ **Treatment** is by behavioral therapy

BRUXISM (TEETH GRINDING)

- Seen in 5-30% of children
- Begin in the **1st 5 years** of life
- Associated with **daytime anxiety**
- **Persistent Bruxism** can manifest as muscular/ temporomandibular joint pain/ dental malocclusion

TREATMENT: Behavioral therapy

BREATH HOLDING SPELLS:

- Results from **immaturity** **of ANS** (AUTONOMIC NERVOUS SYSTEM)
- Begins around **6-18 months**
- **Triggers**: injury, anger, frustration
- **Starts** with a cry & progress to apnea, syncope, tonic posturing
- **2 types** of breath holding spells
  a. **PALLID**- caused by **reflex vagal bradycardia & asystole**
  b. **CYANOTIC** – due to prolonged expiration, apnea, **intrapulmonary shunting** of blood
- **Treatment**: Reassurance; Treatment of co-existing Iron deficiency anemia

TICS & STEREOTYPIES

TICS	STREOTYPIES
Sudden, non-rhythmic, Rapid, **recurrent,** Motor movements or Vocalizations Seen in **TOURETTE SYNDROME**	Stereotyped, **rhythmic, repetitive** movements or patterns of speech with lack of variation over time

AUTISTIC SPECTRUM DISORDERS (A.S.D)

- **Persistent** impairment in reciprocal social communication & interaction & restricted, repetitive patterns of behavior or interest
- RISK FACTORS:
  - Closer spacing of pregnancies
  - Extremely **prematurity** (<26 weeks)
  - Family members with learning/psychological problems
  - Antenatal exposure to **Thalidomide**, valproate, organophosphate
  - Antenatal **Rubella** exposure
- SCREENING TEST:
  – **M-CHAT**: (Modified checklist for autism in toddlers) for 10-30 months
- TREATMENT:
  - **Cognitive Behavior Therapy**
  - Treatment of co morbidities like **Atomoxetine** for **hyperactivity**

- Intra nasal **oxytocin** (upcoming therapy)

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD):

- **Persistent** inattention &/ Hyperactivity / Impulsivity that interferes with functioning/ development of child, present for **atleast 6 months**, in **2 or more settings**, beginning **before 12 years of age**;
- **must not be secondary to another disorder**

RISK FACTORS:

- **Maternal** smoking, alcohol, lead or mercury exposure
- **Genetic** component – **DAT 1 & DRD 4** genes
- **Abnormal Brain** Structure
- **CNS Trauma**
- **Psychologic** Family stress
- **Epilepsy**
- **Tuberous sclerosis, Neurofibromatosis**

EXTRA EDGE:

- **MC Neurobehavioral disorder of childhood** is **ADHD**
- Co-occurs with other emotional, behavioral, language & learning disorders
- Approximately **2% of adults** have ADHD
- 60-80% of children with ADHD continue to have it in adolescence & up to 60% of adolescents exhibit ADHD symptoms into adulthood

TREATMENT:

DRUGS:

- Methylphenidate
- Amphetamine
- Atomoxetine

RETT SYNDROME:

- **X-linked dominant** inheritance
- More common in **girls**
- Most Common gene involved- **MECP-2 gene**
- **Head Circumference is Normal** at birth
- Development – Normal in 1st few months of life

↓

Then, **Deceleration of head growth** occurs

↓ leading to

Acquired microcephaly,

Delayed development

↓ leading to

Loss of purposeful hand movements

↓ causing

Development of stereotypic hand wringing movement

↓

Gait/posture apraxia

RETT SYNDROME

Rett Syndrome **is associated with:**

- Speech problems
- Seizures
- Breathing irregularities
- Intellectual disability

PUBERTY & ADOLESCENCE

ADOLESCENT AGE GROUP:

→ A state of transition from childhood to adulthood

→ W.H.O DEFINITION OF ADOLESCENCE → 10-19 years

- EARLY ADOLESCENCE → 10-13 years
- MID ADOLESCENCE → 14-16 years
- LATE ADOLESCENCE → 17-19 years

→ PUBERTY refers to the **physical aspect of adolescence**

SEQUENCE OF CHANGES IN PUBERTY IN FEMALES:

2-2 ½ years

Thelarche (Breast Development) (1st sign)

↓

Pubarche (development of pubic & axillary hair)

↓

Growth spurt (Peak ↑ in growth velocity)

↓

Menarche (beginning of mensural period)

NOTE – Growth spurt in females occurs just before the onset of **MENARCHE**

SEQUENCE OF CHANGES IN PUBERTY IN MALES:

TESTICULAR ENLARGEMENT (1st sign)

↓

PENILE ENLARGEMENT

↓

PUBIC HAIR

↓

GROWTH SPURTS

↓

AXILLARY HAIR

↓

FACIAL HAIR

Deepening or Ripening of voice

ORCHIDOMETER

➔ ORCHIDOMETER → Device used to measure TESTICULAR SIZE

ASSESSMENT OF PUBERTY IN ADOLESCENT:

➔ Done by TANNER'S STAGING

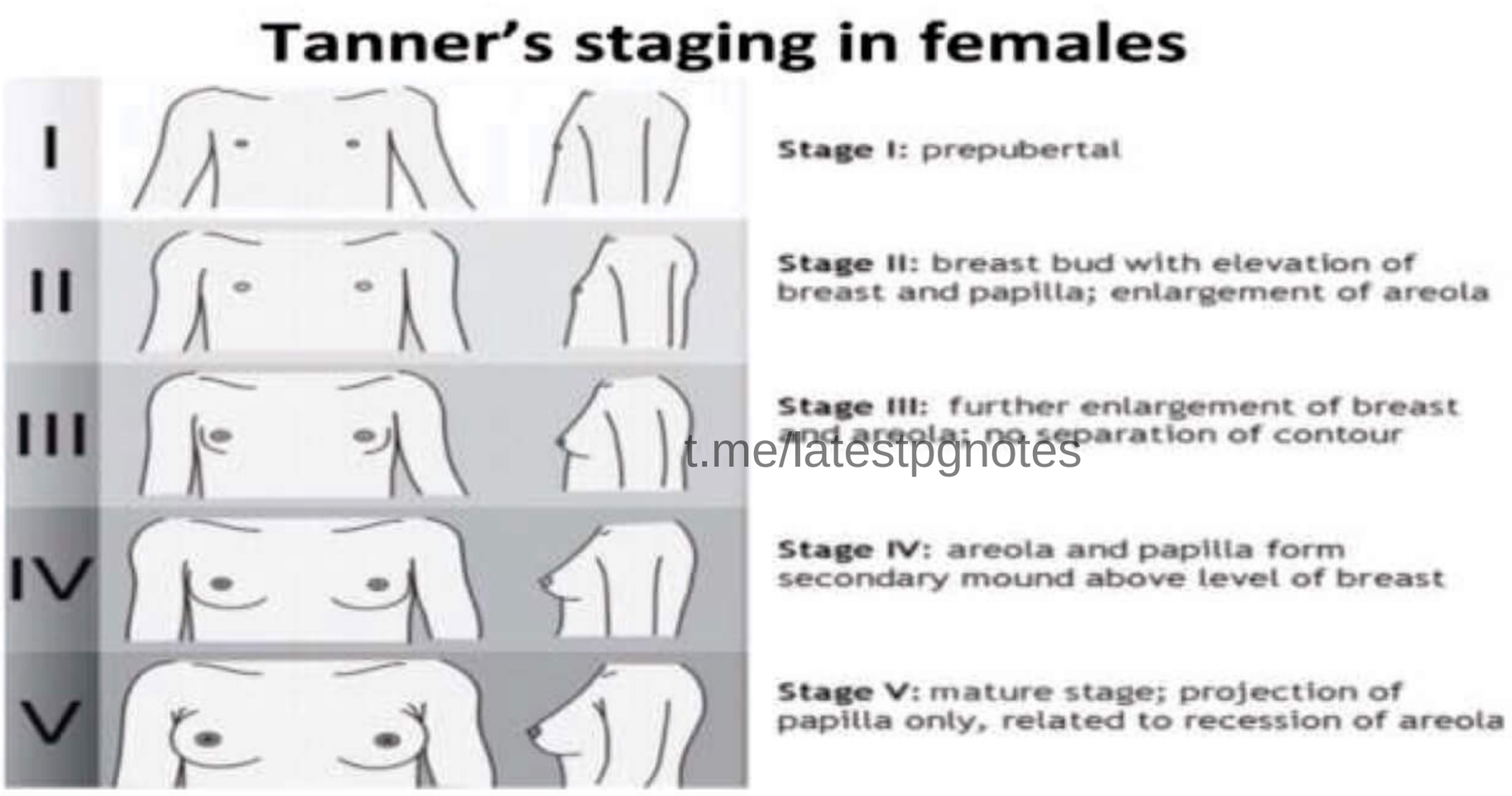
TANNER'S STAGING OR SEXUAL MATURITY RATING (SMR)

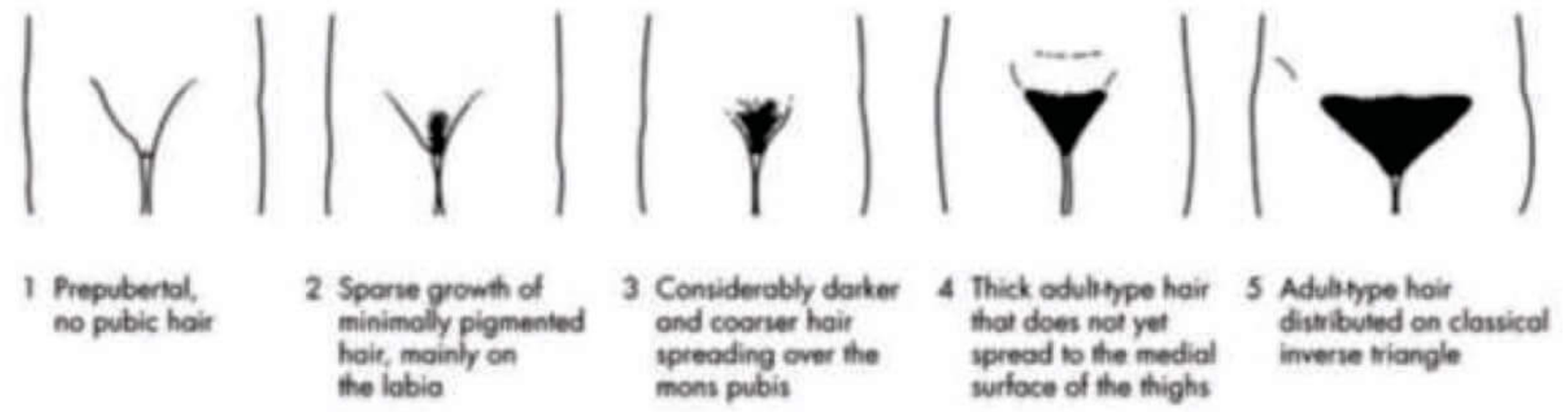
→ Stage 1 to 5

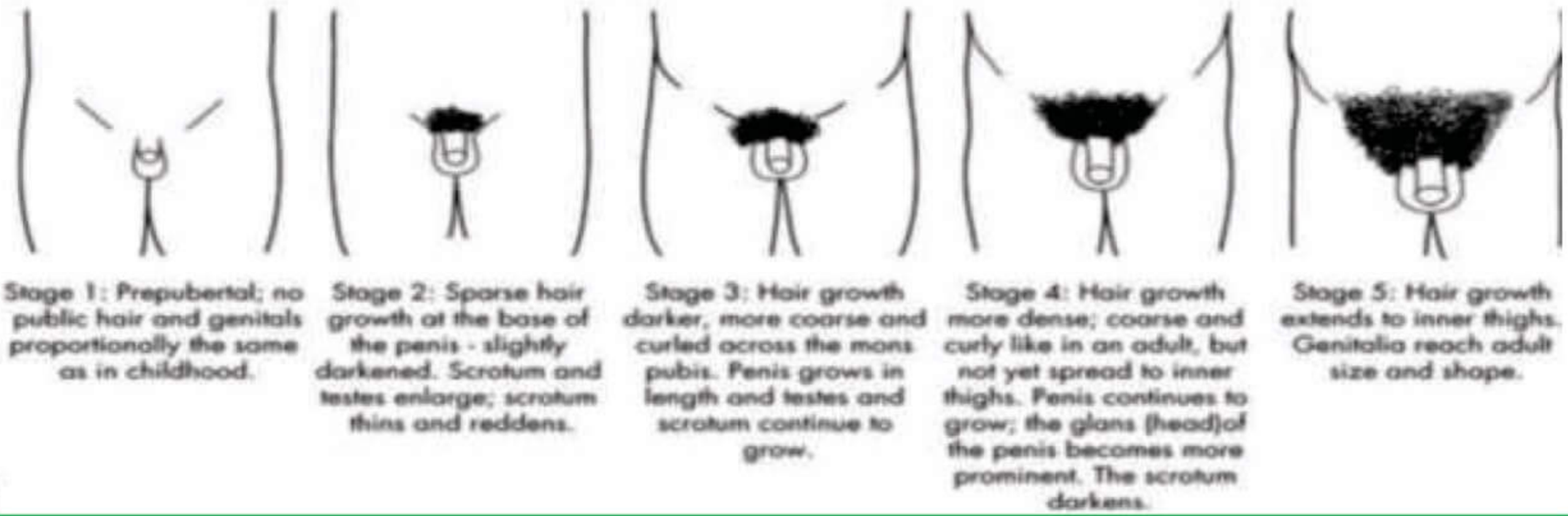
- Stage 1 → pre pubertal stage
- Stage 5 → mature adult

→ PARAMETERS used to access PUBERTY:

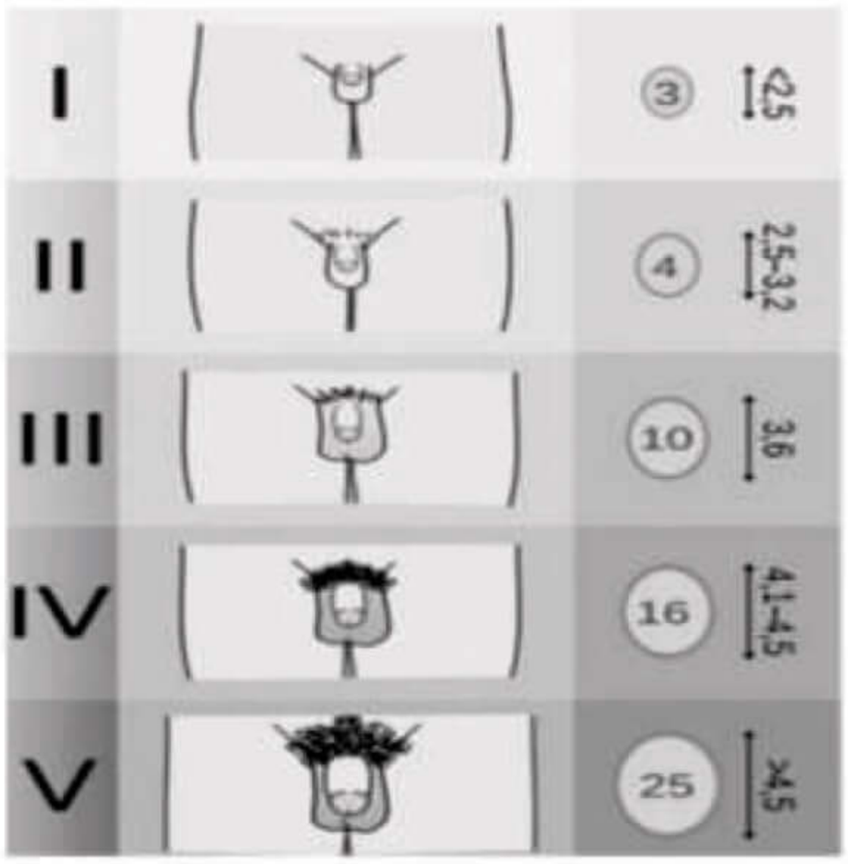
- IN FEMALES→ Based on development of Breast, pubic hairs are used for assessment
- IN MALES → Genitalia (Testis, penis), pubic hairs are used for assessment







Tanner's staging in males



Stage I: prepubertal; testicular size less than 4 cc in volume and 2.5 cm in longest dimension

Stage II: enlargement of scrotum and testes; scrotal skin reddens and changes in texture; growth of testes to 4 cc or greater in volume

Stage III: enlargement of penis (length at first); further growth of testes

Stage IV: increased size of penis with growth in breadth and development of glans; testes and scrotum larger, scrotal skin darker

Stage V: adult genitalia

GROWTH SPURT:

→ Occurs in which stage
- IN GIRLS→ tanner's /SMR stage 3
- IN BOYS→ tanner's /SMR stage 4

→ Growth spurt occurs later & lasts longer in boys/males

→ Height increased by
- Boys → 20-30cm
- Girls → 16-28cm

PROBLEMS IN ADOLESCENT AGE GROUP ('AIMLESS')

→ Accidents (It's the MCC of mortality in adolescent age group)

→ Infections like STD, HIV, Skin infections

→ Mental health problems
- Adjustment & anxiety disorders
- Depression
- Delinquent behavior

→ Low self-esteem and body image issues

→ Eating and nutritional disorders (Anorexia nervosa/ Bulimia nervosa)

→ Sleep disturbances

→ Substance abuse→ Tobacco, Alcohol

NEONATOLOGY

IMPORTANT TERMINOLOGIES AND PRIMITIVE NEONATAL REFLEXES:

INTRODUCTION

NEONATAL PERIOD → 1st 28 days of life

EARLY NEONATAL PERIOD → 1st 7 days of life

→ Day of birth - < 7 completed days

LATE NEONATAL PERIOD → D_7 – 28 days of life

CLASSIFICATION:

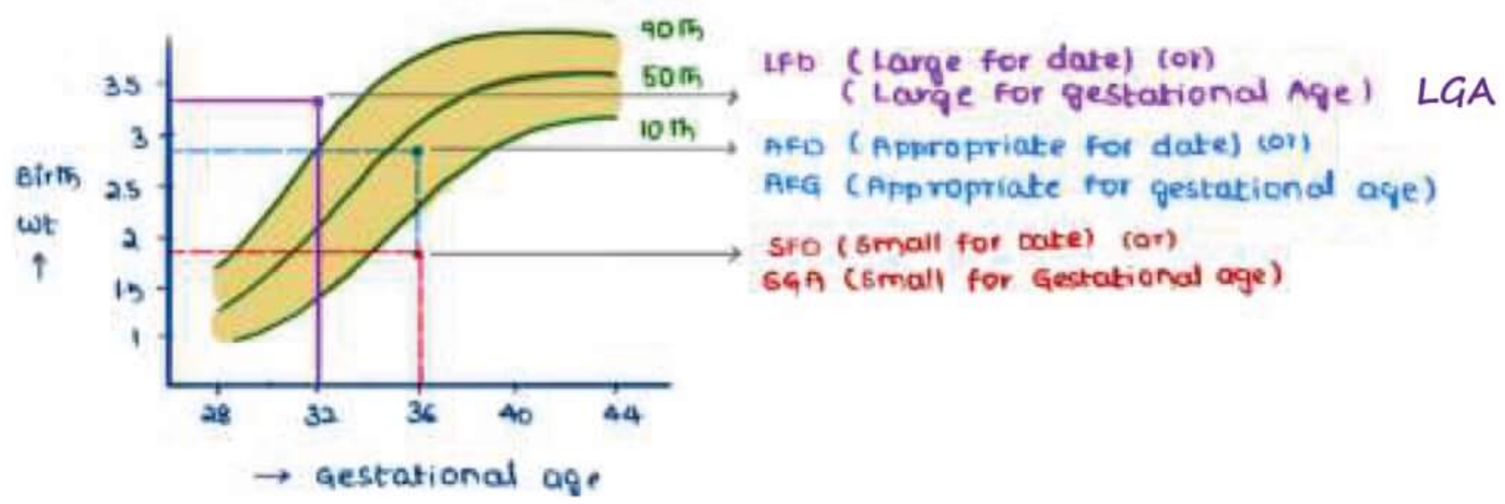
I. **ACCORDING TO THEIR GESTATIONAL AGE** (irrespective of birth weight)

1. TERM → Birth b/w 37 completed weeks to < 42 gestational weeks
2. PRE TERM → Born at <37 weeks of gestation
3. POST TERM → Born at beyond 42 weeks of gestation

ii. **ACCORDING TO BIRTH WEIGHT** (irrespective of gestational age)

1. LBW [low birth weight] → < 2500 gms Birth weight
2. VLBW [Very low Birth weight] → < 1500 gms Birth weight
3. ELBW [extremely low birth weight] → < 1000 gms Birth weight

iii. **ACCORDING TO GESTATIONAL AGE & BIRTH WEIGHT:**



SFD (or) SGA → Birth weight is < 10th percentile of expected, according to Gestational age (GA)

AFD (or) AGA → Birth Weight is between 10th – 90th percentile of expected, according to gestational age

LFD (or) LGA → Birth weight is > 90th percentile or expected, according to GA

IMPORTANT CAUSES FOR LFD NEONATE:

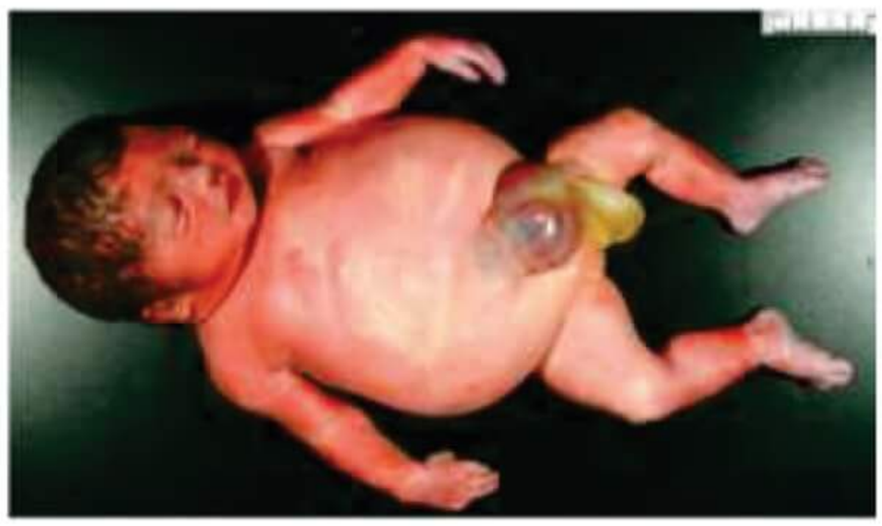
1. Infant of diabetic mother

2. Congenital hypothyroidism

3. Constitutional

4. Soto's syndrome/ cerebral gigantism

5. **Beckwith-wiedemann syndrome**:



- Hemi hypertrophy
- Macroglossia
- Increase risk of tumors (Eg- Wilm's tumor etc)

NORMAL TERM NEONATE:

→ Birth weight of an average Indian baby → 2.8 kg (Ghai → 2.9 kg)

→ **Length** → 50cm

→ **US:LS ratio** → 1.7 – 1.9:1

→ **HC** → 33 – 35 cm

→ **Heart Rate** → 120 – 140 bpm (110-160 bpm)

→ **Respiratory rate** → 40 – 60/ min

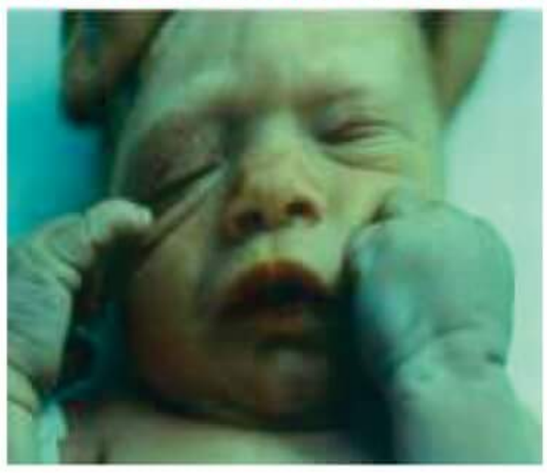
→ **Peripheral cyanosis (Acrocyanosis)** } Normal

→ **Soft systolic murmur** }

→ Central cyanosis at birth } abnormal

→ Jaundice at birth /D_1 }

PERIPHERAL CYANOSIS/ ACROCYANOSIS



PRE TERM NEONATE:

GENERAL	HEAD TO TOE
1. **Lesser subcutaneous fat** → Appears emaciated 2. **Generalized hypotonia** → Extended posture 3. **Skin** → Thin, Translucent & Friable 4. **Abundant lanugo**	1. **Head** appears relatively large 2. **Anterior fontanelle** – Large, wide-open 3. **Ear cartilage** is poorly formed → Soft & deformable ears 4. **Breast buds** < 5 mm size 5. **Genitalia**

5. **Little vernix caseosa** → Cheesy, white, sticky material present all over the body of the neonate	Male → Undescended testes poorly formed scrotum Female → Labial majora widely separated Labia minora clearly visible 6. **Absent deep creases** on the sole

PRIMITIVE NEONATAL REFLEXES:

PRESENT AT BIRTH (Term)	Appears	Disappears
ROOTING REFLEX	32 weeks of gestation	Starts disappearing at 1 month post-natal age
MORO'S REFLEX	28 – 37 weeks	5 – 6 months
PALMER GRASP REFLEX	28 weeks	3 months
ATNR [Asymmetric Tonic Neck Reflex]	35 weeks	5-6 months
PRESENT AFTER BIRTH	Appears	Disappears
STNR [Symmetric Tonic Neck Reflex]	4-6 months	8-12 months
PARACHUTE REFLEX	7-8 months	Persists throughout life
LANDAU REFLEX		
NECK RIGHTING REFLEX		

ROOTING REFLEX

ASYMMETRIC TONIC NECK REFLEX

Q. Which primitive neonatal reflex helpS mother in breast feeding → Rooting reflex

Q. Which primitive neonatal reflex is earliest to disappear → Rooting reflex

MORO'S REFLEX/ EMBRACE EQUIVALENT:

COMPONENTS OF A COMPLETE MORO'S REFLEX:

→ **Symmetric abduction & extension of UL** *along with* **opening of hands** *followed by* **Flexion & adduction of UL** [+] *Extension of head & Trunk, Movement of lower limbs, crying*

- *Begins to appear* → **28 weeks of gestation**
- *1st component to appear* → **opening of hands**
- *Moro's reflex completely appears by* → **37 weeks of gestation**
- **Disappears at** → 5-6 months (Nelson)→ best answer
  → 3-6 months (O.P. Ghai)

→ Abnormal persistence beyond 6 months → CEREBRAL DAMAGE

→ MORO'S REFLEX → IF ONCE DISAPPEARS, NEVER REAPPEARS

CAUSES OF ABSENT MORO'S REFLEX:

➔ **Stage -3** (severe) Hypoxic Ischemic Encephalopathy (HIE)
➔ Down's syndrome
➔ Acute Bilirubin Encephalopathy

CAUSES OF EXAGGERATED MORO'S REFLEX:

➔ STAGE 1 (early/mild) Hypoxic Ischemic Encephalopathy

CAUSES OF ASYMMETRIC MORO'S REFLEX

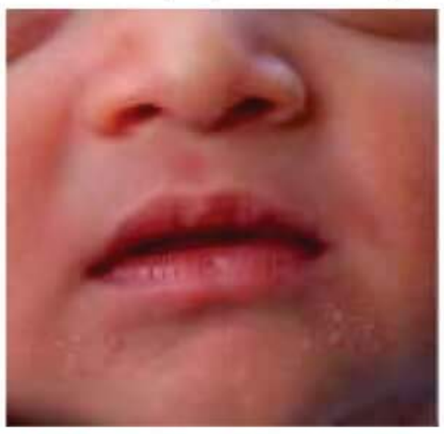
- **NEUROLOGICAL CAUSES**
    1. Erb's palsy [C5, C6 injury]
    2. Congenital hemiplegia
- **SKELETAL CAUSES**
    1. Fracture clavicle
    2. Shoulder joint dislocation

→ **Most common bone to fracture in a neonate** → **CLAVICLE**

IMPORTANT CONDITIONS IN NEONATES NOT REQUIRING ANY SPECIFIC TREATMENT:

SKIN & MUCOSA:

1. **MILIA** → Colourless **papules** d/t plugging of sweat ducts

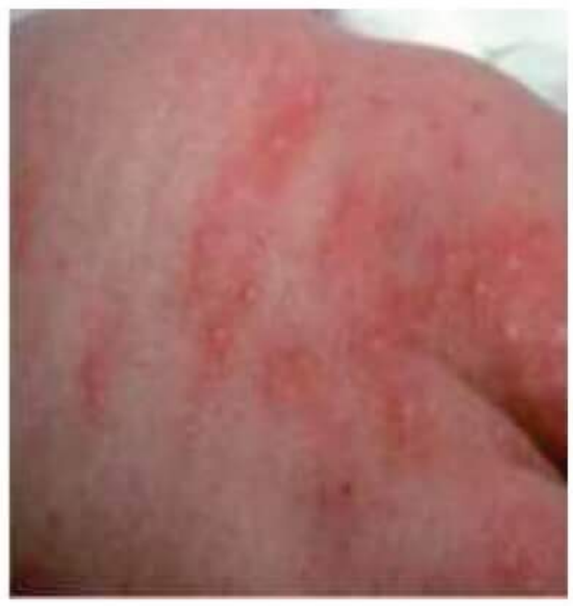


2. **ERYTHEMA TOXICUM NEONATORUM**

→ **Erythematous maculopapular rash** mainly on trunk, seen in 1st week of life

→ d/t immune phenomenon

→ BIOPSY shows Eosinophil filled sterile lesion



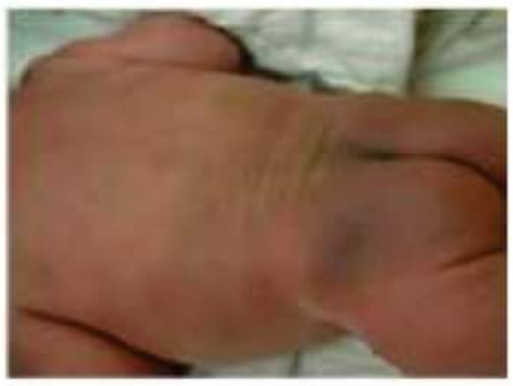
ERYTHEMA TOXICUM

3. **MONGOLIAN SPOTS:**

→ **Bluish black areas** of discoloration

→ Mainly on Lower back, buttocks ,

Back of thighs



MONGOLIAN SPOT

→ d/t migration of **neural crest cells**

4. **STORK BITE/ SALMON PATCH:**

→ **pinkish** colored lesions → capillary hemangiomas

→ In between eye brows/ nape of neck /fore head

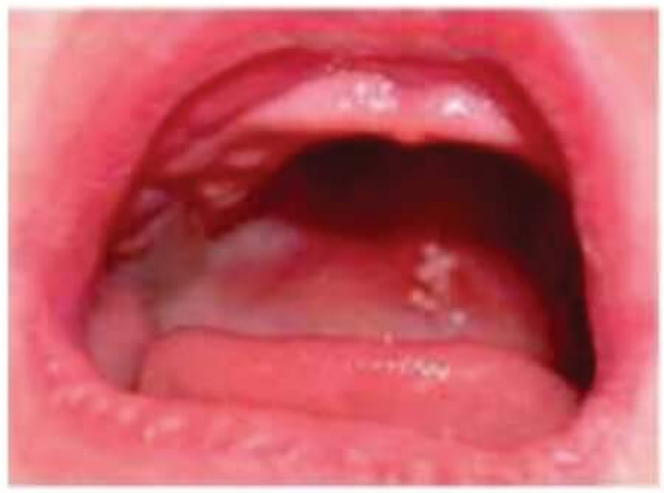
5. EPSTEIN PEARLS:

→ **pearl** like white lesions

→ Hard palate involved

→ epithelial inclusion cysts

EPSTEIN PEARLS



6. ACNE NEONATORUM → d/t maternal androgen

7. SUB CONJUNCTIVAL HEMORRHAGES

8. MASTITIS NEONATORUM:

→ B/L breast engorgement

→ In male/ female neonates

→ D_{2-3} of life

→ d/t effect of maternal hormones

9. VAGINAL BLEEDING:

→ Seen in female Neonates

→ On D3-D5 of life

→ Due to effect of withdrawal of maternal hormones

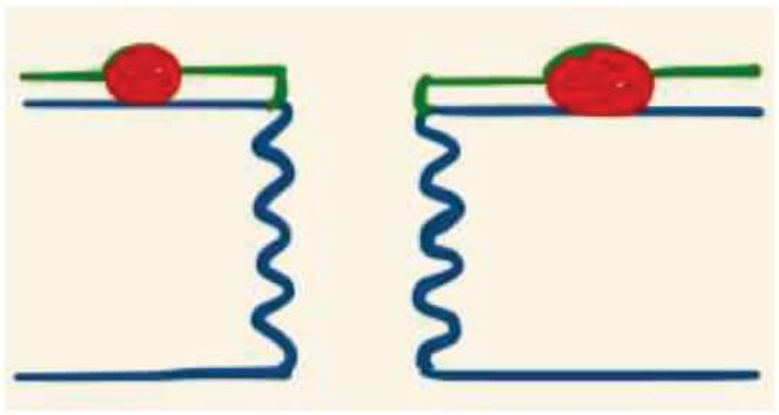
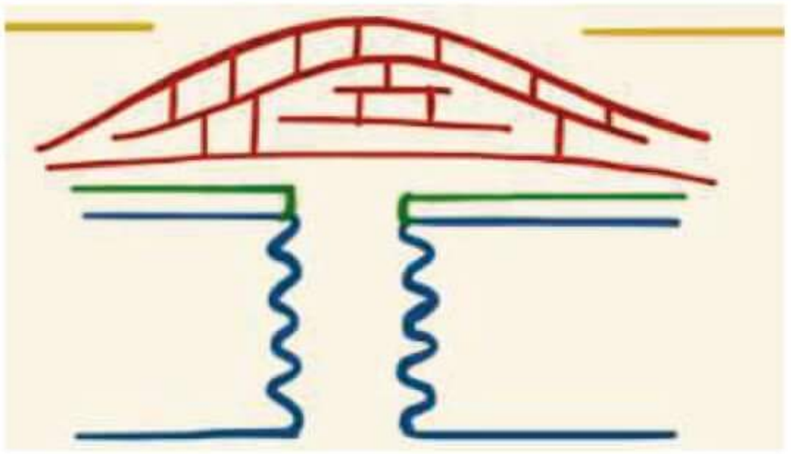
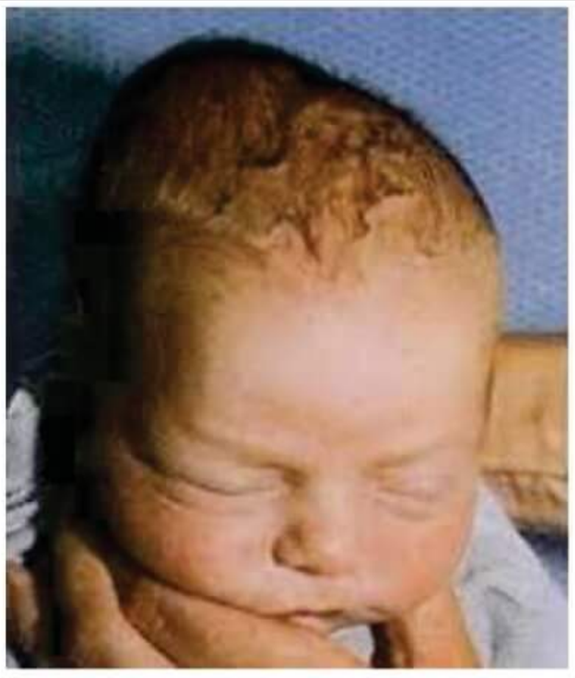
10. HYMENAL TAGS → Skin growth near the vagina opening

11. PHYSIOLOGICAL PHIMOSIS

12. PHYSIOLOGICAL WEIGHT LOSS

→ Term neonates loose upto 10% of birth weight by 3-5 days, regained by D_{10} of life

→ Preterm neonates loose upto 15% of birth weight by 7-10 days, Regained by D_{15} of life

CEPHAL HEMATOMA	CAPUT SUCCEDANEUM
1. Sub periosteal hemorrhage involving cranial bones	1. d/t edema in the layers of scalp
2.  **Does not** cross sutures	2.  Can cross sutures
3. May take 24 hours to appear completely	3. Already present at birth in its maximum size
4. Takes **5-7 weeks** to disappear	4. Disappears by **48-72 hours**
5. Predisposes to neonatal jaundice	5. Does not predispose to neonatal jaundice
	

NEONATAL RESUSCITATION:

NEONATAL RESUSCITATION PROTOCOL:

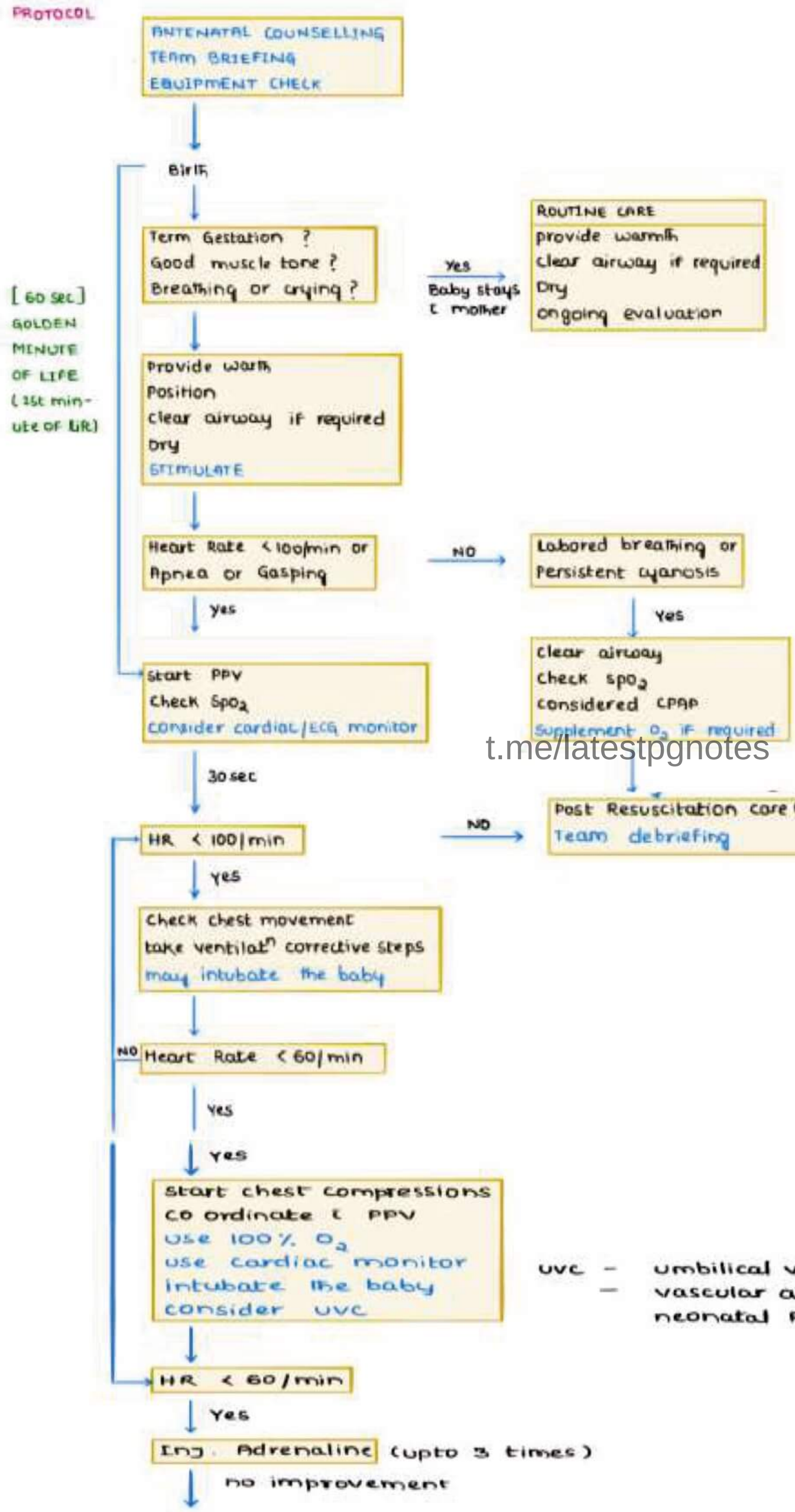
→ Given by **AMERICAN ACADEMY OF PEDIATRICS** (October 2015)

→ 10% of neonates need some resuscitation at birth

→ < 1% require chest compression &/or medications

PROTOCOL

PROTOCOL



UVC – umbilical venous catheterization
– vascular axis of choice during neonatal Resuscitation

Consider → hypovolemia / pneumothorax

→ Hypovolemia → pale, Poor peripheral perfusion, feeble pulses

→ Rx by fluids

- Normal saline [Fluid of choice]

- O group Rh negative blood

- Ringer lactate no longer recommended

→ Pneumothorax

Q suction of Airways → Mouth Followed by Nose

→ Usual size of suction catheter → 12 or 14 f

→ usual pressure of suction → 80 mmHg or 100 cm H_2O [never > 100mm of Hg]

→ Recommended temp. of delivery room → 25° c

→ CPAP → Continuous Positive Airway Pressure

→ PPV → Positive Pressure Ventilation (Bag & mask ventilation)

→ TEAM DEBRIEFING → Question the team members how well they followed the protocol so that they do even better in next time

→ POST RESUSCITATION CARE:

- Start I.V fluids
- Start monitoring the condition of the patient
- Maintain normal temperature
- Maintain normal glucose
- Treatment according to the condition of the baby

RECOMMENDED TARGET O_2 SATURATION:

AGE	TARGET SATURATION
1 minute	60-65%
2 minutes	65-70%
3 minutes	70-75%
4 minutes	75-80%
5 minutes	80-85%
10 minutes	85-95%

POSITIVE PRESSURE VENTILATION:

→ Device used → Self inflating bag & mask **['AMBU' BAG]**

→ Function of reservoir → ↑ O_2 delivered to baby

→ Oxygen delivery depends on O_2 supply & Reservoir

O_2 supply	Reservoir	FiO_2 delivered
–	–	21%
+	–	40%
+	+	90-100%

→ Starts with room air (fio_2 21%) in term neonates

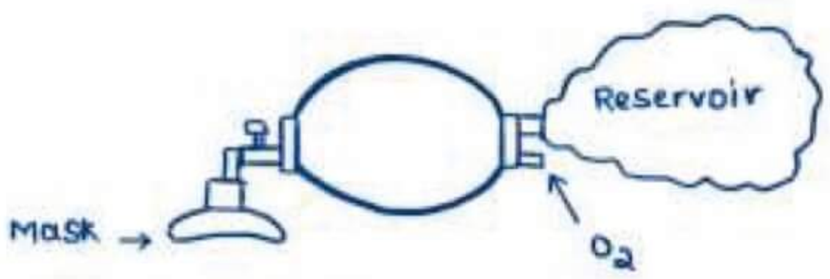
→ Babies born at **< 32 weeks** of gestation → **21-30% fio_2**

→ **Rate** at which PPV done → **40-60 breaths/min**

→ Pressure required to deliver breath to neonate

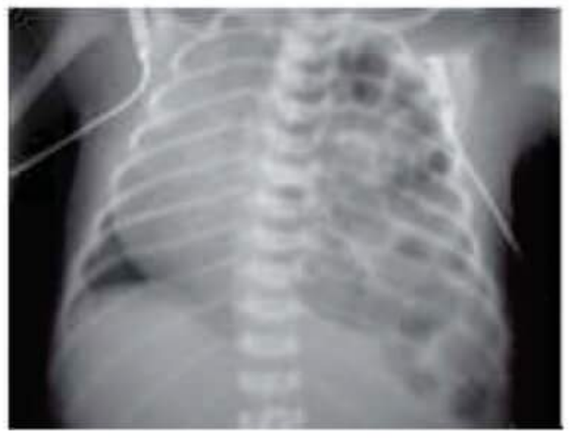
1st breath → **30-40** cm H_2O

Subsequent breaths → **15-20** cm H_2O



Q. Absolute C/I to bag & mask ventilation → **CONGENITAL DIAPHRAGMATIC HERNIA**

CXR FINDINGS:



→ bowel gas shadows in thorax

→ Mediastinal shift

→ Pulmonary hypoplasia

→ **Initiation of PPV** is the single most important step in neonatal resuscitation

Q Most sensitive indicator of effective ventilation → **IMPROVEMENT IN HEART RATE**

VENTILATION CORRECTIVE STEPS:

→ **ENSURE**

- Mask is of appropriate size
- Seal between mask & face should be tight [**E-C CLAMP TECHNIQUE**]
- Head of baby should be slightly **extended**
- Mouth kept slightly open

ENDOTRACHEAL INTUBATION IN NRP:

→ LARYNGOSCOPE [neonatal]:

- With straight blade
- **Size 0 → preterm** neonate
- **Size 1 → Term** neonate

→ ENDOTRACHEAL TUBE SIZE

Birth weight	Gestational age	Size of ET (mm)
< 1000 g	< 28 weeks	2.5 mm
1000-2000 g	28-34 weeks	3 mm
> 2000 g	> 34 weeks	3.5 mm

→ WAYS TO CONFIRM WHETHER ENDOTRACHEAL TUBE IS IN TRACHEA:

1. **B/L** visible **chest rise** with each breath
2. Improvement in vital parameters (H.R, Colour, spo_2)
3. B/L audible breath sounds in chest
4. Misting of ET tube with each breath
5. $ETCO_2$ determination [end tidal CO_2] or CAPNOGRAPHY

→ Recommend method to know whether ET is in Trachea]

→ **CXR-AP view is not useful** for confirming ET tube is in trachea

- It is useful to know the level of ET Tube
  - **Tip of ET Tube** should be at **lower border of body of 2nd thoracic vertebra** in children

CHEST COMPRESSIONS:

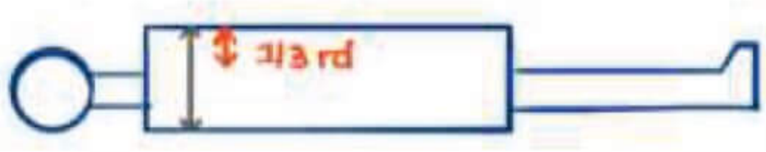
→ SITE → In the midline, on the **lower 1/3rd** of body of sternum (or)

→ In the midline, just **below the line joining 2 nipples**

→ TECHNIQUE → 2 THUMB – ENCIRCLING TECHNIQUE IS PREFERRED OVER 2 FINGER TECHNIQUE

- Because
  - Higher pressure generated
  - Better perfusion
  - Lesser rescuer fatiguability

→ DEPTH: 1/3rd of A.P Diameter of chest



→ RATIO OF CHEST COMPRESSIONS: PPV → 3:1 [90 chest compressions of 30 breaths]

→In 2 seconds → 3 C.C + 1 Breath

INJECTION ADRENALINE:

→ **DOSE** → **0.01** mg/kg/ dose, upto 3 times (0.01-0.03 mg/kg)

Or

0.1 ml/kg/dose of 1:10,000 Adrenaline

→ **1:10,000** → Strength/ concentration of Adrenaline recommended in NRP

→ **PREFERRED ROUTE** → Intravenous through umbilical venous catheter

→ Can be given intratracheally **(0.05-0.1 mg/kg/dose)**, if not able to secure a vascular access

RESUSCITATION OF A BABY BORN THROUGH MECONIUM STAINED LIQUOR (MSL):

Baby born through MSL

↓

Assess

VIGOROUS NEONATE

- HR > 100/ min
- Good muscle tone
- Strong respiratory effort

(-)

NON-VIGOROUS NEONATE

- **DO NOT STIMULATE**
- Put the baby under a warmer
- Do ET intubation & tracheal suction to remove meconium

↓

Proceed as per NRP

- Intra partum suction of mouth & nose, **no longer recommended**

LATEST RECOMMENDATIONS:

→ Routine ET intubation & tracheal suction of all non-vigorous neonates born through MSL is no longer recommended

→ Ensure, at least 1 person, skilled in ET intubation is available at the time of resuscitation of these babies

CONDITIONS IN WHICH DO NOT RESUSCITATE A NEONATE:

1. Anencephaly
2. Confirmed case of Trisomy 13 (Patau syndrome)
3. Gestational Age < **22 weeks**

NEW BORN CARE CORNER SHOULD BE AVAILABLE AT ALL HEALTH FACILITIES WHERE CHILDBIRTH IS TAKING PLACE

DELAYED CORD CLAMPING:

→ Wait for at **least 30 seconds** before clamping umbilical cord

→ Recommended for all stable, term & preterm neonates

→ **ADVANTAGES**:

- Lesser chances of Anemia
- Lesser need of blood transfusion
- Higher **B.P** [lesser chances of shock/hypotension]
- Lesser risk of **NEC** [Necrotizing colitis]
- Lesser risk of **IVH** [Intraventricular haemorrhage]

→ **DISADVANTAGE** → slightly ↑ risk of neonatal jaundice

-A **SINGLE DOSE OF INJ VIT K_1 - 1 mg, Intramuscular** FOR ALL BABIES, AT BIRTH TO PREVENT **'HEMORRHAGIC DISEASE OF NEW BORN'**

-[IF BIRTH WEIGHT < 1 KG, THEN DOSE OF VIT. K → 0.5 mg]

-EARLY INITIATION OF BREAST FEEDING → WITHIN **1 HOUR Of childbirth**

-MAINTAIN NORMAL TEMPERATURE OF THE BABY → **36.5° C - 37.5° C**

-RECORD WEIGHT OF THE BABY

BEFORE DISCHARGE:

→ Immunization -B.C.G, O.P.V, HEP-B

→ Screening for diseases

→ Screen for jaundice

→ Vit. D supplementation (400IU/day)

IUGR AND FEEDING OF PRETERM NEONATE:

DISEASES OF NEWBORN:

More commonly seen in		
PRETERM	SGA/ IUGR	PRETERM/SGA/ IUGR
→ Neonatal sepsis → CNS → intraventricular hemorrhage → area commonly involved → Germinal matrix → Eyes – ROP (Retinopathy Of Prematurity) → Respiratory system- →Respiratory distress syndrome [Hyaline membrane diseases] → Pulmonary hemorrhage → BPD (Bronchopulmonary dysplasia/ chronic lung diseases) → Apnea of prematurity → CVS → PDA (Patent ductus arteriosus) → GI: - Feeding issues - NEC (Necrotizing enterocolitis) - Neonatal jaundice → Anemia of prematurity → Osteopenia of prematurity	→ Polycythemia → Persistent Pulmonary Hypertension Of Newborn → Meconium aspiration syndrome	Hypothermia Hypoglycemia Hypocalcemia Perinatal asphyxia

SGA (Small for gestational age):

→ Birth weight < 10th percentile of expected according to the gestational age.

IUGR (Intra uterine growth restriction):

→ It is a clinical definition

→ Refers to all babies with clinical features of malnutrition or undernutrition like

- ≥ 3 loose skin folds in buttock region
- Emaciated appearance, Peeling of skin

Note:

All SGA babies are IUGR, but all IUGR babies may not be SGA

MORPHOLOGICAL IUGR:

→ Babies with clinical features of malnutrition, but birth weight between **10th – 25th percentile** of expected

→ This baby is **NOT SGA**

SYMMETRIC & ASYMMETRIC IUGR

	Symmetric IUGR	Asymmetric IUGR
1. Time of Insult	1st trimester or early 2nd trimester	Later 2nd or 3rd trimester
2. Usually etiology	→ Genetic → Torch infections	→ Maternal undernutrition → Hypertension → Anemia
3. Effect on cells	No. of cells is ↓	Size of cells are mainly affected
4. Anthropometric parameters	Head circumference, Length, weight Equally affected	Head circumference is usually normal length is less affected than weight
5. Q. Ponderal index (P.I) ↓ Definition: $\frac{Weight\ (g)}{Length\ (cm)3} \times 100$	≥ 2	< 2 Better prognosis

ROP (retinopathy of prematurity):

RISK FACTORS:

1) Prematurity

2) Use of high concentration of O_2

3) Hemodynamically instability

Q. **When to screen for ROP for the 1st time?**

→ At 32 weeks. PMA (Post menstrual age) or 4 weeks postnatal age, whichever is later.

Example:

1) LMP → 26 weeks of gestation + 4 week → 30 weeks (No) PMA → 32 weeks (Yes)

Therefore; will do screening for ROP 6 weeks after birth, for this baby

2) LMP → 30 weeks of gestation + 4 weeks → 34 weeks (Yes)

PMA → 32 weeks (No)

Therefore, will do screening for ROP 4 weeks after birth.

Q Baby born at 28 weeks of gestation, is now 2 weeks old; how much time later will you screen for ROP?

→ LMP → 28 weeks + 4 week's → 32 weeks

PMA → 32 weeks

So, 4 weeks later you will do screen for ROP but baby is already 2 weeks old

Therefore 4 weeks – 2 weeks → 2 weeks

So, in this baby screening for ROP will be done at 2 weeks

FEEDING OF A PRETERM NEONATE:

→ Based on gestational age we decided the preferred initial mode of feeding

Gestational age	Preferred initial mode of feeding	Reason
< 28 weeks	IV fluids ± TPN (total parenteral nutrition)	Gut is too immature
28-31 weeks	Orogastric tube feeding [gavage feeding]	Gut is matured but rooting reflex is not developed
32-34 weeks	Katori spoon feeding or paladai feeding	Coordination between swallowing & breathing not well developed
> 34 weeks	Direct breast feeding.	

Non-nutritive sucking

Trophic feeds

} Can be started even before 34 weeks of gestation if the baby is hemodynamically stable.

NEONATAL SEPSIS:

DEFINITION → Any systemic bacterial infection in a neonate

CLASSIFICATION:

EARLY ONSET SEPSIS:

→ Most commonly seen in 1st 72 hrs of life

→ organisms responsible are usually derived from maternal genital tract like Group B streptococci, E.Coli, Klebsiella

RISK FACTORS:

MOTHER:

→ Maternal fever

→ Foul smelling liquor

→ Pre mature rupture of membranes

DELIVERY:

→ Difficult/ prolonged labour

→ Multiple Per-Vaginal examination

BABY:

→ Low Birth Weight

→ Prematurity

LATE ONSET SEPSIS:

→ Organisms acquired from environment

COMMUNITY ACQUIRED:

- Staphylococcus aureus
- E. coli

HOSPITAL ACQUIRED

- Acinetobacter
- Klebsiella

→ Meningitis is commonly associated

→ **RISK FACTORS:**

- Lack of breast feeding
- Multiple needle pricks
- Superficial infection involving skin or umbilical cord stump
- Low Birth Weight
- Prematurity

6 STEPS OF HAND WASHING

Q. MOST EFFECTIVE/ IMPORTANT METHOD TO PREVENT NEONATAL SEPSIS?

A. **PROPER HAND WASHING OF CARE-GIVERS FOR ATLEAST 2 MINUTES (6 STEPS)**

MOST COMMON ORGANISM RESPONSIBLE FOR NEONATAL SEPSIS:

In India → **Acinetobacter** > klebsiella

In hospitals in India → **Acinetobacter** > klebsiella

In hospitals across the world → **E.coli**

Overall throughout the world → **Group B- streptococcus**

Early onset sepsis (world) → **Group B- streptococcus**

CLINICAL FEATURES:

→ Poor feeding or alteration in established feeding behaviour (earliest)

→ Temperature disturbances (Hypothermia > fever)

→ **Respiratory** → Dyspnea, Hypoxia, Tachypnea

→ **CNS** → Shrill cry, Irritability, Seizures

→ **GI** → Abdominal distension, feed intolerance

→ **Metabolic** → Hypoglycemia, Acidosis

→ **Severe sepsis:**

- Septic shock
- Multiple organ dysfunction
- **Sclerema:** Generalized, non-pitting edema seen in neonates with severe sepsis/ severe hypothermia

DIAGNOSIS:

DEFINITIVE TEST → BLOOD CULTURE

SCREENING TEST → SEPSIS SCREEN

Components → Any **2** out of **5** → +ve sepsis screen

1. **TLC** [Total Leucocyte Count] → **< 5000/mm^3**

2. **ANC** (Absolute Neutrophil Count) → **< 1800/mm^3**

3. **I-T ratio** [Immature: Total neutrophil] → **> 0.2**

4. **Micro ESR** → **>15 mm**

5. **CRP** [C-Reactive Protein] → **> 1mg/dl**

has **High Negative Predictive Valve**

SUPPORTIVE TESTS:

→ Blood glucose

→ CXR

→ Lumbar puncture & CSF study

TREATMENT:

1. SUPPORTIVE CARE

→ Shift to Nursery/ NICU

→ Start IV fluids

→ Maintain normal blood glucose

→ Maintain normal temperature

→ Monitor

2. SPECIFIC TREATMENT:

→ I.V Empirical broad Spectrum antibiotics

- [Inj. Ampicillin + Gentamicin] + [Inj. Cefotaxime, if meningitis presents or suspected]

Sepsis screen	Blood culture	CSF S/O meningitis	Duration of Antibiotics
+	–	–	1 week
±	+	–	2 weeks
±	±	+	3 weeks

NEONATAL HYPOTHERMIA:

DEFINITION → **Axillary temperature < 36.5° C** in a neonate

Q. For how much time should thermometer be kept in axilla, to record temperature accurately → minimum

3 minutes

CLASSIFICATION		AXILLARY TEMPERATURE
Cold stress	→	36 – 36.4° c
Moderate hypothermia	→	32 – 35.9° c
Severe hypothermia	→	< 32° c

Q **Clinical Definition of Cold Stress**– **abdomen** is warm but **soles** are cold to touch

Q. **Hypothermia is more common in neonates, why?**

→ Larger surface area as compared to their body weight

- **maximum heat loss** takes place from head

→ Lesser subcutaneous fat especially in preterm/ SGA/ IUGR

→ Vulnerability to get exposed

→ **Shivering** is **absent**

WAYS BY WHICH NEONATES PROTECT THEMSELVES AGAINST HYPOTHERMIA:

1. NON-SHIVERING THERMOGENESIS: → **most important**

→ d/t the presence of **Brown fat**

→ Lipid deposits richer in **mitochondria**

→ Areas richer in brown fat are

- Axilla
- Groin
- Nape of neck
- Interscapular area , around the kidneys & major blood vessels of abdomen

MECHANISM:

Baby exposed to cold environment

↓

Sympathetic stimulation

↓

Release of **Norepinephrine**

↓

Uncoupling of β oxidation of Fat

↓

Heat generated

2. CUTANEOUS VASOCONSTRICTION: when exposed to cold temperature

3. FLEXED POSTURE

4. HIGHER HEART RATE IN NEONATES → more heat generation

C/F:

-Acidosis
-Hypoglycemia } Multiorgan dysfunction
-Hypoxia

PREVENTION/ TREATMENT

i) WARM CHAIN to prevent Neonatal Hypothermia

→ Thermal care in delivery room (~25° C)

→ Warm resuscitation

→ immediate drying of baby

→ Skin to skin contact

→ Early initiation of breast feeding

→ Bathing postponed

→ Clothing & bedding

→ Rooming in

→ Warm transportation (weakest link)

→ Training & awareness

ii) DEVICES USED:

RADIANT WARMER	INCUBATOR
	
Most important mechanism by which baby gets heated	
Radiation	Convection
Most important mechanism by which heat loss occurs	
Convection	Radiation

iii) **KANGAROO MOTHER CARE**

→ Skin to skin contact between the baby & mother/ care giver

→ **INDICATION** → For all stable LBW Neonates

→ **COMPONENTS:**

- Skin to skin contact → **kangaroo position**
- Exclusive breast feeding
- Early discharge from hospital

→ **ADVANTAGES**

→ Lesser risk of hypothermia

→ Lesser risk of nosocomial infections

→ Lesser risk of neonatal mortality

→ ↑ breast milk output

→ Higher exclusive breastfeeding rates

→ Shortens length of hospital stay

→ Maternal child bonding

Q **Normal** temperature of neonate → **36.5 – 37.5° c**

Q Recommended **Delivery room** temperature → **25° c**

Q Recommended Nursery/ **NICU** temperature → **22 – 26° c**

Q **mcc of neonatal mortality in India** → **Prematurity**

*__Temperature__ of __non-asphyxiated neonates__ is a **strong predictor** of neonatal mortality at __all gestational ages.__

THERMONEUTRAL ENVIRONMENT:

→ Range of temperature in which a neonate has minimum BMR, least O_2 requirement & still the baby is able to maintain a normal body temperature

NEONATAL HYPOGLYCEMIA:

DEFINITION → __Blood__ glucose **< 40 mg/dl** or __plasma__ glucose **< 45 mg/dl**

HIGH RISK NEONATES FOR HYPOGLYCEMIA:

1. SFD (small for date)
2. Preterm neonates
3. IUGR
4. Infant of diabetic mother
5. Large of date neonates
6. Neonatal sepsis
7. Neonatal hypothermia

→ Regular blood glucose monitoring is recommended in high risk neonates at regular intervals (2 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours of life)

C/F:

→ **JITTERINESS** > TREMORS → **most common**

→ Neonatal seizures

→ Cyanosis

→ apnea

→ Lethargy

→ Poor feeding

→ ↑ sweating

TREATMENT:

SYMPTOMATIC:

→ IV **10% dextrose @ 2ml/kg** stat bolus

↓

Continuous IV fluids (GIR @ **6 mg/kg/min**)

↓

Monitor blood glucose; titrate Intra Venous Fluid according to Blood Glucose

ASYMPTOMATIC:

1. **< 20 mg/dl** → Rx as symptomatic case

2. **20 – 40 mg/dl**

→ offer a feed to baby & recheck Blood Glucose after ½ hr – 1 hr

- **CASE 1** → Blood Glucose still **low** → Rx as symptomatic case
- **CASE 2** → Blood Glucose is **normal** → Continue frequent feeding & Blood Glucose monitoring

PERSISTENT HYPOGLYCEMIA

➔ IMPORTANT CAUSES DURING INFANCY

ENDOCRINE CAUSES

1. Congenital hypopituitarism
2. Congenital adrenal insufficiency
3. Congenital **hyper insulinemia** (or) **Nesidioblastosis** (or) **PHHI** (Persistent Hyperinsulinemic hypoglycemia of Infancy)

- Its **mcc of persistent hypoglycemia during infancy**
- **Drugs** used in Rx
  - Diazoxide
  - Octreotide
  - Glucagon
  - Nifedipine
- **Surgery** in focal cases

METABOLIC CAUSES:

1. Glycogen storage disorders [eg- von gierke disease]
2. Galactosemia
3. Hereditary fructose intolerance
4. Mitochondrial disorders
5. Fatty acid oxidation defect

INFANT OF DIABETIC MOTHER:

PATHOPHYSIOLOGY:

PEDERSON'S MATERNAL HYPERGLYCEMIA/ FETAL HYPERINSULINEMIA HYPOTHESIS

Maternal Hyperglycemia

↓

Fetal Hyperglycemia

↓

Fetal hyperinsulinemia → NEONATAL HYPOGLYCEMIA

Insulin Acts As A Growth Factor For Fetus

MACROSOMIA/ LFD

-all organs ↑ in size in IDM

except brain

-**Hairy pinna** **+nt** in IDM

↑ED EXTRA MEDULLARY HEMATOPOIESIS

POLYCYTHEMIA

NEONATAL HYPERBILIRUBINEMIA

PROBLEMS IN IDM

i) **MACROSOMIA/ LARGE FOR DATE BABY:**

→ Difficult/ prolonged labour

→ Perinatal asphyxia

→ ↑ ed chances of birth trauma

ii) **METABOLIC:**

→ Hypoglycemia

→ Hypocalcemia

→ Hypomagnesemia

→ Polycythemia

→ Neonatal jaundice

iii) **RESPIRATORY SYSTEM:**

→ More chances of RDS d/t delayed maturation of surfactant

iv) **CVS**:

→ mc **congenital** abnormality in IDM → **C.H.D** [Congenital heart disease]

→ mc **congenital heart disease** in IDM → **V.S.D**

→ most **specific congenital heart disease** in IDM → **TGA**

v) **CNS:**

→ mc **congenital neurologic** abnormality in IDM → **Neural tube defect**

→ Most **specific neurologic** abnormality in IDM → **Sacral agenesis** or caudal regression syndrome.

→ **Overall most specific** congenital abnormality in IDM → **Sacral agenesis** or caudal regression syndrome

vi) **RENAL** → renal agenesis

→ duplication of ureter

→ Renal vein thrombosis

vii) **GI** → Duodenal atresia

→ **Lazy (small) left colon** syndrome

viii) **LONG TERM PROBLEMS** ["**BOND**"]

→ **B**lindness

→ **O**besity

→ **N**on ketotic hypoglycemia

→ **D**iabetes mellitus

PERINATAL ASPHYXIA [BIRTH ASPHYXIA]:

→ Inability to initiate or sustain breathing

Hypoxia Hypercapnia Acidosis	→	Multiorgan dysfunction especially CNS (HIE hypoxic ischemic encephalopathy)

HIE [HYPOXIC ISCHEMIC ENCEPHALOPATHY]:

Part of brain mc involved in HIE in:

Term neonates → **Para sagittal area** → **Spastic Quadriplegia** (Type of cerebral palsy)

pre term neonates → **Periventricular** area → Periventricular Leukomalacia (PVL) → **Spastic diplegia**

DIAGNOSTIC CRITERIA FOR SEVERE BIRTH ASPHYXIA:

→ **APGAR SCORE**: 0-3 for > 5 minutes

→ Severe acidosis (**cord blood** pH **< 7.0**)

→ Any clinical evidence of **CNS** dysfunction

- Tone abnormalities, seizures etc

→ Any evidence of dysfunction of **atleast 1 organ** other than CNS

- Eg: Renal → Acute Tubular necrosis; Heart → myocardial dysfunction

STAGING OF HIE:

	Stage 1	Stage 2	Stage 3
1. Level of consciousness	Hyper alert	Normal/ depressed	Comatosed
2. Tone	Normal	Mild hypotonia	Severe hypotonia
3. Moro's reflex	Exaggerated	Normal/ depressed	**Absent**
4. Seizures	Not seen	**Present**	Not seen
5. Autonomic involvement	-Generalized sympathetic overactivity -**mydriasis** -↑ Heart rate	-Generalized parasympathetic over activity -**Miosis** -**Bradycardia**	-Both systems are depressed -pupils mid dilated -variable HR
6. Outcome	99% normal	80% Normal	50% die 50% severe neurological sequelae

TREATMENT OF HIE:

1. SUPPORTIVE RX:

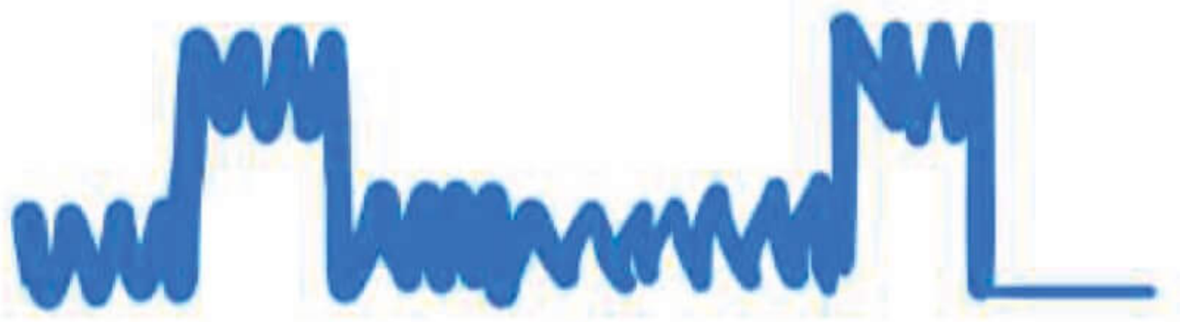
→ NICU

→ IVF

→ (N) Blood glucose & temperature

→ Monitor

- **Tool** used for **bedside monitoring** of neonates with HIE → a **EEG (Amplitude Integrated Electro encephalogram)**



2. LATEST RX MODALITY OR MODERATE TO SEVERE HIE IN NEONATES

→ THERAPEUTIC HYPOTHERMIA → Temp. maintained is → 33.5° c – 34.5° c

3. NEONATAL SEIZURES

→ DOC → phenobarbitone

→ mc type → subtle seizures

→ mc cause → hypoxia

→ Type with best prognosis → Focal clonic seizures

→ Types with worst outcome → myoclonic seizures

→ Preferred initial CNS imaging → Transcranial ultrasound

IMPORTANT SCORES IN NEONATES:

APGAR SCORE

Components	0	1	2
Appearance	Completely blue or pale	Body pink but extremities are blue	Completely pink
Pulse rate	Absent	< 100 min	>100min
Grimace*	No response	Grimaces only	Coughs/ sneezes
Activity	Limp/ flaccid	Some flexion	Actively moving baby
Respiratory effort	None	Slow & irregular	Normal/ strong

***Grimace** → Response to stimulation of oropharynx by a catheter

APGAR score: **Maximum** score → **10** & **minimum** score → **0**

→ **> 7 score** → **Normal**

→ **0 – 3** score → **Severe birth asphyxia**Q

→ APGAR score is usually documented at **1 minute** & **5 minutes** of life

→ Has **no role in neonatal resuscitation**

→ It has **prognostic importance**

SCORES USED TO ASSESS RESPIRATORY DISTRESS IN A:

Preterm neonate → **SILVERMAN** score

Term neonate → **Downe's** score

SILVERMAN SCOREQ

Components	0	1	2
Upper chest retractions	Chest & abdomen rise together	Chest wall lags behind abdomen	Chest wall & abdomen move in opposite direction (see saw)
Lower chest retractions	Absent	Minimal	Marked
Xiphisternal retractions	Absent	Minimal	Marked
Nasal flare	Absent	Minimal	Marked
Grunt	None	Audible only with stethoscope	Audible without stethoscope

→ **maximum** score → **10** & **minimum** score → **0**

→ 0-3 score → Normal; **> 7 score** → **Severe Respiratory Distress**

DOWNE'S SCORE:

COMPONENTS (score → 0, 1, 2)

- ➔ Cyanosis
- ➔ Air entry
- ➔ Respiratory rate
- ➔ Grunt
- ➔ Retractions

RESPIRATORY DISORDERS IN NEONATES:

RESPIRATORY DISTRESS SYNDROME/ HYALINE MEMBRANE DISEASE:

→ Mc cause of respiratory distress in a preterm neonate

- BASIC DEFECT → deficiency of mature surfactant
- SURFACTANT :

  COMPOSITION:

  → DPPC [Di palmitoyl phosphatidyl choline] or lecithin [most imp.]

