1 ASSESSMENT OF GROWTH AND GROWTH CHARTS

Growth

00:00:15

- Growth: Increase in physical size

Embryo	1st 8 weeks of IU life
Fetus	9th week till delivery (birth of baby)
Neonate	1st 28 days of life
Infant	1st year of life
Toddler	1-3 years
Pre school	3-6 years
Adolescent	10-19 years

Growth is assessed using Important Arthropometric parameters

00:03:37

- Anthro: Human
- Pometry: Measurement

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

Mid Arm Circumference (MAC) / Mid Upper Arm Circumference (MUAC)

- It is circumference of the middle point on the arm
- It is the circumference of mid point of distance between acromion process and olecranon process
- While measuring MAC the arm of the child should be hanging loosely by the side.

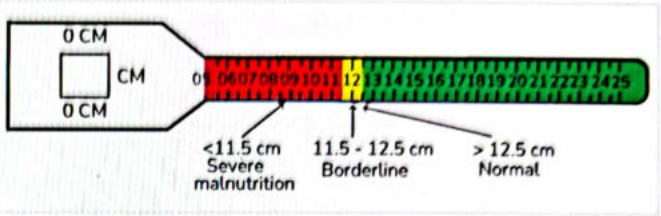
Normal MAC

- Term Neonate: 9-11 cm
- By end of 1st year: 16 cm
- Tanners chart was used previously to get normal value of mid upper arm circumference (MUAC) at different age groups.
- Age independent anthropometric parameters (6months - 5years)

Important Information

- WHO charts are used now
- Between 1-5 year: Increase by 0.25 cm/year so it is regarded as age independent anthropometric parameter

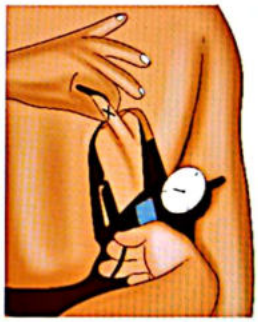
- Device used by health workers to measure MAC: Shakir's Tape, It used for 6 months to 5 years age groups.



Skin fold thickness

00:12:20

- It gives an idea of the amount of subcutaneous fat present in the child.
- Device used to measure it: Harpenden Callipers or Skin fold thickness callipers.
- Areas where skin fold thickness is measured
  - Supra scapular
  - Subscapular
  - Biceps
  - Triceps
- WHO charts are used now to get the normal value of skin fold thickness in various age groups.



Chest Circumference (CC)

- At birth: Head Circumference (HC) > Chest Circumference (CC)
- By 9 months - 1 year: HC = CC
- In a normal child, beyond 1 year of age, CC > HC

Important Information

- If any of the above parameters differ, It indicates underlying Malnutrition

Body Mass Index (BMI)

- Body Mass Index (BMI) = $\frac{\text{Weight (Kg)}}{\text{Height (m)2}}$

BMI

- <5th percentile: Underweight
- >85th percentile: Overweight
- >95th percentile: Obesity

Growth Charts 00:17:38

- Graphical representation of the anthropometric parameters

International Growth Charts

- NCHS Growth Charts (1977)
- CDC Growth Charts (2000)
- WHO Growth Charts (2006) preferred growth chart for under 5 years of age

NCHS: National Center for Health Statistics
CDC: Center for Disease Control & Prevention

WHO Growth Charts 00:20:53

- Preferred growth charts for under 5 years of children all over the world
- Based on MGRS (Multicentre Growth Reference Study)
- Children from 6 different countries across the world were enrolled
- Countries included in MGRS
  - **B - Brazil**
  - **O - Oman**
  - **N - Norway**
  - **G - Ghana**
  - **U - US**
  - **I - India [New Delhi]**

How to Remember?

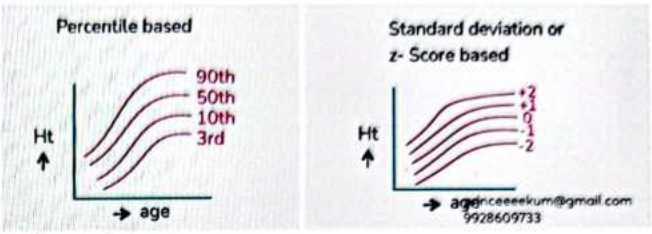
- BONGUI
- Enrolled only those children who are exclusively breastfed in 1st few months of life
- Excluded factors like Maternal smoking & Alcohol
- WHO growth charts include charts for

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

- Separate charts for boys (blue color charts) & girls (pink color charts)

2 types of growth charts are available

Percentile based	Standard deviation or Z-score based



Indian Growth Charts (Local growth charts)

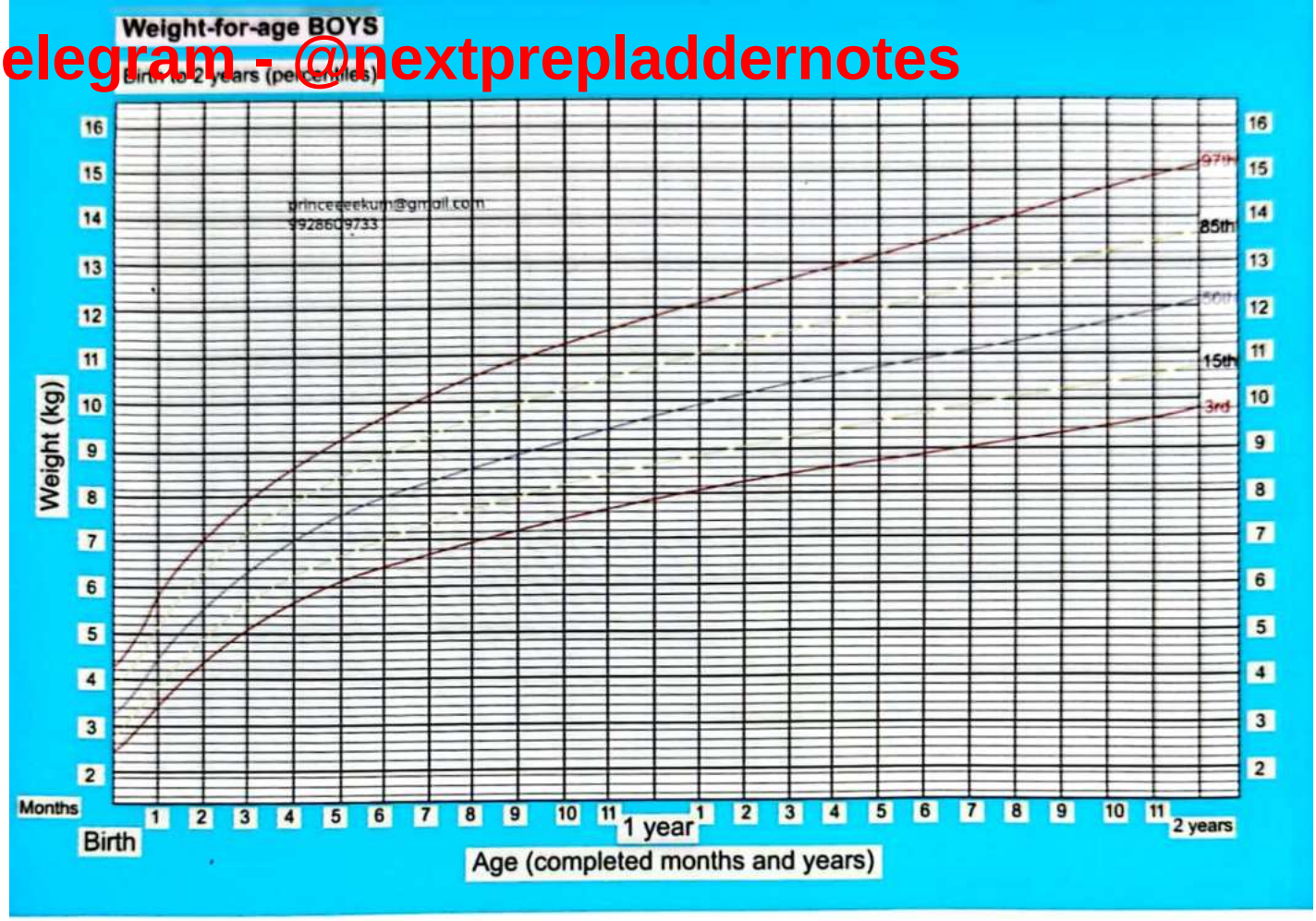
- Preferred beyond 5 years of age
- Different types of Indian Growth charts

1. K.N. Agarwal Charts
2. IAP (Indian Academy of Pediatrics) charts
3. Khadilkar Charts

Important Information

Q. How to assess growth of child?
Ans.

- Decide which anthropometric parameter to use
- Choose appropriate device measure
- Plot on growth chart and compare with normal expected value for that age
- Interpret



ealthy, no advise is given

nalnourished child, Refer for nutritional rehabilitation

ely malnourished. Advice mother to feed calorie dense food

nalnourished, Advice mother for home based care.

2 NORMAL ANTHROPOMETRIC PARAMETERS

Normal Anthropometric Parameters

- Weight
- Height
- Head circumference

Weight

00:00:42

- Device used to measure weight of a child
  - In infants (<10 kg) = Pan type or basket type weighing scale
  - Older children = Platform type weighing scale

Precautions while checking weight of baby

1. Child should be in bare minimum clothes. For small baby remove everything including diaper if possible
2. Tare function should be in weighing machine
3. Entire baby should be in pan and let the weight stabilize

Important Information

- Birth weight of an average in Indian baby: 2.9 Kg.

How the weight increases with age?

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

- Birth weight doubles itself at 5 month of age,
- Birth weight triple itself by 1 year of age

How much is the weight gain in a baby in different age groups?

0-3 month	30g/day
3-6 month	20g/day
6-9 month	15g/day
9-12 month	12g/day
1-3 year	8g/day

Formula for calculating expected weight of Child

- < 1 year = $\frac{x+9}{2}$, where x: age in months
- 1 - 6 year = 2x + 8, where x: age in years
- 7 - 12 years = $\frac{7x-5}{2}$, where x: age in years

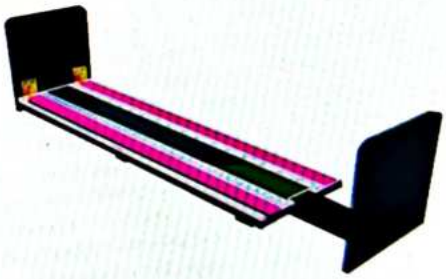
Height (Length)

00:07:05

- Length measured in < 2 years of age child.
  - Device used to measure length: Infantometer
- Height measured in > 2 years of age child.
  - Device used to measure height: Stadiometer

Important Information

- Recumbent length of a child is 0.7 - 1 cm more than the standing height of a child"



Infantometer

Precautions while checking height of baby

1. Remove the footwear
2. Child should stand erect
3. While standing occiput, back of shoulders, buttocks and back of heel should touch the vertical rod behind
4. Remove any cap, hairband, ponytail.
5. Child should look straight in horizontally forward plane
6. In infants ideally 2 persons are required, one will fix the vertical board at the head of child and one will extend the legs of child

Length/ height of child

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

Important Information

- Length of the child ↑ses by 50% in 1st year
- Maximum growth of a child takes place during 1st year of life followed by Puberty
- Height of a child doubles itself or increases by 100% in 4 – 4 ½ years

- Calculation of Expected height of child = (6x + 77) cm, x is age in years
- Example
  - Age of child = 7 years
  - Height of child = 6 x 7 + 77
    = 42 + 77
    = 119 cm

Gain in height or length

Age group	Approx gain in length or Height
0 – 3 months	3.5 cm/month
3 – 6 months	2 cm/month
6 – 9 months	1.5 cm/month
9 - 12 months	1.2 cm/month
1 – 3 years	0.8 - 1 cm/month

Upper Segment: Lower Segment Ratio 00:17:04

- Upper segment: Part of the body above symphysis pubis
- Lower segment: part of the body below symphysis pubis

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

Arm Span 00:18:46

- Measured on outstretched arms 90 degree to the body from tip of middle finger of one hand to tip of middle finger of other hand.
- Almost equal to height of the child.

Important Information

- Arm span almost equal to Height of child, the difference is less than 3 cm

- At age < 10 years, Arm span is 1 – 2 cm less than height of child
- At age >10 years, Arm span more than height of child
- If difference is more than 3 cm, it is abnormal

Head Circumference/ Occipito Frontal Circumference (OFC) 00:20:50

- It is maximum circumference of head from occiput at back to supraorbital area in front of head
- Measured using Non stretchable measuring tape with 'mm' marking
- To be measured to an accuracy of 0.1 cm

Precautions to be taken while measuring head circumference

1. Don't use tailors tape
2. Use non stretchable tape
3. Use overlapping technique
4. Hair accessories to be removed
5. Measure 3 times and maximum reading is taken as OFC

- At Birth, HC: 33 – 35 cm

Time period	Rate of increase in head circumference
0 - 3 months	2 cm/ month
3 - 6 months	1 cm/ month
6 - 12 months	0.5 cm/ month
1 - 3 years	0.2 cm/ month

Q. If Head Circumference at birth is 35 cm. When will it become 43 cm, if everything remains normal?

At birth	35 cm
1 m	37 cm
2 m	39 cm
3 m	41 cm
4 m	42 cm
5 m	43 cm

- An increase in HC by >2 cm/month is due to some underlying pathology. E.g. Hydrocephalus CNS tumour

Brain Development 00:26:54

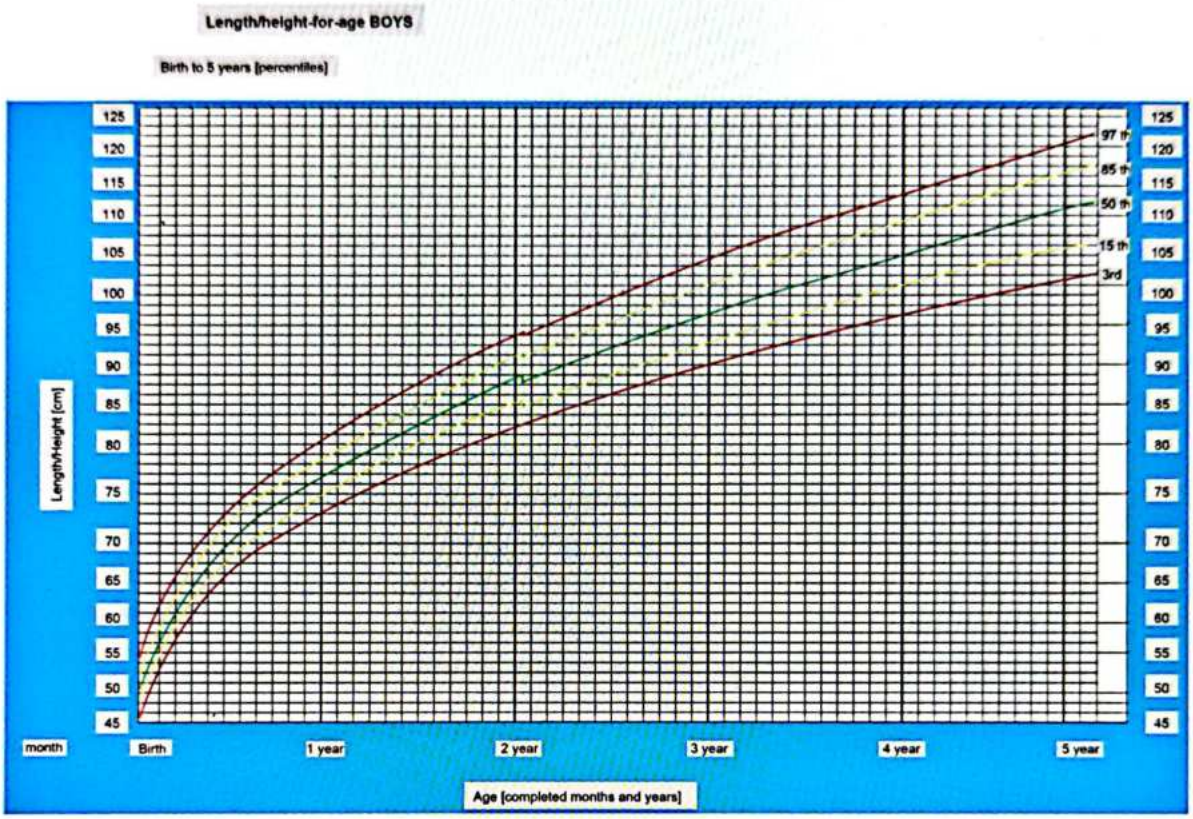
	Size of Brain (% of adult size)
At 1 month	36%
At 1 year of age	72%
At 2 years of age	85%

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

PREVIOUS YEAR QUESTIONS

Q. A mother of a 5-year-old boy feels that he is too tall for his age & she brought him to hospital for evaluation. O/e his height was 108 cm, arm span of 106 cm, upper segment to lower segment ratio 1.2:1. What would be your advice to the mother?

(JIPMER Dec 2019)



A. Order for karyotyping

B. Reassure parents

C. Echocardiography to rule out Marfan syndrome

D. Ophthalmological examination & homocysteine levels

3 SHORT STATURE AND TALL STATURE

Short Stature

00:00:22

Definition

- Height of child < 3rd percentile or < -2 SD of expected, according to age & sex of child

Classification

00:03:40

Classification of short stature:

Type	US: LS ratio
Proportionate SS	Normal
Disproportionate SS	Change
• Short Trunk dwarfism	Decreased
• Short limb dwarfism	Increased

- Proportionate Short Stature: US:LS ratio remains normal or unchanged
- Disproportionate Short Stature: US:LS ratio changes

Important Causes of Proportionate Short Stature

00:05:31

1. Normal Variants
2. Intra-Uterine Causes
3. Post-Natal/Acquired Causes

1. Normal Variants

00:06:44

I. Familial Short Stature

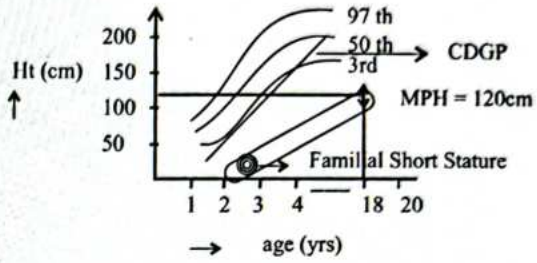
II. CDGP (constitutional Delay in Growth & Puberty)

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

Mid Parental Height (MPH)

00:10:15

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



Important Information

Bone Age: Preferred X rays for its estimation

- In neonates: X-ray Knees
- Infants: X-ray shoulder
- 1 – 13 years: X-ray left hand & wrist

Condition in which Bone Age < Chronological Age

1. CDGP (MC)
2. Congenital hypothyroidism
3. GH deficiency
4. Severe Malnutrition

Important Information

- CDGP is most imp cause of short stature in childhood

2. Intra Uterine Causes

00:23:15

I. IUGR

II. IntraUterine Infections (TORCH)

III. Genetic syndromes

- Turner syndrome
- Down syndrome
- Seckel syndrome (Bird headed dwarfism)

3. Post Natal/Acquired Causes

00:24:46

- Severe Long-Standing Malnutrition
- Any Malabsorption (celiac disease)
- Any Chronic Systemic Disease (chronic kidney disease)
- Endocrine Disorders: GH deficiency, Cushing syndrome (Mc cause is Iatrogenic)
- Psychosocial Dwarfism (maternal deprivation)

GH Deficiency - Short stature, Obesity

00:26:54

- US: LS Ratio is normal

- Bone age < Chronological age
- Dynamic testing
- GH Stimulation Test:
  - Done by using anyone of
    - → Clonidine
    - → Insulin
    - → Arginine

Rx: Recombinant GH therapy (S/E: Pseudotumor cerebri)

Important Causes of Disproportionate Short Stature 00:29:54

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

How to Remember?

- Short Man May Climb high

Important Information

- Alagille Syndrome
  - Neonatal cholestasis
  - Triangular facies
  - Pulmonary stenosis
  - Butterfly vertebra
- Triangular facies also seen in Russell Silver Syndrome

Achondroplasia 00:39:20

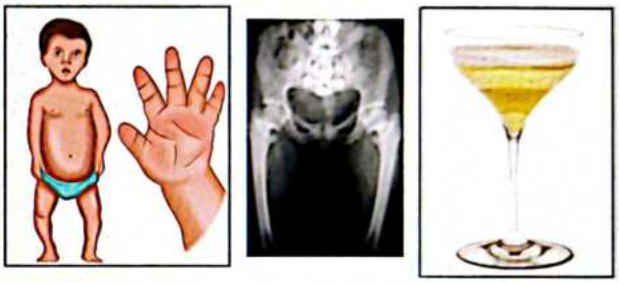
- **A** - Autosomal dominant inheritance
- **C** - Champagne glass pelvis on x ray
- **H** - Hand abnormality (Trident Hand)
- **O** - Obesity
- **N** - Neurological problems
- **D** - Delayed motor milestones
- **R** - Recognized at birth
- **O** - BOwing of legs
- **P** - Proximal limb shortening
- **LA** - LArge head
- **S** - Short stature
- **I** - **Interpedicular** distance b/w vertebra decreases

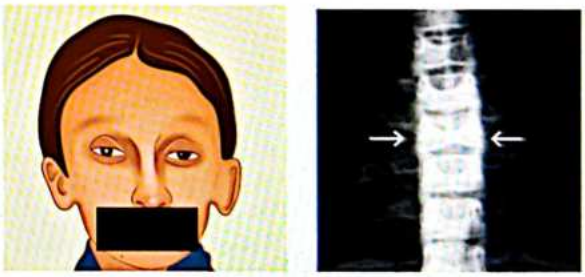
How to Remember?

- ACHONDROPLASI

Important Information

- Gene involved: FGFR 3 gene [Fibroblast Growth Factor Receptor 3 Gene





Osteogenesis Imperfecta/ Brittle Bone Disease 00:45:00

- AD inheritance
- Triad
  - Recurrent fractures / Bony deformity
  - Blue sclera
  - Deafness
- Type-I collagen Defect
- Dentinogenous imperfecta (Dental problem)
- Rx: Bisphosphonates [Pamidronate]

Tall Stature 00:48:14

Definition

- Height of a child > + 2 S.D. of expected, according to age and sex of child.

Causes of Tall Stature in Childhood

1. Constitutional tall stature
2. Exogenous obesity
3. Endocrine causes

- GH excess
- Precocious puberty

Etiology of tall stature

Syndromes

- Klinefelter syndrome (47, XXY)
- Fragile x syndrome
- Marfan syndrome
- Homocystinuria
- Soto's syndrome/ cerebral gigantism
- Beckwith wiedemann syndrome
- Weaver syndrome: Intellectual disability, facial dysmorphism, joint contractures

Important Information

Tall stature during childhood but normal adult height

- Constitutional tall stature
- Exogenous obesity
- Precocious puberty
- Soto's syndrome
- Beckwith wiedemann syndrome

4 ABNORMALITIES OF HEAD SIZE & SHAPE

Abnormalities of Head Size
- Microcephaly
- Macrocephaly

Microcephaly/Small Head 00:00:49

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

Classification
- Primary
- Secondary

Important Causes
- **Primary/Genetic Causes**
  1. **C** - CRI-DU-Chat Syndrome (5p⁻)
  2. **S** - Smith Lemli Opitz Syndrome
  3. **P** - Patau Syndrome (Trisomy 13)
  4. **E** - Edward Syndrome (Trisomy 18)
  5. **F** - Familial
  6. **R** - Rubinstein Taybi Syndrome (microcephaly, nose deformity, broad deviated thumb, congenital heart disease)
  7. **C** - Cornelia De Lange Syndrome (long eye lashes)

How to Remember?
- Cannot See PEFR in Child

- **Structural causes:** Anencephaly, Lissencephaly, Polymicrogyria, Schizencephaly
- **Secondary Causes**

Maternal Causes	Other Causes (related to baby)
1. Alcohol Intake (Fetal Alcohol Syndrome) 2. Smoking 3. Drugs: Phenytoin Intake 4. Phenylketonuria (PKU) 5. Radiation Exposure 6. Infections (TORCH)	1. CNS Infections During Infancy (Meningoencephalitis) 2. Severe Malnutrition in Baby 3. Perinatal Asphyxia/ HIE 4. Inborn errors of metabolism • PKU • Methylmalonic acidemia • Citrullinemia 5. Acquired Microcephaly • **R** - Rett Syndrome (X-Linked Dominant) • **A** - Angelman Syndrome • **S** - Seckel Syndrome (face of child resembles the bird)

How to Remember?
- RAS

Macrocephaly / Large Head 00:10:56

Definition: HC of the child > + 2 SD or Z score of expected, according to age & sex of child

Important Causes
1. **Increased Thickness of Cranial Bones**
- Chronic hemolytic anemia (Thalassemia)
- Osteogenesis imperfecta
- Rickets
2. **Sub-Dural Fluid Collection**
- Present as effusion or empyema sequelae of Meningitis
3. **Megalencephaly (↑ Size of Brian)**
- **B** - Benign familial megalencephaly → runs in families (MCC of megalencephaly in children)
- **A** - Amino acid disorders
  - Maple syrup urine disease (MSUD)
  - Type - I Glutaric aciduria
- **L** - Lysosomal storage disorder
  - Mucopolysaccharidosis, GM1 Gangliosidosis, Taysach's disease,
- **W** - Weaver syndrome
- **A** - Achondroplasia (Short Limb Dwarfism)
- **N** - Neurodegenerative disorder (Regression of milestones)
  - Alexander disease (GFAP gene: Glial fibrillary protein deposition)
  - Canavan disease (ASPA gene: Deposition of NAA in brain)
- **S** - Soto's syndrome/ cerebral gigantism
- **N** - Neurocutaneous disorders (For ex. NF, TS, Sturge weber syndrome)
- **G** – Galactosemia

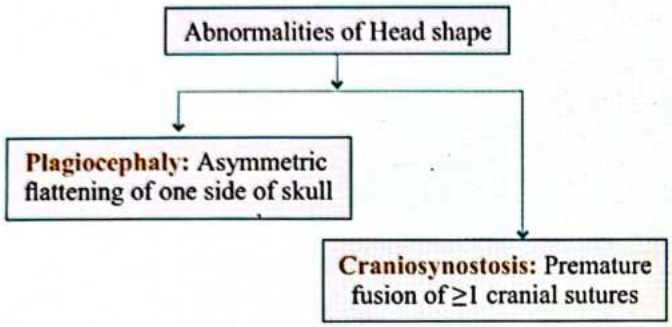
How to Remember?
- BALWAN SiNGh

4. **Hydranencephaly**
- Both Cerebral hemispheres are absent & replaced by fluid filled sacs
- Transillumination is +ve

5. **Hydrocephalus** (↑ in size of ventricles inside brain due to increased production or impaired drainage of CSF)
- Treatment: VP shunt

Abnormalities of Head Shape

00:24:46



Craniosynostosis

- What is it?
  - Premature fusion of one or more cranial sutures
- How to recognize clinically?
  - Abnormal head shape along with palpable ridge in the suture line that is prematurely fused
- Normal sequence of fusion of cranial sutures- **MSCL**
  - Metopic suture (2 months)
  - Sagittal suture
  - Coronal suture
  - Lamboid suture (22-26 months)
  - Frontonasal and frontozygomatic sutures fuse last (Around 6 year)

Types

- **Dolichocephaly (Scaphocephaly)**
  - Elongated head due to premature fusion of sagittal suture
  - Most common type of craniosynostosis
- **Trigonocephaly (triangular in shape)**
  - Premature fusion of metopic suture
- **Turricephaly (Oxycephaly)**
  - Premature fusion of coronal, spheno-frontal, fronto-ethmoid sutures
- **Brachycephaly**
  - Premature fusion of coronal sutures

How to Remember?

- M/C Type of abnormality: Dolichocephaly.

Syndromes Associated with Craniosynostosis

- **Crouzon syndrome**
  - Features of Crouzon syndrome:
    - → Brachycephaly
    - → Bulging eyes
    - → Midface hypoplasia (Cheeks underdeveloped)
- **Apert syndrome**
  - Bulging eyes
  - Antimongoloid slant of eyes
  - Mitten hands due to syndactyly
- **Carpenter syndrome**
- **Pfeifer syndrome**

Fontanelles

00:35:15

	2 most important fontanelles	
	Anterior Fontanelle (AF)	**Posterior Fontanelle (PF)**
Shape	• Diamond	• Triangular
At junction of	• Frontal and parietal bones	• Parietal & occipital bones
Sutures	• At junction of coronal and sagittal sutures	• At junction of sagittal & lambdoid sutures
Closes by	• 18 months of life	• Either closed at birth or admits tip of a finger or closes at 6-8 weeks of life

Examination of Anterior Fontanelle

- Size: 2x2cm
- Level: Slightly depressed & pulsatile
- How to examine: Best Examined by holding baby in upright and calm in sitting position when baby is asleep or feeding

Important Information

- MC cause of bulging AF is Crying/ Irritable child

Bulging Anterior Fontanelle

- Increased ICP e.g.: Meningitis, Intraventricular hemorrhage.

Depressed/ Sunken AF: Dehydration E.g. Diarrhoea

Small AF

- Craniosynostosis (premature fusion of cranial sutures)
- Microcephaly
- Wormian bones/Accessory bones

Causes of Large Anterior Fontanella

- **D - Down syndrome (Trisomy 21)**
- **R - Rickets**
- **O - Osteogenesis imperfecta**
- **P - Prematurity**
- **C – Cleidocranial dysostosis**
- **A - Achondroplasia**
- **T - Trisomy 13, 18**
- **C - Congenital Rubella Syndrome**
- **H – Hydrocephalus/ Hyperthyroidism**

How to Remember ?

- DROPCATCH

princeeeekum@gmail.com
9928609733

PREVIOUS YEAR QUESTIONS

Q. Most common cause of craniosynostosis Ia?
(JIPMER - Nov - 2018)

A. Plagiocephaly
B. Brachycephaly
C. Scaphocephaly
D. Trigonocephaly

Q. Which of the fontanelle is the last to close?
(NEET Jan 2018)

A. Posterior fontanelle
B. Anterior fontanelle
C. Mastoid fontanelle
D. Sphenoidal fontanelle

princeeeekum@gmail.com
9928609733

5 NORMAL & ABNORMAL DENTITION

Normal Dentition

00:00:17

	Primary Dentition Milk/ Temporary Teeth	Secondary Dentition / Permanent Teeth
Begins at	6 months	6 years
1st tooth to erupt	Lower central incisor	1st molar
Last tooth	Second molar	3rd molar (or) wisdom tooth
Completes at	2 and half – 3 years	12 years except the 3rd molar (18-25 years)
Total no. of teeth	20	28-32
Teeth in each quadrant (ICPM)	I C P M	I C P M
	2 1 0 2	2 1 2 3

Sequence in which teeth erupt

00:04:52

- Milk teeth: Central incisor → Lateral incisor → 1st Molar → canine → 2nd molar
- Permanent dentition :1st molar → incisors → canine → premolars → 2 molars

Refer Image 5.1

- Period of Mixed Dentition - 6 TO 12 Years

Abnormalities of Dentition

Delayed Dentition

00:09:09

- When no tooth erupts by the age of 13 months
- **Important Causes**
  1. **F**- Familial
  2. **R**- Rickets
  3. **I**- Idiopathic, Incontinentia pigmenti
  4. **E**- Endocrine
     - Hypopituitarism
     - Hypothyroidism
     - Hypoparathyroidism
  5. **D**- Down syndrome
  6. **C**- Cleidocranial dysostosis
     - Absent clavicles (complete or partial absence)
     - Large anterior fontanelle
     - Delayed closure of anterior fontanelle
     - Supernumerary teeth (also found in Gardner syndrome → precancerous condition of carcinoma of colon)

How to Remember ?

- FRIED CHOP

Natal Teeth

00:13:34

- Baby born with teeth
- Present in following conditions
  1. **Pierre Robin sequence:** Micro or Retrognathia
  2. **Ellis van creveld syndrome**
     - Congenital heart disease
     - Short limb dwarfism
     - Polydactyly
     - Nail abnormalities
  3. **Epidermolysis bullosa** (lethal acantholytic variety)
  4. **Soto's syndrome**

How to Remember ?

- PEES

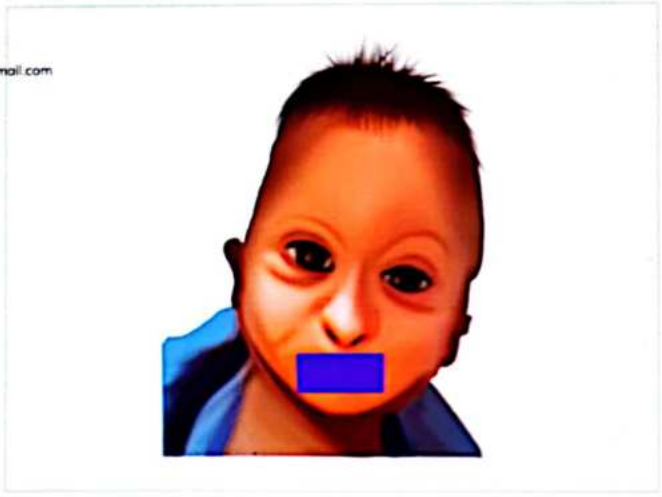
Hutchinson's Teeth

00:15:15

- Notched incisors (Peg shaped)
- Seen in congenital syphilis
- Hutchinson's triad: Hutchinson's teeth, interstitial keratitis, SNHL (Late manifestation of congenital syphilis)

Image Based Practice Questions

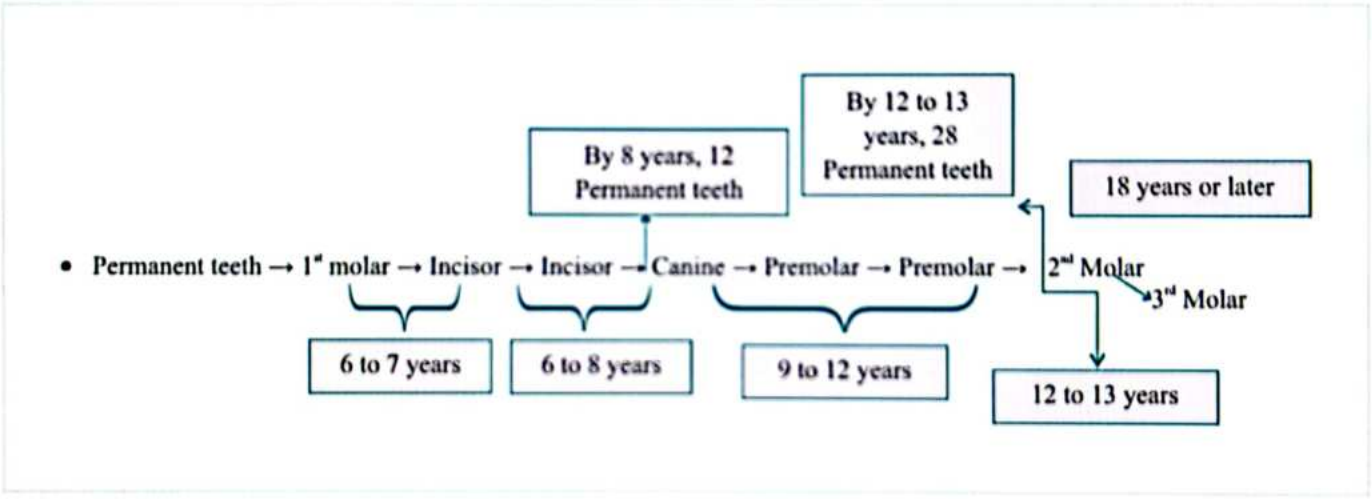
Q. Identify the syndrome in this child with short stature?



Ans. Seckel syndrome (bird headed dwarfism)

- Microcephaly
- Elongated face
- Beak like nose

Image 5.1

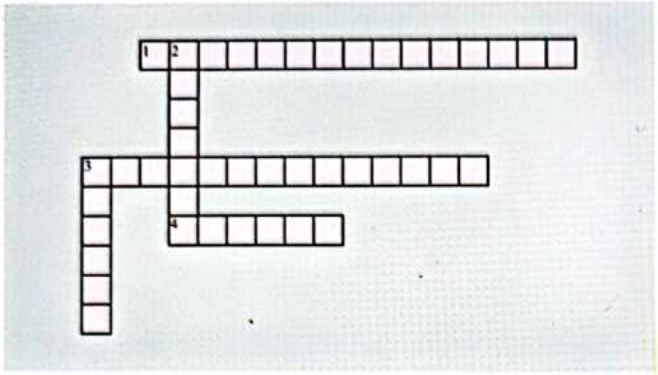


16

CROSS WORD PUZZLES

princeeeekum@gmail.com
9928609733

Crossword Puzzle



Across

1. TOC for Brittle bone disease
3. Soto's syndrome can cause.
4. At 1 year of age, birth weight _____itself

Down

2. A baby is caused an _____at 1st year of life.
3. Most common gene involved in Rett syndrome

6 IMPORTANT MOTOR MILESTONES

Development

Rules of Development

- Continuous process, starting in utero
- Sequence of attainment of milestones remains same
- Depends on neurological status of child
- Cephalo-caudal direction
- Truncal development followed by limb development
- Certain primitive reflexes need to be lost (eg ATNR is lost when child starts crawling)

Domains of Development

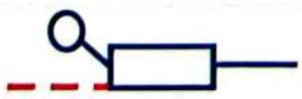
- Gross motor
- Fine motor
- Social
- Language
- Developmental assessment of preterm baby is done using "corrected/adjusted age" till 2 years of age.
  - Corrected/adjusted age = (gestational age + chronological age) - 40 weeks
  - E.g. gestational age = 30 weeks
    → Now age of baby = 12 weeks old
    → Corrected age = (30+12)-40
    = 2 weeks

Gross Motor

00:06:52

In ventral suspension

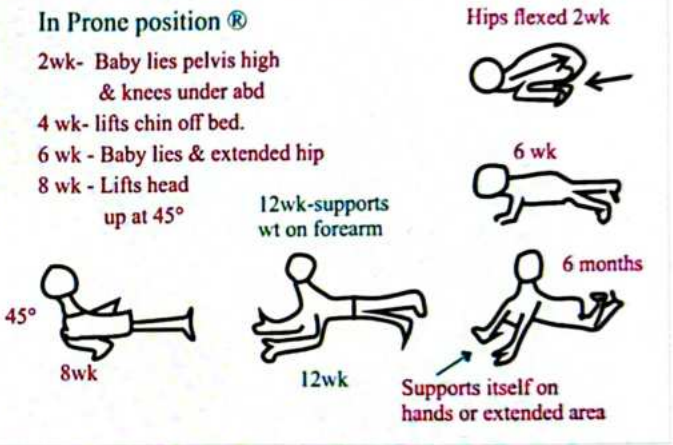
1 month	Head is below the plane of rest of body due to no neck control
2 months	Head in the plane of body, neck control begins to develop
3 months	Head goes above the plane of the body, Neck control develops more



In prone position

00:10:41

2 weeks	Baby lies on bed with high pelvis and knee drawn under the abdomen.
4 weeks	Lifts chin off the bed momentarily
6 weeks	Lies on bed with flat pelvis and extended hips
8 weeks	Lifts face up at 45 degrees
12 weeks	Can bear his weight on forearm with and shoulder lifted off the couch
6 months	Can support his weight on hands or extended arms



Other milestones

4 months	Partial weight bearing when made to stand
5 months	Feet to mouth, complete neck control
6 months	• Sitting with support / sitting in tripod position • Prone to supine
7 months	Supine to prone
8 months	Sitting without support; crawling
9 months	Standing with support
10 months	Creeping
10 - 11 months	• Pivoting • Cruising

1 year (12 months)	• Stand without support • Walk with support • Walk with one hand held
13 months	• Walks without support
15 months	Creep upstairs
18 months	• Goes upstairs & downstairs holding the side railing • Runs • pulls a toy
2 years	• Goes upstairs & downstairs 2 feet per step • Kicks a ball • Walks backwards
3 years	• Goes upstairs with alternating feet & downstairs 2 feet / sleep • Rides a tricycle
4 years	• Goes upstairs & downstairs with alternating feet • Hopping
5 years	• Skipping • Can stand on 1 leg for > 10 sec

Fine Motor

00:24:49

1 month	Hands kept closed
2 months	Hands open intermittently
3 months	Hands kept open Hold an object when placed in hand 'Hand regard' appears (disappears at 20th week) Palmar grasp relfex is lost
4 months	Tries to reach an object, but overshoots
5 months	Bidextrous grasp
6 months	• Unidextrous or palmar grasp
7 months	Transfer objects from 1 hand to another
9 months	Immature/ assisted pincer grasp
12 months	• Mature/ unassisted pincer grasp. • pulls off cap/mittens/socks

Fine Motors milestones (1 to 5 years)

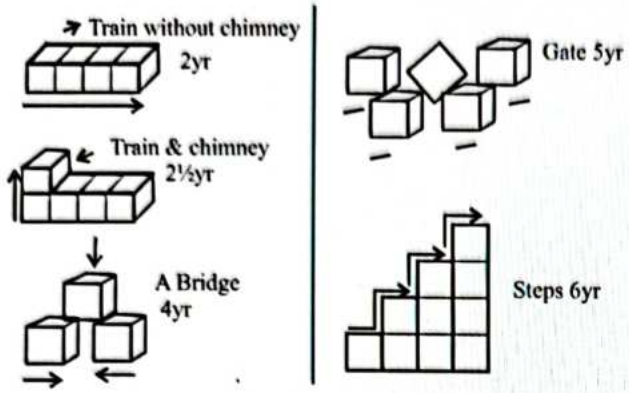
15 months	• Scribbles spontaneously • Feeds self with a cup • tower of 2 cubes
18 months	• Tower of 3 cubes • Feeds self with a spoon • Turn 2-3 pages at a time • Unzips
2 years	• Tower of 6-7 cubes • Can make a train with blocks • Turns a doorknob or unscrew a lid • Turns pages singly • Wears socks and shoes
2.5 years	• Makes a train with chimney
3 years	• Handedness gets established (appears at 24 months and established at 36 months) • Tower of 9-10 cubes • Can dress/undress self except buttons
4 years	• Makes a bridge with cubes • Can button and unbutton • Catches a ball reliably
5 years	• Can tie shoelaces • makes a gate with cubes
6-7 years	• Copies a diamond • Can make steps with cubes

Fine motor milestones 1-5yr age:

DRAWING SKILLS OF A CHILD→

2yr		Copies a straight line at 2Yrs (horizontal or vertical line)
3yr		Copies a circle
4yr		Copies a rectangle or "plus" or "Cross" (4 yr)
5yr		Copies a triangle or tilted Cross or multiplications' sign

MILESTONES RELATED TO CUBES:



Number of cubes put in tower = age x 3

PREVIOUS YEAR QUESTIONS

Q. A 6 year old child with developmental delay, can ride a tricycle, can climb upstairs with alternate feet, but downstairs with 2 feet per step, can tell his name, knows his own sex, but cannot narrate a story. What is his developmental age? (AIIMS May 2019)

A. 3 years
B. 4 years
C. 5 years
D. 2 years

Q. A child transfers objects from one hand to other. What does it imply? (AIIMS June 2020)

A. Visual motor co-ordination
B. Explores small objects
C. Object release
D. Comparison of objects

7 SOCIAL & LANGUAGE MILESTONES

Social

00:00:11

1 month	Looks at the mother intently when talked to
2 months	Social smile
3 months	Recognizes mother
6 months	Mirror play appears
7 months	Stranger anxiety appears
8 months	Object permanence
9 months	Waves bye-bye
10 months	Plays peek a boo
12 months	• Kisses on request • Plays a simple ball game
15 months	• Points to objects • Indicates wet pants } 2 'P's
18 months	• Domestic mimicry • Dry during daytime } 2 'D's
2 years	• Parallel play • Can point to 3-4 body parts • Points to 5-6 familiar objects
3 years	• Joins in play • Knows his name, age, gender • Dry at night usually (Nocturnal enuresis- Involuntary urination at night beyond 5 year of age)
4 years	• Goes to toilet alone • Starts asking questions
5 years	• Starts helping in simple household tasks • Distinguishes morning from evening • Compares 2 weights • Can follow 3 step commands

Language

00:08:12

1 month	Quietens when a bell is rung
2 months	Vocalizes
3 months	Cooing
4 months	Laughs aloud
5 months	Razzing
6 months	Mono-syllablic babbling (ma, ba, da)
9 months	Bi-syllablic babbling (mama, papa but without meaning)
1 year	Speaks 2-3 words with meaning
15 months	Jargon speech
18 months	Vocabulary of 8-10 words with meaning
2 years	• Speaks 2 words sentences • Vocabulary of 50-100 words • Uses pronounces like I, ME, YOU
3 years	• Uses plurals & past tense • Repeats 3 digits, 3 words sentences
4 years	Tells a story/ poem, sings a song
5 years	• Repeats 4 digits • Names 4 colors • Asks meanings of words

Vision

00:13:18

- Birth: can fixate on a red dangling ring and follows it to 45 degrees
- 4 weeks: can follow the red dangling ring to 90 degrees
- 12 weeks: can follow the red dangling ring to 180 degrees
- 3 months: fixates instantaneously on an object shown to him (grasps with eyes)
- Binocular vision: begins to develop by 6 weeks and established by 4 months of age
- 1 year: follows rapidly moving objects

Hearing (Murphy's Sequence)

00:15:35

- Newborns: respond to sound by startle/blinking/crying
- 3-4 months: Turns head towards source of sound

- 5-6 months: Turns head towards source and then downwards if the source of sound is below the level of ears
- 7-8 months: localizes sound produced above the level of ears
- 10 months: looks directly towards the source diagonally

8 DEVELOPMENTAL IMPLICATIONS OF IMPORTANT MILESTONES

Gross Motor Milestone

00:01:15

Milestones	Developmental Implications
Neck control/holding the head steady while sitting	Allow more visual exploration/interaction
Sitting without support	Increasing exploration
Walks alone	Exploration and control of proximity to parents

Fine Motor Milestone

00:03:22

Milestones	Developmental implications
Hand regard	Self-discovery of hands
Grasps a rattle	Object use
Reaches for objects	Visuomotor coordination
Palmar grasp gone	Voluntary release of objects
Transfer objects from one hand to another	Compare objects
Appearance of Pincer grasp/thumb-finger grasp	Able to explore small objects
Scribbling	Visuomotor coordination
Builds a tower of 2 cubes	Uses objects in combination

Social Milestones

00:09:05

Milestones	Developmental implications
Social smile	More active social participation
Follows 1 step command with gesture (7 months)	Nonverbal communication
Points to objects	More interactive communication
Uncovers toys after its hidden	Object permeance i.e., child wants that objects permanently in front of him
Pretends to drink from a cup (1 year)	Symbolic thought
Uses stick to reach toys	Link actions to solve problems

Language Milestones

00:13:44

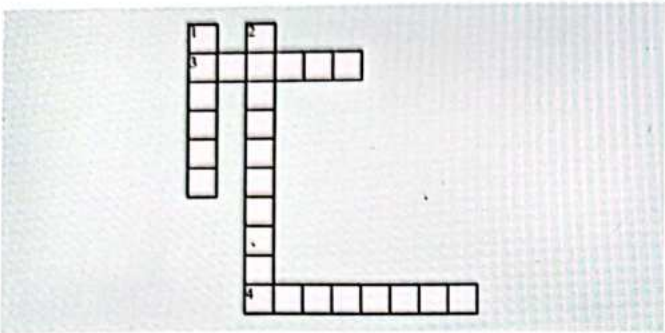
Milestones	Developmental implications
Monosyllabic babbling (6 months)	Experimentation with sound
Follows one step commands without gesture (10 months)	Verbal receptive language (Child understands the meaning of words told to him)
Says 'mama', 'dada'	Expressive language
Speaks first real word (1 year)	Beginning of labelling
Speaks 4-6 words	Acquisition of objects and personal names
Speaks short/2-word sentences	Beginning of grammatization

princeeeekum@gmail.com
9928609733

CROSS WORD PUZZLES

princeeekum@gmail.com
9928609731

Crossword Puzzle



Down

1. At 9 months, a child could _____with support
2. At 5 months, a child could show_____grasp.

Across

3. At 6 month , a child can sit in _____Position
4. _____Can be achieved at 5 yeas of age

9 ABNORMALITIES OF DEVELOPMENT

Abnormalities of Development (3 'D' S) 00:00:10

1. Delay
2. Dissociation
3. Deviancy

1. Developmental Delay 00:00:42

- when a child's development is significantly behind of what is expected

Important Information

- If developmental delay involves 2 or more domains - Global Developmental Delay

2. Developmental Dissociation 00:02:18

- Substantial difference in the rate of development of milestones in 2 or more domains
- Example: Isolated speech delay is a developmental dissociation since only language is hampered while all other domains are normal.

3. Developmental Deviancy

- Developmental milestones occurring out of sequence.
- Example: If Crawling appears before sitting.

Developmental Red Flags 00:05:03

- The upper time limit by which the milestones should usually be attained.

Gross motor	Upper limit	Usual time
Sitting with support	9 months	6 months
Standing with support	12 months	9 months
Walking with support	15 months	12 months

Fine motor	Upper limit	Usual time
Pincer grasp months	12 months	9 months
Scribbling	24 months	15 months

Social	Upper limit	Usual time
Social Smile	6 months	2-3 months
Waving bye-bye	12 months	9 months

Language	Upper limit	Usual time
Babbling	12 months	6 months
Single words	15-16 months	1 year

- If these milestones are not attained by this time, then there is probably some underlying abnormality of development.

Important causes of Development delay ("CDGP PIC") 00:09:02

1. C - Chromosomal abnormalities (Trisomy 21, 13, 18)
2. D - Developmental brain abnormalities (lissencephaly- brain appears smooth due to less gyri & sulci, myelomeningocele)
3. G - Genetic syndromes (Fragile X Syndrome, Rett syndrome, Prader Willi syndrome Nooram syndrome)
4. P - Perinatal factors: Asphyxia, HIE (Hypoxic Ischemic Encephalopathy)
5. P - Postnatal factors and acquired: (CNS Trauma, infections, Hypothyroidism, malnutrition)
6. I - Inborn errors of Metabolism: Maple Syrup Urine Disease, organic Acidemia, Tay sachs disease, GM Gangliosidosis, Mucopolysaccharidosis
7. C - Congenital infections: TORCH group (Toxoplasmosis, Other agents, Rubella, CMV, Herpes)

How to Remember?

- CDGP PIC

Developmental Assessment 00:14:52

Developmental quotient [D.Q.]

- D.Q = Developmental age/Chronological age x 100
- E.g. A child of 6 years of age has attained milestones of that of a 3 year old only. Calculate D.Q.

Solution: DQ = 3yr/6yr x 100 = 50

Screening Tests for Developmental Assessments 00:15:55

1. P - Phatak's Baroda Screening Tests
2. A - Ages & stages questionaire
3. R - Revised DDST (Denver Developmental Screening Test)
4. T - Trivandrum development screening chart

How to Remember?

- PART

Definitive Tests for Intellectual & Developmental Assessment

00:17:06

Name of test	Age group
Vineland adaptive behavior scale II	Birth to 89 years
Bayley scale for Infant development II	1 month-3.5 years
Stanford Binet Intelligence scale	2 years-85 years
Wechsler Intelligence Scale for Children	6 years-17 years

Intelligence Quotient (IQ)

00:18:20

- IQ = Mental age/Chronological age x 100

Degree	IQ Level
• Mild ID	51 – 70
• Moderate ID	36 – 50
• Severe ID	21 – 35
• Profound ID	0 – 20
• Moron	50 – 70
• Imbecile	30 – 50
• Idiot	< 30

- The term mental retardation is no longer used now.
- It has been replaced by term intellectual disability.

Intellectual Disability

- Significant impairment in intellectual functioning, social and adaptive skills

princeeeekum@gmail.com
9928609733

10 BEHAVIOURAL DISORDERS IN CHILDREN

Nocturnal Enuresis 00:00:04

Definition

- Involuntary urination at night beyond 5 years of age irrespective of a boy or a girl
- Epidemiology: M>F
  - Positive family history in 50% cases
    - → If 1 parent had a history of nocturnal enuresis then each child has 44% risk of developing nocturnal enuresis
    - → If both the parent had history of nocturnal enuresis then each child has 77% risk of developing nocturnal enuresis

Types

- Primary nocturnal enuresis: Child who has never attained night time continence
- Secondary nocturnal enuresis: Seen in children who had attained night time continence previously
  - It can be due to any acquired causes
    - → Polyuria due to any reason like Diabetes
    - → Urinary tract infection

Management

- **1st line management**
  - Lifestyle changes
    - → Early dinner
    - → Restrict fluid intake during evening
    - → Restrict intake of sugar or caffeinated products like caffeine
    - → Void bladder before going to bed
  - Motivational therapy – To maintain "Star chart"
    - → Maintain a diary and give child a star for every dry night in a diary
    - → Give the child a reward for having 7-10 stars back to back
    - → It is a type of positive reinforcement
- **2nd line treatment**
  - Bed and alarm technique
    - → Moisture sensing alarm is fitted in the underwear of child
    - → As soon as child begins to void at night that alarm will ring and child will wake up and go to washroom to void
    - → Slowly child will get conditioned to wake up at night by himself, goes to washroom and voids
    - → Hence nocturnal incontinence is avoided
- **3rd line therapy – Pharmacotherapy**
  - Imipramine
  - Oral desmopressin (Nasal desmopressin has a lot of side effects)
    - → It can be used when child is going out for a few days
  - Oxybutynin
- Pharmacotherapy has very high relapse rates so it can be used temporarily in certain conditions like when child is going out for few days
- Lifestyle and behavioural techniques work best and have low relapse rate
- Combination of pharmacotherapy and bed and alarm technique have lowest relapse rate

PICA 00:06:37

- Persistent eating of non-food, non-nutritive substances like paint, cement, chalk, or paper for at least 1 month
- It is more common in children with intellectual disability and autistic spectrum disorder
- It is commonly associated with nutritional anemia, worm infestation
- Treatment: Behavioural therapy

Thumb Sucking 00:08:00

- It is a self-soothing behaviour most commonly seen during infancy
- 25% of children have it at 2 years of age
- If thumb sucking persists at > 5 years of age, it may be associated with
  - Paronychia (Infection around nail bed)
  - Anterior open bite or Dental malocclusion
- Treatment: Behavioural therapy

Bruxism (Teeth Grinding) 00:09:20

- It is seen in 5-30% of children
- It begins in first 5 years of life
- It is associated with increased day time anxiety (can be due to parental separation or going to school)
- Persistent bruxism may be associated with temporo-mandibular joint related problems/pain and dental malocclusion
- Treatment: Behavioural therapy

Breath Holding Spells 00:11:18

- Case scenario: A child 14 month old was crying incessantly and suddenly the child became pale and lifeless. On stimulation the child regain consciousness and child was anemic
- Breath holding spells – Close differential diagnosis of seizures in young children
- It occurs due to immaturity of the autonomic nervous system
- It is most commonly seen between 6-18 months of age

- Triggers
  - Anger
  - Frustration
  - Incessant crying
- It usually begins with a Cry → Syncope → Tonic posturing/ Atonic & lifeless
- Types
  - Pallid spell: It happens because of reflex vagal bradycardia and asystole
    → Baby will become pale for few seconds to minutes
  - Cyanotic spell: It occurs due to prolonged expiration, apnea, intrapulmonary shunting of blood
- Treatment: Reassurance
- Ensure to rule out seizures or any other medical condition
- Case scenarios and clinical history will be typical of breath holding spells
- Reassure the parents and treat any underlying iron deficiency anemia

Tics and Stereotypies

- Tics: Sudden, non-rhythmic, rapid motor movements or vocalisation e.g., Tourette syndrome
- Stereotypies: Stereotypic, rhythmic, repetitive movements or pattern of speech with lack of variation over time

Autistic Spectrum Disorder (ASD) 00:15:41

Definition

- It is defined as persistent impairment in reciprocal social interaction and presence of restricted, repetitive pattern of behaviour or interest
- Child will not smile or hold an eye contact with other people
- Some children will be very intellectual or bright while some of others will have intellectual disability

Risk factors

- Closure spacing of pregnancies
- Extreme prematurity (< 26 weeks of gestation)
- Any family member with learning or psychological disorder
- Antenatal exposure to thalidomide or valproate
- Antenatal exposure to rubella
- Measles immunization is no longer considered as risk factor
- Lot of screen time i.e., long hours on phone, less interaction with parents or friends

Screening test

- M-CHAT (Modified Checklist of Autism for toddlers)

Treatment

- Cognitive behavioural therapy
  - Treatment of associated comorbidities
  - For hyperactivity – Atomoxetine or Methylphenidate
  - More and more social interaction with child is required

Attention Deficit Hyperactivity Disorder (ADHD) 00:20:42

Definition

- Persistent hyperactivity/inattention or impulsivity that interferes with day to day functioning/development of child
- Onset: Before 12 years of age that has been present for at least 6 months in at least 2 different settings (school/home/play area) without any underlying secondary known cause

Epidemiology

- Most common neurobehavioral disorder of childhood
  - 60-80% of children with ADHD will continue to have symptoms till adolescence
  - 60% of adolescents with ADHD will have symptoms till adulthood
  - 2% of adults have ADHD

Risk factors

- Maternal smoking, alcohol, lead exposure, mercury exposure
- Genetic – DAT-1 & DRD-4 gene
- CNS malformation
- CNS trauma
- Psychologic family stress
- Epilepsy
- Neurocutaneous conditions like Tuberous sclerosis & Neurofibromatosis

Management

- Behavioral therapy
- Drugs: Methylphenidate, Amphetamines, Atomoxetine

Rett Syndrome 00:25:42

- It is a condition more common in girls

Important Information

- Inheritance: X-linked dominant inheritance

- Most common gene mutation: MECP2 gene mutation
- Head circumference is normal at birth but later these children develop acquired microcephaly

Developmentally normal in 1st few months of life

↓

Deceleration of head growth (Rate of increase in head circumference goes/slows down)

↓

Acquired microcephaly and developmental delay

↓

Loss of purposeful hand movement &
Appearance of stereotypic hand wringing movement

- Associated problems
  - Seizures
  - Speech problems
  - Breathing irregularities/Apnea
  - Intellectual disability

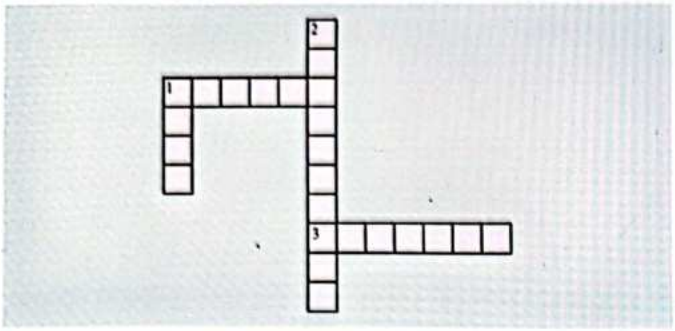
Selective Mutism 00:29:19

- It is a failure of a child to speak in specific social situations, while being able to speak normally in other situations
- E.g., Child speaking normally at home with everyone but at school he does not speak at all
- It is a manifestation of underlying anxiety disorder or excessive shyness or dependency on parents
- There can be history of anxiety symptoms in one or both parents
- Treatment: Behavioural therapy to reduce underlying anxiety

princeeeekum@gmail.com
9928609733

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. 12 months is the upper limit for _____grasp
3. Person with IQ level 30-50 is defined _____

Down

1. Persistent eating of non nutritive substances for > 1 month
2. 24 Months is the upper limit for _____

princeeeekum@gmail.com
9928609733

11 PUBERTY & ADOLESCENCE

Adolescent Age Group 00:00:22

- A state of transition between childhood to adulthood
- W.H.O Definition of Adolescence: 10-19 years
  - Early Adolescence: 10-13 years
  - Mid Adolescence: 14-16 years
  - Late Adolescence: 17-19 years

Sequence of Changes in Puberty in Females

Important Information

- Puberty: Refers to the physical changes in the body during adolescence

Thelarche (Breast Development) (1st sign) 00:01:35
↓
Pubarche (development of pubic & axillary hair)
↓
Growth spurt (Peak ↑ in growth velocity)
↓
Menarche (beginning of menstrual period)

Important Information

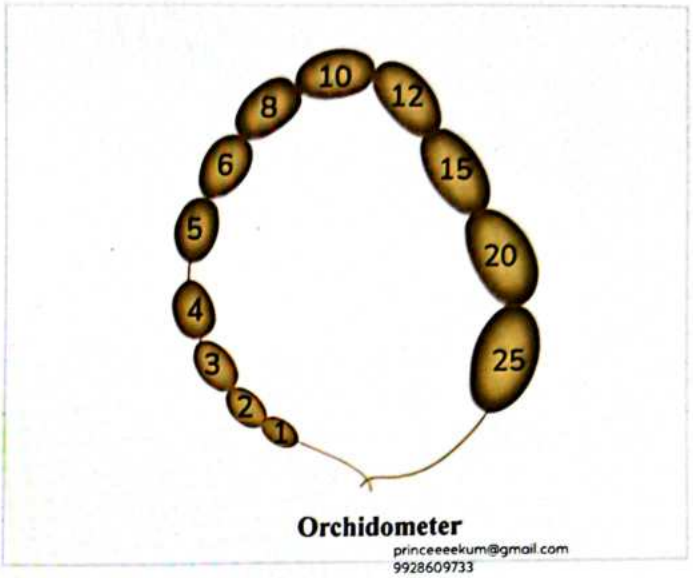
- Growth spurt in females occurs just before the onset of Menarche

Sequence of Changes in Puberty in Males 00:02:30

Testicular Enlargement (1st sign)
↓
Penile enlargement
↓
Pubic hair
↓
Growth spurt
↓
Axillary hair } Deepening or ripening of voice
↓
Facial hair

Orchidometer 00:03:55

- Device used to measure Testicular Size
- The numerical value indicates the volume of testis.



Orchidometer

Assessment of Puberty in Adolescent 00:04:18

- Done by Tanner's Staging or Sexual Maturity Rating (SMR)
- Stage 1 to 5
  - Stage 1: Pre pubertal stage
  - Stage 5: Mature adult
- Parameters used to access Puberty:
  - In Females: Based on development of Breast, pubic hairs
  - In Males: Genitalia (Testis & penis), pubic hairs

Important Facts Related to Puberty & Adolescence 00:11:40

- Earliest neuroendocrine change associated with onset of puberty is → Maturation of GnRH pulse generator.
- Earliest stage of puberty where sperms can be seen in urine of a boy → SMR stage 3
- Bilateral breast tissue growth may be seen in 40 – 65% of males during SMR 2-4, due to excess of estrogenic stimulation

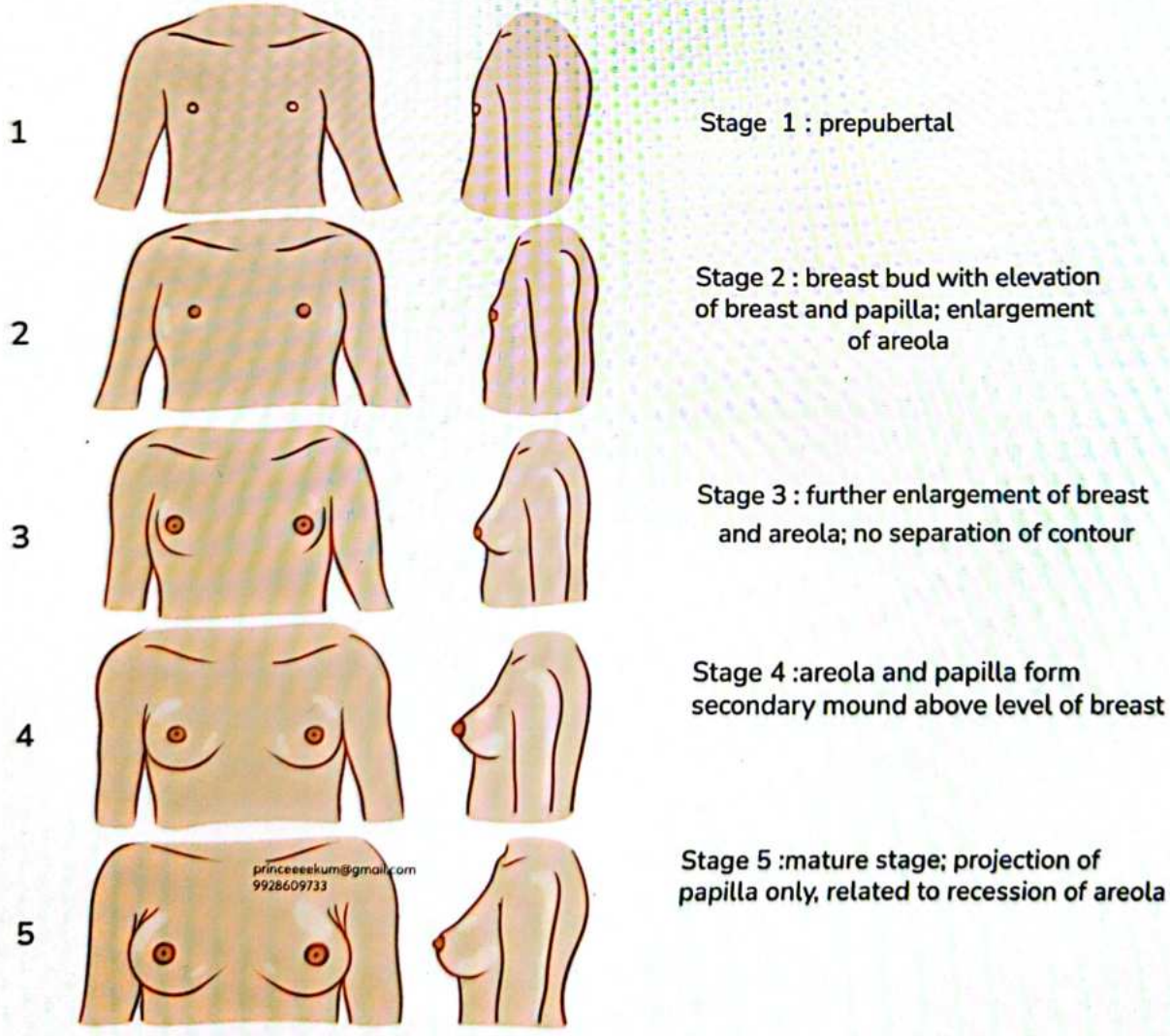
Growth Spurt 00:13:21

- Occurs in which stage
  - In Girls: SMR stage3
  - In Boys: SMR stage 4
- Growth spurt occurs later & lasts longer in boys/males
- Peak height velocity (PHV) during growth spurt is
  - 8-9 cm/yr in females: Attained 6 months before menarche
  - 9-10 cm/yr in males: Continue for 2-3 yrs after females have stopped growing.
- Growth spurt begins distally with enlargement of hands feet followed by arms & legs & finally, chest and trunk.
- After attainment of PHV, males undergo an increase in lean body mass, while females develop a higher proportion of body fat.

Staging of Puberty in Females

00:15:45

Stage	Pubic hairs	Breast
1.	• No pubic hairs	• Pre-pubertal
2.	• Sparse, minimally pigmented hairs, mainly on medial border of labia	• Enlargement of areola, elevation of breast & papilla
3.	• Coarser & darker hairs, spread over mons pubis	• Further enlargement of breast & areola
4.	• Thick, adult type distribution, but does not spread to thighs	• Areola & papilla form a secondary mound
5.	• Adult type distribution, spreading to medial surface of thighs	• Mature stage: • Projection of papilla only



Stage 1 : prepubertal

Stage 2 : breast bud with elevation of breast and papilla; enlargement of areola

Stage 3 : further enlargement of breast and areola; no separation of contour

Stage 4 :areola and papilla form secondary mound above level of breast

Stage 5 :mature stage; projection of papilla only, related to recession of areola

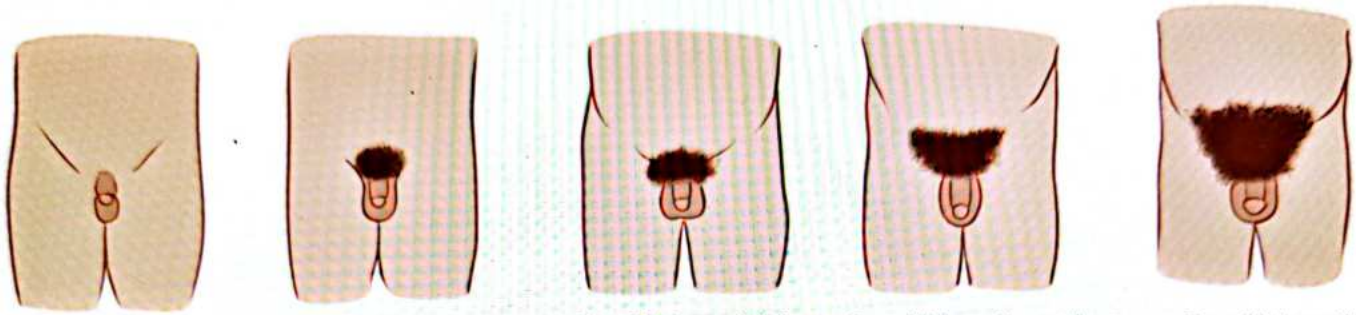
1. Prepubertal, no pubic hair

2. Sparse growth of minimally pigmented hair, mainly on the labia

3. Considerable darker and coarser hair spreading over the mons pubis

4. Thick adult-type hair that does not yet spread to the medial surface of the thighs

5. Adult-type hair distributed on classical inverse triangle



Stage 1.Prepubertal, no pubic hair and genitals proportionally the same as in child

Stage 2.Sparse hair growth at the base of the penis-slightly darkened. Scrotum and testes enlarge, scrotum thins and reddens.

Stage 3.Hair growth darker, more coarse and curled across the mons pubis. Penis grows in and testes and scrotum continue to grow

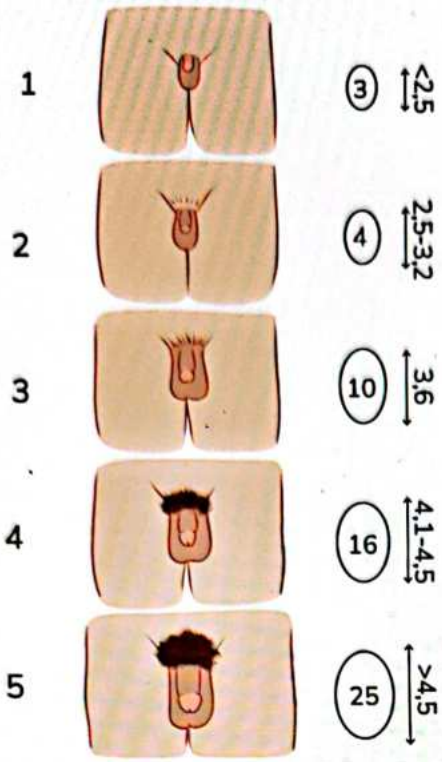
Stage 4.Hair growth more dense; coarse and curly like in an adult, but not yet spread to inner thighs. Penis continues to grow; the glans (head) of the penis becomes more prominent. The scrotum darkens

Stage 4.Hair growth extends to inner thighs. Genitalia reach adult size and shape

Staging of Puberty in Males

00:08:20

Stage	Pubic hairs	Genitalia
1	Absent	• Testicular size < 4 cc or (prepubertal) < 2.5 cm in longest dimension)
2	Sparse hair, at the base of penis	• Enlargement of testes & scrotum; • Scrotal skin reddens • Slight or no enlargement of penis
3	Darker, more coarse and curled	• Further growth of testis • Penis increases in length.
4	More dense, coarse & curly hair	• Tests & scrotum longer • Scrotal skin darker • Penis increases in length & breadth, glans becomes more prominent.
5	Hair growth extends to inner thighs	• Adult genitalia (>20 ml)



Stage 1 :prepubertal; testicular size less than 4cc in volume and 2.5 cm in longest dimensions

Stage 2 :enlargement of scrotum and testes; scrotal skin reddens and changes in texture; growth of testes to 4 cc or greater in volume

Stage 3 :enlargement of penis (length at first); further growth of testes

Stage 4 :increased size of penis with growth in breadth and development of glans; testes and scrotum larger; scrotal skin darker

Stage 5 :adult genitalia

- Menstruation begins :
  - During SMR stage 3-4
  - Average age of menarche: 12-12 1/2
  - Years after onset of thelarche: 2 1/2- 3 years
- Bone growth during adolescence precedes –
  - Bone mineralization→ increase risk of fractures
  - Muscle growth→ increased chances of sprains and Strains.
- In recent times onset of puberty-
  - Occurring at an earlier age
  - More common in girls
- Egocentricity in early adolescence
  - They feel that they are the centre of everyone's attention
- Separation from parents-
  - Hallmark of adolescent development.
  - Adolescents seek more privacy
  - Less times with parents

Problems in adolescent age group:

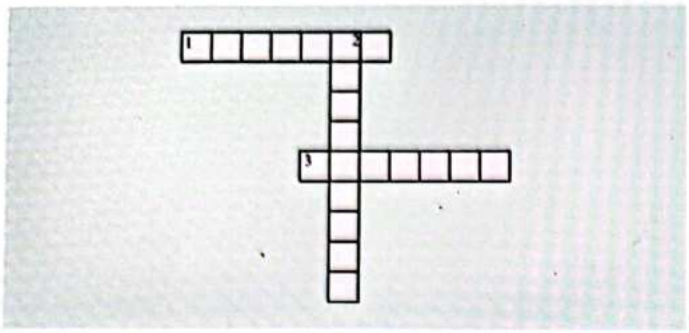
- A – Accident (MC cause of mortality in adolescent age group)
- I – Infection (HIV, STD, Skin disease, TB)
- M – Mental health problems – adjustment & anxiety
- L – Low self esteem & body image issues
- E – Eating disorders
- S – Substance abuse
- S – Sleep disturbances.

How To Remember?

AIMLESS

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. _____is a device used to measure testicular size.
3. Assessment of puberty in adolescent is done by _____ taging.

Down

2. First sign of puberty in females

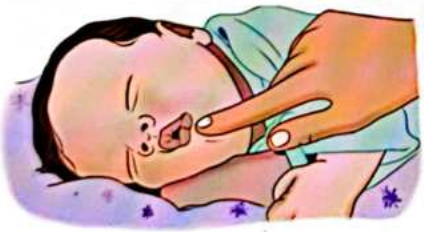
princeeeekum@gmail.com
9928609733

13 PRIMITIVE NEONATAL REFLEXES

Primitive Neonatal Reflexes 00:00:22

Present at Birth (Term)	Appears	Disappears
Rooting Reflex	32 weeks of gestation	Starts disappearing at 1 month post-natal age
Moro's Reflex	28 – 37 weeks	5–6 months
Palmar Grasp Reflex or plantar grasp reflex	28 weeks	3 months
ATNR [Asymmetric Tonic Neck Reflex]	35 weeks	5-6 months
Present After Birth	**Appears**	**Disappears**
STNR [Symmetric Tonic Neck Reflex]	4-6 months	8-12 months
Parachute Reflex	7-8 months	Persists throughout life
Landau Reflex		
Neck Righting Reflex		

Rooting reflex



- It helps in baby in breast feeding
- Earliest to disappear

Asymmetric Tonic Neck Reflex

A comes before S.

How to remember

- A comes before S
  - ATNR is present before birth.
  - STNR is present after birth.

