COMPILED MODULE: GHAI SPECIAL

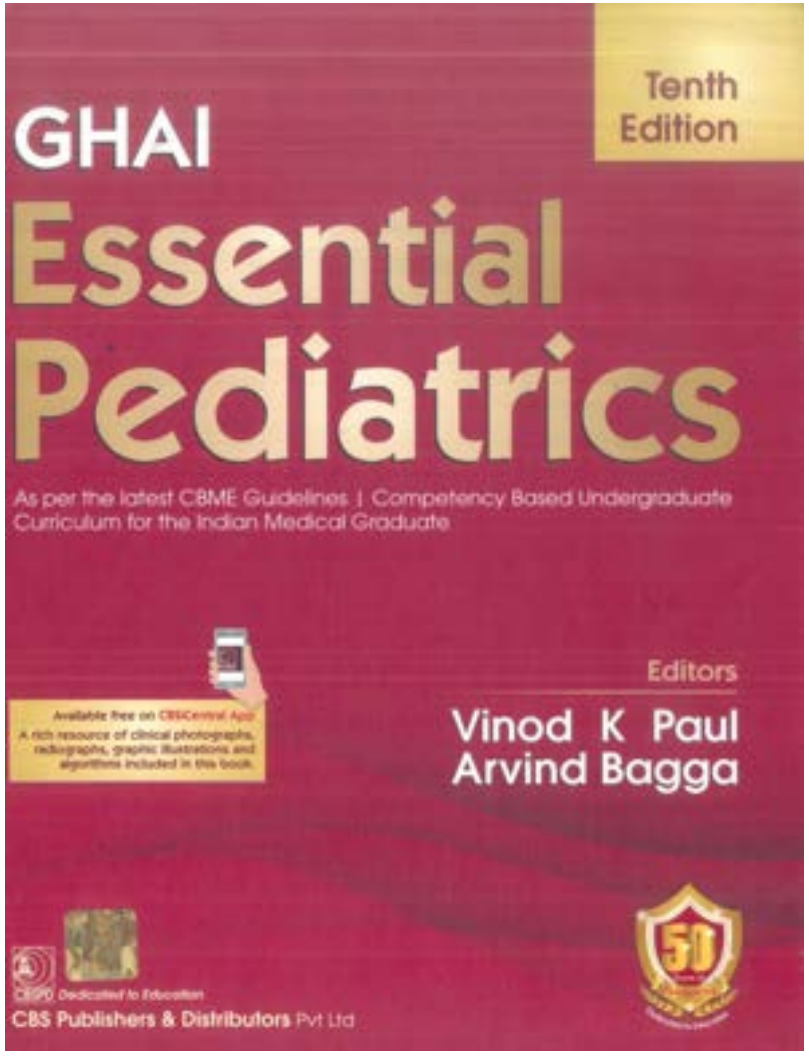


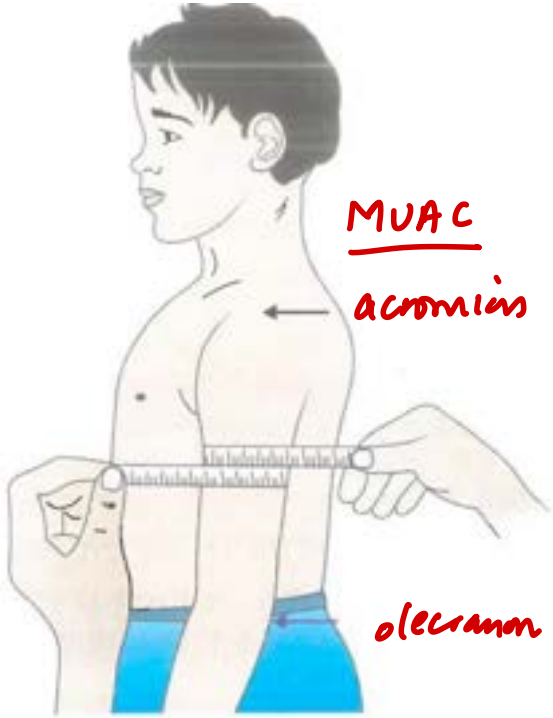
Table 2.1: Periods of growth

Prenatal period	
Ovum	0 to 2 weeks
Embryo	3 to 8 weeks
Fetus	9 weeks to birth
Perinatal period	22 weeks to 7 days after birth
Postnatal period	
Newborn	First 4 weeks after birth
Infant	Birth to <12 months (neonate: Birth to 28 days; post-neonate: 29 days to <1 year)
Toddler	1 year to 36 months
Preschool child	37–72 months
School-age child	73 months–12 years
Adolescence	10–19 years
Early	10–13 years
Middle	14–16 years
Late	17–19 years

The growth pattern of every individual is unique: The order of growth is cephalocaudal and distal to proximal. During fetal life, the growth of the head occurs before that of the neck, and arms grow before the legs. Distal body parts, such as hands, increase in size before the upper arms. In postnatal life, the growth of the head slows down, but limbs continue to grow rapidly.

The seven important causes of under-5 mortality in children in India (with % contribution) are: (i) Prematurity (27%), (ii) neonatal infections (13%), (iii) birth asphyxia (11%), (iv) pneumonia (11%), (v) diarrhea (9%), (vi) congenital anomalies (9%), and (vii) injuries (3%) (Fig. 1.2). The above causes are the proximate conditions that lead to life-threatening situations and death. Poverty, illiteracy, low caste, rural habitat and harmful cultural practices are important determinants of ill-health. Undernutrition is a critical underlying intermediate risk factor of child mortality, associated with about 45% of under-5 child deaths. Undernutrition causes stunting and wasting, predisposes to infections and is associated with adult disorders and low economic productivity.

Fig. 2.7: Method of recording head circumference



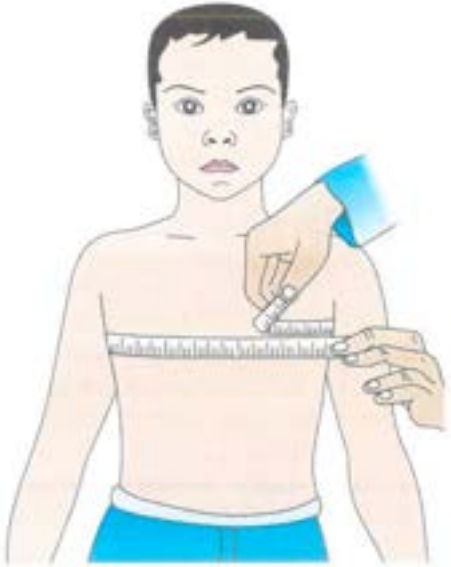
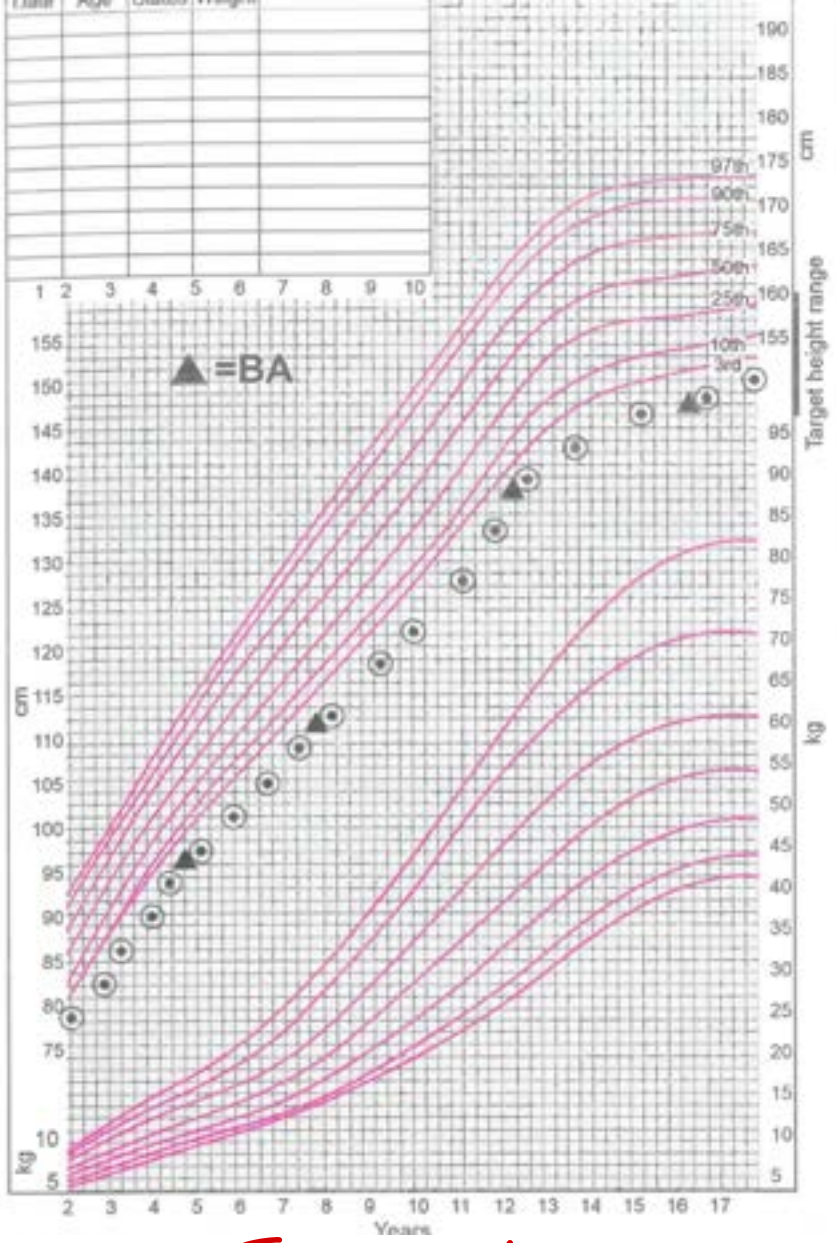


Fig. 2.8: Method of measurement of chest circumference at the level of nipples

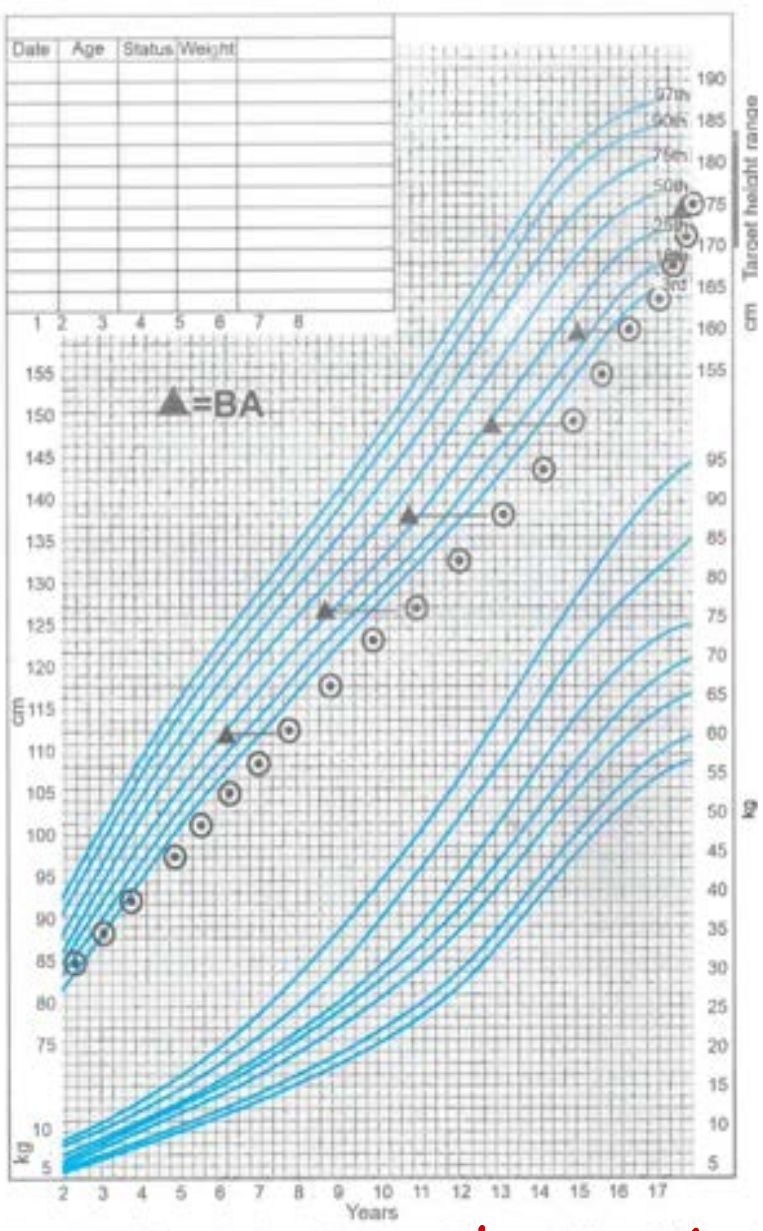
Short stature is defined as height below the third centile or more than two standard deviation scores (SDS) below the median height for age and gender (<–2 SDS) according to the population standard. Two to 3% of children in any given

vertebral anomalies. Arm span is shorter than the length by 2.5 cm at birth, equals height at 11 years, and after that is slightly (usually, <1 cm) greater than height.

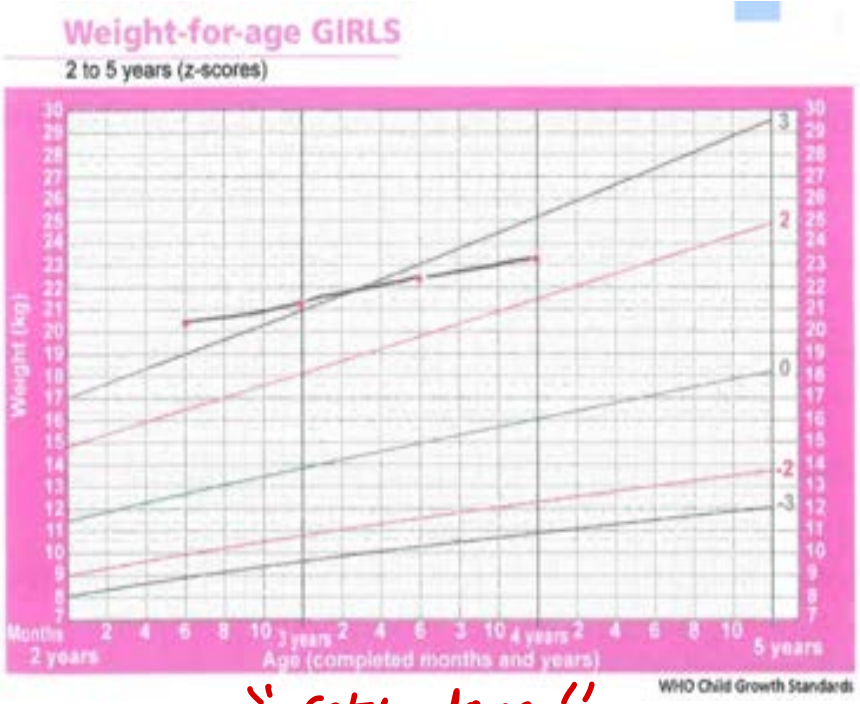
Chest circumference: The chest circumference is about 3 cm less than the head circumference at birth. The circumference of the head and chest are almost equal by the age of 1 year. After that, the chest circumference exceeds the head circumference.