  → Phosphatidyl glycerol

  Cholesterol

  Surfactant proteins → A, B, C, D

*B → most important surfactant protein

SYNTHESIS:

→ **begins** in **fetal lungs** → 20 weeks gestation

→ Begins to appear in **amniotic fluid** → 28-32 weeks of gestation

→ **mature surfactant** in adequate amount → > 35 weeks of gestation

FUNCTION:

→ To ↓ surface tension of alveoli (or)

→ To prevent alveoli from collapsing during expiration

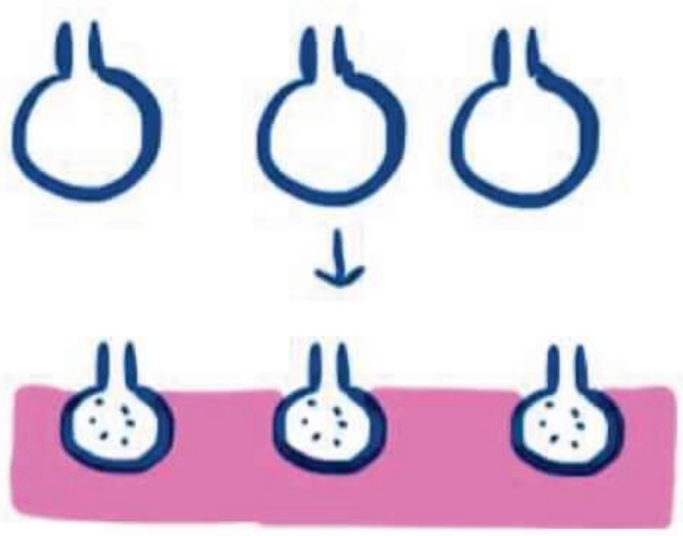
PATHOPHYSIOLOGY OF RESPIRATORY DISTRESS SYNDROME:

Deficiency of mature surfactant

↓

Alveolar collapse
Diffuse alveolar damage
Interstitial edema
Fibrin deposition

→ Eosinophilic **Hyaline Membrane** appearance on **Lung Biopsy**



C/F → A preterm neonate born at **< 35 weeks** of gestation presenting with respiratory distress soon after the birth with typical CXR finding

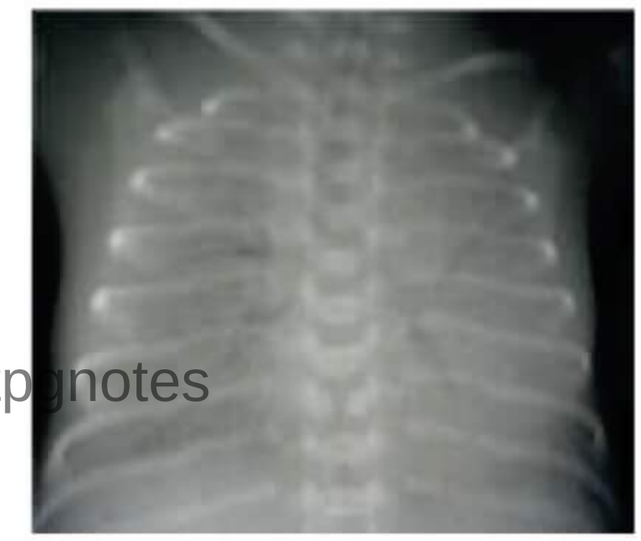
CXR FINDINGS IN RDS:

→ **Ground glass haziness** of lungs

→ Presence of **air bronchogram**

→ Reticulo**granular** or reticulo**nodular** appearance

→ Features of **lung collapse**



DIAGNOSIS:

1. C/F

2. CXR finding

3. **Ways to detect adequacy of surfactant in amniotic fluid:**

   → **L:S Ratio** (Lecithin : sphingomyelin ratio) = **2:1** → mature surfactant
   → **Phosphatidyl glycerol** estimation
   → **Nile blue sulfatase** test → to detect **lung maturity**
   → Shake test

SHAKE TEST:

2. Specific Treatment

a. **Mild RDS** → CPAP (continuous positive airway pressure)

b. **Moderate** → severe RDS

→ Intra Tracheal Surfactant + Respiratory support [CPAP/ mechanical ventilation + O_2]

PREVENTION OF RDS:

ANTENATAL CORTICOSTEROIDS:

→ INDICATION:

- To all pregnant ladies who are expected to deliver between **24 -34 weeks**

→ STEROID OF CHOICE:

- **Inj. Betamethasone** → 12 mg I.M, 2 doses, 24 hrs apart [12x2 = 24] (or)
- **Inj. Dexamethasone** → 6 mg I.M, 4 doses, 12 hrs apart
- Inj. Betamethasone has slightly **Neuroprotective Effect** → Steroid of choice
- Recommended by Indian government → **Inj. Dexamethasone**→ Cheaper & easily available, equally efficacious

→ BENEFICIAL EFFECTS:

- Decrease **RDS**
- Decrease **NEC**
- Decrease **IVH**
- Decrease **neonatal mortality**

→ Does not decrease the risk of neonatal jaundice

NEONATAL PULMONARY ALVEOLAR PROTEINOSIS:

BASIC DEFECT → d/t **deficiency** of Surfactant Protein b

→ Function of surfactant protein B → Forms a thin layer of surfactant in the inner layer of alveoli

CLINICAL FEATURES:

→ A **term** neonate presenting with **severe respiratory distress** soon after birth with CXR showing ground glass haziness

→ No improvement with surfactant therapy

→ H/O similar illness in a previous sibling who died **(Family History)**

MECONIUM ASPIRATION SYNDROME (MAS):

MECONIUM: 1st stool passed by a neonate; **greenish black** in colour; sterile; comprises of

→ Amniotic fluid

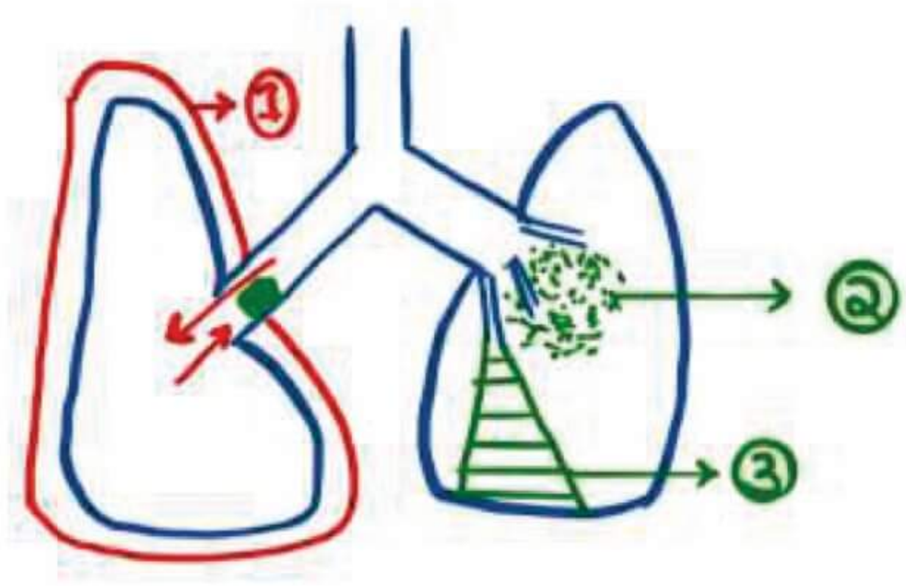
→ Bile

→ Mucus

→ Lanugo

→ Denuded interstitial epithelial cells

→ Water



PATHOPHYSIOLOGY:

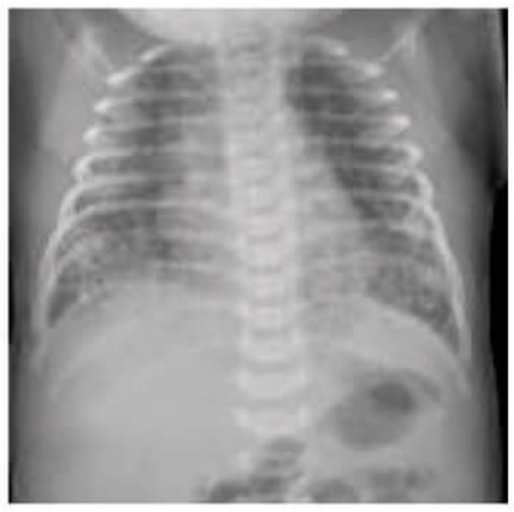
1. Obstructive emphysema [mc & most important]
2. Chemical pneumonitis
3. Segmental collapse or atelectasis

CLINICAL FEATURES:

→ A term SGA/ IUGR baby, born through meconium stained liquor, presents with respiratory distress soon after birth

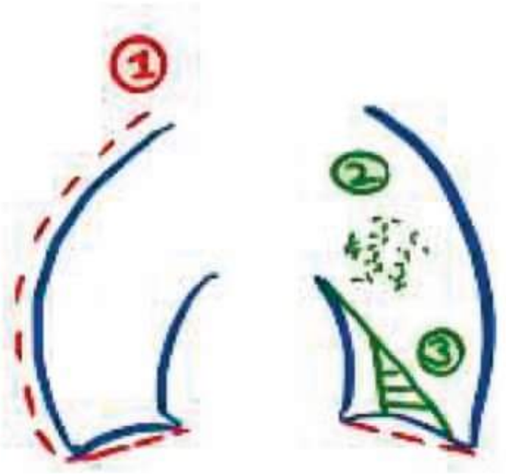
→ **O/E** → AP diameter of chest increased

→ Typical CXR findings



CXR IN MAS:

1. **Hyper inflated lungs** → ↑ ed radiolucency of lungs
   -> flattening of domes of diaphragm
2. Pulmonary infiltrates
3. Segmental collapse



TREATMENT

→ mainly supportive including respiratory support (O_2 ± mechanical ventilation)

→ **In severe cases:**

- Intra tracheal **surfactant**
- **iNO (inhaled Nitric oxide)**

- **High frequency ventilation**
- **ECMO** [Extra Corporeal Membrane Oxygenation]

COMPLICATIONS:

1. Pneumothorax

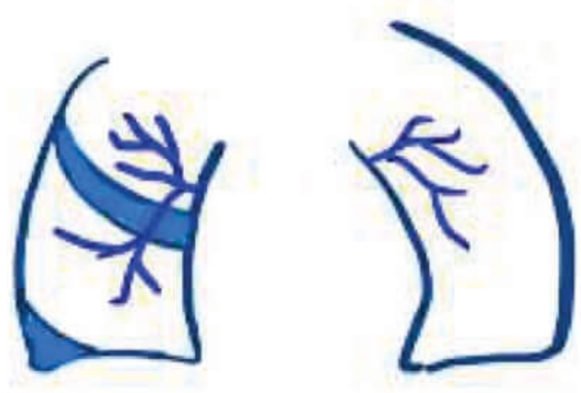
2. PPHN [Persistent pulmonary HTN of New Born]

TTNB [TRANSIENT TACHYPNEA OF NEW BORN]/ DELAYED ADAPTION

Q. MCC of respiratory distress in a term neonate

BASIC DEFECT → Delayed clearance of lung fluids

RISK FACTOR → Delivery by caesarean section



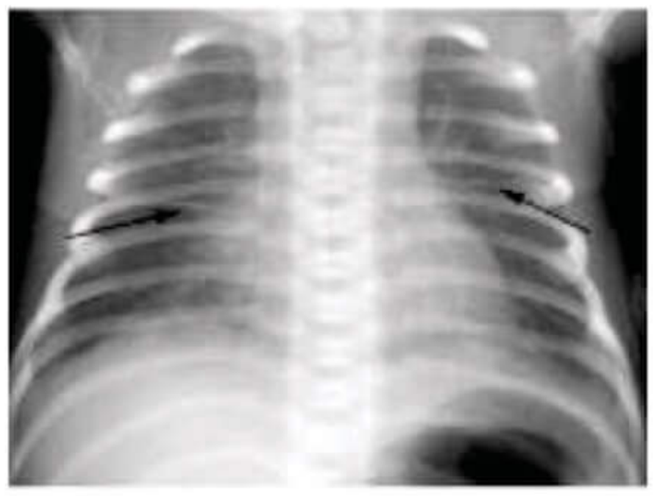
CLINICAL FEATURES:

→ Term/ post term neonates

→ Born by caesarean section

→ Presents with mild respiratory distress, soon after birth that improves Spontaneously in 72 hrs with typical CXR findings

CXR FINDINGS:



- Fluid in **interlobar** fissure
- Pleural effusion
- Perihilar streaking [d/t prominent Broncho vascular marking]

TREATMENT:

→ Mild & self-limiting illness

→ usually no Rx required

→ Distress usually resolves spontaneously in **48-72 hours**

NEONATAL APNEA:

DEFINITION → Cessation of breathing for **atleast 20 sec** or for any duration, in the presence of **bradycardia** or **cyanosis**

IMPORTANT CAUSES:

1. Neonatal sepsis
2. Neonatal hypothermia
3. Neonatal hypocalcemia

4. Neonatal hypoglycemia
5. Polycythemia
6. Neonatal jaundice
7. NEC
8. Apnea of prematurity

→ More preterm the neonate → more chances of apnea of prematurity

→ It is a diagnosis of exclusion

TREATMENT:

1. Respiratory support [CPAP or mechanical ventilation]

2. Look for the cause & treat it

→ **IV antibiotics** for neonatal sepsis

→ **Warm up** for N. hypothermia

→ IV **Ca gluconate** for N. hypocalcemia

→ IV 10% **dextrose** for N. hypoglycemia

→ partial exchange transfusion with normal saline [RxOC] for polycythemia

→ Inj. **Caffeine citrate** [DOC]
Inj. Aminophylline
} for apnea of prematurity

NEONATAL HYPOCALCEMIA:

	Total Ca	Ionised ca
In a **term** neonate	< 8 mg/dl	< 1.2 mmol/L
In a **preterm** neonate	< 7 mg/dl	< 1 m.mol/L

POLYCYTHEMIA:→ Hb > 22 g/dl or Hematocrit > 65% in neonate

BRONCHO PULMONARY DYSPLASIA/ CHRONIC LUNGS DISEASE [CLD]:

Most commonly affects babies born at < 28 weeks of gestation or with birth weight < 1000 gms d/t atelectotrauma, volutrauma, free radicals

DEFINITION:

→ BPD is defined for babies born at **< 32 weeks** gestation, who require **O_2 for 1st 28 days** for their life.

→ Assessed at 36 weeks of PMA [post menstrual age]

→ **Mild BPD** → *No supplemental oxygen required*

→ **Moderate BPD** → *Oxygen required* **< 30%**

→ **Severe BPD** → *oxygen required* **> 30%** / *CPAP / Mechanical ventilation*

CONGENITAL DIAPHRAGMATIC HERNIA:

What is it:

→ *A diaphragmatic defect through which abdominal contents may herniate into thorax*

⊕

→ **Pulmonary hypoplasia**; *Intestinal malrotation*

ASSOCIATED WITH: *Esophageal atresia, Congenital heart diseases, Omphalocele, Trisomy 13, 18*

-Mc type → *posterolateral or Bochdalek variety*

-Mc on **left** *side; Mc in* **females**

CLINICAL FEATURES:

AT Birth, usually presents with a TRIAD:

- *Respiratory distress*
- *Scaphoid abdomen*
- *Mediastinal shift*

Later in life → *Intestinal obstruction*

DIAGNOSIS:

1. *C/F*

2. *Antenatal USG [between 16-24 weeks]*

3. *CXR*

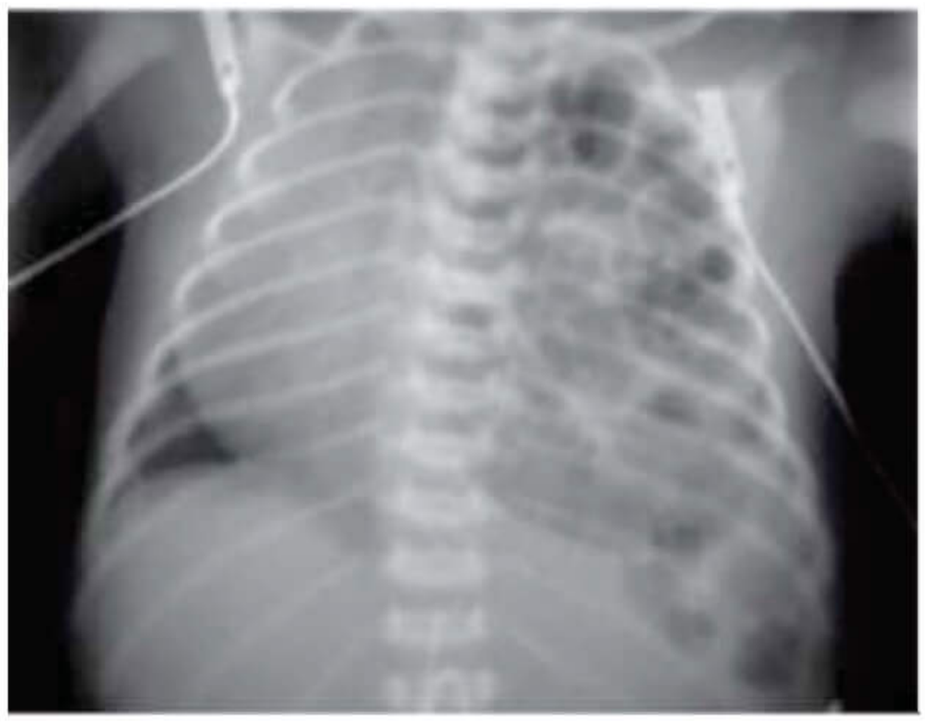
→ **Bowel gas shadows** *in thorax*

→ *mediastinal shift*

→ *Pulmonary hypoplasia*

TREATMENT:

CONGENITAL DIAPHRAGMATIC HERNIA



MEDICAL MANAGEMENT:

Baby with known/ suspected CDH

↓

Severe respiratory distress

Yes

Do Endotracheal intubation

↓

Suspicion of esophageal Intubation (max. cardiac Impulse shifted to right)

↓

1. Confirm position of ET [not by CXR]
2. Remove ET & reintubate

→ Bag & mask ventilation is absolutely C/I

ET in trachea

NO

insert a NG tube

3. CXR to confirm DX

Surgery

PREDICTORS OF POOR OUTCOME IN CONGENITAL DIAPHRAGMATIC HERNIA:

1. Severe pulmonary hypoplasia
2. Lung head ratio [HR] < 1
3. Any malformation associated
4. Symptoms in 1st 24 hrs
5. Liver into thorax
6. ECMO need

Q Mc Cause of mortality in CDH → pulmonary complications/ hypoplasia

NECROTISING ENTEROCOLITIS:

→ Acute intestinal necrosis of unknown etiology

→ **RISK FACTORS:**

1. Pre maturity [single greatest risk factor]→ mean gestational age 30-32 weeks ; 10% cases occur in term neonates
2. Aggressive use of formula feeding
3. Fetal hypoxia
4. Maternal cocaine abuse
5. Absent or reversed end diastolic flow in the umbilical artery on antenatal USG

→ Part of intestine **mc involved** → **Terminal ileum & ascending colon**

MODIFIED BELL'S STAGING OF NEC:

STAGE I [NEC SUSPECT]:

GENERAL FEATURES:

→ Temperature disturbances
→ Apnea
→ Lethargy

ABDOMINAL FEATURES: → Feed intolerance

INVESTIGATIONS:

1. **Abdominal X ray**

→ Normal (or)

→ Mild distention

2. **Stool examination**

→ I_a – **occult** blood in stool

→ I_b – **Fresh** blood in stool

TREATMENT:

→ NPO
→ IV fluids
→ IV antibiotics

} 48-72 hrs & reassess

STAGE II [DEFINITE NEC]:

GENERAL FEATURES:

→ Same as above

ABDOMINAL FEATURES:

→ Absent bowel sounds

→ mild abdominal distention

INVESTIGATIONS:

1. Abdominal X ray

→ IIa → Pneumatosis intestinalis

[air in the wall of intestine]

→ II b → portal vein gas

TREATMENT:

→ NPO
→ IVF + TPN
→ IV antibiotic

} 7-10 days & reassess

STAGE III [Advanced NEC]

GENERAL FEATURES:

→ Shock

→ Bleeding

→ Recurrent

→ Life threatening apnea

ABDOMINAL FEATURES:

→ Abdomen hugely distended & tender

→ Abdominal wall cellulitis

INVESTIGATIONS:

1. Abdominal x ray

→ IIIa → Peritonitis

→ III b → pneumoperitoneum

2. Blood examination

→ Severe acidosis

→ Hyponatremia

→ Refractory thrombocytopenia

Prognosis → 10-30% risk of mortality despite best supportive care

TREATMENT:

→ Same as stage II ⊕

→ IV fluid boluses

→ Inotropes

→ Blood products

→ Mechanical ventilation ⊕

→ Surgery in **III b**

NEONATAL JAUNDICE:

→ Clinical jaundice in neonates is seen at **bilirubin level** ≥ **5 mg/dl**

→ 60 % of term neonates & 80% of preterm neonates have clinical jaundice in **1st week of life**

PHYSIOLOGICAL JAUNDICE	PATHOLOGICAL JAUNDICE
1. Icterus / clinical jaundice never appear in 1st 24 hrs of life	1. May appear in 1st 24hrs of life
2. Always unconjugated; urine does not stain diapers & no pale stools	2. May be conjugated/ unconjugated High colored urine +/- Pale stools may be seen
3. Palms & soles never stained yellow	3. Palms & soles may be stained yellow
4. Clinical jaundice does not persist beyond 2 wks in term neonates & 3 wks in preterm neonates	4. May persist beyond 3 weeks

PHYSIOLOGICAL JAUNDICE:

Reasons

1. Higher production of bilirubin

→ Higher Hb level in neonates

→ Shorter life span of RBCs (90 days vs 120 days)

→ More ineffective erythropoiesis

2. Ineffective carrier mediated uptake of bilirubin by liver
3. Immature **UDP Glucuronyl transferase enzyme** activity
4. ↑sed enterohepatic circulation in neonates

BREAST FEEDING JAUNDICE	BREAST MILK JAUNDICE
→ d/t inadequate breast feeding ↓ Dehydration ↓ Relative polycythemia ↓ Higher bilirubin level	→ d/t substances present in breast milk like pregnanediol & free fatty acids, that interfere with the conjugation of bilirubin

→ **Rx** : Frequent breast feeding	→ **Rx:** Continue breast feeding. Unless the bilirubin level is > 20 mg/dl, when breast feeding only be temporarily withheld.

IMPORTANT CAUSES OF UNCONJUGATED HYPERBILIRUBINEMIA:

↑ PRODUCTION OF BILIRUBIN	↓ CONJUGATION OF BILIRUBIN
1. Hemolytic disorder → Erythroblastosis fetalis [Hemolytic disease of newborn] – MC cause of neonatal jaundice in 1st 24 hrs of life → Hereditary spherocytosis → G6PD deficiency	1. Crigler Najjar syndrome → Deficiency of **UDP glucuronyl transferase** enzyme → **Type I** → **Complete** deficiency → **Type II** → Partial deficiency
2. Polycythemia	2. Gilbert syndrome
3. Delayed cord clamping	3. Down syndrome
4. Cephalhematoma	4. Congenital hypothyroidism

CONJUGATED HYPERBILIRUBINEMIA:

CONJUGATED BILIRUBIN → > 2 mg/dl (or) 20% of total bilirubin

IMPORTANT CAUSES:

NON-OBSTRUCTIVE CAUSES:

1. **Infections**

→ Viral → EBV, CMV, hepatitis
→ Bacterial → Congenital TB [Ghon focus seen in liver], syphilis
→ Parasitic → Toxoplasmosis

2. Toxins → Sepsis, UTI, TPN
3. Metabolic → α1 anti-trypsin deficiency
   Cystic fibrosis
   Tyrosinemia
   Galactosemia
   Hereditary fructose intolerance
4. Idiopathic neonatal hepatitis

→ MC cause of conjugated hyperbilirubinemia in neonates

OBSTRUCTIVE CAUSES:

INTRA HEPATIC CAUSES	EXTRA HEPATIC CAUSES
1. Congenital hepatic fibrosis	1. Extra hepatic biliary atresia (EHBA)
2. Caroli's disease	2. Choledochal cyst
3. Progressive familial intra hepatic cholestasis [PFIC]	3. Stones
4. Alagille syndrome → Triangular facies	4. Stricture

→ Pulmonary stenosis → Butterfly vertebrae	
5. Dubin Johnson syndrome → Pigmented liver [Dark liver]	5. Mass
6. Rotor syndrome	

→ **Screening** test for EHBA → **HIDA Scan** (or) **hepatic scintigraphy**

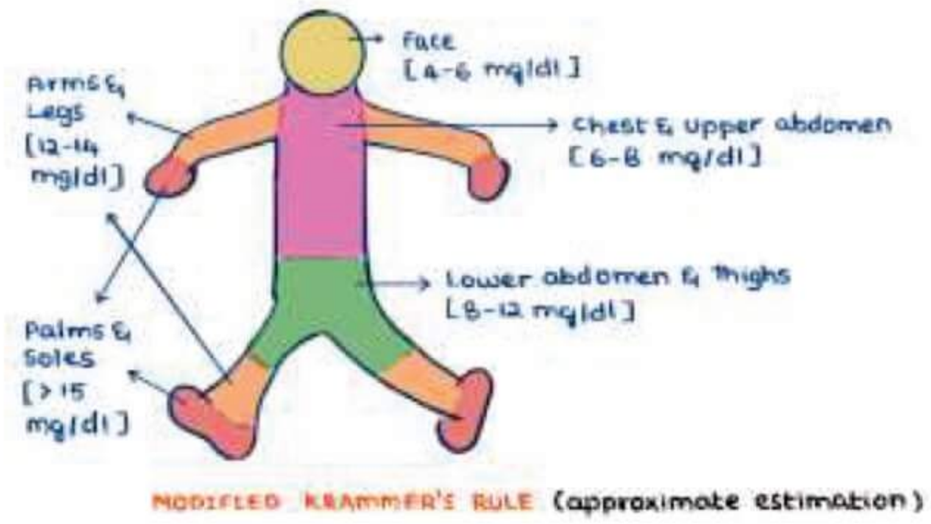
→ Surgery for EHBA

- **KASAI** Procedure [portoenterostomy]
- If done **> 8weeks of life** → **very poor prognosis**

→ **EHBA is the MC indication for liver transplantation in children**

CLINICAL FEATURES OF NEONATAL JAUNDICE

ICTERUS in neonates has a **cephalocaudal** progression



MODIFIED KRAMMER'S RULE (approximate estimation)

→ Bilirubin also measured by

→ Transcutaneous **bilirubinometer**

→ **Blood sample** → Serum bilirubin level

NEUROLOGICAL MANIFESTATIONS:

→ Most Commonly involved part of brain in neonatal jaundice → **Basal ganglia**

→ Type of cerebral palsy seen → **Extra pyramidal type**

→ **KERNICTERUS** = Yellow staining of basal ganglia [previously used term]

ACUTE BILIRUBIN ENCEPHALOPATHY:

Early features [mild] → hypotonia, poor feeding, loss of moro's reflex

↓

Fever, irritability, seizures

↓

Features of Advanced disease (severe) → Hypertonia, opisthotonic posturing, coma, death

CHRONIC BILIRUBIN ENCEPHALOPATHY [SAD MUM]

→ **S**ensorineural hearing loss

→ **A**thetosis

→ **D**ental dysplasia

→ **M**ental retardation

→ **U**pward gaze limitation

TREATMENT OF NEONATAL JAUNDICE:

I. Phototherapy

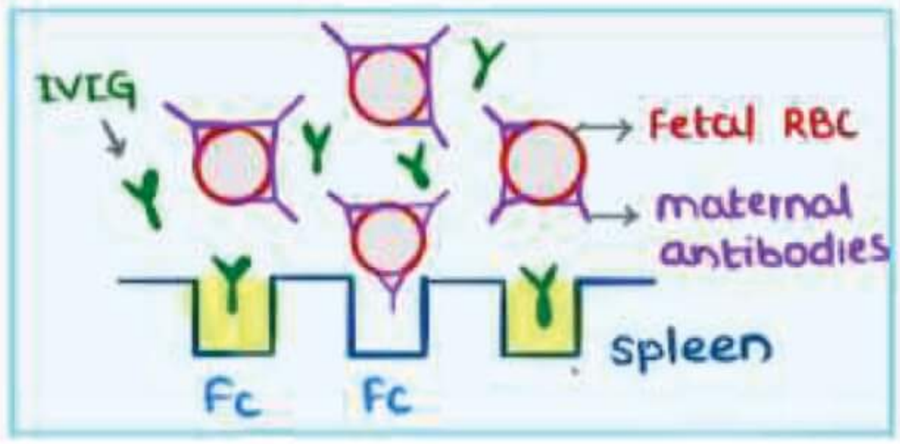
II. Exchange transfusion

III. Drugs

EXCHANGE TRANSFUSION:

→ Used in very severe cases, especially **erythroblastosis fetalis**

→ Double volume exchange transfusion done



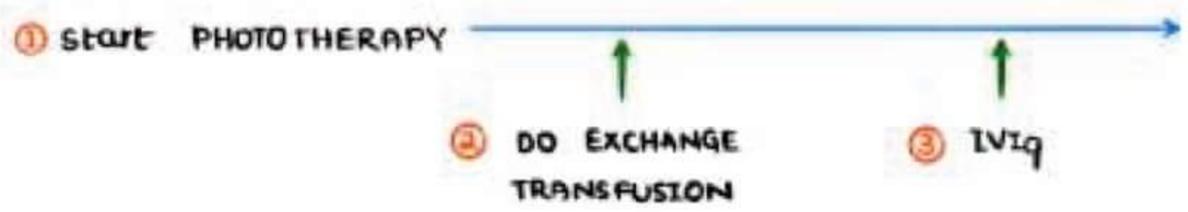
DRUGS:

→ **IV Ig** [Intra venous immunoglobulin]

→ Used in erythroblastosis fetalis

→ Occupies the receptors for FC segment of Ig in reticuloendothelial system & prevents further production of Ig

SEVERE NEONATAL JAUNDICE DUE TO ERYTHROBLASTOSIS FETALIS → TREATMENT (ORDER)



PHOTOTHERAPY:

→ **Most effective** wave length of light used → 450-470 nm

460-490 nm [Ghai 9th]

420-470 nm [Nelson 20th]

→ MECHANISMS BY WHICH PHOTOTHERAPY ACTS

1. PHOTO ISOMERISATION

→ **Bilirubin** → Polar compound → excreted through kidney without conjugation

→ Slow & reversible

2. STRUCTURAL ISOMERISATION

→ Bilirubin → Lumirubin →excreted through kidney without conjugation

→ Faster & irreversible

→ Most important mechanism by which phototherapy acts

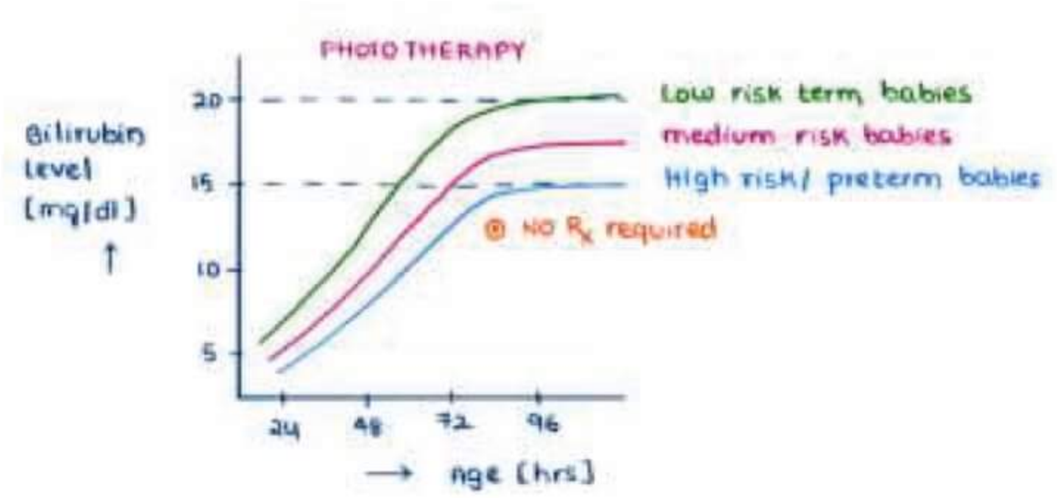
3. PHOTO OXIDATION [lest important]

→ EFFECTIVENESS OF PHOTOTHERAPY DEPENDS UPON

1. Exposed surface area of baby
2. Distance b/w baby & phototherapy unit [30-45 cm]
3. Type of lamp used: **LED lamps > CFL Lamps**
   - Does not depend on skin pigmentation of baby
   - Irradiance should be at least → 30 $\mu m/cm^2/ nm$
   - → Measured using FLUX METER

→ ADVERSE EFFECTS OF PHOTO THERAPY:

1. Bronze baby syndrome
2. Watery diarrhoea
3. Dehydration



4. Hypocalcemia
5. Retinal toxicity
6. Gonadal toxicity or mutations
7. Impaired maternal child bonding

→ IN OTHERWISE HEALTHY TERM NEONATES

AGE	PHOTOTHERAPY CUT OFF	EXCHANGE TRANSFUSION CUT OFF
24-48 hrs	> 15 mg/dl	> 20 mg/dl
48-72 hrs	> 18 mg/dl	> 25 mg/dl
> 72 hrs	> 20 mg/dl	> 25 mg/dl

→ IN PRETERM NEONATE

→ Phototherapy cut off → 1% of birth weight in grams

→ Exchange transfusion cut off → Phototherapy cutoff +5[mg/dl]

PHENOBARBITONE:

→ **Enzyme inducer**

→ ↑ activity UDP glucuronyl transferase enzyme

→ Useful in Crigler Najjar syndrome type II

INDICATIONS OF EXCHANGE TRANSFUSION IN A BABY WITH RH INCOMPATIBILITY:

→ **Cord blood Bilirubin** → **> 5 mg/dl**

→ **Cord blood Hb** → **< 10 mg/dl**

LATEST UPDATES IN NEONATOLOGY:

ANTENATAL CORTICOSTEROIDS

- Not recommended in late preterm neonates (34 weeks to $36^{6/7}$ weeks)
- In peri viable gestation (22 to 24 weeks) decision to be individuated based on capability of NICU & parent's wishes.

GOLDEN HOUR:

-1st hour of life

- Interventions should include:

1) Thermal protection
2) Establishment of FRC of lungs in least invasive manner
3) Avoiding hyperoxia by titrating O2 administration

Antenatal $MgSO_4$ for neuroprotection:

- Indicated for pregnant women ≤ 31 weeks of gestation with imminent preterm birth
- **Effects:**

– Neuroprotection by

→ Anti-inflammatory effects
→ Vasodilation
→ Decreased free radical injury
→ Inhibiting ca^{2f} influx into cells

"COMING IN OF MILK":

- Feeling of breast fullness & milk leakage of nipples
- 59-67 hours after delivery
- Earlier in multiparous
- If it occurs later than 72 hours → called as Delayed onset of lactation

PERINATAL ASPHYXIA:

- Most common cause of still birth
- Severity can be assessed by-
  - → Sarnat & Sarnat staging
  - → Levine's classification
  - → Thompson scare
    - Max (worst) score → 22
    - Score ≥ 15 → Abnormal outcome at 12months of age

PDA IN PRETERM NEONATES:

→ Both Indomethacin & Ibuprofen are equally efficient (70-80%) in preterm ≤ 32 weeks

- Ibuprofen is preferred in view of better safety profile

→ Oral PCM has been shown to be equally efficacious as Ibuprofen

HYPOTENSION IN 1ST 24 HOURS OF LIFE:

- Mean BP < 30 mm Hg
- Mean BP < Gest age in weeks mm Hg

HYPEROXIA TEST:

- Helps to determine whether heart disease is a likely cause in an infant with cyanosis
- Give 100% O_2 for 10 min

  ↓

  PaO_2 **< 50mm Hg** → Highly sensitive of Cyanotic CHD

  PaO_2 **50-150mm Hg** → needs further evaluation

  PaO_2 **> 150 mm Hg or rise in PaO_2 by > 80-120 mm Hg** above base line→ Cyanotic CHD is unlikely

CRITICAL CHD

- Cardiac lesions requiring surgical or catheter-based interventions during infancy
- 25% of all CHD

FEED INTOLERANCE IN NEONATES:

- **Symptoms** → Vomiting, Lethargy, apnoea
- **Signs:**
  - → Abdomen distension / tenderness
  - → Increased gastric residual (>2ml/kg)
  - → reduced / absent bowel sounds
  - → bradycardia or cyanosis

NEC-

L-Arginine → a substrate NO may help in prevention of NEC but no definite recommendation as more evidence required

INVASIVE CANDIDIASIS IN NEONATES:

- Incidence & $\frac{1}{birth\ weight}$
- Most common → C Albicans

INTRACTABLE SEIZURES IN NEONATES ARE SEEN IN

- Pyridoxine deficiency
- Molybdenum co-factor deficiency
- Non ketotic hyperglycinemia (NKH)
- Folinic acid responsive seizures

UMBILICAL ARTERY CATHETERISATION (UAC):

- Most common complication of UAC → **Blanching of 1 leg**

TREATMENT of blanching:

Rewarm the opposite leg with warm towel

↓

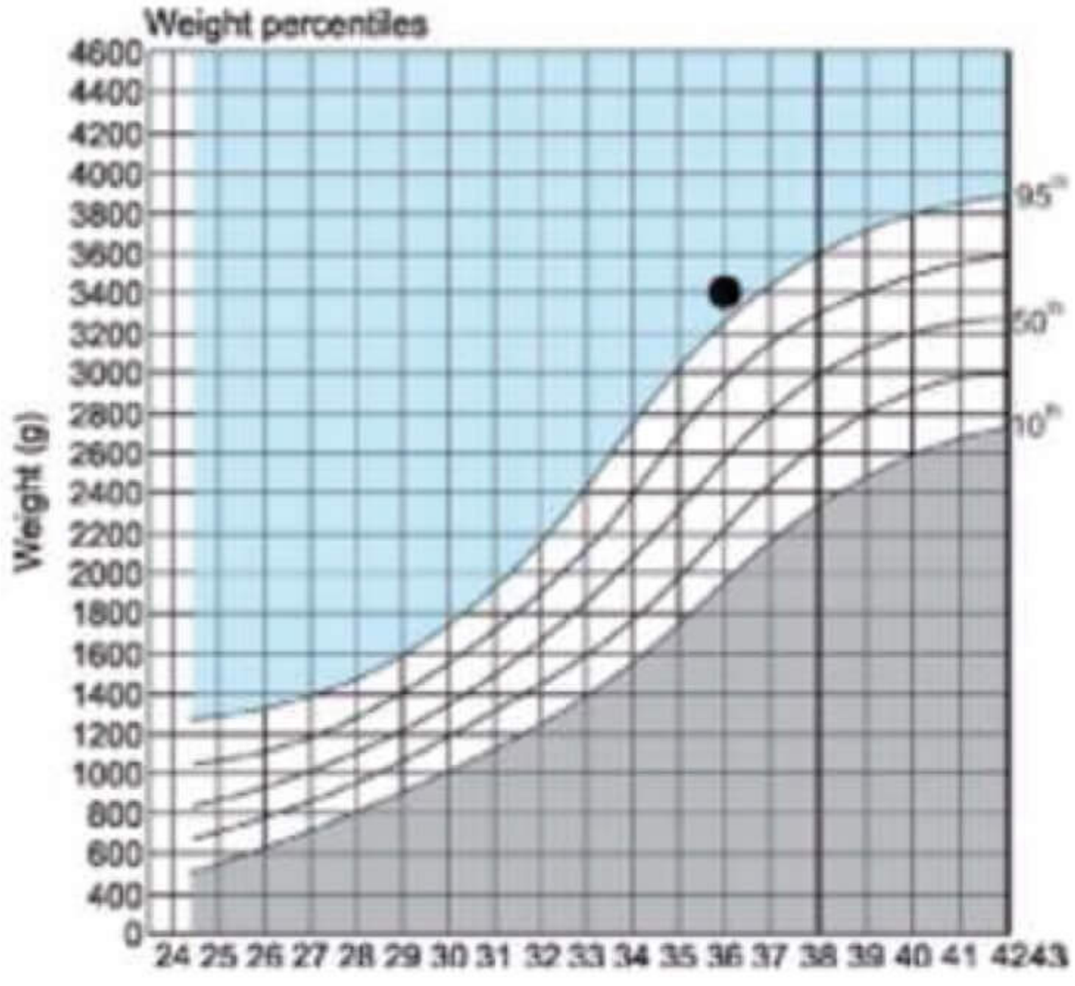
Reflex vasodilation

↓

Colour of opposite limb improves (If doesn't improve then remove UAC)

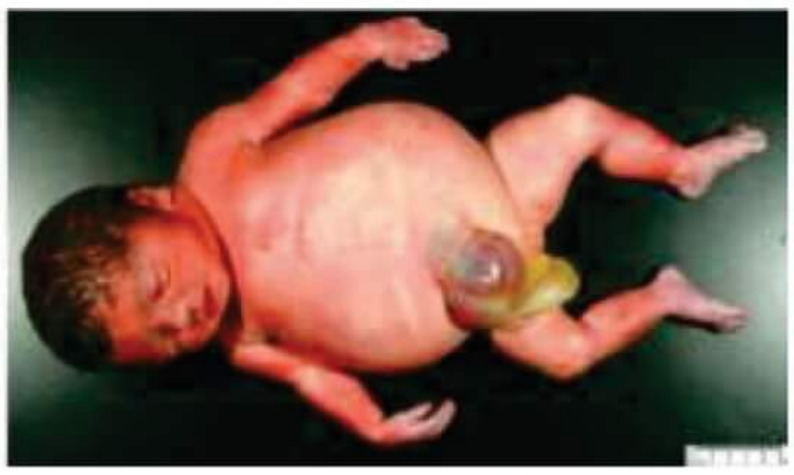
NEONATOLOGY IMAGES:

IBQS:

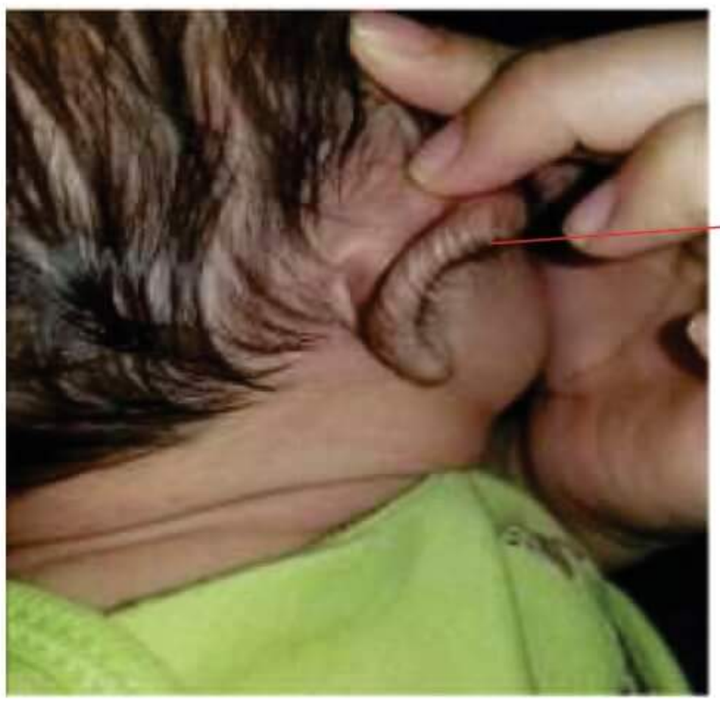


BECKWITH WIEDEMANN SYNDROME:

- Hemi hypertrophy
- Omphalocele
- LFD



INFANT OF DIABETIC MOTHER:



NEUROMUSCULAR MATURITY:

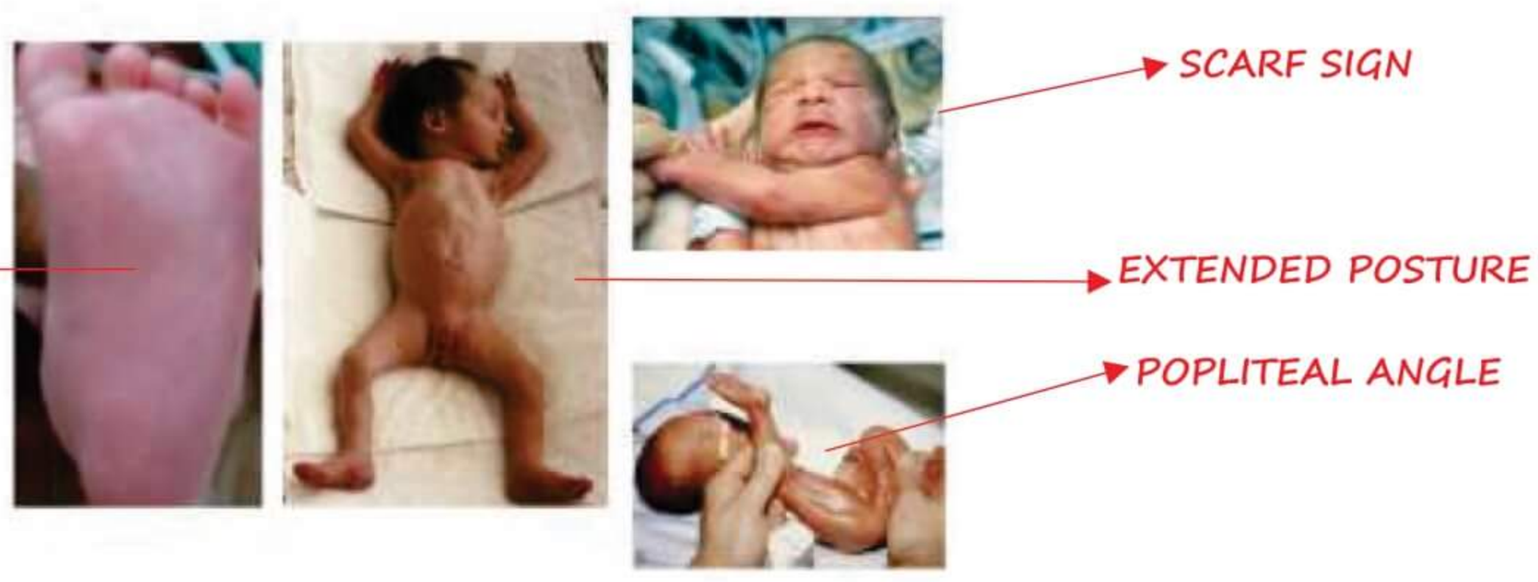
Score	–1	0	1	2	3	4	5
Posture							
Square window (wrist)	> 90°	90°	60°	45°	30°	0°	
Arm recoil		180°	140–180°	110–140°	90–110°	< 90°	
Popliteal angle	180°	160°	140°	120°	100°	90°	< 90°
Scarf sign							
Heel to ear							

PHYSICAL MATURITY

SKIN	Sticky friable, Transparent	Gelatinous, red, translucent	Smooth, pink; visible veins	Superficial peeling and or rash; few veins	Cracking, pale areas; rare veins	Parchment deep cracking; no vessels	Leathery, cracked wrinkled
LANUGO	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	**Maturity Rating**
PLANTAR SURFACE	Heal – toe 40-50 mm; -1 <40 mm:-2	> 50 mm no crease	Faint red marks	Anterior transverse crease only	Creases anterior 2/3	Creases over entire sole	**Score** / **Weeks**
BREAST	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola 1-2 mm bud	Raised areola 3-4 mm bud	Full areola 5-10 mm bud	
EYE / EAR	**Lids fused** loosely -1 Tightly -2	**Lids open** Pinna flat Stays folded	**Slightly curved pinna**, soft; slow recoil	**Well curved pinna**; soft but ready recoil	**Formed and firm** instant recoil	**Thick cartilage;** ear stiff	
GENITALS (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitale (female)	Clitoris prominent, labia flat	Clitoris prominent, small labia minora	Clitoris prominent, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora	

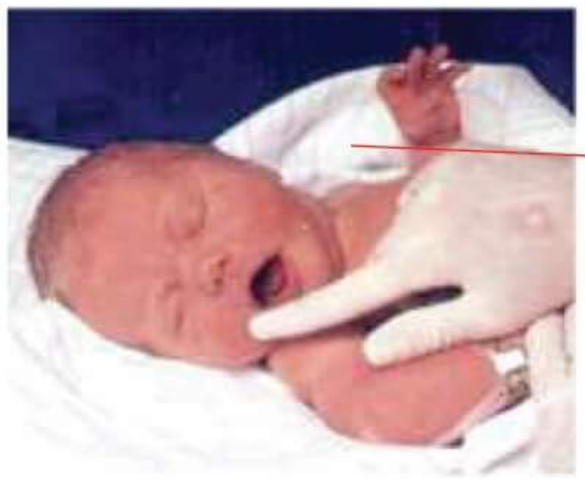
Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

EXPANDED NEW BALLARD SCORE → (20-40 weeks gestational age)

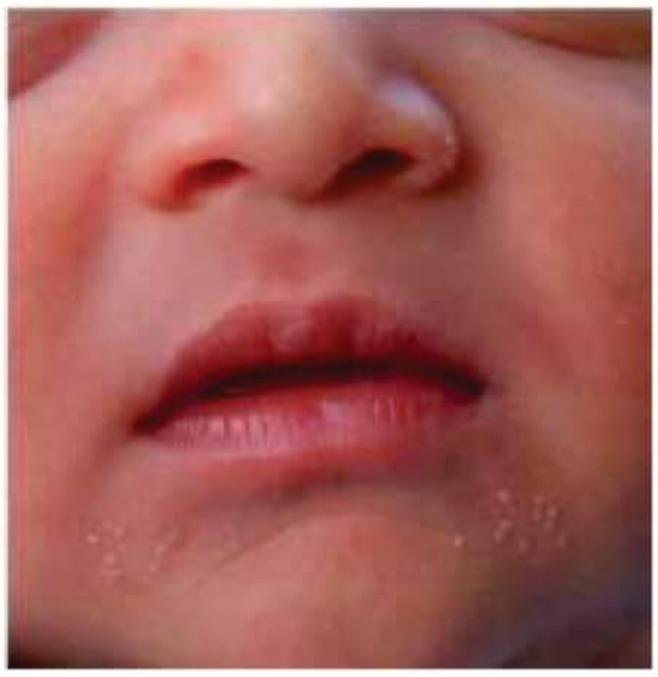


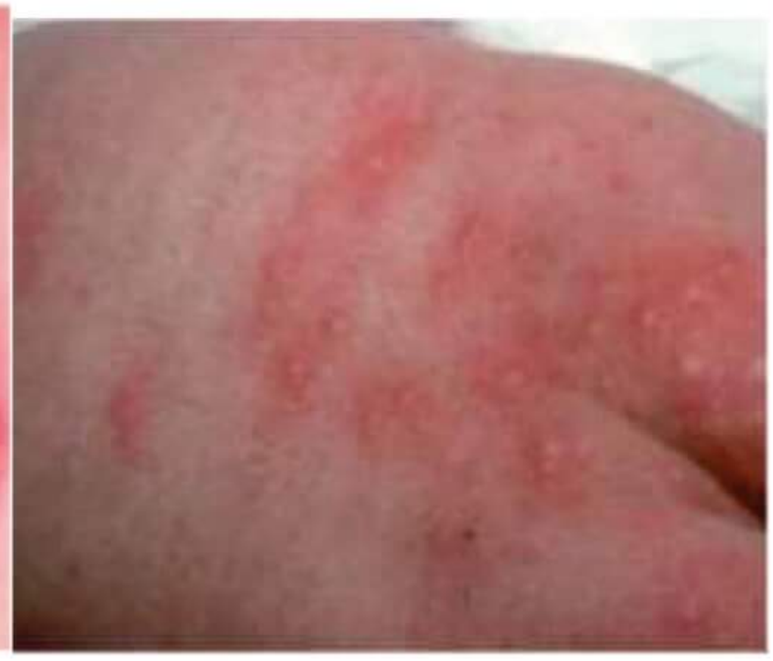
ASYMMETRIC TONIC NECK REFLEX

MORO'S REFLEX



ROOTING REFLEX

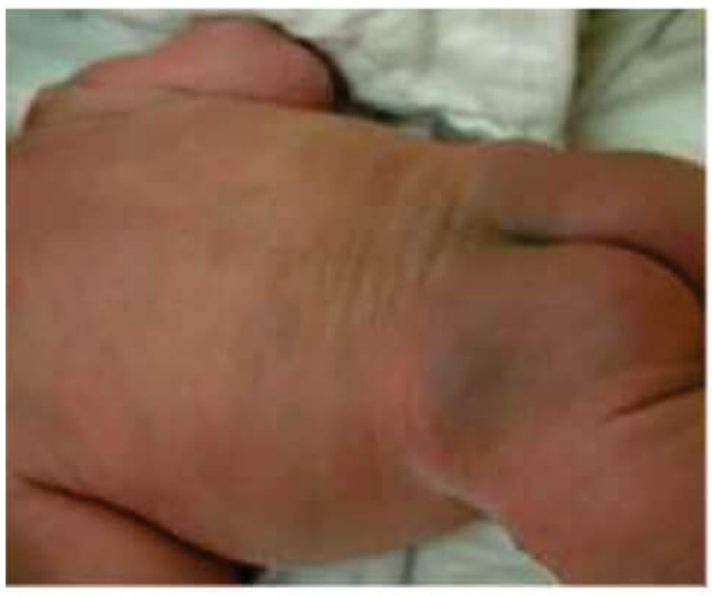


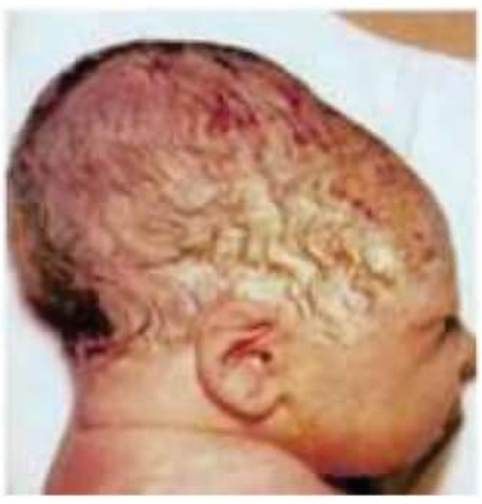


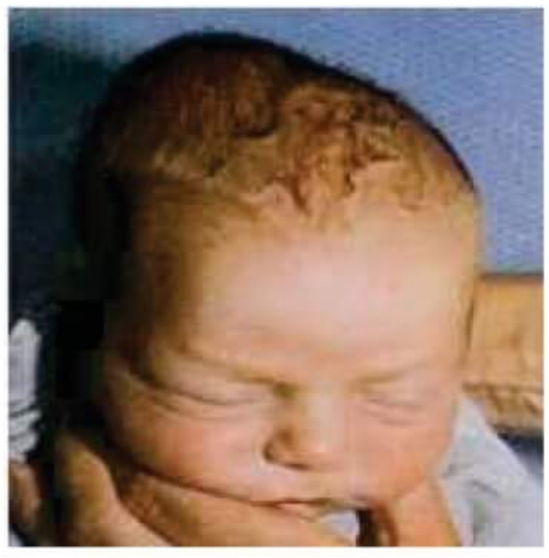
MILIA

EPSTEIN PEARLS

ERYTHEMA TOXICUM NEONATORUM





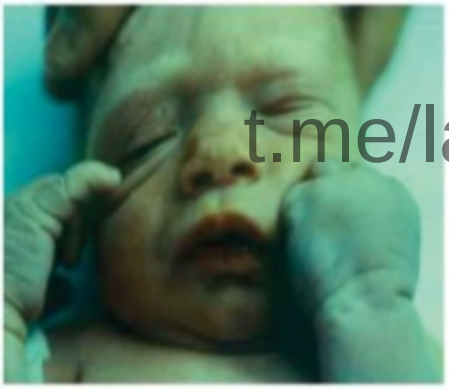


MONGOLIAN SPOTS

CAPUT SUCCEDANEUM

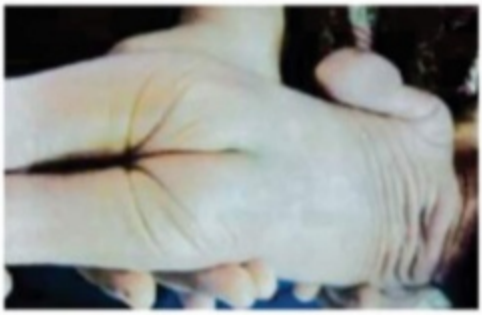
CEPHAL-HEMATOMA

BAG & MASK VENTILATION

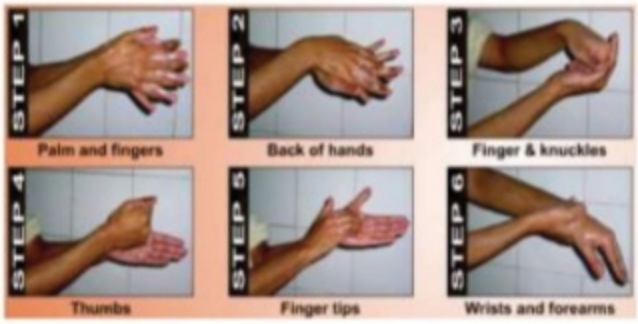


PERIPHERAL/ ACROCYANOSIS

Capillary refill time [Normal- <3sec]



IUGR



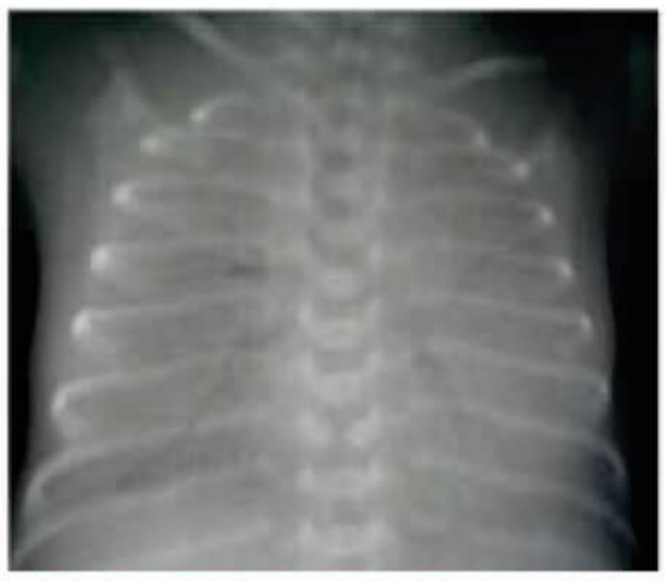
6 STEPS OF HAND-WASHING – Atleast 2 mins

RADIANT WARMER

INCUBATOR

KANGAROO MOTHER CARE

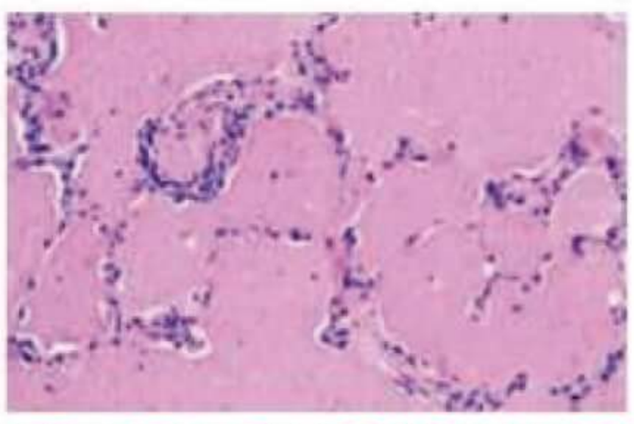
A male neonate delivered at 30 weeks gestation presented with severe distress immediately after birth requiring intubation:



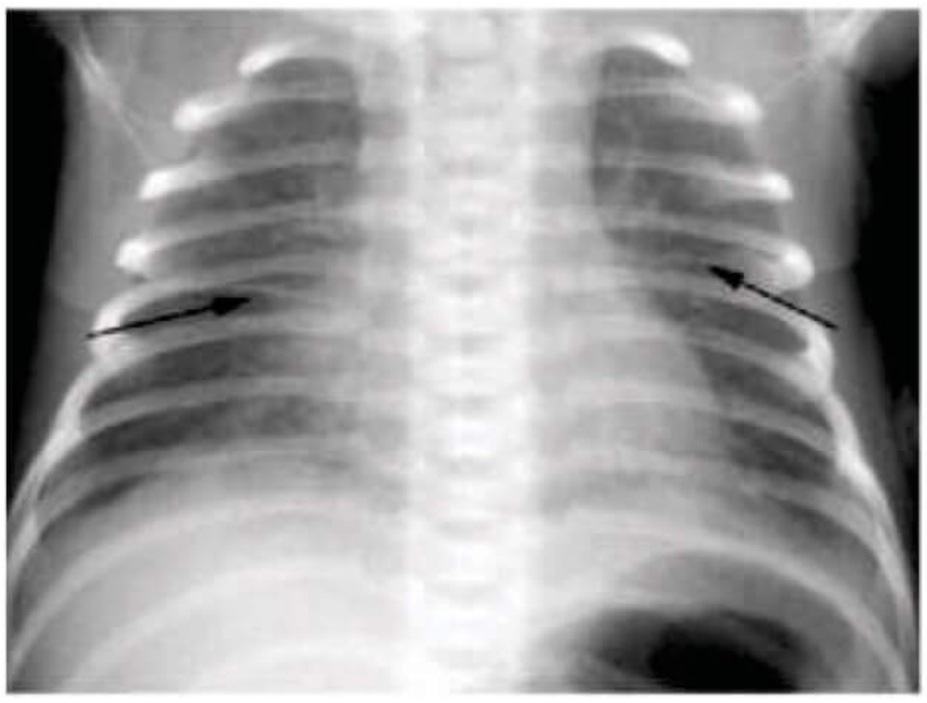
RESPIRATORY DISTRESS SYNDROME

A 3.5 kg newborn born by full-term normal vaginal delivery presented with respiratory distress not responding to surfactant therapy. There is a history of previous sibling's death at one month of age due to respiratory distress. His Postmortem lung biopsy picture is shown.

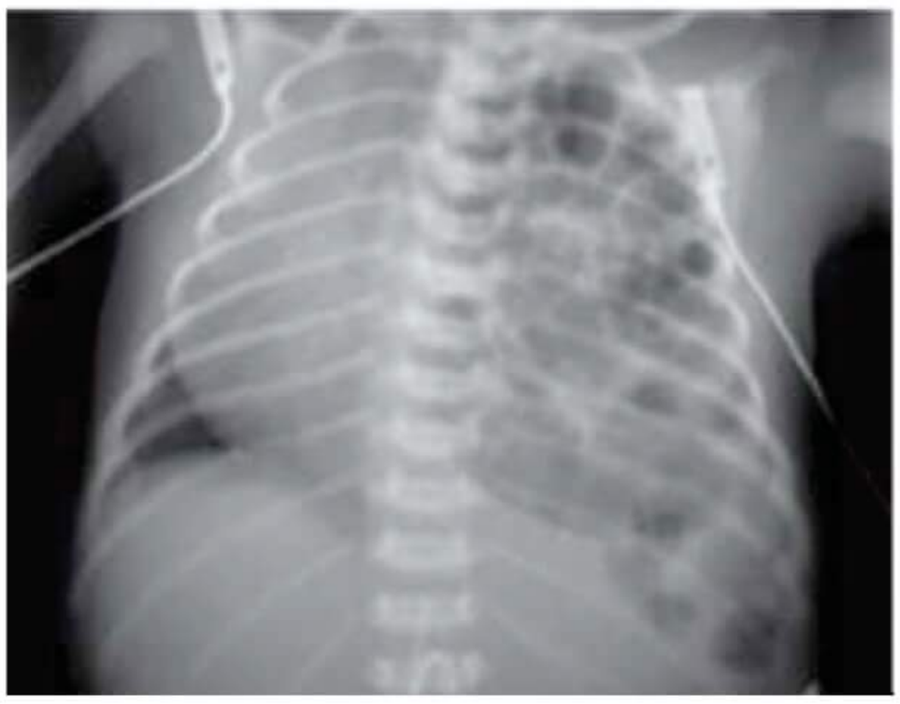
What diagnosis should you suspect?



