NORMAL NEWBORN

Definitions

- New born period : First 28 days
- Early new born : First 7 days
- Late new born : Day 8 - 28
- Average birth weight : 3 kg
  - < 2.5 kg → LBW
  - < 1.5 kg → VLBW
  - < 1 kg → ELBW

- Classification of birth weight according to gestational age
  → SGA (Small for gestational age)
  → AGA (Appropriate for gestational age)
  → LGA (Large for gestational age)

- Intrauterine growth chart:

![Growth Chart Image]

SGA

- Types
  - Normal variant
    - Constitutional
  - Abnormal variant
    - IUGR

- IUGR
  - Evidence of wasting : Loose folds of skin thin umbilical cord
- Causes:

  - Maternal
    - Onset: Late (2nd/3rd trimester)
    - 'Brain sparing'
      (Head size normal, rest → thin)
    - Asymmetric IUGR
      (Good prognosis)

  - Fetal
    - 1st trimester
    - Entire baby appears small
    - Symmetric IUGR

**Ponderal index**

\[ \text{Ponderal index} = \frac{\text{weight (g)}}{\text{length (cm)}^\text{3}} \times 100 \]

- \( > a \) → Symmetrical IUGR
- \( < a \) → Asymmetrical IUGR

**LGA**

- LGA baby, birth weight > 90th percentile
- Common causes:
  - Constitutional
  - Infant of diabetic mother
  - Soto syndrome (cerebral gigantism)
  - Beckwith-Wiedemann syndrome:
    - Hemihypertrophy (one side of child's body is bigger than other)
    - Macroglossia
    - Omphalocele

**Maturity**

- Classification of term babies:
  - Extremely preterm: < 28 wks
  - Very preterm: 28 - 31 wks
  - Moderate preterm: 32 - 33 wks
Late preterm: 34 - 36 wks
- Term babies are also grouped under:
  Early term: 37 - 38 wks

ENBS

- Expanded new Ballard score
- For estimation of gestational age
- Criteria:
  1. Physical appearance
  2. Neuromuscular examination

- Score: -10 to +50

- 20 wks gestation
- 44 wks gestation

- Accuracy: 1 week

- Salient features of differentiation between term and preterm babies:

  ➔ Posture:
  - Term: Flexion
  - Preterm: Extension (↓ tone)

  ➔ Scarf sign:
  - Term: Elbow doesn't cross midline
  - Preterm: Elbow crosses midline

  ➔ Breast bud:
  - Term: > 5 mm
  - Preterm: < 5 mm

  ➔ Genitalia:
  - Male:
    - Term: Rugae ++
    - Testis palpable
  - Preterm:
    - Absent rugae
    - Testis usually not palpable

  - Female:
    - Term: Labia majora covers Labia minora
  - Preterm:
    - Labia majora & Labia minora equally visible
    - Slow
    - Lanugo hair (+ +)

  ➔ Ear recoil:
  - Term: Fast
  - Preterm: Slow

- Post term baby (> 42 wks):
  - Overgrown nails
  - Yellowish staining (meconium stain)
  - Skin wrinkles ++

  ➔ Skin wrinkles are seen in IUGR babies.
ROUTINE NEWBORN CARE AND NORMAL
OBSERVATION IN NEWBORN

Routine newborn care

(i) At birth: 5 cleans - Clean hands
  - Clean surface
  - Clean blade
  - Clean cord clamp
  - Clean cord (umbilical cord)

Note:
- Topical chlorhexidine: used in case of suspicion of contamination.
- Delayed cord clamping: delay by 30-60 sec after birth.
  - Advantages: protects from development of anaemia in later life.
    - Preterms - ↓ risk of intraventricular hemorrhage.
  - Exceptions: in case of emergency situations like birth asphyxia, cord clamping should not be delayed.

(ii) Prevention of hypothermia:
- Delivery room temperature: ~ 25°C
- No free draft of air in the delivery room
- Skin-to-skin contact of baby and mother

(iii) Breastfeeding:
- Should be started as soon as possible preferable within 1 hour of birth.

(iv) Rooming-in:
- Facilitates bonding between mother and baby.

(v) Prophylaxis:
  a. Vitamin K - dose: 0.5mg (birth weight < 1000gm)
     - 1mg (birth weight > 1000gm)
     - route: IM in the anterolateral aspect of thigh
  b. Erythromycin (0.5%) / tetracycline (0%) ointment
    - Preferred
    - To prevent gonococcal conjunctivitis.
  c. Silver nitrate itself causes chemical conjunctivitis. Not used anymore
Normal observation in newborn

(i) Vital Parameters :-
  - Heart rate : 120-160/min
  - Respiratory rule : 40-60 /min
  - Blood pressure : 60/40 mm Hg
  - Temperature : 35.5-37.5°C , more common site : axilla.
  - Capillary Filling Time (CFT) : <3secs, common site : sternum
    - CFT 24secs is shock.

(ii) Cry :-
  - Normal : before/after micturition
  - Abnormal : during micturition (suggestive of urinary tract infection)

(iii) Loss of weight :-
  - Normal : weight loss of about 10% (term) or 15% (preterm)
  during 1st week of life due to loss of extra cellular fluid (ECF).

(iv) Regurgitation (possetting) :-
  - Normal : Regurgitation occurs due to consumption of air with the feeds.
  - Gentle pat (helps the baby to burp) prevents regurgitation

Normal skin findings in a newborn

(i) Erythema toxicum :-
  - Misnomer .
  - Now called as Erythema neonatorum
  - Findings : erythematous papules + pustules .
  - Appears : >24 hours of life
  - Microscopy : Eosinophils (+)

(ii) Milia :-
  - Findings : Epithelial inclusion cyst

(iii) Epstein pearls :
  - Finding : epithelial inclusion cyst
  - site : hard plate , prepuce
  - lesion : white pearly
(iii) Mongolian Sports:
- Finding: Greenish spots
- Site: Sacrum

(iv) Strawberry angiomia:
- Also known as stork bite lesions
- Site: Nape of neck, forehead
- Finding: Reddish lesions

(v) Effect of maternal estrogen on a newborn:
- Engorgement of breast (mastitis neonatorum)
- Acne
- White discharge per vaginum
- Bleeding per vaginum

Head swelling in a newborn

<table>
<thead>
<tr>
<th>Caput Succedaneum</th>
<th>Cephalohematoma</th>
</tr>
</thead>
</table>
| • Cause: prolonged delivery  
  Venous congestion of scalp veins  
  Fluid collection in scalp  
  Swelling: superficial/diffuse  
  Appears: on day 1 | • Cause: instrumental delivery  
  Subperiosteal collection of blood  
  Swelling: deep, localized  
  (Separated by sutures)  
  Appears: after 12-24 hours  
  Complications: - Neonatal jaundice |

(ii) Sub galeal hemorrhage:
- Most severe type of head swelling in newborn.
- Site: Accumulation of blood below galeal aponeurosis.
- Swelling: diffuse
- Cause: Vacuum delivery (improper application of vacuum)
  Complication: ↓ Circulating blood volume
  Shock, pallor

![Diagram of head swelling in a newborn]
# Neonatal reflex

<table>
<thead>
<tr>
<th>REFLEX</th>
<th>ONSET</th>
<th>FULLY DEVELOPED</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmar grasp</td>
<td>26 wk gestation</td>
<td>32 wk gestation</td>
<td>2-3 month postnatal</td>
</tr>
<tr>
<td>Rooting</td>
<td>32 wk gestation</td>
<td>34 wk gestation</td>
<td>Less prominent after 1 month postnatal</td>
</tr>
<tr>
<td>Moro</td>
<td>30-32 wk gestation</td>
<td>37 wk gestation</td>
<td>5-6 months postnatal</td>
</tr>
<tr>
<td>Tonic neck</td>
<td>35 wk gestation</td>
<td>1 month postnatal</td>
<td>6-7 months postnatal</td>
</tr>
<tr>
<td>Parachute</td>
<td>7-8 months postnatal</td>
<td>10-11 months postnatal</td>
<td>Remains throughout life</td>
</tr>
</tbody>
</table>

- Asymmetric tonic neck reflex:
  - When neck is turned towards one side
    - Extension of limbs in the same side, with flexion of limbs in the opposite side.
- Parachute reflex:
  - Protective reflex.
  - Persists throughout life.

**Reflexes that appear after birth:**
- Parachute reflex
- Landau reflex
- Symmetric reflex
- Moro's reflex:
  - Complete Moro's reflex: Extension and abduction followed by flexion and adduction.
Abnormal moro's :-
- Absent moro's reflex in term baby :-
- Congenital malformations
- Hypoxic Ischaemic Encephalopathy (HIE) - a sequelae of birth asphyxia.
- Unilateral moro's :-
  - Nerve - Brachial plexus injury
    - a) Erb's paralysis (C5-C6)
    - b) Klumpke's paralysis (C8-T1)
  - Bone - Fracture or dislocation.
    - Most common bone fracture at birth clavicle
- Moro's > 6 months :-
  - Cause - Cerebral palsy
  - An "immature" brain.

Note :-
- Vernix caseosa : A normal skin finding.
  - Protects the baby from hypothermia.
- Skin probe : continuous temperature monitoring

\[
\text{Weight (gm)} \times 100
\]

\[
\text{Ponderal index} = \frac{\text{Weight (gm)}}{\text{Length (cm)}^3}
\]

- Ponderal's < a: asymmetric IUGR
MANAGEMENT OF LBW BABIES

- Cause of low birth weight (LBW)
  - Preterm
  - SGA - Intrauterine Growth Restriction (IUGR)

Temperature control of babies

- Normal temperature of a new born baby: 36.5 - 37.5°C
- New born baby is prone to Hypothermia.
- A baby can lose temperature by:
  1. Evaporation
  2. Conduction
  3. Radiation ➔ most important source of heat loss.
     M/C site: Head (Large body surface area)
  4. Convection
- LBW babies are ↑ prone to hypothermia due to:
  1. Large size of the head compared to rest of the body.
  2. ↓ Amount of brown fat.
  3. Preterm baby ➔ Extensor posture.

Non-shivering thermogenesis

- Occurs in brown fat.
- Brown fat is ↑ in mitochondria.
- Biochemical mechanism responsible for non-shivering thermogenesis:
  Uncoupling of oxidative phosphorylation.
  Hypothermia ➔ stress for the baby
  Noradrenaline ➔ oxidation ➔ divert the heat ➔ uncoupling
  phosphorylation (ATP)
• m/C site for brown fat: **Nape of neck**

**Classification of Hypothermia**

- Any temperature < 36.5°C : Hypothermia
- Stages: I. Cold Stress : 36 – 36.4°C
  1. Moderate Hypothermia : 32 – 36°C
  2. Severe Hypothermia : < 32°C

**Prevention of hypothermia**

- Baby can be classified into:
  1. Stable Baby
    - KMC (kangaroo mother care), usually indicated for preterm babies 1.8 – 2.5 kg
    - Component of KMC:
      1. Position: upright
      2. Nutrition: breast feeding
      3. Early discharge
    - KMC is stopped when baby attains:
      → Term gestation (37 weeks)
      → Normal weight (> 2.5 kg)
  2. Unstable Baby
    - Warmer (Radiation)
    - Incubator (Convection)

**Nutrition**

1. Enteral Nutrition
   - Breast feeding
   - Breast feeding in preterm babies require proper coordination

**Between:** Rooting → Sucking → Swallowing
- A baby born < 32 weeks gestation:
  - EBM (Expressed Breast Milk) via or/o /naso – gastric tube
  - Measurement of or/o /naso – gastric tube:
  [Diagram]
  - Umbilicus

- A baby born 32-34 weeks gestation
  - No coordination of rooting → sucking → swallowing
  - Mode of nutrition: EBM by
    (a) Palada
    (b) Katori spoon
  - A baby born > 34 weeks gestation
  - Direct breast feeding

II. Parenteral Nutrition
- Indications:
  - <48 weeks
  - Sick baby
- Fluids to be used:
  - <48 hours: 10% Dextrose
    - Add: 60 - 80 ml/kg/day → by 10 - 20 ml/kg/day to a max of 150 ml/kg/day
  - >48 hours: Isolyte - P

Nutritional supplements

- All babies are given vitamin D
- If baby is < 1.5 - 2.5 kg ⇒ vit D + iron supplements (↓ iron stores)

  Started 6 - 8 wks after birth
< 1.5 Kg $\Rightarrow$ vit D + Iron

HMF (Human Milk Fortifier)

Problem faced by LBW babies

- ↑ Risk of birth asphyxia.
- ↓ Stores:
  (a) Hypoglycemia: plasma glucose < 45 mg/dl
  (b) Hypocalcemia: term $\Rightarrow$ < 8 mg/dl
      Preterm $\Rightarrow$ < 7 mg/dl
- Problems faced by preterms and IUGR babies.

<table>
<thead>
<tr>
<th>Preterm</th>
<th>IUGR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematological: Anemia.</td>
<td>↑ production of EPO (Erythropoietin) ↓ Polycythemia</td>
</tr>
<tr>
<td>Problems (&lt;5th percentile)</td>
<td>↓ Hematocrit &gt;65% or (HCT) Hb &gt;22g%</td>
</tr>
<tr>
<td></td>
<td>Treatment:</td>
</tr>
<tr>
<td></td>
<td>1. ↑ Fluids</td>
</tr>
<tr>
<td></td>
<td>2. HCT &gt;75% ↓ Partial Exchange Transfusion</td>
</tr>
<tr>
<td>Respiratory: RDS (Respiratory)</td>
<td>stress $\Rightarrow$ motilin (↑motility of GIT) ↓</td>
</tr>
<tr>
<td>Problems</td>
<td>Distress (Syndrome) release of meconium ↓</td>
</tr>
<tr>
<td></td>
<td>MAS (Meconium Aspiration Syndrome)</td>
</tr>
</tbody>
</table>
Immaturity of organ systems in a preterm

- A baby born in 24 - 34 wks gestation

![24 - 34 wks Brain](image)

- Ventricles are surrounded by capillary group of network → Germinal matrix. It is composed of fragile blood vessels (immature)
- Germinal matrix bleed
  ↓
  Intra ventricular hemorrhage

Apnea of prematurity

- Apnea in new born: cessation of breathing > 20 sec or any duration accompanied by bradycardia or cyanosis.
- Apnea of prematurity:
  - Due to immaturity of respiratory center
  - Usually in Day 2 - Day 7
- Treatment: Drugs:
  1. Caffeine (Drug of Choice)
  2. Theophylline (Narrow Therapeutic Index)
Retinopathy of prematurity

- In preterm baby (<32 wks) exposed to ↑ O₂
- AMA Retrolental Fibroplasia.
- Screening for ROP:
  - <32 wks or <1.5 kg
  - or
  - 32 – 34 wks or 1.5 – 2 kg with any of these problems:
    1. O₂ > 24 hours
    2. CPAP/ventilation
    3. Shock – Inotrope support
    4. Anemia – Blood transfusion
    5. Culture positive sepsis
  - Time for screening: 4 wks after birth or when baby attains:
    - PMA (Post Menstrual Age) – 32 wks (whichever is later).
  - Method of screening: Indirect Ophthalmoscopy.

Hearing loss

- Screening: OAE (Otoacoustic Emission) or Automated Auditory Brainstem Response (AABR)
- BERA is a confirmatory procedure.
NEONATAL RESUSCITATION

- Order of assessment:
  T = Temperature
  A = Airway
  B = Breathing
  C = Circulation

2015 Guidelines for neonatal resuscitation

Initial assessment of newborn:

Cry  Tone  Term of gestation
\[\text{Normal}\]
\[\text{Not crying}\]

1. Dry the baby, provide warmth (radiant warmer)
2. Remove secretion by suction:
   - Mouth followed by nose
     (to prevent aspiration)
3. Position the airway:
   - Slight extension of neck: Sniffing position
4. Tactile stimulation:
   - No cry after initial steps

Assess heart rate and respiratory effort:
- First response of a newborn to hypoxia
  - Bradycardia
Assess heart rate and respiratory effort.

- HR > 100
- Laboured breathing OR
  Central cyanosis.
  ↓
  Supplemental O₂
  • O₂ hood or
    nasal prongs.
  • In preterm (> 32 weeks)
    → CPAP
  Non-invasive.
    • Bag and mask
      ventilation
  Invasive
    • Endotracheal
      intubation.

- HR < 100
  Not breathing.
  ↓
  Positive pressure ventilation (PPV)

- No response to PPV or HR < 60
  ↓
  Chest compression
  +
  ventilation (3:1 ratio)
  No response
  ↓
  Adrenaline

Positive pressure ventilation

- Non-invasive: Bag and mask ventilation.
  • Volume of bag: 240 to 750 ml.
  • Response: ↑ HR. (Most sensitive)
  • No response: do corrective steps.
    • M: mask readjustment
    • R: reposition head.
    • S: suction.
    • O: open mouth.
    • P: ↑ pressure.
    • A: Alternative airway.
  • Rate: 40 - 60/min
  • Pressure:
    1st breath: 30 - 40 cm H₂O.
    Subsequent breath: 15 - 20 cm H₂O.
  • Absolute contraindication: Congenital Diaphragmatic Hernia.

Invasive:
  Endotracheal intubation
  1st step: Laryngoscopy (to visualise glottis)
- Straight blade used
- Size of blade: Preterm - 0
  Term - 1
- ET tube: Uncuffed tube.
  [Cuffed tube → pressure necrosis of trachea.]
- Size of tube:
<table>
<thead>
<tr>
<th>Size</th>
<th>Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 kg</td>
<td>2.5 mm</td>
</tr>
<tr>
<td>1-2 kg</td>
<td>3 mm</td>
</tr>
<tr>
<td>&gt; 2 kg</td>
<td>3.5 mm</td>
</tr>
</tbody>
</table>
- Length of insertion = 6 + weight (kg)
- Best method for confirmation: ETCO₂ (capnography)
- PPV is the most important step in resuscitation.
- During PPV:
  - In term baby: Resuscitate at room air.
  - For pre-term: Start with ai = 30% O₂
    
    Titrate with Spo₂
  - Target saturation in pre-term: 90 : 95%
    (High O₂ % → Risk of retinopathy of prematurity)

**Chest compression and ventilation**

Chest compression:
- Started when HR < 60 even after PPV.
- Techniques:
  a) Two finger technique
  b) Two thumb technique (preferred)
- Ventilation: 100% O₂ given.
  - Compression: Ventilation Ratio
    in 1 minute → 90 compressions and 30 ventilation.
    Ratio → 3 : 1

**Adrenaline**

- Started when HR < 60 even after chest compressions.
- Dose: OJ - 0.3 ml/kg
  (0.01 - 0.03 mg/kg)
  1 : 10,000 solution
- Route: Umbilical vein.
- Note:
  - In babies of opioid-dependent mother, with respiratory depression: Naloxone used.
1 minute - Golden minute of neonatal resuscitation
- Born - not breathing
  ↓ Initial steps
  ↓ PPV
  ↓ 30 seconds.
  Chest compression
  ↓ 30 seconds.
  Adrenaline.

- $\text{SpO}_2$ (pulmonary $\text{SpO}_2$)
  - Measured in right upper arm.
  - 1 minute: 40 - 65%
  - 3 minutes: 70 - 75%
  - 10 minutes: > 85%
- Acrocyanosis in initial minutes after birth: Normal.

Meconium stained liquor (MSL)
03:33:30

Baby born by meconium stained liquor (MSL)
↓
Does not cry
↓
Non-vigorous baby
↓
cries after birth
↓
Vigorous baby
- Keep baby with mother.

Non-vigorous baby:
- HR < 100.
- Poor/no respiratory effort.
- \( \downarrow \downarrow \) Tone
- Management:
  a) Follow usual steps of resuscitation
  b) Early PPV
  c) Routine tracheal suction: Not done.

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.
**APGAR scoring**

<table>
<thead>
<tr>
<th></th>
<th>0 (abnormal)</th>
<th>1</th>
<th>2 (normal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity (Tone)</td>
<td>Extension</td>
<td>Partial Flexion</td>
<td>Complete Flexion</td>
</tr>
<tr>
<td>Pulse rate (HR)</td>
<td>0</td>
<td>&lt; 100 /min</td>
<td>&gt; 100 /min</td>
</tr>
<tr>
<td>Grimace</td>
<td>No response</td>
<td>Grimace</td>
<td>Cry</td>
</tr>
<tr>
<td>Appearance (colour)</td>
<td>Cyanosis</td>
<td>Partial pink</td>
<td>Complete pink</td>
</tr>
<tr>
<td>Respiratory effort</td>
<td>No</td>
<td>Poor</td>
<td>Good /cry</td>
</tr>
</tbody>
</table>

- APGAR done at 1 minute and 5 minutes → low score
  → Repeat at 10 minutes.
- 1 minute score: Overall status of baby at birth.
  APGAR score has no role in predicting the need for resuscitation.
- 5 minute score: Effectiveness of neonatal resuscitation.
  Persistently low APGAR: High risk of neonatal death.
- Normal APGAR: 8 – 10/10
  Low APGAR: ≤ 7/10
NEONATAL SEPSIS

Introduction:
Neonatal sepsis: Bacterial infection affecting the neonates.

Etiology:
most common organism involved
- In India: Klebsiella.
- Worldwide: Group B streptococcus.

Types of neonatal sepsis

<table>
<thead>
<tr>
<th></th>
<th>Early onset sepsis</th>
<th>Late onset sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset:</strong></td>
<td>≤ 72 hrs of birth</td>
<td>&gt; 72 hrs of birth</td>
</tr>
<tr>
<td><strong>Source:</strong></td>
<td>Maternal</td>
<td>Hospital / community acquired</td>
</tr>
<tr>
<td><strong>Risk factors:</strong></td>
<td>Chorioamnionitis,</td>
<td>Unclean hands.</td>
</tr>
<tr>
<td></td>
<td>Foul smelling liquor, PPRM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration of ROM &gt; 72 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Type of infection:</strong></td>
<td>Pneumonia</td>
<td>Septicemia, meningitis</td>
</tr>
</tbody>
</table>

Features of neonatal sepsis

- In any sick baby → suspect sepsis.
- The features are non-specific:
  - ↓ Feeding
  - Child not active
  - Respiratory distress (Pneumonia)
  - Seizures (Meningitis)

In a newborn, sepsis is characterised by Hypothermia not Hyperthermia.
**Diagnosis of sepsis**

- **Blood culture**: Gold standard
- **Sepsis screen in neonate**:
  1. Blood count: ↓ WBC, ↓ Neutrophil
  2. ↑ Immature:total neutrophil ratio (> 10%)
  3. ↑ Micro ESR, positive CRP (c-Reactive protein)

  For a. +ve sepsis screen → 2 out of 3 should be present

- **New marker for neonatal sepsis**: procalcitonin

**Treatment of neonatal sepsis**

- **Empirical antibiotics (initial phase)**
  - Penicillin + aminoglycoside

- **Suspected meningitis**: Add 3rd generation cephalosporin
  - Cefotaxim

- **Duration of treatment**:
  - If sepsis screen +: 5-7 days (1 week)
  - Culture +: 10-14 days (2 weeks)
  - CSF analysis +: 21 days (3 weeks)
BIRTH ASPHYXIA AND HIE

Birth asphyxia

- Asphyxia means not breathing ⇒ Hypoxia.

Criteria for birth asphyxia:
(i) APGAR score 0-3 at ≥ 5 minutes
(ii) Umbilical cord pH < 7
(iii) Brain - HIE (Hypoxic ischemic encephalopathy)
(iv) Multiorgan damage (most common: kidney → acute tubular necrosis)

HIE

Sarnat and Sarnat staging

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mild</td>
<td>moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>CNS</td>
<td>Hyperactive</td>
<td>Depressed</td>
<td>No Function</td>
</tr>
<tr>
<td>Appearance</td>
<td>Active</td>
<td>Lethargic decreased</td>
<td>Comatose</td>
</tr>
<tr>
<td>Sucking</td>
<td>Good</td>
<td>+</td>
<td>No</td>
</tr>
<tr>
<td>Seizure</td>
<td></td>
<td>+</td>
<td>No activity</td>
</tr>
<tr>
<td>ANS</td>
<td>↑ sympathetic mydriasis</td>
<td>↑ Parasympathetic miosis</td>
<td>No activity</td>
</tr>
<tr>
<td>Pupil size</td>
<td></td>
<td>↓</td>
<td>mid-size, poor-light response</td>
</tr>
<tr>
<td>Heart rate</td>
<td>↑</td>
<td>↓</td>
<td>irregular rhythm</td>
</tr>
<tr>
<td>Outcome</td>
<td>100% Normal outcome</td>
<td>80% Sequelae</td>
<td>50% Sequelae</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80% Normal outcome</td>
<td>50% death</td>
</tr>
</tbody>
</table>

- Most common cause of neonatal seizure: HIE

Management of HIE

- Symptomatic treatment
- DOC for neonatal seizures: Phenobarbitone.
- Newer method: Induced hypothermia (therapeutic hypothermia) to ↓ metabolic activity in brain.
Induced hypothermia:

- Types: Selective head cooling
  - Whole body cooling.
- Temperature: 33.5 – 34.5°C
- Criteria:
  1. ≥ 36 week, ≥ 2 kg
  2. Moderate – severe HIE
  3. Within 6 hours after birth
  4. Duration: < 72 hrs. (3 days)

Sequelae of HIE

- Term:
  1. Most common: Selective cortical necrosis
  2. Parasagittal infarct: Spastic quadriparesis
  3. Focal ischemic necrosis: Spastic hemiparesis
  4. Status marmoratus (basal ganglia): Chorea – athetoid
    [mottled / marbled appearance]

- Preterm:
  1. Periventricular leukomalacia: Spastic diplegia (lower limbs)

Parasagittal infarcts

Status marmoratus

Periventricular leukomalacia

Note:
- Investigation of choice for HIE – MRI
NECROTIZING ENTEROCOLITIS

Pathogenesis

- Causes
  1. Prematurity (immaturity of gut)
  2. Asphyxia (vasoconstriction)
     vasoconstriction can also be due to maternal cocaine abuse.
  3. Baby exposed to top feeds (milk other than breast milk)
     Top feeds encourages pathogenic bacterial colonisation

Pneumatosis Intestinalis → Air in wall → Air in lumen

Peritoneum

- Air
- Necrosis
- Pneumatosis Intestinalis
- Bacteria
- Bleeds, abdominal distension, ↓ bowel sounds
- Epithelium

↓ Blood supply

→ G/T of a baby
• Air in intestinal walls: **pneumatosis intestinalis**
• On necrosis air leaks out to:
  → Portal veins: **pneumatosis portalis**
  → Peritoneum: **Pneumoperitoneum**
• If bacteria leaks into peritoneum: **peritonitis**

**Bell’s staging**

- **Stage I** → **Suspect NEC**
  - Intestinal necrosis → bleeds, abdominal distension, ↓ bowel sounds
  - Divided into
    - **Ia:** Occult blood in stools
    - **Ib:** Gross blood in stools
- **Stage II** → **Definite NEC**
  - Air enters intestinal wall
  - Divided into
    - **Iia:** Pneumatosis intestinalis
    - **Iib:** Pneumatosis portalis
  - Triad of findings: Acidosis, hyponatremia, thrombocytopenia.
- **Stage III** → **Advanced NEC**
  - Divided into
    - **Iii a:** Peritonitis, ascites
    - **Iib:** Pneumoperitoneum

**Treatment**

- Up to stage **III a** → **Medical management**
  → Child kept as nil per oral (NPO)
  → Broad spectrum antibiotics
- **Stage III b** → **Surgical management**
  → If baby is very unstable: Peritoneal drainage
  → If baby can be taken for surgery: Laparotomy

**Prevention**

- Antenatal steroids
- **MEN** (minimal enteral nutrition)
  - Baby <38 weeks
  - AKA Trophic feeds
Note

→ Air under diaphragm
↓
Pneumoperitoneum
(Stage III b)
**RESPIRATORY DISORDERS**

**Transient tachypnea of newborn (TTNB)**

- MC cause of respiratory distress in newborn
- Seen in term babies
- In normal vaginal delivery:
  - Squeezing of the baby → Squeezing of lungs → Lung fluid Cleared out
  - Baby breathes freely.

- In LSCS,
  - Lack of squeezing of the lungs
  - Retained lung fluids [Common cause of TTNB]
    - Characterised by fast breathing, respiratory distress
    - Also known as wet lung syndrome.
  - Cleared by the lymphatics
  - Baby becomes normal within 72 hours.