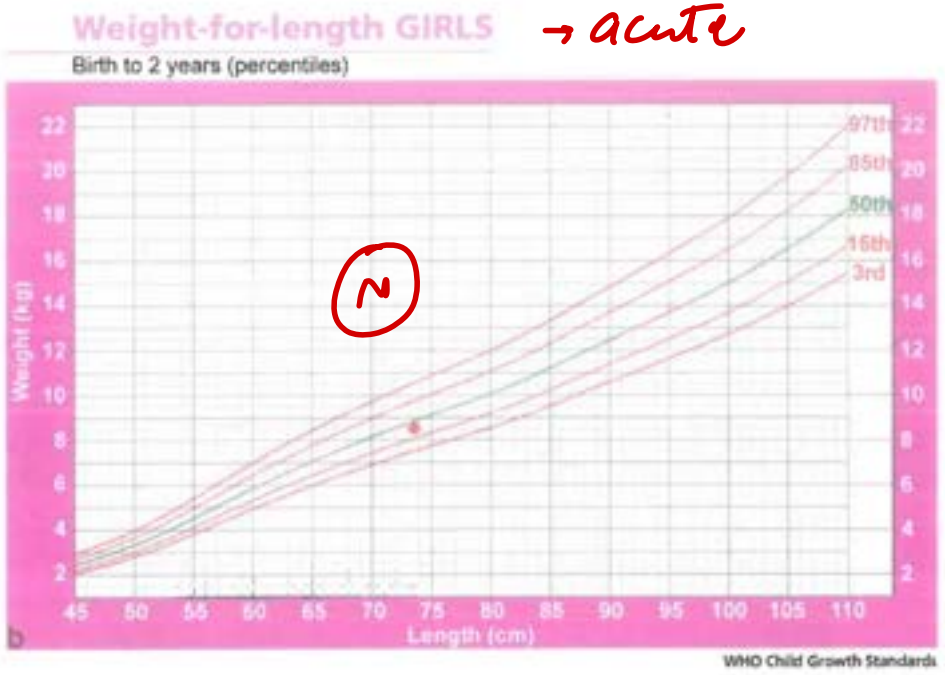
Familial



Constitutional



"Catch-down"



→ acute

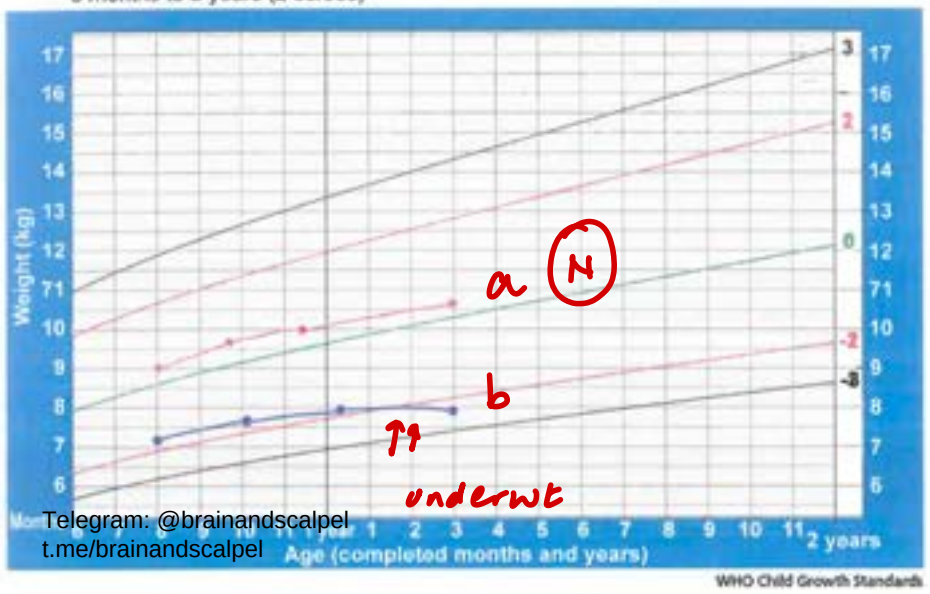
18mm old girl

CHRONIC

Stunted

but

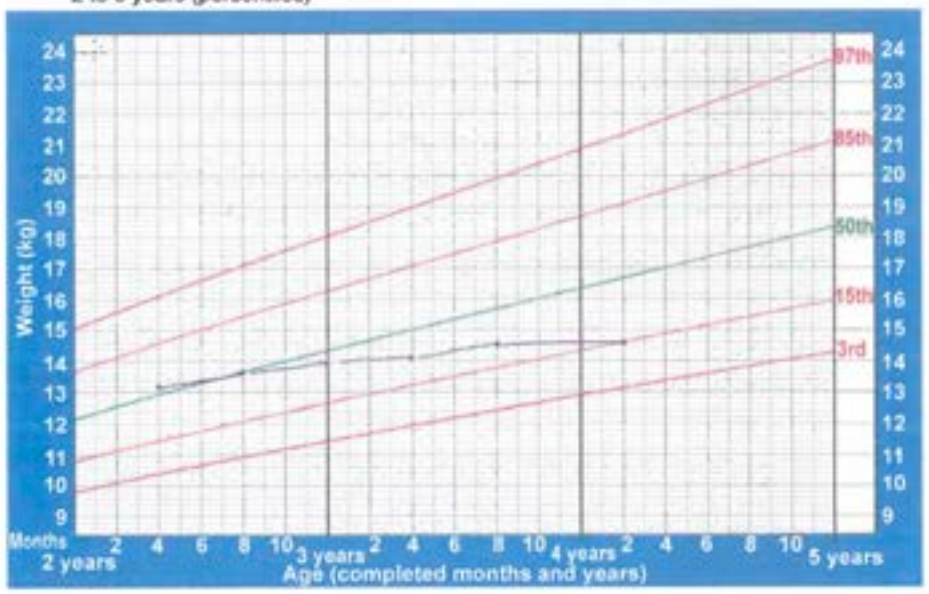
(x) wasting



a (N)

b

↑↑ underwt



Stagnation

↓

recurrent infs/

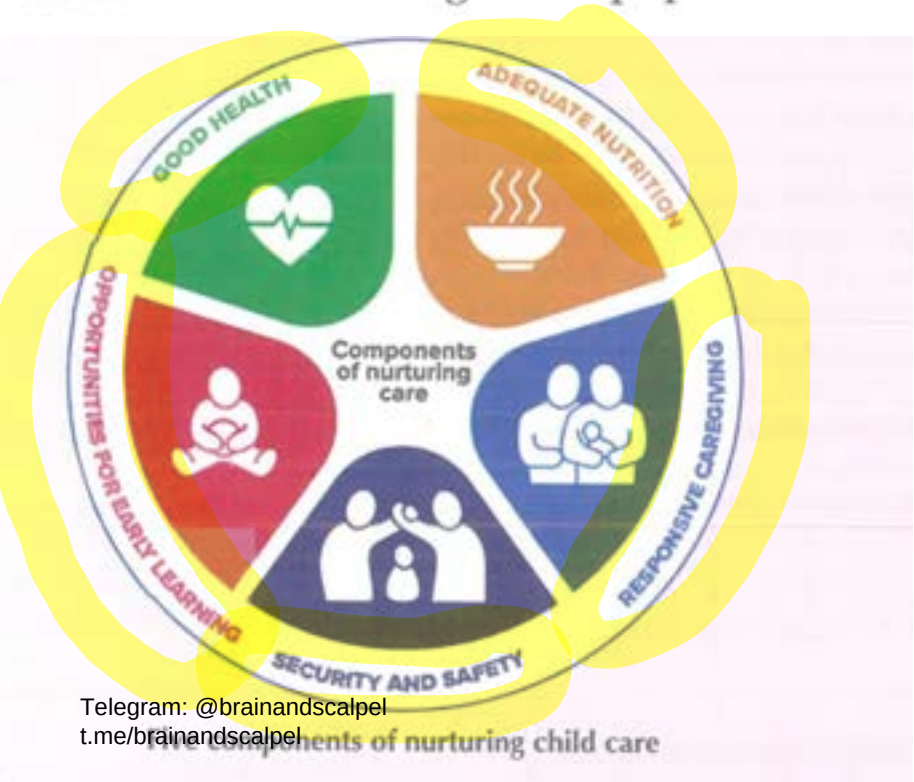
malabsorb^{n}

↳ coliac D

Failure to Thrive

Definition and Epidemiology

Failure to thrive (FTT) is a descriptive term rather than a diagnosis and is used for infants and children up to 5 years of age whose physical growth is significantly less than their peers of the same age and sex. FTT usually refers to weight below the 3rd or 5th centile, failure to gain weight over time, or a change in the rate of growth, such that weight for age or weight for length/ height has crossed two major centiles, e.g. 50th to 10th, over a period of time. The prevalence of FTT varies according to the population sampled.



The components of nurturing child care

Table 2.11: Distinction between constitutional delay in growth and familial short stature

Feature	*Constitutional growth delay*	*Familial short stature*
Height	Short	Short
Height velocity	Normal	Normal
Family history	Delayed puberty	Short stature
Bone age	Less than chronological age	Normal
Puberty	Delayed	Normal
Final height	Normal	Low but normal for target height

Table 18.6: Clinical features of hypothyroidism

Congenital	*Acquired*
Open posterior fontanel	Myopathy and pseudohypertrophy of limb muscles
Umbilical hernia	Enlarged sella
Delayed neurodevelopment	Pseudotumor cerebri
Large tongue	
Common to both congenital and acquired forms	
Growth retardation	
Sallow edematous facies	Pallor
Delayed skeletal maturation	Hypothermia
Delayed dental development	Rough dry skin
Delayed puberty	Hypotonia
Constipation	Protuberant abdomen

Table 18.2: Indications for growth hormone therapy

Growth hormone deficiency in children and adults
Turner syndrome
Chronic renal insufficiency
Prader-Willi syndrome
Small for gestational age who fail to catch-up in growth by 2–3 years of age
SHOX gene mutations and Leri-Weill dyschondrosteosis
Noonan syndrome
Idiopathic short stature

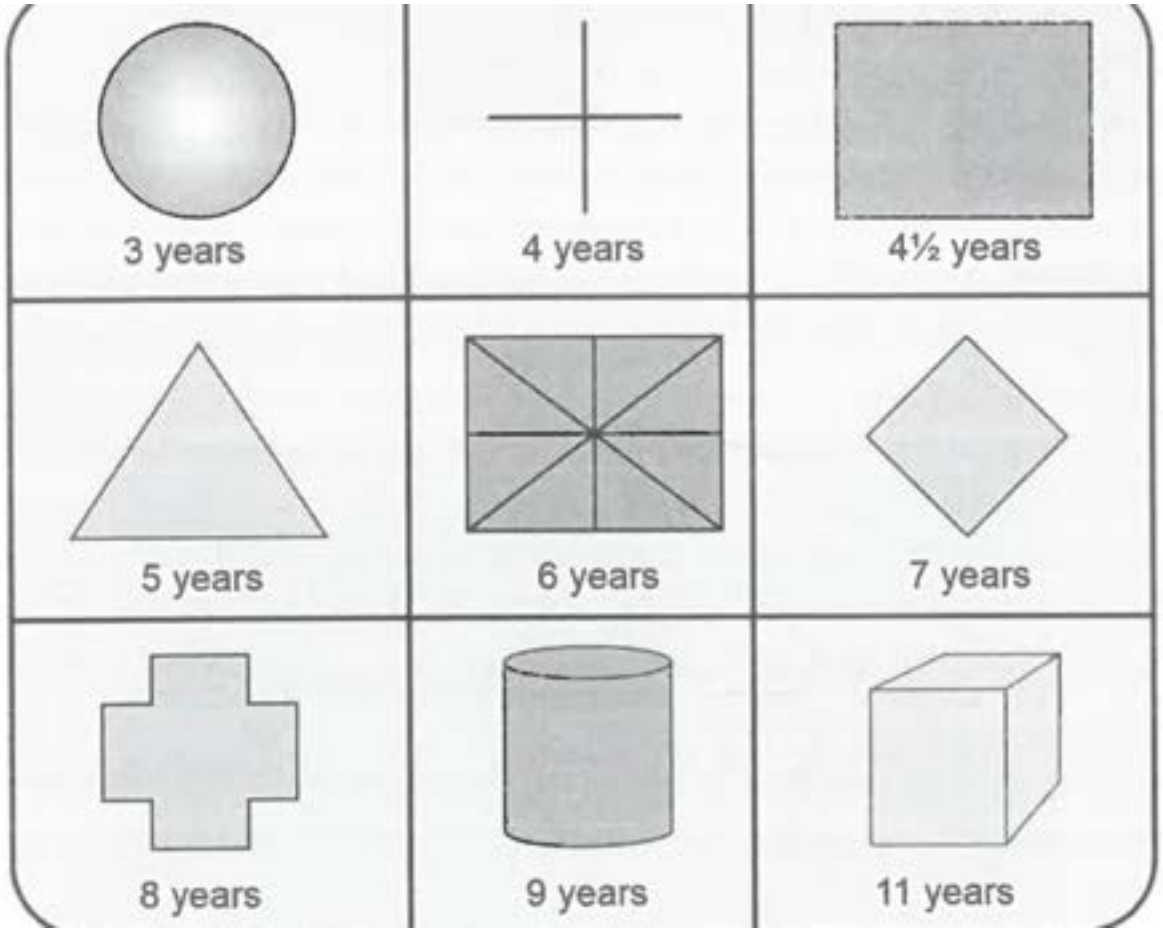


Table 3.5: Upper limit of age for the attainment of **milestones**

Milestone	*Age*
Visual fixation or following	2 months
Vocalization	6 months
Sitting without support	10 months
Standing with assistance	12 months
Hands and knees crawling	14 months
Standing alone	17 months
Walking alone	18 months
Single words	18 months
Imaginative play	3 years

Fig. 3.31). Hand regard is even present in children without vision. Its persistence beyond 20 weeks is abnormal. At 3 to 4 months, the hands of the child come together in the midline as he plays (Fig. 3.32). On dangling a red ring in

Phatak's Baroda screening test: This is India's best-known development testing system that Dr. Promila Phatak developed. It is meant to be used by child psychologists rather than physicians. It is the Indian adaptation of the Bayley development scale and is applied to children up to 30 months.

Ages and stages questionnaire (ASQ-3): It consists of age-based, parent-completed questionnaires for children from one month to 5½ years of age. The questionnaire takes about 10–15 minutes for parents to complete and about 2–3 minutes to score. It assesses the following domains: Communication, gross motor, fine motor, problem-solving, and personal-social.

Denver II: The revised Denver Development Screening Test (DDST) or Denver II was revised in 1992 and assesses child development in four domains, i.e. gross motor, fine motor adaptive, language, and personal-social behavior.

Trivandrum Development Screening Chart (TDSC): It consists of 51 items for children of 0–6 years with items adapted from existing developmental charts/scales. It is primarily a screening tool for use in the community to identify children between 0 and 6 years with developmental delay.

Clinical adaptive test and clinical linguistic and auditory milestone scale (CAT/CLAMS): This easy-to-learn scale assesses the child's cognitive and language skills. It uses parental reports and direct testing of the children from birth to 36 months.

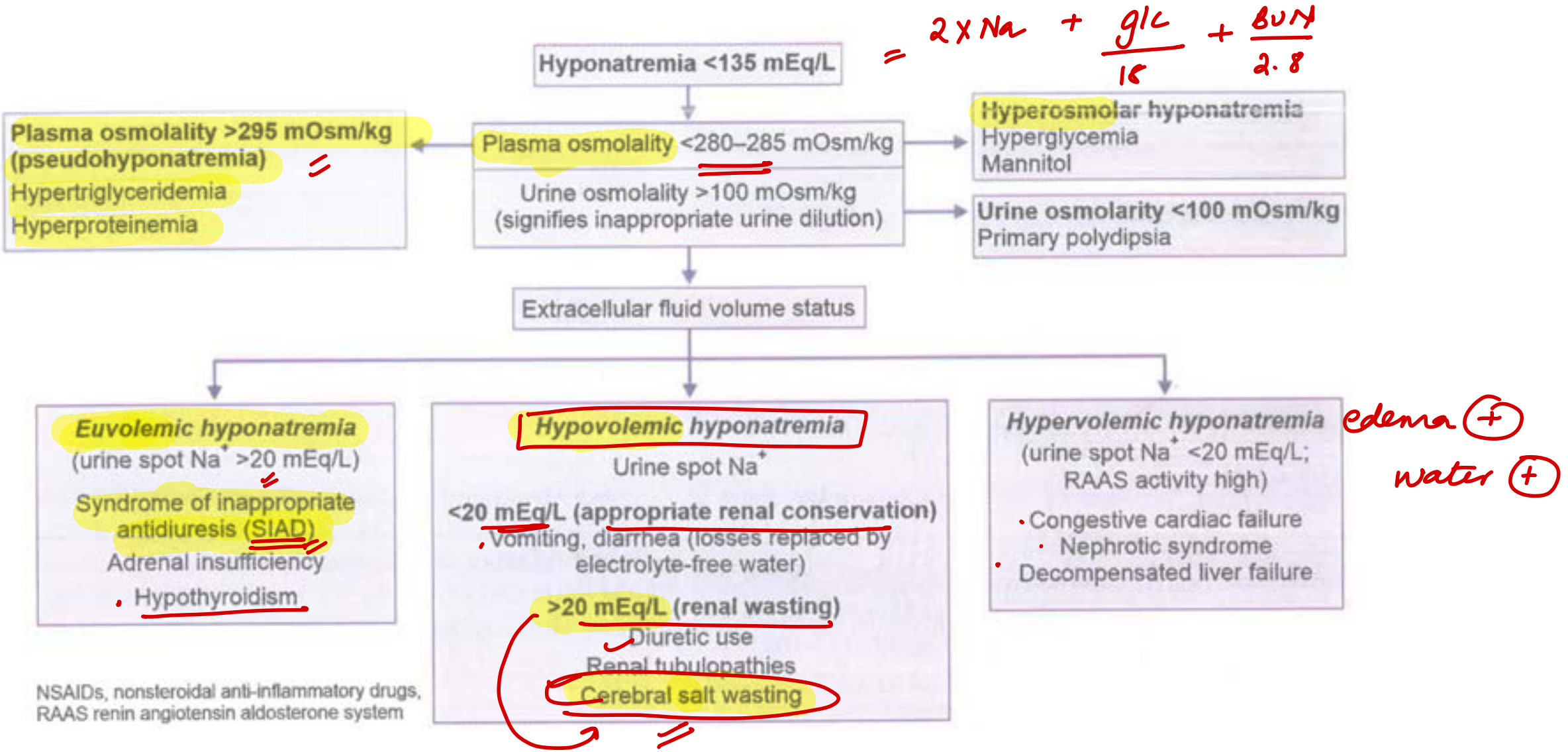
Goodenough-Harris drawing test: The child draws a man in the best possible manner, and the detail of the drawing determines the score of the child (Fig. 3.62; note the mature grip of pen, compare it with immatre grip in Fig. 3.47). One can determine the mental age by comparing scores obtained with a normative sample.