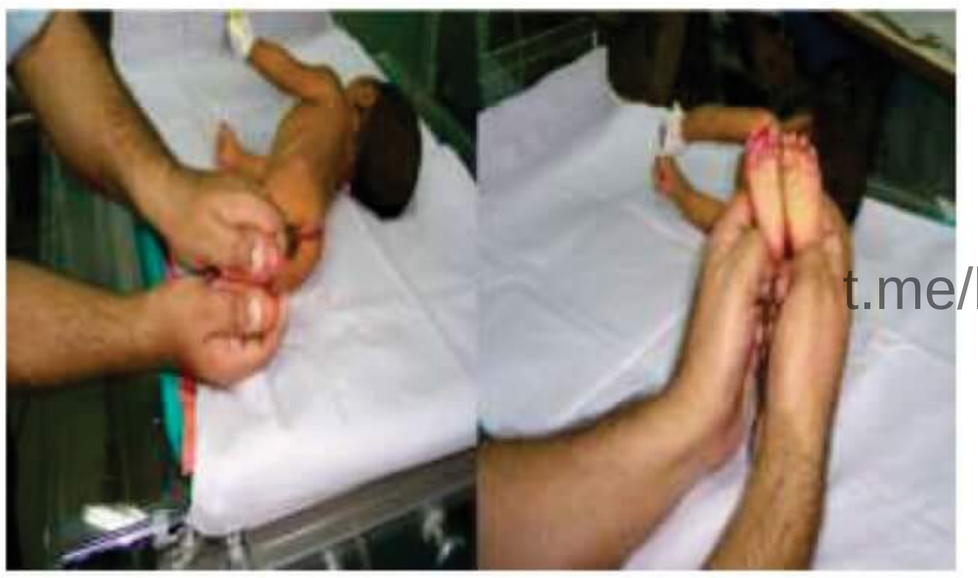
NEONATAL PULMONARY ALVEOLAR PROTEINOSIS



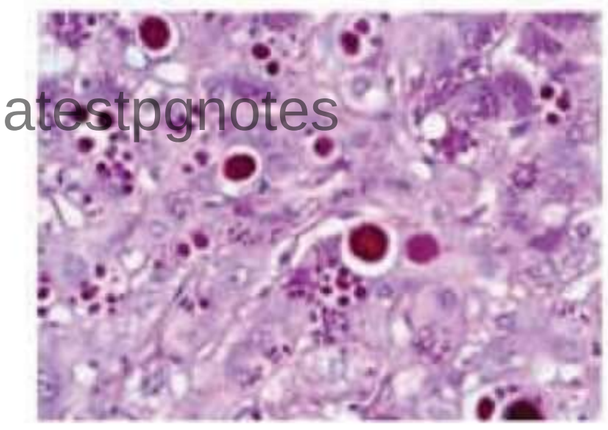
TRANSIENT TACHYPNEA OF NEW BORN



CONGENITAL DIAPHRAGMATIC HERNIA



A 1 month old baby presents with conjugated hyperbilirubinemia, intrahepatic cholestasis and high alkaline phosphatase.
The liver biopsy picture of the baby is shown below:

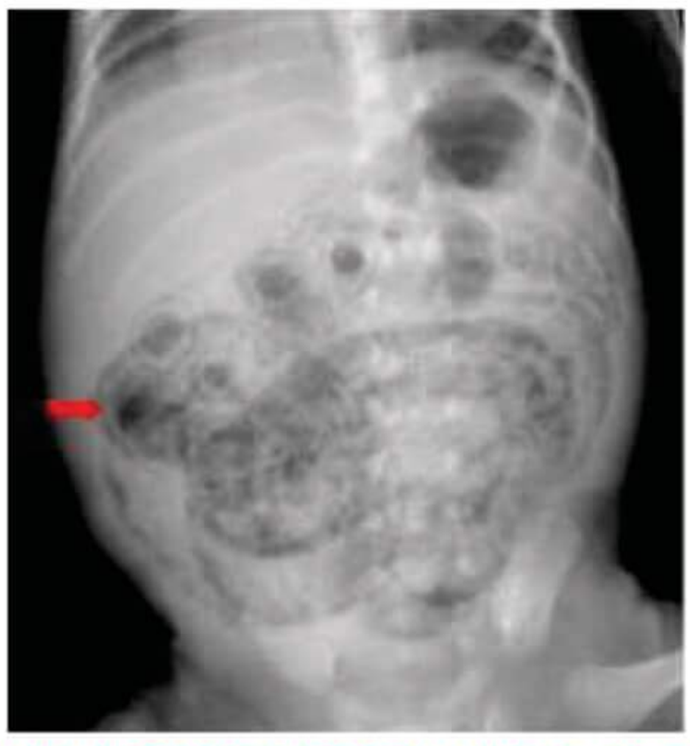


BILIRUBIN LEVEL → 15mg/dl

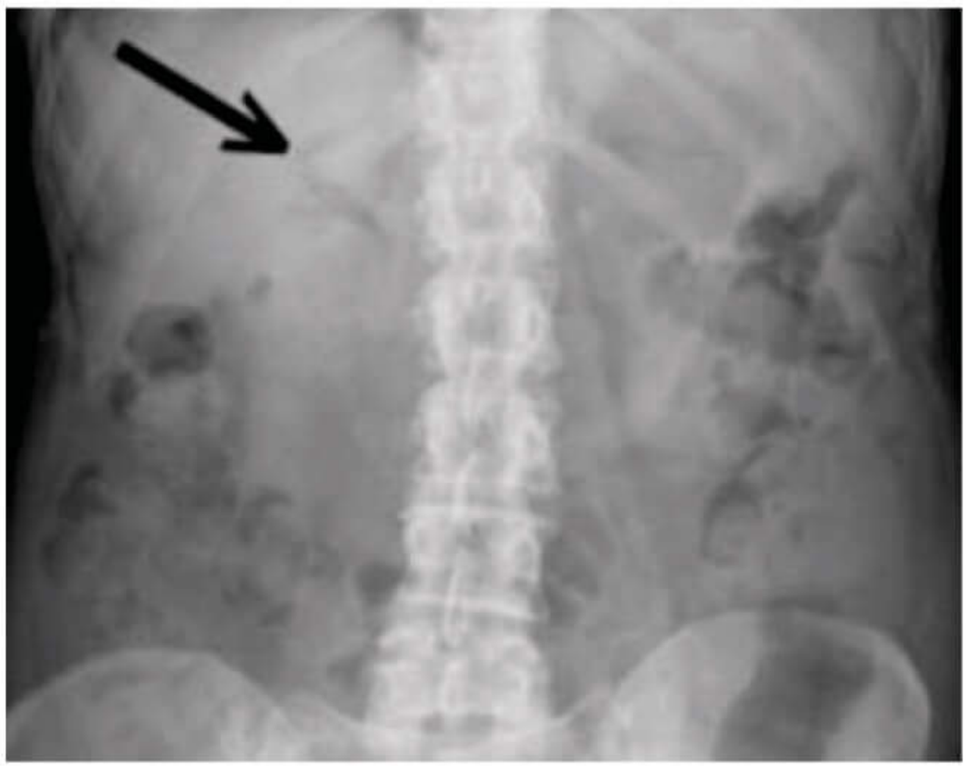
PHOTOTHERAPY → STRUCTURAL

ISOMERIZATION

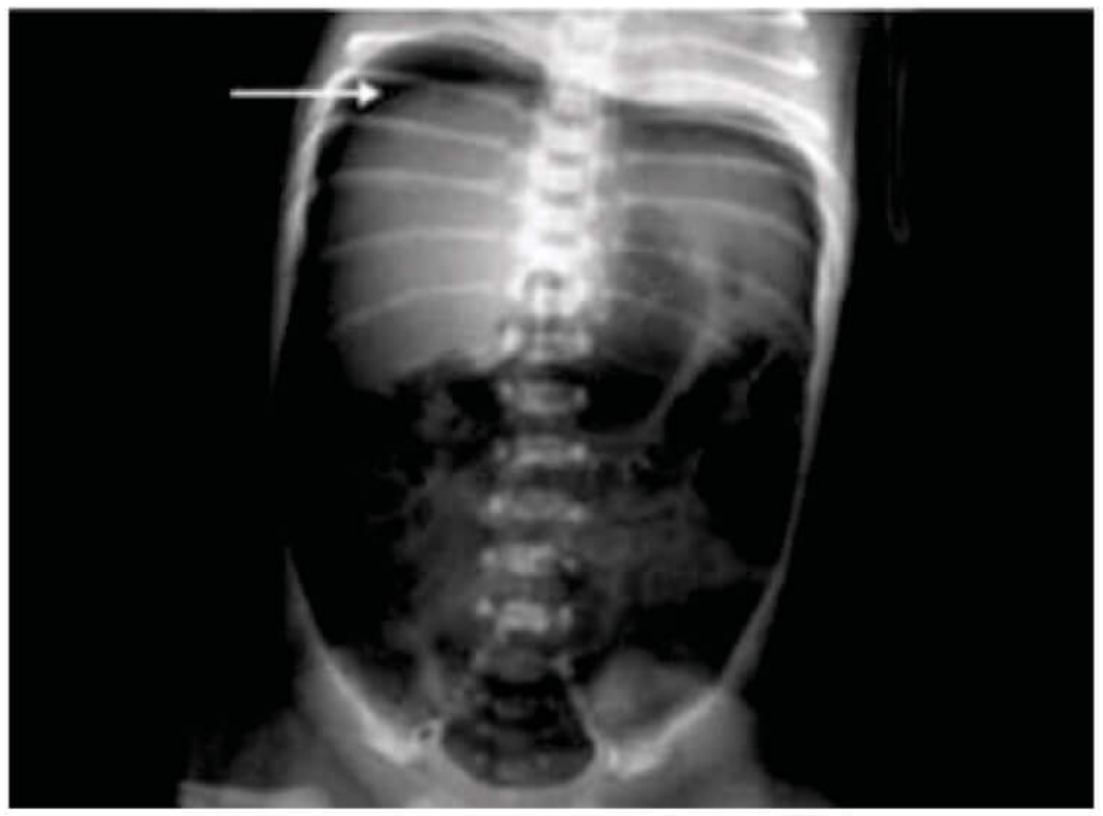
ALPHA-1 ANTI-TRYPSIN DEFICIENCY



PNEUMATOSIS INTESTINALIS → Stage IIa NEC



STAGE II b NEC – PORTAL VEIN GAS SHADOW



STAGE III b NEC – INTESTINAL PERFORATION

NUTRITION & MALNUTRITION

BREAST MILK & BREAST FEEDING:

Breast feeding should be initiated – as soon as possible (or)

- Within 1 hour of child birth

EXCLUSIVE BREAST FEEDING:

- Child should be fed only breast milk, nothing else, not even sips of water unless medically indicated
- Any form of pre-lacteal feeding is absolutely C/I
- Recommended for 6 months exclusively

What should be initiated at 6 months – complementary feeding

→Breast milk output is **maximum** at

- **5-6 months of lactation**

- **730 ml/day**

For how long can expressed breast milk be stored

- At **room temperature** – 8 -10 hrs
- In a **refrigerator** – 24 hrs
- In a **deep freezer** (-20 degree C) – 3 months

REFLEXES HELPING IN BREAST FEEDING

Mother:

1.Milk secretion reflex (by prolactin)

2.Milk ejection reflex (by oxytocin)

Baby:

1.Rooting reflex

2.Suckling reflex

SIGNS OF GOOD POSITIONING WHILE BREAST FEEDING

1.Body of the baby should be well supported

2.Occiput, shoulder & buttocks should be in a straight line

3.Baby should be turned towards the mother

4.Abdomen of baby should touch abdomen of mother

SIGNS OF GOOD ATTACHMENT WHILE BREAST FEEDING

1.Mouth of the baby should be wide open

2.Entire areola should be in baby's mouth except a small upper part that may be visible

3.Lower lip of baby should be everted (turned out)

4.Chin of baby should touch the mother's breast

C/I TO BREAST FEEDING

Related to baby:

1.Galactosemia

2.Lactose intolerance

Related to mother:

Absolute C/I:

- Mother on chemotherapy or radiotherapy

Relative C/I:

-Maternal HIV

-Maternal active untreated TB

-Maternal active varicella

-Maternal active herpes simplex

ADVANTAGES OF BREAST FEEDING FOR BABY:

COMPOSITION:

1. **Carbohydrates**

   •Breast milk is richer in lactose [7g/dL] as compared to cow milk [4.5 g/dl]

   •Breast milk give more energy as carbohydrates to baby

2. **Proteins**

   •Bm contains lesser protein [1g/dl] as compared to cm [3.5 gm/dl]

   •Bm is richer in whey proteins (lactalbumin) which are more easily digestible, as compared to casein in cm

   •Bm contains adequate amount of amino acids like cysteine, taurine, methionine which are adequate for CNS development of baby

3. **Lipids**:

   •Bm is richer in PUFA [poly unsaturated fatty acids] – beneficial for baby

   •Bm contains adequate amounts of DHA [Docosahexaenoic acid – CNS development of baby]

4. **Minerals**:

   •**Ca: phosphate ratio** in Bm is such that, it favors calcium absorption [Cm richer in phosphate – predominantly cm fed baby – more chances of hypocalcemia]

   •**Fe:** present in Bm is more easily absorbable

5. **Vitamins**:

   •Bm contains adequate amount of all vitamins **except** **vitamin D, vitamin K & vitamin B12** [in strictly vegan mothers]

   •Vit K injection at birth prevents hemorrhagic disease of newborn

II. Breast milk contains **anti-infective substances** like

   •**IGF beta [transforming growth factor]** Teach for

   •Phagocytic macrophages P

   •PABA [para amino benzoic acid]

- Lactoferrin — L
- Lysozyme
- Antibodies especially IgA — A
- Anti-staphylococcal factor
- Bifidus factor — B
- Bile stimulated lipase

III. Breast milk protects **against disease** like

- **Neonatal period** – NEC, neonatal sepsis
- **Later in life** – obesity, HTN, diabetes, allergies, dental cares

IV. Bm fed babies have higher IQ

V. Helps in maternal child bonding

VI. Easily available, even in resource limited settings & is free from risk of contamination

VARIANTS IN THE COMPOSITION OF BM:

I. DEPENDING ON TIME AFTER BIRTH:

1. COLOSTRUM:
   - 1st 72 hours of birth
   - Thick and yellowish
   - Rich in Ig, macrophages, proteins
   - Known as 1st immunization of baby
   - Lactose is less
2. TRANSITIONAL MILK:
   - Next 2 weeks
   - Composition is between colostrum & mature milk

3. MATURE MILK:

- Thin & watery
- Richer in lactose & poorer in proteins

II. DEPENDING ON GESTATIONAL AGE:

-Preterm Breast milk richer in

- Sodium S
- Iron I
- Proteins P
- Fat for
- Ig intelligent
- Calories CNS

III. DEPENDING ON EACH FEEDING SESSION

1.FORE MILK:

- at beginning of a feed
- more thin & watery
- satisfies mainly the thirst of the baby

2.HIND MILK:

- At the end of feed
- Richer in fat
- Thicker
- Satisfies hunger of baby

MALNUTRITION:

- **Best indicator of ACUTE MALNUTRITION** – ↓ in weight for height **(Wasting)**
- **Best indicator of CHRONIC MALNUTRITION** – ↓ in Height for age **(Stunting)**

AGE INDEPENDENT ANTHROPOMETRIC INDICES

Name	Formula	Normal	Malnutrition
Kanawati & Mc Laren Index	MAC /HC	0.32-0.33	< 0.25
Rao & Singh's Index	Wt (Kg) / Ht $(cm)^2$ x 100	> 0.14	< 0.14
Dugdale's Index	Wt (kg) /Ht $(cm)^{1.6}$ x 100	0.88-0.97	< 0.79
Quacker's Midarm Circumference Measuring Stick	MAC for a given height		75-85% of expected – malnutrition <75% of expected – severe malnutrition
Jeliff's ratio	HC/CC	For a child > 1 yr age, ratio should be <1	>1 in a child, > 1 yr age

CLASSIFICATIONS OF MALNUTRITION:

1. **IAP CLASSIFICATION:** Based on weight for age & edema

- Normal is **>80%** of expected
- Grades:

I – **71-80%** of expected

II – **61-70%** of expected

III – **51-60%** of expected

IV –**≤50%** of expected

- Add 'K' if edema is present

II. **GOMEZ CLASSIFICATION**: Based on **weight for age**

- N – weight for age **>90%** of expected
- Grades

I (**mild**) – **75-89%** of expected

II (**moderate**) – **60-74%** of expected

III (**severe**) – **<60%** of expected

iii. WHO CLASSIFICATION: Based on **weight for height, height for age & edema**

Weight for height	Height for age
b/w – **2 to -3** Z score or **70-79%** of expected called as **Wasting**	b/w – **2 to -3** Z score or **85-89%** expected called as **Stunting**
-3 Z score or <70% of expected called as **Severe Wasting**	<- 3 Z score or < 85% of expected **Severe Stunting**

- **If edema is present**, add 'edematous' to the category

iv. WELCOME TRUST CLASSIFICATION

- Based on **weight for age & edema**

Weight for age	Edema	Category
60-80% of expected	Absent	Under nutrition
60-80% of expected	Present	Kwashiorkor
<60% of expected	Absent	Marasmus
<60% of expected	Present	Marasmic Kwashiorkar

	Kwashiorkar	Marasmus
Edema	Present	Absent
Appetite	Poor	Voracious Appetite
CNS involvement	Apathy, listless	Active child
Hepatomegaly	Seen	Usually not seen
Skin & hair changes	More common	Less common

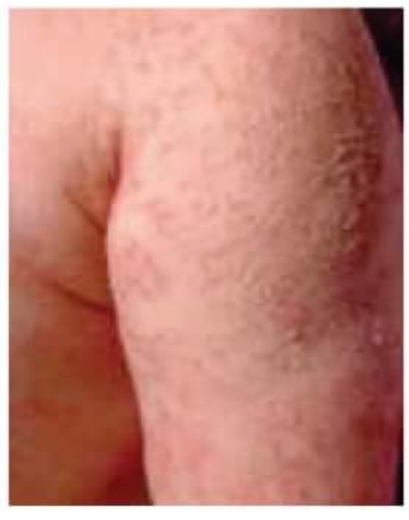
MARASMUS

SEVERE MALNUTRITION:

SKIN CHANGES – flaky paint dermatosis (or) crazy permanent dermatosis

HAIR CHANGES – easy pluckability

-Flag sign



SEVERE ACUTE MALNUTRITION (SAM):

DEFINITION – in a child b/w **6 months to 5 yrs** age, as presence of **any 1 or more** of

- **Weight for ht <-3** Z score or **<70%** of expected or
- **Mid arm circumference <11.5 cm** or
- **Symmetric bipedal edema** of nutritional origin

COMPLICATIONS:

S- **S**ugar deficiency (hypoglycemia) – Blood Glucose <54 mg/dl

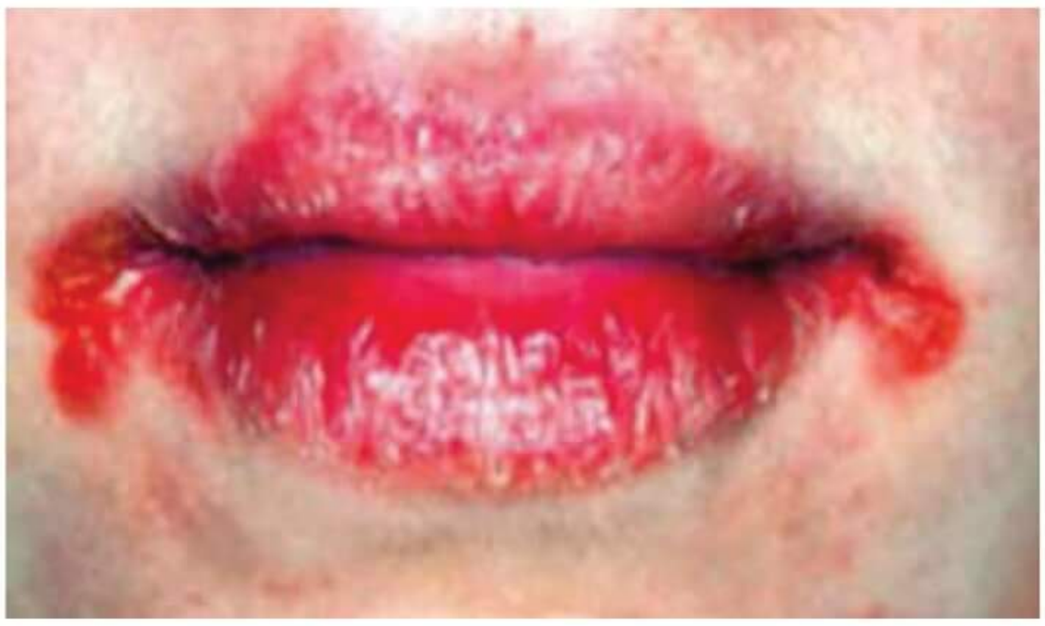
H –**H**ypothermia – rectal temperature <35.5 degree C

I – **I**nfections

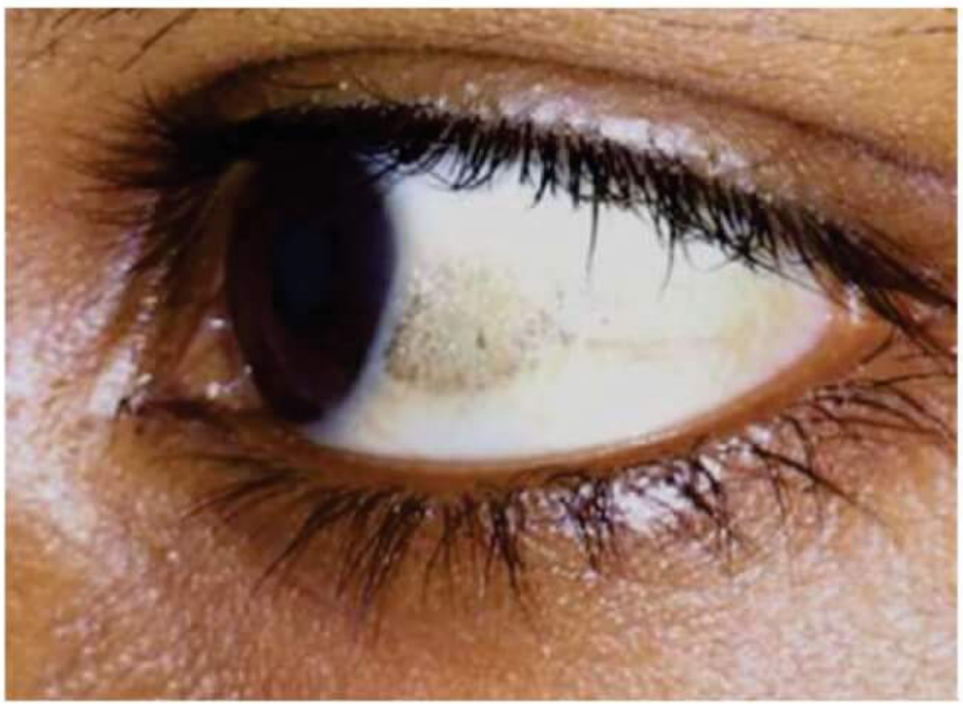
E L– **E**lectrolyte imbalance especially Hyperkalemia

DE - **DE**hydration

D – **D**eficiency of micronutrients



ANGULAR CHEILOSIS (Riboflavin deficiency)



BITOT SPOTS (VIT A deficiency)

SHAKIR'S TAPE

1.**INITIAL HOSPITALIZATION** especially with poor appetite or complications

2.Look for **COMPLICATIONS & RX**

- **Hypoglycemia** – **10%** dextrose
- **Hypothermia** – dry & warm up
- **Infections** – Antibiotics
- **Electrolyte imbalance** – supplement K+, Mg+2
- **Dehydration** – WHO ORS or Resomal (rehydration solution for malnourished child)
- **Deficiency of micronutrients** – supplement multivitamins & minerals, Fe started later

3. **NUTRITIONAL REHABILITATION:**

- Start with **70 – 80 Kcal /kg/day** & **0.7 g/kg /day** **proteins** weight gradually over 1-2 week [prevents refeeding / nutritional recovery syndrome] **150-200 Kcal /kg /day** & **4-5 /kg /day** **proteins** given

CRITERIA FOR DISCHARGE FROM HOSPITAL:

- Child should have **lost edema** & started **gaining weight**
- All infections & micro nutrient **deficiencies** should have been taken **care** of
- Child's **appetite** should have **improved** & be he should be accepting well orally
- Mother /caregiver should be **confident** of taking care of child at home

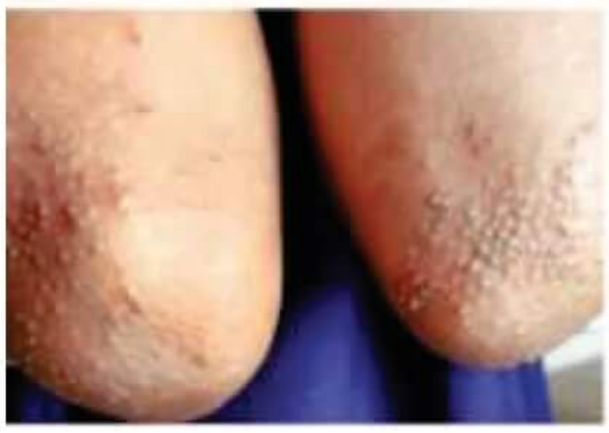
IBQs:

Q. The following **rashes** seen in a previously well 5 months old child can be treated by administration of:

Dx : **Acrodermatitis Enteropathica**

Ans: Treatment by **Zinc**

Q. what is the **skin** condition? It can be seen due to **deficiency** of?



Phrynoderma

Deficiency of vitamins E, B, A, and essential fatty acids

TRAFFIC LIGHT DIET :

CATEGORY	CHARACTERISTIC	EXAMPLES	RECOMMENDED INTAKE
Red	High in calories, sugar & fat	Fatty meats, sugar, sweat beverages, fried food	Reserved for infrequent treats
Yellow	Nutrient dense, but higher in calories & fat	Lean meats, dairy starches, grains	In **moderation**
Green	Low-calorie, high fiber, low fat, nutrient dense	Fruits & vegetables	Without any limitations

RECOMMENDED DAILY ENERGY REQUIREMENT:

Body weight	Recommended daily energy requirement
< 10 kg	100 Kcal/kg
10-20 kg	1000 Kcal + 50 Kcal/kg for each kg **above 10kg**
>20 kg	1500 Kcal + 20 Kcal/kg for each kg **above 20kg**

RECOMMENDED DAILY PROTEIN REQUIREMENT:

Group age	Age	Protein requirement (g/day)
Infants	0-6 months	1.2 g/kg/day
	6-12 months	1.7 g/kg/day
Children	1-3 years	17
	4-6 years	20
	7-9 years	30
	10-12 years	40
Boys	13-15 years	54
Girls	13-15 years	52
Boys	16-17 years	62
Girls	16-17 years	56

FLUID & ELECTROLYTE DISTURBANCES

BODY COMPOSITION & ACID BASE BALANCE:

BODY COMPOSITION

A. TOTAL BODY WATER [TBW]

→ TBW constitutes

- 90% of body weight in early fetal life.
- 75% of body weight at BIRTH
- 60% of body weight by end of 1st year & remains same till puberty

→ Premature infants have higher TBW than term infants.

→ DIVIDED INTO (TBW)

1. ECF volume
2. ICF volume
   - TBW=ECF+ICF

ECF & ICF VOLUME:

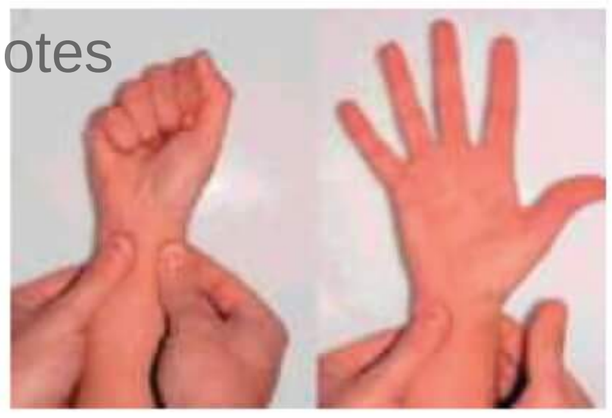
→ In fetus & new born, ECF> ICF volume

→ After birth ECF decreases and ICF increases.

→ By 1year age, ICF: ECF volume approaches adult levels

B. DISORDERS OF ACID BASE BALANCE

Q. What is the name of this test to be done before drawing an arterial blood gas sample:



Ans: ALLEN'S TEST- To assess patency of palmar arch

METABOLIC ACIDOSIS IN CHILDREN [pH< 7.35; primary decrease in HCO_3]

→ Respiratory compensation occurs within 12-24 hrs [ACIDOTIC BREATHING]

→ Expected pCo_2 in metabolic acidosis = 1.5× HCO_3 + 8 ± 2

→ In metabolic alkalosis, pCO_2 increases by 7 for each 10meq/L increase in HCO_3

→ Most common cause of metabolic acidosis in children → DIARRHOEA

METABOLIC ACIDOSIS WITH NORMAL ANION GAP (PURDA)

- Post hypocapnia
- Urinary tract diversions
- Renal tubular acidosis
- Diarrhea
- Ammonium chloride intake

INCREASED ANION GAP METABOLIC ACIDOSIS [KALAM TIP]

- Keto acidosis, Kidney failure
- Lactic acidosis, Liver failure
- Malignancy, Medications

- Tissue hypoxia
- Inborn errors of metabolism
- Poisoning Ex: Ethylene glycol

METABOLIC ALKALOSIS IN CHILDREN [pH>7.45, primary increase in HCO_3]:

- **MC cause- vomit and diuretics**

CAUSES OF METABOLIC ALKALOSIS:

CHLORIDE RESPONSIVE [Urinary chloride **< 15 meq/L**]

- Gastric losses
- Emesis
- Nasogastric suction
- Diuretics [loop or thiazide]
- Elevated CO_2 [post-hypercapnia]

(Emesis, Nasogastric suction, Diuretics, Elevated CO_2) — Volume repletion is necessary for correction of alkalosis

- Raised sweat chloride [cystic fibrosis]

CHLORIDE RESPONSIVE METABOLIC ALKALOSIS (Urinary Cl level < 15 meq/L)

- Characterized by decreased ECF volume & it responds to volume repletion.

Causes: (Cl loss from Gut/kidney/skin)

- **Vomiting/Continuous NG drainage**
- **Congenital Chloride Diarrhea**
- Sweat→ **Cystic fibrosis**
- Kidney losses → **Loop diuretics/Thiazides**

CAUSES OF CHLORIDE RESISTANT METABOLIC ALKALOSIS (Cl> 20meq/L)

Normal BP	High BP ('CL GADA')
- Barter syndrome	(Excess Mineralocorticoid effect)
- Gitelman syndrome	- **C**ushing syndrome
	- **L**iddle syndrome
	- **G**RA (Glucocorticoid remediable Aldosteronism)
	- **A**ME (Apparent mineralocorticoid excess)
	- **D**SD 11β hydroxylase or 17α hydroxylase def.
	- **A**drenal Adenoma/hyperplasia

CUSHING SYNDROME:

- **Excess cortisol**- mineralocorticoid activity leads to hypertension
- MCC is Iatrogenic steroids

LIDDLE SYNDROME/PSEUDOHYPERALDOSTERONISM

→ Autosomal dominant disorder
→ Due to an activating mutation of **Na channel in distal nephron**
→ Because this Na channel is continuously open
→ Features of hyperaldosteronism→ **hypertension**

GLUCOCORTICOID-REMEDIABLE ALDOSTERONISM [GRA]

→ Autosomal dominant

→ **Excess** production of **aldosterone** owing to presence of an aldosterone synthase gene that is regulated by **ACTH**

Treatment:

Glucocorticoids → Inhibits ACTH production by pituitary → Down regulates the inappropriate aldosterone production

AME (Apparent mineralocorticoid excess)

- Due to deficiency of **11B hydroxysteroid dehydrogenase** enzyme

↓

Cortisol → Cortisone in Kidney

Has mineralocorticoid → Effect l/t → Hypertension

No mineralocorticoid effect

Adrenal Adenoma/ Hyperplasia: **Elevated aldosterone** level causes Renal Na^+ & H_2O retention

DISORDERS OF SODIUM & POTASSIUM:

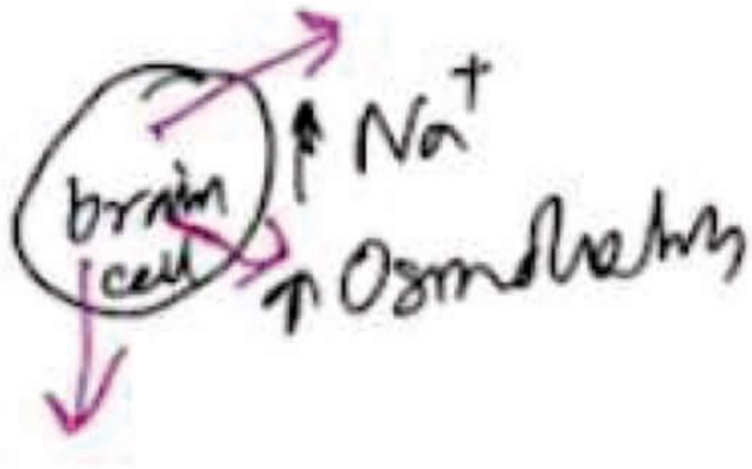
DISORDERS OF SODIUM:

HYPERNATREMIA (Serum **Na^+> 145mg/dl**)

Causes:

Excess Na^+	Water deficit	Water & Na deficits
- Improper feeds	- DI	- GI losses → diarrhea/vomiting
- IV 3 % NaCl	- increased insensible loss	- Cutaneous loss → burns
- $NaHCO_3$	- inadequate fluid intake	- Renal loss→ polyureic phase of ATN
- Hyperaldosteronism		- osmotic diuresis

Q. Most devastating consequence of hypernatremia in children- **BRAIN HEMORRHAGE** (parenchymal/subdural/subarachnoid)



HYPONATREMIA:

Causes:

HYPOVOLEMIC	EUVOLEMIC	HYPERVOLEMIC
- GI/Skin losses	- **SIADH**	- H. failure
- Renal losses	- Hypothyroidism	- Cirrhosis
• Diuretics	- Glucocorticoid deficiency	- Nephrotic syndrome
• Nephronophthisis	- water intoxication	- renal failure
• ARPKD		- Hypoalbuminemia
• Obstructive uropathy		
• CSWS **(Cerebral salt wasting syndrome)**		

PSEUDOHYPONATREMIA → In hyperglycemia, mannitol or sucrose intake

DIAGNOSTIC CRITERIA OF SIADH (SYNDROME OF INAPPROPRIATE ADH)

Presence of-

- Serum Na^+ **< 135meq/l**
- Serum osmolality **<280mosm/kg**
- Urine Na^+ > **30 meq/L**
- Urine osmolality **>100mosm/kg**
- Correction with water restriction

Absence of-

- Renal/adrenal/thyroid insufficiency
- Heart failure/nephrotic syndrome /cirrhosis
- Diuretic ingestion
- Dehydration

DISORDERS OF POTASSIUM:

HYPOKALEMIA → Serum K^+ **< 3.5 meq/L**

Etiology:

- Increased losses of K+ in diarrhea

- Decreased stores e.g. malnutrition
- Shift into intercellular compartment e.g. alkalosis
- Renal e.g. RTA
- Endocrine e.g. Cushing syndrome, Hyperaldosteronism.

Clinical Features:

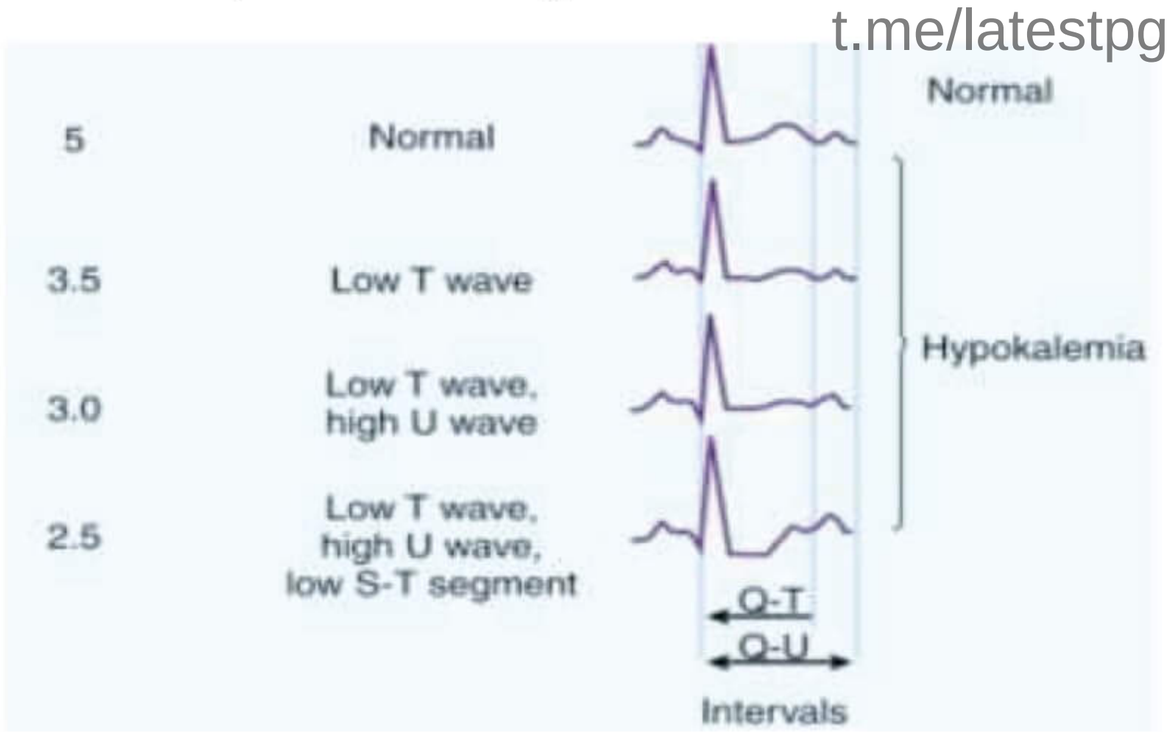
- Muscle weakness –
- Hypotonia
- Constipation
- Paralytic ileus
- Polyurea
- Polydipsia

ECG

3.5meq/L → Flattening of T-wave (1st sign of ECG)

3 meq/L → High U-wave

2.5meq/L → Low ST segment



TREATMENT → K^+ supplementations

Oral

IV –If serum $K^+ < 2.5$ meq/L

– If ECG changes

– If unable to take orally.

Infusion given – peripheral vascular access should not contain $K^+ > 40$ meq/L

HYPERKALEMIA:

- Serum K^+ level > 5.5 meq/L

Etiology:

i. **increase Intake** – oral/IV
   - Blood transfusion

ii. **Spurious Lab value →**
   - Hemolysis
   - Tissue ischemia during sampling
   - Thrombocytosis/leukocytosis

iii. **Transcellular shifts →**
   - Acidosis
   - Hemolysis
   - Rhabdomyolysis
   - Tumor lysis syndrome
   - Malignant hyperthermia
   - Hyperkalemic periodic paralysis
   - Drugs e.g. **digitalis**, Beta blockers, succinyl choline.

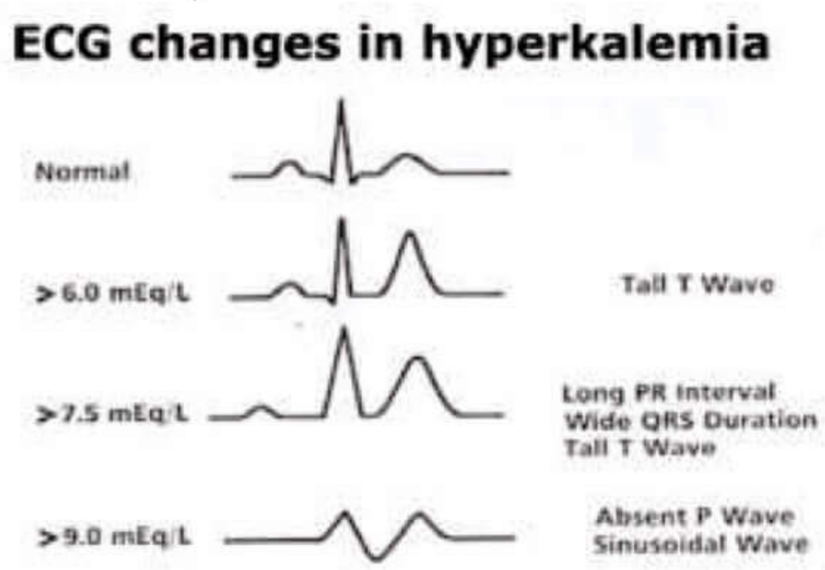
iv. **Decreased excretion:**
   - Renal failure
   - Addison disease
   - **CAH** (21 hydroxylase deficiency)
   - Hyporeninemic hypoaldosteronism
   - Pseudo-hypoaldosteronism
   - Sickle cell disease
   - Drugs e.g. ACE inhibitors, Angiotensin receptor blocker.

ECG changes:

>6meq/L→ Tall T waves

> 7.5 meq/L → long PR internal
   - Wide QRS
   - Tall T-waves

> 8 meq/L → Absent P-waves
   - sinusoidal waves



Rx:

- **Mild** (5.5-6meq/L) → Stop K^+ intake & offending drugs
- **Moderate** (6-8meq/L) → Inj. Sodium Bicarbonate
  - Insulin-glucose infusion

  Severe (>8 meq/L) → Inj. **Ca gluconate** + Rx of moderate Hyperkalemia
- **Refractory Hypercalcemia** → Hemodialysis
- **Long term Rx** → K^+ binding resin

MAINTENANCE OF IV FLUIDS & MANAGEMENT OF SHOCK IN CHILDREN:

How to calculate 24 hr maintenance fluid in children?

- For a child, who cannot be fed enterally.

  How much IV fluid? → HOLIDAY SEGAR METHOD

  For 1st 10 kg → 100ml/kg

  Next 10 Kg → 50ml/Kg

  >20 Kg → 20ml/kg

  E.g. Weight of child – 18 Kg

  1st 10 kg=10× 100=1000ml

  8 kg= 8× 50= 400ml

  1400ml

  So, child needs **1400ml** of IV fluid in 24 hours.

- **Hourly Maintenance fluid rate-**

  <10 kg→ 4ml/kg/hr.

  Next 10 kg → 40ml/hr.+ 2ml/kg/hr.

  Beyond 20 kg → 40ml/hr.+ 20ml/hr.+ 1ml/kg/hr.

  E.g, if weight of child-18kg

  1st 10kg=40ml

  8Kg=16ml

  56 ml/hr.

Recommended **Maintenance fluid** in children=Ds+ 1/2Ns+20Meq/L of K^+

- FLUID REQUIREMENT IN NEONATE-

  - based on birth Weight & day of the life (in ml/kg/day)

BIRTH WEIGHT	D1	2	3	4	5	6	7& BEYOND
<1500gm	80	95	110	120	130	140	150
≥ 1500gm	60	75	90	105	120	135	150

Q. Which fluid?

1st 48 hrs. of life→ 10% dextrose alone

> 48 hrs. → Na^+ & K^+ added

SHOCK:

DEFINITION

An acute syndrome characterized by inability to deliver adequate O_2 to meet the metabolic demands of vital organs & tissue.

TYPES-

1. Hypovolemic
2. Obstructive
3. Distributive

4. Cardiogenic
5. Septic

-**MC cause / type of shock in children – Hypovolemic shock**

-**Hypovolemic Shock** – intravascular fluid loss, through capillary leak

-**Cardiogenic shock**- Myocardial depression, effects of sepsis

- **Distributive shock** (Due to ↓ systemic vs resistance)

-**Septic shock** is a combination of hypovolemia (due to capillary leakage) + cardiogenic + Distributive shock

➔ **Compensatory Mechanism** In early phases of shock-

1. ↑ HR
2. Stroke volume & ↑ vascular smooth muscle tone → to maintain B.P & tissue perfusion.

➔ **MX OF SEPTIC SHOCK IN CHILDREN**

Early identification & treatment with appropriate Antibiotics

➔ **TREATMENT:**

0 min – start **high flow O_2** & establish IV / Intra Osseous access **(Tibial)**

↓

5 min – 1) Push boluses of **20 ml / kg of NS up to 60 ml / kg** unless perfusion improves or rales / Hepatomegaly subsides

2) Correct Hypocalcemia & hypoglycemia

3) Begins Antibiotics

↓

If still **shock not reversed → Fluid Refractory Shock**

↓

15min- Begin **Inotropes eg Dopamine** (DA)

Obtain **central venous access** & airway if needed

- **if resistant**- titrate Epinephrine (EP) (**Cold shock**) or NE (**warm shock**).

↓

Shock not reversed

↓

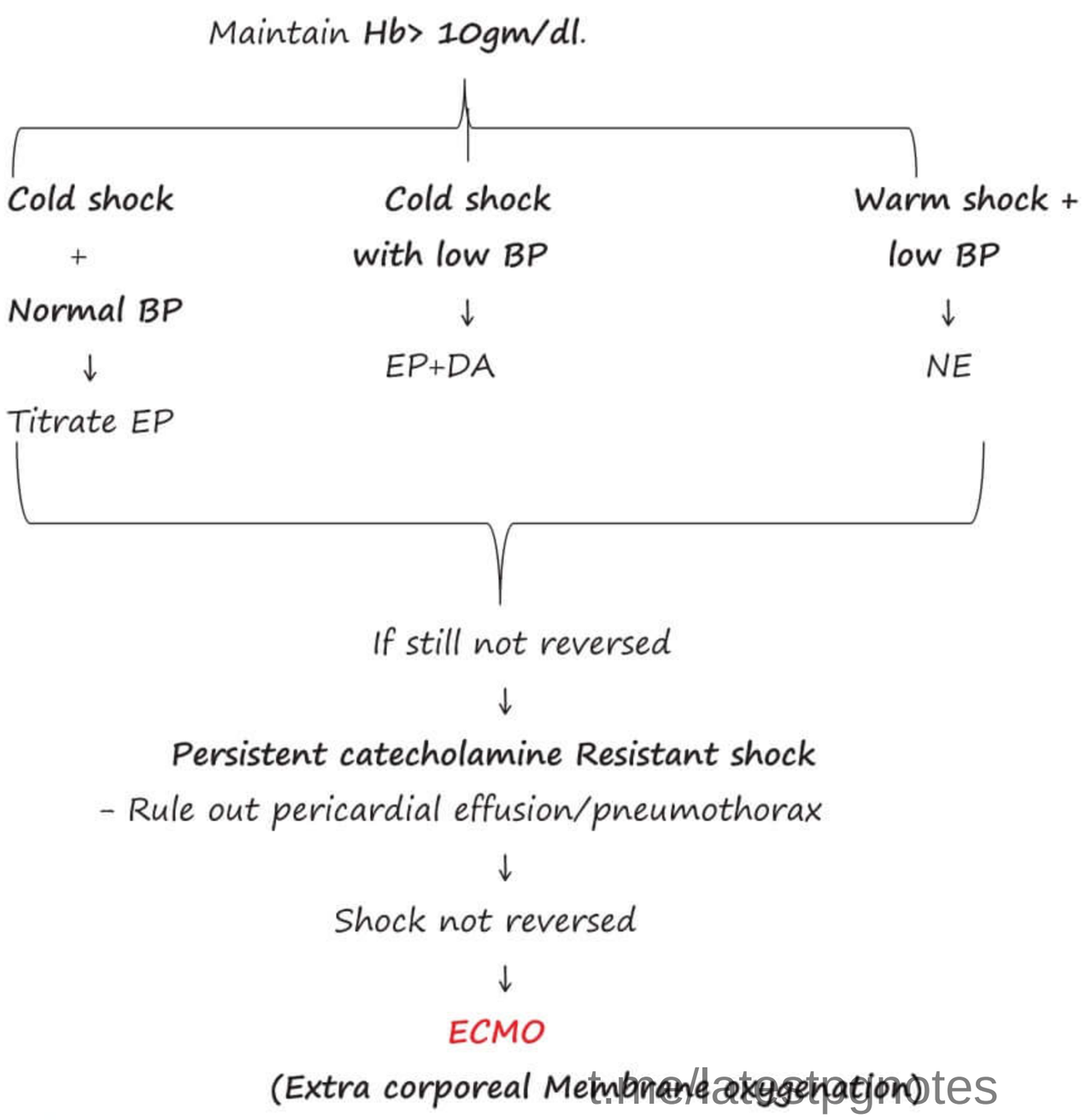
60min- Catecholamine Resistant shock

↓

Begin-hydrocortisone

Monitor CVP

Maintain normal MAP CVP & $SCVO_2$>70%



RECENT UPDATES-

- Protocolized approach **not preferred.**
- **Individualized approach** to suit patient physiology & settings
- CRYSTALLOIDS ARE PREFERRED
- "DERESUSCITATION"
  - Restricting Maintenance fluid after initial resuscitation
  - Use of diuretics

Advantage- More ventilation free days & shorter ICU stay.

MONITORING FLUID RESUSCITATION RESPONSIVENESS-

- **Poor predictors**-HR, SBP, CVP
- **Good bedside predictor**- Hemodynamic changes by passive leg raising.
- **Consistent predictors**- **respiratory variation** in **aortic** blood flow peak velocity.

GENETICS

TYPES OF GENETIC DISORDERS:

CLASSIFICATION:

Type of disorder	Description
Single gene disorders (Mendelian disorders)	Single genes are altered
	Follow mendelian mode of inheritance
	Eg: Hemophilia
Chromosomal disorders	Entire chromosome or segments of them are: Missing Duplicated or altered
	Can affect chromosomal number or structure
	Eg: Down's syndrome
Non-mendelian disorders	1. Trinucleotide repeats 2. Mitochondrial inheritance 3. Genomic Imprinting 4. Gonadal Mosaicism
Multifactorial disorders	Results from a combination of multiple genetic & environmental causes
	Eg: cleft palate Neural tube defects

MENDELIAN DISORDERS:

AUTOSOMAL DOMINANT DISORDERS:

→ Manifest even if only one of the alleles of the abnormal gene is affected

→ At least 1 Parent is affected

→ Examples (HEAVY DOMINANT)

- Hypercholesterolemia, Hereditary spherocytosis, HNPCC
- Ehlers danlos syndrome (except type VI)
- Adenomatous polyposis coli
- Von willebrand disease
- Y- PseudohYpoparathyroidism
- D- Dystrophia Myotonica
- O-Osteogenesis Imperfecta

- Marfan syndrome
- Intermittent porphyria
- Neurofibromatosis 1 and 2
- Achondroplasia, Adult polycystic kidney disease
- Noonan's syndrome
- Tuberous sclerosis

AUTOSOMAL RECESSIVE DISORDERS:

→ Manifest only if both the alleles of the abnormal gene are affected

Examples: (ABCDEFGHI)

- Albinism, Alkaptonuria, Ataxia telangiectasia
- Beta [Thalassemia, Sickle cell anemia]
- Cystic fibrosis, Congenital Adrenal hyperplasia
- Deafness (Sensorineural)
- Emphysema (α – 1 antitrypsin deficiency)
- Friedrich's ataxia
- Gaucher disease, Galactosemia
- Homocystinuria, Hemochromatosis
- Inborn errors of metabolism

X-LINKED RECESSIVE DISORDERS

→ Males are MC affected

→ Affected males have carrier daughters & unaffected sons because they pass their x chromosome to their daughters & Y chromosome to sons

→ Male – to- male transmission excludes x – linkage

→ **Examples:**

- G6PD deficiency — Girls
- Duchenne muscular dystrophy — Do
- Color blindness — care
- Fragile- x – syndrome, Fabry disease — for
- Chronic granulomatous disease — CHAWAL
- Hemophilia A & B, Hunter disease

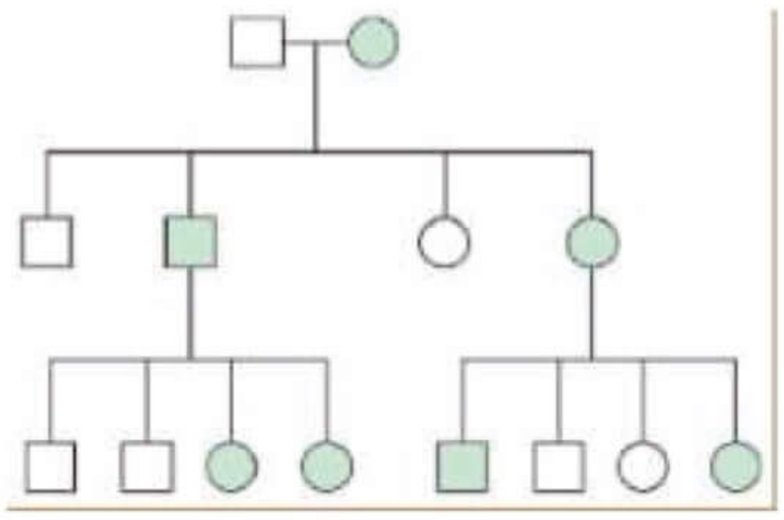
- Agammaglobulinemia
- Wiskott-Aldrich Syndrome
- Albinism
- Lesch – Nyhan syndrome, Lowe syndrome

X-LINKED DOMINANT DISORDERS

→ All daughters, but no sons of an affected male have the disease

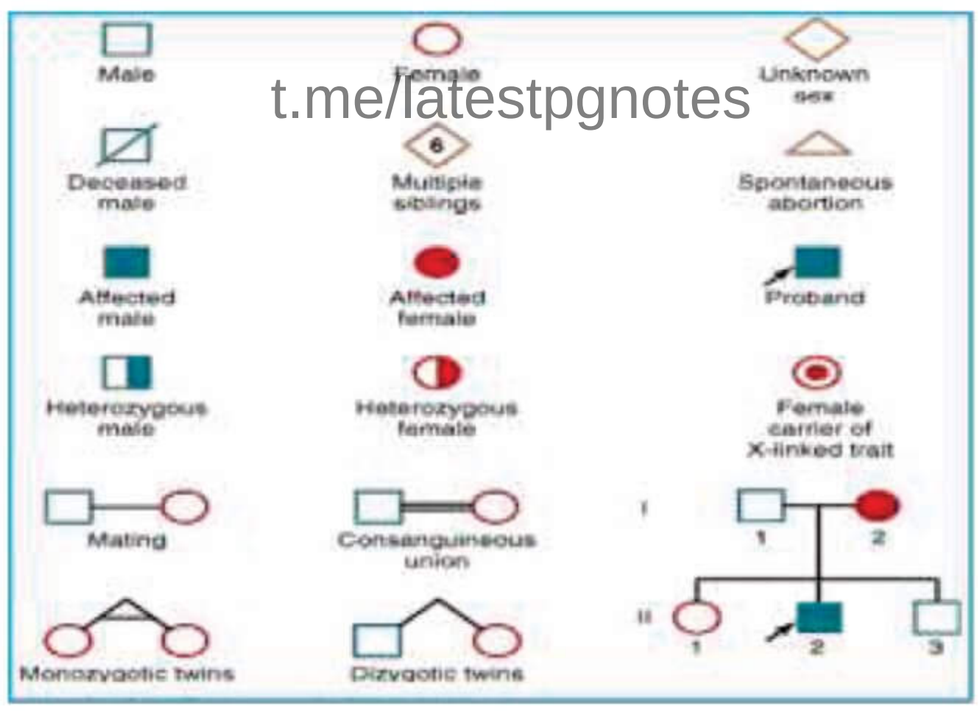
→ **Examples**:

- Red – X- linked hypophosphatemic Rickets
- Rose- Rett syndrome
- For – Fragile x syndrome
- All – Alport syndrome
- Children – Charcot-Marie-Tooth disease



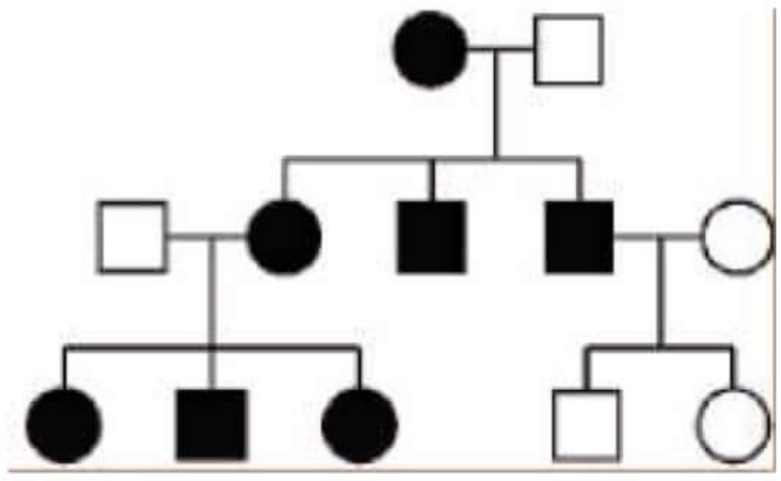
PEDIGREE ANALYSIS:

Important symbols used



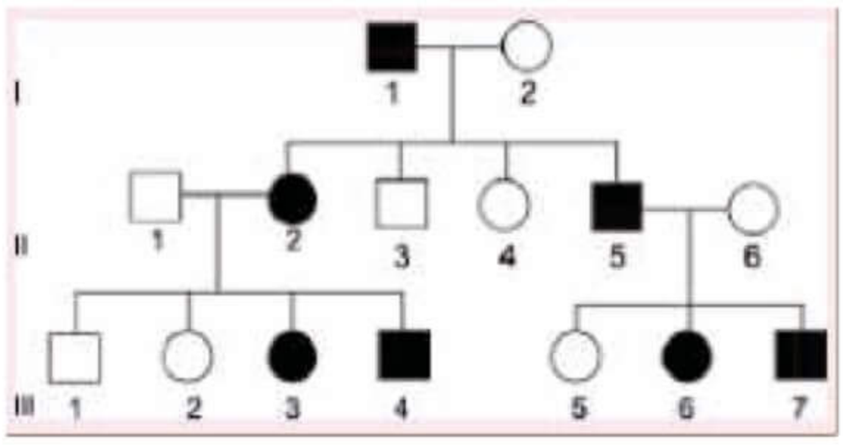
Pattern	Inheritance
All or most children of a mother are affected	Mitochondrial
If at least one of the parents always have the disorder	Dominant
If neither parents has the disorder because they are heterozygous	Recessive
If both males and females are affected, with almost equal frequency	Autosomal
Father to son transmission of trait does not occur	X linked
More males affected: affected sons usually born to unaffected mothers	X linked recessive
More females affected: affected sons must have an affected mother	X linked dominant
It is passed from father to all sons	Y linked dominant

Diagnosis?

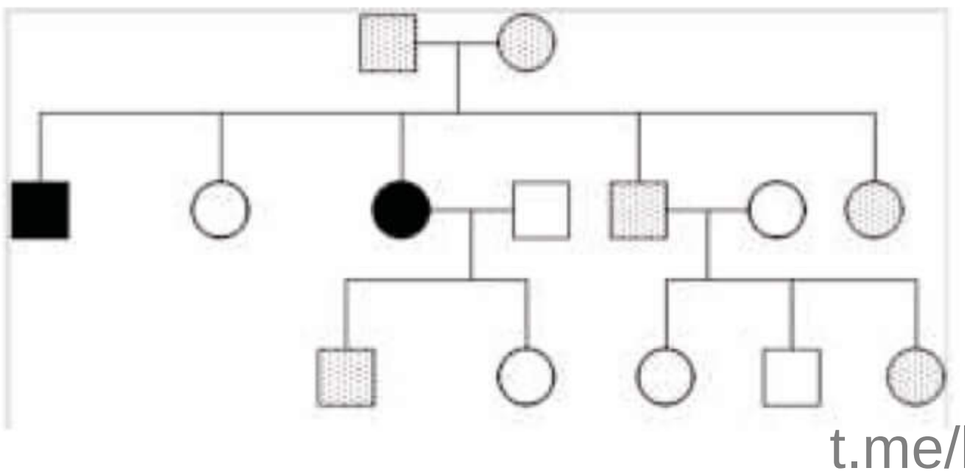


Mitochondrial Inheritance

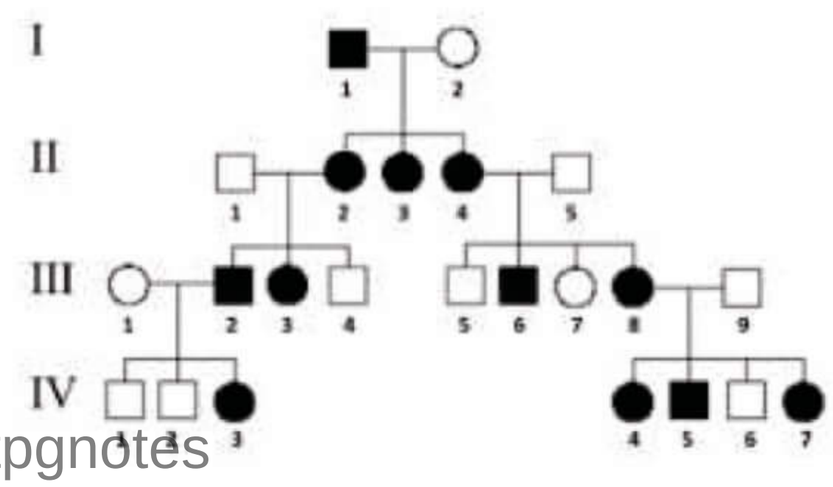
Diagnosis?



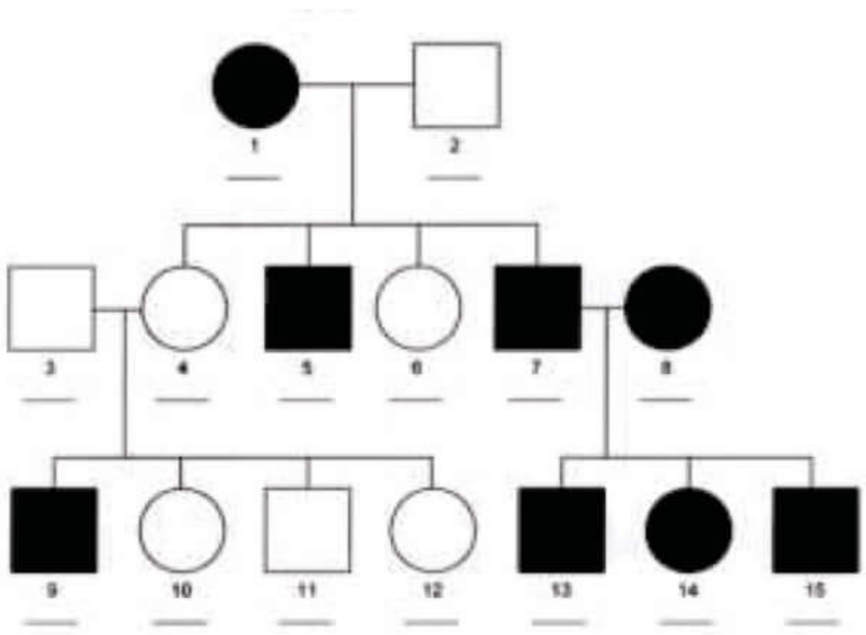
Autosomal Dominant Disorder



Autosomal Recessive inheritance



X-linked Dominant Disorder



X-linked Recessive Pedigree

→ NON-MENDELIAN DISORDERS

1. TRINUCLEOTIDE REPEAT DISORDERS
   - Due to ↑ in no. of Trinucleotide repeats, above a Certain threshold
   - No. Of Repeats usually correlates with the severity the Disease
   - ANTICIPATION Phenomenon is seen
     - Disease manifestation worsen from 1 generation to the Next or it may be observed at an earlier age due to increase in number of Repeats with successive Generation

Examples	Repeats
• Fragile-X-Syndrome	CGG
• Dystrophia Myotonia	CTG
• Huntington Disease	CAG

→ **FRAGILE – X – SYNDROME:**

- Gene involved → FMR 1 (Familial Mental Retardation-1) on Chromosome- X
- 2nd MC Genetic Cause of Intellectual Disability after Down's Syndrome

GENETIC BASIS:

- Normal Population → S- S5 CGG repeat
- Carriers → S5 – 200 Repeats (Premutation stage)

CLINICAL FEATURES:

- Long face
- Hyper extensible joints
- High Arched Palate
- Mitral Valve Prolapse
- Large Mandible
- Large Ears
- Large testis / Macro-orchidism (In post-Pubertal Males)

2. MITOCHONDRIAL DISORDERS

→ Mitochondrial DNA present in cytoplasm

- Exclusively derived from maternal side (Ovum)
- As only head of sperm (from father) contribute in zygote formation

→ Both male & female children born to an affected mother inherit the disease,

- As all of springs receive their mitochondrial DNA from their mother only

→ **HETEROPLASMY** – Presence of both Wild Type (Normal) and Mutated Mitochondrial DNA in same Individual.

→ **THRESHOLD EFFECT** – Minimum Percentage of mutant Mitochondrial DNA, that must be present in a cell for the disease to occur is called Threshold Effect or "Threshold of expression"

Examples (KLMNOP):

Kearn sayre syndrome

→ External ophthalmoplegia

→ Heart Block

→ Retinal Pigmentation

→ Ataxia

MERF

→ Myoclonic epilepsy

→ Ragged red fibers in muscle

→ Ataxia

→ Increased CSF Protein

→sensorineural deafness

→dementia

Leber hereditary optic neuropathy

→B/L subacute or acute painless optic atrophy

NARP

→ Neuropathy

→ Ataxia

→ Retinitis pigmentosa

MELAS

→ Mitochondrial Encephalo-myopathy

→ Lactic Acidosis

→ Stroke like episodes

CPE**O** (Chronic Progressive External Ophthalmoplegia)

→ B/L Ptosis

→ Ophthalmoplegia

→ Proximal Muscle weakness

Pearson syndrome → Pancreatic Insufficiency; Pancytopenia; Lactic Acidosis

1. GENOMIC IMPRINTING

- Gene Expression depends on the parent of origin of the chromosomes.
- Mostly due to Epigenetic Modification of Gene like Methylation of DNA.
- Epigenetic Modification → Alternation in DNA that doesn't Change Nucleotide sequence of DNA

Examples:

- Prader – Willi Syndrome
- Angelman Syndrome
- Russel-silver Syndrome
- Beckwith – Wiedemann Syndrome

Prader-Willi Syndrome	Angelman Syndrome
• Due to Microdeletion / Silencing of Paternal Copy of UBE 3A gene on Chr.15 or • Due to Maternal Disomy	• Aka Happy Puppet syndrome • Due to Micro deletion / silencing of maternal copy of UBE3A gene or • Due to Paternal Disomy

Clinical Features	Clinical Features
• Obesity • Short stature • Intellectual Disability • Hypotonia • Hypogonadism	• A → Ataxia • N → Not Intelligent • G → GTCS (Seizures) • EL → Excessive laughter • MAN → Maternal Gene not there

Imp Points:

- Unilateral Disomy
  - Gene Coming from one of parent gets Duplicated
  - Can be maternal Or paternal
- **Micro deletion**
  - Very small deletion in chromosome that can't be seen on karyotyping

4. GONADAL MOSAICISM

- Due to Mutations that occur Post-Zygotically i.e. after formation of zygote.
- Affects only cells destined to form gonads
- Somatic cells of that person are normal.

We suspect gonadal mosaicism in a case a scenario where →

- More than 1 children are affected with an autosomal Dominant disease like Osteogenesis Imperfecta
- But the parents are Phenotypically Normal.

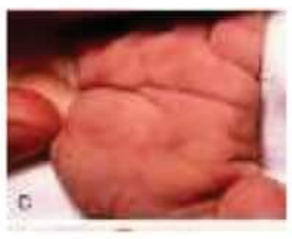
IMPORTANT GENETIC SYNDROMES:

DOWN SYNDROME

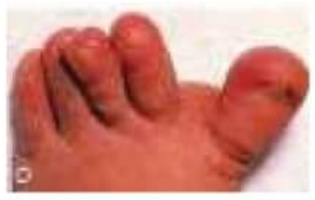
→ Mongoloid slant

→ Epicanthic folds

→ Depressed Nasal Bridge



Simian crease



Sandle Gap

clinodactyly

→ MC chromosomal abnormality seen in Children

→ **Basic defect – 3 copies of Chr. 21 (Trisomy 21)**

→ Incidence → 1:800- 1:1000 live births

→ Genetic basis

→ 95% - Maternal non disjunction (Mc)

→ 3% - Translocation

→ 1-2% - Mosaicism

CLINICAL FEATURES:

CVS

→ Endocardial cushion defects / AVSD (Most Common CHD)

→ VSD, ASD, PDA

→ PAH

GIT

→TEF

→ Duodenal atresia

(mc cause of intestinal obstruction

→Annular pancreas

→Hirschsprung disease

→ imperforate anus

CNS:

→ Lack of Moro's reflex

→ Hypotonia

→ Delayed development / Intellectual disability

IMPORTANT FEATURES (MNEMONIC → I C A PROBLEM Somewhere):

- Incurved 5th finger (clinodactyly) / Intellectual disability
- Congenital heart disease / Congenital hypothyroidism
- Acute leukemia / Alzheimer's disease (early onset) / Atlantoaxial instability / Absent Moro's Reflex / Atresia of Duodenum
- Protruding tongue
- Round face
- Occiput flat / Open, wide fontanelle
- Brushfield spots on Iris / Brachycephaly
- Low (depressed) Nasal bridge, Low tone (hypotonia)
- Epicanthic fold / Ears low set & dysplastic
- Mongoloid slant (oblique palpebral fissure)
- Sandle gap / Simian palmar crease

RISK OF DOWN SYNDROME WITH MATERNAL AGE

→ Risk of having a child with DOWN syndrome increases with increase in maternal age

MATERNAL AGE	INCIDENCE OF DOWN SYNDROME
20 years	1 in 1500
40 years	1 in 30

ANTENATAL SCREENING AND DIAGNOSIS BASED ON RADIOLOGICAL MARKERS (ANTENATAL USG)

- Increased Nuchal fold thickness (>3mm) – **Most sensitive**
- Absent nasal bones
- Cardiac abnormalities
- Duodenal atresia
- Shortened femur

BIOCHEMICAL MARKERS:

FIRST TRIMESTER SCREENING:

Screening method	Detection rate
Maternal age + Biochemical markers (β-HCG , PAPP-A)	70%
Maternal age + Radiology (USG-NT > 3 mm)	80-83%
Combined test: Maternal age + radiology + biochemical markers	82-87%

SECOND TRIMESTER SCREENING

Screening method	Detection rate
Triple test (β-HCG + AFP + Unconjugated Estriol)	67%
Quadruple test (Triple test + Inhibin A)	77%
Integrated test (Best test for Antenatal **Screening** of Down Syndrome) Maternal age + T1 – (NT > 3 mm + PAPP-A) + T2 – (Quadruple test)	94-96%

→ **'HI'**- HCG and Inhibin Levels increase in DOWN SYNDROME

CONFIRMATORY TEST FOR PRE-NATAL DIAGNOSIS OF DOWN SYNDROME: Fetal karyotype

→ Done by Obtaining Fetal Genetic material by following Methods.

Method	Gestation	Remarks
Chorionic villi sampling (CVS)	**11-13 weeks**	↑Risk of Abortions & Fetal limb defects
Amniocentesis	14-16 weeks	Complications →Pregnancy loss →Amniotic fluid leakage →Vaginal bleeding
Cordocentesis (or) Percutaneous Umbilical cord Blood Sampling (PUBS)	17-20 weeks	Fetal blood can be analyzed directly by HPLC after ensuring that there is no maternal contamination

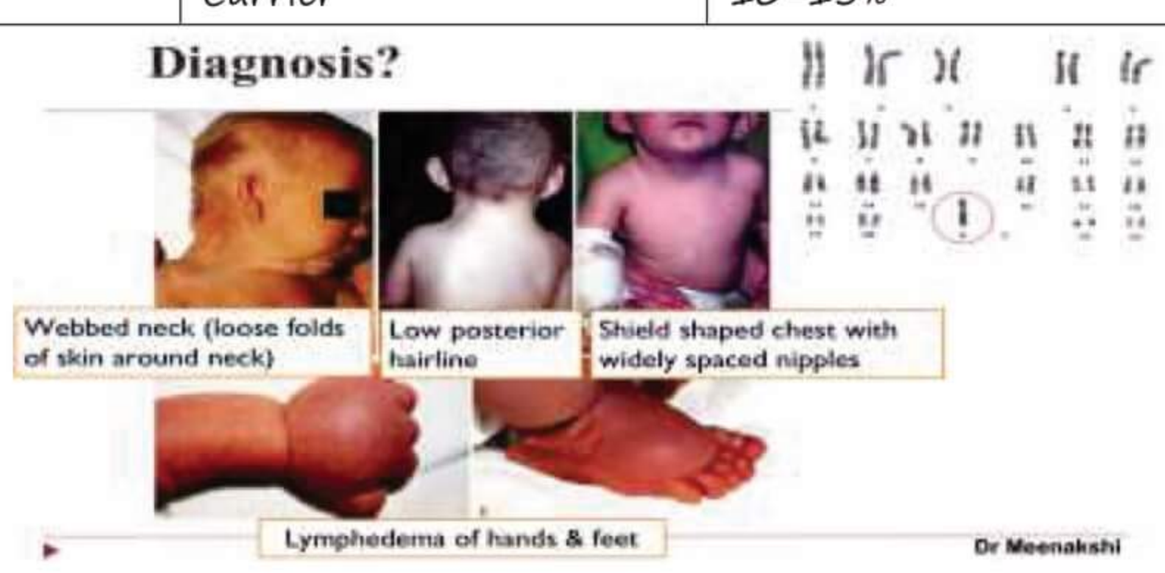
→ All these 3 Procedures have Increased Risk of Abortion.