- Chest x-ray:
  1. Prominent bronchovascular markings / sunburst appearance
  2. Fluid in the interlobar fissure

---

**Respiratory distress syndrome**

- Seen in preterm babies (< 34 weeks of gestation)
- Cause: Surfactant deficiency
  - Collapse of alveoli
  - Deposition of fibrin in the alveoli
  - Also known as Hyaline membrane disease
Chest x-ray:
1. White out / ground glass appearance of lung (due to absence of air entry into the lung)
2. Air bronchogram (due to air in the bronchus & bronchioles)

Feature of RDS:
- Fast breathing > 60 / min
- Retractions
- Grunting / Cyanosis

Silver man score for RDS

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No respiratory distress</td>
</tr>
<tr>
<td>1-3</td>
<td>Mild</td>
</tr>
<tr>
<td>3-6</td>
<td>Moderate</td>
</tr>
<tr>
<td>7+</td>
<td>Severe</td>
</tr>
</tbody>
</table>

**Treatment:**
- **O₂**
- CPAP: Opens collapsed alveoli (PEEP → 5 - 7cm H₂O, FIO₂ → 40 - 70 %)
  - ↑ Functional residual capacity
  - Improved ventilation perfusion ratio

**Surfactant therapy**
Surfactant therapy

- Route of administration: intratracheal
- Methods of administration:
  1. INSURE technique:
     - Intubate → Surfactant → Extubate
  Newer method:
  2. MIST (Minimally invasive surfactant therapy)
  3. LISA (Less invasive surfactant administration)

Earlier animal surfactant was used for therapy
New synthetic surfactant: Lucinactant

Surfactant therapy

\[ \begin{align*}
\text{Prophylactic} & \quad \downarrow \\
\text{Rescue therapy/treatment} & \quad \downarrow \\
\text{Given in preterm (< 28 weeks), before the development of RDS} & \quad \downarrow \\
& \quad \text{After the body developed RDS}.
\end{align*} \]

Prevention of RDS

- Administration of Antenatal steroids
- 24 to 34 weeks of gestation
- Drugs:
  - Dexamethasone → 6mg/dose x 4 doses
    → most common drug in use in India
  - Betamethasone → 12 mg/dose x 2 doses

Uses of antenatal steroids:
- ↓ The occurrence of RDS
- ↓ The occurrence of Necrotising enterocolitis
- ↓ The occurrence of intraventricular hemorrhage
- ↓ The neonatal mortality
Physiology & importance of surfactant

Surfactant

Phospholipids + Protein

Most mature: Lecithin (phosphatidyl choline)

a. Phosphatidyl glycerol

Immature: Sphingomyelin

Test for fetal lung maturity
1. Lecithin : Sphingomyelin (L:S) (> 2:1 - mature lung)
2. Lamellar body count
3. Surfactant : albumin ratio
4. Shake test
   Amniotic fluid + Ethanol in test tube
   Shake
   Bubbles (?) Mature surfactant (?)
   Bubbles ↓/Θ Immature Surfactant / No surfactant

Bronchopulmonary dysplasia

- Also called as chronic lung disease of newborn
- Preterm baby who is oxygen dependant for ≥ 28 days of life

Pulmonary alveolar proteinosis

Normally,
Type A pneumocytes → surfactant to Alveoli

Removed by old surfactant macrophages

In pulmonary alveolar proteinosis (PAP),

Type A pneumocytes

Old surfactant

Removed by macrophages

Alveoli
• Defective surfactant protein (SP-e)
  ↓
Not removed by macrophages

• Defective macrophages
  ↓
Cannot remove surfactant

  ↓
Accumulation of old surfactant in alveoli

  ↓
PRP

• seen in term babies
• Inherited (Autosomal recessive)
• Family history of other siblings being affected
• Chest x ray: Ground glass appearance
  ↓
  1. RDS
  2. PAP
  3. Obstructive TAPVC

Congenital diaphragmatic hernia (CDH) 00:36:57

• Most common type: Bochdalek hernia.
  ↓
Left, posterior defect

• Morgagni hernia:
  - Right & anterior defect.

• Features:
  - Pulmonary hypoplasia, mediastinal shift.
  - ↑ risk of asphyxia
  - Respiratory distress
  - Heart sound of the right hemithorax
  - Sunken abdomen

Management:
  - Baby not crying → Start resuscitation (asphyxia)
    Avoid bag & mask ventilation
- respiratory distress
  0–48 hrs: i) Put nasogastric tube – keep the tube open
  (medical treatment) (decompresses the intestine)
  a) mechanical ventilation
     - Conventional
     - High frequency oscillatory ventilation (HFOV)
     - ECMO (extra corporeal membrane oxygenation)

  after 48 hrs: surgical treatment

- Prognostic factors:
  Pulmonary hypertension
  Liver in hernial sac
  Early onset of respiratory distress
  } Bad prognosis

- Recent advance:
  Feto: fetal endoscopic tracheal occlusion
  Expansion of lungs.
  done in antenatal period.
  ultrasound guided perfusion scope is
  - inverted at 27–30 wks of gestation
    (Long expansion)
  - removed by 34 weeks gestation
    (accelerate the surfactant maturation)
NEONATAL JAUNDICE

Jaundice = Condition of ↑ bilirubin

Heme → Biliverdin → Bilirubin + Albumin
(Conjugated)

Intestine

Conjugated

90%

Gut bacteria

Stercobilinogen

10%

Urobilinogen

Stool

Urine

Excreted

Liver

UDP-GLUCURONYL TRANSFERASE

(UDP - GT)

Conjugated

Physiological Jaundice

- Always ↑ in unconjugated bilirubin
- Causes:
  - Newborn have ↑ Hb → ↑ lysis → Jaundice
  - Immaturity of liver (UDP - GT)
- Features:
  - Cephalo caudal progression - starts from face
    (eyes) last area to get jaundice is palms & soles
  - Never appears on day 1
  - Never exceeds day 7 in term baby, day 14 in preterm baby
  - Never affects palm & sole
  - Never exceeds bilirubin > 15 mg/dl
  - Rise of bilirubin is ≤ 5 mg/day

Modes of estimation of bilirubin:
- Serum bilirubin
- Transcutaneous bilirubinometer
Kramer’s zone

Based on part of body involved in jaundice it is possible to tell approximate bilirubin levels.

1. → Head → 4 - 6 mg/dl
2. → Chest → 6 - 8 mg/dl
3. → Abdomen → 8 - 12 mg/dl
4. → UL & LL → 13 - 14 mg/dl
5. → Palm & sole → 15 mg/dl

Pathological jaundice

- Bilirubin is > 15 mg/dl
- Causes:
  1. ↑ in unconjugated bilirubin
  2. ↑ Production
     - Polycythemia
     - Hemolytic
       - Rh incompatibility (more severe)
       - ABO incompatibility (more common)
       - Hereditary spherocytosis
  3. ↓ Conjugation
     - Absent UDP - GT
       - Criggler - najjar syndrome
  4. Type 1 - No UDP - GT
  5. Type II - deficiency of UDPGT

a) ↑ Conjugated bilirubin
   - Obstructive jaundice (mc cause - Biliary atresia)

Treatment of jaundice

1. Phototherapy
   - Light wavelength → 460 - 490 nm
   - Unconjugated bilirubin → lumirubin → Excreted
     (water insoluble) (water soluble)
   - This is done by following methods
     - Photo isomerization
     - Structural isomerization (bilirubin → lumirubin)
     - Photo oxidation (most important way)
- Types of light used - CFL, LED
  (Better than CFL)
- Irradiance - at least 30 μW/cm²/nm
- Distance between the lamp & baby → 30 - 45 cms.
- Adverse effects:
  - Dehydration (hence feeding is done frequently)
  - Hypocalcemia
  - Bronze baby syndrome

  ↑ Conjugated bilirubin / hepatic dysfunction

  ↓ Phototherapy

  Bilirubin converted to bronze colour pigments

2) Double volume exchange transfusion:
- i.e. : 160 ml/kg
- Type of blood - "O-ve"
- Indications:
  - if cord blood levels of Hb < 10 g, bilirubin > 75 mg,
direct coombs test →
  - Failure of photo therapy to ↓ bilirubin.
  - Severe hemolysis → Immediate transfusion.

3) Drugs
- Phenobarbitone (Enzyme inducer → UDP - GT)
- Metalloporphyrin (Heme oxygenase inhibitors)

  Conversion of Heme → Biliverdin is blocked

Breast feeding v/s Breast milk jaundice

<table>
<thead>
<tr>
<th>Breast feeding jaundice</th>
<th>Breast milk jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Due to ↓ breast feeding</td>
<td>a&quot; week of life</td>
</tr>
<tr>
<td>During 1st week of life</td>
<td>Due to breast milk constituent</td>
</tr>
<tr>
<td>Factors: causing jaundice</td>
<td>like pregnanediol &amp; free fatty acids which inhibit UDP - GT,</td>
</tr>
<tr>
<td>Child predisposed to dehydration</td>
<td>β-glucuronidase ↑ the</td>
</tr>
<tr>
<td>↓ motility of gut</td>
<td>unconjugation of bilirubin</td>
</tr>
<tr>
<td>↑ enterohepatic circulation</td>
<td>Treatment: continue breast feeding</td>
</tr>
<tr>
<td>Treatment: ↑ frequency &amp; duration of breast feeds</td>
<td></td>
</tr>
</tbody>
</table>
Complications of pathological jaundice

**Warning:** Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.

**Kernicterus:**
- ↑ in unconjugated bilirubin (water insoluble)
- Unconjugated bilirubin in high amount is lipid soluble
  - Cross blood brain barrier → Basal ganglia → Kernicterus

- Clinically known as BIND
  (Bilirubin induced neurological damage): it is of 2 types.

  a) Acute: in first 28 days of life.
  - "SLOW" babies have Kernicterus.
  - Seizures
  - Lethargic
  - Opisthotonos → ↑ tone, arching back.
  - Whiny cry / high pitch cry

  b) Chronic:
  - Extrapyramidal type of cerebral palsy
  - Sensorineural deafness
  - Dental dysplasia
  - Upward gaze palsy
NORMAL GROWTH

Definitions:

<table>
<thead>
<tr>
<th>Term</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal:</td>
<td></td>
</tr>
<tr>
<td>• Fertilized ovum (zygote)</td>
<td>First 2 weeks</td>
</tr>
<tr>
<td>• Embryo</td>
<td>2-8 weeks</td>
</tr>
<tr>
<td>• Fetus</td>
<td>9 weeks onward</td>
</tr>
<tr>
<td>Perinatal period</td>
<td>22 wks of gestation to 7 days after birth</td>
</tr>
<tr>
<td>(defines viability of fetus)</td>
<td></td>
</tr>
<tr>
<td>Postnatal</td>
<td></td>
</tr>
<tr>
<td>• Neonate</td>
<td>First 28 days</td>
</tr>
<tr>
<td>• Infancy</td>
<td>First 1 year</td>
</tr>
<tr>
<td>• Toddler</td>
<td>1-3 years</td>
</tr>
<tr>
<td>• Preschool</td>
<td>3-6 years</td>
</tr>
<tr>
<td>• School</td>
<td>6-12 years</td>
</tr>
<tr>
<td>• Adolescent</td>
<td>10-19 years</td>
</tr>
<tr>
<td>- Early</td>
<td></td>
</tr>
<tr>
<td>- Mid</td>
<td></td>
</tr>
<tr>
<td>- Late</td>
<td>10-13 y</td>
</tr>
<tr>
<td></td>
<td>14-16 y</td>
</tr>
<tr>
<td></td>
<td>17-19 y</td>
</tr>
</tbody>
</table>

Puberty

Sequence of pubertal changes:

- In girls:
  - Thelarche → Pubarche → Growth spurt → Menarche.

- In boys:
  - ↑ in testicular volume (measured using orchidometer)
  - Pubarche and penile enlargement
  - Growth spurt (Late)
  - Axillary and facial hair

Tanner’s sexual maturity rating (SMR)

- Stage I – V
  - I: Pre-pubertal
  - V: Adult

Growth spurt:
- in female → stage 3
- in male → stage 4
Growth pattern in different tissues

1. Brain: 90% growth in first 2 years of life

   ![Graph showing brain growth pattern]

   - Periods of growth spurt:
     - Infantile (< 1 yr)
     - Pubertal (> 1a yrs)

2. Somatic growth

   ![Graph showing somatic growth pattern with S-shape]

   - Sigmoid 'S' shape curve

3. Between 4-8 years:
   Physiological lymphoid hyperplasia.

4. Gonadal growth

   ![Graph showing gonadal growth pattern]

   - After 10 years
equal growth spurt

---

* Pediatrics v2.0 * Marrow 4.0 * 2020 * AV
Growth assessment

1. Weight
   - Average birth weight: 3 kg.
   - Weight loss (loss of fluid)
     In term: 10% wt loss → regain birth wt. by 10 days.
     In preterm: 15% wt loss → regain birth wt. by 15 days.
   - Weight gain:
     20-30 g/day - first 3 months
     400 g/month - till 1 year
     2 kg/year → 1 yr till 7 yrs
     3 kg/year → > 7 yrs

   Birth weight doubles by 5-6 months
   triples by 1 year.

2. Height/Length:
   - Length: measured using infantometer
     till age 2 yrs
   - Height: > 2 yrs
     - measured using stadiometer.

   - At birth: 50 cm
   - 1 year: 75 cm
   - 2 yr: 81.5 cm
   - Thereafter, steady ↑ by 6 cm/year.
   - Height doubles by 4 years
     triples by 12 years

3. Head circumference (HC):
   - Occipito - frontal circumference.
   - Measure of brain growth.
   - At birth: 33-35 cm.
     ↑ 2 cm/month × 3 months

   - At 3 months: 41 cm.
     ↑ 1 cm/month × 3 months

   - At 6 months: 44 cm.
At 1 year: 47 cm.
At 2 years: 49 cm.

4. Chest circumference (CC)
   - Indicate nutritional status of child.
   - At birth, HC > CC (3 cm)
     At 1 year: HC = CC
     > 1 year: HC < CC
   - After 1 yr, if CC < HC → malnutrition.
   - At birth, if HC >> CC (> 3 cm difference)
     - Hydrocephalus
     - IUGR (Asymmetric)
     - Preterm.

Mid-Arm Circumference (MAC)

- Age independent measure of malnutrition (between 1-5 years)
- 15-17 cm = Normal
  - < 13.5 cm = Malnutrition
  - < 11.5 cm = Severe malnutrition

Measurement of MAC:
1. Shakir's tape:
   - Green zone - (-
   - Yellow zone - Malnutrition
   - Red zone - Sever malnutrition

2. Bangle test:
   - Bangle of 4cm diameter used to measure MAC
   - If bangle crosses elbow easily → malnutrition (+)

3. QUAC stick
   - Arm circumference stick
   - Compares child's height to MAC

Skinfold thickness

- Harpenden's caliper
  - Used to measure skin-fold thickness
  - Measure of subcutaneous fat.
- Indicator of nutritional status
- Age independent parameter between 1-6 years of age.
  > 10mm - Normal
  < 4mm - Malnutrition.

Growth charts

- Best tool to interpret growth parameters.
  1. WHO growth charts:
     Percentile: position of child with reference to a variable in a given population.

2. Standard deviation charts:
   - 50th percentile: mean value.
   - Standard deviation: deviation of a value from the 50th percentile.

- < 3rd percentile: Low value
- > 97th percentile: High value.

Charts used for growth monitoring:
- Weight for age charts
- Weight for height charts
- Height for age charts
- Head circumference charts
- Skin fold thickness charts
- BMI charts
Dentition

Temporary / Primary

Total number of teeth: 20
First tooth to appear: Lower central incisor
First appears at: approx 6 months
Between 6-12 years: period of mixed dentition

Permanent / Secondary

32
1st molar
6 years
**DISORDERS OF GROWTH**

**Delayed dentition**

- Non - appearance of teeth > 13 months
- Causes:
  - Malnutrition
  - Rickets
  - Hypothyroidism
  - Hypopituitarism
  - Down syndrome

**Short stature**

- Height for age chart < 3rd percentile or < -2 SD
- MPH (mid parental height)
  - Tells the approximate growth potential of child

\[
\text{MPH} = \left[ \frac{\text{Father's height} + \text{Mother's height}}{2} \right] + 6.5 \text{ cm (boy)} - 6.5 \text{ cm (girl)}
\]

- Types
  - Normal variant short stature
  - Pathological short stature
    - Chronic malnutrition
    - Stunting
    - Rickets
    - Chromosomal disorders
    - Endocrine and bone disorders

**Graphs**

- Height vs. Age
  - 3rd Percentile
  - Normal growth velocity
  - Abnormal / absent growth velocity
- Normal variant short stature types:
  - Constitutional short stature  
  - Familial short stature

Height
---
Age

Adult height: Normal
Puberty: Delayed
Bone Age: Delayed

Short
Normal
Normal

Proportionate and disproportionate short stature

- Body proportions
  - Head (vertebral column) ↓ upper segment (US)
  - Pubis (Long Bones) ↓ Lower segment (LS)

- US : LS Ratio
  - Normal:
    - Birth = 1.7 : 1
    - 3 Years = 1.3 : 1
    - 7 - 10 Years = 1 : 1
    - > 10 Years = 0.9 : 1

- Proportionate short stature
  - Normal variant
  - Chromosomal disorders
  - Growth hormone deficiency
  - Malnutrition

- Disproportionate short stature
  - Eg. 1:3 y old child
    - US : LS ratio = 1.7 : 1 (↑)
  - Short limb short stature
    - Achondroplasia
    - Congenital hypothyroidism
    - Rickets
- Eg. 11: 3 yr old child
  LS : LS ratio = 1 : 1 (↓)
  Short + trunk dwarfism
  vertebral anomalies:
  - Spondyloepiphyseal dysplasia
  - Pott's spine (TB)
  - MPS (mucopolysaccharidosis)

Bone age

- Appearance of ossification centres in bone
- New born: Lower end femur + upper end tibia \( \rightarrow \) Knee x-ray
- Infant: Head of humerus \( \rightarrow \) shoulder x-ray
- 1 - 13 years: carpal bones \( \rightarrow \) wrist x-ray
  - 1st carpal bone to appear: Capitate (2 months)
  - 2nd carpal bone to appear: Hamate (2 - 4 months)
- Development of carpal bones:
  - 1 year \( \rightarrow \) 2 carpal bones
  - 2 years \( \rightarrow \) 2
  - 3 years \( \rightarrow \) 3
  - 4 years \( \rightarrow \) 4
  - ...
  - 7 years \( \rightarrow \) 7
- Chronological age (CA): according to date of birth
- Bone age (BA): appearance of ossification centre
- Methods of calculating bone age:
  - Greulich - pyle Atlas (Best)
  - Tanner - white house method
- Delay in bone age BA < CA
  1. Constitutional delay
  2. GH ↓, thyroid hormone ↓ (severe delay)
  3. Chronic malnutrition

Abnormalities in head size

- Microcephaly
  - Head circumference < -3 SD
  - Divided into:
    - Primary (Genetic)
      - Problem is in generation / migration of neuron
    - Secondary (Acquired)
      - Injury to developing brain
      - Torch infection
- Neural tube defect
- Neuronal migration disorder
- Chromosomal
- Familial:
  - AR
  - Low IQ
- Toxin:
  - Alcohol
  - Phenytoin
- Asphyxia at birth
- Post natal
  - Meningitis
  - Intracranial hemorrhage

- Macrocephaly (MC > + a s.d.)

  Skull (Thicker)
  ↓
  Subdural widening
  ↓
  Thalassemia:
  ↓
  Effusion / Empyema
  ↓
  Megalencephaly
  ↓
  Hydrocephalus

- Familial (benign)

- Metabolic:
  - Tay Sachs disease
  - MPS
  - Alexander disease
  - Canavan's disease

Abnormal shapes of head

- Craniosynostosis: premature fusion of suture.
- Whenever suture fuses → skull expands along same direction.
multiple sutural fusion
- Acrocephaly (Tower shaped skull)
- Syndromes associated:

1. Apert syndrome
   Common features:
   - Hypertelorism
   - Hypoplastic mid-face
   - Protruding eyes.

   Differences:
   - CI Syndactyly
   - Cleft palate
   - Low IQ

2. Crouzon syndrome
   -
   - Cleft palate
   - Normal IQ
DEVELOPMENTAL MILESTONES 
AND ASSESSMENT

Developmental milestones: 4 domains
(i) Gross motor
(ii) Fine motor
(iii) Language
(iv) Social

Gross motor milestone

Rule: Cephalo - Caudal progression

<table>
<thead>
<tr>
<th>Age</th>
<th>Milestone Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>Neck holding (head control)</td>
</tr>
<tr>
<td>4-6 months</td>
<td>Rolls over</td>
</tr>
<tr>
<td>6 months</td>
<td>Sits with support, Tripod sitting</td>
</tr>
<tr>
<td>8 months</td>
<td>Sits without support</td>
</tr>
<tr>
<td>10 months</td>
<td>Crawling (abdomen, chest: on ground)</td>
</tr>
<tr>
<td></td>
<td>Stand with support</td>
</tr>
<tr>
<td>11 months</td>
<td>Creeping (abdomen, chest: off ground)</td>
</tr>
<tr>
<td></td>
<td>Cruising (walking sideways while holding onto furniture)</td>
</tr>
<tr>
<td>12 months</td>
<td>Stands without support</td>
</tr>
<tr>
<td>15 months</td>
<td>Walks with support</td>
</tr>
<tr>
<td>18 months</td>
<td>Walks without support</td>
</tr>
<tr>
<td>2 years</td>
<td>Runs</td>
</tr>
<tr>
<td>3 years</td>
<td>Climbs up-stairs (2 foot / step)</td>
</tr>
<tr>
<td>4 years</td>
<td>Rides tricycle</td>
</tr>
<tr>
<td></td>
<td>Climbs up-stairs (1 foot / step)</td>
</tr>
<tr>
<td></td>
<td>Climbs downstairs (1 foot / step)</td>
</tr>
<tr>
<td></td>
<td>Able to hop</td>
</tr>
</tbody>
</table>
Fine motor milestone

<table>
<thead>
<tr>
<th>Age</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>Palmar grasp reflex (hands remain closed)</td>
</tr>
<tr>
<td>4 months</td>
<td>Bidextrous grasp</td>
</tr>
<tr>
<td>6 months</td>
<td>Unidextrous grasp [ulnar (immature)</td>
</tr>
<tr>
<td></td>
<td>Palmar grasp]</td>
</tr>
<tr>
<td>8 months</td>
<td>Radial (mature) palmar grasp</td>
</tr>
<tr>
<td>9 months</td>
<td>Immature pincer grasp (fingers are used to grasp)</td>
</tr>
<tr>
<td>12 months</td>
<td>Mature pincer grasp</td>
</tr>
<tr>
<td>15 months</td>
<td>Able to scribble</td>
</tr>
<tr>
<td>18 months</td>
<td>Able to draw horizontal line (—)</td>
</tr>
<tr>
<td>2 years</td>
<td>Able to draw vertical line (▃)</td>
</tr>
<tr>
<td>3 years</td>
<td>Able to draw circle (○)</td>
</tr>
<tr>
<td>4 years</td>
<td>Able to draw plus (+)</td>
</tr>
<tr>
<td>4 1/2 years</td>
<td>Able to draw square (□)</td>
</tr>
<tr>
<td>5 years</td>
<td>Able to draw triangle (△)</td>
</tr>
<tr>
<td>6 years</td>
<td>Able to draw diamond (◇)</td>
</tr>
</tbody>
</table>

Tower of cubes:
- 15 months - 2 cubes
- 18 months - 3 cubes
- 2 years - 6 cubes
- 3 years - 9 cubes

Dressing and undressing activity:
- 2 years - undressing
- 3 years - dressing and undressing with help
- 5 years - dressing and undressing without help (independent)

Language domain

<table>
<thead>
<tr>
<th>Age</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>Cooing</td>
</tr>
<tr>
<td>4 months</td>
<td>Monosyllable (ma, pa)</td>
</tr>
<tr>
<td>9 months</td>
<td>Bisyllable (mama, papa)</td>
</tr>
<tr>
<td>1 Year</td>
<td>1 - 2 words</td>
</tr>
<tr>
<td>15 months</td>
<td>Jargon speech</td>
</tr>
<tr>
<td>18 months</td>
<td>8 - 10 words</td>
</tr>
<tr>
<td>2 years</td>
<td>2 words sentences</td>
</tr>
<tr>
<td>3 years</td>
<td>Able to tell his name, age, gender</td>
</tr>
<tr>
<td>4 years</td>
<td>Able to tell simple story</td>
</tr>
</tbody>
</table>
Social domain

<table>
<thead>
<tr>
<th>Age</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>Social smile</td>
</tr>
<tr>
<td>3 months</td>
<td>Mother regard</td>
</tr>
<tr>
<td>6 months</td>
<td>Stranger anxiety, Smiles at mirror image</td>
</tr>
<tr>
<td>9 months</td>
<td>Able to wave bye-bye</td>
</tr>
<tr>
<td>10 months</td>
<td>Plays peek-a-boo</td>
</tr>
<tr>
<td>12 months</td>
<td>Plays simple ball game</td>
</tr>
<tr>
<td>15 months</td>
<td>Points to objects</td>
</tr>
<tr>
<td>18 months</td>
<td>Domestic mimicry (mimics house hold activities)</td>
</tr>
<tr>
<td>2 1/2-3 years</td>
<td>Parallel play (plays with kids without interaction)</td>
</tr>
<tr>
<td>4 years</td>
<td>Group play (plays with interaction)</td>
</tr>
<tr>
<td>5 years</td>
<td>Able to discriminate right and left.</td>
</tr>
<tr>
<td></td>
<td>Able to follow 3 step command.</td>
</tr>
<tr>
<td></td>
<td>Able to identify 4 colours.</td>
</tr>
<tr>
<td></td>
<td>Able to repeat 4 digits.</td>
</tr>
</tbody>
</table>

Miscellaneous milestones

- 6 months - Mouthing of objects
- 1 year - Casting (deliberately throwing objects)
- 9 months - Object permanence (able to understand that object continues to exist even when not visible)
- 3 years - Handedness (predominantly using one particular hand for daily activities)

Hand regard
- Child plays with his own hands
  - Appears by 3 months
  - Disappears by 5 months

Vision development:
- Follow object -
  - Newborn: up-to 45°
  - 1 month: up-to 90°
  - 3 months: up-to 180°
- Binocular vision well established by 4 months.
Hearing development:
- Murphy's sequence of hearing
  Response to sound:
  - Newborn: Startling
  - 4 months: looks horizontal at the source of sound.
  - 6 months: looks downward at the source of sound.
  - 7 months: looks upward at the source of sound.
  - 10 months: pivoting (diagonal localisation of sound, can turn diagonally and picks object)

Developmental assessment

1. Pull to sit:
   - Newborn - Head lag
   - By 3 months - no head lag.
2. Ventral suspension:
   - Newborn - Head and limbs drop down.
   - At 2 months - Head at level with the body.
   - Limbs dropped down.
   - At 3 months - Head lifted above the level of the body.
3. In prone position:
   - 0-2 weeks: legs fixed and kept below abdomen.
     Pelvis lifted up.
   - 4-6 weeks: Legs - straight
     Pelvis - straight
   - 3 months:
     - Elbows bent
     - Child bears weight on the forearm.
   - 6 months: Bearing weight on extended arm.

Development Quotient (DQ)

- \( DQ = \frac{\text{Developmental age}}{\text{Chronological age}} \times 100 \)
- \( DQ < 70: \text{Developmental Delay} \)
- Developmental delay in 2 or more domains
  \[ \text{Global developmental delay} \]
  (e.g., Cerebral palsy)
In preterm babies, **corrected age** is used for assessment calculated up to 2 years of age.

* Example: baby born at 32 weeks.
  - Post-natal age: 3 months
  - Corrected age: 1 month
  - Maturity: at 40 weeks

**Tests for Developmental Assessment**

- **Good**: Goodenough Harris draw-a-man test.
- **Doctors**: Denver II test.
- **Treats**: Trivandrum development screening test.
- **Patients**: Phatak's Baroda screening test.

**Definitive tests**:
- **Bayley**: II scale of infant and toddler development.
- **Stanford Binet Intelligence Scale**.
- **Wechsler Intelligence Scale**.
- **Vineland Adaptive Behaviour Scale II**.
BEHAVIOURAL DISORDERS

Temper tantrum

- Between 18 - 36 months of age.
- Temporary.
- Aggressive behaviour (attention seeking).
- Management: Time-out technique.

Pica

- Eating inedible objects for at least 1 month.
- Inappropriate for age of child and cultural practices of community.
- In children < 5 years.
- Common in children with developmental delay.
- Associations:
  a) Iron deficiency.
  b) Chronic lead poisoning.
  c) Parasitic infections.

Thumb sucking

- Age < 4 years: common.
- Age > 4 years:
  - Emotional/social problems.
  - Dental malocclusions.

Breath holding spells

- Starts after 6 months → peaks by 2 years
  ↓
- Settles by 5 years
Stimulus (anger / anxiety / pain)  
↓  
Breath holding (in full expiration)  
↓  
1. Cyanotic spell (common)  
   a. Palid spell.  
   - resembles a seizure  
   - resembles syncope  
   ↓  
   lasts for few seconds  
   ↓  
   Returns to normal  

• Differential diagnosis  
  a) Seizures  
  b) Conduction defect in heart  

• Association: Iron deficiency.

Nocturnal enuresis

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.

• In child > 5 years.  
  • Cause: Delayed maturation of bladder.  
  • Management:  
    - Initial → Non - pharmacological.  
    a) Behavioural modification - Limit fluid intake in the evening.  
    - Avoid caffeinated drinks.  
    - Complete bladder emptying before going to bed.  

b) Alarm therapy.  
   - Drugs: if initial management fails.  
   • Desmopressin (oral).  
   • Anticholinergics - Oxybutynin.  
   - Used if child also has day time enuresis.
BREASTFEEDING

Exclusive breastfeeds: upto 6 months of age.
Complementary feeds: started > 6 months.
Breastfeeds continued till 2 years.