Important Information

Q. Which primitive neonatal reflex helps mother in breast feeding: Rooting reflex

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

MORO'S Reflex/ Embrace Equivalent 00:06:06

- **Components of a Complete Moro's Reflex**
  - Symmetric abduction & extension of upper limbs along with opening of hands followed by Flexion & adduction of

upper limbs
[+]
↓
Extension of head & Trunk,
Movement of lower limbs,
Crying

- Also k\a Embrace Equivalent

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

- Abnormal persistence beyond 6 months indicates Cerebral Damage
- MORO'S Reflex: If once disappears, Never Reappears

Causes of Absent Moro's Reflex

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

Causes of Exaggerated Moro's Reflex

- Stage 1 (early/mild) Hypoxic Ischemic Encephalopathy

Causes of Asymmetric Moro's Reflex

- Neurological Causes
  - Erb's palsy [C5, C6 injury]
  - Congenital hemiplegia
- Skeletal Causes
  - Fracture clavicle in a neonate
  - Shoulder joint dislocation

Important Information

- Most common bone to fracture in a neonate: Clavicle

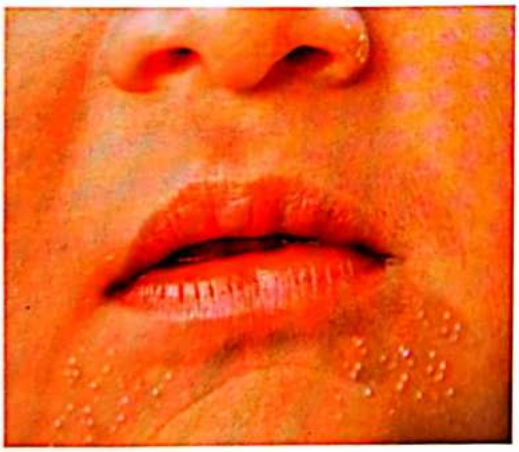
- ATNR is present at birth
- STNR appears after birth
- Parachute relflex persists throughout life

Important Conditions in Neonates Not Requiring Any Specific Treatment

00:15:41

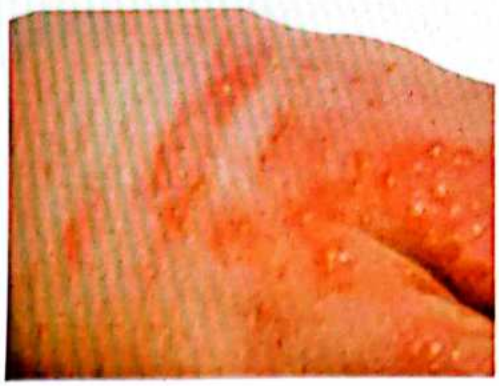
Skin & Mucosa

1. **Milia:** Colourless papules d/t plugging of sweat ducts



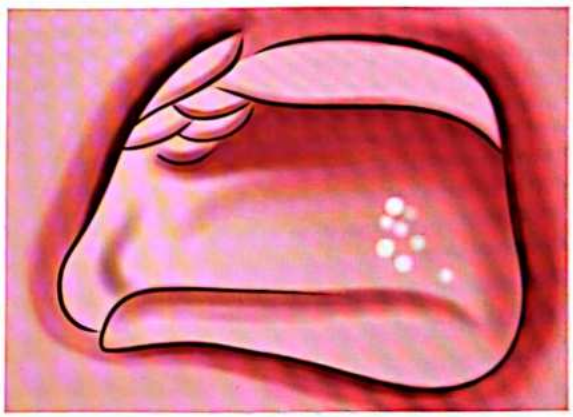
2. **Mongolian Spots**
- Bluish black areas of discoloration
- Mainly on Lower back, buttocks, back of thighs d/t arrest of migration of neural crest cells

3. **Erythema Toxicum Neonatorum**
- Erythematous maculo papular rash mainly on trunk, seen in 1st week of life
- d/t immune phenomenon
- Biopsy shows Eosinophil filled sterile lesion



Erythema Toxicum

4. **Stork Bite/ Salmon Patch**
- Pinkish colored lesions capillary hemangiomas
- In between eyebrows/ nape of neck /forehead
5. **Epstein Pearls**
- Pearl like white lesions
- Hard palate involved
- Epithelial inclusion cysts
6. **Acne neonatorum**
7. **Sub conjunctivalhemorrhage**

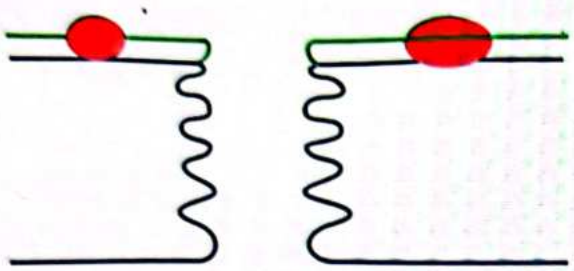


Epstein Pearls

Other Conditions in Neonates Not Requiring any Specific Treatment

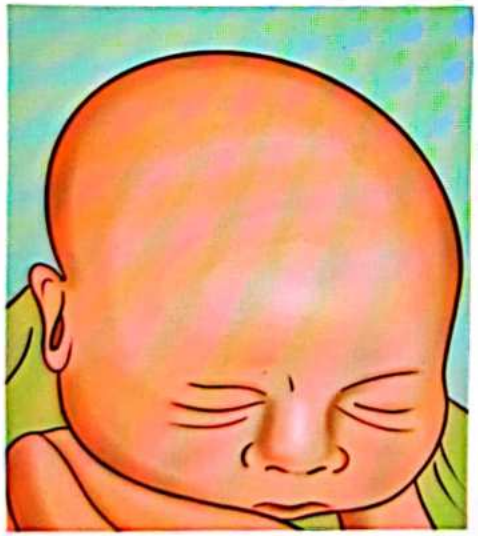
1. **Mastitis Neonatorum**
- B/L breast engorgement
- In male/ female neonates
- Day 2-3 of life
- D/t effect of maternal hormones
2. **Vaginal Bleeding**
- Seen in female Neonates
- On Day 3 - 5 of life
- Due to effect of withdrawal of maternal hormones
3. **Hymenal Tags:** Skin growth near the vagina opening
4. **Physiological Phimosis**

- Subperiosteal hemorrhage involving cranial bones

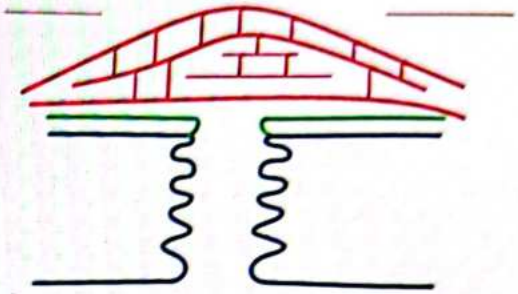


Does not cross midline and swelling is unilateral

- May take 24 hours to appear completely
- Takes 5-7 weeks to disappear
- Predisposes to neonatal jaundice

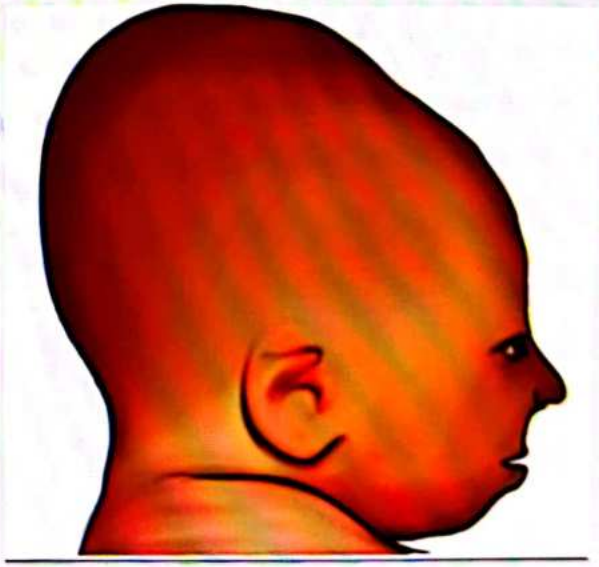


- D/t edema in the layers of scalp



Can cross sutures or mid line

- Already present at birth in its maximum size
- Disappears by 48-72 hours
- Does not predispose to neonatal jaundice



14 NEONATAL RESUSCITATION

Neonatal Resuscitation Protocol (NRP) 00:00:24

- Neonatal resuscitation guidelines came in October 2015
- It is given by the American academy of Pediatrics
- Almost 10% babies require some resuscitation at birth and < 1% requires chest compression and/or medications

Neonatal Resuscitation Protocol

- It starts from the antenatal period
- **Antenatal counselling**: When the mother comes for antenatal visits, at that time mother needs to be counselled for whether there are any risk factors like if mother is high risk or not
  - If mother has a prior history of preterm delivery or abortions
  - If mother have any disease like anemia or some chronic disease or uterine anomalies
  - Counsel and prepare the mother accordingly
- **Team briefing:** A team is formed who will be responsible for taking care of the baby after the birth.
  - Brief the team members about their own individual responsibilities like who will receive the baby or if baby require intubation
- **Equipment check:** Equipment required needs to be checked and ensured if they are working or not
  - Check if the radiant warmer in which the baby is received is working or not or if it is making the atmosphere warm for baby or not
  - Check whether the suction apparatus is working or not
  - If baby requires intubation, appropriate size blades of laryngoscope are available or not, the battery is working or not or if the laryngoscope have proper light or not
- **Once the baby is bora, few questions need to be asked**
  - Whether it is term gestation or not?
  - Whether the baby is breathing or crying or not?
  - Whether the baby has good muscle tone or not?
- **If the answer to all these questions is yes then baby gets routine care i.e.,**
  - Provide warmth to the baby
    - → Take the baby to the neonatal care corner and put the baby in the radiant warmer or in direct skin to skin contact with the mother
  - Clear airway if required
    - → If the baby is having some secretions, wipe it off with gauze piece
    - → But if there is a lot of secretion then suction might be needed to be done
  - Dry up the baby to minimize the heat loss due to evaporation
  - Ongoing evaluation: Monitor the baby to check if there is any respiratory distress developing or not
- **If the answer to any of these questions is no then all the following measures needs to be taken**
  - Provide warmth
  - Position the baby properly to ensure open airway, neck should be kept slightly extended & mouth slightly open
  - Clear airway if required
  - Dry the baby
  - Stimulate the baby i.e., providing physical stimulation by rubbing the back of the baby or flicking the soles of the baby
  - Then assess the baby if the baby has heart rate of < 100/min or apnea or gasping
- **If any of the these is not present then check the baby for**
  - Laboured breathing
  - Persistent cyanosis
    - → All the babies have acrocyanosis or peripheral cyanosis to some extent at birth but if the baby has persistent cyanosis or central cyanosis then some measures are needed
  - But if Laboured breathing or persistent cyanosis is present then do 3C's

1. Clear airway
2. Check SpO_2 (by pulse oximeter)
3. Consider CPAP (Continuous Positive Airway Pressure)
4. Supplement oxygen if required

- **If heart rate < 100/min or apnea or gasping is present then**
  - Start positive pressure ventilation (by self-inflating bag and mask)
  - Check SpO_2 by using pulse oximeter
  - Consider using cardiac or ECG monitor (new entry in latest Neonatal Resuscitation Protocol)
  - Then reassess after 30 sec, if the heart rate is not < 100/min then the baby gets post resuscitation care
  - Also, baby who has laboured breathing and persistent cyanosis which gets improved by CPAP that baby also get post resuscitation care
  - Post resuscitation care: Take the baby in a nursery/NICU, continue monitoring the condition of the baby, start IV fluids, if required oxygen may be given, monitor the baby and treat them accordingly i.e., maintain proper temperature, proper glucose of the baby

- **If the heart rate is still < 100/min despite positive pressure ventilation then**
  - Ensure if the positive pressure ventilation is given properly or not by checking if the chest movement is happening with each breath given or not
  - Take ventilation corrective steps
  - May intubate the baby or do endotracheal intubation
- **Reassess and check if the baby's heart rate is < 60/min or not**
  - If the heart rate is not < 60/min then check whether the heart rate is < 100/min or not, if it is not < 100/min then the baby gets post resuscitation care but if the heart is < 100/min then again check for chest movements, take ventilation corrective step, and may intubate the baby
- **If the heart rate is < 60 /min i.e., the baby has severe bradycardia then**
  - Start chest compressions
  - Continue positive pressure ventilation and coordinate it with chest compressions
  - Positive pressure ventilation and chest compression are done together by 2 people, one will chest compression and other will do positive pressure ventilation e.g., 3 chest compressions then 1 positive pressure ventilation (3CC: 1PPV)
  - Whenever baby require chest compressions and have severe bradycardia, use 100% oxygen
  - Initially positive pressure ventilation can be started with room air if the baby continues to have severe bradycardia, give 100% oxygen
  - Use cardiac and ECG monitor to monitor the heart rate accurately
  - May intubate the baby if not already done
  - Consider securing UVC (Umbilical venous catheterisation) as baby might needs intravenous drugs
  - Reassess, if the baby's heart rate is not < 60/min, then check if baby's heart rate is < 100/min, if it is not < 100/min then baby goes for post resuscitation care but if heart rate is < 60/min then Inj. adrenaline or epinephrine can be given upto 3 times
  - If still there is no improvement, then consider other causes like hypovolemia or pneumothorax
  - For hypovolemia give volume to the baby by giving crystalloids or blood
  - Pneumothorax needs to be appropriately managed and drained

Neonatal Resuscitation Protocol (NRP)

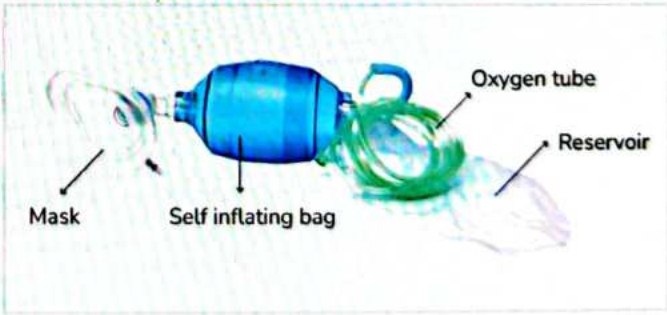
- Target preductal SpO_2 after birth
  - 1 min: 60-65%
  - 2 min: 65-70%
  - 3 min: 70-75%
  - 4 min: 75-80%
  - 5 min: 80-85%
  - 10 min: 85-95%
- Excessive O_2 can also cause damage to baby, increases chances of condition like retinopathy and prematurity

Suction of airways

- Correct order: Mouth followed by nose
- On suction from mouth, vagal stimulation will occur baby will take a deep breath so any oral secretion can get aspirated
- Recommended pressure for the suction: 80mmHg or 100cm of H_2O
- It should never exceed > 100 mmHg
- Recommended temperature of delivery room: ~25° C
- In delivery room baby should be kept in the warmer and the temperature of warmer should be higher than 25° C
- If post neonatal resuscitation is not done properly baby can have life long consequences in the form of cerebral palsy
- In team briefing it can be explained how post resuscitation care could have been done better, what are the things that can be improved and what are things done correctly

Devices used for positive pressure ventilation

- Self-inflating bag and mask
- It is a bag when it is squeezed and released it will inflate on its own, there is no need for extra supply of oxygen or gas to inflate it
- It is recommended for the use of neonatal resuscitation
- Valve provides unidirectional flow of the gases and air
- Reservoir bag and Oxygen may or may not be attached to self-inflating bag



- Function of reservoir: To increase FiO_2 delivered to the baby
- With each breath some oxygen is given to the baby and some oxygen is getting collected into the reservoir so for next breath extra oxygen is given through the reservoir to the baby

O_2 supply	Reservoir	FiO_2 delivered
-	-	21% (room air)
+	-	40%
+	+	90-100%

- Reservoir can either be in the form of bag or in the form of corrugated rubber tubing
- Rate of PPV: 40-60/min (to match the normal physiological breathing rate of new born and their requirements)
- Pressure required to deliver breathe to a neonate
  - For 1st breath: 30-40 cm H_2O
    - → Pressure required for first breath is greater as lungs are totally collapsed and alveoli are also collapsed
  - For subsequent breaths: 15-20 cm H_2O
- Single most important step in neonatal resuscitation: Effective positive pressure ventilation

Important Information

- Absolute contraindication to bag and mask ventilation: Congenital diaphragmatic hernia

- Congenital Diaphragmatic hernia: There is a diaphragmatic defect through which bowel loops herniate into the thorax
- In bag and mask ventilation, mask is covering both nose and mouth so air is going through both trachea and oesophagus so the air going through oesophagus

Most important (Sensitive) indicator of effective positive pressure ventilation:

- Improvement in heart rate

Ventilation corrective steps

- Mask should be of appropriate size
- Seal between mask and face should be tight (E-C clamp technique)
- Head of baby should be slightly extended
- Mouth kept open

Endotrachial intubation in NRP:

- Laryngoscope:
  - With straight blade
  - Size 0 – Preterm neonate
  - Size 1 – Term Neonate

Endotracheal tube size

Birth weight	Gestational weight	Size of ET (mm)
<1000 gm	<28 week	2-5 mm
1000-2000 gm	28-34 week	3 mm
>2000 gm	>34 week	3.5 mm

Ways to confirm whether ET is in Trachea

- Impt: Bilateral visible chest size with each breath
- Auscultation: Bilateral equal breath sounds in chest
- Improvement in vital parameters – HR, SPO2, color
- Misting of ET tube with each breath
- Recommended method – $ETCO_2$ (End tidal CO_2) or capnography

Tip of ET tube should be at:

- The level of lower border of T2

Chest compressions:

- Site
  - In midline on lower 1/3rd of body of sternum
  - Just below the line joining the 2 nipples
- Technique: 2 thumb encircling technique or 2 finger technique
  - Generalized higher pressure
  - Better perfusion
  - Lesser rescuer fatiguability
- Depth: 1/3rd of Antero – posterior diameter
- Ratio of chest compression in PPV 3:1

Important Information

- In 2 seconds : 3CC+1PPV

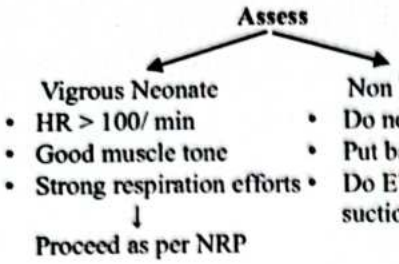
- Injection Adrenaline : 1:10,000
- Dose: 0.1ml/kg of 1:10,000

  Or

  0.01 mg/kg/dose upto 3 doses

  preferred route: Intravenous through umblical venous catheterization
- Can be given intratracheally (if not able to secure intravenous access)

Resucitation of a baby born through Meconium Stained Liquor (MSL)



Latest recommendation about babies born through MSL:

- Routine ET intubation and tracheal suctioning of all non – vigorous babies born through MSL is no longer recommended.
- At least 1 person skilled in ET intubation should be available during resuscitation of this baby.

Conditions in which do not resuscitate of neonate:

- Anencephaly
- Confirmed case of Trisomy 13
- Gestational age <22 weeks

Delayed cord clamping:

- Wait for atleast 30 seconds before clamping cord.
- Recommended for : All stable term and preterm neonate

Advantages

- Lesser changes of Anemia
- Lesser need of blood transfusion
- Lesser risk of short or hypotension
- Lesser risk of NEC (Necrotizing Entero Colitis)
- Lesser risk of IVH (Intra Ventrical Hemorrhage)

Disadvantage

- Slightly more risk of neonatal jaundice

Essential newborn care: Includes immediate care at birth of baby

- Delayed cord clamping
- Through drying
- Assessment of breathing
- Skin to skin contact
- Early initiation of breast feeding
- Thermal care
- Resucitation, whenever needed
- Prevention of Infection
- Check birth weight and gestational age
- Eye care of baby (with sterile swabs)
- Vitamin I mg intra muscularly

Before discharge

- Immunization

1. BCG
2. OPV-O dose
3. Hepatitis B
   - Should be given as soon as possible after birth

- Screening of disease : Do heel prick, take dryy blood spot on (DSB) filter paper
  - This DBS is use to screen for
    - → Congenital hypothyroidism
    - → Congenital adrenaline hyperplasia
    - → Other in born errors
- Screening for Neonatal Jaundice
- Advice Vitamin D 400 IU / day should be given to all babies for 1st year of life

15 IUGR AND FEEDING OF PRETERM NEONATE

Diseases of Newborn 00:00:23

More commonly seen in

Preterm	SGA/ IUGR	Preterm/SGA/ IUGR

• Neonatal sepsis
• **CNS:** intraventricular hemorrhage
  ○ Area commonly involved: Germinal matrix
• **Eyes:** ROP (Retinopathy of Prematurity)
• **Respiratory system**
  ○ Respiratory distress syndrome [Hyaline membrane diseases]
  ○ Pulmonary hemorrhage
  ○ BPD (Bronchopulmonary dysplasia/ chronic lung diseases)
  ○ Apnea of prematurity
• **CVS**
  ○ PDA (Patent ductus arteriosus)
• **GI**
  ○ Feeding issues
  ○ NEC (Necrotizing enterocolitis)
  ○ Neonatal jaundice
• Anemia of prematurity
• Osteopenia of prematurity
	• Polycythemia
	• Persistent Pulmonary Hypertension of Newborn (PPHN)
	• Meconium aspiration syndrome
		• Hypothermia
		• Hypoglycemia
		• Hypocalcemia
		• Perinatal asphyxia (hypoxia)

SGA (Small for Gestational Age) 00:11:50

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

IUGR (Intrauterine Growth Restriction)

- It is a clinical definition
- Refers to all babies with clinical features of malnutrition or undernutrition like
  - ≥ 3 loose skin folds in buttock region
  - Emaciated appearance, Peeling of skin

Important Information

- All SGA babies are IUGR, but all IUGR babies may not be SGA
- Morphological IUGR
  - Babies with clinical features of malnutrition, but birth weight between 10th – 25th percentile of expected
  - So, this baby is Not SGA

Symmetric & Asymmetric IUGR 00:17:00

Refer Table 15.1

- IUGR fetuses do not attain their intrauterine growth potential.

Important causes of IUGR 00:23:14

Refer Table 15.2

Prevention of IUGR 00:26:13

- Balanced energy/ protein supplementation is associated with 30% reduction in risk of IUGR.
- Antiplatelet agents: a/w 10% reduction in risk of IUGR
- Anti-oxidants (Vit. C & Vit. E): No reduction in risk of IUGR

ROP (Retinopathy of Prematurity) 00:28:30

Risk Factors

1. Prematurity
2. Use of high concentration of O_2
3. Hemodynamically instability

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

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

Example

1. LMP: 26 weeks of gestation + 4 week → 30 weeks (No) PMA → 32 weeks (Yes). Therefore, will do screening for ROP 6 weeks after birth, for this baby
2. LMP: 30 weeks of gestation + 4 weeks → 34 weeks (Yes) PMA: 32 weeks (No)

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

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

- LMP: 28 weeks + 4 week's → 32 weeks from LMP
- PMA: 32 weeks
- So, 4 weeks later you will do screen for ROP but baby is already 2 weeks old
- Therefore 4 weeks – 2 weeks → 2 weeks
- So, in this baby screening for ROP will be done 2 weeks later.

Feeding of a Preterm Neonate 00:36:23

- Based on gestational age we decide, the preferred initial mode of feeding

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

Trophic feeds: Can be started even before 34 weeks of gestation if the baby is hemodynamically stable. Here, minimal amounts of orogastric feeding is allowed. It helps in increasing gut immaturity.

Nonnutritive feeds: Babies less than 34weeks of age can be put to feed on breasts. They may or may suck but it helps in increasing milk production and output.

Table 15.1

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

Table 15.2

Maternal Factors	Placental	Fetal
• Underweight mother • Chronic disease • Autoimmune disease • Thrombotic disease (SLE) • Excess caffeine intake • Alcohol / Smoking • Radiation exposure • Teratogen exposure • Uterine anomalies	• Malformation • Infarction • Abruptio placenta • Placenta previa	• Constitutional /familial • Chromosomal anomalies • Congenital malformations • Congenital infection • Multiple gestation

16 FEEDING IN PRETERM NEONATE

Classification of preterm neonates: Born at <37 weeks of gestation

- Extremely preterm <28 weeks
- Early preterm 28 to 34 weeks of gestation
- Late preterm 34 to then <37 week of gestation

Risk factor of preterm birth

Maternal factors

Condition of mother	Previous pregnancy	Present pregnancy
• Young or advanced age • Chr medical illness • Obesity • Anemia/ malnutrition	• Previous preterm birth • Shorter interpreg. Intervals	• Infections (GBS, UTI) • Pre-eclampsia • Polyhydramnios • PROM

Risk factors of Preterm birth

Uterine	Placental	Fetal
• Bicornuate uterus • Incompetent cervix	• Abruptio placentae • Placenta previa • Placental changing	• Fetal distress • Multiple gestation • Erythroblastosis fetalis • Non-immune hydrops

Characteristic of a Preterm Neonate

General	Head to Toe

• Lesser subcut. fat
  ○ Appear emaciated
• Generalised Hypotonia
  ○ Extended posture
• Skin-thin, translucent, friable
• Abundant lanugo but little cervix caseosa
	• Head appears to be relatively large
	• AF: Large and wide open
	• Ear cartilage: Soft and deformeable, ears are poorly formed.
	• Breast buds < 5 mm
	• Genitalia
	  ○ M – Undescended T, poorly formed
	  ○ F – L. Majora widely separated
	  L. minora – clearly visible

- Tool used of assess gestation age in a neonate
  - ENBS (Expanded new ballard score)
  - Used for wide range of gestation (20-44 weeks)

Expanded New Ballard Score

- Physical maturity
- Neuromuscular maturity

Parameters given a score of -1 to 5

- Min. ENBS: - 10
- Max. score: 40
- ENBS - Done between 30 mins to 96 hours
- Useful upto 7 days of life
- Gestation fo corretness of ± 2 weeks

Corrected Gestational Age (CGA) 00:12:05

- GA = (Gestation age at birth + postnatal age) – 40 week
- E.g. What is the corrected gestational age of a baby born at 32 weeks gestation, who is currently 10 weeks old?
  - (32 wk + 10 wk) – 40
    = 2 weeks

Disease more commonly seen in preterm neonates 00:14:14

- Neonatal sepsis
- CNS - Intraventecular hemmorhage (Germinal maxtrix area)
  - Apnea of pre maturity
- Eyes - Retinopathy of prematurity (Screening of ROP at 32 weeks or 4 weeks postnatal)
- CVS - PDA
- Respiratory
  - RDS - Hylaine membrane disease
  - BPD
  - Pulmonary hemmorhage
  - Apena of prematurity
- GIT
  - N&C
  - N.Jaundice
  - Feeding problems
- Anemia of prematurity
- Ostetopenia of prematurity
- N. Hypothermia
- N. Hypoglycemia
- N. Hypocalcemea

Feeding of preterm

00:19:30

Feeding of preterm Neonate	
Gestation age	**Preferred initial mode of feeling**
< 28 week gestation	IVF TPN
28 – 31 week gestation	Orogastric tube feeding or Gavage feeding
32 – 34 week gestation	Katori spoon or Paladai feeding
> 34 week	Direct breast feeding

17 NEONATAL SEPSIS

Definition

It is a clinical syndrome characterized by signs and symptoms suggestive of systemic neonatal infection with or without bacteremia

Classification 00:01:30

- Based on the onset of sepsis, it can be classified into 2 categories
  1. Early onset neonatal sepsis (EOS)
  2. Late onset neonatal sepsis (LOS)

Early onset sepsis

- It begins within the first 72 hours of life
- Organisms responsible are derived from maternal genital tract e.g., Group B streptococcus, E.coli
- Risk factors
  - Maternal: Foul smelling liquor, premature rupture of membrane (24 hrs or more prior to the delivery)
  - During labour: Multiple PV examination (either one unclean vaginal examination or 3 or more clean/sterile vaginal examination)
    → Difficult/prolonged labour (when combined duration of 1st and 2nd stage of labour is > 24 hrs)
  - Fetal: Low birth weight, Prematurity, Perinatal asphyxia

Late onset sepsis

- It has onset in the late neonatal period i.e., beyond the first week of life
- Organisms responsible are derived from environment
  - Community acquired (if baby is staying at home): Staph. aureus, E.coli
  - Hospital acquired/Nosocomial: Acinetobacter, Klebsiella
- It is commonly associated with neonatal meningitis
- In any baby with late onset neonatal sepsis, lumbar puncture must be done to rule out neonatal meningitis as choice and duration of antibiotics is going to be longer.
- Risk factors
  - Nosocomial/hospital acquired
    → Prematurity
    → NICU admission
    → Invasive procedures e.g., IV cannulation, exchange transfusion
    → Mechanical ventilation
    → Use of stock solution in baby with parenteral therapy
  - Community acquired sepsis
    → Poor hygiene
    → Poor cord care
    → Bottle feeding
    → Lack of breast feeding
    → Use of pre lacteal feeds

- Exclusive breastfeeding helps in prevention of neonatal sepsis
- Most effective intervention to prevent neonatal sepsis: Proper hand washing of caregivers
- Remove all the ornaments like rings, bangles, watches
- Fold sleeves above the level of elbow
- Wash your hands; wet your hands, take generous amount of liquid soap, and follow the 6 steps of handwashing for 2 minutes
- **6 steps for hand washing**
  - Wash palm and fingers
  - Wash back of the hands
  - Wash fingers and knuckles
  - Wash thumbs
  - Wash nails/fingertips
  - Wash wrists
- After washing hands, keep your hands upwards to allow draining the material down
- Most common organism responsible for neonatal sepsis
  - In India: Acinetobacter > Klebsiella
  - In hospital in India: Acinetobacter > Klebsiella
  - In hospitals across the world: E.coli
  - Early onset neonatal sepsis: group. B streptococcus (more prevalent in genitalia of mother)
  - Overall, throughout the world: group. B streptococcus

Clinical features of neonatal sepsis

- Earliest manifestation: Poor feeding, alteration in established feeding behaviour
- Temperature disturbances: Hypothermia > Fever
- Metabolic disturbances: Hypoglycemia, Metabolic acidosis, Elevated lactates
- **Systemic manifestations:** Meningitis along with neonatal sepsis
  - CNS manifestations: Shrill cry, irritability, seizures, abnormal posturing
  - Respiratory manifestations: Tachypnea, Hypoxia
    → Features of respiratory distress: retraction, grunting
  - GI manifestations: Abdominal distension, feed intolerance, recurrent episodes of vomiting, necrotising colitis like features can be present
  - Severe sepsis → Septic shock → Multi organ dysfunction
    → DIC: Bleeding manifestations
    → Sclerema: Generalised non pitting edema can be due to severe neonatal sepsis or severe hypothermia in neonates

Diagnosis of neonatal sepsis

- **Confirmatory/Gold standard:** Blood culture
  - Isolation of organism in blood culture
  - Sensitivity pattern based on which treatment is guided
  - It takes 48-72 hrs to blood culture report to come so a screening test is done
- **Screening test:** Sepsis Screen
  - There are 4 components of sepsis screen (TLC is not used now a days as a component of Sepsis screen)
    1. Absolute neutrophil count (ANC): < 1800/mm^3
       → For term neonates: Manroe's chart (to get exact value of ANC for term babies)
       → For Very low birth weight neonates (< 1500 gm): Mouzinho's chart
    2. IT ratio (Immature: Total neutrophil ratio): > 0.2
       → More and more immature neutrophils i.e., myelocytes, metamyelocytes, band cells (u shaped nucleus) come into circulation
    3. MESR (Micro ESR): Quick bedside test: > 15mm suggestive of neonatal sepsis
    4. CRP (C Reactive protein) > 1mg/dl
  - If any 2 out of these 4 parameters are positive then sepsis screen is considered positive
  - Positive sepsis screen gives a very high negative predictive value for neonatal sepsis
  - If sepsis screen is positive then sensitivity for neonatal sepsis: 90-100%
  - But specificity: 80%
  - Positive predictive value: 25%
  - Negative predictive value: 99-100%
  - If the sepsis screen is negative, there is reasonable assumption that baby does not have neonatal sepsis but if there is strong suspicion for sepsis, sepsis screen can be repeated after 12-24 hrs
- **Supportive test can be done: → glucose monitoring for hypoglycemia**
  - Chest X-ray to check for pneumonia
  - Lumbar puncture: For all cases of late onset neonatal sepsis + in those cases of early onset neonatal sepsis where certain neurological symptoms are present and there is suspicion for meningitis

Treatment of neonatal sepsis

A. Supportive care

- NICU admission
- Start IV fluids
- Maintain normal temperature (36.5°C -37°C)
- Maintain Euglycemia
- Maintain normal oxygen saturation of the baby; supplement oxygen if required
- Blood product administration if there is bleeding

B. Specific treatment

- Antibiotics: No role of oral antibiotics in neonatal sepsis
- Start IV broad spectrum empirical antibiotics: Treatment of choice
- Indications for antibiotic therapy
  - In case of early onset sepsis
    → If there is history of foul smelling liquor
    → Presence of 3 or more risk factors for early onset sepsis
    → If there is less than 3 risk factors then baby must present with clinical features suggestive of neonatal sepsis and positive sepsis screen
    → If there is strong clinical suspicion of neonatal sepsis even if sepsis screen is negative and there are no risk factors
  - In case of late onset sepsis
    → Positive sepsis screen
    → Strong clinical suspicion of neonatal sepsis
- Antibiotics given varies upon centre to centre based on prevalent organism in that area and based on antibiogram or antibiotic sensitive pattern of organisms in that area
- 1st line antibiotic therapy: Inj. Ampicillin + Gentamycin
- Cephalosporins have better coverage but they are not given to all babies as it can increase the risk for fungal sepsis and it might have some side effects
- In case of suspicion of meningitis: Inj. Ampicillin + Gentamycin + Inj. Cefotaxime (any 3rd generation cephalosporin)
- Duration of antibiotic therapy: Depends upon the evidence of neonatal sepsis

Sepsis screen	Blood culture	CSF suggestive of meningitis	Duration of antibiotics
-	-	-	3 days; upto 7 days if there is strong clinical suspicion
+	-	-	7-10 days (1 week)
±	+	-	2 weeks
±	±	+	3 weeks

princeeeekum@gmail.com
9928609733

18 NEONATAL HYPOTHERMIA

- Normal axillary temperature of a neonate: 36.5-37.5°C
- Hypothermia: It is defined as a condition when the axillary temperature of a neonate is < 36.5°C
- For measurement of axillary temperature digital thermometer is used (mercury thermometers are not used for safety purposes)

Ways to Assess Temperature of Neonate 00:02:15

1. **Digital thermometer:** It should be kept in axilla for at least 3 minutes to record the axillary temperature perfectly
2. **Thermistor probe:** When the baby is kept in in incubator/radiant warmer, a metallic probe is attached to the skin of the baby usually in upper abdomen, in right hypochondrium area
3. **Touch method**: Crude way to assess the temperature of the baby
   - Examiners dorsum of the hand is used
   - Touch the abdomen of the baby and touch the palm and soles of the baby

Abdomen	Palm and soles	Interpretation
Warm	Warm	Thermal comfort/Euthermia
Warm	Cold	Cold stress
Cold	Cold	Hypothermia

Classification of Hypothermia in Neonates 00:05:52

- It can be classified into 3 categories based on the axillary temperature of the baby

Category	Axillary temperature
Cold stress	36-36.4°C
Moderate hypothermia	32-35.9°C
Severe hypothermia	< 32°C

Thermoneutral environment/Thermoneutral range of temperature

- It is the range of environmental temperature at which the baby has minimal BMR (Basal metabolic rate), least oxygen consumption and the baby can maintain their normal body temperature
- It varies by gestational age and postnatal age
  - For term neonates (>2500gm): 1-2 days of life - 33°C, for ≥3 days - 32°C
- Ideally all babies should be kept in a thermoneutral environment so that all the energy is being used for the growth of the baby
- **How frequently the temperature of a baby should be monitored?**
  - In stable, term babies: Once/day
  - Birth weight 1500gm – 2499 gm: 2 times/day
  - Birth weight < 1500 gm: 4 times/day
  - In sick babies: 1-2 hourly
- **Why hypothermia is more common in neonates?**
  - Neonates have larger body surface area or their body surface area to body weight ratio is more than that of adults hence more heat loss takes place
    → Maximum heat loss takes place from the head of a neonates (neonates have large head at the time of birth, head circumference > chest circumference at the time of birth).
  - Neonates have lesser subcutaneous fat especially in preterm or SGA (Small for gestational age) babies.
  - Neonates have vulnerability to get exposed to cold as they cannot cover themselves
  - Shivering is absent in neonates

Ways by which neonates protect themselves from hypothermia are

- **Non-shivering thermogenesis:** It is due to the presence of brown fat (lipid deposit rich in mitochondria)
  - Areas richer in brown fat
    → Axilla
    → Groin/Inguinal area
    → Nape of neck
    → Interscapular area
  - Mechanism: When the baby is exposed to cold environment, there is sympathetic stimulation in the body of the baby causing release of nor-epinephrine which uncouples the β-oxidation of fat so instead of energy, heat is going to be produced
  - It is the most important mechanism by which the baby protects the themselves against hypothermia
- Cutaneous vasoconstriction on exposure to cold environment so that heat rate loss can be minimized
- Flexed posture in neonates also helps in preservation of body heat
- Higher heart in the neonate (120-140 bpm) → more cardiac output → more oxygenation of the blood → more respiration hence more energy and heat is generated

Clinical features of neonatal hypothermia

- **Early features:** Mainly due to peripheral vasoconstriction
  - Pallor
  - Acrocyanosis/peripheral cyanosis
  - Decreased peripheral perfusion
  - Cool extremities
  - Irritability
- **Late manifestations**
  - Bradycardia
  - Lethargy
  - Apnea
  - Poor feeding
  - Abdominal distension
  - Sepsis like features: Weak cry, emesis
  - Respiratory distress due to increased pulmonary artery pressure
  - seizures
- **In cases of prolonged hypothermia other manifestations are**
  - Hypoglycaemia (as lots of glucose gets used up to produce heat)
  - Metabolic acidosis
  - Elevated lactate values
  - Hypoxia
  - Coagulation abnormalities like thrombocytopenia & bleeding manifestations
  - PPHN (Persistent Pulmonary Hypertension of new born)
  - Acute renal failure
- **Ways to prevent neonatal hypothermia**
  - Warm chain: It refers to series of interlinked steps done just after birth to maintain the normal temperature of a neonate
    - → It includes thermal care in the delivery room
      - Ideal temperature of the delivery room should be 25-28°C
      - Delivery room should be free from drafts of air i.e., done by closing the windows and doors, they should not be frequently opened
      - Ideal temperature of NICU should be between 22-26°C
    - → Warm resuscitation
      - Birthing facilities should have new born care corner which should have at least one radiant warmer
      - Warmer should be switched on 15-30 minutes prior to the expected time of delivery, linen should also be heated in which baby is going to be kept
    - → Immediate drying of the baby is done as to minimize immediate heat loss
    - → Baby should be kept in skin to skin contact with mother so that baby can drive some heat from the body of the mother
    - → Early initiation of breast feeding as comes with higher temperature i.e., the body temperature of the mother
    - → Bathing of the baby should be postponed for at least 2-3 days after the birth
    - → Rooming in: Baby should be kept in the same room as the mother
    - → Bedding in: Baby should in same bed as mother and appropriate clothing of the baby, head of the baby should be covered
    - → Ensure warm transportation if needed
      - It is the weakest link in maintaining the warm chain
    - → Training and awareness generation, all the health workers should be sensitized about the importance of maintaining temperature of neonates, family of the baby should also be educated
  - Thermal care for the preterm neonate
    - → Use of polyethylene, food grade bags to prevent immediate heat loss from the body of the baby just after he is born, before drying and shifting to a warmer or incubator
    - → Incubators are preferred for preterm babies < 32 weeks gestation which will lead to lesser insensitive water losses and lesser evaporation
    - → Servo mode in incubator is preferred in which heater output is guided by the skin temperature of the baby
    - → In pre term neonates born at < 28 weeks gestation, initial humidification upto 80% in first week of life can be done, which is then gradually decreased by 5% every day after first week to minimize the heat loss due to evaporation
      - Humidification is possible in incubator, in which water compartment must be cleaned and dried daily otherwise it is associated with increased risk of pseudomonas sepsis

Devices used to keep baby warm 00:39:48

- **Radiant warmer:** It is an open care system, there is an overhead heating unit which consists of quartz crystal
  - It is readily available, less expensive and should be used in care of all babies
  - Mechanism: Radiation
  - Maximum heat in baby placed in radiant warmer takes place by convection
  - Cling wrap could be used as cover especially for preterm neonates
  - There are 2 modes: Servo mode and manual mode, servo mode is preferred as in servo mode heater output is guided by the body temperature of the baby so the thermostat probe attached to the skin over right hypochondrium will adjust output according the body temperature of the baby
  - Disadvantage: If the probe gets displaced, baby can get overheated

- Manual mode is preferred in
  - → Procedures
  - → Initial heating
  - → Fever
- **Incubator:** It is a closed system
  - Preferred for preterm neonates especially in babies born < 32 weeks gestation
  - Mechanism: Convection
  - Heat loss in incubators happens through radiation

Kangaroo mother care (KMC) 00:45:50

- It is a skin to skin contact between baby and mother or care giver
- Baby is kept inside the clothing of mother or care giver and baby must be wearing cap, mitten, and socks
- It is recommended for all stable low birth weight babies except in sick or very low birth weight babies < 1200 gm initially for few days then gradually starts it
- **Components of KMC**
  - Kangaroo position: Mother should be semi reclining and mother should keep baby in skin to skin contact
  - Kangaroo nutrition: Exclusive breastfeeding is done as and when required on demand to baby kept in mother's cloth
  - Early discharge from hospital and follow up
- **Advantages of KMC**
  - Decreased risk of neonatal hypothermia
  - Decreased risk of nosocomial sepsis
  - Decreased risk of neonatal mortality
  - Decreased length of hospital stay
  - Higher exclusive breast feeding rates
  - Better growth of the baby
- It should be done for minimum 1 hour per session

Treatment of neonatal hypothermia

- Cols stress
  - Remove wet clothes and cover the baby adequately
  - Warm environment should be ensured
  - Baby should be kept in skin to skin contact with mother
  - Exclusive breast feeding should be encouraged
  - Monitor the temperature of the baby frequently
- Moderate hypothermia
  - All the above measures should be taken and extra heating source for the baby is provided in the form of radiant warmer or incubator or room heater
- Severe hypothermia: Axillary temperature of baby is < 32°C
- Initial rapid rewarming is done using manual mode till baby's temperature reaches 34°C followed by slow rewarming till baby's temperature reaches 36.5°C
  - Take measures to decrease the heat loss of baby by using caps, mittens, and socks, remove wet clothing
  - Start IV fluid 10% dextrose as babies with prolonged hypothermia can end up having prolonged hypoglycaemia
  - Oxygen inhalation is also given if required
  - Inj. Vit K should also be given as bleeding abnormalities or coagulation abnormalities can be associated with severe hypothermia
  - If baby is not improving look for and treat neonatal sepsis
- Temperature of a non-asphyxiated neonate is a strong predictor of neonatal mortality, across all gestational ages

Neonatal Hyperthermia 00:57:42

Definition

- It is defined as axillary temperature > 37.5°C in a neonate
- **Aetiology**
  - Too hot environment
  - Too many clothes
  - Dehydration
  - Sepsis

Clinical features

- Hot, flushed skin
- Irritability initially
- Tachypnea and tachycardia
- Later the baby may develop lethargy, seizures or features of shock can develop

Management of hyperthermia

- Keep the baby in a room with temperature 25-28°C, away from any heat source
- Undress or remove any extra clothing from the baby
- Continue frequent breastfeeding
- If temperature is > 39°C, do sponging with tap water, give paracetamol 10-15mg/kg can also be given

19 NEONATAL HYPOGLYCEMIA

Definition

- Blood glucose < 40 mg/dl or plasma glucose < 45 mg/dl
- According to WHO: blood glucose <45mg/dl

High Risk Neonates for Hypoglycemia 00:02:08

- SFD (small for date)/IUGR/Preterm
- Large for date neonates /infant of diabetic mother
- Neonatal hypothermia
- Neonatal sepsis

- Regular blood glucose monitoring is recommended in high risk neonates at regular intervals (2 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours of life). Blood glucose values are lowest b/w 1-3 hours of life.

Clinical Features 00:05:29

- Jitteriness > Tremors (most common)
- Jitteriness stops on holding the limb but seizures do not.
- Neonatal seizures
- Lethargy
- Poor feeding
- Apnea, cyanosis
- Stupor, coma
- Increased sweating
- Sudden pallor
- Cardiac arrest

Treatment 00:07:10

Symptomatic

IV 10% dextrose @ 2ml/kg stat bolus
↓
Continuous IV fluids (@ GIR of 6 mg/kg/min)
↓
Monitor blood glucoses and titrate GIR according to Blood Glucose value (GIR= glucose infusion

Asymptomatic

1. BG < 20 mg/d→I start IVF @ GIR of 6mg/kg/min –continue blood glucose monitoring and titrate GIR according to blood glucose levels
2. BG 20 – 40 mg/dl Offer a feed to baby & recheck Blood Glucose after ½ hour– 1 hour

- **Case 1**: Blood Glucose still low → start IVF @ GIR of 6 mg/kg/min – continue blood glucose monitoring and titrate GIR according to BG value
- **Case 2**: Blood Glucose is normal → Continue frequent feeding & Blood Glucose monitoring
- Maximum dextrose concentration that can be given via a peripheral access = 12.5%

Persistent Hypoglycemia 00:12:35

Endocrine Causes

- Congenital hypopituitarism
- Congenital adrenal insufficiency
- Congenital hyperinsulinemia (or) Nesidioblastosis (or) PHHI (Persistent Hyperinsulinemic hypoglycemia of Infancy)
- It is mcc of persistent hypoglycemia during infancy
- Drugs used in Rx
  - Octreotide (s/c injection)
  - Diazoxide
  - Glucagon
  - Nifedipine
- Surgery in focal cases

Metabolic Causes

- Glycogen storage disorders [eg- von gierke disease aka type-I GSD]
- Galactosemia
- Hereditary fructose intolerance
- Mitochondrial disorders
- Fatty acid oxidation defect

Infant of Diabetic Mother 00:19:18

- Complications and congenital malformations are more in babies born to mothers with pre-existing diabetes than those with GDM.

Pathophysiology 00:20:52

- Pederson's Maternal Hyperglycemia/ Fetal
- Hyperinsulinemia Hypothesis

Maternal Hyperglycemia
↓
Fetal Hyperglycemia
↓
Hyperplasia and hypertrophy of fetal pancreatic beta cells
↓
Fetal hyperinsulinemia → Neonatal Hypoglycemia
↓
Insulin acts as a Growth Factor for Fetus

princeeeekum@gmail.com
9928609733

Macrosomia LFD	extra medullary Hematopoiesis	RDS in Infants
• All organs ↑ in size in IDM except brain Hairy pinna • +nt in IDM	• Polycythemia • Neonatal • Hyperbilirubinemia	• Insulin inhibits cortisol mediated • maturation of surfactant

Problems in IDM

00:26:52

Macrosomia/ Large for Date Baby

- Difficult/ prolonged labour
- ↑ed chances of birth trauma

→ Perinatal asphyxia/HIE

Metabolic

- Hypoglycemia: presents in 1st 24 hours
- Hypocalcemia
- Hypomagnesemia presents later
- Polycythemia
- Neonatal jaundice

CVS

- Increased risk of CHD
- Mc congenital abnormality in IDM: C.H.D (Congenital heart disease)
- Mc congenital heart disease in IDM: V.S.D
- Most specific congenital heart disease in IDM: TGA (Transposition of great arteries)

Respiratory System

- More chances of RDS due to delayed maturation of surfactant

CNS

- Mc congenital neurologic abnormality in IDM: Neural tube defects
- Most specific neurologic abnormality in IDM: Sacral agenesis or caudal regression syndrome.
- Overall most specific congenital abnormality in IDM: Sacral agenesis or caudal regression syndrome

Renal

- Renal agenesis
- Duplication of ureter
- Renal vein thrombosis

GI

- Duodenal atresia
- Lazy (small) left colon syndrome

Long Term Problems

- B - Blindness
- O - Obesity
- N - Non ketotic hypoglycemia
- D - Diabetes mellitus

20 PERINATAL ASPHYXIA

Definition: Inability to initiate or sustain breathing

Pathophysiology

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

- **Part of brain mc involved in HIE in**
  - Term neonates → Para sagittal area → Spastic Quadriplegia
  - Pre term neonates → Periventricular area → Periventricular Leukomalacia (PVL) → Spastic diplegia

Diagnostic Criteria for Severe Birth Asphyxia 00:05:19

All of the following are required

- Apgar Score: 0-3 for > 5 minutes
- Severe acidosis (cord blood pH < 7.0)
- Presence of any clinical evidence of CNS dysfunction
  - E.g.: Tone abnormalities, seizures, changes in sensorium etc.
- Presence of any evidence of dysfunction of at least 1 organ other than CNS
- Example
  - Renal: Acute Tubular necrosis, renal vein thrombosis
  - Heart: myocardial dysfunction, CCF, arrythmias
  - Pulm: pulmonary hypertension
  - GIT: NEC
  - Hemat: coagulation abnormalities
  - Metabolic: hypoglycemia, acidosis
  - Subcutaneous fat necrosis

Staging of HIE 00:09:42

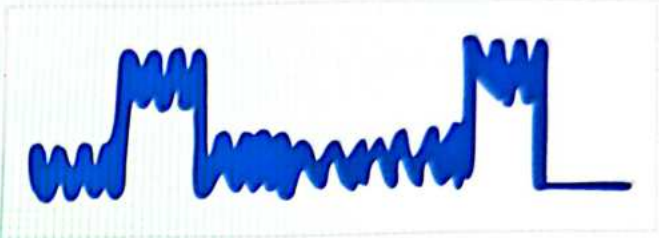
- Sarnat and Sarnat
- Levene's staging
- Thompson score
  - Maximum score = 22
  - Score of ≥ 15 is suggestive of poor outcome

Refer Table 20.1

Treatment of HIE 00:16:48

1. Supportive Care

- NICU admission
- IVF
- Maintain euglycemia & normothermia
- Monitor the baby
- Tool used for bedside monitoring of neonates with HIE → aEEG (Amplitude Integrated Electroencephalography)



2. Latest Rx Modality for neonates with Moderate to Severe HIE

- **Therapeutic Hypothermia**
  - Temp. maintained is 33.5° c –34.5° c
  - Preferred in babies > 35 weeks gestation
  - Decreases mortality and neuromorbidity
  - Due to some side effects, done at tertiary care centre.

3. Neonatal Seizures treatment

- DOC: phenobarbitone
- 2nd line: levetiracetam
- Mc type: subtle seizures
- Mc cause: hypoxia
- Type with best prognosis: Focal clonic seizures
- Types with worst outcome: myoclonic seizures
- Preferred initial CNS imaging: Transcranial ultrasound (cranio sonogram)

Table 20.1

Parameters	Stage 1 (Mild HIE)	Stage 2 (Moderate HIE)	Stage 3 (Severe HIE)
1. Level of consciousness	Hyper alert/irritable	Normal/depressed (lethargic)	Comatosed
2. Tone	Normal	Mild hypotonoia	Severe hypotonia
3. Moro's reflex	Exaggerated	Normal/depressed	Absent
4. Seizures	Not seen	Present	Not seen
5. Autonomic involvement	• Generalized sympathetic overactivity mydriasis • Increased heart rate	• Generalized parasympathetic overactivity • Miosis • Bradycardia	• Both systems are depressed • Pupils mild dilated • Variable HR
6. Prognosis	• 99% normal outcome	• 80% normal outcome	• 50% die • 50% severe neurological sequelae

21 IMPORTANT SCORES IN NEONATE

1. APGAR Score

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

- **Grimace:** Response to stimulation of oropharynx by a catheter/feeding tube
- **APGAR score**
  - Maximum score: 10
  - Minimum score: 0
  - >7 score: Normal
  - 0–3 score: Severe birth asphyxia Q
  - APGAR score is usually documented at 1 minute and 5 minutes of life
  - Has no role in neonatal resuscitation
  - It has prognostic importance

Scores used to assess respiratory distress

- Preterm neonate: Silverman score
- Term neonate: Downe's score

Silverman Score

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

- Maximum score: 10 & minimum score 0
- 0-3 score: Normal
- >7 score: Severe Respiratory Distress

Downe's Score

00:00:18

Components	0	1	2
C - Cyanosis	Absent	Present in room air	Present at FiO2 greater than or equal to 40%
A - Air entry	Normal	Decreased	Barely audible
R - Respiratory rate	<60/min	60-80/min	>80/min
G - Grunt	Absent	Audible only with stethoscope	Audible without a stethoscope
R - Retractions	None	Mild	Severe

- Min Score: 0
- Max Score: 10
- >7: Severe Respiratory distress

Crib Score

Clinical Risk Index for Babies 00:22:21

- Score used to predict mortality of neonates in ICU
- Compares performance of different NICU.

Snap Score

Score for Neonatal Acute Physiology

- Uses 34 parameters (vital signs and investigation findings)
- Predicts morbidity and mortality for neonates

22 RESPIRATORY DISORDERS IN NEONATES

Respiratory Distress Syndrome/ Also Known as Hyaline Membrane Disease (HMD)

00:00:22

- Mc cause of respiratory distress in a preterm neonate

Basic Defect

- Deficiency of mature surfactant

Surfactant

- Composition is
  - DPPC [Dipalmitoyl phosphatidylcholine] or lecithin [most imp. component]
  - Surfactant proteins A, B, C, D
  - B: most important surfactant protein
  - Phosphatidyl glycerol
  - Cholesterol
  - Surfactant is produced by type 2 Alvelor cells

Synthesis

- Begins in fetal lungs: 20 weeks gestation
- Begins to appear in amniotic fluid: 28-32 weeks of gestation
- Mature surfactant in adequate amount: > 35 weeks of gestation

Function

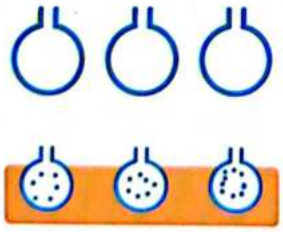
- To decrease surface tension of alveoli i.e. it prevents alveoli from collapsing during expiration

Pathophysiology of Respiratory Distress Syndrome

00:04:45

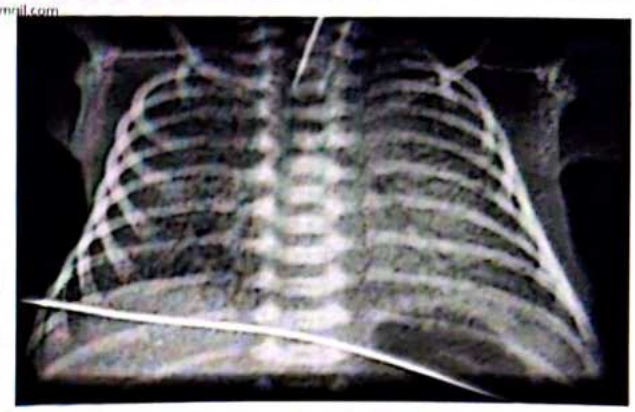
- Deficiency of mature surfactant
  - Alveolar collapse
  - Diffuse alveolar damage
  - Interstitial edema
  - Fibrin deposition

} Eosinophilic Hyaline Membrane appearance on Lung Biopsy



Clinical features

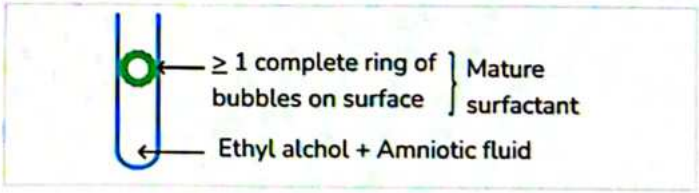
- A preterm neonate born at < 35 weeks of gestation who presents with respiratory distress soon after the birth with typical CXR picture



Diagnosis

- Clinical features
- CXR findings
  - Ground glass haziness of lungs
  - Presence of air bronchogram
  - Reticulogranular or reticulonodular appearance
  - Features of lung collapse and crowding of lungs
- Ways to detect adequacy of surfactant in amniotic fluid:
  - L:S Ratio (Lecithin: sphingomyelin ratio) > 2:1 → mature surfactant
  - Shake test

Shake Test



- Phosphatidyl glycerol estimation
- Nile blue sulphatase test- to detect lung maturity

Treatment of RDS

- Supportive care
  - NICU
  - O_2 Support
  - IV fluid
- Mild RDS: CPAP (continuous positive airway pressure)
- Moderate to severe RDS
  - Intratracheal Surfactant +Respiratory support [CPAP/ mechanical ventilation + O_2] INSURE Technique.

Prevention of RDS

Antenatal Corticosteroids

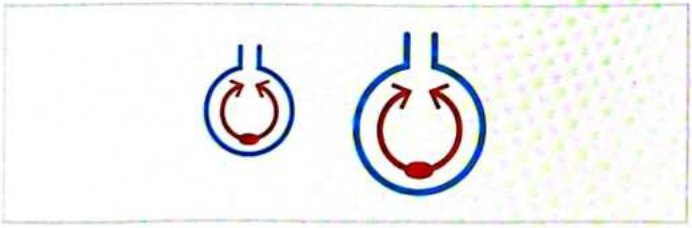
- Indication

- To all pregnant ladies who are expected to deliver between 24 -34 weeks of gestation.

- Contraindication
  - Clinical chronioaninoitis
- Steroid of Choice
  - Inj. Betamethasone: 12 mg I.M, 2 doses, 24 hrs apart [12 x 2 = 24] (or)
  - Inj. Dexamethasone: 6 mg I.M, 4 doses, 12 hrs apart [6 x 4=24]
  - Inj. Betamethasone has slightly more neuroprotective effect: Steroid of choice
  - Recommended by Indian government → Inj. Dexamethasone: Cheaper & easily available, equally efficacious
- Beneficial Effects
  - Decrease RDS
  - Decrease IVH
  - Decrease NEC
  - Decrease neonatal mortality
- Does not decrease the risk of neonatal jaundice

Neonatal Pulmonary Alveolar Proteinosis 00:17:37

- Basic Defect: d/t deficiency of Surfactant Protein B Which forms a thin layer of surfactant in the inner layer of alveoli

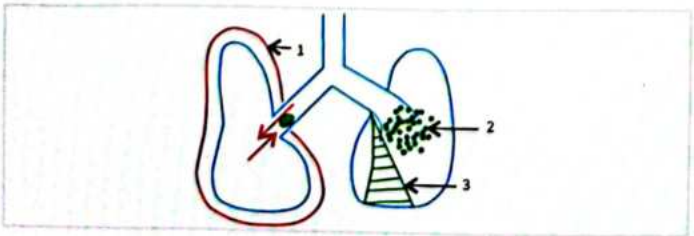


Clinical Features

- A term neonate presenting with severe respiratory distress soon after birth with Chest X-Ray showing ground glass haziness with H/O similar illness in a previous sibling who died (Family History positive)
- No improvement with surfactant therapy

Meconium Aspiration Syndrome (MAS) 00:20:25

- **Meconium:** 1st stool passed by a neonate; greenish black in colour; sterile; comprises of
  - Amniotic fluid
  - Bile (bile pigments and salts)
  - Mucus
  - Lanugo
  - Denuded interstitial epithelial cells
  - Water



Pathophysiology 00:43:42

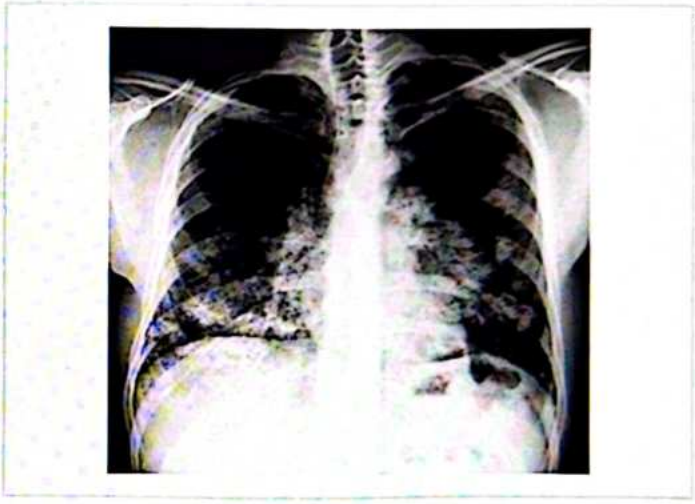
- Obstructive emphysema [m/c & most important] - Hyperinflated lungs
- Chemical pneumonitis
- Segmental collapse or atelectasis

Clinical Features 00:48:07

- A term neonate SGA/ IUGR baby, born through meconium stained liquor, presents with respiratory distress soon after birth with increased AP diameter of chest and typical CXR findings.

Chest X-Ray in MAS

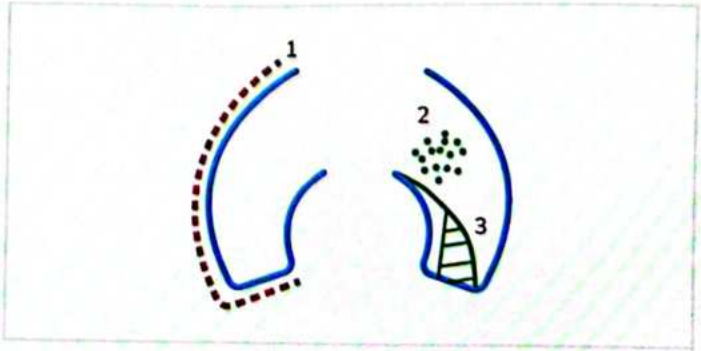
- Hyper inflated lungs
  - Increased radiolucency of lungs
  - Flattening of domes of diaphragm



- Hetrogenous Pulmonary infiltrates
- Segmental collapse

Treatment

- Mainly supportive including respiratory support (O_2 ± mechanical ventilation)
- In severe cases of MAS
  - Intra tracheal surfactant
  - iNO (inhaled Nitric oxide)
  - High frequency ventilation
  - ECMO [Extra Corporeal Membrane Oxygenation]



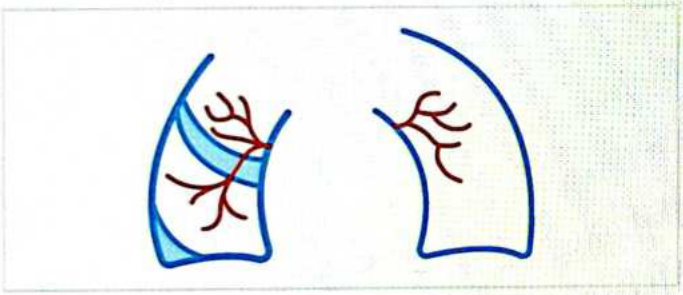
Complications
- Pneumothorax
- PPHN [Persistent pulmonary HTN of New Born]

TTNB (Transient Tachypnea Of New Born) 00:28:27
- MCC of respiratory distress in a term neonate

Basic Defect
- Delayed clearance of lung fluids
- TTNB is also called "delayed adaptation"

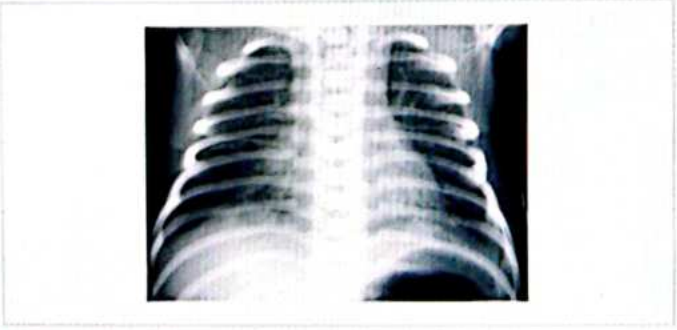
Risk Factor
- Delivery by caesarean section

Clinical Features
- Term baby
- Born by caesarean section
- Presents with mild respiratory distress, soon after birth that improves Spontaneously in 72 hours with or without typical CXR findings



CXR Findings
- Fluid in interlobar fissure
- Pleural effusion
- Perihilar streaking [prominent Broncho vascular markings]

Treatment
- Usually no Rx required
- Distress usually resolves
- Spontaneously in 48-72 hours



Neonatal Apnea 00:30:20

Definition
- Cessation of breathing for at least 20 sec or for any duration, in the presence of either bradycardia or cyanosis, in a neonate.

Etiology
1. Neonatal sepsis
2. Neonatal hypothermia
3. Neonatal hypocalcemia
4. Neonatal hypoglycemia
5. Neonatal hyperbilureinema
6. Polycythemia
7. Neonatal jaundice
8. NEC
9. Apnea of prematurity due to CNS immaturity

- More preterm the neonate: more chances of apnea of prematurity
- It is a diagnosis of exclusion

Treatment
- Respiratory support (CPAP or mechanical ventilation)
- Look for the cause & treat it
  - IV antibiotics for neonatal sepsis
  - IV 10% dextrose for N. hypoglycemia
  - Warm up for N. hypothermia
  - IV Ca gluconate for N. hypocalcemia
  - Partial exchange transfusion with normal saline (Treatment of choice) for polycythemia
  - For NEC →NPO, IV fluids
  - Neonate jaundice- phototherapy and exchange of fluids
  - Inj. Caffeine citrate (DOC): for apnea of prematurity
  - Inj. Aminophylline: is alternate for apnea of prematurity

Neonatal Hypocalcemia 00:35:30

	Total Ca	Ionised Ca
In a term neonate	< 8 mg/dl	< 1.2 mmol/L
In a preterm neonate	< 7 mg/dl	< 1 mmol/L

- **Polycythemia:** Hb >22 g/dl or Hematocrit > 65% in neonate, (blood is viscous)

Bronchopulmonary Dysplasia/ Chronic Lung Disease [CLD] 00:39:00
- Most commonly affects babies born at < 28 weeks of gestation or with birth weight < 1000 gms
- Due to atelectotrauma, volutrauma, free radicals = > Injury of lungs

Definition
- BPD is defined for babies born at < 32 weeks gestation, who require O_2 for 1st 28 days of their life.
- Assessed at 36 weeks of PMA [post menstrual age]
- Mild BPD: No supplemental oxygen required
- Moderate BPD: Oxygen required < 30%

- Severe BPD: oxygen required > 30%/ CPAP / Mechanical ventilation

Congenital Diaphragmatic Hernia 00:42:10

- A diaphragmatic defect through which abdominal contents may herniate into thorax
  +
- Pulmonary hypoplasia
- Intestinal malrotation

Other defects Associated with

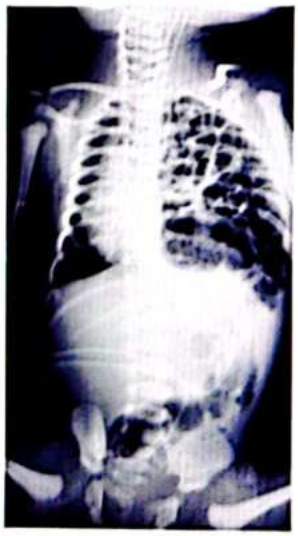
- Esophageal atresia
- Congenital heart diseases
- Omphalocele,
- Trisomy 13, 18
- Mc type of CDH → Postero lateral or Bochdalek variety
- Mc on left side; Mc in females

Clinical Features

- At Birth, usually presents with a triad of -
  - Respiratory distress
  - Scaphoid abdomen (abdominal contents go into thorax)
  - Mediastinal shift
- Later in life: Intestinal obstruction (due to associated malrotation)

Diagnosis

- Clinical features
- Antenatal USG [between 16-24 weeks]
- Chest X-Ray
  - Bowel gas shadows in thorax
  - Mediastinal shift
  - Pulmonary hypoplasia



Congenital diaphragmatic hernia

Treatment Refer Flow Chart 22.1

Important Information

- Bag and Mask ventilation is absolutely contra-indicated in CDH

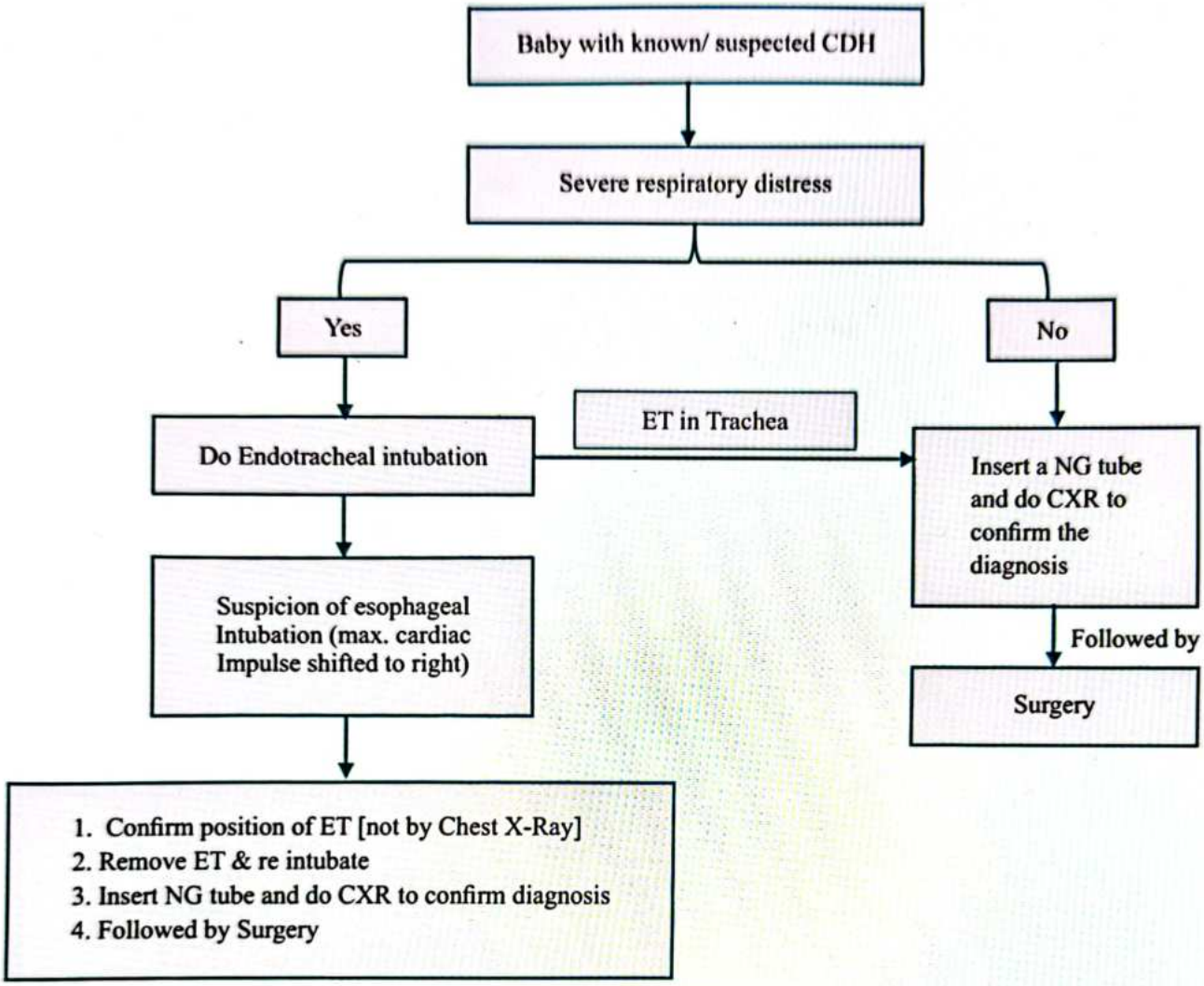
Predictors of Poor Outcome in Congenital Diaphragmatic Hernia

- Severe pulmonary hypoplasia
- Lung head ratio (LHR) < 1
- Any major malformation associated
- Symptoms in 1st 24 hrs
- Liver herniation into thorax
- Need of ECMO

Important Information

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

Flow Chart 22.1



PREVIOUS YEAR QUESTIONS

Q. In a preterm baby with respiratory distress syndrome, which type of cell is deficient? (NEET JAN 2020)

A. Type 1 alveolar cell
B. Type 2 alveolar cell
C. Alveolar capillary endothelial cells
D. Bronchial mucosal epithelial cells

Q. When can one diagnose acute respiratory distress in a child? (NEET JAN 2018)

A. Within 7 days of known insult
B. Respiratory failure not fully explained
C. No left ventricular dysfunction
D. All of the above

23 NECROTISING ENTEROCOLITIS (NEC)

Q. What is NEC?

Ans. It is an acute intestinal necrosis of unknown aetiology

- The part of intestine most commonly involved in NEC: Terminal ileum and ascending colon
- **Risk factors for NEC**
  - Most important risk factor: Prematurity
    → < 10% cases of NEC occur in term babies
    → Mean gestational age at which the NEC occurs: 30-32 weeks of gestation
  - Aggressive use of formula feeding and lack of breastfeeding
  - Fetal hypoxia
  - Maternal cocaine abuse
  - Absent or reversed end diastolic flow in umbilical artery on antenatal USG

Modified Bell's staging of NEC

Stage I (NEC suspect)

General features

- Temperature disturbances like fever or hypothermia
- Apnea
- Lethargy

Abdominal features

- Feed intolerance
- Blood in stools

Investigation

- Abdominal X-ray: Normal or mild intestinal dilatation
- In stage IA: Occult blood positive in stool
- Stage IB: Fresh blood present in stool of the baby

Treatment

- Keep baby nil per oral
- IV fluids
- IV antibiotics (for sepsis)

} 48-72 hrs then reassess

Stage II (Definitive NEC)

General features

- Same as Stage I

Abdominal features

- Absent bowel sounds
- Mild abdominal distension

Investigation

- Abdominal X-ray:
  - Stage IIA: Pneumatosis intestinalis (Air in the wall of the intestine)
  - Stage IIB: Portal vein gas

Treatment

- Nil per oral
- IV fluids
- IV antibiotics

} 7-10 days

- Start Total parenteral nutrition and then reassess

Stage III (Advanced NEC)

- Most severe form of NEC

General features	Abdominal features
• Shock • Bleeding manifestations • Life threatening apnea	• Huge abdominal distension and tender • Abdominal wall cellulitis

Investigations	Treatment
• Stage IIIa: Peritonitis on USG or Abdominal X-ray • Stage III b: Pneumoperitoneum (due to intestinal perforation)	• Same as Stage II • IV fluids bolus (for shock) • Blood products (for bleeding) • Intubation or mechanical ventilation (Life threatening apnea) • In Stage III b for intestinal perforation: Surgery • Palliative procedure if condition of baby is not suitable for surgery o Insert glove drain from which the faecal matter of baby can be drained from peritoneal cavity

- **Triad of blood investigations findings in NEC**
  - Severe metabolic acidosis
  - Hyponatremia
  - Refractory thrombocytopenia (persisting)

Prognosis of NEC: Poor

- Mortality/ death: 10-30% cases despite best supportive care

24 NEONATAL JAUNDICE

- 60 % of term neonates & 80% of preterm neonates have clinical jaundice in 1st week of life.
- Clinical jaundice in neonates is seen at bilirubin level > 4- 6 mg/dl
- M/c/c of readmission of a neonate discharged from a hospital: Neonatal jaundice
- M/c/c of neonatal morbidity in 1st week: Neonatal Jaundice

Physiological jaundice v/s Pathological Jaundice 00:02:56

Physiological jaundice	Pathological jaundice
• Icterus/clinical jaundice never appear in 1st 24hrs of life	• Clinical jaundice may appear in 1st 24 hrs of life
• Always unconjugated; urine does not stain diapers and no pale stools	• May be conjugated/unconjugated. High coloured urine; pale stools may or may not be seen
• Palms and soles never stained yellow	• Palms and soles may be stained yellow
• Clinical jaundice doesn't persist beyond 2 weeks in term neonates and 3 weeks in preterm neonates	• May persist beyond 3 weeks

Why does Physiological Jaundice of newborn occur? 00:08:00

- Higher production of bilirubin
  - Higher Hb level in neonates
  - Shorter life span of RBCs (90 days vs 120 days).
  - More ineffective erythropoiesis
- Ineffective carrier mediated uptake of bilirubin by liver
- Immature UDP Glucoronyl transferase enzyme activity
- ↑ sed enterohepatic circulation in neonates

Breastfeeding Jaundice v/s Breast Milk Jaundice 00:11:38

Refer Table 24.1

Important Causes of pathological jaundice

A. Unconjugated Hyperbilirubinemia 00:15:29

↑ Production of Bilirubin	↓ Conjugation of Bilirubin
• Hemolytic disorders o Erythroblastosis fetalis [Hemolytic disease of newborn] → MC cause of neonatal jaundice in 1st 24 hrs of life o Hereditary spherocytosis o G6PD deficiency	• Crigler Najjar syndrome o Deficiency of UDP glucuronyl transferase enzyme o Type I: Complete deficiency o Type II: Partial deficiency (Rx: phenobarbitone - enzyme inducer)
• Polycythemia	• Gilbert syndrome
• Delayed cord clamping	• Down syndrome
• Cephalhematoma	• Congenital hypothyroidism
• Infant of diabetic mother	-

B. Conjugated Hyperbilirubinemia 00:20:51

- Conjugated Bilirubin > 2 mg/dl (or) 20% of total bilirubin

Non-Obstructive Causes

- **Infections**
  - Viral: EBV, CMV, hepatitis
  - Bacterial: Congenital TB [Ghon focus seen in liver]
  - Parasitic: Toxoplasmosis
- **Toxins**
  - Sepsis, UTI, TPN
- **Metabolic**
  - Tyrosinemia
  - Galactosemia
  - Hereditary fructose intolerance
  - Alpha 1 antitrypsin deficiency
  - Cystic fibrosis
- **Idiopathic neonatal hepatitis**
  - MC cause of conjugated hyperbilirubinemia in neonates

Obstructive Causes

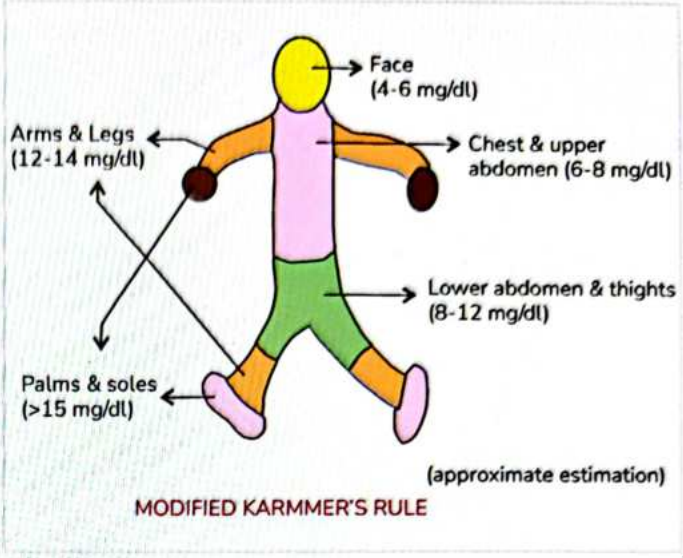
Intra Hepatic Causes	Extra Hepatic Causes
Congenital hepatic fibrosis	Extra hepatic biliary atresia (EHBA)
Caroli's disease	Choledochal cyst
Progressive familial intra hepatic cholestasis	Stones
Alagile syndrome(bile duct paucity syndrome) • Triangular facies • Butterfly vertebrae • Pulmonary stenosis	Stricture
Dubin Johnson syndrome • Pigmented liver(Dark liver)	Mass
Rotor syndrome	

- Screening test for EHBA: HIDA Scan (or) hepatic scintigraphy
- Surgery for EHBA
  - KASAI Procedure [portoenterostomy]: favourable results if done < 8weeks of life
- EHBA is the MC indication for liver transplantation in children

Clinical Features of Neonatal Jaundice 00:31:08

- Icterus in neonates has a cephalocaudal progression
- Ways to detect neonatal jaundice
  - Clinical examination: Modified Krammer's rule
  - Transcutaneous bilirubinometer
    - → Advantages: Avoids blood sampling
    - → Disadvantage: Not very reliable in
    - a. 1st 24 hours of life
    - b. Gestational age <35 weeks
    - c. Baby on phototherapy
    - d. Bilirubin >12-14mg/dl
  - Serum bilirubin level

Modified Krammer's Rule



MODIFIED KARMMER'S RULE

	Lemon Yellow (mg/dl)	Orange Yellow (mg/dl)
Face	5-7	7-9
Chest and upper abdomen	7-9	9-11
Lower abdomen and thighs	9-11	11-14
Arm and legs	11-13	14-16
Palms and soles	13-15	>/=17

Neurological Manifestations 00:38:44

- Most Commonly involved part of brain in neonatal jaundice: Basal ganglia
- Type of cerebral palsy seen: Extra pyramidal type
- Kernicterus = Yellow staining of basal ganglia [previously used term]

Acute Bilirubin Encephalopathy

- **Early features [mild]**: hypotonia, poor feeding, loss of moro's reflex

↓

Fever, irritability, seizures

↓

- **Features of Advanced disease (severe)**: Hypertonia, Opisthotonic posturing, coma, death

Chronic Bilirubin Encephalopathy

- **Mnemonic: SADMUM**
  - S - Sensorineural hearing loss
  - A - Athetosis
  - D - Dental dysplasia dental enamel changes)
  - M - Mental retardation
  - U - Upward gaze limitation

Treatment of Neonatal Jaundice 00:55:08

I. Phototherapy

II. Exchange transfusion

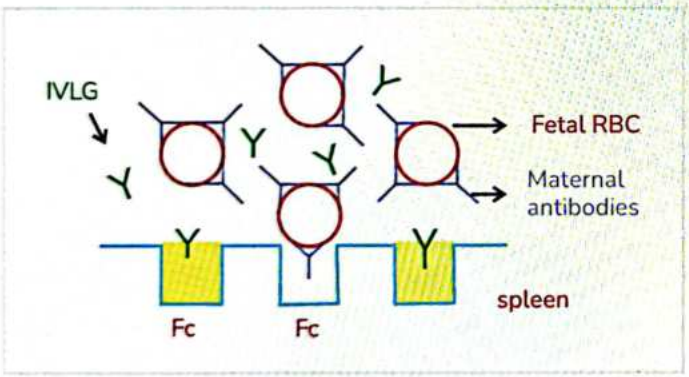
III. Drugs

Exchange Transfusion

- Used in very severe cases, especially Erythroblastosis Fetalis
- Double volume exchange transfusion done

Drugs

- IV Ig (Intravenous immunoglobulin)
  - Used in Erythroblastosis fetalis
- Occupies the receptors for FC segment of Ig in reticuloendothelial system & prevents further production of Ig



- Phenobarbitone
  - Severe Neonatal Jaundice Due to Erythroblastosis Fetalis Treatment Order:

Start Phototherapy
↓
Do exchange transfusion
↓
IVIg

Phototherapy 00:48:28

- **Most effective wavelength of light used**
  - 460-490 nm [Ghai 9 and AIIMS NICU protocol]
  - 420-470 nm [Nelson 20]
- **Mechanisms by Which Phototherapy Acts**

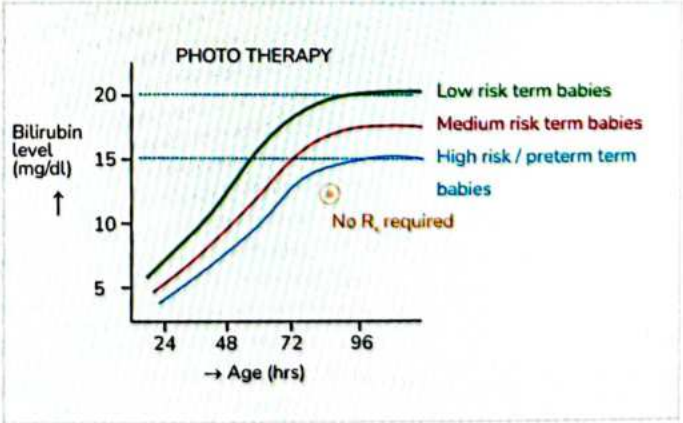
1. Photo Isomerisation
   - Bilirubin → Polar compound → excreted through kidney without conjugation
   - Slow & reversible

2. Structural Isomerisation
   - Bilirubin → Lumirubin → excreted through kidney without conjugation
   - Faster & irreversible
   - Most important mechanism by which phototherapy acts

3. Photo Oxidation [least important]
   - Irradiance should be at least 30 micro W/cm 2/nm
     → Measured using flux meter
   - Effectiveness of Phototherapy Depends Upon
     → Exposed surface area of baby
     → Distance b/w baby & phototherapy unit [30-45 cm]
     → Type of lamp used: LED lamps > CFL Lamps
   - Effectiveness does not depend on skin pigmentation of baby

Adverse Effects of Photo Therapy 00:57:00

- Bronze baby syndrome
- Dehydration
- Watery diarrhea
- Hypocalcemia
- Retinal toxicity
- Gonadal toxicity or mutations
- Impaired maternal child bonding



In Otherwise Healthy Term Neonates

Age	Phototherapy Cut off	Exchange Transfusion Cut off
24-48 hrs	>15 mg/dl	>20 mg/dl
48-72 hrs	>18 mg/dl	>25 mg/dl
>72 hrs	>20 mg/dl	>25 mg/dl

In Preterm Neonate

- Phototherapy cut off → 1% of birth weight in grams
- Exchange transfusion cut off → Phototherapy cutoff +5 [mg/dl]
  - E.g., birth weight = 1400 gm
  - Phototherapy cutoff = 1% of 1400 = 14 mg/dl
  - Exchange transfusion cutoff = 14+5 = 19 mg/dl
- Indications of exchange transfusion in a baby with RH incompatibility
  - Cord blood Bilirubin: > 5 mg/dl
  - Cord blood Hb: < 10 mg

Table 24.1

Breast feeding jaundice	Breast Milk Jaundice
• D/t inadequate Breastfeeding ↓ Dehydration ↓ Relative polycythemia ↓ Higher bilirubin level	• D/t substances present in breast milk like pregnanediol & free fatty acids, that interfere with the conjugation of bilirubin
• Rx: Frequent breastfeeding	• Rx: Continue breastfeeding. Breast feeding may be temporarily withheld if bilirubin >20mg/dl.