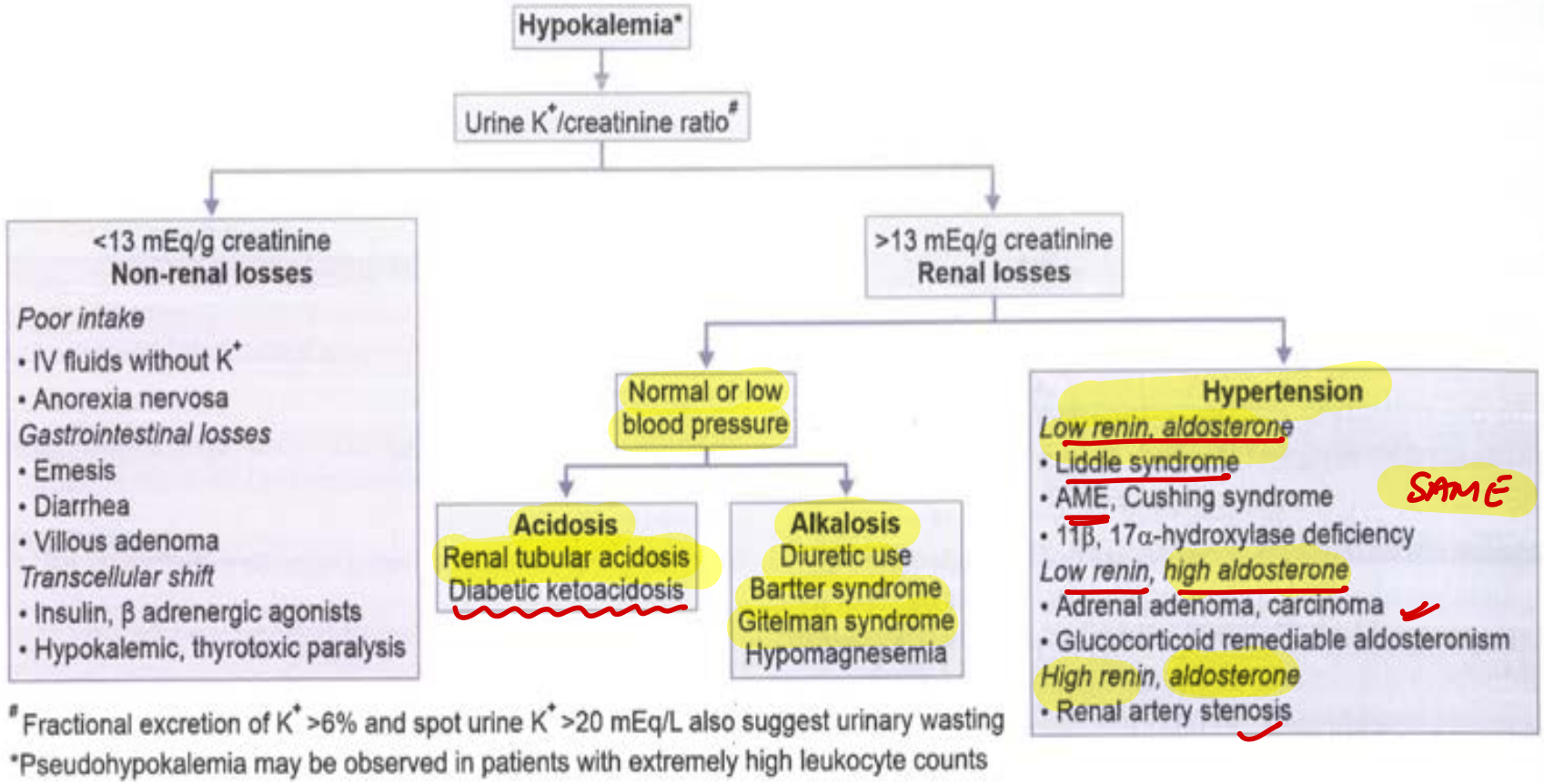
Table 3.6: Scales for definitive testing of intellect and neurodevelopmer

Name of the test	*Age range*	*Time taken to administer*
Bayley Scale for Infant Development IV	16 days to 42 months	30–70 min
Wechsler Intelligence Scale for Children IV	6 to 17 years	65–80 min
Stanford-Binet Intelligence Scales, 5th edition	2 to 85 years	50–60 min
Vineland Adaptive Behavior Scale III	0 to 90 years	20–60 min
Development Assessment Scale for Indian Infants (DASII)	Birth–30 months	45–60 min

screening

confirmatory





Fractional excretion of K^+ >6% and spot urine K^+ >20 mEq/L also suggest urinary wasting

*Pseudohypokalemia may be observed in patients with extremely high leukocyte counts

The transtubular potassium gradient (TTKG) accounts for the confounding effect of urine concentration on interpretation of urine K^+ excretion. TTKG is the ratio of K^+ concentration in the lumen of the cortical collecting duct to that of the plasma; an indirect indicator of aldosterone activity. It is calculated as follows.

TTKG = (urine potassium × plasma osmolality)/(serum potassium × urine osmolality)

This test cannot be applied when the urine osmolality is less than the serum osmolality or in cases of poor distal tubular Na^+ delivery (urine Na^+ <25 mEq/L). Normal TTKG varies between 6 and 12. It should rise to >10 in patients with hyperkalemia. A value <5 signifies inappropriate aldosterone effect. An increase in TTKG >7 after administration of physiologic dose of fludrocortisone suggests mineralocorticoid deficiency; <7 suggests resistance.

The urinary K^+ to creatinine ratio can be used to assess K^+ handling by the kidneys; the near-constant rate of creatinine secretion in urine helps in correction for variation in urine concentration. A K^+: creatinine ratio <13 mEq/g creatinine (or <2.5 mEq/mmol creatinine) suggests an appropriate response to gastrointestinal K^+ loss, remote use of diuretics, decreased dietary intake, and K^+ shift into cells. Higher ratios imply an inappropriate response by the kidney. While cumbersome to collect, a 24-hour excretion of >25–30 mEq/day of K^+ in a hypokalemic patient also implies renal wasting.

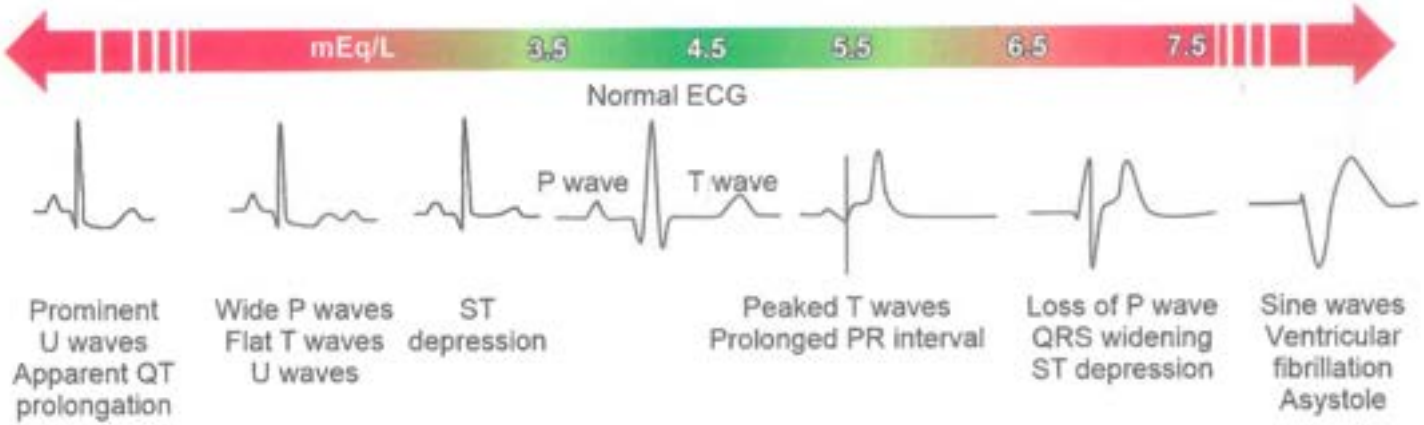


Table 6.8: Causes of hyperkalemia

Decreased losses

Acute kidney injury or chronic kidney disease

Renal tubular disorders: Pseudohypoaldosteronism, urinary tract obstruction

Medications: ACE inhibitors, angiotensin receptor blockers, potassium sparing diuretics, NSAIDs, heparin

Adrenal insufficiency: Congenital/acquired

Increased intake

Intravenous or oral K^+ intake, packed red cells transfusion

Extracellular shift

Acidosis, low insulin state, medications (β-adrenergic blockers, digitalis, succinylcholine, fluoride), hyperkalemic periodic paralysis, malignant hyperthermia

Cellular breakdown

Tumor lysis syndrome, rhabdomyolysis, crush injury, massive hemolysis

Box 6.4: Treatment of Hyperkalemia

- Prompt discontinuation of K^+-containing fluids and medications that lead to hyperkalemia
- Stabilize myocardial cell membrane to prevent cardiac arrhythmia. Use IV 10% calcium gluconate at 0.5–1 mL/kg over 5–10 minutes under cardiac monitoring. Discontinue, if bradycardia develops
- *Enhance cellular uptake of potassium*

  Regular insulin and glucose IV: 0.3 U regular insulin/g glucose over 2 hr

  Sodium bicarbonate IV: 1–2 mEq/kg body weight over 20–30 minutes

  β-adrenergic agonists (salbutamol, terbutaline) nebulized or IV
- *Total body potassium elimination*

  Sodium polystyrene sulfonate (Kayexalate) oral/per rectal: 1 g/kg (max. 15 g/dose) oral or rectal enema in 20–30% sorbitol

  Loop or thiazide diuretics (if renal function is maintained)

  Kidney replacement therapy (hemodialysis or peritoneal dialysis): For severe symptomatic hyperkalemia, particularly in patients with impaired kidney function or tumor lysis syndrome

  Primary or secondary hypoaldosteronism: Maintenance steroids and fludrocortisone

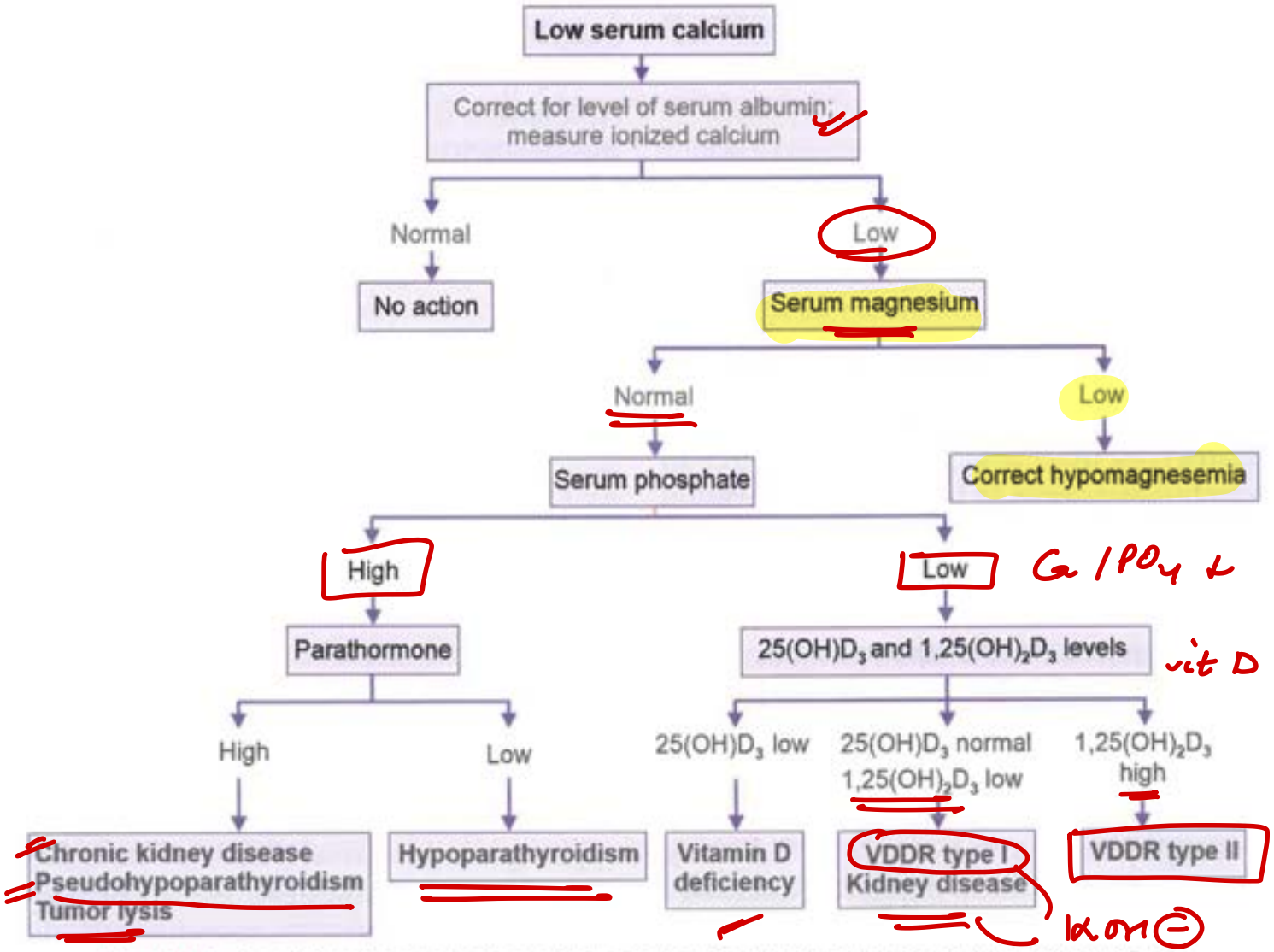
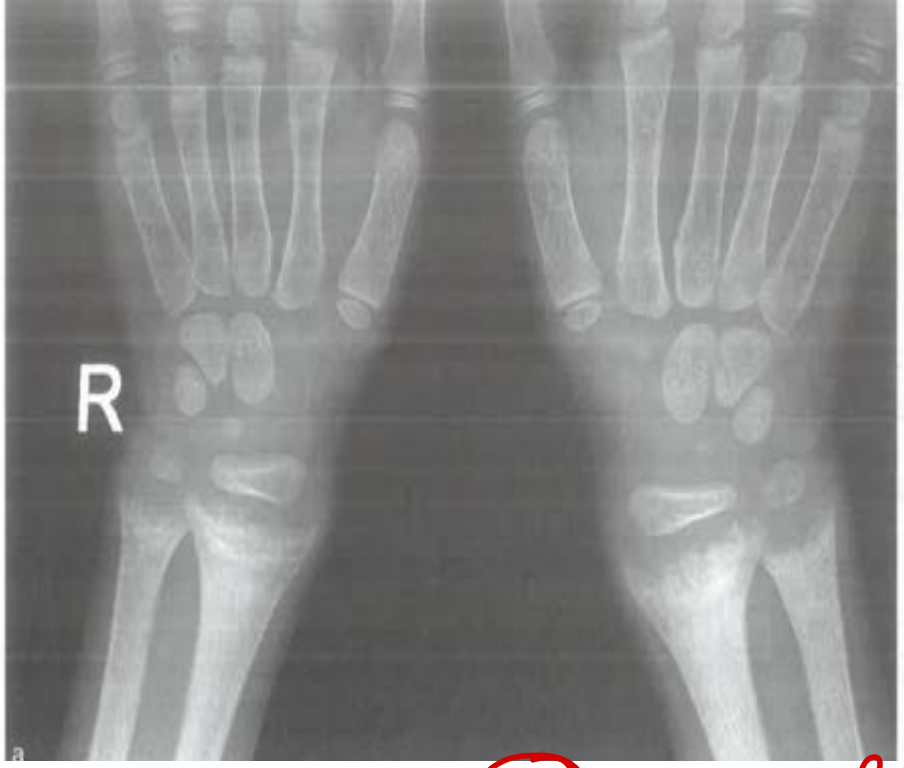
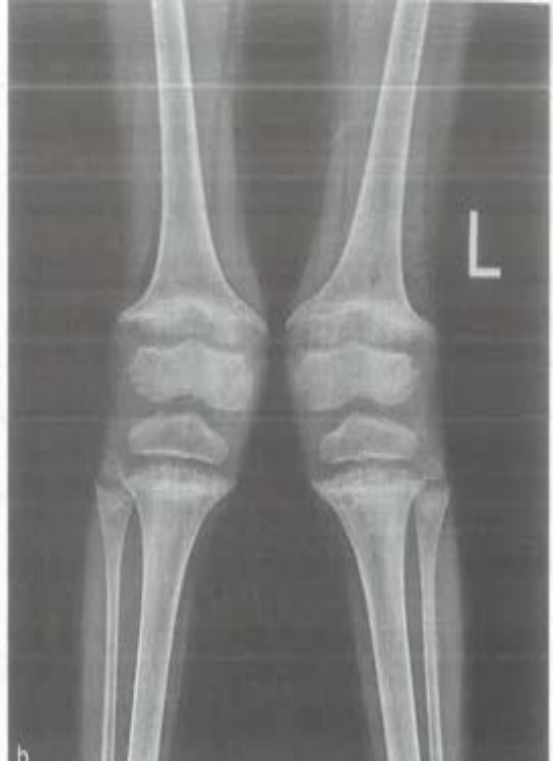


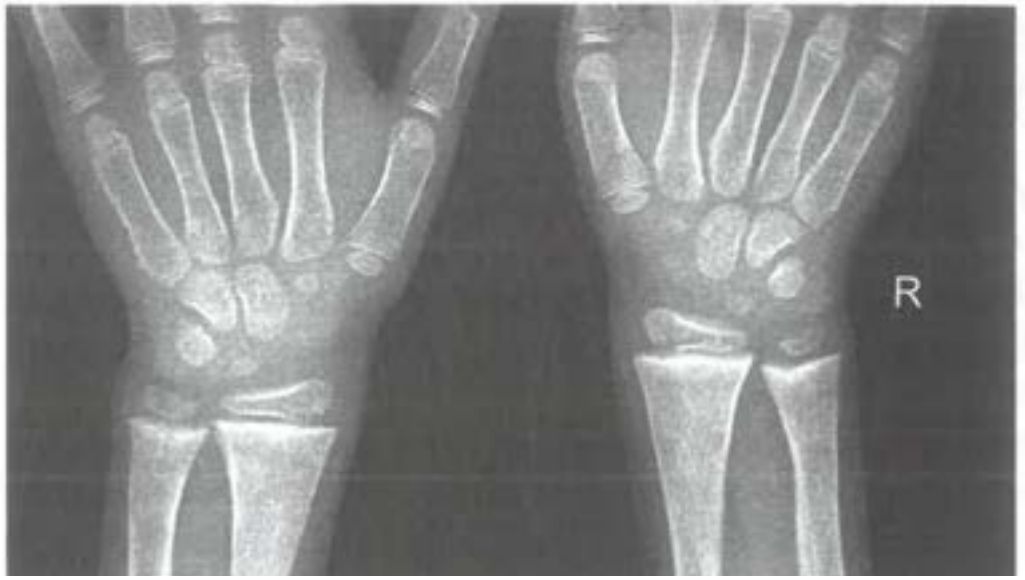
Fig. 6.10: Algorithm for evaluation of hypocalcemia. VDDR vitamin D dependent rickets