Case Scenario – **A Couple Already has a child with Down syndrome. How to predict Recurrence risk of Down syndrome in Next Pregnancy ?**

Karyotype of affected child	Karyotype of parents		Recurrence risk
	Father	Mother	
Trisomy 21	N	N	~ 1%
Translocation 21q 21q	N	N	~ 1%
	Either parent carrier		100%
Translocation of Chr 21 with Other Chromosome	N	N	~1%
	Carrier	N	1-3%
	N	Carrier	10-15%

Q. Which is true about Turner syndrome?

a. Normal stature
b. Normal puberty
c. Normal fertility
d. Normal intelligence



Ans. D. Normal intelligence

TURNER SYNDROME:

→ Basic defect is 45 XO

→ Always seen in Females

→ Female is Infertile

→ Short stature & webbed neck

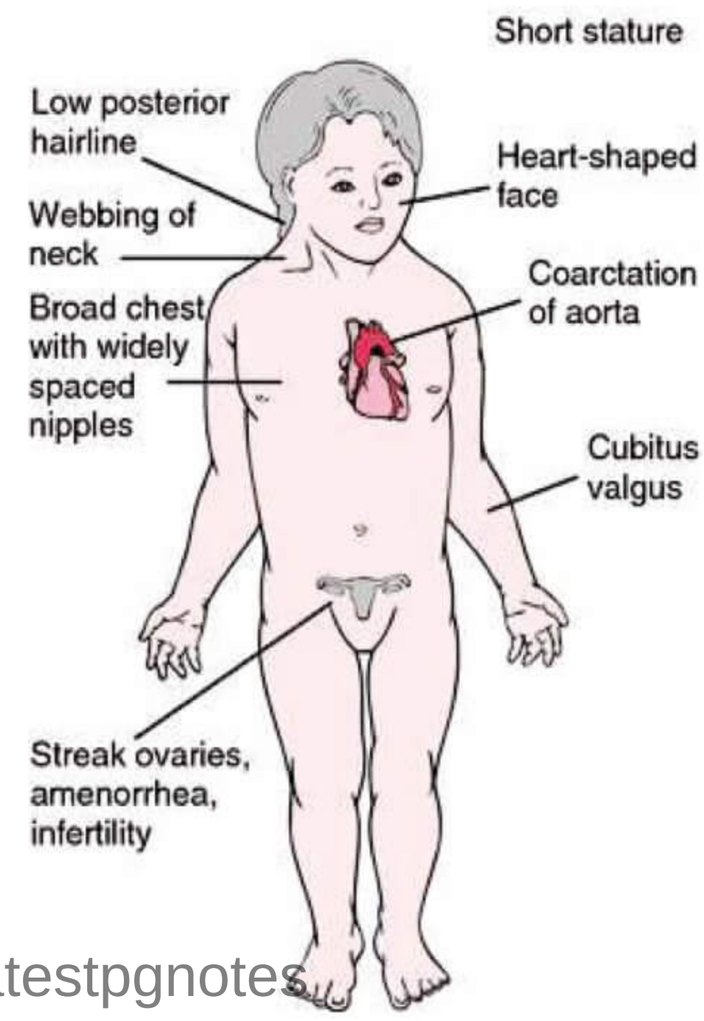
→ No intellectual disability

→ Bicuspid aortic valve (50%) (MC)

→ Coarctation of aorta (30%)

→ Aortic stenosis

→ Mitral valve prolapse



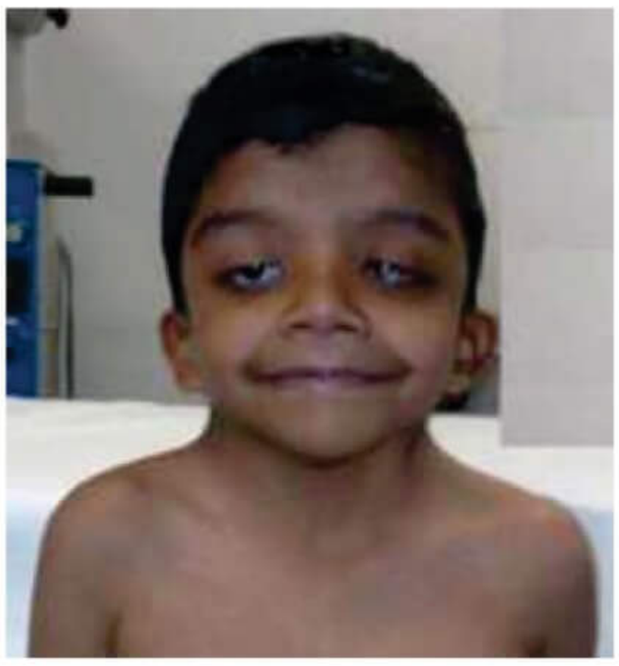
→ Short 4th metacarpal

IMPORTANT FEATURES (MNEMONIC – See There Is A Baby Clown)

- Short stature, Sensorineural hearing loss, Short 4th metacarpal
- Amenorrhea (Primary)
- Barr body absent; No. of Barr body = No of X-chromosome -1; Normal Female = 2-1 =1; Male = 1-1=0; In Turner =1-1=0
- Cardiac anomalies, Cystic hygroma
- Lymphedema of Hand and Feet, Low Thyroid
- Ovaries Underdeveloped (Streak Ovaries)
- Webbed neck
- Nipples widely placed, SHIELD shaped chest

OTHER GENETIC SYNDROMES:

NOONAN'S SYNDROME



→ Autosomal dominant, Normal karyotype

→ PTPN 11 gene (mc), Fertile

→ can be seen in both boys & girls

→ Short stature, webbed neck

→ Antimongoloid slant eyes (Opposite of Down syndrome

→ Cubitus valgus

→ Clinodactyly, Cryptorchidism

→ Supra valvular Pulmonary Stenosis (mc Congenital Heart Disease in Noonan's), HOCM, ASD

→ **Intellectual disability present**

SIMILARITIES WITH TURNER SYNDROME:

- Webbed neck

- Short stature

- Cubitus valgus

DIFFERENCES FROM TURNER SYNDROME:

- Delayed puberty but fertility is normal whereas infertility seen in Turner syndrome

- Intellectual disability not seen in Turner but seen in Noonan syndrome

- Seen in both boys and girls

- Karyotype is normal

EXTRA EDGE:

- In Noonan syndrome, Congenital heart disease is seen in 80% children (More common than in TURNER SYNDROME)

- Incidence of Congenital Heart disease in Turner Syndrome is 3 times more common in those with WEBBED NECK as compared to those without WEBBED NECK.

TRISOMY 18 (EDWARDS SYNDROME) (MNEMONIC- ROCKY MOUNTAIN)

Rocker bottom foot

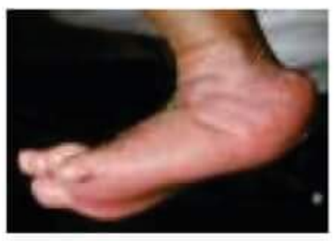
Overlapping fingers

Cardiac defects

Kidney malformations

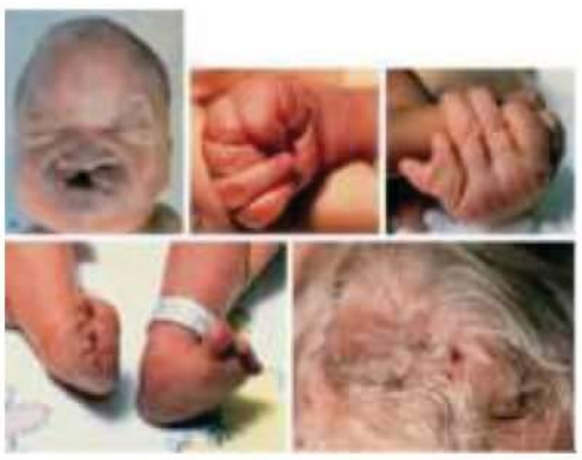
Y – Microcephal**Y**

Mental retardation



TRISOMY 13 (PATAU SYNDROME)

More severe craniofacial & midline defects than trisomy 18 or 21

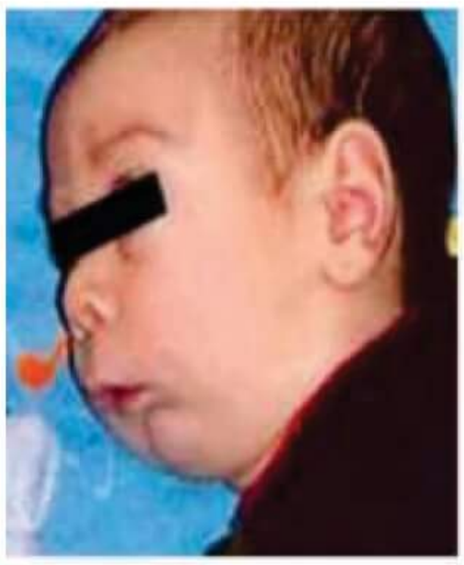


IMPORTANT FEATURES (MNEMONIC – CMC DOCTOR OPD)

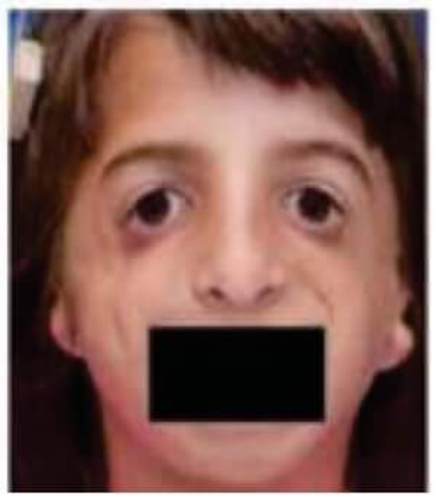
- **C**utis aplasia
- **M**icrophthalmia, **M**icrocephaly
- **C**ongenital Heart disease
- **D**eafness
- **O**thers (Renal Abnormalities)
- **C**left Lip and **C**left Palate
- **T**risomy 13
- **O**cular Hypotelorism
- **R**ib abnormalities
- **O** – h**O**l**O** prosencephaly
- **P**olydactyly
- **D**evelopmental delay

IMAGES OF SOME IMPORTANT GENETIC SYNDROMES:

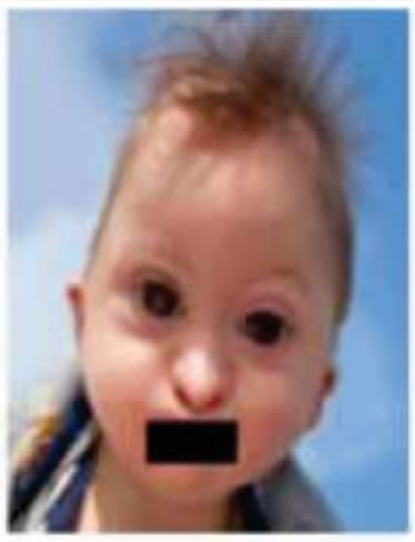
Pierre robin syndrome



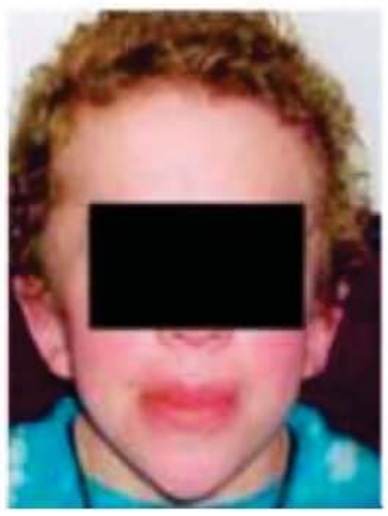
Treacher Collin syndrome



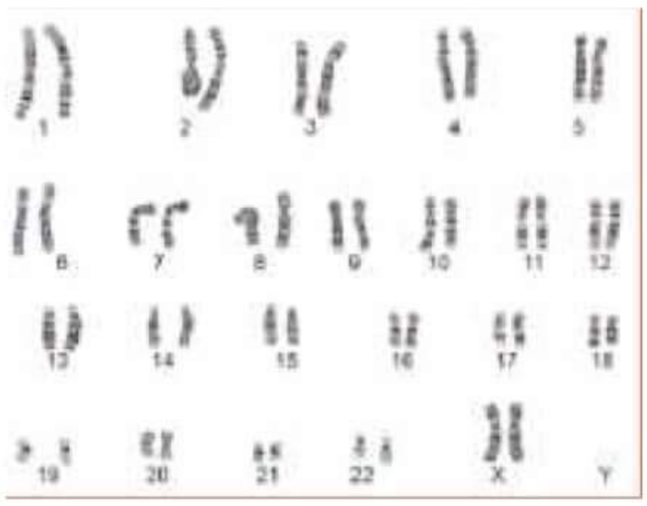
Seckel syndrome



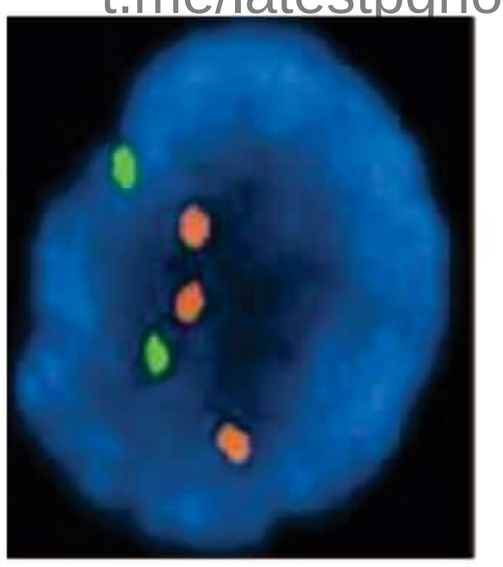
Russel silver syndrome



IMPORTANT DIAGNOSTIC TOOLS:

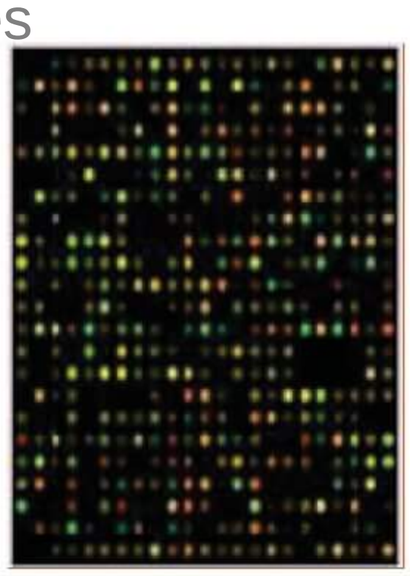


Karyotyping



FISH

(Flourescent In Situ Hybridization)



Microarray

INBORN ERRORS OF METABOLISM

DISORDERS OF CARBOHYDRATE METABOLISM:

Think 'METABOLIC': High index of suspicion is a must; if missed may prove fatal

Q. When to Suspect a Metabolic Disorder?

IN NEONATES & INFANTS

→ Deterioration after a period of apparent normalcy

→ Rapidly progressive encephalopathy +/- seizures

→ Sepsis like presentation with negative sepsis screen

→ Persistent / Recurrent vomiting; peculiar body fluids / urine odour

→ Significant family history

→ Parental consanguinity

→ Multiple Abortions

→ Siblings with similar illness

→ Investigations → Severe metabolic acidosis, ketosis & hypoglycemia

IN OLDER CHILDREN:

→ Rapidly progressive encephalopathy +/- seizures

→ Persistent / Recurrent vomiting; peculiar body fluids / urine odour

→ Significant family history

→ Episodic presentation

→ Worsening with Intercurrent Illness

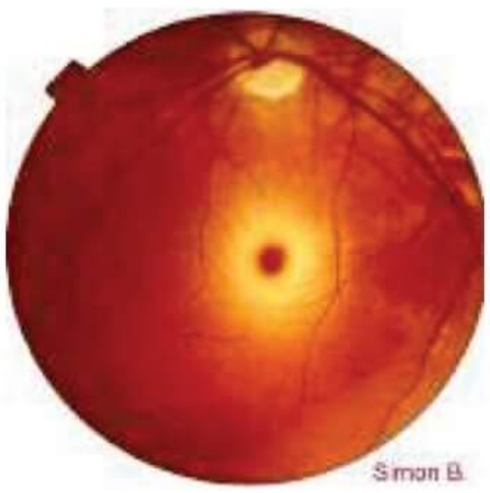
→ Ataxia / Other CNS manifestations

→ Multisystemic Involvement

→ Investigations → Severe metabolic acidosis, ketosis & hypoglycemia

CLINICAL POINTERS FOR SPECIFIC INBORN ERROR METABOLIC SYNDROMES:

Clinical finding	Disorders
Coarse facies	Lysosomal disorders (Mucopolysaccharidosis), GM 1 gangliosidosis
Cataract	Galactosemia, Wilson disease, Diabetes mellitus
Retinitis pigmentosa	Mitochondrial disorders
Cherry red spot	GM 1 gangliosidosis, Niemann Pick disease, Tay Sachs disease
Eczema / Alopecia	Biotinidase deficiency, Multiple carboxylase deficiency
Abnormal kinky hair	Menke disease
Hypopigmentation	Phenyl ketonuria, albinism



Cherry Red Spot

DISORDERS OF CARBOHYDRATE METABOLISM:

→ Glycogen storage diseases

→ Galactosemia

→ Hereditary Fructose Intolerance

GLYCOGEN STORAGE DISEASES (GSD)

IMPORTANT GLYCOGEN STORAGE DISEASE:

LIVER GLYCOGENOSES

Liver Glycogenoses	Enzyme deficiency
I Von Gierke disease	Glucose 6 phosphatase
III Cori disease	Debranching enzyme
IV Anderson disease	Branching enzyme
VI Hers disease	phosphorylase

→ Muscle may also be involved in Cori's Disease

MUSCLE GLYCOGENOSES:

Type	Name	Enzyme Deficiency
II	Pompe Disease	α-1,4 Glucosidase
V	Mc Ardle Disease → MC GSD in Adolescents /Adults	Muscle Phosphorylase
VII	Tarui Disease	Phosphofructokinase

[2+5 =7; MC GSD IN ADOLESCENCE → MCARDLE DISEASE]

Q. Child with recurrent hypoglycemic attacks & hepatosplenomegaly is likely to have

A. Von Gierke Disease

VON GIERKE DISEASE:

Most common GSD in children

→ Autosomal recessive

→ Type 1a → Glucose 6 phosphatase deficiency

→ Type 1b → Translocase deficiency

→ **CLINICAL FEATURES:**

→ Recurrent Hypoglycemia +/- seizures

→ Hepatomegaly

→ Easy Bruising

→ Doll like facies

→ **INVESTIGATION FINDINGS IN VON GIERKE'S DISEASE:**

→Hypoglycemia → Hyperuricemia

→Lactic acidosis → Hyperlipidemia

→ **DEFINITIVE DIAGNOSIS**

→ Liver Biopsy

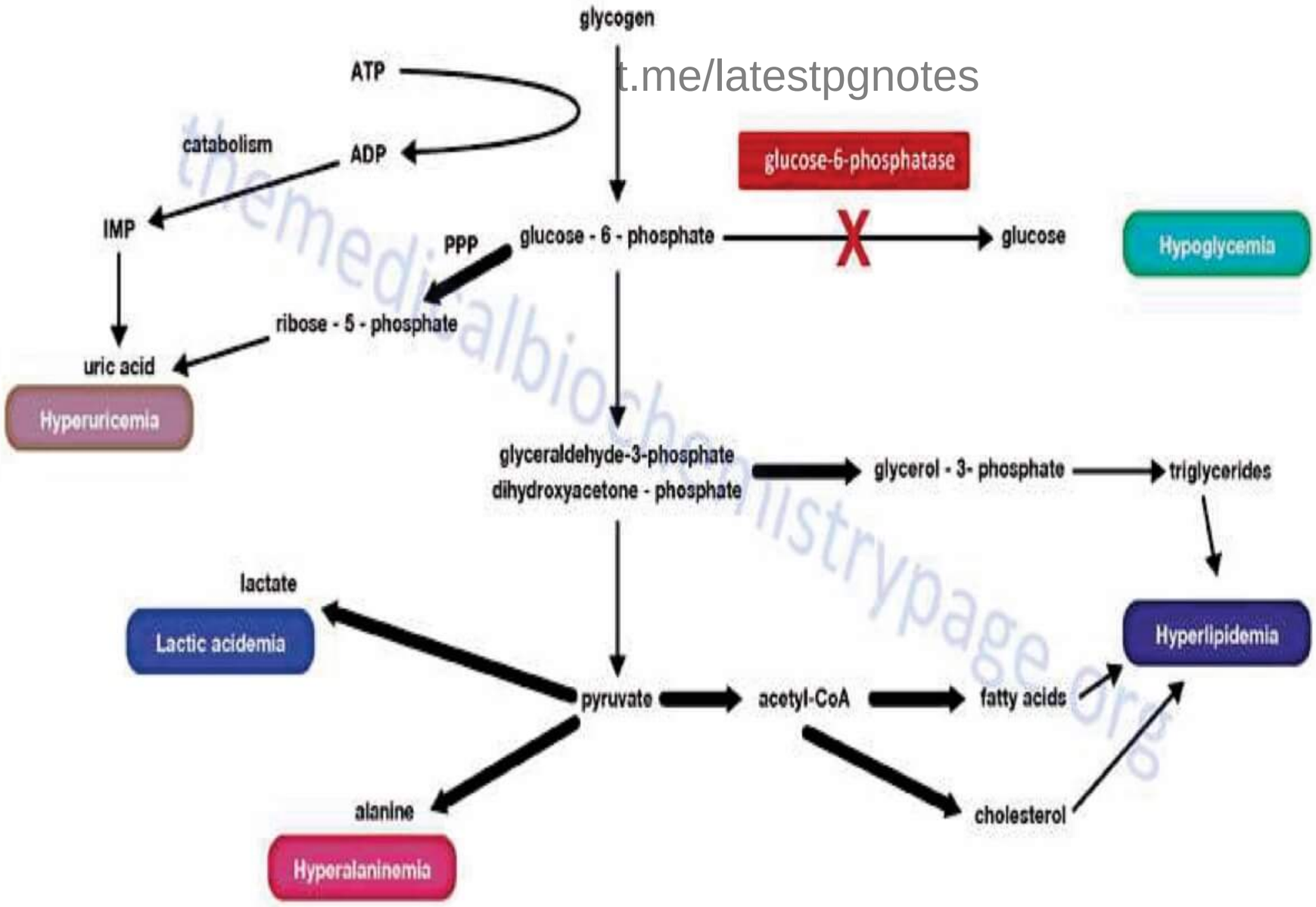
- → Gene based tests

→ **COMPLICATIONS**

- → Hepatic Adenomas
- → Pulmonary HTN
- → Renal stones
- → Proteinuria
- → Hypertension

→ **Treatment**

- → Frequent feeding
- → Corn starch diet



→ Both Type I and Type III GSD have Hepatomegaly, Hypoglycemia & Hyperlipidemia

DIFFERENCES BETWEEN TYPE I & TYPE III GSD

	Type I GSD	Type III GSD
Kidneys	Enlarged, spleen normal	Normal, splenomegaly seen
Muscles	Not involved	May be involved
CPK levels	Normal	May be elevated
LFT	Usually normal	Transaminitis & fasting ketosis +
Lactate	Elevated	Usually normal
Effect of glucagon	No rise in blood glucose, but lactate level rises	2 hr after meal - ↑ in blood glucose After fast – no increase
Liver Biopsy	Distension of Hepatocytes by Glycogen and Fat	Fibrosis and Paucity of Fat

POMPE DISEASE:

→ **Enzyme Deficiency** – Acid Maltase or α-1,4 Glucosidase

→ **Clinical Features**:

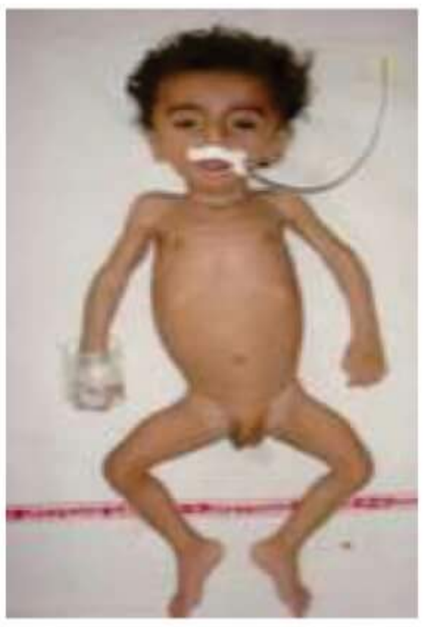
→ Hypotonia

→ Cardiomegaly

→ Hepatomegaly

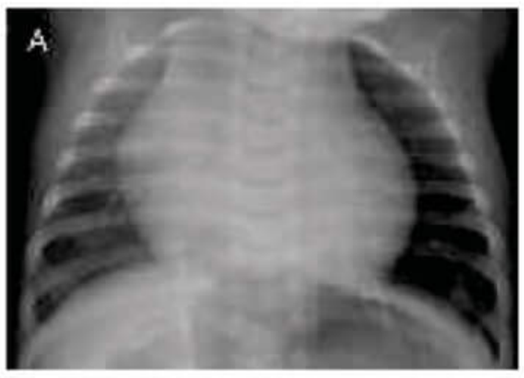
→ Coarse facies

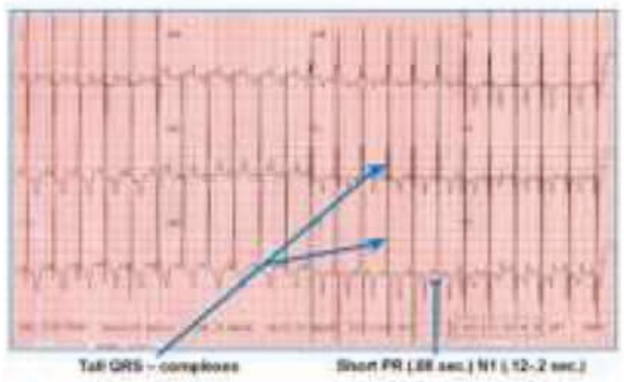
→ **Treatment** – ERT (Enzyme Replacement Therapy)



Floppy Child

Head Lag





Cardiomegaly

GALACTOSEMIA:

- Autosomal Recessive
- Deficiency of
    - GALT (Galactose 1 PO4 Uridyl transferase) (MC)
    - Galactokinase
    - Epimerase

PATHOPHYSIOLOGY:

- Milk → Lactose → Glucose + **Galactose**
- Galactose can't get digested in body due to Enzyme Deficiency
- **Breast feeding is Contraindicated** in Confirmed cases of Galactosemia
- **GALT Deficiency** → Accumulation of Galactose-1-Phosphate which is Toxic to Kidney, Brain and Liver
- **Galactokinase Deficiency** → Accumulation of Galactose and Galactitol which is Toxic to Eye

→ CLINICAL FEATURES:

- Jaundice
- Hepatomegaly
- Seizures +/- MR
- Cataract (Might be the only manifestation of Galactokinase Deficiency)
- Diarrhoea / vomiting
- Failure to thrive
- Sepsis with E.coli is common in children with Galactosemia

DUARTE VARIANT OF GALACTOSEMIA

- Quite Common
- Due to Single Amino Acid Substitution
- 50 % of Normal Enzyme Activity Present

- These Children usually remain Asymptomatic
- No Clinical significance of this Condition
- Diagnosis:
  - Reducing Substances in Urine Positive (detected by Benedict's Test)
  - Direct Enzyme assay
  - Prenatal Diagnosis is also Possible

→ TREATMENT:

- Avoid Milk and Milk Products
- Use Lactose free formulas

HEREDITARY FRUCTOSE INTOLERANCE

→ **Enzyme deficiency** – Aldolase-B or Fructose-1,6 Bisphosphate Aldolase

→ PATHOPHYSIOLOGY –

- Due to Aldolase B Enzyme Deficiency, there is accumulation of Fructose 1 Phosphate as Fructose metabolism is Hampered.
- Fructose 1 Phosphate so accumulated is Toxic to body (mainly Liver)
- Symptoms appear on intake of Fructose
- Child has Aversion to sweet food

→ CLINICAL FEATURES

- Hypoglycemia
- Jaundice
- Hepatomegaly
- Vomiting

→ DIAGNOSIS:

- Reducing substance in urine → Positive-Benedict's test
- Assay of Aldolase B activity in Liver
- Gene based Diagnosis available

→ TREATMENT → Complete Elimination of sucrose and Fructose from diet

DISORDERS OF AMINO ACID METABOLISM:

1. ORGANIC ACIDEMIAS

- Multiple carboxylase deficiency
- Maple syrup urine disease (MSUD)

2. UREA CYCLE DISORDERS

3. DISEASES OF PHENYLALANINE PATHWAY

- Phenylketonuria
- Alkaptonuria
- Tyrosinemia

4. OTHERS

- Hartnup disorder
- Homocystinuria

ORGANIC ACIDEMIAS:

CLINICAL FEATURES

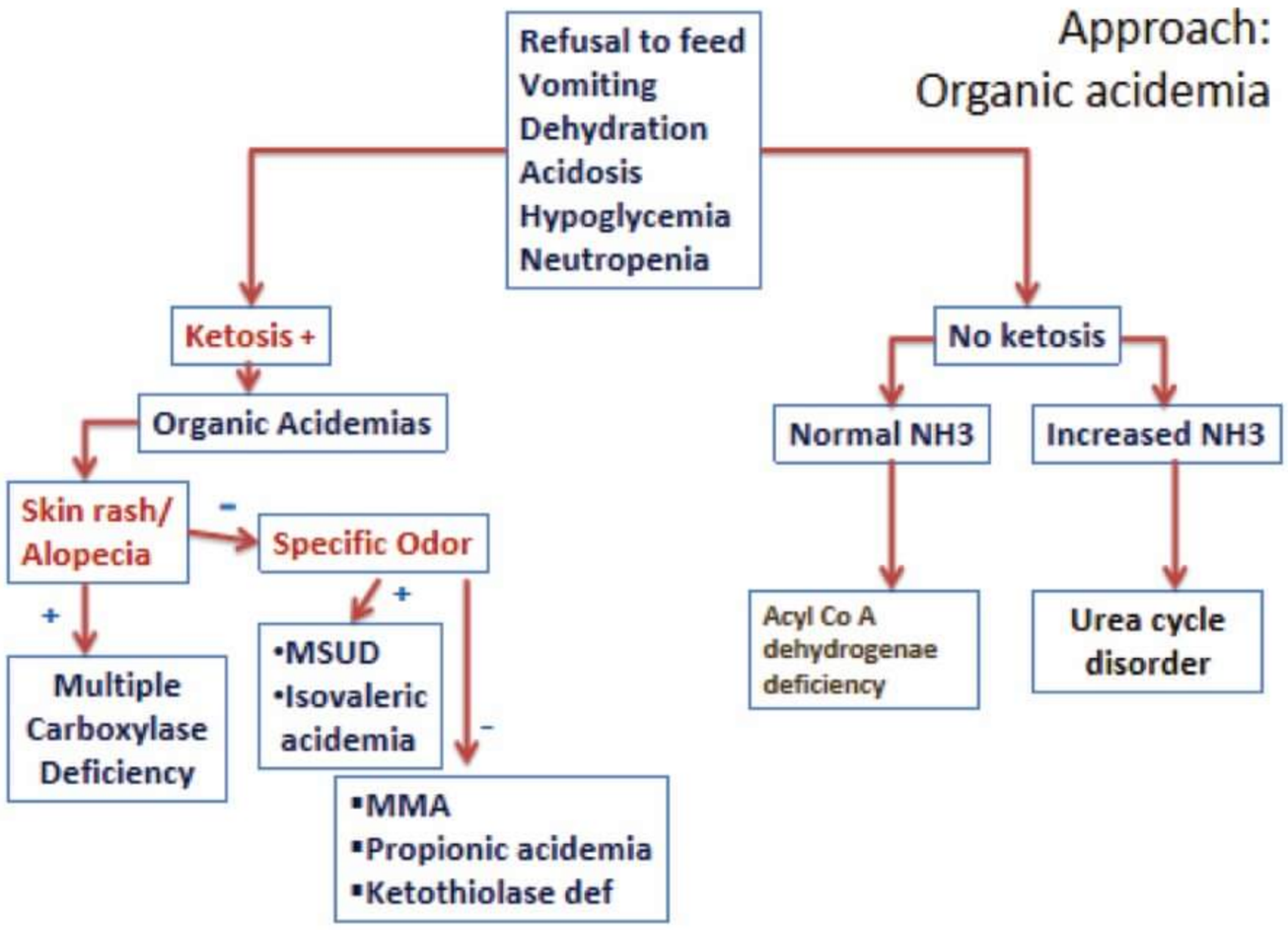
→ Lethargy, poor feeding, coma, vomiting, seizures, developmental delay, dystonia, specific odours.

INVESTIGATION FINDINGS:

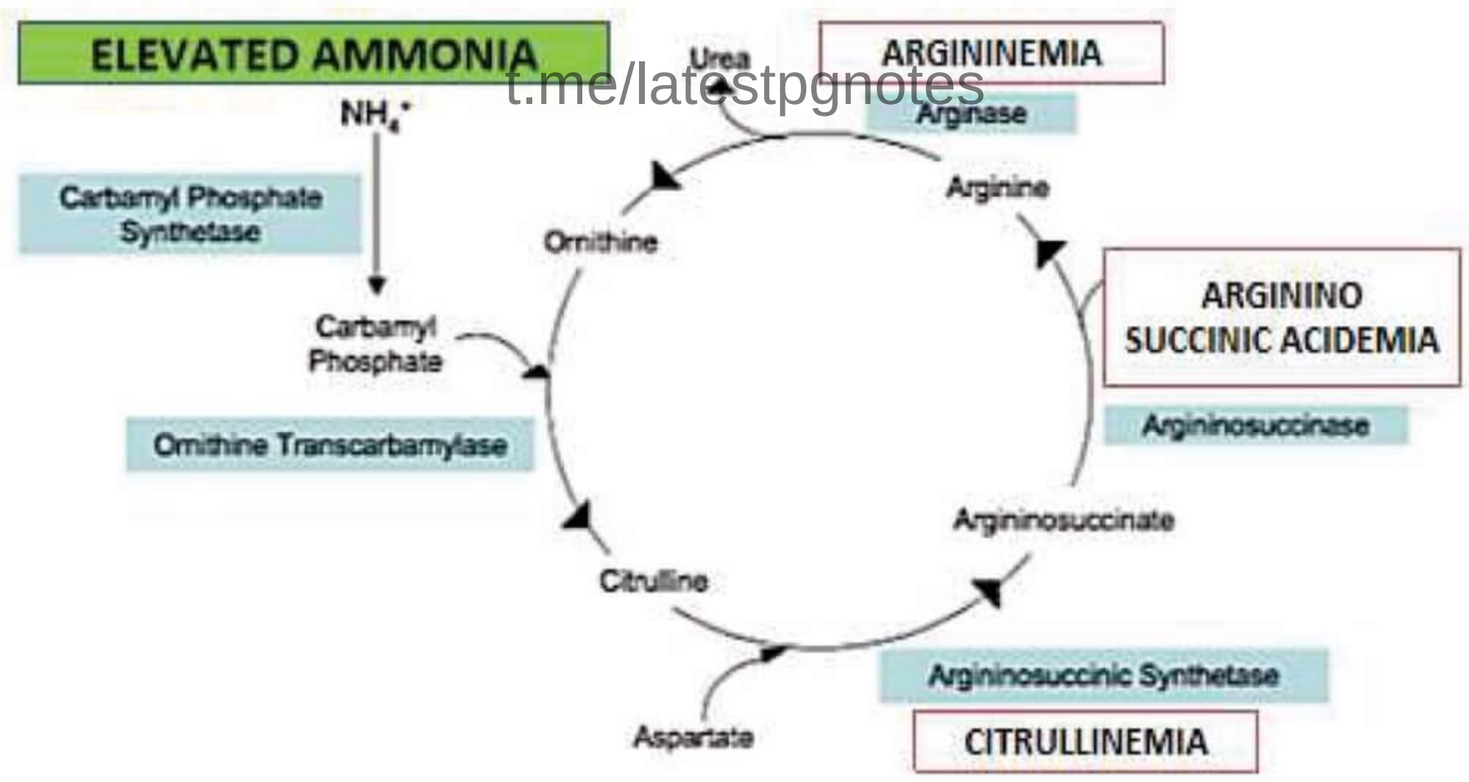
- Metabolic acidosis, lactic acidosis, Ketosis, Hyperammonemia, Hypoglycemia
- Neutropenia
    - Methyl malonic acidemia
    - Isovaleric Acidemia
    - Propionic Acidemia

IEMS WITH PECULIAR ODOUR

IEM	Urine ODOUR
Glutaric acidemia	Sweaty feet
Maple syrup urine disease	Maple syrup or Burnt Sugar
Tyrosinemia	Boiled cabbage
Multiple carboxylase	Tomcat
Phenyl ketonuria	Mousy or musty

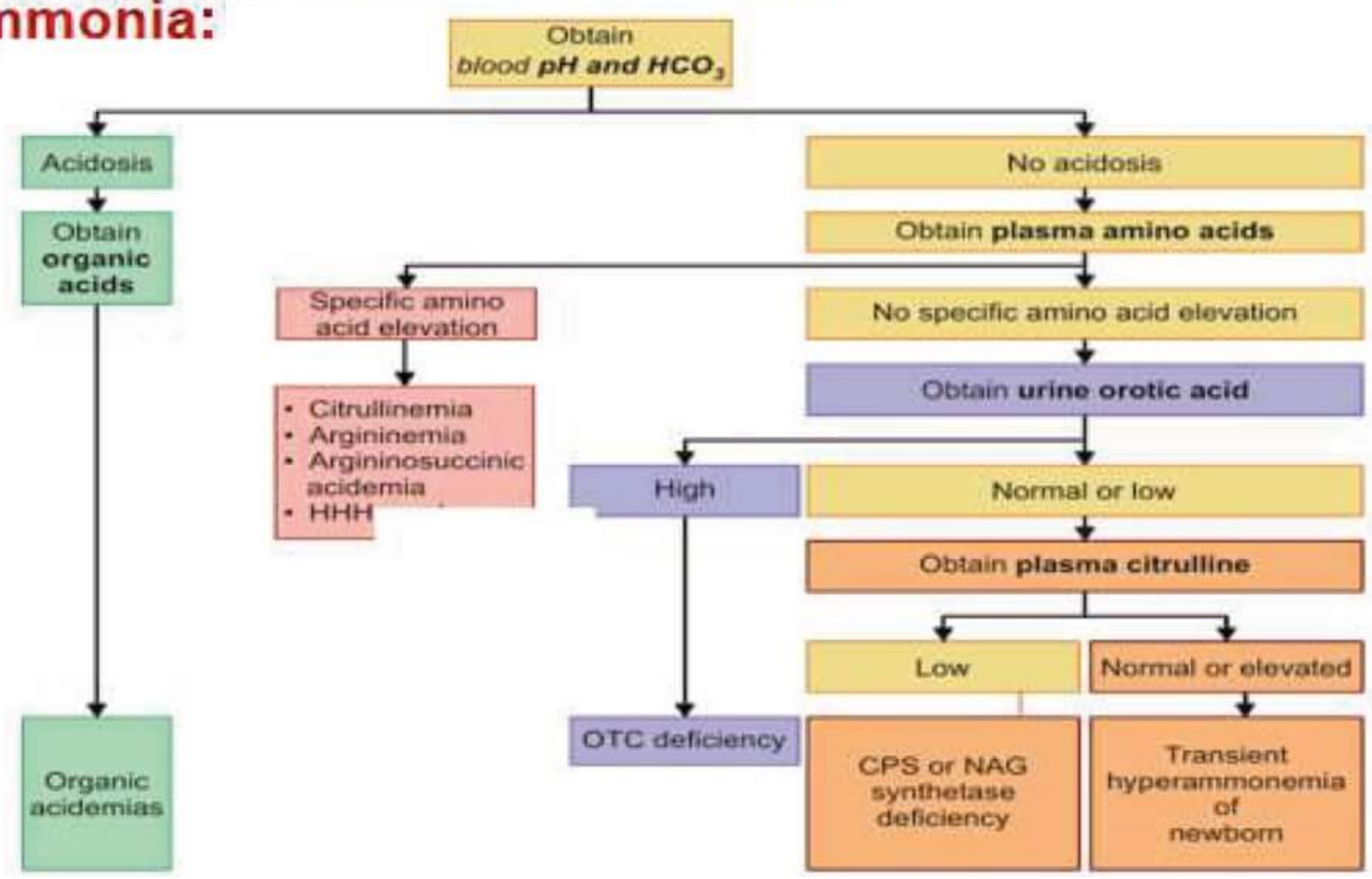


UREA CYCLE and IT'S DEFECTS:



Urea cycle & its defects

Approach to a child with elevated Ammonia:



TREATMENT OF ELEVATED AMMONIA

→ Phenyl Acetate

→ Arginine

→ Hemodialysis

→ Peritoneal dialysis

Q. An Infant with seizures, poor feeding & skin rashes and Alopecia. On Investigation: Metabolic acidosis, ↑ blood ketones & normal NH3. Diagnosis?

A. Multiple carboxylase deficiency

MULTIPLE CARBOXYLASE DEFICIENCY:

→ Autosomal Recessive

→ Tomcat urine odour

→ Confirmed by Enzyme assay in lymphocytes

→ Rx – **Biotin**

MAPLE SYRUP URINE DISEASE (MSUD)

→ Autosomal Recessive

→ Disorder of Branched Chain Amino Acids

→ Deficiency of Alpha keto acid dehydrogenase

→ accumulation of Branched chain amino acids Leucine, Isoleucine and Valine

→ Sweet mousy odour of Maple syrup in body fluids

DIAGNOSIS

→ marked ↑ in leucine, Isoleucine, Valine in plasma & urine → by HPLC or Electrophoresis

→ **DNPH test** → Yellow

→ **Ferric chloride test** – Blue

→ SCREENING TEST FOR IEM ARE

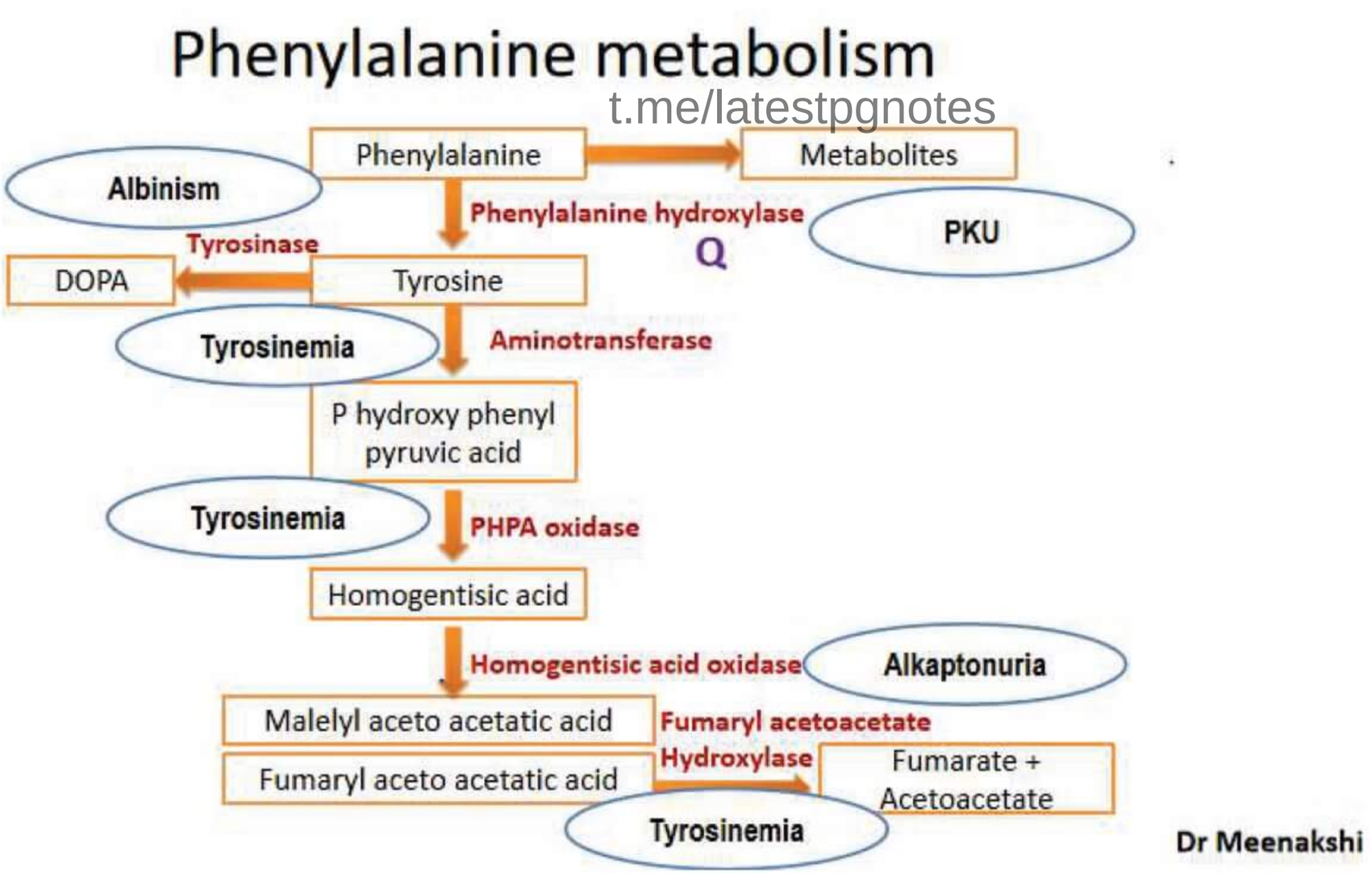
→ Tandem mass spectrometry (TMS) → done on Dried Blood Spots

→ Gas Chromatography Mass Spectroscopy (GCMS) → Done on Urine

Q. A child has microcephaly, blue eyes, fair skin, mental retardation.

Fecl3 test is positive. Diagnosis?

A. Phenylketonuria



PHENYLKETONURIA (PKU)

→ Autosomal recessive disease due to deficiency of Phenylalanine Hydroxylase

→ Phenylalanine metabolites like phenylacetate, Phenylpyruvate increase→ **Tyrosine becomes Essential amino acid**

Q. **Children born to Mothers with PKU have**

→ Microcephaly

→ Mental Retardation

→ Growth Retardation

→ Congenital Heart disease

Q. **Clinical features of PKU**

→ Blonde hair, Blue Iris, Fair skin

→ Musty / Mousy body odour

→ Microcephaly

→ Intellectual disability due to Toxic levels of Phenylalanine and Insufficient Tyrosine

→ Growth Retardation

→ Dental Enamel Changes

→ Irritability, Tremors, Convulsions, Hypertonia

Diagnosis

→ $FeCl_3$ test with urine → Green colour (Detects Phenylalanine in urine)

→ Guthrie's test → Detects phenylalanine in serum

→ ↑ levels of Phenylalanine and its Metabolites like Phenylacetate and Phenyl pyruvate

Treatment

→ Low Phenylalanine diet as soon as possible

→ Adequate intake of Tyrosine should be ensured

Q. **Darkening of Urine on standing seen in**

A. **Alkaptonuria**

ALKAPTONURIA:

→ Autosomal recessive disease due to deficiency of Homogentisic acid Oxidase

CLINICAL FEATURES

→ Ochronosis (Dark spot on Sclera / Ear cartilage)

→ Arthritis

→ Darkening of urine on standing (oxidation of Homogentisic Acid)

→ High incidence of Heart ds (mitral / aortic valvulitis/ calcification)

TYROSINEMIA:

TYROSINEMIA TYPE I:

→ MC type of Tyrosinemia

→ Severe disease of kidney, liver & peripheral nerves

→ Deficiency of Fumaryl Acetoacetate Hydrolase (FAH)

→ ↑ Serum AFP & Succinyl Acetone in serum & urine

→ **Treatment** – Nitisinone (inhibits Tyrosine degradation at 4-HPPD)

TYROSINEMIA TYPE II:

→ Autosomal recessive

→ Deficiency of Tyrosine aminotransferase

→ Palmar / plantar hyperkeratosis

→ Corneal ulcers & Intellectual disability seen

TYROSINEMIA TYPE III:

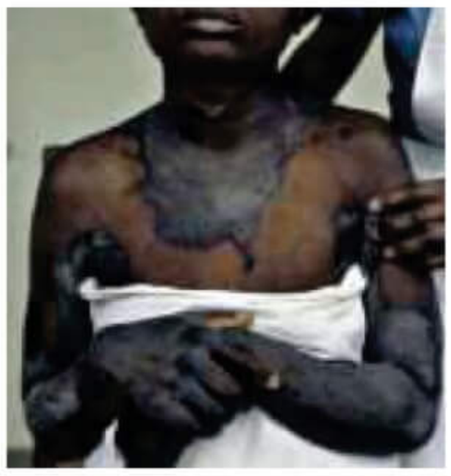
→ Deficiency of 4 Hydroxy phenyl pyruvate deoxygenase (4 HPPD)

HARTNUP DISEASE:

→ Defect in transport of mono-amino mono carboxylic amino acids by intestinal mucosa & renal tubules

→ Autosomal recessive

→ Defect in SLC6A19 gene on chr 5p 15



→ **CLINICAL FEATURES**

→ Most children remain asymptomatic

→ Cutaneous Photosensitivity & Pellagra like rash

→ **ON INVESTIGATION**

Amino aciduria restricted to neutral amino acids *eg.* Valine, Leucine, Phenylalanine, Tyrosine, Tryptophan

→ **Rx** – **Nicotinic acid** or **Nicotinamide**

- **High Protein diet**

HOMOCYSTINURIA

→ Classical type is due to deficiency of Cystathionine β-synthase

→ can also be caused by

→ Defect in Methylcobalamin formation

→ Deficiency of MTHFR (Methylene Tetra Hydro Folate Reductase)

→ **Clinical features**

→ Failure to thrive

→ Developmental delay

→ Ectopia Lentis

→ Intellectual Disability

→ Behavioral Disorders

→ Seizures

→ **Skeletal abnormalities resembling Marfan syndrome** seen like tall stature, Arachnodactyly, Scoliosis, Pectus excavatum etc

→ **COMPLICATIONS**

Homocystinuria is a Procoagulant state

→ Recurrent Stroke

→ Spontaneous Pneumothorax

→ Acute Pancreatitis

→ **DIAGNOSIS**

→ ↑ Methionine & Homocysteine in blood and body fluids

→ Enzyme assay in liver biopsy /skin fibroblasts

→ DNA analysis

→ **TREATMENT**

→ High doses of vitamin B6(Pyridoxine) & folic acid

→ Restriction of Methionine intake

→ Cysteine supplementation

LYSOSOMAL STORAGE DISEASES:

Disease	Enzyme deficiency	Clinical features
GM 1 Gangliosidosis	β galactosidase	Cherry Red spot + Visceromegaly + Skeletal lesions +
Gaucher disease	Glucocerebrosidases	Visceromegaly + Skeletal lesions +
Neimann pick disease	Sphingomyelinase	Cherry Red spot + Visceromegaly + No skeletal lesions
Tay sachs disease	Hexosaminidase A	Cherry red spot + No visceromegaly No skeletal lesions

MUCOPOLYSACCHARIDOSES (MPS)

Type	Name	Enzyme Deficiency	Clinical features
I	Hurler / Scheie disease	α-L-Iduronidase	Coarse face + corneal clouding + ID + hepatosplenomegaly + bony changes
II	Hunter disease	Iduronate sulfate sulfatase	Same as above but **No Corneal Clouding**
III	San fillipo disease	Heparan S sulfamidase	Only Mental Retardation
IV	Morquio disease	N acetyl galactosamine Sulfate sulfatase	Bony abnormalities severe & corneal clouding may be present
VI	Moroteaux Lamy ds	Aryl sulfatase B	Same as Morquio + coarse facies + visceromegaly
VII	Sly disease	β glucuronidase	HSM + Bony Abnormalities

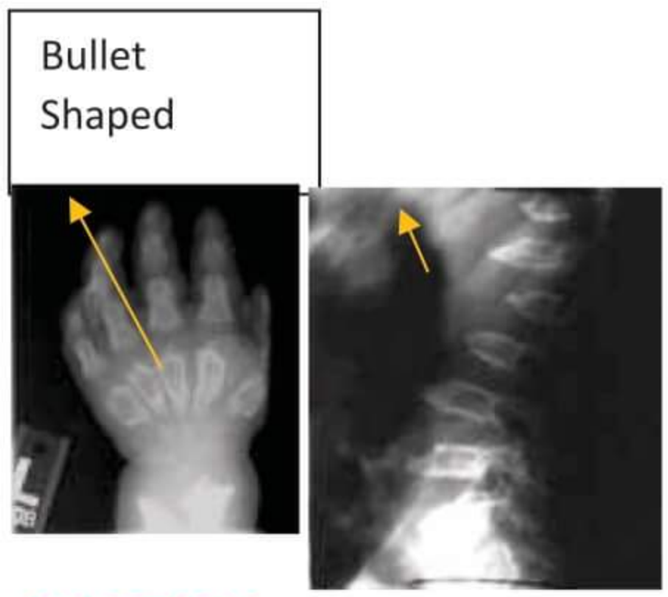
→ All Mucopolysaccharidosis are Autosomal Recessive except Hunter disease (x linked inheritance)

DYSOSTOSIS MULTIPLEX:

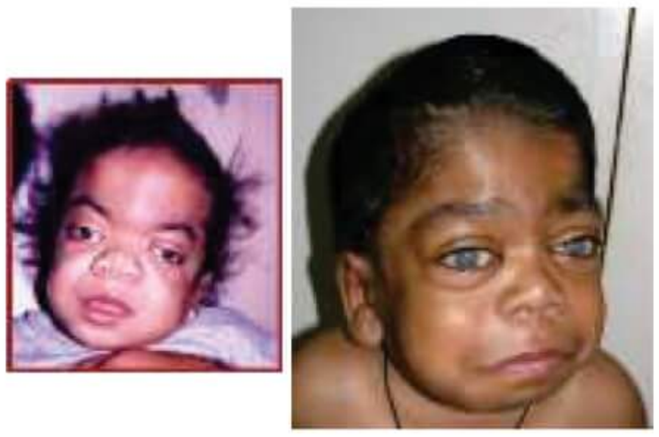
➔ PROXIMAL ENDS OF METACARPALS ARE BULLET SHAPED

➔ ANTERIOR BREAKING OF VERTEBRAL BODIES

➔ SHORT TRUNK DWARFISM



DYSOSTOSIS MULTIPLEX



Mucopolysaccharidosis

ANTERIOR BREAKING

NIEMANN PICK DISEASE (NPD)

➔ **Type A & B** results from deficient acid sphingomyelinase, encoded by a gene on Chr 11 (Autosomal Recessive)

Type A:

- Rapidly progressive neurodegenerative disorder
- Hepatosplenomegaly, Lymphadenopathy
- Psychomotor Retardation evident by 6 months
- Regression and Death by 3 years

Type B:

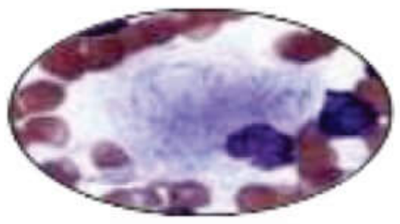
- Non-neuronopathic form in children & adults
- Hepatosplenomegaly, Cherry Red spot
- Pulmonary involvement (diffuse reticular or finely nodular infiltration on CXR)

Type C:

- Neuronopathic form that results from defective cholesterol transport
- Often presents with prolonged Neonatal Jaundice

GAUCHER'S DISEASE

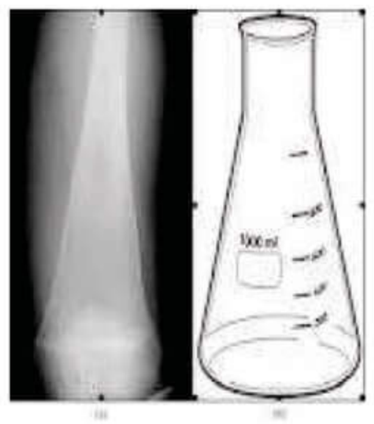
- Autosomal recessive due to deficiency of glucocerebrosidase
- Mc lysosomal storage disease
- Accumulation of glucocerebroside inside cells



Gaucher Cell

CLINICAL FEATURES: Hepatosplenomegaly, Bone pains/ pathologic fractures, Bruising (Thrombocytopenia) & Anemia, Neurological features +/-

Erlenmeyer Flask



Deformity

(wrinkled paper appearance of cytoplasm)

DIAGNOSIS

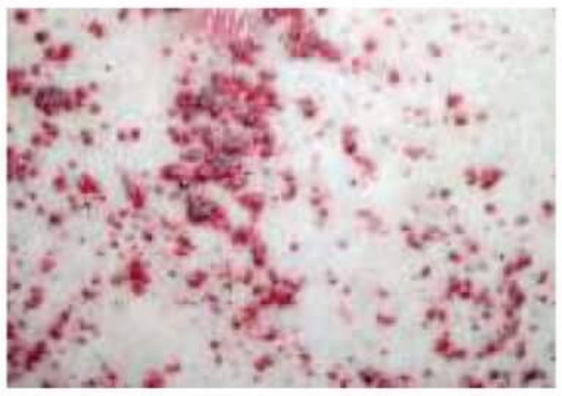
- Deficiency of **glucocerebrosidase** in **leukocytes / fibroblasts**
- **Gaucher cells in bone marrow**
- X ray long bones – **Erlenmeyer flask deformity**

TREATMENT:

- Enzyme Replacement Therapy
- Stem cell Transplantation

METABOLIC DISEASES FOR WHICH ENZYME REPLACEMENT THERAPY (ERT) IS AVAILABLE

- Gaucher disease
- Pompe disease (GSD type II)
- Hurler syndrome (MPS type I)
- Maroteaux lamy disease (Type VI MPS)
- Fabry disease



FABRY DISEASE:

- Deficiency of α galactosidase
- X – linked recessive
- **Angiokeratomas** are most dense between umbilicus & knees, in "**Bathing Trunk Area**"
- **Pain** is the most debilitating symptom
- Vascular diseases of kidney, Brain & Heart develop

LESCH NYHAN disease

- Hypoxanthine guanine phosphoribosyl transferase (HGPRT) deficiency
- X linked inheritance
- Asymptomatic at birth; Developmental delay & Neurologic signs including dystonia, spasticity & dysarthria;
- **Self -injury is an important feature;**
- Serum levels of uric acid > 5 mg/dl
- Definitive Dx – Analysis of HGPRT enzyme
- Rx – High fluid intake, Alkalization & Allopurinol

Q. 5 year male presented with fever for 10 days, for which child was given some medication. He has developed anorexia & vomiting for last 3 days, altered sensorium for 1 day. The mother gave h/o of seizure 1 day back. O/E B/L crepts, no pallor or icterus, liver palpable – 2 cm BCM, Blood glucose 45 mg%, Hemogram – Normal , PT raised. What is diagnostic possibility?

A. Reye's syndrome

REYE'S SYNDROME / JAMSHEDPUR FEVER:

- Acute metabolic disorder resulting in generalized mitochondrial dysfunction due to inhibition of fatty acid oxidation
- Characterized by
  → Fatty liver

→ Encephalopathy

→ Sometimes Fatty Infiltration of Kidneys

- Jaundice is infrequent in Reye's syndrome
- Seizures occur in >80% patients
- Also known as "Jamshedpur fever"
- **Drugs, toxins, virus, IEM can precipitate**
- Virus → Influenza A & B, Varicella, Adeno, Coxsackie A **(not caused by RSV)**
- Encephalopathy (liver damage & cerebral edema)
- Prognosis is poor (25-70% mortality)

DISEASES OF IMMUNE SYSTEM

PRIMARY IMMUNODEFICIENCY:

DEFINITION: A group of disorders characterized by **impaired ability** to produce a **normal immune response**

When to suspect:

Infections occurring at-

- **Unusual sites** e.g. liver, brain
- **Unusual pathogens** e.g. Pneumocystis jiroveci, Burkholderia
- **Unusual severity**

TYPES

1. Primary **antibody** deficiency
2. **Cellular** and combined immunodeficiency
3. **Phagocytic** cell disorders

PRIMARY ANTIBODY DEFECTS:

- Bruton's X linked agammaglobulinemia
- Common variable immunodeficiency (CVID)
- Selective IgA deficiency
- Hyper IgM syndrome
- IgG subclass deficiency

X LINKED AGAMMAGLOBULINEMIA / BRUTON DISEASE

DEFECT:

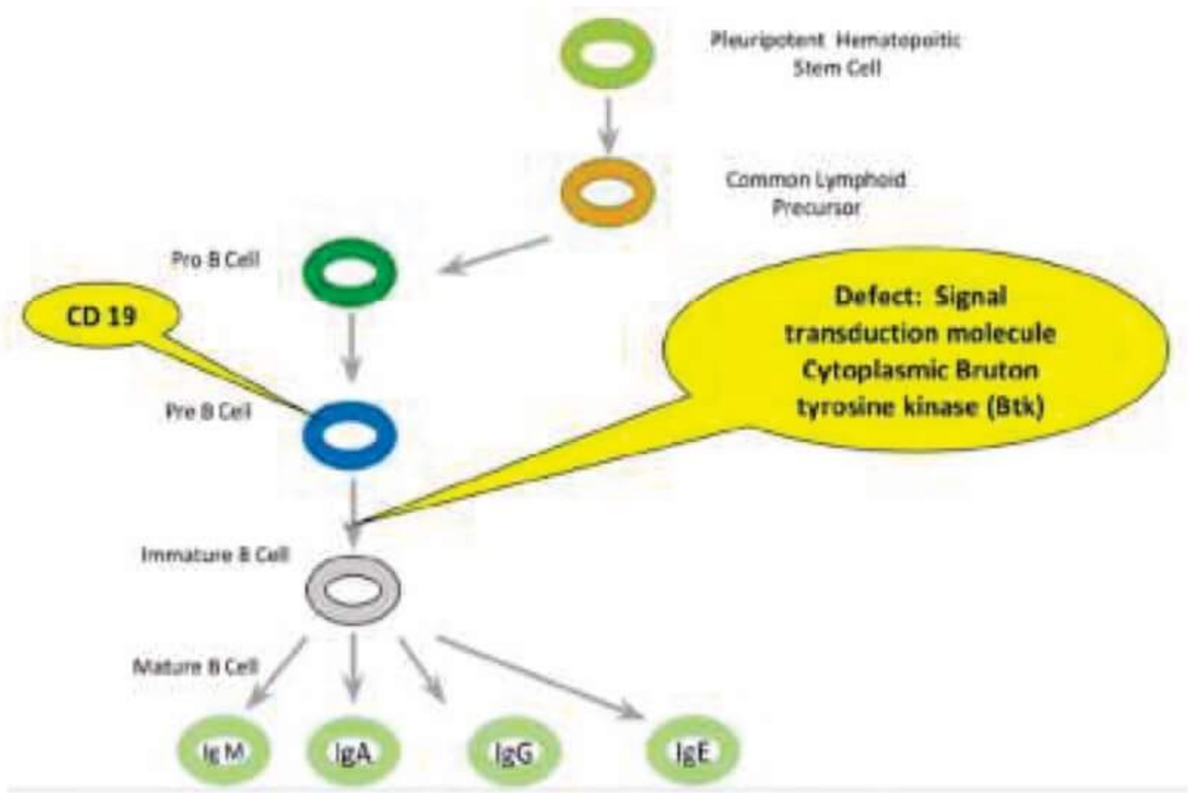
➔ BTK gene on Chr Xq 21.22 mutation (BTK protein Tyrosine kinase is needed to transduce signal from Ig receptor complex of pre B Cell)

↓

Pre B-Cell cannot deliver signals

↓

Maturations stops at this stage



CLINICAL FEATURES: -

Usually present at **6-18months** of age

- More common in **males**
- Tonsils & adenoids **absent**
- Lymph node **not palpable**

DIAGNOSIS-

increased B cells, T cells are normal-

- Plasma cells **absent**
- **Low** Ig level
- Germinal centers of LN underdeveloped

CVID (COMMON VARIABLE IMMUNE DEFICIENCY)

DEFECT:

Inability of B cells to differentiate into plasma cells due to defect in-

- **BAFF** (B cells Activation Factor for TNF-R)
  → BAFF helps in survival & differentiation B cells
- **ICOS** (Inducible co-stimulator)
- → T cell activation & interaction of T & B cells

DIAGNOSIS:

- **Hypogammaglobulinemia** with normal B cells

-LN may be normal or enlarged

COMPLICATIONS: increased risk of **B cells lymphoma**, autoimmune disease

SELECTIVE IGA DEFICIENCY

- **Most common type of immune deficiency**- Selective IgA deficiency

DEFECT –

Impaired differentiation of naive B cells into IgA producing plasma cells-

C/F- increased **sinopulmonary infection**-

DIAGNOSIS – decreased IgA levels

COMPLICATION – increased risk of malignancy & auto immune disease

HYPER IGM SYNDROME:

- **Inability** of B cells to **class switch** to IgG, IgA & IgE antibodies
- Can be AR or X Linked recessive
  Loss of function of **CD40** on B cells
- Due to Loss of **AID** (Activation Induced Cytidine Deaminase) required for class switching

DIAGNOSIS –

- **Low** IgG, IgA and IgE
- Normal / **High** IgM

IgG SUBCLASS DEFICIENCY

- Normal total serum IgG but decreased level of 1 of the subclasses
- **Most common subtypes** in **children** is IgG_2 deficiency while in **adults** in **IgG3** deficiency

CELLULAR & COMBINED IMMUNODEFICIENCY DEFECT

- SCID
- Hyper IgE syndrome '
- Wiskott Aldrich syndrome
- Ataxia telangiectasia
- Di George syndrome

SEVERE COMBINED IMMUNODEFICIENCY

DEFECT:

X linked → Cytokine receptor gamma chain defect

IL7 defect → T cell affected

IL15 defect → NK cell affected

AUTOSOMAL RECESSIVE

- **ADA** deficiency→ loss of common lymphoid precursor of B & T cells due to accumulation of **deoxyadenosine**-toxic to immature lymphocytes
- **JAK- 3** defect
- **IL- 7** receptor defect

C/F-

- Present in **1st few month** of life
- Recurrent/ persistent **diarrhea**, **pneumonia**, **otitis media**, sepsis.
- Persistent **mucocutaneous candidiasis**
- **Live vaccine organism** (BCG, OPV, Rota) can cause severe/ fatal infections

DIAGNOSIS:

- Absolute lymphocyte count**< 2500/mm³**
- T cells make up **< 20%** of total lymphocyte
- ↓ Antibody levels
- **Lymph node** – Depleted T&B cells zones
- **Thymus** – small devoid of lymphoid cells

CONFIRM: Identification of specify gene defect

RX:

- **HSCT**
- Gene therapy
- **PEG-ADA** for ADA defect SCID

HYPER IgE SYNDROME (JOB SYNDROME)

- Mutation in **stat3 gene → IL- 17 defect**
- **AD** inheritance

CLINICAL FEATURES

Characteristic facies:

→ **Coarse** face

→ Permanent **forehead**

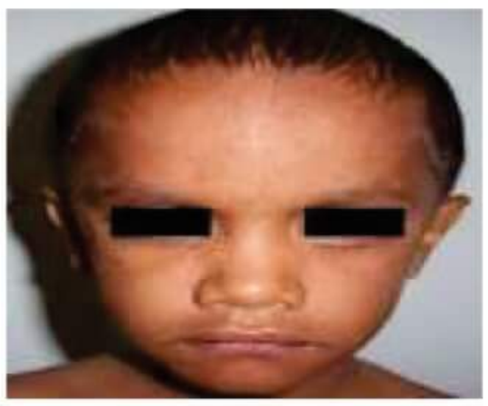
→ Deep set eyes

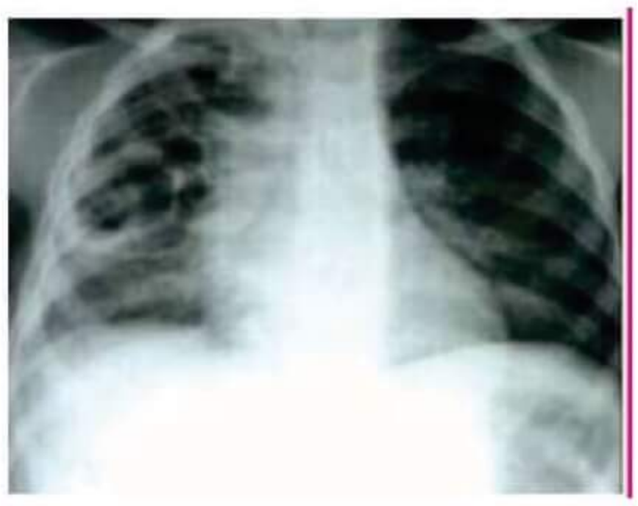
→ Broad nasal bridge

→ Fleshy nasal tip

→ Hemihypertrophy

- **Recurrent abscesses** – Skin/ lungs





Most common – Staph aureus f/b Candide albicans

DX:

- IgE > 2000 IU/ml (IgG, A, M- normal IgD increased)
- Blood & sputum eosinophilia

WISKOTT ALDRICH SYNDROME

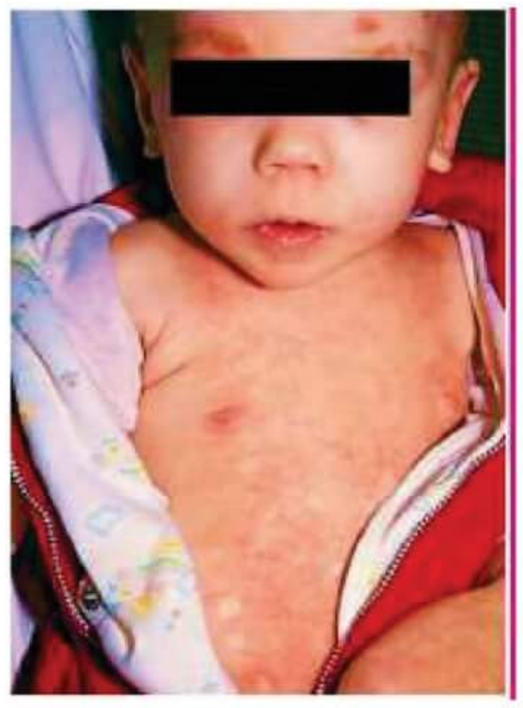
- X linked
- Defect in WASP gene (Chromosome X p 11)

↓

Links membrane receptor to cytoskeletal protein

↓

Defect leads to defective cell migration & signal transduction



CLINICAL FEATURES

TRIAD of → Eczema
TRIAD of → Recurrent infections
TRIAD of → Thrombocytopenia with small platelets

DIAGNOSIS -

- Platelets – small & decreased number
- IgM → Low
- IgE & IgA → Elevated

ATAXIA TELANGIECTASIA

- Due to defect in ATM gene (chromosome 11q), which is a sensor of DNA damage

↓

Defective DNA repair & abnormal V, D, J recombination

↓

Abnormal iso type switching & Increased cancer risk

C/F-

- Ataxia
- Oculocutaneous telangiectasia
- Immunodeficiency
- Increased sensitivity to ionizing radiation & defect. DNA repair
- Increased risk of lymphocytic malignancies & adenocarcinoma

DIAGNOSIS- Low IgA, IgE and IgG2 levels

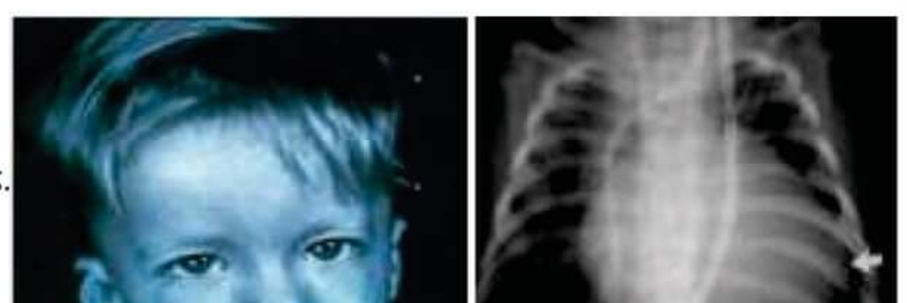
DIGEORGE SYNDROME (VELO CARDIOFACIAL SYNDROME)

- Chromosome 22q11 microdeletion

↓

Failure of development of 3rd & 4th pharyngeal pouches.