25 ERYTHROBLASTOSIS FETALIS

Erythroblastosis Fetalis: Aka 'Hemolytic Disease of Newborn' (HDN) 00:00:20

- Basic defect: Due to trans placental passage of maternal antibodies against paternally derived RBC antigens, which causes increased RBC destruction in the neonate/ Infant.
- ABO incompatibility is the MC cause of HDN, but it is usually a much milder illness, as compared to Rh incompatibility.

Erythroblastosis fetalis due to Rh incompatibility 00:04:33

- Rh: c, C, D, E, e
- RhD Ag is responsible for 90% cases of Rh incompatibility

Pathophysiology of HDN (Rh incompatibility) 00:06:03

1 st pregnancy

- Mother Rh –ve
- Father Rh + ve
- Fetus Rh + ve

↓

Fetal blood may enter maternal blood during delivery or abortion or intrauterine invasive procedure

↓

Ig M Ab against Rh antigen form in mother

Newborn remains safe (because IgM does not cross placenta Next exposure to even a smaller dose of Rh Ag will produce rise in anti Rh IgG

Mother Gets sensitised

Next/ subsequent pregnancies (In Rh incompatibility) 00:13:32

- Mother Rh –ve (already sensitised)
- Father Rh +ve
- Fetus is Rh +ve

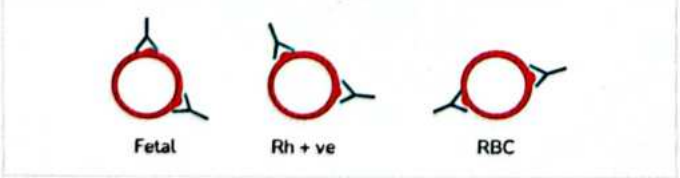
Repeat encounter with fetal RhD Ag

↓

Rapid production of anti Rh IgG Ab by mother

↓

Maternal anti Rh IgG crosses placenta & reaches fetus & binds to fetal RBCs

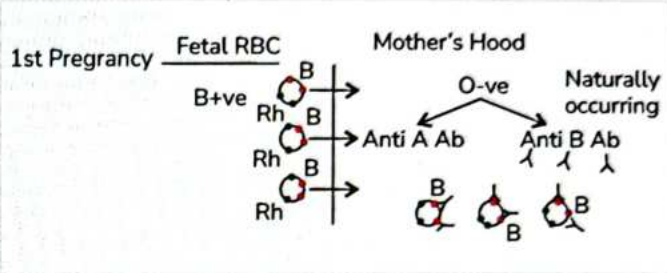


Are destroyed by RE system of fetus

↓

Hemolysis of fetal/ Neonatal RBCs (HDN)

- Severity of Rh incompatibility worsens with subsequent pregnancies due to repeated immune stimulation.
- If the mother & fetus are both ABO & Rh incompatible (Less severe) mother is partially protected against sensitization by RhD Ag due to rapid removal of fetal RBCs, by mother's pre-existing anti-A or Anti B IgM Ab.



- Injection of anti Rh Ig into Rh –ve mother both-during pregnancy & immediately after delivery of each Rh +ve baby, reduces the risk of HDN due to Rh incompatibility

Clinical features of HDN 00:27:27

- Varying severity based on
  - Immunogenicity of Blood Group Ag
  - Amount of blood transferred
  - Immune response of mother
- Mildest: only lab evidence of hemolysis
- Severe cases

Refer Table 25.1

Hydrops fetalis 00:34:15

- Presence of abnormally excessive fluid in 2 or more fetal compartments e.g. skin, pleural cavity, pericardium, peritoneal cavity, placenta, amniotic fluid.
- Immune: Mediated Hydrops in Erythroblastosis fetalis.
- In Severe HDN
  - Hypoglycemia: due to hypertrophy of pancreatic islet cells & hyperinsulinemia
  - Petechiae/ purpura: due to decreased platelet production & DIC
  - CNS damage: due to Kernicterus

Investigation Findings 00:37:59

- Maternal & Neonatal ABO & Rh blood grouping
- Direct coomb test (usually positive)
- Anemia (Hb & Hematocrit)
- ↑ Reticulocyte count
- PS → Polychromasia with ↑ nucleated RBCs
- ↑ed unconjugated bilirubin
- ↑ed LDH

During pregnancy (When mother Rh negative & father Rh positive)

- Fetal Rh status may be detected by
  - CVS
  - Amniocentesis or
  - Testing of fetal DNA in maternal circular (non-invasive)
- Severity of fetal anemia may be measured by
  - PUBS (Percutaneous Umbilical Blood Sampling) or
  - Doppler ultrasound of middle cerebral artery (MCA) of fetus

Etiology 00:46:00

- Immune Erythroblastosis fetalis (Rh incompatibility)
- Non-Immune
- **Mnemonic: ABCDEFGHIK**
  - A - Anemia: - α thalassemia
  - B - Bone ds: Osteogenesis Imperfecta, skeletal dysplasias
  - C - CNS- Encephalocele, Intracerebral Hemorrhage
  - C - Cardiac
  - Structural: HLHS, Endocardial cushion defect, Cardiomyopathies
  - Arrhythmias: Congenital Heart block, SVT, A. fibrillation
  - C - Chest / Thorax: Diaphragmatic hernia, mediastinal teratomas
  - C - Cancer/Tumors: Neuroblastoma, Hepatoblastoma, Sacrococcygeal Teratomas
  - D - Diseases of Lymphatic system: Cystic hygroma, lymphangiectasias
  - E - Errors of metabolism: Gaucher's disease, NPD, MPS
  - F - Flow related: Twin- Twin tx, Thrombosis of umbilical or renal vein
  - G - Genetic causes: Trisomy 13, 18, 21, Noonan syndrome.
  - H - Hepatic causes: congenital Hepatic fibrosis.
  - I - Infections: Toxoplasma, Syphilis, Rubella, CMV, Parvo, Leptospirosis
  - I - Infant of Diabetic mother
  - K - Kidney: Congenital Nephrosis

Table 25.1

Severe Hemolysis		
• Compensatory hyperplasia of erythropoietic tissue in fetus/ newborn • Massive Hepatosplenomegaly	If Hemolysis exceeds compensatory capacity of body ↓ Severe Anemia (Hb < 5-7 g/dl in fetus) ↓ • Pallor • Cardiac decompensation (cardiomegaly, respiratory distress) • Circulatory collapse • Anasarca(generalized edema) • Hypoalbuminemia due to hepatic dysfunction	• Jaundice usually within 1st 24 hrs of life

26 LATEST UPDATES IN NEONATOLOGY

Antenatal Corticosteroids 00:00:53

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

Golden hour 00:02:24

- 1st hour of life is called the golden hour.
- Interventions should include

1. Thermal protection
2. Establishment of FRC of lungs in least invasive manner
3. Avoiding hyperoxia by titrating O_2 administration.

Antenatal MgSO4 for neuroprotection 00:03:58

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

Effects

- Neuroprotection by
  - Anti-inflammatory effects
  - Vasodilation
  - Decreased free radical injury
  - Inhibiting ca2+ influx into cells

Coming in of Milk 00:06:00

- Feeling of breast fullness & milk leakage from nipples, as perceived by mother.
- 59-67 hours after delivery
- Earlier in multiparous
- If it occurs later than 72 hours: called as Delayed onset of lactation

Perinatal Asphyxia 00:07:38

- Most common cause of stillbirth
- Severity can be assessed by
  - Sarnat & Sarnat staging
  - Levine's classification
  - Thompson score
    - → Max (worst) score: 22
    - → Score ≥ 15 is suggestive of Abnormal outcome at 12 months of age with PPV of > 92%

PDA in Preterm Neonates 00:09:21

- Both Indomethacin & Ibuprofen are equally efficacious (70-80%) in preterm ≤ 32 weeks
  - Ibuprofen is preferred in view of better safety profile
- Oral PCM has been shown to be equally efficacious as Ibuprofen

Hypotension in 1st 24 Hours of Life 00:11:19

- Mean BP < 30 mm Hg
- Mean BP < Gestational age in weeks (mm Hg)

Hyperoxia Test 00:12:20

- Helps to determine whether heart disease is a likely cause in an infant with cyanosis
- Give 100% O2 for 10 min
  - ↓
  - PaO2 < 50mm Hg → Highly sensitive of Cyanotic CHD
  - PaO2 50-150mm Hg → needs further evaluation
  - PaO2 > 150 mm Hg or rise in PaO2 by > 80-120 mm Hg above base line → Cyanotic CHD is unlikely

Critical CHD 00:14:48

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

Feed Intolerance in Neonates 00:15:35

- Symptoms: Vomiting, Lethargy, apnea
- Signs
  - Abdomen distension / tenderness
  - Increased gastric residual (>2 ml/kg)
  - Reduced / absent bowel sounds
  - Bradycardia or cyanosis

NEC 00:17:04

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

Invasive Candidiasis in Neonates 00:17:48

- Incidence is inversely proportional to the Birth Weight
- Most common: C albicans

Intractable Seizures in Neonates are Seen in 00:18:34

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

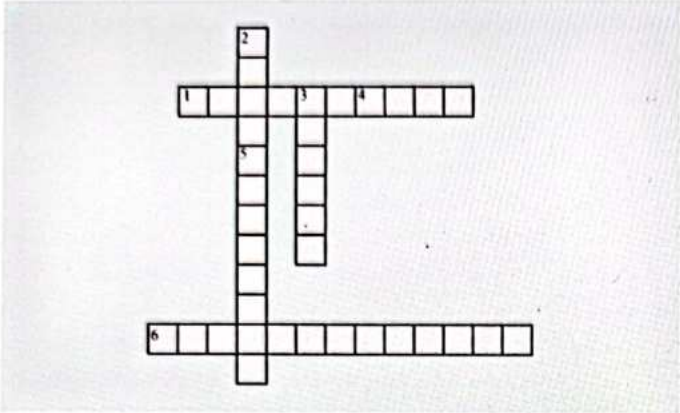
Umbilical Artery Catheterisation (UAC) 00:20:09

- Most common complication of UAC: Blanching of l leg
- Treatment of blanching

Rewarm the opposite leg with warm towel
↓
Reflex vasodilation
↓
Colour of opposite limb improves (If doesn't improve in 5 min, then remove UAC)

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. _____Score is used to assess gestational age in neonate.
4. _____is the most important component in surfactant
6. Steroid of choice in prevention of respiratory distress syndrome.

Down

2. Beckwidth – Wiedemann syndrome carries increased risk of _____tumor.
3. Hariequin ichthyrosis is associated with mutation in _____gene
5. Scoring system used to assess respiratory distress in preterm neonate.

27 BREAST MILK & BREAST FEEDING

Initiation of Breast Feeding 00:00:37

- As soon as possible
  (or)
  Within 1 hour of childbirth (born either by normal vaginal delivery or c-section)

Exclusive Breast Feeding 00:03:20

- Recommended for first 6 months of life exclusively. Child should be fed only breast milk, nothing else, not even sips of water unless medically indicated
- Any form of pre-lacteal feeding is absolutely contraindicated.
- One of the most important intervention to decrease neonatal and childhood mortality

What should be initiated at 6 months

- Complementary feeding
- It is defined as semi-solid, energy dense food, given in addition to breast feeding.

Characteristics of food items used for complementory feeding 00:06:15

- **Mnemonic: AFASS**
  - A - Acceptable
  - F - Feasible
  - A - Affordable
  - S - Sustainable
  - S - Safe

When is the breast milk output maximum 00:07:12

- At 5-6 months of lactation
- Approx. 730 ml/day

Factors affecting breast milk output 00:08:00

- **Milk output increased by**
  - Thought of baby
  - Sight of baby
  - Sound of baby
- **Milk output decreased by**
  - Pacifiers
  - Bottle feeding
  - Formula / top feeding
  - Lack of night time feeding
  - Incomplete emptying of breasts
  - Cracked /sore nipples
  - Drugs: Dopamine agonists: Bromocriptine, cabergoline

Storage of expressed breast milk (EBM) 00:11:26

- At room temperature (25 degree Celsius): 8-10 hrs
- In a refrigerator (2-8 degree Celsius): 24 hrs
- In a deep freezer (-20 degree Celsius) used in breast milk banks: 3 months

Reflexes Helping in Breast Feeding 00:12:44

- **Baby**

1. Rooting reflex
2. Suckling reflex

- **Mother**

1. Milk secretion reflex (mediated by prolactin)
2. Milk ejection reflex (mediated by oxytocin)

Signs of Good Positioning While Breast Feeding 00:15:25

1 Body of the baby should be well supported.
2 Entire body of the baby should be turned towards the mother.
3 Occiput, shoulders and buttocks of baby should be in a straight line.
4 Abdomen of baby should touch the abdomen of the mother.

Signs of Good Attachment While Breast Feeding 00:17:15

1 Mouth of the baby should be wide open.
2 Entire areola should be in baby's mouth except a small upper part that may be visible.
3 Lower lip of baby should be everted /turned out.
4 Chin of the baby should touch the mother's breast.

Contraindications to Breast Feeding 00:19:55

- Related to baby

1. Galactosemia
2. Lactose intolerance

- Related to mother
  - Absolute contraindications
    → Mother on chemotherapy or radiotherapy
  - Relative contraindications
    → Maternal HIV
    → Maternal active varicella zoster (HHV-3) involving nipple area
    → Maternal active herpes simplex involving nipple area
    → Maternal active untreated tuberculosis

→ Breast abscess

Maternal Medications contraindicated during lactation

00:24:26

- Antineoplastic agents
- Cyclosporine (immunomodulator)
- Lithium
- Certain antibiotics: Tetracycline, chloramphenicol
- Drugs decreasing breast milk production
  - Mnemonic: **A B C**
    - → A - Amphetamine
    - → B - Bromocriptine
    - → C – Cocaine

Important Information

- Pre-lacteal feeding is absolutely contraindicated due to the risk of clostridial sepsis.

Advantages of Breast Feeding for Baby 00:27:50

1. **Composition:** Composition of the breast milk is perfectly suitable for the baby.

i. **Carbohydrates**

- Breast milk is richer in lactose [7gm/dL] as compared to cow's milk [4.5 gm/dl]
- Breast milk (lactose) gives more energy as carbohydrates to baby.
- Galactose formed from lactose forms galactocerebrosides which are required for the central nervous system development.
- Lactose helps in calcium absorption.
- Lactose helps in development of lactobacilli in the intestine.

ii. **Proteins**

- Breast Milk contains lesser protein [1gm/dl] as compared to cow's milk [3.5 gm/dl] which poses lesser solute load on kidneys.
- Breast Milk is richer in whey proteins (lactalbumin) which are much more easily digestible as compared to casein in cow's milk.
- Breast Milk contains adequate amount of amino acids like cysteine, taurine, methionine which are required for CNS development of the baby.

iii. **Lipids**

- Breast Milk is richer in PUFA [poly unsaturated fatty acids] – beneficial for the baby
- Breast Milk contains 30 time more DHA (Docosahexaenoic acid) than cow's milk which is required for CNS development of the baby.

iv. **Minerals**

- Calcium: phosphate ratio in Breast Milk is such that it favors calcium absorption. [Cow's Milk is richer in phosphate which hinders calcium absorption so increasing the chances of hypocalcemia in the baby]
- Iron: present in Breast Milk is not in much quantity but is much more easily absorbable than the one present in cow's milk.

v. **Vitamins**

- Breast Milk contains adequate amounts of all vitamins except vitamin D, vitamin K & vitamin B12 [in strictly vegan mothers].
- All infants should receive 400 IU of vitamin D daily throughout the first year of life.
- All neonates should receive single dose of Vit K 1 mg dosage intramuscularly at birth to prevent hemorrhagic disease of newborn.

vi. **Water Content**

- Breast milk has 88% water approximately equal to cow's milk
- This water content is adequate to meet the demands of baby in 1st 6 months

2. **Breast milk contains certain substances that protect the baby against infection**

- Mnemonic: **(P L A B)2**
  - P - Phagocytic macrophages
  - P - PABA [para amino benzoic acid]
  - L - Lactoferrin
  - L - Lysozyme
  - A - Antibodies especially IgA
  - A - Anti-staphylococcal factor
  - B - Bifidus factor
  - B - Bile stimulated lipase

3. **Breast milk protects against diseases like**

- Neonatal period: NEC, neonatal sepsis
- Later in life: obesity, HTN, diabetes, allergies, asthma, dental caries
- Breast Milk fed babies have higher IQ.
- Breast milk helps in maternal and child bonding.

- Breast milk is safe, free from contamination, easily available even in resource limited settings.

Variations in the composition of breast milk 00:46:35

I. Depending on Time After Birth

A. Colostrum

- During the 1st 72 hours after the birth of the baby
- Thick, yellowish colored milk
- Produced in small quantity
- Rich in immunoglobulins, macrophages, proteins
- Known as 1st immunization of the baby
- Contains lesser lactose (so less sweeter) than normal breast milk

B. Transitional Milk

- During the next 2 weeks
- Composition is in between colostrum & mature milk

C. Mature Milk

- Thin & watery
- Richer in lactose (more sweeter) than colostrum
- Poorer in proteins

II. Depending on Gestational Age

- Preterm Breast milk richer in
  - Mnemonic: **S I P For Intelligent CNS**
    - → S - Sodium
    - → I - Immunoglobulins
    - → P - Proteins
    - → F - Fat
    - → I - Iron
    - → C - Calories
- But has lesser lactose.

III. Depending on Each Feeding Session

Fore Milk	Hind Milk
• At the beginning of a feed • More thin & watery • Satisfies mainly the thirst of the baby	• At the end of a feed • More thicker and calorie dense • Richer in fat • Satisfies the hunger of the baby

PREVIOUS YEAR QUESTIONS

Q. Breast feeding is contraindicated in (JIPMER Dec 2019)
A. MDR TB
B. Zika virus infection
C. Hep B Infection
D. Mastitis with abscess

Q. Amount of protein present in 100 ml of breast milk? (JIPMER May 2019)
A. 2.2 gm
B. 1.1 gm
C. 0.55 gm
D. 3.39 gm

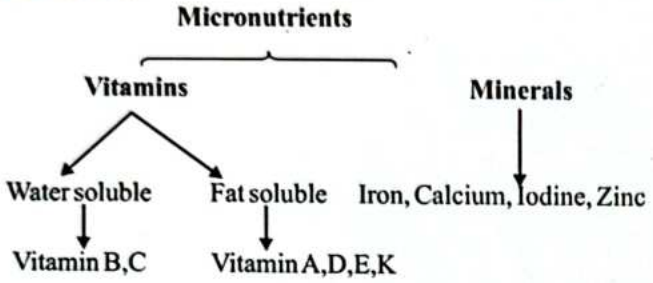
Q. Fat content of breast milk? (JIPMER Dec 2019)
A. 2.4%
B. 3.4%
C. 4.4%
D. 5.4%

28 MICRONUTRIENTS IN HEALTH AND DISEASE

What are micronutrients?

- There are the substances needed in miniscule amount but they are very important in facilitating the action of various enzymes and hormones in our body and required for proper growth, development and functioning of our body

Classification



Vitamin A

00:02:34

Normal function

- It ensures normal vision
- It plays an important role in
  - Cell and tissue differentiation
  - Embryonal and neonatal development
  - Reproduction

RDA (Recommended Dietary Allowance) of VIT A: (µg of Retinol equivalent)

- In Infancy: 400µg of Retinol equivalent/day
- In childhood: 600µg of Retinol equivalent/day
- In adolescence: 900µg of Retinol equivalent/day

Dietary sources of Vitamin A

- Plant sources
  - Carotenoids: Found in yellow, orange vegetables and fruits like carrots, pumpkin, green leafy vegetables like Spinach, broccoli
- Animal sources
  - Retinyl Palmitate: Fish oil, milk, meat

Clinical features of Vit A deficiency

- **Epithelial changes:** Dry, scaly hyperkeratotic patches on arms, shoulder, legs, and buttocks (Toad like skin)
  - Toad like skin can also be seen in essential fatty acid deficiency
- **Eye lesions:** WHO classification
  - Earliest symptom: Night blindness
  - Earliest sign: Conjunctival Xerosis (Drying of conjunctiva)

WHO classification of eye lesions due to Vitamin A deficiency (X-Xerophthalmia)

- XN: Night blindness
- X1A: Conjunctival Xerosis/Dryness
- X1B: Bitot's spot
  - Bitot's spot are the triangular spots on the sclera with base of the triangle near the cornea or towards the cornea
- X2: Corneal Xerosis
- X3: Corneal ulceration/Keratomalacia
  - X3A: Involvement of < 1/3rd of cornea
  - X3B: Involvement of > 1/3rd of cornea
- XS: Corneal Scars

Treatment of Vitamin deficiency

Age	Oral Vitamin A dose
< 6 months	50,000 IU
6 months-1 year	1,00,000 IU
>1 year	2 lac IU
Therapeutic dose	0 (at first contact), 24 hrs and 4 weeks later

Hypervitaminosis A

- It is due to excess intake of a single large dose or larger doses for several weeks
- It can present with features of pseudotumor cerebri i.e., there can be headache, vomiting, irritability, papilledema on fundus examination
- There can be desquamating itchy skin, hepatosplenomegaly
- In chronic cases X-ray shows: Hyperostosis involving long bones
- If vitamin A is taken during pregnancy, it can have teratogenic effects on fetus (still births, congenital malformations)

National Vitamin A Prophylaxis Program 00:11:39

- 9 mega doses of vitamin A starting at 9 months age with measles vaccine
- 1st dose: 9 months, dose – 1 lac IU
- 2nd dose: 18 months, dose – 2 lac IU
- Then it is given every 6 months upto the age of 5 years

Vitamin B-Complex 00:12:33

- Normal function: It works as coenzyme in important enzyme reaction involved in mechanism of carbohydrates, fats, and nucleic acid

- So, deficiency of Vitamin B complex can cause multiple manifestations

Vitamin	RDA	Dietary sources
Thiamine (B1)	0.4 mg/1000 kcal	Unpolished rice, oats, legumes, wheat, meat
Riboflavin (B2)	04-1.2mg/1000 kcal	Milk, green leafy vegetables, sprouts, legumes, meat
Niacin (B3)	6-8 mg/1000 kcal	Milk, green leafy vegetables, sprouts, legumes, meat
Pyridoxine (B6)	0.3-1 mg/day	Banana, wheat germ, rice, sunflower seeds
Cobalamin (B12)	0.3-0.5 mg	Milk, meat, eggs (not found in plant sources)
Folate	0.5-1 mg	Green leafy vegetables, citrus fruits, papaya
biotin	1-10 mg	Fruits, organ meats

Clinical features due to Vitamin B deficiency

Thiamine deficiency

- Predominantly, it is due to intake of polished rice, GI, or liver disease
- In thiamine deficiency: Beri-Beri
  - Wet Beri-Beri: There can be features of congestive cardiac failure like edema, respiratory distress
  - Dry Beri-Beri: Neurological features like irritability, weakness of lower limbs, DTRs (Deep tenson reflexes) may be diminished.

Niacin deficiency

- It gives rise to Pellagra
- Pellagra is a disease of 4D's
  1. Diarrhoea
  2. Dermatitis: Photosensitivity, rashes on sun exposed area like Casel's necklace (hyperpigmented rash in the neck area)
  3. Dementia (early onset)
  4. Death
- Pellagra like rash can be seen in metabolic disorders like Hartnup disease (impaired transport of neutral amino acid)

Pyridoxine deficiency

- Pyridoxine deficiency in neonatal or infantile period can lead to refractory seizures
- If a child is having refractory seizures which is not getting controlled despite giving multiple antiepileptics, think of pyridoxine deficiency and a trial dose of pyridoxine 100 mg can be given
- Older children can have peripheral neuropathy, anemia, or dermatitis
- Drugs can predispose to pyridoxine deficiency like Isoniazid

Riboflavin (Vit B2) deficiency

- Riboflavin deficiency can cause
  - Glossitis
  - Cheilosis: Inflammation of lips
  - Angular stomatitis: Painful lesions near the angle of the mouth
  - Seborrheic dermatitis along the nasolabial folds
  - Photophobia

Cobalamin deficiency

- Haematological manifestation: Megaloblastic anemia
- Neurological manifestation: Subacute combined degeneration of spinal cord

Folate deficiency

- It can give rise to
  - Megaloblastic anemia
  - Growth restriction
  - Glossitis
- Folate deficiency during pregnancy can give rise to neural tube defects in baby like myelocoele, meningomyelocele

Biotin deficiency

- Biotin deficiency can cause
  - Alopecia
  - Skin rashes like periorificial scaly dermatitis
  - Conjunctivitis
  - Glossitis
  - Anorexia, vomiting
  - Neurological manifestations: Developmental delay or seizures

Vitamin C (Ascorbic Acid) 00:22:18

Normal function

- It helps in the formation of collagen
- It is required for the maintenance of
  - Normal connective tissue & wound healing
  - Bone formation or osteoid formation
- It helps in Iron absorption from gut by reducing the ferrous to ferric state

RDA of vitamin C

- In infants: 30-40 mg/day
- In children: 40-70 mg/day

Dietary sources of Vitamin C

- Citrus fruits like orange, lime
- Vegetables like cauliflower, cabbage, cucumber, spinach

- Breast milk contains adequate Vitamin C for the baby so there are lesser chances of breast fed babies to develop scurvy but cow milk is poor in Vitamin C, so babies fed with cow milk have more chances of developing scurvy
- Deficiency of Vitamin C causes: Scurvy
- Collagen is backbone of blood vessels, in scurvy due to improper collagen synthesis, blood vessels become fragile resulting in bleeding everywhere like
  - Gum bleeding
  - Subperiosteal hemorrhage of long bones cause painful pseudo paralysis of lower limbs so there is crying on touching
  - Scorbutic rosary i.e., prominence of the costochondral junction which is sharper, tender, and angulated as compared to rachitic rosary

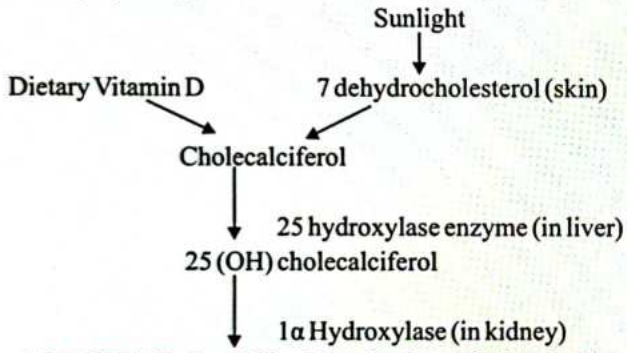
Treatment

- Vitamin C supplementation 100-200 mg daily is required

Vitamin D

00:26:40

Normal physiology



- Vitamin D deficiency can be due to
  - Deficient diet
  - Deficient sunlight exposure
  - Due to liver problem
  - Due to some kidney problem
  - There can be resistance at the level of receptors also

1,25, $(OH)_2$Cholecalciferol (Calcitriol)
↓
Vitamin D receptors

- Vitamin D receptors in
  - Intestine: Cause increase Ca and phosphate absorption
  - Parathyroid gland: Supress parathormone level
  - Bones: Upregulates Osteocalcin, Osteopentin
  - It also activates Rank 1 ligand which leads to increased osteoclast activity which further causes increased bone turn over
- All these helps in increasing the Ca and phosphate level in the blood
- Resistance at the level of Vitamin D receptors can cause VDDR Type II (Vitamin D Dependent Rickets Type II)

RDA of Vitamin D

- In infants: 400 IU
- In older children: 600 IU
- It is now recommended that all babies must be given Vitamin D supplementation 400IU/day throughout infancy or 1st year of life
- Vitamin D level in breast milk: 40 IU/L but Recommended Dietary Allowance is 400 IU so it is important to supplement Vitamin D in infancy

Sources of Vitamin D

- Exposure to sunlight
- Non vegetarian sources: Fish oil, egg yolk
- Vitamin fortified milk, cereals, bread etc
- Vitamin D deficiency causes Rickets

Hypervitaminosis D

00:33:14

- Children with rickets have deformities even if biochemic part is corrected by supplementing Vitamin D, the deformities take a long time to recover so parents may get impatient and visit several physicians and multiple times Vitamin D mega doses are prescribed so children can end up with Hypervitaminosis D
- Hypervitaminosis D is going to present with Hypercalcemia (Excess blood calcium level > 11mg/dl)
- CNS manifestation: Confusion, Psychosis, Coma, Seizures
- Cardiac manifestations: Hypertension and arrythmias
- GI manifestations: Constipation, pain abdomen
- Renal manifestations: Impaired renal concentrating mechanism causing polyuria & dehydration
  - Excess calcium can be deposited in the renal parenchyma giving rise to Nephrocalcinosis and Nephrolithiasis

Treatment of Hypervitaminosis D

- Fluid therapy/hydration
- Forced diuresis by Furosemide
- Bisphosphonates (Also used in osteogenesis imperfecta)
- Calcitonin: It will bring down the level of calcium
- Steroids

Vitamin E

00:35:35

Function: It acts as an antioxidant

RDA

- It is required more in preterm babies
  - In preterm neonates: 5-10 IU/kg/day
  - Term neonates: 0.5 IU/kg/day
  - Children: 5-10 IU/day
  - 1 mg Tocopherol = 1.5 IU

Dietary sources
- Vegetable oil, seeds, nuts, green leafy vegetables

Causes of Vitamin E deficiency
- Prematurity
- Severe malnutrition
- Fat malabsorption seen in conditions like cystic fibrosis or cholestatic liver disease

Clinical features of Vitamin E deficiency
- Cerebellar disease
- Posterior column dysfunction
  - Both Cerebellar disease and Posterior column dysfunction can lead to loss of deep tendon reflexes followed by ataxia
- Retinal disease

Treatment of Vitamin E deficiency
- Vitamin E supplementation

Vitamin K
00:38:24

Normal function
- It has a very important role in coagulation cascade because it acts as a cofactor for enzyme Gamma Glutamyl Carboxylase which performs the post translational carboxylation of coagulation factors II, VII, IX, X required by the coagulation pathway to function properly

Sources
- Vitamin K_1 (Phytonadione): Usually present in plant sources like vegetable oils, nuts, seeds, green leafy vegetables etc
- Vitamin K_2 (Menaquinone): Mainly synthesized by the intestinal bacteria

RDA
- In new born: 3-5 µg/day
- In older children: 10-30 µg/day
- Dose of Vitamin K at birth: 1 mg intramuscularly to all babies as it is a fat soluble vitamin it stays in body for long time

Vitamin K deficiency
- In neonates: Haemorrhagic disease of new born (now known as Vitamin K deficiency bleeding)
- In older children: Bruising or mucocutaneous bleeding
- Investigations: Both PT and aPTT are prolonged
  - In milder cases, PT and aPTT may not be prolonged only PIVKA (Proteins induced in Vitamin K absence) levels are elevated

Treatment of Vitamin K deficiency
- In neonates: 1 mg Vit K injection IM
- In older children: 2.5-5 mg
- Prothrombin time should start decreasing within 6 hrs of Vitamin K Inj. and should be normalised by 24 hrs
- For severe life threatening bleeding: Give fresh frozen plasma (replenish coagulation factors levels immediately)
- Vitamin K toxicity in preterm neonates: Can precipitate neonatal jaundice and kernicterus

Iron
00:44:54

Dietary sources

- Vegetarian sources: Spinach, beans, broccoli, nuts, jaggery, raisins, lentils, soyabean, tofu
- Animal sources: Meat, seafood, eggs
- If dietary sources are not available, cooking food in iron utensils can increase the iron content of the food

RDA
- 1-9 yrs.: 6-11 mg/day
- Adolescents: 11-19 mg/day
- Requirement is more in females than males due to menstrual losses
- Deficiency: Iron deficiency anemia (IDA)
- IDA is one of the most common nutritional disorders especially in developing countries like India

Aetiology of Iron deficiency anemia
- It can be due to dietary Iron deficiency
  - Inadequate intake
- Impaired absorption
- Cases of Celiac disease
- Increased Iron losses due to worm infestation like hookworm infestation, Schistosomiasis, Inflammatory Bowel Disease, GI bleeds.
- Increased requirement during infancy and puberty

Clinical features of Iron deficiency anemia
- **Symptoms**
  - Pallor
  - Essy fatigue
  - Generalised weakness
  - Poor appetite
  - Lethargy
  - Irritability
- **Signs**
  - Pallor: It can be demonstrated on lower palpebral conjunctiva, Palms of the child (Palmar creases become less prominent and they are almost not visible if the Hb level is < 7 gm/dl), nail beds, general skin surface, dorsum of tongue

Treatment of Iron deficiency anemia
- Iron supplementation: 3-6mg/kg/day for minimum of 3 months

- It can be given in the form of Iron tablets, syrups
- In refractory cases where GI tolerance is very poor, injectables can be given
- Advise Iron rich diet to be taken

Response to treatment in Iron deficiency anemia

- Within 24 hrs: Improvement in general condition i.e., decreased irritability, improved appetite
- By 48-72 hrs: Reticulocytosis appears which peaks at 5-7 days
- By 4-30 days: There is increase in Hb level
- 1-3months: For the replenishment of stores

Calcium

00:51:00

It plays role in

- Coagulation cascade
- Nerve conduction
- Muscle function
- Hormone action (Ca is a second messenger)

Dietary sources

- Milk and milk products like yoghurt, cheese
- Nuts, legumes, spinach, cabbage, broccoli
- Fortified food items

RDA of calcium

- In infants: 250 mg/day
- 1-10 years: 500 mg/day
- Pubertal growth spurt (adolescents): 1000 mg/day

Deficiency of Calcium leads to

- Rickets
- Increased irritability
- Seizures
- In neonates: Apnea, poor feeding, jitteriness
- Older children: Numbness, tingling of limbs and tetany

Treatment of hypocalcemia

- Acute: Inj. Ca gluconate
- Chronic: Oral calcium supplements

Zinc

00:55:13

Normal function

- It helps in > 200 enzymatic reactions
- As a component of Zinc finger protein, it regulates gene transcription, participates in nucleic acid metabolism, protein synthesis and cell growth
- As a part of superoxide dismutase, it also has antioxidant action

Dietary sources

- Mainly animal sources like meat
- Vegetarian sources: Nuts
- Dietary phytates decrease the bioavailability of zinc

RDA (Recommended Daily Allowance):

- In normal children: 3.5-5 mg/day
- In malnourished children: 2-4 mg/kg/day

Causes of Zinc deficiency

- Increased requirements e.g., in Infancy and adolescence
- Malnutrition
- Malabsorption
- Recurrent or chronic diarrhoea
- Prolonged Total parenteral nutrition (TPN) or IV fluids

Clinical features of Zinc deficiency

- Acrodermatitis Enteropathica
- Poor physical growth
- Alopecia
- Anemia
- Diarrhoea
- Impaired wound healing
- Impaired immune function
- Delayed sexual maturation and hypogonadism in adolescence

Acrodermatitis Enteropathica

- It is an autosomal recessive disorder due to defect in SLC39A4 gene which leads to impaired zinc absorption in intestine
- **It can present in early infancy with**
  - Various types of skin lesions which can be vesiculobullous , dry scaly or erythematous around the orifices and in acral region
  - Alopecia
  - Eye changes like conjunctivitis, blepharospasm/blepharitis, and photophobia
  - Diarrhoea
  - Anemia
  - Poor growth

Treatment of Zinc deficiency

- Zinc supplementation
  - In inherited deficiency like Acrodermatitis Enteropathica: 3 mg/kg/day (lifelong)
  - In acquired cases: 0.5-1 mg/kg/day (till the cause is taken care of)

Iodine

01:03:44

Normal function

- It is essential for the formation of thyroid hormones required for the growth and development including bone development and skeletal maturation especially in fetus and in first 3 years of life

Dietary sources of Iodine

- Sea foods/plants
- Uncooked Iodised salt
- Dairy products like milk, yoghurt, and cheese
- Figs, almond, sesame seeds

Important Information

- RDA of Iodine
  - Birth to 5 years age: 90 µg/day
  - 6-12 years: 120 µg/day
  - Adolescents and adults: 150 µg/day

Features of Iodine deficiency

- Fetal life: Still births, congenital abnormalities, Increased perinatal mortality
- In neonates and infants: Hypothyroidism and goitre
- In older children: Goitre, growth restriction, short stature, impaired mental function, and other features of hypothyroidism like constipation, obesity etc.

Prevention of Iodine deficiency

- Previously it was known as National Goitre Control Program and now it is renamed as National Iodine Deficiency Disorders Control Program
- Under this program, universal Iodisation of salt is recommended
- Target Iodine content of salt recommended: 30 ppm at manufacturing level and 15 ppm at distribution level

29 MALNUTRITION

- **Mal:** Abnormal, **Nutrition**: Intake of food
- Best indicator of Acute Malnutrition: ↓ in weight for height (Wasting)
- Best indicator of Chronic Malnutrition: ↓ in Height for age (Stunting)
- Cardinal determinants of undernutrition
  1. Low birth weight (LBW)
  2. Infections
  3. Less dietary intake (food)

Age Independent Anthropometric Indices 00:05:30

Refer Table 29.1

Important Information

- Mild arm circumference is age independent parameter in age group of 1-5 year

Classification of Malnutrition 00:10:52

I. IAP Classification: Based on weight for age and edema

- Normal is weight for age >80% of expected
- Grades

I	71-80% of expected
II	61-70% of expected
III	51-60% of expected
IV	≤50% of expected

- Add 'K' to the category if edema is present
- E.g., wt. for age = 55% with edema so grade is III K

II. Gomez Classification: Based on weight for age

- Expected weight = 50th percentile of Harvard standard
- It is the oldest classification.
- It has prognostic value for hospitalized children.
- Normal - weight for age >90% of expected
- Grades

I. (Mild): 75-89% of expected
ii. (Moderate): 60-74% of expected
iii. (Severe): < 60% of expected

III. WHO Classification: Based on weight for height, height for age & edema

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

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

IV. Waterlow classification: based on weight for height, height for age

V. Welcome Trust Classification

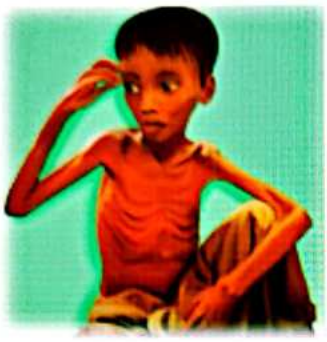
princeeeekum@gmail.com
9928609733

- Based on weight for age & edema

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

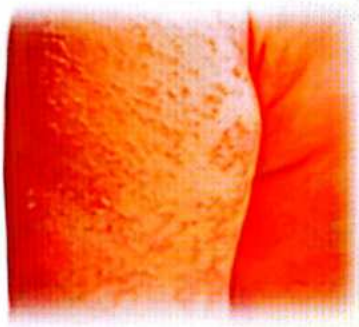
Kwashiorkor v/s Marasmus 00:24:38

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



Severe Malnutrition

- **Skin Changes:** Flaky paint dermatosis (or) crazy permanent dermatosis



- **Hair Changes**
  - Flag sign: alternate bands of hyperpigmented and hypopigmented hair
  - Easy pluckability
  - Sparse hair
- **Flag sign**

Severe Acute Malnutrition (SAM) 00:29:20

Definition: In a child b/w 6 months to 5 yrs age, as presence of any 1 or more of the following

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

Complications 00:32:02

- **Mnemonic: SHIELDED**
  - S - Sugar deficiency (hypoglycemia) – Blood Glucose <54 mg/dl
  - H – Hypothermia – rectal temperature < 35.5 degree C
  - I – Infections
  - EL – Electrolyte imbalance especially Hypokalemia
  - DE - Dehydration
  - D – Deficiency of micronutrients

Management for SAM 00:36:52

1. **Initial Hospitalization especially with poor appetite or complications**
2. **Look for Complications & treat**

- Hypoglycemia
  - Asymptomatic: 50 ml of 10% dextrose orally or by NG tube
  - Symptomatic: 5 ml/kg of 10% dextrose IV
- Hypothermia
  - Remove wet clothing
  - Cover appropriately
  - Heating device can be used
- Infections: Antibiotics (oral/iv)
- Electrolyte imbalance: Supplement K+, Mg+2
- Dehydration
  - oral: Re So Mal (rehydration solution for malnourished child)
  - iv fluids (if child is in shock)
- Deficiency of micronutrients – supplement multivitamins & minerals, Fe started later

3. **Nutritional Rehabilitation**

- Start with:

70 – 80 Kcal/ kg/ day & 0.7 g/ kg/ day proteins

↓ Gradually over 1-2 week [to prevent refeeding / nutritional recovery syndrome]

(Upto 150 – 200 kcal/ kg day) (4 – 5/ kg/ day proteins)

Initially	Kcal(each 100 ml)	Protein (each 100 ml)
Initially F-75 diet started:	75	1 gm
Later F-100 (catch up diet)	100	3 gm

RUTF (ready to use therapeutic food)

- Energy dense, semisolid, minerals and vitamins rich food
- Peanut paste, milk solids, sugar, vegetable oils with added minerals and vitamins.
- 100 gm of RUTF has 543 kcal of energy and 15 gm protein

Criteria for Discharge from Hospital

- Child should have lost edema & started gaining weight
- All infections & micro nutrient deficiencies should have been taken care of
- Child's appetite should have improved & he should be accepting well orally

- Mother /caregiver should be confident of taking care of child at home

Failure to respond to treatment

- **Primary failure**
  - Failure to regain appetite by D4
  - Failure to start losing edema by D4
  - Presence of edema on D10.
  - Failure to gain at least 5 gm/kg/day by D10.
- **Secondary failure**
  - Failure to gain at least 5 gm/kg/day for 3 consecutive days during rehabilitation phase.

Poshan Abhiyan 00:53:04

- Prime minister's overarching scheme for holistic nutrition.
- Launched in march 2018.
- Proper nutrition ensured to baby in 1st 1000 days of life.
- Goal
  - Decrease prevalence of stunting and undernutrition by 2% per annum
  - Decrease nutritional anemia by 3% per annum.

Table 29.1

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

PREVIOUS YEAR QUESTIONS

Q. Which of the following if normal rules out PEM? (NEET Jan 2020)
A. Skin fold thickness
B. ECF fluid
C. Lean body mass
D. Serum potassium

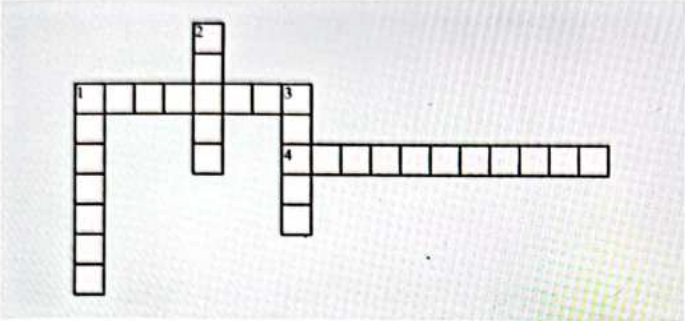
Q. An anganwadi teacher takes weight and height of 4-year-old child and find out that height for age is < - 2 SD, likely cause is?
A. Chronic malnutrition
B. Acute malnutrition
C. Recent infection
D. No malnutrition

Q. Severe acute malnutrition as per WHO criteria? (NEET Jan 2019)
A. Weight for age - 2 SD less than median
B. Weight for height – 2 SD less than median
C. Weight for age – 3 SD less than median
D. Weight for height – 3 SD less than median

Q. All are diagnostic criteria for 'severe acute malnutrition' (SAM) except? (JIPMER Nov 2018)
A. Weight for age < - 3 Z score
B. Mid upper arm circumference (MUAC) < 115 mm
C. Presence of bipedal edema
D. Presence of visible severe wasting

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. Both indicator of chronic malnutrition
4. Vit K2 is also known as

Down

1. _____tape is used to measure mid – arm circumference
2. Spots counted by Vit. A deficiency
3. _____classification is based on weight for age.

30 BODY COMPOSITION & ACID BASE BALANCE

Body Composition

Total Body Water [TBW]

00:00:31

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

Important Information

- After puberty, males have slightly more total body water than females.
- Preterm neonates have higher TBW than the term neonates.

- TBW is divided into
  1. ECF volume
  2. ICF volume i.e. TBW = ECF + ICF

ECF & ICF Volumes

- In fetus & newborn, ECF > ICF volume
- After birth ECF decreases and ICF increases.
- At around 1 year of age, ECF and ICF approach adult values.

Osmolality

00:04:28

- It is defined as concentration of the solute per unit weight of the solvent. It is expressed as mosm/kg.
- Normal plasma osmolality = 285-295 mosm/kg
- Normal urine osmolality = upto 1200-1400 mosm/kg (reached at or beyond 1 year of age)

Important Information

- Calculation of plasma osmolality = 2[sodium] + glucose/18 + BUN/2.8

Cases

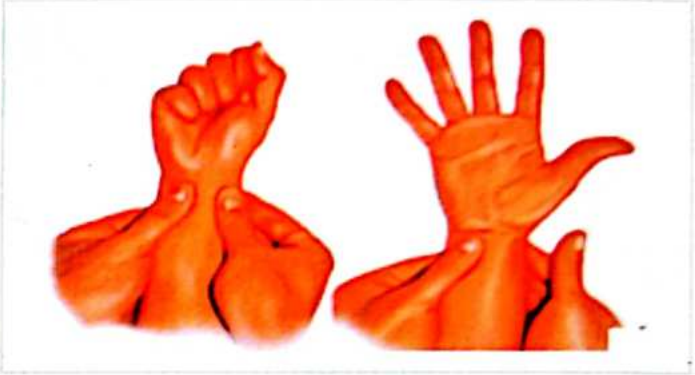
00:07:10

Plasma osmolality	Urine osmolality	Diagnosis
1. Increased	Increased	Dehydration/water deprivation
2. Decreased	Increased	SIADH
3. Increased	Decreased	DI

Disorders of Acid Base Balance

00:10:00

- Detected through ABG analysis (arterial blood gas)
- Ideal site: Radial artery



- Before hand Modified Allen's Test is done to assess patency of palmar arch
- Blood is drawn using 1 ml/2 ml syringe.
- ABG sample is processed as soon possible after its collection.

Normal Values

- pH = 7.35 - 7.45
- Pco2 = 35 - 45 mmHg
- pO2 = 80 – 100 mmHg
- HCO3 = 22 – 28 meq/L

1. Acidosis

00:12:54

- It is pH < 7.35
- Causes
  - Metabolic: due to excess HCO_3^- loss or H^+ retention
  - Respiratory: due to CO_2 retention

A. Metabolic Acidosis in Children

00:14:05

- pH < 7.35 due to primary decrease in HCO_3^-
- It is corrected by Respiratory compensation (Acidotic breathing) which begins within minutes and is maximum by 12-24 hrs.

- Expected pCo_2 in metabolic acidosis = $(1.5 \times HCO_3^-) + 8 \pm 2$
- Example: In a pt of metabolic acidosis, the HCO_3^- levels are 10 meq/L. Calculate the expected Pco2.
  Solution: 1.5 x 10 + 8 +/-2
  = 15 + 8 +/-2
  = 23 +/-2
  = 21 – 25 mmHg
- Important causes of metabolic acidosis in children
  - High anion gap metabolic acidosis
  - Normal anion gap metabolic acidosis

Important Information

- ANION GAP(AG) = Na - (HCO3 + Cl)
- Normal AG = 8-12meq/L

Metabolic Acidosis with Normal Anion Gap

- **Mnemonic: PURDA**
  - P - Post hypocapnia
  - U - Urinary tract diversions
  - R - Renal tubular acidosis
  - D - Diarrhea - most common cause
  - A - Ammonium chloride ingestion

Metabolic Acidosis with increased anion gap

- **Mnemonic: KaLaM TIP**
  - K - Keto acidosis, Kidney failure
  - L - Lactic acidosis, Liver failure
  - M - Malignancy, Medications (Metformin)
  - T - Tissue hypoxia (shock)
  - I - Inborn errors of metabolism
  - P - Poisoning by Ethylene glycol

B. Respiratory Acidosis

00:21:49

- pH <7.35 primarily due to CO_2 retention
- It occurs due to respiratory compromise leading to CO_2 retention due to
  - Decrease in central respiratory drive
  - Paralysis of respiratory muscles (intercostal muscles and diaphragm)
  - Lung parenchymal/airway disease
  - Progressive neuromuscular disease
  - Scoliosis (restrictive lung disease)
- Compensation is by metabolic alkalosis i.e. kidneys compensate by increasing HCO_3 retention/resorption which begins in 6-12 hours and is maximum by 3-5 days. HCO_3 is resorbed and H ions lost as NH4 ions from the body.
- For every 10 mmHg increase in PCO_2, there is 4meq/L rise in HCO_3.
- Treatment of respiratory acidosis is assisted ventilation (NIV/IMV)

Metabolic Alkalosis in Children

00:27:55

- pH >7.45 due to primary increase in HCO_3
- MC causes
  - Vomiting (HCL loss, Relative rise in HCO_3)
  - Diuretics use.
- Types

i. **Chloride Responsive metabolic alkalosis**
  - Urinary chloride < 15 meq/L
  - Decrease in ECF volume
  - It responds to volume repletion by normal saline.
  - **Etiology:** (Cl or fluid loss from Gut/kidney/skin)
    - → Gut losses: vomiting /continuous NG drainage/congenital chloride diarrhoea
    - → Sweat losses: Cystic fibrosis
    - → Kidney losses: Loop diuretics (furosemide) /Thiazides

ii. **Chloride Resistant Metabolic Alkalosis**
  - Urinary chloride >20 meq/L
  - Non responsive to volume repletion by normal saline.

Normal BP	High BP
• Barter syndrome • Gitelman syndrome	• **Mnemonic: CLGADA** o C - Congenital adrenal hyperplasia (11 beta hydroxylase/17 alpha hydroxylase deficiency) o L - Liddle syndrome o G - GRA (Glucocorticoid remediable Aldosteronism) o A - AME (Apparent mineralocorticoid excess) o D - Disorders of sexual development o A - Adrenal Adenoma/ carcinoma

Liddle Syndrome

00:34:17

- Autosomal dominant condition
- Due to an activating mutation of Na channel in distal nephron
- These Na channels remain continuously open
- Leading to sodium retention and thus hypertension

Glucocorticoid Remediable Aldosteronism [GRA]

00:35:14

- Autosomal dominant condition
- Aldosterone synthase gene becomes regulated by ACTH.
- **Treatment:** Glucocorticoids → Inhibits ACTH production by pituitary → decreased aldosterone production so hypertension decreases.

Apparent Mineralocorticoid Excess (AME)

00:37:10

- Due to deficiency of 11 Beta hydroxysteroid dehydrogenase enzyme

↑↑ Cortisol —✕→ ↓↓cortisone (in kidney)

- Cortisol Has mineralocorticoid activity which leads to hypertension

B. Respiratory alkalosis

00:38:46

- Primarily due to CO2 washout leading to hyperventilation

Causes

- High fever
- Sepsis
- Bronchial asthma
- CNS disorders
- Overventilated of intubated child

- Compensation is metabolic acidosis which begins in few hours but takes few days to establish.
- Clinical features are those of the underlying disease.
- Alkalosis promotes binding of calcium to albumin leading to decreased fraction of ionized calcium in blood.
- So, the child can present with features of hypocalcemia i.e. tingling, paranesthesia's, tetany, seizures, palpitations.

31 DISORDERS OF SODIUM AND POTASSIUM

Disorders of sodium

00:00:05

- **Hypernatremia:** Serum sodium level > 145 meq/L
- **Hyponatremia:** Serum sodium level < 135 meq/L
- **Pseudohyponatremia:** No actual hyponatremia but low sodium values in reports due to other factors

Hypernatremia

Definition

- Serum sodium level > 145 meq/L

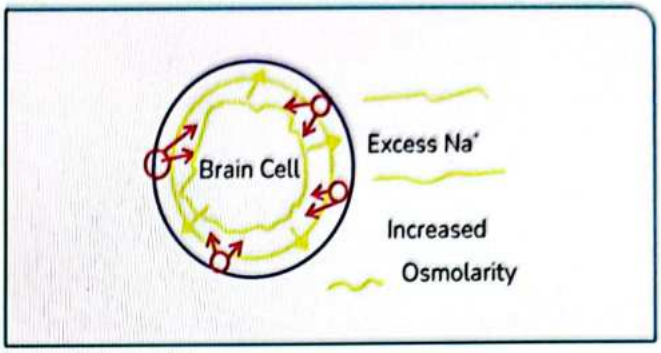
Etiology

Excess sodium intake	Water deficit	Sodium and water loss (Water loss > Sodium loss)
• Salt-rich diet • IV 3% NaCl (Hypertonic saline) • Sodium bicarbonate (Oral or Iv) • Hyperaldosteronism: More and more sodium retention in body	• Diabetes Insipidus (Central or nephrogenic) • Increased insensible loses • Inadequate fluid intake	• GI losses: Vomiting or diarrhoea • Cutaneous losses: Burns involving large body surface area • Renal losses: Polyuric phase of Acute Tubular Ne crosis • Osmotic diuresis: Free water loss

- Hyponatremia can predispose to seizures

Important Information

- Most devastating consequences of hypernatremia in children
  - Due to excess sodium in interstitial fluid, the fluid will come out from brain cells
  - Brain cells gets shrunken and become smaller
  - As a result, sheer force will be exerted on these blood vessels which will then be pulled apart from layers of covering outside the brain leading to brain hemorrhage
  - Brain hemorrhage: Subarachnoid bleed, Dural bleed or parenchymal hemorrhage



Hyponatremia

00:05:50

Definition

- Serum sodium level < 135 meq/L

Classification

- Depending upon blood circulation/fluid volume in body
  - Hypovolemic
  - Euvolemic
  - Hypervolemic

Etiology

Refer Table 31.1

SIADH (Syndrome of inappropriate ADH)

Pathophysiology

- Because of effect of ADH, there will be less or no diuresis

So, lesser urine is produced

↓

More concentrated urine (Urine sodium and urine osmolality are high)

↓

Lesser urine produced, more water is retained in body

↓

Serum sodium & serum osmolality is low, BP – normal

Diagnostic criteria of SIADH

Presence of	Absence of
• Serum sodium level: < 135 meq/L • Serum osmolality: < 280mOsm/kg (Normal-290mOsm/kg) • Urine sodium: > 30meq/L • Urine osmolality: > 100mOsm/kg • Correction with water restriction	• Renal/thyroid/adrenal insufficiency • Cirrhosis/nephrotic syndrome/heart failure • Dehydration • Diuretic ingestion

Treatment
- Water restriction
- Treatment of underlying cause
- Newer drugs: Tolvaptan

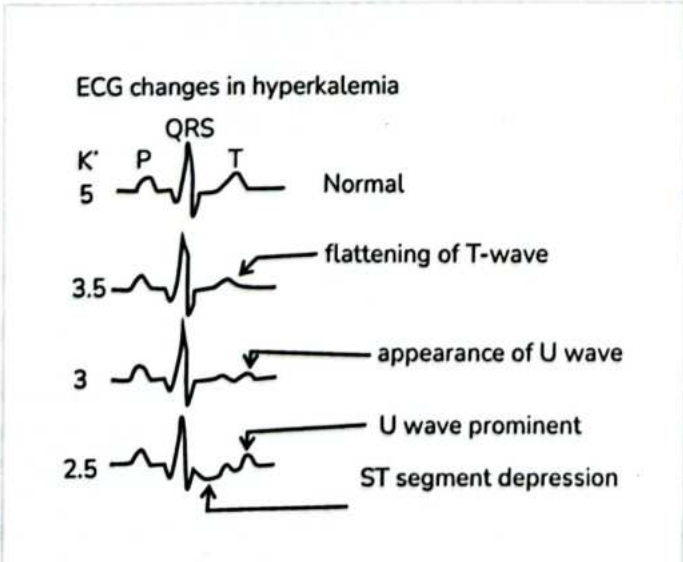
Pseudohyponatremia
- Falsely low sodium values seen in
  - Hyperglycemia
  - History of mannitol or sucrose intake
  - Diabetic ketoacidosis (DKA)

Disorders of Potassium
00:13:16
- Normal serum potassium level: 3.5-5.5 meq/L
- Hypokalemia (low serum potassium level): < 3.5 meq/L
- Hyperkalemia (high serum potassium level): > 5.5 meq/L

Hypokalemia
Etiology
- Increase potassium losses from body: Diarrhoea
- Malnutrition (low muscle mass, low potassium level, low total body potassium)
- Renal losses: RTA (Renal Tubular Acidosis)
- Endocrine conditions: Cushing syndrome, Hyperaldosteronism (sodium is absorbed and potassium is secreted)
- Movement of potassium into intracellular compartment e.g., Alkalosis

Clinical features
- Hypotonia
- Muscle weakness (Potassium level: < 2.5 meq/L)
- Constipation (Impaired gut movement) - Paralytic ileus
- Association with polyuria & polydipsia (in case of Renal Tubular Acidosis)

ECG changes



Treatment of hypokalemia
- Supplement K^+
  - Orally: Pot Klor, fruit juices, coconut water
  - IV supplementation: Serum potassium level < 2.5 meq/L
    → ECG changes
    → Unable to take orally

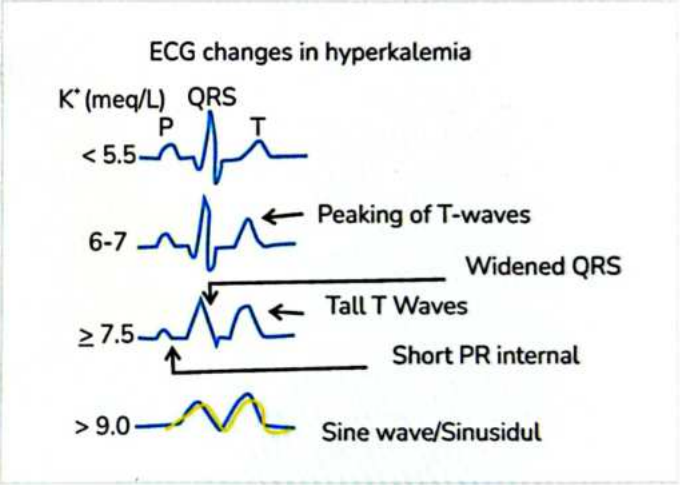
Important Information
- Maximum K^+ concentration that can be given via peripheral vascular access: 40 meq/L

Hyperkalemia
00:19:05
- Serum K^+ value: > 5.5 meq/L

Etiology

Refer Table 31.2

- **ECG changes**



Treatment of hyperkalemia
- **Mild (K^+ level: 5.5 – 6/6.5 meq/L)**
  - Stop K^+ in IV fluids
  - Stop any offending drug (causing renal injury and hyperkalemia)
  - Add salbutamol nebulisation
- **Moderate to severe cases**
  - Give Inj. Calcium gluconate: Stabilise membrane and prevent arrythmias
  - Inj. Sodium bicarbonate: Reduce K^+ level by moving potassium intracellularly
  - Inj. Insulin-dextrose infusion, as insulin alone will cause hypoglycemia
  - Salbutamol nebulisation
- A child with CKD (Chronic kidney disease): Long term treatment
  - Potassium binding raisins like Kayexalate, K-bind

- Avoid potassium rich diets like fruits, juices, coconut water

- Refractory cases (no improvement despite medical therapy)
  - Hemodialysis/Peritoneal dialysis (Renal replacement therapy)

Table 31.1

Hypovolemic	Euvolemic	Hypervolemic
• GI/skin losses • Renal losses: Can be due to o Intake of diuretics o Underlying renal conditions: → Nephronophthisis → ARPKD (Autosomal recessive polycystic kidney disease) → CSWS (Cerebral salt wasting syndrome): Sodium loss through urine	• SIADH (Syndrome of inappropriate antidiuretic hormone) • Glucocorticoid deficiency • Hypothyroidism	• Conditions with lots of third spacing or edema • Total fluid in body is increasing but fluid in intravascular compartment may not be much o Cardiac failure o Cirrhosis of liver o Nephrotic syndrome o Hypoalbuminemia o Renal failure

Table 31.2

Increased intake	Spurious lab value (Falsely elevated K^+ level due to certain conditions)	Transcellular shifts (Total K^+ level in body is not high)	Decreased excretion
• Blood transfusion (especially in stored blood)	• Hemolysed sample before analysis • Tissue ischemia during sampling o Tight tourniquet in young child o In younger children holding limb for sample collection is enough • Thrombocytosis/Leucocytosis (in stored sample): High platelet and WBC count	• Acidosis • Hemolysis • Rhabdomyolysis • Tumor lysis syndrome/Acute tumor lysis syndrome (ATLS) • Hyperkalemic periodic paralysis • Drugs: Digitalis, β – blockers, Succinyl choline • Malignant hyperthermia	• Renal failure o Acute kidney injury o Chronic kidney disease • Adrenal insufficiency o Addison disease o CAH (due to 21 hydroxylase deficiency) • Hypoaldosteronism • Sickle cell disease • Drugs: ACE inhibitors, Angiotensin receptor blockers

32 IV FLUIDS IN HEALTH AND DISEASE

How to calculate 24 hr maintenance fluid in 00:00:18

- For a child, who cannot be fed enterally.
- Calculation of IV fluids for maintenance is calculated by Holiday Segar Method

Body wt.	Fluid	Hourly maintenance fluid rate
For 1st 10 kg	100 ml/ kg	4 ml/kg/hr
Next 10 Kg	50 ml/ Kg	40 ml/hr + 2 ml/kg/hr x (wt - 10 kg)
Beyond 20 Kg	20 ml/ kg	40 ml/hr + 20 ml/hr + 1 ml/kg/hr x (wt - 20 kg)

- **Example**
  - Weight of child = 18 Kg
  - For 1st 10 kg = 10 X 100 = 1000 ml
  - For next 8 kg = 8 X 50 = 400 ml
  - So, child needs 1400 ml of IV fluid in 24 hours
- **Example of Hourly Maintenance fluid rate**
  - If weight of child = 18 kg

$$= 40 + 2 \times (18 - 10)$$
$$= 40 + 2 \times 8$$
$$= 56 \text{ ml/hr}$$

Important Information

- Usual maintenance fluid in children = D5+ ½ NS + 20 Meq/L of K+

Fluid requirement in Neonate 00:06:13

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

Birth Weight	D1	2	3	4	5	6	7 & Beyond
<1500 gm	80	95	110	120	130	140	150
1500 gm	60	75	90	105	120	135	150

Important Information

Q. Which fluid?

- 1st 48 hrs. of life: 10% dextrose alone
- After 48 hrs.: Na^+ & K^+ added

Shock 00:10:00

Definition

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

Types

1. Hypovolemic
2. Obstructive
3. Distributive
4. Cardiogenic
5. Septic

Important Information

- MC cause / type of shock in children: Hypovolemic Shock

- Septic shock is a combination of
  - **Hypovolemia**: Due to capillary leakage
  - **Cardiogenic**: Due to myocardial dysfunction
  - **Distributive shock**: Due to decreased system vascular resistance

Compensatory mechanisms in early phases of shock 00:13:55

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

Cornerstone of Rx of septic shock in children 00:14:47

- Early identification
- Treatment with appropriate Antibiotics

Treatment of child with shock 00:15:36

0 min: Start high flow O_2 & establish IV/ Intra Osseous access (Tibial)

↓

5 min

i. Push boluses of 20 ml / kg of isotonic/ normal saline NS up to 60 ml/ kg until perfusion improves or rales/ Hepatomegaly appears
ii. Correct Hypocalcemia & hypoglycemia
iii. Begins Antibiotics (broad spectrum)

↓

If still shock not reversed

↓

Fluid Refractory Shock

↓

15 min

i. Begin Inotropes (Dopamine)
ii. Obtain central venous access & airway if needed
iii. If not improving titrate epinephrine (Cold shock) or Norepinephrine (warm shock).

↓

Shock not reversed

↓

Catecholamine Resistant Shock

↓

60 min

i. Begin hydrocortisone
ii. Monitor CVP
iii. Maintain normal MAP-CVP & $SCVO_2$ > 70%
iv. Maintain Hb> 10gm/dl.

Cold shock + Normal BP	Cold shock with low BP	Warm shock + low BP
↓	↓	↓
Titrate Epinephrine	Epinephrine + Dobutamine	Titrate Norepinephrine

If shock still not reversed

↓

Persistent catecholamine Resistant shock

↓

- Rule out pericardial effusion/ pneumothorax

↓

Shock not reversed

↓

ECMO

(Extra corporeal Membrane oxygenation)

Recent updates

00:26:06

- Protocolised approach not preferred.
- Individualized approach to suit patient physiology & settings.
- Crystalloids Are Preferred
- **"Deresuscitation"**
  - Restricting Maintenance fluid after initial resuscitation
  - Use of diuretics
  - Advantage: More ventilation free days & shorter ICU stay (faster recovery)

Monitoring Fluid Resuscitation Responsiveness

00:28:52

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

Burns in children

00:31:06

- 'Burns': caused by dry heat
- 'Scalds': caused by wet heat e.g hot water/ steam
- MC cause of burns in children 5-14 yr of age: flame injury.
- Scald burn is MC in children < 4 yr age

Indications of hospitalization in burns

- Burns involving > 10% of Body Surface Area.
- 3rd degree burns (full thickness burns involving epidermis, dermis & subcutaneous tissue)
- Electric burns due to high tension wires.
- Chemical burns
- Inhalational injury (regardless of Body Surface Area involved)
- Suspected child abuse or neglect.

Estimation of BSA involved in burns in children

- Varies in different age groups.
- May use BSA (Body Surface Area) charts eg
  - Modified Lund & Browder chart
  - Shriners Hospital Chart, Boston.
- 'Rule of nines' – in adults and children > 14 yrs age.
- In small burns (<10% of BSA), 'rule of palm' may be used → area from the wrist crease to the finger crease (palm) in a child 1% of BSA (body surface area)

Fluid Resuscitation in a child with burns

00:37:27

- Parkland Formula: 4ml/ kg/ % BSA burned in 24 hours

  ↓ ½ in 1st 8 hours ↓ Remaining in next 16 hours

- Fluid of choice: Ringer Lactate
- In the next 24 hours: Reabsorption of edema fluid and diuresis occurs.
  - ½ of the fluid infused in 1st day
  - RL in 5% dextrose preferred.