Table 6.9: Causes of hypocalcemia

Neonatal:	Early (within 48–72 hours after birth) or late (3–7 days after birth) neonatal hypocalcemia; prematurity; infant of diabetic mother; neonates fed high phosphate milk
Parathyroid:	Aplasia or hypoplasia of parathyroid glands, DiGeorge syndrome, idiopathic; pseudohypoparathyroidism; autoimmune parathyroiditis; activating mutations of calcium sensing receptor
Vitamin D:	Deficiency; resistance to vitamin D action; acquired or inherited disorders of vitamin D metabolism
Others:	Hypomagnesemia; hyperphosphatemia (excess intake, CKD); malabsorption; metabolic alkalosis; hypoproteinemia; acute pancreatitis
Drugs:	Prolonged therapy with frusemide, corticosteroids or phenytoin







Stress xx

RICKETS

while metaphyseal line

Healing rickets

earliest :

Table 8.4: Treatment guidelines for nutritional rickets

Age	*Daily dose of vitamin D_3 for 12 wks*[a]	*Alternative intermittent dose regimen*[b]	*Daily calcium supplementation*[c]	*Daily maintenance dose*[d]
<6 months	2000 IU	Not recommended	30–75 mg/kg/day	400 IU
6–12 months	2000 IU	Equivalent of 2000 IU/day may be given on a weekly or monthly basis	30–75 mg/kg/day	400 IU
>12 months	3000 IU	60,000 IU every 2 weeks for 5 doses	30–75 mg/kg/day (up to 500 mg)	600 IU

Reassess after 12 weeks

Table 6.10: Causes of hypercalcemia

Neonates

- Neonatal primary hyperparathyroidism (HPT; nonsyndromic or syndromic), secondary HPT
- Familial hypocalciuric hypercalcemia
- Excessive supplementation of calcium
- William syndrome, Down syndrome, hypophosphatasia, idiopathic infantile hypercalcemia

Older children

- HPT (parathyroid adenoma, autosomal dominant hereditary HPT, multiple endocrine neoplasia type 1; tertiary HPT in CKD or during therapy for hypophosphatemic rickets).
- *Malignancies:* Non-Hodgkin or Hodgkin lymphoma, Ewing sarcoma, neuroblastoma, Langerhans cell histiocytosis, rhabdomyosarcoma, acute leukemia.
- *Granulomatous disease:* Sarcoidosis, tuberculosis, polyangiitis with granulomatosis.

Others: Vitamin D or A intoxication; thiazide diuretics, milk-alkali syndrome; dietary phosphate deficiency; subcutaneous fat necrosis; thyrotoxicosis; retinoic acid therapy, prolonged immobilization, Jansen metaphyseal dysplasia.

Corrected calcium = [4 – plasma albumin in g/dL] × 0.8 + measured serum calcium

A child with SAM may be considered to have completed treatment when:

- There is no edema for at least 2 weeks, plus
- Weight-for-height (or length) reaches –2 SDS or higher on WHO growth standard or mid-upper-arm circumference is more than 12.5 cm

Table 7.15: Norms for supplementary nutrition in ICDS

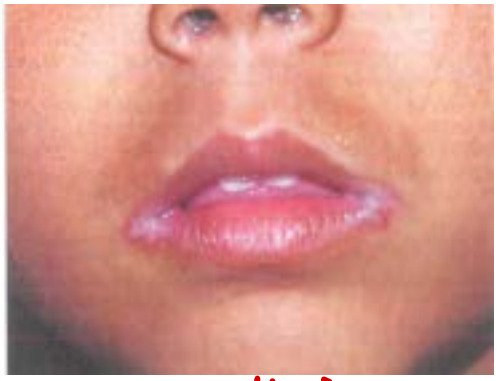
Beneficiaries	*Energy (kcal)*	*Protein (g)*
Children (6 to 72 months)	500	12–15
Severely malnourished children (SAM) (6 to 72 months)	800	20–25
Pregnant women and lactating mothers	600	18–20

Source: http://icds-wcd.nic.in/icds/icds.aspx

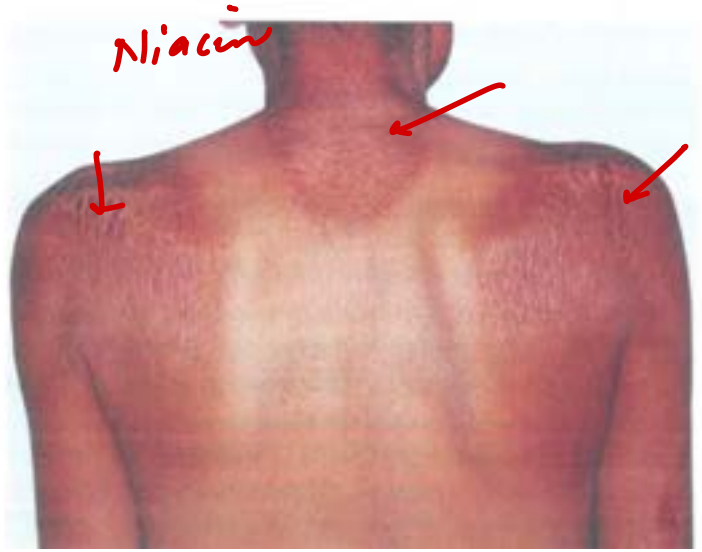
Table 8.1: WHO classification of xerophthalmia

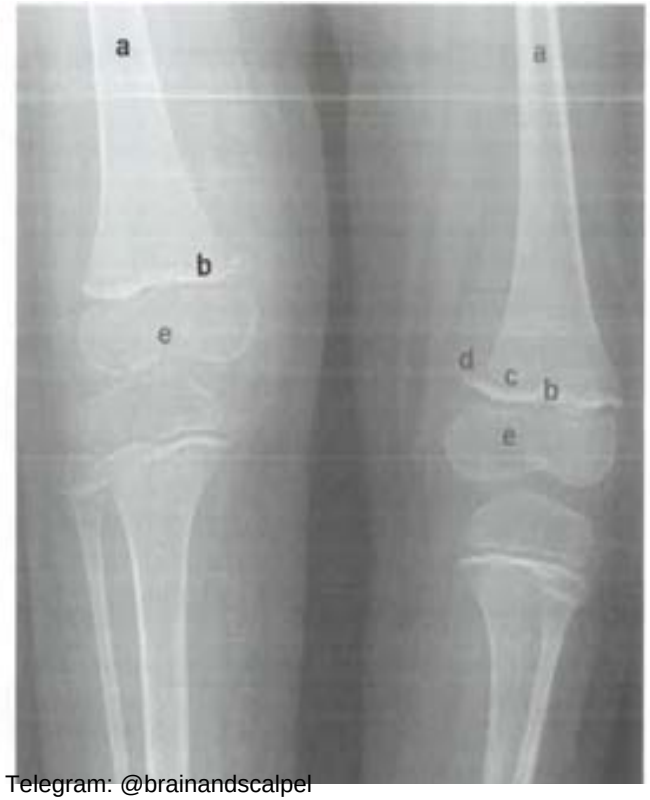
Primary signs	*Secondary signs*
X1A Conjunctival xerosis	XN. Night blindness
X1B Bitot's spots	XF. Fundal changes
X2 Corneal xerosis	XS. Corneal scarring
X3A Corneal ulceration (<1/3 of cornea)	
X3B Corneal ulceration (>1/3 of cornea)	

- earliest sign

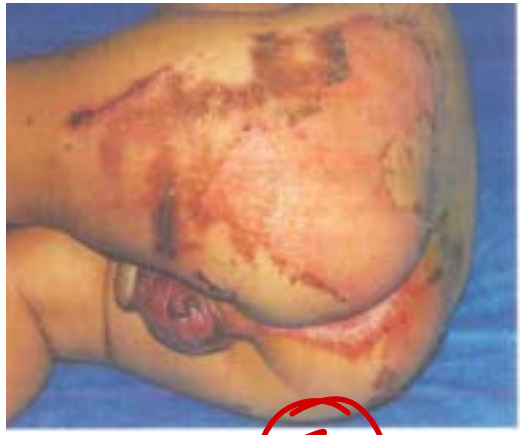


Riboflavin B2

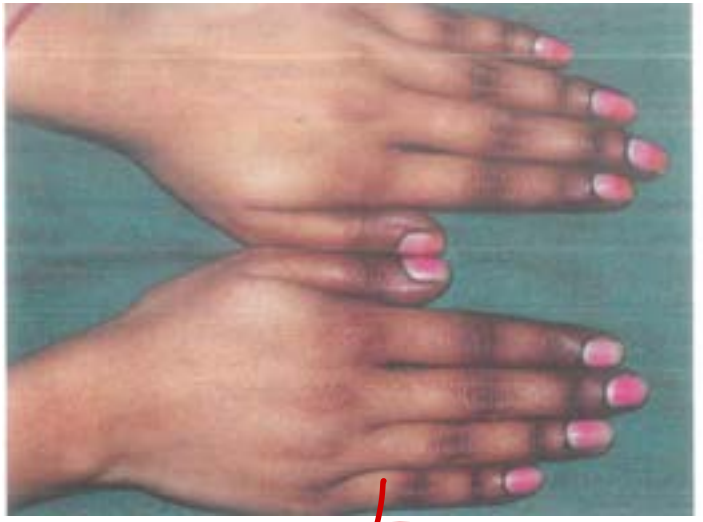




Scurvy
a - pencil thin cortex
b - Frenkel
c - Trummerfield
d - Pelkan spur
e - Wimberger



Zn



B12

Acrodermatitis enteropathica is an autosomal recessive disorder of severe zinc deficiency, caused by impaired intestinal absorption due to defect in intestinal zinc transporter protein, ZIP4. It presents in early infancy, with vesicobullous, dry, scaly or eczematous skin lesions chiefly in the periorificial (around the mouth and perineum), buttocks and acral areas (Fig. 8.11). Alopecia

SLC39A4

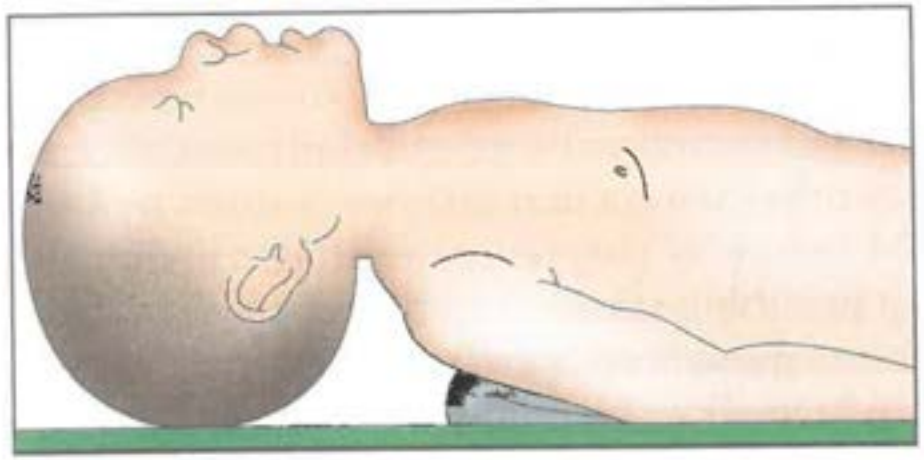


Fig. 9.4: Rolled towel under the shoulders

The indications of ET intubation during resuscitation are: (i) If the neonate's heart rate is less than 100 bpm despite 30 seconds of effective PPV, (ii) when prolonged BMV is required, (iii) when BMV is ineffective, (iv) when chest compression is needed, and (v) when a diaphragmatic hernia

Table 9.3: Ventilation corrective steps (MR SOPA)

Action	*Condition*
Inadequate seal	Re-apply **m**ask
Blocked airway	**R**eposition the infant's head
Blocked airway	Clear **s**ecretions by suction
Blocked airway	Ventilate with mouth slightly **o**pen
Inadequate pressure	Increase **p**ressure slightly
Consider **a**lternate airway	Blocked **a**irway (endotracheal tube)

For suctioning, the catheter size should be 12 or 14 Fr. Keep the suction pressure around 80 mm Hg (100 cm H_2O) and no more than 100 mm Hg (130 cm H_2O). Do not insert the catheter too deep in the mouth or nose as the stimulation of the posterior pharynx can cause vagal response resulting in bradycardia or apnea.

M → N

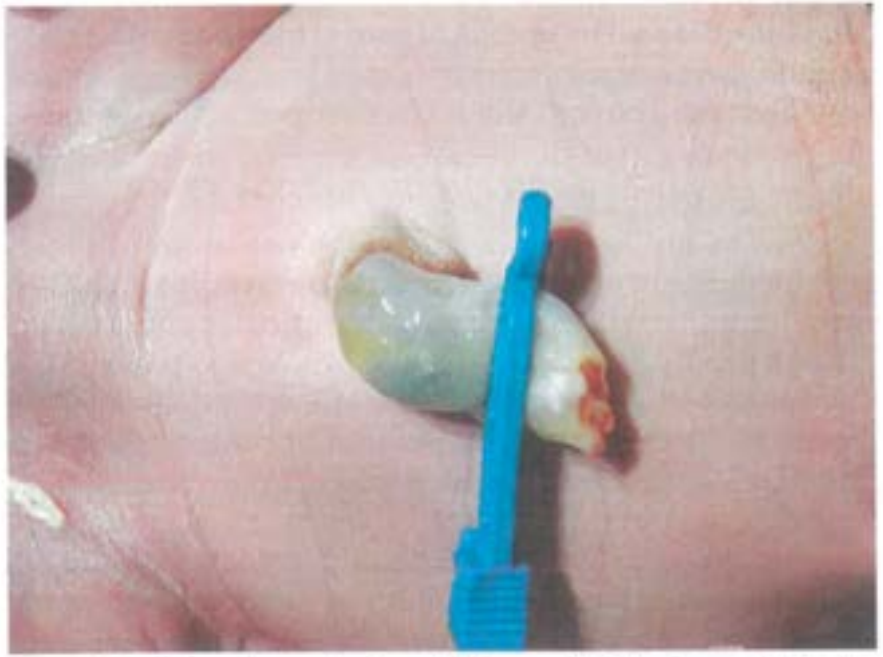


Fig. 9.13: Correct application of the umbilical clamp. Note the clamp should leave 1.2 cm of the cord length on each side of it

- Difficulty in feeding or poor feeding
- Convulsions
- Lethargy (movement only when stimulated)
- Fast breathing (RR >60/min)
- Severe chest indrawing
- Temperature of more than 37.5°C or below 35.5°C
- Yellow soles (severe hyperbilirubinemia)

Fig. 9.15: Danger signs in newborns

Adequate attachment:
Mouth wide open
Only small part upper areola visible
Lower lip everted
Chin touch mother's breast

bf

Position of the baby

i. Baby's *whole body is supported*, not just the neck or shoulders
ii. Baby's *head and body are in one line* without any twist in the neck
iii. Baby's *body turned towards the mother* (abdomens of the neonate and the mother touching each other)
iv. Baby's *nose is at the level of the nipple.*

v. *Foremilk* is the milk secreted at the start of a feed. Watery and high in proteins, sugar, vitamins, and minerals, it quenches the baby's thirst.
vi. *Hindmilk* comes later and is richer in fat, providing more energy and a sense of satiety. For optimum growth, the neonate needs fore- and hindmilk. Therefore, the neonate should empty the breast before switching to the other.

paladai or gastric tube. EBM can be stored for 6–8 hours at room temperature, 24 hours in a refrigerator, and 3 to 6 months in a freezer at –20°C.

- No breastfeeding problems and the mother can breastfeed the neonate well. The adequacy of feeds can be determined by:
  - Passage of urine 6 to 8 times every 24-hour
  - Neonate sleeping well for 2–3 hours after feeds.

Table 9.28: Levene classification for hypoxic-ischemic encephalopathy

Samat - Samat

Feature	*Mild*	*Moderate*	*Severe*
Consciousness	Irritability	Lethargy	Comatose
Tone	Hypotonia	Marked hypotonia	Severe hypotonia
Seizures	No	Yes	Prolonged
Sucking/respiration	Poor suck	Unable to suck	Unable to sustain spontaneous respiration

Modified from: Levene MI.The asphyxiated newborn infant. In: Levene MI, Lilford RJ, eds. Fetal and Neonatal Neurology and Neurosurgery. Churchill Livingstone, Edinburgh 1995;405–26.

The following features differentiate jitteriness from seizures are:

1. Absence of eye deviation or fixed gaze, heart rate changes. → jitteriness
2. Rhythmic tremors with equal to and fro movements. The frequency is 7 to 10 per second—no fast and slow components. In contrast, a clonic seizure is slower (1–2 per second), and the to and fro movements have rapid and slow components.
3. The tremors are usually stimulus sensitive, precipitated by hunger, crying, or loud noise, and stopped by gentle restraint. → jitteriness

The screen has an excellent negative predictive value for ruling out CCHD.

Hearing Screen

Normal hearing is critical for normal speech development. Routine screening can help early detection of hearing loss and facilitate the timely provision of hearing aid.

Hearing screening is performed at discharge/after 24 hours in neonates of 34 weeks or greater gestation. Perform screening in neonates lesser than 34 weeks once they complete 34 weeks of gestation. The screening tool could be either otoacoustic emissions (OAE) or automated auditory brainstem responses (AABR) for normal neonates. However, both OAE and AABR should be used for high-risk neonates (Fig. 9.81). For those who fail the first screening, a repeat after 48 to 72 hours reduces the false positivity rate (two-step screening). Finally, a diagnostic auditory brainstem response (ABR) is performed to confirm the hearing loss. Such neonates need a hearing aid or cochlear implant by 6 months of age and speech rehabilitation. Any neonate with a normal hearing screen should be re-screened, if they develop any illness that can impair hearing, such as meningitis, if there is any parental concern for hearing, or if there is any red flag sign of normal speech development.