Physiology of breastfeeding

- Reflexes:
  - In mother:
    a) Prolactin reflex: Galacto poiesis (milk production)
    b) Oxytocin reflex: Galacto kinesis (milk ejection)

  - In baby:
    a) Rooting reflex
    b) Sucking reflex
    c) Swallowing reflex

Properties of breast milk:

A. Immunological properties:
   - Rich in IgA.

<table>
<thead>
<tr>
<th>Component of breast milk</th>
<th>Protect against</th>
</tr>
</thead>
<tbody>
<tr>
<td>P - Para amino benzoic</td>
<td>malaria</td>
</tr>
<tr>
<td>acid</td>
<td>E - coli</td>
</tr>
<tr>
<td>L - Lactoferrin</td>
<td>E - coli</td>
</tr>
<tr>
<td>A - IgA</td>
<td>Giardia</td>
</tr>
<tr>
<td>B - Bifidus Factor</td>
<td></td>
</tr>
<tr>
<td>Gile salt lipase</td>
<td></td>
</tr>
</tbody>
</table>

B. Bioactive substances:
   - Epidermal growth factor
   - Transforming growth factor -β
      { maturation of intestinal epithelium.

Advantages of breast milk:

- Energy: 67 Kcal / 100 ml.
- Carbohydrates: High in breast milk.
  Predominant: Lactose → Glucose + Galactose.
  - Provide energy
- Lactoferrin
- Lactobacillus

- **Proteins**: Low in breast milk. Predominant: whey protein eg: Lactalbumin, lactoglobulin.
  - easily digested
  - essential for brain growth (Taurine, cysteine)
- Cow milk: Predominant → Casein
  - Can cause constipation and cow milk protein allergy (CMPA)

- **Fats**: ↑ PUFA.
  - DHA (docosahexaenoic acid)
  - Arachidonic acid

### Deficiencies in breast milk

- Vit. K and D
- Vit B₉ (mother - strict vegetarian)
- Micronutrients → Iron.
- Iron in breast milk is better absorbed than cow milk.

- Term baby: Adequate stores.
- Preterm baby: Inadequate stores. Supplementation needed.

### Contraindications

- **Absolute**
  - Lactose intolerance
  - Galactosemia
  - Mother on radiation/chemotherapy.

- **Relative**
  - Maternal infection:
    - a) HIV
    - b) TB
    - (Mother not taking R₉, R₉ duration < 2 weeks)
    - c) Varicella
    - d) Herpes simplex
Composition and types

Birth  3 days  14 days

Colostrum  Transitional  Mature milk.

- ↑ IgA
- ↑ Vit. A, D, E, K

Milk produced by mother of preterm baby:
- ↑ Sodium
- Iron
- Immunoglobulins
- Proteins
- Sugar (Calories)

‘Preterm babies drink in SIPS’

Foremilk & hindmilk.

- Foremilk
  - Watery
  - Satisfies thirst
  - ↑ Protein, carbohydrates

- Hindmilk
  - ↑ Fats
  - Satiety

Storage of expressed breast milk:
- Room temp: 6 - 8 hours
- Refrigeration: 24 hrs
- Freezer (-20°C): 3 months.

Nutritional requirements of a baby

1. Protein:
   - < 5 years: 20 g/day
   - 5 - 10 years: 30 g/day
   - Early adolescence 40 g/day
   - Middle and late adolescence: 50 g/day

2. Calorie requirement: (daily)
   - First 10 kg: 100 kcal/kg
   - 0 - 20 kg: 1000 kcal + 50 kcal/kg
   - > 20 kg: 1500 kcal + 20 kcal/kg.
MALNUTRITION BASICS & SAM

WHO classification of malnutrition

- Malnutrition
  - Based on duration
    - Acute
      - Weight affected "wasting"
    - Chronic
      - Height affected "stunting"
  - Based on severity (growth chart)
    - Moderate
      - Height is affected
      - -2 to -3 S.D (standard Deviation)
    - Severe
      - < -3 S.D

- If bilateral "pedal edema" \( \oplus \) → it is severe malnutrition
- It is a diagnosis of exclusion

Growth charts used for:
- Acute malnutrition → weight for height chart
- Chronic malnutrition → height for age chart

Severe acute malnutrition (SAM)

Diagnostic criteria:
1) Weight for height \( \rightarrow < -3 \text{ S.D} \)
2) Bilateral pedal edema
3) Mid arm circumference (MAC) \( < 11.5 \text{ cm} \) (from 6 months to 5 yrs age)

If any 1 of above criteria is satisfied, SAM is diagnosed.

Management of SAM

In SAM, Assess:
1) Appetite Test:
   - Offer food to Child
   - Accepting \( \rightarrow \) good \( \rightarrow \) community management / food / appetite / supervised home management
   - Not Accepting \( \rightarrow \) poor \( \rightarrow \) management at hospital / food / appetite / hospital
a) Edema - Anasarca
b) Medical complications
   - Triad of factors
     - Associated with mortality in children
   - S - sugars (Hypoglycemia)
   - H - Hypothermia
   - I - Infections
   - EL - Electrolyte imbalance
   - DE - Dehydration
   - D - Deficiencies (micronutrients)

- Appetite - good
  - No anasarca
  - No medical complication
  - Community / supervised home management

- Appetite - poor
  - Anasarca
  - Medical complication
  - Hospital management

Management of SAM: 2 phases

- Rehabilitation (2 - 6 weeks) - a "m" phase
- Stabilization phase: all complications are managed
  a) Hypoglycemia: blood sugar < 50 mg/dl
     - Treatment
       - Asymptomatic - oral fluids at 50 ml of 10% dextrose / breast feeds
       - Symptomatic - IV fluids 5 ml/kg of 10% dextrose
  b) Hypothermia: Rectal temperature < 35.5°C
  c) Infections: M. organism → gram -ve
     - Treatment - empirical antibiotics = penicillin + Aminoglycosides
       - In septic shock or meningitis or Not responding to empirical antibiotics
       - For > 48 hrs = cefotaxime + Aminoglycosides
d) Electrolyte imbalance:
- Child prone for - Hypokalemia & Hypomagnesemia in SAM
- When plasma sodium is measured in SAM → it gives falsely lowered sodium levels (due to edema). But the body stores of sodium are high. ∴ restrict sodium in diet.

e) Dehydration:
- Oral → give ORS / ReSoral (rehydration solution for malnourished).
- IV fluids = RL + 5% Dextrose (if oral intake is poor)

f) Deficiencies:
Children with SAM require the micronutrients twice the amount of RDA (recommended dietary allowance) except vit A which is given in normal dose.

Prophylactic vit. A Dose:

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 month</td>
<td>50,000</td>
</tr>
<tr>
<td>6 - 12 month</td>
<td>100,000</td>
</tr>
<tr>
<td>&gt; 12 month</td>
<td>200,000</td>
</tr>
</tbody>
</table>

In treatment of vit. A deficiency:
Day 0, 1 and then 2 weeks later → same dose as per the age group.

Correction of iron deficiency: Not done on first week of treatment, as active infection & malnutrition interfere with iron absorption.

Feeding in SAM

- Falls under Rehabilitation
  B - Begin feeding
  E - Energy dense feeds
  S - Stimulation
  T - Transfer of home diet

- Start with low feeding & gradually ↑ it.
  Start with: 80 K cal/kg/day
  Gradually ↑ 10 - 20 K cal/kg/day
  Max → start with 150 - 200 K cal/kg/day
  Protein → start with 0.8 - 1 g/kg/day
  Up to 4 - 6 g/kg/day

Pediatrics • v2.0 • Marrow 4.0 • 2020 • AV
Refeeding syndrome:
- Complication of starting feeds with a high calorie diet.

- R/o A Nutritional Rehabilitation Syndrome
  - High calorie diet ➔ ↑ insulin ➔ shift of ions in cell
  - Investigation:
    Lab hallmark: Hypophosphatemia.
    Clinical hallmark: ↑ in edema

Types of Diet in SAM:
- F - 75:
  - 75 kcal /100 ml
  - 0.9 g protein /100 ml
- F - 100:
  - 100 kcal /100 ml
  - 2.9 g protein /100 ml
- RUTF (Ready to use therapeutic food)
  ➔ Peanut paste + sugar + milk solids + vegetable oil
  - It is an oily paste
  - Palatable for children

Criteria for discharge of child in SAM

- No edema for at least 2 weeks.
- Weight for height ➔ reached ≥ 50 (or)
  mid arm circumference reaches at least 12.5 cm
MARASMUS AND KWASHIORKOR

Introduction - kwashiorkor

- “Kwashios” means displaced child
- Onset around 1 year of age
- Child usually does not receive a nutritious diet.
  - Feed: calorie rich diet such as - rice, cereals, plantains, starchy eruel
  - :: Kwashiorkor child has severe protein deficiency.

Difference between kwashiorkor and marasmus

<table>
<thead>
<tr>
<th></th>
<th>Marasmus</th>
<th>Kwashiorkor</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Onset</td>
<td>• Shortly after birth</td>
<td>• ≥ 1 year</td>
</tr>
<tr>
<td>(ii) Deficiency</td>
<td>• Calorie ↓↓</td>
<td>• Protein ↓↓</td>
</tr>
<tr>
<td>(iii) Edema</td>
<td>• Alert</td>
<td>++</td>
</tr>
<tr>
<td>(iv) Appearance</td>
<td>• Good</td>
<td>• Lethargic</td>
</tr>
<tr>
<td>(v) Appetite</td>
<td>• Good</td>
<td>• Poor / Absent</td>
</tr>
<tr>
<td>(vi) Prognosis</td>
<td>• absent</td>
<td>• Poor</td>
</tr>
<tr>
<td>(vii) Additional feature</td>
<td>absent</td>
<td>• present</td>
</tr>
</tbody>
</table>

Additional features in kwashiorkor:

a) Fatty liver: due to impaired synthesis of lipoprotein
b) Crazy pavement dermatosis
c) Flaky paint dermatosis
   Peeling of hyperpigmented patches.
Marasmic and kwashiorkor child

(i) Marasmic child:
- Alert child
- Visible wasting (prominent ribs)
- Monkey facies (wrinkles)
- Baggy pant appearance (Loose buttock folds)

(ii) Kwashiorkor child
- Lethargic child
- Edema masks wasting
- Flag sign (alternate black and white hair)
- Fatty liver
- Flaky paint dermatosis.
**FAT - SOLUBLE VITAMINS**

**Vitamin A:**

- Recommended dietary allowance (RDA)
  - Infant: 400 mcg
  - Child: 600 mcg

<table>
<thead>
<tr>
<th>Functions of vitamin A</th>
<th>Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Eye:</td>
<td>- Defective dark adaptation (early) ↓ if untreated Night blindness</td>
</tr>
<tr>
<td>→ Rhodopsin (dark adaptation)</td>
<td></td>
</tr>
<tr>
<td>→ Corneal and conjunctival epithelium protection</td>
<td>- Dryness (xerosis)</td>
</tr>
</tbody>
</table>

- Eye:
  - Bitot spots

Protection of:
- Skin epithelium
- Gastrointestinal epithelium
- Respiratory epithelium

- xA - Conjunctival xerosis
- xB - Bitot spots (hyperkeratinised silvery plaques)
- xC - Corneal xerosis
- xD - Keratomalacia < 1/3rd cornea (thinning of cornea)
- xE - Keratomalacia > 1/3rd cornea
- xS - Scar in cornea
- xF - Fundal changes

Dry skin (toad skin or phrynoderma)

Recurrent respiratory and gastrointestinal infections

**Treatment:**

**Dosage:**
- Age < 6 months: 50,000 IU
  - 15 months: 1 lakh IU
  - >12 months: 2 lakh IU

Schedule - Day 0, day 1, day 14.
Hypervitaminosis A:
- Cause: Rupture of lysosomes
- C/F: Pseudotumor cerebri
  - Alopecia, hepatosplenomegaly
  - Hyperostosis of bone

Vitamin D

- Sunshine vitamin
- UV-B rays (sun) → skin → 7-dehydrocholesterol
  ↓ as hydroxylase (liver)
  Cholecalcidiol
  or
  (25-hydroxycholecalciferol)
  ↓ 1α-hydroxylase (kidney)
  Cholecalcifrol (active form)
  or
  (1, 25-dihydroxycholecalciferol)

kidney

GIT

Bone

Absorption of
Ca²⁺ and Po₄³⁻

Bone mineralization

Growth plate mineralization:
- Composition of growth plate -
  - Chondrocytes
    ↓ hypertrophy
    Apoptosis (Ca²⁺, Po₄³⁻ required)
    ↓ mineralization
  - Diaphysis
  - Metaphysis
  - Growth plate

Vitamin D deficiency:
↓ Calcium → ↑ Parathyroid hormone 
  → stimulates → Normalisation 
  (PTH) Osteoclasts of Ca²⁺ 
  ↓ Loss of Po₄³⁻ 
  (↓ absorption in kidney and GIT)
Pathophysiology:–
1) ↓ mineralization → weak bones → deformities
2) Chondrocyte hypertrophy → widening at the end of long bones.

Clinical features:–
- Short stature
- In head – Cranial tubas: soft consistency of bones called
  “Ping pong” ball consistency
  - Wide opened anterior fontanelle
- In chest – Rachitic rosary (swelling at costochondral joints)
  - String of beads appearance
  - Harrison’s sulcus
- In Extremities:–
  - Upper → enlargement of the wrist.
  - Lower → Genu varum (Bowling of the legs) – mc
  - Genu valgum (knock knees)
  - Wind swept deformity (valgus + varum)

Investigations:–
- ↓ or normal Ca²⁺
- ↑ PTH
- ↓ PO₄³⁻
- ↑ ALP
- X-ray – mc – wrist
  - Changes: – ↓ Fraying
    - ii) Splaying
    - ii) Cupping

Diagnosis:–
- ↓ as hydroxy cholecalciferol (as (OH)₂ D₃)
- Cholecalcitriol → cannot be measured in lab.
Treatment:

Dose: 3-6 lakh IU → stoss therapy (oral or intramuscular) or
2000 IU/day x 12 weeks (preferred nowadays)

After 4 weeks of completing treatment
repeat x-ray
if responding
Show - Healing white line of rickets
if not responding
refractory rickets

Refractory rickets:

- Conditions associated -
  1) Hypophosphatemic rickets
  2) Vit D dependent rickets
  3) CKD associated - Hyperphosphatemia.
  4) RTA associated (Renal tubular acidosis)
     → Proximal / distal - associated acidosis.

Hypophosphatemic rickets:

Normally → FGF-23 → inhibits renal tubular absorption of $p_{o_{5}}^{2-}$
Lost in urine ($p_{o_{5}}^{2-}$)
Causes hypophosphatemia.

Phex gene → endopeptidase
lyses
FGF-23
Prevents hypophosphatemia.

1) X - linked dominant condition - Defect Phex gene → cause.
   hypophosphatemia - mc cause of inherited rickets.

2) Autosomal dominant condition - Resistance to action of
   endopeptidase

3) ↑ Production of FGF-23 → in Benign mesenchymal bone tumors.
Vitamin D dependent rickets
- Two types: Type I
  - Deficiency of 1α-hydroxylase
Type II
  - Defect of receptor for vitamin D

Vitamin E
- Most powerful antioxidant
- Deficiency - mc in preterm ➔ Hemolysis, posterior column defects

Vitamin K
- Activates clotting factors - II, VII, IX, X
- If given as prophylaxis ➔ prevents ➔ Hemorrhagic disease of newborn (HDN)
  - Early / classic onset (Day 1-14)
    - Risk factor - home delivery
    - Site:
      - GI tract
      - Bleeding from umbilical stump
  - Late onset (2-12 weeks)
    - Severe form of bleeding e.g. intracranial bleed
    - Cause:
      - Malabsorption
      - Severe liver dysfunction (neonatal cholestasis)

- If HDN occurs at / soon after birth
  - due to maternal intake of drugs like: warfarin, phenytoin
WATER SOLUBLE VITAMINS & TRACE ELEMENT DISORDERS

Vitamin C Deficiency

- Deficiency: Scurvy
  [Common in children consuming pasteurized milk]
- Role of vitamin C:
  Maturation of Collagen
  Skin  Blood vessels  Bone
  (Formation of osteoid matrix)
- Features of Scurvy (due to defect in collagen):
  1. Bleeding:
     - Bleeding gums
     - Subperiosteal bleeding
     Pseudoparalysis
     [Child adopts a frog-leg posture]
     Hip, Knee: flexed
     Foot: rotated outwards
     - Perifollicular bleeds.
  2. Rosary in chest:
     - Sharp/angled enlargement at the costochondral junction
     - Painful lesions
     [DD: Rickets - round and painless lesions at costochondral junction]
- X-ray features:
  D osteoid matrix, Normal mineralisation
  1) Pencil thin cortex
  2) Frenkel's line: calcification at the end of long bone
  3) Trümmerfeld's zone: radiolucent zone below the Frenkel's line
  4) Wimberger's sign: Ring shaped calcification
  5) Pelkin's spur/fracture: Small portion of the bone gets detached at the end.
Other Water Soluble Vitamin Deficiency

i) Thiamine ($B_1$) deficiency:
   - Deficiency known as Beri beri
   - Common in population consuming polished rice

   Beri beri
   ↓
   Wet
   Cardiac edema
   ↓
   Dry
   - No edema
   - Neurological manifestation
     - Neuropathy

   - In infants: Wernicke's encephalopathy
     ↓
     Triad: Confusion, Ataxia, opthalmoplegia.

ii) Riboflavin ($B_2$) deficiency:
    Characterised by
    - Recurrent oral ulcers
    - Stomatitis, cheilitis, glossitis
    - Corneal vascularisation

iii) Niacin ($B_3$) deficiency:
    - In association: 1) maize based diet
      a) Hartnup's disease
      b) Carcinoid syndrome

    - Classical manifestation: Pellagra (40's)
      - Diarrhoea
      - Dermatitis: Sun exposed areas - Casal's necklace
      - Dementia
      - Death

iv) Pyridoxine ($B_6$) deficiency:
    1) Peripheral neuropathy
    2) Refractory neonatal seizures
Trace Elements Disorder

(i) Selenium

- Deficiency
  - Keshan's Cardiomyopathy
  - Kashin-beck's Endemic osteochondropathy

- Selenium excess: Garlicky odour, metallic taste

(ii) Copper Disorder:

<table>
<thead>
<tr>
<th>Wilson's</th>
<th>Menke's</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive</td>
<td>X-linked recessive</td>
</tr>
<tr>
<td>ATP 7B gene</td>
<td>ATP 7A gene</td>
</tr>
<tr>
<td>odourless, lustreless, brittle hair (Menke's kinky hair disease)</td>
<td></td>
</tr>
</tbody>
</table>

(iii) Zinc

- Functions of Zinc
  - Somatic growth
  - Gonadal growth
  - Hair growth
  - Wound healing
  - Epithelialisation of GIT

- Deficiency
  - Short stature
  - Delayed puberty
  - Alopecia
  - Delayed wound healing
  - Diarrhoea

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.
- Acrodermatitis enteropathica:
  - Severe form of zinc deficiency
  - Seen in infants
  - Autosomal recessive disorder (zinc transport)
  - SCL 39A4 gene is affected.
  - Manifestations:
    * Recurrent diarrhoea
    * Skin - periorificial symmetrical rash.
BASIC GENETICS

Types of genetic disorders

1. Chromosomal (MC type)
2. Single gene disorders
   - Cystic fibrosis
   - α - 1 Anti trypsin deficiency
3. Non-mendelian inheritance
   a) Mitochondrial inheritance
   b) Trinucleotide repeat disorders
   c) Genomic imprinting
4. Multifactorial inheritance
   a) Congenital heart diseases
   b) Neural tube defects
   c) Cleft lip / palate

Pedigree

- Family tree
- Indicates pattern of inheritance

Basic symbols:
- Δ - Miscarriage / Abortion
- ■ - Proband
  (First person to come to medical attention)
- ○ - Autosomal carrier
- ○ - X-linked recessive carrier
- △ - Dizygotic twins
- △ - Monozygotic twins

Rules to identify inheritance pattern:
1) At least 1 parent of diseased child is affected → Dominant inheritance
2) Parents unaffected (carriers), child affected (diseased) → Recessive
3) Males and females equally affected → Autosomal
4) Father affected, all daughters affected → X-linked dominant
   only males affected → X-linked recessive
5) Affected mother, all children affected (irrespective of gender) → mitochondrial inheritance.

   only ovum contributes mitochondrial DNA

   eg:

   a) All generations affected → dominant.
   males & females affected → autosomal.

   Dominant inheritance

   b) Child affected, parent unaffected → recessive.
   Both genders affected → autosomal.

   Recessive inheritance.

   c) All generations affected → dominant.
   Father affected, daughters affected → X-linked.

   X-linked

**Autosomal dominant disorders**

- Dominant job hunting
- Dystrophia myotonica
- Osteogenesis imperfecta
- Marfan's syndrome
- Intermittent porphyria (AIP)
- Noonan's syndrome
- ADPKD, Achondroplasia
- Neurofibromatosis
- Tuberous sclerosis
- Job's syndrome (Hyper IgE syndrome)
- Huntington's chorea.
Autosomal recessive disorders

- A - Albinism
- B - β - thalassemia
- C - Cystic fibrosis
- D - Deafness (SNHL)
- E - Emphysema (α - 1 antitrypsin deficiency)
- F - Friedreich ataxia
- G - Galactosemia
- H - Homocystinuria
- S - Sickle cell anemia

X - linked recessive disorders

- Butcher’s father had a beautiful gold watch.
- Bruton agammaglobulinemia
- Fabry disease
- Hunter’s disease / Hemophilia A and B
- G6PD deficiency
- Ocular albinism
- Lesch - Nyhan syndrome.
- Duchenne muscular dystrophy
- Wiskott - Aldrich syndrome
- **X - linked recessive : Only in males.**

X - linked dominant disorders

- X - linked (Familial) hypophosphatemic rickets
- Incontinentia pigmenti

Non - mendelian inheritance

- **Mitochondrial disorders:**
  - mother affected, all children affected
    1. MELAS : mitochondrial encephalopathy, lactic acidosis, stroke - like episodes
    2. MERRF : myoclonic epilepsy with ragged red fibres
  3. NARP : Neuropathy Ataxia Retinitis pigmentosa
  4. LHON : Leber’s Hereditary optic Neuropathy
Trinucleotide repeat disorders:

- Fragile X syndrome: CGG repeats
- Myotonic dystrophy: CTG
- Huntington’s disease: CAG

Genomic imprinting disorders:

Genomic imprinting: Out of a gene copies, only 1 is expressed.
- Deletion of expressed gene
  - No active gene
  - Genomic imprinting disorder

Eg: Deletion of Chromosome 15

Prader-Willi syndrome (Paternal chromosome deletion)
- Obesity
- Hypogonadism
- Small hands/feet
- Almond shaped eyes

Angelman syndrome (Maternal chromosome deletion)
- Severe intellectual disability
- Ataxia
- Uncontrolled seizures
- Inappropriate laughter
  - Happy puppet
GENETIC DISORDERS

Trisomy 21

- a/ k/a Down’s syndrome
- In 95% cases, cause: Maternal Meiotic non disjunction
- 4% cases: Robertsonian translocation (Acrocentric translocation)
- 1% cases: Mosaicism.
- Features:
  - Face: Mongoloid slant of eyes
  - Iris - Brushfield’s spots
  - Epicanthal folds
  - Flat facies
  - Brachycephaly
  - Low set ears
  - Protruding tongue - due to small mandible
- Hands: Simian crease (single transverse crease)
- Foot: Sandal gap
- Internal association:
  1) Congenital heart defect (MC - endocardial cushion defect)
  2) GIT - MC - Atresia (MC - duodenal atresia)
     - Other - Anular pancreas, Hirschsprung disease.
  3) Congenital hypothyroidism
  4) Tumors (MC - Acute lymphoblastic leukemia) - in children < 3 yrs
  - MC is Acute myeloid leukemia (AML - M)
  5) Presenile Alzheimer’s Disease
  6) Atlanto axial / Atlanto occipital subluxation
     - Have low IQ
     - Hypotonia seen in newborn period itself.

Antenatal diagnosis of Down’s syndrome:
- USG - Nuchal thickness > 3 mm
- Markers - FAPP - A (Pregnancy Associated) → ↓
  - Plasma Protein - A]
    - β - hCG → ↑
    - AFP (Alpha fetoprotein) → ↓
    - Unconjugated estriol → ↓
    - Inhibin A → ↑

Double test: done at 1st trimester. PAPP-A + β hCG
Triple test: β hCG + AFP + unconjugated estriol
Quad test: β hCG + AFP + unconjugated estriol + Inhibin A 3rd trimester
**Karyotyping:**
- Best way to identify Down’s during antenatal period
- Done by: Chorionic villous sampling, Amniocentesis (has risk of fetal miscarriage)

**CFF - DNA (Cell free fetal DNA sequencing):**
- Non invasive prenatal testing (NIPT)
- Sample collected from maternal circulation

**Recurrence:**
- In maternal meiotic non disjunction → 1%
- Advanced maternal age → 4%
- Robertsonian translocation → 7 - 10%
  - t(14;21)
  - t(21;13)
  - t(21;11)

**Trisomy 18**

- **K/ a. Edward syndrome**
  - 21st mc trisomy
  - Rocker bottom feet
  - Due to prominent calcaneum
  - Overlapping fingers
  - Microcephaly with prominent occiput
  - Risk of congenital heart disease (CHD) → VSD, ASD

**Trisomy 13**

- **K/a. Patau syndrome**
  - Associated with highest incidences of CHD
  - Features:
    - Polydactyly
    - Aplasia cutis
    - Terrible face (cleft lip / palate)
    - Anomalies of heart (80% → CHD)
    - Urinary (renal) anomalies
Turner's syndrome

- Absent X in females
- Genetic makeup 45 XO, seen only in girls, IQ is normal

- Features:
  - Short neck, web neck
  - Broad (Shield) chest
  - CHD (MC - Bicuspid aortic valve > Coarctation of Aorta)
  - Streak ovaries
  - Universal feature - Short stature
  - In neonatal period → associated with lymphedema of hands and feet
  - PS: if lymphedema in neck - Cystic hygroma
  - Widely spaced nipples

Noonan syndrome:

- Autosomal dominant
- Seen both in boys and girls
- PTPN 11 defect
  (Protein Tyrosine Phosphatase Non receptor) gene.
- Low IQ
- CHD associated: Pulmonary stenosis, Hypertrophic obstructive cardiomyopathy, Atrial septal defect.
- Girls → delayed puberty
- Boys → Cryptorchidism

Klinefelter syndrome

- Seen in males
- Genetic makeup 47 XXX
- Features:
  - Small undescended testis
  - Testosterone → Aromatase, Estrogen, hence develop feminine character – Gynaecomastia, feminine pubic hair, delayed puberty, tall stature, infertile due to azospermia.

Fragile x syndrome

- mc inherited condition with low IQ (Intellectual disability)
- Trinucleotide repeat → CGG
- X-linked recessive
- Defect - Fmr 1 gene
- Features:
  - Elongated face - large ears
  - Prominent chin
  - Macro - orchidism
  - Low IQ
  - ↑ Autism

Anticipation - onset of features of disease at an early age in the next generation.
DISORDERS OF CARBOHYDRATE METABOLISM

Galactosemia

- It is due to the deficiency of following enzymes:
  i) Galactokinase
  ii) Galactose-1-phosphate uridylyl transferase (GALT) - MC - classic variety
  ii) Epimerase
- C/F starts with introduction to breast milk (Lactose is present)
- C/F - In Liver - neonatal cholestasis
  In Eye - 'oil drop' cataract
  In Kidney - Acute tubular necrosis
- E. coli → cause of sepsis (associated with death)

Hereditary fructose intolerance

- It is due to deficiency Aldolase & enzymes
- C/F - starts after 6 months (Complementary feed → fruits have Fructose)
- Clinical manifestations are similar to Galactosemia → except Cataract.

Glycogen storage disorders (GSD)

Liver

- During fasting state
  Glycogen (stored) → Glucose
- C/F - fasting hypoglycemia
  Hepatomegaly

Muscle

- During exertion
  Glycogen → Glucose
- C/F - exertional fatigue
Types of GSD:
- Liver GSD MC than muscle GSD

<table>
<thead>
<tr>
<th>Liver</th>
<th>Muscle</th>
</tr>
</thead>
</table>
| • Type I - von Gierke disease  
  (Glucose-6-phosphatase deficiency)  
  mc type - overall |
| • Type III - Cori’s disease  
  (Branching enzyme deficiency)  
  It can involve muscle |
| • Type IV - Andersen disease  
  (Debranching enzyme deficiency)  
  C/F - Cirrhosis  
  (Not hepatomegaly)  
  Bad prognosis |
| • Type VI - Her’s disease  
  (Liver phosphorylase deficiency) |
| • Type II - Pompe disease  
  (Acid maltase / α-glucosidase deficiency) |
| • Type IV - mc Ardle disease  
  (Muscle phosphorylase deficiency)  
  mc type in muscle |
| • Type VII - Tarui’s disease  
  (Phosphofructokinase deficiency) |

Von Gierke disease

- Glucose - 6 - phosphate → Glucose ↓  
  × Glucose-6-phosphatase deficiency  
  Alternate pathway
  | Pentose phosphate Pathway (PPP) |
  | ↓ Ribose - 5 - phosphate |
  | ↓ Purine |
  | Uric acid |

- C/F - i) Round “doll-like” facies  
  ii) Hypoglycemia (Fasting)  
  iii) Hepatomegaly  
  iv) Hyperuricemia  
  v) Lactic acidosis  
  vi) Hyperlipidemia
• Treatment:
  i) Frequent feeding
  ii) Uncooked Starch (Slow release of glucose over 6 - 8 hrs) -
      in the night time.