PREVIOUS YEAR QUESTIONS

Q. Not a feature of severe dehydration? (AIIMS June 2020)

A. Child thirsty

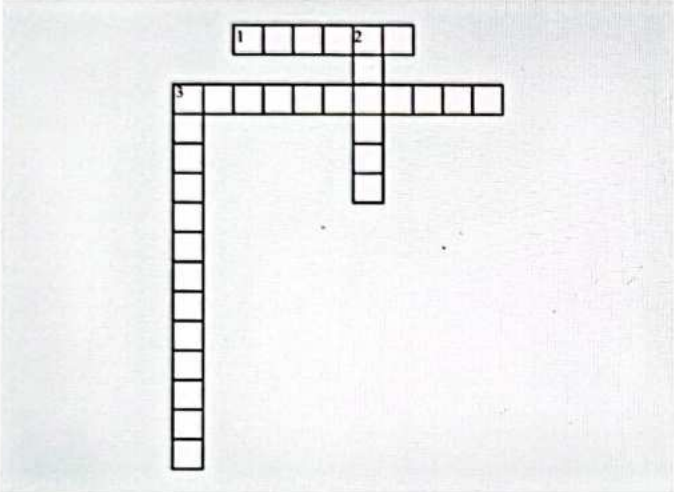
B. Drowsy child

C. Skin retract very slowly

D. Sunken fontanelles

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. Ideal site for ABG analysis
3. Flatting of T craves is the 1st ECG sign in _____

Down

2. This test is done to assess patency of palmour arch
3. Brain hemorrhage is the most devasting consequence of _____

princeeeekum@gmail.com
9928609733

33 TYPES OF GENETIC DISORDERS

Classification of Genetic Disorders 00:00:05

- Chromosomal disorders
  - Disorders where the entire chromosome is affected either chromosome number or structure
- Single gene disorders/Mendelian disorders
  - Follows Mendelian pattern of inheritance
- Multifactorial inheritance
  - Disorders where apart from genetic factors, environmental factors also play a very important role e.g cleft palate,neural tube defects
- Non-Mendelian disorders
  - E.g., Trinucleotide repeat disorders, Gonadal mosaicicm,genomic imprinting,mitochondrial inheritance
  - These disorders do not follow typical Mendelian pattern of inheritance

Chromosomal disorders

- Disorders where either the structure or the number of chromosomes is affected
- Chromosomes are large chunk of genetic materials (Total no of chromosomes in human – 46)
- Chromosome can either be missing, duplicated, or altered in some form
- E.g., Down syndrome: Trisomy 21 (3 copies of Chr. 21 instead of 2)
  - Turner syndrome: 45, XO (Female with single X chromosome)

Single gene disorders/Mendelian disorders

- These disorders follow typical Mendelian pattern of inheritance
- Autosomal dominant (Sex chromosomes are not involved, somatic chromosomes are involved)
- Autosomal recessive
- X-linked recessive
- X-linked dominant
- Y-linked conditions: Very rare

Non-Mendelian disorders

- Trinucleotide repeat disorders
- Mitochondrial disorders/Mitochondrial pattern of inheritance
- Genomic imprinting
- Gonadal mosaicism

Multifactorial disorders

- Disorders where apart from genetic factors, host related factors and environmental factors also plays a very important role
- E.g., Cleft lip, cleft palate, Neural tube defects, Diabetes, Hypertension

Mendelian Disorders 00:05:32

- Single gene disorders which follow typical Mendelian pattern of inheritance

Autosomal dominant disorders

- Dominant gene: Even only one allele is abnormal, disease is going to manifest
- For each gene there are 2 allele

ABCD 1 gene

- Autosomal dominant disorders are those disorders that manifest even if one of the alleles of a gene is affected (both the alleles need not to be affected)
- How to identify a dominant disorder?
  - In dominant disorders either of the parents is also affected by the same disorder (at least 1 parent is affected)
- Examples of autosomal dominant disorders: **HEAVY**
  - Hereditary spherocytosis, Hypercholesterolemia
  - Ehlers Danlos syndrome
  - Achondroplasia
  - Von Willebrand disease
  - Pseudohypoparathyroidism
- Other autosomal dominant disorders: **DOMINANT**
  - Dystrophia Myotonica (Myotonic dystrophies)
  - Osteogenesis imperfecta (most types are autosomal dominant)
  - Marfan syndrome
    - → Clinical presentation- tall stature, arm span increased, arachnodactyly
    - → Skeletal manifestations: Pectus excavatum
  - Intermittent porphyria
  - Noonan syndrome
  - Adenomatous polyposis coli (pre-cancerous condition for carcinoma colon)
  - Neurocutaneous conditions – Neurofibromatosis and Tuberous sclerosis (runs in families)

Autosomal recessive disorders

- Disorders that manifest only if both the copies/alleles of a gene are affected
- If both the parents are carrier than only the children will manifest this disease

ATP 7B gene

- Wilson disease caused by ATP 7B gene is going to manifest only if both the copies/alleles of this gene are abnormal
- Parents are usually the carrier
- If one of the parents is affected then all the babies will be carriers of that disorder even if the other parent is normal
- Examples of autosomal recessive disorder: **ABCDEGH**
  - Albinism, Alkaptonuria
  - β-Thalassemia
    → If both the parents have thalassemia trait then each baby have 25% risk of being affected
  - Cystic fibrosis, Congenital adrenal hyperplasia
  - Deafness (Congenital Sensorineural deafness)
  - Emphysema caused by α_1 antitrypsin deficiency
  - Gaucher disease, Galactosemia
  - Homocystinuria (classical variety)
- Mucopolysaccharidosis – Autosomal recessive inheritance
- Most of the metabolic disorders have autosomal recessive inheritance

X-linked recessive disorders

- These are sex chromosome (X) linked recessive disorders
- Predisposition: Males are more commonly affected

Males	Females
↓	↓
46, XY	46, XX

- Since males have single X chromosome, and if that chromosome is abnormal then also disease is going to manifest as there is no other normal copy of X chromosome
- Female – 2 X chromosomes, even if 1 X chromosome is affected, there is another normal copy of same gene on another X chromosome
- Females are usually not affected in X-linked recessive disorder
- All daughters of an affected male are going to be carriers
- Father to son transmission is not seen as son receives Y chromosome from father and X chromosome from mother
- Father to son transmission rules out X-linked inheritance
- Examples of X-linked recessive disorders: **Girls Do Care For CHAWAL**
  - G6PD (Glucose-6-Phosphate Dehydrogenase) deficiency
    → RBCs can get hemolysed very easily
    → Avoid notorious drugs which precipitates hemolysis
  - **Duchenne muscular dystrophy (DMD)**
  - Colour blindness (more common in males)
  - Fabry disease (Lysosomal storage disorder)
  - Chronic granulomatous disease (CGD - Immunodeficiency condition)
    → Screening test – Nitroblue tetrazolium test (NBT)
    → Confirmatory test – Dihydro rhodamine (DHR) assay
  - Hemophilia A and B
  - Hunter disease (Type 2 MPS)
  - Agammaglobulinemia/Bruton's disease

Important Information

- Wiskott-Aldrich syndrome
  - Thrombocytopenia, small sized platelets, eczema like skin rash, recurrent infections
  - WASP gene is affected
  - Albinism
  - Lesch Nyhan syndrome
    → Self-mutilation
    → Uric acid accumulates in body
- History: Child is affected and there is history that mother's brothers (mama) is also affected with same disorder (commonly seen in X-linked recessive inheritance pedigrees)
- When can females manifest X-linked recessive disorders?
  - Female – 2 X chromosomes, even if 1 X chromosome is affected, there is another normal copy of same gene on another X chromosome
  - Female manifest X-linked recessive disorder if they have single X chromosome i.e., 45, XO
  - **Turner syndrome:** 45, XO
  - Unfavourable lyonization
    → Normally, in females one of the X chromosomes get randomly inactivated and other remains active
    → So, if X chromosome carrying abnormal allele remains active and normal one gets inactivated then the female can manifest the disease

X-linked dominant disorder

- More commonly seen in females
- Female karyotype: 46, XX
- Dominant gene: Manifest only if one of the alleles is abnormal/affected
- So, if one X chromosome is affected and other X chromosome is normal – Disease is still going to manifest
- Male karyotype: 46,XY
- If the only X chromosome in males is affected then this condition becomes lethal and they succumb in utero
- All daughters of an affected male have the disease but all sons are normal
- Father to son transmission is not seen

- Father to son transmission in pedigree rules out X-linked inheritance
- Examples of X-linked dominant disorders: **CARR**
  - Charcot Marie tooth disease – Peripheral neuropathy, Pes Cavus
  - Alport syndrome (controversial)
  - Rett syndrome
  - Rickets: X-linked Hypophosphatemic rickets
    → PHEX gene is affected (PHEX- Phosphate regulating endopeptidase X-linked)

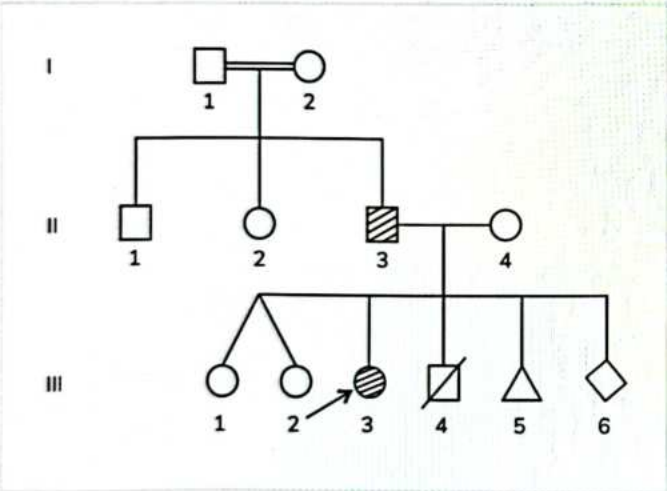
Pedigree

00:30:32

Q. What is pedigree?

- Diagrammatic representation that shows the inheritance of various genetic trait through different generations in a family

Drawing of a pedigree

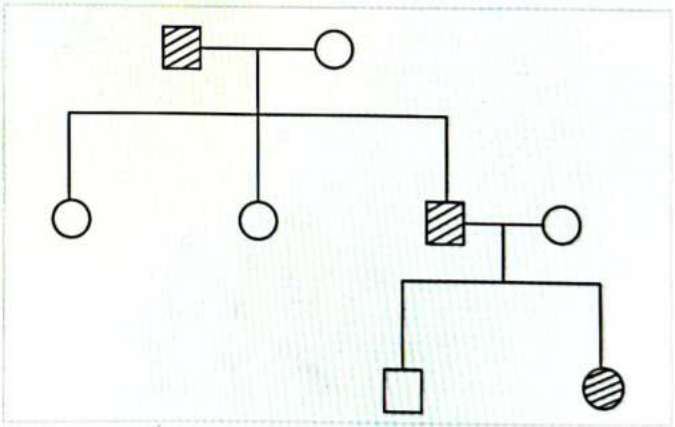


- □ - Represents male
- ○ - Represents female
- Roman numerals I,II,III indicates - Various generations
- Arabic numeral 1,2,3 represents – Number of individuals in a particular generation
- □—○ - Represents consanguinity i.e., marriage in blood relation
  - Proportion of genetic disorder is more in family if there is consanguinity
  - Various degree of consanguinity – 1st degree, 2nd degree, 3rd degree and so on
- △ - Represents spontaneous abortion
- ◇ - Represents unknown sex i.e., unable to categorise whether it is male of female
  - Can be the case with a child with ambiguous genitalia, or the when the sex of the fetus is not known
- ▨, ◍ - Represents affected individual (male & female respectively)
  - ↗ Arrow represents proband i.e., individual due to whom this family has been brought to attention
- ⩚ Represents monozygotic twins, with no line in between represents dizygotic twins
- ☒ - Represents deceased individual
- for genetic disorders - 3 generations need to be depicted in pedigree
- 3rd generation in this pedigree shows - Normal monozygotic twins, affected female, deceased male , spontaneous abortion, child with ambiguous genitalia
- Affected father (2nd generation), other siblings normal
- Father's parents have a history of consanguinity

Important Information

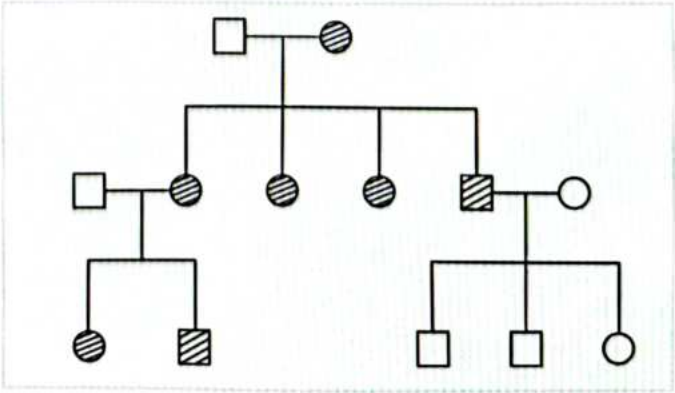
- 3 golden rules of pedigree analysis
  1. If at least 1 parent of the affected child has disease: Dominant inheritance
  2. Father to son transmission: Rules out X-linked inheritance
  3. If all children of an affected female are diseased: Mitochondrial inheritance

Examples



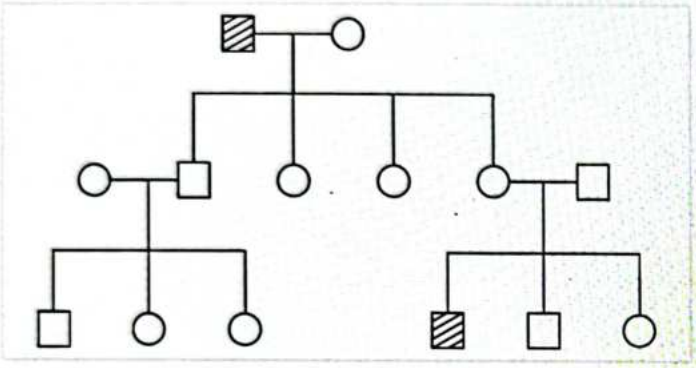
- Grandfather, father, and daughter is affected: Dominant inheritance
- Father to son transmission seen: Autosomal dominant inheritance

Q. Identify the mode of inheritance?



- For 1st generation: female is affected, all her children are affected
- For 2nd generation
  - Male is affected but his children are not affected
  - Female is affected and all her children are affected
- Interpretation: Mitochondrial inheritance

Q. Mode of inheritance?



- Male is affected but parents are unaffected: Recessive pedigree
- Father's father is affected
- There is no father to son transmission
- Interpretation: X-linked recessive inheritance
- X-linked recessive inheritance runs more commonly in males e.g., Hemophilia, Duchene muscular dystrophy

Non-Mendelian Disorders

00:39:10

A. Trinucleotide repeat disorder

- These disorders are due to increase in the number of trinucleotides repeats above a certain threshold
- More the number of repeats, more the severity of disease
- **"Anticipation" phenomenon**: Disease manifestations worsen or appear at an earlier age in subsequent generations
  - It occurs because of increase in nucleotide number with each generation
  - E.g., if father had 200 nucleotides repeat for a particular disorder, then his daughter may have 250 repeats then daughter's son may have 300 repeats so disease tend to worsen with each generation

Examples

Name of disorder	Repeats
Huntington disease	CAG
Myotonic dystrophy	CTG
Fragile X syndrome	CGG

Fragile X syndrome

00:43:58

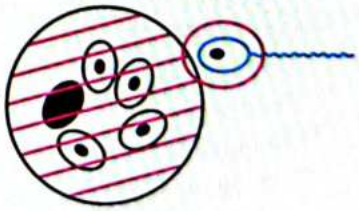
- Gene involved – FMR-1 (Familial mental retardation) gene on X chromosome

Genetic basis	No. of CGG repeats
Normal population	5-55
Carriers	55-200 (premutation)
Fragile X syndrome	>200 repeats

- In premutation stage: No clinical features are seen
  - In females, it is associated with premature ovarian failure
- 10% of female may have intellectual disability/low IQ
- It is more common in males
- **Clinical features**
  - Long face
  - Large ears
  - Large mandible/Prominent jaw
  - High arched palate
  - Hyperextensible joints
  - Mitral valve prolapse
  - Macro-orchidism/large testes: Seen in adolescent age group
  - Intellectual disability (developmental delay, mental retardation)

B. Mitochondrial disorders

- All children of an affected female have the disease
- In all cells of body, there is nucleus containing nuclear DNA and mitochondria containing mitochondrial DNA present in cytoplasm



- When sperm penetrates ovum, only head of sperm enters the ovum
- Head of sperm contains DNA material from father
- Rest entire part of cell is formed from mother
- When zygote forms entire ovum goes from mother and only head of sperm comes from father i.e., all mitochondrial DNA material/nuclear material comes from mother in the baby
- **Heteroplasmy:** Presence of both wild type (Normal) and mutated mitochondrial DNA in same individual
- **Threshold effect:** The minimum percentage of mitochondrial DNA required for the manifestation of disease

- **Examples: KLMNOP**
  - K - Kearns Sayre syndrome
  - L - Leber's hereditary optic neuropathy
  - M - MELAS (Mitochondrial Encephalo-myopathy, Lactic acidosis, Stroke like episodes)
    → Stroke like episode cause neurological deficit
  - M - MERRF (Myoclonic epilepsy, Ragged red fibre)
  - N - NARP (Neuropathy, Ataxia, Retinitis pigmentosa)
  - O - CPEO (Chronic progressive external ophthalmoplegia)
  - P - Pearson syndrome: Bone marrow involvement, pancytopenia, pancreatic involvement

C. Genomic Imprinting

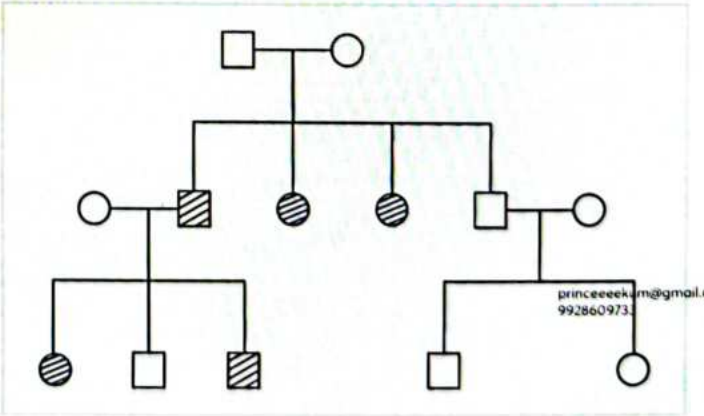
- It is due to parent specific inactivation of certain genes
- Genomic imprinting refers to alteration in DNA without any change in nucleotide sequence
- It occurs due to epigenetic phenomenon
- Epigenetic changes – Alteration in DNA without any change in nucleotide sequence
- There is differential gene expression depending on the parent of origin
- Epigenetic change usually responsible is methylation of DNA
- Prader Willi syndrome – It is due to paternal gene silencing or imprinting
- Angelman syndrome – It is due to maternal copy of the gene silencing or imprinting

Examples

Prader Willi syndrome	Angelman syndrome
• Paternal copy of gene o Deleted or o Silenced or • Maternal disomy o Two copies of maternal allele have formed, no copy from father	• Maternal copy of gene o Deleted or o Silenced or • Paternal disomy o Both copies from father instead of mother
• Gene involved – UBE 3A gene on Chromosome 15	• Gene involved – UBE 3A gene on Chromosome 15
• Clinical features o Obesity o Short stature o Intellectual disability o Hypotonia o Hypogonadism (delayed puberty) o Typical dysmorphism → Almond shaped eyes → Tapering fingers/ digits	• Also known as Happy puppet syndrome: Children have happy demeanour • **Clinical features: ANGELMAN** o Ataxia o Not intelligent/ Intellectual disability o GTCS o Excessive Laughter (Episodes of laughter similar to gelastic seizures in hypothalamic hamartoma) o Maternal gene Not there

D. Gonadal mosaicism

- It is a condition that occurs due to mutation that happens after zygote formation
- Somatic cells are unaffected but gonadal cells/germ cells are affected
- Somatic cells are unaffected: Individual remains asymptomatic
- Gonadal cells affected: Multiple children can be affected



- Couple is asymptomatic, but their multiple children are affected: Dominant pedigree
- Interpretation: Gonadal mosaicism
- One of the parents might be harbouring such a mutation that is not present in somatic cell but might be present in germ cell i.e., why their multiple offspring are affected

34 IMPORTANT GENETIC SYNDROMES

Down Syndrome

00.00.10

- It is the most common chromosomal abnormality seen in children
- Basic defect: There is 3 copies of chromosome 21 instead of 2 i.e., also known as Trisomy 21

Genetic basis

- 95% cases of Down syndrome - Trisomy 21 which is due to maternal meiotic non disjunction (most common) i.e., separation of chromosomes does not take place properly during maternal meiosis
- 3% cases – Translocation i.e., translocation of chromosome 21 with chromosome 21 or translocation of chromosome 21 with another chromosome like chromosome 14 or 15
- 1-2% cases – Mosaicism
  - Mosaicism: It means presence of > 1 different cell line in the same individual i.e., some cell will have trisomy 21, some cell may have monosomy 21 and some cells may have normal chromosomal structure
  - Individuals with mosaicism have less severe clinical features
- The risk of having a child with Down syndrome increases with increase in maternal age

Maternal age	Risk of having child with Down syndrome
20 years	1 in 1500
40 years	1 in 30

- Most common congenital heart disease in a child with Down syndrome: Endocardial cushion defect/AVSD (Atrioventricular septal defect)
- Most common cause of intestinal obstruction in a child with Down syndrome: Duodenal atresia
  - On X-ray: Double bubble sign is seen
- Important clinical features of Down syndrome: **I C A PROBLEM Somewhere**

  - I - Intellectual disability/Mental retardation, Incurved little finger/Clinodactyly
  - C - Congenital heart diseases, Congenital hypothyroidism (Thyroid profile needs to be checked regularly)
  - A - Atlantoaxial instability, Acute leukemia especially Myeloid leukemia (M7 variety), Alzheimer's disease (Early onset), Atresia of duodenum, Absent Moro's reflex
    → Atlantoaxial instability i.e., Cervical spine is unstable so it needs to be checked before participating in contact sports or surgery requiring general anaesthesia as it requires extension of neck
    → Absent Moro's reflex: Due to hypotonia limbs are limp and loose
  - P - Protruding tongue
  - R - Round face
  - O - Occiput flat; Open, large sized anterior fontanelle
  - B - Brush field spots on Iris, Brachycephaly (Head shape - Squarish)
  - L - Low tone, Low /depressed nasal bridge, Low set ears/Dysplastic ears
  - E - Epicanthic folds/Fold of skin over medial canthus
  - M - Mongoloid slant of eyes
  - S - Sandal gap i.e., increased gap between great toe and rest of the toes, Simian crease

- Diagnosis of child with Down syndrome:
  - By distinct clinical features
  - For confirmation of Down syndrome– Karyotype or FISH (Fluorescence in situ hybridization) is done
    → It shows 3 copies of chromosome 21

- Antenatal screening for Down syndrome
  - Radiological markers
    → In 1st trimester, increased nuchal fold thickness (> 3mm) is a very high risk
    → For nuchal thickness, scan is done at 11 weeks of gestation in 1st trimester
    → Soft markers: Shortened femur, absent/hypoplastic nasal bones (in 2nd trimester)
    → Cardiac anomalies
    → Duodenal atresia

Important Information

- Biochemical markers
  - 1st trimester (T_1): β-HCG, PAPP-A (Pregnancy Associated Plasma Protein A)
  - 2nd trimester (T_2)
    →Triple test: β-HCG, Unconjugated estriol, α-fetoprotein
    →Quadruple test: β-HCG, Unconjugated estriol, α-fetoprotein, Inhibin
- Biochemical Markers that increase in down syndrome: HI
  - HCG
  - Inhibin
- Rest all the biomarkers are going to decrease in Down syndrome

- **Integrated test**: it is a test which takes in account certain factors from 1st trimester as well as 2nd trimester along with maternal age
  - → Maternal age + T_1 (Nuchal thickness + PAPP-A levels) + T_2 (Quadruple test)
  - → All these values are used for calculated risk or composite risk in Down syndrome
  - → It is the best screening test for Down syndrome in the antenatal period
  - → It has pick up rate of > 95% cases for Down syndrome
- **NIPS (Non-Invasive Prenatal Screening Test)/NIPT (Non-Invasive Prenatal Test)**
  - → Cell free fetal DNA circulating in mother's blood is used to diagnose aneuploidies like Down syndrome
  - → 8 to 10 ml of mother's blood is taken
  - → Major chromosomal abnormalities can be easily diagnosed or screened by this test
  - → Limiting factor for this test was its cost and it was not easily available but now a days it is routinely offered to all the mothers at high risk or higher age

- **Confirmatory test for pre-natal diagnosis of Down Syndrome**: Fetal karyotype
  - Procedure for women in early pregnancy (11-13 weeks of gestation): CVS (Chorionic Villous Sampling)
  - At 14-16 weeks of gestation: Amniocentesis can be done
  - At 17-20 weeks of gestation: Cordocentesis can be done

- All these 3 procedures; CVS, Amniocentesis, Cordocentesis are invasive procedure
  - They carry risk of abortion
  - It is only offered to mothers at high risk based on screening test or previous child with Down syndrome

Q. A couple already has a child with Down syndrome. How much will be the recurrence risk of Down syndrome in the next pregnancy?

Ans. It depends upon the karyotype of affected child and the karyotype of parents

Refer Table 34.1

Turner Syndrome

00:23:26

- Basic defect: 45, XO
- It is always seen in females
- Most common congenital heart disease: Bicuspid aortic valve > Coarctation of aorta
- Clinical features: **See A Baby Clown**
  - S - Short stature, Short 4th metacarpal, Sensorineural hearing loss
  - A - Amenorrhea (Primary)
  - B - Barr body absent
- Number of Barr bodies in any individual = Number of X chromosome - 1
  - Normal males: 1-1 = 0
  - Normal females: 2-1 = 1
    - → Take a sample from buccal area and see under microscope, a dark or dense in nucleus is seen which is a Barr body
  - Turner syndrome females: 1-1 = 0
    - → Female with absent Barr body
  - C - Cardiac abnormalities, Cystic hygroma, Cubitus valgus
  - L - Low posterior hair line, Lymphedema of hands and feet, Low thyroid
  - O - Ovaries streak shaped/underdeveloped, Rudimentary nucleus
  - W - Webbed neck
  - N - Nipples are widely spaced on a shield shaped chest, Normal intelligence

Q. Which of the following is true about Turner Syndrome?
A. Normal height
B. Normal intelligence
C. Normal puberty
D. Normal fertility

Trisomy 18 (Edward syndrome)

00:30:07

- Important clinical features: **ROCKY Mountain**
  - R - Rocker bottom foot i.e., foot is convex from below like a rocking chair
  - O - Overlapping fingers or toes
  - C - Cardiac anomalies
  - K - Kidney malformations
  - Y - Microcephaly
  - M - Mental retardation/Intellectual disability

Trisomy 13 (Patau syndrome)

00:31:38

- It is more severe disorder than Trisomy 18
- Important clinical features: **CMC OPD**
  - C - Cutis aplasia i.e., scalp defects
  - M - Microcephaly
  - C - Congenital heart diseases, Cleft lip, and palate
  - O - Holoprosencephaly i.e., cerebral hemispheres and ventricular system are not cleaved properly and are fused to each other to varying degree
  - P - Polydactyly (Post axial polydactyly more common)
  - D - Developmental delay, Intellectual disability

Noonan syndrome

00:33:38

- It has autosomal dominant inheritance
- It is one of the disorders of the group called as RASopathies, Ras map kinase pathway is involved
- Most common gene involved: PTPN 11 gene

- There is a microdeletion in PTPN 11 gene, the deletion is so small that it cannot be seen in Karyotype. So, karyotype is usually normal in these individuals
- It can be seen in both boys and girls
- Similarities between Noonan syndrome and Turner syndrome
  - Short stature
  - Webbed neck
  - Cubitus valgus
  - Increased risk of congenital heart disease
- Difference between Noonan syndrome and Turner syndrome

Noonan syndrome	Turner syndrome
• Autosomal dominant inheritance • Karyotype – Normal (microscopic deletion) • It can be seen in both boys and girls • Intellectual disability present • Delayed puberty but fertility is preserved	• Do not follow any inheritance pattern • Karyotype – 45, XO • It is seen only in girls • Normal intelligence • Infertile (Streak ovaries and rudimentary uterus)

- Most common congenital heart disease in Noonan syndrome: Pulmonary stenosis (Supravalvular) or Pulmonary tract outflow obstruction
- Children with Noonan syndrome have more congenital heart diseases more commonly than Turner syndrome
- Children with webbed neck in turner syndrome have more chances of having congenital heart disease.

Marfan Syndrome

00:37:40

- It has autosomal dominant inheritance
- It is a multisystem disorder with involvement of the connective tissues
- Most common genetic abnormality is due to mutation in FBN 1 (Fibrillin 1) gene
  - This protein is essential for connective tissue formation and proper functioning of connective tissue

Clinical features

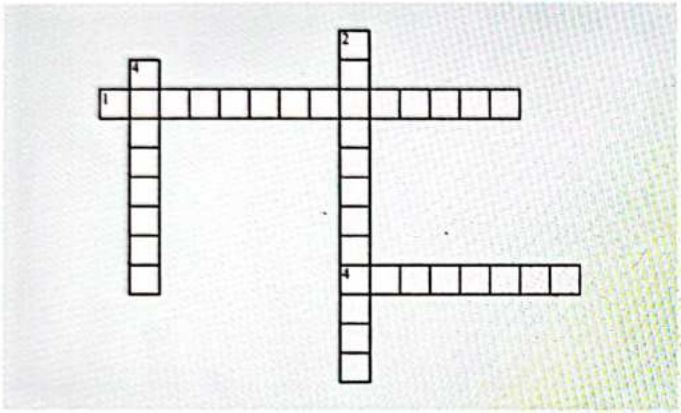
- Skeletal abnormalities: Tall stature, arachnodactyly, chest wall abnormalities like pectus excavatum, pectus carinatum, thumb sign (On folding thumb it will protrude beyond the ulnar border of palm) or wrist sign positive, Increased joint laxity
- CVS abnormalities: Aortic route dilatation, Mitral insufficiencies, Arrythmias
- Eye abnormalities: Ectopia lentis or subluxation of the lens of the eye, Blindness
  - MSL: In Marfan syndrome, dislocation of lens is in Superolateral direction
  - In homocystinuria dislocation of the lens of the eye is in Inferomedial direction
  - In homocystinuria there is hypercoagulability of blood so there is more chances of stroke
- Pulmonary involvement: Increased risk of pneumothorax
- To diagnose Marfan syndrome clinically, Ghent criteria is used

Table 34.1

Karyotype of affected child	Karyotype of father	Karyotype of mother	Recurrence risk
Trisomy 21	• Normal	• Normal	• ~ 1% i.e., same as that of general population
t(21;21)	• Normal • If either of parent is a carrier for t(21;21)	• Normal	• ~ 1% • 100% (Parents needs to be counselled)
Translocation of Chr. 21 with another chromosome (14 or 15)	• Normal • Carrier • Normal	• Normal • Normal • Carrier	• ~ 1% • 1-3% • 10-15%

CROSS WORD PUZZELS

Crossword Puzzle



Across

1. _____ Disorders is a remit of a combination of multiple genetic & environmental causes.
3. Which syndrome is also known as "Happy Puphet Syndrome"?

Down

2. Presence of both wild type (normal) & mutated mitochondrial DNA in the same individual is known as ?
4. Most common cause of intestinal obstruction in Down's syndrome is _____ atresia.

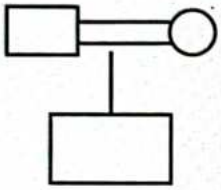
princeeeekum@gmail.com
9928609733

35 DISORDERS OF CARBOHYDRATE METABOLISM

When to suspect a metabolic disorder?

In neonates and infants –

- Deterioration after a period of apparent normalcy
- Rapidly progressive encephalopathy ± seizures
- Recurrent vomiting, peculiar body fluid odor.
- Neonatal sepsis is like a presentation with negative sepsis screen.
- Significant family history:
  - Consanguinity



  - Multiple abortions
  - Siblings with similar illnesses.

In older children

- Episodic presentation
- Worsening with intercurrent illness
- Ataxia/other CNS manifestation
- Multisystemic involvement

Investigations: Metabolic acidosis, ketosis, hypoglycemia.

Clinical pointers in different metabolic disorders.

- Coarse facies – MPS, GM, gangliosidase.
- Cataract – Glactosemia, DM, Wilson disease
- Retinitis pigmentosa – Mitochondrial disorders
- Cherry red spot
  - GM, gangliosidases
  - Niemann pick disease.
  - Tay sach disease
- Eczema/Alopecia – Biotinidase deficiency, Multiple carboxylase deficiency
- Hypo pigmentation: Phenyl ketonuria, Albinism
- Abnormal kidney hair – Menke's disease
- Glycogen storage disease
- Galactosemia
- Hereditary fructose intolerance

Glycogen Storage Disease

00:12:04

- There is defect in storage of glycogen and related compounds in these group of disorders

Glycogen storage disease

Liver glycogenosis | Muscle glycogenosis

Liver glycogenesis

- Glycogen and its products are mainly deposited in liver
  - Liver is mainly affected
  - Hepatomegaly, liver is firm and enlarged

Muscle glycogenosis

- Muscles are predominantly affected
- **Liver glycogenesis:** Liver is predominantly affected though muscle involvement can also be there

Type	Name of the disease	Enzyme deficient
I	Von Gierke disease (most common in younger age group)	Glucose 6 Phosphatase
III	Cori disease	Debranching enzyme
IV	Anderson disease	Branching enzyme
VI	Her's disease	Hepatic phosphorylase

Muscle glycogenosis: 2+5=7

Type	Name of the disease	Enzyme deficient
II	Pompe disease	Acid maltase/α-1,4-glucosidase
V	Mc Ardle disease (Most common GSD to present in adolescents)	Muscle phosphorylase
VII	Tarui disease	Phosphofructokinase

- Mc Ardle disease
  - Because of muscle involvement, there are features of rhabdomyolysis, myoglobinuria, urinary manifestations, muscle cramps
  - It can lead to renal failure

Von Gierke disease (Type-I GSD)

00:17:50

- Most common GSD among children
- Inheritance – Autosomal recessive

Types

- Ia – Glucose 6 phosphatase deficiency

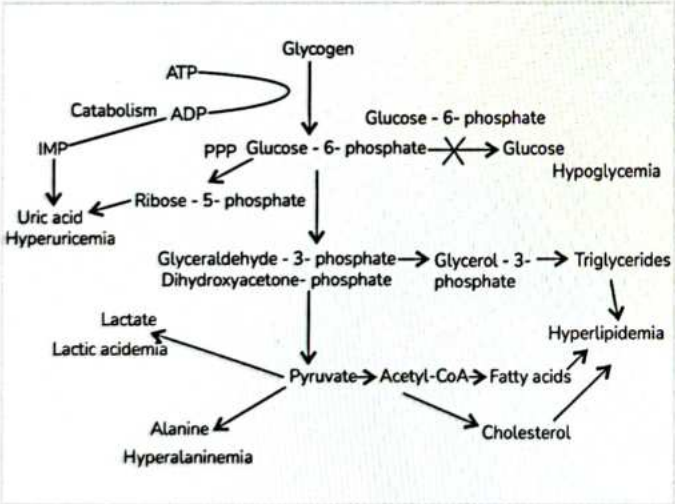
- 1b – Translocase deficiency (deficiency of transporter, transporting Glucose 6-phosphate inside microsome)

Glycogen
↓ Enters microsome
Glucose 6 phosphate ⟶ Glucose & Ribose 5-P
Glucose 6 phosphatase

Clinical features

- Presents in infancy or early childhood
- Recurrent hypoglycemia, Early morning hypoglycemia (due to less feeding at night) leading to lethargy or seizures
- Hypertriglyceridemia
  - Doll like facies: Chubby cheeks
- Abdominal distension (hepatomegaly)
- Clinical presentation: A 6 month old child having doll like chubby looking facies and huge abdominal distension. Mother complaints that child is having early morning lethargy or seizures. Investigations -

Metabolic pathway



Biochemical Investigation

- Due to deficiency of G 6-Phosphatase
  - Glucose-6-P ⟶ Glucose - Causing Hypoglycemia
- Glucose-6-P gets accumulated excessively in body
- By pentose phosphate pathway
  - Glucose 6-P ⟶ Ribose 5-P
- Excess of glucose 6-P, Ribose 5-P break down to produce excess of uric acid causing Hyperuricemia
  - Elevated uric acid levels
- Hyperuricemia can cause renal shutdown, renal stones, arthritis
- Glycolysis
  - ↑Glucose 6-P ⟶ ↑ Glyceraldehyde-3-P & Dihydroxyacetone-P ⟶ ↑ Pyruvate ⟶ ↑Lactate, Alanine
  - Elevated lactic acid levels
- Excess acetyl CoA ⟶ ↑ Fatty acid & ↑ Cholesterol
- ↑Glyceraldehyde-3-P ⟶ ↑ Glycerol 3-P ⟶ ↑ Triglycerides ⟶ **Hyperlipidemia**

Definitive diagnosis

- Liver biopsy: Shows deposition of glycogen & fat
- Gene based study: Demonstrate genetic mutation

Complications

- Huge hepatomegaly can lead to hepatic adenoma
- Systemic/pulmonary hypertension
- Renal involvement: Renal stones, proteinuria
- Monitor these patients for any complications

Treatment

- Corn starch diet
  - Give slow sustained source of glycogen or glucose to the body
  - Use uncooked corn starch like corn flour dissolved in water can be fed to baby
  - Prevent recurrent episodes of hypoglycemia
- Frequent feeding: To prevent hypoglycemia
- Treatment of comorbidities
  - For elevated uric acid levels: Give allopurinol
  - For elevated lipid levels: Give statins (lipid lowering drugs)

Q. A 2 year old child presents with recurrent episodes of hypoglycemia. On examination, the child is found to have hepatomegaly. On investigation, the child has hyperlipidemia and elevated CPK levels. What is the probable diagnosis?

- There is low blood sugar (hypoglycemia), hepatomegaly, hyperlipidemia seen in Von Gierke disease
- But muscle involvement is usually not seen in Von Gierke disease
- Presence of elevated CPK levels indicate possible muscle involvement
- Probable diagnosis – Cori disease (Type III GSD)

Refer Table 35.1

Pompe disease/Type II GSD

- Predominantly muscle involvement
- Enzyme deficient – Acid maltase/ α-1,4-glucosidase
- Clinical features
  - Hypotonia (Skeletal muscle involvement)
  - Cardiomegaly (Hypertrophic cardiomyopathy) - Elevated CPK level, ECG changes - shortened P-R interval, tall QRS complexes)
  - Coarse looking facies
  - Hepatomegaly

- Infantile variety: Very severe, patient succumb if proper treatment is not given
- Juvenile variety: Less severe
- Treatment: Enzyme replacement therapy
  - Patients can have symptom free life

Galactosemia

Deficiency of

1. Galactose-1-Phosphate-Uridyl transferase (GALT): Classical type
2. Galactokinase
3. Epimerase

Pathophysiology

- Milk → Lactose → Glucose & Galactose (cannot be digested)
- Galactose and its toxic metabolites get accumulated in body causing various manifestations
- Any form of milk and lactose containing products are contraindicated in confirmed case of galactosemia
- Even breastfeeding is contraindicated
- **In GALT deficiency**, there is accumulation of Galactose 1-Phosphate (toxic product) - Toxic to liver, kidney, and brain
- **In galactokinase deficiency**, there is accumulation of galactose and galactitol (toxic to eye)
  - Congenital cataract is most important manifestation of galactokinase deficiency
  - Galactokinase deficiency can present with bilateral cataract alone

Clinical features of galactosemia

- **Hepatic involvement**
  - Jaundice
  - Hepatomegaly
- **GI manifestations**
  - Diarrhoea
  - Vomiting
- **Failure to thrive**
- **CNS manifestations**
  - Seizures
  - Intellectual disability
- **Bilateral congenital cataract (in galactokinase deficiency)**
- **Renal tubular manifestations**
- **Sepsis with E.coli (very common)**

Duarte variant of galactosemia

- It is quite common, not very severe condition
- 50% of normal enzyme activity is present
- Usually, remains asymptomatic
- It is due to single amino acid substitution
- No clinical significance, these children have normal intelligence

Diagnosis of galactosemia

- Reducing substance in urine – positive (Benedict's test)
- Direct enzyme (GALT) assay
- Demonstration of genetic mutation – Prenatal diagnosis is possible

Treatment

- Lactose free diet
- All milk and milk products are avoided
- Soya based formulas can be given (lactose free infant feeding formulas)
- Breastfeeding contraindicated in confirmed case of galactosemia

Hereditary fructose intolerance 00:30:37

- Enzyme deficient – Aldolase B or Fructose 1,6 bisphosphate aldolase

Pathophysiology

Fructokinase Aldolase B

Fructose → Fructose 1-Phosphate → DHAP + Glyceraldehyde

- Due to deficiency of aldolase B
  - Fructose 1-Phosphate accumulates in body (toxic)

Sugar ⟶ Sucrose ⟶ Glucose and fructose

- Any sweets ingestion can cause disease manifestation
- All sweet items and fructose containing items should be avoided

Clinical features

- Aversion to sweet foods
  - As children are not able to digest sweet foods and they have adverse manifestations
- Jaundice
- Diarrhoea
- Hepatomegaly
- Failure to thrive
- Deposition of fructose -phosphate is toxic to liver (mainly)

Diagnosis

- Reducing substance positive in urine (Benedict's test)
- Liver biopsy
  - Aldolase B enzyme assay in liver biopsy sample

- Gene based diagnosis (non-invasive)
  - Whole axon sequencing is done by next generation sequencing and demonstrate mutation responsible for hereditary fructose intolerance

Treatment

- Ensure fructose free diet
- Complete elimination of sweet food (sucrose and fructose) items
- Cough syrup can not be prescribed in these children for cough
  - Cough syrup contains sucrose and fructose which can cause manifestations instead crushed tablets are given

Table 35.1

	Type I GSD/Von Gierke disease	Type III GSD/Cori disease
Kidneys	Enlarged; spleen – normal	Normal; Splenomegaly may be present
Muscles involvement	Not seen	Seen
CPK levels	Normal	Elevated
LFT	Normal	SGPT, SGOT levels elevated - Transaminitis & fasting ketosis present
Lactate/ Lactic acid level	Elevated	Normal (Usually)
Effect of glucagon	No rise in blood glucose but lactic acid levels may increase	In fed state: Increase in glucose level In fasting state: No increase in blood glucose level
Liver biopsy	Distension of hepatocytes by glycogen and fat deposition	Fibrosis; Paucity of fat

36 DISORDERS OF AMINO ACID METABOLISM

Disorders of Phenylalanine Pathway

00:00:25

princeeeekum@gmail.com
9928609733

- Phenylketonuria
- Alkaptonuria
- Tyrosinemia

Phenylalanine pathway

Phenylalanine
↓ Phenylalanine hydroxylase
DOPA ← (Tyrosinase) Tyrosine
↓ Melanin synthesis
↓ T. aminotransferase
4–OH Phenyl pyruvate
↓ 4 HPPD (Hydroxy Phenyl pyruvate dioxygenase)
Homogentisic acid
↓ Homogentisic acid oxidase
Maleylacetoacetate → Fumarylacetoacetate → (FAH) Fumarate + Acetoacetate

- **Phenylketonuria**: There is deficiency of phenylalanine hydroxylase causing accumulation of phenylalanine in body
  - Accumulation of phenylalanine will cause brain damage, CNS manifestations and gets converted into metabolites like phenyl acetate & phenyl pyruvate which can be detected in urine and blood
  - Due to deficiency of tyrosinase, DOPA is not getting formed causing hypopigmentation
- **Albinism**: One of the causes of albinism is deficiency of enzyme tyrosinase
  - Like phenylketonuria, in Albinism, due to deficiency of tyrosinase, DOPA is not getting formed causing hypopigmentation
- **Tyrosinemia**: It can be due to deficiency of any of the 3 enzymes

1. Tyrosine aminotransferase
2. Fumarylacetoacetate hydroxylase
3. 4 HPPD (Hydroxy phenyl pyruvate dioxygenase)

- **Alkaptonuria**: It is due to deficiency of homogentisic acid

Phenylketonuria (PKU)

00:04:25

- It is a metabolic disorder with autosomal recessive inheritance
- There is deficiency of enzyme phenylalanine hydroxylase
- There is accumulation of phenylalanine, phenylacetate and phenyl pyruvate

Important Information

- Tyrosine becomes an essential amino acid in phenylketonuria.
- Essential amino acid: Amino acids which can not be synthesized in human body and has to be taken from outside
- Normally tyrosine is not an essential amino acid but in phenylketonuria due to deficiency of enzyme phenylalanine hydroxylase, tyrosine is not synthesized in body making it an essential amino acid
- Excessive accumulation of phenylalanine can cause brain damage

Clinical features of PKU

- Hypopigmentation: Blond hair, fair skin, blue iris
- CNS manifestation: Intellectual disability, seizures, microcephaly, hypotonia, irritability
- Mousy/musty body odour
- Growth restriction
- Dental enamel changes
- Children born to mothers with phenylketonuria might have
  - Growth restriction
  - Intellectual disability
  - Microcephaly
  - Congenital heart disease

Diagnosis of phenylketonuria

- Typical case scenario with clinical features
- Biochemical test
  - FeCl, test with urine: Gives green colour (detects excess amount of phenylalanine)
  - Guthrie's test: Detects phenylalanine in serum
  - Plasma/Urine HPL: Detects increased amount of phenylalanine and their metabolites like phenyl acetate and phenyl pyruvate

Management of phenylketonuria

- Low phenylalanine diet
- Supplement tyrosine as it is not getting synthesized in body (Ensure adequate intake of tyrosine)
- Children can have near normal life with these diets

Alkaptonuria

00:12:29

- It is an autosomal recessive disorder

Deficiency of enzyme homogentisic acid oxidase
↓
Polymers of homogentisic acid (Black colour Alkapton bodies) accumulates
↓
Ochronosis (Dark coloured spots on sclera and ear cartilage)

- Excessive polymers of homogentisic acid are secreted in

urine which on oxidation gives black coloured urine or darkening of urine on standing

Clinical features of Alkaptonuria

- During childhood, the only manifestation is darkening of urine on standing otherwise the child remains asymptomatic or mother complains of grey coloured diaper
- Ochronosis: Dark spots on sclera or ear cartilage
- Arthritis: Due to deposition of homogentisic acid polymer usually involving spine and large joints like shoulder, knees
  - On X-ray: Osteoarthritis like changes is seen including calcification of the intervertebral disc with occasional flares
- Cardiac involvement: Mitral or Aortic valvulitis

Treatment of alkaptonuria

- Ensure low phenylalanine and tyrosine diet
- Nitisinone reduces production of homogentisic acid by inhibiting 4-HPPD enzyme
- Manage comorbidities like arthritis symptomatically

Tyrosinemia 00:17:08

- Tyrosinemia is of three types:
  - Type I (Commonest): It is due to deficiency of enzyme Fumarylacetoacetate hydroxylase (FAH)
  - Type II: It is due to deficiency of enzyme Tyrosine aminotransferase
    → Clinical features: Palmar or plantar hyperkeratosis, corneal ulcers, and intellectual disability
  - Type III (Least common): It is due to deficiency of enzyme 4-HPPD (4 – Hydroxy Phenyl Pyruvate Dioxygenase)
    → Nitisinone acts on enzyme 4-HPPD

Tyrosinemia Type I

- It is most common type of tyrosinemia; due to enzyme Fumarylacetoacetate hydroxylase (FAH)
- Due to deficiency of FAH, there are some systemic manifestations of liver, kidneys, and peripheral nerves
- Liver manifestation: Hepatomegaly, features of liver dysfunction like jaundice, bleeding manifestation
  - On investigation: Prolonged prothrombin time and INR which cannot be corrected by Vitamin K administration
- These babies are usually very sick
- Investigation: Increased AFP (Alpha fetoprotein level) and urinary succinyl acetone levels
- These children also have increased risk of hepatic tumours
- Treatment: Nitisinone or Anti-BC and Supportive care

Organic Acidaemia 00:20:53

- These are the group of disorders with non-specific clinical manifestation
- Clinical presentation: Poor feeding, failure to thrive, lethargy, seizures, intellectual disability, or developmental delay, skin and hair changes
- On investigation: Acidosis, elevated lactate, ketosis (may or may not present)
- These babies have a peculiar body odour

IEMs with peculiar odour

IEM (Disorder)	Urinary odour
Multiple carboxylase deficiency	Tomcat urine odour
Glutaric aciduria	Sweaty feet odour
Tyrosinemia	Boiled cabbage
Phenylketonuria	Mousy or musty body odour
MSUD (Maple syrup urine disorder)	Maple syrup or Burnt sugar body odour

- These odours can be found by going near the child or from the ear/earwax of child or from urine of child
- Investigation findings in organic acidaemia's
  - Metabolic acidosis
  - Elevated lactic acid levels
  - Ketosis
  - Hypoglycemia
  - Neutropenia is seen in organic acidemias like MMA (Methyl Malonic acidemia), Propionic acidemia and Isovaleric acidemia
  - Recurrent infections

Q. An infant present with seizures, poor feeding, skin rash and alopecia. On investigation, metabolic acidosis, increased blood ketones and normal NH_3 are seen. What should be used for treatment?

Ans. These are the features of Multiple carboxylase deficiency (Organic acidemias), there is Tom cat urine odour

- In multiple carboxylase enzyme, biotin is a cofactor therefore if there is any problem related to biotin, skin and hair changes are seen like alopecia, skin rashes
- Treatment: Biotin is given

Maple Syrup Urine Disease (MSUD) 00:26:15

- Basic defect: Deficiency of enzyme alpha keto acid dehydrogenase
- Because of which branched chain amino acid (Leucine, Isoleucine, and valine) are not getting metabolized
- Accumulation of branched amino acid in body fluids and excretion in excess amount in urine

- Hence Maple syrup or burnt sugar odour of urine

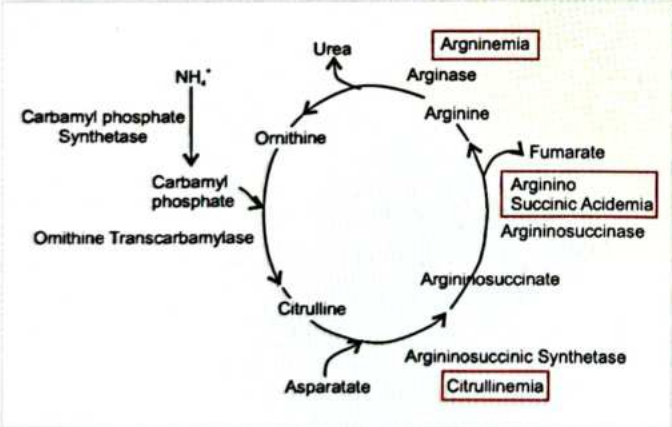
Diagnosis of MSUD

- HPLC (High performance liquid chromatography) of plasma or urine: Increased level of Leucine, Isoleucine and Valine
- $FeCl_3$ test: Gives blue colour in MSUD
- DNPH (Dinitrophenylhydrazine): Gives yellow colour

Important Information

- Screening test for Inborn Errors of metabolism are:
  - TMS (Tandem Mass Spectrometry): Done on dried blood spots
    - → Heel prick is done and some blood spots are taken on special filter paper so punching holes from blood spots, use small aliquot (process it) to diagnose more than 50 metabolic disorders
    - → It can be easily collected, transported, and stored
  - GCMS (Gas chromatography mass spectroscopy) of urine

Urea Cycle and its Defects 00:30:48



- A part of urea cycle takes place in mitochondria and a part takes place in cytoplasm
- There is hyperammonaemia as ammonia is not converting into urea so there are elevated ammonia levels
- If there is deficiency of Ornithine transcarbamylase, ornithine will decrease and urinary orotic acid will increase
- Deficiency of Argininosuccinate synthetase will cause accumulation of citrulline as it is not getting converted into arginosuccinate and this disorder will be known as Citrullinemia
- Deficiency of argininosuccinase will cause accumulation of arginosuccinate and this disorder is known as Argininosuccinic aciduria
- Deficiency of arginase will cause accumulation of arginine and this disorder is known as Argininemia
- When ammonia is elevated, plasma or urine HPLC is done
- If any specific amino acid is highly elevated than disorders are
  - Elevated Citrulline: Citrullinemia
  - Elevated arginine: Argininemia
  - Elevated argininosuccinic acid: Argininosuccinic acidemia
- If non-specific amino acids are elevated, urine orotic acid is done
  - If urine orotic acid is high – OTC (Ornithine transcarbamylase) deficiency
  - If urine orotic acid is normal/low, then check plasma citrulline and if plasma citrulline is also low then it can be carbamyl phosphate deficiency
  - But if plasma citrulline is normal, then it is Transient Hyperammonaemia of new born
- In all the defects of urea cycle, ammonia levels are highly elevated except in arginase deficiency
- Management of hyperammonaemia: Phenylacetate, Arginine, Benzoate
  - In refractory cases: Peritoneal or Hemodialysis
- Hyperammonaemia can cause altered sensorium, developmental delay, coma, lethargy

Clinical presentation

- These disorders can present in episodic manner with child being well in between and then there can episodes of vomiting, seizures, altered sensorium

Other Amino Acid Disorders

- Hartnup disease
- Homocystinuria

Hartnup Disease 00:36:53

Basic defect

- It is an autosomal recessive disorder
- There is defect in SLC6A19 gene on Chr. 5
- There is defect in transport of mono amino mono carboxylic or neutral amino acid by renal tubules and intestinal mucosa

Clinical features

- Most of the children remain asymptomatic
- But if symptomatic, there is cutaneous photosensitivity and pellagra like rash involving the neck area (Casals necklace)

Investigation

- Urine and plasma HPSC: Amino aciduria restricted to neutral amino acid like Valine, Leucine, Phenylalanine, Tyrosine and Tryptophan
- Demonstrate the defect in SLC6A19 gene

Treatment

- Nicotinic acid or Niacin or Nicotinamide

- High protein diet

Homocystinuria 00:40:02

- Classical type of homocystinuria is caused by deficiency of cystathionine β synthetase
  - Pyridoxine is a cofactor for cystathionine β synthetase
- Other types are caused due to defect in methyl cobalamin metabolism
- It can also be due to deficiency of MTHFR (Methylene tetra folate reductase)

Clinical features of homocystinuria

- Failure to thrive
- Developmental delay, Intellectual disability
- Seizures, behavioural disorders
- Skeletal abnormalities resembling Marfan syndrome like tall stature, arachnodactyly, pectus excavatum, pectus carinatum
- Ectopia lentis/subluxation of lens of eye in inferomedial direction (In Marfan syndrome direction is superolateral)
- Recurrent episodes of stroke due to hypercoagulable state

Complications of Homocystinuria

- Recurrent episodes of stroke
- Spontaneous pneumothorax
- Acute pancreatitis

Diagnosis of homocystinuria

- Increased level of homocysteine and methionine in blood and body fluids
- Enzyme assay (cystathionine β synthetase) in liver biopsy or skin fibroblasts
- DNA analysis to demonstrate pathogenic variation in genes involved

Treatment of homocystinuria

- High doses of pyridoxine (Vit B_6) and folic acid
- Restrict methionine intake
- Cysteine supplementation

37 LYSOSOMAL STORAGE DISORDERS

Important Lysosomal Storage Disorders

Refer Table 37.1

Gaucher Disease

00:02:17

- It is the most common lysosomal storage disorder seen in children.

Deficiency of enzyme Glucocerebrosidase

↓

Accumulation of glucocerebrosides in various cells of the body

↓

Accumulation in cytoplasm gives cytoplasm "Crumpled tissue paper" appearance

↓

Gaucher cells

- Gaucher cells accumulate in various parts of the body
  - Accumulation in spleen: Splenohepatomegaly
  - Accumulation in bone: Pancytopenia causing bone pains and pathological fractures
  - Accumulation in nervous system: Neurological involvement

Important Information

- **Clinical features of Gaucher disease**
  - Some children may remain asymptomatic
  - But children with symptoms usually have
    - → Splenohepatomegaly: One of the causes of massive splenomegaly that it can even cross the umbilicus
    - → Pancytopenia: Anemia; easy fatiguability, lassitude, lethargy
      - Leukopenia: Recurrent infections
      - Thrombocytopenia: Bleeding manifestations
    - → Bone pains and pathological fractures
    - → Lytic lesions of long bones known as Erlenmeyer flask bone deformity
    - → Neuronal involvement may or may not be present
      - Neurological involvement is absent in type 1
      - Type 2 & 3 can have some neurological involvement

Diagnosis of Gaucher disease

- Characteristic clinical presentation
- Bone marrow aspiration ± biopsy: Gaucher cells with characteristic "Crumple tissue paper" appearance of cytoplasm
- Demonstrate the deficient glucocerebrosidase enzyme activity in the leucocytes or skin fibroblast
- X-ray of long bones: Erlenmeyer flask deformity

Treatment of Gaucher disease

- Enzyme replacement therapy is available
  - With this therapy, organomegaly decreases, pancytopenia improves and these children can have a near normal life
  - Enzyme replacement therapy is costly so funds are required to manage it
- Supportive care
  - These children require regular blood transfusion
  - Treatment of infections
  - For bleeding, give platelets
- Hematopoietic stem cell transplantation plays a potential role

Diseases for which Enzyme Replacement therapy is available

- Gaucher disease
- Type II glycogen storage disorder/Pompe disease
- Mucopolysaccharidosis Type I (Hurler disease), Type II (Hunter disease) and Type VI (Maroteaux-Lamy syndrome)
- Fabry disease
- Niemann Pick disease (Recently available)
- Morquio disease

Niemann Pick disease

00:09:25

- There are 3 types of Niemann Pick disease
- Type A and B results from deficiency of enzyme acid sphingomyelinase for which gene is encoded on chr. 11
- It has autosomal recessive inheritance

Type A Niemann Pick disease

- It is rapidly progressive neurodegenerative disorder
- Clinical features: Hepatosplenomegaly, Lymphadenopathy, and death usually by 3 years of age

Type B Niemann Pick disease

- It is a non-neuronopathic form
- This form can be seen in children as well as adults
- Hepatosplenomegaly is usually seen
- Cherry red spot is present

- Chest X-ray shows pulmonary infiltrates in the form of diffuse reticular opacities

Type C Niemann Pick disease

- It is a neuronopathic disorder where neurological features are seen that results from defective cholesterol transport
- It often presents with prolonged neonatal jaundice
- Recently enzyme replacement therapy for Niemann pick disease is available

GM1 gangliosidosis 00:12:47

- It is an autosomal recessive disorder
- It is due to deficiency of enzyme β-galactosidase
- As a result, GM1 ganglioside accumulates in various cells of the body including neurological system
- It can have infantile/juvenile/adult presentation
- Infantile type is the most severe type with onset before 6 months and death in the early childhood
- It can also present with hydrops fetalis
- Clinical presentation: Splenohepatomegaly, bony manifestations, neuro regression, cherry red spot, and death in early childhood

Tay Sach disease 00:14:23

- It is due to deficiency of enzyme Hexosaminidase
- It is a neurodegenerative disorder with progressive CNS dysfunction
- The most common and most severe form of Tay Sach disease is infantile
- Clinical presentation: Reduced vision, exaggerated startle, neuroregression, seizures and death usually occur in early childhood
- Splenomegaly is usually not present in Tay Sach disease
- It has an autosomal recessive inheritance

Mucopolysaccharidosis (MPS) 00:15:48

Refer Table 37.2

Clinical features of Hurler disease

- Child with coarse facies i.e., puffy looking facies, periorbital puffiness, depressed nose bridge, prominent philtrum, protruding tongue
- Intellectual disability/mental retardation
- Corneal clouding
- Hepatosplenomegaly
- Copious nasal discharge, airway problems
- Bony abnormalities: Dysostosis multiplex - proximal tapering of metacarpals or bullet shaped metacarpals, anterior beaking of the vertebral body, J shaped Sella turcica
- Cardiac abnormalities

Clinical features of other Mucopolysaccharidosis

Refer Table 37.3

Inheritance pattern

- All type of MPS have autosomal recessive inheritance except Type II MPS (Hurler disease) which has X-linked recessive inheritance
- Most of the lysosomal storage disorders have autosomal recessive inheritance except Fabry disease which has X-linked recessive inheritance

Fabry disease 00:23:30

- Basic defect: Deficiency of enzyme α-Galactosidase
- It has X-linked recessive inheritance
- Most characteristic clinical feature: Angiokeratoma - reddish pinpoint spots which are non-blanching and present mainly on bathing trunk area i.e., it is present between umbilicus and knees most densely
- Other clinical feature:
  - Hyperhidrosis or excessive sweating
  - Corneal or lenticular opacities
  - Acroparaesthesias
  - Pain which is severe and debilitating due to involvement of nerves
  - Vascular disease of brain/heart/kidney develops
- Enzyme replacement therapy is now available for Fabry disease

Miscellaneous/Other Inborn Errors of Metabolism 00:25:56

Lesch Nyhan syndrome

- Basic defect: Deficiency of HGPRT (Hypoxanthine Guanine Phospho Ribosyl Transferase) enzyme
- This enzyme helps in recycling of the building blocks of DNA and RNA
- It has an X-linked recessive inheritance

Clinical features

- It can be asymptomatic at birth
- Subsequently, Developmental delay and other neurological features like dystonia, dysarthria, and spasticity
- Self-Injury/Self-Mutilation

Diagnosis

- Increased level of uric acid, due to excess turn over of purine, pyrimidine, DNA, RNA
- There is deficiency of HGPRT enzyme

Treatment

- Because uric acid levels are very high use
  - Allopurinol
  - Alkalinization

- High fluid intake

Menke Disease

00:28:58

- It is caused by mutation in ATP 7A gene
- Mutation in ATP 7B gene cause Wilson disease
- ATP 7A gene is a gene encoding copper transporting ATPase
- So, there is impaired copper metabolism and less copper levels are found in liver and brain but high copper levels are found in fibroblasts and enterocytes

Clinical features

- Progressive cerebral degeneration or neurodegeneration
- Seizures
- Feeding difficulties
- Failure to thrive
- Hypothermia
- Apnea
- Characteristic hair abnormalities: Woolly or fuzzy hair
  - On hair microscopy: Trichorrhexis nodosa i.e., breakages in the hair shaft
    → Pilli torti i.e., twisting of hairs at different places
- It has poor prognosis and in classical form of disease, death usually occurs by 3 years of age

Wolman Disease

00:32:09

- Basic defect: It is an autosomal recessive disorder

Mutation in LIPA gene

↓

Deficiency of lysosomal acid lipase

↓

Accumulation of triglycerides and cholesterol esters in various cells

Clinical features

- Hepatosplenomegaly
- Jaundice
- Vomiting
- Diarrhoea

Diagnosis

- Plain X-ray abdomen: Bilateral adrenal gland calcifications is seen

Table 37.1

Disease	Cherry red spot	Visceromegaly	Skeletal involvement
Gaucher disease	Absent	Present	Present
Niemann Pick disease	Present	Present	Absent
GM_1 gangliosidosis	Present	Present	Present
Tay Sach disease	Present	Absent	Absent

Table 37.2

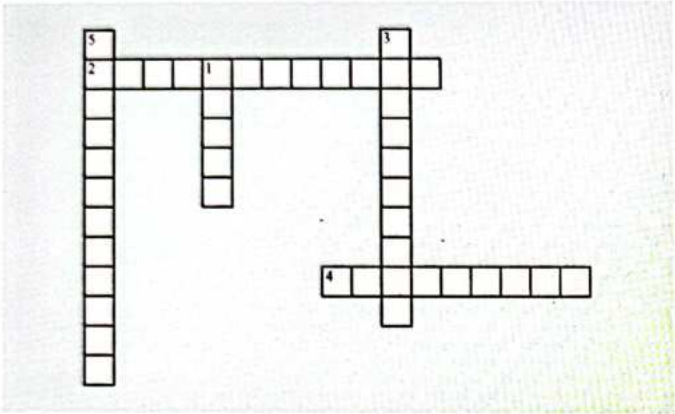
Type	Name	Enzyme deficient
I	Hurler disease(more severe)/Scheie disease (milder severe)	α-L-Iduronidase
II	Hunter disease	Iduronate Sulfate sulfatase
III	Sanfilippo disease	Heparin-S-Sulfamidase
IV	Morquio disease	N-acetyl-galactosamine Sulfate Sulfatase
VI	Maroteaux-Lamy disease	Aryl Sulfatase B

Table 37.3

Disease	Clinical features
Hunter disease	Same clinical features as Hurler disease but there is no corneal opacity
San Filippo disease	Mainly presents with Intellectual disability/mental retardation, behavioural problems
Morquio disease	Bony abnormalities are most prominent
Maroteaux-Lamy disease	Same as Morquio disease + Coarse facies + Visceromegaly

CROSS WORD PUZZLES

Crossword Puzzle



Across

2. _____is an Autosomal recessive disease due to the deficiency of Homogentisic acid Oxidase.
4. Which is the most common glycogen Storage disease in children ?

Down

1. Which disease is caused due to the deficiency of the enzyme "Acid Maltase or α-1.4 Glucosidase"?
3. TOC for Tynosinemia ?
5. _____is an autosomal recessive condition with GALT & Galactokinase deficiencies.

princeeeekum@gmail.com
9928609733

38 PRIMARY IMMUNODEFICIENCY

Primary Immunodeficiency

Definition

- A group of disorders characterized by impaired ability to produce a normal immune response

When to suspect

- Infections occurring at
  - Unusual sites e.g. liver, brain
  - Unusual pathogens e.g. Pneumocystis jiroveci, Burkholderia
  - Unusual severity

Types 00:02:33

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

1. Primary Antibody Defects 00:02:43

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

Bruton's Disease / X-Linked Agammaglobulinemia (XLA) 00:04:25

Defect

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

  ↓

  Pre B-Cells cannot deliver signals

  ↓

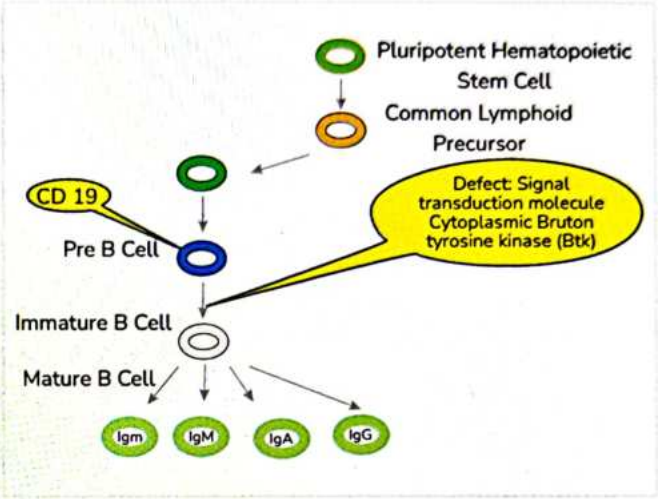
  Maturation stops at this stage

Clinical Features

- Usually present at 6-18 months of age
- More common in males
- Tonsils & adenoids absent
- Lymph nodes not palpable

Diagnosis 00:07:19

- Decreased B cells, T cells are normal
- Plasma cells absent
- Low Ig levels
- Germinal centers of LN underdeveloped



CVID (Common Variable Immune Deficiency) 00:08:04

Defect

- Inability of B cells to differentiate into plasma cells due to defect in-
  - BAFF (B cells Activation Factor for TNF-R)
    → BAFF helps in survival & differentiation of B cells
  - ICOS (Inducible co-stimulator)
    → Helps in T cell activation & interaction of T & B cells

Diagnosis

- Hypogammaglobulinemia with normal B cells
- Lymph Nodes may be normal or enlarged

Complications

- Increased risk of B cell lymphomas, autoimmune diseases

Selective IGA Deficiency 00:11:22

- **Most common type of immune deficiency:** Selective IgA deficiency
- **Defect**: Impaired differentiation of naive B cells into IgA producing plasma cells.
- **Clinical features**: Increased sinopulmonary infections.
- **Diagnosis:** Decreased IgA levels
- **Complications:** Increased risk of malignancy & autoimmune diseases.

Hyper IGM Syndrome 00:13:25

- Inability of B cells to class switch to IgG, IgA & IgE antibodies
- Can be AR or X Linked recessive
- Loss of function of CD40 on B cells

- Due to Loss of AID (Activation Induced Cytidine Deaminase) required for class switching

Diagnosis
- Low IgG, IgA and IgE
- High IgM

IgG Subclass Deficiency 00:15:45
- Normal total serum IgG but decreased levels of 1 of the subclasses
- Most common subtypes in children is IgG_2 deficiency while in adults in IgG3 deficiency

2. Cellular & Combined Immunodeficiency Defect 00:16:42
- SCID
- Hyper IgE syndrome
- Wiskott Aldrich syndrome
- Ataxia telangiectasia
- Di George syndrome

Severe Combined Immunodeficiency 00:17:31
Defect
- **X linked:** Cytokine receptor gamma chain defect
  - IL7 defect: T cell affected
  - IL15 defect: NK cell affected
- **Autosomal Recessive**
  - ADA deficiency: Loss of common lymphoid precursors of B & T cells due to accumulation of deoxyadenosine-toxic to immature lymphocytes
  - JAK-3 defect
  - IL-7 receptor defect

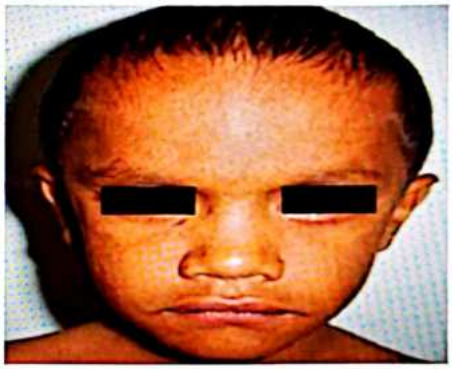
Clinical features
- Presents in 1st few months of life
- Recurrent/ persistent diarrhea, pneumonia, otitis media, sepsis.
- Persistent mucocutaneous candidiasis
- Live vaccine organism (BCG, OPV, Rota) can cause severe/ fatal infections

Diagnosis
- Absolute lymphocyte count < 2500/mm^3
- T cells make up < 20% of total lymphocytes
- ↓ Antibody levels
- Lymph node: Depleted T&B cells zones
- Thymus: small, devoid of lymphoid cells
- **Confirmation:** Identification of specific gene defect

Treatment
- HSCT
- Gene therapy
- PEG-ADA for ADA deficient SCID

Hyper IgE Syndrome (Job Syndrome) 00:23:44
- Mutation in stat 3 gene: IL-17 deficiency
- AD inheritance

Clinical Features
- Characteristic facies
  - Coarse face
  - Prominent forehead
  - Deep set eyes
  - Broad nasal bridge
  - Fleshy nasal tip
  - Hemihypertrophy
- Recurrent abscesses: Skin/ lungs
  - Most common: Staph aureus > Candida albicans



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

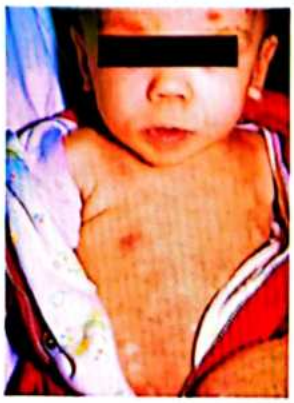
Wiskott Aldrich Syndrome 00:26:50
- X linked
- Defect in WASP gene (Chromosome X p II)

↓

Links membrane receptor to cytoskeletal proteins

↓

Defect leads to defective cell migration & signal transduction



Clinical Features

- Eczema
- Recurrent infections
- Thrombocytopenia with small platelets

} Triad

Diagnosis

- Platelets: Small & decreased in number
- IgM: Low
- IgE& IgA: ElevAted

Ataxia Telangiectasia

00:29:42

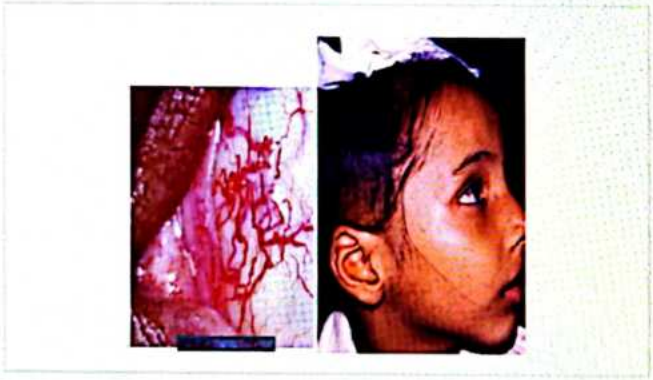
- Due to defect in ATM gene (chromosome 11q), which is a sensor of DNA damage

↓

Defective DNA repair & abnormal V, D, J recombination

↓

Abnormal isotype switching & Increased cancer risk



Clinical features

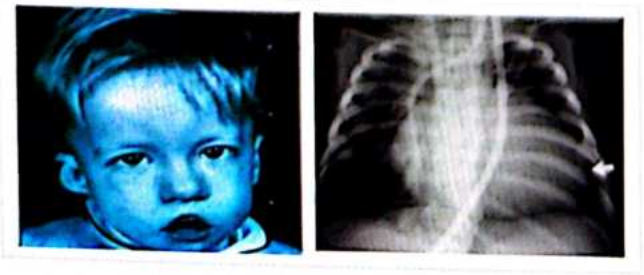
- Ataxia
- Oculocutaneous telangiectasia
- Immunodeficiency: Recurrent infections
- Increased sensitivity to ionizing radiation & defect. DNA repair
- Increased risk of lymphocytic malignancies & adenocarcinoma

Diagnosis

- Low IgA, IgE and IgG2 levels

Digeorge Syndrome (Velo Cardiofacial Syndrome)

00:33:24



- Chromosome 22q11 microdeletion → Failure of development of 3rd & 4th pharyngeal pouches.

↓

a. Hypoplasia of Thymus: Decreased T cells.
b. Parathyroid Hypoplasia: Hypocalcemia
c. Ultimo-branchial body: Defect in heart & great vessels

'CATCH–22

22q11 deletion

- C - Cardiac Anomaly
- A - Abnormal face (Hypertelorism, antimongoloid slant, Short philtrum, mandibular hypoplasia)
- T- Thymic hypoplasia
- C- Cleft palate
- H- Hypocalcemia

Diagnosis

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

3. Phagocyte Dysfunction

00:38:01

- Chronic Granulomatous Disease (CGD)
- Leukocyte Adhesion Defect (LAD)
- Chediak Higashi Syndrome

Chronic Granulomatous Disease (CGD)

00:38:13

- X linked or AR
- Mutation in genes involving NADPH oxidase

Clinical features

- Recurrent infections with catalase positive organisms like staph aureus, Serratia marcescens.
- Granuloma Formation is a hallmark
  - Can cause pyloric outlet or bladder outlet or ureteric obstruction.
  - Intestinal granulomas resembles Crohns Disease

Diagnosis

- NBT (Nitro blue Tetrazolium Test)
- Flow cytometry using Dihydrorhodamine: Definitive test

Leukocyte Adhesion Deficiency (LAD)

00:41:32

Disease	Deficiency	Defect
LAD I	• Beta 2 integrin family is deficient or defective	• Integrins: Adhesion of leukocytes to endothelium (CD 11) and β (CD1B) chain
LAD II	• Fucosylated carbohydrate ligands for selectins [sialyl lewis x] are absent	• Selectins: Cellular margination and rolling

Clinical features

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

Investigations

- Neutrophilic leukocytosis (TLC>25000/mm^3)
- LAD1: Absence of CD11& CD 18 by flow cytometry
- LAD2: Lack of Sialyl Lewis X

Chediak Higashi Syndrome 00:45:28

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

↓

Uncontrolled fusion of Lysosomes with each other

↓

Giant Granules

- Melanosomes are oversized

Delivery to keratinocytes & hair follicles is compromised

↓

Hypopigmented hairs

Clinical features

- light skin & Silvery hair
- Frequent infections
- Neuropathy, ataxia
- Impaired platelet aggregation
  - Due to deficiency of dense granules containing ADP and serotonin
  - Prolonged BT with normal Platelet count but platelet function is affected.

On Investigation

- Progressive neutropenia & abnormal platelets, neutrophils & NK cells function.
- Large inclusions in all nucleated cells (with wright/ peroxidase stains) in peripheral smear & BM

Treatment

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

Complication

- HLH (Hemophagocytic Lympho-histiocytosis)

PREVIOUS YEAR QUESTIONS

Q. All of the following are true for selective IgA deficiency EXCEPT? (JIPMER Dec 2019)

A. Can occur due to phenytoin administration

B. Intestinal giardiasis is rare

C. IgG2 subclass deficiency

D. Antibodies to IgA may occur

Q. Which of the following primary immunodeficiency present during the neonatal period? (JIPMER Dec 2019)

A. Hyper IgE syndrome

B. Chronic granulomatous Disease

C. Leukocyte adhesion defect

D. Ataxia telangiectasia

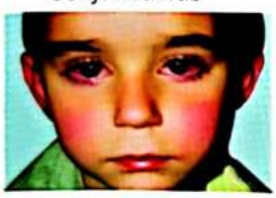
39 VASCULITIC DISORDERS IN CHILDREN

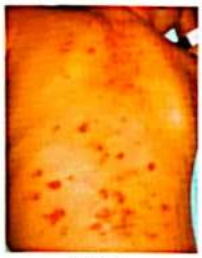
Henoch Schonlein Purpura (HSP) 00:00:03

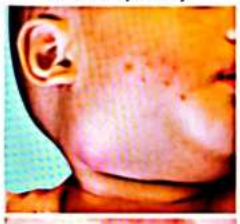
- Palpable purpura with presence of 1 or more of
  - Diffuse abdominal pain
  - Arthritis or arthralgia
  - Any biopsy showing IgA deposition
    → Renal Involvement: Glomerulonephritis is seen in 1/3 of patients
  - Thrombocytopenia Absent

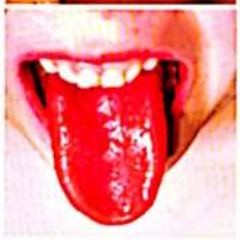
Treatment

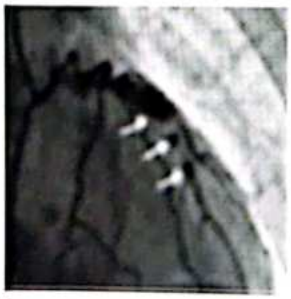
- Most of the cases are self-limiting
- Severe cases - corticosteroids











Kawasaki Disease 00:03:32

Diagnostic Criteria

- Fever for > 5 days with any 4 out of 5- "CREAM" features
- **C** - B/L non-purulent Conjunctivitis
- **R** - Rash involving trunk
- **E** - Erythema & Edema of palms & soles along with desquamation
- **A** - Adenopathy (Unilateral, cervical)
- **M** - **Mucositis** (Strawberry Tongue)

Investigations

- No diagnostic test
- Leukocytosis, thrombocytosis, elevated ESR or CRP
- Coronary artery aneurysm (Giant > 8mm in diameter) is an important complication but the incidence has decreased due to early diagnosis and treatment.

Important Information

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

Treatment

- IVIg: As soon as diagnosis is made to prevent complications.
- Aspirin: High dose f/b low dose.
- Corticosteroids if persistent fever despite IvIg.

Juvenile Dermatomyositis (JDMS) 08:00:00

- MC Inflammatory myositis in children
- Proximal muscle weakness +characteristic rash

Diagnostic Criteria of IDMS

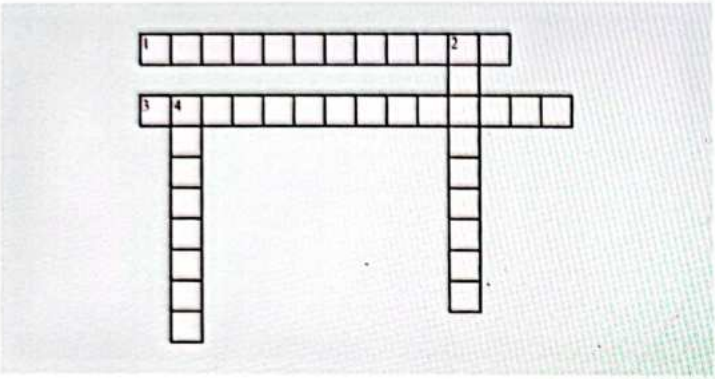
- Classical rash (Heliotrope rash and Gottoron papules) + 3 out of the following
  - Weakness symmetric, proximal muscles
  - Elevated muscle enzymes - CPK, SGOT, IDH
  - EMG changes- Fibrillation, sharp waves
  - Muscle biopsy - Necrosis, inflammation

Treatment of IDMS

- Steroids
- Weekly Methotrexate

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. _____is the most common type of immune deficiency.
3. _____syndrome is an autosomal recessive condition due to the Mutation " Lyst Gene" on chromosome 1q

Down

2. _____formation is a hallmark of chronic Granulomatous disease.
4. Which syndrome is caused as a result of the loss of activation induced cytidine Deaminase required for class switching?

40 IMPORTANT VIRAL DISEASES IN CHILDREN

Measles 00:00:09

- Measles is caused by measles virus (RNA virus) belonging to family Paramyxoviridae
- Incubation period: 8-12 days
- It remains communicable from 3 days before to 4-6 days after the onset of rash
- Receptor for measles virus: CD 150 and PVRL 4
- Pathognomonic pathological feature: Presence of multinucleate Warthin Finkel Dey giant cells

Clinical features

- Prodromal phase (Child has wet kind of look): Fever, conjunctivitis, coryza
- Koplik spot (Reddish spots with white centre): It is present on inner side of cheek on the buccal mucosa
  - It can also be present in conjunctiva and vaginal mucosa
- Rash of measles typically begins from behind the ear and then spreads to the rest of the body
  - Rash is erythematous maculopapular rash which is confluent at places
  - Rash usually appears on day 4 of fever and rash fades in 7 days in same progression as it appears leaving behind a brownish discolouration
- Most common complication: Otitis media
- Most common cause of death: Pneumonia
  - After measles, cell mediated immunity of child decreases and child is prone to infections like respiratory infections, pneumonia, diarrhoea
  - So, Vitamin A is often used in treatment of measles, it helps in mucosal immunity
- Rare, fatal, long term complication: SSPE (Subacute Sclerosing Pan Encephalitis)

SSPE (Subacute Sclerosing Pan Encephalitis)

- It is rare, fatal, long term complication of measles
- It develops 7-13 years after 1° measles infection
- Initially it is characterised by decreasing school performance, then there is appearance of myoclonic jerks, sudden falls, choreoathetosis, dystonia and rigidity
- It is a neurodegenerative disorder with progressive downhill course
- No good treatment is available till date
- Diagnosis: CSF and Blood anti-measles antibody is done

Rubella (German Measles) 00:05:31

- It is a mild exanthematous illness caused by Rubella virus (RNA) belonging to Togaviridae family
- Incubation period: 14-21 days
- It becomes communicable from 5 days before to 6 days after the onset of rash

Clinical features

- Prodrome phase: Low grade fever, sore throat, malaise, and headache
- Rash begins on face and spread centrifugally
- Forcheimer spots on soft palate and uvula
- Posterior auricular lymphadenopathy
- Rubella is mild and self-limiting illness and usually it improves in 3-5 days.

Chicken Pox (Varicella) 00:07:42

- Chicken pox/Varicella is cause by varicella zoster virus (DNA virus) belonging to Herpesviridae family
- Incubation period: 10-21 days

Clinical feature

- There is fever along with rash which begins on first day of fever itself
  - Rash is pleomorphic i.e., presence of various kinds of lesions at the same time e.g., presence of papules, macules, vesicles, pustules all at same time
  - Child with varicella remains infective till all vesicles have crusted
- **Complications of varicella infection**
  - Secondary bacterial infections of the skin lesions
  - Purpura fulminans – Life threatening condition
  - Reye syndrome – There is hepatic dysfunction
  - Neurological complication: **STOMA**
    - → S - Stroke
    - → T - Transverse myelitis
    - → O - Optic neuritis
    - → M - Meningoencephalitis
    - → A - Ataxia

Erythema Infectiosum 00:10:30

- It is caused by Parvovirus B19
- Incubation period: 4-28 days

Clinical features

- Low grade fever, headache, malaise, upper respiratory tract infection
- **Characteristic feature:** "Slapped cheek" appearance of rash

Other diseases caused by Parvo virus

- Transient aplastic crisis: It can be caused spontaneously or in some children with underlying diseases like sickle cell

- Papular purpural gloves and socks syndrome: There is involvement of distal part of extremities

Hand Foot Mouth Disease (HFMD) 00:12:03

- Most common cause of HFMD is Coxsackie A16 virus

Clinical features

- Low grade fever
- Presence of blisters in the oral cavity
- Palmar/Plantar pustule
- It is a mild and self-limiting illness and resolves usually in 5-7 days

Roseola Infantum 00:12:56

- It is caused by HHV (Human Herpes virus) 6A or 6B
- It is a condition where Nagayama spots may be seen
- Characteristic feature: High grade fever and rash appears when the fever subsides

Mumps 00:13:41

- It is a viral infection where there is acute onset unilateral or bilateral parotid swelling along with fever
- Most common complication: Aseptic meningitis
- It is a very infectious disease so various children in the same locality suffer from mumps at the same time
- In adolescent male with mumps, orchitis may be seen
- It is a self-limiting illness and no specific treatment is required

Poliomyelitis 00:14:55

- It is caused by polio virus (RNA virus) belonging to Picornaviridae family
- There are 3 distinct serotypes: P_1, P_2, P_3

Clinical features

- 90-95% cases of polio are mild and inapparent and they give a protective immunity
- In 5% cases, non-paralytic flu like illness is seen
- In < 1% cases, there is paralytic poliomyelitis

HIV in children 00:16:33

- Perinatal treatment has decreased the parent to child transmission of HIV to < 2%
- Caesarean section is no longer recommended just for prevention of parent to child transmission, it is done only if an obstetrics indication is present.

- **Diagnosis of HIV in infants and children**
  - In infants or neonates investigations that can be done are
    - → HIV RNA PCR
    - → HIV DNA PCR
    - → HIV culture
    - → There is no role of antibody testing
    - → Test for parents HIV status
  - In breast fed babies, retesting should be done at least 12 weeks after stopping breast feeding
  - In older children > 18 months of age, antibody demonstration by ELISA/Western blot test can be done
  - A positive test needs to be confirmed at least twice
- **Prophylaxis for infant born to mother with HIV**
  - Nevirapine +/- Zidovudine given for at least 6 weeks, for breast fed child it is given for at least 12 weeks
  - If safe, sustainable replacement feeding is available, avoid breastfeeding
  - In low resource setting, exclusive breast feeding is recommended as benefits of breastfeeding far outweighs the risks
- **Treatment of HIV in children**
  - ART (Anti-retroviral therapy) should be given to all children with HIV irrespective of their WHO clinical stage or CD4 count
  - If it cannot be given to all children then high priority groups are
    - → Children < 2 years of age
    - → WHO Stage 3 or 4
    - → Children < 5 years of age with CD4 count < 25% or < 750/mm^3
  - Cotrimoxazole prophylaxis against for pneumocystis carinii or pneumocystis jirovecii infection should be given for all children with HIV

Age	Preferred 1st line treatment
Infants < 2 weeks of age	Zidovudine + Lamivudine + Nevirapine
Children < 3 years of age	Abacavir/Zidovudine + Lamivudine + Lopinavir/Ritonavir
3-10 years of age	Abacavir + Lamivudine + Efavirenz
Adolescents	Tenofovir + Lamivudine + Efavirenz

H_1N_1 infection 00:24:08

- It is a viral infection by influenza virus
- Drug of choice: Oseltamivir

Refer Table 40.1

- It is given twice daily for 5 days for treatment and for prophylaxis it is given once a day

Table 40.1

Age	Dose of oseltamivir
Infants	3mg/kg/dose
< 15 kg	30 mg/dose
15-23 kg	45 mg/dose
24-40 kg	60 mg/dose
>40 kg	75 mg/dose

41 COVID-19 IN CHILDREN

Covid-19 in Children

1. Caused by: 00:00:36

a. SARS-CoV2 (Severe Acute Resp. syndrome - corona virus 2): Possibly originated in bats

b. Pandemic began in Wuhan, China in Dec 2019

2. Modes of Transmission 00:02:06

a. Direct inhalation of infected droplets produced during coughing/ sneezing by an infected person.

b. Contact with surfaces and fomites, soiled by infected respiratory secretions.