OAE → abN → Repeat OAE → abN → BERA

34w
6mon
9mon

max-6mm → hearing aid ↓x

CI min age : 9mm

Pediatric Cochlear Implantation

Cochlear implant directly stimulates the residual cochlear nerve cells in the spiral ganglion (cochlea). The US FDA approved pediatric cochlear implantation for children with bilateral severe to profound sensorineural hearing loss (≥70 dB hearing loss) with unsatisfactory benefit from hearing aid use for at least 3–6 months. As early introduction of sound is crucial to develop processes for sound awareness and speech development in the auditory cortex, and hence hearing should be aided as early as possible. The minimum age for cochlear implant has been reduced to 9 months by US FDA. Evaluation before surgery includes computed tomography and magnetic resonance imaging to assess anatomy of the inner ear and to confirm the presence of cochlear nerve. Multielectrode implants that provide information across various frequencies are positioned sequentially along the cochlea to allow sound to be coded and transmitted for the entire sound spectrum (Fig. 14.8). The implant risks damage with strong magnetic fields and caution is advised with MR scanning. Most current implants are safe for MR scanners up to 3.0 Tesla.

Common indications

1. Respiratory distress in preterm neonates due to respiratory distress syndrome (RDS), transient tachypnea, and pneumonia
2. Apnea of prematurity despite methylxanthine therapy
3. Following extubation in preterm VLBW infants
4. Airway instability such as laryngomalacia, tracheomalacia and bronchomalacia

Contraindications to CPAP

- Severe cardiovascular instability
- Poor respiratory drive
- Progressive respiratory failure ($PaCO_2$ levels >60 mm Hg and/or PaO_2 <50 mm Hg)
- Congenital malformations, e.g. tracheoesophageal fistula
- Congenital diaphragmatic hernia

How to set up

- *Initiation:* CPAP 5 cm H_2O, FiO_2 titrate to maintain SpO_2 90–95%

Surfactant production starts around 20 weeks of life and peaks at 35 weeks gestation. Therefore, any neonate less than 35 weeks is prone to develop RDS. The primary abnormality is surfactant deficiency. Surfactant, produced

SRT is indicated in preterm neonates with moderate to severe RDS. SRT can be given as rescue therapy to treat established RDS or prophylactic therapy in neonates less than 28 weeks. SRT has a synergistic action with CPAP. A preterm neonate with respiratory distress is treated initially with CPAP. The SRT is administered, if the RDS is severe enough to require FiO_2 of 40% or greater while on CPAP.

SRT decreases the duration and level of respiratory support in neonates and improves outcomes. Traditionally, the neonates were intubated, given surfactant in four or five boluses through an endotracheal tube, and later extubated after a few hours to days. Many neonates can now be INtubated, given SURfactant, and rapidly Extubated (InSurE approach) to CPAP, avoiding mechanical ventilation. Lately, giving surfactant using a thin catheter inserted in the trachea under vision has obviated the need for intubation, thus avoiding complications of intubation.

LISA

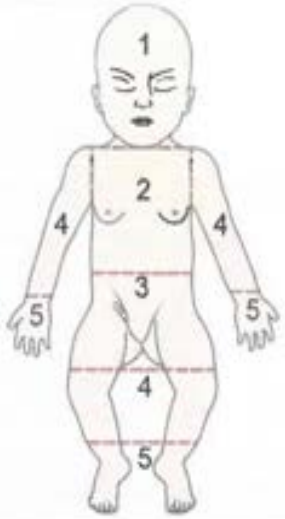
Table 9.4: Appropriate endotracheal tube size

Inner diameter of tube (mm)	*Weight (g)*	*Gestational age (weeks)*
2.5	<1000	<28
3.0	1000–2000	28–34
3.5	2000–3000	34–38
4.0	>3000	>38

$$\text{Tracheal tube size (in mm)} = \frac{\text{(Age in years)}}{4} + 4$$

A neonatal laryngoscope with straight blades of sizes 0′ (for preterm neonates) and '1' (for term neonates) is required for intubation. Before intubating, the appropriate blade is attached to the laryngoscope handle, and the light is turned on.

Visual assessment of jaundice (Modified Kramer Rule)



Kramer zones	Approximate TSB level
1. Face and neck	5–7 mg/dL
2. Chest and upper abdomen	7–9 mg/dL
3. Lower abdomen and thighs	9–11 mg/dL
4. Legs and arms/forearms	11–13 mg/dL
5. Palms and soles	13–15 mg/dL

Fig. 9.67: Dermal zones for estimation of total serum bilirubin levels

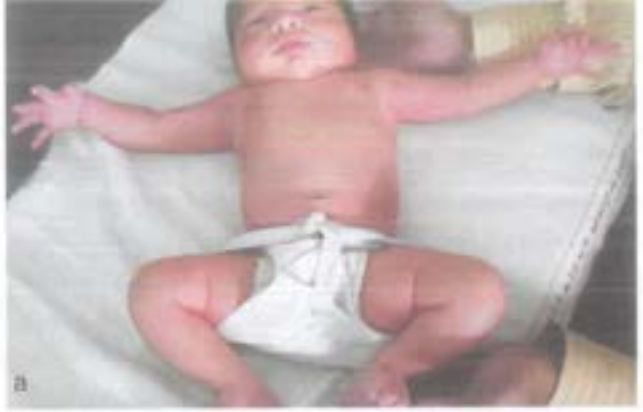
Breastfeeding Jaundice (BFJ)

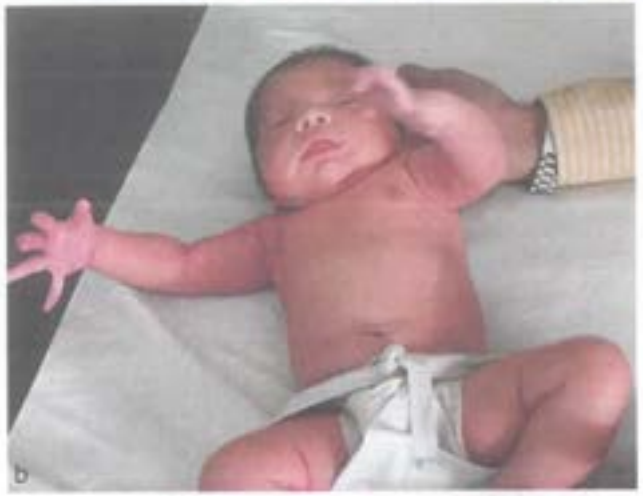
Many neonates have higher TSB values due to inadequate breastfeeding. Such neonates have excess weight loss, and jaundice appears in the later part of the first week and can persist into the third and fourth week of life. This excess jaundice results from inadequate breast milk intake that promotes enterohepatic circulation. The BFJ is, therefore, more aptly termed "suboptimal intake hyperbilirubinemia." Maternal conditions, such as improper breastfeeding technique, breast engorgement, cracked or sore nipples, illness or fatigue, and neonatal factors, such as late preterm gestation (34 to 36 weeks), and ineffective sucking, can cause ineffective breastfeeding and, consequently, BFJ. Ensuring optimum breastfeeding would help decrease this kind of jaundice.

Breast Milk Jaundice (BMJ)

Approximately 2–4% of exclusively-breastfed term neonates have TSB over 10 mg/dL beyond the third-fourth week of life. Breast milk jaundice (BMJ) is possible in neonates if the jaundice is unconjugated type (not staining nappies); and other causes for prolongation hyperbilirubinemia such as inadequate feeding, continuing hemolysis, extravasated blood, G6PD deficiency, and hypothyroidism have been ruled out.

Breast milk contains high concentrations of beta-glucuronidase, which deconjugates bilirubin excreted in the intestine after conjugation by the liver. Most such neonates would not have a dangerous level of TSB and do not require any treatment. The mothers would be able to continue breastfeeding their neonates. There is no need to stop breastfeeding for diagnosis or treatment of BMJ.





Primary neonatal reflexes: To elicit the Moro reflex, raise the baby's head slightly and drop it suddenly while the hand still supports the neonate. The response consists of the opening of the hands and extension and abduction of the upper extremities, followed by anterior flexion (embracing) of the upper extremities with an audible cry (Fig. 9.33a and b). The hand opening is present by 28 weeks, extension and abduction by 32 weeks, and anterior flexion by 37 weeks. Moro reflex disappears by 3–6 months in normal infants. The most common cause of depressed or absent Moro reflex is a generalized disturbance of the central nervous system. An asymmetrical Moro reflex indicates root plexus injury

MORO'S :

Congenital Rubella

Transmissibility is highest in the first trimester, and so is the rate of fetal disease (90% at <11 weeks). The fetus is completely spared, if infection occurs beyond 16 weeks. The classical triad of congenital rubella syndrome consists of deafness, cataract and congenital heart disease (commonly patent ductus arteriosus). Expanded rubella syndrome comprises delayed manifestations such as diabetes mellitus and renal disease have also been described. Diagnosis is by demonstration of positive rubella IgM in cord or neonatal blood. No treatment exists. A unequivocal diagnosis of rubella in the first trimester of pregnancy is an indication for maternal termination of pregnancy. Preconceptual counselling should include testing women for rubella IgG and vaccinating them with MR or MMR if IgG is negative.

Congenital/Perinatal CMV

Congenital CMV is reported to be the commonest congenital infection in developed countries. The rate of transmission of CMV from mother to baby depends on whether it is primary maternal infection or reactivation/reinfection in the mother. The overall transmission rate with primary infection is 30% and 10% of all babies infected are symptomatic. The transmission risk with reactivation or reinfection is only 1% and only 5–10% of infected babies are symptomatic. But since the total numbers of reactivations and reinfections are higher than primary infections, these contribute to half the burden of congenital CMV. In India where 99% of the mothers are CMV IgG positive, congenital infections are due to reactivations/reinfections. CMV transmission and fetal disease occur throughout pregnancy. Congenital CMV can affect all organ systems; periventricular calcification is characteristic of CMV (Fig. 11.33). Babies who are asymptomatic at birth can manifest later with sensorineural deafness. The diagnosis of congenital CMV can be confirmed by a positive IgM or urine CMV PCR in the first 2 to 3 weeks of life. The sensitivity of IgM is low and a negative IgM does not rule out CMV. A positive CMV IgM/urine CMV PCR after the first 2–3 weeks of life can also occur due to postnatal transmission and is not specific for diagnosis. Antiviral treatment with ganciclovir is indicated in patients with neurologic involvement, progressive disease and deafness. The treatment duration is 6 weeks and should be followed with oral valganciclovir for up to 6 months.

Table 11.5: WHO criteria for diagnosis of MIS-C

0–19-year-old child with fever >3 days

AND Two of the following

- Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet)
- Hypotension or shock
- Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP)
- Evidence of coagulopathy (PT, PTT, elevated d-dimers)
- Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)

AND

- Elevated ESR, C-reactive protein, or procalcitonin

AND

- No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes

AND

- Evidence of COVID-19 (RT-PCR, antigen test or serology positive) or likely contact with patients with COVID-19

QQ

Mx → IVIG / aspirin / steroid

Multisystem Inflamm Sx in Children

· COVID-19

- Kawasaki-like
- Toxic shock Sx like
- Febile inflamm like

Table 10.10: Vaccination beyond early childhood

Other at-risk groups	Adolescents	Healthcare workers	Pregnant women	Elderly (>50 years)	Comment
Diphtheria	Yes	Yes	Yes	Yes	*If previously unimmunized:* One dose of Tdap, followed ≥4 weeks later by two doses of Td given 6–12 months apart; then one dose of Td every 10 years (and one dose of Td during each pregnancy)
Tetanus	Yes	Yes	Yes	Yes	*If previously immunized:* One dose of Tdap, followed by Td every 10 years (and a dose of Td during each pregnancy)
Hepatitis B	Consider	Yes	Yes	No	*If previously unimmunized or lacking seroprotection*[1]: Three doses (20 µg or 1 mL each) at 0, 1 and 6 months; confirm seroprotection after 1–2 months
Pneumococcal	No	Yes	No	Yes	One dose of PCV13, followed ≥8 weeks later by one dose of PPSV23; repeat PPSV23 once after ≥5 years if first dose of PPSV23 was given at <65-yr-old
Influenza	No	Yes	Yes	Yes	One dose of the inactivated vaccine annually (only once in pregnant women)
MMR	Consider	Yes	Postpartum	No	*If previously unimmunized or lacking seroprotection:* Two doses ≥4 weeks apart
Varicella	Consider	Yes	No	No	*If previously unimmunized:* Two doses of varicella vaccine ≥4 weeks apart
Shingles/zoster	No	No	No	Yes	Two doses of zoster vaccine 2–6 months apart
SARS-CoV-2	Yes	Yes	Yes	Yes	Two doses, followed by booster, as per national schedule for the specific vaccine
HPV	Yes	No	No	No	As per schedule
Specific risks (children or adults, including healthcare workers)					
Travel to endemic areas					Cholera, yellow fever, Japanese encephalitis and rabies
High risk of exposure to specific pathogens					Typhoid, polio, rabies and/or meningococcal vaccines

[1]An anti-HBs antibody titer of ≥10 mIU/mL is considered seroprotective

Table 10.11: Vaccination of previously unimmunized child

IAP

Visit	*At evaluation*	*After 1 month*	*After 2 months*	*After 6 months*
Age ≤7 years	BCG Oral poliovirus DTwP/DTaP Hepatitis B	Oral poliovirus DTwP/DTaP Hepatitis B	Oral poliovirus Measles-containing vaccine Typhoid	DTwP/DTaP Hepatitis B
Age >7 years	Tdap Hepatitis B	Td Hepatitis B	Measles-containing vaccine Typhoid	Td Hepatitis B

Td diphtheria pertussis with reduced content of diphtheria; DTaP diphtheria tetanus acellular pertussis; DTwP diphtheria tetanus whole cell pertussis; Tdap tetanus toxoid with reduced content of diphtheria and pertussis; BCG Bacillus Calmette-Guérin

Protective efficacy of a vaccine is its ability to protect against disease, asscssed as follows:

$$\text{Efficacy} = \frac{\text{Rate of disease in unvaccinated} - \text{Rate of disease in vaccinated persons}}{\text{Rate of disease in unvaccinated persons}} \times 100$$

Live viral vaccines (measles, rubella) and toxoids are more efficacious than BCG and killed bacterial vaccines.

Following chemotherapy, live vaccines are contraindicated, at least up to 6 months after the end of chemotherapy. Non-live vaccines are also best deferred until that time point, to provide sustained protection. All children should receive the inactivated influenza vaccine annually and complete immunization with hepatitis B vaccine, even during chemotherapy. Post-treatment immunization depends on the pre-chemotherapy immunization status.

Household contacts may transmit infection to immuno-compromised children. Hence, they should be immunized with live vaccines against common or serious pathogens in order to provide indirect protection to the index patient, e.g. varicella and MMR vaccines. However, household contacts should not receive those live vaccines in which the organism may be transmitted to the patient (e.g. oral poliovirus vaccine); they should instead receive an alternative killed vaccine, if feasible (e.g. IPV).

until after 4 weeks of stopping corticosteroid therapy. Live vaccines may be given, if corticosteroids are given for <14 days, in lower doses, on alternate days, or by inhaled, topical or intra-articular routes. Wherever possible, vaccination should be completed prior to initiation of chemotherapy, immunosuppressive drugs or radiation. Live vaccines are not given for 3 months after such treatment; inactivated vaccines during therapy might need to be repeated.