Pompe's and Mc Ardle disease

Pompe's disease:
  • α-glucosidase enzyme deficiency
  • It affects skeletal muscle and cardiac muscle

  ↓
  Cardiomyopathy
  (Due to glycogen accumulation)
  ↓
  Cardiac failure

• Treatment:
  ↓ Enzyme replacement therapy

Mc Ardle disease:
  • Mc type of muscle GSD.
  • C/F:
    i) Exertional fatigue.
    ii) Muscle cramps
    iii) ↑Creatinine kinase levels (Due to necrosis of muscles)
    iv) Myoglobinuria (Myoglobin in urine)
DISORDERS OF PROTEIN METABOLISM

Suspect: sick newborn

↓

1st suspect: sepsis
↓ if ruled out

Suspect: IEM (Inborn errors of metabolism)

Sick newborn

↓

Ammonia levels

↓

High

↓ ABG

↓

ABG: Normal
Ammonia: high

↓ Urea cycle defect

↓ Organic acidemia

↓ Normal

↓ ABG

↓

Aminoacidopathies

Aminoacidopathies - Phenylketonuria

Phenylketonuria:

Normally: Phenylalanine \( \xrightarrow{\text{Phenylalanine hydroxylase}} \) Tyrosine

Phenylketonuria: deficiency of phenylalanine hydroxylase

↑ Phenylalanine \( \xrightarrow{\text{phenylalanine hydroxylase}} \) ↓ tyrosine

- metabolites of phenylalanine
  - Phenylacetate ⇒ mousy/musty odour urine
  - Phenyllactate
  - Phenylpyruvate
- ↑ Phenylalanine: Toxic to brain - microcephaly
  - Low IQ
  - Seizures
• ↓ tyrosine → ↓ melanine (Skin: fair / blonde, Sclera)

Treatment: Low phenylalanine diet
- Tetrahydrobiopterin (BH₄) - cofactor for phenylalanine hydroxylase
- Sapropterin (synthetic BH₄)

Alkaptonuria

- Tyrosine metabolic pathway
  Tyrosine
  ↓ Aminotransferase
  4 - OH phenylpyruvate
  ↓ Dioxygenase
  Homogentisic acid
  ↓ Homogentisic acid oxidase
  Maleylacetoacetic acid
  ↓ Isomerase
  Fumarlylacetooacetic acid
  ↓ Fumaryl acetooacetate hydrolase
  Fumarate
  ↓ Acetoacetate

Causes: deficiency of homogentisic acid oxidase
- ↑ Homogentisic acid
  ↓ Alkaptonuria

Features: Black urine
- Black pigment deposits
  - Sclera / Pinna
  - Synovium (Ochronosis)

Treatment:
- Nitisinone - inhibits dioxygenase
- Vitamin C supplement - Prevents ochronosis

Tyrosinemia:
- 3 types - 1) Type 1, Type II, Type III tyrosinemia.

1) Type I tyrosinemia:
  - Cause: ↓ Fumarylacetooacetate hydroxylase
    - ↑ Fumaryl acetooacetate
    - ↓ enters alternate pathway
    - ↑ Succinylacetone

Urine colour

Pediatrics • v2.0 • Marrow 4.0 • 2020 • AV
• Diagnosis: ↑ excretion of succinyl acetone
• Toxicity: liver, nerves, kidney
• Also known as hepatorenal tyrosinemia
• Treatment: Nitisinone

(i) Type II tyrosinemia:
• Cause: ↓ Aminotransferase
• Features: Palmoplantar Keratoderma
  : Corneal ulcer / erosions

Homocystinuria

• Cause: ↓ Cystathionine B synthase
• Features: Similar to marfan’s syndrome * Tall stature
  * Long slender fingers
  * Lens dislocation

<table>
<thead>
<tr>
<th></th>
<th>Homocystinuria</th>
<th>Marfan’s syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Autosomal recessive</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td><strong>IQ</strong></td>
<td>Inferior</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Lens dislocation</strong></td>
<td>Joint stiffness</td>
<td>Superior</td>
</tr>
<tr>
<td><strong>Joints</strong></td>
<td></td>
<td>Ligament laxity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(: ↑ Range of movements)</td>
</tr>
</tbody>
</table>

• More prone to recurrent stroke due to thromboembolism
• Treatment: Betaine, Vitamin B₆

Urea cycle defects

Cause: Hyperammonemia
↓
Cerebral edema

Treatment:

↓ excretion of ammonia
  - Sodium benzoate / Phenyacetate
↓ Production / ↓ release of ammonia from liver
  - L - Arginine
Disorders:
1. Ornithine transcarbamylase (OTC) defect
   - Most common
   - X-linked disorder
2. Carbamoyl phosphate synthase (CPS) - 1 defect
   - Most severe

Investigations:
- Urine orotic acid: ↑ OTC defect
- ↓ CPS - 1 defect

**Organicacidemia**

Disorders: Isovaleric acidemia.
Propionic acidemia.
MSUD (maple syrup urine disease)
Multiple carboxylase deficiency

Features: Acidosis, Ketosis
- Lactate level
  - Increased
    - Multiple carboxylase
      * Skin rash (+) (Perioral)
      * Alopecia (+)
    - Other acidemia
  - Normal
    - MSUD

- Propionic: * Sweaty feet odour
- Isovaleric

**Maple syrup urine disease**

- Cause:
  - Branched chain amino acid (BCAA) metabolism defect
  - Complex - (Branched chain Keto acid) BCKA dehydrogenase defect
  - Normally, BCAA (Valine, Isoleucine, Leucine)
    - ↓ BCAA aminotransferase
    - BCKA dehydrogenase
    - Acyl CoA derivatives
- Features:
  - Cerebral edema
    \[ \text{↑ BCKA ⇒ inhibits kreb's cycle} \]
    \[ \downarrow \text{↓ ATP ⇒ Na, K ATPase} \]
    \[ (\text{Intracellular Na}^+, \text{H}_2\text{O accumulation}) \]
    \[ \downarrow \text{Cerebral edema} \]
  - Cerebral depression
    \[ \text{↑ Leucine ⇒ inhibits tyrosine, tryptophan} \]
    \[ \downarrow \text{Cerebral depression} \]
  - Maple syrup odor
    \[ \text{↑ Isoleucine ⇒ Sotolone} \]
    \[ \downarrow \text{urine : maple syrup (Caramel odour)} \]
- Investigations = Yellow white precipitate
  - BCKA + 2, 4 DNP (Chimotryphyl hydrazine) reagent
    \[ \downarrow \text{Yellow white precipitate} \]
LYSOSOMAL STORAGE DISORDERS

- Hepatosplenomegaly is a common feature of all the lysosomal storage disorders.

**Gaucher's disease**

- **m. c. type**
- **Deficiency of glucocerebrosidase.**

**Features:**
1. **CNS:** microcephaly, seizures, developmental delay.
2. **Hepatosplenomegaly.**
3. **Skeletal:** expansive lytic bone lesions.
   - At end of long bones
   - Cause pain / pathological fractures
   - Erlenmeyer flask deformity on x-ray
   - Pancytopenia
4. Crumpled / wrinkled tissue paper appearance (characteristic feature)

**Treatment:**
- Enzyme replacement therapy.

**Niemann - Pick disease**

- **↓ Sphingomyelinase**

**Features:**
- Neurological manifestations (seizures, microcephaly)
- Hepatosplenomegaly.
- Cherry - red spots.
- Splenic aspirate.
Nucleus pushed to periphery
- Foamy appearance / Foam cell appearance

Treatment:
- Enzyme replacement therapy

D/D for cherry red spot:

Cherry trees never grow tall in sand.

CRAO:
- Trauma (Berlin's edema)
- Neuramin - pick disease
- GM1 gangliosidosis (β 1 galactosidase deficiency)
- Tay - Sach's disease (Hexosaminidase A deficiency)
- Sandhoff's disease (Hexosaminidase A & B deficiency)

Fabry disease

- ↓ α - galactosidase
- Features:
  - Angiokeratomas (vascular swellings in skin)
  - Below umbilicus to knee → Bathing trunk area
  - Painful neuropathy
  - Corneal erosions
  - Maltese cross appearance in urinary sediment

Treatment:
- Enzyme replacement therapy

Mucopolysaccharidosis (MPS)

Types:
- MPS I: Hurler's disease
  - Scheie's
  - Hunter's disease
  - Sanfilippo
  - Morquio
  - Maroteaux - lamy
  - Sly

Enzyme deficiency:
- α - Iduronidase
  - Iduronate sulphatase
  - Heparin sulfamidase
  - N-acetyl galactosamine sulfatase
  - Aryl sulphatase - B
  - P - glucuronidase
- **m.c. type**: Type III
- I, II & VI types: Enzyme replacement therapy

Features:

1. Abnormal facies:
   - Broad forehead
   - Flat nasal bridge
   - Upturned nose
   - Cloudy cornea

- Cloudy cornea - Absent in Hunter's disease
  (X - linked recessive)
  [Rest are autosomal recessive]

2. Skeletal lesions: Dysostosis multiplex
   - Bullet shaped metacarpals
   - Beaking of vertebrae
- Marked in type IV

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.
COMMON VIRAL INFECTIONS

Measles

Clinical manifestations:

Prodromal phase
- fever
- 3 'c'- cough
- coryza
- conjunctivitis

On Day 2
- KOPLIK SPOTS appear
  (Sandlike lesions surrounded by redness)

On Day 4
- Rash appears
  (maculopapular rash),
  behind the ears 1st and face and spreads down.

On Day 8
- Rash starts disappearing and leaves
  behind brownish
  Pigmentation.

Complication:

Acute
- MC - otitis media
- Most severe - Pneumonia
deue to secondary bacterial infections
- Pneumonia caused by measles virus - Hecht pneumonia,
  (less common).

Chronic
- SSPE (subacute Sclerosing Pan Encephalitis)
- Myoclonic seizures
Varicella

- On day 1 - fever
  - Vesicle initially appear on trunk
  - Dew drops on a rose petal appearance (vesicle filled with clear fluid and surrounded by redness)
  - Pleomorphic vesicles (different sizes of the vesicles)

- MC complication: Secondary bacterial infections
- It can spread from mother → fetus by two ways:
  - Intrauterine
  - Perinatal
    - Affects the baby during development
    - Has severe clinical presentation
      - i) Limb hypoplasia
      - ii) Scar skin - CICATRIX
    - MC mode of spread
    - At risk period:
      - If mother gets infected within 5 days before delivery
      - 2 days after delivery

Rubella

Clinical feature → fever
  - Rash (similar to measles), present between day 0 – 3 days
  - Cervical lymphadenopathy - Occipital lymphadenopathy posterior lymphadenopathy
In pregnancy (1st trimester) - severe
   → Triad- Cataract, (MC - salt and pepper retinopathy)
       Sensorineural deafness
       Congenital heart defects - MC - ARVD, other → PS
       VSD

Late onset complications- i) Progressive Rubella Panencephalitis
                          (PRP)
       ii) Type 1 Diabetes mellitus
            iii) Thyroiditis and hypo thyroidism.

Exanthema subitum and erythema infectiosum

1) Exanthema subitum
   a) a/Ka Roseola infantum
   b) Caused by HHV-6/HHV-7
   c) Characteristic feature: Rash appears only after fever subsides

<table>
<thead>
<tr>
<th>Fever (-)</th>
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<tbody>
<tr>
<td>0 3 4</td>
</tr>
<tr>
<td>Fever (+)</td>
</tr>
<tr>
<td>Rash (+)</td>
</tr>
</tbody>
</table>

   It has strongest association with febrile seizures.
   Exanthem - Presence of red coloured lesions in /u/ula /palate -
               called Nagayama spots.

2) Erythema infectiosum :
   a) Caused by parvovirus B19
   b) C/F- Erythema (flushing) over cheeks called slapped check
      Spreads to extremities
      Central clearing (Lacy / Reticulate pattern)
Complications:
- Aplastic crisis $\rightarrow$ Suppression of bone marrow
- Arthralgia $\rightarrow$ in adolescent and adults
- In pregnancy - Hydrops fetalis

Cytomegalovirus and toxoplasmosis

<table>
<thead>
<tr>
<th>Cytomegalovirus (CMV) infection</th>
<th>Toxoplasmosis infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ risk of transmission in 3rd trimester</td>
<td>↑ risk of transmission in 3rd trimester</td>
</tr>
<tr>
<td>No clinical manifestations</td>
<td>C/F - Chorioretinitis</td>
</tr>
<tr>
<td>MC TORCH infection</td>
<td>- Intracranial calcification</td>
</tr>
<tr>
<td>If affected in 1st trimester</td>
<td>(Diffuse calcification)</td>
</tr>
<tr>
<td>C/F - microcephaly</td>
<td>- Hydrocephalus</td>
</tr>
<tr>
<td>Low IQ</td>
<td>Prevention: Spiramycin of transmission</td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>Intracranial calcification</td>
</tr>
<tr>
<td>(Periventricular calcification)</td>
<td></td>
</tr>
</tbody>
</table>

Mumps

- Painful enlargement of - Parotid (unilateral/bilateral)
  - Ear lobe pushed upward and outward
  - Sublingual and submandibular glands.
- Isolation: Till swelling has subsided.
Complications:-
- MC - Aseptic meningitis
- Orchitis - in postpubertal age group (never leads to infertility, but can be associated with pancreatitis, oophoritis - in females).

Hand Foot Mouth disease (HFMD)

- Occur in children < 6 years.
- Highly contagious
- Characterised by papulo-vesicular lesions of hand, foot and mouth.
- Can also involve buttocks / genitals.
- Caused by - Coxsackie virus A16, Enterovirus 71
- Self limiting condition, resolves by 4-5 days.

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COMMON BACTERIAL INFECTIONS

Scarlet fever

- Caused by - Group A,B hemolytic streptococci
- C/F - fever
  - Sore throat (Pharyngitis) + Strawberry tongue
  - Rash called “Sandpaper rash”
    - Appears on day 2 of illness
      - Starts in face palms and spreads downwards
      - Sares palms and soles
      - Pastia’s lines (rash becomes concentrated and
        Forms lines)
- Treatment - Penicillin for 10 days

Diphtheria and pertussis

1. Diphtheria.
   - Incubation period - 2-4 days
   - Three forms of diphtheria - pharyngeal (mc)
     - Laryngeal - brassy cough
     - Nasal - serosanguinous nasal
discharge.

- Pharyngeal form
  C/F - Sick looking
  - High grade fever
  - Sore throat → Pseudo membrane - adherent
    - Necrosis + exudates caused by diphtheria toxin
  - Enlarged cervical lymph nodes - “bull neck” appearance.
Treatment:
- Penicillin/Erythromycin (if allergic to penicillin)
- Diphtheria antitoxin
- After treatment → give active immunisation (DPT vaccine)

2. Pertussis
- Caused by - Bordetella pertussis/para pertussis
- Incubation period - 1-2 weeks
- C/F:

<table>
<thead>
<tr>
<th>Catarrhal Phase</th>
<th>Paroxysmal Phase</th>
<th>Convalescent Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 weeks</td>
<td>2-6 weeks</td>
<td>&gt; 6 weeks</td>
</tr>
<tr>
<td>Highly infectious</td>
<td>Whooping cough</td>
<td></td>
</tr>
</tbody>
</table>

- Antibodies against Pertussis are not transferred from mother to fetus.
- If Pertussis occurs in child < 6 months - Whooping cough (−)
  - Recurrent apnea
  - ↑ Risk of mortality
- Locht - Nasopharyngeal Swab
- Treatment - Macrolides (Azithromycin preferred, Erythromycin → Pyloric stenosis S/E).
Congenital Syphilis

Early onset (< 2 yrs)
- Rash (copper coloured)
  - Involves palms and soles
- Hepatosplenomegaly / lymphadenopathy
- Osteochondritis / Periostitis
  (Pseudoparalysis)
- Snuffles (excessive rhinitis
  Causing continuous discharge)

Late onset (> 2 yrs)
- Hutchinson's triad:
  - Hutchinson teeth
    (Notched incisors)
  - Interstitial Keratitis
    (Deafness)
- Mulberry molars
- Rhagades (Fissure
  around mouth)
- Saber shin
  (Bowing of tibia)
- Clutton's joint
  (Painless joint swelling
  → Knee)
- Saddle nose
  deformity.

Diagnosis:
- VDRL / RPR test
TB AND HIV INFECTIONS: GUIDELINES

TB suspect:
- Fever and/or cough > 2 weeks
- Weight loss (OR) no weight gain
- Contact with case of active TB.

Evaluation: Manoux test.

Chest X-ray.

Chest X-ray findings:
1. Primary complex: Subpleural focus of consolidation + draining
   Lymphatics + enlarged hilar lymph nodes.
2. Miliary shadows
3. Cavities
4. Pleural effusion.

Chest X-ray

Suggestive of TB

Confirmatory tests

Non-suggestive

Antibiotics for 7-10 days

Reassess.

Confirmatory tests:
Specimen: Sputum
- Gastric aspirate (early morning sample)
  → in young children.
Tests: AFB staining
- Culture: Mycobacterial growth indicator tubes (MGIT)
- Rapid test: CENFATT (cartridge based nucleic acid
  amplification test)
  → detect rifampicin sensitivity

Treatment guidelines

<table>
<thead>
<tr>
<th>Category</th>
<th>Intensive Phase</th>
<th>Continuation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>2 HRZE</td>
<td>4 HRE</td>
</tr>
<tr>
<td>[New cases]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R&lt;sub&gt;x&lt;/sub&gt; duration: 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category II</td>
<td>2 HRZES + 1 HRZE</td>
<td>5 HRE</td>
</tr>
<tr>
<td>R&lt;sub&gt;x&lt;/sub&gt; duration: 8 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Baby born to TB +ve mother

- **MC mode of spread:** postnatal
- Breastfeeding can be continued.
- Mothetrs not taking ATT
  - or
  - Taken ATT < 2 weeks \{ Direct breastfeeding is contraindicated \}

- **Isoniazid** prophylaxis - for 6 months (total)
  - Reassess after 6 weeks
    - no signs / symptoms of TB
      - Continue INH
    - signs / symptoms of TB
      - confirm diagnosis
      - start ATT

- **BCG:** given after INH prophylaxis is completed.

Baby born to HIV +ve mother

- **Modes of spread:**
  - Intrapartum
  - Breastfeeding

- Breastfeeding: can be continued, not combined with formula feed (↑ risk of HIV)

**Diagnosis:**

1. **ELISA:** not recommended till 18 months
   - (maternal antibodies persist up to 18 months)
2. < 18 months:
   a) HIV - PCR (Best method)
      - (RNA + proviral DNA)
   b) P4 antigen
   c) Culture.
**Prophylaxis and treatment**

1. **Anti-retroviral therapy**:
   - Nevirapine
   - High risk cases: Add Zidovudine
     
     a) Mother not taking ART
     b) Mother taking ART < 4 weeks
     c) Newly diagnosed
     d) High maternal viral load
        (RNA > 1000 copies / ml)

2. **Cotrimoxazole prophylaxis**.
   - Against Pneumocystis infection.
   - Continued till HIV diagnosis is excluded, up to at least 6 weeks after stopping breastfeeds.

**Treatment**

- Once diagnosis is confirmed → All children treated.
- **HAART**: 2 NRTI + 1 NNRTI (or protease inhibitor)
  
  Zidovudine, Efavirenz, Lamivudine

- < 3 years of age: Lopinavir - Ritonavir used instead of Efavirenz
- Hb < 9 g/dl: Abacavir instead of zidovudine.
CONGENITAL ANOMALIES OF GIT

Tracheoesophageal fistula (TEF)
- most cases of is associated with esophageal atresia.
- Gross classification of TEF.

- Type C:
  → Proximal esophageal atresia + distal TEF
  → m/C type
- Type E:
  → Pure TEF

- Clinical features:
  - Polyhydramnios
  - Recurrent vomiting → Aspiration
  - Excessive frothy salivation
- X-Ray:
  - Coiling of nasogastric tube
  - VACTERL association:
    V → vertebral anomalies
    A → Anal atresia
    C → Congenital heart defects
    T → Tracheoesophageal fistula
    E → Esophageal atresia
    R → Renal anomalies
    L → Limb defects

IHPS
- Infantile Hypertrophic pyloric stenosis
- Hypertrophy: circular muscles in the pylorus region
- Erythromycin usage in 1st 2 wks after birth is associated with IHPS
- Features:
  - Recurrent non-bilious vomiting - 2 weeks after birth
  - ‘Olive shaped’ epigastric swelling (after vomiting)
  - vGP (visible gastric peristalsis)
**Diagnosis:**
- Based on ultrasound abdomen:
  -> Thickness of pylorus muscle > 4mm
  -> Canal length > 16mm

- When infant vomits:
  -> $H^+$, $Cl^-$ are cleared out -> Hypochloremic metabolic alkalosis
    
    Kidneys try to reabsorb $H^+$ in exchange for $H^+$ -> Hypokalemia

    Recurrent vomiting

    Hyponatremia with dehydration

    Paradoxical aciduria

- Treatment:
  -> Surgery: Ramstedt's pyloromyotomy

**Duodenal atresia**

- Bilious vomiting without abdominal distension.
- Classical finding: Double bubble sign (x-ray)
- Treatment: Duodeno-duodenostomy
- 30% of cases are associated with Down syndrome

**Meckel’s diverticulum**

- MC anomaly: 2% of world population
- Remnant of vitellointestinal duct
- Rule of 2:
  -> Size: 2 inches (5cm)
→ Location: A few centimeters from ileocecal junction
→ Lined by: A mixture of ectopic mucosa (gastric, pancreatic)
→ Blood in stool (painless) → currant jelly stool

→ Age: < 2 years
→ Incidence: 2 times more common in males
• 100: *99m* Tc - pertechnetate scan
  Pertechnetate has affinity for gastric mucosa (dark areas in the scan)
• Treatment: Diverticulotomy

**Hirschsprung’s disease**

• Aka. aganglionosis
• Gut motility disorder (causes constriction)
• M/C affected segment: Rectosigmoid
• Characteristic presentation:
  → Delayed passage of meconium
  - PR examination: Empty rectum
  - Rush of meconium on withdrawal of finger
  - Anorectal manometry: Failure of relaxation of internal anal sphincter
• 100: Rectal biopsy
  → Marker: Acetylcholine esterase
  → Hypertrophied nerve fibres
DIARRHOEA

Types:
- Acute Diarrhoea: < 7 days
- Persistent Diarrhoea: > 14 days
- Chronic Diarrhoea: > 14 days - Non Infectious Cause

Etiology:
- m<sub>e</sub> - Rota Virus
- m<sub>e</sub> - bacteria associated with diarrhoea in children
  ETEC (Entero Toxigenic E. Coli)
- Dysentry - Blood in stools, m<sub>e</sub> cause - Bacterial
  Organism - Shigella Flexure
  Treatment - 3rd generation Cephalosporin

Assessment and management of dehydration

<table>
<thead>
<tr>
<th>Types of Dehydration</th>
<th>Features</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dehydration</td>
<td>loose stools</td>
<td>Plan A: ORS (10 - 20 ml/kg)</td>
</tr>
<tr>
<td></td>
<td>no other complaints</td>
<td>Everytime child passes stools, replace ongoing loss</td>
</tr>
<tr>
<td>Some Dehydration</td>
<td>intense thirstiness</td>
<td>Plan B: Replacement of ongoing loss + correct dehydration (75 ml/kg ORS over 4 hours) + Daily maintenance fluids</td>
</tr>
<tr>
<td></td>
<td>irritable child</td>
<td></td>
</tr>
<tr>
<td>Severe Dehydration</td>
<td>child is lethargic</td>
<td>Plan C: IV fluids (RL &gt; NS)</td>
</tr>
<tr>
<td></td>
<td>skin pinch =&gt; 2 sec</td>
<td></td>
</tr>
</tbody>
</table>

Daily maintenance fluid: Holiday - Segar formula.
- Tells us how much is the daily formula fluid for a child.
  \[
  \text{wt (kg)} \quad \text{fluid (ml/kg)}
  \]
  \[
  \begin{align*}
  0 - 10 & \quad 100 \\
  10 - 20 & \quad \oplus 50 \\
  > 20 & \quad \oplus 20
  \end{align*}
  \]

Plan C: In severe dehydration 100 ml/kg fluid is lost.
This fluid is replaced into 3 parts: first 30 ml, then 70 ml.

<table>
<thead>
<tr>
<th>Age</th>
<th>30 ml/kg</th>
<th>70 ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 yr</td>
<td>over 1 hr</td>
<td>5 hrs</td>
</tr>
<tr>
<td>&gt; 1 yr</td>
<td>over 1/2 hour</td>
<td>2.5 hrs</td>
</tr>
</tbody>
</table>
**ORS**

**Low osmolarity ORS by WHO**
- Total Osmolarity is 245 mmol/l
  - Na - 75 mmol/l, K - 20 mmol/l, Glucose - 75 mmol/l
  - Cl - 65 mmol/l, Citrate 10 mmol/l

Along with ORS, zinc supplementation is given.
- It promotes re-epithelization of GI tract.

Dose of zinc,

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 month</td>
<td>10mg/day</td>
</tr>
<tr>
<td>&gt; 6 month</td>
<td>20mg/day</td>
</tr>
</tbody>
</table>

**Persistent Diarrhoea**

- Diarrhoea of > 14 days with infectious cause
- Etiopathogenesis →
  - Common in children with malnutrition
  - Exclusive use of Antibiotics for long duration
  - Infections → Enterotoxigenic E. coli
  - Enterotoxigenic E. coli
  - Entero aggregatory E. coli
  - Crypto sporidium

\[ a^2 \text{ lactose intolerance} : \text{caused due to persistent diarrhoea.} \]

Persistent Diarrhoea → Sluffing of tips of intestinal villi

\[ \downarrow \]

↓ Lactase

\[ \downarrow \]

Lactose from milk gets converted to

\[ \downarrow \]

Lactic acid

\[ \downarrow \]

Perianal excoriation

\[ \downarrow \]

Gaseous stools

Diet advice →
- Low lactose / No lactose diet
  - milk soyj
  - milk cereal
  - Avoid milk

Pediatrics • v2.0 • Marrow 4.0 • 2020 • AV
OTHER GI DISORDERS

Gastroesophageal Reflux Disease (GERD)

- Presence of gastroesophageal reflux causing real problem in child
- Pathologic if child has:
  - Recurrent aspirations (recurrent respiratory pneumonitis)
  - Failure of thrive

Diagnosis:
- Esophageal pH monitoring - if pH < 4 for most period in 24 hrs suggests GERD
- Multichannel intraluminal impedance monitoring - new and better investigation

Treatment:
- Initially non pharmacological
  - Small frequent feeds
  - Thickening of the feeds
  - Positioning
    - When awake
    - Prone
    - While sleeping
    - Supine with minimal head end elevation

- If non pharmacological treatment fails pharmacological
  - PPIs (proton pump inhibitors) is the drug of choice
  - In refractory GERD → Surgery → Fundoplication

Foreign bodies in Esophagus

- In children < 3 years
  - me - coins, toys, batteries (dangerous)

If foreign body in esophagus is:
  - Blunts objects and asymptomatic
    - Observe for 24 hours
  - Impacted (> 24 hours)
    - Symptomatic (especially respiratory)
    - Battery ingestion

If foreign is:
  - Rx - immediate endoscopic removal
Acute intestinal obstruction

- mc cause of obstruction in children - Intussusception (Telescoping of one portion of the intestine into other portion of the intestine)
- mc site - ileo-colic
- Age group - 9 - 12 months → due to complementary feeds

Causes peyer's patch hypertrophy
(Acts as lead point, resulting in intussusception)

Clinical features :-
- Severe abdominal pain
- Vomiting
- Painful bleeding per rectum
  (Due to necrosis)
  ↓ If untreated
- Gangrene

Diagnosis :-
- USG - Abdoman → shows → Target sign (Donut sign)

Treatment :-
- USG - guided Reduction of intussusception
  → Air insufflation (safest method)
  → Water (hydrostatic reduction)
  → Barium

Celiac disease

- A / K / A gluten hypersensitivity (T cell mediated)
- Chronic inflammation of small intestine
- Chief substance: Gluten, Source: wheat (major)
- Common in wheat eating population
- Genetic association: HLA-DQA
  HLA-DQ8
- Other associated conditions: Type I diabetes mellitus
  Autoimmune thyroiditis
  Down and turner syndrome

Clinical features :-
- Chronic diarrhoea.
- Failure to thrive
• Anemia (Refactory anemia)
• Extra intestinal features:
  i) Dermatitis herpetiformis
  ii) Non Hodgkin's lymphoma (Cause of mortality)

Diagnosis:

Biopsy (or) Serology

↓

• Findings → Villous atrophy
  → Inflammatory cells ++
  → Crypt hyperplasia

• Sensitive → Anti tissue transglutaminase antibody
• Specific → Anti endomysial antibody (EMA)

* Investigation of choice - Biopsy
* Resolution of symptoms after stopping the gluten exposure for 12 weeks

Treatment:

• Life long restriction of gluten containing diet
• Diet to be avoided: Barley, Rye, Wheat, Contaminated oats

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.
LIVER DISORDERS

Inherited Hyperbilirubinemia:
   a) unconjugated hyperbilirubinemia -
      • Crigler Najjar syndrome
      • Gilbert syndrome
   b) Conjugated Hyperbilirubinemia -
      • Dubin Johnson syndrome
      • Rotor Syndrome

Crigler Najjar syndrome
- Autosomal recessive
- 2 types: 1) Type I:
   - Absence of UDP-GT (UDP - Glucuronyl Transferase)
   - Highly fatal disease in newborn
   - Management - intensive photo therapy or exchange transfusion
   - Liver transplant → good outcome
- 2) Type II:
   - Deficiency of UDP-GT
   - Treatment: Phenobarbital (induce UDP-GT)

Gilbert syndrome
- Main cause of inherited jaundice in children
- ↓ Level of UDP-GT
- Usually asymptomatic
- Jaundice developed during intercurrent illness
- No specific treatment required

Dubin Johnson
- Due to ↓ excretion of conjugated bilirubin into bile duct
- Liver biopsy show brownish black deposit in liver.
- No specific treatment required

Rotor
- ↓ Excretion of conjugated bilirubin into bile duct
- Liver biopsy is○
- Here ↓ storage capacity for binding anions in the liver
- No treatment required
Neonatal cholestasis

- ↑ Level of conjugated bilirubin
- Conjugated bilirubin > 1 mg/dl or > 20% total bilirubin
  It is known as conjugated hyperbilirubinemia

- Causes:
  - Extra Hepatic Biliary Atresia [ EHBA ] - mc condition
  - Neonatal Hepatitis :
    • Usually idiopathic
    • Sometimes a" to metabolic disorders → galactosemia,
      Tyrosinemia, α-antitrypsin deficiency
      ( mc metabolic disorder affecting liver )
    • a" to TORCH infection and Neonatal sepsis.
    • Genetic syndrome → Alagille syndrome :
      Neonatal cholestasis with Triangular facies, Pulmonic
      stenosis.
  - Liver biopsy show : lobule - disarray ; Inflammatory cells Θ,
    Hepatocellular necrosis Θ
  - It is suspected if neonatal jaundice persist > 2 weeks after birth
  - Features :
    • Clay coloured stools ( pale )
    • High coloured urine

- Investigations :
  • USG abdomen - Show fibrosis
    at the region of bile duct
    ↓
    " Triangular cord sign "
  • HIDA scan - only stains liver
    It is a screening test
  • Liver Biopsy - Shows bile
    ductular proliferation and bile
    accumulates but hepatic lobules normal

- Treatment :
  • Definitive - liver transplantation
  • Surgical - Kasai procedure
    a/k/a Hepaticojejunostomy

mc indication for liver transplantation in children → EHBA
Wilson's disease

- Autosomal recessive
- Defect in chr 13, codes for gene ATP7B → which codes for copper transporting ATPase
- This will ↓ Ceruloplasmin, causing ↑ levels of free copper.