↓



a. **Hypoplasia of Thymus** → **Decreased** T cells.

b. **Parathyroid Hypoplasia** → **Hypocalcemia**

c. **Ultimo-brachial body** → Defect in **heart** & great vessel

'CATCH – 22--- 22q11 deletion

C- **C**ardiac Anomaly

A **A**bnormal face (Hypertelorism, antimongoloid slant, Short Philtrum, mandibular hypoplasia)

T- **T**hymic hypoplasia

C- **C**left palate

H- **H**ypocalcemia

DIAGNOSIS

- **CXR**- **Absent** thymic shadow
- **Blood** → **Decreased CD 3** T Cells, increased B cells, decreased IgA, IgE↑
- **Lymph node** → Para cortical area depletion

PHAGOCYTE DYSFUCNTION

→ Chronic Granulomatous Disease (CGD)

→ Leukocyte Adhesion Defect (LAD)

→ Chediak Higashi Syndrome

CHRONIC GRANULOMATOUS DISEASE (CGD)

→ X linked or AR

→ Mutation in genes involving **NADPH oxidase**

C/F:

Recurrent infection with catalase positive organisms like staph aureus, Serratia marcescens.

Granuloma Formation is a hallmark

↓

- Can cause pyloric outlet or bladder outlet or ureter obstruction.
- Intestinal granulomas **resembles** **Crohns Disease**

DX-

- **NBT** (Nitro blue Tetrazolium Test)
- Flow cytometry using **Dihydrorhodamine**

LEUKOCYTE ADHESION DEFICIENCY (LAD)

Disease	Deficiency	Defect
LAD I	Beta 2 – integrin family is deficient or defective	Integrins : Adhesion of leukocytes to endothelium α (CD11) & β (CD18) chain
LAD II	fucosylated carbohydrate ligands for selectins [sialyl Lewis x] are absent	Selectins : cellular margination & rolling

C/f:

- **Delayed fall** of umbilical card stump
- Signs of inflammation are **absent**
- Pus **does not** form

INVESTIGATIONS:

- Neutrophilic leukocytosis (TLC>25000/mm³)
- LAD1- Absence of CD11 & CD 18 by flow cytometry
- LAD2- Lack of Sialyl Lewis X

CHEDIAK HIGASHI SYNDROME

- AR, Mutation of LYST gene on chromosome 1q (regulates vesicle transport)

  ↓

  Uncontrolled fusion of Lysosomes with each other

  ↓

  Giant Granuloma
- Melanosomes are oversized

  → delivery to keratinocytes & hair follicles in compromised

  ↓

  Hypopigmented hairs

C/F;

- light skin & Silvery hair
- Frequent infections
- Neuropathy, **ataxia**
- Impaired platelet aggregation
- (due to deficiency of dense granules containing adp and serotonin

  → Prolonged BT with normal Platelet count, platelet function is affected.

INVESTIGATION

- **Progressive neutropenia** & **abnormal platelet**, neutrophil & NK function,
- **Large inclusions** in all nucleated cells (**wright/ peroxidase stains**) in Peripheral smear & BM

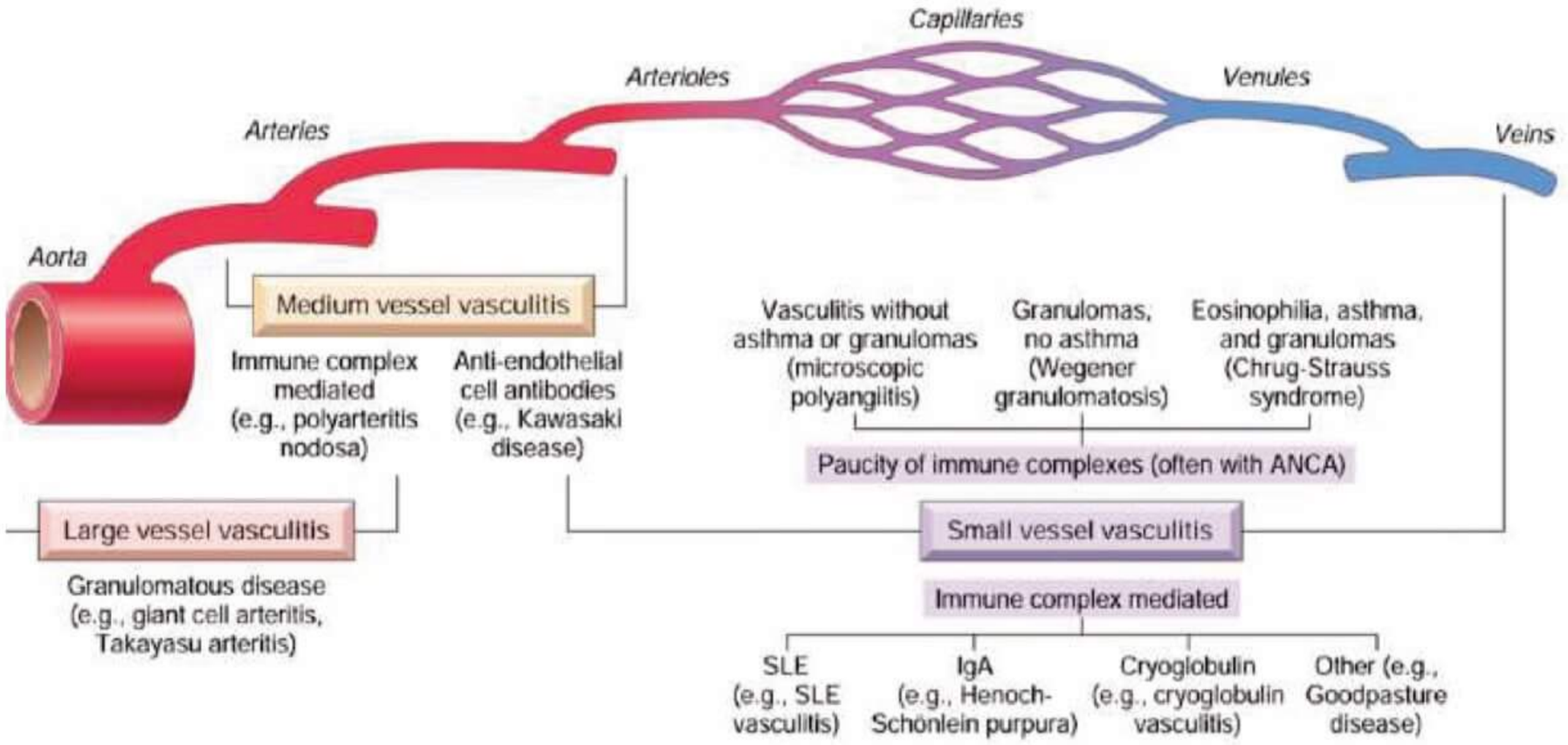
Rx:

- High doses of vitamin C
- HSCT (hematopoietic stem cell transplant)

COMPLICATION:

- HLH (Hemophagocytic Lympho-histiocytosis)

VASCULITIC DISORDERS IN CHILDREN:

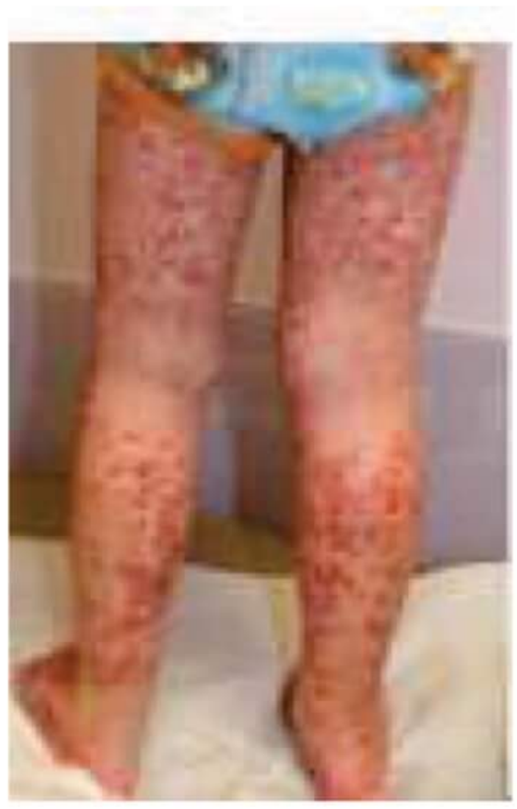


CLASSIFICATION:

- **LARGE VESSEL VASCULITIS** -Giant cell arteritis
  - Takayasu arteritis

- **MEDIUM VESSEL VASCULITIS**:
  - Anti-endothelial cell absent- Kawasaki disease
  - Immune complex mediated-Polyarteritis nodosa.
- **SMALL VESSEL VASCULITIS**

Immune Complex mediated	Pauci Immune
- HSP	- Microscopic Polyangitis
- SLE	- Wegener Granulomatosis
- Good Pasteur disease	- Churg Strauss Syndrome



HENOCH SCHOENLEIN PURPURA (HSP)

- **Palpable purpura** with presence of **1 or more of**
  - Diffuse abdominal pain
  - Arthritis or arthralgia
  - Any **biopsy** showing **IgA** deposition

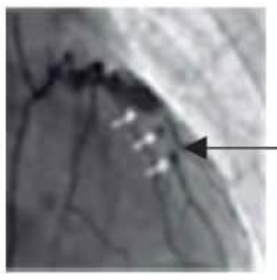
- **Renal** Involvement

Glomerulonephritis is seen in **1/3** of patients

Thrombocytopenia **Absent**

Q. **Identify the disease this child with fever for 6 days is suffering from?**

A. Kawasaki disease.



Coronary Artery Aneurysm

KAWASAKI DISEASE:

DIAGNOSTIC CRITERIA:

- **Fever** for > 5days with any **4** **out of 5** - "C R E A M" features:
- **Mnemonic** → "C R E A M"
  - C B/L non-purulent Conjunctivitis
  - R Rash involving **trunk**
  - E Erythema & Edema of palms & soles
  - A Adenopathy
  - M Mucosal involvement (STRAWBERRY TONGUE)

    - No diagnostic test
    - Leukocytosis, thrombocytosis, increased ESR or CRP

- **Coronary Artery Aneurysm** (**Giant** > **8mm** in diameter) is an important **complication.**

- Scarlet fever is a close D/D of Kawasaki disease

TREATMENT:

Iv Ig- as soon as diagnosis made to prevent complications

- **Aspirin**- High dose f/b low dose
- **Steroids** if persistent fever despite IvIg.

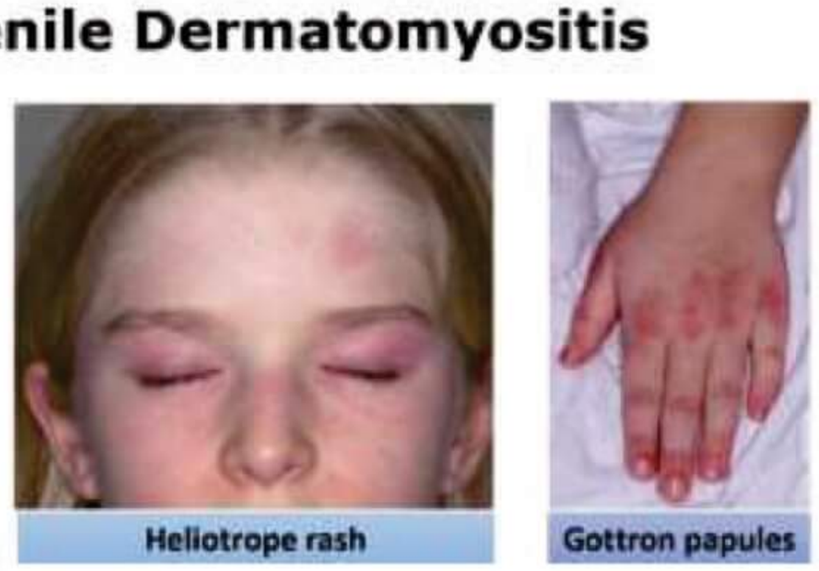
JUVENILE DERMATOMYOSITIS:

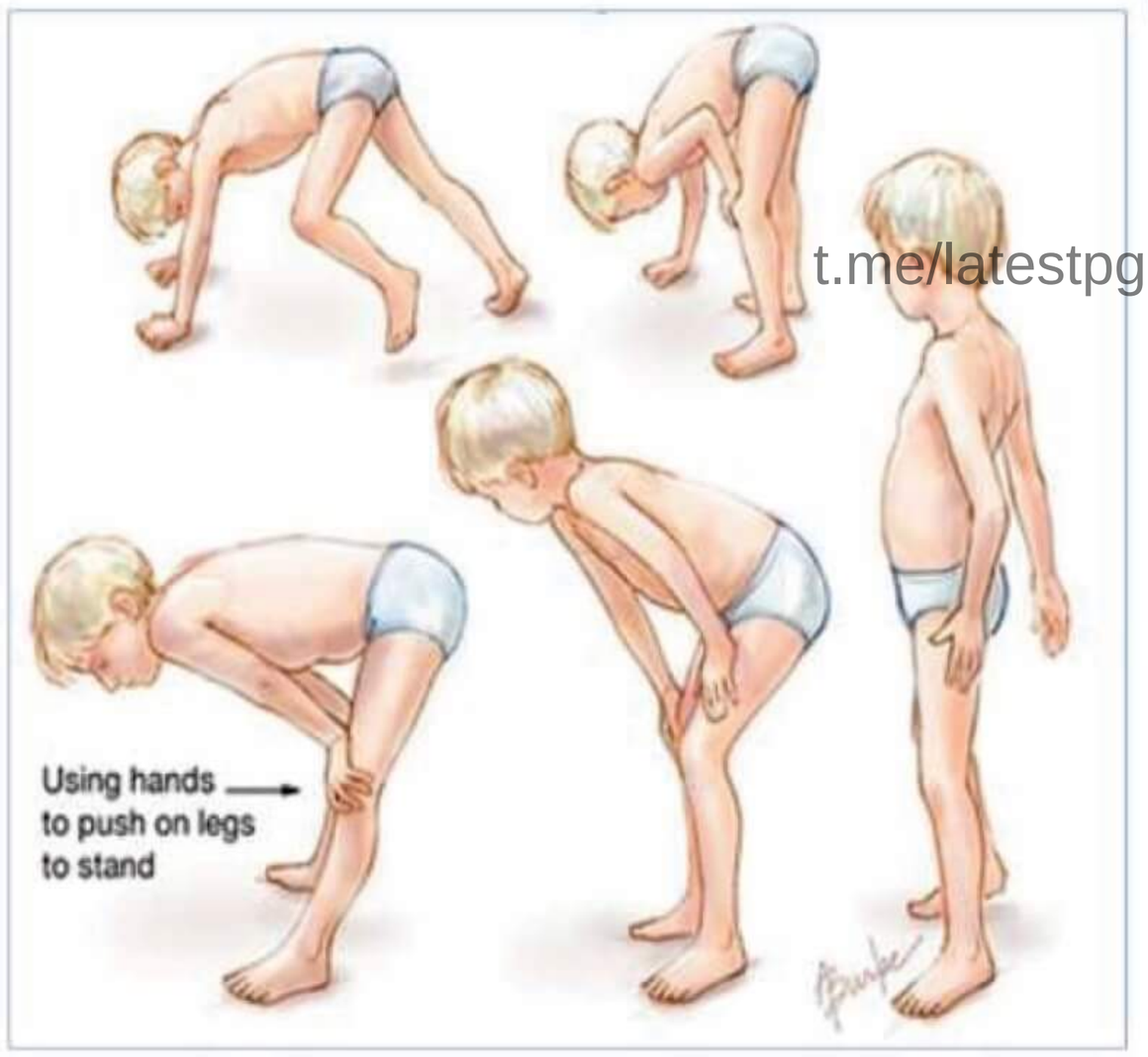
Symmetric proximal muscle weakness.

GOWER sign seen + ve

-Muscle tenderness

-Esophageal and respiratory muscles also affected





GOWER SIGN

INVESTIGATIONS:

- **Elevated** muscle enzymes (CPK, SGOT, LDH)
- **MRI**- Active sites of disease and increases sensitivity of muscle biopsy and EMG
- **EMG**- myopathy and muscle fibre **necrosis**
- **Nerve Conduction Studies** -**Normal** unless severe muscle necrosis and atrophy present
- **Muscle biopsy** done when diagnosis is in doubt

INFECTIOUS DISEASES

IMPORTANT VIRAL DISEASES IN CHILDREN:

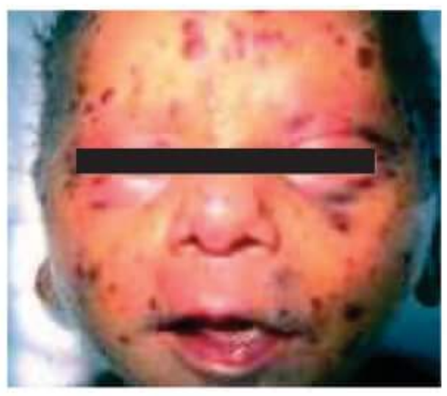
RUBELLA (GERMAN MEASLES OR 3-DAY MEASLES)

- Mild, exanthematous disease
- Rubella Virus, (SS RNA) → Family Togaviridae
- Incubation period → 14-21 Days
- Communicable 5 days before to 6 days after rash
- Prodrome of low-grade fever, sore throat, red eyes, headache & lymphadenopathy
- Rash begins on face & neck & spreads Centrifugally
- Forchheimer spots on soft palate may be present.

CONGENITAL RUBELLA SYNDROME:

Gestational age	Risk of congenital defects	Frequency of congenital infection
Before 11 weeks	90%	70-80%
11-12 weeks	33%	70-80%
13-14 weeks	11%	30-54%
15-16 weeks	24%	10-25%

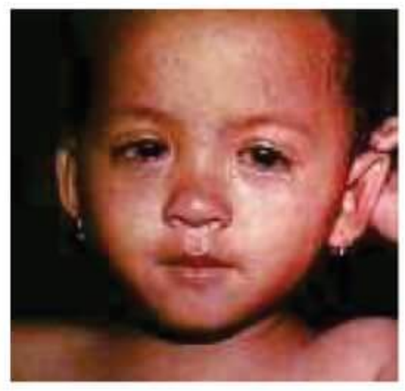
- Hearing loss
- Heart defects (MC – PDA, least common – ASD)
- IUGR
- Microcephaly & Brain Calcification
- Salt & Pepper Retinopathy
- Cataract, glaucoma
- Interstitial pneumonitis
- Hepatosplenomegaly
- Thrombocytopenia



Blueberry muffin lesions

MEASLES

- SS RNA Virus; Family – Paramyxoviridae & genus – Morbillivirus
- Incubation period → 8-12 Days
- Communicable 3 days before to 4-6 days after onset of rash
- Fusion of infected cells → multinucleated warthin finkeldey giant cells (pathognomonic for measles)
- Prodromal phase → Fever, conjunctivitis, Coryza
- **Koplik Spots** on inner cheeks, vagina, conjunctiva at the levels of 1st & 2nd molars
- Receptors for measles virus: CD150 & PVRL4.
- Rash begins behind the ears & Spreads downwards
- Rash fades in 7 days in the same progression as it evolved
- MC complication is otitis media



- MC cause of death: pneumonia

SUB ACUTE SCLEROSING PANENCEPHALITIS (SSPE)

- Rare fatal severe long-standing Complication of Measles
- Begins 7-13 years after primary measles infection
- Results from a persistent infection with an altered measles virus that is harbored intracellularly in the CNS

STAGE	FEATURES
1st	Subtle changes in behaviour / school performances (EEG N)
2nd	Massive myoclonus but consciousness in maintained
3rd	Choreoathetosis, dystonia, rigidity & altered sensorium
4th	Loss of critical centers that support breathing, HR & BP

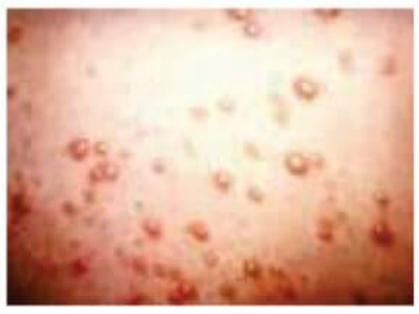
DIAGNOSIS:

- Compatible clinical course & at least 1 of the following:
  1. measles antibody in CSF.
  2. EEG findings (burst suppression episodes)

CHICKEN POX (VARICELLA)

- Varicella Zoster virus, DNA Virus, herpes family
- Mode of Infection → Air bone or direct contact with skin
- Period of Infectivity → from 24-48 hrs before rash
  → Until all the vesicles are crusted

Secondary Attack Rate → 80%



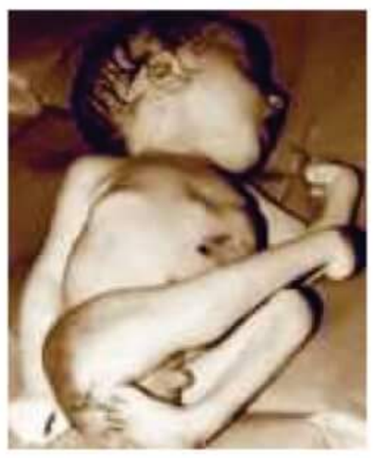
pleomorphic rash

CLINICAL FEATURES:

- Pleomorphic Rash appears 24-48 hrs after prodromal symptoms
- Evolves into papules, clear vesicles & then crusted

COMPLICATIONS:

- Secondary bacterial infections
- Purpura fulminans
- Meningoencephalitis
- Cerebellar ataxia
- Transverse myelitis
- Optic neuritis
- Stroke
- Reyes Syndrome



congenital varicella syndrome

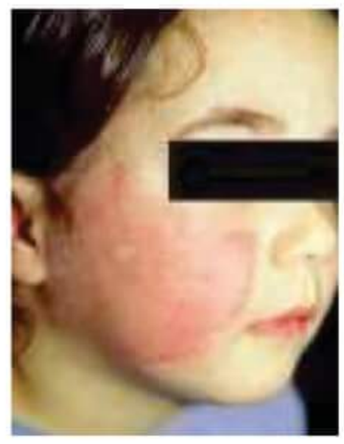
CONGENITAL VARICELLA SYNDROME

- Seen in 0.4% of babies infected in 1st & 2% in 2nd trimester
- Cicatricial skin scarring in a zoster – like distribution
- Limb hypoplasia, law birth weight
- CNS abnormalities (microcephaly, seizures & ID)
- Eye (Chorioretinitis, Microphthalmia & Cataracts)
- Renal abnormalities (hydronephrosis)

- Autonomic disturbances (neurogenic bladder, swallowing dysfunction)

ERYTHREMA INFECTIOSUM:

- Self-limited, exanthem of childhood
- Caused by → Parvovirus B 19
- Incubation period → 4 - 28 days
- Prodromal phase → Low grade fever, headache & URTI
- Hallmark → Slapped cheek rash



slapped cheek appearance

DISEASES CAUSED BY PARVO VIRUS

- Erythema infectiosum
- Transient arrest of erythropoiesis aplastic crisis
- Popular purpuric "gloves and socks" syndrome

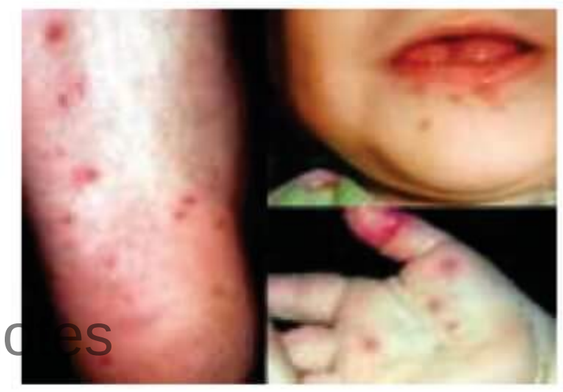
Q. A 2.5 Child presents with low grade fever, oral ulcer & fluid rashes on limbs. Diagnosis?

HAND FOOT MOUTH DISEASE:

MC Cause: Coxsackie A16, Enterovirus 71

Spreads by direct contact / fomites

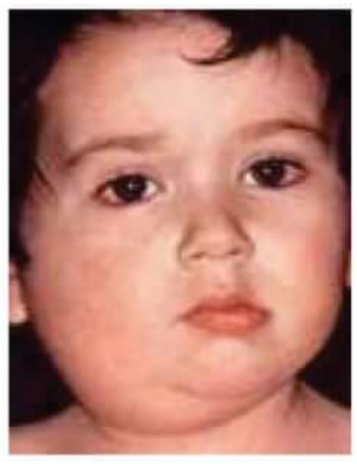
Usually resolves in 4-5 Days



ROSEOLA INFANTUM:

- Caused by HHV6A & 6B.
- Nagayama spots are seen.
- the rash appears when the fever subsides.

MUMPS:



- Acute Self-limiting infection
- Fever, B/L or U/L parotid swelling
- Spreads by respiratory droplets
- Incubation period → 12-25 Days
- Infective from 7 days before and 7 days after the onset of parotid swelling.
- Orchitis common in adolescent males
- MC complication is – Aseptic meningitis.

POLIOMYELITIS:

- Non-enveloped, RNA virus of Picornaviridae family
- 3 biogenetically distinct serotypes → types 1, 2, 3
- Spreads from GIT to CNS → aseptic meningitis & poliomyelitis
- 90-95% infectious are inapparent → protective immunity
- Non-paralytic influenza (flu) like illness in 5% of infections
- Paralytic polio occurs in 1 in 1000 infectious in infants to 1 in 100 infections in adolescents (very rare)

HIV IN CHILDREN;

- Perinatal Treatment → Fetal infection <2%

- Most imp factor that influences maternal to child HIV transmission is level of maternal viraemia.

****Caesarean Section is no longer recommended for Prevention of parent to child transmission & is to be done only if there is an obstetric indication .**

DIAGNOSIS OF HIV IN INFANTS & CHILDREN

- Ig A or Ig M anti-HIV in infants circulation → Indicated HIV infection
- In any child > 18 months of age, demonstration of IgE antibody to HIV by ELISA & Western blot should have antibody testing performed 12 weeks following cessation of breast feeding.
- HIV DNA or RNA PCR or HIV Culture are useful in young infants, to reach to a definitive Diagnosis.
- In breast fed infants, re-testing should be done 12 weeks after cessation of breast feeding.

PROPHYLAXIS FOR INFANTS BORN TO MOTHER WITH HIV

- Nevirapine +/- zidovudine for 6 weeks (12 weeks if breast fed)
- if replacement feeding is readily available & safe, breast feeding is avoided.
- in low resource setting, benefits outweigh the risks.

HIGH RISK INFANTS ARE DEFINED AS THOSE BORN TO WOMEN WITH HIV INFECTION:

- Who have received < 4 weeks of ART at the time of delivery, or
- With Viral load >1000 copies/mL in 4 weeks before delivery, or
- Detected (for the 1st time) during pregnancy or breastfeeding

WHO RECOMMENDATION REGARDING BREAST FEEDING IN HIV-INFECTED MOTHER

- Where replacement feeding is readily available & safe, Breast feeding should be avoided
- In law-resources countries, the benefits of breast feeding out-weighs the risk of HIV transmission

LATEST WHO RECOMMENDATION FOR HIV TREATMENT IN CHILDREN

- ART (Anti-retroviral treatment) should be initiated in all children living with HIV, regardless of WHO clinical stage or CD 4 count
- < 2 yrs age or with who clinical stage 3 or 4
- < 5 yrs with CD_4 count < 750 / mm^3 or < 25%
- > 5 yrs with CD_4 count < 350 cells / mm^3

} High priority groups

HIV TREATMENT IN CHILDREN

Age group	Preferred 1st line ART regimen
Infant < 2 weeks	Zidovudine + Lamivudine + Nevirapine
Children < 3 yrs	Abacavir (or Zidovudine) + Lamivudine + Lopinavir / Ritonavir
Children 3-10 yrs	Abacavir + Lamivudine + Efavirenz
Adolescents	Tenofovir + Lamivudine (or Emtricitabine) + Efavirenz

H1N1 INFECTION:

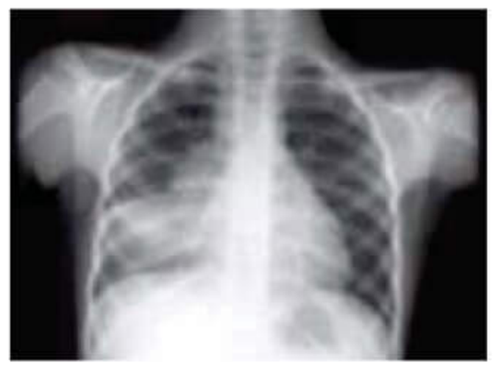
- Oseltamivir given twice daily for 5 days for : → Infants : 3 mg/kg/dose
  → < 15 kg : 30 mg
  → 15-23 kg : 45 mg
  → 24-40 kg : 60 mg
  → >40 kg : 75 mg

IMPORTANT BACTERIAL DISEASES IN CHILDREN:

TB IN CHILDREN

Q. A 4-yrs child presented with cough persisting for 1 month & lowgrade fever. There was a history of contact with TB. What is the Chest X ray of this child suggestive of?

a. Pleural effusion
b. Miliary TB
c. Cavitation
d. Primary TB



- MC age group in children : <5yrs
- MC forms of TB in children → pulmonary TB
- MC extrapulmonary form of TB in children: TB lymphadenitis
- Primary TB: Ghon's focus in lungs.
- Diagnosis → C/F, CXR, demonstration of M. Tuberculosis

DIAGNOSIS

- Demonstrated bacteriological evidence for TB from sputum, gastric aspirate, induced sputum, BAL
- History of contact with TB patient.
- CBNAAT (cartridge based nucleic acid amplification test)
- microscopy
- A positive tuberculin skin test / Mantoux test is defined as an induration > 10 mm, measured 48-72 hrs after intradermal injection with tuberculin 2 TU
- **No role in Dx**
  - Serology (IgM, IgG, IgA against MTB antigens)
  - BCG test
  - IGRAs

Recent updates – treatment of /TB in children

First line:

Type of TB case	Treatment regimen in IP	Treatment regimen CP
New	(2) HRZE	(4) HRE
Previously treated	(2) HRZE	(4) HRE

Treatment is same for both.

Only pyrazinamide is stopped in CP.

Daily treatment is given for all pediatric patients.

Drug sensitivity testing for atleast rifampicin should be conducted in previously treated patients.

Don't wait for DST results to start the treatment.

Daily Doses of:

- Rifampicin → 15 mg/kg (max 600 mg/day)
- Isoniazid → 10 mg/kg (max 300 mg/day)
- Ethambutol → 20 mg/kg (max 1500 mg/day)
- Pyrazinamide → 30-35 mg/kg (max 2000 mg/day)
- Streptomycin → 15 mg/kg (max 1g/day)

Isoniazid prophylaxis is recommended for children less than 5 yrs age who have history of contact with TB patient after ruling out disease in them.

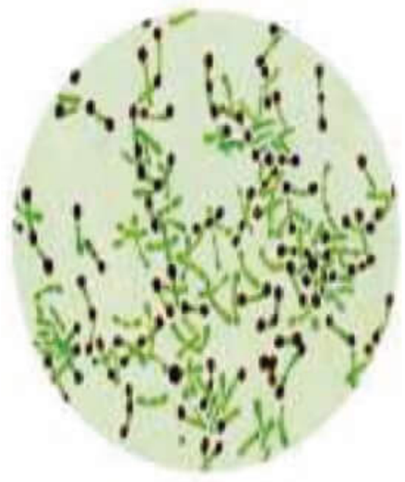
INDICATION OF STEROIDS IN TB:

- Prednisolone 1mg/Kg/Day, Tapered Over 6-8 wks
- Indications: severe cases like-
  - Tuberculous meningitis
  - Pericarditis & pericardial effusion
  - Massive Pleural Effusion

DIPHTHERIA:

- Acute toxic infection caused by Corynebacterium diphtheriae
- Incubation period → 2-4 Days
- Universal early symptom → Sore throat
- Fever (only in 50%), dysphagia, hoarseness, malaise or headache seen
- Shallow ulceration of external nares and upper lip is characteristic.
- Soft tissue edema and lymphadenopathy.
- Hoarseness, Stridor & croupy cough can occur d/t infection of larynx/tracheal bronchi
- **A dense necrotic coagulum of organisms, epithelial cells, fibrin, WBCs & RBCs form, advances & becomes a gray-brown, leather like adherent pseudomembrane.**
- Pseudo membrane can extend to uvula, soft palate, posterior oropharynx or glottic areas
- Paralysis of palate & hypopharynx is an early soft palate, posterior oropharynx or glottic areas
- Paralysis of palate & hypopharynx is an early local effect of diphtheritic toxin
- Toxin absorption can lead to systemic manifestation
  - Kidney tubule necrosis
  - Thrombocytopenia
  - Cardiomyopathy
  - Demyelination of nerves

DIAGNOSIS:



- Sample → a portion of membrane along with underlying exudate
- Direct Smear Using Gram Stain, Albert stain or specific fluorescent antibody
- Culture isolates of Coryneform organisms should be identified to the species level & toxigenicity & antimicrobial susceptibility tests should be performed

COMPLICATIONS:

CARDIAC	NEUROLOGIC
- Toxic Cardiomyopathy in 10-25% patients & 10-25% patients & causes ≥ 50% deaths - 1st evidence is tachycardia disproportionate to fever, during 2nd-3rd wk of illness: - Prolonged P-R interval & St-T Wave changes seen	- paralysis Soft palate (2-3 wks) - Weakness of post. Pharyngeal, laryngeal & facial nerves nasal quality in voice, difficulty in swallowing & risk of aspiration - Cranial neuropathy oculomotor & ciliary paralysis Squint/blurred vision (5th wk) - Symmetric polyneuropathy (10 days – 3 m) after oropharyngeal infection distal muscle weakness with diminished deep tendon reflexes

TREATMENT:

- Specific antitoxin (as soon as possible) is the mainstay of therapy
- Antibiotic therapy is not a substitute for antitoxin .
- **Antimicrobial therapy**
  - Halts toxin production
  - Treats localized infection
  - Prevents transmission
- C. diphtheriae is susceptible to
  - Penicillins
  - Erythromycin
  - Clindamycin
  - Rifampicin
  - Tetracycline
- Asymptomatic case contacts should receive antimicrobial Prophylaxis regardless of immunization status, using benzathine penicillin G or erythromycin

PERTUSSIS

- Caused by Bordetella pertussis or B. Parapertussis
- 3 Stages:

- **Catarrhal stage (1-2 wk)**: Congestion, rhinorrhea, low-grade fever, sneezing, lacrimation & conjunctival suffusion.
- **Paroxysmal stage (2-6 wk)**: Dry, Intermittent, irritative hack with paroxysms of uninterrupted cough on a single exhalation, eyes bulging & a loud whoop follows as inspired air traverse the still partially closed airway. Post-tussive emesis is common
- **Convalescent stage (>6 wk)**: The number, severity, and duration of episodes diminish.
  - Attack rate is as high as 100% in susceptible individuals
  - Hallmark – dry paroxysmal cough

INVESTIGATIONS:

- Leukocytosis (15000-100000 / ML) (absolute lymphocytosis)
- Confirmation by culture/PCR/serology.

TREATMENT:

- Macrolides (Azithromycin/erythromycin)

COMPLICATIONS:

- Apnea
- Otitis media
- Pneumonia
- Sequelae of forceful coughing

TETANUS:

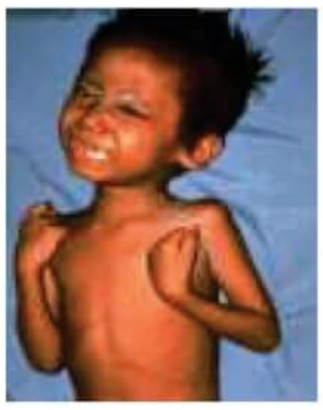
An acute, spastic paralysis, caused by neurotoxin of clostridium tetani, a motile, gram +ive, spore forming anaerobe

MODE OF INFECTION:

Neonatal Cases → occurs in infants whose mothers are not immunized

Non-neonatal cases → a/w a penetrating wound inflicted by a dirty object or unsterile injection

Incubation Period → Typically 2-14 days, may be a months

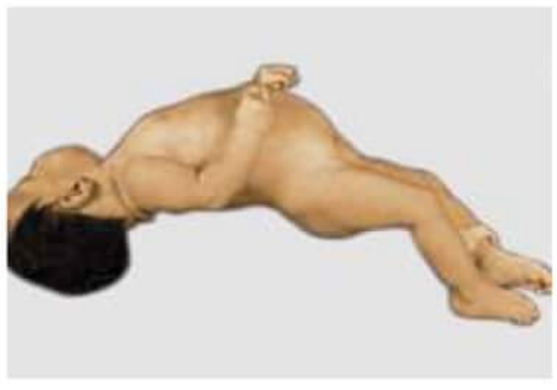


Generalised Tetanus

- MC presenting symptom → Trismus or Lock Jaw d/t masseter muscle spasm
- Headache, restlessness & irritability
- Stiffness, difficulty chewing, dysphagia, neck muscle spasm & risus sardonicus
- Opisthotonus (arched posture)

NEONATAL TETANUS

- Manifests (in 3-12 days of birth)
- Progressive difficulty in sucking & swallowing
- Irritability & excessive crying
- Paralysis, stiffness & rigidity, spasm without opisthotonus



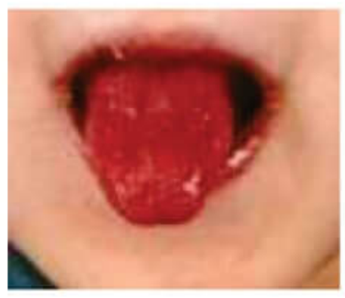
Neonatal tetanus

TREATMENT

- Eradication of C. tetani & anaerobic wound environment, neutralization of tetanus toxin, control of seizures
- Surgical wound debridement to remove anaerobic growth conditions
- Tetanus Ig → asap to neutralize toxin
- Penicillin G → antibiotic of choice
- Metronidazole, erythromycin or tetracycline for penicillin-allergic patient
- All patients with generalized tetanus need muscle relaxants (Diazepam)

SCARLET FEVER:

- Caused by Group A Streptococcus
- Pharyngitis & strawberry tongue is seen
- Erythematous rash appears 24-48 hr after onset
- Kawasaki disease is a close differential Diagnosis
- Identification of GAS in the pharynx -confirms Diagnosis



strawberry tongue

CONGENITAL INFECTIONS

1. CONGENITAL TOXOPLASMOSIS

- Occurs when a women acquires primary infection during pregnancy.
- Risk of fetal infection increases with each trimester of pregnancy.

  1st trimester → Risk is 15%

  2nd trimester → Risk is 25%

  3rd trimester → Risk is 60%
- Severity of fetal infection is greater is early pregnancy.
- C/F
  - Chorioretinitis
  - Hydrocephalus
  - Cerebral calcifications

  } triad
- Small for gestational age
- Prematurity
- Hydrops fetalis
- Persistent jaundice
- Thrombocytopenia

2. CONGENITAL TB

- Primary / Ghon Focus is in liver
- C/F :

  → Hepatomegaly

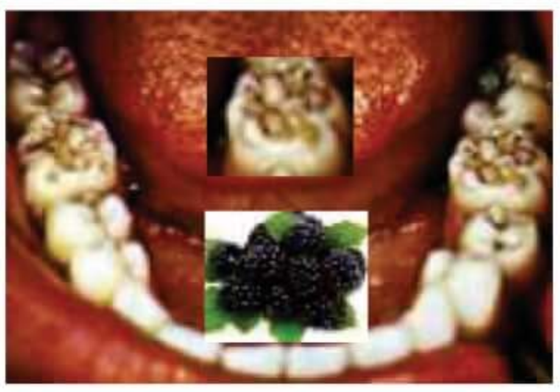
→ Conjugated hyperbilirubinemia

- The neonate can acquire postnatal infection from the mother but that will be by aerosol route.

3. CONGENITAL SYPHILIS

- Results from transplacental transmission, or during birth, by contact with infectious lesions.
- Transmission during early pregnancy can result in
  - Fetal loss
  - Prematurity
  - LBW
  - Still birth
  - Neonatal death
- **Early signs of congenital syphilis**
  - Hepatosplenomegaly
  - Jaundice
  - Diffuse lymphadenopathy
  - Painful osteochondritis & periostitis
    ↓
    Pseudoparalysis
  - Mucocutaneous erythematous, maculopapular rash or vesiculobullous rash
  - Followed by desquamation, involving hands & feet

- **Late signs of congenital syphilis**
  - Olympian brow → Prominent forehead
  - Sabre shins → anterior bowing of tibia
  - Higoumenakis sign → Thickening of medial 1/3rd of clavicle
  - Hutchinson's Triad
    - Hutchinson teeth
    - Interstitial keratitis
    - Sensorineural deafness
  - Mulberry molars
  - Saddle nosh
  - Rhagades (Scars in spoke like fashion from mouth)
  - Cluttons joints → Painless joint swelling involving the knees.



- **Prevention for syphilis**
  - Prenatal screening for syphilis
  - Untreated cases → 100% risk of transmission

4. CONGENITAL RUBELLA

- Risk of congenital defects & frequency of congenital infections is highest before 11 wks of gestation

- C/F

  C – Cataract
  D – Deafness
  C – Congenital heart disease
  } Triad

  Note : M/C congenital heart defect in congenital rubella

  ↓

  PDA (Patent ductus arteriosus)

  Least common is → Atrial septal defect (ASD)

  - Glaucoma & salt & pepper retinopathy
  - IUGR, microcephaly
  - Hepatosplenomegaly
  - Thrombocytopenia
  - Blue berry muffin lesions

5. CONGENITAL CMV

- 90% of infected infants are asymptomatic
- In symptomatic infants

  ↓

  C/F Hepatosplenomegaly
  Jaundice
  Petechiae
  Microcephaly
  Chorioretinitis
- Most important longterm sequelae is → **Hearing loss**
- Diagnosis of CMV infection
  - Recovery of replicating virus &/or

    Viral nucleic acid within 3wk of life → Saliva / Urine / Blood
- Urine is the best specimen for this diagnosis by CMV PCR
- Methods → Viral culture

  PCR

  If microscopy
- CMV IgM → Less sensitivity
- Rx → Ganciclovir

6. CONGENITAL VARICELLA

- Seen in 0.4 % of babies infected is 1st trimester

  2% of babies infected in 2nd trimester
- C/F
  - Cicatricial skin scarring in a zoster like distribution

- Limb hypoplasia
- LBW

CNS → Microscopy, seizures, ID

EYE → Chorioretinitis, microphthalmia, cataract

Renal → Hydronephrosis

Autonomic dysfunction → Swallowing dysfunction

Diagnosis:

- H/o varicella during pregnancy
- C/F in baby
- Demonstrate anti varicella IgM is baby

IMMUNIZATION

→ Latest Immunization schedule
→ Additional vaccines in IAP guidelines
→ Mission Indradhanush
→ General principles
→ AEFI
→ Important points about individual vaccine
→ Practical case scenario
→ FAQs

1. LATEST NATIONAL IMMUNIZATION SCHEDULE (NIS): 2019

At birth – BCG, OPV_0, Hep B- Birth dose

↓ ↓ ↓

Maximum age can be given Upto 1 year Of age. till 1st 15 days of life within 24 hrs.

At 6 weeks- OPV_1, Penta-I, f-IPV, Rota-I, PCV 1

↓ ↓ ↓

Till 5 years Of age D.P.T Hep B, with OPV, Should begin not later than 1 yr. of age.

- **At 10 weeks**- OPV_2, $Penta_2$, $Rota_2$
- **At 14 weeks** – OPV_3, $Penta_3$, $Rota_3$, IPV_2, PCV_2
- **At 9 completed months** → MR, PCV Booster, JE. Vit-A. months

→ **At 16-24 months** → DPT_B, MR_2, OPV_B, JE_2 $VitA_2$

– Vit-A-total no. of doses- 9

- Starts from 9th month.

- Should be given up to 5yrs of age.
- Every 6 Monthly given.

→ **At 5-6 Years**→ DPTB_2 (No OPV)

→ **At 10 & 16 years** → Td (instead of TT)

FULLY IMMUNIZED CHILD-

→ Child received all vaccines by NIS till 1 year of age.

- 3 dosed of OPV
- 3 dosed of Penta
- 2 doses of I-IPV
- 1 dose of MR
- 3 doses of Rota
- 3 dosed of Penta
- 1st dose of JE

COMPLETELY IMMUNIZED CHILD-

→ Received all vaccines till 2 years of age.

- Above vaccines + MR 2nd dose
  - DPT – B_1
  - OPV- B
  - JE- 2nd dose

2. **ADDITIONAL VACCINES IN IAP GUIDELINES**

→ Typhoid conjugate vaccine

→ HEP A

→ Varicella

→ HPV

3. **MISSION INDRADHANUSH**

→ Launched by Ministry of Health & Family welfare

→ On 25th Dec 2014

→ To improve full immunization coverage from 65% in 2014 to go % over Next 5 Yrs.

→ It included vaccines against-

1. TB
2. Diphtheria
3. Pertussis
4. Tetanus
5. Polio
6. Measles
7. Hep B

4. **GENERAL PRINCIPLES OF IMMUNIZATION IN CHILDREN**

→ Any number of vaccines – live or killed may be given on the same day, maintaining a gap of at least 5 cm between different vaccines.

→ Inactivated or killed vaccines can be given any time in relation to any live / killed vaccine.

→ If Missed on a single day, a gap of at least 4 weeks should be there between any 2 live vaccines.

5. **AEFI – ADVERSE EVENTS FOLLOWING IMMUNIZATION**

→ Any untoward medical occurrence which follows immunization but does not necessarily have a causal relationship

CLASSIFICATION OF AEFI

I) **VACCINE RELATED:**

→ Vaccine product related – AEFI caused or precipitated by a vaccine, due to or more inheritant properties of vaccine product.

→ Vaccine quality defect related reaction due to, or more quality defects in vaccine

Vaccine related reactions can be:

→ Common / Minor reactions – Local pain, swelling

→ Serious reaction – Death, disability, Hospitalization or cluster (2 or more cases in a geographical area.)

→ Severe – neither minor nor serious

E.g Anaphylaxis, Persistent cry

II) **PROGRAM ERROR** – caused by inappropriate vaccine handling, prescription or administration.

III) **INJECTION REACTION** – Due to anxiety about injection. Eg. syncope

IV) **CO-INCIDENTAL EVENT** – Caused by something other than vaccine product, program error or injection reaction. E.g Sudden infant Death syndrome following any vaccination.

6. **INDIVIDUAL VACCINES –**

1. **BCG –**

Live attenuated vaccine; Strain – Copenhagen (Danish 1331) or Pasteur

Light sensitive vaccine

Lyophilized form available; NS is used as diluent

Dosage: 0.05 ml → Intradermal route

Induces CMI

Protects against severe forms – TB meningitis / Disseminated TB

S/E: BCG Lympadenitis, osteitis

2. **POLIO-**

OPV or sabin – live

IPV or salk – killed

Bivalent OPV – P_1 & P_3 – Bivalent

P_2 – Globally discontinued in April 2016

- WHO advocates at least, 1 dose of IPV in national immunization schedule.
- WHO no longer advocates OPV only schedule because IPV protects from wild polio virus as well as polio caused by cVDPV-2

VAPP – VACCINE ASSOCIATED PARALYTIC POLIO: Cases of AFP, which have residual weakness 60 days after onset of paralysis & from whose sample of stool, vaccine related but not wild virus isolated.

VDPV – VACCINE DERIVED POLIO VIRUS: Arise due to mutation & recombination of vaccine derived polio virus in human gut which are 1-15 % divergent from parent vaccine strain.

3. **Hep B vaccine –**

Birth dose to prevent Hep B transmission from mother to baby.

Should be given within 24 hours

Hep B Status of Mother		Intervention
1. HBsAg positive	→	HB Ig & HBV within 12 hours of birth Completes Hep B vaccines at 2, 6 months
2. HBsAg Unknown	→	HBV within 12 hours comes, HBsAg positive → HBIg within 7 days of life Complete Hep B vaccine at 2 & 6 months
3. HBsAg negative	→	Complete Hep B at 0 & 6, 10, 14 weeks.

4. **DPT**

Most adverse effects are due to pertussis component

Severe – 1) Persistent inconsolable screaming

2) Seizures

3) Hypotonic Hyporesponsive episodes

4) Encephalopathy

5) Anaphylaxis

C/I of DPT – 1) Progressive neurological illness

2) Anaphylaxis to previous DPT

3) Encephalopathy within 7 days of vaccination.

Catch- up: < 7 years – DPT of – 0,1,6 months

> 7 years – Tdap at presentation, F/b Td at 1 & 6 months

5. MEASLES & RUBELLA

Measles - live attenuated vaccine; Edmonton Zagreb strain

Diluent – Distilled water

6. PNEUMOCOCCAL VACCINE-

Conjugate vaccine (PCV)

- 13 valent
- Can be given at < 2 years of age

Polysaccharide vaccine

- 23 valent
- Beyond 2 years of age
- low immune memory
- No herd immunity.

Recommendation about immunization prior to splenectomy-

1. Hib
2. Pneumococcal
3. Meningococcal

At least 2 weeks before splenectomy

7. ROTAVIRUS VACCINE-

→ live oral vaccines

→ 6,10 & 14 weeks (maximum age→ 1 year)

Strain- 116E strain of Indian origin

S/E – Intussusception

8. HEP A VACCINE-

Live vaccine- 12-23 months

Inactivated V- 2 doses 6 months apart

- starting at 1 year of age

9. INFLUENZA VACCINE-

- Inactivated V- whole virus/ split product
- live attenuated-Nasal spray
- Regime- 2 doses IM, 4 weeks apart f/b 1 dose annually
- Strains in 2018-2019 Influenza vaccine-
  - A/ Michigan /H.N.
  - A/ Singapore /H_3N_2
  - B/Colorado [Victoria lineage]
  - B/ Phukat [yamegeta lineage]

10. TYPHOID-

1. **vi capsular polysaccharide vaccine: -**

(not immunogenic < 2year age)

No immune memory efficacy 50-60%

Recommended ≥ 2year age f/b revaccination every 2-3 years.

2. **Conjugate vaccine-**
   - can be given 6 m age onwards
   - single dose
   - efficacy ~ 90%

An unimmunized child who had enteric fever should be given 4 weeks after full recovery.

11. **VARICELLA-**
   - live attenuated
   - OKA strain
   - SC- 2 doses → 15 months, 4-6 years
   - IAP recommends to all children with no previous H/o varicella
   - for post-exposure prophylaxis, should be given preferably within 3 days of exposure but Potentially up to 5 days of exposure

12. **HPV-**

1. Quadrivalent- Gardasil
   HPV-6,11,16,18
2. Bivalent- Cervarix
   HPV- 16 & 18

99-100% efficacy against vaccine type related genital warts & vaginal & vulval Neoplasia.
Minimum age- 9 years
Catch up- 13-45 years

7) PRACTICAL CASE SCENARIOS –

Q- If a child has upper respiratory infection on due date of vaccination, what to do?
- Minor illness are not C/I for vaccination
- Give the vaccine
- To be postponed only during serious illness

Q- Vomiting after OPV:
- If vomiting within 30 minutes → repeat OPV

Q- Lapsed immunization:
- No need to restart vaccine series, regardless of the time elapsed
- Give vaccine due as per schedule.

Q- Preponed immunization:
- If given 5 or more days before due date, that dose is not counted
- You have to repeat it.

Q- Unknown immunization status:

- Child should be considered unimmunized & vaccinated accordingly

Q- What vaccines should be given to an unimmunized child?

- MR
- DPT (>7 years – T dap)
- Hib (<5 years)
- OPV (<5 years)
- BCG (<1 years)
- Hep B (<1 years)

8) FAQs-

• **Vaccines CI in Egg allergy-**

- Yellow fever vaccine
- Influenza vaccine

• **Vaccines causing thrombocytopenia-**

- Measles vaccine

• **Strains included in meningococcal Vaccine**

- A, C, Y, W-135

• **Heat sensitive vaccines-**

- OPV, Reconstituted BCG, Measles vaccine

• **Light sensitive vaccine-**

- Measles vaccine, BCG, Rota, JE vaccine

• **Freeze sensitive vaccine-**

- Hep B, Pentavalent, TT, DPT vaccine

• **VVM – Vaccine Vial Monitor**

- Heat sensitive label that indicates cumulative heat exposure over time.

If color of inside square lighter than outside circle

↓

We can use the vaccine

VVM – 7 → Number indicates Number of days the vaccine remains potent when exposed to 37°C

• Test done to check for cold damage to Vaccine due to freezing → "Shake test"

• **Open Vial Policy (OVP):** It allows the reuse of partially used multi-dose vials in subsequent immunization sessions (up to 4 weeks) provided-

- Expiry date not reached
- Cold chain maintained
- Date of opening the vial mentioned
- Aseptic technique used to withdraw vaccine
- Vaccine vial septum not submerged in water
- **Open Vial Policy – can be applicable for-**
  - DPT
  - PCV
  - TT
  - Hep B
  - pentavalent
  - OPV
  - IPV

- **'Open vial policy' Not applicable for-**
  - MR
  - BCG
  - Rota
  - JE

• **Vaccines recommended in adolescents-**
  - T dap
  - Td
  - TT
  - HPV
  - Influenza
  - JE
  - Pneumococcal
  - Rabies

*** Cocoon Strategy-**

- Vaccination of persons from immediate environment of persons who are susceptible to disease but cannot be immunized

• **Recommended sequence in which vaccine should be given-**

- Oral → Intradermal → SC → IM
- O.P.V, Rota, FIPV, MR, Pentavalent

PEDIATRIC CARDIOLOGY

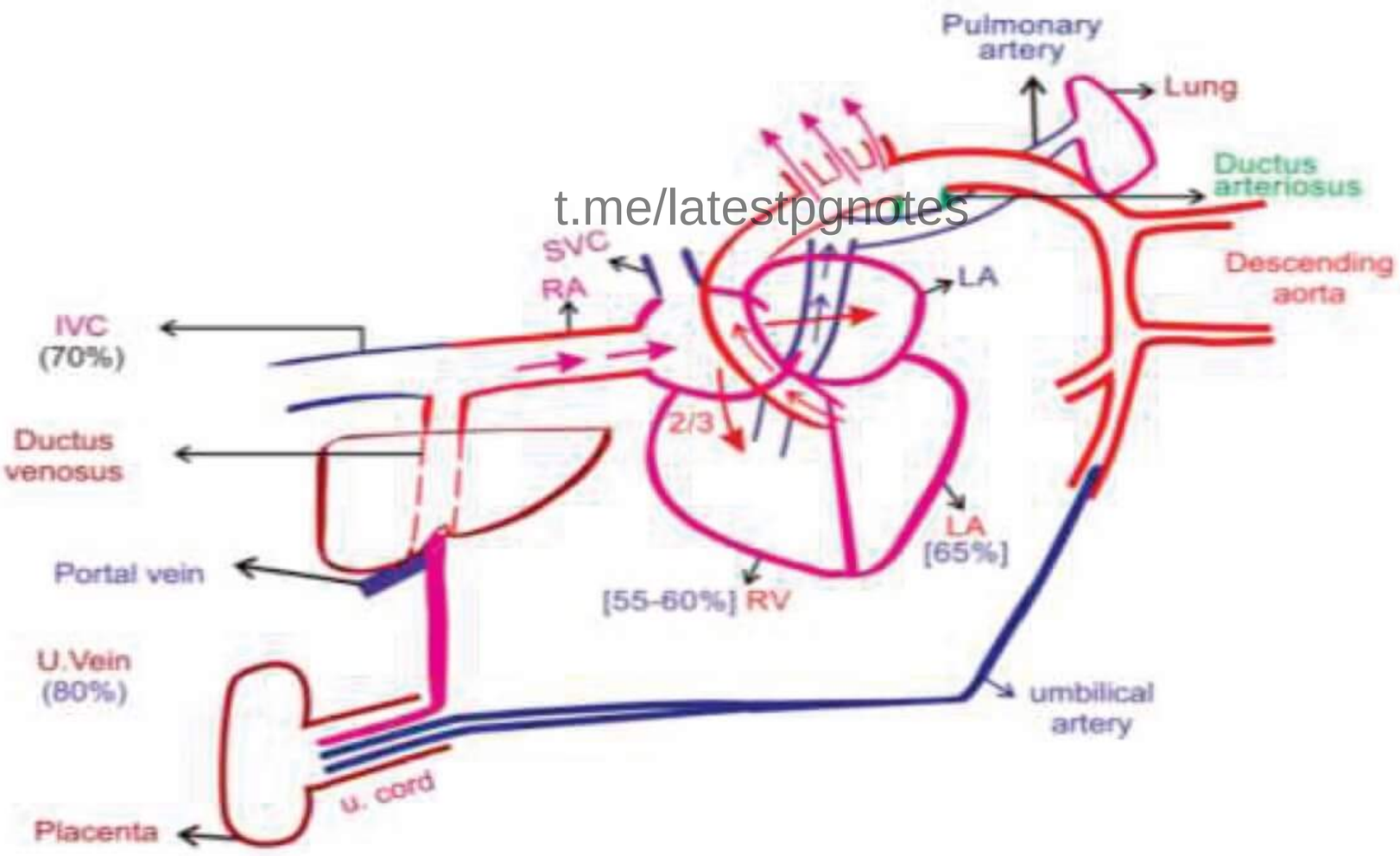
FETAL CIRCULATION & CLASSIFICATION OF CONGENITAL HEART DISEASES

DIFFERENCES BETWEEN FETAL CIRCULATION & ADULT CIRCULATION

1. Source of O_2
   - → Fetal circulation → Placenta
   - → Adult circulation → Lungs
2. In fetal life, lungs are collapsed & pulmonary vascular resistance is very high
   - → very little blood goes to lungs
3. Ductus arteriosus
4. Ductus venosus
5. Foramen ovale

} important for fetal circulation

Q. 4 chambered structure of heart appeared by → 6th week of IUL



UMBILICAL CORD

- → contains 1 vein & 2 arteries
- → umbilical vein carries oxygenated blood (SpO_2 → 80%)
- → single umbilical artery associated with increased risk of renal anomaly
- → Delayed fall of umbilical cord seen in Leukocyte adhesion defect (a form of immunodeficiency)

SATURATION OF O_2 IN

- → Umbilical vein → 80% (maximum in the entire body of fetus)
- → Inferior vena cava (IVC) → 70% (seen in deoxygenated blood also so saturation level falls)

→ LV → 65%

→ RV → 55-60%

→ Umbilical artery → very low

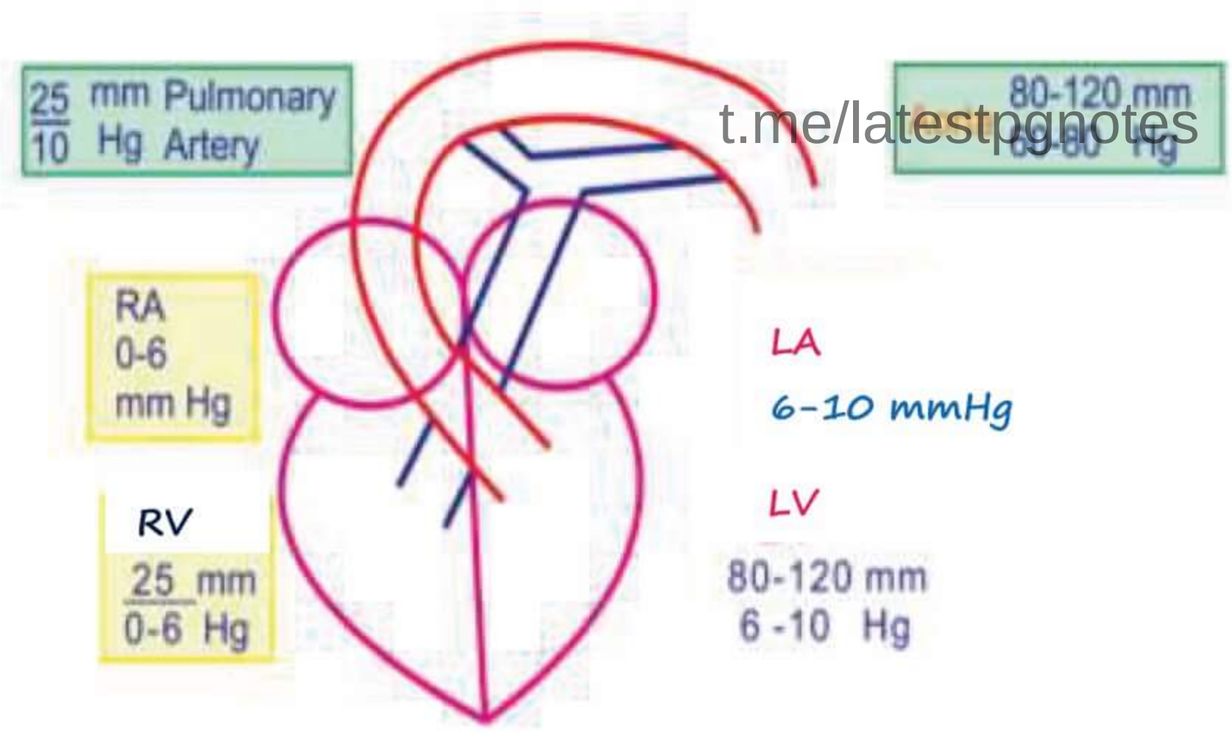
CHANGES IN CIRCULATION AT or AFTER BIRTH:

1. Lungs become the source of O_2
2. Pulmonary vascular resistance decreases → Blood flow to lung increases
3. Systemic vascular resistance increases (pressure in left side of heart increases)
4. Foramen ovale closes
5. Ductus venosus closes by D_7 of life
6. Ductus arteriosus closes (PROSTAGLANDINS plays an important role)
   - Functional closure → immediately after birth (due to smooth muscle contraction)
   - Anatomical closure → D_{10}-D_{21} of life (due to proliferation of cells of intima of ductus arteriosus)

Q. When does Ductus arteriosus closes?

Ans. Anatomical > Functional i.e DAY 10-21 > Immediately after birth

PRESSURES IN DIFFERENT CHAMBERS OF HEART IN ADULT CIRCULATION



→These pressures are normally get established by 2-3 weeks of age

→ In presence of VSD or PDA, these pressures get established by 6-10 weeks age

NADA'S CRITERIA

→ Predicts presence of congenital heart disease

→ 1 major or 2 minor criteria indicates possibility of Congenital Heart Disease

MAJOR CRITERIA

→ Systolic murmur ≥ Grade 3

→ Any diastolic murmur

→ Cyanosis

→ Congestive heart failure

MINOR CRITERIA

→ Systolic murmur < Grade 3
→ Abnormal S_2
→ Abnormal BP
→ Abnormal ECG
→ Abnormal Chest X-ray

CONGENITAL HEART DISEASES:

→ Multifactorial inheritance
→ Arise usually between 3rd -8th week of IUL
→ Genetic basis is most strong for Holt oram syndrome
→ TGA & Left side lesions are slightly more common in boys
→ ASD, VSD, PDA & Pulmonary stenosis more common in Girls

CLASSIFICATION OF CONGENITAL HEART DISEASES

(BASED ON PATHOPHYSIOLOGY)

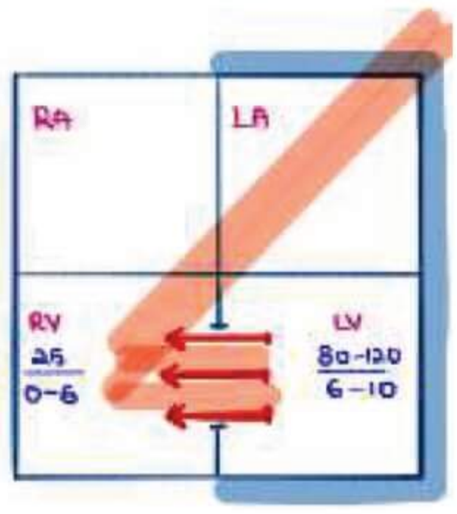
CLASSIFICAITON OF CONGENITAL HEAT DISEASES				
L → R shunt	Complete mixing of blood of L & R side	Parallel Circulation	DUCTUS DEPENDENT	
• VSD • ASD • PDA	• Truncus arteriosus • TAPVC	TGA	SYSTEMIC CIRCULATION	PULMONARY CIRC
			• Critical AS • Severe coarctation of aorta • Interrupted aortic arch • HLHS	• Severe PS • Severe TOF • Pulm. atresia • Tricuspid atresia • Ebstein anomaly

IMPORTANT ACYANOTIC CONGENITAL HEART DISEASES

VENTRICULAR SEPTAL DEFECT

→ MC congenital heart disease in children
→ MC congenital acyanotic heart disease in children
→ MC congenital heart diseases affected by infective endocarditis in children
→ 90% VSDs involve membranous part (10% muscular part)

HEMODYNAMICS OF VSD:



Auscultation Findings:

→ Pansystolic murmur (blood moves from left to right with a gush)

→ In large VSD

→ delayed diastolic murmur in mitral area

→ ejection systolic murmur in pulmonary area

Chambers enlarged → LEFT ATRIUM & LEFT VENTRICLE. Since excess blood goes into lungs through pulmonary circulation it comes back also into LA → LV (enlarged)

CLINICAL FEATURES

→ Recurrent episodes of pneumonia [Tachypnea]

→ Heart failure & failure to thrive (child doesn't gain weight adequately)

→ Usually presents at 6-10 weeks

ECG Findings:

→ LAD [Left axis deviation] [normally all babies at birth have right axis deviation]

→ Left ventricular hypertrophy

Chest X-ray findings:

→ Cardiomegaly with LV apex (moves down & out)

→ Pulmonary plethora d/t excess blood going to lungs

TREATMENT:

MEDICAL Management

1.Treatment of Heart failure

→ Digoxin

→ Furosemide

SURGICAL Management

Closure of VSD by DACRON PATCH

INDICATIONS

1. Heart failure refractory to medical management
2. If pulmonary blood flow (QP) is more than double of systemic blood flow (Qs) [Qp : Qs> 2:1]

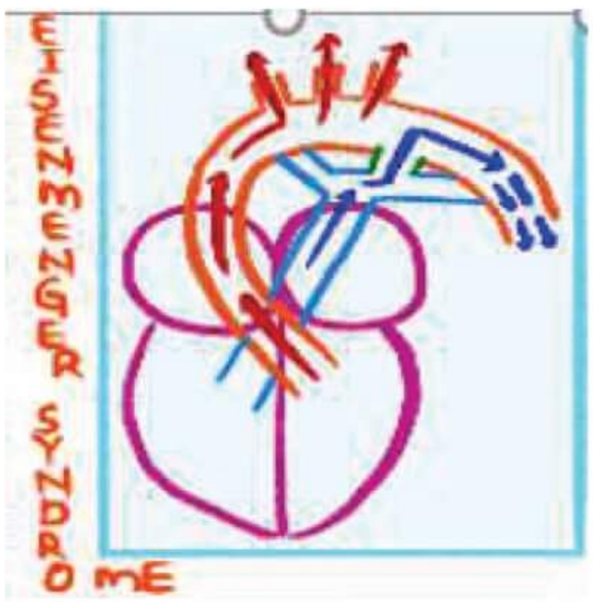
2. Treatment of pneumonia with antibiotics & supportive care
3. Nutritional rehabilitation

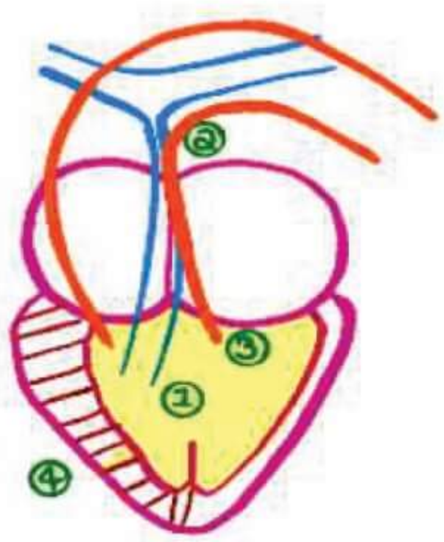
COMPLICATIONS OF VSD:

1. Infective endocarditis → VSD + fever + Clubbing without cyanosis
2. Eisenmenger syndrome → VSD + Clubbing + Cyanosis [no fever]

EISENMENGER SYNDROME:

→ Reversal of shunt at the level of VSD/ASD/PDA due to irreversible pulmonary vascular obstructive changes





PATHOPHYSIOLOGY:

VSD [Left → Right]
↓
Excess pulmonary blood flow
↓
Hyperkinetic pulmonary hypertension[reversible]
↓
Irreversible pulmonary vascular obstructive changes
[obstructive pulmonary HTN]
↓
Rt ventricular hypertrophy
↓
Pressure in RV increases
↓
When RV increases > LV pressure
↓
Right → Left shunt
↓
Cyanosis & clubbing

ATRIAL SEPTAL DEFECT (ASD)

➔ 2 MAIN TYPES:

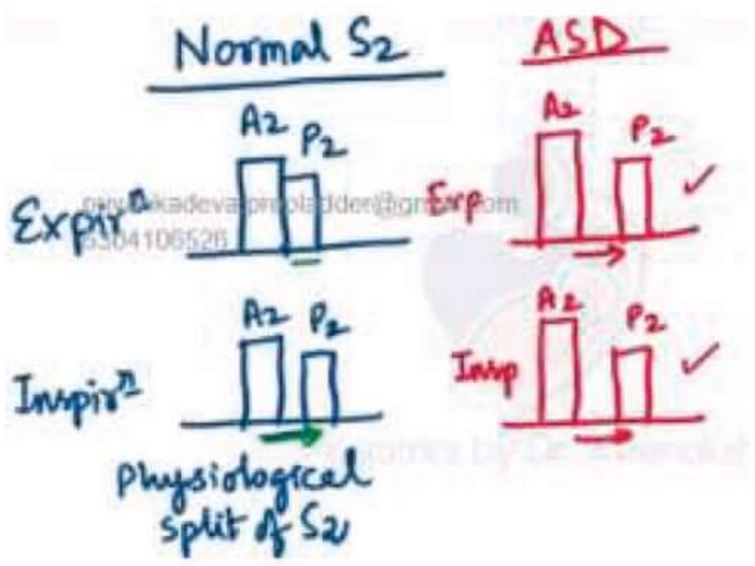
→OSTIUM PRIMUM

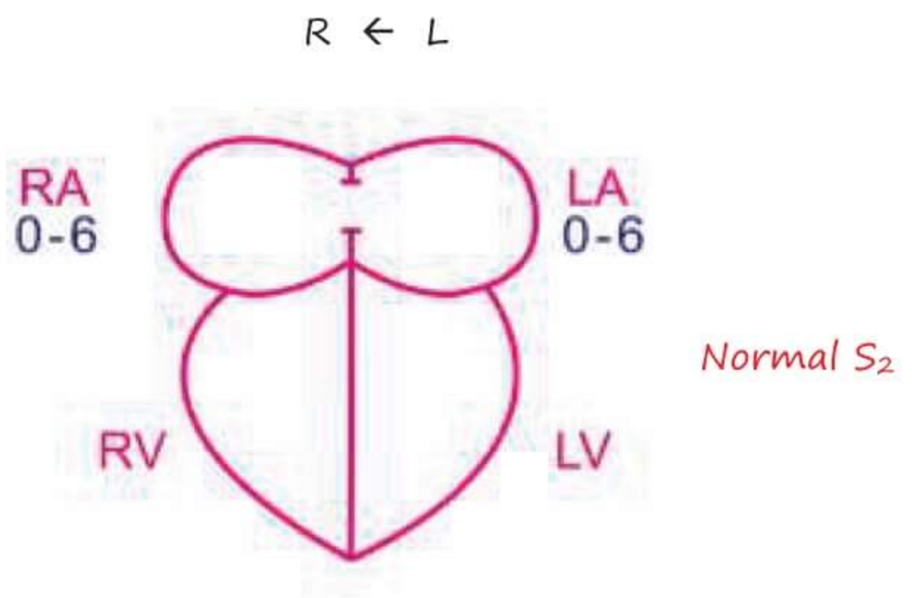
→OSTIUM SECUNDUM [MC Type]

OSTIUM SECUNDUM ASD

HEMODYNAMICS:

→ Shunt remains silent in ASD (No Murmur)





Normal S_2

→ During inspiration, Right side of heart has more blood
→ Right ventricle takes more time to empty than left ventricle, P_2 come later (as Right atrium has more blood) → Physiological split of S2

In ASD

→ Irrespective of inspiration or expiration, Right atrium has more blood (as it is receiving blood from Superior Vena cava, Inferior Vena cava and Left Atrium) than left atrium

→ Right ventricle takes more time to empty, P_2 comes later

→ WIDE, FIXED SPLIT of S2

→ LARGE ASD PRODUCE MURMURS LIKE

→ Diastolic murmur in tricuspid area

→ Ejection systolic murmur in pulmonary area

CLINICAL PRESENTATION:

SMALL ASD → asymptomatic throughout life

LARGE ASD → same as VSD

INVESTIGATIONS:

1. ECG FINDINGS

→ Right axis deviation in ostium Secundum ASD

→ Left axis deviation in ostium Primum ASD

TREATMENT:

ASYMPTOMATIC → no treatment required

SYMPTOMATIC → same as VSD

Congenital heart disease which is least commonly affected by Infective endocarditis → **ASD**

- **CONGENITAL RUBELLA SYNDROME**

C → Cataract

D → Deafness

C → Congenital heart disease → Most common → **PDA**; Least common → **ASD**

-SYNDROMES ASSOCIATED WITH ASD [MNEMONIC → 'PETER FED HER']

1. Pierre Robin Sequence
2. TAR [Thrombocytopenia Absent Radius] Syndrome
3. Fetal Alcohol syndrome
4. Ehler Danlos Syndrome
5. Down Syndrome
6. Holt-Oram syndrome
7. Ellis van Creveld Syndrome
8. Rubinstein Taybi syndrome

→ Atrial Septal Defect is not associated with Turner syndrome

→ Atrial Septal Defect is not a component of TOF

→ Atrial Septal Defect is a component of Trilogy of Fallot & Pentalogy of Fallot

→ **Pentalogy of Fallot** → TOF + ASD

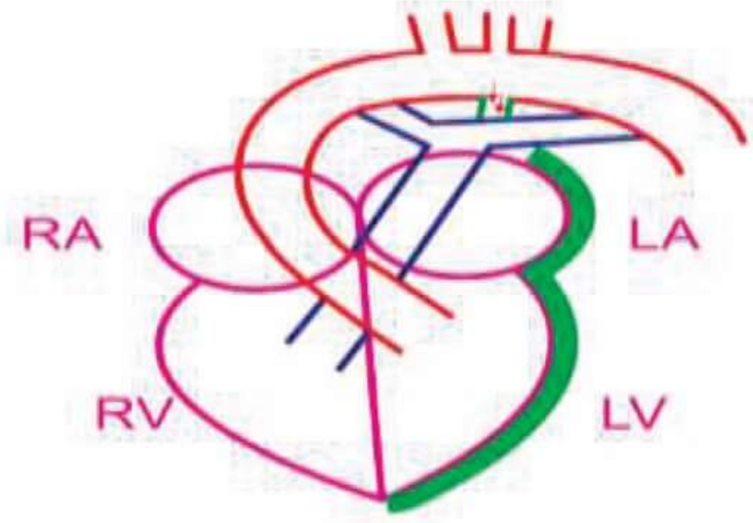
→ **Trilogy of Fallot** → Pulmonary Stenosis + Atrial Septal Defect + Right Ventricular Hypertrophy

PATENT DUCTUS ARTERIOSUS:

→ Ductus arteriosus connects aorta to pulmonary artery

→ Hypoxia & prematurity predispose to PDA

HEMODYNAMICS



Aorta 80-120 mm
60-80 Hg

25 mm Pulmonary
10 Hg Artery

1. AUSCULTATION → Continuous machinery murmur – 'drrrr sound' (as huge difference between pressures in aorta & pulmonary artery)
2. Left side of heart enlarged
   (LA+LV increased in size)
   *(excess blood from ascending aorta enters pulmonary artery into lungs)

CLINICAL PRESENTATION → same as VSD

Term Neonates → presents at 6-10 weeks

Preterm Neonates→ presents at 1st week

INVESTIGATIONS → CXR & ECG findings are same as VSD

TREATMENT:

For term babies → same as VSD

I. **Medical Management**
   → Treatment of heart failure
   → Treatment of pneumonia
   → Nutritional rehabilitation

II. **Surgical Management**
   → Ligation of PDA
   → Coil embolization of PDA
   → Indications of Surgery:
      → Heart failure refractory to medical Management
      → Q_p (Pulmonary blood flow): Q_s (Systemic blood flow) > 2:1
   → **DOC** for medical closure of PDA in preterm neonate → PG Inhibitor [Indomethacin; Ibuprofen]

DIFFERENTIAL CYANOSIS IS SEEN IN PDA with REVERSAL OF SHUNT [EISENMENGER SYNDROME]

→ No cyanosis in upper limbs (as oxygen blood goes us there)

→ Cyanosis in lower limbs (mixing of blood with deoxygenated blood)

TETRALOGY OF FALLOT (TOF)

➔ MC congenital cyanotic heart disease in children

4 COMPONENTS

1. Large, unrestricted VED
2. Pulmonary infundibular stenosis
3. Overriding of aorta
4. Right ventricular hypertrophy

CLINICAL FEATURES:

- Cyanosis
- Clubbing
- Polycythemia
- Cyanotic spells
- Heart failure is not seen in TOF, unless it is complicated by
  - Anemia
  - Infective endocarditis
  - Myocarditis
  - Systemic hypertension

AUSCULTATION:

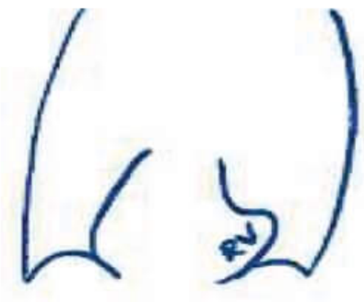
- Ejection systolic murmur in pulmonary area
- Single S_2 (P_2 is soft & inaudible)

Severity of TOF α Severity of Cyanosis

$$\alpha \frac{1}{\textbf{Intensity \& duration of murmur}}$$

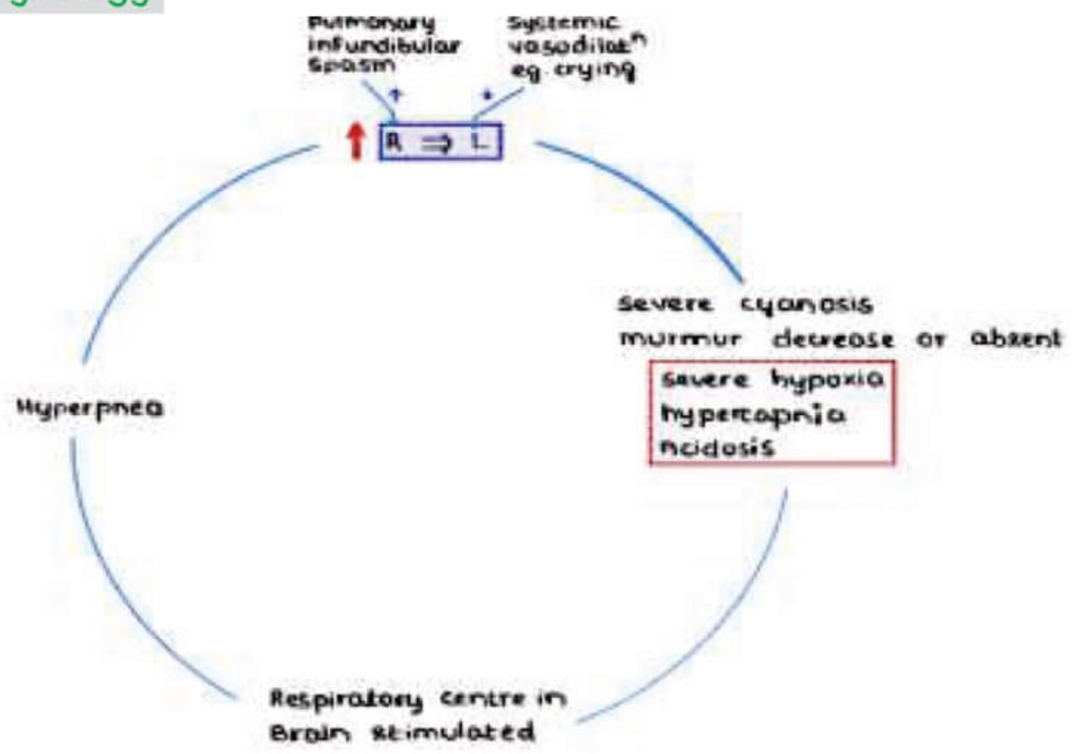
INVESTIGATIONS:

1. CxR:
   - Boot Shaped Heart (or) 'Cor En Sabot' Appearance
   +
   Pulmonary Oligemia



CYANOTIC SPELL OR TET SPELL

Pathophysiology:



TREATMENT:

1. Moist O_2 inhalation
2. Inj. Sodium Bicarbonate
3. Morphine
4. Ketamine
5. ∝ agonists (Phenylephrine)
6. B blockers (Propranolol)
7. Squatting or knee chest position helps aborting cyanotic spell

→ No role of Calcium & Isoprenaline (β agonist) in the treatment of cyanotic spell

SURGICAL TREATMENT OF TOF:

Definitive Sx → VSD closure + Repair of Pulmonary stenosis

Shunt Sx → Connection b/w pulmonary artery & aorta or its branch (**Mnemonic:**"BaS WahA Pahucha Do")

- Blalock Taussig shunt → Subclavian artery
- Waterston's Shunt → Ascending Aorta
- Pott's Shunt → Descending Aorta

Pink TOF → Milder pulmonary stenosis → Cyanosis is less obvious

OTHER CONGENITAL HEART DISEASES

TRUNCUS ARTERIOSUS:

→ Single common trunk from which pulmonary artery & aorta arise

→ Rt sided aortic arch is commonly a/w truncus arteriosus

→ 22 q deletion commonly associated [CATCH 22]

→ Conotruncal abnormalities

→ Abnormal facies

→ Thymic hyperplasia

→ Cleft palate

→ Hypocalcemia

TAPVC / TAPVR [TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION / RETURN]

Basic defect → Pulmonary veins instead of draining into the left atrium, drain, either directly or indirectly into right atrium

3 types:

	Supra cardiac	Cardiac	Infracardiac
Pulm. Vein drains into	SVC Lt. Innominate vein	Rt. Atrium coronary sinus	IVC Hepatic veins Portal veins
	MC type		Always obstructive

→ Obstructed TAPVC presents with heart failure even in 1st wk of age

CXR in TAPVC:

→ Supra-cardiac TAPVC → **'Figure of 8' or 'snow man' appearance**

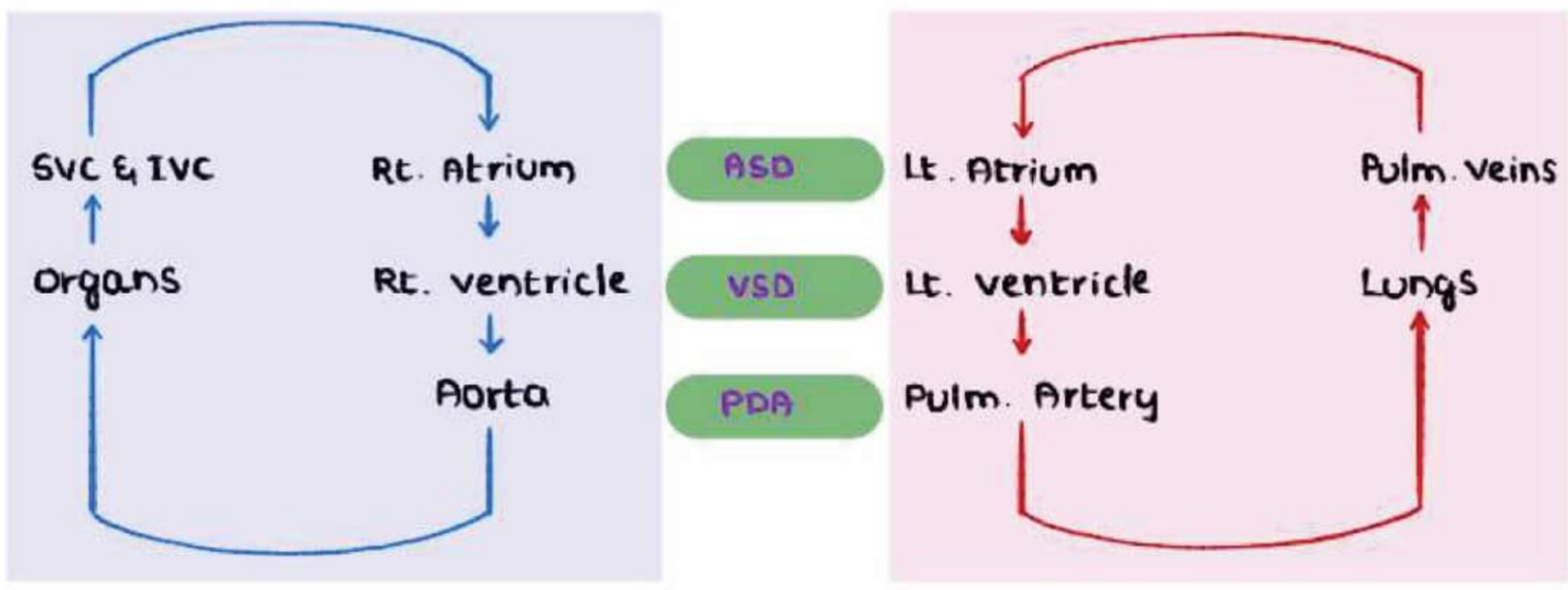
→ Obstructed TAPVC → Ground glass haziness of lungs

TGA /TGV [TRANSPOSITION OF GREAT ARTERIES / VESSELS]

→ Basic defect → Pulmonary artery instead of arising from Rt. Ventricle, arise from left ventricle.

→ Aorta instead of arising from Lt ventricle, arises from Rt ventricle

→ **PARALLEL CIRCULATION (D – TGA)**



L – TGA or corrected TGA → Usually comes to notice due to other associated heart defects

→ CXR → **"Egg on side" appearance**

→ MC congenital cyanotic heart disease presenting in neonatal period of early infancy → TGA

TREATMENT:

1. PGE_1 analogue [Alprostadil] → Keeps ductus arteriosus open
2. Balloon atrial septostomy / Rashkind procedure
   → Emergency procedure
3. Arterial switch operation / Jatene's repair
   → Definitive surgery

COARCTATION OF AORTA

→ Juxta ductal part of aorta is mostly involved

→ Medial wall of aorta is usually spared

→ Clinical presentation

→ Severe coarctation → Heart failure in neonate with B/L feeble or impalpable femoral pulses

→ Hypertension

→ milder disease: intermittent claudication of lower limbs

CXR:

Figure of 3 &

Notching of inferior margin of 3^{rd} – 9^{th} ribs usually seen >3 years age

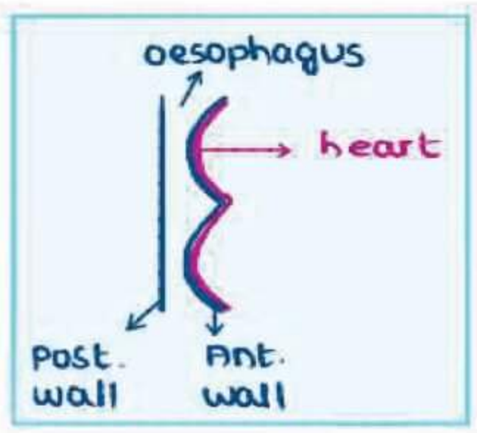
CONTRAST ESOPHAGOGRAM AND BARIUM SWALLOW:

E sign

TREATMENT:

→ Balloon angioplasty

→ Anti hypertensives for hypertension

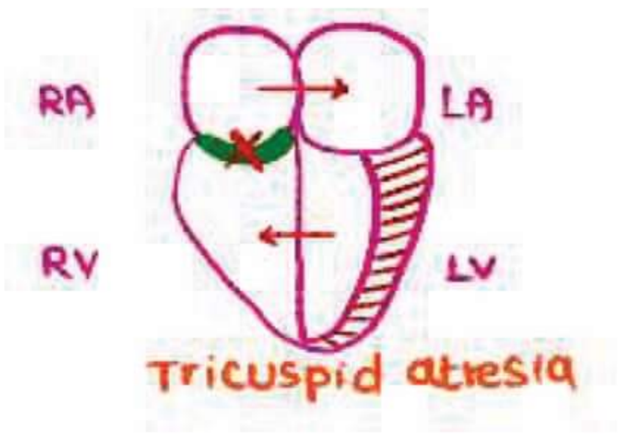


HLHS [HYPOPLASTIC LEFT HEART SYNDROME]

→ MC congenital heart disease causing mortality in 1st wk of life

TRICUSPID ATRESIA:

→ Congenital cyanotic heart disease with left axis deviation on ECG → Tricuspid atresia



EBSTEIN ANOMALY

PATHOPHYSIOLOGY:

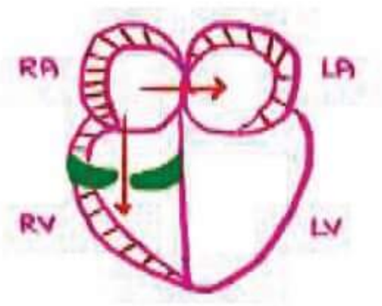
Downward displacement of tricuspid valve

↓

Atrialization of right ventricle

+

Functionally abnormal tricuspid valve

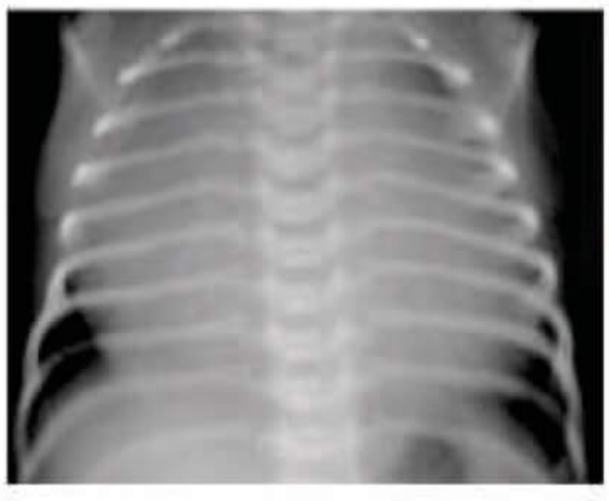


→ Huge cardiomegaly seen, especially Rt atrium [RA, LA, RV also involved]

CXR →Box shaped heart

ECG →Himalayan P waves

Box shaped heart



Himalayan P waves

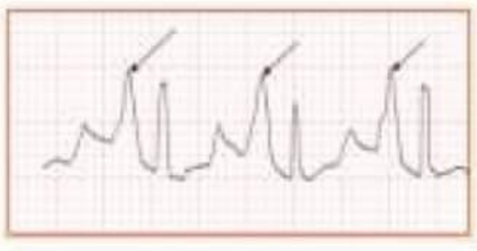
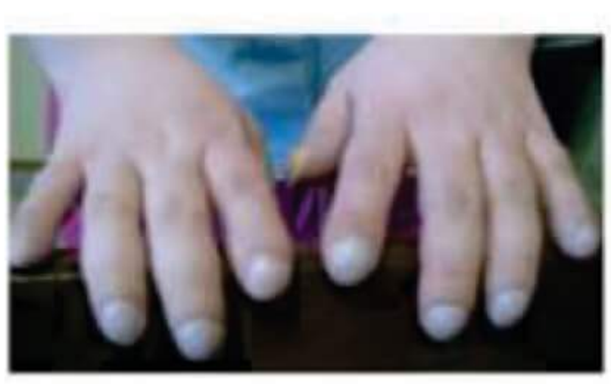


IMAGE BASED QUESTIONS

A child with VSD develops these findings.

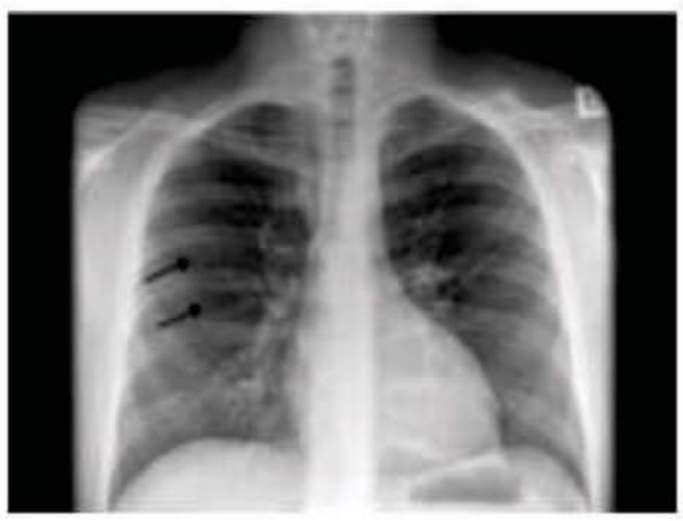
There is no history of fever. What is the most probable cause?

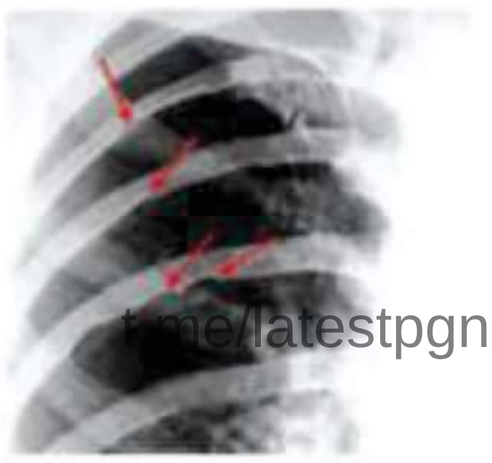


EISENMENGER SYNDROME

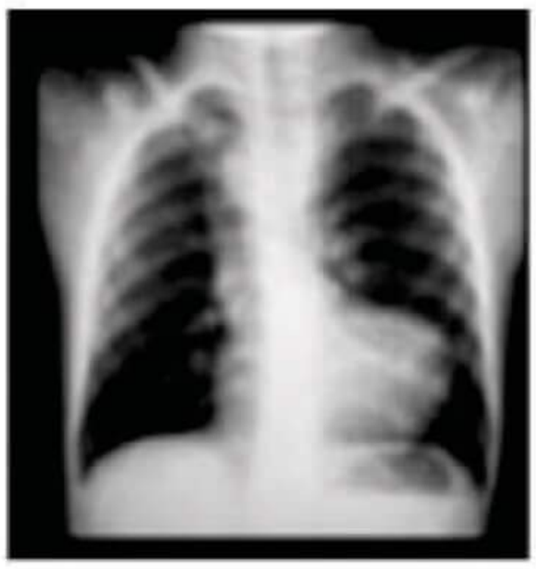
A 6 year child presented with hypertension.

What could be the cause?

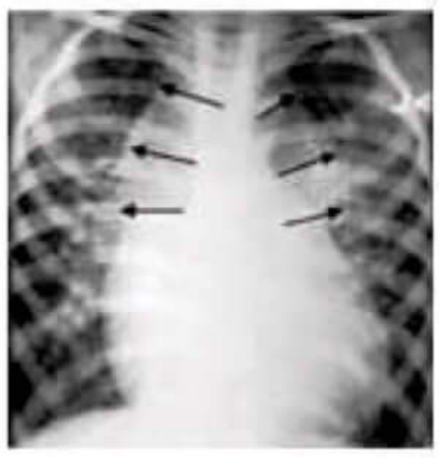




COARCTATION OF AORTA

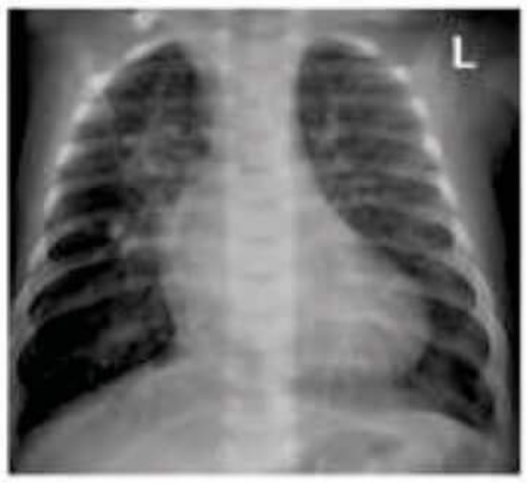


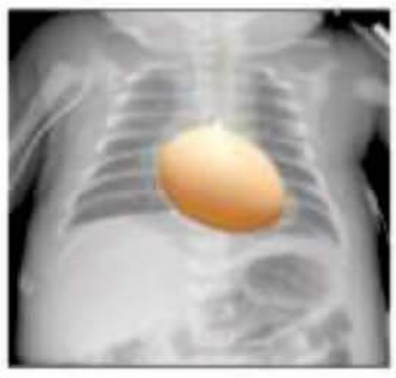
TETRALOGY OF FALLOT



SUPRACARDIAC TAPVC

TGA (Transposition of great arteries





TIMING OF HEART FAILURE

1st week	1-4 weeks	> 1 month
Ductus dependent	PDA in preterm's	PDA in terms
Systemic circulation → Severe coarctation of Aorta → Interrupted aortic arch → HLHS	VSD with coarctation	VSD
	Truncus arteriosus	Non obstructive TAPVC
Obstructive TAPVC	TGA with VSD	Endocardial cushion defect
TGA with intact ventricular septum		
Ebstein anomaly		

PEDIATRIC HEMATOLOGY AND ONCOLOGY

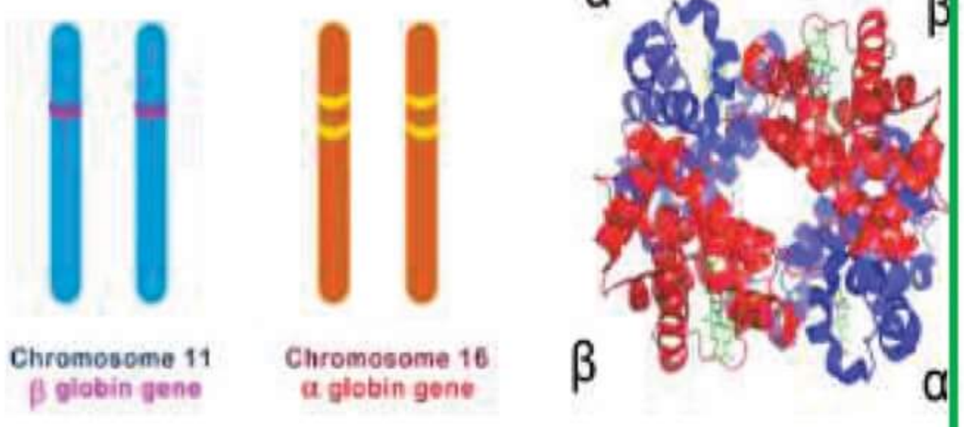
IMPORTANT HEMATOLOGICAL DISORDERS IN CHILDREN:

NORMAL ERYTHROPOIESIS:

NORMAL HUMAN HEMOGLOBINS:

	Hemoglobin	-Structural formula
Adult	Hb-A	$\alpha_2\beta_2$ 97%
	Hb- A_2	$\alpha_2\delta_2$ 1.5-3.2%
Fetal	Hb-F	$\alpha_2\gamma_2$ 0.5-1%
Embryonic	Hb-Gower 1	$\zeta_2\varepsilon_2$
	HB-Gower 2	$\alpha_2\varepsilon_2$
	Hb- Portland	$\zeta_2\gamma_2$

HEMOGLOBIN



Major sites of HEMATOPOIESIS:

Yolk sac - Starts from 3rd week till 10-12th week

Liver - Starts at 6-8th week, ceases by 2nd trimester

Bone marrow- Starts from 2nd trimester onwards

EXTRA EDGE:

Normal life span of RBC

120 days → Older children

90 days → term neonates

40-60 days → pre term neonates

ANEMIAS IN CHILDREN (WHO DEFINITION)

Children 6 months – 5 years → Hb < 11 g/dl

Children 6-14 years → Hb < 12 g/dl

IMPORTANT ONE LINERS

→ Most common cause of anemia in children → Iron deficiency

→ Most common mutation in hereditary spherocytosis → Ankyrin

→ Chromosomal breakage analysis is used in Dx of → Fanconi anemia

→ Auto splenectomy seen in → Sickle cell disease

→ Most common structural hemoglobinopathy → Sickle cell disease

Anemia (Pallar, lethargy)

↓

Hepatosplenomegaly

Absent

No Petechiae
- Iron deficiency anemia
- Megaloblastic Anemia
- Pure red cell aplasia
- Lead poisoning
- Chronic kidney disease

Petechiae Present
- Aplastic Anemia
- Bleeding disease
- Coagulation disease
- DIC

Present

↓

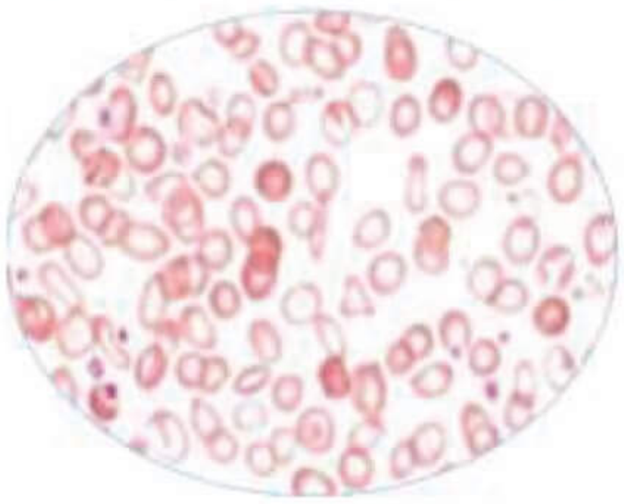
Lymphadenopathy

Absent
- Thalassemia
- Sickle cell disease

Present
- Leukemia
- Infection
- Infiltrative Disorders

IRON DEFICIENCY ANEMIA

- **MC CAUSE OF nutritional disorder in the world**
- MC cause of anemia in the world



ETIOLOGY

Decreased iron intake • Inadequate diet • Impaired absorption: Celiac disease **Increased iron loss** • Gastrointestinal bleeding, varices • Hookworm, Schistosomiasis, Trichiasis, Gastritis • Hiatal hernia • **Inflammatory bowel disease**, Meckel's • Milk-induced enteropathy (infants)	**Inadequate presentation to erythroid precursors** • Atransferrinemia • Anti-transferrin receptor antibodies **Abnormal iron balance** • Aceruloplasminemia • Autosomal dominant hemochromatosis due to mutations in ferroportin **Increased requirements** • Infancy

CLINICAL FEATURES: Smooth tongue, pica, koilonychia

PS: Microcytic Hypochromic Anaemia & anisocytosis, target cells, pencil cells

D/D	IDA	B Thalassemia minor	Anaemia of Chronic disease
RDW	Increased	Normal	Normal/Increased
S. iron	Decreased	Normal/Increased	Decreased
S. ferritin	Decreased	Normal/Increased	Increased
TIBC	Increased	Normal	Decreased
Mentzer Index:	>14	<13	

MENTZER INDEX:

$$= \frac{MCV\ (FL)}{RBC\ count\ (\frac{million}{ml})}$$

TREATMENT

→ 3-6 mg/kg/ day of elemental iron in 2-3 divided closes

→ Maximum dose: **150-200mg** of elemental Iron daily

→ Iron is continued for 8 weeks after blood values normalized

→ For IV correction, total amount of Iron needed

= body weight [kg]× [15-patient's Hb]× 2.3. + 500mg

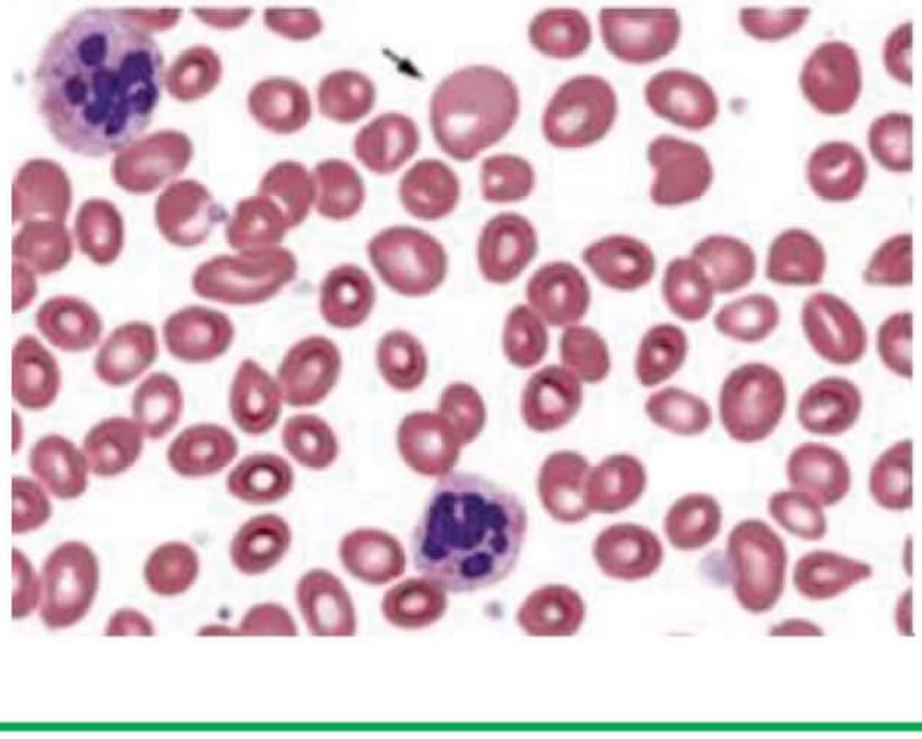
RESPONSE TO TREATMENT IN IRON DEFICIENCY ANEMIA

Time after Iron administration	Response
12-24 hours	Decreased irritability, **increased appetite**
48-72 hours	**Reticulocytosis**, peaks at 5-7 days post treatment
4-30 days	**Increase in Hb** level (best measure)
1-3 months	Repletion of stores

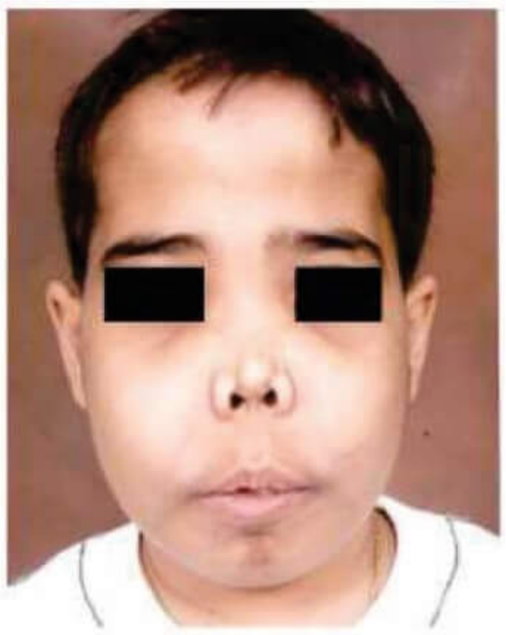
MEGALOBLASTIC ANAEMIA:

On Peripheral smear: Anisopoikilocytosis, **Macro ovalocytes, Hyper segmented neutrophils**

TREATMENT: Vitamin B12 and Folic acid



BETA-THALASSEMIA



DEFECT-Decreased production of Beta globin chains.

COMMON MUTATIONS IN INDIA-

- IVS 1-5 G → C
- IVS 1-1 G→ T
- Codon 41/42
- Codon 819
- 619 by deletion

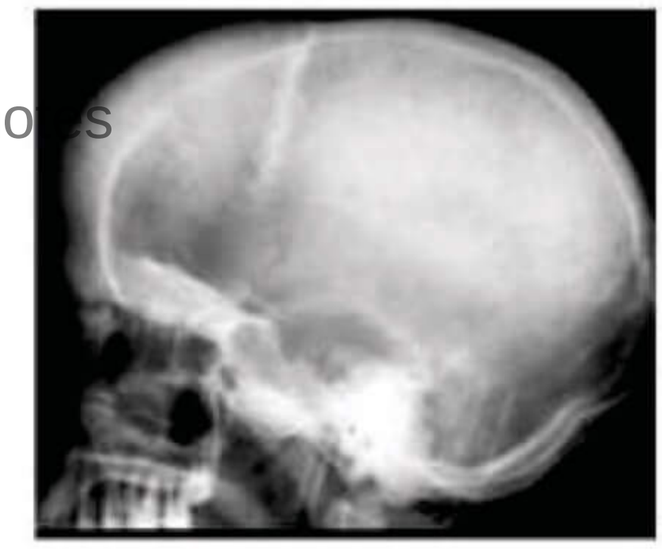
CLASSIFICATION:

Thalassemia trait- Heterozygous state - **Mild** Anemia ($HbA_2 \geq 3.5\%$)

Thalassemia intermediate (B^0/B^+) – **Moderate** anaemia, Hepatosplenomegaly – HbF elevated

Thalassemia major (B^0/B^0) - **Homozygous severe** anaemia, HSM – HbF markedly elevated

Regular transfusions requirement



CLINICAL FEATURES:

- Haemolytic Facies- Frontal prominence
  - depressed bridge of nose
  - maxillary prominence
- Hepatosplenomegaly (d/t extramedullary hematopoiesis)

INVESTIGATION:

- Lat. X Ray skull → **"Hair on End"" or "Crew Cut appearance"**
- Elevated LDH, Unconjugated bilirubin.

TREATMENT OF THALASSEMIA

1. **BLOOD TRANSFUSIONS**: To maintain pretransfusion Hb level between 9.5-10.5 g/dL
2. **Drug of choice** for transfusional hemosiderosis in thalassemia
   → Sub cutaneous Deferoxamine + oral Deferiprone/Deferasirox
3. The only **curative** treatment for thalassemia major → Hematopoietic stem cell transplantation (**HSCT**)

IRON CHELATION THERAPY: Usually started when serum ferritin > **1000 ng/ml**

a) **Deferoxamine** → Parenterally (IV or SC)

Effective in reverting hepatic & cardiac iron deposition.

b) **Deferiprone** – 1st oral chelator.

Adverse effects → Agranulocytosis, GI side effects, arthritis

c) **Deferasirox** – Oral drug, Effective in decreasing cardiac iron burden & lowering serum ferritin.

COMPLICATIONS:

Endocrine → Osteoporosis, Short stature, delayed puberty, Hypothyroidism, Hypogonadism, D.M

Cardiac → Heart failure, pericardial effusion, DCM

GI – Transaminitis

Other- Infections, allergies

SICKLE CELL ANEMIA

➔ **MC Structural Hemoglobinopathy**

→ Point mutation in 6th codon of β-globin gene so there is replacement of glutamate with valine

→ Production of Hb with abnormal physiochemical properties that promotes polymerization of deoxygenated Hb

HETEROZYGOUS TRAIT- sickle cell trait –protects against falciparum

HOMOZYGOUS TRAIT- sickle cell disease

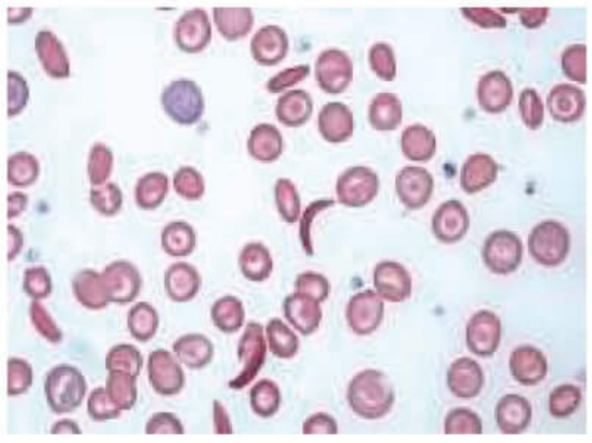
PATHOPHYSIOLOGY:

On Deoxygenation -- HbS forms long polymers

↓

- RBC membrane damage
- Microvascular obstruction leading to ischemia & tissue damage.
- Hemolysis in Reticuloendothelial system

CLINICAL FEATURES:



→ Hand foot syndrome or **dactylitis** of bones of hands and or feet

→ **Priapism** [in 45% of affected male] & erectile dysfunction

→ **Stroke** & **retinopathy** → loss of visual acuity & blindness

→ **Auto splenectomy** d/t splenic INFARCTS (Spleen not palpable)

→ Chronic **hemolysis** → Generalised impairment of growth

→ Renal Involvement → **papillary necrosis & hyposthenuria**

→ cardiomegaly

→ Infections mainly by → encapsulated bacteria

DIAGNOSIS:

→ **SICKLING TEST** → mixing a blood sample with metabisulfite or dithionate induces sickling of RBCs, if HbS is present.

→ **Howell- Jolly bodies** due to asplenia

→ Spleen biopsy → **Gamma Gandy bodies**

→ Hb Electrophoresis to detect HbS- **CONFIRMATION**

TREATMENT:

→ Avoid infections & prompt correction of any inflammation

→ Pneumococcal & HIB vaccination early in life

→ Acute painful crisis → vigorous hydration & analgesia

→ **Hydroxyurea** for patients with severe symptoms (increase HbF levels)

→ Bone marrow transplantation, gene therapy

FANCONI ANEMIA:

- AR inheritance
- Abnormal chromosomal fragility

(demonstrated using Diepoxybutane or Mitomycin C)

CLINICAL FEATURES:

- Most common → Hyperpigmentation, café au lait spots
- Short stature
- Absent radius, hypoplastic thumb.
- Facies → Microcephaly, small eyes, epicanthic folds, abnormal ears.
- Renal/ CNS/GIT malformations

COMPLICATIONS:

Increased risk of tumors like squamous cell Carcinoma of Head/ Neck/Esophagus.

TREATMENT: - Transfusions

- HSCT (definitive treatment)
- Androgens (Example: Oxymetholone) → **latest update**

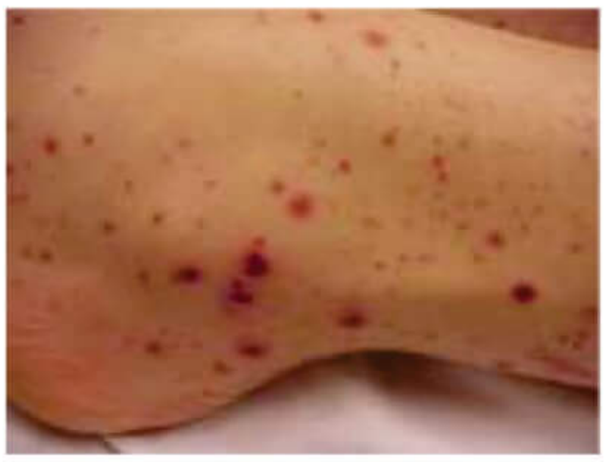
BLEEDING & COAGULATION DISORDERS:

ITP (IDIOPATHIC/IMMUNE THROMBOCYTOPENIC PURPURA)

- In an otherwise well child, generated onset of petechiae & purpura.
- H/o preceding viral illness 1-4 week ago.
- Examination- Petechiae present; no other abnormalities
- Disorder due to antibodies against Gp Ib/IX and Gp IIb/IIIa

INVESTIGATION:

- Platelet counts < 20,000/mm³
- Coagulation profile normal
- Platelet size normal/ increased
- BM- Increased megakaryocytes
- HIV & COOMBS test → important



TREATMENT

→ Platelet transfusion → usually avoided unless life threatening bleeding is present
→ IVIg
→ IV anti D therapy → used in **Rh positive patients**
→ Prednisolone → for 2-3 weeks or till platelet count > 20,000/mm³
→ Splenectomy → in severe/ **refractory/ life threatening ITP**
→ Rituximab → induces remission in 30-40% children & has been used as an Alternative to splenectomy

HEMORRHAGIC DISEASE OF NEWBORN (HDN):

(Now called "Vitamin K" deficiency bleeding)

Classification:

EARLY ONSET	CLASSICAL DISEASE	LATE ONSET
Age – 0-24 hrs	2-7 days	1-6 months
Etiology – Maternal drugs	– Vitamin K deficiency	– Cholestasis
Or risk – of Phenytoin	– Breast feeding	– Abetalipoproteinemia
Factor – Rif, INH		– Warfarin ingestion

PREVENTION/ TREATMENT: Inject Vit K 1mg intra muscularly to all neonates at birth

HAEMOPHILIA A:

➔ Deficiency of Factor VIII
➔ X linked recessive → more common in males

- Mild (>5%)
- Moderate (1-5%)
- Severe (<1% factor level)

CLINICAL FEATURES – Bleeding, Hemarthrosis (**earliest joint involved** – ankle, also seen in knee joint)

INVESTIGATION– Increased APTT, normal PT, BT, platelet count.

TREATMENT:

➔ Factor VIII replacement.
➔ If not available – use Fresh frozen plasma (FFP)

HEMATOLOGICAL MALGNANGES IN CHILDREN

- **ALL**
- **AML**
- **Hodgkin Disease**
- **LCH**

→ Leukemia is the most common malignant neoplasm in childhood
→ Factors predisposing to childhood leukemias are:

- Down's syndrome
- Kostmann syndrome
- Fanconi anemia
- NF1
- Bloom syndrome

- Shwachman diamond syndrome
- Li fraumeni syndrome
- Alkylating agents
- PNH

MNEMONIC → "DAUGHTER KE FATHER NE BOY KO SLAP KIA"

ALL (ACUTE LYMPHOBLASTIC LEUKEMIA)

- B cell ALL is more common than T- Cell ALL
- Superior mediastinal syndrome is more common in adolescent boys with T-Cell ALL

FAB Classification

L_1	L_2	L_3
Size → Small cells	Large, heterogenous	Large, Homogenous
Cytoplasm → Scant	Variable	Abundant
Nucleoli → small & inconspicuous	Large	Prominent

C/F-

- Usual duration of symptoms → days to weeks.
- Pallor, fatigue, petechiae, bleeding, infection, fever, bone-pain.
- O/E – Lymphadenopathy, hepatosplenomegaly

DIAGNOSIS-

- BM aspirate > 20% leukemic lymphoblasts
- Immunophenotype → Pre-B/ B/ T cell

TREATMENT

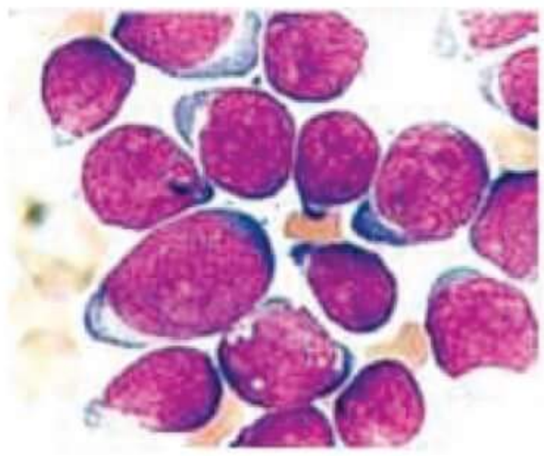
- **Induction** → 4-6 weeks (Vincristine, Anthracycline, Prednisolone, L- Asparaginase)
- **CNS prophylaxis** → Intrathecal Methotrexate ± Radiotherapy
- **Intensification** – Methotrexate, L- Asparaginase, Cyclophosphamide
- **Maintenance phase** – 2-2.5 years – oral 6- MP & Methotrexate

Prognosis	Good	Bad
Age	2-8 years	< 1 years or > 10 years
Initial TLC	< 20000/mm^3	>50000/mm^3
SEX	Females	Male
Cytogenetics	Hyper ploidy	Hypo ploidy, t (9:22)
MRD (Minimal Residual disease) on day 29	< 0.01 %	>0.01%

AML (ACUTE MYELOID LEUKEMIA)

CLINICAL FEATURE

- Pallor, fatigue, petechiae, bleeding, infection, fever, bone-pain
- DIC in M_3
- Chloromas in M_2
- Gingival involvement in M_4 , M_5



TYPES:

M0- **Minimally differentiated**

M1- AML **without maturation**

M2- AML **with maturation**

M3- **APML** (Acute Promyelocytic Leukemia)

M4- **Myelomonoblastic** Leukemia

M5- **Monoblastic** Leukemia

M6- **Erythrocytic** Leukemia

M7- **Megakaryoblastic** Leukemia

DIAGNOSIS:

- **Auer rods** positive in M_2, M_3, M_4 & MPO positive
- NSE positive M_3, M_4, M_5 (Monoblasts)

STAINS USED:

Myeloblasts are positive for MPO, Sudan Black B

Monoblasts are positive for NSE (Non-Specific Esterase)

TREATMENT:

- Ara C (Cytosine Arabinoside)
- Anthracyclines (Doxorubicin)

For APML use

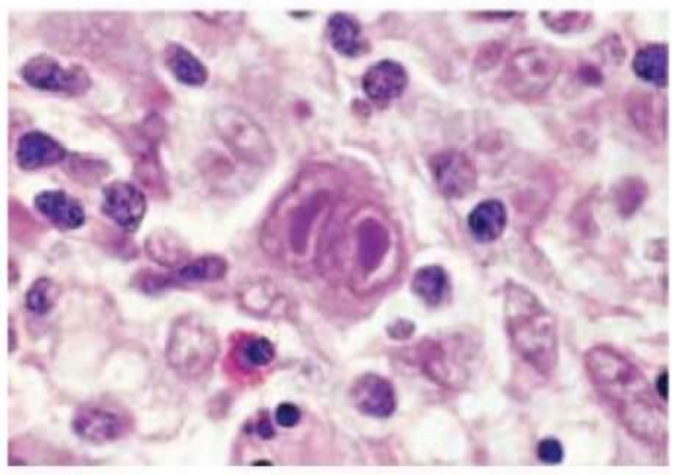
- ATRA (All trans Retinoic Acid)
- Arsenic

HODGKIN's DISEASE:

CLINICAL FEATURES: Fever, lymphadenopathy, hepatosplenomegaly

- **Types**

Nodular	**Classical**
Lymphocyte Predominance	- Lymphocyte rich
– Lymphocyte depletion	
– Mixed cellularity	
- Nodular sclerosis	



ANN ARBOR STAGING:

I- Single LN or extra lymphatic site involved

II- 2 or more LN regions on **same** side of diaphragm involved

III- LN regions on **both** sides of diaphragm involved

IV- Diffuse to Disseminated disease

TREATMENT- 'ABVD'

A- Adriamycin (Doxorubicin)

B – Bleomycin
V – Vinblastine
D – Dacarbazine

LANGERHANS CELL HISTIOCYTOSIS:

-Due to excess proliferation of dendritic cells.

TYPES:

- **Eosinophilic granuloma** → Localized disease & eosinophilia
- **Hand Schuller Christion disease** → Lytic bone defects, DI, Exophthalmos
- **Letterer siwe disease** → Multiple foci & organs involvement

C/F:

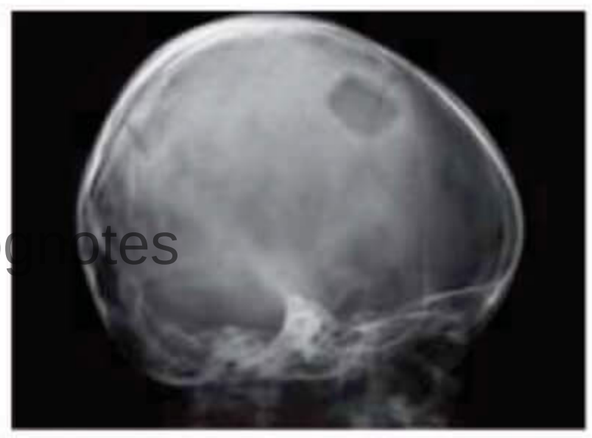
- **Localized** → Osteolytic bone lesions (**punched out lesions**) → skull & mastoid involved → chronic ear discharge
- **Scalp** -Seborrheic dermatitis
- **Pancytopenia** → increased extra medullary haematopoiesis → hepatosplenomegaly
- **Lung involvement** – Pneumothorax
- **Pituitary involved** → DI & GH deficiency

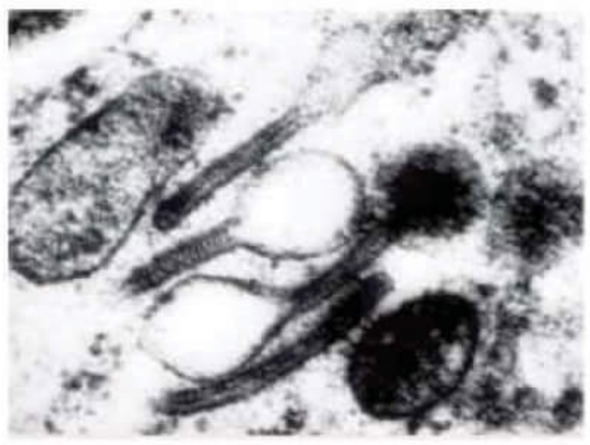
DIAGNOSIS:

Biopsy → CD/a or S-100
EM → Tennis racket shaped Birbeck granule

TREATMENT:

- **Localized** – Steroids, Radiation, Curettage
- **Multifocal**- Vinblastine, Etoposides, Prednisolone





TUMORS OF INFANCY & CHILDHOOD:

RETINOBLASTOMA:

→ MC primary intra ocular tumor in children
→ 60% are acquired
→ 40% are hereditary
→ Caused by inactivation of RB1 gene on Chr 13q 14
→ Arises from the inner layer of retina
→ It's overgrowth can lead to vitreous seeding & retinal detachment, necrosis & calcification.
→ MC presentation → Leukocoria
→ Earliest presentation → Strabismus

→ Most common route of spread → Direct spread through optic nerve

→ Most common secondary tumor following retinoblastoma

→ Osteosarcoma

→ Soft tissue sarcoma

→ Malignant Melanoma

DIAGNOSIS

→ Ophthalmoscopy under EA is the mainstay of Dx

→ CT Scan → Demonstrates presence of calcifications

→ MRI is preferred to rule out trilateral retinoblastoma syndrome

Trilateral retinoblastoma = B/L retinoblastoma + tumor of pineal gland

TREATMENT

1. **Chemotherapy**
   - Carboplatin, vincristine, etoposide
   - For reduction of tumor size

     ↓ F/b

     Laser photocoagulation for small tumor

     Cryotherapy for large tumors
2. **Enucleation** → Only for tumors with no possibility of vision restoration
3. **Radiotherapy** → reserved for resistant cases

NEUROBLASTOMA:

→ MC abdominal tumor of childhood

→ 98% cases are sporadic

2% cases are familial

→ Most frequently diagnosed tumor of infancy [<1yr of age]

→ 90% Neuroblastomas produce catecholamines → vanillyl-mandelic acid [VMA] & homovanillic acid

SITE OF TUMOR:

→ Adrenal medulla [MC site]

→ Along the sympathetic chain > pelvis, neck & brain [cerebral neuroblastomas]

CLINICAL FEATURES:

→ Depends on tumor site & extent of disease

→ **Metastatic disease**

→ Fever

→ Irritability

→ Failure to thrive

→ Bone pain

→ Bluish subcutaneous nodules

→ Orbital proptosis

→ Periorbital ecchymoses

→ **Localized disease** → Asymptomatic mass or Cognitive dysfunction

→ **Catecholamine producing** → Hypertension, Profound secretory diarrhea

→ **Extensive tumors** → Tumor lysis syndrome, DIC

STAGING:

Stage	Definition
1	Localized tumor with **complete gross excision** with ipsilateral **lymph nodes negative**
2A	Localized tumor with **incomplete gross excision**; with **lymph nodes negative**
2B	Localized tumor with ipsilateral nonadherent **lymph nodes positive** for tumor
3	**Unresectable** unilateral tumor infiltrating **across the midline**, with or without regional lymph node involvement
4	Any primary tumor with **dissemination of distant lymph nodes; bone; bone marrow, liver skin**, and other organs (except as defined for stage 4S)
4S	**Localized primary tumor** (as defined for stage **1, 2A, or 2B**), with **dissemination limited to skin, liver, and bone marrow,** (limited **to infants < 1 year of age**)

PROGNOSTIC FACTORS:

Variable	Favorable	Unfavorable
Stage	Stage 1, 2A, 2B, 4S	Stage 3, 4
Age	<18 months	> 18 months
Schwannian stroma & gangliocytic differentiation on histology	Present	Absent
Mitosis – karyorrhexis index	<200/5000 cells	>200/5000 cells
DNA ploidy	Hyper-diploid	Near – diploid
N-MYC	Not amplified	Amplified
Chromosome 17q gain	Absent	Present
Chromosome 1p loss	Absent	Present
Chromosome 11q loss	Absent	Present
TRKA expression (Accha)	Present	Present
TRKB expression (Bura)	Absent	Present
Telomerase expression	Low or absent	Highly expressed

TREATMENT:

1. **Low risk disease**
   → Surgeries for stage 1 and 2 , and observation
   → For stage 4S with cure rates generally >90% without further therapy
2. **Intermediated risk disease**
   → Surgery, chemotherapy ± radiotherapy
   → Chemotherapy → Cisplatin or carboplatin, Cyclophosphamide, Etoposide & Doxorubicin
3. **High risk neuroblastoma** [Survival rate ~ 25-35%]
   → High dose chemotherapy with autologous stem cell rescue
   → Surgery, radiation, & 13- cis – retinoic acid [isotretion]
   → Induction chemotherapy: Cyclophosphamide, Topotecan, Doxorubicin, vincristine, Cisplatin & Etoposide

WILM'S TUMOR

→ MC primary renal tumor of childhood

→ Peak incidence → b/w 2-5 years

→ **MC initial clinical presentation** for WT is incidental discovery of an asymptomatic abdominal mass by parents while bathing or clothing or by a physician during routine examination

→ Can present as

→ **Synchronous**-Both kidneys involved simultaneously

→ **Metachronous**- Kidneys affected one after the other

→ CONGENITAL MALFORMATIONS WITH INCREASED RISK OF WILMS TUMOR

WAGR syndrome (33% risk)Q	**Denys – Drash syndrome** (90% risk, Maximum risk)Q	**Backwith – Wiedemann syndrome** (BWS)
WT1 gene: Chr 11 p13Q Wilms tumor, Aniridia, Genital anomalies, and mental Retardation	Gonadal dysgenesisQ (male pseudohermaphroditism) Early – onset nephropathy (diffuse mesangial sclerosis)Q increased risk of gonadoblastomaQ	Organomegaly: MacroglossiaQ, hemihypertrophyQ, omphalocele, and abnormal large cell in the adrenal cortex (**adrenal cytomegaly**) Genomic imprintingQ is the causative mechanism

STAGING:

Stage I	**Tumor confined to the kidney and completely resected. Renal capsule, vessels or lymph nodes** not involved
Stage II	**Tumor extend beyond the kidney** but is **incompletely resected with negative margins** and **lymph nodes.** At least 1 of the following has occurred: **(a) penetration of renal capsule, (b) invasion of renal sinus vessels**
Stage III	**Residual tumor present** following surgery confined to abdomen, including gross or microscopic tumor, spillage of tumor preoperatively or intraoperatively, biopsy prior to nephrectomy, **regional lymph node metastases**; tumor implants on peritoneal surface; extension of tumor thrombus into inferior vena cave and heart
Stage IV	**Hematogenous** metastases (lung, live, bone, brain, etc.) or **lymph node metastases outside the abdominopelvic region**
Stage V	Bilateral renal involvement by tumor

TREATMENT:

→ Nephrectomy alone may be sufficient for patients < 2 yr age with stage I disease & a tumor weighing <550 g

→ **Stage I or II** → chemotherapy with 2 drugs

→ Vincristine and Dactinomycin

→ every 1-3wk for total of 18wk regimen (EE4A)

→ **Stage III or IV** → Chemotherapy with 3 drugs & radiotherapy

- Vincristine, doxorubicin & actinomycin

- Every 1 – 3 wk, total 24 wks [regimen DD4A]

→ Regional LN metastasis, residual diseases after surgery, or tumor rupture, lung metastases → Radiation therapy.

→ Presence of loss of heterozygosity at 1p & 16 q confers an adverse prognosis

→ Patients with diffuse anaplasia have a poor outcome

SACRO – COCCYGEAL TERATOMA (SCT):

→ Teratoma arises from sacrococcygeal region

→ Arise from totipotent cells from node of hensen at anterior aspect of coccyx, by 2nd to 3rd weeks of gestation

→ Mostly mixed solid / cystic, although purely cystic types occur in 15%

CLASSIFICATION

→ Benign [mature] → 60-70%

→ Malignant [immature]

COMPLICATIONS

→ Anemia, dystocia, tumor rupture

→ Ureter obstruction, Gastrointestinal obstruction

→ Compression of underlying nerves

→ Fetal incontinence

→ High output cardiac failure from AV shunting

→ Hydrops fetalis

TREATMENT & PROGNOSIS:

→ SCT can be benign or malignant depending on whether mature or immature

→ Those presenting in older infants tend to have a higher malignant potential while those presenting in utero have poor prognosis d/t complications.