3. Incubation Period

- 2-14 days (Median IP: 5 days)

4. Clinical features 00:03:59

a. Similar to any acute resp. viral infection.

b. Fever, cough, breathlessness, sore throat, fatigue, malaise.

c. Nasal symptoms (e.g. coryza) are less common.

d. Children usually have milder symptoms as compared to adults who get infected.

e. Infants & younger children → more chances of severe manifestations.

f. Those with severe ds → usually develop complications like hypoxemia or hypoperfusion by the end of first week

g. Possible acute complications in children

→ ARDS
→ Myocarditis
→ Septic shock
→ DIC
→ AKI
→ Liver dysfunction

5. PIMS-TS 00:08:10

a. Paediatric Inflammatory Multisystem Syndrome, Temporally associated with SARS-Cov-2

b. It is a hyper inflammatory syndrome seen in some children (Due to immune injury mediated by antibody dependent enhancement response).

c. C/F

→ Persistent fever
→ Evidence of inflammation
→ Mucocutaneous changes (rash, conjunctivitis, periorbital edema)
→ Single/ Multi-organ dysfunction in the absence of any other known infections.
→ May deteriorate rapidly & child may need intensive care support.
→ May have RT PCR negative but Ab positive

6. Whom to suspect for infection with SARS CoV2? 00:13:32

a. In all hospitalized children with acute respiratory illness (Fever & cough and/or shortness of breath)

or

b. Asymptomatic, direct contacts of a lab confirmed case

7. Lab diagnosis: 00:14:56

a. Preferred sample

→ In Non intubated children: Upper resp. tract sample (nasopharyngeal & Oropharyngeal swabs) – transported in VTM (Viral Transport Media) on ice
→ Intubated patient: Bronchoalveolar Lavage (BAL) or endotracheal aspirate preferred.

b. Preferred diagnostic test → RT-PCR (Reverse Transcriptase Polymerase Chain Reaction)

8. Rx: 00:18:10

a. Mild illness (No resp. difficulty, feeding well and SpO_2 > 92%): Home based supportive care

→ Fever control using PCM
→ Ensure adequate hydration
→ Explain danger signs
→ Duration of isolation recommended → 14 days from symptoms onset or afebrile for 72 hrs whichever is later.

b. Moderate-severe illness: Hospitalization

h. Indications of hospitalization:

i. Resp. distress

→ SpO_2 < 92% on room air
→ Shock/ poor peripheral perfusion
→ Poor oral intake
→ Lethargy in neonates and infants
- Seizures/ encephalopathy

ii. Management in hospital

→ IV fluids
→ Symptomatic Rx
→ Antimicrobials in suspected septic shock
→ Respiratory support
- O_2
- HFNC (High Flow Nasal cannula)
- Mechanical ventilation (intubation using video Laryngoscope)

→ Hydroxychloroquine (In moderately severe cases)
→ Remdesivir
→ Tocilizumab (anti-IL6)
→ For PIMS-TS

- IVIg
- Steroids
- Immunomodulators.

42 IMPORTANT BACTERIAL DISEASES IN CHILDREN

Tuberculosis In Children

00:00:24

- MC age group in children: < 5 years
- MC form of TB in children: Pulmonary TB
- MC extrapulmonary form of TB in children: Tubercular lymphadenitis
- Primary TB: Ghon's focus seen in lungs
- Diagnosis
  - History of contact with TB patient
  - Clinical features: Low-grade fever, constitutional symptoms, area specific features
  - Demonstrate bacteriological evidence for TB from sputum/ gastric aspirate/ BAL
    - → CBNAAT (cartridge based nucleic acid amplification test)
    - → Microscopy
  - A positive tuberculin skin test / Mantoux test is defined as an induration > 10 mm, measured 48-72 hrs after intradermal injection with tuberculin 2 TU
    - → No role in Dx
  - Serological tests (IgM, IgG, IgA against MTB antigens)

Important Information

- BCG test and IGRAs have no role in diagnosis of TB

- Recent updates in treatment of TB in children

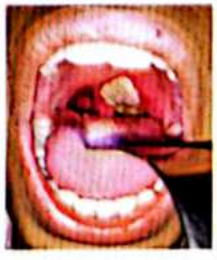
First line regimen		
Type of TB case	Treatment regimen in IP	Treatment regimen in CP
New	(2) HRZE	(4) HRE
Previously treated	(2) HRZE	(4) HRE

  - Treatment is same for both.
  - Only pyrazinamide is stopped in CP.
  - Daily treatment is given for all pediatric patients.
  - Drug sensitivity testing for atleast rifampicin should be conducted in previously treated patients.
  - Don't wait for DST results to start the treatment.
  - Daily Doses of
    - → Rifampicin: 15 mg/kg (max 600 mg/day)
    - → Isoniazid: 10 mg/kg (max 300 mg/day)
    - → Ethambutol: 20 mg/kg (max 1500 mg/day)
    - → Pyrazinamide: 30-35 mg/kg (max 2000 mg/day
  - Steroids are added in severe cases.
  - Prednisolone 1mg/Kg/Day, Tapered Over 6-8 wks
- **Indications**
  - Tuberculous meningitis
  - Pericarditis & pericardial effusion
  - Massive Pleural Effusion
  - INH prophylaxis is recommended for children less than 5 years of age who have H/o contact with active TB patient after ruling out disease in them.

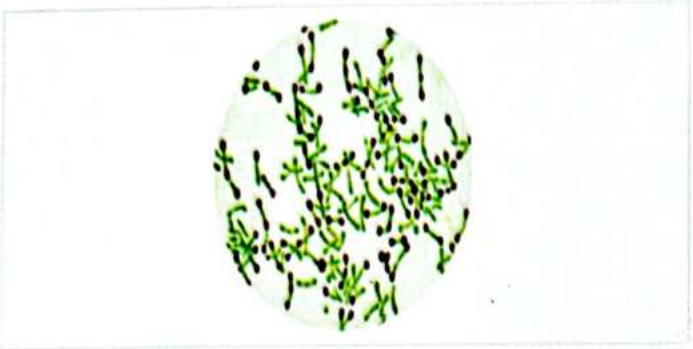
Diphtheria

00:11:50

- Acute toxic infection caused by Corynebacterium diphtheriae
- Incubation period: 2-4 Days
- Clinical features
  - Universal early symptom: Sore throat
  - Fever (only in 50%), malaise, headache
  - Dysphagia, hoarseness
  - Stridor & croupy cough
- O/E: A dense necrotic coagulum of organisms, epithelial cells, fibrin, WBCs & RBCs forms and advances to become a gray-brown, leather like adherent pseudomembrane.
- Pseudo membrane can extend to uvula, soft palate, posterior oropharynx or glottic areas
- Effects of diptheritic toxin
  1. Local effects
     - → Paralysis of palate & hypopharynx
  2. Systemic effects
     - → ATN
     - → Cardiac involvement
     - → Thrombocytopenia
     - → Demyelination of nerves



- **Diagnosis**
  - Sample: A portion of membrane along with underlying exudate
  - Stained using Albert stain or specific fluorescent antibody
  - Culture & antimicrobial susceptibility tests



- **Treatment**
  - Specific antitoxin (as soon as possible) is the mainstay of therapy
  - Antibiotic therapy is not a substitute for antitoxin (penicillin/ erythromycin/ clindamycin/ rifampicin/ tetracycline
    → To Halt toxin production
    → To Treat localized infection
    → Prevents transmission
- Management of Contacts of a Child with Diptheria

A. Isolation and monitoring
- All the household contacts and persons who had intimate respiratory or physical contact with patient, should be closely monitored for the illness for atleast 7 days.
- Cultures from any lesions appearing on nose, throat or skin should be sent for diagnosis.

B. Chemoprophylaxis
- Should be given regardless of the immunization status of contacts.
- Single dose of inj. Benzathine penicillin G (6 lakh units IM for < 6 years age and 12 lakh units IM for > 6 years age)
- Erythromycin (40-50mg/kg/day) in 4 divided doses for 10 days is an alternate.
- Azithromycin is an another alternate.

C. Vaccination
- Given to immunized individuals who have not received a booster dose in last 5 years.
- Children who have not received their 4th dose of diphtheria containing vaccine should be vaccinated.
- Those who have received < 3 doses of diphtheria toxoid or have uncertain immunization status are immunized with age appropriate diphtheria containing vaccine.

Important Information
- < 7 years : DPT
- > 7 years: Tdap

- Complications of Diphtheria 00:31:48

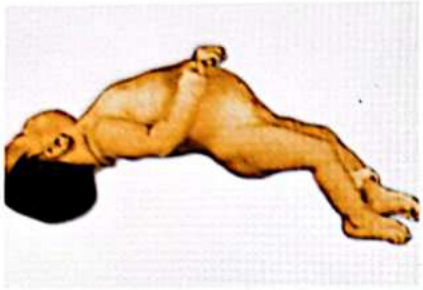
Cardiac	Neurological
• Toxic cardiomyopathy o Seen in 10-25% patients. o Causes = >/ 50% deaths. o 1st evidence: disproportionate tachycardia to degree of fever o Prolonged PR interval and ST-T changes	• Paralysis of soft palate (in 2-3 weeks of Onset of illness) • Weakness of posterior pharyngeal, laryngeal and facial nerves (nasal intonation of voice) • Oculomotor and ciliary paralysis (in 5 weeks of illness) • Symmetric polyneuropathy (within 10 days- 3 months of illness) o Distal weakness and Decreased DTRs.

Pertussis 00:31:48
- Caused by Bordetella pertussis or B. Parapertussis
- 3 Stages
  - Catarrhal stage (1-2 wk): Rhinorrhea, lacrimation.
  - Paroxysmal stage (2-6 wk): Dry, uninterrupted paroxysmal, hacking cough with inspiratory whoop.
  - Convalescent stage (>6 wk): The number, severity, and duration of episodes diminish.
- Attack rate is as high as 100% in susceptible individuals
- Investigations
  - Leukocytosis (15000-100000 / ML) (absolute lymphocytosis)
  - Confirmation by culture/PCR/serology.
- Treatment
  - Macrolides (Azithromycin/erythromycin)
- Complications
  - Apnea
  - Otitis media
  - Pneumonia
  - Sequelae of forceful coughing

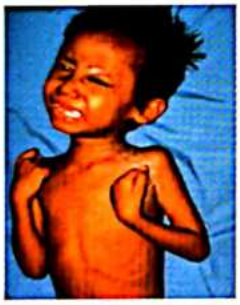
Tetanus 00:35:38
- An acute, spastic paralysis, caused by neurotoxin of clostridium tetani. (a motile, gram +ve, spore forming anaerobe).
- 2 Types
  1. Neonatal Cases: babies born to unimmunized mothers and with unhygienic delivery

2. Non-neonatal cases: a/w penetrating injury with dirty object or unsterile injection or otogenic infection

- Incubation Period: 2-14 days
- Clinical features
  - Neonatal Tetanus
    - → Manifests within 3-12 days of birth
    - → Progressive difficulty in sucking & swallowing
    - → Irritability, excessive crying
    - → Paralysis, stiffness & rigidity, spasm without opisthotonus



  - Generalised Tetanus
    - → MC presenting symptom: Trismus or Locked Jaw d/t masseter muscle spasm
    - → Headache, restlessness & irritability
    - → Stiffness, difficulty chewing, dysphagia
    - → Risus sardonicus (typical facial grin)
    - → Opisthotonus (arched posture)

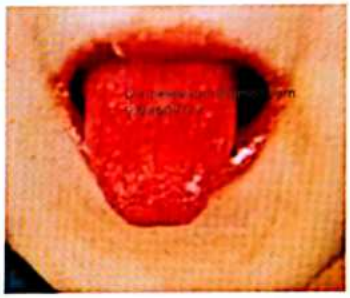


- **Treatment**
  - Eradication of C. tetani & anaerobic wound environment.
  - Surgical wound debridement if required.
  - Tetanus Ig to neutralize the toxin
  - Control of seizures: antiepileptics
  - Penicillin G → antibiotic of choice
  - Metronidazole, erythromycin or tetracycline for penicillin-allergic patient
  - All patients with generalized tetanus need muscle relaxants (Diazepam)

Scarlet Fever

00:42:45

- Caused by Group A Streptococcus
- Pharyngitis & strawberry tongue
- Erythematous rash
- Kawasaki disease is a close differential Diagnosis of strawberry tongue
- Identification of GAS in the pharynx-confirms Diagnosis



43 CONGENITAL INFECTIONS

Congenital Toxoplasmosis 00:00:09

- Congenital toxoplasmosis is seen in a baby if a mother acquires primary toxoplasma infection during pregnancy
- Risk of fetal infection increases with each trimester

Trimester	Risk of infection
1st trimester	15%
2nd trimester	25%
3rd trimester	60%

- Severity of fetal infection is greater is fetus is affected earlier in pregnancy

Clinical features

- **Mnemonic: CHC**
  - Chorioretinitis
  - Hydrocephalus
  - Cerebral calcification (Detection on Non contrast CT head)

Other features

- Small for gestational age
- Prematurity
- Hydrops fetalis i.e., generalised anasarca
- Persistence jaundice
- Thrombocytopenia
- Congenital infections in baby are mostly caused by TORCH group of organisms
- T in TORCH is for Toxoplasmosis

Prevention

- Early diagnosis of infection and treatment of mother
- Treatment of mothers is by sulphadiazine's

Congenital TB 00:03:23

- In congenital TB, primary/ghon focus is in liver
- In tuberculosis occurring in children or older individuals primary focus is usually in lungs

Clinical features

- Hepatomegaly
- Conjugated hyperbilirubinemia
- Pulmonary involvement may or may not be present
- Disseminated tuberculosis in severe cases
- Most common mode of infection to baby is through mother
  - Postnatally: Aerosol mediated

Congenital Syphilis 00:04:31

- Organism causing syphilis infection: Treponema pallidum
- Modes of transmission
  - Transplacental transmission during pregnancy
  - During birth by contact with infectious lesions
- Transmission during early pregnancy can lead to
  - Still birth
  - Fetal loss
  - Low birth weight
  - Neonatal death
  - Prematurity

Early signs of congenital syphilis

- Hepatosplenomegaly
- Jaundice
- Diffused lymphadenopathy
- Painful lesions like osteochondritis & periostitis can lead to pseudoparalysis
- Skin lesions: Mucocutaneous erythematous maculopapular or vesiculobullous lesions (involving hand and feet) followed by desquamation (shedding/scaling)

Important Information

- Late signs of congenital syphilis: From head to toe
  - Olympian brow (prominent forehead)
  - Saddle nose
  - Hutchinson's triad
    - → Hutchinson's teeth (notched incisors)
    - → Interstitial keratitis
    - → Sensory neural deafness
  - Rhagades: Spoke like lesion/moving out scars
  - Higoumenakis' sign i.e., thickening of the medial 1/3rd or sternal end of clavicle
  - Clutton joints involving knee (painless)
  - Sabre shins i.e., anterior bowing of tibia

Prevention

- Prenatal screening for syphilis by VDRL test for every woman
- Screening for lesions
- Untreated cases have ~ 100% risk of transmission

Congenital Rubella 00:11:14

- Risk of transmission of infection and frequency of congenital infection is earliest before 11 weeks of gestation

Important Information

- Clinical features: CDC
  - Congenital bilateral cataract
  - Deafness (Sensory neural hearing loss)
  - Congenital heart diseases
    - → Most common: PDA (Patent Ductus Arteriosus)
    - → Least common: ASD (Atrial Septal Defect)
    - → Others like VSD, pulmonary stenosis

Other clinical features

- Microcephaly, IUGR
- Glaucoma, Salt and pepper retinopathy
- Hepatosplenomegaly
- Jaundice
- Thrombocytopenia
- Blueberry muffin lesion: Bluish red nodular lesions is a characteristic of congenital rubella

Congenital CMV Infection 00:13:53

- 90% of infected babies with CMV (Cytomegalovirus) are asymptomatic
- There is no use of routine screening

In symptomatic infants clinical features are

- Microcephaly
- Chorioretinitis
- Hepatosplenomegaly
- Jaundice
- Petechiae
- Most important long term sequalae of congenital CMV infection: Sensory neural hearing loss
- Congenital CMV infection is one of the most common non syndromic causes of hearing loss

Diagnosis

- Demonstrate replicating virus in any type of samples from baby within first 3 weeks
  - PCR/Viral culture: Best sample - urine sample
    - → It can be done using saliva or blood sample
  - CMV IgM: It can also provide some indirect clue about whether the baby is infected or not

Treatment for symptomatic patients

- Ganciclovir

Congenital Varicella 00:16:12

- It is seen in 0.4% of babies of mothers who get infected in 1st trimester and 2% of those are infected in 2nd trimester

Clinical features

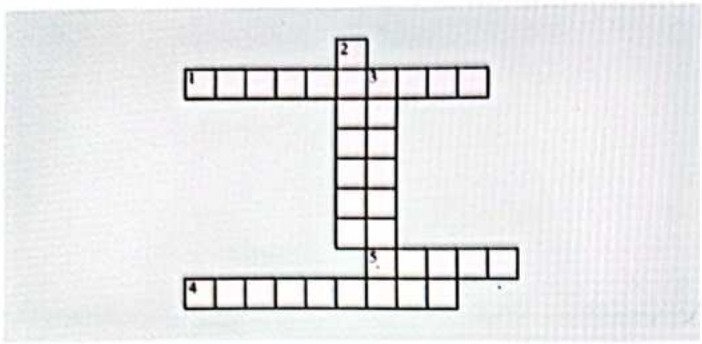
- Cicatricial scarring in zoster like or dermatomal distribution around umbilicus
- Limb hypoplasia
- Low birth weight
- CNS involvement: Microcephaly, developmental delay, intellectual disability, seizures
- Eye involvement: Chorioretinitis, cataract, microphthalmia (small eye)
- Renal involvement: Hydronephrosis
- Autonomic dysfunction: Swallowing dysfunction, neurogenic bladder

Diagnosis of congenital varicella infection

- If a mother has a history of varicella infection during pregnancy
- Suggestive clinical features in a baby
- Demonstrate Anti-varicella IgM in a baby

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. Which common disease in children has the following clinical feature: Pleomorphic Rashi Simultaneous presence of various types of skin lesions like papules, vesicles, pustules.
4. ___TB is the most common form of TB in children
5. Which infectious disease has "Aseptic meningitis" as the most common complication?

Down

2. 'Koplite spots' on inner cheeks, vaginal mucosa, conjunctiva is a clinical feature of which common communicable disease?
3. _____Spots are seen in Roseola infantum ?

princeeeekum@gmail.com
9928609733

44 IMMUNIZATION

General Concepts

00:00:17

General principles of Immunization

- Any number of vaccines (live or killed) can be given on the same day, maintaining a gap of at least 5 cm between the vaccination sites (to identify which vaccine have adverse effect)
- Inactivated or killed vaccine can be given at any time with respect to other vaccine
- 2 or more live vaccine can be given on the same day - if not, then a gap of at least 4 weeks should be there between them (so that immunogenicity of vaccine is not affected)

Latest National Immunization Schedule

At birth	OPV-0, BCG, Hep-B – birth dose
6 weeks	Penta -1, OPV-1, Rota-1, f-IPV, PCV-1
10 weeks	Penta-2, OPV-2, Rota-2
14 weeks	Penta-3, OPV-3, Rota -3, f-IPV-2, PCV - 2
9 months	MR-1, PCV booster, JE-1, Vit A-1, f-IPV-3
16-24 months	MR-2, DPT-booster, OPV-booster, JE-2, Vit A -2
2 years	Typhoid vaccine (not given in all states)
5-6 years	DPT booster
10-16 years	Td, Td

- OPV (Oral polio vaccine) – Given orally 2 drops
- BCG site – Left upper arm given intradermally

Important Information

- Hep-B: Given intramuscularly on anterolateral aspect of thigh
  - If mother is Hep-B positive, it helps in prevention of transmission of hepatitis B from mother to children
  - It is now recommended to be given along Vit K in the delivery room immediately after birth
  - Earlier the vaccine is given, the better protection it gives against transmission

- Pentavalent vaccine – Combination of 5 vaccines
  - DPT + Hep-B + Hib
- OPV is not given beyond 5 years of age

Additional Vaccines recommended by IAP (Indian Academy of Pediatrics)

- Hep-A
- Varicella
- HPV (Human Papilloma Virus) vaccine
- Typhoid vaccine: Given at 2 years of age
- **Fully immunized child:** A child who has received all vaccines recommended by NIS (National Immunization Schedule) till 1 year of age
  - Child should have received
    - → OPV + OPV-O – 3 doses
    - → Pentavalent - 3 doses
    - → Rotavirus - 3 doses
    - → f-IPV - 2 doses
    - → PCV - 3 doses
    - → BCG
    - → MR – 1 dose
    - → JE – 1 dose
    - → Hep B – birth dose
- **Completely immunized child:** A child who has received all vaccines recommended by NIS till 2 years of age
  - Vaccines given till 1 year of age +
    - → MR – 2nd dose
    - → DPT – booster
    - → OPV – booster
    - → JE – 2nd dose

Practical case scenarios

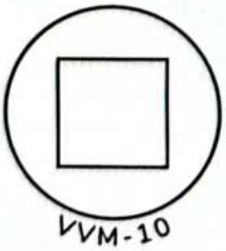
- **If a child has cough & cold on day of vaccination, what to do?**
  - Continue immunization as per schedule
  - Minor cough and cold is not a contraindication for vaccination
- **If a child vomits after OPV, what to do?**
  - If child has vomited immediately or within 30 minutes, repeat the dose
  - If vomiting occurs more than 30 minutes after OPV dose, no need to repeat the dose (as it is assumed that dose must have been absorbed through intestine)
- **If there is lapsed immunization, what to do?**
  - There is no need to restart the entire immunization schedule from beginning
  - Give all the vaccines due by that age but have not been received by the child
  - E.g., A baby received vaccines at due at 6 weeks and 10 weeks and then the baby did not come for vaccination at 14 weeks, baby came directly at 9 months for vaccination schedule, give all vaccination that are due but child has not yet received

→ So, at 9 months for that baby - MR + Vaccines due at 14 weeks of age i.e., Penta-3, OPV-3, Rota -3, f-IPV-2, PCV-2

- **If immunization is preponed e.g., if parents have to travel out of station and immunization is due on 16th of August but because they must travel, they took immunization on 9th of August, what to do?**
  - If immunization is preponed by 5 days or more, that dose is not counted and it must be repeated
  - But if it preponed by 2 or 3 days, no need to repeat the dose
- **If immunization status of child is unknown, what to do?**
  - Consider the child as **unvaccinated/unimmunized** appropriately
  - Vaccines that need to be given at 1st visit of an unimmunized child
    - → MR-1 (> 9 months age)
    - → BCG & Penta (if child is <1 year of age)
    - → OPV and Hib (if child is < 5 years of age but > 1 year of age)
    - → DPT (if child is < 7 years of age)
    - → dTap (first visit), followed by Td on 2nd and 3rd visit – for child > 7 years of age
- **Which vaccines should be given to an unimmunized child?**
  - Depends on the age at which the child has presented
- Vaccines contraindicated in egg allergy
  - When vaccines are cultured, egg yolk medium is used
  - Vaccines contraindicated are
    - → Influenza vaccine
    - → Yellow fever vaccine
- Vaccine that can cause thrombocytopenia – Measles vaccine
  - There is no significant association with autism spectrum disorder
- Strains included in meningococcal vaccine – A, C, Y, W-135
- Heat sensitive vaccine – OPV, reconstituted BCG, Measles vaccine princeeeekum@gmail.com 9928609733
- Light sensitive vaccine (Have dark/amber coloured vials/ampules)– BCG, Measles, Rotavirus, JE
- Freeze sensitive vaccine: T series vaccine - TT, DPT, Pentavalent Hep-B

Vaccine Vial Monitor (VVM) 00:20:38

- It is a heat sensitive label that indicates the cumulative heat exposure over time to that vaccine vial



- If colour of inside square is lighter than the outside circle – Use the vaccine if the expiry date has not passed
- Number written beside VVM like VVM-10 indicates the number of days that vaccine remains potent if kept at room temperature or 37°

- If the inside square colour is lighter than outside circle colour – Use vaccine, if the expiry date has not passed
- If colour of square is same as outside circle – Do not use the vaccine
- If colour of square is darker than the outside circle – Do not use vaccine
- Test done to check for cold damage to the vaccine due to freezing: Shake test

} These vaccines vial have sustained damage due to heat exposure

  - Shake the vial and let it stand for sometime
  - If the sediments settle down, do not use the vaccine
  - It is used to know whether the vaccine has incurred cold damage due to freezing or not

Open vial policy

- It is used to prevent vaccine wastage as much as possible
- Certain vaccine vials can be reused for upto 4 weeks provided certain conditions are met
- E.g., 10 dose vaccine vial of tetanus toxoid vaccine given to one patient does not need to be discarded, it can be reused 4 or 10 days later for another patient provided certain conditions are met

Conditions to be met for open vial policy

- Expiry date of vaccine have not yet reached
- Cold chain has been maintained properly
- All aseptic technique has been followed to withdraw vaccine from vial
- Vaccine vial septum has not been submerged in water
- Date of first time opening of vial is clearly mentioned on the label

Open vial policy

Applicable for: PPT H	Not applicable for: BMR J
• Polio vaccine • PCV • Tetanus containing vaccine o Pentavalent o DPT o TT o Td • Hep B	• BCG • Measles/Measles containing vaccine (MR) • Rotavirus • JE

- Vaccine that can be given in adolescents
  - Tdap
  - Td
  - TT
  - HPV
  - JE (in endemic area)
  - Influenza (in high risk individuals)
  - Pneumococcal
  - Rabies (for pre and post prophylaxis exposure)
  - Yellow fever vaccine (for international travel)
- **Cocoon strategy**
  - Vaccination of persons from immediate environment surrounding a child who is susceptible to a disease but cannot be immunized (like making a shield or cocoon around the child)
  - E.g., A child with severe immunodeficiency , live vaccines cannot be given, so the other family members of that child who are healthy should be immunized against disease e.g., measles vaccine can be given to immediate family which further decreases the chances of exposure of child to that disease
- Recommended sequence in which vaccines should be given to a child in single visit: Start with least painful one
  - Oral (OPV/Rota) → Intradermal (BCG/f-IPV) Subcutaneous (Measles) → IM (Penta) (Least painful) → (Most painful)
- Vaccines are given at certain site to know whether the child have received vaccine of National Immunization Schedule or not, if mother is not able to tell
  - Based on time and site where it is administered it can be identified to some extent which vaccine was given e.g., BCG scar is checked on left upper arm

Adverse Events Following Immunization (AEFI) 00:35:09

Definition

- Any untoward medical occurrence that follows immunization, but that does not necessarily have any causal association with the usage of vaccine

Classification of AEFI

1. Vaccine related

2. Program error
   - It is caused due to inappropriate vaccine handling, preparation, or administration
   - E.g., Proper diluent not used for vaccine or aseptic precaution not taken while withdrawing vaccine or vaccine not given at proper site
   - It is preventable adverse effect by proper training of health care givers

3. Injection reaction
   - It is due to anxiety about injection and not because of injection like syncope

4. Co-incidental event
   - AEFI caused by something other than vaccine product, program error or injection reaction
   - E.g., SIDS (sudden infant death syndrome) following immunization
   - Vaccine related AEFI can be
     - Vaccine product related i.e., caused, or precipitated due to one or more component of vaccine itself
       → E.g., Preservative in vaccine causing adverse effects
     - Vaccine quality defect related
       → It is due to defective quality of vaccine
   - All the adverse effects following immunization (AEFI) needs to be reported and then investigated by DIOs (District Immunization officers)

Clinical classification of vaccine reaction

- Common/Minor reactions: Local pain, redness, fever
- Serious reaction
  - Reaction resulting in either of the 4 things
    → Death
    → Disability
    → Hospitalization (in case of seizures)
    → Cluster of 2 or more cases in a geographical area
- Severe reaction
  - Reaction that is neither minor nor serious and can be treated in OPD
  - E.g., Child having persistent cry following immunization

Immunization in Special Situations 00:45:07

- HIV positive children
  - In asymptomatic HIV positive children, all vaccines can be given except OPV
  - In symptomatic children with HIV, all live vaccines are contraindicated while all killed vaccines can be given
- Immunocompromised child (including child on oral steroids/chemotherapy)

- These children should not receive any live vaccine till at least 1 month after discontinuation of steroids or chemotherapy
  - → It can cause that disease (against which vaccination is given) due to low immunity
- Killed vaccine can be safely given (immunogenicity might be doubtful)
- Pneumococcal vaccines and annual influenza vaccines must be given
- Sibling of these children should not receive transmissible live vaccine like OPV
  - → Oral polio virus is going to be shed in stools and these children with household contact can get infected

- For a child on corticosteroids, Immunization schedule:
  - Needs to be modified if - Child is on oral steroids at a dose of ≥ 2 mg/kg/day or receiving ≥ 20 mg/day prednisolone
  - Does not need to be modified if – Child is on inhaled corticosteroids (bronchial asthma) or topical steroids or ointment or cream (dermatological condition)
- **Immunization of a child with**
  - Primary immunodeficiency
    - → In all children with severe immunodeficiency whether it is B cell group i.e., X-linked agammaglobulinemia or severe T cell immune deficiency like SCID (Severe Combined Immunodeficiency) – All live vaccines are contraindicated
  - Planned splenectomy
    - → Certain conditions like hereditary spherocytosis, hypersplenism, thalassemia or Gaucher disease with massive spleen and hypersplenism, refractory ITP
    - → Ensure at least 2 weeks before a planned splenectomy, child should have been immunized against capsulated organisms like pneumococcus, meningococcus & Hemophilus influenzae (As spleen protects against these capsulated organism)
    - → For pneumococcal vaccine – PCV (give immune memory) + Polysaccharide vaccine should be given (protects against all 23 strains of pneumococcus)
- **Immunization of child with known coagulation disorder (e.g., Hemophilia)**
  - There is formation of large bruises on site of intramuscular injection and sometime bleeding may not stop after injection
  - Give vaccines subcutaneously instead of intramuscularly so chance of formation of hematoma is less e.g., Hib, Pneumococcal polysaccharide vaccines
  - Schedule immunization, shortly after administration of factor therapy (factor 8 in case of hemophilia)
  - Use smaller size needle (23 G or even smaller than that)
  - Apply firm pressure at injection site for at least 5-10 minutes as to stop bleeding quickly
- **Immunization of babies born preterm**
  - All vaccines can be given at chronological age as recommended by National Immunization Schedule
  - Birth vaccines – BCG and OPV-0 are given after initial stabilization (preferably at time of discharge)
  - So other vaccines will also be delayed by 4 weeks according to general principle of immunization
  - Hep B is given as soon as possible after birth to prevent vertical transmission from mother to child along with Vit K

45 INDIVIDUAL VACCINE

BCG (Bacillus Calmette Guerin) vaccine 00:00:07

- Calmette and Guerin are first scientists who invented BCG vaccine
- Against bacteria: Mycobacterium tuberculosis
- Strain commonly used: Copenhagen (Danish 1331) or Pasteur strain
- **3Ls**
  - Live attenuated vaccine
  - Light sensitive (comes in dark ampoule)
  - Lyophilised vaccine (comes in powder form and needs to be dilute with diluent)
- **Diluent**: Normal saline is used as diluent (supplied along with vaccine vial)
  - Distilled water is not used as it will irritate the skin
- **Dosage**
  - 0.05 ml till 1 month of age
  - Beyond 1 month: 0.1ml
- Route of administration: Intradermal

Important Information

- Site for BCG vaccine: Left upper arm
- BCG scar is checked over left upper arm

- Maximum age till BCG can be given as per NIS guidelines: 1 year
  - In India as tuberculosis is endemic condition so by 1 year of age all the children would have been exposed to blood TB virus in some way or another
  - IAP used to recommend BCG vaccine till 5 years of age but according to NIS it is to be given till 1 year of age
- Normal response following BCG vaccination
  - Papule → Ulcerate → Crust formation → Scar formation (by age of 6-8 weeks)

- Adverse effects
  - Suppurative lymphadenitis (common)
    → Lymph nodes of left axilla becomes enlarged and beocme pus filled
  - BCG osteitis (bone infection)
  - Disseminated BCG infection (in immunodeficient child)

- Protective effect: 0-80%
  - It does not give protection against pulmonary COX much
  - It protects mainly against severe forms of TB i.e., TB meningitis or disseminated TB
  - It does not give protection against TB infection

Polio vaccines 00:05:33

- **2 types**
  - OPV (Oral polio vaccine)/Sabin: Live attenuated vaccine
  - IPV (Injectable polio vaccine)/Salk: Killed vaccine
- Strains of polio virus used in OPV: P_1 & P_3
- P_2 strain was globally discontinued in April 2016
- **WHO recommendations**
  - P_2 strain to be no longer used in OPV
  - Only P1 and P3 strains are used in OPV
  - WHO no longer recommend an OPV only schedule; at least 1 dose of IPV should be there in NIS
- IPV not only protects against polio virus but it also protects against disease caused by vaccine derived polio viruses

VAPP (Vaccine Associated Paralytic Polio)

- Cases of AFP (Acute flaccid paralysis) having residual weakness 60 days after the onset of paralysis & from whose stool samples vaccine related polio viruses have been isolated

VDPV (Vaccine Derived Polio Virus)

- Arise due to mutation and recombination of the vaccine polio virus in human gut
- They are 1-15% divergent from parent vaccine strain

Hepatitis-B vaccine 00:08:54

- Route of administration: Intramuscular, on anterolateral aspect of thigh
- Dosage: Birth dose: As soon as possible after birth
  - It helps in prevention of transmission of hepatitis B infection from mother to baby
  - Subsequent dosage is given as part of Pentavalent vaccine according to NIS at – 6,10,14 weeks
- If the mother is Hepatitis B positive
  - Hep B vaccine is given immediately after birth to the baby
  - Hep B immunoglobulin ideally within 12 hours after birth
  - Complete Hep B vaccination series at 2 & 6 months

DPT vaccine 00:12:03

- DPT vaccine protects against 3 diseases
  - Diphtheria
  - Pertussis
    → Whole cell: It is in NIS (National Immunization schedule)
    → Acellular: Risk of adverse effects is less
  - Tetanus

Dosage

- 6 weeks, 10 weeks, 14 weeks
  - Booster: 16-24 weeks
  - 2nd booster: 5-6 years
  - It is given as a part of pentavalent vaccine according to NIS

Route of administration

- Intramuscular, on anterolateral aspect of left thigh

Adverse effects

- Local effects: Redness, pain at site of injection
- Systemic effects: Fever
- Severe adverse effects
  - Persistent inconsolable cry (> 3 hours)
  - Seizures
  - Hypotonic hyporesponsive episodes
  - Encephalopathy/altered sensorium
  - Anaphylaxis

Contraindications to DPT vaccines

- Progressive neurological illness
- Cerebral palsy (static neurological illness) - Not a contraindication to DPT vaccine
- Anaphylaxis to a previous dose of DPT vaccine
- Encephalopathy within 7 days of previous dose of DPT vaccine

Recommended catch up schedule for children who did not receive DPT vaccine

- < 7 years of age: DPT is given at 0,1,6 months
- > 7 years of age: Tdap (lesser dose of Diphtheria and Pertussis) at first visit
  - Followed by Td & Td: 0,1,6 months

Case scenario: A 5 year old unimmunized child developed Diphtheria. He has a 3 year old unimmunized sibling contact. Whether any vaccination against Diphtheria is needed for sibling?

- Diphtheria is a life threatening illness
- Children die or some have residual neurological deficit or some cardiac problems
- If any contact has received at least 4 doses of Diphtheria containing vaccine such that the last dose was given within last 5 years - No further immunization is required
- Remaining vaccination according to immunization schedule is required to be completed
- But because of this exposure no extra immunization is required
- So, this immunized child should have received dosage at – 6, 10, 14 weeks and booster – 16-24 months (4 dosage)
- If the child was unimmunized or have received < 4 doses of Diphtheria containing vaccine then additional dose of DPT would have been required as a post exposure prophylaxis for this child

Pentavalent vaccine 00:19:48

- Component of pentavalent vaccine used in National Immunization Schedule
  - Diphtheria
  - Pertussis
  - Tetanus
  - Hepatitis B
  - H. influenzae type B
- Dosage, route, and site of administration: 0.5 ml intramuscularly at anterolateral aspect of left thigh at 6, 10, 14 weeks according to NIS

Measles vaccine

- Type of vaccine: Live-attenuated vaccine
- Strain: Edmonston Zagreb stain
- Diluent: Distilled water
- Route: Subcutaneous route (right upper arm)
- Recommended age: 9 completed months – 12 months of age

- In case of measles outbreak: Measles vaccine can be given between 6-9 months of age as post exposure prophylaxis
  - Dose given before 9 completed month age is not counted as part of NIS
  - If a dose of measles vaccine is given before 9 months, it is still required to be given at 9 months and booster dose – 16-24 months

- Adverse effects
  - Local effects: Pain, redness, tenderness
  - Fever
  - Mild measles like illness (rashes)
  - Thrombocytopenia

Pneumococcal vaccine 00:17:51

- There are 2 types of pneumococcal vaccine

PCV (Pneumococcal conjugated vaccine)	PPV (Pneumococcal polysaccharide vaccine)
• Previously available - 7, 10 valent vaccines • Currently - 13 valent vaccine available	• Contains 23 strains of pneumococcus

• It is a part of NIS	• Not a part of NIS
• Given to all children at 6 weeks, 14 weeks, and 9 months	• Given to high risk individuals o Child undergoing splenectomy o Immunocompromised child o Underlying respiratory conditions o Chronic illness
• Advantage: Can be given at < 2 years of age	• Can only be given beyond 2 years of age
• It produces good immune memory	• No good immune memory

- Advantage of PPV: It protects against 23 strains of pneumococcus
  - It gives much wider protection than PCV

- Recommendation about pneumococcal vaccine in our National Immunization schedule
  - PCV: 13: 6, 14 weeks & booster dose at 9 months
  - Dose: 0.5 ml given at anterolateral aspect of right thigh
  - Catch up immunization schedule – till 1 year of age
  - Route of administration of both PCV & PPV: Intramuscular

Rotavirus vaccine

00:21:00

- Recently introduced in National Immunization Schedule
- Dosage: 6, 10, 14 weeks
- Type of vaccine- Live attenuated oral vaccine
- Recently, 116 E strain of rotavirus is found in AIIMS NICU
  - It is now used to produce Indian rotavirus vaccine
- Adverse effects
  - Intussusception
- Rotavirus vaccine is contraindicated if child has history of intussusception
- Catch up immunization schedule: Permissible upto 1 year of age

Hepatitis A vaccine

- It is not a part of National Immunization Schedule
- But Indian Academy of Pediatrics recommend that it should be given to all healthy children
- Type of vaccines
  - Live vaccine: Single dose
    → Age of administration for live vaccine: 12-23 months
  - Inactivated vaccine: 2 doses required 6 months apart
    → First dose is given at 1 year of age

Typhoid vaccine

- **Types**
  - Vi Capsular polysaccharide vaccine (Used previously)
  - Typhoid Conjugate vaccine (newer vaccine)

Typhoid VI Capsular polysaccharide vaccine

- It can be given only beyond 2 years of age
- No good immune memory → Repeat dose is required every 3 years
- Efficacy: 50-60%

Typhoid conjugate vaccine

- It can be given at ≥ 6 months of age
- Single dose is given
- Efficacy: 90%

Case scenario: A child who has not received typhoid vaccine develops enteric fever. How much time later can you vaccinate the child against typhoid?

- It can be given 4 weeks after full recovery

Varicella vaccine

- Type of vaccine: Live-attenuated vaccine
- Strain used: Oka strain
- Route of administration: Subcutaneous
- Dosage
  - 1st dose: 15 months of age
  - 2nd dose: 4-6 years of age
- IAP recommendations
  - It should be given to all children with no previous history of varicella
- For post- exposure prophylaxis
  - Ideally given within 3 days of exposure, but can be given upto 5 days following exposure to prevent development of varicella infection

HPV (Human Papilloma Virus) vaccine

- It is a recombinant DNA vaccine
- **Types**
  - Quadrivalent vaccine (Gardasil)
    → It protects against HPV serotype 6,11,16,18
  - Bivalent vaccine (Cervarix)
    → It protects against HPV serotypes: 16,18
- Protective efficacy: 99% against vaccine type related genital warts & vulvar and vaginal neoplasia
- Minimum age at which HPV vaccine recommended: 9 years
- It should be started before first sexual activity
- HPV should be given to all female children
- Maximum age for catch up schedule: 13-45 years of age
- Recommendation according to WHO SAGE (Strategic Advisory Group of Expert/ Committee) protocol for HPV vaccination (April 2022)
  - For 14-19 years old girls - Either 1 or 2 doses of HPV vaccine can be given

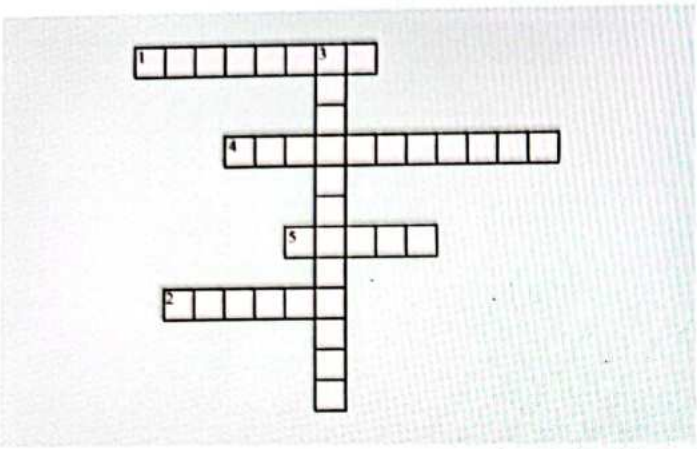
Influenza vaccine

00:36:24

- Types of vaccine
  - Inactivated vaccine: Whole virus/Split product
  - Egg based vaccine
  - Cell culture vaccine (for egg allergic individuals)
  - Recombinant technology derived vaccines
  - Nasal live attenuated vaccine (not available in India)
- Regime for inactivated vaccine: 2 doses intramuscular, 4 weeks apart followed by annually
- Every year strains of Influenza vaccine changes based on WHO recommendation
- Annual influenza vaccine should be given to all the high risk individual like elderly immunocompromised children, or children with chronic disease
- Latest WHO recommendation for the Influenza vaccine composition for 2022-23 for northern hemisphere
  - A/Wisconsin/588/2019 (H_1N_1)
  - A/Darwin/6/2021 (H_3N_2)
  - B/Austria/1359417/2021 (B/Victoria Lineage)
  - B/Phuket/3073/2013 (B/Yamagata lineage)

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. In DPT vaccine, most adverse effects are due to _____compound
2. Strategy in which people from the immediate environment of persons who are susceptible to a disease but cannot be immunized are vaccinated is known as?
5. ____test is done to check for cold damage to vaccine due to freezing?
4. What is the route of administration of BCG vaccine?

Down

3. Which mission was launched by Ministry of Health & Family Welfare, Government of India on 25th Dec 2014?

princeeeekum@gmail.com
9928609733

46 FETAL CIRCULATION& CLASSIFICATION OF CONGENITAL HEART DISEASES

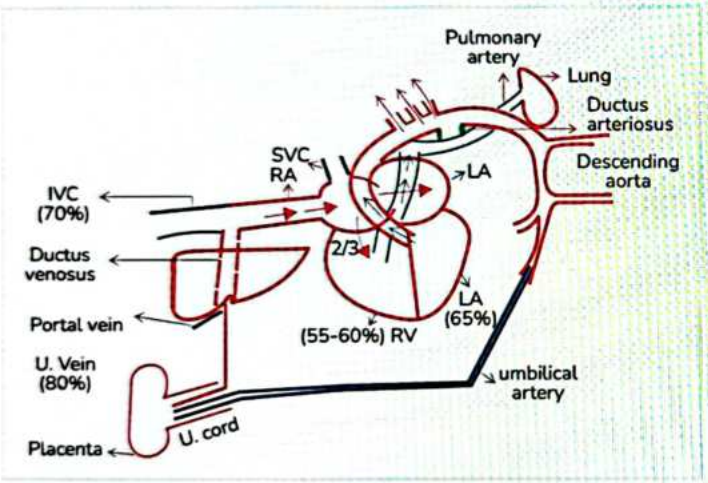
Differences Between Fetal Circulation & Adult Circulation 00:01:24

1. Source of O_2
   - Fetal circulation: Placenta
   - Adult circulation: Lungs
2. In fetal life, lungs are collapsed & pulmonary vascular resistance is very high: very little blood goes to lungs
3. Ductus arteriosus
4. Ductus venosus } Important for fetal circulation
5. Foramen ovale

Important Information

- Chambered structure of heart appeared by 6th week of IUL

Fetal Circulation 00:04:10



Umbilical cord

- Contains 1 vein & 2 arteries
- Rudimentary allantois, remnant of omphalomesenteric duct
- Wharton jelly.
- Umbilical vein carries oxygenated blood (SpO2 - 80%)
- Single umbilical artery
  - 5-10/1000 births
  - Associated with increased risk of renal anomaly
  - MC in twin pregnancy
  - Trisomy 18
- Delayed fall of umbilical cord seen in Leukocyte adhesion defect (a form of immunodeficiency)

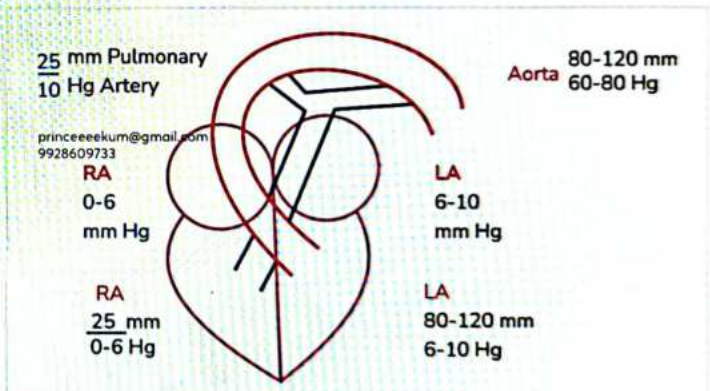
Saturation of O_2 in fetal circulation

- Umbilical vein: 80% (maximum in the entire body of fetus)
- Inferior vena cava (IVC): 70% (seen in deoxygenated blood also so saturation level falls)
- LV: 65%
- RV: 55-60%
- Umbilical artery: very low

Changes in circulation at or after birth 00:23:48

1. Lungs become the source of O_2 instead of placenta
2. Pulmonary vascular resistance decreases: Blood flow to lung increases(systolic murmur)
3. Systemic vascular resistance increases
4. Foramen ovale closes
5. Ductus venosus closes -forms ligamentum venosus, Funtional closure: 10-96 hrs, Anatomical closure: 2-3 weeks
6. Ductus arteriosus closes- forms ligamentum arteriosus (PROSTAGLANDINS plays an important role)
   - **Functional closure:** immediately after birth at 10-15 hrs (due to smooth muscle contraction)
   - **Anatomical closure:** D15-D21 Up to 3 months of life (due to proliferation of cells of intima of ductus arteriosus)

Pressures in Different Chambers of Heart in Adult Circulation 00:30:41



- These pressures normally get established by 2-3 weeks of age
- In presence of VSD or PDA, these pressures get established by 6-10 weeks age

Nada's Criteria 00:35:39

- It is used to assess the presence of congenital heart disease
- 1 major or 2 minor criteria indicates possibility of Congenital Heart Disease

Major Criteria

- Systolic murmur ≥ Grade 3
- Any diastolic murmur
- Cyanosis
- Congestive heart failure

Minor Criteria

- Systolic murmur < Grade 3
- Abnormal S_2
- Abnormal BP
- Abnormal ECG
- Abnormal Chest X-ray

Important Information

Hyperoxia Test

- To see the presence of CHD now a days.
- Put the baby under O2 by hood (100%)-do ABG analysis: if paO2 > 150 mmHg, then CHD is ruled out

Classification of Congenital Heart Diseases

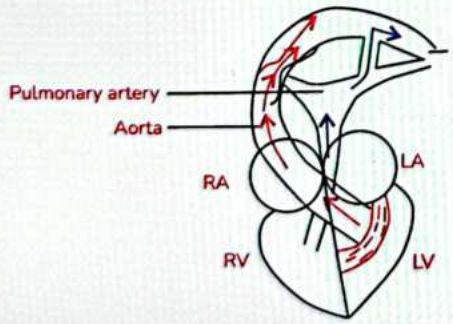
00:40:45

Classification of congenital heart diseases

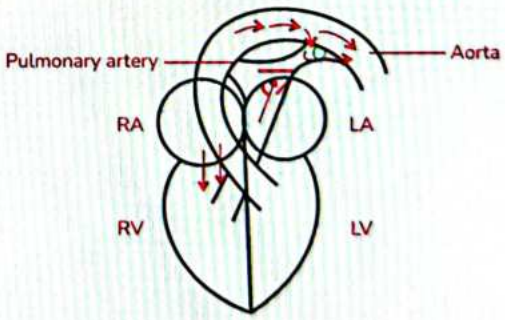
L → R shunt	Complete mixing of blood of L & R side	Parallel Circulation	Ductus Dependent	
			Systemic circulation	Pulmonary circ
• VSD • ASD • PDA (Note: R to L Eisenmenger syndrome)	• Truncus arteriosus • TAPVC (total anomalous pulmonary venous connection)	• TGA	• Critical AS • Severe coarctation of aorta • Interrupted aortic arch • HLHS (CHD MC causes mortality in 1st week of life)	• Severe PS • Severe TOF • Pulm. atresia • Tricuspid atresia • Ebstein anomaly

Ductus Dependent

Systemic circulation



Pulmonary circulation



princeeeekum@gmail.com
9928609733

PREVIOUS YEAR QUESTIONS

Q. In a fetus, highest O_2 concentration is found in? (NEET JAN 2020)

a. IVC
b. SVC
c. LV
d. AA

Q. Most oxygenated fetal vessel? (JIPMER Nov 2018)

a. Umbilical artery
b. Ductus arteriosus
c. **Umbilical vein**
d. Ductus venosus

princeeeekum@gmail.com
9928609733

47 IMPORTANT ACYANOTIC CONGENITAL HEART DISEASES

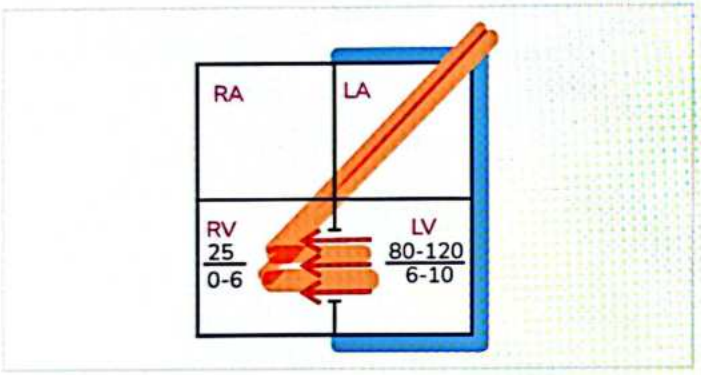
Ventricular Septal Defect

00:00:31

- MC congenital heart disease in children
- MC congenital acyanotic heart disease in children
- MC congenital heart diseases affected by infective endocarditis in children
- 90% VSDs involve membranous part (10% muscular part)

Parts of ventricular septum
- Membranous → 90% of VSDs
- Muscular part

Hemodynamics of VSD



Auscultation Findings

- Pansystolic murmur (blood moves from left to right with a gush)
- In large VSD additional murmurs
  - Delayed diastolic murmur in mitral area
  - Ejection systolic murmur in pulmonary area
- Chambers enlarged in VSD: Left Atrium & Left Ventricle. (Since excess blood goes into lungs through pulmonary circulation, it comes back into LA so LA & LV enlarged)

Clinical features

- Tachypnea
- Recurrent episodes of pneumonia
- Heart failure & failure to thrive (child doesn't gain weight adequately)
- Usually presents at 6-10 weeks

ECG Findings

- Left axis deviation [normally all babies at birth have right axis deviation]
- Left ventricular hypertrophy

Chest X-ray findings

- Cardiomegaly with LV apex (moves down & out)
- Pulmonary plethora d/t excess blood going to lungs

Treatment

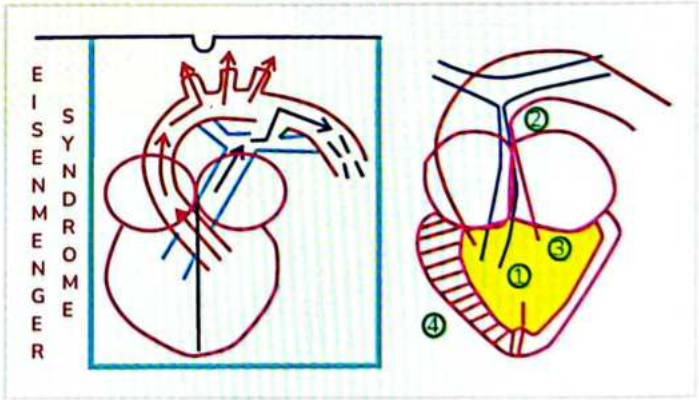
Medical management	Surgical management
1. Treatment of Heart failure • Digoxin • Diuretics (Furosemide) management 2. Treatment of pneumonia with Antibiotics & supportive care 3. Nutritional rehabilitation	• Closure of VSD by DACRON PATCH Indications 1. Heart failure refractory to medical 2. If pulmonary blood flow (QP) is more than double of systemic blood flow (Qs) [Qp: Qs> 2:1]

Complications of VSD

1. Infective endocarditis: VSD + fever + Clubbing without cyanosis
2. Eisenmenger syndrome: VSD + Clubbing + Cyanosis [no fever]

Eisenmenger Syndrome

00:17:38



Definition

- Reversal of shunt at the level of VSD/ASD/PDA due to irreversible pulmonary vascular obstructive changes

Pathophysiology

VSD [Left → Right]
↓
Excess pulmonary blood flow
↓
Hyperkinetic pulmonary hypertension[reversible]

↓
Irreversible pulmonary vascular obstructive changes [obstructive pulmonary Hypertension]
↓
Rt ventricular hypertrophy
↓
Pressure in RV increases
↓
When RV increases >LV pressure
↓
Right → Left shunt
↓
Cyanosis & clubbing

Clinical features of Eisenmenger Syndrome

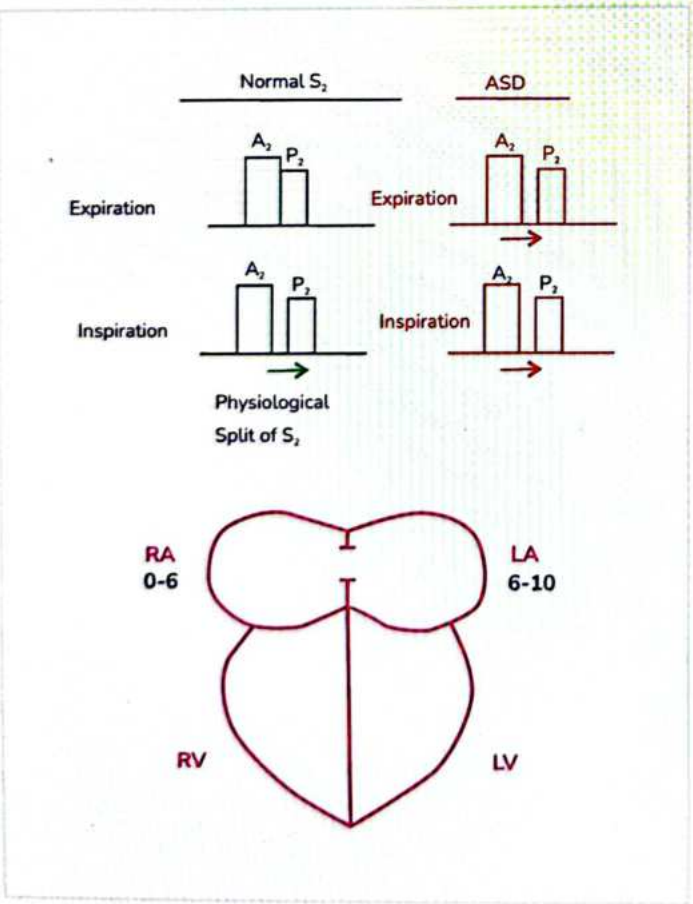
- Cynosis and clubbing in a child with Acyanotic congenital heart disease like VSD
- Reversal of shunt does not occur TOF

Atrial Septal Defect (ASD) 00:24:02

- **2 Main Types**
  1. OSTIUM PRIMUM lower part of atrial septum
  2. OSTIUM SECUNDUM [MC Type] upper part of atrial septum

Hemodynamics

- Shunt remains silent in ASD (No Murmur)



- Large ASD Produce Murmurs
  - Diastolic murmur in tricuspid area
  - Ejection systolic murmur in pulmonary area

- Irrespective of inspiration or expiration, Right atrium has more blood (as it is receiving blood from Superior Vena cava, Inferior Vena cava and Left Atrium)
- Right ventricle takes more time to empty, P_2 comes later
- Wide, Fixed Split of S2 : also in TAPVC, RBBB

Clinical Presentation

- Small ASD: Asymptomatic throughout life
- Large ASD: Same as VSD

Investigations

ECG findings

- Right axis deviation in ostium Secundum ASD
- Left axis deviation in ostium Primum ASD

Treatment

- Asymptomatic and small: no treatment required
- Symptomatic: same as VSD

Important Information

- Congenital heart disease which is least commonly affected by Infective endocarditis: ASD

Important Information

Congenital Rubella Syndrome

- Cataract
- Deafness
- Congenital heart disease (MC is PDA, Least common is ASD)

Syndromes Associated with ASD

- **Mnemonic: PeTAR FED HER**
  1. P - Pierre Robin Sequence
  2. TAR - TAR [Thrombocytopenia Absent Radius] Syndrome
  3. F - Fetal Alcohol syndrome
  4. E - Ehler Danlos Syndrome
  5. D - Down Syndrome
  6. H - Holt-Oram syndrome
  7. E - Ellisvan Creveld Syndrome
  8. R - Rubinstein Taybi syndrome

Important Information

- Atrial Septal Defect is not associated with Turner syndrome
- Atrial Septal Defect is not a component of TOF
- Atrial Septal Defect is a component of Trilogy of Fallot & Pentalogy of Fallot
- Pentalogy of Fallot TOF + ASD
- Trilogy of Fallot Pulmonary Stenosis + Atrial Septal Defect + Right Ventricular Hypertrophy

Patent Ductus Arteriosus

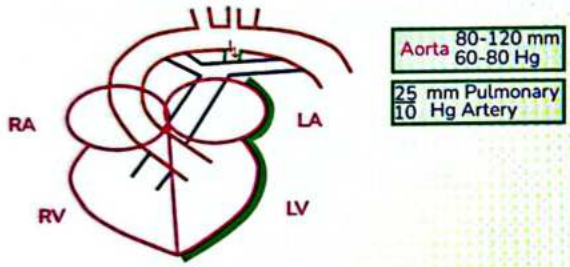
00:45:47

- Ductus arteriosus connects aorta to pulmonary artery

Factors

- Hypoxia
- Prematurity predispose to PDA

Hemodynamics



Auscultation

- Continuous machinery murmur - 'drrrr sound' (as huge difference between pressures in aorta & pulmonary artery)
- Left side of heart enlarged (LA+LV increased in size) (excess blood from ascending aorta enters pulmonary artery into lungs)

Clinical Presentation

- **Term Neonates and infants:** presents at 6-10 weeks (Same as VSD)
  - Tachypenea
  - Tachycardia
  - Failure to thrive
  - Features of heart failure
- **Preterm Neonate**: presents at 1st week (Hyper dynamic circulation, Bovdy pulses)

Investigation

- **CXR**
  - Cardiomegaly with LV apex (moves down and out)
  - Pulmonary plethora due to excess blood going to lungs.
- ECG findings are same as VSD

Treatment

- For term babies same as VSD

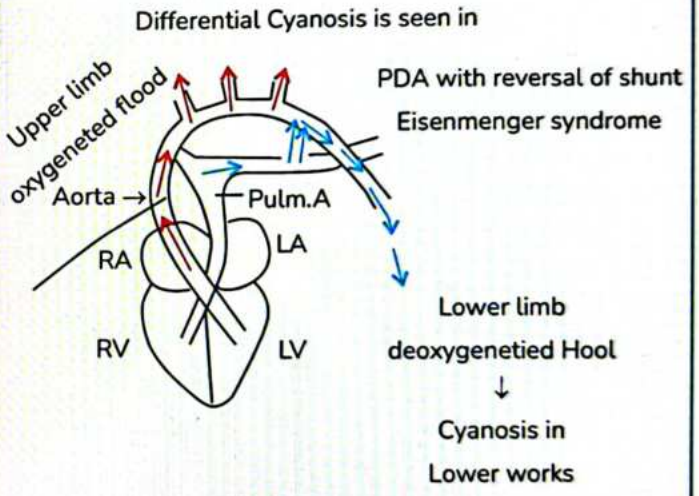
I. **Medical Management**
   - Treatment of heart failure
   - Treatment of pneumonia
   - Nutritional rehabilitation

II. **Surgical Management**
   - Ligation of PDA
   - Coil embolization of PDA via cardiac catherisation
   - Indications of Surgery
     → Heart failure refractory to medical Management
     → Qp (Pulmonary blood flow): Q,(Systemic blood flow) >2:1

Important Information

Differential cyanosis is seen in pda with reversal of shunt [Eisenmenger Syndrome]

- No cyanosis in upper limbs (as oxygen blood goes us there)
- Cyanosis in lower limbs (mixing of blood with deoxygenated blood)



- DOC for medical closure of PDA in preterm neonate: PG Inhibitors [Indomethacin; Paracetamol, Ibuprofen- preferred due to less side effects]

princeeeekum@gmail.com
9928609733

PREVIOUS YEAR QUESTIONS

Q. On repair of VSD, the patient will show improvement in which of the following? (AIIMS JUNE 2020)

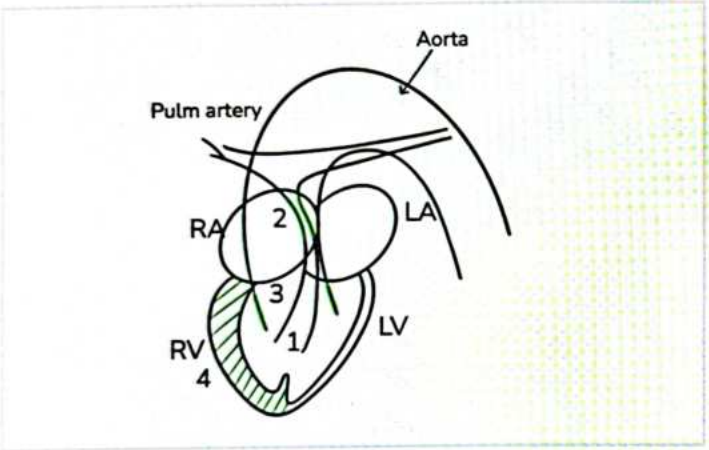
A. Arrythmia
B. Heart block
C. Respiratory alkalosis
D. Failure to thrive

48 TETRALOGY OF FALLOT (TOF)

TOF
- MC congenital cyanotic heart disease in children

4 Components
1. Large, nonrestricted VSD
2. Right ventricular outflow tract obstruction (RVOT) or pulmonary stenosis (infundibular or subpulmonic>valvular)
3. Overriding of aorta
4. Right ventricular hypertrophy

Pathophysiology
- Cyanosis because lesser blood going to lungs and getting oxygenated.
- Mixing of blood of left and right ventricle



Timing of presentation & severity will depend on
- Degree of pulmonary stenosis
- Ductus arteriosus open or not

Clinical features
a. Cyanosis(central) due to hypoxia:spo2=75-85%
b. Clubbing
c. Polycythemia
d. Cyanotic spells
e. Dyspnoea on exertion (improves on squatting)
f. Heart failure is not seen in TOF, unless it is complicated by
   - Anemia
   - Infective endocarditis
   - Myocarditis
   - Systemic hypertension

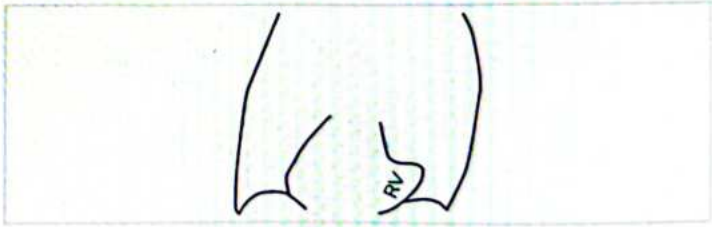
Age of presentation depends on severity
- Mild PS: pink TOF
- Mild to mod.TOF: present after 1st few months of life
- Severe TOF: cyanosis even at birth
- **TOF with pulmonary atresia:** blood goes to the lungs via ductus arteriosus(PDA) or via MAPVA (multiple aorto-pulmonary collateral arteries)
- Cyanotic spells MC in infants with mild TOF because compensatory polycythemia not yet developed

CVS examination
a. RVH: Precordial bulge
b. RV type of apex(upturned apex)
c. Auscultation
   - Ejection systolic murmur in pulmonary area
   - Single S_2 (P_2 is soft & inaudible)
   - In severe TOF/TOF with pulmonary atresia= continuous murmur (due to collaterals)
- Severity of TOF: α Severity of Cyanosis

$$:\alpha \frac{1}{\text{Intensity \& duration of murmur}}$$

Complications of TOF
a. Cerebral thrombosis: due to polycythemia & dehydration (in <2 yrs)
b. Cerebral abscess: in > 2 yrs
c. Bacterial endocarditis

Investigations
1. CxR: Boot Shaped Heart (or) 'Cor En Sabot' Appearance
   +
   Pulmonary Oligemia



2. ECG: RVH pattern
3. 2D ECHO with doppler is confirmatory of TOF

Cyanotic Spell or Tet Spell

Pathophysiology
Refer Diagram 48.1

Treatment of cyanotic spell
1. Moist O_2 inhalation (decreases pulmonary vascular resistance)
2. Inj. Sodium Bicarbonate (to neutralize acidosis)
3. Morphine

4. Ketamine (increases systemic vascular resistance)
5. Alpha agonists (Phenylephrine)
6. Beta blockers (Propanolol): decreases pulmonary infundibular spasm, used as prophylactic medicine

7. Squatting or knee chest position helps aborting cyanotic spell: increases systemic vascular resistance, decreases venous return to right side of heart
8. PRBCs transfusion

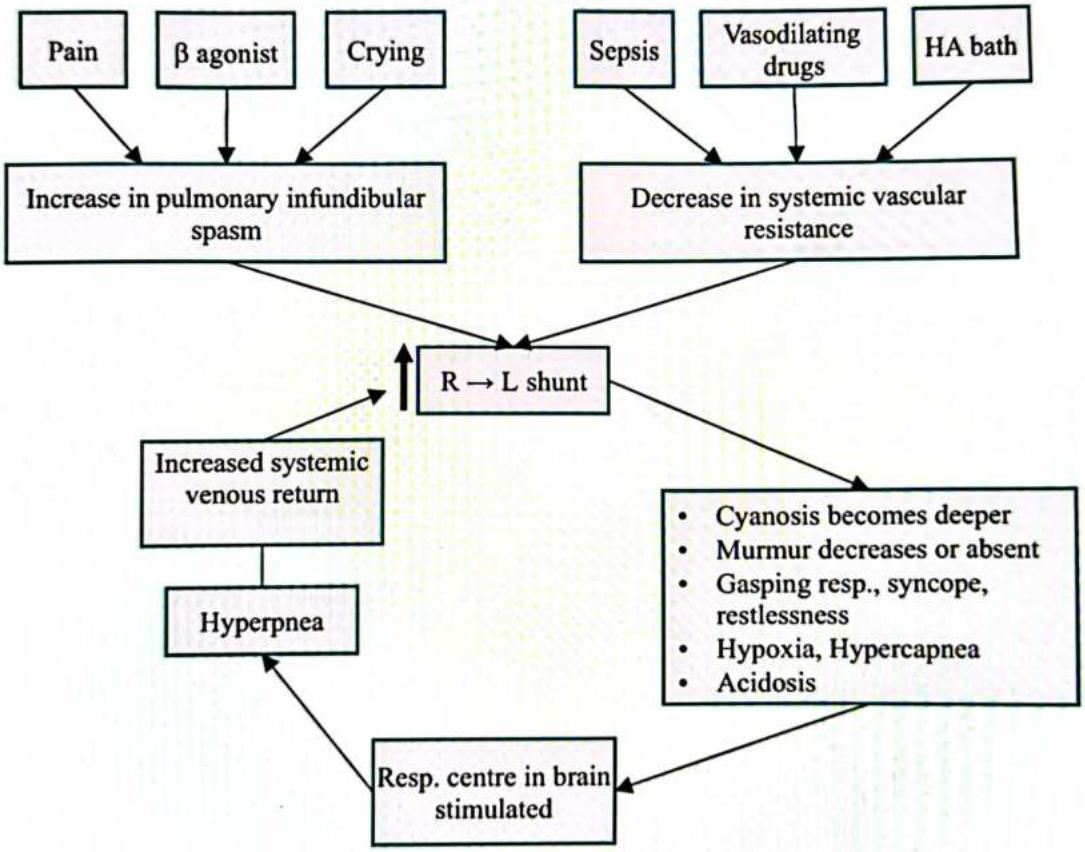
Surgical Treatment of TOF

- Definitive (corrective) Sx → VSD closure + Repair of Pulmonary stenosis
- Shunt (palliative) Sx → Connection b/w pulmonary artery & aorta or its branch
  - **B** - **B**lalock Taussig shunt: **S** - **S**ubclavian artery
  - **W** - **W**aterston's Shunt: **A** - **A**scending Aorta
  - **P** - **P**ott's Shunt: **D** - **D**escending Aorta

How to remember

- BaSWahAPahucha Do

Diagram 48.1



49 RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

- Mc acquired heart disease in children in developing countries: RHD
- ARF/RHD is strongly associated with antecedent group A streptococcal pharyngitis (with strains M1,3,5,6,18,29)
- Pathogenesis: immune mediated

Modified Jone's criteria (2015) 00:03:10

Low risk	Moderate to high risk
• Incidence= <2/lakh school going children	• Incidence= >2/lakh school going children
• Rhd prevalence= <1/1000	• Rhd prevalence= >1/1000

Major criteria

1. Carditis (clinical or subclinical):50-60%
2. Arthritis(low risk population: polyarthritis, moderate to high risk population: polyarthritis, monoarthritis, polyarthralgia): 75%
3. Chorea (syndenham's chorea): 10-15%
4. Erythema marginatum: 1%
5. Subcutaneous nodules: <1%

Minor criteria

1. Polyarthralgia (low risk population), monoarthralgia (moderate to high risk population)
2. Fever
3. Increased ESR/CRP
4. Prolonged PR interval

Essential criteria: Evidence of antecedent group A streptococcal infection (increased or rising ASO titres)

Modified Jone's criteria

- Initial episode of RF = 2 major or 1 major + 2minor criteria
- Recurrence of RF = 2 major or 1 major+2 minor or 3 minor

Important Information

- Mc manifestation of RF: arthritis f/b carditis (mitral valve f/b aortic valve)

Treatment of ARF 00:15:01

- A course of antibiotics: 10 days of oral amoxicillin or penicillin or single dose of IM benzathine penicillin (azithromycin in penicillin allergy)
- Aspirin: 50-70 mg/kg/day initially
- Corticosteroids: carditis + CCF/ cardiomegaly
- Bed rest: carditis

Primary prophylaxis 00:17:17

- Any streptococcal pharyngitis: appropriate antibiotics should be started within 9 days of onset of illness to prevent RHD (poverty/overcrowding: risk factors for ARF/RHD)

Secondary prophylaxis

- Inj. Benzathine penicillin IM 6 lakh IU in children ≤ 27 kg
- Inj. Benzathine penicillin IM 1.2 million IU in 27 kg every 3-4 weeks
- Till when secondary prophylaxis
  - Without carditis: 5 yr or till 21 yr age, whichever is later
  - With carditis but without residual heart disease: next 10 yr or till 21 yr, whichever is later
  - With residual heart disease: next 10 yr or 40 yr of age, whichever is later

50 OTHER CONGENITAL HEART DISEASES

princeeeekum@gmail.com
9928609733

Classification of cong. heart ds

L→R	Complete mixing of flood of L&R side	Parallel circulation	Ductus dependent	
VSD ASD PDA	• Truncus arteriosus • TAPVC	TGA	Systemic	Pulmonary
			- Critical AS - Severe coarctation - Interrupted aortic arch - HLHS	- Severe PS - Severe TOF - Pulm. atresia - Tricuspid atresia - Ebstein anomaly

Truncus Arteriosus

00:01:10

- Single common trunk from which pulmonary artery & aorta arise
- 22 q deletion commonly associated [CATCH 22]
  a. Conotruncal abnormalities
  b. Abnormal facies
  c. Thymic hypoplasia
  d. Cleft palate
  e. Hypocalcemia
- Rt sided aortic arch is commonly a/w truncus arteriosus

Tapvc / Tapvr [Total Anomalous Pulmonary Venous Connection / Return]

00:04:35

- **Basic defect:** Pulmonary veins instead of draining into the left atrium, drain either directly or indirectly into right atrium

3 types

	Supra cardiac	Cardiac	Infra cardiac
Pulmonary Veins drain into	• SVC • Lt. Innominate vein	• Rt. Atrium coronary sinus	• IVC • Hepatic veins • Portal veins
	• MC type		• Always obstructive

- Obstructed TAPVC presents with heart failure even in 1st wk of life

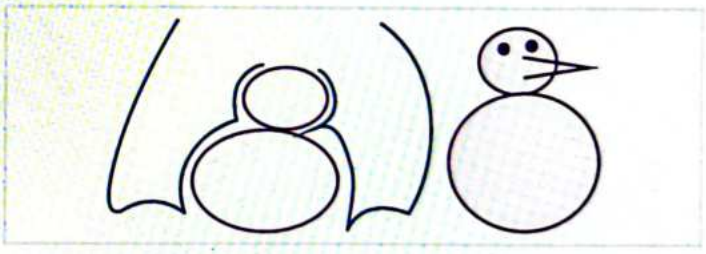
Timing of heart failure in CHDs

00:10:40

1st week	1-4 weeks	> 1 month
• Ductus dependent Systemic circulation o Severe coarctation of aorta o Interrupted aortic Arch o HLHS	• PDA in preterms	• PDA in terms
• Obstructive TAPVC	• VSD with coarctation	• VSD
• TGA with intact Ventricular septum	• Truncus arteriosus	• Non - obstructive TAPVC
• Ebstein anomaly	• TGA with VSD	• Endocardial cushion Defects

CXR in TAPVC

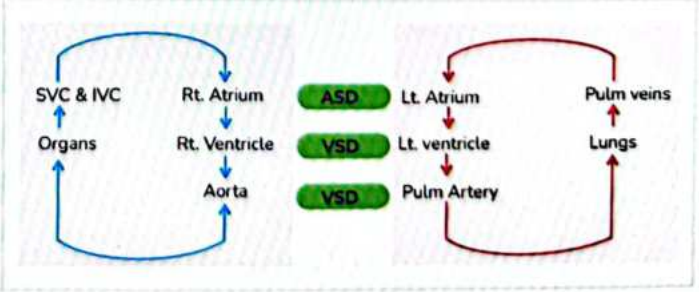
a. Supra-cardiac TAPVC: 'Figure of 8' or 'snow man' appearance
b. Obstructed TAPVC (ground glass haziness of lungs)



TGA/TGV [Transposition of Great Arteries / Vessels]

00:17:14

- **Basic defect:** Pulmonary artery instead of arising from Rt. Ventricle, arise from left ventricle and aorta instead of arising from Lt ventricle, arises from Rt ventricle
- Parallel Circulation (D – TGA)



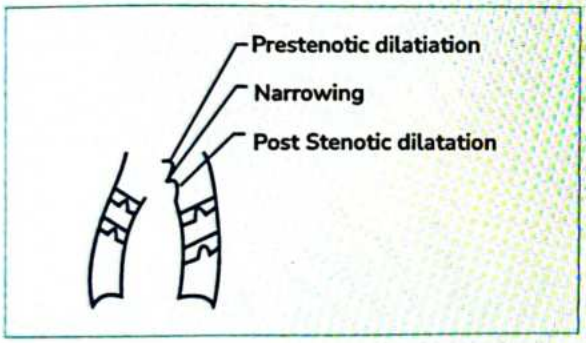
- L – TGA or corrected TGA: Usually comes to notice due to other associated heart defects
- CXR: "Egg on side" appearance
- MC congenital cyanotic heart disease presenting in neonatal period early infancy is TGA

Treatment

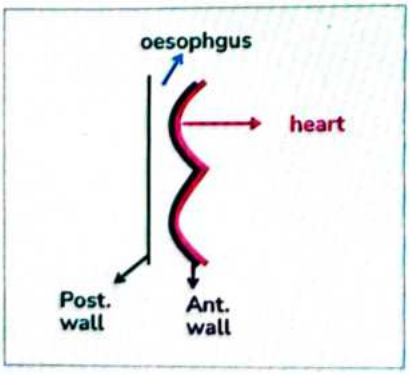
- PGE_1 analogue [Alprostadil] → Keeps ductus arteriosus open
- Balloon atrial septostomy / Rashkind procedure: Emergency procedure
- Arterial switch operation / Jatene's repair: Definitive surgery

Coarctation of Aorta 00:30:46

- Juxta ductal part of aorta is mostly involved
- Medial wall of aorta is usually spared
- Clinical presentation
  - Severe coarctation: Heart failure in neonate with B/L feeble or impalpable femoral pulses
  - Hypertension in later life
  - Milder disease: intermittent claudication of lower limbs



- **CXR:** Figure of 3 appearance and Notching of inferior margin of 3rd – 9th ribs usually seen >3 years age
- **Contrast Esophagogram and Barium Swallow:** E sign



Treatment

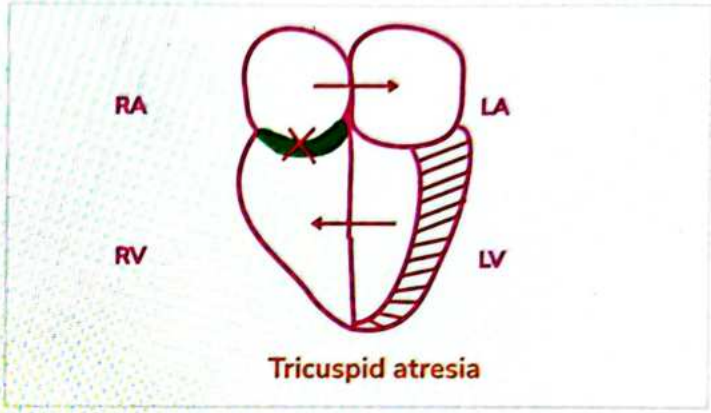
- Balloon angioplasty
- Anti hypertensives for hypertension

HLHS [Hypoplastic Left Heart Syndrome] 00:39:53

- MC congenital heart disease causing mortality in 1st wk of life since LV is poorly developed.