- Manifestation:
  - Chronic liver disease (mc pediatric presentation)
  - Neuro psychiatric manifestation (mc adult presentation)
  - Kayser - fleischer rings at descememt membrane of cornea
  - Sunflower cataract
  - Coombs Negative Hemolytic Disease: hemolysis due to release of excess free copper from damaged hepatocytes (worst outcome)

- Investigations:
  - Screening test - Serum ceruloplasmin levels → ↑
  - Urine copper levels → ↑
  - Diagnostic test - Liver Biopsy
    - Findings: copper of > 250 mcg / gram of liver

- Treatment:
  - Chelating agent - D - Penicillamine, Trientine
  - Maintenance - Zinc (↓ GI absorption of copper)
  - Definitive - Liver transplantation

Portal hypertension

- Normal pressure in portal venous system venous system 5-10 mmHg
- In portal hypertension it is > 12 mm Hg
- Causes:
  - Extra hepatic portal venous obstruction (EHPVO)
    - In neonates: omphalitis
    - Older children: peritonitis, Hypercoagulable state (Protein C or S deficiency)
- Salient features: Liver size, Liver enzymes, LFT, Clinically no evidence of chronic liver disease
- Clinical features: Huge splenomegaly, Ascites, upper GI bleeding (due to esophageal varices)

- Management of esophageal varices:
  - Treat upper GI bleed - IV fluids, Vasopressin - Terlipressin
    - Somatostatin - Octreotide
    - Sengstaken Blackmore tube
  - Definitive Treatment - Endoscopic sclerotherapy
    - Methylene blue - Ethanolamine
CONGENITAL ANOMALIES OF RESPIRATORY SYSTEM

**Choanal atresia**

- Obstruction can be:
  1. Bony (90%)
  2. Membranous (10%)
- Symptomatic only if bilateral
- Classical condition associated with Choanal atresia: **Cyclical cyanosis** (when mouth is closed → Child tums irritable, cries → opens mouth → cyanosis disappears)
- Best investigation: HRCT
- Charge syndrome
  - Associated with choanal atresia
  - AD
  - CHD 7 gene affected
  - It represents:
    - C → Coloboma
    - H → Heart defects
    - A → Atresia (choanal)
    - R → Retardation (Growth)
    - G → Genital anomalies
    - E → Ear anomalies

**Laryngomalacia**

- m/C anomaly of larynx
- ‘malacia’ → softness
- Structures affected: Epiglottis (most), arytenoids, aryepiglottic folds
- **Omega (Ω) shaped epiglottis**
  - when a child lies in supine position → Airway narrows → Stridor
  - A/H/A congenital laryngeal stridor
  - Benign condition, improves with age
  - Excellent prognosis
  - Treatment: Reassurance
  - Resolution: 1 - 1/2 years
Dysgenesis

- Abnormal development
- Hypoplasia > aplasia.
- Common associations with pulmonary hypoplasia:
  1. Congenital diaphragmatic hernia
  2. Potter syndrome
  3. Asphyxiating thoracic dystrophy (Jeune's syndrome)

Congenital Pulmonary Airway Malformation (CPAM)

- Congenital pulmonary airway malformation
- Previously known as CCAM (congenital cystic adenomatoid malformation.)
- M/C cystic lung malformation
- X-ray features:
  - Many cyst like spaces in lung field
  - Closely resembles that of CDH (congenital diaphragmatic hernia.)

- In CDH, intestines enter the thoracic cavity
  - In CPAM → CLEAR diaphragm outline is seen
  - In CDH → clear diaphragm outline is not seen

Exit procedure

- Exutero Intrapartum Treatment
- Modified c-section. Incision made on abdomen
- After the head and shoulder delivery, airway of baby is secured
- Umbilical cord is not cut.
- Indicated for congenital anomalies causing severe airway obstruction.
Pulmonary sequestration

- 'Sequestration' ➔ Separation
- Can be:
  1. Intrapulmonary (↑ common)
     a. Extrapulmonary
- Sequestrated lung segment doesn't communicate with bronchus.
- Blood supply is from systemic blood vessels
- Venous drainage is into RA via IVC or PV
- Has tendency to cause recurrent infections
- Diagnosis: CT with contrast.

CLE

- Congenital Lobar Emphysema
- m/C: left lobe
PNEUMONIA

- Pneumonia in children can be:
  - Bacterial
    - m/C cause: Pneumococcus
    - Neonates: E.Coli > Group B Streptococci
    - Other organisms:
      → Staphylococcus aureus
      → Hemophilus influenzae
      → Atypical
        • Mycoplasma pneumoniae (m/C)
        • Chlamydia pneumoniae
  - Viral
    - m/C: Respiratory syncytial virus (RSV)

Revised WHO guidelines for diagnosis and management of pneumonia

- For management at community level:
  - Categories:
    → No pneumonia
      - Fever, cough, cold
    → Pneumonia
      - Fast breathing ±
        Chest indrawing (without hypoxia.)
      - Oral antibiotic: Amoxicillin
    → Severe Pneumonia
      - Chest indrawing (with hypoxia.)
        or
        One of the danger signs:
        → Not feeding
        → Lethargic
        → Cyanosis / convulsions
      - Refer to hospital immediately
Respiratory system

- Fast Breathing:
  - < 2 months: Respiratory rate > 60 / min
  - 2-12 months: Respiratory rate > 50 / min
  - > 12 months: Respiratory rate > 40 / min

X-Ray features

- Streptococcus pneumoniae → Lobar consolidation
- Staphylococcus infection
  → Microabscess formation → Pneumatocele (air containing cavity in lung)
  - Differential diagnosis of pneumatocele:
    1. Staphylococcus infection
    2. Klebsiella infection
    3. Hydrocarbon pneumonitis
→ Patchy consolidation
- Mycoplasma → Interstitial pattern (bilateral)
  Interstitial pattern is also associated with RSV

IMNCI

- Integrated management of Neonatal and Childhood Illness
- Colour coding:
  - Pink → Severe pneumonia.
  - Yellow → Pneumonia.
  - Green → No pneumonia.
- X-Ray:
  → Lobar consolidation
  → Probable organism: Streptococcus pneumoniae

Note:

X-Ray finding: Bilateral pattern of pneumonia.
Causative organism: Mycoplasma pneumoniae.
OTHER RESPIRATORY DISORDERS

Acute epiglottitis

- Severe
- M. C organism: H. influenza type B
- Features: - Toxic child
  - High grade fever
  - Stridor, open mouth breathing + excess salivation
  - Tripod position
- Laryngoscopy: Cherry red epiglottis
- Lateral X-ray neck: Thumb sign
- Treatment: 3rd generation Cephalosporins
  Airway management

Acute laryngotracheobronchitis (ALTB)

- Also called croup.
- M. C organism: parainfluenza virus
- Features:
  - Stridor
  - Brassy (barking) cough.
  - Relatively well child.
- X-ray: Steeple sign.
- Treatment: Corticosteroids (Dexamethasone)
  ↓ airway inflammation.
- Severe croup: Hypoxia / Stridor at rest.
  Rx: Add Adrenaline nebulisation

Acute bronchiolitis

- Due to respiratory syncytial virus.
- First episode of wheeze in child < 1yrs following an upper respiratory tract infection.
- X-ray: Hyperinflation of lung fields.
- Associated with ↑ mortality in children with co-morbidities.
Foreign body in airway

- Common in young children (toddlers, infants)
- Sudden onset of any respiratory complaint.
- M/C Object: peanuts

- X-ray finding:
  1. Complete obstruction: collapse of lung
  2. Partial obstruction: airtrapping during expiration

  → Hyperinflation of lung.

- X-ray detects only radio-opaque objects.

Management:
- Immediate removal.

Upper airway foreign body:

1. Heimlich maneuver.
   - Epigastric thrust, backwards and upwards
   - Only in child > 1 year.

2. In infants (< 1 yrs)
   - Child in prone position
     → 5 back blows
     → Child in supine position
     → 5 chest thrusts
   - Alternate between back blow and chest thrust to expel the foreign object.

Lower airway foreign body
- Rigid bronchoscopy guided removal.

Asthma

- Hyper-responsiveness of airway → Bronchoconstriction (wheeze)
- At least 3 episodes (to diagnose)
- Reversible

\[
\text{Allergen} \quad \downarrow \quad \text{Th}_2 \text{ cells} \quad \downarrow \\
\text{IgE-mediated mast cell activation} \quad \downarrow \\
\text{Airway response} \quad (\uparrow \text{mucus}) \quad \} \quad \text{Early phase}
\]

- Only early phase response: Intermittent variety.

Late Phase: repeated attacks
- Recruitment of inflammatory cells \rightarrow \text{Persistent inflammation}
- Early morning hours: Exacerbation of symptoms

Diagnosis:
- Clinical features
- Peak expiratory flow rate:
  - measured using peak flow meter
  - in: > 80%
  - Asthma: < 80% of expected
  - < 20% diurnal variation.
- FEV\(_1\) \downarrow
- FEV\(_{25-75}\) \downarrow: most sensitive
  - Signifies air exhaled from alveoli and small bronchioles

management:
- Intermittent type: Infrequent symptoms
  - Short acting \(\beta\) agonists
    - (salbutamol)
    - (as and when required)
- Persistent: Frequent symptoms

1. Mild: At least 2/month at day
   1 episode/month at night
   - Low dose
     [Budesonide, Beclometasone,
      Fluticasone]

2. Moderate: Daily symptoms
   - Medium dose inhaled steroids
   - Low dose steroids + long acting
     β-agonists (LABA)
     (Salmeterol, Formotrol)

3. Severe: Daily, Continuous symptoms
   - Limitation of physical
     activity
   - High dose steroids
     + LABA

**Second Line Medication:**

1. Leukotriene modifiers:
   - Synthesis inhibitors: Zileuton
   - Receptor antagonist: Montelukast

2. Most cell stabilizers: Cromolyn

Newer drugs:
- For refractory asthma

- Omalizumab
  - Anti-IgE antibody
  - Subcutaneous
  - Children > 6 years of age

- Mepolizumab
  - Reslizumab
  - Anti-IL-5

- Dupilumab - anti IL-4 (Receptor antagonist)

**Modes of drug delivery:**
- Inhalation
  1. Metered Dose Inhaler (MDI)
     - In small children, spacer & face mask are used
Other delivery Systems:
Dry powder inhaler
- For children > 5 years.

Cystic fibrosis

- Defect in chromosome 7q.
- CFTR gene defect (Cystic fibrosis Transmembrane regulator protein)
  codes for a channel that liquefies secretions.
- Defective CFTR channel → mucoviscidosis (Thick mucus)

manifest as:
1. Recurrent respiratory tract infections
   - m.c. cause: staph. aureus
   - Pseudomonas (mucoid colony producing stain)
   - Burkholderia (↑ mortality)

2. GI symptoms
   - Earliest manifestation
   - Thick meconium

     Delayed passage of meconium

     Neonates: Meconium ileus
     Older children: Constipation.

Other manifestations:
- B/L absence of vas deferens → Azoospermia.
- Pancreatic insufficiency → Deficiency of vitamin A, D, E, K
- ↑ in sweat chloride levels (Salty sweat)

Diagnosis:

Lab: ↑ sweat chloride > 60 meq / L
   on atleast a occasions
   OR
   a Cystic fibrosis mutations
   OR
   Abnormal transepithelial nasal potential difference.
Treatment:

- Symptomatic treatment
- Newer drugs:
  - CFTR modulators
  - Potentiator: Ivacaftor
  - Corrector: Lumacaftor
ACYANOTIC HEART DISEASE

Fetal circulation

- Placenta is responsible for the oxygenation of the blood. (Lungs do not play any role)
- Oxygenated blood is carried by umbilical vein.
- Blood flow direction: umbilical vein → Ductus venosus → inferior vena cava.
- Before birth:

  RV → PA → Aorta
  (Right ventricle) → (pulmonary artery)

  RA → LA
  (Right Atrium) → (Left Atrium)

  Foramen Ovale

- Changes occurring after birth:

  Placenta is cut off
  Umbilical vein closes

  Breathing
  O₂ in to lungs
  Pressure (↑ Systemic vascular resistance)

  Closure of Ductus
  Pulmonary artery pressure ↓
  RA pressure ↓
  RV pressure ↓

  Closure of Foramen Ovale

  Umbilical cord clamped

  Aortic pressure ↑
  LA pressure ↑
  LV pressure ↑

- Closure of Ductus arteriosus due to:
  - Reversal of pressure between pulmonary artery and left Aorta.
  - Presence of O₂ in circulation

- Closure of foramen ovale due to:
  - Reversal of pressure between right Atrium and left Atrium.
Order of closure:
- Closure can be of two types:
  (1) Anatomical closure
    (a) Functional closure
- Functional closure:

Umbilical Artery → umbilical vein → Ductus venosus → Foramen ovale → Ductus Arteriosus Closes

<table>
<thead>
<tr>
<th>Functional</th>
<th>Anatomical</th>
</tr>
</thead>
<tbody>
<tr>
<td>within 24 hrs</td>
<td>2-3 weeks</td>
</tr>
</tbody>
</table>

Acyanotic congenital heart defects

Types of lesion:

- Mixing lesion
  - Classical lesion
  - L → R shunt
    - Eg: 1. VSD
    - 2. ASD
    - 3. PDA

- Obstructive lesion
  - Obstructive to systemic blood flow
    - A/K/A Duct dependent systemic circulation
  - Eg: 1. Congenital Aortic stenosis
    - 2. Interrupted Aortic Arch
    - 3. Coarctation of Aorta
    - 4. Hypoplastic left Heart syndrome
    - Treatment: PGE1 infusion

VSD

- Ventricular septal defect
- m/C congenital heart defect

Types:
- Perimembranous VSD (m/C)
- Muscular VSD
  - 'Swiss cheese' pattern defect is seen in muscular VSD.
- Outlet VSD
- Inlet VSD

**Characteristic Features:**
- Shunt murmur: Pansystolic murmur $\rightarrow$ left 4th intercostal space (Parasternal)

$\rightarrow$ RV/RA Roger's murmur

- Flow murmur (in large VSD)

$\rightarrow$ Types:
1. Ejection systolic murmur (more blood through normal valve $\rightarrow$ situation like pulmonary stenosis)
2. Delayed diastolic murmur (more blood through normal valve situation like mitral stenosis)

$\rightarrow$ As a result, left side of heart gets overloaded
- X-ray: enlarged left side of heart
- ECG: Left axis deviation with left ventricular hypertrophy
- Treatment: patch closure of VSD

$\rightarrow$ Indications:
1. Features of congenital cardiac failure
2. Qp: Qs (pulmonary: systemic blood flow) ratio $> 2:1$

**Complications of VSD**

1. Flow in pulmonary artery $\rightarrow$ pulmonary congestion $\rightarrow$ recurrent respiratory infections
2. Congestive cardiac failure (Flow in PA $\rightarrow$ Lungs $\rightarrow$ Heart)
   VSD presents with congestive cardiac failure at: 6 - 10 wks after birth.
3. Infective endocarditis
   VSD is the MC CHD to be associated with infective endocarditis
4. Eisenmenger's syndrome
   - VSD is the earliest CHD to be associated with Eisenmenger's syndrome.
• VSD : ↑ PA Size (more blood) → Vascular remodelling
  ↓ Size of PA (↑ resistance) => progressive Process
  Right ventricular Hypertrophy
  Closure of PA
  Reversal of Shunt
  \[ R \rightarrow L \]
  Cyanosis

• Development of Eisenmenger’s syndrome is a contraindication for surgical.

**ASD**

- Atrial septal defect
- Types:
  - Ostium primum (defect in septum primum)
  - Ostium secundum (defect in septum secundum) (m/c)
  - Sinus venosus defects
  - Coronary sinus defects
- Features:
  - No shunt murmur (no significant pressure difference between LA and RA)
  - Flow murmur is present
    → Delayed Diastolic murmur
    → Ejection systolic murmur
  - Splitting of 2nd heart sound : wide, fixed split of \( S_2 \)
  \( S_2 \) : Normal, 
  Inspiration : \( A_2 - P_2 \) (no split)
    → \( A_2 - P_2 \) (wide gap) (↑ venous return)
  → \( S_2 \) : ASD, 
  Inspiration : \( A_2 - P_2 \) (wide gap) [↑ blood in RA]
    Inspiration : \( A_2 - P_2 \) (wide gap)
  - Major conditions showing wide split \( S_2 \):
    → ASD
    → TAPVC (Total Anomalous Pulmonary Venous Connections)
    → RBBB (Right Bundle Branch Block)
• ECG
  - ASD → Right Axis Deviation
  - Ostium primum ASD → Left Axis Deviation
    → Left anterior fascicular block: depolarisation vector moves through left posterior fascicle.
    → Associated with mitral insufficiency.

Surgery in ASD

• To prevent late onset complications
• In a child with:
  ASD < 8 mm → observe till preschool age
  ASD > 8 mm or
  Symptomatic or
  < 8 mm (which persists > 6 years of age)

PDA

• Patent Ductus Arteriosus
• More common in:
  - Preterm babies (↓ maturity, ↑ chance for hypoxia)
  - Females
  - Congential Rubella syndrome
• Features:
  → Continuous murmur → 'machinery murmur'
  → Location: 2nd left intercostal space (parasternal)

  Gibson's Area

• Differential Diagnosis for continuous murmur:
  1. PDA
  2. A-V malformation
  3. RSOV (Ruptured sinus of Valsalva)
  4. Aortopulmonary window
  5. Collaterals in coarctation of Aorta.
• Management:

Preterm (< 2 wks)
- Medical Treatment
  - PG inhibitors
  - Ibuprofen
  - Indomethacin

Term
- Surgery (catheter based)
  - Occluder / coil

Coarctation Of Aorta (COA)

- m/c: Juxta ductal / post ductal

- Features:
  - Severe: shock + cardiac failure in new born
  - m/c presentations:
    - ↓ blood flow to lower limbs
    - m/c: intermittent claudication
    - Feeble pulse (femoral)
    - Hypertension (↑ blood flow in upper limbs)

- Chest X-ray:
  1. ‘g’ sign
  2. Barium study of esophagus:
     - Reverse z’ sign / ‘e’ sign

  NORMAL
  COA

3. Collaterals:
   - Intercostal arteries dilate → indentation ribs → inferior rib notching
   - > 10 years of age
   - Ribs (4 - 9)
• Treatment: Balloon dilatation ± stenting

Hypoplastic left heart syndrome

• Involves:  → mitral valve atresia
  → LV Hypoplasia.
  → Ascending aorta + Arch hypoplasia.
• Presents with: shock + cardiac failure in newborn
• m/C CHD to present with cardiac failure in 1st week of life
• Definitive Treatment: Norwood procedure.
CYANOTIC CONGENITAL HEART DEFECTS

Cyanotic Congenital heart defects

Two categories

Obstruction to Pulmonary blood flow

↑ased pulmonary blood flow

Conditions:
1. Tetralogy of fallot - Late onset
2. Tricuspid atresia
3. Ebstein's anomaly

early onset

• R2 - PGE, infusion
• Called as Duct dependant pulmonary circulation

Tetralogy of fallot

• Characterised by - i) Sub pulmonary / infundibular stenosis
  ( Primary cause, incomplete stenosis
  ( Reason for late presentation )
  ii) Overriding of aorta
  iii) Ventricular septal defect (VSD)
  ( Large, non restrictive )
  iv) Right ventricular hypertrophy (RVH)

• Presents in children > 6 months
• C / F - i) Failure to thrive
  ii) Single S2 heard
  iii) Ejection systolic murmur
• Complication - i) Polycythemia → Thromboembolism
  a) Brain abscess
  b) Hypercyanotic Spells.
Hypercyanotic spells:

- Exertion
- Spasm of infundibulum
  - \( R_x \) - Beta blockers
- ↑ Venous Return
  - \( R_x \) - Squat → Femoral vein
  - Compression → ↓ venous return
  - in infants - knee chest position
- Hyperventilation
- Hypoxia, acidosis
  - \( R_x \) - \( O_2 \), NaHCO₃
  - (Sodium bicarbonate)
- Stimulation of Respiratory centre
  - \( R_x \) - morphine

- Additional \( R_x \) for hypercyanotic spells - \( \alpha \) - agonist
- \( \text{un x-ray} \) - Boot shaped heart (due to RVH → causes upturned apex)

Treatment:
- Shunting procedure to improve pulmonary blood flow
- Blalock - Taussing shunt - Synthetic communication between subclavian artery and pulmonary artery
- Modified Blalock - Taussing shunt - communication between subclavian artery and pulmonary artery
  - mc method used.
  - Synthetic material used: Gore - Tex
- Waterston shunt - Communication between ascending aorta and pulmonary artery
- Pott's shunt - Communication between descending aorta and pulmonary artery
Shunting procedure:

Tricuspid atresia

- Blood from veins (SVC, IVC)
- Right atrium → blood shunted through foramen ovale → Left atrium → blood from pulmonary veins
- Overloaded & enlarged
- Due to tricuspid atresia
  - Reduced blood entry
- Right ventricle (becomes smaller in size)
- Left ventricle (overloaded & enlarged)

- In ECG → Left axis deviation
- Temporary treatment - PGE infusion
- Definitive treatment - Shunting procedure:
  - Two shunts
  - Glenn shunt
    - SVC is connected to pulmonary artery
  - Fontan shunt
    - IVC is connected to pulmonary artery
Ebstein’s anomaly

- Displacement / prolapse of the tricuspid valve
  - Atrialization of right ventricle
  - Stenosis of tricuspid valve
- On x-ray: Box shaped heart (due to enlarged right atrium)
- Antenatal exposure of lithium → predisposes to develop Ebstein’s anomaly
- Mc condition associated:
  - Wolf Parkinson White syndrome (Bundle of pre-excitation fibres)
    - Predispose to develop arrhythmias
    - Mc arrhythmia: PSVT (paroxysmal supraventricular tachycardia)
- ECG findings:
  - i) short PR interval
  - ii) wide QRS
  - iii) Delta wave

Truncus arteriosus

- Single arterial trunk arising from right ventricle and left ventricle + associated VSD
- It is a part of conotruncal defects (DiGeorge syndrome)
- Treatment - Rastelli procedure
  - Close VSD
  - Divide the single arterial trunk into two
    - Pulmonary artery and aorta
  - Connect the pulmonary artery with a conduit to the right ventricle

Truncus arteriosus → Rastelli procedure
Transposition of great arteries (TGA)

- This is called parallel circulation
- TGA + intact ventricular septum presents with severe cyanosis + congestive cardiac failure (CCF)
- MC type of TGA → TGA + VSD
  \[ \downarrow \]
  Less severe cyanosis + CCF
  Late presentation (6-8 weeks) after birth
- On x-ray Egg on a string appearance
- Treatment:
  1) PGE infusion
  2) Rashkind atrial septostomy (create an opening between left and right atrium)
  3) Definitive treatment - Arterial switch procedure
  \[ \downarrow \]
  RV to AV Jatene operation
  done at 2-4 weeks of age

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.
**Total anomalous pulmonary venous connection (TAPVC)**

- Pulmonary veins draining into right atrium (RA)
  - Three types

<table>
<thead>
<tr>
<th>Supra cardiac</th>
<th>Cardiac</th>
<th>Intra cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pulmonary vein forms ➔ vertical vein ➔ innominate vein ➔ joins SVC ➔ drains into RA</td>
<td>- pulmonary vein directly drains into RA</td>
<td>- Pulmonary vein ➔ join Portal vein or hepatic vein ➔ Drains into IVC ➔ drains into RA</td>
</tr>
<tr>
<td>- mc type</td>
<td>- features similar to supra cardiac TAPVC except figure of 8 sign</td>
<td>- Associated with obstruction of pulmonary veins (due to ductus venosus obliteration)</td>
</tr>
<tr>
<td>- RA (overloaded), blood drains through ASD (atrium septal defect) to left atrium</td>
<td>- cyanosis + CCF + (less severe) features of ASD (wide, fixed splitting of s₂)</td>
<td>- severe pulmonary congestion due to obstruction</td>
</tr>
<tr>
<td>- mixing of deoxygenated blood with oxygenated blood ➔ cyanosis + CCF + (less severe)</td>
<td>- x-ray - figure of 8/snowman sign (due to dilated SVC)</td>
<td>- on x-ray - ground glass appearance, (DO₂ - respiratory distress)</td>
</tr>
</tbody>
</table>
ARF AND INFECTIVE ENDOCARDITIS

Acute rheumatic fever

- Following a group A Streptococcus infection.
- Progression:
  - Sore throat (pharyngitis); 5 - 15 years
  - Molecular mimicry
  - 2 - 4 weeks
  - Rheumatic fever
- Probability of sore throat developing into rheumatic fever: 0.3 - 3%
- Preceding history of sore throat → 50% cases

Modified Jones criteria (2015)

- India: moderate to high risk population, when:
  - Incidence of Rheumatic fever > 2 / 1,00,000 population
  - Prevalence of Rheumatic heart disease > 1 / 1000 population

Major criteria:
- Carditis
  - Pancarditis
  - Clinical or subclinical (echo) carditis → 90% cases
- Arthritis
  - Early, 15% cases
  - Monoarthritis or polyarthritis (large joints) or polyarthralgia
  - Migratory
  - Good response to aspirin
  - Pain is out of proportion
- Erythema marginatum
- Subcutaneous nodules → late (at insertion of tendons)
- Sydenham's chorea → last

Minor criteria:
- Monoarthritis
- Fever ≥ 38°C
- ESR ≥ 50 mm in 1 hour
- CRP > 3 mg/dl
- P-R interval prolongation
For diagnosis of rheumatic fever:
- It requires: 2 major
  or
  1 major + 2 minor criteria.
- In case of recurrence: 3 minor

Treatment of ARF

- Bed rest
- Penicillin X 10 days
- Steroids / Aspirin
  - Steroids are drug of choice
  - Duration: 12 weeks

Prophylaxis
- Penicillin / macrolides
- Duration:
  1. Without carditis: For next 5 years / till 18 years of age whichever is longer
  2. With carditis: For next 10 years / till 25 years of age whichever is longer
  3. Residual valve problem (RHD) or following surgery: Lifelong

Infective endocarditis

- Etiology
  - *Streptococcus Viridans*: Subacute bacterial endocarditis.
  - *Staphylococcus aureus*
  - *Enterococci*

- Features:
  - Fever ≥ 5 days
  - Valves are usually affected

  NEUTROPHILS, MACROPHAGES
  VEGETATIONS (HALLMARK)
  MITRAL VALVE
  BACTERIA

  HEART
- The vegetation causes:
  - Embolic phenomenon (vascular)
  - Janeway lesion
  - Splinter hemorrhages
  - Septic infarct
  - Immunological phenomenon
  - Glomerulonephritis
  - Osler's nodes
  - Roth spots

Duke’s criteria

- Criteria
  - Major
    1. Separate (+) blood cultures
    2. Echocardiography:
       - Vegetation
       - Valvular regurgitation
       - Abscess / valve dehiscence
  - Minor
    1. Predisposing factors
    2. Fever
    3. Immunological
    4. Vascular
    5. Single (+) blood culture
    6. Echocardiography - not meeting major criteria

- For diagnosis of infective endocarditis:
  - 2 major criteria
    or
  - 1 major + 3 minor criteria
    or
  - 5 minor criteria

Treatment

- 3rd generation cephalosporin or vancomycin
  + Aminoglycoside
- Duration: 4 - 6 weeks

Prophylaxis

1. Prosthetic heart valves
   a. Prior history of infective endocarditis
   b. Unrepaired heart defects
   c. Repaird heart defects
      - Residual defect
      - First 6 months following repair
   d. Cardiac transplant
CONGENITAL ANOMALIES OF RENAL SYSTEM

Classification of congenital anomalies in Renal System:
- Parenchymal anomalies
- Obstructive uropathy

**Parenchymal anomalies**

i) mCDM - multi Cystic Dysplastic Kidney
   - Cysts formed instead of normal renal parenchyma
   - Condition associated with enlargement of kidney
   - Cause palpable abdomen - mass at loin / flank
   - Most cause of palpable abdominal mass in newborn
   - Usually unilateral - in 15% of cases causes
     Contralateral vesico urethral reflux
   - Usually undergoes Spontaneous involution by 5 to 7 years of age

ii) ARPKD - Autosomal Recessive Polycystic Kidney disease.
   - Defect in Chromosome 6, Coding for PKHD1 gene, which codes for the protein Fibrocystin (Polyductin)
   - Usually Bilateral Cyst.
   - Usually associated with Significant ↓ ↓ in renal function
   - Due to Blood vessels Compression
     → Local ischemia
     this releases Renin → RAA system
       Angiotensin
       Aldosterone
       Hypertension
   - It is also associated with Hepatic cyst, leading to fibrosis

iii) Bilateral Renal Agenesis:
   - Causes severe Oligohydramnios.
   - Leading to fetal Compression
     Potters Syndrome:
     Features: i) Potters facies
       ii) Lung hypoplasia.
       iii) Limb abnormalities (eg: CTEV)
IV) Horse Shoe Kidney: lower pole of kidney fused with each other.
   - M_3 associated with Turner’s Syndrome
   - Complications -
     • ↑ risk of Wilms’ Tumor
     • Stones, hydronephrosis

Obstructive Uropathy

1) Pelvic Ureteric Junction Obstruction:
   - M_3 condition among Obstructive uropathy.
   - Antenatal presentation - Hydronephrosis
   - Usually Unilateral, M_3 at Left side.
   - Usually resolves Spontaneously in post natal period.
   - On post natal USG; remains unresolved → DTPA / MAG → 3 scan

   If significant ↓ ↓ in renal function of affected kidney

   Correction of PUJ Obstruction
   K/A Andersen Heyne’s Pyeloplasty

a) Ureterocele

3) Posterior Urethral Valves:
   - Most severe form of Obstructive Uropathy
   - Usually affects Boys
   - Often has postnatal presentation.
     - Dribbling of urine during micturition
   - Complication: Recurrent UTI → vesicourethral reflux
   - Diagnosis: Micturating Cysto Urethrogram (MCU)
   - Treatment: Relieve Obstruction by putting feeding tube.
     (use of Foley’s catheter can precipitate bladder spasm)
Vesico ureteric reflux

- Reflux of urine from bladder back into ureter
- Features → ↑ risk of recurrent UTI
  Reflux nephropathy

Diagnosis: MCU

Helps in grading of VUR
5 Stages:
I  - Partial VUR
II  - Complete VUR
III - Dilated ureter
IV - Grossly dilated ureter with Tortuosity
V  - Renal pelvis outline is damaged

management: Prophylactic Antibiotics to prevent UTI
- Grade I & II → give Prophylactic Antibiotic till age of 1 year
- Grade 3 to 5 → till age of 5 year.