Box 10.10: Rotavirus Vaccines

Vaccine name	Rotavac	RotaTeq	Rotarix	Rotasiil
Name by type	Indian neonatal (116E); human bovine monovalent	Human bovine pentavalent (RV5)	Human monovalent (RV1)	Bovine pentavalent; thermostable
Number of strains	1	5	1	5
Schedule[1]				
National program	3 doses at 6, 10 and 14 weeks	Not included	Not included	Not included
IAP 2021	3 doses at 6, 10 and 14 weeks	3 doses at 6, 10 and 14 weeks	2 doses at 6 and 10, or 10 and 14, weeks[2]	3 doses at 6, 10 and 14 weeks
Dose, route	5 drops, oral	2 mL (liquid), oral	1 mL (lyophilized); 1.5 mL (liquid), oral	2.5 mL, oral
Catch up	National program: Up to 1 year of age IAP 2021: Give the first dose before 16 weeks of age and complete the schedule by 32 weeks of age			
Adverse reactions	Fever, diarrhea, vomiting, cough, rhinitis, rash, irritability; intussusception is rare			
Contraindication	Past history of intussusception; severe immunodeficiency			
Precaution	Postpone vaccination during ongoing diarrhea or moderate illness			
Storage	2–8°C (except Rotasiil, which can be stored at <25°C); protect from heat; use within 4 hours of reconstitution or opening			

Box 10.9: Pneumococcal Vaccines

Type	Pneumococcal conjugate (PCV13: Prevenar 13®; PCV10: Synflorix®, Pneumosil®)	Pneumococcal polysaccharide (PPSV23: Pneumovax®)
Dose, route	0.5 mL; intramuscular	0.5 mL; intramuscular or subcutaneous
Site	Anterolateral thigh or deltoid	Deltoid
Schedule		
National program	Three doses at 6 weeks, 14 weeks and 9 months	Not recommended
IAP 2021	Three doses at ≥6 weeks age; given ≥4 weeks apart; one booster at 15–18 months[1]	Only in high-risk category[2]: One dose ≥8 weeks after primary course with conjugate vaccine; repeat once after 5 years, if risk persists[3]
Catch up (IAP)	At 7–11 months: Two doses ≥4 weeks apart; one booster at 15–18 months[1] At 12–23 months: Two doses ≥8 weeks apart[1] At 24–59 months: One dose[4] ≥60 months: One dose[4], if high risk[2]	Use only if high risk[2] and ≥2 years old
Adverse reactions	Fever, local pain, soreness, malaise	Local pain, redness, soreness (30–50%)
Contraindication	Anaphylaxis after previous dose	Anaphylaxis after previous dose
Storage	2–8°C; do not freeze	2–8°C

Box 10.14: Varicella Vaccine

Dose, route	0.5 mL, subcutaneously
Site	Anterolateral thigh or upper arm
Schedule	
National program	Not included
IAP 2021	All children, especially high-risk categories; following exposure to varicella; and adolescents/adults without evidence of immunity[1]: Two doses 3–6 months apart, with first given at 15–18 months (minimum 12 months)[2]
Catch up	Complete two doses ≥3 months apart (≥4 weeks apart, if ≥13-yr-old), if lacking evidence of immunity[1]
Adverse reactions	Fever, rash, local pain or redness; mild rash after 2–3 weeks (5%)
Contraindications	Anaphylaxis after previous dose; immunodeficiency; active leukemia or lymphoma; during immunosuppressive therapy
Precautions	Moderate to severe illness; thrombocytopenia; recent receipt of blood products or immunoglobulins; therapy with aspirin
Storage	Freeze dried, lyophilized; 2–8°C; protect from light; use within 30 minutes of reconstitution

and in adolescents (≥12 years)

Box 10.13: Typhoid Vaccines

	Typhoid conjugate (PedaTyph, Typbar-TCV, TyphiBEV)	**Vi capsular polysaccharide (Typbar, Vactyph, Biovac)**	**Live attenuated Ty21a (no Indian brands)**
Dose; route	0.5 mL (25 µg[1]); IM	0.5 mL (25 µg); SC or IM	Oral; capsule
Site	Anterolateral thigh or deltoid	Anterolateral thigh or deltoid	Oral
Schedule			
National program	Not included	Not included	Not included
IAP 2021	(Preferred) One dose at ≥6 months of age	(If conjugate vaccine not available) One dose at ≥2 years	Not available; 3 doses at >5 years (based on ability to swallow)
Booster doses	No[2]	Every 3 years	Every 3 years
Catch up	One dose, up to 18 years	One dose at ≥2 years	Any age
Adverse reactions	Local pain, swelling, redness; fever	Local pain, swelling, redness; fever	Abdominal discomfort, fever
Contraindication	Anaphylaxis after previous dose	Anaphylaxis after previous dose	Immunodeficiency
Storage	2–8°C	2–8°C; do not freeze	2–8°C

Box 10.19: Yellow Fever Vaccine

Type	Live attenuated (17D-204)
Dose, route	0.5 mL, subcutaneous
Site	Anterolateral thigh or upper arm
Schedule	
National program	Not included
IAP 2021	Single dose ≥10 days before travel to endemic areas; revaccinate after 10 years
Indications	Residence in, or travel to, endemic area; age >9 months
Adverse reactions	Mild (20–30%): Fever, headache and myalgia
Contraindication	Age <6 months; symptomatic HIV or CD4 <15% or <200/mm³; primary or secondary immunodeficiency; radiation; malignancy; organ transplantation; chemotherapy; anaphylaxis after a previous dose; allergy to a vaccine component
Precaution	Age 6–9 months or >60 years; pregnancy and lactation; asymptomatic HIV or CD4 ≥15% or 200–499/mm³; family history of vaccine-associated adverse effects
Storage	2–8°C; use within 30 minutes of reconstitution

Box 10.15: Influenza Vaccines

	Inactivated vaccine	**Live attenuated vaccine**
Dose, route	0.5 mL (15 µg); intramuscular	0.25 mL in each nostril
Site	Anterolateral thigh or upper arm	Intranasal using *accuspray* device
Schedule		
National program	Not included	Not included
IAP 2021	All children >6 months to 5-yr-old; children >5-yr-old with high-risk category[1] First time vaccination: 6 months to 9-yr-old: Two doses ≥4 weeks apart[2] ≥9-yr-old: Single dose Subsequently: Annual revaccination with one dose, preferably before rainy season[3]	All healthy children 2–18 years old First time vaccination: 2–9 years old: Two doses ≥4 weeks apart[2] ≥9 years old: Single dose Subsequently: Annual revaccination with one dose, preferably before rainy season[3]
Adverse reactions	Mild (10–35%): local pain, fever, nausea; severe (rare): anaphylaxis; Guillain-Barre syndrome[4]	Runny nose, headache, wheeze, myalgia, fever, sore throat, vomiting
Contraindications, precautions	Anaphylaxis after a previous dose, intake of egg or chicken, or thiomerosal; use cautiously in children with suspected chicken or egg allergy	Severe allergy after any influenza vaccine; high risk categories[1]
Storage	2–8°C; do not freeze	2–8°C; do not freeze

Box 10.12: Japanese B Encephalitis Vaccine

	Live attenuated cell culture derived SA-14-14-2	Inactivated cell culture derived SA-14-14-2 [IC51]	Inactivated Vero cell culture derived Kolar [82156XY]
Dose, route	0.5 mL; subcutaneous	1–3 yr: 0.25 mL; ≥3 yr: 0.5 mL; intramuscular	0.5 mL; intramuscular
Site	Anterolateral thigh, upper arm	Anterolateral thigh, upper arm	Anterolateral thigh, upper arm
Schedule			
National program	Only endemic areas; two doses at 9 and 16–18 months; also adults	Not used	Not used
IAP 2021	Recommended in endemic areas; not available in the private sector	Recommended in endemic areas; ≥1 yr-old; two doses ≥4 weeks apart	Recommended in endemic areas; ≥1 yr-old; two doses ≥4 weeks apart; timing of booster not determined
Catch up	Up to 15 years; adults	Any age	Any age
Adverse reactions	Fever, malaise; hypersensitivity (rare)	Less common: Fever, pain, malaise	Uncommon

The attributes of the most commonly used vaccines are compared in Table 10.5. The three vaccines that have been licensed for use in India's national program are Covishield (Serum Institute of India), Covaxin (Bharat Biotech) and CorBEvax (Biological E), sanctioned for use in patients ≥18-yr-old, ≥15-yr-old, and 12–14-yr-old, respectively **(Box 10.20)**. Other vaccines authorized in India for emergency use (EUA) in children ≥12-yr-old include ZyCov-D (Zydus Cadila) and Covovax (Serum Institute of India). Vaccines commonly used in children elsewhere, but not yet licensed or marketed in India, include BNT162b2 (Pfizer), mRNA-1273 (Moderna), and Gam-COVID-Vac (Sputnik). Recently, the intranasal vaccine iNCOVACC (Bharat Biotech) was approved in India for >18-yr-olds.

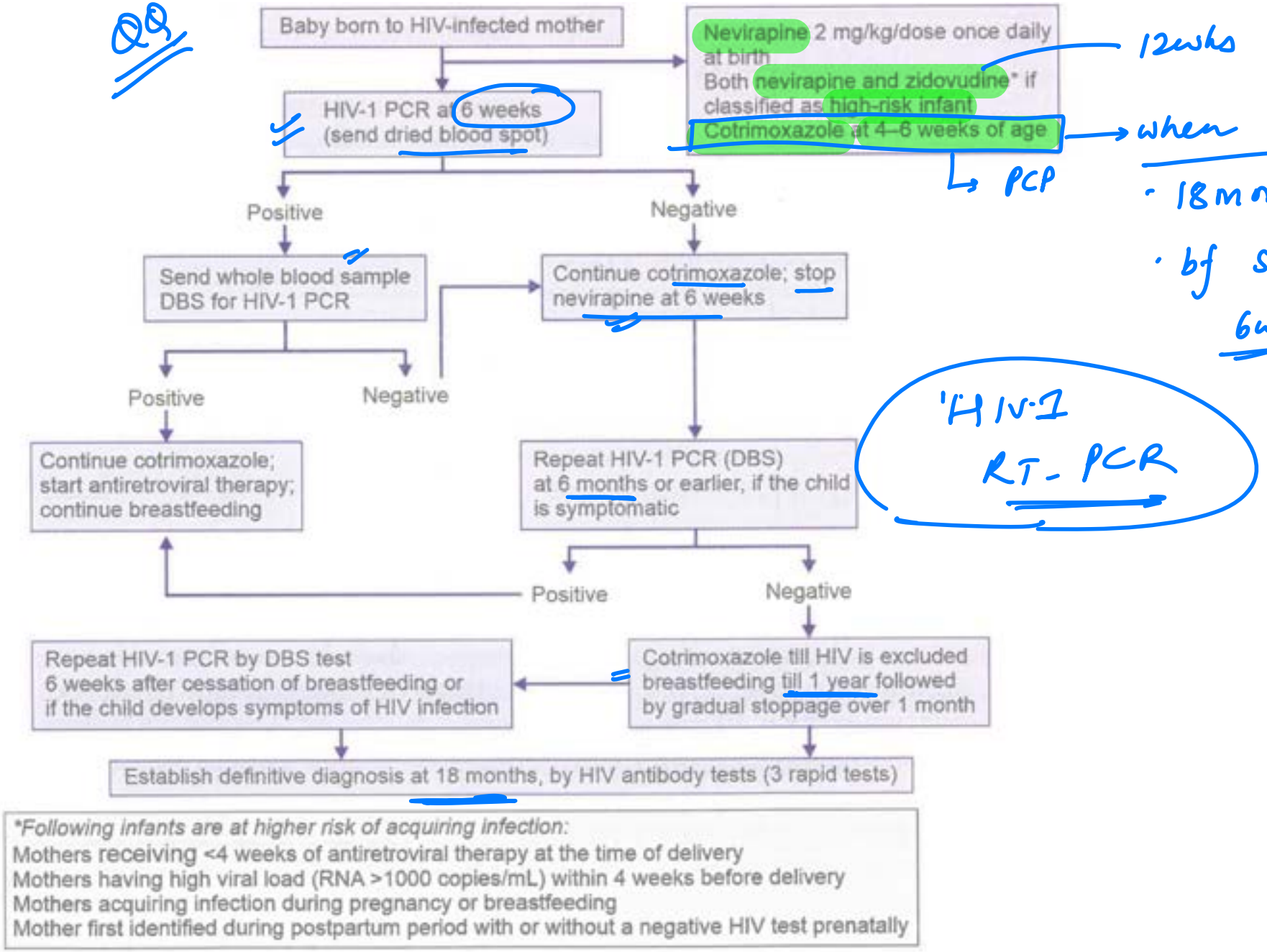


Fig. 11.18: HIV diagnosis in children <18 months with HIV-total nucleic acid-PCR. DBS dried blood spot

Table 11.9: First-line antiretroviral regimens for infants and children with HIV infection

	Regimen
Age less than 6 years, and body weight less than 20 kg	Abacavir + Lamivudine + Lopinavir/ritonavir (ALL+LPV/r)
Age between 6 and 10 years, and body weight between 20 kg and 30 kg	Abacavir + Lamivudine + Dolutegravir (ALD)
Age more than 10 years, and body weight more than 30 kg	Tenofovir + Lamivudine + Dolutegravir (TLD)

Note:

- Any infant or child initiated on any regimen must be based on body weight; refer to NACO guidelines for weight-band dosage charts to determine the appropriate doses.
- On every visit, check body weight of the infant/child before writing the prescription. Even though the drug regimen remains the same, drug dosages have to be modified according to change in body weight.

Intrapartum interventions: Artificial rupture of membranes should be avoided, unless medically indicated. Delivery should be by elective cesarean section at 38 weeks before onset of labor and rupture of membranes. Procedures increasing exposure of child to maternal blood should be avoided.

Breastfeeding: The risk of HIV infection via breastfeeding is highest in the early months of breastfeeding. Factors that increase likelihood of transmission include detectable levels of HIV in breast milk, presence of mastitis and low maternal CD4+ T cell count. Exclusive breastfeeding has been reported to carry a lower risk of HIV transmission than mixed feeding and risk of mortality in non-breastfed infants in resource-limited settings is increased. Currently, exclusive breastfeeding is recommended during the first months of life. WHO recommends that the transition between exclusive breastfeeding and early cessation of breastfeeding should be gradual and not an "early and abrupt cessation".

OBG → NVD

Till 1 yr exclusive BF

6mon - complement

Table 15.9: Stepwise treatment of asthma

	Symptoms	*Treatment*	
Step 4: Severe persistent	Continuous Limited physical activity	High dose inhaled steroids + long-acting beta agonists	Refer to specialist for consideration of omalizumab and tiotropium
Step 3: Moderate persistent	Daily use β_2 agonist; daily episodes affect activity	Low dose inhaled steroids + long-acting beta agonists or medium dose inhaled steroids	
Step 2: Mild persistent	Low grade symptoms twice a month, or once night-time awakening per month	Low dose inhaled corticosteroids with short-acting beta agonists SOS	
Step 1: Intermittent	Infrequent Asymptomatic and normal PEFR between attack	Short-acting beta-2 agonists (SABA) along with inhaled steroids SOS	

Table 15.6: Assessment of symptom control of asthma

Characteristics	*Controlled (all of the following)*	*Partially controlled (any measure present in any week)*	*Uncontrolled*
Daytime symptoms	None (twice a week or less)	More than twice per week	Three or more features of partly controlled asthma present in any week
Limitation of activity	None	Any	
Nocturnal symptoms, awakening	None	Any	
Need for reliever or rescue drugs	None (less than twice a week)	More than twice per week	

Table 15.11: Common clinical features of cystic fibrosis (%)

0–2 years	
Meconium ileus ✓	10–15
Obstructive jaundice ✓	
Hypoproteinemia, anemia	
Bleeding diathesis	
Heat prostration, hyponatremia	
Undernutrition	
Steatorrhea	85
Rectal prolapse	20
Bronchitis, bronchiolitis	
Staphylococcal pneumonia	
2–12 years	
Malabsorption	85
Recurrent pneumonia	60
Nasal polyposis	6–36
Intussusception	1–5
>13 years	
Chronic pulmonary disease	70
Clubbing	
Abnormal glucose tolerance	20–30
Diabetes mellitus	7
Chronic intestinal obstruction	10–20
Focal biliary cirrhosis	
Portal hypertension	25
Gallstones	4–14
Azoospermia	98

QQ

bile strictures xx

GBS pharyngitis

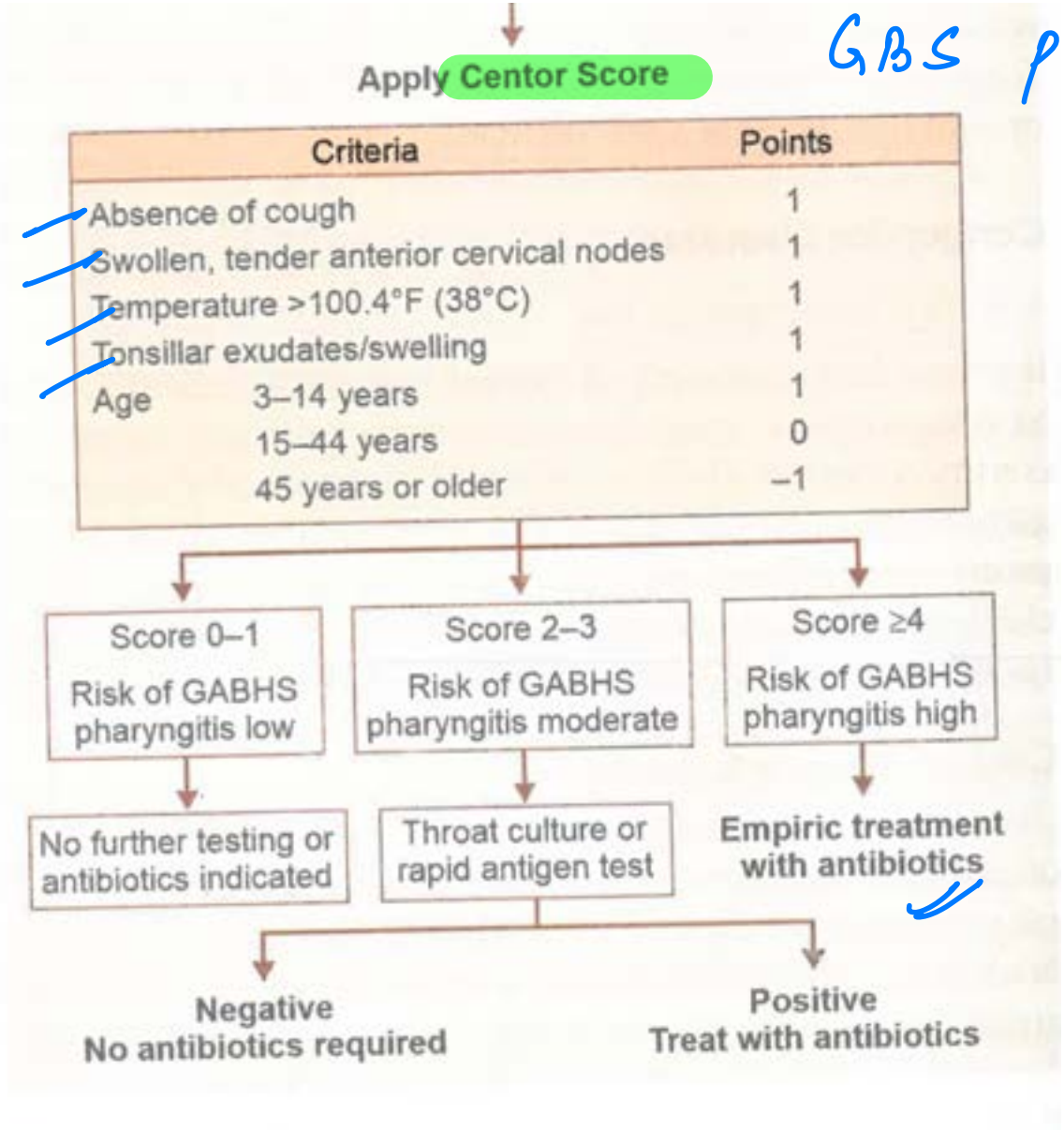


Table 17.6: Indications for kidney biopsy in acute glomerulonephritis (GN)