Tricuspid Atresia 00:41:40

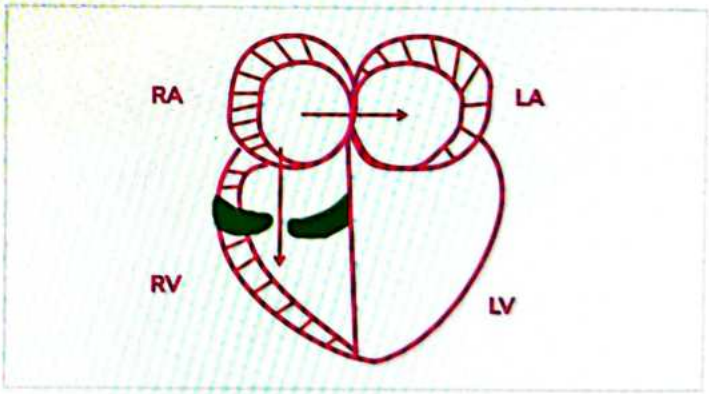
- Congenital cyanotic heart disease with left axis deviation on ECG → Tricuspid atresia



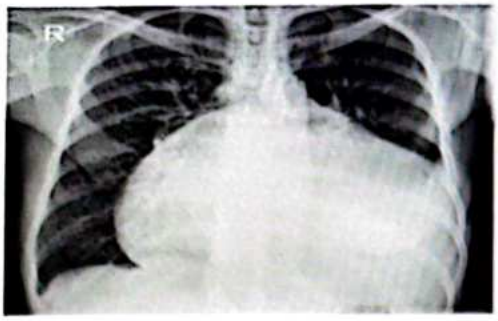
Tricuspid atresia

Ebstein Anomaly 00:43:51

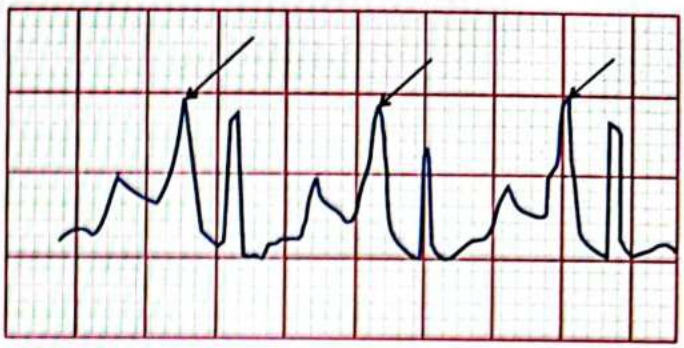
Downward displacement of tricuspid valve
↓
Atrialization of right ventricle
+
Functionally abnormal tricuspid valve



- Huge cardiomegaly seen, especially Rt atrium [RA, LA, RV also involved]
- **CXR:** Box shaped heart
- **ECG:** Himalayan P waves



Box shaped heart



Himalayan P waves

PREVIOUS YEAR QUESTIONS

Q. Pulmonary plethora in a child with cyanosis, is seen in? (NEET Jan 2020)

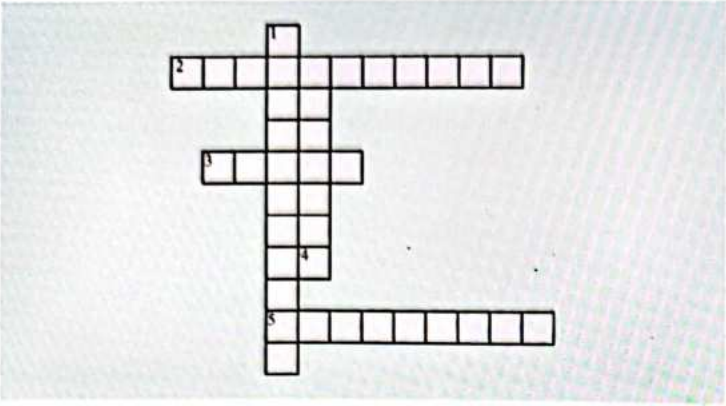
a. TOF
b. TAPVC
c. Coarctation of aorta
d. Tricuspid atresia

Q. A 6 yr old child presents with hypertension. On examination, lower limb pulse was feeble, upper limb pulse was normal. On chest x-ray, notching is seen. What is the probable diagnosis?

a. ASD
b. Bicuspid aortic valve
c. PDA
d. Coarctation of aorta

CROSS WORD PUZZLES

Crossword Puzzle



Across

2. Ventricular septal defect + clubbing + cyanosis (Nofeuer) indicates which syndrome?
3. Ductus arteriosus connects _____ to pulmonary artery?
5. ____ is the most common manifestation of rheumatic fever.

Down

1. _____ septal defect is the most common congenital heart disease affected by infective endocarditis in children.

Up

4. Which anomaly shows a 'Box-shaped heart' on CXR and 'Himalayan P wakes' in ECG?

princeeeekum@gmail.com
9928609733

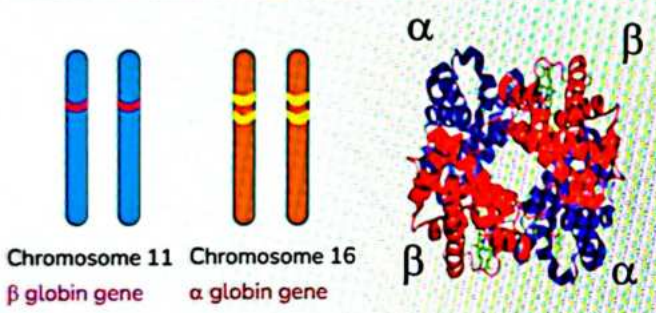
51 IMPORTANT HEMATOLOGICAL DISORDERS IN CHILDREN

Normal Erythropoiesis

00:00:16

- **Normal human haemoglobins**

	Hemoglobin	Structural formula
Embryonic	Hb-Gower 1	$\zeta_2\varepsilon_2$
	HB-Gower 2	$\alpha_2\varepsilon_2$
	Hb- Portland	$\zeta_2\gamma_2$
Fetal	Hb-F	$\alpha_2\gamma_2$ (0.5-1%)
Adult	Hb-A	$\alpha_2\beta_2$ (97%)
	Hb- A_2	$\alpha_2\delta_2$ (1.5-3.2%)



Hemoglobin

Major Sites of Hematopoiesis

00:03:12

- Yolk sac: Starts from 3rd week till 10-12th week
- Liver: Starts at 6-8th week, ceases by 2nd trimester
- Bone marrow: Starts from 2nd trimester onwards

Important Information

Normal life span of RBC

- Older children & adults: 120 days
- Term neonate: 90 days
- Preterm neonate: 60 days

Anemias in Children

00:05:18

WHO definition

- Children 6 months – 5 years: Hb < 11 g/dl
- Children 6-14 years: Hb < 12 g/dl
- Approach to anemia in children

Pallor, lethargy
↓
Hepatosplenomegaly
↓
Absent

No Petechiae	Petechiae Present
• Iron deficiency anemia	• Aplastic Anemia
• Megaloblastic Anemia	• Bleeding disease
• Pure red cell aplasia	• Coagulation disease
• Lead poisoning	• DIC
• Chronic kidney disease	

Present
↓
lymphadenopathy

Absent	Present
• Thalassemia	• Leukemia
• Sickle cell disease	• Infection
	• Infiltrative
	• Disorders

Iron Deficiency Anemia

00:10:08

- Mc cause of nutritional disorder in the world
- MC cause of anemia in the world

Etiology

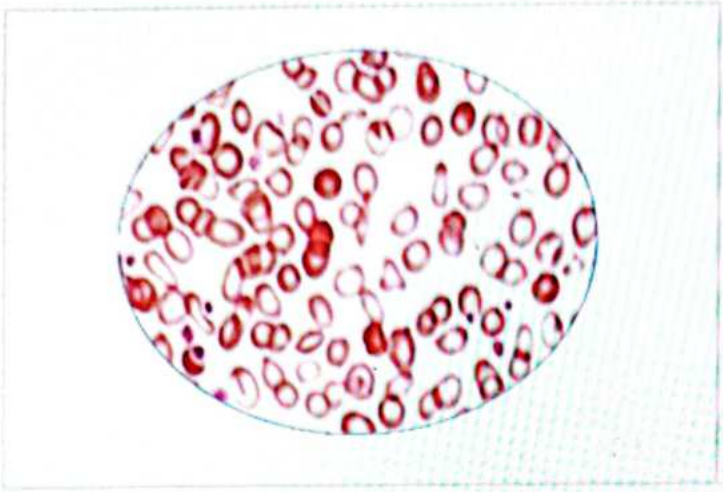
- Decreased iron intake
  - Inadequate diet
- Impaired absorption: Celiac disease
- Increased iron loss
  - Gastrointestinal bleeding
  - Inflammatory bowel disease
- Increased requirements
  - infancy, puberty
- Inadequate presentation to erythroid precursors
  - Atransferrinemia

Clinical Features

- Pallor: generalised weakness, lethargy
- Smooth and shiny tongue
- Pica
- Koilonychia

Diagnosis

- PS: Microcytic, Hypochromic Anaemia, anisocytosis, target cells, pencil cells



Important Information

Microcytic, hypochromic anemia also in:

- Thalassemia
- Anemia of chronic disease eg., RA, osteomyelitis, papillary necrosis
- Lead poisoning
- Sideroblastic anemia

00:16:54

D/D of microcytic, hypochromic anemia	IDA	B Thalassemia minor / trait	Anaemia of Chronic disease
RDW	Increased	Normal	Normal/ Increased
S. iron	Decreased	Normal/ Increased	Decreased
S. ferritin	Decreased	Normal/ Increased	Increased
TIBC	Increased	Normal	Decreased
Mentzer Index	>14	<13	

Important Information

$$\text{Mentzer Index} = \frac{\text{MCV (FL)}}{\text{RBC count } (\frac{\text{million}}{\text{ml}})}$$

Treatment of IDA 00:20:16

- 3-6 mg/kg/ day of elemental iron
- Maximum dose: 200mg of elemental Iron daily
- Children with iron overdose infection with Yersina Enterocolitica
- Only 10% of oral dose gets absorbed
- For IV correction, total amount of Iron needed = (body weight [kg] × [15 - patient's Hb] × 2.3) + 500mg

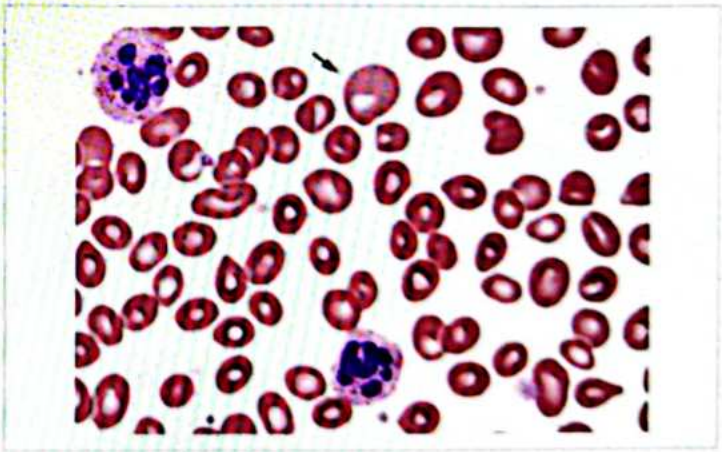
Response to treatment in iron deficiency anemia 00:22:32

Time after Iron administration	Response
12-24 hours	Decreased irritability, increased appetite
48-72 hours	Reticulocytosis appears, peaks at 5-7 days post treatment
4-30 days	Increase in Hb level (best measure)
1-3 months	Repletion of stores

Megaloblastic Anaemia 00:25:04

- Due to Vit B12 or folic acid deficiency
- On Peripheral smear: Large oval shape RBCs Macro ovalocytes, Hyper segmented neutrophils (>5 lobes in 5% neutrophils)

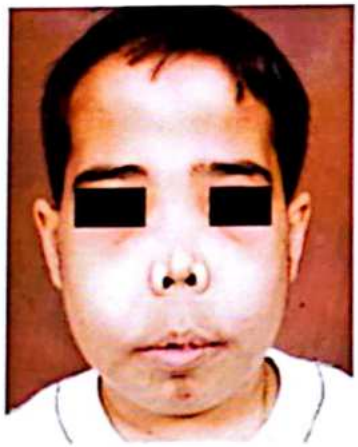
Treatment: Vitamin B12 and Folic acid



Beta -Thalassemia 00:26:35

Defect: Decreased production of Beta globin chains.

- Common Mutations in India
  - IVS 1-5 G→C
  - IVS 1-1 G→T
  - Codon 41/42
  - Codon 819
  - 619 by deletion



Classification

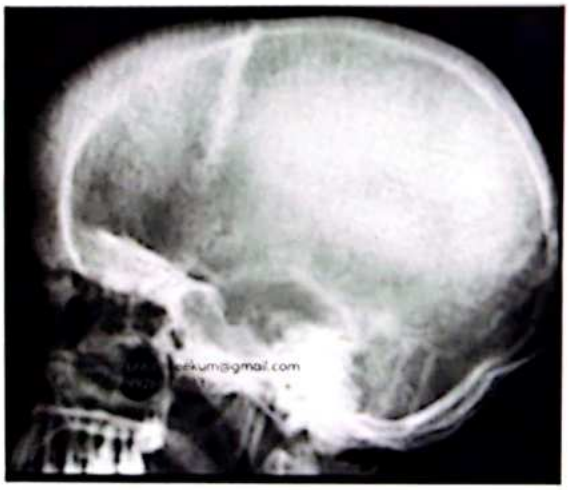
- **Thalassemia trait/ minor:** Heterozygous state, Mild Anemia (HbA2≥ 3.5%, HbF is normal)
- **Thalassemia intermediate** (β^0/β^+): Moderate anaemia, Hepatosplenomegaly: HbF elevated
- **Thalassemia major** (β^0/β^0): severe anaemia, hemolytic facies: HbF markedly elevated regular transfusions requirement

Clinical features

- Haemolytic Facies
  - Frontal prominence
  - depressed bridge of nose
  - maxillary prominence
- Hepatosplenomegaly (d/t extramedullary hematopoiesis)

Investigation

- Lat. X Ray skull: 'Hair on End' or 'Crew Cut appearance'



- Hemolytic anemia
  - Low Hb, low MCV, low MCH (thalassemia major)
  - Increased LDH
  - Increased unconjugated bilirubin
- PS: microcytic, hypochromic anemia, target cells, Howel jolly bodies, poikilocytosis
- Osmolar fragility: decreased (NESTROFT- Naked Eye Single Tube Red Cell Osmotic Fragility Test)
- Coombs test -ve (+ve in immune hemolytic anemias)
- Hb HPLC (high performance liquid chromatography) or Hb electrophoresis:
  - HbA decreased
  - HbA2 increased
  - HbF increased

  } beta thalasemia major
- Definitive diagnosis: globin gene mutation- helps in prenatal diagnosis in next pregnancy

Treatment of Thalassemia 00:37:47

- **Repeated Blood Transfusions**: To maintain pretransfusion Hb level between 9.5-10.5 g/dL
- The only curative treatment for thalassemia major: Hematopoietic stem cell transplantation (HSCT)
- Iron Chelation Therapy: Usually started when serum ferritin >1000 ng/ml
  - Desferrioxamine: Parenterally (IV or SC)
    → Effective in reverting hepatic & cardiac iron deposition.
  - Deferiprone: 1st oral chelator.
    → Adverse effects Agranulocytosis, GI side effects, arthritis
  - Deferasirox: Oral drug, Effective in decreasing cardiac iron burden & lowering serum ferritin.

Complications of thalassemia and its therapy 00:41:54

- Endocrine: Osteoporosis, Short stature, delayed puberty, Hypothyroidism, Hypogonadism, D.M
- Cardiac: Heart failure, pericardial effusion, DCM
- GI: Transaminitis
- Other- Infections, allergies

Alpha Thalassemia

- Normal $\alpha\alpha/\alpha\alpha$
- Alpha trait $-\alpha/\alpha\alpha$
- Alpha thalassemia $--/\alpha\alpha$
- Non immune hydrops $--/-\alpha$
- Free beta and gamma chains: β4 & λ4 (tetramers) – precipitate in RBCs and hemolysis occurs

Sickle Cell Anemia 00:45:50

- MC Structural Hemoglobinopathy
- Point mutation in 6th codon of β-globin gene so there is replacement of glutamate with valine
- Production of Hb with abnormal physiochemical properties that promotes polymerization of deoxygenated Hb
- **Heterozygous Trait**: sickle cell trait –Protects against falciparum
- **Homozygous Trait**: sickle cell disease

Pathophysiology

On Deoxygenation, HbS forms long polymers

↓

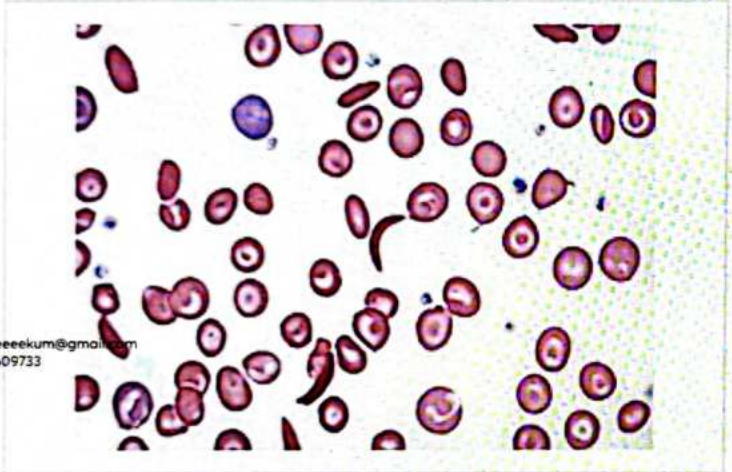
RBC membrane damage

Microvascular obstruction leading to ischemia & tissue damage.

Hemolysis in Reticuloendothelial system

Clinical Features

- Usually presents after 6 months of age
- Anemia: pallor, generalized weakness
- CNS: stroke
- Retinopathy
- Hand foot syndrome (dactylitis of hands & foot)
- Priapism (in 45% of affected male) & erectile dysfunction
- Auto splenectomy due to splenic infarcts: predisposes to infection by encapsulated organisms
- Renal papillary necrosis



Important Information

- Infection is M/C cause of death in children < 3 yrs of age

Important Information

Crises in sickle cell disease

- vaso occlusive crisis:painful
- aplastic crisis: parvovirus B19
- hemolytic crisis
- splenic sequestration
- acute chest syndrome

Diagnosis

- PS: evidence of hemolysis, sickle cells, Howel Jolly bodies
- (SICKLING TEST: mixing a blood sample with metabisulfite or dithionate induces sickling of RBCs, if HbS is present)
- Spleen biopsy: Gamma Gandy bodies
- Hb Electrophoresis to detect HbS peak or HPLC
- Confirmatory test: genetic defect checked

Treatment

- Maintain hydration
- Avoid infections & do immunisation
- Acute painful crisis: analgesia
- blood transfusion
- Hydroxyurea for patients with severe symptoms (increases HbF levels)
- Bone marrow transplantation
- gene therapy

Important Information

- HbD: in punjabi/sindhis
- HbE: in Bengal/ NE states

Fanconi Anemia 01:02:43

- AR inheritance
- Abnormal chromosomal fragility (demonstrated using Diepoxybutane or Mitomycin C)

Clinical Features

- Most common Hyperpigmentation, café au lait spots
- Short stature
- Absent radius, hypoplastic thumb.
- Facial dysmorphism: Microcephaly, small eyes, epicanthic folds, abnormal ears.
- Renal/ CNS/GIT malformations

Complications: Increased risk of tumors like squamous cell Carcinoma of Head/ Neck/Esophagus.

Treatment

- Transfusions
- HSCT (definitive treatment)

Aplastic Anemia 01:05:24

- Inherited/acquired condition with pancytopenia with hypo/acellular bone marrow

Clinical features

- Pancytopenia
  - Anemia:pallor, easy fatiguability,
  - Thrombocytopenia: bleeding manifestations
  - Leukopenia: fever, recurrent infections
- No lymphadenopathy
- No hepatosplenomegaly

Diagnosis

- CBC: pancytopenia
- PS: normocytic, macrocytic, decreased platelets, decreased WBCs
- Bone marrow: fat globules

Treatment

- Treat the cause
- Steriods
- Immunosuppressanta
- Antithymocyte globulin
- Transfusion
- Hsct

Q. A boy after playing football complaining and abdominal pain. He also had a history of hand swelling in past. On USG, he has shrunken spleen. What is the likely diagnosis of this patient? (NEET Jan 2020)

a. Sickle cell anemia

b. IDA

c. Acute pancreatitis

d. Intermittent porphyria

princeeeekum@gmail.com
9928609733

52 BLEEDING & COAGULATION DISORDERS

ITP (Idiopathic/Immune Thrombocytopenic Purpura)

00:00:20

- What is it?
  - Immune-mediated quantitative disorder of platelets

C/F

- Peak age : 1-4 yr
- Sudden onset petechiae/ bleeding manifestation in an otherwise well child, generated onset of petechiae & purpura.
- H/o preceding viral illness 1-4 week ago.
- 20% of children and 50% of adolescent who present with acute ITP leads to chronic ITP
- Chronic ITP more common in adult females

Investigation:

- Platelet count low: < 1 lakh/mm3
- Anemia +/-
- Coagulation profile normal(PT, aPTT)
- Platelet size normal/ increased
- BM- compensatory Increase in megakaryocytes
- HIV/ COOMBS test/ ANA

Treatment

- Platelet transfusion: usually avoided unless life threatening bleeding is present
- IVIg
- Anti D antibody: used in Rh positive patients
- Steroids
- Splenectomy: in severe/ refractory/ life threatening ITP
- Rituximab
- Agents that stimulate thrombopoiesis: Eltrombopag, Romiplostin

Neonatal Alloimmune Thrombocytopenia

00:08:55

- Caused by maternal Antibodies against fetal platelets Antigens inherited from father
- Ag MC responsible: HPA1a> HPA5b
- Maternal Antibodies cross placenta & destroy platelets fetus
- 50 % of cases are in 1st pregnancy
- C/F:
  - bleeding is severe in affected neonates
  - Even ICH is common

Hemorrhagic Disease Of Newborn (HDN)

00:11

- Now called "Vitamin K" deficiency bleeding (VKDB)

Classification

Refer Table 52.1

C/F: Petechiae, gum bleeding, ICH

Investigation: Increased PIVKA

Prevention/ Treatment: Inject Vit K 1mg intramuscularly to a neonates at birth

- In a child with hemarthrosis give Factor VIII replacement
- till the joint effusion subsides
- Factor VIII replacement

Haemophilia A

00:15:3

- Deficiency of Factor VIII
- X linked recessive: more common in males

Classification

- Mild (>5%)
- Moderate (1-5%)
- Severe (<1% factor level)

Clinical Features

- Bleeding, Hemarthrosis (earliest joint involved: ankle fb knee joint)

Investigation

- Increased aPTT but normal PT, BT, platelet counts, low factor VIII levels

Treatment

- Factor VIII replacement.
- If not available – use Fresh frozen plasma (FFP)

Hemophilia B

00:19:46

- XLR
- Due to deficiency of factor IX
- Cryoprecipitate cant be used in hemophilia B

Factor 12 Deficiency 00:20:39

- Elevated aPTT
- No bleeding symptoms

Factor 13 Deficiency 00:21:18

- Normal aPTT, PT, thrombin time, fibrinogen level
- Urea clot lysis test +ve
- C/F: bleeding from umbilical cord stump, recurrent epistaxis, hematuria, hematochezia

VWD 00:23:04

- VWF is carrier of factor VIII
- Intrinsic pathway affected: increased aPTT
- VWF helps in platelet adhesion to wall of vessel: increased BT
- Desmopressin is helpful in Type 1 VWD

Table 52.1

	Early onset	Classical disease	Late onset
Age	0-24 hrs	2-6 weeks	1-6 months
Etiology	• Maternal drugs e.g. Phenytoin, Rifampicin, INH	• Vitamin K deficiency • Exclusively Breast feed baby born at home	• Cholestasis • Abetalipoproteinemia • Warfarin ingestion

- Initially non-specific features: anorexia, irritability, fever
- Severe bone/joint pains
- Organ involvement: lymphadenopathy, hepatosplenomegaly, testicular involvement, neurological features
- Respiratory distress: due to severe anemia or compression of airways by enlarged lymph nodes.

Clinical differentiation b/w AML and ALL

	ALL	AML
CNS infiltration	++	+
Testicular infiltration	++	+
mediastinal LN	++	+
chloromas	-	++ (M2> M5)
gum hypertrophy	-	++ (M5)
DIC	-	++ (M3 variety)

Diagnosis

1. ≥ 20% blasts in peripheral blood or bone marrow examination is essential to diagnose ALL & AML

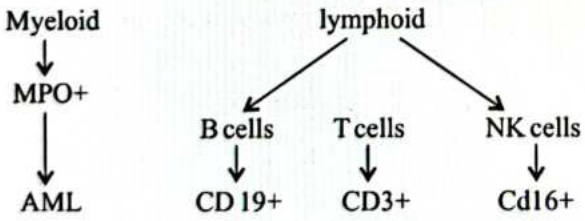
- Except
  - t(8;21)
  - t(15;17)
  - inv 16

  } irrespective of the % of blasts, it is AML.

2. Cytochemistry

- ALL: PAS+
- AML: MPO & SBB (SUDAN BLACK B-STAIN)
- Auer rods seen

3. Immunophenotyping: blasts (CD 34+)



Treatment of ALL: for 2.5 yrs to 3 yrs

A. Induction
   - V - Vincristine
   - P - Prednisolone
   - L - L-asparaginase
   - A - Anthracycline

B. CNS Prophylaxis
   - Intrathecal chemotherapy eg MTX +/- cranial irradiation

C. Consolidation/ intensification
   - M - Methotrexate
   - C - Cyclophosphamide
   - L - L- asparaginase
   - A - Ara-C

D. Maintenance
   - To prevent relapse
   - Daily 6-MP & weekly MTX
   - Given for long term

Treatment Of AML

Drugs used:

- Ara-C (cytosine arabinoside)
- Anthracycline (doxorubicin)
- Arsenic
- ATRA (All Trans Retinoic Acid)

Prognostic Markers In ALL

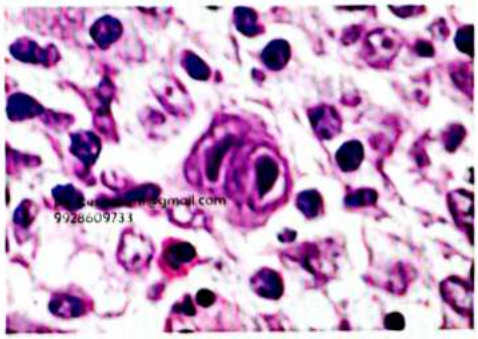
00:31:18

Characteristic	Good	Bad
Age	2-9 years	≤ 1 years or ≥ 10 years
Race	Whites	Blacks
Gender	Females	Males
TLC	< 10,000/micro L	>2 Lac/micro L
FAB WHO	L1 t (12;21) Hyperploidy	L3 t (5;14), t (9;22) Hypoploidy
Phenotypically Remission	Early Pre-B-cells ≤14 days	Mature B cells, T cells ≥28 days
MRD (Minimal Residual disease)	< 0.01 %	>0.01%

Hodgkin's Disease

00:36:02

- Clinical Features: Fever, lymphadenopathy, hepatosplenomegaly



Types	
Nodular	**Classical**
• Lymphocyte Predominant	• Lymphocyte rich • Lymphocyte depletion • Mixed cellularity • Nodular sclerosis

Ann Arbor Staging

I - Single LN or extra lymphatic site involved
II - 2 or more LN regions on same side of diaphragm involved
III - LN regions on both sides of diaphragm involved
IV - Diffuse or Disseminated disease ±LN involvement.

Treatment-'ABVD'

- **A** - Adriamycin (Doxorubicin)
- **B** - Bleomycin
- **V** - Vinblastine
- **D** - Dacarbazine

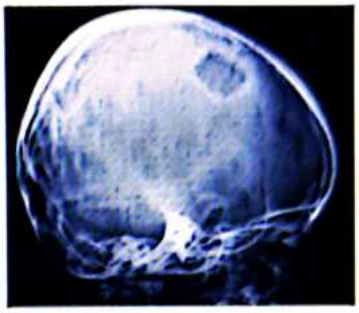
Langerhans Cell Histiocytosis

00:40:02

- Due to excess proliferation of dendritic cells.
- Types
  a. Eosinophilic granuloma → Localized disease & eosinophilia
  b. Hand Schuller Christian disease → Lytic bone defects, DI, Exophthalmos
  c. Letterer siwe disease → Multiple foci & organs involvement
- Clinical features
  a. Localized → Osteolytic bone lesions (punched out lesions) → skull & mastoid involved → chronic ear discharge
  b. Scalp - Seborrheic dermatitis
  c. Pancytopenia → increased extra medullary haematopoiesis → hepatosplenomegaly
  d. Lung involvement – Pneumothorax

a) Pituitary involved → DI & GH deficiency

- Diagnosis
  a. Biopsy: CD1a or S-100
  b. EM: Tennis racket shaped Birbeck granules
- Treatment
  a. Localized: Steroids, Radiation, Curettage
  b. Multifocal: Vinblastine, Etoposide, Prednisolone



Punched out lesion On skull

Birbeck granules On Electron Microscopy

53 HEMATOLOGICAL MALGNANCIES IN CHILDREN

- ALL
- AML
- Hodgkin Disease
- LCH

Acute Leukemia

00:00:33

- most common malignancy in children
- in children ALL > AML
- B-ALL > T-ALL
- Superior mediastinal syndrome is MC in adolescent boys with T-ALL.
- Genetic syndromes predisposing to development of acute leukemias in children
  - Down syndrome
  - Diamond Blackfan syndrome
  - Kostmann syndrome
  - Fanconi anemia
  - NF1
  - Bloom syndrome
  - Shwachman diamond syndrome
  - Li fraumeni syndrome
  - Ataxia telegiectasia
  - PNH (paroxysmal nocturnal hemoglobinuria)

How to Remember?

- Daughter Ke Father Ne Boy Ko SLAP Kia

All (Acute lymphoblastic leukemia) Classification

00:04:53

A. FAB Classification (previously used)

- Morphological classification
  - L1: small cells with min. cytoplasm
  - L2: small and large cells with predominant nucleoli and variable cytoplasm
  - L3: large cells with vacuolated cytoplasm

B. WHO classification of ALL (used now)

1. ALL with recurrent cytogenetic aberrations

Good prognosis	Poor prognosis
• t(12;21)	• t(5;14)
• Hyperdiploidy	• t(9;22)
• (trisomy 4,10,17)	• hypodiploidy

2. ALL NOS (not otherwise specified)
   - L1
   - L2
   - L3

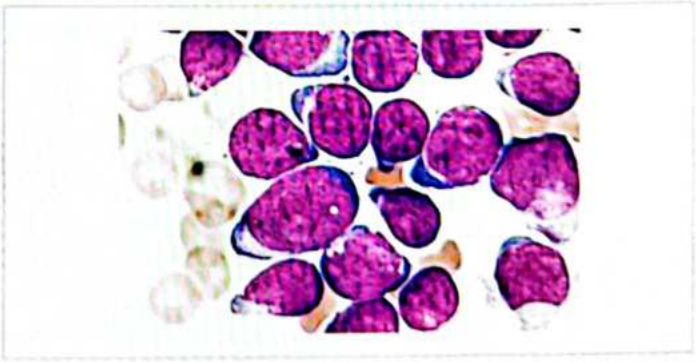
AML (acute myeloid leukemia)

WHO Classification:

1. AML with recurrent cytogenetic aberrations

Good prognosis	Poor prognosis
t(8;21) M2	t(1;22)
t(15;17) M3	t(6;9)
inv 16 M4	FLT 3 mutation
CEBPA mutation NPM-1 mutation	

2. AML with myelodysplastic changes: poor prognosis
3. AML- therapy related- poor prognosis
4. AML in Down syndrome(M7)/GATA-1 mutation – good prognosis
5. AML-NOS : M0-M7 (FAB classification)
   - M0 - minimally differentiated cells
   - M1 - without maturation
   - M2 - with maturation
   - M3 - acute promyelocytic leukemia
   - M4 - myelomonocytic
   - M5 - monocytic
   - M6 - erythroid leukemia
   - M7 - Megakaryo Blastic leukemia



Clinical features

- Pancytopenia
  - Anemia: easy fatiguability, pallor
  - Thrombocytopenia: bleeding
  - Leukopenia: recurrent infections

54 TUMORS OF INFANCY & CHILDHOOD

Retinoblastoma

00:00:32

- MC primary intra ocular tumor in children
- 40% are hereditary
- Caused by inactivation of RB1 gene on Chr 13q14
- MC presentation → Leukocoria (white eye reflex)
- Most common route of spread → Direct spread through optic nerve
- Most common secondary tumor following retinoblastoma
  - Osteosarcoma > Soft tissue sarcoma > Malignant Melanoma

Important Information

- Trilateral retinoblastoma = B/L retinoblastoma + tumor of pineal gland

Neuroblastoma

00:03:25

- MC abdominal tumor of childhood
- 98% cases are sporadic
- Most frequently diagnosed tumor of infancy [<1yr of age]
- 90% Neuroblastomas produce catecholamines → vanillyl-mandellic acid [VMA] & homovanillic acid

Site of Tumor

- Adrenal medulla [MC site]
- Along the sympathetic chain, brain [cerebral neuroblastomas]
- Adrenal medulla [MC site]

Clinical Features

- Depends on tumor site & extent of disease.
  - Localized disease: asymptomatic mass
  - Catecholamine producing: Hypertension, secretory diarrhoea
  - Extensive tumor: acute tumor lysis syndrome(ATLS), DIC
  - Metastatic disease: bluish subcutaneous nodules, orbital proptosis, periorbital ecchymoses, bone pains.

Staging

Refer Table 54.1

Prognostic factors

	Favorable	Unfavorable
Stage	Stage 1, 2A, 2B, 4S	Stage 3, 4
Age	<18 months	> 18 months
DNA ploidy	Hyper-diploid	Near-diploid
N-MYC	Not amplified	Amplified
TRKA expression (Accha)	Present	Absent
TRKB expression (Bura)	Absent	Present

Treatment

- Combination of surgery, chemo and radio therapy depending on extent of involvement.

Wilm's Tumor

00:13:01

- MC primary renal tumor of childhood
- Peak incidence → b/w 2-5 years
- MC initial clinical presentation for WT is incidental discovery of an asymptomatic abdominal mass by parents while bathing or clothing the child.
- Can present as
  - Synchronous: Both kidneys involved simultaneously
  - Metachronous: Kidneys affected one after the other

Congenital malformations with increased risk of wilms tumor

WAGR syndrome	Denys- Drash syndrome (90% risk, maximum risk)	Beckwith-Wiedemann syndrome (BWS)
Wilms tumor, Aniridia, Genital anomalies, mental Retardation	Gonadal dysgenesis (male pseudohermaphroditism), diffuse mesangial sclerosis, increased risk of gonadoblastoma	LFD, Organomegaly: macroglossia, hemihypertrophy, Omphalocele, Abnormal large cells in the adrenal cortex (adrenal cytomegaly) • Genomic imprinting is the causative mechanism

princeeeekum@gmail.com
9928609733

Staging

Stage I	Tumor confined to the kidney
Stag II	Tumor extends beyond the kidney, penetration of renal capsule ± invasion of renal sinus vessels
Stage III	Residual tumor present following surgery with regional lymph node metastasis.
Stage IV	Hematogenous metastasis (lung, live, bone, brain, etc.) or lymph node metastasis outside the abdominopelvic region
Stage V	Bilateral renal involvement by tumor

Treatment

- Surgery with or without chemo or radio therapy depending on the extent of the disease.

SACRO – Coccygeal Teratoma (SCT) 00:20:42

- Teratoma arising from sacrococcygeal region.
- Arises from totipotent cells from node of Hensen, by 2nd to 3rd weeks of gestation.
- Mostly mixed solid / cystic.
- Classification
  a. Benign [mature]: 60-70%
  b. Malignant [immature]
- Complications
  a. Ureter obstruction
  b. Gastrointestinal obstruction
  c. Anemia, tumor rupture
  d. Compression of underlying nerves – incontinence
  e. High output cardiac failure (from AV shunting)
  f. Hydrops fetalis
- Treatment & Prognosis
  - Surgical excision ± chemotherapy

Brain Tumors 00:23:20

- MC solid malignancy of childhood
- 2nd MC malignancy in children (after leukemia)
- Risk factors:
  - cranial exposure to ionizing radiation
  - Hereditary syndromes

Syndromes Associated With Brain Tumors 00:25:10

Refer Table 54.2

Refer Flow Chart 54.1

Important Information

- MC CNS tumor in children: Pilocytic Astrocytoma
- Most aggressive CNS tumor in children → Medulloblastoma
- MC CNS tumor in children < 1 yr age: Choroid Plexus Tumor

Clinical Features 00:40:02

Depend on tumor location, size, age of child

1. Supratentorial tumors (cortical tumors)
   - Subtle behavioral changes
   - Lateralized defects: focal motor weakness, seizures
   - Premature hand preferences (due to weakness of the other side of body)
   - Features of raised ICT: headache, vomiting, irritability, bulging fontanelles
2. Infratentorial tumors
   - Gait disturbances
   - Vision problems, diplopia, nystagmus
   - Headache, vomiting, papilledema
3. Tumors of brainstem
   - Gaze palsy, multiple CN palsies, UMN defects
4. Optic pathway tumors
   - Decreased visual acuity, visual field defects
5. Suprasellar tumors
   - Obesity
   - Abnormal growth velocity
   - Diabetes insipidus
   - Hypothyroidism
   - Delayed/ precocious puberty
   - Galactorrhea

Some Syndromes

1. Diencephalic syndrome 00:45:43

- Failure to thrive
- Emaciation despite normal caloric intake
- Normal or happy affect
- Seen in infants/ young children
- With hypothalamic or pituitary tumors

2. Parinaud syndrome 00:47:12

- Seen in pineal region tumors
- Paresis of upward gaze
- Pseudo Argyll Robertson pupil (accommodation reflex present but not light reflex)
- Nystagmus to convergence
- Eyelid retraction

Pilocytic Astrocytoma 00:49:12

- WHO grade I tumor

- Indolent clinical course
- MC location: Cerebellum > optic pathway
- On ME: Rosenthal fibers
- Radiology: contrast enhancing nodule within the wall of a cystic mass.
- Due to activation of MAPK pathway.
- Surgery is the primary treatment ± radiotherapy and/or chemotherapy.

Medulloblastoma 00:52:01

- WHO grade IV tumor.
- Embryonal tumor or PNET (primitive neuroectodermal tumor)
- Always arises from cerebellum.
- MC genetic abnormality: 17p deletion.
- Median age: 5-7 years.
- HPE: small, round blue cells with Homer Wright Rosettes
- Neuroimaging: solid, homogenous contrast enhancing lesion in posterior fossa causing obstruction to 4th ventricle & hydrocephalus.
- Dissemination through the CSF is a common complication: giving rise to nodular masses at some distance away from the primary tumor called as "Drop Metastases"
- Chang staging used for it previously.
- Patient < 4 yr age & those with dissemination at diagnosis: Poor prognosis

Treatment

- Surgery + chemotherapy + radiotherapy (multimodal)
- Radiotherapy is avoided in children < 3 yr age, to prevent severe neurologic sequelae & endocrine dysfunction.

Craniopharyngioma 00:59:43

- WHO Grade I Tumor
- Arises from suprasellar region
- 2 histologic types
  a. Adamantinomatous (MC)
  b. Papillary
- Clinical features
  - Endocrinologic: Growth failure, delayed sexual maturation
  - Vision: Decreased visual acuity & visual field defects
- Neuroimaging: solid tumor with cystic areas containing fluid ± calcifications
- Treatment
  - Surgery is the primary treatment.
  - No role of chemotherapy

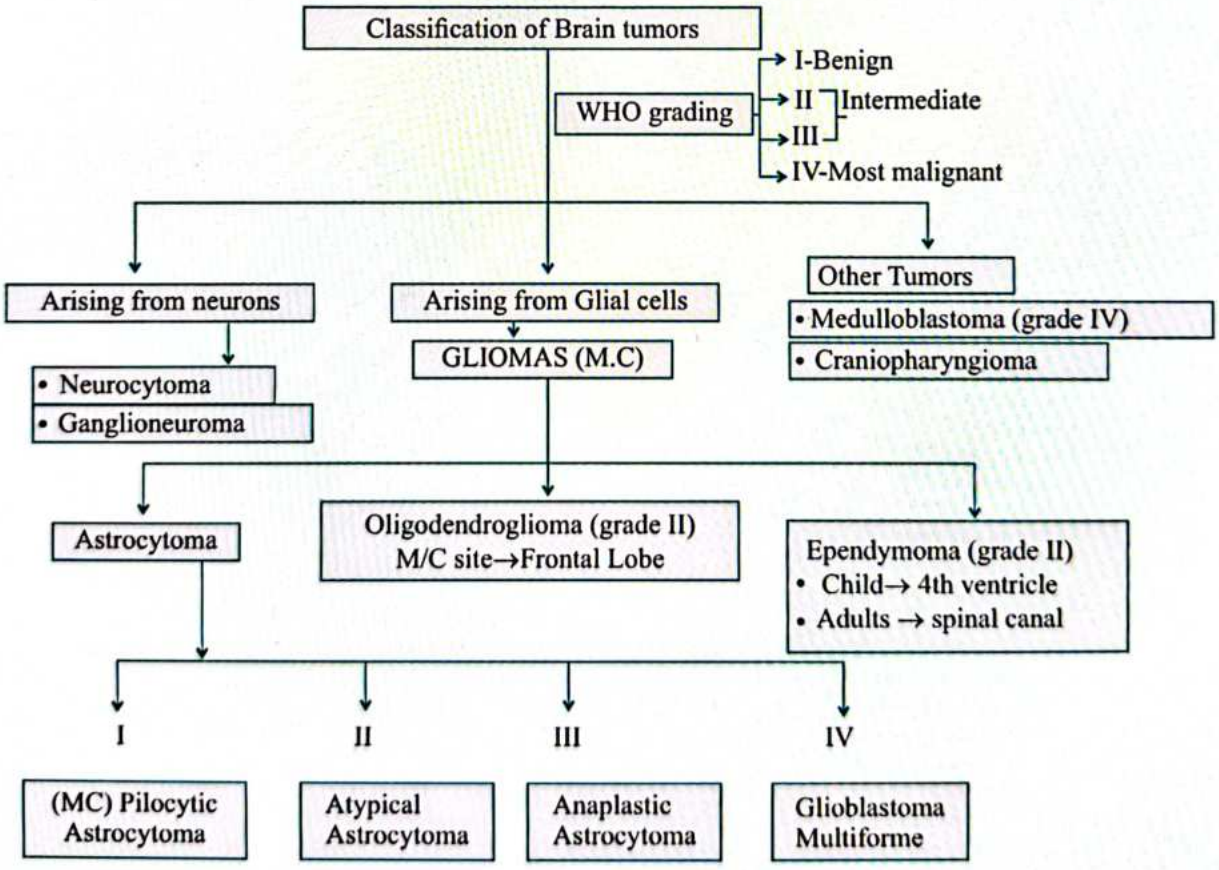
Table 54.1

Stage	Definition
1	Localized tumor with complete gross excision with lymph nodes negative
2A	Localized tumor with incomplete gross excision; with lymph nodes negative
2B	Localized tumor with ipsilateral lymph nodes positive for tumor
3	Unresectable tumor infiltrating across the midline, with or without regional lymph node involvement
4	Any primary tumor with dissemination to distant lymph nodes; bone; bone marrow, liver skin, and other organs
4S	Localized primary tumor (as defined for stage 1, 2A, or 2B), with dissemination limited to skin, liver, and bone marrow (limited to infants < 1 year of age)

Table 54.2

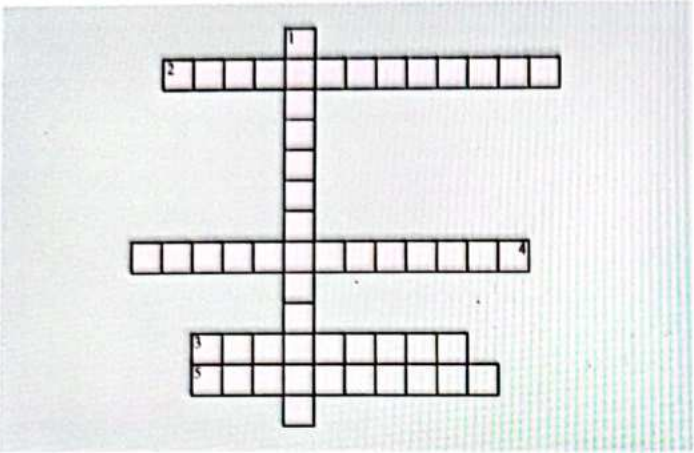
Syndrome	Tumors associated	Chromosome	Gene
Neurofibromatosis type 1 (autosomal dominant)	Optic gliomas, astrocytoma, neurofibromas, malignant peripheral nerve sheath tumors	17	NF1
Neurofibromatosis type 2 (autosomal dominant)	Vestibular schwannomas, meningioma, spinal cord ependymoma, spinal cord astrocytoma	22	NF2
Von – Hippel – Lindau (autosomal dominant)	Hemangioblastoma	3	VHL
Tuberous sclerosis (automal dominant)	Subependymal giant cell astrocytoma, cortical tubers	9 and 16	TSC1 TSC2
Li-Fraumeni (autosomal dominant)	Astrocytoma, primitive neuroectodermal tumor (PNET)	17	TP53
Cowden syndrome (autosomal dominant)	Dysplastic gangliocytoma of the cerebellum	10	PTEN

Flow Chart 54.1



CROSS WORD PUZZLES

Crossword Puzzle



Across

2. Which is the most common malignancy in children?
3. Langerhans cell histocytosis is due to the excess proliferation of _____cells.
4. Most common infra ocular tumour seen in children?
5. Sacro – coccygenl teratoma arises from _____cells from nude of Hensen, by 2nd to 3rd week of gestation.

Down

1. ____Anemia is due to Vit B12 & Idic acid deficiency.

55 DISORDERS OF GASTROINTESTINAL SYSTEM INCLUDING DIARRHOEA

A. **Esophageal disorders**
1. GERD
2. EA & TEF
3. FB esophagus

B. **Disorders of stomach and intestine**
1. Hypertrophic pyloric stenosis
2. Acute Diarrhea
3. Persistent Diarrhea
4. Lactose intolerance
5. Celiac disease
6. Inflammatory Bowel disease
7. Hirschsprung disease
8. intussusception
9. Bowel atresia
10. Peutz jegher syndrome

C. **Liver disease in children**
- N. hepatitis
- Biliary atresic
- Portal Hypertension and EHPVO
- Wilson disease

Esophageal Disorders

1. Gastro Esophafeal Reflux Disease [GERD] 00:03:07
- MC esophageal disorder in children
- Physiological GERD may be seen in infancy & resolves in upto 90% by 12 months age
- Pathologic GERD: Clinical manifestations because of frequent or persistent GER producing respiratory symptoms, esophagitis related symptoms, or nutritional effects (failure to thrive).

Diagnosis
1. Contrast esophagogram (Barium swallow) → poor sensitivity & specificity → but gives clue about achalasia or esophageal strictures
2. 24 hours Esophageal pH monitoring → quantitative & sensitive documentation of acidic reflux episodes
3. Endoscopy for erosive esophagitis / strictures.
4. GER scan – Radionucleotide scintigraphy
5. Multichannel intraluminal impedance measurement - a cumbersome test for understanding esophageal function

Treatment
- Positioning: Prone/ upright position

2. Pharmacotherapy
- Anti-acids
- H_2 receptor antagonists eg., Ranitidine
- PPIs eg., omeprazole, Pantoprazole

3. Surgery: Fundoplication for intractable GERD with refractory esophagitis

2. Esophageal Atresia (EA) & Tracheoesophageal Fistula (TEF) 00:08:47
- 5 types based on presence & location of EA & TEF
- Mc type is type C: Here proximal end is blind distal end has presence of TEF

Clinical features
- H/O of polyhydramnios during the antenatal period
- Neonate has frothing, excessive drooling
  - Coughing with feeds
  - Cyanosis
  - Respiratory distress

Important Information
- H-type Fistula may present later in life with recurrent pneumonia due to aspiration.

EA and TEF comprise a part of 'VACTERL' association
- V – Vertebral anomalies
- A – Anal Atresia
- C – Cardiac defects
- TE – Tracheoesophageal fistula
- R – Renal and radial anomalies
- L – Limb defect

Diagnosis
- Inability to pass orogastric or nasogastric tube
- On X-ray: Coiled tube in upper esophagus
- Prenatal USG

Treatment: Surgical Repair

3. Foreign Body (FB) in Esophagus 00:14:17
- Majorities of FB ingestions occur b/w 6 months & 3 years
- MC FB: Coins & small toy items

- Plain radiographs of neck, chest & abdomen (AP and lateral views)

Treatment

- Asymptomatic blunt object & coins can be observed upto 24 hours, anticipating passage into the stomach.
- Sharp objects, button batteries or respiratory symptoms require endoscopic visualization and early removal.

Disorders of Stomach and Intestine

1. Hypertrophic Pyloric Stenosis 00:16:42

Clinical Feature

- Infants with forceful, projectile, non-bilious vomiting presenting between 2-6 weeks of age

On Examination

- Visible peristalsis from left to right.
- Mobile olive shaped mass which is palpable (Best in MID-GASTRIC AREA)
- Easiest to palpate just after an episode of vomiting

Important Information

- 1st born male are MC affected
- Maternal erythromycin intake during pregnancy is a risk factor

Diagnosis

- Hypokalemic metabolic alkalosis with paradoxical aciduria
- USG is sensitive and specific method for diagnosis
- Upper G.I contrast studies shows STRING SIGN or DOUBLE TRACT or SHOULDER Sign

Treatment: Isotonic saline with Potassium to correct dehydration.

Definitive Treatment: RAMSTED'S pyloromyotomy

2. Acute Diarrhea 00:21:16

- **Definition**: Passage of 3 or more liquid or watery stools in a day
- MC cause of diarrhea in children: Rota virus

Important Information

- MC cause of constipation in children → functional or habitual due to improper toilet training
- MC cause of vomiting in a neonate → aerophagy

- Important consequence of Diarrhoea in children are – Dehydration and malnutrition

Assessment of Dehydration in a Child with Diarrhea

Refer Table 55.1

- If patient has 2 more signs including at least "1 sign" then the child has severe or some dehydration

Management of Acute Diarrhea in Children

1. **Hydration**

i. No dehydration [PLAN A]: Replacement of ongoing losses by WHO ORS [5-10 ml/kg 1 loose stool]

ii. Some dehydration [PLAN B]: 75 ml/kg over 4 hours [if cannot accept orally, give IV fluid]

STANDARD ORS (used previously)

- Osmolarity -311
- Sodium -90 mEq/L

COMPONENTS OF REDUCED OSMOLARITY ORS (or) NEW WHO ORS [in mmoL/L]

- Glucose -75
- Sodium -75
- Potassium -20
- Chloride -65
- Citrate -10
- Osmolarity -245

COMPONENTS OF ReSoMAL [Rehydration solution for malnourished child] [mmol/L]

- Glucose -125
- Sodium -45
- Potassium -40
- Chloride -70
- Citrate -7
- Magnesium
- Zinc
- Copper

iii. Treatment of severe dehydration: (PLAN C): [100 ml/kg]

Age	1st 30ml / kg	NEXT 70 ml / kg	Total over
< 1 year	over 1 hour	Over 5 hours	6 hour
> 1 year	over ½ hour	Over 2 ½ hours	3 hour

Fluid of choice for severe dehydration

- Ringer lactate in 5% Dextrose> Ringer lactate or normal saline

Important Information

- Dextrose containing fluid alone should not be used

1. Zinc: Reduces duration and severity of diarrhea in children from developing countries.
- DOSE: 2-6-month age: 10 mg/day
  6-month age: 20 mg/day
  } Duration in 10-14 days
2. Mantain Normal Diet
3. No Role of antibiotics except in
- Suspected bacterial infections like dysentery (blood, mucus in stool), cholera (rice watery stool)
- Severe malnutrition

3. Persistent Diarrhea in Children 00:38:45

Definition: Diarrhea that start as an acute episode and lasts for at least 14 days

Management

a. Correction of dehydration
b. Supplement zinc, vit A
c. Dietary modification
- Initial Diet A (Reduced lactose diet)
- Second Diet B (Lactose free diet with reduced starch)
- Third Diet C (Monosaccharide- based diet)

4. Lactose Intolerance in Children 00:41:14

Types

1. **Congenital / Primary**: Due to mutation of lactose gene on chromosome 2, very rare type
2. **Acquired / Secondary**
- More common type
- Post infectious (following diarrhea)
- Inflammatory
- Radiation
- Drugs

Clinical Features

- Diarrhea, abdominal pain & vomiting, especially on intake of milk products
- Perianal excoriation because of acidic stools

Diagnosis

- Reducing substances positive in stool
- Improvement of symptoms on exclusion of milk & milk products from diet
- Decreased lactase activity in small intestinal biopsy

Treatment

- Avoid milk, skimmed milk & milk products like ice cream, skimmed milk
- Curd / yoghurt may be given

5. Celiac Disease [Gluten Sensitive Enteropathy] 00:44:38

- It is T-Cell mediated autoimmune disorder in which intolerance to wheat, (or rye/barley/oats) containing gluten occurs.

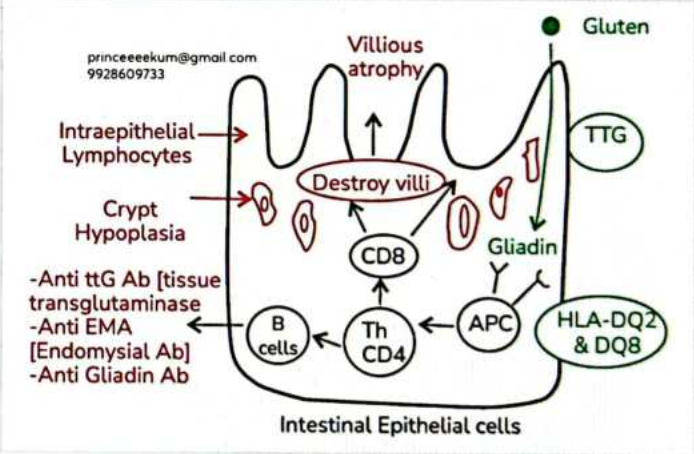
Important Information

- Oats are relatively safer in patients with celiac disease.

Pathogenesis

1. Environmental factor due to Gliadin [Component of gluten]
2. Genetic factors associated with HLADQ2 & HLADQ8 haplotypes
3. Immunological factors

- Anti TTG (Tissue Trans Glutaminase)
- Anti Endomysial Antibody (EMA)
- Anti DGP (Deaminated gliadin peptide)



Clinical Features

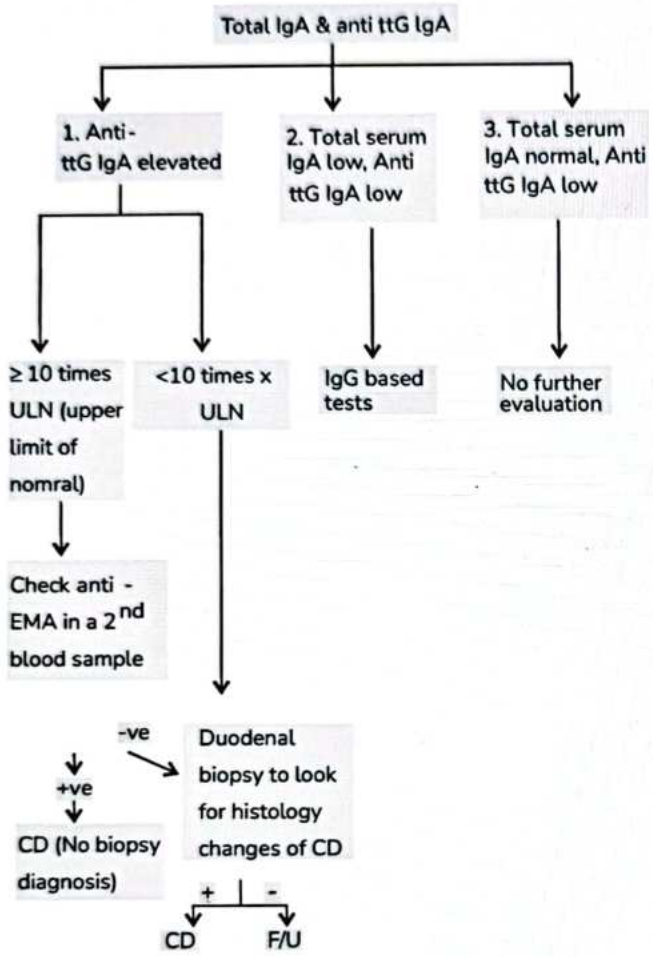
Refer Table 55.2

Important conditions associated with Celiac Disease

- Mnemonic: **Doctor Don't WAIT Today**
  - Dermatitis herpetiformis - Doctor
  - Down syndrome - Don't
  - William's syndrome - W
  - Addison's disease - A
  - Ig A deficiency - I
  - Turner syndrome - T
  - Type 1 DM - Today

Diagnosis

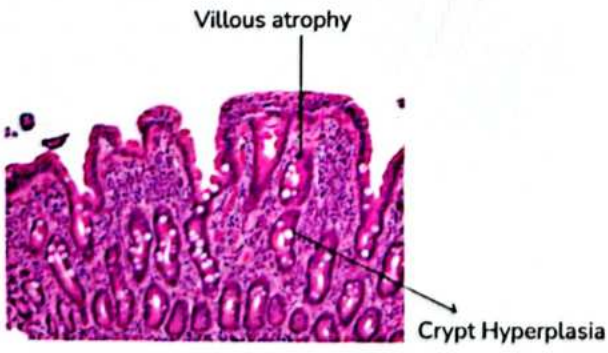
- Latest ESPGHAN (European society for Ped. Gastroent. Hepatology & Nutrition) guidelines 2019
- For initial screening for CD: combination of total serum IgA is more accurate than other tests.



Important Information

- HLA DQ2 or DQ8 testing & presence of symptoms are not obligate criteria for "NO-Biopsy" diagnosis of CD.

- Duodenal biopsy in CD



- Intestinal biopsy: Marsh grading
  - 0, 1: normal
  - 2,3: CD
- Findings: villous atrophy, crypt hyperplasia, lymphocytes infiltration

Treatment

- Lifelong gluten free diet

6. Inflammatory Bowel Disease

- Chronic recurrent disease characterized by intestinal inflammation

2 Types

1. Ulcerative Colitis: Involves the Rectum
2. Crohn's disease
- Skip lesions
- Non caseating granuloma
- Rectum is usually spared

Clinical Feature: Depends on site of involvement & severity

Ulcerative Colitis

- Involvement of rectum causes TENESMUS, Fecal urgency, Blood in stool
- Involvement of sigmoid colon causes constipation
- Involvement of descending colon causes Bloody diarrhea with pus and abdominal pain

Crohn's Disease

- Ileocolitis (involvement of Ileum and colon): causes recurrent abdominal pain and diarrhea
- Jejunoileitis: Malabsorption, low grade fever, steatorrhea, weight loss
- Colitis and Perianal involvement: cause fever, hematochezia stricture & fistula formation-

Important Information

- Rectum is usually spared in Crohn's ds
- MC part involved in CROHN'S: Terminal Ileum

Investigation of IBD

- Anemia + leukocytosis
- Increased ESR and CRP
- pANCA elevated in 60-70% cases of U. Colitis
- ASCA (Anti – Saccharomyces cerevisiae Ab) elevated in 60-70% cases of Crohn's disease

Treatment

- 5-Amino salicylic acid (5-ASA)
- Glucocorticoids
- Cyclosporin
- Azathioprine
- In mild Ulcerative colitis: Sulfasalazine
- In severe cases where strictures / fistulas are present: Surgery required

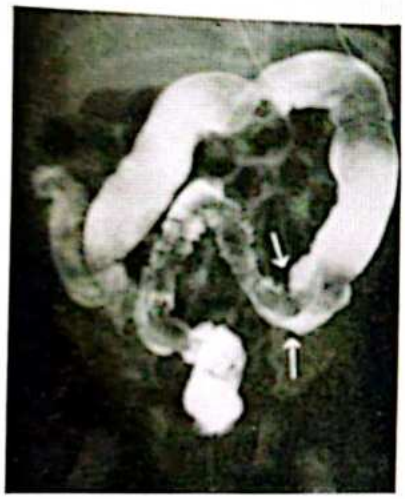
7. Hirschsprung Disease 01:12:40

- A.k.a Congenital Aganglionic Megacolon
- what is it? Occurs due to premature arrest in the descent of neural crest cells, which form the ganglions in the intestine.

Pathogenesis

a. Recto sigmoid colon involved in 80% cases.
b. No peristalsis/infolding
c. Not able to relax: dilatation of proximal normal band

- Absence of ganglion cells



Clinical features

- Neonates may present with failure to pass (or delayed passage) of meconium (greenish-black due to bile pigments), abd. distension, bilious vomiting, feed intolerance

↓

- Dilatation of proximal normal bowel & increasing Abdominal Distension

↓

- Intraluminal pressure increases

↓

- Decreased blood flow, deterioration of mucosal barrier & stasis

↓

- Proliferation of bacteria

- Enterocolitis (fever, toxic look, sepsis)

Diagnosis

- Rectal suction biopsy: gold standard
  - Absence of ganglion cells
  - Presence of hypertrophy of nerve trunks: Acetylcholinesterase or Calretinin staining
- Anorectal manometry: internal anal sphincter fails to relax in response to rectal dilatation
- Unprepared contrast enema: an abrupt transition zone between the normal dilated proximal colon & a small caliber obstructed, distal aganglionic segment.

Treatment

- surgery (surgical resection of involved segment, anastomosis of normal segment)
- Enterocolitis: IV antibiotics
- General supportive care

Important Information

- MC cause of lower intestinal obstruction in neonates: Hirschsprung disease

8. Intussusception 01:30:25

- Definition: When 1 portion of Elimentary tract is telescoped into an adjacent segment

Clinical Feature

- Sudden onset severe paroxysmal colicky pain/ excessive crying + currant jelly stools + tender, sausage shaped palpable mass in abdomen

Important Information

- MC cause of intestinal obstruction in 3 month - 6 year of age: Intussusception
- MC type: ILEOCOLIC
- Swollen peyer's patches in response to GI infection or introduction of new food can predispose to intussusception

Diagnosis

- USG has good sensitivity in diagnosis.
- Barium enema shows COILED Spring Sign Or Claw Sign

9. Bowel Atresia 01:33:57

- DUODENAL ATRESIA accounts for 25-40% of cases.
- HALLMARK of duodenal atresia: Bilious vomiting without abdominal distention
- H/O polyhydramnios in 50% cases
- On x-ray abdomen: Double Bubble Sign

10. Peutz – Jegher Syndrome 01:35:17

- A.D inheritance
- Patients with positive family history
- Mucocutaneous pigmentation seen

- Polyps mainly in small intestine(MC in Jejunum> Ileum > Duodenum)
- Extensive G.I Hamartomatous polyposis
- Maybe colonic/ gastrin polyps are present
- These polyps leads to abdominal cramping and bleeding

Important Information

- This disease predisposes to cancer of breast, colon, rectum and reproductive organs.
- Lifetime risk of cancer in these patients is 47-93%.
- GI surveillance with upper & lower GI endoscopies is recommended beginning in childhood by 8 years of age or when symptoms occur.

Table 55.1

Parameters	No dehydration	Some dehydration	Severe dehydration
Sensorium	Well alert	"Restless, irritable"	"Lethargic, floppy"
Eyes	Normal	Sunken	Very sunken & dry
Tears	Present	Absent	Absent
Mouth & tongue	Moist	Dry	Very dry
Thirst	Drinks normally, not thirsty	"Thirsty, drinks eagerly"	"Drinks poorly/ not able to drink"
Skin pinch	Goes back quickly	"Goes back slowly"	"Goes back very slowly"

Table 55.2

Clinical features of celiac disease		
System	**Manifestation**	**Possible cause**
GIT	Diarrhea, abdominal distension, Vomiting, anorexia, Failure to thrive, aphthous Stomatitis	Atrophy of small Bowel mucosa causing malabsorption
Hematology	Anemia	Iron & other vitamins Malabsorption
Skeletal	Rickets, osteoporosis, dental Enamel hypoplasia	Ca/ vit D Malabsorption
Muscular	Atrophy	Malnutrition
Neurology	Peripheral neuropathy, Irritability, seizures	Thiamine, vit B 12 Deficiency
Endocrine	Short stature	Malnutrition, ca/ Vit d deficiency
Immunology	Hyposplenism	Not known

56 IMPORTANT LIVER DISORDERS IN CHILDREN

I. Unconjugated Hyperbilirubinemia 00:00:58

Increased production	Decreased conjugation

• Hemolytic disorders
• Ineffective erythropoiesis
	• Gilbert syndrome
	  ○ Mild deficiency of UDP GT enzyme
	  ○ Increase during stress, fasting, fatigue
	• Criggler Najjar syndrome
	  ○ Type I: Severe, complete absence of UDPGT
	  ○ Type II: Milder illness with decreased UDP GT

II. Conjugated Hyperbilirubinemia 00:04:59

Dubin Johnson Syndrome

- Impaired excretion of conjugated bilirubin due to mutation in canalicular multidrug resistance protein 2 (MRP-2)
- Dark pigmentation of liver.

Rotor Syndrome

- Decreased hepatic uptake, storage & Decrease biliary excretion of bilirubin.

PFIC (Progressive Familial Intrahepatic cholestasis)

- Severe cholestatic jaundice beginning in childhood
- 3 types: GGT enzyme level elevated only in PFIC type 3

Biliary Atresia (Extra Hepatic Biliary Atresia/EHBA)

- Screening test: HIDA Scan (hepatic scintigraphy)
- Surgery: Kasai procedure. It has good outcome if done <8 weeks of age.

Important Information

- MC indication of liver transplant in children: Biliary atresia.

- A very close Differential of EHBA is neonatal hepatitis

Refer Table 56.1

III. Portal Hypertension in Children 00:17:28

- Elevation of portal pressure >10-12mm Hg
- Due to obstruction to portal blood flow, anywhere along the course of portal venous system.

Causes

A. Prehepatic (Presinusoidal)

- Due to portal vein obstruction from any cause.
- Portal vein thrombosis is the MC cause of extrahepatic portal hypertension
- Neonates: Omphalitis, UVC, dehydration, sepsis
- Older children: Appendicitis, peritonitis, inflammatory bowel disease, Hypercoagulable state.

Important Information

- Most common cause of portal hypertension in children: EHPVO (Extrahepatic portal venous obstruction)

B. Intrahepatic (Sinusoidal)

Important Information

- MC intrahepatic cause of portal hypertension in children: Cirrhosis

- Important causes of Cirrhosis in children:
  - ○ Biliary atresia
  - ○ Chronic viral hepatitis
  - ○ Autoimmune hepatitis
  - ○ Metabolic liver disease
    → In some children, non-cirrhotic portal fibrosis (NCPF)

C. Post-hepatic (Post-sinusoidal)

- Budd Chiari syndrome
- Veno-occulsive disease

Budd Chiari Syndrome 00:25:14

- Due to obstruction to Hepatic veins anywhere between the efferent hepatic veins to the entry of IVC into right atrium
- Due to
  - ○ Hypercoagulable structure
  - ○ Malignancy
  - ○ Inflammation bowel disease
  - ○ Bechet syndrome

Veno-Occulsive Disease 00:27:10

- MC cause of hepatic venous obstruction in children
- Occlusion of centrilobular venules or sub lobular hepatic veins

- It occurs most frequently in BM transplant recipients after total body irradiation.

Clinical features of portal hypertension

- Bleeding is the most common presentation of portal hypertension in children.
- Splenomegaly
- Ascites
- Growth failure
- Cyanosis, Clubbing, dyspnea (hepatopulmonary syndrome)

Viral Hepatitis in Children 00:30:16

Clinical Features

- Jaundice/icterus
- Tender hepatomegaly ± Splenomegaly ± Lymphadenopathy
- Extrahepatic features eg., arthritis, rash – MC in Hep B/C
- Acute Liver Failure
  - Bleeding
  - Altered sensorium
  - Elevated PT, unresponsive to Vitamin K.

Hepatitis A

- Highly contagious
- Feco-oral route
- Mean incubation period -3 week

Hepatitis B

- Incubation period: 45-160 days(av. 120 days)
- In children, most important risk factor for acquisition of HBV is perinatal exposure to HBsAg positive mother.
- Risk of transmission is greatest if
  - Mother is HBeAg positive
  - High maternal HBV viral load
  - Delivery of a prior infant who developed Hep B despite of prophylaxis
- Prophylaxis
  - Both Hep B Ig & Hep B vaccine should be given within 12 hours of delivery Prevents Hep B infection in neonates in >95% cases.

Chronic Hep B

- Risk of developing Chronic Hep B (HBs Ag positive for >6months) is inversely related to the age of acquisition of infection.
  - Risk of Chronic Hep B in:
    → Children < 1 year: 90%
    → Year: 30%
    → Adults: 2%
  - 1-5% cases may develop fulminant Hepatitis
  - Risk increased if
    → Co-infection/super infection with HDV
    → Host is immunocompromised.

Treatment of HEP B in children:

- Acute-Supportive
- Chronic Hep B: Rx required for patients with immune- active form of disease
- Drugs used
  - IFN alpha 2b
  - Pegylated Interferon alpha 2
  - Lamivudine
  - Adefovir, Tenofovir
  - Entecavir

Hepatitis-C in children

- Most common mode of transmission is perinatal.
- Most common Hepatitis to cause Chronic Inflammation: Hep C
- Rx for Chronic Hep C: Pegylated IFN alpha 2b & Ribavirin.

Hepatitis E

- Affects older patients
- Feco-oral transmission
- Most severe in pregnant females.

Wilson Disease 00:44:45

- Autosomal recessive
- ATP 7B gene mutation (Chr 13q 14)
- Decreased biliary copper excretion & accumulation of copper in hepatocytes.

Clinical Features

- Hepatic: Hepatomegaly, Hepatitis, liver failure, portal hypertension, ascites
- Hematologic: hemolytic anemia
- CNS: Tremors, dysarthria, dystonia, chorea.
- Eye: KF ring (Kayser Fleischer ring) & Sunflower cataract.
- Renal: Fanconi syndrome, renal failure

Investigation

- Decreased Serum ceruloplasmin level.
- Serum free copper level may be elevated
- Urinary copper excretion increased
- Hepatic copper content > 250 microgm/gm of dry liver weight
- KF ring: On slit lamp exam of eye.

Treatment

- Restrict dietary copper intake
- Avoid liver, shellfish, nuts, chocolates
- Use Cu chelating agents like

- d-penicillamine
- Zinc
- Trientine

Reye Syndrome

00:51:24

- Acute metabolic disorder resulting in generalized mitochondrial dysfunction due to inhibition of fatty acid oxidation.
- Also known as "Jamshedpur Fever".
- Fatty liver & encephalopathy seen
  - Cerebral edema
  - Hepatic encephalopathy
- Reye syndrome can be precipitated by
  - Drugs (NSAIDS)
  - toxins
  - IEM
  - Viruses e.g.: Coxsackie V, Influenza V, Adeno V, Varicella V (not by RSV).

Clinical Features

- Features of hepatic dysfunction- Hypoglycemia, Bleeding (prolonged PT) But Jaundice is rare.
- Seizures & encephalopathy seen in > 80%

Case Scenario:

- A 3-year male child with fever 5 days was given some medication (Aspirin), developed anorexia, vomiting, altered sensorium, Seizures; O/E: No jaundice but hepatomegaly seen
- On Investigation: Hypoglycemia, prolonged PT
- Diagnosis: Reye syndrome

Prognosis: Poor (Mortality 25-70% cases)

Table 56.1

	Neonatal Hepatitis	Biliary Atresia
1. Onset	• Anytime in neonatal period	• By end of 1st week of life.
2. Severity	• Mild to moderate Jaundice	• Moderate to severe Jaundice
3. Color of stool	• Variable	• Clay colored
4. Alkaline Phosphatase	• Usually normal	• Increased
5. USG abdomen	• Identifies choledocholithiasis or choledochal cysts	• "Triangular cord sign"
6. HIDA scan	• Radioactivity seen in intestine	• No radioactivity in intestine
7. Liver biopsy	• Distortion of lobular architecture, giant cells, inflammation.	• Bile ductular proliferation; portal or peri-lobular edema & fibrosis.
8. Operative cholangiogram	• Normal	• Usually determines presence & size of obstruction.

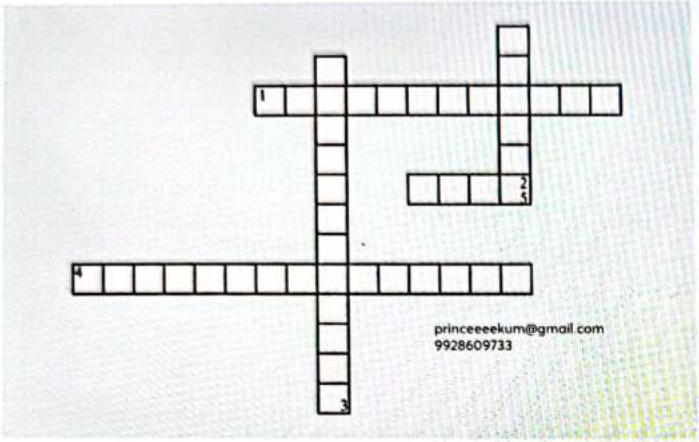
PREVIOUS YEAR QUESTIONS

Q. In a neonate on phototherapy, bilirubin is converted into?
(AIIMS June 2020)

A. Biliverdin
B. Lumirubin
C. Urobilin
D. Stercobilin

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. Involvement of sigmoid colon causes _____in ulcerative colitis
4. The condition in which 1 portion of alimentary tract is telescoped into an adjacent segment is known as?
5. Which syndrome is also known as 'Tamshedpur fever'?

Up

2. ____is mostly spared in Crohn's disease
3. Which disease is also known as 'congenital Aganglionic Megacolon?

57 IMPORTANT RESPIRATORY DISORDERS IN CHILDREN

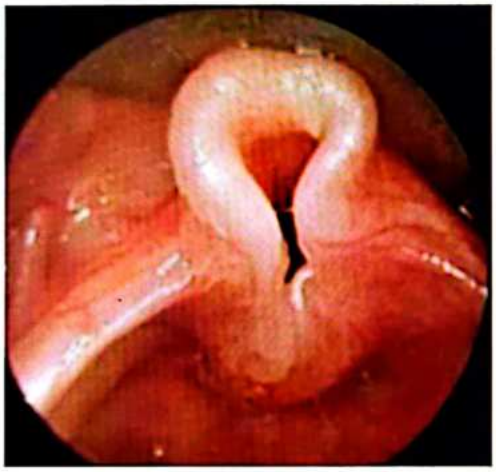
Differnece between Pediatric & Adult Airway 00:00:26

In Infant & Children

- Large head, short neck & large tongue
- Larynx is more anterior & cephalad
- Epiglottis is relatively long, 'floppy' & U-shaped
- Carina is at T_2 [T_4 in adults]
- Narrowest part of airway in children
  - At cricoid cartilage (Previous)
  - At Subglottis (Latest)

Congential Malformations of Airways 00:01:52

Laryngomalacia



- Mc causes of stridor in infants
- Stridor is exacerbated by crying, agitation or feeding
- Stridor Improves when the baby sleeps in prone position
- **Symptoms** appear in 1st 2 weeks of life, gradually increase in severity up to 6 months.
- **Diagnosis** confirmed by flexible laryngoscopy: Omega shaped epiglottis is seen

Congenital Lung Malformations 00:03:36

1. Pulmonary Hypoplasia

- Defective development of 1 or both lungs

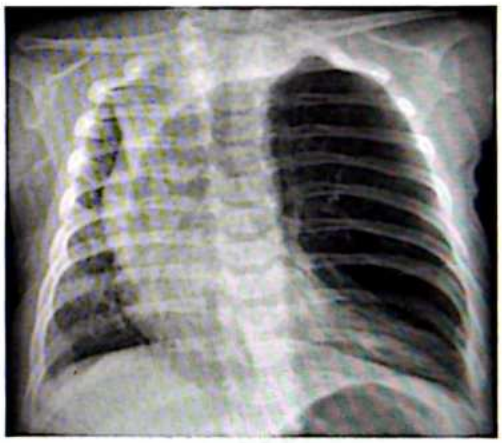
2. Pulmonary Sequestration 00:04:01

- Discrete areas of lung tissues that lack any connection with airway system.
- These areas get Abnormal Blood supply from aorta
- 2 types of pulmonary sequestration

Extra lobar type	Intra lobar type (MC)
• Present External to lungs • Causes mass affect Compressing the lung • Venous return occurs Through IVC	• Occurs inside the lung • Manifests due to localized infections or Bronchiectasis • Venous return occurs through pulmonary veins

1. Congenital Lobar Emphysema [CLE] 00:06:55

- Over distention of 1 or more lobes of lung
- Left upper lobe is Most commonly involved
- Mediastinal shift
- Atelectasis/collapse of ipsilateral normal lobe of lung
- May present in neonatal period with tachypnea, dyspnea & cyanosis
- Surgery may be required in symptomatic cases



2. Congenital Cystic Adenomatoid Malformation [CCAM] or Congenital Pulmonary Airway Malformation [CPAM] 00:09:02

- Now known as CPAM (Congenital-Pulmonary Airway Malformation)
- Basic defect-Hamartomatous/ Dysplastic lung tissue, usually confined to 1 lobe
- Present in infancy with
  - Respiratory distress
  - Recurrent respiratory infections
  - Pneumothorax
- On chest X-ray: cystic mass, sometimes with MEDIASTINAL SHIFT

- Congenital diaphragmatic hernia is a close differential diagnosis
- Surgery is indicated in symptomatic cases

Foreign Body Aspiration 00:11:06

- Most common in older infant & toddler (1-3 yr)
- Most common objects food items e.g. peanuts, toys, balloons.
- Most serious complication: complete obstruction of airway.

Clinical Features

- Initial event: Violent coughing, choking & gagging immediately after intake.
- Asymptomatic phase: FB becomes lodged, reflexes fatigue & irritating symptoms subside.

Complications

- Complete obstruction of airway (most serious): Atelectasis
- Erosion of bronchus: Hemoptysis
- Secondary infection: Fever & cough

Diagnosis

- Sudden onset choking/coughing episodes accompanied by new onset wheezing
- CXR: unilateral hyperinflated lungs due to obstruction emphysema.
  - Normal in 15-30% cases
  - Opaque FB seen in 10-25%
- **Treatment:** Prompt removal of FB by rigid bronchoscopy

58 BRONCHIAL ASTHMA

Definition: It is a chronic inflammatory disorder of airways, characterized by airway hyperresponsiveness, leading to recurrent episodes of reversible airway obstruction causing respiratory symptoms like wheezing, cough, shortness of breath, chest tightness.