- If UTI after prophylaxis (or) despite prophylaxis → Break through UTI
  → Restart prophylaxis
- In grade 3 to 5 → despite prophylaxis if UTI
  → Surgical correction of VUR

Ectopia Vesicae / Bladder Exstrophy
**Prune Belly Syndrome / Eagle - Barret Syndrome:**

- Wrinkled skin over abdomen, due to deficient abdominal muscles.
- Condition is associated with:
  - Undescended testis
  - Mega ureter
  - Mega bladder
URINARY TRACT INFECTION (UTI)

UTI in Children:
- Most common cause: E. coli.
- Generally, F > M; ascending infections occur through the urethra.
- In infants: M = F (Source of infection - Hematogenous infection)

Types of UTI

<table>
<thead>
<tr>
<th>Upper UTI</th>
<th>Lower UTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ Pyelonephritis</td>
<td>→ Cystitis</td>
</tr>
<tr>
<td>→ Clinical Features (C/F):-</td>
<td>→ Urethritis</td>
</tr>
<tr>
<td>• Sick looking child</td>
<td>• C/F:</td>
</tr>
<tr>
<td>• High grade fever</td>
<td>• Relatively well child</td>
</tr>
<tr>
<td>• Pain in flank or loin</td>
<td>• Mild abdominal pain</td>
</tr>
<tr>
<td>• Constitutional symptoms</td>
<td>• Pain during micturition</td>
</tr>
<tr>
<td>→ A/W/A Complicated UTI</td>
<td>→ A/W/A Simple/Uncomplicated UTI</td>
</tr>
<tr>
<td>i) High risk of renal damage</td>
<td>i)</td>
</tr>
<tr>
<td>ii) In children &lt; 1 yr</td>
<td>ii)</td>
</tr>
<tr>
<td>hematuria spread</td>
<td>of infection.</td>
</tr>
<tr>
<td>of infection.</td>
<td></td>
</tr>
<tr>
<td>→ Treatment - IV antibiotics</td>
<td>→ Treatment - Oral antibiotics</td>
</tr>
</tbody>
</table>

Diagnosis of UTI

- Gold standard investigation - urine c/s
Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>i) mid stream clean</td>
<td>≥ 10^5 CFU / ml</td>
</tr>
<tr>
<td>Catch urine sample</td>
<td></td>
</tr>
<tr>
<td>ii) urethral catheterization</td>
<td>&gt; 5 x 10^4 CFU / ml</td>
</tr>
<tr>
<td>iii) Supra pubic aspiration</td>
<td>Any number of bacteria grown</td>
</tr>
<tr>
<td>(Best method)</td>
<td></td>
</tr>
</tbody>
</table>

Additional investigations

i) Kidney damage :-  ii) Renal anomalies :-  iii) General screening

→ Common till the Age of 5 years  → * Posterior orethral valve

→ Specific test - DMSA Scan  → * Vescoureteral reflex

→ Common till the  → Test - USG

→ Specific test - age of 1 year

→ Test - MCU

(micturating Cystourethrogram)

Routine investigations :-
- In children < 1 yr - USG, DMSA, MCU
- In children between 1 - 5 years - DMSA, USG
- In children > 5 yr - USG
GLOMERULAR DISORDERS

Nephrotic Syndrome

- Definition:
  - Proteinuria: Urine protein > 40 mg/m²/hour
    - Urine protein: creatinine (P/C) ratio > 2
  - Hypoalbuminemia (albumin < 3.5 g/dl)
  - Edema (anasarca)
  - Hyperlipidemia (serum cholesterol > 200 mg/dl)

- Causes:
  a. Minimal change disease
  - Overall most common cause of nephrotic syndrome.
  - Loss of foot process of podocytes
    \[\downarrow\]
    - Visible only through electron microscopy
  - Excellent response to steroids
  b. Focal segmental glomerulosclerosis (FSGS)
  c. Membranous nephropathy
  d. Membranoproliferative glomerulonephritis (MPGN)
  e. Congenital nephrotic syndrome (≤ 3 months)
    \{Steroid resistant
    - No response to steroids
    \[\times\]
    8 weeks

- Congenital nephrotic syndrome:
  - Cause defect in NPHS-1/2, WT-1 gene
  - Normally, podocytes: A protein
    - Podocin: NPHS-1
    - Nephrin: NPHS-1 (Finnish type nephrotic syndrome)
  - Antenatal: \[\uparrow\] α-feto protein
  - WT-1 gene associated with
    - Denys drash syndrome
    - Ambiguous genitalia in male
    - \[\uparrow\] Risk of wilm’s tumor

- Other definitions:
  i. Frequent relapse: >2 relapse in 6 months (or) > 4 relapse in 12 months.
  ii. Steroid dependent: > a relapse while on alternate day steroid therapy (or) within 14 days of stoppage of steroids.
Treatment and complications of Nephrotic syndrome

a) Treatment :-
- Steroids
  - Commonly used steroid: **Prednisolone**
  - Dose - daily dose for 6 weeks + Alternate dose for 6 weeks.
- Steroid resistant cases:
  - Cyclosporine / tacrolimus
- Steroid dependent cases:
  - Steroid sparing agents - Cyclophosphamide and levamisole

b) Complications :-
- **Thrombosis** : due to ↑ fibrinogen production (especially cerebral and renal vein thrombosis)
- Spontaneous bacterial peritonitis (**SBP**): most common cause
  Streptococcus pneumoniae

Nephritic Syndrome / Glomerulonephritis

- Hallmark feature: microscopic hematuria.
  (> 5 RBC's / high power field)
  - Dysmorphic RBC
  - RBC cast
- Mild proteinuria
- Edema
- Hypertension

Post Streptococcal Glomerulonephritis (PSGN)

- Most common cause of glomerulonephritis
- PSGN can occur once in a lifetime
- Course: Following upper respiratory tract infection (URT1) by Group
  A β hemolytic streptococi (sore throat)

  Lag period ↓ 1-2 weeks

  deposits immune complex in kidney

  ↓

  PSGN

- Clinical feature: hematuria (after 1 - 2 weeks of URT)
- Most common age group: 5 - 15 years (school going children)
Ig-A Nephropathy

• **Aka Berger’s disease**
  • IgA levels are normal, but there is IgA deposition in glomeruli.
  • Most common cause of chronic glomerulonephritis
  • Clinical feature: Recurrent gross hematuria.
  • Age: Adolescent age
  • URTI 1-2 days→ hematuria.
  • Treatment: Angiotensin converting Enzyme (ACE) inhibitors
    - Controls proteinuria, hypertension
    - Omega-3 polyunsaturated fatty acid (PUFA)
    - ↓ Inflammation
    - Corticosteroids
    - ↓ Inflammation and proteinuria.

Familial Nephritis

(i) Thin glomerular basement disease:
  • Benign, Autosomal dominant disorder.
  • Feature: Persistent hematuria.
  • Good survival rate

(ii) Alport’s syndrome:
  • X-linked recessive disorder
  • Systemic features
    - Anterior lenticonus
    - Sensorineural hearing loss.
  • Abnormal COL4A5 (α5 chain of type IV collagen).
  • Microscopy - Basket - weaving appearance
    - Thickening and thinning of glomerular basement membrane
    - Associated lamellations
INHERITED TUBULAR DISORDERS

- Characteristic features of tubular disorders:
  - Polyuria
  - Polydipsia
  - Dehydration

Bartter Syndrome

- Usually present in young children
- Normal renal function, Normal Blood pressure
- Defect in: Ascending limb of Loop of Henle

LUMEN

Na-K-Cl cotransporter

Na⁺, Cl⁻

K⁺, Cl⁻

ROMK Channel

Ca²⁺

Basal side

Cl⁻ channel

- Loss of function in:
  - Na-K-Cl cotransporter
  - ROMK (Renal outer membrane K⁺) Channel
  - Cl⁻ channel
- When Na-K-Cl cotransporter is affected → Ca²⁺ gradient is affected.
  Ca²⁺ absorption is also affected
  Hypocalciuria => Nephrocalcinosis
- When Cl⁻ channels in cochlea are affected → SNHL (sensory Neural Hearing Loss)
- In the distal part of collecting duct, body tries to conserve Na⁺, in return it secretes K⁺, H⁺ → Hypokalemic Metabolic Alkalosis
**Gitelman Syndrome**

- Usually presents in older children
- Defect in: Distal convoluted tubule (DCT)

- Loss of function in:
  - Na-Cl cotransporter
  - TRPM6 Channel (Transient Receptor Potential M6)
- It leads to Hypokalemic metabolic Alkalosis
- ↑ Excretion of mg²⁺ → Hypomagnesemia

**Liddles Syndrome**

- Defect in: Collecting duct
- AD inheritance characterised by Activating Mutation

- ↑ Na⁺ in blood → Hypertension
- As a result K⁺ gets secreted into Lumen → Hypokalemic alkalosis
Nephronophthisis

- AR
- In young children
- Mutation in NPHP gene
- Problem:
  Tubular inflammation $\rightarrow$ Atrophy $\rightarrow$ ESRD (End Stage Renal Disease)
- Associated manifestation:
  - Ciliopathy - Situs inversus
  - Retinitis pigmentosa - Senior Loken Syndrome
  - Cerebellar hypoplasia - Joubert Syndrome

Medullary Cystic Kidney Disease

- AD
- In adults
- Genes affected: mckd1
  - mckd 2
- Not associated with any extra renal complications.
RENAL FAILURE

Acute Kidney Injury (AKI)
Definition: ↑ in S. Creatinine > 0.3 mg/dl or >1.5 times from baseline
- Urine output: < 0.5 ml/kg/hr x 6 hours

Causes of AKI

1. Pre-renal:
   - Due to hypoperfusion (i.e., Cause)
     - Dehydration
     - Blood loss
     - Shock

2. Renal:
   - Parenchymal diseases: Acute glomerulonephritis (AGN)
     Hemolytic uremic syndrome (HUS)
   - Tubular necrosis: Acute tubular necrosis (ATN)
     Acute interstitial necrosis (AIN)
   - Vascular: Renal vein thrombosis

3. Post-renal: obstruction

Hemolytic uremic syndrome (HUS)
- D (+) HUS: Diarrhea, ↑ Hemolysis, ↑ S. creatinine (uremia)
  mediated by shiga toxin,
  Associated with: E. coli (O 157, H7)
  Shigella
- D (-) HUS: due to inherited complement defect.

Complications

- Fluid overload → Pulmonary edema.
- Anemia (due to hemodilution).
- Electrolyte disturbances:
  a) Hyperkalemia.
  b) Metabolic acidosis
  c) Hypocalcemia.
  d) Hyponatremia.
management of hyperkalemia:
- K⁺ > 6 mEq/L: Exchange resins (Exchange Na⁺ for K⁺)
  Sodium polystyrene sulfonate (Kayexalate)
- K⁺ > 7 mEq/L: 10% calcium gluconate (slow iv)
  Stabilizes the myocardium
  Shift K⁺ to intracellular compartment
  - Insulin glucose infusion
  - Na₂HCO₃

- Persistent hyperkalemia - Hemodialysis

Chronic kidney disease (CKD)

Definition:
1. Structural (anomalies) or functional (persistent proteinuria, hematuria) abnormalities, for > 3 months.
2. GFR < 60 ml/min/1.73 m² body surface area.

Staging:

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;90 (hyper filtration stage)</td>
</tr>
<tr>
<td>2</td>
<td>60 - 90</td>
</tr>
<tr>
<td>3</td>
<td>30 - 59</td>
</tr>
<tr>
<td>4</td>
<td>15 - 39</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15 (or) patient dependant on dialysis</td>
</tr>
</tbody>
</table>

Complications:

1. Anemia.
   - Normocytic normochromic
   - Due to ↓ erythropoietin
   - R₉ : Darbepoeitin alfa (subcutaneous)

2. Renal osteodystrophy:
   - Also called osteitis fibrosa cystica
3. Rickets
   - Due to 1-α hydroxylase deficiency
   - $R_x$: Vit D supplementation
   - Associated with hyperphosphatemia. ($R_x$: phosphate binders)

4. Short stature
   - $R_x$: recombinant human growth hormone.

5. Hypertension
   - $R_x$: ACE inhibitors. (preferred)
     Angiotension receptor blockers.
NEUROMUSCULAR DISORDERS

Introduction

- Classification of neuromuscular disorders based on the area affected.

1. Anterior horn cell → Neuronopathy
   - Spinal muscular atrophy
   - Polio
2. Neuron → neuropathy
   - Guillain barre syndrome
3. Neuromuscular junction
   - myasthenia gravis
4. Muscle fibres
   - Muscular dystrophy

Spinal muscular atrophy

- Autosomal recessive
- Defect in chromosome 5q
- Gene responsible SMN1 (survival motor Neuron gene)
  - SMN1 gene is non-functional due to defect in EXON 7.

- Features:
  - Types:
    1. Type 0
       - Most severe
       - Mostly associated with in-utero death
    2. Type 1
       - Classical types called as werdnig hoffman disease
       - Presents within 0-6 months of life.
       - Characteristic presentations:
         1. Floppiness → ragged doll appearance
         2. ↓ absent deep tendon reflexes
         3. Sparing of extra ocular muscles
         4. Fasciculations (tongue)
       - Important cause of death: Aspiration pneumonia.
3. Type 2
   • Called as pubovitz disease
   • Presents within 6 - 18 months

4. Type 3
   • Called as kugelberg welander disease
   • Presents within > 18 months
   • Least severe

SMN gene mutations

- New treatment approaches:
  1. Gene therapy
     - The gene is inserted into adenovirus (vector) and is integrated with host genome.
  2. Exon skipping technology
     - Anti sense oligonucleotide is introduced.
     - As a result of which non-functional SMN2 gene is converted to a partly functional gene.
     - When antisense oligonucleotide is introduced in SMN2 gene, it covers up EXON 7 (defective). As a result, EXON 7 is skipped during translation.
     - Drug used in exon skipping: Nusinersen

Guillain barre syndrome

- Also called as acquired inflammatory demyelinating polyneuropathy
- Neuropathy develops post-infectious, which is 1-6 weeks after infection due to diarrhoea (jejuni) of mycoplasma (pneumonia)
- mostly mediated by anti ganglioside antibodies: Anti Gm I
  Anti GQ I

- Features:
  - Ascending paralysis (Landry's paralysis)
    - Lower limbs → trunk → upper limbs → face, bulbar muscles
    - Its a symmetrical paralysis
    - Sparing of extraocular muscles
  - Autonomic involvement
  - Mild sensory involvement
  - CSF Analysis: Albumino - cytological dissociation (and week)
    - Protein ↑ cell count is normal (< 50/ cu. mm)
  - ↓ In nerve conduction velocity.

- Variants
  - AMAN (Acute motor axonal neuropathy)
  - AMSAN (Acute motor and sensory axonal neuropathy)
  - Miller Fischer syndrome
    - Characterised by ataxia, areflexia, ophthalmoplegia
    - Associated with anti GQ I
  - Treatment: I. V. I. G (intravenous immunoglobulin)
    plasmapheresis

Myasthenia gravis

- Ach receptor anti bodies are responsible, as they
  Bind to ach receptors and prevent Ach from meeting the receptor.

- Characteristic feature: muscle weakness
  - Skeletal muscles
  - Extra ocular muscles (earliest)
    - Ptosis
    - Diurnal (↑ in evening)
    - Fluctuating
    - Worsens with activity

- Test: 1. Edrophonium test
  - Edrophonium is a Ache inhibitor
    (↑ Contraction of muscles)
  - The test looks for improvement in signs
  - In a child, < 1 year there is ↑ risk of arrhythmias associated
    with edrophonium. therefore neostigmine is used instead.
  2. Electromyogram: shows decremental response on repeated
    nerve stimulation.
3. Antibodies
   - Ach receptor antibody
   - Anti-musk antibody (muscle specific kinase)
     Source: Thymus

- Treatment:
  - Cholinesterase inhibitors
  - Pyridostigmine (drug of choice)
  - Steroids - Thymectomy

Duchenne muscular dystrophy

- X-linked recessive
- Defect in X-chromosome which codes for protein, Dystrophin (helps to mediate muscle contraction)
- Defect is in Xp21

   Frameshift  missense
   ↓          ↓
  Duchenne muscular dystrophy  Becker's dystrophy
                          (less severe)

- Features:
  - Before the age of 5 years
  - Delay in walking (proximal group of muscles)
  - Waddling gait
  - Pseudohypertrrophy (muscles get destroyed, replaced by fibro-fatty deposition)
  - Gower's sign (not a specific sign) → Seen in condition with proximal muscle weakness.
  - Mild intellectual disability
- Complications: Respiratory insufficiency cardiomyopathy → Death

- Treatment
  - Steroids (↓ apoptosis): Prednisolone
deflazocort
  - Exon skipping (etepliren)
Becker's muscular dystrophy
- Late onset > 5 year
- Slow progression
- Early onset cardiomyopathy

Facioscapulohumeral dystrophy
- Autosomal dominant
- In puberty
- Affects facial, shoulder girdle and proximal arm muscles
- Winging of scapula → Asymmetrical
- Facial muscles are affected : Expressionless face
- Biceps and triceps are affected, deltoid and forearm are not affected → popeye arm appearance
- Associated features : Deafness
  Coat's disease (Exudative retinopathy)

Emery - Dreifuss muscular dystrophy
- X - linked recessive
- Defect in nuclear proteins : Emerin, laminin
- Contracture precedes weakness
- Upper limbs → Proximal group of muscles affected
- Lower limbs → Distal group of muscles affected

Limb girdle muscular dystrophy
- Autosomal dominant or recessive
- Defect in proteins : Sarcomere and calpain - 3
- Proximal muscles are more affected than distal muscles
- Sparing of : Facial muscles
  Extra ocular muscles
  Pharyngeal muscles.
Summary:
1. Duchenne muscular dystrophy
2. Emery Dreifuss muscular dystrophy
3. Limb girdle muscular dystrophy
4. Facioscapulohumeral dystrophy
Neural tube defects

Cause: failure of closure of neuropore
Types: Cranial, caudal (more common)

Caudal neural tube defects:

1. Spina bifida occulta
   - Posterior vertebral fusion defect
   - Common site: L₅ - S₁
   - Asymptomatic

2. Meningocele
   - Meninges (lining the spinal cord) forms a cavity

3. Meningomyelocoele
   - Meninges forms a cavity with spinal nerve roots in it.

Cranial neural tube defects:

- Anencephaly
- Encephalocele
- Iniencephaly
(i) Anencephaly
  - Underdeveloped cranial vault
  - Absence of brain

(ii) Encephalocele
  - Cavity formed outside the skull with contents of brain matter in it.

(iii) Iniencephaly
  - Occipital bone defect + fusion of cervical vertebrae
    \[ \Downarrow \]
    Retrosflexion of cervical spine

Combined neural tube defect:
  - Craniorachischisis
    - Cranial defect + caudal defect
    - Most severe

Risk factors for neural tube defects:
  A multifactorial inheritance
  - Folic acid deficiency
  - Infants born to diabetic mother
  - Anti-convulsants (valproate, phenytoin)
  - Trisomy 13, 18

**Diagnosis of neural tube defect**

<table>
<thead>
<tr>
<th>Antenatal period</th>
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</thead>
<tbody>
<tr>
<td>Ultrasoundography</td>
</tr>
<tr>
<td>Earliest: Anencephaly (10 - 12 weeks)</td>
</tr>
<tr>
<td>Sensitivity: Alpha fetoprotein (screening)</td>
</tr>
<tr>
<td>Specific: Acetylcholine esterase</td>
</tr>
</tbody>
</table>

Periconceptional folic acid supplementation:
  - Supplementation: 1 month before conception to 3 months after conception
  - Dose: Normal pregnancy - 400 \( \mu \)g (\( = 0.4 \) mg)
  - Previously affected child - 4000 \( \mu \)g (\( = 4 \) mg)

**Warning:** Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with additional medical videos.
Neuronal migration disorder

a. Lissencephaly
   - Also known as agyria.

b. Schizencephaly
   - A split brain (cleft-like partition inside the brain).

c. Porencephaly
   - Small cyst-like structures.

d. Polymicrogyria.
   - Multiple folds (gyri) which are unusually small.

e. Agenesis of corpus callosum:
   - Corpus callosum: connects right and left cerebral hemispheres.

• Signs:
  - Horns of lateral ventricle
    : Normally, arranged like a bow tie
    : Agenesis, arranged parallel – racing car sign

  - Mouse head sign
    : Dilatation and indentation of 3rd ventricle

Racing car sign
Holoprosencephaly
Cause: failure of division of fore brain (prosencephalon)
External manifestation
  a) Serve form
     - Cyclopia (single eye)
     - Proboscis
  b) Mid form
     - Cleft lip

Note: Spina bifida occulta - a neural tube defect with maximum viability

Hydrocephalus

- ↑ CSF

Causes

Obstructive  Non obstructive
- ↑ Production
  - Choroid plexus papilloma.
- ↓ Absorption
  - Sub arachnoid hemorrhage
  - Pus (Tubercular / pyogenic meningitis)

Obstructive
(i) Aqueductal stenosis (most common)
  - Usually congenital
  - Acquired - causes: Mumps, toxoplasmosis

(ii) Arnold - chiari malformation - type II
  - Herniation of
    : Pons
    : medulla
    : Vermis
    : 4th ventricle
    { into cervical spinal canal

(iii) vein of galen malformation
- Associated with CCF
  (Congestive cardiac failure)

(iv) Dandy walker malformation
- Failure of opening of foramen magendie  \( \rightarrow \) Ballooning of 4th ventricle

Dandy walker

Clinical features and management of hydrocephalus

Clinical features:
- Head size: Large
- Fontanel: Bulged
- Tense
- No pulsations
- Prominent scalp veins
- Wide separation of sutures
- Sunset sign - exposure of upper sclera.
- Crack pot resonance on percussion of skull

In case of an older child:
- ↑ ICT (intra cranial tension)
  - Papilledema
  - Projectile vomiting

Management:
- a) Shunt: ventriculo - peritoneal shunt (most common)
  - ventriculo - atrial shunt

- b) Drugs: ↓ CSF production - Acetazolamide
  Normal intra cranial pressure (ICP): Infant - < 5 mmHg
  : Children - < 15 mmHg

First line management:
- 1) Head end elevation (30°)
- 2) Controlled hyperventilation  \( \rightarrow \) Vasoconstriction  \( \rightarrow \) ↓ ICP
  \( (\text{PaCO}_2: 35 - 40 \text{ mmHg}) \)
3) Osmotic diuretics
   : mannitol → ↓ blood viscosity → improves cerebral perfusion
   : 3% hypertonic saline
4) Sedatives: Barbiturates

Second line management:
1) Decompressive craniectomy
2) Induced coma / hypothermia
3) Therapeutic CSF drainage
SEIZURE DISORDERS

- Increased electrical activity in brain.

Types

Generalized
- GTCS (MC) Seizures
- Absence Seizures
- Myoclonic Seizures

Focal
- with intact awareness
- with impaired awareness

- GTCS: Generalised tonic Seizures.

Febrile seizures

- 6 m - 5 years
- no neurological defects.
- Types:
  a) Simple (typical)
     - Single episode of GTCS
     - Lasts < 15 mins
     - Occur within 24 hours of fever onset.
  b) Complex (Atypical)

Indications for lumbar puncture:
- Suspected meningitis
- Unimmunised / H. influenza B or pneumococcus immunization status unknown.

Treatment:
- Benzodiazepines i.v
- Paracetamol.

Prevention:
Intermittent prophylaxis: Oral clonazepam / diazepam.
- Not recommended routinely.
Indications:
- Recurrent (≥ 3 episodes in 6 months)
- 1st episodes at age ≤ 18 months
- Family history

Absence seizures

- Short duration (<30 sec)
- Brief episodes of inattention
- Common in school-going children
- EEG: 2Hz spike and wave pattern
- Precipitated by: Hyperventilation
- Treatment: Sodium valproate, lamotrigine

Myoclonic seizures

- Fast clonic movement on awakening
- In adolescents
- Also called: juvenile myoclonic epilepsy
- Janz syndrome: repeated myoclonic seizures.
- Precipitated by: lack of sleep/alcohol.
- EEG: 4-6 Hz poly spike and wave discharges
- Treatment: Sodium valproate

West syndrome

- In child <1 year.
- Spasm of neck flexors → Salaam spells.
- Low IQ.
- EEG: Hypsarrhythmias (High voltage spikes in a chaotic background)

Types:
- a) Cryptogenic (Idiopathic)
  - Normal development before seizure onset.
  - Poor outcome.
- b) Symptomatic (Secondary)
  - Developmental delay
  - Favourable outcome.
Treatment:
- ACTH (immunomodulatory effect)
- In tuberous sclerosis: vigabatrin.

Lennox - Gastaut syndrome (LGS) 00:17:06
- 2 to 12 years
- Multiple seizure types
- EEG: 1-2 Hz spike and wave pattern
- Treatment: Sodium valproate.

Benign Rolandoic (Centrotemporal) Epilepsy 00:18:22
- Focal seizures
- EEG: Spikes from central part of temporal region
- Resolves by adolescence
- Treatment: Carbamazepine

Dravet syndrome 00:19:49

1st year: Febrile seizures
↓
and year: Afebrile seizures
( multiple seizure types )
↓
Developmental delay
and refractory seizures.