Systemic features

- Fever, rash, joint pain, pulmonary symptoms, heart disease; history of recurrences
- Absence of serologic evidence of streptococcal infection; normal C3 in acute stage of illness
- Features of both GN and nephrotic syndrome
- High blood urea and creatinine, or anuria requiring dialysis

Delayed resolution

- Oliguria, hypertension, azotemia beyond 7–10 days
- Gross hematuria persisting beyond 3–4 weeks
- Nephrotic range proteinuria beyond 2 weeks
- Low C3 levels beyond 12 weeks

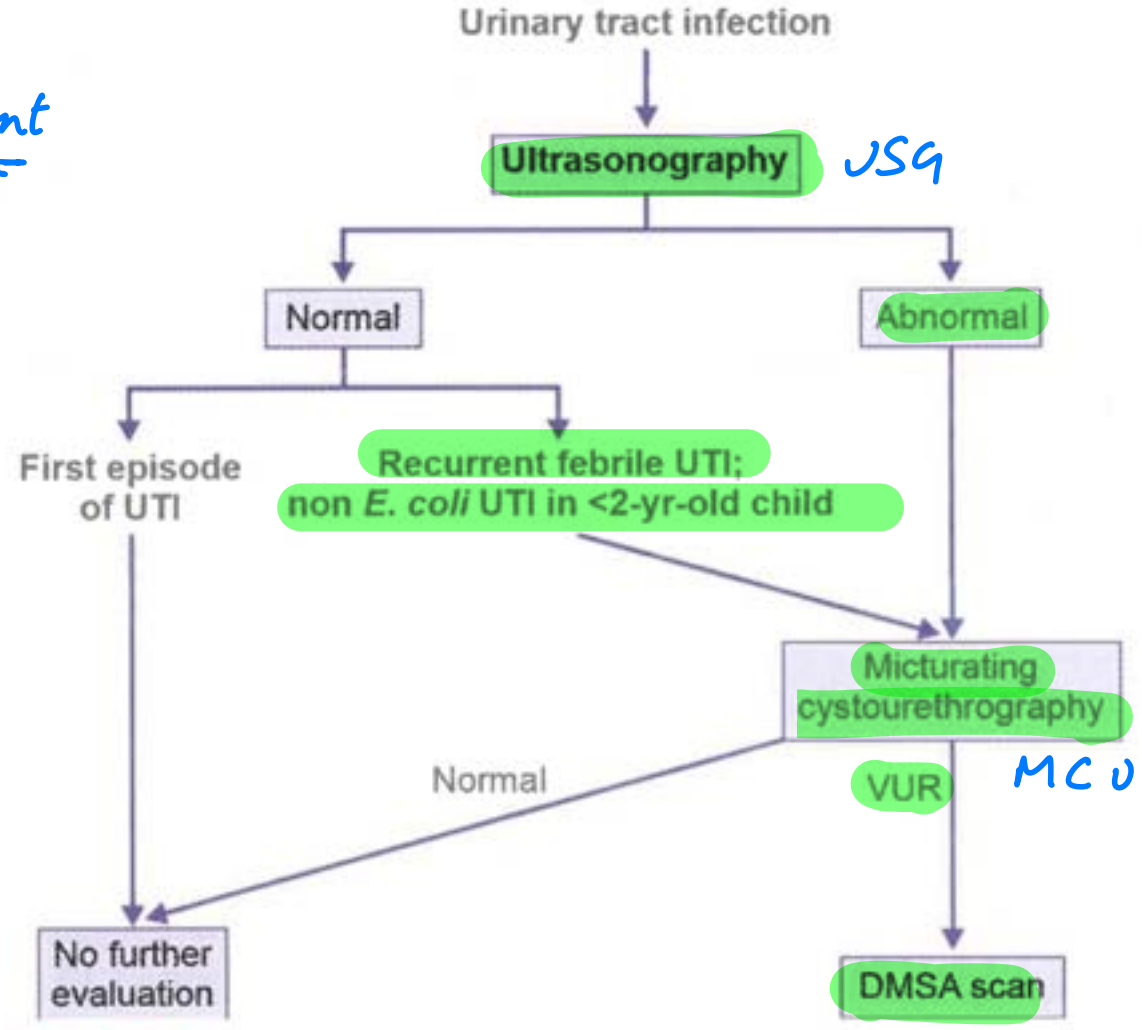


Table 17.3: Features that distinguish glomerular from non-glomerular hematuria

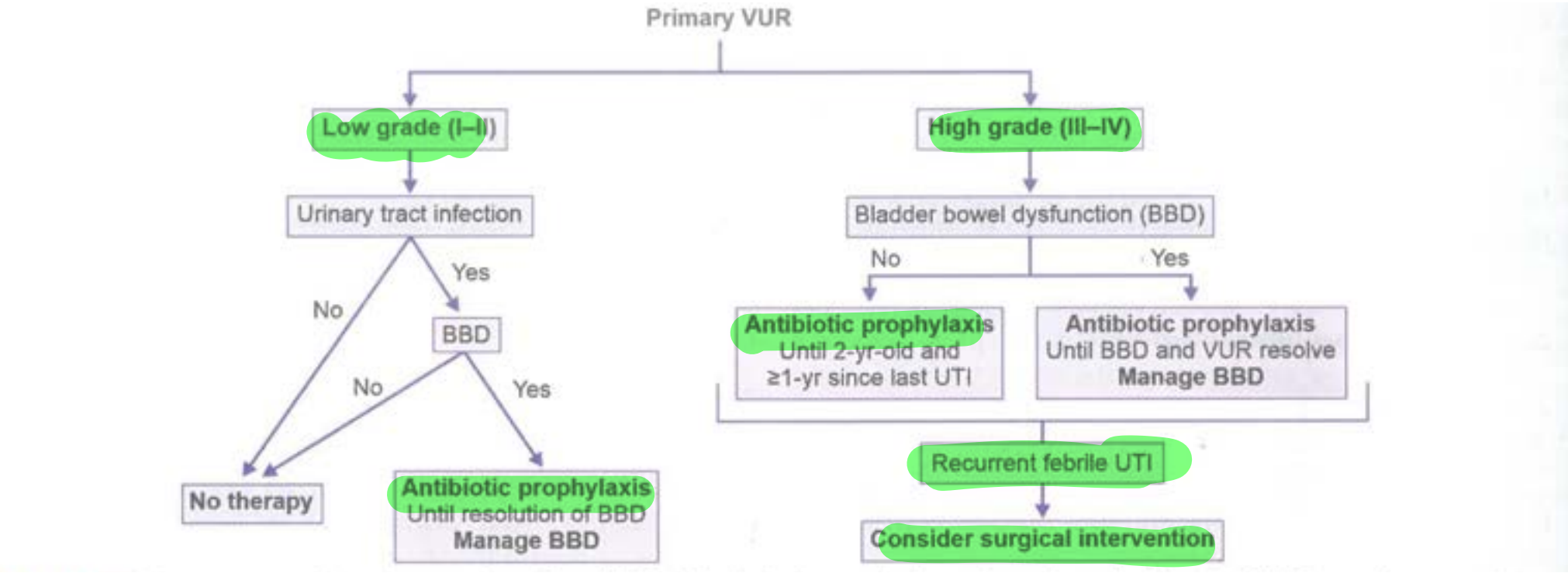
Features	*Glomerular causes*	*Non-glomerular causes*
Dysuria	No	Suggests urethritis or cystitis
Systemic complaints	Edema, pharyngitis, rash, arthralgia	Fever (UTI), loin pain (calculi)
Family history	Deafness, kidney failure (Alport syndrome)	Calculi (hypercalciuria, uricosuria)
Hypertension, edema	Common	Rare
Association with exercise	Absent	Nutcracker syndrome
Abdominal mass	Absent	Wilms tumor, obstructive uropathy, polycystic kidney disease
Urine color	Brown, tea, or cola	Bright red, clots
Proteinuria	2+ or more	Trace, 1+
Dysmorphic red cells	>20%	<15%
Red cell casts	Common	Absent
Crystals	Absent	May suggest calculi
Hypercalciuria or hyperuricosuria	Absent	May suggest calculi

UTI urinary tract infection

QQ

lower urinary tract

LRV



ENURESIS

Enuresis is defined as normal, nearly complete evacuation of the bladder at a wrong place and time at least twice a month after 5 years of age. Enuresis should be differentiated from continuous or intermittent incontinence or dribbling. The bed is soaking wet in the former, compared to loss of urine without normal bladder emptying in the latter. Enuresis is usually functional while continuous or daytime incontinence is often organic.

More than 85% children attain complete diurnal and nocturnal control of the bladder by 5 years. The remaining

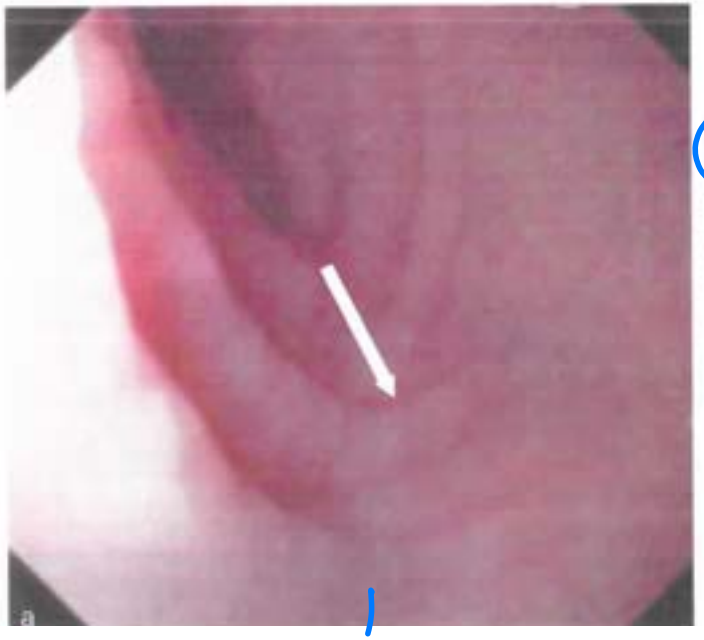
→ R/O organic → reinforcement / alarm ∞ → ↓ × → Pharmacotherapy → Nasal Desmopressin, TCA - Imipramine

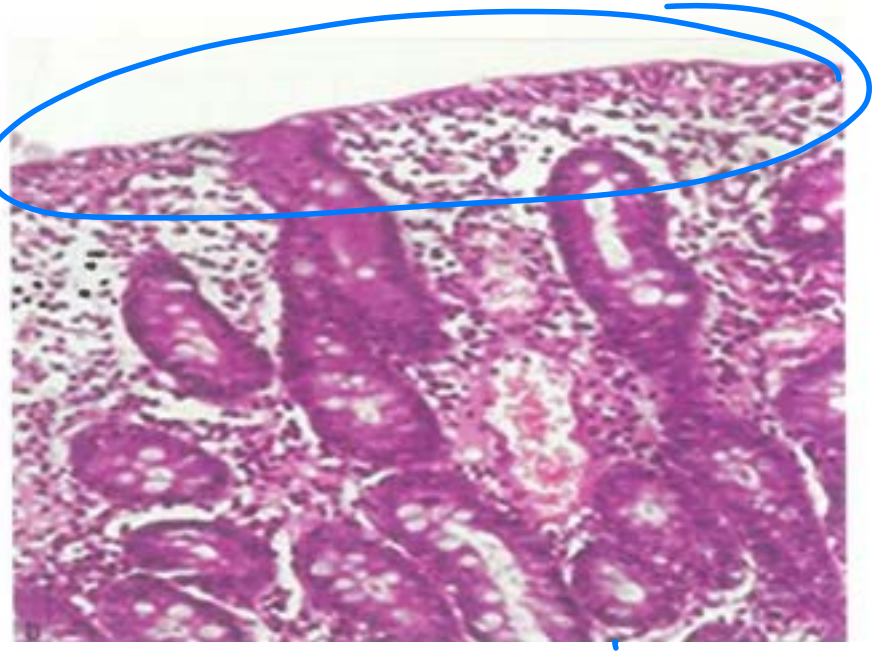
Table 12.16: Differentiating small bowel from large bowel diarrhea

Features	*Small bowel diarrhea*	*Large bowel diarrhea*
Stool volume; color	Large; pale	Small; normal
Blood in stool	No	Usually present
Rectal symptoms, e.g. urgency, tenesmus	No	Yes
Steatorrhea (greasy stools); smell	Yes; offensive smell	No; normal
Carbohydrate malabsorption	Yes, explosive stools	No
Protein malabsorption	Yes	No
Pain (if any)	Periumbilical, no reduction after stool	Hypogastric, reduced after passage of stool
Nutrient deficiency	Frequent	Can occur due to blood loss

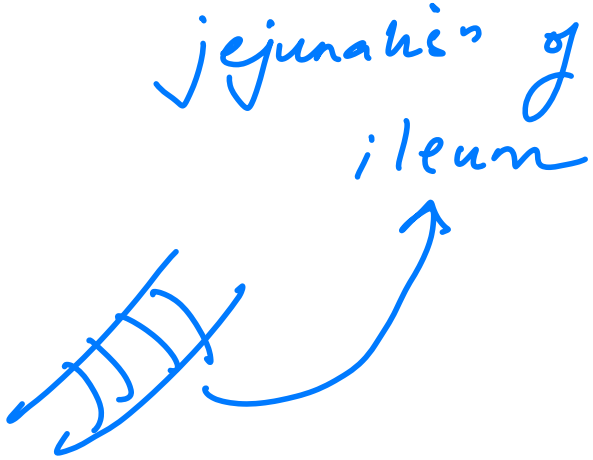
Table 12.17: Clues to important causes of chronic diarrhea

Cow milk protein allergy	• Onset of diarrhea after introduction of cow or buffalo milk or formula • Rectal bleeding (due to colitis) • Anemia; failure to thrive • Family history of allergy or atopy • Response to milk withdrawal
Lymphangiectasia	• Nonpitting pedal edema suggesting lymphedema • Recurrent anasarca • Hypoalbuminemia and hypoproteinemia • Lymphopenia • Hypocalcemia
Cystic fibrosis	• History of meconium ileus • Predominant or associated lower respiratory tract infections • Severe failure to thrive • Clubbing • History of sibling deaths • High sweat chloride (>60 mEq/L)
Immunodeficiencies	• Predominant fever • Recurrent infections involving other sites • History of sibling deaths • Organomegaly • Opportunistic infections on stool examination





Scalloping of duodenal Celiac Disease



Celiac Disease

This is an enteropathy caused by permanent sensitivity to gluten in genetically susceptible subjects. Nearly 99% of patients are positive for the human leukocyte antigen-DQ2 or -DQ8. Celiac disease is the most common cause of chronic diarrhea in children over 2 years of age in North India. High-risk groups include type 1 diabetes mellitus, Down syndrome, selective IgA deficiency, autoimmune thyroid disease, Turner syndrome, Williams syndrome, autoimmune liver disease and first-degree relatives of patients with celiac disease.

The main investigations required for making a diagnosis include:

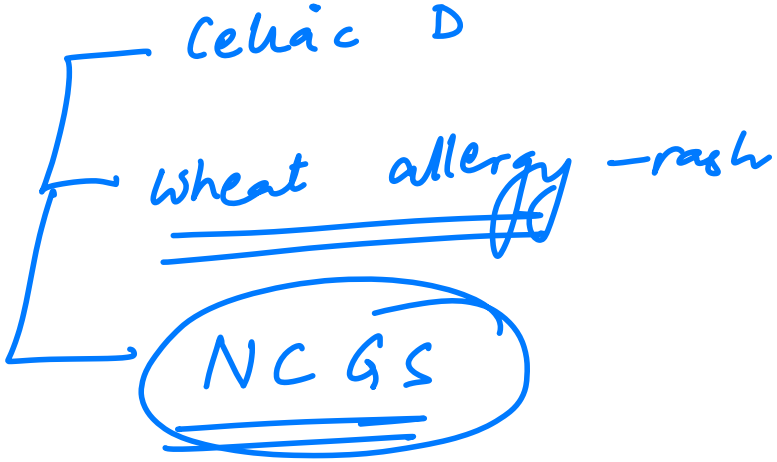
Serology: IgA antibody against tissue transglutaminase (tTG) is an ELISA-based test, with high sensitivity (92–100%) and specificity (91–100%) and is recommended for initial testing. IgA antiendomysial antibody is an equally accurate test (sensitivity 88–100%; specificity 91–100%), but is difficult to perform and not readily available. Serology helps in making a diagnosis of celiac disease and also in assessing compliance to dietary therapy.

Upper GI endoscopy and histology: The endoscopy may be normal or show absence of folds or scalloped duodenal folds (Fig. 12.20a). Multiple biopsies should be taken from the second/third part of duodenum and also from the duodenal bulb. The characteristic histological changes in celiac disease are increased intraepithelial lymphocytes (>30/100 enterocytes), increased crypt length, partial to total villous atrophy, decreased villous to crypt ratio and infiltration of plasma cells and lymphocytes in lamina propria (Fig. 12.20b). Both serology and biopsy should be done when the subject is on a normal gluten-containing diet.

The diagnostic criteria have been changing in recent years with differences in recommendations between children and adults. Traditionally, the diagnosis of celiac disease required the following:

i. Clinical features compatible with diagnosis
ii. Positive intestinal biopsy
iii. Positive serology and
iv. Unequivocal response to gluten-free diet (GFD) within 12 weeks of its initiation.