Types

00:03:15

- Atopic type: more common
  - Associated with allergic rhinitis, atopic dermatitis
- Non-atopic type: triggered by viral respiratory infections, cold air, exercises

Etiology

00:05:22

1. Genetic factors

- Chr 5 : IL4, IL 5, IL 13
- Polymorphisms of ADAM 33: proliferation of smooth muscles
- Beta 2 adrenergic receptor gene variant
- IL 4 receptor gene variant

2. Environment factors

- Hygiene hypothesis: childhood exposure to germs & infections helps immune system to develop
- Dust, animal danders, smoke

3. Prenatal risk factors

- Maternal malnutrition
- Maternal smoking
- Maternal infections
- Stresses
- Use of antibiotics

Triggers

- Viral resp. infections
- Exposure to animals, dust, moulds, pollens
- Smoke: Chullah/incense sticks/tobacco
- Air pollutants/aerosols
- Drugs: aspirin, beta blockers (cause bronchospasm)
  - Aspirin inhibit cox and decrease PGE2

Pathophysiology

Refer Flow Chart 58.1

Refer Flow Chart 58.2

Clinical Features

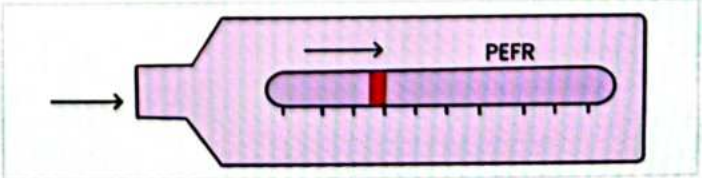
- **Classical symptoms:** cough, shortness of breath, wheeze, chest tightness
  - More at night or early morning
  - Triggered by allergens, exercise, cold air
  - Worsened with viral resp. infections
- **Severe disease:** cyanosis, altered sensorium
- **Signs of allergic disease:**
  - Skin rashes: eczema, atopic dermatitis
  - Dennie lines: B/L lower eyelid skin folds
  - Allergic salute: nasal crease
  - Allergic shiners: dark circles/ pigmentation under eyes due to congestion of nose& sinuses
  - Mouth breathers: rhinitis with nasal polyps, enlarged adenoids, DNS

Respiratory Examination

- **Severe cases:** pulsus paradoxus
- Inspection
  - Signs of increased work of breathing
  - Hyperinflated chest
  - Tripod positioning
  - Grunting
  - Inability to speak full sentences
  - Cyanosis
- Percussion
  - Hyperresonant chest
- Auscultation
  - Prolonged expiration with wheezing

Investigations

- Pulmonary function tests (PFTs) or spirometry
  - Possible only in children < 5 yr age
  - Evidence of variable expiratory airflow limitation
  - FEV1/FVC :low(80%)
  - Bronchodilator responsiveness or reversibility: FEV1 increases by 12% of baseline value after inhaling a bronchodilator
  - FEV1 increases by > 12% of predicted after 4 weeks of anti inflammatory therapy
  - Average diurnal variability of PEFR(peak expiratory flow rate) >13%
- Peak expiratory flow meters



- Portable, hand held, economic devices
- Used at home for monitoring expiratory airflow obstruction
- Fall of 20-30% from baseline: impending/ current exacerbation

D/D of bronchial asthma

- Young infants: GERD, aspiration, bronchiolitis
- 6 months to 3 yrs: bronchiolitis, transient wheezers, FB aspiration, CHD
- >3 years: transient wheeze, CHD

Treatment of asthma in children

- Identify & eliminate exacerbating factors
- Education of patients & parents
- Pharmacological therapy (Reliever& controller)

A&B

- House should be kept clean & dust free
- Wet mopping of floor & other items should be done
- Carpets, curtains, stuffed furniture- should be cleaned periodically
- Adolescent patients & parents to refrain from smoking
- Avoid strong odours: incense sticks, perfumes, wet odour
- To avoid areas that were unoccupied & closed for some days

C. Pharmacological treatment

1. Classify severity
2. Assess risk of exacerbation
3. Select medication
4. Select appropriate device & route
5. Follow up

1. Classification of asthma severity

Refer Table 58.1

2. Assess risk of exacerbation

- Uncontrolled asthma symptoms
- Medication related: ICS not prescribed, poor technique, poor compliance, high SABA use
- Co- morbidities: obesity, GERD, sinusitis, food allergies
- Exposure to smoke
- Socio economic issues
- Blood/ sputum eosinophilia
- Ever been to ICU or intubated for asthma

3. Stepwise approach to treatment

- In each step: avoid/ control triggers
- Reliever medication in all steps inhaled beta agonists eg, salbutamol
- Stepwise controller medication
  - Step 1: As per latest GINA (global initiative for asthma, 2019), all patients of asthma should receive ICS, either symptom driven or daily (because SABA doesnot protect against severe exacerbation & regular/ frequent use of SABA increases risk of exacerbation)
  - Step 2: Daily low dose ICS or daily LTRA
  - Step 3: Daily low dose ICS+LABA or daily LTRA + low dose ICS or medium dose ICS
  - Step 4: Medium dose ICS+ LABA or high ICS or add on ipratropium or LTRA
  - Step 5: High dose ICS +LABA
    → Refer for phenotypic assessment & add on treatment
    → Oral low dose steroid

- **SABA** - Short acting β agonist
- **L-ICS** - Low dose inhalational corticosteroid
- **M-ICS** - Medium dose inhalational corticosteroid
- **H-ICS** - High dose inhalational corticosteroid

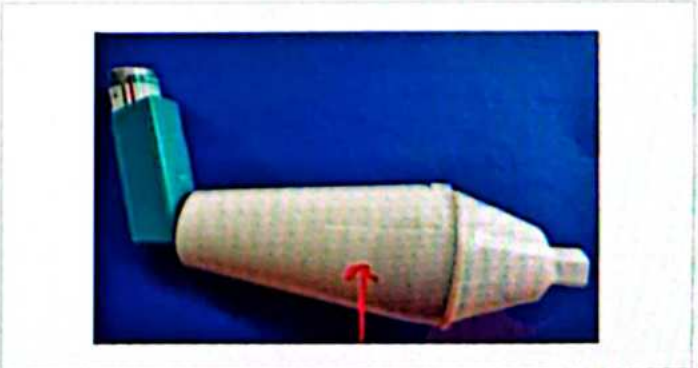
4. Devices used

a. Metered dose inhaler (MDI)

- Blue: bronchodilator
- Red: steroid

b. MDI + spacer

- Lesser coordination required
- Less impaction of drug in oropharynx



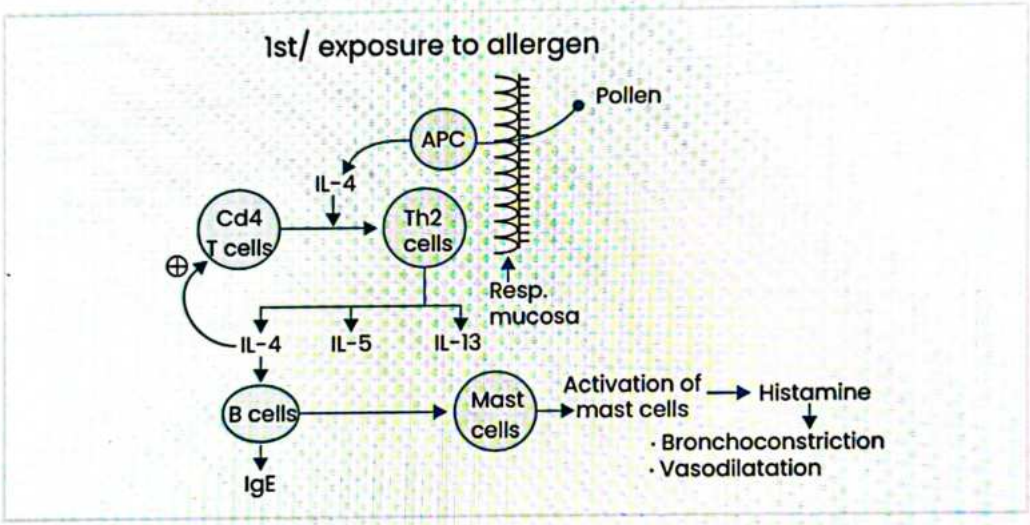
c. Using a mask

- MDI + spacer + baby mask: in children < 4 yrs

5. Follow up

- Assess technique on each visit
- Check for drug compliance
- Check asthma symptoms daily
- Classify into well/ partially/poorly controlled

Flow Chart 58.1



Flow Chart 58.2

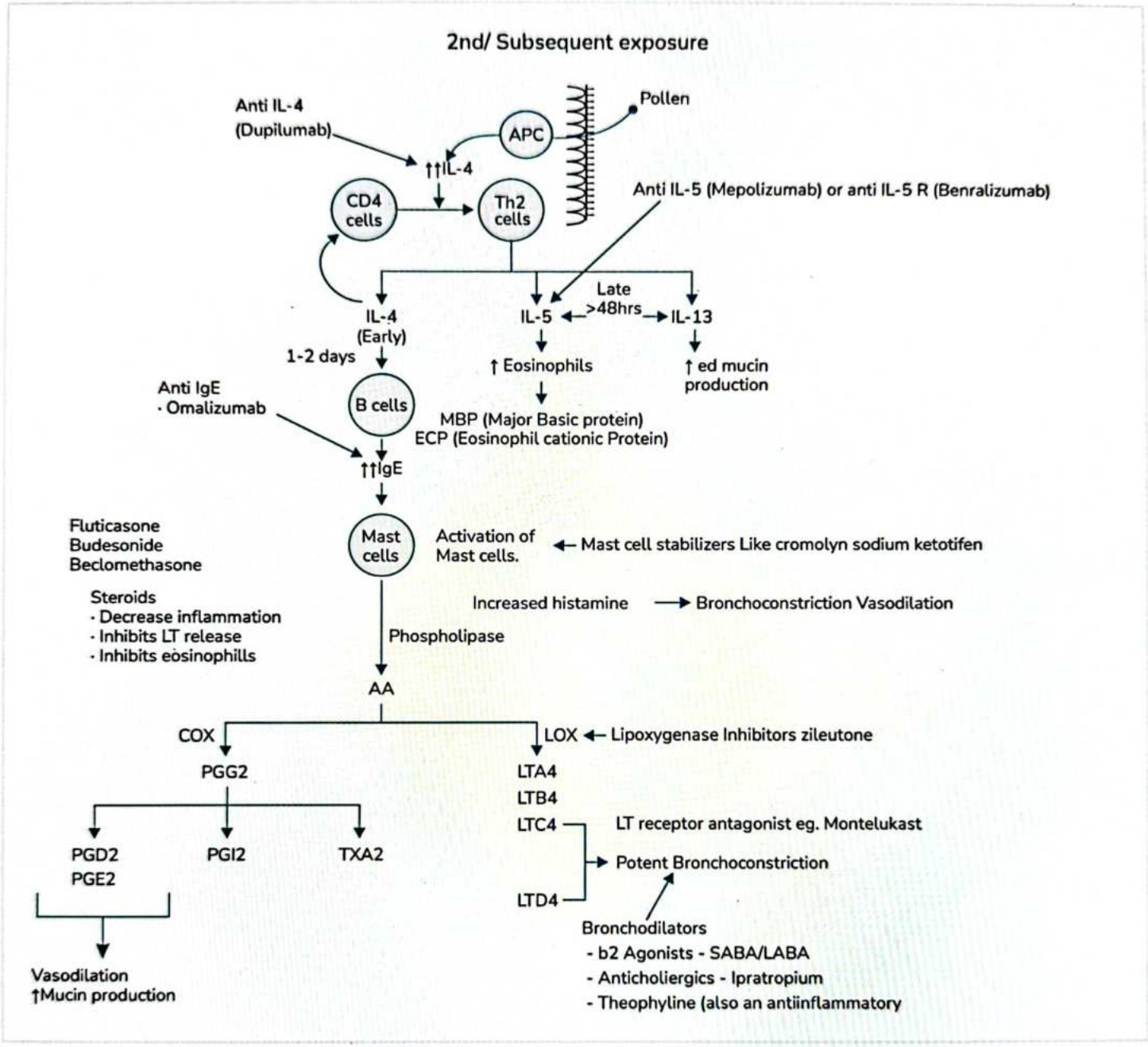


Table 58.1

Severity	Day time symptoms	Night time symptoms	FEV_1	No. of acute exacerbation/ year
Intermittent	< 2/ week	< 2 month	> 85%	≤1/year
Mild persistent	> 2/ week but not daily	3 – 4/ month	> 80%	≥ 2/ year
Mod persistent	Daily	> 1/ week	60 – 80%	
Severe persistent	Continuous	More frequent	< 60%	

PREVIOUS YEAR QUESTIONS

Q. All are indicative of pediatric asthma except?

(AIIMS June 2020)

A. Increase in FEV1 more than 15% after bronchodilator

B. AM:PM variation in FEV1 more than 15%

C. FEV1 decreases more than 15% after exercise

D. FEV1/FVC less than 80%

59 INFECTIONS OF AIRWAYS & LUNGS

- Common cold
- Acute pharyngitis
- Acute Epiglottitis
- Acute laryngotracheobronchitis
- Acute Bronchiolitis
- Pneumonia

Important Information

- MC case of acute coryza/common cold in children: Rhinovirus

Acute Pharyngitis

00:01:17

- MC cause in children: Streptococcus pyogenes
  - Viral cause: **Adenovirus**
- When to suspect streptococcal pharyngitis
  - Acute onset pharyngitis
  - High grade fever
  - Tonsillar exudates
  - Palatal Petechiae
  - Tender cervical lymphadenopathy

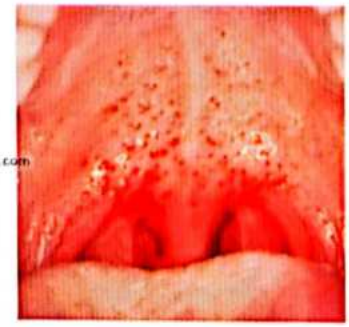
Diagnosis: Throat swab RADT (Rapid Ag Detection test) or Culture

Treatment: Penicillin / amoxicillin for 10 days

Complications

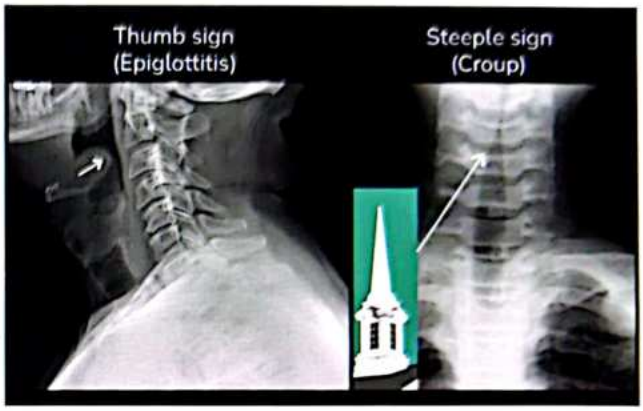
	Prevention by Antibiotics
Peritonsillar abscess	Yes
Acute Rheumatic fever	Yes
Acute post streptococcal GN	No

- Antibiotics also prevent transmission of infection to others
- Antibiotics given how many days within the onset of illness of streptococcus pharyngitis prevents rheumatic fever: 9 days of onset.



Acute Epiglottitis

00:08:12



- MC organism responsible
  - Previously, H influenza type b (Unvaccinated)
  - In Vaccinated children, currently
    - → Streptococcus pyogenes
    - → Streptococcus pneumonia
    - → Staph aureus

Clinical Features

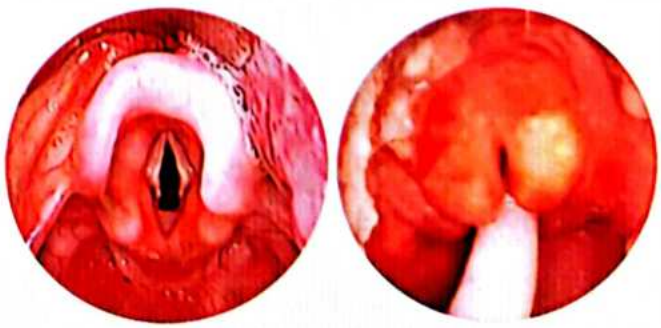
- Acute onset high grade fever
- Throat pain
- Drooling of saliva
- Respiratory distress
- Muffled voice
- Stridor

Diagnosis

- 'Cherry Red' Epiglottis on laryngoscopy
  - 'Thumb sign' on lateral X-ray neck

Treatment

- Supportive care + IV 3rd generation cephalosporin for 7-10 days



Acute Laryngotracheobronchitis (CROUP) 00:12:34

- MC ORGANISM: Parainfluenza virus

Clinical features:

- Starts with a viral prodrome & progresses to stridor, barking cough& respiratory distress. It has lesser acute onset & less severe course than acute epiglottitis

Diagnosis: CXR 'STEEPLE SIGN' due to narrowing of upper airway

Treatment

- Supportive care, including O_2.
- Single dose dexamethasone – Oral / IM
  - Effective, even in mild cases
  - Reduces the need & duration of hospitalization
- Moderate to Severe cases (Stridor at rest, Hypoxia, severe respiratory distress)
  - Supportive care + single dose dexamethasone + Nebulized Epinephrine is used
- Antibiotics are not recommended as it is viral illness

Acute Bronchiolitis 00:17:47

- MC age group: 6 months – 2 years
- MC agent – RSV (Respiratory syncytial virus)
- Other etiological agents – Influenza Virus, parainfluenza virus, Adenovirus

Clinical Features Viral prodrome (low grade fever) f/b tachypnea, retractions & hypoxemia

O/E: Hyperinflated chest & audible wheeze & Crepitation

Treatment

- Supportive: Moist O_2, IV fluids
- Specific Rx: Nebulized Ribavirin indicated only in immunocompromised children& infants on ventilator

Prevention: Palivizumab (in high risk situations)

Pneumonia 00:21:22

- It is leading infectious cause of death in children, worldwide accounting for 15% of all deaths of under 5 children
- MC cause of bacterial pneumonia in children: Streptococcus Pneumoniae
- 2ND MC cause of bacterial pneumonia in children: H. Influenza
- MC cause of viral pneumonia in children: RSV (Respiratory Syncytial Virus)
- MC cause of pneumonia in neonates: GBS > E.Coli
- MC cause of pneumonia in infants with HIV: Pneumocystis jiroveci

Approach To A Child [Cough Or Difficulty In Breathing] 00:24:14

- Latest IMNCI [integrated management of neonatal & childhood illness] guidelines

Assess

- Count breath in 1 minute
- Look for chest indrawing
- Look & listen for stridor & wheeze
- Look for any danger sign

Fast Breathing

- <2 months -> 60/min
- 2-12 months -> 50/min
- 1-5 years -> 40/min

General Dangerous Signs

- Persistent vomiting
- Unconsciousness
- Convulsions
- Inability to drink or breast feed
- Lethargy
- If wheezingis there along with fast breathing & chest indrawing, give a trial of rapid acting Inhaled Bronchodilators upto 3 times 15-20 min apart & reassess for fast breathing & chest indrawing.

Signs	Classify as	Treatment
• Any general danger sign or stridor in a calm child	• Severe Pneumonia or Very Severe Disease	• Give 1st dose of Inj Ampicillin & Gentamycin & refer urgently to hospital
• Either chest indrawing or fast breathing	• Pneumonia	• Give oral Amoxycillin x 5 days • If wheezing present, inhaled bronchodilator x 5days • Soothe the throat & relieve cough with a safer remedy • If cough > 14 days or recurrent wheeze → refer for evaluation of TB or bronchial asthma • Advise the mother when to return immediately • Follow up in 2 days • If the o_2 saturation <90% → refer urgently
• No signs of pneumonia or very severe disease	• No Pneumonia or cough or cold	• Steps 2 to 5 plus follow up in 5 days

PREVIOUS YEAR QUESTIONS

Q. A child presents with high grade fever, stridor and develops swallowing difficulty with drooling of saliva. Along with airway management, which of the following is given?
(AIIMS June 2020)

A. IV antibiotics
B. Steroids
C. Nebulized racemic epinephrine
D. Diphtheria anti toxin

Q. Steeple sign is seen in?
JIPMER Nov 2018)

A. Influenza
B. Croup
C. Laryngomalacia
D. Acute epiglottis

60 CYSTIC FIBROSIS

Genetic Basis 00:00:12

- CFTR gene [CF transmembrane Conductance Regulator]
- Chromosome 7q 31.2
- Δ F508 mutation: Most common mutation worldwide
  - In india: 19-56% of cases
- Autosomal recessive

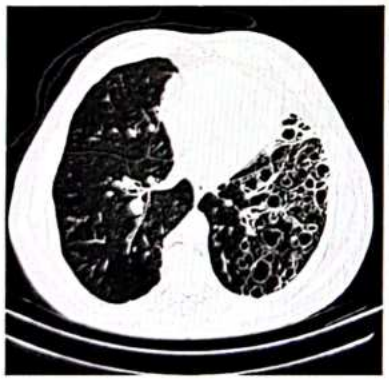
Pathophysiology 00:02:26

- Epithelial cells of bronchioles
  - Na^+ and Cl^- channel is defective and does not gets secreted in Lumen resulting in thick and viscous respiratory secretions leading to infection such as recurrent pneumonia.
- Epithelial cells of skin
  - Na^+ and Cl^- does not get absorbed therefore Cl^- level increases in sweat

Clinical Features 00:04:32

Respiratory

- Recurrent pneumonia
  - Early cases Staph. Aureus, H. influenza
  - Later colonization by pseudomonas
  - Mucoid Transformation of pseudomonas
    → Burkholderia capacia is pathognomic organism



- Eventually develop
  - Bronchiectasis
  - Atelectasis
  - Sinusitis
  - Nasal Polyps

Gastrointestinal manifestation 00:00:02

- Recurrent diarrhea
- Steatorrhea
- Failure to thrive
- Meconium ileus [new born]
- Distal intestinal obstruction syndrome in older children
- Rectal prolapse

Pancreas

- Exocrine pancreatic insufficiency
- Acute / chronic pancreatitis

Liver

- Cholestasis
- Biliary cirrhosis

Genitourinary system

- Azoospermia
- Infertility

Nutritional problems in CF

- Failure to thrive
- Hypoalbuminemia
- Vitamin deficiency
- Salt depletion
- Metabolic alkalosis

Diagnostic criteria of CF 00:10:49

- Clinical features characteristic of CF
  OR
- History of CF in sibling
  OR
- +ve NB screening for CF [IRT- ImmunoReactive Trypsinogen]

AND

- Sweat chloride (>60 mmol/L) on 2 or more occasions
  OR
- 2 mutations detected in CFTR gene
  OR
- Abnormal nasal transepithelial Potential difference

Treatment 00:13:34

For respiratory issues

- Bronchodilators
- Nebulised Hypertonic saline
- DNase inhalation
- Chest physiotherapy
- Respiratory support
- Antibiotics [inhaled /oral / IV]

Nutritional management

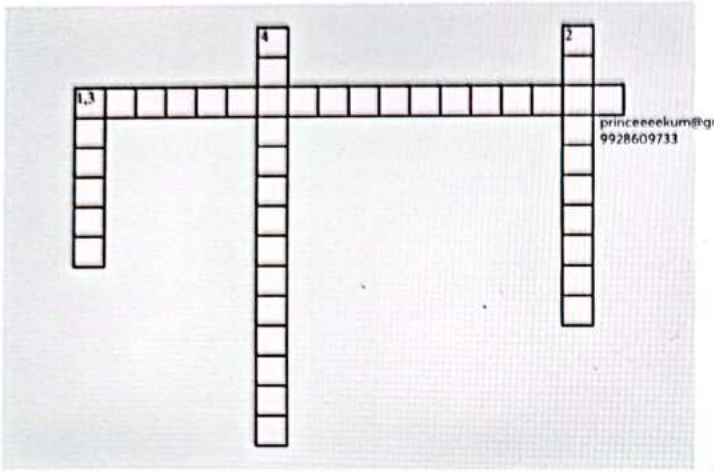
- High calorie diet
- Fat soluble vitamin
- Pancreatic enzyme supplement (creon)

Treatment of complication of such as

- Meconium ileus
- DIOS
- Appendicitis
- Rectal prolapse

CROSS WORD PUZZLES

Crossword Puzzle



Across

3. Respiratory syncytial virus is the most common agent of?

Down

1. Which is the most common type of Bronchial Asthma?
2. What is the viral cause of acute pharyngitis?
4. ____Virus is the most common organism causing. Acute Laryngotracheobronchitis (CROUP)

61 NORMAL STRUCTURE AND FUNCTION OF KIDNEY IN CHILDREN

Structure of Kidney

- Any disease leads to progressive loss of nephrons: renal insufficiency

	Length of kidney	weight of kidney
Newborn	6 cm	24 gm
Children up to (5 years)	8.5 cm	24-150 gm
Adults	>/= 12 cm	150 gm

Development of Kidneys

- Begins at 6 week of Intrauterine life
- Mesonephric (Wolffian duct) → Ureteral bud → metanephric blastoma
- In humans, formation of nephrons is complete by 34-36 weeks of gestation
- Approximately, 1 million nephrons in each kidney.
- There is functional maturation & tubular growth till the kidney continues to grow (till 18-20 years)

Function of Kidney 00:02:20

- Function of kidney is best assessed by GFR
- Glomerular filtration begins at 6 weeks of gestation
- GFR increases till renal growth ceases.
- Unit of GFR is ml/min/1.73m^{2}BSA
- To compare GFR in children & adults, GFR is standardized to body surface area (1.73m^2 of a 70 kg adult)
- Even after correction for BSA, GFR doesnot reach adult value until 2-3 yr of age

Age	Normal GFR (ml/min/1.73m2 BSA)
Preterm neonate	10
Term neonate	20-40
2-3 year	120 Adult value

Ways to assess kidney function 00:04:58

1. BUN level: affected by hydration & nitrogen balance of body
2. Creatinine level: depends on muscle mass & GFR (kidney function may deteriorate by 50 % before significant rise in creatinine)
3. Cystatine
4. Inulin clearance

Bedside assessment of GFR

- **Schwartz formula eGFR** = $\frac{\text{K x Ht (CM)}}{\text{Serum creatinie (mg/dl)}}$ where k= 0.413 in children

Urine concentrating ability

Urine concentrating ability (mosm/kg)	
Preterm	500
Term	500-700
1 year	1200-1400 (adult value)

- Normally, small plasma molecules E.g., Electrolytes(Na,K) glucose, phosphate, urea, creatinine are freely filtered across the glomerulus, while larger molecules eg., albumin, globulin are retained in circulation.

62 ACUTE & CHRONIC KIDNEY DISEASE

Acute Kidney Injury 00:00:20

Definition: Abrupt loss of kidney function, such that

- Increase in serum creatinine by ≥0.3 mg/dl from baseline within 48 hours
  or
- Increase in serum creatinine by ≥ 50% within prior 7 days
  or
- Urine volume ≤ 0.5 ml/kg/hr from ≥ 6 hrs

KDIGO staging of AKI 00:04:20

- (KDIGO: Kidney disease improving global outcomes)

Stage	Serum creatinine	Urine output
1	• ≥ 0.3 mg/dl increase or 1.5-1.9 times baseline	• < 0.5 ml/kg/hr for 6-12 hrs
2	• 2-2.9 times baseline	• < 0.5 ml/kg/hr for ≥ 12 hrs
3	• ≥ 3 times baseline (or) serum creatinine ≥ 4 mg/dl (or) indication of RRT (dialysis) (or) eGFR < 35 ml/min/1.73m^2	• < 0.3 ml/kg/ml for ≥ 24 hrs (or) Anuria for ≥12 hrs

Types of AKI & its Etiology 00:10:46

1. Prerenal AKI
2. Intrinsic Renal AKI
3. Post Renal AKI

1. Prerenal AKI

- Due to diminished effective circulating blood volume
- Inadequate renal perfusion: Decreased GFR
- Example
  - Dehydration (Diarrhea)
  - Hemorrhage
  - Cardiac failure
  - Burns
  - Sepsis

2. Intrinsic Renal AKI

- Due to Renal Parenchymal damage by Hypoxia / Ischemia & nephrotoxic insults
- Example
  - Glomerulonephritis (PSGN, LUPUS, HSP)
  - Hemolytic Uremic Syndrome (HUS)
  - Renal vein thrombosis
  - Toxins & Drugs Eg: Aminoglycosides, Amphotericin B vancomycin, cisplatin, cyclosporine
  - Tumor infiltration
  - ATLS
  - Snake bite

3. Post Renal AKI

- Obstruction of Urinary tract
- Relief of obstruction leads to recovery of Renal function except in associated renal dysplasia (or) Prolonged obstruction
- Example
  - Posterior urethral valve
  - B/L Pelvic-Ureteric 3 Junction obstruction
  - Urolithiasis
  - Abdominal tumors
  - Neurogenic bladder

Diagnosis 00:20:13

- History of AKI in an infant with vomiting & Diarrhea → 'Prerenal AKI'
- Male neonate with B/L Hydronephrosis & Palpable urinary bladder → PUV
- 6-7yr old with pharyngitis, Edema, Hypertension and Hematuria - acute Glomerulonephritis
- Critically ill child on multiple drugs → Acute tubular Necrosis

Refer Table 62.1

Complications of AKI 00:28:20

- **Metabolic**
  - Hyperkalemia – Arrthymias
  - Metabolic Acidosis
  - Hypocalcemia
  - Hyponatremia
  - Hyper phosphatemia
- **Cardia pulmonary**
  - Pulmonary edema
  - Heart failure
  - Severe hypertension
- **Hematologic**
  - Anemia
  - Bleeding
- **Neurologic**
  - Irritability
  - Seizure
  - Encephalopathy

Treatment of AKI 00:32:10

- Monitor urine output (Bladder catheterization)
- Relieve urinary obstruction (If any)
- If no fluid overload (or) Heart failure then fluid challenge NS 20ml/kg over 30 mins
- Diuretics considered after ensuring adequacy of circulating blood volume, If no response to diuretics → stop
- Patients with normal intravascular volume fluid is given in 24 hrs called AKI regime
  - Insensible loss (400ml/m^2/24 hrs) + Replacement of urine output volume by volume

↓

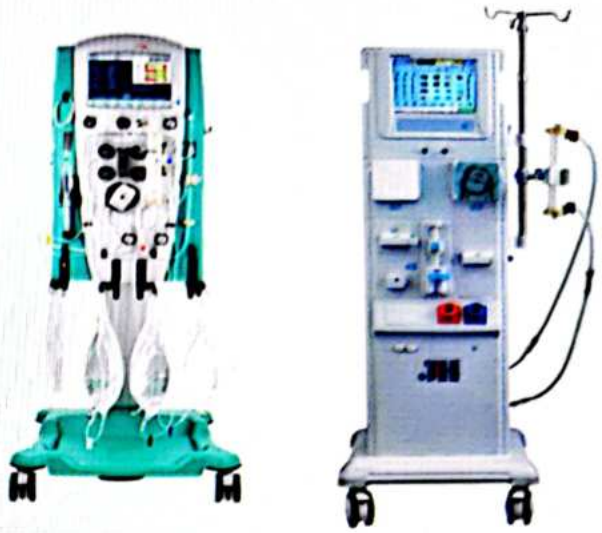
- Avoid & stop any nephrotoxic drugs if possible or modify their dosage

Treatment of complications 00:38:20

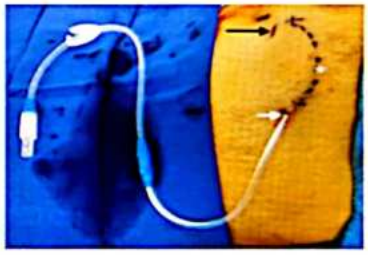
Hyperkalemia	• IV Gluconate, IV NaHCO3, Inj insulin Dextrose
Metabolic Acidosis	• Give NaHCo3 only if PH < 7.15 (or) HCO3 level < 8mEq/L
Hypocalcemia	• Decrease phosphate levels ± IV calcium
Hyponatremia	• Restriction of fluid ± Hypertonic saline if symptomatic (or) very severe
Hypertension	• Anti-Hypertensive Eg: Amlodipine, Labetolol

Renal replacement Therapy (RRT) 00:41:52

- **Indications**
  - Volume overload with pulmonary Edema
  - Refractory Hyperkalemia
  - Severe refractory Metabolic acidosis
  - Uremic encephalopathy/pericarditis
- **Modalities of RRT**
  - Intermittent Hemodialysis: Hemodynamically stable patients
  - Peritoneal Dialysis: neonates & infants
  - Continuous Renal Replacement Therapy (CRRT): Preferred in Hemodynamically unstable critically ill patients in ICU setting



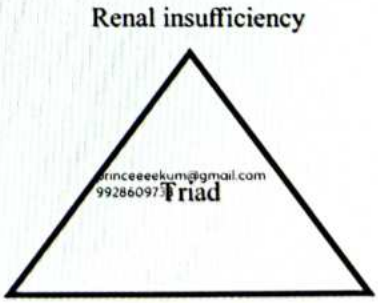
CRRT Machine



Hemodialysis machine Peritoneal dialysis

Hemolytic Uremic Syndrome 00:53:44

- Most common Thrombotic Microangiopathy in children
- Endothelial injury in the causes of HUS



Microangiopathic Hemolytic Anemia Thrombocytopenia

2 types of HUS

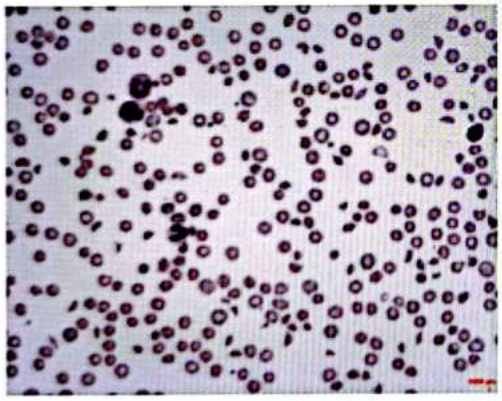
Classical (D HUS)	Atypical (D-HUS)
• Secondary to infection by shigatoxin producing E coli (0157:H7) or shigella dysentery	• Excess of activation or insufficient inhibition alternative complement pathyway
• Secondary to infection by streptococcus pneumonia, malaria, HIV parvovirus	• E.g.: Factor H deficiency factor I deficiency Anti-factor H Ab

Clinical features

- MC in preschool / school age children
- Onset 5-7 days after bloody diarrhea & Fever
- Sudden pallor, weakness, petechial, bleeding, Deceased urine output

Investigative findings

- Anemia-Rapidly progressive; increased LDH
- Thrombocytopenia
- Peripheral smear: Schistocytes
- Urine: Microscopic hematuria & mild proteinuria
- Elevated urea/creatinine



Treatment of HUS

- RRT
- Plasmapheresis
- IVIG
- Steriods
- Eculizimab (anti C5 Ab): blocks terminal complement pathway

Renal Vein Thrombosis (RVT) 01:02:41

- Begins in intra renal venous circulation

Occurs in

- Neonates/infants: Asphyxia, dehydration, shock, sepsis, central venous catheter
- Older children: Nephrotic syndrome, (CHD, Hypercoagulable states sepsis)

Clinical features

- Sudden onset gross hematuria with unilateral (MC) (or) B/L flank masses
- May present with Microscopic hematuria, flank pain hypertension

Diagnosis

- USG- Marked renal Enlargement
- Radio Nucleotide scan (DTPA)- Little (or) no filling in the affected kidney
- Doppler of renal vein & IVC – confirm the diagnosis

Treatment

- Supportive
- B/L: Tissue plasminogen activation and/or unfractionated heparin

Chronic Kidney Disease 01:07:30

Definition

A patient has CKD if either of the following is present:

1. Kidney damage ≥ 3 months as defined by structural or functional abnormalities of the kidney with / without decrease in GFR manifested by one of the following:
   - Any abnormalities in composition of blood (or) urine
   - Any abnormalities on imaging tests (or)
   - Abnormalities in kidney biopsy
2. GFR < 60 ml/min 1.73 M^2 for > 3 months

Staging of CKD 01:11:08

Stage	GFR (ml/min/1.73 m^2)
1	≥ 90
2	60-89
3	30-59
4	15-29
5	< 15 (or) on Dialysis

Etiology of CKD

01:12:13

Glomerular	Non glomerular
Door Camp	
• D - Dysplastic kidney • O - Obstructive uropathy • O - Oxalosis • R - Reflux nephropathy • C - Cystinosis • A - ARPKD, ADPKD • M - Medullary cystic kidney • P – Pyelonephritis	• Chronic glomerular nephritis • Alport syndrome • Lupus nephritis • HUS • HSP Nephritis • IGA Nephropathy • MGN • MPGN

Clinical features

01:15:33

Growth restriction (short stature)	• Anemia, inadequate nutrition, • Renal osteodystrophy
Anemia	• Decreased Erythropoietin, • Iron & vitamin B12 deficiency
Bleeding	• Uremic platelet dysfunction
Infection	• Defective granulocyte function
Hypertension	• Volume overload, increase rennin production
Renal osteo-dystrophy	• Decreased calcitriol, hypocalcemia, hyperphosphatemia, Hyper para- thyroidism

Investigative findings

01:18:45

Increased urea & creatinine	• Decreased GFR
Hyperkalemia	• Decreased GFR, metabolic acidosis
Hyponatremia	• Solute diuresis
Metabolic acidosis	• Impaired HCO3 reabsorption, decreased acid excretion
Urine concentrating defect	• Solute Diuresis & tubular damage

Treatment of CKD

01:20:40

- Supportive

Nutritional rehabilitation	• Adequate calories + Micronutrients
Treatment of anemia	• Inj Erythropoietin, Fe, Multivitamins
Anti- hypertensives	• ACE inhibitors, ARB's
Renal osteodystrophy	• Calcitriol
Phosphate binders	• Eg Caco3, Ca Acetate, sevelamer
K+ binding resins	• Kayexalate
RX of metabolic acidosis	• Sodium Bicarbonate tablets

- Adjust drug according to GFR
- RRT
  - Intermittent HD
  - Continues Ambulatory Peritoneal dialysis
  - Renal transplantation

Table 62.1

Lab parameters	Pre renal AKI	Renal AKI
Urine specific Gravity	>1.020	<1.010
Urine osmolality	>500 mosm/kg	< 350 mosm/kg
Urine Na	>20 meq/L	>40 meq/L
Fractional excretion of sodium $FeNa = \frac{U_{Na} \times P_{cr}}{P_{Na} \times U_{cr}} \times 100$	<1% (<2.5% in neonates)	>2% (>10% in neonates)

63 CONGENITAL ABNORMALITIES OF GENITOURINARY TRACT

Normal Renal Development 00:00:10

- Begins in 5th week of Intrauterine life
- Ureteral bud arises from mesonephric (wolffian) duct and Penetrates metanephric Blastema
- Metanephric Blastema: Undifferentiated mesenchyme on nephrogenic ridge

Unilateral Renal Agenesis 00:01:59

- Absent kidney development on one side
- Secondary to defect of wolffian duct / ureteral bud / Metanephric blastema
- Increased incidence in neonates with 'single Umbilical artery'

Assoicated genitourinary abnormalites

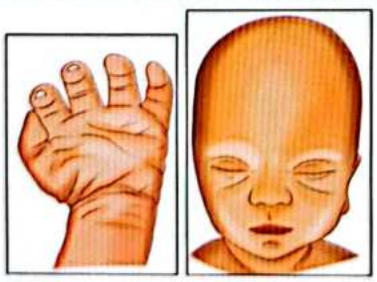
- **Males**
  - Absent ipsilateral vas deferens
  - Contralateral (verico Ureteric reflux)
- **In Females**
  - Meyer Rokitansky kuster Hausen (MRKH) Syndrome: Vaginal aplasia, uterine Mal-development
- Contralateral kidney undergoes compensatory Hypertrophy

Important Information

- **Renal Aplasia**: A small lump a non-Functioning tissue is seen capping the ureter

Potter Syndrome/Sequence 00:05:31

- B/L renal agenesis (incompatible with life)
- Clinical features
- **Mnemonic: POTTER**
  - P – Pulmonary Hypoplasia (MC cause of mortality in Potter syndrome)
  - O - Oligohydramnios
  - T – Twisted Facial Dysmorphism
  - T – Twisted skin (wrinkled skin)
  - E – Extremities anomaly
  - R – Renal agenesis B/L (Primary anomaly)

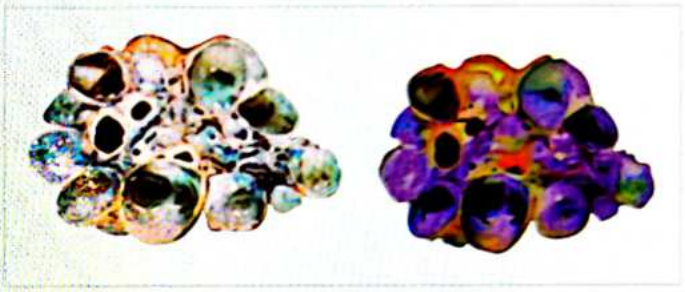


Potter facies

- Eyes widely separated
- Epicanthic folds
- Depressed Bridge of nose
- Low set ears
- Receding chin

Multi Cystic Dysplastic Kidney (MCDK) 00:08:34

- Entire kidney is dysplastic and replaced by multiple cysts of varying sizes and are non-functional
- Usually unilateral
- Non-Inherited disorder
- B/L MCDK is not compatible with life
- MCDK is the most common cause of abdominal mass in newborn.
- Increased risk of Wilm's tumor



Ask-Upmark Kidney 00:10:36

- Aka segmental Hypoplasia
- Kidneys with one or more deep groves on the lateral convexity under which parenchyma consists of tubules resembling those in thyroid gland
- Most patients have severe hypertension

↓

May even require Nephrectomy

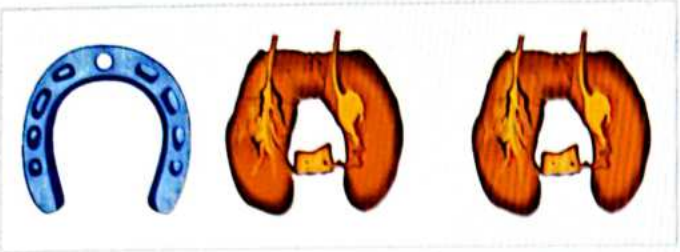
Simple Renal Cysts 00:11:40

- Usually diagnosed incidentally
- Mostly Asymptomatic and No Rx required
- Further evaluation may be warranted for
  - Septations
  - Irregular margins
  - Cluster of cysts
  - Calcifications

Horse Shoe Kidney 00:12:55

- Fusion of lower poles of both kidneys in midline
- Common in Turner syndrome
- Chances of Wilm's Tumor are 4 times more common than general populations

- Nephrolithiasis and hydronephrosis are important complications (due to compression of ureters by isthmus)



Autosomal Recessive Polycystic Kidney (ARPKD)

00:14:38

- Gene-PKHD1 Gene (Polycystic kidney and Hepatic disorders)
- Fibrocystin-Autosomal recessive inheritance
- Both kidneys are markedly enlarged with innumerable cysts throughout cortex and Medulla
- M/E: Dilated ectatic collecting ducts which radiate from the medulla to cortex

Pathophysiology

- Progressive Interstitial fibrosis and tubular Atrophy

↓

Renal Failure

- Bile duct Proliferation and Ectasia leading to progressive Hepatic fibrosis

Clinical feature

- Antenatal USG - Oligohydramnios & B/L enlarged kidneys
- Infant

a. B/L flank masses in early infancy, Respiratory distress, severe Hypertension, oliguria and AKI

b. 50% develop ESRD (End Stage Renal Disease) by 10 years of age

- Hepatic fibrosis: Portal Hypertension, varices, Hepatosplenomegaly, Ascending Cholangitis and thrombocytopenia

Investigation

- USG Abd → Markedly enlarged and uniformly hyperechogenic kidneys with poor corticomedullary differentiation

Treatment

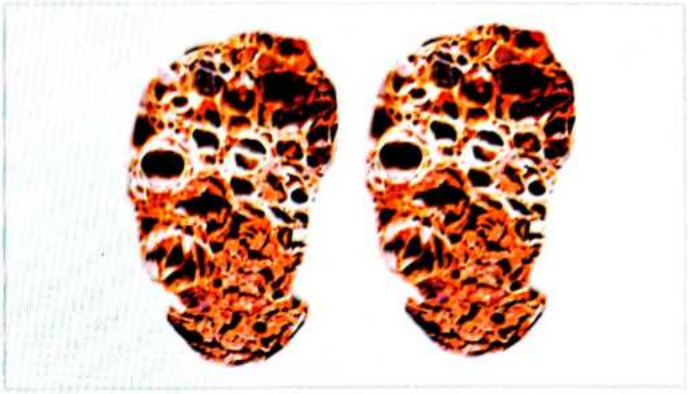
- Supportive

Autosomal Dominant Polycystic Kidney Disease 00:18:49

- MC inherited kidney disease
- Multisystem disease (cysts in liver, pancreas, spleen and brain: saccular cerebral aneurysm)

Genes

- PKD1 Gene on ch16- polycystin (more severe)
- PKD2 Gene on ch 4- polycystin 2
- B/L enlarged kidneys with large cortical & Medullary cysts, arising from all regions of Nephron



Clinical features

- Symptomatic MC in 4th or 5th decade
- Hematuria (gross or Microscopic)
- B/L Flank pain
- Abdominal mass
- Hypertension
- UTI may be seen in children

Dx

- USG – B/L enlarged kidneys with Macrocysts in a patient with an affected 1st degree relative
- Screening USG - may be normal in:
  - <20%. by 20yrs age
  - <5% 30yr age

Treatment

- Supportive
- HTN treatment: ACE inhibitors, ARBs

Nephronophthesis 00:22:01

- NPHP 1-9 Genes (Nephrocystin-AR)
- Renal fibrosis, Tubular atrophy and Cyst formation
- One of the common causes for ESRD in children & Adolescents

Clinical feature

- Polyuria
- Failure to thrive
- Anemia
- Later Hypertension and edema
- ESRD

Bladder Exstrophy 00:23:16

- M:F-2:1
- Severity: Epispadias (Male) to complete exstrophy of cloaca (exposure of entire hindgut and bladder)

Clinical feature

- Urinary Bladder protrudes from Anterior abdominal wall and its Mucosa is exposed
- Umbilicus displaced downwards
- Pubic rami widely separated
- Rectus Muscles separated
- In males -Complete Epispadias, undescended testis, Inguinal Hernia common
- Anus displaced anteriorly and/or Rectal prolapsed (both males and females)

Consequence

- Total urinary incontinence
- Increased Risk for bladder adenocarcinoma

Treatment

- Cover the defect with a plastic wrap to keep the Mucosa moist
- Surgery

Ectopic Ureter 00:27:17

- A condition where the ureter instead of terminating into the urinary bladder terminates at a different site.

Common sites

- Female: urethra, vestibule, vagina
- Males: posterior urethra, prostatic utricle, seminal vesicle

Clinical feature

- Incontinence/continuous dribbling of urine
- Infections
- Hematuria
- Flank pain
- Vaginal discharge

64 NEPHRITIC & NEPHROTIC SYNDROMES

Nephritic Syndrome

00:00:20

Definition

- Sudden onset of gross Hematuria(cola coloured urine) & Proteinuria (nephritic range), edema, Hypertension with or without Renal Dysfunction
- Nephritic Range Proteinuria
- To detect proteinuria in children, take morning sample & do Urine protein: urine creatinine
- Most common cause of nephritic syndrome in children → PSGN (Post streptococcal Glomerulo nephritis)
- Hematuria in a child

Number of days after URI	Probable underlying diagnosis
1 – 2 days	IgA nephropathy
1 – 2 weeks	PSGN

Up: Ucr	Dipstick
<0.2 normal	nil or trace
0.2-2 Nephritic range Proteinuria	1^+ or 2^+
>2 nephrotic range (or) massive proteinuria	3^+ or 4^+

Important Information

- MC cause of Nephritic syndrome in children – PSGN (Post streptococcal Glomerulonephritis)
- It is one of the most common syndrome cause of gross hematuria in children

Hematuria in a child	
No of Days after URI	Probable underlying diagnosis
1-2 days	IgA Nephropathy
1-2 weeks	PSGN

PSGN (Post streptococcal Glomerulonephritis)

00:04:00

- Follows infection by nephritogenic strains of group A β hemolytic streptococcus causing Pharyngitis (M1, 4, 25) (or) skin infection (M_{49})

Pathophysiology

- Deposition of immune complexes with streptococcal antigen & complement activation
- Antibodies against them cross react with Glomerular antigens due to molecular mimicry

Clinical features

- MC age: 5-12 years
- Symptoms usually appear 1-2 weeks after URI & 3-6 weeks after Skin infections
- Nephritic picture: coca colored urine, edema, proteinuria, oliguria
- Severe cases: AKI , renal function test may be deranged
- Acute phase usually resolves in 6-8 weeks

Diagnosis

- Urine examination: proteinuria (1+ to 2+, Up:Uc of 0.1-2) RBCs and RBC casts
- C_3 Levels decreased in in 90% of patients
  - Normal in 6-8 weeks of onset
- Increased ASO (Anti Streptolysin O) titer following pharyngitis

  } Evidence of prior Streptococcal infection
- ↑Anti DNASe B following Pyoderma
- **Indications of Renal biopsy in PSGN**
  - AKI
  - Nephritic-Nephrotic presentation
  - Normal C_3 at the beginning
  - C/F &/or elevated C_3 levels persisting even > 2 months after of illness
- **Renal Biopsy finding in PSGN**
  - **Light microscopy**: Neutrophilic infiltration in Glomeruli & diffuse mesangial proliferation
  - **Electron microscopy**: 'Sub epithelial humps" (below podocytes)

Treatment

- Diuretics
- Early antibiotics do not eliminate the risk of glomerulonephritis
- Salt & water restriction
- Anti – hypertensive
  - Eg: Ca channel blockers, ACE inhibitors

Prognosis
- Complete recovery seen in >95% children
- Chronic Glomerulonephritis 2-4 %
- RPGN in 1%

1. Rapidly progressive glomerulo Nephritis (RPGN)
- Rapid loss of Renal function following GN

3 Types

I	II	III
Anti GBM Ab Mediated	Immune complex mediated	Pauci Immune (ANCA +ve)
• Good pastuer syndrome	• PSGN • IgA Nephropathy • HSP nephritis	• Churg strauss syndrome • Microscopic poly angiitis • Wegner's Granulomatosis

Clinical features in RPGN
- AKI
  - Oliguria/Anuria
  - Raised renal function test
  - Bleeding manifestations
- Many presents as nephritic syndrome may present as Nephrotic syndrome
- Hypertension & Loin pain

Investigation
- **Urine**
  - Hematuria & Proteinuria
  - Serum C_3 level normal usually
- **Kidney biopsy**
  - Mesangial Proliferation & IgA deposits in mesangium

Kidney Biopsy finding

Hallmark	• Epithelial Crescents (crescentric GN) involving ≥ 50% of glomeruli ↓ Later, fibrous crescents	• Proliferation of parietal epithelial cells of Bowman capsule.

Treatment
- Corticosteroids
- Cyclophosphamide
- Plasmapheresis

2. IgA nephropathy 00:21:24
- Aka Berger's disease
- It is the MC chronic glomerular disease in children

Clinical features
- Males > Females
- Gross Hematuria recurrent episodes within 1-2 days following URI

Treatment: Is supportive
- BP control (ACE inhibitors & ARB)

Prognosis
- Progressive disease in 20-30% adults, 15-20 years after onset

3. Alport syndrome 00:24:44
- Aka Hereditary nephritis

Genetics
- ~85% patients have x linked: COL_4A_5 Gene
- ~15% patients have AR: COL_4A_3, COL_4A_4 Gene
- Mutation in Gene encoding type IV collagen which is an important component of Basement membrane

Clinical features

Kidneys	Eyes	Ears
• Proteinuria • Hematuria	• Anterior Lenticonus (Pathognomic) • Corneal erosions • Macular flecks	• B/L – Sensory neural hearing Loss (not congenital) in 90% of males with X- linked disease

Diagnosis
- Family history
- Screening urinalysis of 1st degree relative

- Audiogram
- Ophthalmic examination
- **Kidney biopsy**
  - Light microscopy: progressive Glomerular Sclerosis, Tubular atrophy, Interstitial Inflammation
  - Electron Microscopy: "Basket weave appearance", Due to splitting of Glomerular basement membrane
  - Genetic Diagnosis: possible mutation in COL_4A, Gene
- **Skin biopsy**
  - Absent epidermal basement membrane staining for , chain of type IV collagen in Hemizygous males (Pathognomonic for X – linked Alport syndrome)

Treatment

- ACE inhibitors & ARBs
- **Prognosis**
  - Risk of end stage Renal disease is high among male Hemizygotes
  - ESRD seen at <30 years in 75% hemizygotes

Nephrotic Syndrome

00:31:45

- Nephrotic range/massive proteinuria (Up: Ucr >2 or ≥ 3 protein on dipstick testing)
- Generalized edema (MC presenting symptom)
- Hypoalbuminemia
- Hyperlipidemia

Congenital nephrotic Syndrome

- Manifests at birth or within First 3 months of life

Etiology

Refer Table 64.1

Genetic defects

Genes	Protein	Phenotype
NPHS1	Nephrin	Congenital nephrotic syndrome (finish variety)
NPHS2	Podocin	FSGS SRNS
NPHS3	PLCE1	SRNS (Steroid resistant nephrotic syndrome)
WTI	Under phenotype in adjacent box	

Syndromes associated with congenital nephrotic syndrome

1. Denys Drash syndrome: WT1 gene
2. Frasier syndrome: WT1 gene
3. Pierson syndrome: LAMB 2 gene
4. Nail patella syndrome: LMX1B gene
5. Galloway Mowat syndrome

Important Information

- MC cause of Nephrotic syndrome in children – minimal change disease (in 2-6 yrs)
- Kidney biopsy
  - LM|: Normal
  - EM: Effacement of foot process of Podocytes
- M/C cause of Nephrotic Syndrome in Adolescent: FSGS
- M/C cause of ESRD in Adolescent: FSGS

Clinical features of nephrotic syndrome

1. **Edema**

Begins usually as puffiness around eyes(Periorbital edema)
↓
Pedal edema (pitting)
↓
Generalized edema (MC presenting symptom)
↓
Anasarca (pleural effusion, Peritoneal collection)

2. Increased susceptibility to infections

- Loss of Ig & complement factors lost in urine
- Mainly by Encapsulated organisms Eg: Pneumococcus
- Cellulitis, SBP (Spontaneous Bacterial Peritonitis)

3. Hypercoagulability

- Increased risk of thrombosis
- Due to Hemoconcentration & vascular stasis, loss of protein S & Antithrombin III in urine

Investigations in Nephrotic syndrome

- Morning urine sample-up: ucr >2 or ≥3+ protein on Dipstick and hyaline casts
- Low serum albumin: 2.5g/dl
- Increased lipid levels (TG & cholesterol)
- Usually urea/creatinine initially normal
- In children presenting with first episode of nephrotic syndrome >10 yrs age at onset of illness investigate for
  - ANA
  - C3
  - Anti ds DNA
  - Hepatitis B, C
  - HIV
  - Kidney Biopsy

Indications of kidney Biopsy in Nephrotic Syndrome

- Children < 1 year or > 10years age at onset of illness
- Family H/O nephritic Syndromes Present
- Presence of extra renal findings: rash/arthritis/anemia
- Acute or chronic Renal insufficiency
- Hypertension
- Gross hematuria

Treatment of Nephrotic syndrome in children

- DOC for initial episode of Nephrotic syndrome in a child: Prednisolone
- **Dose:** 2mg/kg/day or 60 mg/m^2/ day daily for 6 weeks f/b 1.5 mg/kg/day or 40mg/m^2/day every alternate day for 6 weeks (80%-90% children respond within 2-3 weeks)
- **Response to Rx:** Remission within initial 4wk of steroid therapy
- **Relapse**:Recurrence of nephrotic range protienuria and Increased morning urine up: ucr ≥2 (or) urine Protein ≥3+, for 3 consecutive days, in a child with NS. who had previously gone into remission
- **Frequently Relapsing NS: (FRNS):** 2 or more relapses within 6 months of initial treatment (or) 4 or more relapse within 12 months
- **In frequent Relapsing Nephrotic Syndrome: (IFRNS):** Frequency of Relapses is less than that of FRNS
- **Steroid dependent nephrotic syndrome (SDNS):** Relapse during steroid tapering or within 2 weeks of stopping steroids
- **Steroid resistant Nephrotic Syndrome: (SRNS):** Absence of remission within 4 weeks of daily steroid therapy

Treatment based on type of nephritic syndrome

1. **IFRNS**
- Treat each relapse
- Prednisolone 2mg/kg/day till remission or 60mg/m2/day till remission every alternate day for 4 weeks
2. **FRN (or) SDNS:** Tappering doses of alt day steroids

Steroid threshold	Steroid threshold
<0.5 mg/kg alternate day ↓ Continue long term alternate dose alternate day prednisolone for 18 months	>0.5 mg/kg alternate day (or) features of steroid Toxicity use steroid sparing drugs ↓ • Levamisole • Oral cyclophosphamide • Mycophenolate Mofetil

3. **SRNS**
- Usually caused by FSGS in 80% cases
- DOC:Calcineurin inhibitors (Cyclosporine/Tacrolimus)
4. **Refractory cases:** Rituximab (Anti CD2O)
5. **Supportive care**
- Severe edema
  - Salt &/or fluid restriction
  - Albumin infusion f/b Furosemide cautiously
- Hyperlipidemia
  - Limit dietary fat intake
- Infection
  - Treat with Antibiotics
  - SBP:MC cause is streptococcus Pneumoniae
  - Rx: 3rd gen cephalosporins iv

Prevention of infection by Immunization

- Respiratory Pneumococcus
- Annual influenza vaccination

Table 64.1

Primary/idiopathic	Secondary	Hereditary
• Minimal change disease (MCD)	• SLE	• Mutation in genes encoding critical component of Glomerular filtration apparatus
• Focal segmental Glomerulo sclerosis FSGS	• HSP	
• Membrano- proliferative Glomerulonephritis (MPGN)	• Malignancy (leukemia/ Lymphoma)	
• Membranous nephropathy	• Infections (Hep B, HIV, Malaria)	
	• Drugs-NSAIDS, Penicillamine, Rifampicin	

PREVIOUS YEAR QUESTIONS

Q. A 3 yr girl with generalized edema, shortly after recovery from an upper respiratory infection. Lab studies reveal marked albuminuria, hypoalbuminemia & hyperlipidemia. Prior similar episodes responded to steroid. What is the diagnosis? (NEET Jan 2020)

A. FSGS

B. MGN

C. MCD

D. PSGN

65 OBSTRUCTIVE AND INFECTIVE DISORDERS OF URINARY TRACT

Obstructive Uropathy

Pelvi Ureteric Junction Obstruction (PUJD) 00:00:10

- Most common in males
- May be seen as fetal hydronephrosis on Antenatal USG
- Severe if A-P diameter of Pelvis of kidney is
  - >10 mm in 2nd trimester
  - >15 mm in 3rd trimester
- SFU grading system (society for fetal urology): for hydronephrosis

C/F of PUJ Obstruction

- Palpable unilateral renal mass in a neonate or infant With or without heamturia
- Older children, abdominal / flank/ back pain
- B/L in 10% cases UTI after backpain

Treatment

- Pyeloplasty

Posterior Urethral Valves (PUV) 00:04:30

- Important causes of Distal urinary tract obstruction in Boys

Pathophysiology

- Obstruction at level of PUV
- Prostatic Urethra Dilatation
- Bladder muscle undergoes Hypertrophy (to relieve obstruction & allow passage of urine)

Consequences of PUV

- VUR is seen in 50% of patients
- Mild Hydronephrosis to severe renal dysplasia
- Oligohydramnios & pulmonary Hypoplasia in severe Cases(fetal life)

Clinical features

- Neonates / infants: weak urinary stream with straining during micturation distended & palpable urinary bladder
- Older infants & children: Failure to thrive with Recurrent episodes of UTI / sepsis with or without uremia

Diagnosis

- Antenatal USG in severe cases: Bilateral Hydronephrosis with Distended bladder & oligohydramnios
- Post natal investigation
  - USG
  - Contrast VCUG (Voiding cysto – urethrogram) or MCUG (micturating cysto-urethrogram)
  - DMSA scan

Treatment

- Transurethral ablation/fulguration of PUV valveleaflets
- Vesicostomy in severe cases
- Sepsis/ UTI: IV antibiotics
- Uremia: Dialysis

Nephrolithiasis 00:09:42

- Underlying metabolic cause in 50-75%
  - Hypercalciuria with hypercalcemia
  - Idiopathic hypercalciuria (MC in children)
  - Hyperuricemia (ATLS, von Gierke ds)
  - Hyperoxaluria
  - Cystinosis

Clinical features

- Microscopic or gross hematuria
- Other features depending on position of calculus
  - Ureter/Renal pelvis: severe flank or Abdomen pain (renal colic)
  - Distal ureter: dysuria, urgency & Frequency
  - Urethra: Dysuria & voiding difficult

Diagnosis

- Abdominal X-ray – Radio opaque calculi
- USG and Spiral CT of abdomen & pelvis
- Urine Ca – Hypercalciuria
  - Urine Ca > 4mg/kg in 24 hrs
    or
  - Urine Ca – urine cr > 0.2 in children, > 0.7 in infants
  - Uric acid levels

Treatment of Idiopathic Hypercalciuria

- High fluid intake
- Avoid high protein diet
- Dietary Ca2 not restricted
- Thiazide diuretics – increased Ca reabsorption

Prune Belly Syndrome 00:21:22

- MC in males
- aka Eagle Barrett Syndrome or Triad Syndrome

Triad

- Deficient abdominal wall muscles
- Undescended testis
- Urinary tract anomalies due to severe urethral obstruction in fetal life (Very large urinary bladder with massive dilation of ureters & upper tracts & Patent urachus)
- Most patients also have VUR

- Limb anomalies & scoliosis may be associated

Vesico – Ureteric Reflux (VUR) 00:18:26

Definition

- Retrograde flow of urine form urinary bladder to the ureters & pelvis, at rest or during micturition

Pathophysiology

Pathogenic organism if present in bladder can reach the renal parenchyma

↓

Infection, inflammation & scaring of kidneys

↓

Reflux Nephropathy

↓

Renal insufficiency

↓

ESRD

- Grading of VUR: Based on appearance of urinary Tract on contrast VCUG

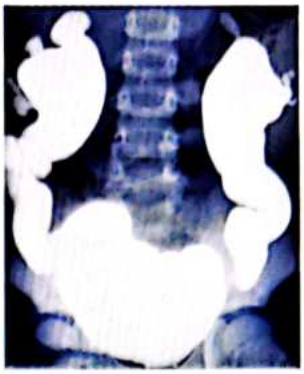
Refer Diagram 65.1

Clinical feature

- VUR is usually discovered during evaluation of UTI
- Asymptomatic or isolated fever or Fever + Abdominal pain + dysuria
- Bladder ♂ Bowel dysfunction seen in 50% of children with VUR
- 35% of siblings of children with VUR also have it
- VUR Grade I & II may resolve spontaneously as the child grows

Diagnosis

- Contrast VCUG(Voiding cystourtethrography
- Radionuclide: cystogram



- DMSA Scan useful in renal scarring

Treatment

- Goal: Prevent VUR related pyelonephritis & renal injury
- Continuous Antibiotic prophylaxis is recommended for VUR in
  - Children < 1 yr of age
  - Those with Bowel/bladder dysfunction
  - Those with H/O febrile UTI

Other treatment modalities

- Endoscopic deflux injection at uretero – vesical junction
- Surgical ureteral reimplantation

Urinary Tract Infection (UTI) 00:28:24

- MC in children <1 yr age
- More common in girls than boys beyond 1st yr of life
- MC cause of UTI in children E-coli > klebsiella & proteus

2 types

1. **Pyelonephritis**
2. **Cystitis**

Pyelonephritis (Most serious infection in <2yr who have fever without focus)	Cystitis
• Upper renal collecting system involved • Abdominal/black/flank pain	• Only bladder involved
• Fever toxic/sick	• Dysuria, frequency
• Nausea, vomiting	• Urgency
• Neonate – poor feeding, Irritability, Jaundice, Weight loss	• Supra pubic pain, Incontinence

Risk factors for recurrent UTI

- Female sex
- Children <6m
- Obstructive uropathy
- Severe VUR
- Voiding dysfunction/Bladder-Bowel dysfunction
- Constipation
- Repeated catheterization

Diagnosis

- Urine microscopy
  - PUS cells (>5/HPF) bacteria
- Dipstick: Leucocyte esterase and Nitrite +ve
- Urine culture
  - Clean catch midstream urine sample: >10^5 CFU/ml significant

Treatment

- Oral antibiotics in older or uncomplicated UTI
- Antibiotics iv in <3 months & with complicated UTI

Recommended Imaging in children with UTI

Age < 1 year	Age > 1 year
• USG Ku B • DMSA scan • MCU	USG Ku B ↓ Abnormal DMSA Scan ↓ Abnormal MCU

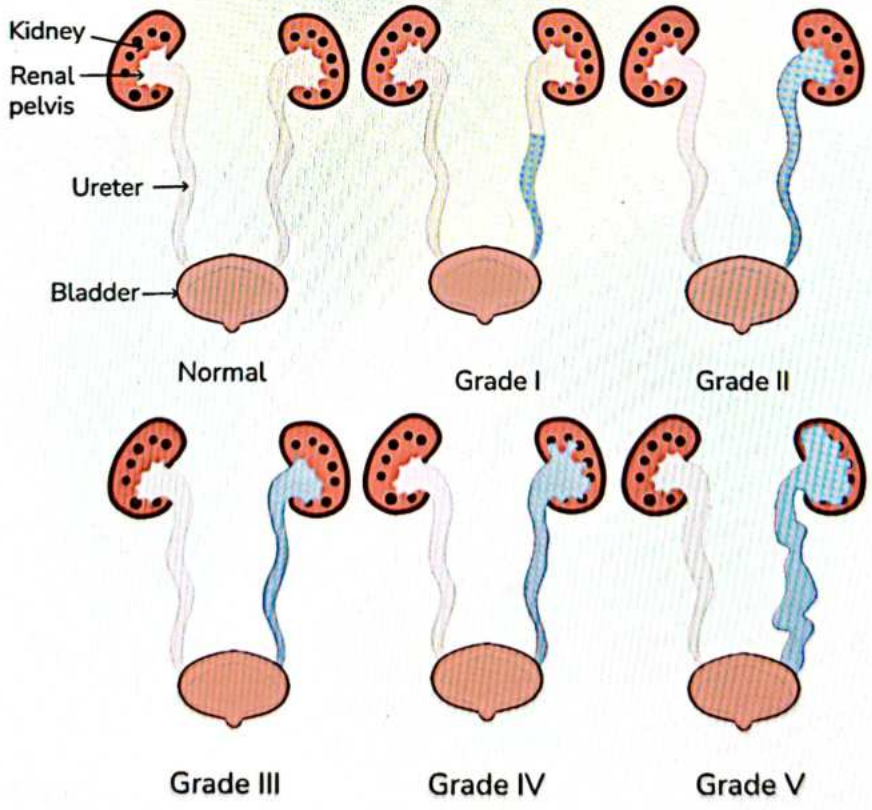
Indications of prophylactic antibiotics in children with previous H/o UTI

- VUR
- Bowel/bladder dysfunction
- Recurrent UTI
- Pending complete radiology investigation especially in infancy

Complicated UTI

- Sick looking
- Dehydration
- Poor feeding
- High grade fever

Diagram 65.1



66 RENAL TUBULAR DISORDERS

- **Definition:** Non anion gap metabolic acidosis, due to renal tubular dysfunction with usually a normal GFR
- **Types**

1. Proximal (Type II) RTA
2. Distal (Type I) RTA
3. Combined proximal & distal (Type III) RTA
4. Hyperkalemic (Type IV)

Proximal RTA 00:02:30

- Due to defective HCO_3 Resorption from proximal tubule
- Can be isolated HCO_3 wasting or more commonly as a part of Fanconi syndrome

A. Fanconi Syndrome

- Global Proximal tubular dysfunction → Low molecular weight proteinuria, Aminoaciduria, Glycosuria, Phosphaturia
- **Causes of Fanconi syndrome:**
  - **G** – Galactosemia
  - **L** – Lowe syndrome
  - **O** – CystinOsis
  - **B** – Wilson disease
  - **A** – Amyloidosis
  - **L** – Lead

How to Remember?

- Global

B. Cystinosis 00:07:02

- Mutation in CTNS gene (for cystinogen)

↓

Defective metabolism of cysteine

↓

Accumulation of cysteine & form of cystine (dimers of cysteine)

- Effects on organs

Refer Table 66.1

Diagnosis

- Cystine crystals in cornea
- Increased leukocytes cystine content

Treatment

- Cysteamine (Converts cystine to Cystene)

C. Lowe syndrome 00:10:08

- aka Occulocerebrorenal syndrome
- congenital cataract, Mental retardation, Fanconi syndrome
- X – linked OCRL 1 gene
- **C/F of Proximal RTA**
  - Polyuria
  - Dehydration
  - Hypotonia
  - Failure to thrive
  - General muscle weakness
  - Vomiting
  - Constipation
  - Rickets especially in Fanconi syndrome (d/t phosphaturia)

Distal RTA (Type IV) 00:12:07

- More common than proximal RTA
- Impaired secretion of H+ ions in distal tubules
  - Urine pH cannot be decreased to <5.5 despite sever M. acidosis
  - Compensatory ↑K^+ Secretion

↓

Hypokalemia

  - Ca^{2+} & Phosphate released from bone to buffer Extracellular H^+

↓

↓resorption of Ca^{2+} & phosphate

↓

Hypercalciuria

↓

Nephrocalcinosis & Nephrolithiasis

- C/F
  - Same as proximal RTA plus Nephrolithiasis & nephrocalcinosis
- Distal RTA is MC 1^o in children
- Can occur 2^o to drugs(amphotericin B, ifosfamide), Wilson ds, sickle cell anemia

00:18:04

Refer Table 66.2

Type IV RTA 00:23:21

- Due to impaired aldosterone production (Hypo – aldosteronism) or impaired renal responsiveness to aldosterone (Pseudo hypoaldosteronism)

Impaired K+ excretion in distal tubule	H+ ATPase are not able to function
↓	↓
Hyperkalemia	Metabolic acidosis

Barter Syndrome 00:25:15

- A group of disease characterized by Hypokalemic, Hypochloremic, Metabolic alkalosis with hypercalciuria & salt wasting
- UAG (UA-UC) : Urine Na^+ + Urine K^+ - Urine Cl^-
  Indirect estimation of Urinary $NH4^+$ exaction

Type	Gene	Inheritance
I	NKCC2	AR
II	ROMK1	AR
III	CLC kb	AR
IV	CLC ka CLC kb	AR
V	MAGED2	X – linked recessive

Clinical Features

Antenatal (Type I, II, IV)	Classical Type III – Milder
• aka Hyper PGE syndrome	• Recurrent Polyuria & Dehydration
• More severe disease	• Failure to thrive
• Maternal polyhydramnios	• Chronic constipation
• Prematurity	• Non specific fatigue & dizziness
• Severe salt wasting → Dehydration & Sometimes Hypotension	• Muscle cramps (Hypokalemia)
• Hearing loss (Type IV)	• BP usually normal

Investigation

- Severe Hypokalemia ($K+ < 2.5$)
- Metabolic alkalosis
- Urea/creatinine levels usually normal, urine Ca^{2+} & Cl^- are ↑ed.
- PGE levels elevated in antenatal form
- **USG – Nephrocalcinosis in types I & II**

Treatment

- Prevent dehydration & maintain nutrition
- K^+ supplementation
- Indomethacin – Inhibits PGE (May be effective in antenatal form)

Gitelman Syndrome 00:34:53

- Hypokalemic Hypochloremic metabolic alkalosis with Hypocalciuria & Hypomagnesmia
- Defect in gene encoding NCCT (Nacl contrasporter) in DCT
- Presents at late age with recurrent muscle cramps

Dent Disease 00:36:36

- X – linked proximal tubulopathy
- Loss of functional mutation CLCN5 Gene that encode renal Cl^-/H^+ antiporter.
- LMW proteinuria, Hypercalciuria & features of Fanconi syndrome
- Nephrolithiasis, Nephrocalcinosis, Renal failure

Table 66.1

Kidney	Eyes	Liver	Brain	Others effects
• Severe tubular dysfunction • Growth failure	• Retinopathy • Photophobia • Decreased visual acuity	• Hepato-Splenomegaly	• Swallowing dysfunction • Muscle weakness	• Hypothyroidism • Delayed sexual maturation

Table 66.2

	Proximal RTA	Distal RTA
1. Urine PH	<5.5	>5.5
2. Global Proximal tubular dysfunction	Can be seen	Not seen
3. Fractional excretion of HCO_3 ($FeHCO_3$)	>10-15%	2-5%
4. (U-B) Co_2	Normal (>20 mmHg)	Low
5. Urine anion Gap	Negative	Positive
6. Nephrocalcinosis Nephrolithiasis	-	++

67 CONGENITAL CNS MALFORMATIONS & HYDROCEPHALUS

Neural Tube Defects 00:00:32

- d/t failure of proper closure of neural tube
- They have multifactorial inheritance
- Examples
  - Meningocele
  - Meningomyelocele
  - Anencephaly
  - Spina bifida occulta
  - Iniencephaly
  - Encephalocele
- Diagnosis
  - Antenatal USG
  - Maternal serum or Amniotic Fluid α feto protein level
  - Acetylcholinesterase levels

Important Information

- Mc congenital neurologic abnormality in children is NTDs

Prevention of NTD'S

- Folic Acid Supplementation
  a. Dose
  - 400 µg/ day or 0.4 mg/ day in all women of childbearing age
  - 4000 µg/ day (4 m / day) in high-risk women

  b. When should it be started?
  - Should be started at least 1 month before conception

  c. Folic acid supplementation decreases the risk of NTDs by approx.70%
- Risk of recurrence
  a. With 1 affected child with NTD: 3-4%
  b. With 2 previous affected children: 10%

Hydrocephalus 00:07:30

- **Definition:** Enlargement of ventricles inside the brain, either d/t ↑ production or impaired drainage of CSF

Types 00:08:52

I. Communicating Hydrocephalus
- Causes
  - **C** - Choroid plexus papilloma
  - **A** - Achondroplasia
  - **M** - Meningeal malignancy or metastasis
  - **P** - Post hemorrhagic

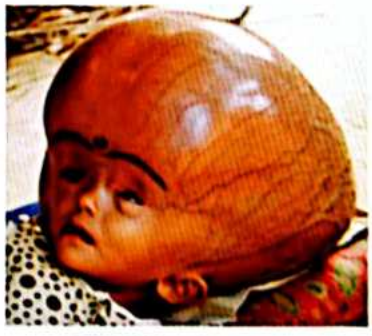
How to Remember?
- CAMP

II. Non – Communicating / Obstructive Hydrocephalus
- Causes
  - **M** - Mass lesion (ICSOL)
  - **A** - Abscess
  - **A** - Aqueductal stenosis
  - **A** - Arnold Chiari malformation
  - **D** - Dandywalker malformation
  - **H** - Hematoma
  - **I** - Infections (Toxoplasma, mumps, Neurocysticercosis)
  - **V** - Vein of Galen malformation

How to Remember?
- MAAADHIV

  - Neonate
    → Heart failure with bounding pulse
    → Large, bulging anterior fontanella
    → Cranial bruit on auscultation over ant. fontanella

- Treatment of Hydrocephalus
  - Medical RX
    → Acute: 3% NaCl or mannitol
    → Chronic: Acetazolamide or Glycerol
  - Surgical RX
    → VP shunt (ventriculoperitoneal shunt)
    → Endoscopic 3rd ventriculostomy (for aqueductal stenosis)



68 SEIZURES IN CHILDREN

A. Seizures Febrile Seizures

00:00:15

- MC cause of seizures in children < 5 Years of age
- Definition: Seizure + significant fever (> 100. 4°F) without any evidence of CNS infection in the age group of 6 months – 5 years

Types

Simple febrile seizures	Complex febrile seizures (3Fs)
• Generalized seizures • Lasts <15 minutes • No recurrence within 24 hrs	• F - Focal seizures • F - Fifteen minutes or longer • F - Frequent (recurrence may be seen)

Management

- In cases where seizure last >5 minutes
  a. Home Mx:
     → Rectal diazepam or
     → Buccal/ nasal midazolam
     → Put the child in recovery position (left lateral position)
  b. Hospital Mx
     → IV lorazepam or midazolam
- No long-term anti epileptics are recommended in the Mx of simple type febrile seizure
- Control of fever

Factors Increasing Risk of Recurrence

00:08:14

- Age <1 yr
- Temperature 39-39C (100.4-102.2 F)
- Duration of fever < 24 hrs
- Family history of Febrile seizures
- Complex febrile seizures
- Lower serum Na levels at the time of presentation

Risk Factors for Epilepsy in A Child with Febrile Seizures

00:10:28

Risk factors	Risk for epilepsy (%)
Simple febrile seizures	1%
Recurrent febrile seizures	4%
Complex febrile seizures	6%
Fever of < 1 hr before febrile seizure	11%
Family H/O epilepsy	18%
Complex febrile seizure (focal)	29%
Neurodevelopment abnormalities	33%

Status Epilepticus in Children

00:14:30

- Definition: Any seizure lasting for >5 min or multiple episodes of seizures without gaining consciousness in between or a child brought with ongoing seizures to a medical facility
- Management
  - It is a Medical emergency
    → A – Airway
    → B – Breathing
    → C – Circulation
  - Get an IV Access
  - Rule out hypoglycemia & hypocalcemia
  - IV lorazepam or midazolam
    ↓ Seizure persisting
    Inj. Phenytoin (20 mg / kg) loading dose
    ↓ seizure persisting
    Repeat inj. phenytoin (10 mg/kg)
    ↓ seizure persisting
    Inj valproate or
    Inj levetiracetam or
    Inj phenobarbitone

B. Epilepsy

00:20:01

- At least 1 unprovoked seizure with either seizure recurrence or sufficient clinical or EEG abnormality

Epilepsy Syndromes with Good Prognosis

- Benign neonatal seizures → neonatal period, Fifth Day Fits
- Benign infantile seizures → during 1st year
- Benign childhood epilepsy with centrotemporal spikes or Rolandic epilepsy: 3-13 yrs
- Childhood absence epilepsy: 5-8 yrs
- Juvenile myoclonic epilepsy: 12-18 yrs

Childhood Absence Epilepsy

- No aura or post ictal phase
- Lip smacking / eye fluttering
- Precipitated by hyperventilation
- EEG: 3Hz spike & wave pattern
- DOC: Ethosuximide& valproate

Juvenile Myoclonic Epilepsy

- Adolescent
- Myoclonic jerks

- Drops objects (drop attacks)
- prominent during early morning
- Doc: Valproate

Important Information

- Doc for focal seizures in children → oxcarbazepine> carbamazepine

Epilepsy Syndrome with Poor Prognosis

- Ohtahara syndrome: Infancy
- Rasmussen syndrome: 6-12 yrs
- Dravet syndrome: Infancy
- Lennox Gastaut syndrome (LGS): 3-10 yrs
  - Developmental delay / intellectual disability
  - Multiple types of seizures
  - Difficult to control despite multiple antiepileptics
  - EEG: 1-2 Hz slow wave & spike pattern
- Evolution of syndromes
  - Ohtahara syndrome → WEST syndrome → LGS

West Syndrome

- Triad of
  - Infantile spasms (Salaam Attacks/flexor spasms)
  - Developmental delay
  - Hypsarrhythmia (on EEG)

  → DOC: Inj ACTH (adreno corticotropic hormone)

  → DOC: For west syndrome in a child with tuberous sclerosis: Vigabatrin

Break Through Seizures

- A child who is a known case of seizure disorder on antiepileptics, present again with an episode of seizure

Management

- 1st drug: Inj. Lorazepam/ midazolam
- If the child is not on maximum dose of any antiepileptic, then give half the loading dose of same antiepileptic

Dose Range

- Valproate - 20-50 mg/kg/day
- Phenytoin - 5-8 mg/ kg/day
- Phenobarbitone - 3-5 mg/kg/day (Doc for neonatal seizures)

PREVIOUS YEAR QUESTIONS

Q. Vitamin deficiency causing neonatal seizures? (AIIMS JUNE 2020)

A. Pantothenic acid
B. Pyridoxine
C. Thiamine
D. Riboflavin

Q. Drug of choice for absence seizures? (INICET NOV 2020)

A. Ethosuximide
B. Valproate
C. Carbamazepine
D. Phenytoin

Q. About Juvenile myoclonic epilepsy, all are true except? (AIIMS Nov 2019)

A. Valproate is contraindicated
B. Lamotrigine can be given
C. Phenytoin is not the preferred drug
D. Polygenic inheritance

Q. Which of the following epileptic syndromes will not present during infancy? (JIPMER Dec 2019)

A. Ohtohara syndrome
B. West syndrome
C. Lennox-Gastaut syndrome
D. Dravet syndrome

Q. A 1 yr old child was brought with sudden onset multiple spasms. On examination he had shagreen patch and 4 hypomelontic macules on extremities. What is the drug of choice for this seizure type? (JIPMER Dec 2019)

A. Carbamazepine
B. Phenytoin
C. Vigabatrin
D. Steroids

69 DISORDERS WITH CNS INVOLVEMENT AND BRAIN DEATH

A. Cerebral Palsy

00:00:28

Definition: A group of disorders of movement & posture, causing activity limitation, d/t non –progressive disturbances that occurred in the developing fetal or infant brain

Types of CP	Area of brain involved
1. Spastic diplegia	• Periventricular Area (PVL: Periventricular, Leukomalacia or PVHI-(Periventricular hemorrhagic infarct)
2. Spastic quadriplegia	• Multicystic encephalopathy • Parasagittal brain injury
3. Spastic hemiplegia	• MCA territory infarct
4. Dyskinetic or Extra pyramidal CP	• Basal ganglia (neonatal jaundice/kernicterus)
5. Hypotonic CP	• Cerebellar lesion

B. CNS Infections In Children

Acute Bacterial Meningitis 00:06:52

Etiology

	In India	In world
Neonates	• E. Coli • Acinetobacter > E.coli , klebsiella	• Grp B streptococci > E. coli. > Listeria monocystogenes
Infants and Older children	• Strept pneumoniae • N. Meningitidis • H. influenzae	• Strept. pneumoniae

Risk factors

- Young infants due to lack of pre-existing immunity to pathogens causing meningitis
- Recent colonization with pathogenic bacteria
- Close contact with individual having invasive infection with pathogenic organisms

Important Information

- Risk of pneumococcal meningitis is increased in those with congenital or acquired CSF leak e.g., lumbar dural sinus, cribriform plate defects , middle / inner ear fistulas, skull fractures

Clinical Features of Meningitis 00:12:25

A. Non-specific features: fever, anorexia, poor feeding, tachycardia, hypotension, petechia, purpura
- Older children: headache, myalgiae & arthralgia

B. Signs of meningeal irritation:
- Nuchal rigidity
- Meningeal signs
  - I. Kernig's sign
  - ii. Brudzinski' sign

} not consistently present in children < 12-18 month age

C. Features of raised ICT
- i. Cytotoxic edema
- ii. Vasogenic edema
- iii. Interstitial edema

} all 3 seen

- Headache, vomiting
- Bulging fontanelle
- Widening of sutures
- Oculomotor or abducens nerve palsy
- Hypertension + bradycardia
- Decorticate or decerebrate posturing

D. Fundus examination: papilledema – more common in complicated meningitis or an underlying chronic process eg., brain abscess or subdural empyema.