- Due to de-novo mutations in SCN1A gene (α1 subunit of Na+ Channel)
OTHER NEUROLOGICAL DISORDERS

Cerebral palsy (CP)

- Characterised by insult to developing brain, results in changes in posture, tone, movement.
- A/V/a static encephalopathy
- mc association - Birth asphyxia, others - trauma, infection (meningitis)
- Classification based on changes in tone:

  ↓

  Hypotonic
  ↓
  - Severe mental retardation

  spastic
  ↓
  (sc)
  - ↑ tone

  Choreo - athetoid / Extrapyramidal CP
  ↓
  - Basal ganglia affected
  - mc cause - Kernicterus
  - C/F - Chorea, low IQ

Spastic CP:

<table>
<thead>
<tr>
<th>Quadruplegia</th>
<th>Diplegia</th>
<th>Hemiplegia</th>
</tr>
</thead>
</table>
Meningitis

- **MC cause - Bacterial infection**

**Pyogenic meningitis:**

- **MC organism overall - Streptococcus pneumoniae**
- **MC organism in < 2 months of age - E. coli**
- **C/F - High grade fever**
  - Seizures
  - Signs of meningeal irritation
    - Neck stiffness
    - Brudzinski’s Sign (neck flexion elicits hip and knee flexion)
    - Kernig’s sign (hip and knee flexed, first and extension of knee causes pain)

**Diagnosis:**

- **CSF analysis → Findings →** Turbid fluid
  - ↑ Cells (Neutrophils)
  - Protein ↑
  - Sugar ↓ (Hypoglycorrhachia)
- Other tests → Gram staining, culture of CSF.

**Complications:**

1) Seizures - **MC**
2) ↑ Intracranial pressure
3) Subdural effusion
4) Hydrocephalus (due to pus blocking the subarachnoid space)

**Sequela of Pyogenic meningitis → Sensorineural deafness**

- Brainstem evoked response audiometry is performed to assess deafness

**Treatment:**

* Drug of choice → IV Ceftriaxone → If no improvement → Add Vancomycin in > 48 hrs
* Corticosteroids → Dexamethasone

↓

Two uses →

1) ↓ ses inflammation → ↓ edema → ↓ intracranial pressure
2) ↓ ses incidence of sensorineural deafness
Tuberculous (TB) meningitis

- Rich focus in brain (TB focus) → Rupture → Thick basal exudate
  ↓
  Blocks subarachnoid space
  ↓
  Hydrocephalus

- Most severe form of tuberculosis in children
- C/F - 3 stages:

<table>
<thead>
<tr>
<th>Prodromal</th>
<th>meningitis</th>
<th>Comatose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, irritability</td>
<td>Fever, seizures</td>
<td>only 50% survival rate</td>
</tr>
<tr>
<td>100% good outcome</td>
<td>Abnormal CSF findings</td>
<td>In surviving patients</td>
</tr>
<tr>
<td>80% survival rate</td>
<td>60% neurological sequelae</td>
<td>- 60% neurological sequelae</td>
</tr>
<tr>
<td>↓ 50% of them will have neurological sequelae</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- CSF findings → 'cob - web' appearance (due to ↑ sed fibrin)
- Tests → ↑ sed ADA (Adenosine deaminase levels)
  IGRA (Interferon gamma release assay)

Viral meningitis

- A/k/a aseptic meningitis
- Etiology: mc virus - worldwide - Enteroviruses
  - India - Japanese encephalitis virus

Culex is the most common vector for the virus

Mosquito bites transmit the JE virus

JE virus multiplies mainly in pigs and waterbirds as its main reservoirs.

There is no person-to-person transmission of the virus.

- Amplifier host - pigs and waterbirds
- Dead-end host - man
- CSF finding -
  - clear fluid
  - ↑ sed lymphocyte count
  - mild ↑ protein
  - N - sugar
  - Ig in ELISA - IOD
- In MRI - Thalamus, basal ganglia changes seen.

Neurocutaneous syndromes

neurofibromatosis (NF):-

Two types

- NF - 1
  - Autosomal dominant
  - Chromosome - 17
- NF - 2
  - Chromosome - 22
  - B/L Acoustic neuroma - McN association

- Atleast 6 cafe - au-lait macule
  (hyperpigmented lesions)
  Should be ≥ 5mm size prepubertal
  ≥ 15mm size postpubertal
- Axillary/ groin freckling - pathognomonic finding
- Lisch nodules
- ≥ 10 more neurofibroma (or)
  atleast one plexiform neurofibroma
- Skeletal manifestations -
  anterior bowing of tibia
  dysplasia of sphenoid bone
- Optic nerve glioma - MC tumor
- Atleast one first degree relative affected
- Diagnosis: -
  Atleast any two of the
  above findings should be present
Tuberous sclerosis

- Autosomal dominant
- Ash leaf macule (First finding) (hypopigmented lesion)
- Shagreen patch
- Adenoma sebaceum (tumor of sweat glands) in adolescent
- Subungual fibroma (tumor beneath the nail)
- Characterised by defect in two genes:
  - TSC-1 (Tuberous sclerosis complex)
    - Present in chromosome 9
    - Code for tuberin
      - associated with cortical tubers
    - Subependymal giant cell astrocytoma (SEGA)
  - TSC-2
    - Present in chromosome 16
      - Hamartin
        - Present in chromosome 16
        - Present in chromosome 16
          - Associated with
            - Retinal hamartoma
            - Renal angiomalyplipoma
            - Cardiac rhabdomyoma

- Vigabatrin - Doc in infantile spasm + tuberous sclerosis

Sturge - Weber syndrome

- It is due to sporadic gene mutation in chromosome - 9
- C/F - Hemangioma (port - wine stain)
  (in face - Trigeminal nerve distribution)
  - Glaucoma (mc C/F - in eye)
  - Leptomeningeal angioma
    - Calcify in brain
    - Tram track calcification

Scanned with CamScanner
Brain death in children

- Prerequisites before declaring brain death:
  * Done by two qualified persons at two time period (24-48hrs apart)
  * Reversible causes (hypothermia, shock, drugs, sedatives, neuromuscular blocking agents, CNS depressants) should be excluded

- Criteria for brain death:
  
  brainstem reflexes → Apnea test
  
  - Absent pupillary reflex
  - Absent corneal reflex
  - Absent oculocephalic reflex (Doll's eye response)
  - Absent oculovestibular reflex
  - Absent pharyngeal gag reflex

  Test is (+) if there is absence of breathing effort / respiratory drive when the paco₂ > 60 mm Hg or > 30 mm Hg from baseline.

  (To determine paco₂ → AETG is done)
PITUITARY DISORDERS

Hypopituitarism

Deficiency of pituitary hormones

- Etiology:
  - Congenital (common)
  - Developmental:
    - Aplasia / Anencephaly
  - Acquired
    - Trauma
    - Tumour
      - MC: Cranio-Pharyngioma
    - Infiltration
      - (Sarcoidosis)
    - Irradiation to Pituitary
  - Genetic:
    - PROP-1 gene
    - HESX-1 gene
    - Mutation

- Features of congenital hypopituitarism:
  - Mid facial hypoplasia
  - Cleft lip
  - Single maxillary central incisor

In Newborns: Hypoglycemia, Jaundice, micropallus, Small undescended testis.

Order of deficiency of hormones in hypopituitarism:

GH > LH, FSH > TSH > ACTH

- Treatment:
  - Replacement therapy:
    - Steroids are replaced first then thyroxine
    - If Thyroxine is given first → it can precipitate Adrenal crisis.

Growth hormone deficiency [Isolated]

- It can be a part of hypopituitarism also.
- Features:
  - Normal at birth
  - Retardation starts after 1 yr age.
  - Doll like facies
Proportionate short stature
Delayed bone age / dentition
Delayed puberty

- Screening investigations :
  - IGF - 1 (Insulin Growth Factor - 1) : ↓
  - IGFBP3 (IGF Binding Protein - 3) : ↓

- Diagnostic investigation :
  Growth Hormone (GH) stimulation test
  ↓
  Clonidine
  Insulin
  Glucagon,
  Arginine
  \{ agents used for stimulation \}

- Treatment :
  Administration of recombinant GH (Expensive)

Uses of recombinant GH [ "GTCS in Prader - Willi syndrome " ]
- E → GH deficiency
- T → Turner's syndrome
- C → CKD
- S → SGA (>2 yrs)
- SHOX mutation

Diabetes insipidus (DI)

- Due to ADH (Antidiuretic hormone) / Vasopressin

Produced in the hypothalamic supra optic nuclei
Discharged into posterior pituitary

- Normally ,
  ADH released → Acts on the kidneys (V2 receptor)

Expression of Aquaporin

↓ Urine output.
Diabetes Insipidus (DI)

Central (Neurogenic)
- Sufficient ADH - not produced from the CNS

Nephrogenic
- Due to defect in kidney

- v2 Receptor related
- X-linked Inheritance

- Aquaporin related
- Autosomal recessive inheritance

- Feature:
  Polyuria: urine output > 5 mL/kg/hr or > 2 L/m²/day

- Investigations:
  - Plasma osmolality - Normal
  - Urine osmolality - < 300 mOsm/kg
  - Water deprivation test
    - Normal
    - Plasma osmolality ↑
    - Urine osmolality ↑
  - DI
    - Plasma osmolality ↑
    - Urine osmolality ↓

- Administration of ADH
  - Response
    - Urine osmolality ↑
    - Central DI
  - No response
    - Nephrogenic DI

- Treatment:
  - Central DI: Desmopressin
  - Nephrogenic DI: Thiazide + Amlodipine
THYROID DISORDERS

Hypothyroidism

- Congenital
- Acquired

Congenital hypothyroidism:
- Etiology:
  - Thyroid dysgenesis: mc cause
    - Sporadic condition
    - Not associated with goiter
    - Thyroid dysshormogenesis:
      - 2nd mc cause
      - Autosomal recessive
      - Goiter

- Features:
  - Lethargy
  - Hoarse cry
  - MacroGLOSSIA
  - Umbilical hernia
  - Dry skin
  - Wide open fontanelle
  - Delayed passage of meconium
  - In the first week of life - They are asymptomatic
    (Due to maternal thyroxine)

- Investigations
  - Thyroid function test
    \[ \downarrow \text{free } T_4, \uparrow \text{TSH} \]
  - X-ray ➔ skull ➔
    1) Wormian bones ➔
      (Intrasutural bones)

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.
a) Long bones → epiphyseal dysgenesis.

**USG/CT/99™ scan:**

- No uptake of radionuclide
- Uptake in different location
- Upset uptake of radionuclide
- USG
- Ectopic thyroid
- Thyroid dys hormogenesis
- Gland present
- Absent
- Thyroid gland
- Maternal antibody
- Aplasia
- (Transient condition)

- Screening test: serum TSH.
  - Done: 2-4 days after birth (72 hrs)
- Treatment:
  - Thyroxine (10-15 mcg/kg)
  - Response: T₄ ↑ (first change) after 1 week of treatment; later TSH normalizes after 4 weeks

**Endemic cretinism**

- Condition of severe iodine deficiency
- The mother is also iodine deficient
- a types:
  - Neurologic type: severe intellectual disability, spasticity, seizures, deaf mutism, palpable goiter
  - Myxedematous type: moderate intellectual disability, goiter, myxedematous facies (loss of lateral eyebrow, dull face, dry coarse skin)

**Pendred’s syndrome**

- Problem in chr 7, codes for pendrin (PDS). It’s a chloride transporter
- This chloride transporter is expressed in:
  - Thyroid (hormone synthesis)
  - Cochlea
- Clinical features:
  - Hypothyroidism
    - Goiter: soft, diffusely enlarged gland
    - SNHL (due to distension of endolymphatic sac)
    - Mondini's deformity

Acquired hypothyroidism

- More common in adolescent girls
- More cause: Hashimoto's thyroiditis

- Clinical feature: Growth retardation (1st feature to appear)
  - Constipation
  - Dry skin
  - Weight gain despite poor appetite
  - Goiter - diffuse, firm, nontender
DISORDERS OF ADRENAL GLAND

Congenital adrenal hyperplasia

- MC adrenal disorder in children
- It is the deficiency of the following enzymes:
  - i) 11β - hydroxylase (MC)
  - ii) 17α - hydroxylase
  - iii) 17β - hydroxylase
  - iv) 3β - HSD (Hydroxysteroid dehydrogenase)

Cholesterol metabolism in adrenal

**Example**: if 11β hydroxylase is deficient

ADRENAL 

- Cholesterol 
- Dehydroepiandrosterone 
- Androsterone 
- Aldosterone

PITUITARY 

- ACTH 
- Cortisol 
- Testosterone 

Pediatrics • v2.0 • Marrow 4.0 • 2020 • AV

Scanned with CamScanner
Manifestations of enzyme deficiencies

i) \( \alpha \)-hydroxylase

\[ \text{↓ Aldosterone} \quad \text{↓ cortisol} \quad \text{↑↑ Testosterone} \]

\[ \rightarrow \text{Hypotension, shock} \quad \rightarrow \text{hypoglycemia} \quad \rightarrow \text{in males: precocious puberty} \]

\[ \rightarrow \text{Salt wasting - Hyponatremia} \quad \rightarrow \text{in females: virilization (Ambiguous Genitalia)} \]

\[ \rightarrow \text{Hyperkalemia} \]

- It is an Autosomal recessive disorder
  
  Prenatally → reduce virilization in female fetus

  at 6 weeks

  Dexamethasone given (cross placenta and ↓ ACTH)

  Chorionic villus sampling (to determine gender of the fetus)

  male

  female

  Stop dexamethasone

  continue dexamethasone

- Screening test at birth → 17\(-\)hydroxyprogesterone level

  It elevated

  Suggests CAH

Cholesterol → 17\( \delta \)Pregnene-3\( \alpha \)-ol → 17\( \alpha \)Hydroxy pregnenediol → 17\( \alpha \)Hydroxypregnenolone → 17\( \beta \)Hydroxypregnenolone → DHEA → DHEAS

Cholesterol → Pregnenolone \rightarrow 17\( \alpha \)-Hydroxy pregnenolone → 17\( \alpha \)-Hydroxypregnenolone → DHEA → DHEAS

Testosterone → 17\( \beta \)-Hydroxysteroid → Androstenedione

Cortisol → 11\( \beta \)-Hydroxy cortisol → 11\( \beta \)-Hydroxy cortisol

i) \( \beta \)-hydroxylase

\[ \rightarrow \text{↓ Aldosterone, ↓ cortisol, ↑ testosterone} \]
Deoxycorticosterone ↑ it has mineralocorticoid activity ↓
- Hypertension
- ↑ Na⁺, ↓ K⁺

Cholesterol

- SCC

Pregnenolone → 17β Hydroxyprogrenolone → DHEA → DHEAS

- 18-HSD

Progestrone → 17β Hydroxyprogesterone → Androstenedione

- 21-HSD

Deoxycorticosterone → 11-Deoxycorticosteron → Testosterone

- 18-HSD

Corticosterone → Cortisol

- 11β-HSD

Aldosterone

iii) 17β-hydroxylase
- ↓ Cortisol ↓ testosterone ↑ Aldosterone

Hypoglycemia.

- In males:
  → Ambiguous
  Genitalia in a male

Cholesterol

- SCC

Pregnenolone → 17β Hydroxyprogrenolone → DHEA → DHEAS

- 18-HSD

Progestrone → 17β Hydroxyprogesterone → Androstenedione

- 21-HSD

Deoxycorticosterone → 11-Deoxycorticosteron → Testosterone

- 18-HSD

Corticosterone → Cortisol

- 11β-HSD

Aldosterone

iv) 3β - HSD
- ↓ Aldosterone ↓ Cortisol

Hypotension

- Hypoglycemia.

- Testosterone

- Due to
  DHEA → DHEAS
  (weak androgen)

- In males
  → Virilization

- In females
  → Mild virilization
Cushing syndrome

Cushing syndrome (excessive glucocorticoids)

- **ACTH Dependent**
  - In children > 7 yrs
  - Cause:
    - Pituitary adenoma
      - (Cushing disease)
    - Ectopic ACTH - Neuroblastoma (MC)

- **ACTH Independent**
  - In children < 7 yrs
  - Cause:
    - Adrenal tumor
      - In infants - malignant Adrenocortical tumor

Clinical features:
- Cushingoid facies
  - Obesity - buffalo hump (due to more fat accumulation in shoulder).
- Abdominal striae
- Hypertension
- Decreased bone density
- HC / earliest feature - growth retardation

Diagnosis:

1. Screening test:
   - Overnight dexamethasone - fail to suppress level cortisol in Cushing syndrome.
   - 24 hour urine free cortisol - increased in Cushing syndrome
i) confirmatory test —

**Low dose**

Dexamethasone

\[ \text{ACTH} \]

- 
  - **< 5 pg/ml**
  - ACTH Independent
  - **> 15 pg/ml**
  - ACTH dependent

- **High dose**
  - Dexamethasone
  - ACTH Suppressed
    - Pituitary Adenoma
  - No ACTH suppression
    - Ectopic ACTH Secreting tumor

- **interior Petrosal sinus sampling**

To find out source of ACTH
DIABETES, PARATHYROID AND PUBERTAL DISORDERS

Hypoparathyroidism:

- Characterised by low PTH (parathyroid hormone) → ↓ calcium

Causes:
- Dysgenesis of parathyroid gland - DiGeorge syndrome
  ↓
  Poor development of 3rd / 4th branchial arch
- Iatrogenic - during thyroid surgery
- Autoimmune destruction of parathyroid gland - APECED
  ↓
  Autoimmune Polyendocrinopathy (Addison’s / adrenal and PTH)
  Candidiasis
  Ectodermal Dystrophy

- In neonates:
  i) Birth asphyxia
  ii) Prematurity
  iii) Infant of a diabetic mother

Clinical features:
- Latent tetany
  ↓
  Signs to elicit
  ↓
  Chvostek’s sign
  Trousseau sign
- Hypocalcaemic seizures
- Delayed dentition

Treatment:
- Calcium supplements
Pseudohypoparathyroidism

- PTH - normal or increased
- Defective ER (G protein coupled receptor)
  \(-\xi\alpha\) (\(\xi\) stimulatory alpha)
  ER \(\xi\alpha\)
  GPCR \(\xi\alpha\)
  ↓
  cAMP
  ↓
  CAMP
- Autosomal dominant disorder
- Characterised by Albright’s Hereditary Osteodystrophy - phenotypic.

Clinical features:
- Short, round facies
- Stocky build
- Short 4th and 5th metacarpals (knuckle - knuckle - dimple - dimple sign)
- Biochemical features → hypocalemia.
  On giving PTH → No ↑ in cAMP
- Depending on inheritance pattern
  ↓
  If maternal inheritance
  ↓
Pseudohypoparathyroidism
  (Both phenotypic and biochemical features present)
  ↓
  Normal biochemical features
  ↓
  Albright’s Hereditary Osteodystrophy
  ↓
Pseudopseudohypoparathyroidism
  (Only phenotypic features Present)

Delayed puberty

- > 13 years in girls
- > 14 years in boys
- Overall MC cause - constitutional delay
Other causes: -

Central

Hypogonadotropic hypogonadism

Syndromes associated:
- KAL-1 Kallmann syndrome
- Prader willi syndrome
- Laurence Moon Biedi Bardet Syndrome
  
  ○ C/♀: obesity
  ○ Polydactyly
  ○ Retinitis pigmentosa.

Peripheral

Hypogonadotropic hypogonadism

Syndromes associated:
- Turner syndrome
- Klinefelter syndrome
- Premature ovarian failure
  
  → In males -
    i) 5α reductase deficiency
    ii) AIS - androgen insensitivity syndrome

Precocious puberty

- <8 years in girls
- <9½ years in boys
- Causes (central more than peripheral)

Central

Girls

functioning tumor

→ Ovary

Boys

functioning tumor

→ Testis

→ Adrenal

→ hCG secreting tumor - germinoma

→ CAH:
  
  - 11β-hydroxylase deficiency - Café-au-lait
  - 11α-hydroxylase - Polyostotic Fibrous dysplasia

Girls

McCune Albright Syndrome

In girls - Idiopathic

In boys - Hypothalamic hamartoma

(Gelastic seizures)
Premature variants of precocious puberty
- Development of any one of the sexual characteristics:

<table>
<thead>
<tr>
<th>Thelarche</th>
<th>Pubarche</th>
<th>Menarche</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>1st sign of puberty</td>
<td>Premature Pubarche</td>
<td>Premature Menarche</td>
</tr>
<tr>
<td>Early thelarche</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Regular follow up (Because patients might develop after features of puberty early)</td>
<td>Familial variant</td>
<td>Not at all due to premature Puberty</td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td>R/O - Local causes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Foreign body</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Sexual abuse</td>
<td></td>
</tr>
</tbody>
</table>

Diagnosis:
- LH/FSH
- Bone age

Treatment:
- Treat underlying cause
- GnRH analogue
  Desensitises GnRH receptors and downregulates the receptors
  ↓
  LH/FSH

Diabetes mellitus (DM)
- mc type - Type 1 DM (autoimmune destruction of Β cells in the pancreas)
  ↓
  Insulin deficiency
- Important associations:
  i) HLA DR3/DR4
  ii) Mumps
  iii) Congenital Rubella Syndrome (late onset of DM)

Symptoms:
- Polyuria, polydipsia, polyphagia
Diagnosis:
- Any of the symptoms + any one of the following:
  1) Postprandial/random blood sugar ≥ 200 mg/dl
  2) Fasting blood sugar ≥ 126 mg/dl
  3) HbA1c >6.5%
- For performing glucose tolerance test → glucose: 1.75/1 kg given.

Treatment
- Insulin.
  - Dose: Pre pubertal 0.6 w/kg/day
  - post pubertal 1.2 w/kg/day

Types of insulin

<table>
<thead>
<tr>
<th>Rapid acting</th>
<th>Short acting</th>
<th>Intermediate acting</th>
<th>Long acting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eg: Lispro, aspart, glulisine</td>
<td>Eg: Regular insulin; given 20 mins before meals</td>
<td>Eg: NPH (Neutral Protamine Hagedorn) Duration of action - 12-18 hrs</td>
<td>Eg: Insulin detemir</td>
</tr>
<tr>
<td>Drug of choice - Toddler</td>
<td>Drug of choice - Adults or older children</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Administration of insulin

- Target - HbA1c < 7.5%
- Two regimens
  - Basal bolus regimen
  - Best regimen
  - Mimics physiological insulin secretion
  - Disadvantage - require multiple doses.
- Mixed split regimen
  - Short acting + intermediate acting
  - Given two times a day:
    - Before breakfast (1/3)
    - Before dinner (2/3)
Neonatal diabetes

- Onset of diabetes mellitus before 3 months of age
- Rare condition

Cause: activating mutation of the gene coding for $K_{ATP}$ channel

- Always open
- Calcium channel always closed
- No release of insulin

Treatment: sulfonylureas (closes $K_{ATP}$ channel) - drug of choice.
HEMATOLOGICAL MALIGNANCIES

Acute Lymphoblastic Leukemia (ALL)

- ALL - most common type of leukemia in children and most common malignancy overall in children.
- Peak age - 2 to 5 yrs
- Boys > Girls
- Risk factors:
  - A - Ataxia telangiectasia
  - B - Bloom's syndrome
  - C - severe Combined Immuno - deficiency
  - D - Down syndrome
  - E - Environmental factors (like radiation exposure)
  - F - Li Fraumeni syndrome, Fanconi's anaemia

- Types of ALL:
  - (i) progenitor B cell (pre B- cell) - 85% cases
  - (ii) T- cell
  - (iii) mature B- cell

- Features of ALL:
  - (i) Bone pain
  - (ii) Decrease in cell count - Anaemia, thrombocytopenia, leukopenia.
  - (iii) Infiltration - Hepatosplenomegaly
    - Lymphadenopathy
    - Mediastinal mass -> SVC Syndrome
    (more commonly associated with T- cell type)

- Diagnosis of ALL:
  - Bone marrow aspirate - >25% lymphoblast
### Standard risk and high risk

<table>
<thead>
<tr>
<th></th>
<th>Standard risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>2-10 yrs</td>
<td>&lt;1 yr, &gt;10 yrs</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td><strong>Features:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organomegaly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS features</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Initial WBC count</strong></td>
<td>&lt;50,000/cumm</td>
<td>&gt;50,000/cumm</td>
</tr>
<tr>
<td><strong>Subtypes</strong></td>
<td>Pre-B cell</td>
<td>Mature B-cell</td>
</tr>
<tr>
<td><strong>Genetic factors</strong></td>
<td>Hyperdiploidy, Trisomy 4, 10</td>
<td>Hypodiploidy, t(9;22) - Philadelphia, t(4;11) - &lt;1 yr - Infantile leukemia</td>
</tr>
</tbody>
</table>

**Intermediate risk** - T-cell type of ALL

**Treatment of ALL**

1. **Induction phase:**
   - Prednisolone
   - Asparaginase
   - Anthracycline
   - Vincristine

   - **In high risk:** Minimal Residual disease - (+) at the end of induction phase
   - Minimal Residual Disease - Minimal number of blasts present even at the end of induction phase.
     - Done using flow cytometry, PCR.

2. **Prophylactic CNS therapy:**
   - Intrathecal methotrexate

3. **Consolidation phase (intensification phase):**
   - Methotrexate
   - Epipodophyllotoxin
   - Cyclophosphamide
   - Cytosine - Arabinoside

4. **Maintenance phase:**
   - Methotrexate
   - 6 - mercaptopurine

**Acute myeloid leukemia (AML)**

- 2nd most common type of leukemia in children.
• **Diagnosis of AML:**
  Bone marrow aspirate – >20% myeloblasts.

• **Types of AML:**

<table>
<thead>
<tr>
<th>FAB</th>
<th>Name</th>
<th>Genetic variation and prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>Dedifferentiated / minimally differentiated</td>
<td>Deletion of 17q – poor prognosis</td>
</tr>
<tr>
<td>M1</td>
<td>Myeloblastic without maturation</td>
<td>t(8;21)</td>
</tr>
<tr>
<td>M2</td>
<td>Myeloblastic with maturation</td>
<td>t(15;17) – good prognosis</td>
</tr>
<tr>
<td>M3</td>
<td>Promyelocytic</td>
<td>Inversion – 16</td>
</tr>
<tr>
<td>M4</td>
<td>Myelomonocytic</td>
<td></td>
</tr>
<tr>
<td>M5</td>
<td>Monocytic</td>
<td></td>
</tr>
<tr>
<td>M6</td>
<td>Erythroleukemic</td>
<td></td>
</tr>
<tr>
<td>M7</td>
<td>Megakaryocytic</td>
<td>Down’s syndrome – good prognosis</td>
</tr>
</tbody>
</table>

• **Features of AML:**
  - Features similar to ALL
  - Except: no lymphadenopathy, no hepatosplenomegaly.
  - But, M4 AND M5 have associated hepatosplenomegaly.

- M3: increased risk of DIC
- M4: Gum hypertrophy
- Accumulation of myeloperoxidase: chloroma

Gum hypertrophy
Chloroma

**Leukemia and Down’s syndrome**

- Down’s syndrome has increased risk of leukemia.
- Most common leukemia overall – ALL
- Most common leukemia in age < 3 yrs – AML
- Transient myeloproliferative disorder:
  - New born
  - Myeloblast +
  - Hepatosplenomegaly
  - GATA-1 mutation
  - 20% cases develop leukemia.
Hodgkin's Lymphoma

- **Bimodal distribution:** 2nd - 3rd and 5th - 6th decade
- **Clinical presentation:**
  - Painless cervical
    Lymphadenopathy
- **Lymph node:** Firm, rubbery
- **Diagnosis:** Excision biopsy
- **Symptoms (Constitutional):**
  - Weight loss > 10% in 6 months
  - Night sweats
  - Fever

- **Types of Hodgkin's lymphoma:**
  1. Classical
     (CD - 15, CD - 30)
  2. Nodular - lymphocyte predominant
     (CD - 20, CD - 45)
- Nodular sclerosis
- Mixed cellularity
- Lymphocyte depletion
- Lymphocyte - rich

  - Nodular sclerosis is more common in developed countries
  - Mixed cellularity is more common in India.

- **Classical:** Reed sternberg cell
- **Nodular:** popcorn cell

**Modified Ann Arbor Staging**

- **Stage I:** Single lymphnode (LN)
- **Stage II:** a or more LN (one side of diaphragm)
- **Stage III:** LN on both sides of diaphragm
iv: Extranodal spread
   A: No B symptoms
   B: B symptoms (+)
   X: Bulky tumor (> 10 cm)
   E: Extension to (adjacent) extra-lymphatic site

Treatment of Hodgkin’s Lymphoma:
   ABVD chemotherapy regime - Adriamycin
   - Bleomycin
   - Vinblastine
   - Dacarbazine

Non-Hodgkin’s Lymphoma

- Absence of R-S cell
  Adult
  Low-grade
  Nodal
  child hood
  high grade
  Extra - nodal
    - Abdomen
    - Mediastinum

- Types: B-cell (i) Burkit (m/c)
  (ii) Diffuse large B cell
  (iii) Anaplastic large cell
  T cell - Lymphoblastic lymphoma
    (like ALL) - more common in India.
  - Burkit’s is associated with:
    (i) Epstein Barr virus
    (ii) Malaria

St. Jude staging system
- Localised (low risk)
  i: single tumor (site/node), excluding GI/mediastinum
  ii: multiple LN (one side of diaphragm)
    Single GI (resectable)
- Advanced (high risk)
  iii: Extensive GI involvement (non-resectable)
    Mediastinal involvement, paraspinal/epidural tumor
  iv: stage iii + CNS involvement and/or Bone marrow involvement.