→ Malignant changes may be commoner in males

→ Treatment: **Surgical excision** + coccygectomy with additional chemotherapy for malignant tumors

BRAIN TUMORS:

→ **2nd MC malignancy** in childhood & adolescence

→ Histologically gliomas accounts & for majority of tumors including malignant tumors

→ Hereditary syndromes & cranial exposure to ionizing radiation are associated with a higher incidence of brain tumor

SYNDROMES ASSOCIATED WITH BRAIN TUMORS

SYNDROME	TUMORS ASSOCIATED	CHROMOSOME	GENE
Neurofibromatosis type 1 (autosomal dominant)	Optic pathway gliomas, astrocytoma, malignant peripheral nerve sheath tumors, neurofibromas	17q11	NF1
Neurofibromatosis type 2 (autosomal dominant)	Vestibular schwannomas, meningioma, spinal cord ependymoma, spinal cord astrocytoma, hamartomas	22q12	NF2

Von – Hippel – Lindau (autosomal dominant)	Hemangioblastoma	3p25-26	VHL
Tuberous sclerosis (autosomal dominant)	Subependymal giant cell astrocytoma, cortical tubers	9q34 16q13	TSC1 TSC2
li- Fraumeni (autosomal dominant)	Astrocytoma, primitive neuroectodermal tumor	17q13	TP53
Cowden (autosomal dominant)	Dysplastic gangliocytoma of the cerebellum (Lhemitte – Duclos disease)	10q23	PTEN

→ During 1st yr of life, supra tentorial tumors predominate & include choroidal plexus complex tumors & teratomas

→ In children 1 – 10 yrs, infratentorial tumors predominate mostly juvenile pilocytic astrocytoma & medulloblastoma

→ After 10 yrs age, supra tentorial tumors again predominate, with diffuse astrocytomas most common

Q **Most aggressive tumor in children → Medulloblastoma**

Q **MC tumor in children → Pilocytic astrocytoma**

PILOCYTIC ASTROCYTOMA

→ Localized astrocytoma
→ WHO grade I tumor
→ Occurs in children
→ Indolent clinical course
→ Localized in Cerebellum > 3rd ventricle, optic nerve
→ Biphasic tumor
→ Rosenthal fibers & eosinophilic granular bodies are seen

MEDULLOBLASTOMA

→ WHO grade IV tumor
→ Embryonal tumor or PNET
→ Occurs predominantly in children & exclusively in cerebellum
→ Dissemination through the CSF is common complication → giving rise to nodular masses at some distance from the primary giving rise to nodular masses at some distance from the primary tumor called as "DROP METASTASES"
→ Treatment → Exquisitely radiosensitive

CRANIOPHARYNGIOMA

→ Adamantinomatous variant predominates in childhood
→ Endocrinological abnormalities like growth failure, delayed sexual maturation often seen
→ Visual changes can occur
→ Sx is the primary Rx, no role of chemotherapy

PEDIATRIC GASTROINTESTINOLOGY

DISORDERS OF GI SYSTEM INCLUDING DIARRHEA

A. ESOPHAGEAL DSIORDERS

1.GASTRO ESOPHAFEAL REFLUX DISEASE [GERD]:

→ MC esophageal disorder in children

→ PHYSIOLOGICAL GERD in infancy resolves in upto 90% by 12 months age

→ PATHOLOGIC GERD

→ Clinical manifestations because of frequent or persistent GER producing respiratory symptoms, esophagitis – related symptoms, or nutritional effects (failure to thrive)

DIAGNOSIS:

1. **Contrast esophagogram** (Barium swallow) → poor sensitivity & specificity

→ but gives clue about achalasia or esophageal strictures

2. **24 hours Esophageal pH monitoring** → quantitative & sensitive document of acidic reflux episodes
3. **Endoscopy** for erosive esophagitis / strictures.
4. **GER scan** – Radionucleotides scintigraphy
5. **Multichannel intraluminal impedance measurement** - a cumbersome test can be done foe understanding esophageal function

MANAGEMENT:

1.Conservative therapy & life style modification

→ Thickening of feeds

→ Positioning -prone/ upright position

2.Pharmacotherapy

→ Anti acid

→ H_2 receptor antagonist eg: Ranitidine

→ PPI & [omeprazole, Pantoprazole]

3.Surgery -fundoplication, for intractable GERD with refractory esophagitis

2.ESOPHAGEAL ATRESIA & TRACHEOESOPHAGEAL FISTULA (TEF):

- 5 types based on pressure & location of EA & TEF
- **Mc type is type C** – Here proximal end is blind distal end has presence of TEF

CLINICAL FEATURE:

1. H/O of **polyhydramnios**
2. Neonate has frothing, excesses drooling

- Coughing with feeds
- Cyanosis
- Respiratory distress

EXTRA EDGE:

H-type Fistula may present later in life with recurrent pneumonia due to aspiration

EA and TEF comprise a part of 'VACTERAL' association

V – **Vertebral anomalies**

A – Anal Atresia
C – Cardiac defects
TE – Tracheoesophageal fistula
R – Renal and radial anomalies
L – Limb defect
DIAGNOSIS: - Inability to pass orogastric or nasogastric tube
– **On X-ray**: Coiled tube in upper esophagus
– Prenatal USG
TREATMENT: - Surgical Repair

3.FOREIGN BODY IN ESOPHAGUS

→ Majorities of FB ingestions occur b/w **6 months & 3 years**
→ Coins & small toy items are **mc** ingested
→ DIAGNOSIS:
→ H/O FB ingestion
→ Plain AP radiographs of neck, chest & abdomen, along with lateral Views
→ TREATMENT:
→ **Endoscopic** visualization & **removed** using FB retrieving instrument
→ Sharp objects, disk button batteries or respiratory symptoms require **Urgent removal**
→ **Asymptomatic** blunt object & coins can be observed upto 24 hours, to allow it pass into stomach

B. DISORDERS OF STOMACH AND INTESTINE:

1. HYPERTROPHIC PYLORIC STENOSIS

CLINICAL FEATURE: Infants with forceful, projectile, non-bilious vomiting presenting between 2-6 weeks of age
ON EXAMINATION:
→Visible peristalsis from left to right
→Mobile olive shaped mass which is palpable (**Best** in MID-GASTRIC AREA)
→**Easiest** to palpate just after an episode of vomiting
NOTE: →1st born male are MC affected
→**Maternal erythromycin** intake during pregnancy is a risk factor
DIAGNOSIS:

- Hypokalemic metabolic alkalosis with paradoxical aciduria
- **USG** is sensitive and specific method for diagnosis
- **Upper G.I contrast studies** shows **STRING SIGN** or **DOUBLE TRACT** or **SHOULDER SIGN**

TREATMENT: Isotonic saline with Potassium to correct diarrhea
DEFINITIVE TREATMENT: RAMSTED'S pyloromyotomy

2. ACUTE DIARRHEA:

DEFINITION: Passage of 3 or more liquid or watery stools in a day

→ **MC cause of diarrhea in children** → **Rota virus**

→ **MC cause of constipation in children** → functional or habitual due to improper toilet training

→ **MC cause of vomiting in a neonate** → aerophagy

→Important consequence of Diarrhoea in children are – Dehydration and malnutrition

ASSESSMENT OF DEHYDRATION IN A CHILD WITH DIARRHEA:

Parameters	No dehydration	Some dehydration	Severe dehydration
Sensorium	Well alert	"Restless, irritable"	"Lethargic, floppy"
Eyes	Normal	Sunken	Very sunken & dry
Tears	Present	Absent	Absent
Mouth & tongue	Moist	Dry	Very dry
Thirst	Drinks normally, **not thirsty**	**"Thirsty, drinks eagerly"**	**"Drinks poorly/ not able to drink"**
Skin pinch	Goes back quickly	"Goes back slowly:	"Goes back very slowly"

If patient has 2 more signs including at least "1 sign" then the child has severe or some dehydration

a. MANAGEMENT OF ACUTE DIARRHEA IN CHILDREN

1. WHO ORS / Hydration

→ No dehydration [PLAN A] → Replacement of ongoing losses [5–10 ml/kg 1 loose stool]

→ Some dehydration [PLAN B] → **75 ml / kg** over 4 hours [if oral unable then can give IV fluid]

PREVIOUSLY USED, STANDARD ORS:

Osmolarity → 311

Sodium → 90 mEq/L

COMPONENTS OF REDUCED OSMOLARITY ORS (or) NEW WHO ORS [in mmoL/L]

Glucose → 75

Sodium → 75

Potassium → **20**

Chloride → **65**

Citrate → 10

Osmolarity → 245

COMPONENTS OF ReSoMAL [Rehydration solution for malnourished child] [mmollL]

Glucose → 125

Sodium → **45**

Potassium → **40**

Chloride → 10

Citrate → 7

Magnesium → 3

Zinc → 0.3

Copper → 0.045

TREATMENT OF SEVERE DEHYDRATION [100 ml / kg]:

Age	1st 30ml / kg	NEXT 70 ml / kg
< 1 year	over 1 hour	Over 5 hours → 6 hour
> 1 year	over ½ hour	Over 2 ½ hours → 3 hour

Fluid of choice for severe dehydration:

→ **Ringer lactate in 5% Dextrose** > Ringer lactate or normal saline

NOTE: Dextrose containing fluid alone should not be used

2. **ZINC** – reduces duration and severity
   → DOSE → **2-6-month age**: 10mg/day
   ≥ **6-month age**: 20mg/day
   Duration in 10-14 days
3. **CONTINUE NORMAL DIET**
4. No Role of antibiotics except in

- suspected bacterial infections like dysentery (blood, mucus in stool), cholera (rice watery stool)
-also in severe malnutrition

3. PERSISTENT DIARRHEA IN CHILDREN:

Persistent diarrhea: Diarrhea that start as an acute episode and lasts for **atleast 14 days**

MANAGEMENT:

INITIAL DIET A [Reduced lactose diet]

→ Examples

a. Milk rice gruel
b. Milk sooji gruel
c. Rice with curd
d. Dalia

} 65-70% children response to this diet

SECOND DIET B [Lactose free diet with reduced starch]

→ About 65-70% of children improve on the initial diet 'A', diet 'B' for remaining

THIRD DIET C [Monosaccharide – based diet]

→ 80-85% of patients recover on initial diet 'A' OR 'B', rest started on diet 'C'

4. LACTOSE INTOLERANCE IN CHILDREN

TYPES:

1. **Congenital / Primary** → due to mutation of lactose gene in **chromosome 2**, very rare type
2. **Acquired / Secondary** → **post infections** following diarrhea, due to infection or adverse effects of drugs and radiations (More common type)

CLINICAL FEATURE:

→ Diarrhea, abdominal pain & vomiting, especially on intake of milk products

→ Perianal excoriation because of acidic stools

DIAGNOSIS:

→ **Reducing substances positive in stool**

→ Confirmed by improvement of symptoms on exclusion of milk

→ **Decreased lactase activity** in small intestine **biopsy**

TREATMENT:

→ Avoid milk, skimmed milk & milk products like ice cream;

→ Curd / yoghurt may be given

5. CELIAC DISEASE [GLUTEN SENSITIVE ENTEROPHATHY]

→ A T-Cell mediated autoimmune disorder in which intolerance to wheat, rye, barley, oats containing gluten

ETIOLOGY:

1. Environmental factor due to Gliadin [Component of gluten]
2. Genetic factors associated with **HLADQ2 & HLADQ8** haplotypes
3. Immunological factors

→ Anti TTG (Tissue Trans Glutaminase)

→ Anti Endomysial Antibody (EMA)

→ Anti DGP (Deaminated gliadin peptide)

CLINICAL FEATURES:

SYSTEM	MANIFESTATION
GIT	Diarrhea, abdominal distension, vomiting, anorexia, failure to thrive, **aphthous stomatitis**
Hematologic	Anemia
Skeletal	Rickets, osteoporosis, enamel hypoplasia of teeth
Muscular	Peripheral neuropathy, epilepsy, irritability
Endocrine	Short stature, secondary hyperparathyroidism
Dermatologic	Dermatitis herpetiformis, alopecia areata, erythema nodosum

IMPORTANT CONDITIONS ASSOCIATED WITH CELIAC DISEASE

→ Dermatitis herpetiformis	**Doctor**
→ Down syndrome	**Don't**
→ William's syndrome	**W**
→ Addison's disease	**A**
→ Ig A deficiency	**I**
→ Turner syndrome	**T**
→ Type 1 DM	**Today**

DIAGNOSIS:

<u>**In Symptomatic patient**</u>

↓

1st line test: Anti TTG IgA + Total serum IgA

↓

Anti TTG IgA if negative

↓

Look at total serum IgA

- **If Normal** → Celiac disease unlikely
- If **reduced** → Perform anti TTG IgA

If anti TTG IgA positive

If < 10 times upper Of normal → Perform UGI Endoscopy & Duodenal Biopsy

If > 10 times of normal → Perform **HLADQ2** & **DQ8** and anti **EMA** test → If both test positive Then celiac disease is confirmed (So Duodenal biopsy is Not required)

TREATMENT :

→ Lifelong gluten free diet

6. INFLAMMATORY BOWEL DISEASE:

- **Chronic recurrent** disease characterized by intestinal inflammation

2 TYPES:

1. Ulcerative Colitis: **Involves the RECTUM**
2. Crohn's disease: **Skip lesions**

- **Non caseating granuloma**
- Rectum is usually spared

CLINICAL FEATURE: Depends on site of involvement & severity

ULCERATIVE COLITIS:

→ Involvement of **rectum** causes TENESMUS, Fecal urgency, Blood in stool

→ Involvement of **sigmoid colon** causes constipation

→ Involvement of **descending colon** causes Bloody diarrhea with pus and abdominal pain

CROHN'S DISEASE:

→ **Ileocolitis** (involvement of Ileum and colon): causes recurrent abdominal pain and diarrhea

→ **Jejunoileitis**: Malabsorption, low grade fever, steatorrhea weight loss

→ **Colitis and Perianal involvement**: cause fever, hematochezia stricture & fistula formation

→**MC part involved in CROHN'S: TERMINAL ILEUM**

INVESTIGATION OF IBD

- Anemia of leukocytosis are seen
- Increased ESR and CRP levels
- **PANCA** elevated in 60-70% cases of **U. Colitis**
- **ASCA** (Anti – Saccharomyces cerevisiae Ab) is elevated is 60-70% cases of **Crohn's disease**

TREATMENT:

- 5- Amino salicylic acid
- Glucocorticoids
- Cyclosporin
- Azathioprine

In **mild** Ulcerative colitis: **SULFASALAZINE**

In **severe** cases where strictures / fistulas are present: Surgery required

7. HIRSCHSPRUNG DISEASE

- a.k.a **CONGENITAL AGANGLIONIC MEGACOLON**

CLINICAL FEATURE: Delayed passage of meconium

- Bilious vomiting
- Abdominal distension
- Sometimes complication
  - Intestinal perforations
  - Rectal Bleeding

DIAGNOSIS: On Barium Enema – a) Contracted involved segment become Narrow
b) Dilated normal Proximal segment

DEFINITE DIAGNOSIS: **Intestinal biopsy**

- **ABSENCE of GANGLION CELLS**
- NERVE TRUNK HYPERTROPHY
- **INCREASED ACETYCHOLINESTERASE** activity in involved segment

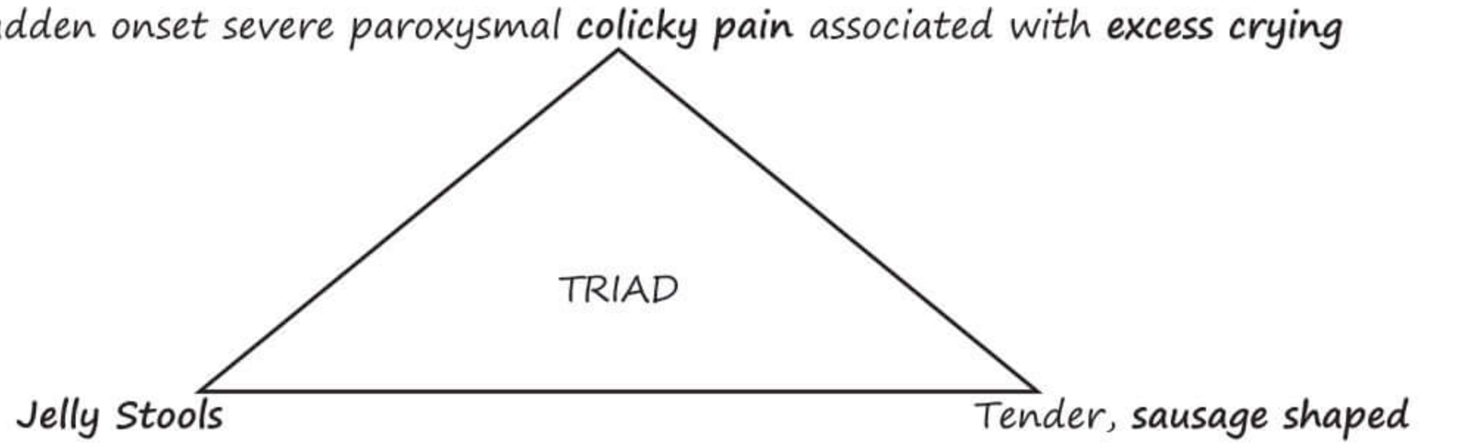
TREATMENT: Surgery [surgical resection of involved segment, anastomosis of normal segment]

8. INTUSSUSCEPTION:

When 1 portion of alimentary tract is telescoped into an adjacent segment

CLINICAL FEATURE:

Sudden onset severe paroxysmal **colicky pain** associated with **excess crying**



EXTRA EDGE:

- **MC cause of intestinal obstruction** in **3 month – 6 year of age**: INTUSSUSCEPTION
- **MC type: ILEOCOLIC**
- Swollen peyer's patches in response to GI infection or introduction of new food can predispose to intussusception

DIAGNOSIS:

- USG has good sensitivity

- Barium enema shows called **SPRING or CLAW SIGN**

9. BOWEL ATRESIA

MC type is **DUODENAL ATRESIA** which accounts for 25-40% of cases.

HALLMARK of duodenal atresia: Bilious vomiting without abdominal distention

- H/O **polyhydramnios** in 50% cases
- On x-ray abdomen: **DOUBLE BUBBLE SIGN**

10. PEUTZ – JEGHER SYNDROME:

- **A.D** inheritance
- Patients with **positive family history**
- Mucocutaneous pigmentation can be seen
- Polyps mainly in small intestine **(MC in JEJUNUM > ILEUM > DUODENUM)**
- Extensive G.I HAMARTOMATOUS polyposis
- Maybe colonic/ gastrin polyps are present
- These polyps leads to abdominal cramping and bleeding

EXTRA EDGE:

- This disease predisposes to cancer of **breast, colon, rectum** and **reproductive organs.**
- Life time risk of cancer in these patients is 47-93% so GI surveillance with upper & lower GI endoscopies is recommended beginning in childhood by **8 years of age** or when symptoms occur

IMPORTANT LIVER DISORDERS IN CHILDREN:

. 1. UNCONJUGATED HYPERBILIRUBINEMIA

Increased production

Ineffective erythropoiesis

Hemolytic disorders

Decreased conjugation

- **Gilbert syndrome** -mild deficiency of UDPGT
  - increase during stress, fasting

-**Crigler Najjar syndrome**

Type I→ Severe; complete absence of UDPGT

Type II→ Milder illness with decreased UDPGT

II. CONJUGATED HYPERBILIRUBINEMIA

DUBIN JOHNSON SYNDROME:

→ Impaired excretion of conjugated bilirubin due to mutation in canalicular multidrug resistance **protein 2.**

→ **Dark pigmentation of liver.**

ROTOR SYNDROME:

→ Decreased hepatic uptake & storage & decreased biliary excretion of bilirubin.

PFIC (Progressive Familial Intrahepatic cholestasis)

→ Severe cholestatic jaundice beginning in childhood

→ **3 types**-GGT enzyme level elevated only in PFIC type 3

BILIARY ATRESIA:

→ **Screening test**→ HIDA Scan (hepatic scintigraphy)

→ **Surgery**→ Kasai procedure

- (<8-week age)
- Better prognosis

→ MC indication of liver transplant in children→ Biliary atresia.

	Neonatal Hepatitis	Biliary Atresia
1. Onset	Anytime in neonatal period	By end of 1st week of life.
2. Severity	Mild to moderate J	Moderate to severe J
3. Color of stool	Variable	Clay colored
4. Alk. Phosphatase	Usually normal	Increased
5. USG abdomen	Identifies choledocholithiasis or cysts	"Triangular cord sign"
6. HIDA scan	Radioactivity scan in intestine	No radioactivity in intestine
7. Liver biopsy	Distortion of lobular architecture, giant cells, inflammation.	Bile ductular proliferation; portal or peri-lobular edema & fibrosis.
8. Operative cholangiogram	Normal	Usually determines presence & size of obstruction.

III. PORTAL HYPERTENSION IN CHILDREN

→ Elevation of portal pressure >10-12mm Hg

→ Due to obstruction to portal blood flow, anywhere along the course of portal venous system.

CAUSES

A. Prehepatic (Presinusoidal)

→ Due to portal vein obstruction from any cause.

→ Portal vein thrombosis is the MC cause of extrahepatic portal hypertension

→ Neonates → Omphalitis, UVC, dehydration, sepsis

→ Older children → Appendicitis, peritonitis, inflammatory bowel disease, Hypercoagulable state.

Q- Most common cause of portal hypertension in children → EHPVO (Extrahepatic portal venous obstruction)

B. Intrahepatic (Sinusoidal)

Q. Mc intrahepatic cause of portal hypertension in children → Cirrhosis

Important causes of Cirrhosis in children:

→ biliary atresia

→ Chronic viral hepatitis

→ Autoimmune hepatitis

→ Metabolic liver disease

→ In some children, non-cirrhotic portal fibrosis (NCPF)

C. **Post-hepatic (Post-sinusoidal) causes**

→ Budd Chiari syndrome

→ Veno-occulsive disease

BUDD CHIARI SYNDROME

→ Due to obstruction to Hepatic veins anywhere between the efferent hepatic veins to the entry of IVC into right atrium

Due to –

- Hypercoagulable structure
- Malignancy
- Inflammation bowel disease
- Bechet syndrome

VENO-OCCULSIVE DISEASE

→ **MC cause of hepatic venous obstruction in children**

- Occlusion of **centrilobular venules** or sub lobular hepatic veins
- It occurs most frequently in BM transplant recipients after total body irradiation.

CLINICAL FEATURES OF PORTAL HYPERTENSION:

→ **Bleeding is the most common presentation of portal hypertension in children.**

→ Splenomegaly

→ Ascites

→ Growth failure

→ Cyanosis, Clubbing, dyspnea (hepatopulmonary syndrome)

VIRAL HEPATITIS IN CHILDREN

CLINICAL FEATURES:

- Jaundice
- Tender hepatomegaly ± Splenomegaly ± Lymphadenopathy
  - Extrahepatic features

E.g. arthritis, rash – Mc in Hep B/C

ACUTE LIVER FAILURE-

→ Bleeding

→ Altered sensorium

→ Elevated Patient, unresponsive to Vitamin K.

Hepatitis A:

→ Highly contagious

→ Feco-oral route

→ Mean incubation period -**3 week**

Hepatitis B: Incubation period -**45-160 days**

→ **In children**, most important risk factor for acquisition of HBV & perinatal exposure to HBsAg positive mother

→ **Risk of transmission is greatest if →**

- HBeAg positive
- High maternal HBV viral load
- Delivery of a prior infant who developed Hep B despite prophylaxis

PROPHYLAXIS:

➔ Both Hep B Ig & Hep B vaccine should be given within 12 hours of delivery

➔ Prevents Hep B inf in neonates in > 95% cases.

CHRONIC HEP B:

➔ Risk of developing Chronic Hep B (**HBs Ag positive for >6m**) is inversely related to the age of acquisition of infection.

-Risk of Chronic hep b in:

Children < 1year → 90%

1-5 year → 30%

Adults → 2%

- 1-5% cases may develop fulminant Hepatitis

Risk increased if →

→ Co-infection/super inflammation with HDV

→ Host is immunocompromised.

RX OF HEP B IN CHILDREN:

→ **Acute**- Supportive

→ **Chronic Hep B** – Rx required for patients with immune active form of disease

- **Drugs used**→
  - IFN & 2b
  - Pegylated Interferon 2
  - Lamivudine
  - Adefovir, Tenofovir
  - Entecavir

HEPATITIS-C IN CHILDREN:

→ Most common mode of transmission is perinatal.

→ Most common Hepatitis to cause Chronic Inflammation → Hep C

→ Rx for Chronic Hep C→ Peg IFN 2b & Ribavirin.

Hepatitis E – affects older patients

→ Feco-oral transmission

→ Most severe- in pregnant female.

WILSON DISEASE:

→ Autosomal recessive

→ **ATP 7B gene** mutation (Chr 13q 14)

→ Decreased biliary copper excretion & accumulation of copper in hepatocytes.

CLINICAL FEATURES:

→ **Hepatic**- Hepatomegaly, Hepatitis, liver failure, portal hypertension, ascites

→ **Hematologic**- hemolytic anemia

→ **CNS**- Tremors, dysarthria, dystonia, chore.

→ **Eye**- **KF ring (Kayser Fleischer ring) & Sunflower cataract.**

→ **Renal**- Fanconi syndrome, renal failure

INVESTIGATION:

→ Decreased Serum ceruplasmin level.

→ Serum free copper level may be elevated

→ Urinary copper excretion increased

→ Hepatic copper content > **250mg/g** of dry liver weight

→ KF ring- On slit lamp exam of eye.

TREATMENT:

→ Restrict dietary copper intake

→ Avoid liver fish, shellfish, ruts, chocolates

→ Use Cu chelating agents like

- d- penicillamine
- Zinc
- -Trientine

REYE SYNDROME

→ Acute metabolic disorder resulting in generated mitochondria dysfunction due to inhibition of fatty acid oxidation.

→ Also known as "JAMSHEDPUR FEVER"

→ Fatty liver & encephalopathy seen

- Cerebral edema
- Hepatic encephalopathy

→ Reye syndrome can be <u>precipitated</u> by

- drugs,
- toxins,
- IEM,
- viruses e.g. – Coxsackie V, Influenza V, Adeno V, Varicella V (not by RSV).

CLINICAL FEATURES:

Hepatic dysfunction- Hypoglycemia, Bleeding (prolonged patient)

But Jaundice rare.

- **Seizures & encephalopathy seen in > 80%**

CASE SCENARIO-

A 3-year male child with fever 5 days was given same medications (Aspirin) → developed anorexia, vomiting, altered sensorium, Seizures; **O/e**: No jaundice but hepatomegaly seen

ON INVESTIGATION → Hypoglycemia, prolonged Prothrombin time

Diagnosis: Reye syndrome

PROGNOSIS: Poor (Mortality 25-70% cases)

PEDIATRIC RESPIRATORY SYSTEM

IMPORTANT RESPIRATORY DISORDERS IN CHILDREN

PEDIATRIC AIRWAY:

→ Large head, short neck & large tongue

→ **Larynx** is more anterior & cephalad

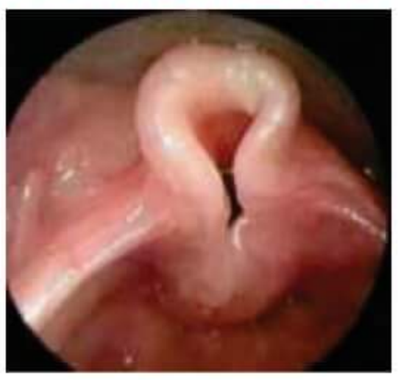
→ **Epiglottis** is relatively **long, 'floppy'** & **U – shaped**

→ **Carina** is at T_2 [T_4 in adults]

→ **Narrowest part of airway in children**→ at cricoid cartilage (PREVIOUS)
at **SUBGLOTTIS** (LATEST)

CONGENTIAL MALFORMATIONS OF AIRWAYS & LUNGS:

LARYNGOMALACIA



→ **Mc causes of stridor in infants**

→ Stridor is exacerbated by crying, agitation or feeding

→ Stridor Improves when the baby sleeps in prone position

→ **Symptoms** appear in 1st 2 weeks of life, gradually increase in severity up to 6 months.

→ **Diagnosis** confirmed by flexible laryngoscopy

- omega shaped epiglottis is seen

CONGENITAL LUNG MALFORMATIONS:

1. **PULMONARY HYPOPLASIA**: Defective development of 1 or both lungs
2. **PULMONARY SEQUESTRATION:**

→ Discrete areas of lung tissues that lack any connection with airway system.

→ These areas get Abnormal Blood supply from aorta

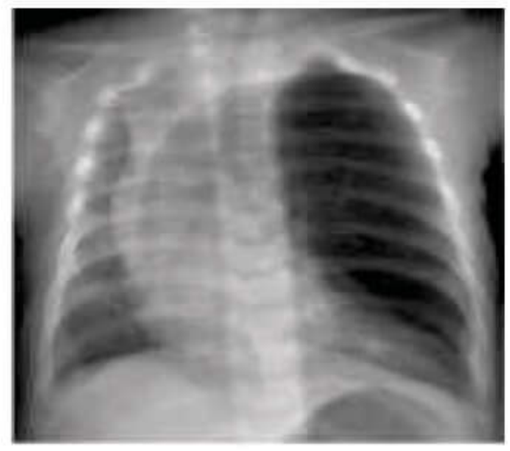
2 Types of pulmonary sequestration

Extra lobar type	**Intra lobar type(MC)**
– Present External to lungs	– Occurs within the lung
– Causes mass affect Compressing the lung	– Manifests due to localized infections or BRONCHIECTASIS
– Venous return occurs Through IVC	– Venous return occurs through pulmonary veins

3. **CONGENITAL LOBAR EMPHYSEMA [CLE]**

→ Over distention of **1 or more lobes** of lung

→ **Left upper lobe is Most commonly involved**



→ **Atelectasis/collapse** of ipsilateral normal lobe of lung

→ May present in **neonatal** period with tachypnea, dyspnea & cyanosis

→ **Surgery** may be required in symptomatic cases

4. **CONGENITAL CYSTIC ADENOMATOID MALFORMATION [CCAM] OR CONGENITAL PULMONARY AIRWAY MALFORMATION [CPAM]**

→ Now known as **CPAM (Congenital-Pulmonary Airway Malformation)**

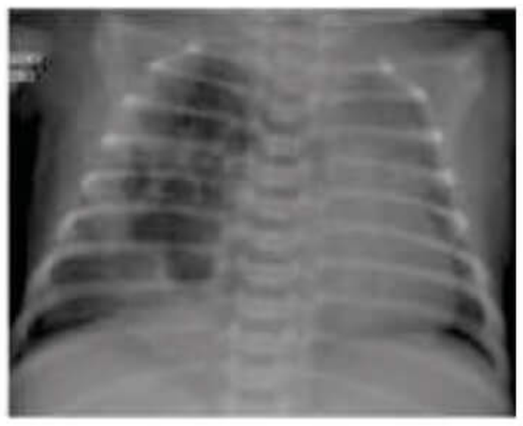
→ Hamartomatous / Dysplastic lung tissue, usually confined to 1 lobe

→ Present in infancy with

→ Respiratory distress

→ Recurrent respiratory infections

→ **PNEUMOTHORAX**



→ On **chest X-ray** cystic mass, sometimes with MEDIASTINAL SHIFT

- Congenital diaphragmatic hernia → close differential diagnosis

→ **Surgery** is indicated in symptomatic cases

FOREIGN BODY ASPIRATION:

- **Most common** in older infant & toddler
- **Most common objects** → food items e.g. peanuts, toys, balloons.
- **Most serious complication** → complete obstruction of airway.

CLINICAL FEATURES:

- **Initial event** → Violent coughing, choking & gagging immediately after intake.
- **Asymptomatic interval** → FB becomes lodged, reflexes fatigue & irritating symptoms subside.

COMPLICATIONS-

- Complete obstruction of airway **(most serious)**→ **Atelectasis**
- Erosion of bronchus → **Hemoptysis**
- Secondary infection → **fever & cough**

DIAGNOSIS:

- **Sudden** onset choking/coughing episodes accompanied by new onset wheezing
- **CXR – unilateral** hyperinflated lungs due to obstruction emphysema.
  - Normal in 15-30% cases
  - Opaque FB seen in 10-25%

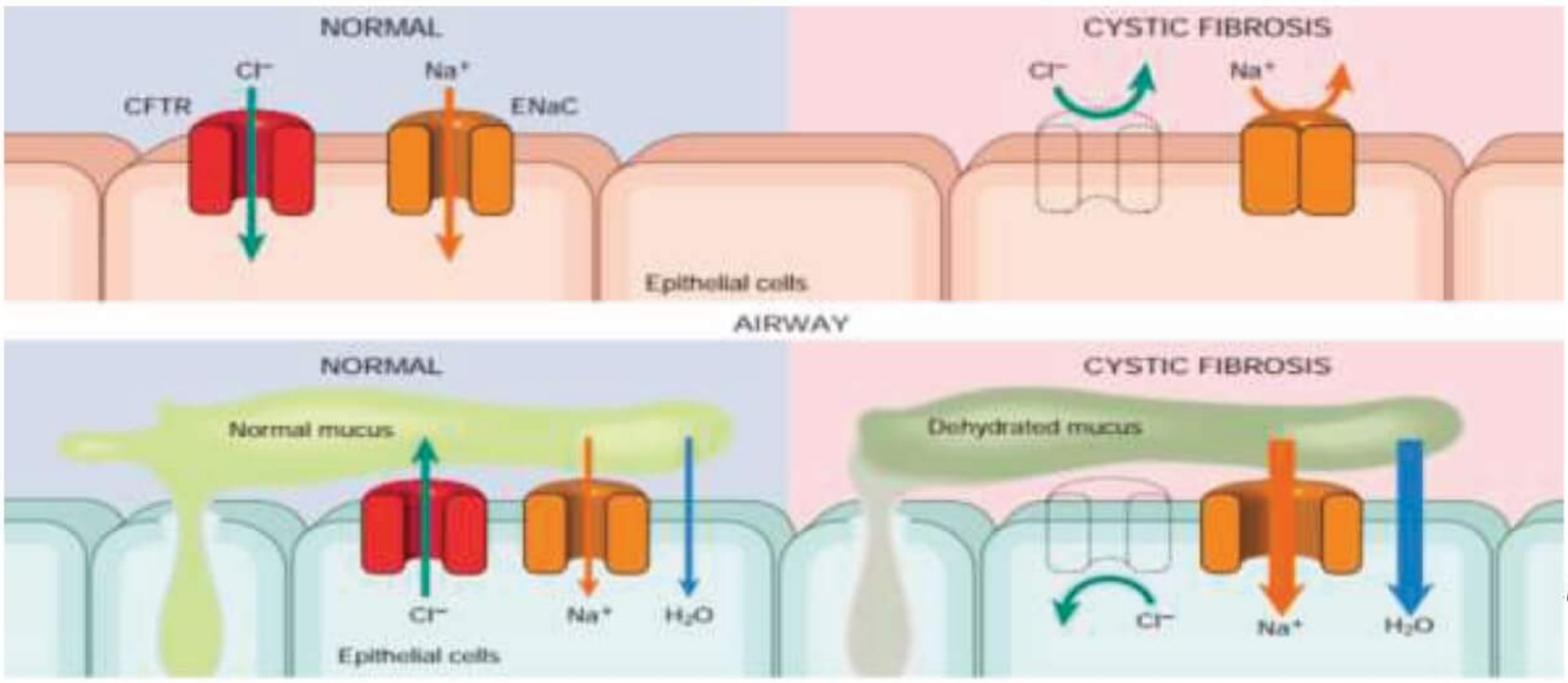
TREATMENT – Prompt removal of FB by rigid bronchoscopy

CYSTIC FIBROSIS:

- Autosomal recessive disease, Chromosome 7q
- **Primary defect** → Abnormal function of an epithelial **Chloride channel** encoded by CFTR gene (CF Transmembrane Conductance regulator gene) on Chromosome **7q 31.2**

- Others defects in-
    - K^+ channels (Kir 6.1)
    - Epithelial Na channels (ENaC)

PATHOPHYSIOLOGY:



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CLINICAL FEATURES:

A. Respiratory tract

- Recurrent Infections→
    - **Staph aureus**, H. influenzae first (mc)
    - Colonization by **Pseudomonas aeruginosa**

↓

Undergo mucoid transformation in CF airways

- **Burkholderia capacia**- as pathognomonic organism of CF.
- Bronchiectasis, atelectasis, nasal polyps can be seen

B. **Genitourinary**: Azoospermia & Infertility

C. **GI & Nutritional abnormality**:

Intestinal – Meconium Ileus

- DIOS (Distal intestinal obstruction syndrome)
- Rectal prolapse
- Recurrent, persistent /chronic diarrhea/ steatorrhea

Pancreas – Exocrine Insufficiency

-Recurrent acute/chronic pancreatitis.

Hepatic – Biliary Cirrhosis

- prolonged neonatal Jaundice

Nutrition- Failure to thrive, hypoproteinemia, Vitamin deficiencies, salt depletion, metabolic alkalosis

DIAGNOSTIC CRITERIA OF CF:

→ Require the presence of One or more characteristic phenotypic features
  → A history of cystic fibrosis in a sibling **OR**
  → A positive newborn screening test result on IRT (Serum Immunoreactive Trypsinogen)

Any of the above AND

→ **Increased sweat chloride [> 60 mmol/L]** concentration on 2 or more occasions **OR**
→ Identifications of two cystic fibrosis mutations **OR**
→ Demonstration of abnormal nasal transepithelial potential difference

TREATMENT:

A. **Pulmonary:** - Bronchodilators
   - Hypertonic saline
   - Human recombinant DNase inhalation
   - Aerosolized -oral/IV antibiotics
   - Chest physiotherapy
   - Respiratory support (PPV) if required

B. **Nutrition:** - High Calorie Diet

   - Pancreatic enzyme supplements
   - Fat Soluble Vitamins
   - Mineral Supplements.

C. **Rx of bowel complication:** e.g. meconium ileus, pancreatitis, appendicitis, rectal prolapse etc.

BRONCHIAL ASTHMA

DEFINITION → **Reversible obstruction** to the air flow due to hyper responsive of airways to various stimuli

TRIGGERS

→ Infection
→ Dust
→ Allergy
→ Cold air
→ Exercise
→ Stress

CLINICAL FEATURES

→ Recurrent cough
→ **Wheezing** episodes
→ Respiratory distress
→ More at night
→ Family history positive

DIAGNOSIS

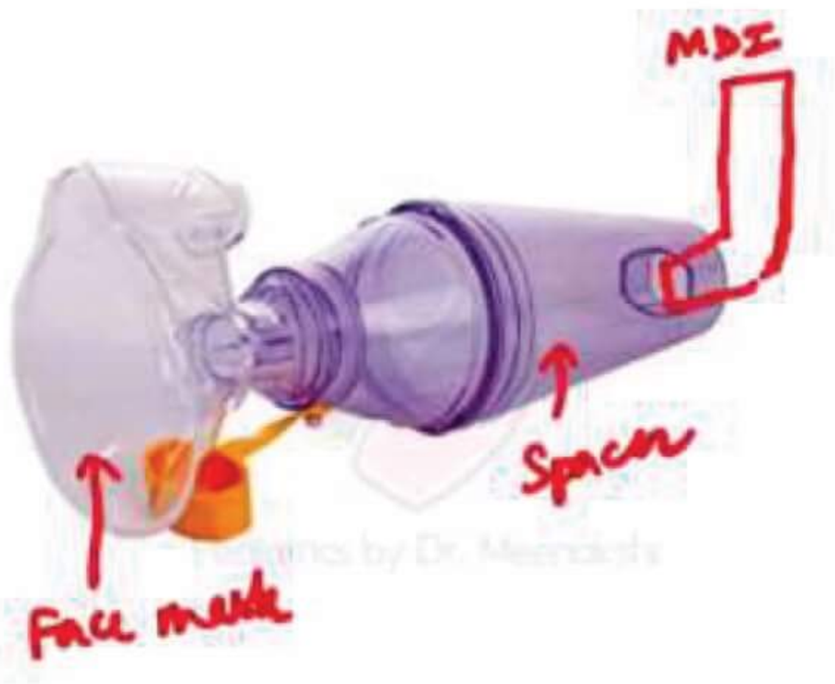
1. Clinical diagnosis

2. Investigations
   → Absolute eosinophilic count
   → **IgE** level
   → **PFT** [Pulmonary function Test]
      →**FEV1**
      →**FEV25-75** – more sensitive indicator of airway obstruction
      →**FEV1/FVC < 0.8**
      →**PEFR** [Peak expiratory flow rate]
         → Diurnal variation > 20% in PEFR
         → Improvement of > 20% after giving a bronchodilator

TREATMENT

→ Identify & **eliminate triggers**
→ **Education** of patients & parents
→ **Pharmacological** therapy
   → Bronchodilators → Salbutamol, Ipratropium
   → Steroids → Inhaled / oral
   → Mast Cell Stabilizers → Cromolyn sodium
      → Montelukast / Zafirlukast
      → Useful in seasonal exacerbation & exercise induced asthma
   → Theophylline
   → **Anti IgE antibody** → Omalizumab
      → Useful in moderate to severe cases of allergic asthma in

- child >12 yrs of age
   → **First line of Rx**→ Inhalational therapy
      → **Preferred device** →Pressured MDI(Meter Dose Inhaler)± Space ± Face mask(for child< 4 yrs of age)



→ **Nebulization** may be used in those children who are not able to use MDI & spacer

→ STEP WISE TREATMENT

Step	Day time frequency	Night time frequency	Treatment
1	< 1 / wk	< 2 / month	SABA SOS
2	> 1/wk but < 1 / day	> 2 / month	SABA + L – ICS or Leukotriene modifier
3	Daily use of β agonist	> 1 / month	SABA + M – ICS + LABA
4.	**Continuous limitation** of physical activity	**Frequent**	SABA + HICS + LABA ± oral steroids

SABA → Short acting β agonist
L – ICS → Low dose inhalational corticosteroid
M – ICS → Medium dose inhalational corticosteroid
H – ICS → High dose inhalational corticosteroid

INFECTIONS OF AIRWAYS & LUNGS:

- Common cold
- Acute pharyngitis
- Acute Epiglottitis
- Acute laryngotracheobronchitis
- Acute Bronchiolitis
- Pneumonia

Q-MC case of acute coryza/common cold in children – RHINOVIRUS

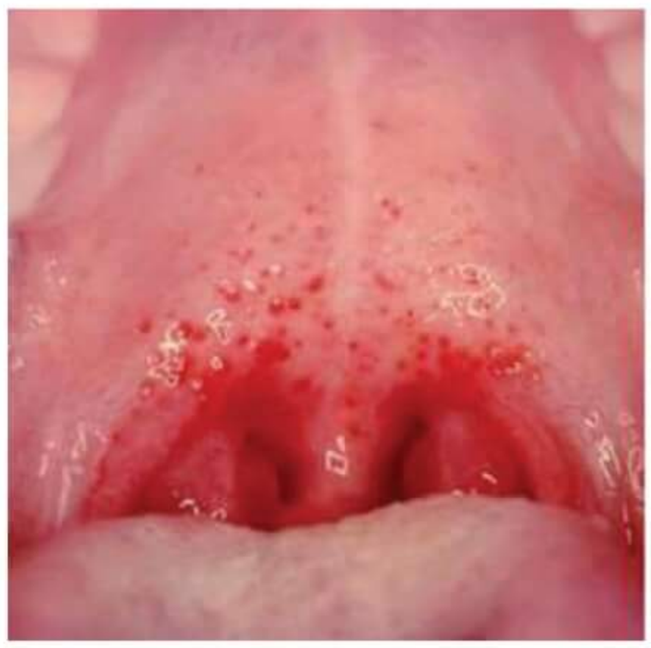
ACUTE PHARYNGITIS:

Q- MC cause in children→ Streptococcus pyogenes

Viral cause →Adenovirus

Q-When to suspect streptococcal pharyngitis

- Acute onset pharyngitis
- High grade fever
- Tonsillar exudates
- Palatal Petechiae
- Tender cervical lymphadenopathy



DIAGNOSIS – Throat swab RADT (Rapid Ag Detection test) or Culture

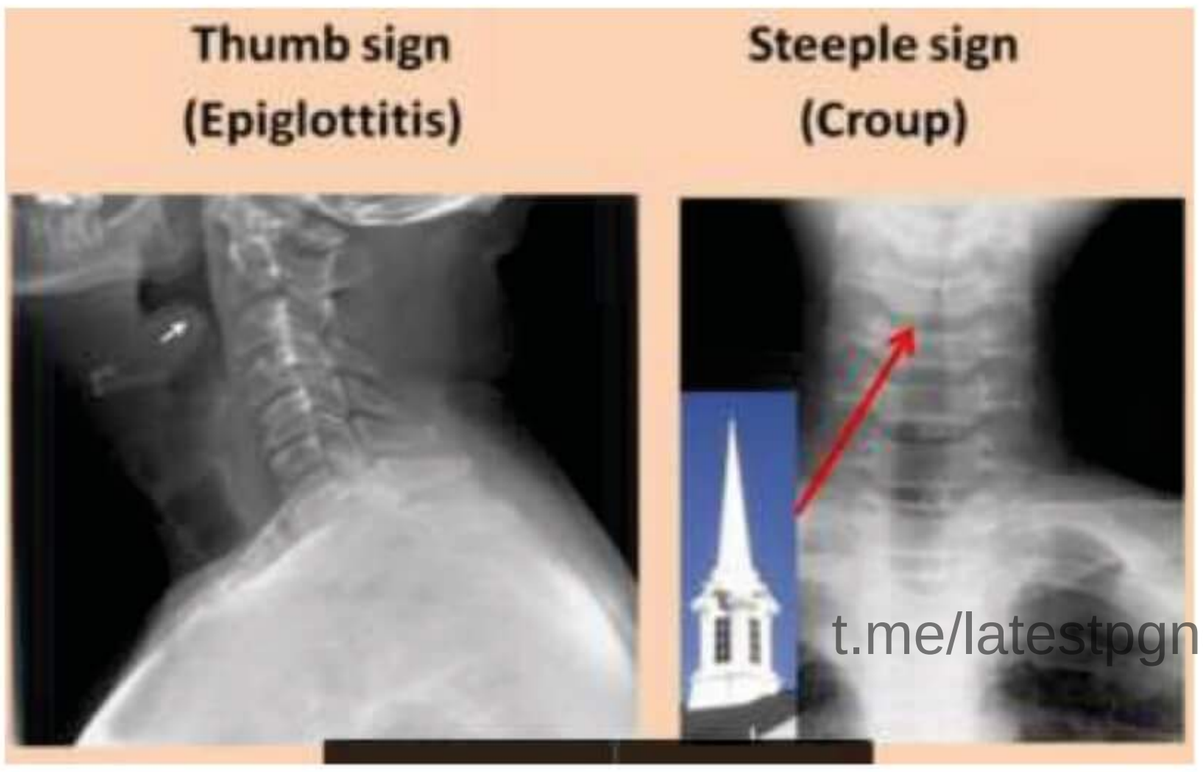
TREATMENT – Penicillin / amoxicillin for 10 days

COMPLICATIONS –	PREVENTION BY ANTIBIOTICS
• Peritonsillar abscess	Yes
• Acute Rheumatic fever	Yes
• Acute post streptococcal GN	NO

→ Antibiotics also prevent transmission of infection to others

→ Antibiotics given how many days within the onset of illness of streptococcus pharyngitis presents rheumatic fever – 9 days of onset.

ACUTE EPIGLOTTITIS:



Q – MC organism responsible –

- Previously, H influenza type b (Unvaccinated)
- In Vaccinated children, currently –
  - streptococcus pyogenes
  - streptococcus pneumonia
  - Staph aureus

C/F

- Acute onset high grade fever
- Throat pain
- Drooling of saliva
- Respiratory distress
- Muffled voice
- Stridor

DIAGNOSIS

- 'Cherry Red' Epiglottis on laryngoscopy
- 'Thumb sign' on lateral X-ray neck

TREATMENT

- Supportive care + IV 3rd generation cephalosporin for 7-10 days

ACUTE LARYNGOTRACHEOBRONCHITIS (CROUP)

Q- MC ORGANISM - Parainfluenza virus

C/F – Starts with a **viral** prodrome & progresses to stridor, **barking cough** & respiratory distress. It has lesser acute onset & less severe course than acute epiglottitis

DIAGNOSIS – CXR 'STEEPLE SIGN' → due to narrowing of upper airway

RX – 1) **Supportive care**, including O_2

2) **Single dose dexamethasone** – Oral / IM

- Effective, even in mild cases
- Reduces the need & duration of hospitalization

MODERATE TO SEVERE cases (Stridor at rest, Hypoxia, severe respiratory distress)

- Supportive care + single dose dexamethasone + Nebulized Epinephrine is used
- Antibiotics are not recommended as it is viral illness

ACUTE BRONCHIOLITIS

- MC age group – **6 months – 2 years**
- MC agent – RSV (Respiratory syncytial virus)

Other etiological agents – Influenza Virus, parainfluenza virus, Adenovirus

C/F – Viral prodrome (low grade fever) f/b tachypnea, retractions & hypoxemia

O/E – Hyperinflated chest & audible wheeze & Crepitation

Rx

- **Supportive** – Moist O_2 , IV fluids
- **Specific Rx** – Nebulized Ribavirin

  Indicated only in immunocompromised children & infants on ventilator
- **Prevention** – Palivizumab (in high risk situations)

PNEUMONIA:

➔ It is leading infectious cause of death in children, worldwide accounting for 15% of all deaths of under 5 children

- MC cause of bacterial pneumonia in children – STREPTOCOCCUS PNEUMONIAE
- 2ND MC cause of bacterial pneumonia in children – H. INFLUENZA
- MC cause of viral pneumonia in children – RSV (Respiratory Syncytial Virus)
- MC cause of pneumonia in neonates – GBS > E.Coli
- MC cause of pneumonia in infants with HIV – Pneumocystis jiroveci

APPROACH TO A CHILD [COUGH OR DIFFICULTY IN BREATHING]

Latest IMNCI [integrated management of neonatal & childhood illness] guidelines

ASSESS

→ Count **breath in 1 minute**

→ Look for **chest indrawing**

→ Look & listen for **stridor & wheeze**

→ Look for any **danger sign**

Fast Breathing

< 2 months → ≥ 60/ min

2-12 months → ≥ 50 / min

1-5 years → ≥ 40/ min

GENERAL DANGEROUS SIGNS

→ Persistent vomiting

→ Unconsciousness

→ Convulsions

→ Inability to drink or breast feed

→ Lethargy

→ If **wheezing** is there along with **fast breathing & chest indrawing**, give a **trial** of rapid acting **Inhaled Bronchodilators** upto 3 times 15-20 min apart & reassess for fast breathing & chest indrawing.

SIGNS	CLASSIFY AS	TREATMENT
Any general danger sign or stridor in a calm child	SEVERE PNEUMONIA or VERY SEVERE DISEASE	Give 1st dose of Inj Ampicillin & Gentamycin & refer urgently to hospital
Either chest indrawing or fast breathing	PNEUMONIA	1. Give oral Amoxycillin x 5 days 2. If **wheezing** present, inhaled bronchodilator x 5D 3. Soothe the throat & relieve cough with a safer remedy 4. **If cough > 14 days** or recurrent wheeze → refer for evaluation of TB or bronchial asthma 5. Advise the mother when to return immediately 6. **Follow up in 2 days** if the o_2 saturation <90% → refer urgently
No signs of pneumonia or very severe disease	NO PNEUMONIA or cough or cold	Steps 2 to 5 ⊕ Follow up in 5 days

PEDIATRIC NEPHROLOGY

ACUTE & CHRONIC KIDNEY DISEASE:

RENAL FUNCTION IN CHILDREN:

GLOMERULAR FILTRATION RATE (GFR)

Age	Normal GFR (ml/ min / 1.73 m^2)
Preterm neonate	→ 10
Term neonate	→ 20-40
2 yrs	→ 120 (adult value)

SCHWARTZ FORMULA

- Formula used to assess renal function

$$\text{Estimated GFR} = \frac{K \times Ht\ (cm)}{Sr.Creatine\ (mgldl)} \qquad K = \text{Constant } (0.42)$$

URINE CONCENTRATING ABILITY (MOSM/kg)

→ Pre term neonate → 500

→ Term neonate → 500-700

→ 1 yr age → 1200-1400 (Adult value)

ACUTE KIDNEY INJURY (AKI)

Definition → Increase in serum creatinine by ≥0.3 mgldl or by ≥50% or oliguria < 0.5 ml/kg/hr for > 6 hrs

ETIOLOGY

Pre Renal	Renal	Post – Renal
→ dehydration	→ PSGN	→ PUJ obstruction
→ hemorrhage	→ SLE, HSP	→ PUV
→ Sepsis	→ HUS	→ Urolithiasis
→ Heart Failure	→ Acute Tubular Necrosis	→ Tumor
	→ Renal Vein Thrombosis	
	→ Tumor lysis syndrome	

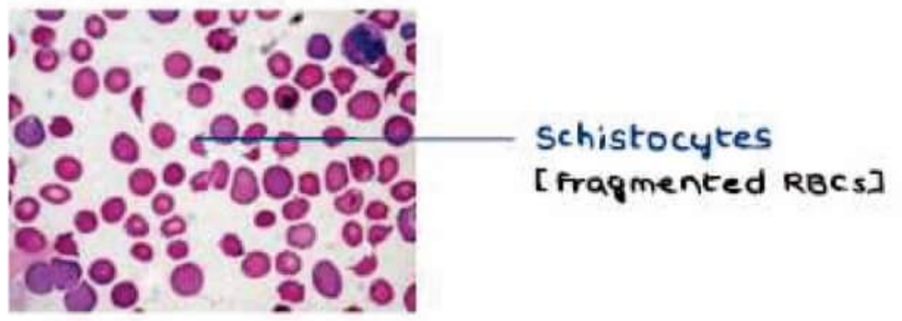
LIFE THREATENING COMPLICATIONS OF AKI

- Hyperkalemia → Arrhythmias
- Fluid overload → Pulmonary edema & Heart Failure
- Sever hyponatremia
- Severe hypertension
- Uremia
- Severe Anemia
- Severe Acidosis

} Encephalopathy

Q. A 4 yr child presented with decreased urine output for last 20 hours & petechial spots over the body there was a history of diarrhea 2 wks to this. Investigation revealed a Hb level of 7 g/dl, TLC 11,800/mm³, Platelet count 35,000/mm³. His PS findings are shown. What is the diagnosis?

a. Malaria
b. Idiopathic thrombocytopenic purpura
c. Acute tubular necrosis
d. Hemolytic Uremic syndrome



HEMOLYTIC UREMIC SYNDROME (HUS)

- A thrombotic microangiopathy causing vascular injury
- TRIAD
  1. Hemolytic anemia
  2. Thrombocytopenia
  3. Renal dysfunction

→ 2 TYPES

1. TYPICAL (D + HUS)
   - 2° to infection by shigella dysenteriae or shiga like toxin producing E. Coli (O157 : H7)
2. ATYPICAL HUS
   - d/t inappropriate activation or insufficient inhibition of alternate complement pathway

- TREATMENT
  - → Dialysis
  - → Therapeutic plasma exchanges/plasma phresis
  - → Immune suppression- steroids
  - → IV Ig
  - → Eculizumab → blocks terminal complement pathway

PERITONEAL DIALYSIS

HEMODIALYSIS MACHINE

CHRONIC KIDNEY DISEASE (CKD)

Definition → Any structural or functional kidney impairment, that persists for at least 3 months

STAGES		GFR (ML / MIN / 1.73 M²)
I	→	> 90
II	→	60-89
III	→	30-59
IV	→	15-29
V	→	< 15 or any patient on RRT (Renal Replacement Therapy)

TREATMENT

→ RRT (Renal Replacement therapy) → R_x of hyperphosphatemia → Nutritional Rehabilitation
→ R_x of anemia → R_x of mineral bone disease → Micronutrient supplementation

CONGENITAL ANOMALIES OF GENITOURINARY TRACT

1. POTTER'S SEQUENCE

→ PRIMARY DEFECT → b/L Renal agenesis

→ FEATURES

Pulmonary hypoplasia (MCC of death)

Oligohydramnios

Twisted (Wrinkled) skin

Twisted Face (flat facies,retrognathia , low set ears , eyes widely separated)

Extremity deformities

Renal agenesis

Washerman hand appearance

Potter's Facies

TWISTED FACE

→ Flat facies → Low set ears

→ Retrognathia → Eyes widely separated

2. MULTICYSTIC DYSPLASTIC KIDNEY (MCDK)

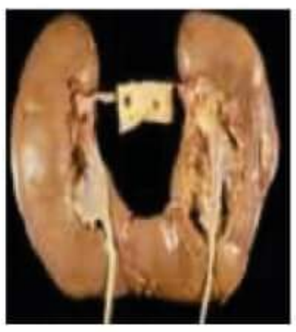
- Entire Kidney is dysplastic, non-functional & replaced by cysts
- Usually U/L
- MC cause of abdominal mass in neonate
- a/w hypertension & wilm's tumor

3. AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD)

- Renal Collecting duct dilatation + Biliary ectasia
- Gene affected is → PKHD1 (chr 6p 12)
- Can present during infancy with enlarged kidneys, hypertension and renal failure
- Older children →Hepatomegaly and portal hypertension

4. HORSE SHOE KIDNEY

- Lower poles of kidneys fuse
- a/w turner syndrome
- ↑ risk of nephrolithiasis & hydronephrosis



5. ALPORT SYNDROME

- X linked recessive (MC mode of inheritance) → COL 4 A5 gene affected
- Characteristic abnormality of glomerular capillary basement membrane
- Presents with proteinuria & persistent microscopic hematuria or recurring episodes of gross hematuria

+

Sensorineural hearing loss

+

Ocular abnormality

(Anterior lenticonus, retinopathy or cataract)

6. BLADDER EXTROPHY


Classical bladder extrophy

→MC in males

→CLASSICAL BLADDER EXTROPHY

- → Bladder mucosa exposed
- → Umbilicus displaced down
- → Pubic rami widely separated
- → Accompanied by epispadias in both males and females
- → Anus displaced anteriorly

→ IF UNREPAIRED

- → Urinary incontinence
- → Bladder cancer

NEPHRITIC & NEPHROTIC SYNDROMES

NEPHRITIC SYNDROME:

- Hematuria, Hypertension, proteinuria (Urine Protein: Urine Creatinine → 0.2-2)

PSGN (POST STREPTOCOCCAL GLOMERULO NEPHRITIS)

- → MC age group → 5-12 yrs
- → Secondary to β hemolytic streptococcal Infection of throat or skin by the nephritogenic Strains
- → Elevated Also or anti Dnase B titre
- → Serum C_3 levels usually low, return to normal in 6-8 wks.

- HEMATURIA IN A CHILD
  - → 1-2 wks after URI → PSGN
  - → 1-2 Days after URI → Ig A nephropathy or Berger's disease

→TREATMENT → Symptomatic & supportive therapy

NEPHROTIC SYNDROME:

DEFINITION:

- → Generalized edema
- → Hypoalbuminemia
- → Hyperlipidemia
- → Massive proteinuria
  - Single morning spot sample urine

↓

UP:U_C > 2:1
Or
Urine protein ≥, 3+
} Massive or Nephrotic range proteinuria

Minimal change disease (MC cause in children)

GENETIC DEFECT:

- MC genetic defect in congenital nephrotic syndrome → NPHS 1 (nephrin)
- Mc genetic defect in idiopathic steroid resistant nephrotic syndrome
  - NPHS 2 (Podocin)

IMPORTANT DEFINITIONS:

Relapse →Up: U_C > 2:1 (or) Urine Pr. ≥3+ for 3 Consecutive days, in a child who was in remission

FRNS (FREQUENTLY RELEASING NS)

→ ≥, 2 relapse in 6 months or

→ ≥, 4 relapse in 12 months

SDNS (STEROIDS DEPENDENT NS)

- 2 Consecutive relapses during steroid R_1 or within 14 days of stopping steroids

SRNS (STEROID RESISTANT NS)

- Absence of remission despite only use of steroid for 8 wks

TREATMENT:

Child presents with 1st episode of NS

Rule out hematuria, azotemia, hypertension

DOC- Prednisolone (6+6 regime)

Dose- 2mg/Kg/daily *6 weeks

1.5 mg/Kg/Alternate day *6 weeks

1. **INFREQUENTLY RELAPSING NEPHROTIC SYNDROME (IFRNS)**
   - R_1 of each relapse
   - Prednisolone
     - Dose → 2 mg/Kg/daily till remission F/b 1.5 mg / kg / alternate day X 4 wks

2. **FREQUENTLY RELAPSING OF STEROIDS DEPENDENT NS**
   - Steroids threshold < 0.5 mg/kg/alt. days
     - Continue low dose alternate day prednisolone for 9-18 months
   - Steroid threshold > 0.5 mg/kg on alternate days or steroid toxicity
     - Levamisole
     - Oral cyclophosphamide
     - MMF (Mycophenolate Mofetil)
3. **STEROID RESISTANT NS**
   - DOC → Calcineurin Inhibitors (Cyclosporine or Tacrolimus)
   - Severe or refractory cases → Rituximab

COMPLICATION OF NS

- ↑ Risk of Infectious (cellulitis, spontaneous bacterial peritonitis)
- ↑ Risk of coagulopathy / thrombosis

RENAL TUBULAR & OBSTRUCTIVE DISORDERS:

→ Renal tubular acidosis
→ Bartter and gitelman syndrome
→ Juvenile nephronophthisis
→ Diabetes insipidus

RENAL TUBULAR ACIDOSIS (RTA):

DEFINITION

→ Defective acidification of urine d/t
→ Defective excretion of H+ ion in distal tubule (Distal or type I RTA) or
→ Defective absorption of HCO3- in proximal tubule (Proximal or type II RTA)
→ GFR remains normal

CLINICAL FEATURES

→ Failure to thrive
→ Vomiting
→ Constipation
→ Generalized muscle weakness
→ Rickets

+

→In distal RTA

→ Polyuria
→ Polydypsia
→ Nephrocalcinosis
→ Nephrolithiasis

INVESTIGATIONS

→ Normal anion gap acidosis
→ Urea & Creatinine → Normal
- **Proximal RTA**
  1. $FEHCO_3$ [Fractional excretion of HCO_3]
  2. TRP [Tubular reabsorption of phosphate]
→ Distal RTA → U – B CO_2

BARTTER & GITELMAN SYNDROME

- Hypokalemic metabolic alkalosis in both

BARTTER SYNDROME:

→ Hypercalciuria
→ Salt wasting and hyponatremia
→ Polyuria, polydipsia at 3-5 years of age
→ Anemia, rickets and growth retardation
→ End Stage Renal Disease (ESRD) by 8-13 yrs of age

DEFECT IN BARTTER SYNDROME:

- NKCC2($Na^+K^+2Cl^-$)

- ROMK (K^+ Channel)
- Chloride channel

TYPES OF BARTTER SYNDROME

- 5 types (I to V)
- Autosomal Recessive except type IV
- Types I, II & IV → Antenatal type
- Type III → Classical type

Treatment OF BARTTER SYNDROME

- K Supplementation
- Indomethacin

GITELMAN SYNDROME

- Hypocalciuria
- Hypomagnesemia

DEFECT IN GITELMAN SYNDROME

- Mutation in NCCT (NaCl to transporter) in distal tubule

JUVENILE NEPHRONOPHTHISIS

→ Impairment of urinary concentration
→ Polyuria, Polydypsia at 3-5 yrs of age
→ Anemia, rickets and growth retardation
→ End stage renal disease (ESRD)by 8-13 yrs of age

DIABETES INSIPIDUS

DEFINITION →Polyuria d/t ↓ action of ADH (anti diuretic Hormone)

2 TYPES

- Central DI → deficiency in the section of ADH (1° or 2° to tumor, trauma, infection etc)
- NEPHROGENIC DI
  → d/t renal tubular unresponsiveness to ADH (anti diuretic hormone)
  → Inherited → X linked Recessive (MC)
  → Acquired → 2° to drugs, obstruction, sickle cell disease, chronic pyelonephritis

CLINICAL FEATURES

→ Irritability
→ Failure to thrive
→ Recurrent episodes of dehydration
→ Fever
→ Constipation

WATER DEPRIVATION TEST:

→Helps to differentiates
→ Psychogenic polydipsia from DI
→ Central DI Vs nephrogenic DI

OBSTRUCTIVE LESIONS OF URINARY TRACT:

PUJ Obstruction

- MC cause of hydronephrosis in children
- MC in boys
- Usually unilateral

VESICO URETERIC REFLUX (VUR) INDUCED PYELONEPHRITIS

- MC cause of Renal Scarring in children

POSTERIOR URETHRAL VALVE (PUV)

→ MC cause of lower urinary tract infections in boys

→ H/O straining while micturition or abnormal urinary stream

→ E. Coli → most common cause of UTI in children

VESICO URETERIC REFLUX (VUR)

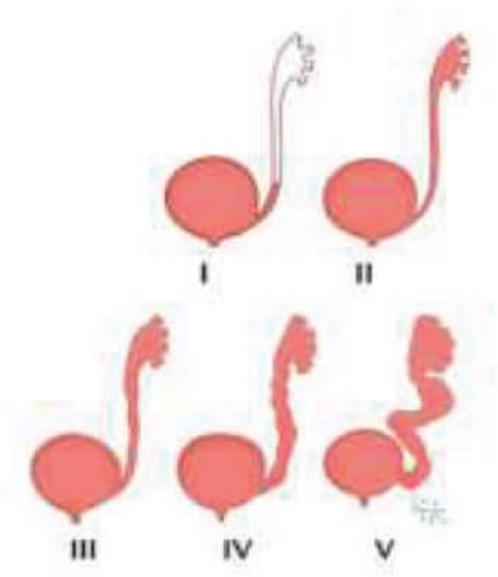
DEFINITION

→ Retrograde flow of urine from bladder to ureters & or kidneys, at rest or during micturition

ASSOCIATED WITH PUJ obstruction & PUV

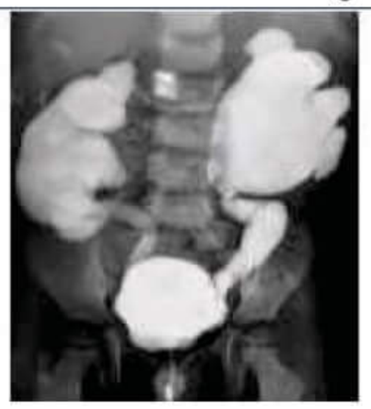
GRADING OF VUR:

Grade	Description
I	Reflux into the non-dilated ureter
II	Reflux into the upper collecting system in non-dilated ureter
III	Reflux into dilated ureter
IV	Reflux into grossly dilated ureter
V	Massive reflux with ureteral dilation, tortuous effaced calyces



DIAGNOSIS

1. Micturating cysto urethrogram



B/L dilated renal pelvis & ureter

2. Radionuclide Cystogram

More sensitivity than MCU lesser radiation exposure does not give good idea about structural involvement

POSTERIOR URETHRAL VALVE

ON MCU

- Treated by fulguration of PUV
- Dilated posterior urethra

TREATMENT OF VUR

1. Continuous antibiotic prophylaxis
2. Surgery

1. Continuous Antibiotic prophylaxis Indications

→ < 1 yr age

→ Grade 3-5 VUR with H/o Febrile UTI

→ Associated bladder bowel dysfunction

2. SURGERY

→ Ureteral Reimplantation

→ Indication → Break through UTI despite on continuous antibiotic antibiotic prophylaxis

NEPHROLITHIASIS:

ETIOLOGY

- Underlying metabolic cause in 50-75%
  - → Hypercalciuria with hypercalcemia
  - → Idiopathic hypercalciuria (MC cause in children)
  - → Hyperuricemia (Von Gierke disease, Tumor lysis syndrome)

HYPERCALCIURIA in children

→Urine Calcium > 4 mg/Kg in 24 hrs (or)

Urine Ca: Urine Creatine > 0.2

- R_x OF IDIOPATHIC HYPERCALCIURIA
  - → High fluid intake
  - → Avoid high protein diet
  - → Thiazide diuretic → ↑ Ca reabsorption
  - → Dietary Calcium is not restricted

PEDIATRIC NEUROLOGY

CONGENITAL CNS MALFORMATIONS & HYDROCEPHALUS

NEURAL TUBE DEFECTS

- d/t failure of proper **closure** of **neural tube**
- They have **multifactorial** inheritance
- **Examples**:
  1. Meningocele
  2. Meningomyelocele
  3. Anencephaly
  4. Spina bifida occulta
  5. Iniencephaly
  6. Encephalocele

DIAGNOSIS

- Antenatal **USG**
- Maternal serum or **Amniotic Fluid α feto protein** level
- **Acetylcholinesterase** levels
- **Mc congenital neurologic abnormality in children**

PREVENTION OF NTD'S

FOLIC ACID SUPPLEMENTATION

→ DOSE

- **400 µg**/ day or **0.4** mg/ day in all women of child bearing age
- **4000 µg**/ day (4 m / day) in high risk women

→Should be started at **least 1 month** before conception

→**Risk of recurrence**

- With **1 affected child** with NTD → **3-4%**
- With **2 previous affected** children → **10%**

SPINA BIFIDA OCCULTA

→Defect lies in vertebra

→Usually overlying skin is normal, but sometimes tuft of hair or a sinus or dimple may be present

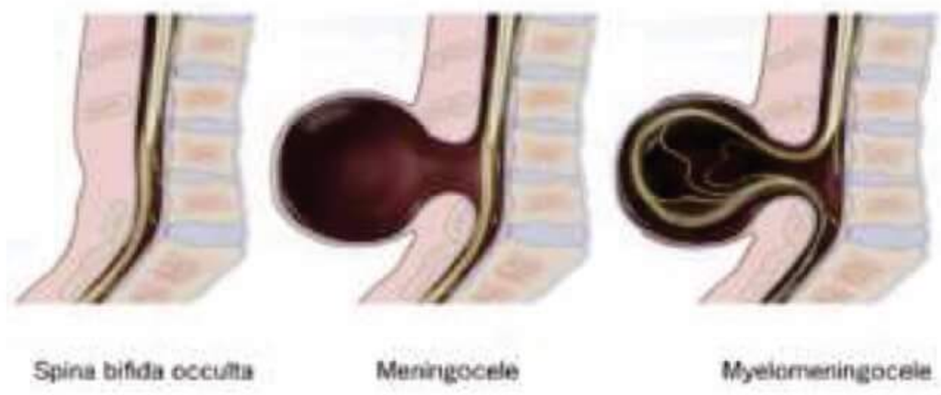
→No Rx required

MENINGOCELE

→Sac of meninges which is empty inside is formed

→**No neural component** inside the sac

→**Transillumination** is **positive**



MYELOMENINGOCELE

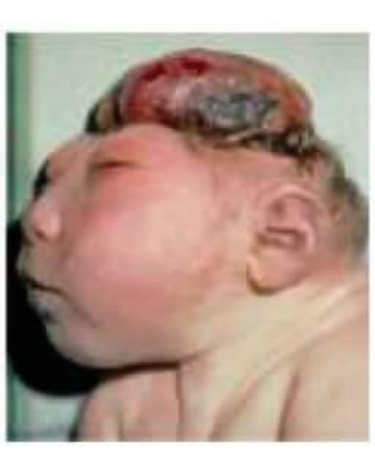
→Sac of meninges with **neural components present**

→**Most commonly** involves the **lumbosacral** region of spine

ANENCEPHALY:

→Fatal condition

→**Resuscitation** is **not advocated**



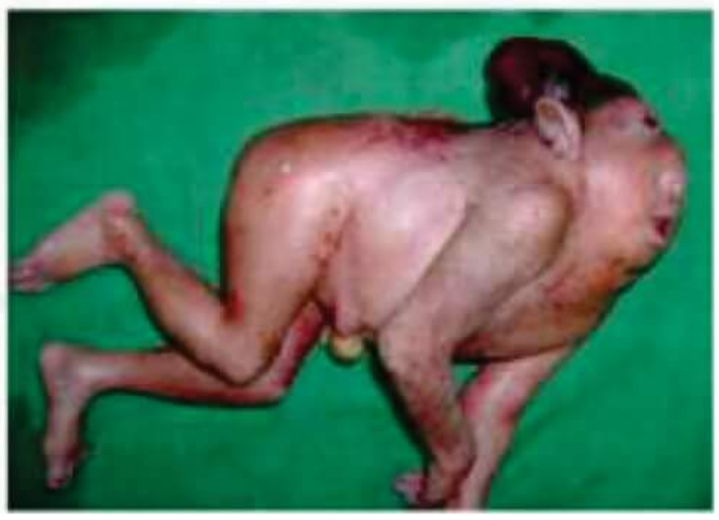
INIENCEPHALY

→Brain & upper part of spinal cord are **absent**

→**Absent** neck

→**Retroflex head**

INIENCEPHALY



HOLOPROSENCEPHALY

Incomplete midline separation of cerebral hemispheres

TYPES:

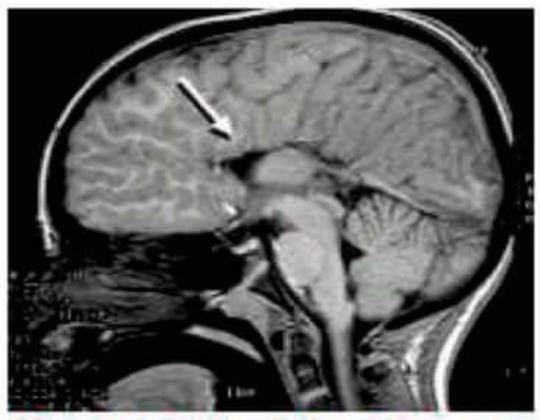
- Alobar (**most severe**)
- Semi lobar (less severe)
- Lobar (least severe)

LISSENCEPHALY

- Smooth appearance of brain

AGENESIS OF CORPUS CALLOSUM

- Agenesis of corpus callosum
- a/w **AICARDI** syndrome



Agenesis of corpus callosum

HYDROCEPHALUS

DEFINITION – Enlargement of ventricles inside the brain, either d/t ↑ production or impaired drainage of CSF

TYPES

COMMUNICATING HYDROCEPHALUS

CAUSES

1. **C**horoid plexus papilloma — **C**
2. **A**chondroplasia — **A**
3. **M**eningeal malignancy or metastasis — **M**
4. **P**ost hemorrhagic — **P**

NON – COMMUNICATING / OBSTRUCTIVE HYDROCEPHALUS

CAUSES

1. **M**ass lesion (ICSOL) — **M**
2. **A**bscess — **A**
3. **A**queductal stenosis — **A**
4. **A**rnold Chiari malformation — **A**
5. **D**andy walker malformations — **D**
6. **H**ematoma — **H**
7. **I**nfections (**Toxoplasma, mumps, Neurocysticercosis**) — **I**
8. **V**ein of Galen malformations — **V**

TREATMENT OF HYDROCEPHALUS:

MEDICAL RX

→Acute → 3% NaCl or mannitol

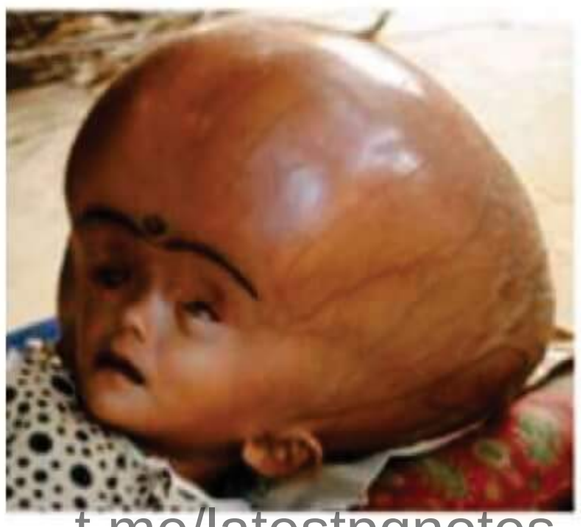
→Chronic → Acetazolamide or Glycerol

SURGICAL RX

→VP shunt (ventriculo peritoneal shunt)

→Endoscopic 3rd ventriculostomy for aqueductal stenosis

HYDROCEPHALUS →

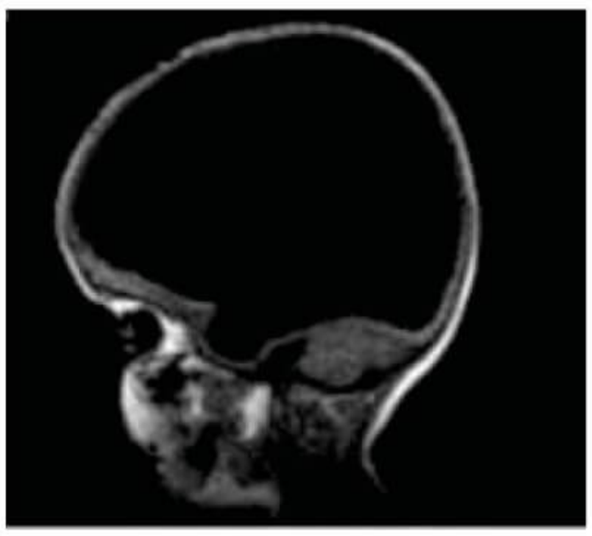


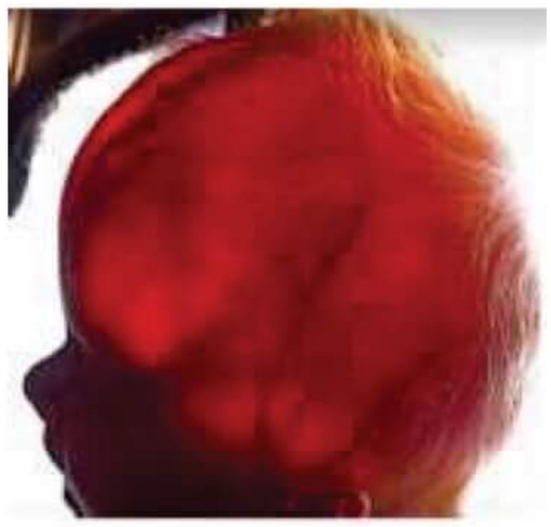
→Cracked pot (or) MAC EWAN'S sign

→Large head with venous prominences

→SETTING SUN SIGN

HYDRANENCEPHALY



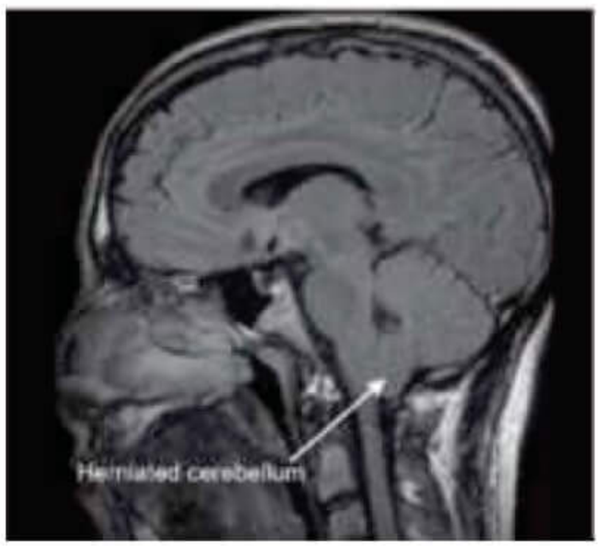


→Absence of cerebral hemispheres

→Replaced by fluid filled sac

→Transillumination +ve

ARNOLD CHIARI MALFORMATION



Herniation of cerebellum into **foramen magnum**

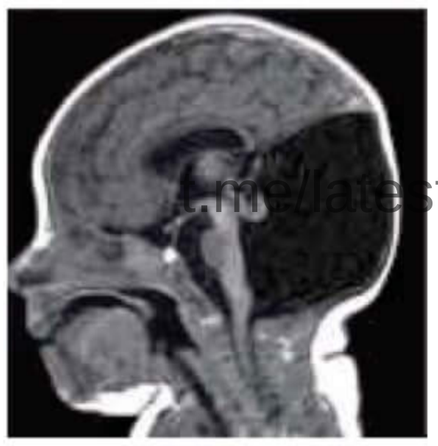
2 TYPES

Type I → **Not a/w hydrocephalus**; Usually presents in **adolescent** age group.