E. Focal neurological signs may be seen
- Seizures: due to cerebritis, infarction, electrolyte disturbances
- Altered sensorium

Diagnosis 00:20:09

- Lumbar puncture: CSF study
  - Neutrophilic pleocytosis (cell count > 1000/mm3 with 75-95% neutrophils)
  - Increased proteins
  - Decreased CSF glucose (<50% of serum glucose)
  - Gram stain & culture sensitivity
- Contraindications to LP
  - Evidence of increased ICT
  - Severe cardiopulmonary compromise eg., shock requiring prompt resuscitation

Treatment 00:23:13

- Prompt initiation of empirical antibiotics
  - IV 3rd gen. cephalosprin (ceftriaxone) + vancomycin
  - CSF becomes sterile 24-48 hrs after starting appropriate antibiotics
  - Duration: 10-14 days
- Corticosteroids: inj. Dexamethasone helps in decreasing cytokine mediated CNS injury
  - It decreases risk of hearing loss in meningitis due to H. influenzae
  - Should be started 1-2 hr before antibiotics & used for 48 hrs

Complications

- Subdural empyema
- SIADH
- DIC

Prognosis

- Highest mortality with meningitis is seen when etiology is pneumococcus
- MC neurologic sequaele following acute bacterial meningitis in children: Sensorineural hearing loss (due to cochlear or auditory nerve inflammation)

Tubercular Meningitis 00:28:46

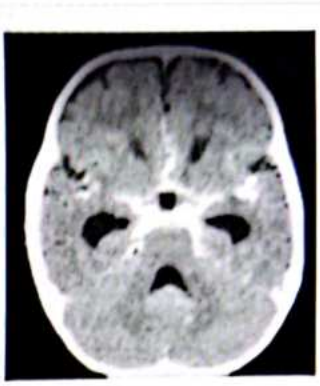
- One of the most severe forms of TB
- Pathogenesis

Primary infection
↓
Bacillemia
↓
Seeding of meninges (RICH's FOCI)
↓
Rupture
↓
Tubercular meningitis

Clinical Features

- Prodromal stage (fever, anorexia, vomiting, irritability)
- Focal deficits, seizures, meningeal signs
- Coma, neurological sequelae

Investigations



1. CNS Imaging (CECT Head)
- Enhancement of basal meanings/ basal exudates
- Hydrocephalus
- tuberculoma with perilesional edema

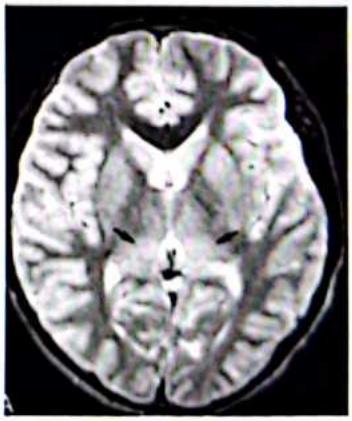
2. CSF Study
- Opening pressure elevated
- Cell count: 500/mm3 (lymphocytic predominance)
- Elevated proteins& Low glucose
- Cob-web coagulum

Treatment

- ATT + Steroids

Japanese Encephalitis 00:34:12

- MC cause of encephalitis in children in India (world → enterovirus)
- MC age group affected: 5-15 years
- Vector: Culex tri taeniorhynchus



Clinical Features
- Prodromal stage (fever, headache, vomiting, Diarrhoea)
- Encephalitic stage → seizures, focal deficits, features of ↑ ICT
- 3rd stage: extrapyramidal sequelae, death

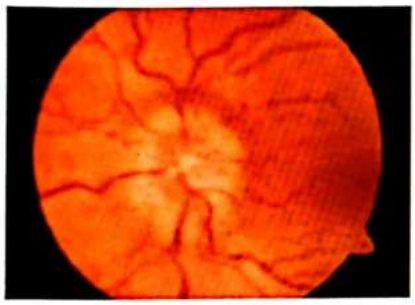
Diagnosis
- CSF study: elevated proteins & normal glucose
- JE specific IgM ELISA in serum & CSF
- CNS Imaging: B/L thalamic lesions

Treatment
- Supportive Rx

C. Intracranial tension

00:38:14

- Normal ICP (mm Hg)
  - Neonates: <5
  - Infants: 6-15
  - Older children: 10-15
- Cerebral Perfusion Pressure (CPP) = MAP – ICP
  - MAP: Mean Arterial Pressure
  - ICP: Intra Cranial Pressure
- Normal CPP (mm Hg)
  - 2-6 yrs: 50
  - 7-10 yrs: 55
  - 11-16 yrs: 65



Important Information
- In neonates and infants with open AF, papilledema is not seen.

Management
1. Fluid of choice: Normal Saline (Isotonic Fluid)
2. Supportive
   - Elevation of head end
   - Midline positioning
   - Sedation and analgesia
   - Controlled mechanical ventilation
3. Osmolar agents: Mannitol or hypertonic saline (3% NaCl)
4. Refractory cases Mx
   - Decompressive craniectomy
   - Phenobarbitol infusion
   - Hypothermia
   - Lumbar CSF drainage
5. Long term Mx: Oral Acetazolamide or glycerol

D. Brain death

00:46:52

- **Definition**: Irreversible cessation of all functions of entire brain including brain stem
- Brain Death in Children Is Usually due to Trauma or asphyxial brain injury
- 3 Key Components of Dx of Brain Death

1. Irreversible coma with a known cause
2. Absence of brain stem reflexes (light reflex, corneal reflex, gag reflex)
3. Apnea: Absence of respiratory efforts in response to an adequate stimulus (PCO_2 > 60 mm Hg)
   - All these Findings must remain consistent for 2 examinations separated by an observation period of
     → 24 hrs in neonates
     → 12 hrs in infants & older children

- Findings seen occasionally compatible with dx of brain death
  - Respiration like movements
  - Sweating & flushing
  - BP may remain normal without pharmacological support
  - DTRs elicitable
  - Superficial Abdominal reflexes elicitable
- Features incompatible with the dx of brain death
  - Decerebrate/ Decorticate posturing
  - Presence of Seizures
  - Extensor or flexor response to painful stimulus

PREVIOUS YEAR QUESTIONS

Q. Indication for lumbar puncture in child with febrile seizures are all except? (JIPMER Nov 2018)

A. All infants < 6 months

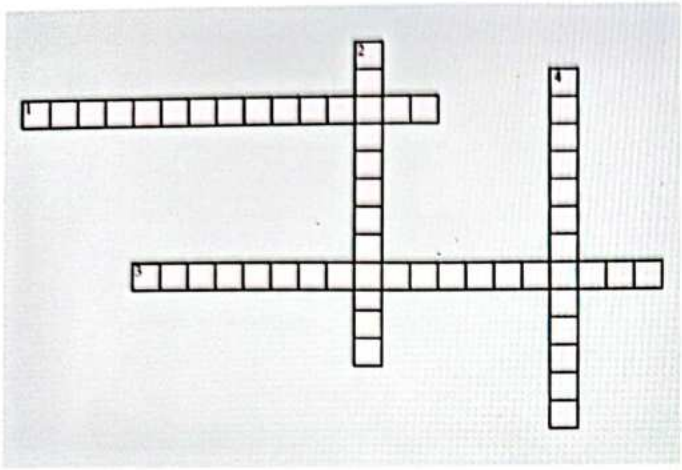
B. Children 6-12 months with no Hib & pneumococcal vaccination

C. Severely ill infants with clinical signs & symptoms

D. Infants pretreated with antibiotics

CROSS WORD PUZZLES

Crossword Puzzle



Across

1. Name of the condition in which lower poles of both kidneys are fused in the midline.
3. ASK- Upmark Kidney is also known as?

Down

2. ____Is a condition in which the kidney can be present as a small lump of non-functioning tissue ?
4. Multi cystic Dysplasic kidney is the most common cause of _____in newborn?

princeeeekum@gmail.com
9928609733

70 DISORDERS OF MUSCLES IN CHILDREN

Muscular Dystrophy 00:00:22

Definition

- A group of inherited disorders involving muscles with progressive muscle damage

Types of muscular dystrophy

1. DMD (Duchenne Muscular Dystrophy)
2. BMD (Becker Muscular dystrophy)

- Gene affected: Dystrophin gene; one of the largest gene found in humans and it is present on ChrXp21
- **Mode of inheritance:** X-linked recessive inheritance

Refer Table 70.1

Clinical features of DMD and BMD

- **Symptoms**: Progressive proximal muscle weakness i.e., weakness involving thigh muscles, arm muscles
  - There may be history of delayed walking
  - Frequent falls while walking
  - Waddling gait
  - Early weakness of neck flexors causing difficulty in raising the head
- Family history of multiple siblings or maternal Uncles are affected
- Gradually these patients become non-ambulatory i.e., wheel chair bound
- Clinical features after loss of ambulation
  - Kyphoscoliosis
  - Weakness of upper limbs
  - Bulbar weakness
  - Weakness of intercoastal muscle and diaphragm
  - Cardiomyopathies and arrythmias

Clinical signs in DMD and BMD

- It is most commonly seen in boys, females are rarely affected but females are affected when there is unfavourable lyonization or turner syndrome (single X chromosome)
- On examination: Pseudohypertrophy of calf muscles are seen, it gives inverted bottle appearance
- Valley sign positive: It is a groove like depressed area in between pseudo hypertrophied deltoid and infraspinatus muscles
- **Gower sign positive:** If a child with DMD and BMD (proximal muscle weakness) is asked to get up from sitting position, he will first take help of hand and put them on ground and take support of his legs and slowly taking help from himself, the child will get up
- There can be exaggerated lumbar lordosis
- These children can have varying degrees of intellectual disabilities
- Cardio-respiratory compromise is usually the most common cause of mortality in these children

Investigations findings in muscular dystrophy

- Serum CPK levels (Normal - < 160 U/L): Markedly elevated; > 10,000 U/L
  - This is often used as screening and first line investigation
- Confirmatory test: Demonstration of mutation in dystrophin gene
  - It can be done by multiplex PCR or MLPA (Multiplex Ligation Probe Dependent Amplification)
- Muscle biopsy: It is no longer used/preferred
  - On light microscopy: Necrosis and Regeneration of muscle fibres are seen
  - On special staining: Absent or reduced staining for dystrophin is seen
- Prenatal genetic diagnosis can also be done if one of the siblings is affected and mother is carrier for DMD
- Chorionic villous sampling or amniocentesis can be done during pregnancy and dystrophin gene mutation is looked for

Treatment of muscular dystrophy

- Supportive care including physiotherapy, taking care of cardio-respiratory issues
- Corticosteroids: It decreases the progression of the disease but it can not cure the disease
  - It will improve the muscle strength and prolongs the ambulation
  - Prednisolone or Deflazacort can be used
  - Side effects: Weight gain, Hypertension, Cataract
- Newer drugs: Eteplirsen (axon skipping drug)
  - It binds with RNA and skips over the defective axon and it restores the reading frame so shorter but potentially functional dystrophin protein is produced

Myotonic Dystrophy 00:16:45

- It is a trinucleotide repeat disorder
- Genetic basis: It is due to abnormal increase in number of CTG repeats (to > 80) in DMPK gene on chr19
- Hallmark: Myotonia; It is the delayed relaxation of muscles or muscles to contract
  - It can be manifested in various ways like ask the patient to hold one hand with other and release immediately, in healthy individual it is released immediately but in in case of myotonic dystrophy it will take some time to release the hand

- Use a percussion hammer and percuss on thenar eminence, a depression will form and it will take some time to come back
- Similarly, if the tongue of patient is percussed, depression is formed in that area and it will take some time to come back

- Antenatal manifestation: There is a possibility of decreased fetal movements and polyhydramnios

Other clinical features of myotonic dystrophy

- Facies: Inverted v shaped upper lips and bitemporal hollowing
- Flat thenar and hypothenar areas on the palm
- Deep grooves between fingers
- Tongue can be thin and atrophied
- Proximal muscle undergoes atrophy: Gower sign positive

Facio Scapulo Humeral Dystrophy 00:21:05

- There is asymmetric facial weakness
- Winging of scapula is an early finding
- There is atrophy of biceps and triceps with sparing of deltoid and forearm muscles giving it the "Popeye" arm appearance
- Hearing loss
- Retinal involvement

Limb Girdle Muscular Dystrophy 00:23:18

- It mainly affects the muscles of hip and shoulder girdles
- Predominantly lower limb weakness is seen in children and as weakness progresses, deep tendon reflexes get diminished
- There is cardiac involvement and these children are normal intellectually

Congenital Muscular Dystrophy 00:24:33

- It usually presents in neonatal period or infancy
- It usually presents with hypotonia, weakness, Arthrogryposis, bulbar dysfunction, and respiratory insufficiency

Congenital Myopathies 00:25:50

Definition

- It is a non-progressive, inherited disorders involving muscles, with typical subcellular abnormalities on muscle biopsy

Types of congenital myopathies

- Central core disease
- Centro nuclear myopathy
- Congenital fibre type Disproportion myopathy
- Nemaline myopathy

Clinical features

- Floppy infant: Limbs lie loose giving a frog leg posture
- Hypotonia
- Static or non-progressive muscle weakness
- Decreased or absent deep tendon reflexes
- Respiratory insufficiency
- Feeding difficulties
- Contractures can be present

Investigations

- CPK levels: Normal or mildly elevated
- EMG: Myopathic pattern
- Muscle biopsy gives specific diagnosis as which congenital myopathy it is

Acute Flaccid Paralysis 00:30:15

- It refers to rapid onset progressive weakness with absence of spasticity or other upper motor neuron signs in children < 15 years of age
- Common underlying causes
  - **Guillian Barre Syndrome:** Mainly there is lower limb weakness which can progress upwards and there are absent deep tendon reflexes
    → CSF albumino cytological disassociation
    → NCV (Nerve conduction velocity) helps in diagnosing this condition
    → IVIG is the preferred treatment
  - Acute poliomyelitis: Previously it is used to be very common cause of acute flaccid paralysis but it has been almost eradicated
  - Transverse myelitis: Bilateral over limb weakness along with a sensory level and girdle like sensation
  - Traumatic neuritis
  - Post-Diphtheritic polyneuropathy

Disorders of Neuromuscular Junction

Myasthenia gravis 00:32:42

- Basic defect: It is a chronic autoimmune disease or post synaptic motor end plate leading to abnormal neuromuscular transmission or blockade
- Release of Ach at synaptic cleft is normal but receptors/motor end plates are less sensitive as numbers of receptors for the binding of Ach are less available because presence of antibodies against those receptors

Clinical feature

- 20% cases of myasthenia gravis are present during childhood or adolescence
- Hallmark: Fatiguable weakness i.e., initially when child wakes up, he is ok but as the day progresses and there is usage of muscle, child get fatigued
- Most patients have ptosis and ophthalmoplegia but pupillary reflexes are normal
- "Peep sign" positive: Ask the child to forcibly close the eyes

and after time the cornea will gets exposed or peep from inside because of fatiguable weakness
- Bulbar weakness leading to nasal intonation of voice, difficulty in swallowing
- Limb weakness can be proximal and symmetrical
- Respiratory muscles can be involved in myasthenic crisis
- "Ice pack" test is a bedside test in which during ptosis ice pack is put over eyes and after sometime eyes can open properly

Investigations
- **Edrophonium testing:** when edrophonium is given in a patient with MG, there is transient improvement within 10 seconds persisting upto 120 seconds (2 minutes)
- Neostigmine test can also be used, it shows response in 10-15 minutes
- Both these tests increase the Ach level at the synaptic cleft so it can act
- On EMG, repeated nerve stimulation test will show weakness of > 10%, it shows a decremental response
- Child can be tested for anti- Ach receptor antibody testing; it is expensive and not readily available and
- Anti-MUSK (Muscle specific kinase) levels can be estimated

Treatment
- Use cholinesterase inhibitors like Pyridostigmine
- Low dose steroids or steroid spring agents like azathioprine, cyclosporine, cyclophosphamide or MMF (Mycophenolate mofetil) can be used
- Thymectomy can be done in refractory seropositive patients

Disorders of Anterior Horn Cells
Spinal muscular atrophy (SMA) 00:42:15
- Basic defect: It is an autosomal recessive disorder due to mutation in SMN1 gene (Survival motor neuron gene) on chr5
- Types of SMA based on clinical features and severity

Types 0,1,2,3
- **Type 0 is the most severe type which presents during fetal life and most children do not survive**
- **Type 1 (Werdnig Hoffman disease): It manifests during infancy**
  - There is profound hypotonia, flaccid weakness
  - These babies never learn to sit, neck control also comes later
  - Global areflexia
  - Respiratory muscle weakness and swallowing dysfunction leading to recurrent aspirations and pneumonia
  - **Hallmark:** Presence of tongue fasciculations
- **Type 2 SMA**
  - Onset: 16-18 months of age
  - These children are usually able to sit unaided but never able to stand so they are often wheelchair bound
  - Kyphoscoliosis, tremors (polyminimyoclonus can be seen), poor swallowing and respiratory insufficiency
- **Type 3 SMA:** Least severe form
  - It usually presents at > 18 months of age
  - These children are usually able to walk but there is global areflexia, fasciculations and tremors

Treatment
- Supportive treatment: Ensure adequate nutrition and prevent obesity as these children are going to be non-ambulatory
- Address the respiratory/swallowing and respiratory issues, sometimes in younger child tube feeding or nasogastric tube feeding is required to prevent recurrent aspirations and pneumonias
- Newer drugs: Neusinersin; it is an antisense oligonucleotide
  - It is given intrathecally through lumbar puncture
  - Risdiplam: It is an Oral drug to be taken daily

Table 70.1

	DMD (More severe)	BMD
Onset of weakness	< 5 years of age	>6 years of age
Progression	Rapid	Slower
Mutations responsible	Frame shift mutation	In-frame mutations/Substitutions
Non-ambulatory by	9-10.5 years of age	>15 years of age
Cardio-respiratory problems	Late onset	Early onset of myalgia, rhabdomyolysis, and respiratory distress

71 RICKETS

Rickets

Definition:

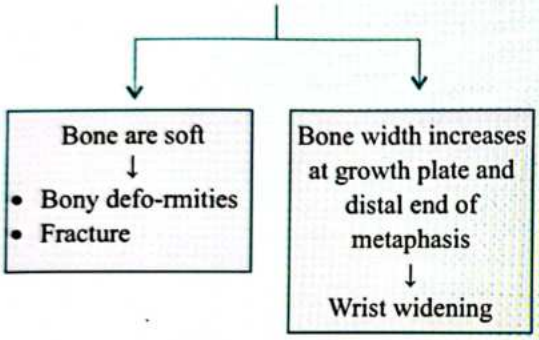
- It is a disease of growing bones due to defective mineralisation of the bone matrix at the growth plate in children, before fusion of epiphysis.

Pathophysiology of Rickets 00:01:18

Defective mineralisation of bones matrix at growth plate

↓

Growth plate cartilage and osteoid continue to expand, but mineralisation is inadequate



Etiology of Rickets 00:03:17

- MC cause of Rickets is nutritional deficiency of Vitamin D

Nutritional Rickets	Refractory Rickets
• Vit D deficiency o Congenital deficiency o Inadequate dietary intake o Malabsorption o Liver/ Kidney Disease • Ca deficiency • Phosphate deficiency	• Rickets that does not show response to the usual treatment of nutritional Rickets o VDDR types I and II o Hypophosphatemic Rickets o Chronic kidney disease (CKD): ↑ Phosphate level o Renal tubular acidosis (proximal / distal) o Oncogenous/ Tumor induced →Some benign mesenchymal tumor: Secrete FGF-23 → Phosphaturia & hypophosphatemia

Clinical Features of Rickets 00:07:23

I. General

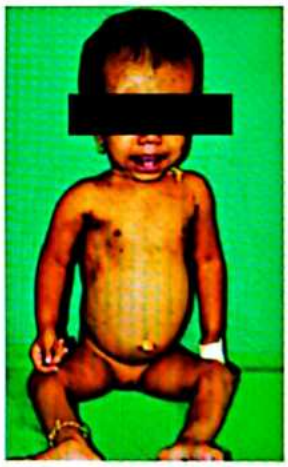
- Failure to thrive
- Protruded abdomen
- Listlessness
- Increased risk of respiratory infections: Softening of ribs, impairs air movement during respiration
- Increased risk of fractures

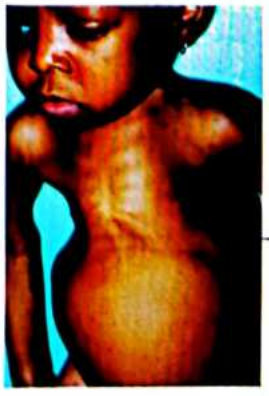
II. Head and Face

- Craniotabes: Due to softening of cranial bones; also seen in OI, congenital syphilis, hydrocephalus, prematurity
- Frontal and parietal bossing
- Large AF and delayed closed of AF
- Delayed dentition and dental caries

III. Chest

- Rachitic rosary: Bleeding of costochondral junctions
- Harrison sulcus: Due to pulling of softened ribs by diaphragm

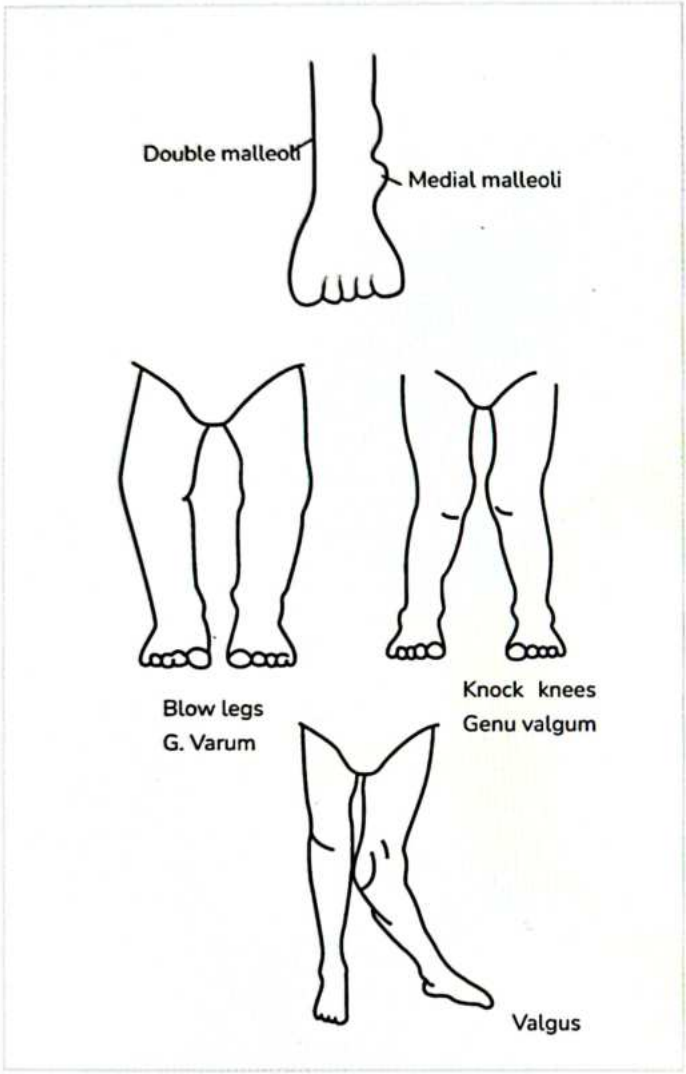




Harrisons sulcus

IV. Limbs

- Wrist widening
- Genu varum or valgum deformity
- Windswept deformity
- Bowing of tibia
- Double malleoli



V. Hypocalcaemia

- Tetany
- Seizures
- Stridor
- Trousseau sign (more specific)
- Chvostek sign

Investigations

00:12:11

- Serum calcium Normal or low
- Serum: Normal or Low
- PTH
- Alkaline phosphatase: High
- 25 (OH) Vit D3: Low (< 10 ng/ml or < 30 nmol/L) (Normal: > 20 ng/ml or > 50 nmol/L)

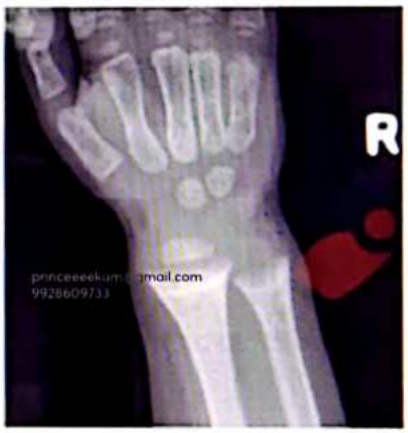
Refer Table 71.1

Diet (*Cholecalciferol*)
↓25 Hydroxylase (Liver)
25-OH-Vit D,
↓1 hydroxylase (kidney)
1, 25, (OH), Cholecalciferol
↓
Vit D, receptors

Radiological Features of Rickets (X–Ray Wrist or Knees)

00:19:35

- 1° change due to loss of normal zone of provision calcification adjacent to metaphasis → blurring of metaphyseal margin → "Fraying"
- Cartilage hypertrophy → widening of growth plate → splaying
- Soft bones → cupping
- Generalized reduction in bone mineral density: Osteoporosis



Treatment

00:20:55

Vit D	Calcium	
Neonates and infants: 2000 IU/day	+ 500 mg/day	Minimum 3 months f/b maintenance dose of Vit D and Ca
1 – 18 yr: 3000 – 6000 IU/day	+ 600 – 800 mg/day	

- Alternatively, for infants > 3 m age, 60,000 IU weekly for 6 weeks

VDDR (Vitamin D Dependent Rickets)

00:22:47

- AR inherited Rickets
- Usually manifests during infancy

VDDR Type I

- Due to deficiency of 1 alpha hydroxylase which converts 25(OH)vit D3 into 1,25(OH)2 Vit D3 Which is the active form of vit D

Investigations

- Decreased blood Ca levels
- Normal to low phosphate levels
- Increased alkaline phosphatase levels
- Normal 25(OH) vit D3 level
- 1,25 (OH)2 vit D3 level markedly low despite of hypocalcemia.
- **Rx:** Calcitriol + Calcium +/- Phosphate

VDDR Type II: Vit D resistant rickets

- End organ resistance to 1, 25 (OH)2 Vit D3 At the level of receptors

Clinical Features

- Early onset Rickets
- High prevalence of alopecia and ectodermal defects (oligodontia, Milia, Epidermal cysts)

Investigations

- Hypocalcaemia and hypophosphatemia
- Secondary hyper PTH
- Elevated 1, 25 (OH)2 Vit D3 Level

Treatment

- Large dose of Ca2+ for prolonged period
- Responses to Rx not satisfactory

Familial Hypophosphatemic Rickets 00:26:41

- X lined dominant inheritance (XLD)
- Gene: PHEX gene (Phosphate regulating gene with Homology to an Endopeptidase on X chromosome)

↓

Normally produce an endopeptidase, that is responsible for breakdown of FGF-23

Pathophysiology

Mutation of PHEX gene

↓

Increased in FGF – 23 levels

Excessive renal loss of phosphate ↓ Hypophosphatemia	Decreased activity of renal α1 hydroxylase ↓ Low blood level of 1, 25 $(OH)_2$ Vit D3 despite hypophosphatemia

Clinical features

- Lower limb deformities are common
- Skull deformities and dental abnormalities seen
- Absent symptoms of Hypocalcaemia

Investigations

- S. calcium: Normal / Mildly decreased
- S Phosphate: Low (1.5 – 3 mg/dl); urine phosphate → increased
- Alk phosphate : increased
- PTH – normal
- 1, 25 $(OH)_2$ Vit D_3 level: inappropriately low for the serum phosphate

Treatment

- High doses of oral phosphate and Vit D3 (Calcidiol)

Important Information

Q. A 6 yr old female presenting with joint deformities had received multiple course of Vit D with no improvement. Her lab values are given below.
- Calcium: 9.5 mg/dl
- Phosphorous: 1.6 mg/dl
- Alkaline phosphates: 814 IU with normal serum parathyroid hormone, electrolytes creatine

A. Vit D dependent rickets type 1
B. Vit D dependent rickets type 2
C. Hypophosphatemic rickets
D. CRF

Table 71.1

S. Ca	$S.PO_4$	Alk Phos	25(OH) Vit D_3	1,25,(OH) Vit D_3	PTH	
↓ -	↓ -	↑	↓ -	↓ -	↑ -	Nutritional Rickets
↓ -	↓ -	↑	(N)	↓	↑ -	VDDR Type 1
↓ -	↓ -	↑	(N)	(↑)	↑	VDDR Type 2
N -	↓	↓ -	N -	N -	N/↑ -	Hypophosphatemia Rickets
N/↓	↑ -	↑ -	N -	N/↓ -	N/↑ -	Chronic Kidney ds

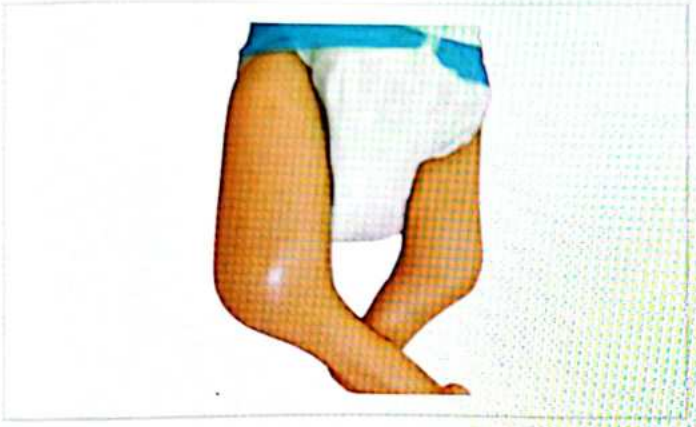
72 IMPORTANT DISORDERS INVOLVING BONES IN CHILDREN

Scurvy

00:00:21

Basic defect

Deficiency of Vit C
↓
Defective collagen synthesis (vit C is required for collagen synthesis)
↓
Increased vascular fragility



Risk Factors: Child predominantly fed on cow's milk

Clinical Features

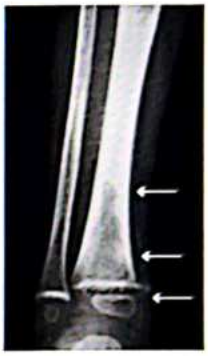
- Gum bleeding
- Petechiae
- Sub periosteal hemorrhage involving long bones
  - Painful pseudo paralysis
  - Crying on touch

Important Information

Scorbutic Rosary	Rachitic Rosary
• Feature of scurvy ○ Sharp & angulated ○ Tender & painful	• Features of rickets ○ Rounded ○ Not painful

Diagnosis: X Ray features of scurvy

- Pencil thin outline of cortex
- Sub periosteal hemorrhage
- Wimberger sign (ring shaped epiphysis)
- Pelkan spur (bony spur)
- Trümmerfeld zone
- White line of Fraenkel
- Ground glass appearance of bones
- Treatment of scurvy
  - Vit C supplementation
  - Diet rich in vit C (citrus fruits)



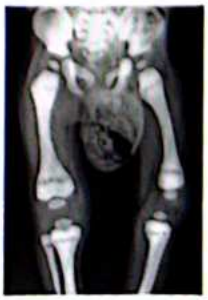
Osteopetrosis / Marble Bone Disease

00:07:18

- Defect: mutation in CLCN7gene
- leads to defective resorption of bones
  ↓
  increased density of bones

Clinical Features

- Neurological problems due to compression of nerves
- Deafness
- Bone marrow infiltration: pancytopenia-anemia, bleeding, infections
- Increased extramedullary hematopoiesis: Large head, hepatosplenomegaly
- X ray findings in osteoporosis
  - Increased density of bones
  - Bone within bone appearance



Osteogenesis Imperfecta 00:11:51

- Defect: type 1 collagen defect
- 12 types → type I – V have autosomal dominant inheritance

Important Information

- M/C mode of inheritance in osteogenesis imperfecta: AD

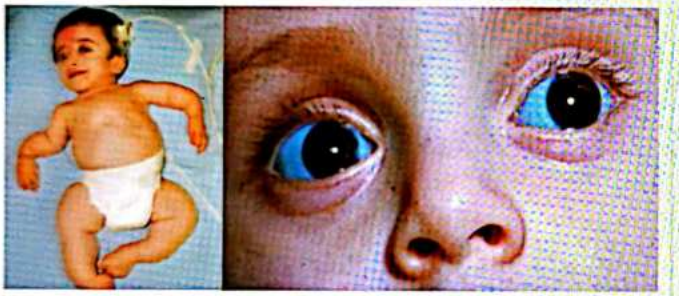
- Types I & IV have subtypes
  - A -nt
  - B +nt

  } abnormal translucent teeth(Dentinogenous Imperfecta)

Clinical Features

- Triad: Blue sclera, deafness, bony deformities
- Hyperextensible joints
- Dental manifestations
- Family history in parents / siblings +ve

Treatment: Bisphosphonates like pamidronate



Phocomelia 00:17:11

- Limbs resemble flippers of a seal
- Maternal intake of thalidomide during pregnancy is a risk factor
- Short proximal segments of limbs

Infantile Hyperostosis (Caffey's Disease) 00:18:58

- M/C in early infancy (around 10 weeks)
- M/C involved bone: mandible f/b clavicle, ulna

Clinical Features

- Sudden onset irritability
- Painful soft tissue swelling with wood like induration but minimal warmth & redness (suppuration is absent)
- a/w fever, anemia
- Episode can last from 2 weeks to 3 months

X – ray: Cortical thickening of underlying bones

On investigation: Increased ESR & alkaline phosphatase anemia & thrombocytosis

Treatment : Indomethacin& prednisolone

JIA (Juvenile Idiopathic Arthritis) 00:22:09

- Definition: Arthritis of ≥ 1 joints , lasting for at least 6 weeks , in a child < 16 yrs of age

Types

1. Oligo articular: 4 or less joints involved; mc type a/w Uveitis/ iridocyclitis; more in girls
2. Poly articular: >4 joints involved
3. Systemic onset: Fever, rash, hepatosplenomegaly

Important Information

- Arthritis in SLE is Non- erosive arthritis

Reactive Arthritis 00:25:07

- Joint inflammation caused by sterile inflammation reaction following a recent entropathic or urogenital infection.
- Pathogenic organisms mainly responsible are:
  a. Entropathic infection, Salmonella, Shigella flexneri, Yersisnia enterocolitis, Campylobacter jejuni
  b. Urogenital infection, Chlamydia trachomatis
- 75% patients with reactive arthritis are HLA-B27 + ve

Clinical Features

- Symptoms often begin 3 days to 6 weeks following infection
- Asymmetric oligoarthritis with predilection for lower limbs
- Enthesitis: in 90 % patients
- Fever, fatigue, malaise seen
- HLA-B27 +ve : Increased risk of symptomatic uveitis
- Less common features: Sterile pyuria, conjunctivitis, optic neuritis
- C/F may last from weeks to months

Diagnosis

- There is no single test for reactive arthritis
- ESR, CRP, platelet count may be elevated
- Imaging: normal/non-specific

Treatment

- Physical therapy
- NSAIDs
- Intra articular steroid injection in severe cases

PREVIOUS YEAR QUESTIONS

Q. Repolarization in isolated muscle fiber proceeds from:

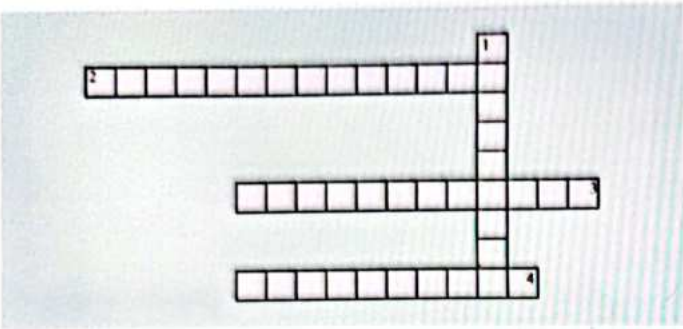
(PGI Dec 98)

A. Epicardium to endocardium
B. Endocardium to epicardium
C. Left to right
D. Right to left

Note: For individual myocardial cells (fibers) depolarization and repolarization proceed in the same direction. However, for the entire myocardium, depolarization proceeds from innermost layer (endocardium) to outermost layer (epicardium), whereas repolarization proceeds in the opposite direction. The exact mechanisms of this well-established asymmetry are not fully understood.

CROSS WORD PUZZLES

Crossword Puzzle



Across

2. ECG Shows ____ in case of West syndrome?
3. DOC for childhood absence epilepsy?
4. DOC for west syndrome in a child with tuberous sclerosis.

Down

1. What is the Drug of choice for juvenile myoclonic Epilepsy?

73 DISORDERS OF PITUITARY

A. Multiple Pituitary Hormone Deficiency 00:00:36

Genetic
- HESX1 gene
- PTX2 gene
- LHX3 gene
- LHX4 gene
- PROP1 gene
- POU1F1 gene

Acquired

1. **Brain damage**
- Trauma
- Neurosurgery
- Radiation

2. **Tumors**
- Pituitary adenoma
- Craniopharyngioma
- Meningioma
- Glioma

3. **Infections**
- Brain abscess
- Meningoencephalitis

4. **Others**
- Hemochromatosis
- Histiocytosis
- Perinatal insult
- Auto immune disorders

Important Information
- Order in which Pituitary Hormones are Usually Affected
- GH > Gonadotropins (LH & FSH) >TSH >ACTH
- While treating, Corticosteroids should be started before supplementing thyroxine in multiple pituitary hormone deficiency

B. Isolated GH Deficiency 00:07:25
- Can be genetic or acquired
- Birth weight & length are normal
- US:LS ratio normal
- Delayed

1. Bone age
2. Dentition
3. Puberty
4. Milestones

} More common in multiple hormone deficiency

- Hypoglycemia
- Frontal bossing
- High pitched voice
- Short stature

Situations in which growth hormone (GH) deficiency can be seen 00:10:20
- Physiology of GH secretion

Hypothalamus
↓← GHRH receptor

Pulsatile secretion of GHRH (Growth hormone releasing hormone)
↓
GH receptor ← Receptor insensitivity to GHRH
(+)↓(-)
Ghrelin → ↓ ←(Somatostatin)

Pulsatile secretion of GH from somatotrophs in pituitary ← GH deficiency due to mutations
↓
GH receptor ← Mutation leading to resistance of receptors to GHRH (Laron syndrome)
↓
Increased synthesis of IGF-1 (somatomedin or insulin like growth factor-1) from liver and growth plate in children
↓
IGF 1 circulates bound to IGF – BP3

	GHRH	GH	IGF-1
GHRH deficiency	Low	Low	Low
Receptor insensitivity to GHRH	N/ increased	Low	Low
GH deficiency due to mutations		Low	Low
Mutation leading to receptor resistance		N/ increased	Low

Q. A child with short stature, normal GH level but low IGF-1 levels. What is the possible cause of it?

Ans. Receptor resistance to GH

Diagnosis

1. GH stimulation test

- Done using insulin(MC used), arginine, clonidine, glucagon, levodopa
- Peak GH level <10 ng/ml → GH deficiency
  - Done for decreased bone age
  - Decreased growth velocity

} In presence of other C/F as discussed

Treatment

- Recombinant GH injections given subcutaneously
- Should be given for a period of atleast 1-2 years for the results to be apparent
- Effective only if epiphyseal fusion/ closure of long bones has not occurred

Adverse Effects of Gh Therapy

- Pseudotumor cerebri
- Gynecomastia
- Impaired glucose tolerance

C. GH Excess

00:29:58

- Results in overgrowth or gigantism during childhood
- After fusion of epiphysis: Acromegaly
- Coarse facies
- large tongue
- Prognathism (protruded lower jaw)
- thick skin
- broad nose
- headache &visual field defects

Best screening test

- IGF 1 LEVEL

Treatment

- Somatostatin analogues (Octreotide)
- GH Receptor antagonist (Pegvisomant)

D. Diabetes Insipidus

00:33:15

- Polyuria &polydipsia
- Polyuria → urine output > 5ml/kg/hr or >2L/m²/24 hr
- Either d/t vasopressin deficiency (central DI) or insensitivity at the level of kidney (Nephrogenic DI)

Etiology

Central DI	Nephrogenic DI
• Genetic • Acquired • Trauma • Congenital malformations • Tumors (LCH) • Drugs (chemotherapy)	• Genetic • Acquired • Hypercalcemia • Hypokalemia • Drugs • Kidney disease • Sickle cell Disease

Mechanism of Action

Vasopressin (ADH) synthesized in supra optic & para ventricular nuclei of hypothalamus

↓

Posterior pituitary

↓

V2 receptors in renal tubules

↓

Insertion of aquaporin 2 water channels into apical/ Luminal membrane

Diagnosis

- Low urine osmolality (<600 mosm/L) in association with high plasma osmolality [>300 mosm/L)
- Water deprivation test → Differentiates psychogenic polydipsia from DI
- Vasopressin response test → To differentiate central DI & nephrogenic DI
- On giving vasopressin exogenously, ↑in urine osmolality by >50% of base line indicates Central DI

Treatment of DI

- Central DIvasopressin Analogue (desmopressin)
- Nephrogenic DI: Thiazide, Indomethacin & salt Restrictions

MEN (Multiple Endocrine Neoplasia) Syndromes

00:44:24

MEN 1 (Wermer Syndrome)

- Gene on chromosome 11 → MEN 1 gene → menin
- 3 'P' affected
  - P – Pituitary hyperplasia/adenoma
  - P – Parathyroid hyperplasia/adenoma
  - P – Pancreatic hyperplasia/adenoma/Neuroendocrine tumor

How to Remember?

- PPP

MEN 2 A (Sipple Syndrome)

- Gene affected: RET gene on chr10
- Features
  - H - Hirschsprung disease
  - A - Amyloidosis
  - P - Pheochromocytoma
  - P - Para thyroid hyperplasia / adenoma
  - Y - ThYroid carcinoma (medullary)

How to Remember?

- HAPPY

MEN 2B

- Features
  - P - Pheochromocytoma
  - M - Medullary thyroid carcinoma
  - M - Mucosal & GI neuromas
  - M - Marfanoid features

How to Remember?

- PPPM

74 DISORDERS OF THYROID IN CHILDREN

princeeeekum@gmail.com
9928609733

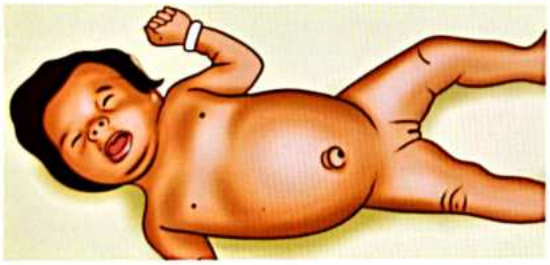
A. Congenital Hypothyroidism 00:00:32

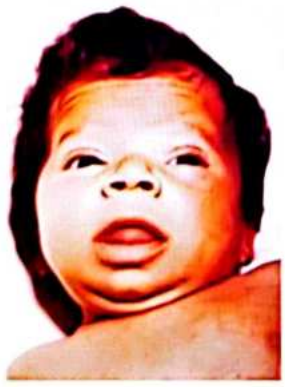
- MC preventable/ treatable cause of mental retardation/ intellectual disability in children
- Incidence: 1 in 1000 newborns

Etiology

- Thyroid dysgenesis: mc cause of congenital hypothyroidism
- Thyroid dyshormonogenesis: mc cause of congenital hypothyroidism in a child with goitre
- Pendred syndrome
  - Due to mutation in PDS gene on chr 7 → codes for pendrin (SLC 26A4) which is a chloride-iodide transporter, important in hearing and thyroid pathway.
  - Hearing Loss (SNHL) + Goitre & Hypothyroidism
- Iodine deficiency
- Hypothalamic pituitary dysfunction
- TSH receptor blocking antibody (usually transient)

Clinical Features





- Birth weight & length usually normal
- Wide open Anterior fontanelle and Posterior fontanelle
- Prolonged physiological jaundice (earliest sign sometimes)
- Myxedematous facies: Large, protruded tongue
- Skin: Dry & scaly
- Hypotonia, hypothermia, hoarse cry
- Constipation
- Abdominal distension
- Umbilical hernia
- In Untreated Cases
  - Delayed development
  - Intellectual disability (not seen in neonatal period)
  - Delayed dentition
  - Short stature
  - Delayed puberty
  - Delayed bone maturation (Bone age < Chronological age)

Diagnosis

- Primary hypothyroidism:
  - TSH usually > 100 mu/L
  - T4 level: Low
- Central hypothyroidism: Low TSH, T3 and T4 levels

Treatment

- Oral Levo thyroxine (early morning with empty stomach)
- Newborn: 10-15 mg/kg/day

Prevention: Universal newborn screening for cong. Hypothyroidism

- At birth, with umbilical cord blood
- Heel prick: dried blood spots (between 48-72 hours of life)
- Should not be done in 1st 1-2 days, to avoid TSH surge
- Most sensitive approach → check for T4 & TSH

B. Acquired hypothyroidism 00:15:34

- MC in girls
- MC cause is auto immune thyroiditis
- Also associated with
  - Down syndrome
  - Turner's syndrome
  - Celiac disease
  - T1 DM

Clinical Features

- Firm & nodular goitre
- Short stature
- Cold intolerance
- Lethargy
- Constipation
- Delayed dentition
- Delayed puberty (some may have pseudo precocious puberty)
- Bradycardia
- Myopathy/ pseudohypertrophy of muscles
- Heart failure (in severe cases)

Treatment

- Thyroxine
- Dose (Decreases with increase in age)

1. 1-3 yrs age: 4-6 mg/kg/day
2. 10-16 yrs age: 2-4 mg/kg/day

C. Endemic cretinism

00:19:38

- Most serious consequence of Iodine deficiency

2 Types

1. Neurologic type
2. Myxedematous type

1. Neurological Cretinism

- Deaf: Mutism
- Squint
- Spasticity & rigidity → gait problems
- Intellectual disability

2. Myxedematous Cretinism

- Retarded psychomotor development
- Short stature
- Coarse facial features
- Myxedema

Prevention

- Adequate Iodine intake (fortification of food with iodine)
- RDA of Iodine

1. For children <10 yrs: 40-120 µg/day
2. For children > 10 yrs: 150 µg/day

D. Hyperthyroidism

- Rare

00:23:34

- Suspected in children with
  - Weight loss (unexplained)
  - ↑ appetite
  - Tremors
  - Warm extremities
  - Heat intolerance Diarrhoea
  - ↑ sweating
  - Anxiety
- Eye signs are not commonly seen in children.

Treatment

- Propylthiouracil is usually avoided in children(due to risk of hepatotoxicity)
- Methimazole & Propranolol are used

Neonatal Thyrotoxiuosis

- Due to maternally acquired thyrotropin receptor stimulated antibody
- Disappears in 2-4 months
- Neonates - tachypnea, tachycardia, LBW, irritability Heart failure
- Treatment: Symptomatic management

Q. Most sensitive test for thyroid dysfunction in newborn
(JIPMER DEC 2019)

a. Total T3
b. Total T4
c. TSH
d. Free T3

princeeeekum@gmail.com
9928609733

75 ADRENAL DISORDERS

A. Adrenal physiology
B. Congenital adrenal hyperplasia
C. Adrenal insufficiency
D. Cushing syndrome
E. Aldosterone excess
F. Pheochromocytoma

A. Adrenal Physiology 00:00:59

- steroid hormones are synthesized in adrenal cortex. Predominantly cortisol is synthesized by fetal adrenal gland.

Pathways of adrenal steroidogenesis

Refer Flow Chart 75.1

- Cholesterol is precursor all steroid hormones.
- StAR protein → Steroidogenic acute Regulatory protein that transports cholesterol into mitochondria.
- 3β- HSD → 3β- hydroxyl steroid dehydrogenase
- ACTH plays an important role in regulation of glucocorticoids & sex steroid synthesis
- Mineralocorticoid production regulated by :
  - Intravascular volume
  - K^+ level
  - Renin Angiotensin system

Important Information

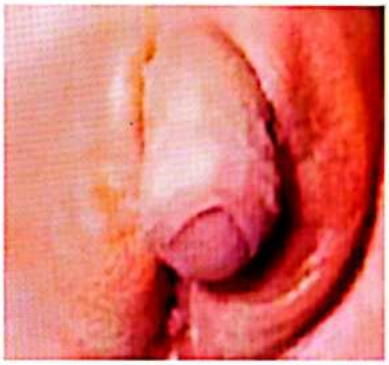
- ACTH is not important in the regulation of mineralocorticoid

B. Congenital Adrenal Hyperplasia (CAH) 00:09:43

- A Group of autosomal recessive defects in steroid hormone synthesis, characterized by deficiency of some hormones & excess of steroid precursors
- CAH is the Mc adrenal disorder seen in children.
- Mc cause of CAH: 21 hydroxylase deficiency
- 2nd mc cause of CAH: 11 β hydroxylase deficiency

21 Hydroxylase Deficiency 00:12:47

- **Features**
  - Deficient aldosterone
    → Salt wasting
    → Dehydration
    → Hyperkalemia
  - Deficient glucocorticoids
    → Hypoglycemia
    → Shock
  - Excess sex steroids: Ambiguous genitalia in female neonate
    → In male, genitalia is normal but this increased testosterone is a very important cause of precocious puberty.



Ambiguous genitalia in Female

- **Lab diagnosis**
  - Hyperkalemia
  - ↑ 17 hydroxy progesterone levels (very imp. Screening test for diagnosis of 21 hydroxylase deficiency)
  - Genetic diagnosis: Mutation on chr 6
    → Confirmatory
    → Useful in pre natal diagnosis in next pregnancy
- **Treatment**
  - Hydrocortisone (Life long replacement)
  - Fludrocortisone (Life long replacement)
  - ↑ salt intake
  - ↑ dose of glucocorticoids in times of stressful conditions (surgery, fever)
  - Doc for antenatal Rx of CAH → Dexamethasone
  - In a couple with previous case of CAH neonate, start dexamethasone as soon as next pregnancy is diagnosed to prevent virilization of female.

11 β Hydroxylase Deficiency 00:25:04

- **Features**
  - Excess mineralocorticoids (due to deoxycorticosterone) → Hypertension, hypokalemia
  - Excess 11 deoxy cortisol → No features of glucocorticoid deficiency
  - Excess sex steroid → Ambiguous genitalia in females

Important Information

- Ambiguous genitalia in female with HTN : 11 beta hydroxylase deficiency

3 β Hydroxy Steroid Dehydrogenase Deficiency (3 βSHD)

(This enzyme is common to all the three pathways) 00:30:28

- **Features**
  - Deficient mineralocorticoids: Salt wasting, dehydration, hyperkalemia
  - Deficient glucocorticoids: Hypoglycemia, shock
  - Deficient sex steroids: Normal genitalia in females
    → Under virilization (ambiguous genitalia) in males

17 Hydroxylase Deficiency 00:35:01

- Excess mineralocorticoids: Hypertension, hypokalemia
- No features of glucocorticoid deficiency
- No sex steroids
  - Normal genitalia in females
  - Undervirilization (ambiguous genitalia) in males

	Ambiguous genitalia in Female	Undervirilization in Males
With salt wasting & Hyperkalemia	• 21 hydroxylase deficiency	• 3 β hydroxy steroid dehydrogenase deficiency
With Hypertension	• 11 β hydroxylase deficiency	• hydroxylase 17 deficiency

C. Adrenal Insufficiency 00:41:51

- **Primary (Adrenal Defects)**
  1. Autoimmune/Addison disease
  2. Infections: TB, HIV
  3. Adrenal Hemorrhage (Waterhouse Friedrichsen syndrome)
  4. CAH d/t 21 hydroxylase / 3 βHSD deficiency
  5. StAR defect → lipoid CAH
- **Secondary (↓ACTH)**
  1. Congenital malformations (Holoprosencephaly)
  2. Genetic defects
  3. Acquired insults (Neuro Sx, Radiotherapy)
  4. Tumors
  5. Discontinuation of steroids after prolonged Rx
- **Clinical features**
  - Dehydration
  - Lethargy
  - Vomiting
  - Salt craving
  - Hypotension
  - Hyperpigmentation seen in primary Adrenal insufficiency
- **Investigations**
  - Hypoglycemia
  - Hypernatremia
  - Hyperkalemia
  - Hemoconcentration
  - ↑ hematocrit
- **Treatment**: Hydrocortisone, Fludrocortisone

D. Cushing Syndrome 00:48:16

- Mc cause of adrenocortical hyperfunction in children
- Cushing disease (different from cushing syndrome): Hypercortisolism caused by ACTH producing pituitary tumor

Etiology

Acth dependent	Acth independent	Exogenous administration
1. Hypothalamic Lesions	• Adrenal adenoma / carcinoma	• Glucocorticoids
2. Pituitary lesions- adenoma	• Pigmented nodular hyperplasia	• ACTH
3. Ectopic source • Neuroblastoma • Wilm's tumor • Carcinoid	• Mc cune Albright syndrome	• Mc cause of Cushing syndrome in children→ iatrogenic / exogenous administration of steroids

- **Clinical features**
  - Obesity, striae
  - Moon facies, buffalo hump are rare
  - Short stature
  - Hypertension
  - Hirsutism
  - Delayed puberty
  - Bone pains
  - Muscle weakness
  - Behavioural problems
- **Diagnosis**
  1. Screening test
     - Assessment of diurnal cortisol rhythm
     - Overnight Dexamethasone suppression test
     - 24hr free Urine cortisol
  2. Confirmatory test: Low dose dexamethasone suppression test
     - ACTH Levels
       → < 5 pg/ml: ACTH independent cause
       → 15 pg/ml: ACTH dependent cause
       → 100 pg/ml: Ectopic ACTH production

3. Inferior petrosal sinus sampling → best test to identify the source of ACTH production

- **Treatment**
  1. Surgical Mx: Resection of pituitary/adrenal lesions.
  2. Medical Mx: Metyrapone, Ketoconazole, Mitotane.

E. Aldosterone Excess (Hyper Aldosteronism) 01:02:20

- **Primary Aldosteronism/ Conn Syndrome**
  - Adrenal adenoma of Hyperplasia
  - Glucocorticoid remedial Aldosteronism (GRA)
  - d/t genetic defect: aldosterone becomes regulated by ACTH
- **Secondary Hyperaldosteronism** (Activation of renin angiotensin pathway)
  - Renal artery stenosis
  - Renin secreting tumor
  - Congestive cardiac failure
  - Liver disease
  - Nephrotic syndrome
- **Pathophysiology**
  - Excess Na & H_2O absorption → Hypertension
  - Excess K^+ & H^+ loss → Hypokalemic metabolic alkalosis, generalized muscle weakness
- **Diagnosis**

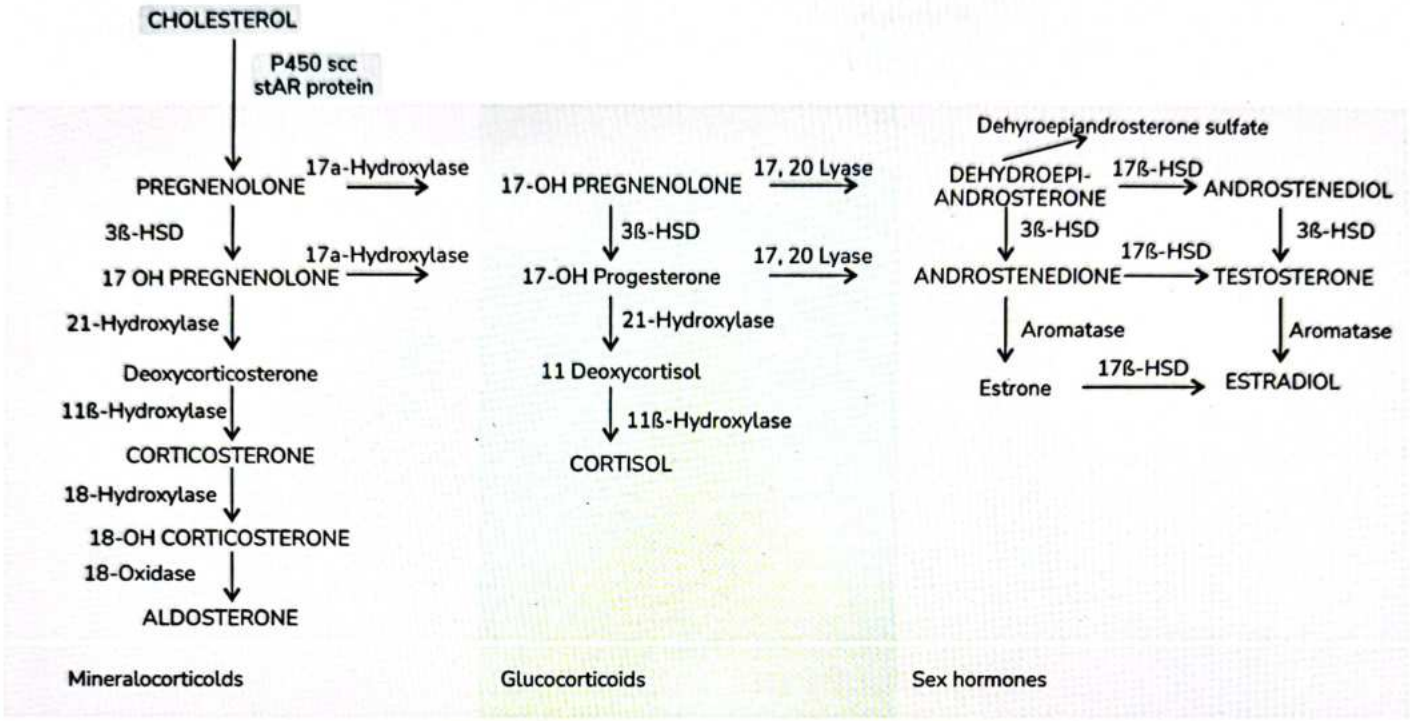
Renin	Aldosteronism	
Low	High	1°
High	High	2°
Low	High (Decreases after giving steroids)	GR A

- **Treatment**
  - Salt Restriction
  - Aldosterone antagonist (Spironolactone)

F. Pheochromocytoma 01:10:30

- A catecholamine secreting tumor that arises from chromaffin cells of abdominal sympathetic chain / Peri adrenal area/ thoracic cavity
- Rare in children
- More likely to be bilateral than adults
- Co-exist with
  - Neurofibromatosis
  - VHL syndrome
  - MEN syndrome type II
- **Diagnosis**: ↑ urinary VMA (vanillyl mandelic acid) & metanephrines.
- **Treatment**: surgical removal
- Pre-op alpha blockade with prazosin

Flow Chart 75.1



princeeeekum@gmail.com
9928609733

PREVIOUS YEAR QUESTIONS

Q. A 3 week neonate with ambiguous genitalia presented with Na =127meq/L, K= 6meq/L with BP 52/24 mmHg & was managed with IV fluids. What is the next step in management? (AIIMS MAY 2019)

A. Spironolactone
B. Hydrocortisone administration
C. Antibiotics
D. Calcium gluconate

76 DISORDERS OF PUBERTY

Disorders of Puberty
A. Precocious puberty
B. Delayed puberty

Important Information
- Breast development beyond Tanner stage II &testicular volume beyond 4 ml indicate the onset of puberty

Precocious Puberty 00:02:09

Definition: Onset of puberty before the age of 8 yrs in girls & Less than 9 and half years in boys
- Precocious puberty is more common in girls

2 Types
1. Central Precocious Puberty (Gonadotropin Dependent)
2. Peripheral Precocious Puberty (Gonadotropin Independent)

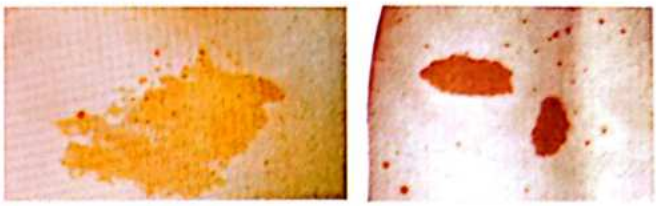
Important Information
- Central> peripheral in girls

Etiology in girls 00:05:24

1. Central Precocious Puberty (Gonadotropin Dependent)
- Idiopathic (more common in girls)
- Infections: TB, meningitis
- Injuries: Trauma, neuro Sx, Radiotherapy
- Tumors: Hypothalamic hamartoma (Gelastic seizures)
- CNS malformations
  - → Arachnoid cyst
  - → Hydrocephalus
  - → Septo-optic dysplasia

2. Peripheral Precocious Puberty (Gonodotropin Independent)
- Hypothyroidism
- Ovarian estrogen excess (cyst, tumor, Mc cune Albright syndrome)
- Adrenal estrogen excess
- Exogenous estrogen exposure

McCune Albright Syndrome
- Triad of
  - Precocious puberty
  - Café au lait spots
  - Polyostotic fibrous dysplasia
- Occurs due to somatic activating mutation of stimulatory G-protein



Café au lait spots

- Endocrine Abnormalities
  - Hyperthyroidism
  - Rickets
  - GH excess
  - Precocious puberty

Etiology in boys 00:12:25

1. Central Precocious Puberty
- Causes are the ones similar to seen in girls.
- Organic causes are more common in boys

2. Peripheral Precocious Puberty
- Excess androgen production from testis or adrenal is with prepubertal LH levels
- CAH d/t 21 hydroxylase or 11β hydroxylase deficiency (MC cause of peripheral precocious puberty in boys)
- Adrenal tumors → adenoma/ carcinoma
- Testicular tumors → Seminoma/Germinoma
- Testo toxicosis → activation of LH receptors
- HCG secreting tumors → Hepatoblastoma/ germinoma
- Exogenous intake of androgens

Diagnosis
- LH is a better indicator of puberty than FSH
- LH levels > 0.6 mu/L or LH/ FSH ratio >1 indicates development of puberty
- Advanced bone age
- Imaging to rule out CNS/gonadal/ adrenal tumors. MRI is better diagnostic modality.

Treatment
- Rx the underlying cause
- Long acting GnRH analogues (Leuprolide)

Delayed Puberty 00:21:12
- More common in boys

Definition

- Girls: Lack of secondary sexual characters by 13 yrs age or absence of menarche by the age of 16 yrs or within 5 yrs after onset of puberty
- Boys: Lack of pubertal changes by 14 yrs of age

Etiology

A. Hypogonadotrophic Hypogonadism (LH & FSH → low) causes same in both boys and girls

- Transient Conditions
  - → Chronic systemic illness (CKD, Chronic liver Disease)
  - → Severe malnutrition
  - → Endocrine causes (hypothyroidism, type 1 DM)
- Permanent Causes
  - → Isolated delayed puberty
    - Genetic mutations →KAL 1 (Kallmann Syndrome), GnRH Receptor, DAX-1 gene
    - Syndromes →Prader Willi Syndrome, Laurence Moon Syndrome
  - → MPHD (multiple pituitary hormone disease)
    - Injury
    - Infiltration by tumors- LCH
    - Genetic – PROP1,LH
    - CNS malformation
    - Trauma

B. Hypergonadotrophic Hypogonadism (LH & FSH → High)

- **Girls**
  - → Gonadal dysgenesis (Turner Syndrome)
  - → Steroidogenic defect (StAR deficiency, aromatase deficiency, 17 hydroxylase deficiency)
  - → Ovarian insult (surgery / radiotherapy)
  - → Autoimmune ovarian failure
  - → LH & FSH receptor resistance
- **Boys**
  - → Chromosomal abnormalities (Klinefelter Syndrome)
  - → Steroidogenic defects (17α hydroxylase deficiency)
  - → Testicular insults (trauma, chemotherapy, radiotherapy)
  - → Malformations (cryptorchidism)
  - → Inefficient testosterone action (5α reductase deficiency)
  - → Resistance to testosterone action (androgen insensitivity syndrome)

Investigations

- Screen for systemic diseases
- LH, FSH levels
- Karyotype

Treatment

- HRT to be initiated beyond 12 yrs in girls & 14 yrs in boys, to initiate & maintain sexual character & to prevent osteoporosis

77 DISORDERS OF SEXUAL DEVELOPMENT (DSD)

00:00:45

Germ cells

- (arise from coelomic epithelium of hindgut & midgut & migrate to Gonadal Ridge by 4-6 weeks of gestation)

↓

Bipotential Gonad

- DAX 1: Suppresses androgen synthesis
- WNT 4: Stimulates expression of DAX 1

- Most important in development of testis: SRY (Sex determining region on Y chromosome)
- SOX9
- WT1 gene

OVARY

↓

- Presence of Estrogen & Absence of AMH (Anti Mullerian Hormone)

↓

- Mullerian development into Fallopian tubes, uterus & upper 2/3 of vagina

TESTIS

↓

Sertoli cells

↓

AMH

↓

Regression of Mullerian ducts

Leydig cells

↓

Testosterone

Wolffian development

5 reductase

↓

DHT (Di hydro Testosterone)

↓

Male external genital development

00:10:56

DSD

46, XX DSD

1. Androgen excess

- CAH (21 hydroxylase or 11 hydroxylase deficiency)
- Placental aromatase def
- Maternal virilising tumors
- Mat. Androgenic drug

2. Abnormal gonad

↓

- Ovotesticular DSD

46, XY DSD

Disorder of Androgen synthesis or action

1. CAH
   - Star def
   - 3β HSD def
   - 17β HSD def
   - 17,20 Lyase def
2. 5α reductase deficiency
3. Androgen insensitivity syndrome
4. Smith Lemli Opitz syndrome

Abn. Gonadal development

1. Gonadal dysgenesis
2. Gonadal regression
3. Ovotesticular DSD

Sex chromosome DSD

1. 45,XO
2. 47,XXY

Androgen Insensitivity Syndrome (AIS) 00:24:24

- Previously called 'Testicular Feminisation Syndrome'
- Basic defect – Resistance to androgens
- It is the MC form of 46, XY DSD
- X linked recessive inheritance
- Clinical features
  - Clinical spectrum ranging from phenotypic females (complete AIS) to males with ambiguous genitalia & undervirilization to normal appearing males with infertility (partial AIS)

CAIS

- Genetic males appear females at birth
- External genitalia is female
- Vagina ends blindly in a pouch
- Uterus is absent (due to effect of AMH by testis)
- Testis are usually intra-abdominal, but may be in inguinal canal
- At puberty:
  - Normal development of breast & female habitus (Testosterone acted upon by aromatase to form Estradiol)
  - But menstruation does not occur.
  - Sexual hair is absent
  - Girl with primary amenorrhea, normal breast development but absent axillary / public hairs → Suggestive of CAIS

Partial AIS

- Wide variety of phenotypic presentation ranging from perineoscrotal hypospadias, Bifid scrotum, Cryptorchidism, Clitoromegaly & labial fusion
- At puberty lack of facial hair or voice change

Diagnosis

- Karyotype: 46,XY
- Presence of Testis
- Normal or elevated Testosterone or DHT

Treatment

- Genetic counseling
- In CAIS with female body habitus
  - Testis are removed
  - Replacement therapy with estrogen at puberty

78 TYPE 1 DIABETES MELLITUS & OBESITY IN CHILDREN

Type 1 DM

- MC type in children → type 1 DM
- Diagnostic Criteria

  Symptoms of DM (polyuria/polyphagia/polydipsia)

  +

  FBS ≥ 126 mg/dl (or)

  RBS/PP ≥ 200 mg/dl (or)

  HbA1c ≥ 6.5%
- Dose of glucose for doing OGTT in children → 1.75g/kg of ideal body wt (maximum 75 g)
- RxOC type 1 DM → Insulin
- Dose of insulin
  - Prepubertal children: 0.6 – 0.8 U/kg/day
  - Pubertal age group: 0-1.2 U/kg/ day

Examples of different Insulins 00:03:59

- Rapid acting: Lispro, Aspart
- Short acting: Regular
- Intermediate acting: NPH
- Long acting: Glargine, Detemir, Degludec

- 2 Regimes (target HbA_{1c} <7.5%)
  - **Basal Bolus Regime**
    - → Long acting → 40-50% of total daily dose (TDD)
    - → Rapid acting → 50-60% of TDD in 2-3 divided closes
  - **Mixed Split Regime**
    - → 2/3rd before breakfast
      - 2/3 intermediate acting (NPH)
      - 1/3 short acting
    - → **1/3rd after dinner**
      - 2/3 intermediate acting (NPH)
      - 1/3 short acting
- Screening for Complications like nephropathy should be started:
  - After 5 yrs of diagnosis in pre pubertal children
  - After 2 yrs of diagnosis in pubertal children

Obesity 00:08:38

- **Definition**: A condition of excess fat deposition in the body to the extent that health may be impaired.
- **Diagnosis**: BMI (Body Mass Index)
  - $BMI = \frac{wt(kg)}{Ht(m)2}$
  - For obesity
    - → BMI >/= 95th percentile for age & sex is diagnosed as obesity.
    - → BMI: 85th to 95th percentile according to age & sex is overweight
- Parameters useful in diagnosing obesity

Parameters useful for diagnosis of obesity 00:12:20

Clinical parameters	Investigations

• BMI
• Skin fold thickness
• Waist circumference and waist hip ration
	• Density based methods (based on Archimedes principle)
	  ○ Air displacement plethysomography
	• Scanning methods:
	  ○ E.g.: DEXA, CT scan, MRI scan
	• Bioelectrical impedance methods

Etiology 00:17:01

Refer Table 78.1

Prader willi syndrome

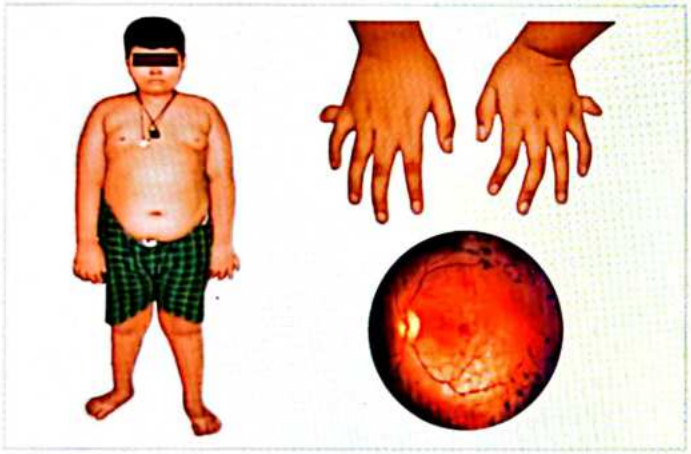
- Facial dysmorphism in the form of narrow bifrontal diameter of head, almond shaped palpebral fissures, downturned mouth.
- Can be seen as a result of genomic imprinting or uniparental disomy in chromosome 15
- In infancy, severe hypotonia and feeding problems
- Later: Excessive eating and morbid obesity.
- Hypogonadism and short stature seen.
- Cognitive impairment and delayed molar or language milestones

Laurence Moon Bardet Biedel Syndrome:

Features:

1. Obesity
2. Retinal pigment changes (H/O vision Problems)
3. Post axial polydactyl

L - Learning Disability
A - } Sound as obesity
U - }
R - Retinal pigmentation changes
E - Renal abnormalities
N - No. Of digits increased (Polydactyly)
C
E - Extra features (Hypogonadism, DM, Hepatic Fibrosis)



How to distinguish constitutional obesity from pathological obesity

	Characteristics	Constitutional obesity	Pathological obesity
1.	Distribution of fat	Generalised	Central
2.	Height	Normal or tall	Usually short stature
3.	Bone age	Normal or advanced	Usually less
4.	Dysmorphism	(-)nt	(+)nt
5.	Mental ability (Mental function)	Normal	Impaired (Usually)
6.	Family H/O obesity	Common	May not be seen (uncommon)

Complications of Obesity

00:34:13

- Insulin resistance (acanthosis nigricans, DM)
- Metabolic syndrome(hyperlipidemia, HTN, diabetes)
- Non-alcoholic fatty liver disease (NAFLD)
- Gall stones
- Obstructive sleep apnoea

Prevention and Treatment of Obesity

00:36:19

- **Prevention**
  - Healthy lifestyle
  - Decrease consumption of junk food
  - Excess food should not be taken
  - Increased physical activity

Treatment

1. Dietary modification: Traffic light diet recommended

Traffic light diet

- Red light _____
  - High in calories, sugar and fat
  - e.g. Fatty meats, sugar, fried foods
- Yellow light: _____
  - Nutrient dense, but rich in cal. and fat
  - e.g. dairy, starches & grains
- Green light: _____
  - Low calorie, high fibre, low fat
  - e.g. fruits, vegetables, cereals and legumes
- Red: Avoid
- Yellow: Limited Intake
- Green: UNLIMITED QUANTITY of food can be taken

2. Increase physical activity
3. Orlistat: Gastric lipase inhibitor
4. Metformin: for insulin resistance
5. Bariatric Sx: laparoscopic adjustable banding (only in those with morbid obesity, where other measures have failed)

Table 78.1

A. Constitutional (> 90% causes)

- d/t imbalance b/w energy intake & expenditure
- No organic/ underlying cause
- normal development; tall for age

B. Pathological / organic

i. Endocrine

- Cushing syndrome
- GH deficiency
- Hypothyroidism

ii. Genetic syndromes

- Prader Willi syndrome
- Laurence moon syndrome (obesity, polydactyly and retinal pigment changes)
- Beckwith Wiedemann syndrome

iii. Hypothalamic

- Injury
- Radiotherapy
- Tumors

iv. Drugs

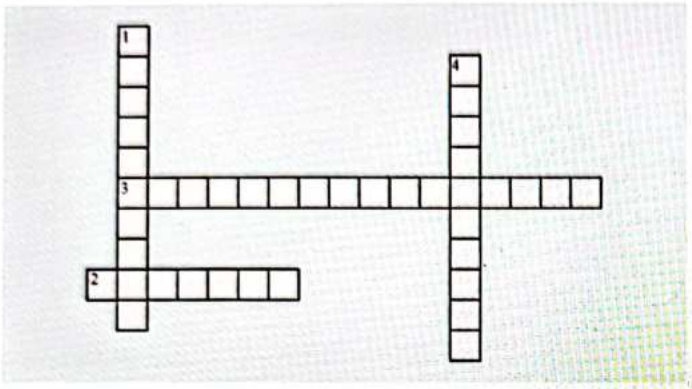
- Steroids
- Antiepileptics
- Estrogen

v. Monogenic disorders

- Leptin deficiency or resistance
- Melanocortin 4 receptor defects

CROSS WORD PUZZLES

Crossword Puzzle



Across

2. Bone disorder caused by vitamin D deficiency in which there is defective mineralization of bones matrix of growth plat.
3. ____ is a chronic autoimmune disease post synaptic motor end plate leading to abnormal neuro-muscular transmission or blockade.

Down

1. Bone disorder in which the limbs resemble flippers of a seal?
4. ____ gene is affected in both Duchenne muscular dystrophy (DMD) & Becker muscular Dystrophy (BMD).

princeeeekum@gmail.com
9928609733