Histiocytosis X

- Langerhans cell histiocytosis (LCH)
  - Non - malignant
  - Spectrum of disorder - single → multi system involvement.
Skull - Lytic lesion

Seborrhoeic scalp lesions

- Other features
  - Ear discharge
  - CNS: infiltration of pituitary stalk - Diabetes insipidus

Spectrum of LCH
- Eosinophilic granuloma - isolated bony lesion (lytic lesion in skull)
- Hand - Schuller Christian disease

Calvarial bone defect

Diabetes Insipidus
Exophthalmos

- Letterer - Siwe disease - multi-system disorder.
- Diagnosis - Biopsy
  (i) Electron microscopy:

Birbeck granules

Birbeck granules - tennis racket shaped

(i) Immunohistochemistry
  CD markers: CD 1a, CD 207 (langerin + ), S - 100

- Treatment:
  - Single lesion: curettage, intralesional steroidal therapy
  - Multi-system: chemotherapy (steroid, vinblastine, mercaptopurine)
OTHER MALIGNANCIES

Brain Tumor

- 2nd most common tumor overall and
- most common solid tumor.

Brain tumor

- Neurons
  - medulloblastoma.
- Glial cells
  - astrocytes - astrocytoma.
  - oligodendrocytes - oligodendroglioma.
  - Ependymal cells - ependymoma.
- Meninges
  - meningioma.

Brain tumor

- Most common tumor overall: astrocytoma (benign)
- Most common malignant tumor: medulloblastoma.

Clinical features of brain tumor

(i) Supratentorial
- Age: <1 yr, >10 yrs
- Features: focal seizures
  - Frontal lobe - speech impairment
  - Personality
  - Temporal lobe - speech impairment
  - Occipital lobe - vision impairment
  - Pituitary - hypopituitarism

(ii) Infratentorial
- Most common location of brain tumor in general in children
- Most common: posterior fossa.
- Age: 1 - 10 yrs
- Features: ↑ ICP - Early morning headache, vomiting,
  Papilledema, Hydrocephalus
Astrocytoma

- Most common brain tumor overall
- Most common location: cerebellum
- Most common type: JPA (Juvenile pilocytic astrocytoma)
  - Biopsy: Rosenthal fibres
- Benign tumors (WHO grade I)
- Treatment of astrocytoma: Surgery

Medulloblastoma

- Most common location: cerebellum
- Malignant tumor I (WHO grade IV)
- Spread (highly): extra neuronal sites, known as “drop metastasis”.
- Treatment of medulloblastoma: surgery + Radiotherapy

Craniopharyngioma

- A supratentorial tumor
- Cause: remnant of Rathke’s pouch
- Most common endocrine dysfunction: Growth hormone deficiency
- Clinical features: delayed puberty
  - Visual field defect - bitemporal hemianopia
- Characteristic feature: cystic lesions
  - CT brain: Calcifications

Neuroblastoma

- Neuroblastoma is
  - Most common intra-abdominal tumor
  - Most common malignancy in infancy (≤1 yr)
- Origin: Neural crest cells
- Site: 1st most common: supra renal (Adrenal medulla)
  - 2nd most common: Paravertebral sympathetic ganglia
- Genetics
  - Hyperdiploidy: Good prognosis
  - N: myc oncogene amplification: Poor prognosis
  - LOH (Loss of heterozygosity): Ip, Ip, Hq: Poor prognosis
- Clinical Features
  (i) **Raccoon eyes**
  - Periorbital swelling and ecchymosis

(iii) **Horner’s syndrome**
  - Ptosis
  - Anhydrosis
  - Miosis

( iii) **Paraneoplastic**
  - Opsoclonus - myoclonus ataxia (irregular movement of eyes and lips)
  - Vasoactive intestinal polypeptide (VIP) secretion which is associated with watery diarrhoea, hypokalemia.
  - Characteristic feature: calcification

Suprarenal mass - calcification

- Tumor markers:
  - Vanillyl mandelic acid (VMA)
  - Homovanillic acid (HVA)
  - Neuron specific enolase (specific marker)

International Neuroblastoma Staging System (INSS)
- Stage I: Completely resectable
- Stage 2: Incomplete resection
  - 2a: LN
  - 2b: Lymph node involvement
- Stage 3: Crosses midline
- Stage 4: Disseminated tumor
  - 4s: Infants, Stage 1 or stage 2 + dissemination to skin/liver/bone marrow
  - 4S has good prognosis.

Treatment:
(i) Localised: surgery
(ii) Advanced: surgery + chemotherapy + radiation

Drugs: Cisplatin, Cyclophosphamide, Vincristine, Teniposide.
Wilm’s tumor

- Wilm’s tumor
  - Most common renal malignancy
  - 2nd most common intra-abdominal tumor

- Age group: 2-5 yrs
- Risk factors
  1. Congenital malformations

  ![horse shoe kidney](image1.png)  ![cryptorchidism](image2.png)  ![hypospadias](image3.png)

  ![hemi hypertrophy](image4.png)

(ii) Syndromes

a. WT-1 gene (11p 13)
   - WAGR Syndrome - Wilm’s Tumor
     - Aniridia
     - Genito-urinary anomaly
     - Mental Retardation
   - Denys-Drash syndrome - mesangial sclerosis (early onset nephrotic syndrome
     - Male pseudohermaphroditism

b. WT - 2 gene (11p 15.5)
   - Beckwith Wiedmann syndrome - Hemi hypertrophy,
     - Macroglossia,
     - Earlobe creases,
     - Omphalocele

  ![macroglossia](image5.png)

  ![earlobe creases](image6.png)
• Clinical Features
  (i) Characteristic: asymptomatic abdominal mass
  (ii) Unexpected hypertension/hematuria.
• Staging of Wilms’ tumor:
  i: Confined to kidney, completely excised
  ii: Extends outside kidney, completely excised
  iii: Limited to abdomen, lymph node involvement +
  iv: Distant hematogenous metastasis
  v: Bilateral kidney
• Treatment of Wilms’ tumor: Surgery + Chemotherapy
  • Drugs:
    - Vincristine
    - Actinomycin

Warning: Not all points are covered in the notes, especially conceptual explanations. Please use the notes in conjunction with Marrow Edition 4 videos.

Summary
• Most common tumor overall: ALL
• 2nd most common tumor / most common solid tumor: Brain tumor (MC: Astrocytoma)
• MC malignant brain tumor: Medulloblastoma
• MC tumor infancy: Neuroblastoma.
• MC renal tumor in childhood: Wilms’ tumor
RHEUMATOLOGICAL DISORDERS

Juvenile Idiopathic Arthritis (JIA)

- Chronic arthritis (≥ 6 weeks)
- Age of onset ≤ 16 yrs

- Types of JIA:
  1) Systemic onset JIA:
     - Arthritis + fever + systemic features (Any one)
     - Fever: ≥ 2 weeks.
       - Quotidian fever
       - Temperature ≥ 39°C at least once a day followed by return of temperature to the baseline.

- Systemic features:
  - Evanescent salmon rash
  - Not present throughout the day
  - Generalised lymphnode enlargement
  - Hepatosplenomegaly
  - Serositis

a) Oligoarticular JIA:
  - ≤ 4 joints involved
  - Common in girls
  - MC type of JIA
  - Most children have antinuclear antibody (ANA)
    - this ↑ risk of uveitis

b) Polyarticular JIA:
  - Joints involved: ≥ 5
  - < 6 yr age = Asymmetrically affected
    - Rheumatoid factor (RF)
    - No rheumatoid nodules.
  - > 6 yr age = Symmetrically affected
    - RF
    - Rheumatoid nodules
4) Psoriatic JIA:
- Features of psoriasis (or) any of the following:
  - Dactylitis
  - Fitting of nails
  - First degree relatives affected with this condition.

5) Enthesitis related JIA:
- Enthesis = place where ligament & joint get attached to the bone.
- HLA-B27
- In adulthood - can develop ankylosing spondylitis

Treatment of JIA:
- First choice → NSAID

  Intra articular steroids (triamcinolone)
  → DMARD (Disease modifying anti- rheumatic drugs)
  → Methotrexate

Juvenile dermatomyositis

- Inflammation of skin & muscle
- Essential features:
  - Heliotrope rash
  - Gottron's papule

- Other features: any 3 out of 4 should be present
  - Symmetrical proximal muscle weakness
    - Gottron's sign
    - ↑ muscle enzymes: creatine kinase / aldolase
    - Electromyogram: features suggestive of myopathy
    - Muscle biopsy: muscle fiber necrosis.
"Diagnosis of juvenile dermatomyositis is done if heliotrope rash / gottron’s papule is present along with 3 of the other features."

- Other finding:
  - Shawl sign
  - Mechanics hand

Erythematous rash over sun exposed area.

Thick erythematous & scaly rashes over the palm.

- Treatment:
  - Methylenepridolone - to treat the inflammation
  - For maintenance - methotrexate

Kawasaki Disease

- Medium vessel vasculitis - (Coronary artery)
- MC vasculitis disorder
- Early feature:
  - Fever \( \geq 5 \) days
  - CREAM
    - Mucosal changes - strawberry tongue

A-Conjunctivitis, B- Strawberry tongue, C- Single cervical lymphadenopathy, D-Rash, E- Edema & erythema of legs, F- Skin peeling from fingertips, G- Reactivation in BCG scar region, H- Perianal desquamation.

- Diagnosis: fever \( \geq 5 \) days + atleast (4/5) among CREAM
  - (or) Echocardiography show any abnormality
- Treatment:
  - Treatment of choice - Intravenous immunoglobulins
  - Aspirin - Anti-inflammatory

**Henoch - schonlein purpura**

- Small vessel vasculitis
- **Palpable purpura with normal platelet count.**
  - (Seen at gravity dependent areas like lower limb & buttock region)

- **Diagnosed when purpura is present,**
  - along with one of the following features:
    - Abdominal pain
    - Arthritis / Arthralgia
    - Renal findings (Hematuria and/or proteinuria)
    - Skin/Renal biopsy → IgA depositions.
ANEMIA IN CHILDREN

WHO definition of anemia:
Based on hemoglobin (Hb)
Levels as per the age group

<table>
<thead>
<tr>
<th>Age group</th>
<th>Hemoglobin cut-off (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months - 5 years</td>
<td>11</td>
</tr>
<tr>
<td>5 - 11 years</td>
<td>11.5</td>
</tr>
<tr>
<td>&gt; 12 years</td>
<td>12</td>
</tr>
</tbody>
</table>

Iron deficiency anemia

m/c condition causing anemia in children - iron deficiency
m/c micro nutrient deficient all over the world - iron

Causes of iron deficiency in children:
• ↑ Demand - growth spur
• ↓ Absorption - malabsorption [m/c - hookworm infestation]

Age group - 9 months - 24 months
In first 6-9 months → no anemia d/t iron stores
derived from mother at last trimester of pregnancy

Associations in clinical situations:
• Temper tantrum
• Breath holding spells
• Pica
• Restless leg syndrome

C/F- • pallor
• koilonychia

Treatment:
Most economical & effective form of iron - ferrous sulfate. Earliest response following iron treatment is clinical in the form of subjective improvement

First hematological finding following iron therapy

⇒ Reticulocytosis

response to iron therapy

<table>
<thead>
<tr>
<th>TIME AFTER IRON ADMINISTRATION</th>
<th>RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-24 hr</td>
<td>Replacement of intracellular iron enzymes; subjective improvement; decreased instability; increased appetite</td>
</tr>
<tr>
<td>36-48 hr</td>
<td>Initial bone marrow response; erythroid hyperplasia</td>
</tr>
<tr>
<td>48-72 hr</td>
<td>Reticulocytosis, peaking at 5-7 days</td>
</tr>
<tr>
<td>4-30 days</td>
<td>Increase in hemoglobin level</td>
</tr>
<tr>
<td>1-3 mo</td>
<td>Repletion of stores</td>
</tr>
</tbody>
</table>
Megaloblastic anemia

Cause: Vit B₉ deficiency or folate deficiency or both

Cause for Vit B₉ deficiency:
- Person on pure veg diet
- Autoimmune - pernicious anemia
- Intrinsic factor deficiency
- Metabolic disorders:
  - Orotic aciduria
  - Methylmalonic acidemia
  - Homocystinuria
- Thiamine responsive megaloblastic anemia (TRMA)

Cause for folate deficiency:
- Goat milk consumption
- Improper utilization of folic acid due to
  - 6 mercaptopurine
  - Methotrexate
  - Trimethoprim

Features:
- Hyperpigmentation - knuckles
- Neurological features - loss of position & vibration sense
  (Earliest change) - in Vit B₉ deficiency
  "Neurological symptoms can precede pallor"

Inherited pancytopenia

Fanconi's anemia: Autosomal recessive
- Defect in DNA repair
- Features: 3'5' - Short stature
  Skeletal malformations
  Skin pigmentation - hyperpigmentation
  (Café-au-lait macules)
- Treatment:
  - HSCT (Hematopoietic stem cell transplant)
  - Palliative - oral androgens

Hereditary spherocytosis

- Autosomal dominant
- Defect in RBC cytoskeleton

Abnormal shape of RBC
"Spherocyte"
Ankyrin - MC defect
Spectrin - most severe defect
- RBC destruction in spleen
Recurrence episodes of - Anemia + jaundice

Treatment - • Folic acid (life long supplementation)
  • Splenectomy - improve anemia & normalize RBC survival.

Splenectomy in children: deferred until age of 5 years because it ↑ risk of encapsulated infections like H. influenza, pneumococci, Streptococcus pneumoniae.

• Vaccination against these organisms is a must before splenectomy
• Penicillin prophylaxis is required

Sickle cell anemia

Defect: β globin chain of Hb at 6th position
Glutamine is replaced by valine
Hence HbS levels ↑
HbS - undergo sickling in dehydration, hypoxia etc.

RBC membrane

- It causes “Blockage of microvasculature”
Clinical Features:
- Crisis - sudden event caused due to sickling
  - Vaso-occlusive - pain & swelling
    First → Dactylitis
  - Aplastic - usually due to parvovirus B19 infection
  - Sequestration - in spleen;
    sudden ↑ in spleen size; ↓ Hb (> 2 gl/dl from base line)
- Neurological: stroke
- Kidney: papillary necrosis
- Infarct: spleen - Auto splenectomy
- ↑ Recurrent infection (Encapsulated bacteria)
  → Osteomyelitis (staph aureus > salmonella)

Treatment:
- Hydration
- Analgesia
- Blood transfusion - aplastic / sequestration crisis
- Exchange transfusion - stroke. (↑ HbA)

Long term management: hydroxyurea → ↑ HbF to protect RBC from sickling.

β Thalassemia

Disease of varying severity with ↓ or absent β globin chains

Types:
- β Thalassemia trait
- Thalassemia intermedia
- Thalassemia major aka transfusion dependent form of thalassemia

“Ineffective erythropoiesis”: Destruction of erythroid cells in bone marrow

- Extramedullary hematopoesis

↑ Organomegaly

Bony deformities

- Hemolytic / chipmunk facies; d/t maxillary hyperplasia and prominent incisor

- “Hair on end” appearance of skull on x-ray; d/t widening of diploic spaces in skull

Treatment:
- Blood transfusion - “Hyper transfusion Regimen”
  - Pretransfusion Hb → 9.5 - 10.5 g/dL
High pretransfusion Hb:
- For better growth
- Improvement in bone deformities
  
  **Risk** - Iron overload → managed with chelation therapy

**Chelation therapy:** Deferoxamine (S/C)

- Deferiprone
- Deferasirox (oral)

To be started when ferritin > 1000 ng/ml

**Curative:** HSCT
BLEEDING DISORDERS

Bleeding disorders - introduction

- If there is a cut in the skin leading to bleeding, the changes which happen to stop bleeding are:
  
  Vasoconstriction  \(\rightarrow\) platelet plug \(\rightarrow\) Coagulation
  
  (vessels) \(\rightarrow\) (Formation) \(\rightarrow\) (Clotting factors)

- Defects:
  - Hereditary hemorrhagic Telangiectasia
  - Osler - Weber - Rendu
  - Scurvy
  - Vasculitis

- Bleeding disorders approach

<table>
<thead>
<tr>
<th>Finding</th>
<th>Disorders of coagulation</th>
<th>Disorders of platelets or vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Petechiae</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>- Deep dissecting hematomas</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>- Superficial ecchymoses</td>
<td>Single; large</td>
<td>multiple; small</td>
</tr>
<tr>
<td>- Hemarthrosis</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>- Delayed bleeding</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>- Bleeding from superficial cuts and scratches</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Idiopathic thrombocytopenic purpura

- Also called as immune thrombocytopenic purpura (ITP)
- Antibody mediated
- Usually in age group 1-7 years
- Types: Acute (m. c. type)
  - Chronic (persists > 6 months)
Acute ITP

- Typical presentation:

Non-specific
Viral infection
- Petechiae, purpura in a previously well child
- No splenomegaly, no lymphadenopathy
- Treatment:
  - > 20,000 / µL
    - No active bleed
    - Observation
  - < 20,000 / µL
    - Active bleed
    - IVIG (Intravenous immunoglobulins)
    - (Prevent destruction of antibody coated platelets)
    - Steroids
    - Anti-D (Rh+ children)

Platelet Function Disorders

- Platelet receptor function:
  - GP IIb/IIIa
  - GP Ib
  - Endothelium
  - Subendothelium
  - VWF

  - Aggregation
  - Adhesion

- a major platelet function disorders:

  - Glanzmann's thrombasthenia
  - Bernard soulier syndrome
    - Defect in GP IIb/IIIa
    - Defect in GP Ib
    - Defect in platelet aggregation
    - Defect in platelet adhesion
    - Normal platelet number
    - ↓ platelet number
    - Normal sized platelets
    - ↑ sized platelets
Von Willebrand disease

- MC inherited bleeding disorder worldwide
- Functions of von willebrand factor (vWF):
  1. Carrier for factor B
  2. Helps in attachment of platelet to endothelium
- Types:
  1. Type I
    - ↓ vWF (MC)
    - Treatment: Desmopressin
  2. Type II
    - Impaired function of vWF
    - Treatment: vWF concentrates
  3. Type III
    - Absent vWF
    - Treatment: vWF concentrates

Hemophillia

- Types: Hemophilia A → Factor VIII deficiency
  Hemophilia B → Factor IX deficiency
- Hallmark Feature: Recurrent hemarthrosis
- Target joint: A joint which is prone to recurrent hemarthrosis
- Treatment: Factor replacement

<table>
<thead>
<tr>
<th>Hemophilia, A</th>
<th>Hemophilia, B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of factor</td>
<td>Amount of factor</td>
</tr>
<tr>
<td>required</td>
<td>required</td>
</tr>
<tr>
<td>% desired rise x body weight (kg) x 0.5</td>
<td>% desired rise x body weight (kg) x 1.4</td>
</tr>
</tbody>
</table>

- % rise is estimated based on severity of bleeding:
  - Severe bleed (CNS) → 100 %
  - Less severe bleed → 30 - 50 %

- If factor replacement is not available, alternative treatment options:
  - Fresh frozen plasma or
  - Cryoprecipitate (does not contain factor IX)
SHOCK

- Inadequate delivery of oxygen to tissue
- Metabolic demands of tissue are not met.

Stages of shock:

1. Uncompensated shock:
   - Restlessness
   - Tachycardia: earliest sign
   - Mild tachypnea
   - Capillary filling time (CFT) >3 sec.
     [Normal CFT: ≤2 seconds]

2. Compensated shock:
   - Drowsiness
   - Oliguria
   - CFT >5 sec.
   - Hypotension
   - Narrow pulse pressure.
   - Cold extremities.

3. Irreversible shock:
   - Unresponsive
   - Anuria
   - Apnea
   - Bradycardia
   - BP unrecordable

Types of shock

1. Hypovolemic shock - most common:
   - Due to decreased circulating blood volume.
2. Cardiogenic shock: impaired cardiac contractility
3. Distributive shock:
   - Blood volume normal
   - Due to vasodilation, pooling of blood occurs within blood vessels
     leading to inadequate supply to tissues.
     - Seen in allergy
4. Septic shock:
   - Associated with infections
- Combination of all 3 types of shock.
- Types:
  a) Cold (common)
    - Low cardiac output + high systemic vascular resistance (SVR)
      * Cold extremities
      * Feeble pulse
      * CFT prolonged
  b) Warm
    - High cardiac output + low SVR.
      * Warm extremities
      *Bounding pulse
      * Flash capillary refill

Management of shock

- Early recognition
- Vigorous treatment
- Initial treatment of choice:
  - Intravenous fluids
  - Fluids preferred: crystalloids (NS → Preferred)
    - 20 ml/kg over 5-10 minutes
  - If response is inadequate, it is known as fluid refractory shock
  - Inotropes are to be used.
    - Initial inotrope: Dopamine (10 μg/kg/min)
      - Upto 15 μg/kg/min.
      - No response
      - Assess the patient
  - Warm shock
    - Administer norepinephrine
    - No response
    - Fluid and inotrope refractory shock
      - Give hydrocortisone
  - Cold shock
    - Administer epinephrine

- Cold shock with normal BP:
  - Vasodilators or type 3 phosphodiesterase inhibitors
    (Like Milrinone) can be used.
Other measures:

1. In severe acidosis (pH < 7)
   - NaHCO$_3$ 1-2 mEq/kg to be given
2. Treatment of hypoglycemia / hypocalcemia.
3. Aggressive treatment of infections (in septic shock)
   - 3rd generation cephalosporin
     + Aminoglycoside
CARDIOPULMONARY RESUSCITATION

Pediatric life support

Done during "Cardiopulmonary Arrest"

→ Less common in Children
→ Is often d/t Respiratory failure
→ (or) Terminal Stage of Shock

Sequence of CPR:
( in Children ) Assessment → Circulation → Airway → Breathing

Assessment

- Done to confirm cardiac arrest
- In an unresponsive Child → • Absent Breathing
  • Abnormal Breathing
- Pulse (≤ 10 Sec)

Compression

- Done in an effort to maintain circulation
- Depth — should be 1/3rd of AP diameter of chest
- Rate — 100-120/min (Push hard, Push fast)

Technique:
- Child < 1 year
  "Two Thumb Technique"
- Child 1-8 years
  "Heel of one hand"
Child > 8 years ➔ Heel of a hand
with interlocking of finger)

“Avoid xiphoid process” – during
compression

Airway

modes to keep the airway open:

- Jaw Thrust
- Chin lift

- Fingers placed on underside/angle of jaw –
it is lifted upwards and outwards.
- Head tilt and Chin lift
  - Not done in case of head
  and neck trauma.

Breathing

manual ventilation

Non invasive (bag and mask)

Invasive (endotracheal intubation)

Bag and mask –

- Bag volume – 240-750ml
  depending on age of child.

Endotracheal intubation –

- Most effective way of manual
  ventilation

Size of Endotracheal Tube (ET):

\[
\text{Size ET (in mm)} = \frac{\text{Age (years)}}{4} + 4
\]

Depth of insertion of ET tube: 3 x Size of ET
Vascular access

- Largest accessible vein has to be used.
- MC used vein - femoral vein.
- If not possible - intraosseous access
  → Site: below and medial to tibial tuberosity.
  Avoid - growth plate.

![Diagram of femur and tibia](image)

CPR: protocol (algorithm)

Unresponsive

→ Access Breathing/Pulse (≤ 10 Sec)

No breathing, Pulse → CPR

- Ratio: 30:2 - 1 rescuer
  (Compression/ventilation)
  15:2 - 2 rescuer
- After Amin, connect AED
  (Automatic External Defibrillator)

No breathing, Pulse

→ Provide - Rescue Breath

- 1 breath every 3-5 sec
- Recheck pulse every 2 min
- Pulse → Start compression
- Pulse ≤ 60/min; signs of poor perfusion → CPR
**AED:** Automatic External Defibrillator
- Can assess Rhythm

**Shockable**
- Ventricular tachycardia
- Ventricular fibrillation

**Non-Shockable**
- Asystole
- PEA (Pulseless Electrical Activity)

**Shock** ($2J/kg$)
(total shock should not exceed $10J/kg$

**Reversible Causes:**

**4 H’s**
- Hypovolemia
- Hypothermia
- Hypoxia
- Hyperkalemia

**4 T’s**
- Tension Pneumothorax
- Tamponade (Cardiac)
- Toxin / Drug
- Thromboembolism (Pulmonary)
**IMMUNODEFICIENCY DISORDERS**

Primary immunodeficiency disorder:

- **T - cell**
  - DiGeorge syndrome
  - Selective immunoglobulin deficiency disorder
  - Hyper IgM syndrome

- **B - cell**
  - Agammaglobulinemia

- Combined immuno deficiency disorder
  - Severe combined Immunodeficiency Disorder (SCID)
  - Wiskott Aldrich
  - Ataxia telangiectasia

**DiGeorge syndrome**

- **T - cell immunodeficiency disorder**
- Cause: Abnormal development of 3rd and 4th branchial arch
  
  → Thymic hypoplasia / aplasia
  
  → T - cell immunodeficiency

- **Characteristic features:**
  - C - Congenital heart Defect (Conotruncal anomalies)
  - A - Abnormal facies (Short philtrum, Antimongolid slant, Folded ears)
  - T - T - cell immunodeficiency
  - C - Cleft lip / palate
  - H - Hypocalcemia
  - aa - Microdeletion of 22q 11.2

**B - Cell immunodeficiency disorders**

(i) X - linked Agammaglobulinemia
(ii) Selective immunodeficiency disorder
(iii) Hyper IgM syndrome
(i) X-linked Agammaglobulinemia (XLA):
- Cause: Bruton's tyrosine kinase deficiency
- XLA is also known as Bruton's agammaglobulinemia.
- Clinical features:
  - Absent / Small tonsils, adenoids, lymph nodes.
  - Recurrent pyogenic infection (Encapsulated bacteria: streptococcus pneumoniae, Hemophilus influenza type B, meningococcus).
- Treatment: periodic replacement of (Ig's) immunoglobulins iv every 3-4 weeks.

(ii) Selective immunodeficiency disorder:
  a.) isolated IgA deficiency:
    - most common primary (1%) immunodeficiency disorder
  b.) IgE subclass deficiency:
    - IgE1: Diphtheria, Tetanus infection
    - IgE2: Recurrent encapsulated bacterial infection
    - IgE3: Increased risk of viral infection
    - IgE4: Increased risk of parasitic infection

(iii) Hyper IgM syndrome:
- Cause: deficiency of CD40 ligand.

\[
\theta
\]

\[\text{B-cell} \rightarrow \text{IgM} \xrightarrow{\text{class switching}} \text{IgA / IgD / IgE}\]

- ↑ Risk of pneumocystis carinii infection

Combined immunodeficiency disorder

(i) SCID
- Severe combined Immuno Deficiency disorder
- X-linked recessive (only males are affected)
- Cause: mutation in common γ (gamma) chain of IL-2 γ
- Features:
  - Recurrent infection since birth
  - Absent tonsils, adenoid, thymus.
- Treatment:
  - Bone marrow transplantation
  - Gene therapy
(ii) Wiskott Aldrich syndrome:
- X-linked recessive disorder
- Cause: mutation in XP 11.22 - 11.23 (WASP - Wiskott Aldrich syndrome protein)
- Feature:
  - Triad: Recurrent infection, Thrombocytopenia, (microplatelets), Eczema.
  - Elevated levels of IgA, IgE.
- Treatment: Bone marrow transplantation

(iii) Ataxia Telangiectasia:
- Cause: mutation in chromosome 11q
- Feature:
  - Initial: ataxia
  - Dilated blood vessels
  - Recurrent infection → Death of the child
- Chromosomal instability → ↑ risk of cancer
- Tumour marker: Alpha fetoprotein

Miscellaneous disorders

(i) Macrophage disorders:
(a) Leukocyte adhesion defect (LAD):
  - Cause: defect in β1 integrin (LAD type I) - most common
    - Defect in selectin (sialyl Lewis X receptor)
  - Clinical feature:
    - Recurrent infection (absence of pus)
    - Delayed fall of umbilical cord
  - Diagnosis: flow cytometry - deficiency of CD18
(b) Chronic Granulomatous Disease:
  - X-linked recessive
  - Defect in NADPH oxidase
  - Features: Recurrent abscess formation
    - Especially by catalase +ve organisms like Staphylococcus, Serratia, fungi (candidiasis)
  - Screening test: Nitroblue tetrazolium (NBT test)

No colour change → Colour change
- Change in colour indicate presence of NAOPH oxidase
- No change in colour indicates absence of NAOPH oxidase
- Confirmatory test: Dihydro - rhodamine assay (DHR assay)

(i) Complement defects:
- Early: C₃ - C₅ - Recurrent bacterial infection
- Late: C₅ - C₉ - Recurrent Neisseria infection
- C₁ esterase inhibitor deficiency:
  - Hereditary Angioneurotic edema
  - Autosomal dominant disorder
  - Recurrent non-itching edema