→ Presents with headache, urinary problem

Type 2 → **a/w hydrocephalus**, myelomeningocele; presents early

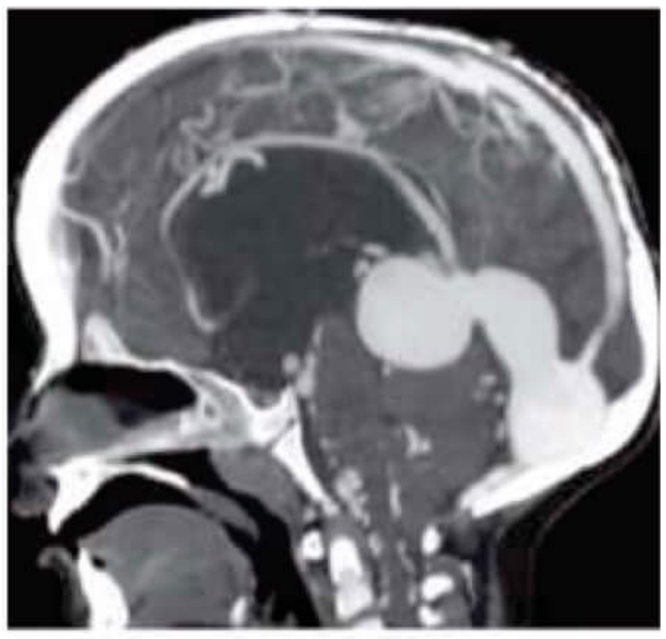
DANDY WALKER SYNDROME:



→**Dilated 4th** ventricle

→Cerebellar vermis hypoplasia

VEIN OF GALEN MALFORMATION: Suspect in a neonate with Heart failure with bounding pulses; Large, **bulging AF** (Ant. Fontanelle) & **Cranial bruit heard** on auscultation over AF



→Vessel involved is → median **prosencephalic** vein of markowsky (precursor of vein of Galen)

→**Onset** → 11-13 weeks of gestation

NEUROCUTANEOUS SYNDROMES & SEIZURES IN CHILDREN:

Skin & CNS involvement is seen in neurocutaneous syndromes

STURGE WEBER SYNDROME

→**Port wine stain** of face involving the **ophthalmic** & **maxillary** division of trigeminal nerve

→**Contralateral** focal seizures seen

→Intracranial **calcification**

→Glaucoma

NEUROFIBROMATOSIS

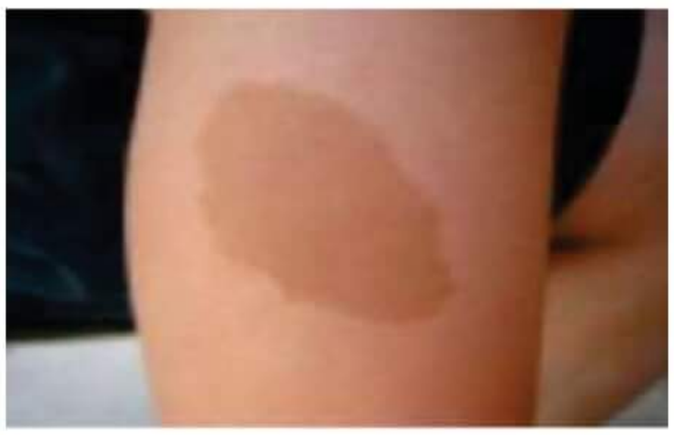
→Autosomal Dominant

→**Café–au lait spot**

→**Lisch nodule**

→**NF 1** → chromosome **17** involved

→**NF 2** → chromosome **22** involved



Café au lait spots

Lisch nodules

DIAGNOSTIC CRITERIA FOR NF 1 (2 OUT OF 6 REQUIRED TO DX)

F – **F**reckling in axillary or inguinal area

L – **L**isch nodules (2 or more)

O – **O**ptic glioma (mc tumor a/w NFI

Re – **Re**lative affected (1st degree)

N – Neurofibroma (2 or more) or 1 plexiform neuroma

Ce – Café all lait spots

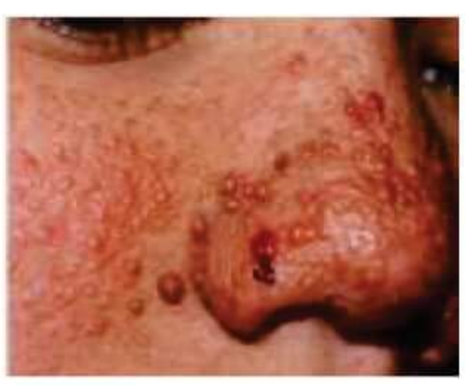
- 6 or more
- **>5 mm** size in **pre pubertal age** group
- **>15 mm** size in **older age** group

TUBEROUS SCLEROSIS

-Intellectual disability

-Seizures

-Skin Manifestations



Adenoma sebaceum Shagreen patch Ash leaf macules

- Adenoma sebaceum
- Shagreen patch
- Hypomelanotic/Ash leaf macules

GENETIC DEFECTS

→TSC 1 gene on chromosome 9

→TSC 2 gene on chromosome 16

MAJOR CRITERIA (AT LEAST 2 NEEDED TO DX)

Pulmonary lymphangio leiomyomatosis	P
Ungual fibroma	U
Shagreen patch	S
Hypomelanotic macules (≥3)	H
Cardiac rhabdomyoma	C

Angiomyolipoma of kidney A

Retinal hamartoma R

Facial angiofibroma F

Astrocytoma (giant cell) A

Subependymal nodules S

Tubers (cortical) T

SEIZURES & EPILEPSY:

FEBRILE SEIZURES:

MC cause of seizures in children < 5 Years of age

DEFINITION → seizure + significant fever (> 100. 4°F) without any evidence of CNS infection in the age group of 6 months – 5 years

TYPES:

SIMPLE FEBRILE SEIZURES	COMPLEX FEBRILE SEIZURES (3Fs)
Generalized seizures	Focal seizures
Lasts **<15 minutes**	Fifteen minutes or longer
No recurrence **within 24 hrs**	Frequent (recurrence may be seen)

MANAGEMENT:

In cases where seizure last >5 minutes

Home Mx:

-Rectal diazepam or

-Buccal/ nasal midazolam

-Put the child in recovery position (left lateral position)

Hospital Mx

-IV lorazepam or midazolam

- **No long-term** anti epileptics are recommended in the Mx of simple type febrile seizure
- Control of fever is done

FACTORS INCREASING RISK OF RECURRENCE

- Younger age
- Shorter duration of fever
- Lower temperature
- Family history of Febrile seizure

To reduce risk of recurrence of febrile seizure → **intermittent prophylaxis**

- Oral **clobazam** (or) **diazepam** (for 1st 3 days of fever)
- **Paracetamol** (Antipyretics) do not decrease the risk of recurrence

RISK FACTORS FOR EPILEPSY IN A CHILD WITH FEBRILE SEIZURES

- H/o complex febrile seizures
- Neuro developmental abnormality
- Shorter duration of fever before seizure occurs
- Family H/O epilepsy

STATUS EPILEPTICUS IN CHILDREN

DEFINITION

•Any seizure lasting for >5 min or multiple episodes of seizures without gaining consciousness in between or a child brought with ongoing seizures to a medical facility

MANAGEMENT

It is a Medical emergency

A – Airway

B – Breathing

C – Circulation

→ get an **IV** Access

→ Rule out **hypoglycemia** & **hypocalcemia**

→IV **lorazepam** or midazolam

↓ seizure persisting

Inj. **Phenytoin** (**20 mg / kg**) loading dose

↓ seizure persisting

Repeat inj. phenytoin (10 mg/kg)

↓ seizure persisting

Inj **valproate** or

Inj **levetiracetam** or

Inj **phenobarbitone**

EPILEPSY

→At least **1 unprovoked seizure** with either seizure recurrence or sufficient clinical or EEG abnormality

→EPILEPSY SYNDROMES WITH GOOD PROGNOSIS

1. **Benign neonatal seizures** → neonatal period, **FIFTH DAY FITS**
2. **Benign infantile seizures**→ during **1st** year
3. **Benign childhood epilepsy** with centrotemporal spikes or Rolandic epilepsy → **3-13 yrs**
4. **Childhood absence epilepsy** → **5-8 yrs**
5. **Juvenile myoclonic epilepsy** → **12-18 yrs**

CHILDHOOD ABSENCE EPILEPSY

- **No aura** or post ictal phase
- **Lip smacking / eye fluttering**
- Precipitated by **hyperventilation**
- **EEG**→ 3Hz **spike & wave** pattern
- **DOC**→ Ethosuximide & valproate

JUVENILE MYOCLONIC EPILEPSY

- **Adolescent**
- Myoclonic jerks
- **Drops** objects(drop attacks)
- prominent during early morning
- **Doc** → Valproate

Doc for focal seizures in children → oxcarbazepine > carbamazepine

EPILEPSY SYNDROME WITH POOR PROGNOSIS

1. **OHTAHARA** syndrome → infancy (Ohtahara syndrome→ WEST syndrome→ LGS)
2. **RASMUSSEN** syndrome → 6-12 yrs
3. **DRAVET** syndrome → infancy
4. **LENNOX GASTAUT** syndrome (LGS) → 3-10 yrs

→Developmental delay / intellectual disability

→Multiple types of seizures

→Difficult to control despite multiple antiepileptics

→**EEG** → 1-2 Hz slow wave & spike pattern

WEST SYNDROME

Triad of

- Infantile spasms (**SALAAM ATTACKS**)
- Developmental delay
- **Hypsarrhythmia** (on EEG)

DOC→ Inj ACTH (adreno corticotropic hormone)

DOC for **west** syndrome in a child with **tuberous sclerosis** → Vigabatrin

BREAK THROUGH SEIZURES

→A child who is a known case of seizure disorder on antiepileptics, present again with an episode of seizure

MANAGEMENT

1.**1st drug** → inj. Lorazepam/ midazolam

2.If the **child** is **not** on **maximum dose** of any antiepileptic, then **give half the loading dose** of same antiepileptic

	DOSE RANGE	
Valproate	→	20-50 mg /kg/day

Phenytoin → 5-8 mg/ kg/day

Phenobarbitone → 3-5 mg/kg/day (Doc for neonatal seizures)

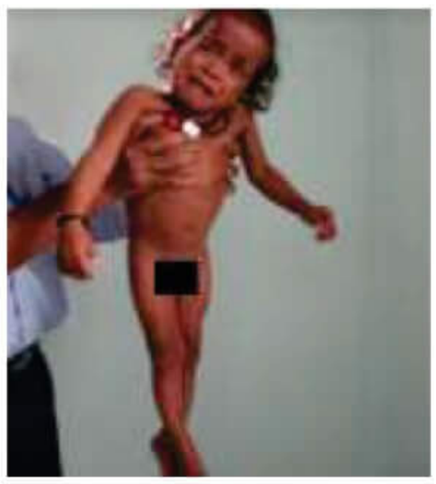
OTHER DISORDERS WITH CNS INVOLVEMENT:

CEREBRAL PALSY

DEFINITION:

A group of disorders of movement & posture, causing activity limitation, d/t non –progressive disturbances that occurred in the developing fetal or infant brain

SPASTIC DIPLEGIA CP



Types of CP	Area of brain involved
1.**Spastic diplegia**	→ periventricular area (**PVL** – periventricular leukomalacia) OR **PVHI**-(Periventricular hemorrhagic infarct)
2.**Spastic quadriplegia**	→ multicystic encephalopathy Parasagittal brain injury
3.**Spastic hemiplegia**	→ MCA territory infarct
4.**Dyskinetic** or **Extra pyramidal** CP	→ Basal ganglia (neonatal jaundice/kernicterus)
5.**Hypotonic** CP	→ Cerebellar lesion

TREATMENT → multidisciplinary treatment

- Physiotherapy
- Vision & hearing to be taken care of
- Early stimulation
- Structured play therapy

CNS INFECTIONS IN CHILDREN

ACUTE BACTERIAL MENINGITIS

Mc Organism Responsible

	IN INDIA	IN WORLD
NEONATES	E. Coli	Grp B streptococci> E. Coli > Listeria
INFANTS& OLDER CHILDREN	Strept pneumoniae N. meningitidis N. influenza	Strept. Pneumoniae

CLINICAL FEATURES IN NEONATES & INFANTS

- Irritability
- Shrill cry
- Seizures
- Tense, **bulging** anterior fontanelle

TREATMENT → **DOC** → IV 3rd generation **cephalosporins** (ceftriaxone)

TUBERCULAR MENINGITIS

→One of the **most severe forms of TB**

PATHOGENESIS

Primary infection

↓

Bacillemia

↓

Seeding of meninges (**RICH's FOCI**)

↓

Rupture

↓

Tubercular meningitis

CLINICAL FEATURES

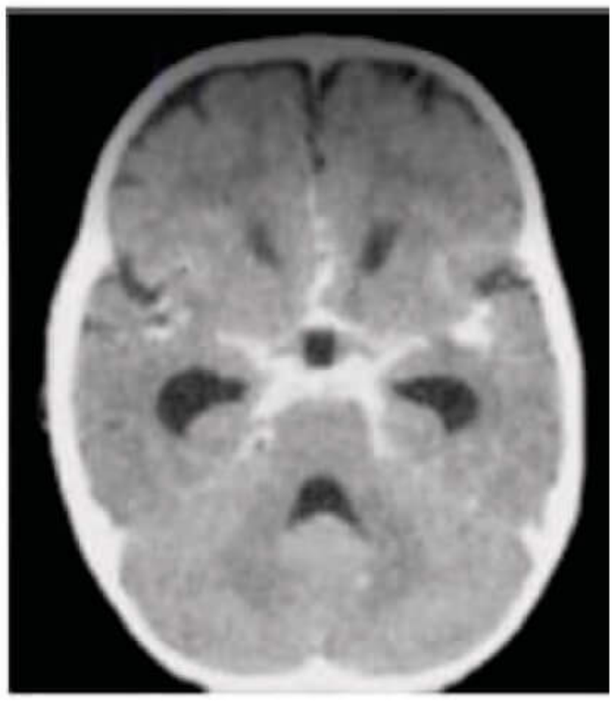
STAGES

1. **Prodromal** stage (fever, anorexia, vomiting, irritability)

2. **Focal** deficits, seizures, meningeal signs

3. Coma, **neurological sequelae**

INVESTIGATIONS



1. **CNS IMAGING (CT Head)**

- Enhancement of basal meanings
- Hydrocephalus
- tuberculoma with perilesional edema

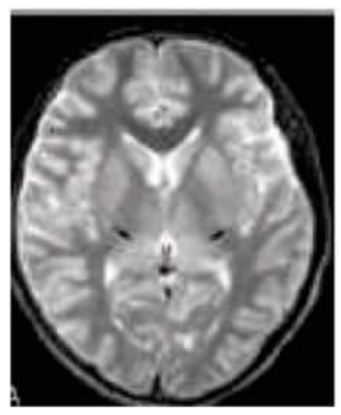
2. **CSF STUDY**

- Opening pressure **elevated**
- Cell count → **500/mm³** (**lymphocytic** predominance)
- Elevated proteins& Low glucose
- **Cob-web coagulum**

TREATMENT – ATT + Steroids

JAPANESE ENCEPHALITIS

B/L thalamic lesions



- **MC cause of encephalitis in children in India** (world → enterovirus)
- **MC age** group affected → **5-15 yrs**
- **Vector → Culex tri taeniorhynchus**

CLINICAL FEATURES

1. **prodromal** stage (fever, headache, vomiting, Diarrhoea)
2. **encephalitic** stage → seizures, focal deficits, features of ↑ ICT
3. **extra pyramidal** sequelae, death

DIAGNOSIS

1. **CSF study** → elevated proteins & normal glucose
2. JE specific **IgM ELISA** in serum & CSF
3. **CNS Imaging** → B/L thalamic lesions

TREATMENT → supportive Rx

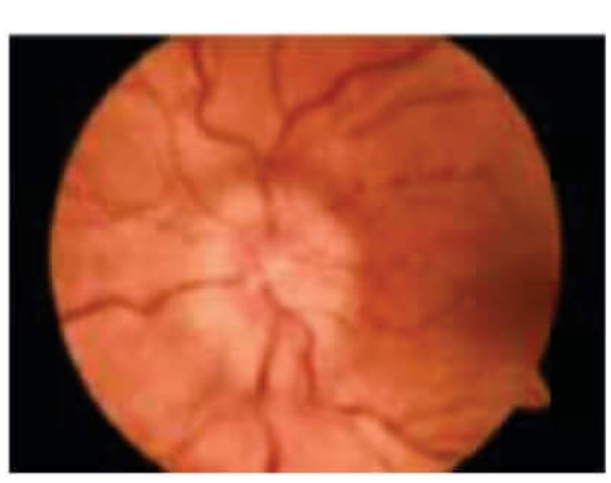
RAISED INTRACRANIAL TENSION:

→ Normal ICP (mm Hg)

1. Neonates → <5
2. Infants → 6-15
3. Older children → 10-15

Most commonly an agitated child has ↑ICP

CEREBRAL PERFUSION PRESSURE (CPP) = MAP – ICP



- MAP – mean arterial pressure
- ICP – Intra cranial pressure

Papilledema= ↑ ICT

Normal CPP (mm Hg)

- 2-6 yrs → 50
- 7-10 yrs → 55
- 11-16 yrs → 65
- In neonates and infants with open AF, papilledema is not seen.

MANAGEMENT

1. **Fluid of choice** → Normal Saline (Isotonic Fluid)
2. **Supportive** → Elevation of head end

   Midline positioning

   Sedation and analgesia

   Controlled mechanical ventilation
3. **Osmolar agents** → Mannitol or hypertonic saline (3% NaCl)
4. **Refractory cases Mx**

- Decompressive craniectomy
- Phenobarbitol infusion
- Hypothermia
- Lumbar CSF drainage

5. **Long term Mx** → Oral Acetazolamide or glycerol

BRAIN DEATH:

DEFINITION → Irreversible cessation of all functions of entire brain including brain stem

BRAIN DEATH IN CHILDREN IS USUALLY DUE TO

→Trauma or asphyxial brain injury

3 KEY COMPONENTS OF Dx OF BRAIN DEATH

1. **Irreversible coma** with a known cause

2. **Absence of brain stem reflexes** (light reflex, corneal reflex, gag reflex)

3. **Apnea** → absence of respiratory efforts in response to an adequate stimulus (PCO2>60 mm Hg)

→All these Findings must remain consistent for 2 examinations separated by an observation period of

- **24 hrs** in neonates
- **12 hrs** in infants & older children

FINDINGS SEEN OCCASIONALLY COMPATIBLE WITH DX OF BRAIN DEATH

- Respiration like movements
- Sweating & flushing
- **BP may remain normal** without pharmacological support
- **DTRs elicitable**
- **Superficial Abdominal reflexes elicitable**

FEATURES INCOMPATIBLE WITH THE DX OF BRAIN DEATH

- Decerebrate/ Decorticate posturing
- Presence of Seizures
- Extensor or flexor response to painful stimulus

MUSCULOSKELETAL DISORDERS IN CHILDREN

DISORDER OF MUSCLES IN CHILDREN:

I MUSCULAR DYSTROPHY

→Inherited disorders of muscle with progressive muscle damage

DUCHENNE MUSCULAR DYSTROPHY (DMD)

→**mc inherited neuromuscular disease in children**

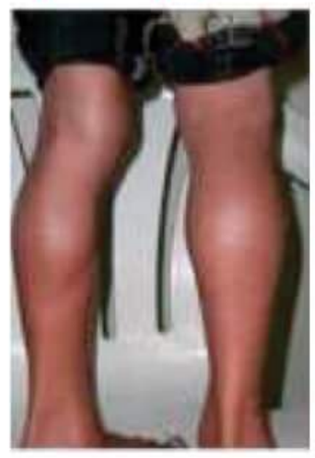
→**gene** involved → **dystrophin** gene (Xp 21) – one of the **largest gene**

→**X linked recessive** inheritance

CLINICAL FEATURES

1. More common in **males**
2. Family history present
3. **Pseudohypertrophy** of calf muscles

Pseudo-hupertrophy of calf muscles



4. Cardiac involvement
5. Recurrent respiratory infection

→ cause of death (around 20 years of age)

6. Proximal muscle weakness in limbs
7. Intellectual disability
8. 'GOWER SIGN' is positive

→Not specific

→Usually appears at 3 yrs age

DIAGNOSIS:

1. Serum **CPK** levels (creatinine phosphokinase levels)
    - Normal → 160 U/L
    - Very high levels → >10000 U/L

2. **PCR** for dystrophin gene

3. Muscle **biopsy**

2. BECKER MUSCULAR DYSTROPHY

→Similar to DMD

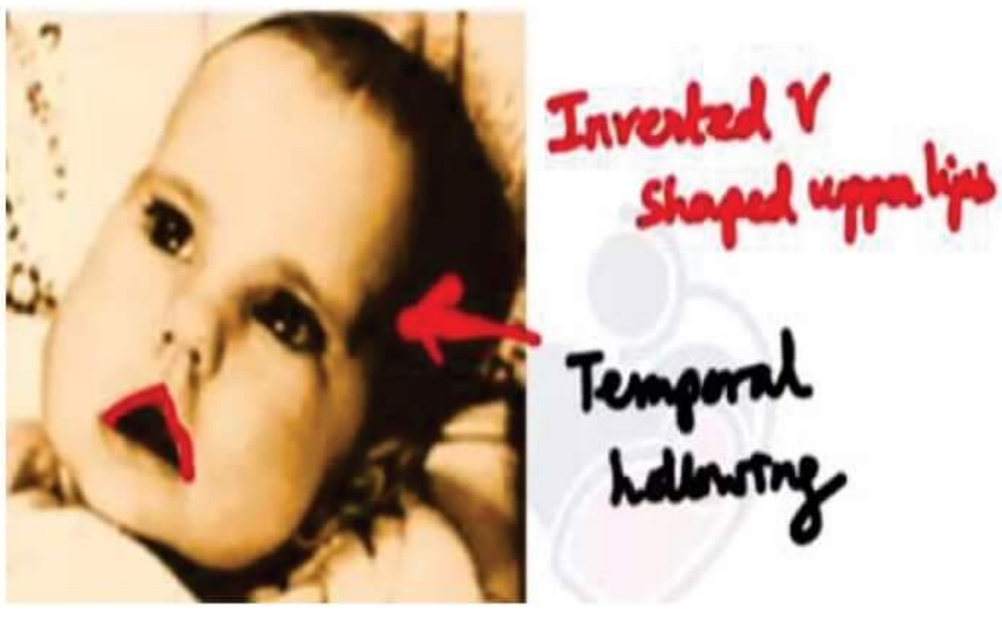
→Milder illness; presents later; has more protracted course

3. FACIOSCAPULOHUMERAL DYSTROPHY

- **Winging** of **scapula**
- Weakness of facial muscles
- **Atrophy** of biceps, triceps and deltoid
- Hearing loss & retinal changes
- **Gower sign** is positive

4. MYOTONIC DYSTORPHY

- d/t ↑ed no. of CTG repeats
- **myotonia** i.e. delayed relaxation of muscles after contraction
- facial abnormalities present → MYOTONIC FACIES



1.**inverted V – shaped upper lip**

2.**temporal hollowing**

II CONGENITAL MYOPATHY

→**non-progressive** inherited disorders involving muscles, where sub cellular abnormalities seen on muscle biopsy

ex: 1. **C**entro nuclear myopathy

2. **N**emaline Rod myopathy

3. **M**yotubular myopathy

4. **C**ongenital fibre type disproportion myopathy

III SPINAL MUSCULAR ATROPHY (SMA)

- d/t degeneration of motor neurons
- **Gene** involved → survival motor neuron(**SMN**) gene on **Chr 5**
- Tongue fasciculations are characteristic
- Generalized weakness
- **Absent Deep tendon reflex**
- Diaphragmatic involvement occurs lately

TYPES

0 → Most severe from: Presents at birth

1 → Infantile

2 → Late infantile

3 → Juvenile

DIAGNOSIS

1. **CPK** levels are **normal**

2. SMN gene abnormality demonstration

3. **Pre natal diagnosis** is possible

IMPORTANT DISORDERS INVOLVING BONES IN CHILDREN:

1. RICKETS

DEFINITION → A disease of growing bone d/t defective mineralization of the bone matrix

ETIOLOGY

I. VITAMIN D RELATED CAUSES

1. Nutritional vitamin deficiency
2. Congenital deficiency
3. Malabsorption
4. Liver disease
5. **VDDR 1** (vit D Dependent Rickets) (d/t **1α hydroxylase** def.)
6. **VDDR 2** (d/t resistance of receptors to the action **of 1, 25 $(OH)_2$ (vit D3)** (active form)
7. Chronic kidney disease

→ elevated phosphate levels

II. RENAL LOSSES

1.**Hypophosphatemic rickets**- due to **PHEX** gene
2. Tumor induced rickets
3. Mc Cune Albright syndrome
4. Fanconi disease
5. Dent disease
6. Distal RTA

HYPOPHOSPHATEMIC RICKETS

→d/t **PHEX** gene defect

→PHEX gene is phosphate regulating gene with homology to endopeptidases on X chromosome

→**X linked dominant** inheritance

→↑ **FGF 23** production → ↑ excretion of phosphate → Inhibits 1 α hydroxylase activity

III. CALCIUM DEFICIENCY

→Low intake

→Pre maturity

→Malabsorption

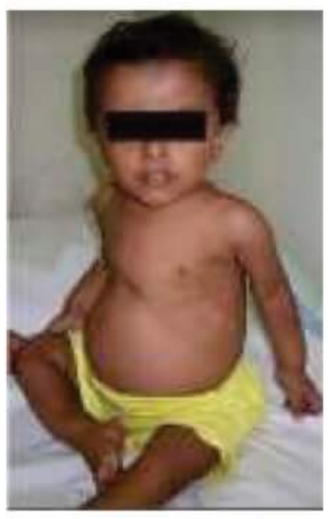
IV. PHOSPHATE DEFICIENCY

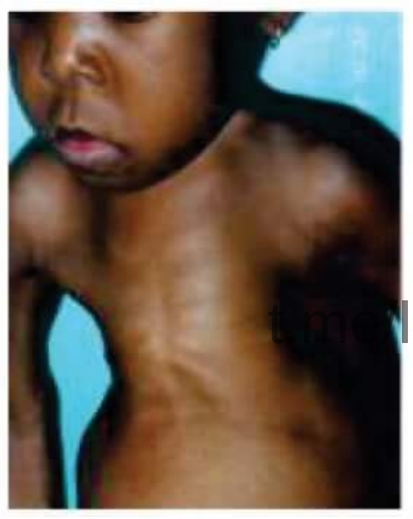
→Inadequate intake

→Pre maturity

→Aluminium containing antacids

CLINICAL FEATURES





HARRISON'S SULCUS

I. GENERAL

- Failure to thrive
- Protruded abdomen
- Listlessness
- ↑Risk of respiratory infections
- ↑Fractures

II. HEAD

- Craniotabes
- Frontal bossing
- Parietal bossing
- Large AF
- Delayed closure of AF
- Delayed dentition

III. CHEST

- Rachitic rosary
- Harrison's sulcus

IV. LIMBS

- Wrist widening
- Genu varum or valgum
- **Wind swept** deformity
- **Double malleolus**
- Bowing of tibia

V. HYPOCALCEMIA

- Tetany
- Seizures
- Stridor

DIAGNOSIS:

1. Biochemical

→Ca

→Phosphate (low/ normal except in chronic kidney disease)

→Alkaline phosphatase (elevated in all cases)

→25OH Vit D_3 level

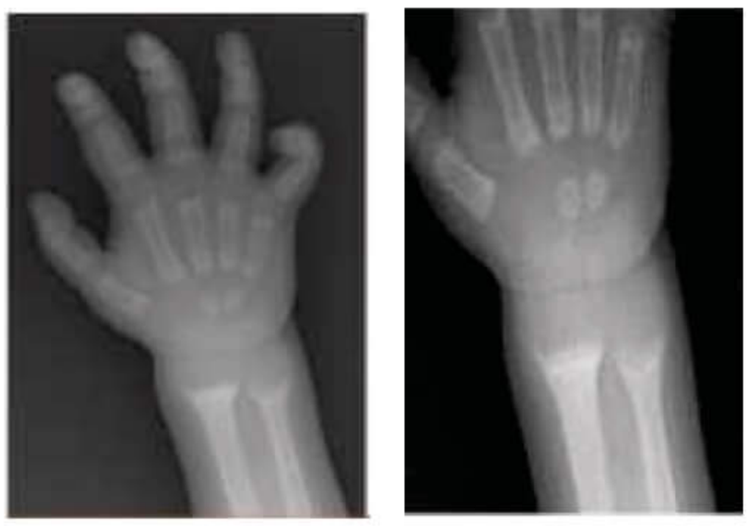
→PTH

2.Radiological X-RAY of wrist:

→**Cupping** (concavity)

→**Fraying** (irregularity)

→**Splaying** (widening) of ends of long bones



TREATMENT

VITAMIN D SUPPLEMENTATION

→STOSS THERAPY

→ 3 Lac - 6 Lac units of **cholecalciferol** → Previously used (toxic)

→Single **IM** injection of **3 lac units** (or)

→**60,000 U** per sachet x 6 (once every week)

2. SCURVY

PATHO PHYSIOLOGY

Deficiency of **Vit C**

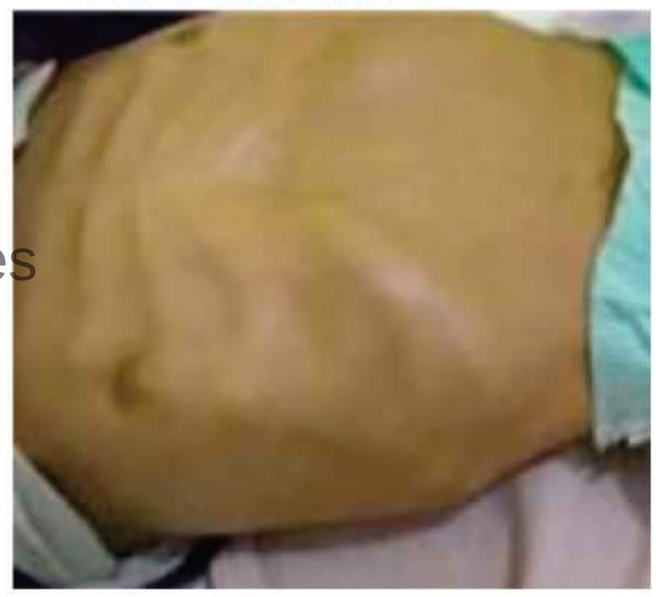
↓

Defective **collagen synthesis**

RISK FACTOR → child predominantly cow milk fed

CLINICAL FEATURES

SCORBUTIC ROSARY



→Gum bleeding

→**Petechiae**

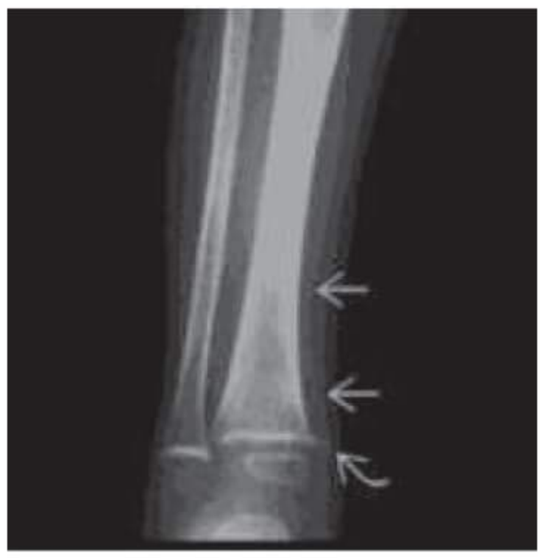
→Irritability

→Sub periosteal hemorrhage involving long bones

- **Painful pseudo paralysis**
- Crying on touch

DIAGNOSIS

X Ray



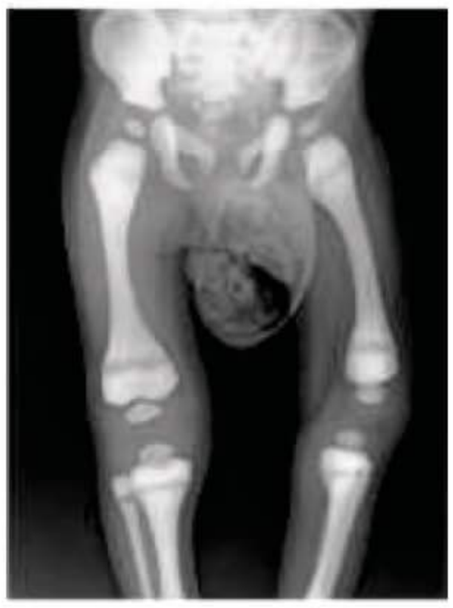
- **Pencil thin** outline of cortex
- Sub periosteal hemorrhage
- **Wimberger sign** (ring shaped epiphysis)
- **Pelkan spur** (bony spur)
- **Trümmerfeld zone**

RACHITIC ROSARY → Rounded

SCORBUTIC ROSARY: Sharp & angular, Painful & tender

OTHER BONE DISORDERS INVOLVING THE BONES

OSTEOPETROSIS / MARBLE BONE DISEASE



→**Bone with in bone** appearance

→↑es density of bones

→d/t mutation in **CLCN 7** gene

→ leads to defective resorption of bones

- neurological problems present
- large heads
- hepatosplenomegaly
- pancytopenia
- deafness

OSTEOGENESIS IMPERFECTA

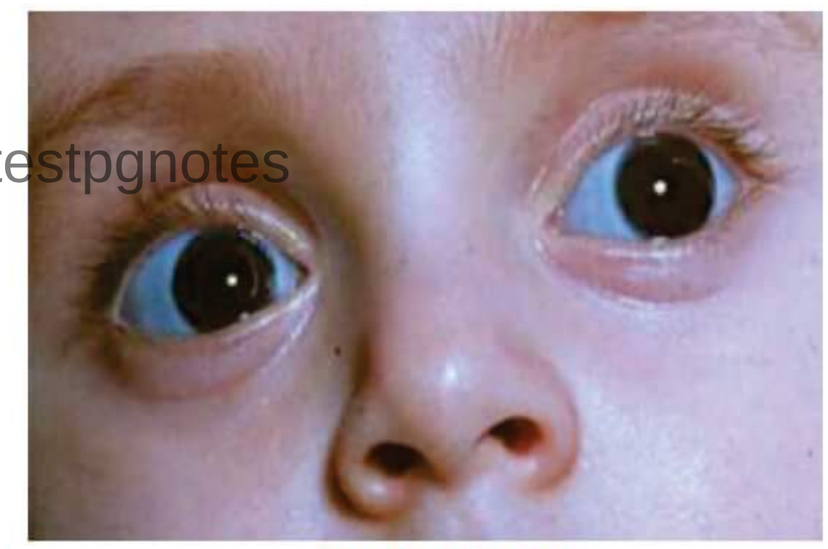
TRAID

1.Bony deformities

2.Blue sclera

3.DeafnesS

BONE DEFORMITIES



BLUE SCLERA

-d/t type **1** collagen defect

→**12 types** → type **I – IV autosomal dominant** inheritance e

• **Dentigerous** imperfecta present

•**Hyperextensible** joints

TYPES

Types **I** & **IV divided** into

A → dentigerous imperfect **absent**

B → dentigerous imperfect **present**

TREATMENT → Bisphosphonates like pamidronate

ACHONDROPLASIA

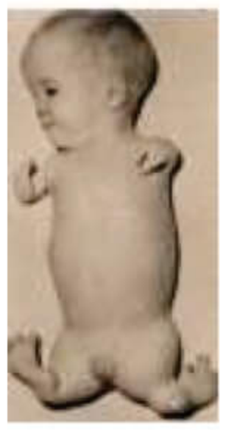
- Short limb dwarfism
- trident hand
- Champagne glass pelvis

PHOCOMELIA

•Risk factor → antenatal exposure to thalidomide

•Short proximal segments of limbs

•Limbs resemble flippers of a seal



phocomelia

JIA (JUVENILE IDIOPATHIC ARTHRITIS)

• Arthritis of ≥ **1 joints**

• Lasting at least **6 weeks**

• In a child **< 16 yrs age**

TYPES

1. **Oligo articular** → 4 or less joints involved; **mc type**

Uveitis/ iridocyclitis; more in girls

2. **Poly articular** → >4 joints involved

3. **Systemic onset** → fever, rash, hepatosplenomegaly

SLE → **Non- erosive arthritis**

PEDIATRIC ENDOCRINOLOGY

DISORDERS OF PITUITARY:

A. MULTIPLE PITUITARY HORMONE DEFICIENCY

GENETIC

1. HES x 1 gene
2. PT x 2 gene
3. LH x 3 gene
4. LH x 4 gene
5. PROP 1 gene
6. POU1F1 gene

ACQUIRED

1. **Brain damage** d/t
   - Trauma
   - Neurosurgery
   - Radiation
2. **Tumors**
   - Pituitary adenoma
   - Craniopharyngioma
   - Meningioma
   - Glioma
3. **Infections**
   - Brain abscess
   - Meningoencephalitis
4. **Others**
   - Hemochromatosis
   - Histiocytosis
   - Perinatal insult
   - Auto immune disorders

ORDER IN WHICH PITUITARY HORMONES ARE USUALLY AFFECTED

GH > Gonadotropins (LH & FSH) >TSH >ACTH

WHILE TREATING, **Corticosteroids** should be started **before** supplementing thyroxine in multiple pituitary hormone deficiency

B. ISOLATED GH DEFICIENCY

- Can be genetic or acquired
- Birth weight & length are **normal**
- US:LS ratio **normal**
- **Delayed**
  1. Bone age
  2. Dentition
  3. Puberty
  4. Milestones

  More common in multiple pituitary Hr deficiency
- Hypoglycemia
- **Frontal bossing**
- **High pitched voice**
- **Short stature**

DIAGNOSIS:

1. **GH stimulation test**
   - Done using insulin, arginine, clonidine, glucagon
   - Peak GH level **<10 ng/ml** → **GH deficiency**
2. Bone age < Chronological age

Treatment: – Recombinant GH injections **subcutaneously**

IMPORTANT ADVERSE EFFECTS OF GH THERAPY

1. Pseudotumor cerebri
2. Gynecomastia
3. Impaired glucose tolerance

C. GH EXCESS

- Results in overgrowth or **gigantism** during **childhood**
- After fusion of epiphysis → **ACROMEGALY**
- **Coarse** facies,
- large **tongue**,
- Prognathism(protruded lower jaw)
- thick skin,
- broad **nose**,
- headache & **visual field defects**

Best screening test → IGF 1 LEVEL

TREATMENT → Somatostatin analogues (**Octreotide**)

→ GH Receptor antagonist (**Pegvisomant**)

D. DIABETES INSIPIDUS

- Polyuria & **polydipsia**
- **Polyuria** → urine output > 5ml/kg/hr or >2L/m^2/24 hr
- Either d/t vasopressin deficiency (**central DI**) (or) insensitivity at the level of kidney (**Nephrogenic DI**)

ETIOLOGY

CENTRAL DI	NEPHROGENIC DI
1. Genetic	1. Genetic
2. Acquired	2. Acquired
3. Trauma	3. **Hypercalcemia**
4. Congenital malformations	4. **Hypokalemia**
5. Tumors (LCH)	5. Drugs
6. Drugs (chemotherapy)	6. Kidney disease
	7. Sickle cell Disease

MECHANISM OF ACTION

Vasopressin (ADH) synthesized in **supra optic & para ventricular nuclei** of hypothalamus

↓

Posterior pituitary

↓

V2 receptors in renal tubule

↓

Insertion of aquaporin 2 water channels into apical/ Luminal membrane

DIAGNOSIS

- **Low urine osmolality** (<600 mosm/g) in association with **high plasma osmolality** [>300 mosm /kg)
- **Water deprivation test** → differentiates **psychogenic polydipsia** from DI
- **Vasopressin response test** → to differentiate **central** DI & **nephrogenic** DI

- On giving vasopressin exogenously , ↑ in urine osmolality by > 50% of base line indicates **Central DI**

TREATMENT OF DI

CENTRAL DI → vasopressin Analogue (**desmopressin**)

NEPHROGENIC DI → **Thiazide**, Indomethacin & salt Restrictions

MEN (MULTIPLE ENDOCRINE NEOPLASIA) SYNDROMES

MEN 1 (WERMER SYNDROME):

- Gene on chromosome **11** → MEN 1 gene → **menin**
- 3 'P' affected

P – Pituitary **hyper**plasia/adenoma

P – Parathyroid **hyper**plasia/adenoma

P – Pancreatic **hyper**plasia/adenoma/Neuroendocrine tumor

MEN 2 A (SIPPLE SYNDROME)

→Gene affected → **RET** gene on **chr 10**

→ FEATURES

H → Hirschsprung disease

A → Amyloidosis

P → Pheochromocytoma

P → Para thyroid hyperplasia / adenoma

Y → Thyroid carcinoma (**medullary**)

MEN 2B

FEATURES

P → Pheochromocytoma

M → Medullary thyroid carcinoma

M → Mucosal & GI neuromas

M → Marfanoid features

DISORDERS OF THYROID IN CHILDREN:

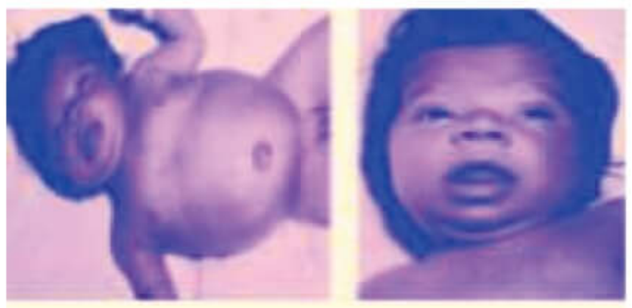
A. CONGENITAL HYPOTHYROIDISM

- mc preventable/ treatable cause of mental retraction/ intellectual disability in children
- Incidence → 1 in 1000 newborns

ETIOLOGY

1. Thyroid **dysgenesis** → mc cause of **congenital hypothyroidism**
2. Thyroid **dyshormonogenesis** → mc cause of **congenital hypothyroidism in a child with goitre**
3. **PENDRED syndrome**
   - d/t PDS gene on **chr 7** → codes for **pendrin** (SLC 26A4) which is a **chloride-iodide transporter**, important in hearing and thyroid pathway.
   - **Hearing Loss + Goitre & Hypothyroidism**
4. **Iodine** deficiency
5. Hypothalamic pituitary dysfunction
6. TSH receptor blocking antibody (usually transient)

CLINICAL FEATURES



- Birth weight & length usually **normal**
- **Wide open** Anterior **fontanelle** and Posterior **fontanelle**
- **Prolonged** physiological jaundice (earliest sign sometimes)
- **Myxedematous facies**
- Large, protruded **tongue**
- **Skin** → dry & scaly
- **Hypotonia**, hypothermia, hoarse cry
- Constipation
- Abdominal distension,
- Umbilical hernia
- **IN UNTREATED CASES**
  1. Delayed development
  2. Intellectual disability (not seen in neonatal period)
  3. Delayed dentition

4. Short stature
5. Delayed puberty
6. Delayed bone maturation (Bone age < Chronological age)

- **DIAGNOSIS**
  1. T4 level → **low**
  2. **Primary hypothyroidism** → TSH usually **> 100** mu/L
  3. **Central** hypothyroidism → **low** TSH levels
- **TREATMENT →** Oral **Levo thyroxine** (early morning with empty stomach)
- **PREVENTION →** Universal newborn **screening** for cong. Hypothyroidism
  - At birth, with umbilical cord blood
  - **Heel prick** → dried blood spots (b/w 2-4 days age)
  - **Should not be done in 1st 1-2 days, to avoid TSH surge**
  - **Most sensitive approach** → check for T4 & TSH both

B. ACQUIRED HYPOTHYROIDISM

- **MC in girls**
- MC **cause** is **auto immune thyroiditis**
- Also **associated** with
  1. Down syndrome
  2. Turner's syndrome
  3. Celiac disease

CLINICAL FEATURES

- Firm & **nodular** goitre
- Short stature
- Cold intolerance
- Lethargy
- Constipation
- Delayed dentition
- **Delayed puberty** (some may have pseudo precocious puberty)
- **Bradycardia**
- Myopathy/ **pseudohypertrophy of muscles**
- **Heart failure** (in severe cases)

Treatment – Thyroxine

DOSE (decreases with increase in age)

1. 1-3 yrs age → 4-6 mg/ kg/ day
2. 10-16 yrs age → 2-4 mg/kg/day

C. ENDEMIC CRETINISM

- **Most serious consequence of Iodine deficiency**

- 2 TYPES
    1. Neurologic type
    2. Myxedematous type

1. NEUROLOGICAL CRETINISM
    - Deaf – mutism
    - Squint
    - Spasticity & rigidity →gait problems
    - Intellectual disability

2. MYXEDEMATOUS CRETINISM
    - Retarded psychomotor development
    - Short stature
    - Coarse facial features
    - Myxedema

PREVENTION – Adequate Iodine intake (fortification of food with iodine)

- RDA of Iodine
    1. For children **<10 yrs** → 40-120 µg/day
    2. For children **≥ 10 yrs** → 150 µg/day

D. HYPERTHYROIDISM **(rare)**
- Suspected in children with
    1. Wt. loss
    2. ↑ appetite
    3. Tremors
    4. Warm extremities
    5. ↑ sweating
    6. Anxiety

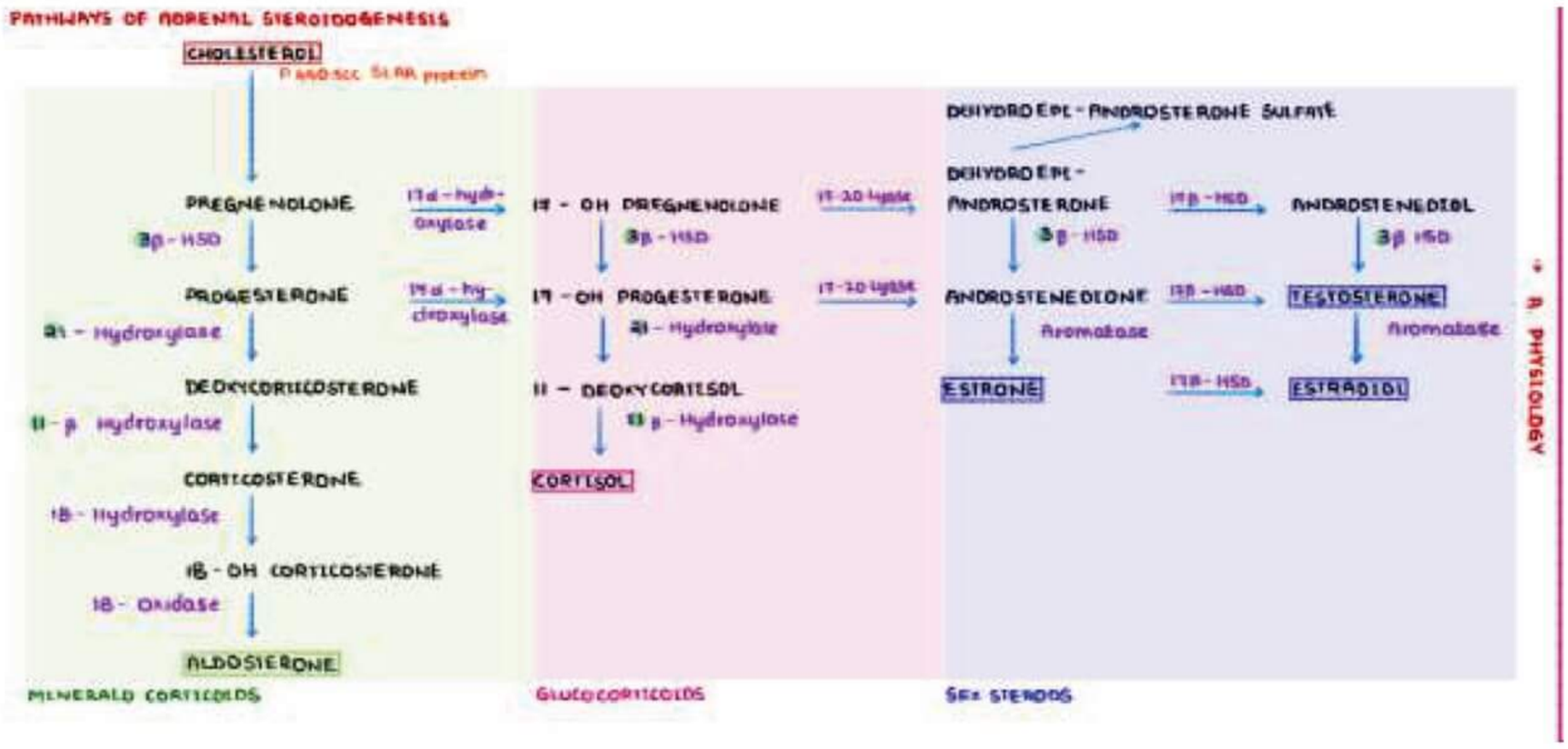
Eye signs are **not** commonly seen in children.

- TREATMENT
    1. Propylthiouracil is usually avoided in children
    2. **Methimazole & Propranolol** are used

ADRENAL DISORDERS:

A. PHYSIOLOGY- steroid hormones are synthesized in adrenal cortex. Predominantly cortisol is synthesized by fetal adrenal gland.

PATHWAYS OF ADRENAL STEROIDOGENESIS



- *Cholesterol is precursor all steroid hormones.*
- *StAR protein → steroidogenic acute Regulatory protein that transports cholesterol into mitochondria.*
- *3β- HSD → 3β- hydroxyl steroid dehydrogenase*
- *ACTH plays an important role in regulation of* ***glucocorticoids & sex steroid synthesis***
- ***Mineralocorticoid production*** *regulated by :*

-Intravascular volume

-K^+ level

-Renin Angiotensin system

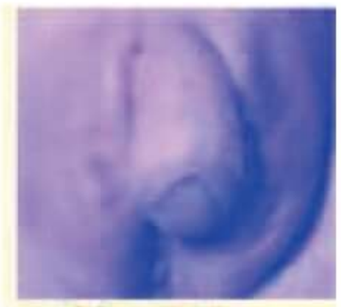
B. CONGENITAL ADRENAL HYPERPLASIA (CAH)

- *Group of* ***autosomal recessive*** *defects in steroid hormone synthesis, characterized by deficiency of some hormones & excess of steroid precursors*
- ***CAH*** *is the mc adrenal disorder seen in children.*
- *mc cause of CAH →* ***21 hydroxylase deficiency***
- *2nd* ***mc*** *cause of CAH →* ***11 β hydroxylase deficiency***

21 HYDROXYLASE DEFICIENCY

Features:

1. *Deficient* ***aldosterone***
   - *Salt wasting*
   - *Dehydration*
   - *Hyperkalemia*
2. *Deficient* ***glucocorticoids***
   - *Hypoglycemia*
   - *Shock*
3. ***Excess*** *sex steroids – ambiguous genitalia in female neonate*



In male, genitalia is normal but this is a very important cause of precocious puberty.

LAB DIAGNOSIS

1. Hyperkalemia
2. ↑ 17 hydroxy progesterone levels
3. Genetic diagnosis →mutation on chr 6

→ **Confirmatory**

→ Useful in **prenatal diagnosis** in next pregnancy

TREATMENT

- Hydrocortisone (Lifelong replacement)
- Fludrocortisone (Lifelong replacement)
- ↑ **salt intake**
- ↑ **dose of glucocorticoids** in times of stressful conditions(surgery, fever)
- Doc for **antenatal** Rx of CAH → **Dexamethasone**
- In a couple with previous case of CAH neonate, start dexamethasone as soon as next pregnancy is diagnosed to prevent virilization of female.

11 β HYDROXYLASE DEFICIENCY:

FEATURES

1. **Excess mineralocorticoids**(due to deoxycorticosterone)→ Hypertension, hypokalemia
2. **Excess 11 deoxy cortisol** → **No features** of glucocorticoid deficiency
3. **Excess sex steroid** → Ambiguous genitalia in **females**

3β HYDROXYL STEROID DEHYDROGENASE DEFICIENCY (3 βSHD)

FEATURES

1. **Deficient mineralocorticoids** → Salt wasting, dehydration, **hyperkalemia**
2. **Deficient glucocorticoids** → Hypoglycemia, shock
3. **Deficient sex steroids** → **Normal genitalia** in females
   → Under virilization (ambiguous genitalia) in males

17 HYDROXYLASE DEFICIENCY

- **Excess mineralocorticoids** → Hypertension, hypokalemia
- No **features of glucocorticoid deficiency**
- No **sex steroids** → normal genitalia in females

→ under virilization (ambiguous genitalia) in males

	Ambiguous genitalia in Female	Under virilization in Males
With salt wasting & Hyperkalemia	21 hydroxylase deficiency	3 β hydroxyl steroid dehydrogenase deficiency
With Hypertension	11 β hydroxylase deficiency	17 hydroxylase deficiency

C. ADRENAL INSUFFICIENCY

PRIMARY (ADRENAL DEFECTS)

1. Autoimmune or **Addison** disease
2. **Infections** → TB, HIV
3. Adrenal Hemorrhage (**WATERHOUSE FRIEDRICHSEN** syndrome)
4. **CAH** d/t 21 hydroxylase / 3 βHSD deficiency
5. **StAR** defect → **lipoid CAH**

SECONDARY (↓ ACTH)

1. **Congenital** malformations (Holoprosencephaly)
2. **Genetic** defects
3. **Acquired** insults (Neuro Sx, Radiotherapy)
4. Tumors
5. **Discontinuation of steroids** after prolonged Rx

CLINICAL FEATURES

- Dehydration
- Lethargy
- Vomiting
- **Salt craving**
- Hypotension
- **Hyperpigmentation** seen in **primary** Adrenal insufficiency

INVESTIGATIONS

- Hypoglycemia
- **Hyper**natremia
- **Hyper**kalemia
- Hemoconcentration
- ↑ hematocrit

TREATMENT: Hydrocortisone, Fludrocortisone

D. CUSHING SYNDROME

- mc cause of adrenocortical hyperfunction in children
- **Cushing disease**(different from cushing syndrome)
    1. **Hypercortisolism** caused by ACTH producing pituitary tumor

ETIOLOGY

ACTH DEPENDENT	ACTH INDEPENDENT	EXOGENOUS ADMINISTRATION
1.Hypothalamic Lesions	Adrenal adenoma / carcinoma	Glucocorticoids
2 Pituitary lesions- adenoma	Pigmented nodular hyperplasia	ACTH
3.Ectopic source -Neuroblastoma -Wilm's tumor -Carcinoid	Mc cune Albright syndrome	mc cause of Cushing syndrome in children → iatrogenic / exogenous administration of steroids

CLINICAL FEATURES

- Obesity, striae
- Moon facies, buffalo hump are rare
- Short stature
- Hypertension
- Hirsutism
- Delayed puberty
- Bone pains
- Muscle weakness
- Behavioural problems

DIAGNOSIS

1. **Screening test**
    - Assessment of **diurnal cortisol rhythm**
    - Overnight **Dexamethasone suppression** test
    - 24hr free **Urine cortisol**
2. **Confirmatory test** → low dose dexamethasone suppression test

ACTH LEVELS

< 5 pg/ ml → ACTH **independent** cause

> 15 pg/ ml → ACTH **dependent** cause

> 100 pg/ ml → Ectopic ACTH production

- Inferior petrosal sinus sampling → best test to identify the source of ACTH production

TREATMENT

1. Surgical Mx → Resection of pituitary/adrenal lesions.
2. Medical Mx → Metyrapone, Ketoconazole, Mitotane.

E. ALDOSTERONE EXCESS (HYPER ALDOSTERONISM)

PRIMARY ALDOSTERONISM/ CONN SYNDROME

1. Adrenal adenoma of Hyperplasia
2. Glucocorticoid remedial Aldosteronism (GRA)
    - d/t genetic defect aldosterone becomes regulated by ACTH

SECONDARY HYPERALDOSTERONISM (Activation of renin angiotensin pathway)

1. Renal artery stenosis
2. Renin secreting tumor
3. Congestive cardiac failure
4. Liver disease
5. Nephrotic syndrome

PATHOPHYSIOLOGY

- Excess Na & H_2O absorption→ Hypertension
- Excess K^+ & H^+ loss → Hypokalemic metabolic alkalosis, generalized muscle weakness

DIAGNOSIS

RENIN	ALDOSTERONISM	
Low	High	1°
High	High	2°
Low	High Decreases after giving steroids	GRA

TREATMENT

- Salt Restriction
- Aldosterone antagonist (Spironolactone)

F. PHEOCHROMOCYTOMA

- A **catecholamine** secreting **tumor** that arises from **chromaffin cells** of abdominal sympathetic chain / Peri adrenal area/ thoracic cavity
- Rare in children
- More likely to be **bilateral** than adults
- **Co-exist** with
    1. Neurofibromatosis
    2. VHL syndrome
    3. MEN syndrome type II
- **DIAGNOSIS** → ↑ urinary **VMA** (vanillyl mandelic acid) & metanephrines.
- **TREATMENT** → surgical removal

    Pre-operative α blockade with **prazosin**

DISORDERS OF PUBERTY:

Breast development beyond **Tanner stage II** & **testicular volume beyond 4 ml** indicate that onset of puberty

A. PRECOCIOUS PUBERTY

DEFINITION → onset of puberty **before** the age of **8 yrs** in **girls** & **9 ½ yrs** in **boys**

- Precocious puberty is **more common in girls**

2 TYPES

1. CENTRAL PRECOCIOUS PUBERTY (GONADOTROPIN DEPENDENT)
2. PERIPHERAL PRECOCIOUS PUBERTY (GONADOTROPIN INDEPENDENT)

Central> peripheral in girls

1. CENTRAL PRECOCIOUS PUBERTY (GONADOTROPIN DEPENDENT)

- ETIOLOGY (GIRLS)
    1. **I**diopathic (more common in girls)
    2. **I**nfections → TB, meningitis
    3. **I**njuries → Trauma, neuro Sx, Radiotherapy
    4. **T**umors → Hypothalamic hamartoma (**Gelastic seizures**)
    5. **C**NS malformations
        - Arachnoid cyst
        - Hydrocephalus
        - Septo-optic dysplasia

2. PERIPHERAL PRECOCIOUS PUBERTY (GONADOTROPIN INDEPENDENT)

→ETIOLOGY (girls)

- **Hypothyroidism**

- **Ovarian** estrogen excess (cyst, tumor, Mc cune Albright syndrome)
- **Adrenal** estrogen excess
- **Exogenous** estrogen exposure

MC CUNE ALBRIGHT SYNDROME

- Triad of
  - **Precocious puberty**
  - **Café au lait spots**
  - **Polyostotic fibrous dysplasia**
- Occurs due to somatic activating mutation of **stimulatory G- protein**
- Endocrine Abnormalities
  - Hyperthyroidism
  - Rickets
  - GH excess
  - Precocious puberty

ETIOLOGY OF PRECOCIOUS PUBERTY IN BOYS

1. CENTRAL PRECOCIOUS PUBERTY

- causes are the ones similar to seen in girls.

- Organic causes are more common in boys

2. PERIPHERAL PRECOCIOUS PUBERTY

- **Excess androgen production** from testis or adrenal is with prepubertal LH levels
  - **CAH** d/t **21 hydroxylase or 11β hydroxylase deficiency** (mc cause of peripheral precocious puberty in boys)
- **Adrenal** tumors → adenoma/ carcinoma
- **Testicular** tumors → Seminoma/Germinoma
- **Testo toxicosis** → activation of LH receptors
- **HCG** secreting tumors → Hepatoblastoma/ germinoma
- **Exogenous** androgen exposure

DIAGNOSIS

- LH is a better indicator of puberty than FSH

- LH levels > 0.6 mu/L or
- LH/ FSH ratio >1 indicates development of puberty
- Advanced bone age
- **Imaging** to rule out CNS/gonadal/ adrenal tumors. MRI is better diagnostic modality.

TREATMENT

- Rx the underlying cause
- Long acting **GnRH analogues** (**Leuprolide**)

A. DELAYED PUBERTY

- **More common in boys**

DEFINITION

- **Girls** → **lack** of secondary sexual characters by **13 yrs** age or absence of menarche by the age of **16 yrs** or within **5 yrs** of **onset** of puberty
- **Boys** → **lack** of pubertal changes by **14 yrs** of age

ETIOLOGY:

A. HYPOGONADOTROPHIC HYPOGONADISM (LH & FSH → low) same in both boys and girls

TRANSIENT CONDITIONS

- Chronic systemic illness (CKD, Chronic liver Disease)
- Severe malnutrition
- Endocrine causes (hypothyroidism, type 1 Dm)

PERMANENT CAUSES

- **Isolated delayed puberty**
  - **Genetic** mutations → **KAL 1** (**Kallmann Syndrome**), GnRH Receptor, DAX -1 gene
  - **Syndromes**→ Prader Willi Syndrome, Laurence Moon Syndrome
- **MPHD** (multiple pituitary hormone disease)
  - Injury
  - Infiltration by tumors- **LCH**
  - **Genetic** – PROP1,LH
  - Malformations
  - trauma

B. HYPERGONADOTROPHIC HYPOGONADISM (LH & FSH → High)

GIRLS:

- Gonadal dysgenesis (**Turner Syndrome**)
- **Steroidogenic** defect (StAR deficiency, aromatase deficiency, 17 hydroxylase deficiency)
- **Ovarian** insult (surgery / radiotherapy)
- **Autoimmune** ovarian failure
- LH & FSH **receptor** resistance

BOYS:

- Chromosomal abnormalities (**Klinefelter Syndrome**)
- **Steroidogenic** defects (17α hydroxylase deficiency)
- **Testicular** insults (trauma, chemotherapy, radiotherapy)

- Malformations (**cryptorchidism**)
- Inefficient testosterone **action** (5α reductase deficiency)
- **Resistance** to testosterone action (androgen insensitivity syndrome)

INVESTIGATIONS

- Screen for systemic diseases
- LH, FSH levels
- Karyotype

TREATMENT → **HRT** to be initiated **beyond 12 yrs** in **girls** & **14 yrs** in **boys**, to initiate & maintain sexual character & to prevent osteoporosis

TYPE 1 DIABETES MELLITUS & OBESITY IN CHILDREN:

- **MC type in children → type 1 DM**
- **DIAGNOSTIC CRITERIA**

Symptoms of DM (polyuria/polyphagia/polydipsia)

+

FBS ≥ 126 mg/dl (or)

RBS/PP ≥ 200 mg/dl (or)

HbA1c ≥ 6.5%

- **Dose** of glucose for doing OGTT in children → **1.75g/kg** of ideal body wt (**maximum 75 g**)
- **RxOC** type 1 DM → **Insulin**
- **DOSE OF INSULIN**
  - **Prepubertal** children → **0.6 – 0.8 U/kg/day**
  - **Pubertal** age group → **0-1.2 U/kg/ day**
- **EXAMPLES**
  - **Rapid** acting → Lispro, Aspart
  - **Short** acting → Regular
  - **Intermediate** acting → NPH
  - **Long** acting → Glargine, Detemir, Degludec
- **2 Regimes** (target HbA_{1c} **<7.5%**)
  - BASAL BOLUS REGIME
    - **Long** acting → 40-50% of total daily dose (TDD)
    - **Rapid** acting → 50-60% of TDD in 2-3 divided closes
  - MIXED SPLIT REGIME
    - **2/3rd before breakfast**

- 2/3 intermediate acting (NPH)
- 1/3 short acting

- **1/3rd after dinner**
  - **2/3 intermediate acting** (NPH)
  - **1/3 short** acting

- SCREENING FOR COMPLICATIONS like nephropathy should be started:
  - **After 5 yrs** of diagnosis in **pre pubertal children**
  - **After 2 yrs** of diagnosis in **pubertal children**

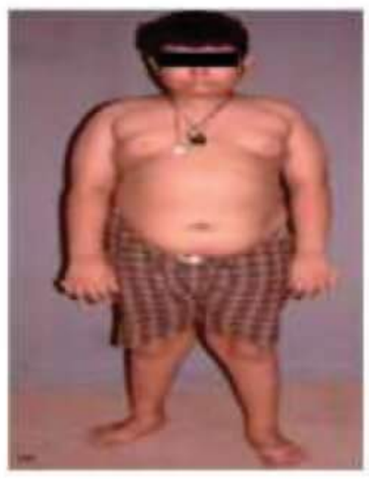
OBESITY:

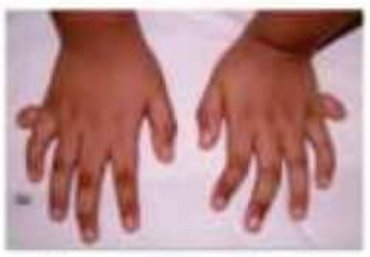
DEFINITION of obesity:

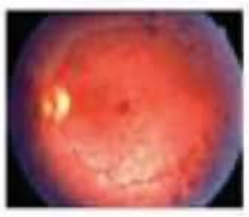
- Obesity → BMI > 95th percentile for age
- Over weight → BMI > 85th percentile for age

OTHER PARAMETERS FOR OBESITY

- Wt for height → >120% of expected value
- Skin fold thickness → >85% of expected value
- Waist circumference & waist hip ratio







ETIOLOGY

Constitutional	
d/t **imbalance** b/w energy intake & expenditure **no** organic cause tall for age normal development	
Pathological / organic	
Endocrine	Genetic syndromes
Cushing syndrome GH deficiency Hypothyroidism	Prader Willi syndrome Laurence moon syndrome (obesity, polydactyly and retinal pigment changes) Beckwith Wiedemann syndrome
Hypothalamic	Drugs
Injury Radiotherapy Tumors	Steroids Antiepileptics Estrogen
Monogenic disorders	
Leptin deficiency or resistance Melanocortin 4 receptors defects	

COMPLICATIONS

1. Insulin resistance
2. Metabolic syndrome
3. Type II DM
4. **Non-alcoholic fatty liver disease** (NAFID)
5. Gall stones
6. Obstructive sleep apnoea

TREATMENT :

RED → AVOID

YELLOW → LIMIT INTAKE

GREEN → UNLIMITED QUANTITY

1. **Dietary** modification – traffic light diet recommended
2. Increase **physical activity**
3. ORLISTAT → **Gastric lipase inhibitor**
4. METFORMIN → for insulin resistance
5. **Bariatric Sx** → laparoscopic adjustable banding