Celiac disease should be differentiated from nonceliac gluten sensitivity (NCGS) which is a condition in which gluten ingestion leads to GI and non-GI symptoms but the patients does not have celiac disease or wheat allergy (i.e. no enteropathy, negative serology). Gluten challenge is required to make a diagnosis of NCGS.



There are two kinds of reactions to cow milk: (i) Immediate (IgE mediated). It occurs within minutes of milk intake and is characterized by vomiting, pallor, shock-like state, urticaria and swelling of lips. (ii) Delayed (cell mediated): It has an indolent course and presents mainly with GI symptoms.

Clinical Features

The chief presentation is with diarrhea with blood and mucus. Depending upon the site and extent of involvement, the child may have small bowel, large bowel or mixed type diarrhea. In an Indian study, 40% children presented with bloody diarrhea, 33% watery and 7% with a mixed type of diarrhea. Uncommonly reflux symptoms and hematemesis may be present. Respiratory symptoms (allergic rhinitis and asthma) and atopic manifestations (eczema, angioedema) may be seen in 20–30% and 50–60% cases, respectively. Iron deficiency anemia, hypoproteinemia and eosinophilia are commonly present.

Diagnosis

In patients with GI symptoms, non-IgE-mediated CMPA is more common. The gold standard for diagnosis is the elimination and challenge test. Typically, the symptoms subside after withdrawal of milk and milk products and recur after re-exposure to milk. Eosinophilia and family history of atopy are suggestive. Sigmoidoscopy (aphthous ulcers and nodular lymphoid hyperplasia, Fig. 12.21a) and rectal biopsy (plenty of eosinophils, Fig. 12.21b) can be used in patients with only gastrointestinal symptoms. Skin prick test and specific IgE levels are useful for IgE-mediated CMPA.

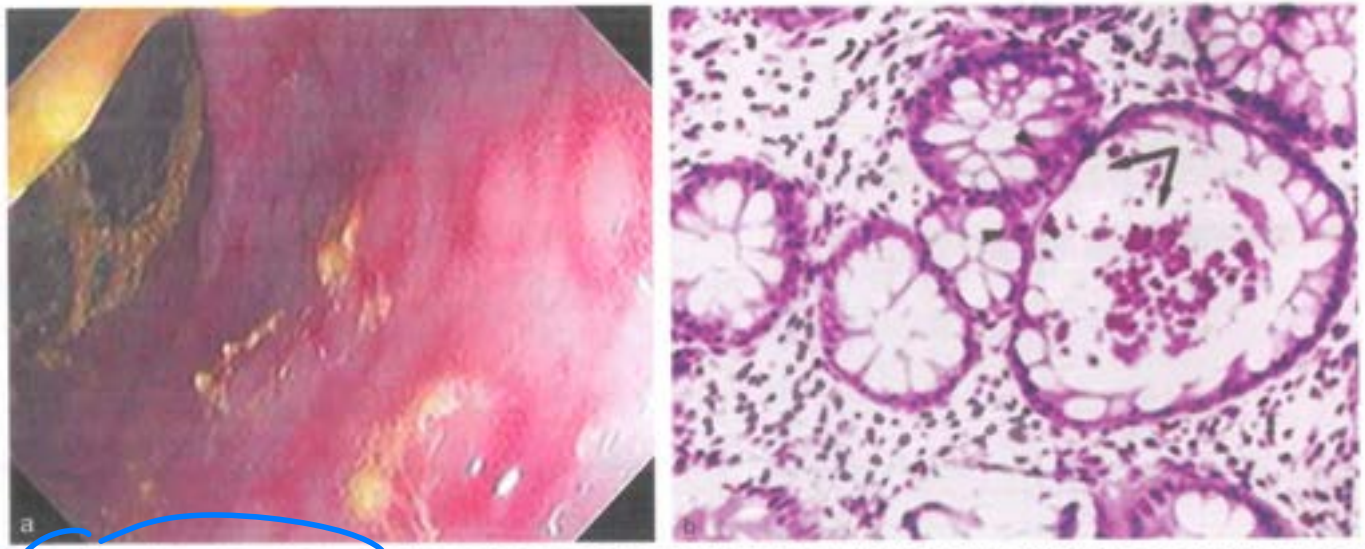


Fig. 12.21: Cow milk protein allergy: (a) Sigmoidoscopy showing aphthous ulcers; (b) Rectal biopsy showing eosinophilic infiltration with crypt abscess

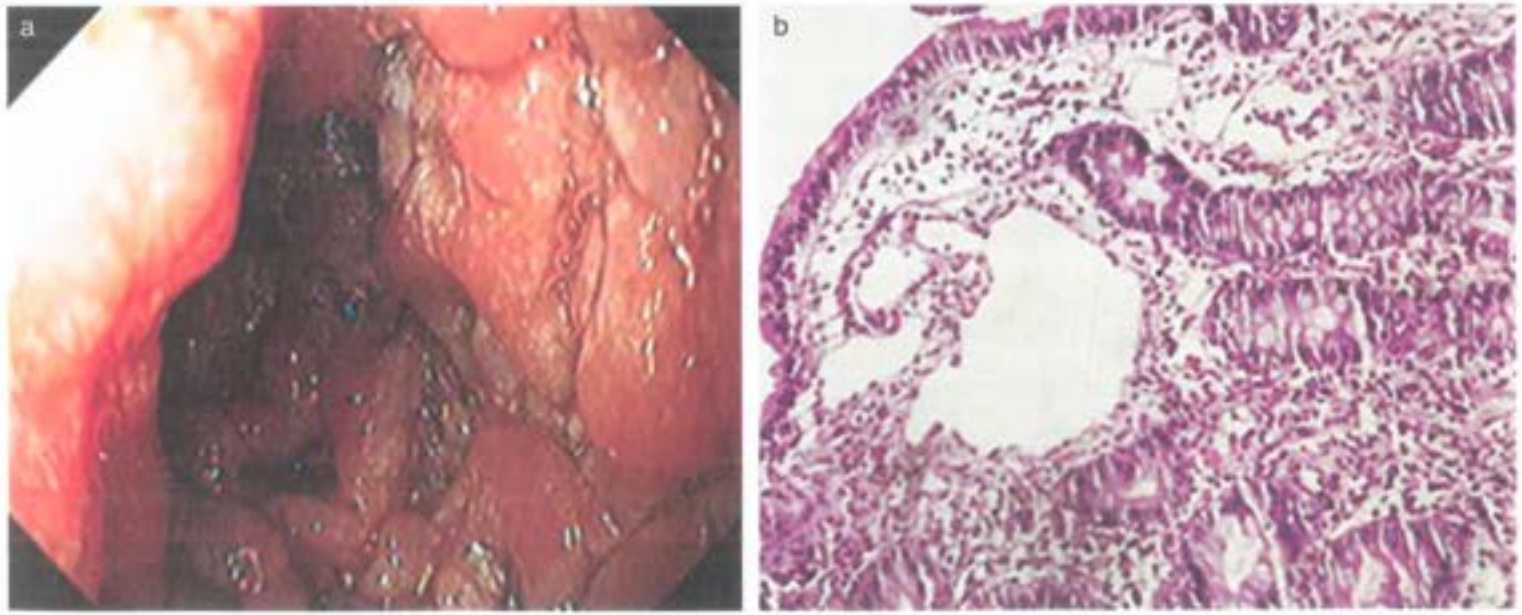


Fig. 12.22: Intestinal lymphangiectasia: (a) Upper gastrointestinal endoscopy showing snow-flake appearance; (b) Duodenal histology shows dilated lacteals

Cyclic Vomiting

This is defined as occurrence of stereotypic episodes of intense nausea and vomiting satisfying the following criteria:

- Minimum 5 episodes, or 3 attacks in 6 months time
- Episodic intense nausea and vomiting, lasts 1-hr to 10 days, separated by ≥1 week
- Stereotypical
- Vomiting >4 times/hr, for ≥1 hr
- Return to baseline health between episodes
- Not attributed to other metabolic, neurologic or gastrointestinal disorders

Typically, the attacks begin in early morning with symptoms of autonomic surge, e.g. lethargy, pallor, mild fever, headache, tachycardia, hypertension, diarrhea and abdominal pain. Most subjects have onset in preschool or school age. Family history of migraine and/or motion sickness is noted in 30–40% cases. Symptoms may overlap with abdominal migraine. Age <2 years at onset or presence of alarm features like attacks precipitated by fasting/high protein meal, presence of abdominal distension/bilious vomiting/severe pain, or altered mentation (confusion/ severe irritability) needs exclusion of other causes by appropriate investigations.

Functional Constipation

Functional constipation (FC) is defined by the presence of at least two or more of the following criteria for >1 month: (i) Two or fewer defecations per week; (ii) at least 1 episode of fecal incontinence per week after the acquisition of toileting skills; (iii) history of retentive posturing; (iv) history of painful or hard bowel movements; (v) presence of a large fecal mass in the rectum or on per

diameter stools that may obstruct the toilet (applicable only for children who use the Western type of toilet).

Table 12.4: Differences between functional constipation and Hirschsprung disease

Feature	*Functional constipation*	*Hirschsprung disease*
Passage of meconium	Normal	Delayed
Onset of symptoms	Beyond 1 year of age	Within infancy
Encopresis	Yes	No
Stool withholding behavior	Yes	No
Episodes of enterocolitis	No	Yes
Growth failure	No	Yes
Abdomen	Not distended; may have palpable fecoliths	Distended
Per rectal examination	Soft to hard stools present	Empty rectum with gush of stools on removing the finger
Barium enema	Rectum larger than sigmoid; ratio >1	Rectosigmoid ratio <1; transition zone seen
Anorectal manometry	Rectoanal inhibitory reflex present	Rectoanal inhibitory reflex absent
Rectal biopsy	Ganglion present	Ganglion absent

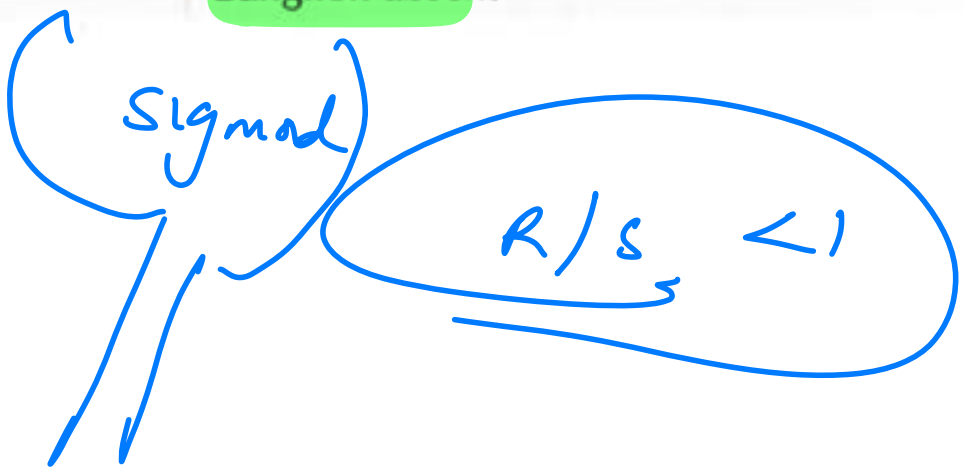


Table 20.10: Differentiating common causes of acute flaccid paralysis

	Poliomyelitis	*Guillain-Barré syndrome*	*Transverse myelitis*	*Traumatic neuritis*
Fever	Present; may be biphasic	May have a prodromal illness	May have a prodromal illness	Absent
Symmetry	Asymmetric	Symmetrical	Symmetrical	Asymmetric
Sensations	Intact; may have diffuse myalgias	Variable	Impaired below the level of the lesion	Impaired in distribution of the affected nerve
Respiratory insufficiency	May be present	May be present	May be present	Absent
Cranial nerves	Affected in bulbar and bulbospinal variants	Usually affected	Absent	Absent
Radicular signs	May be present	Present	Absent	Absent
Bladder, bowel complaints	Absent	Transient, late; due to autonomic dysfunction	Present, early	Absent
Nerve conduction	May be abnormal	Abnormal	Normal	Abnormal
Cerebrospinal fluid	Lymphocytic pleocytosis; normal or increased protein	Albuminocytologic dissociation	Variable	Normal
MRI spine	Usually normal	Usually normal	Characteristic changes	Normal

Finding	*Likely diagnosis*
Spike followed by slow waves	Interictal pattern of epilepsy
3 Hz spike and wave discharges; provoked by hyperventilation	Absence epilepsy
Chaotic high voltage record with multifocal spikes (hypsarrhythmia)	West syndrome
Brief bursts of polyspikes with photosensitivity	Juvenile myoclonic epilepsy
Spike wave complexes in Rolandic areas	Benign epilepsy with centrotemporal spikes
Generalized periodic epileptiform discharges	Subacute sclerosing panencephalitis
Lateralized periodic epileptiform discharges	Herpes simplex encephalitis

↳ temporal lobe

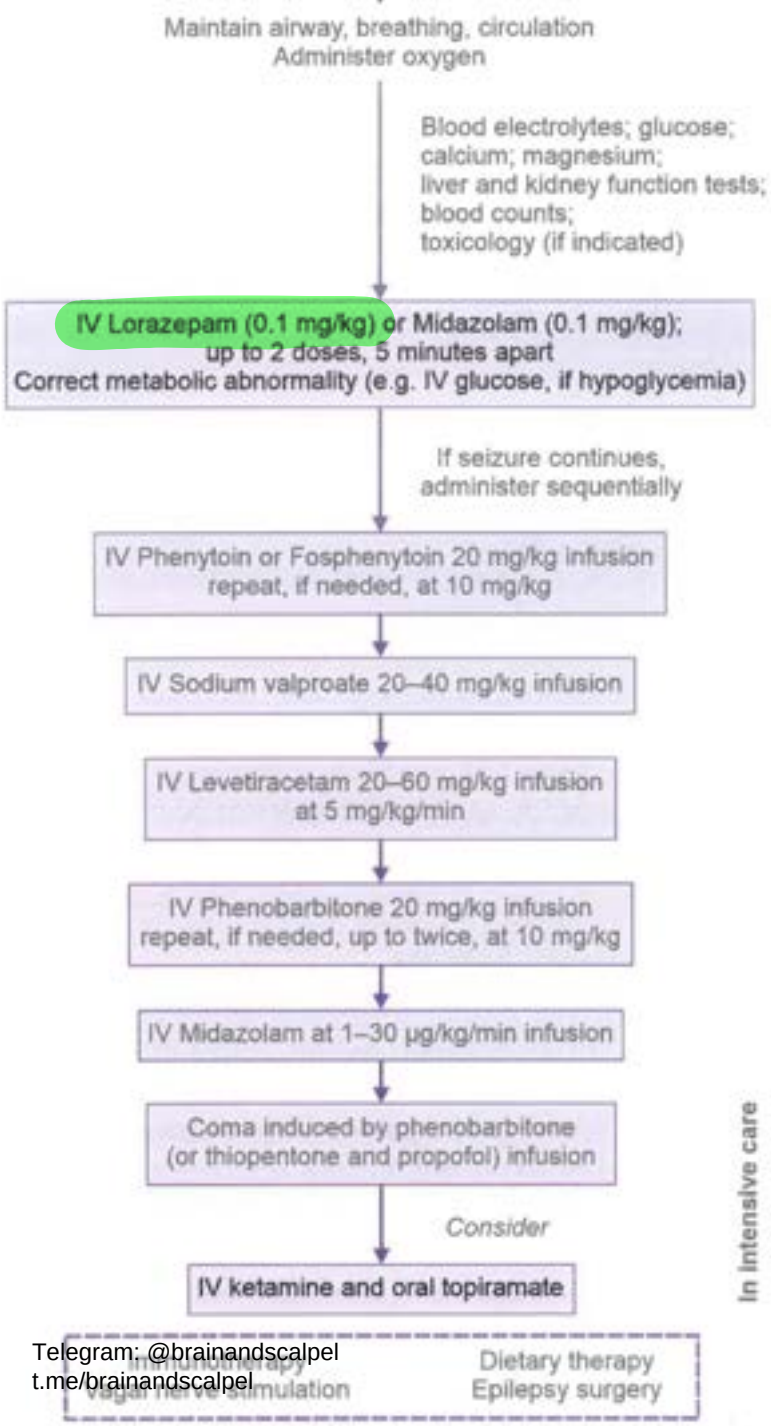


Table 20.4: Clinical classification of SMA

SMA type	*Age of onset*	*Motor milestones*	*Lifespan*
0	Prenatal	None	Few weeks; <6 months
1 (Werdnig-Hoffmann disease)	<6 months	Head held unaided	<2 years
2 (Dubowitz disease)	<18 months	Sits independently, cannot stand	2nd-3rd decade
3 (Kugelberg-Welander disease)	>18 months	Stand and walk independently	Normal life expectancy
4	Adolescent or adult onset	Ambulatory, may complain of muscle pain and fatigue	Normal life expectancy

Spinal Muscular Atrophy

AHC

This is an autosomal recessive disease caused by a mutation in the survival motor neuron 1 (*SMN1*) gene at chromosome 5q13.2. This region also carries *SMN2* gene, the copy number of which acts as a main modifier of the various clinical phenotypes. Both genes encode the SMN protein of anterior motor horn cells. In healthy individuals, the *SMN1* is responsible for the functional SMN protein, while *SMN2* produces 10–20% of the full length SMN protein and ~80% of a non-functional product that lacks exon 7 (Fig. 20.4). In ptients with SMA, the *SMN1* is lost due to pathogenic variations or deletions. *SMN2* remains and the small amount of full length SMN protein is sufficient for survival. The number of *SMN2* copies correlates with disease severity, with a lower copy number being linked to more severe types of SMA.

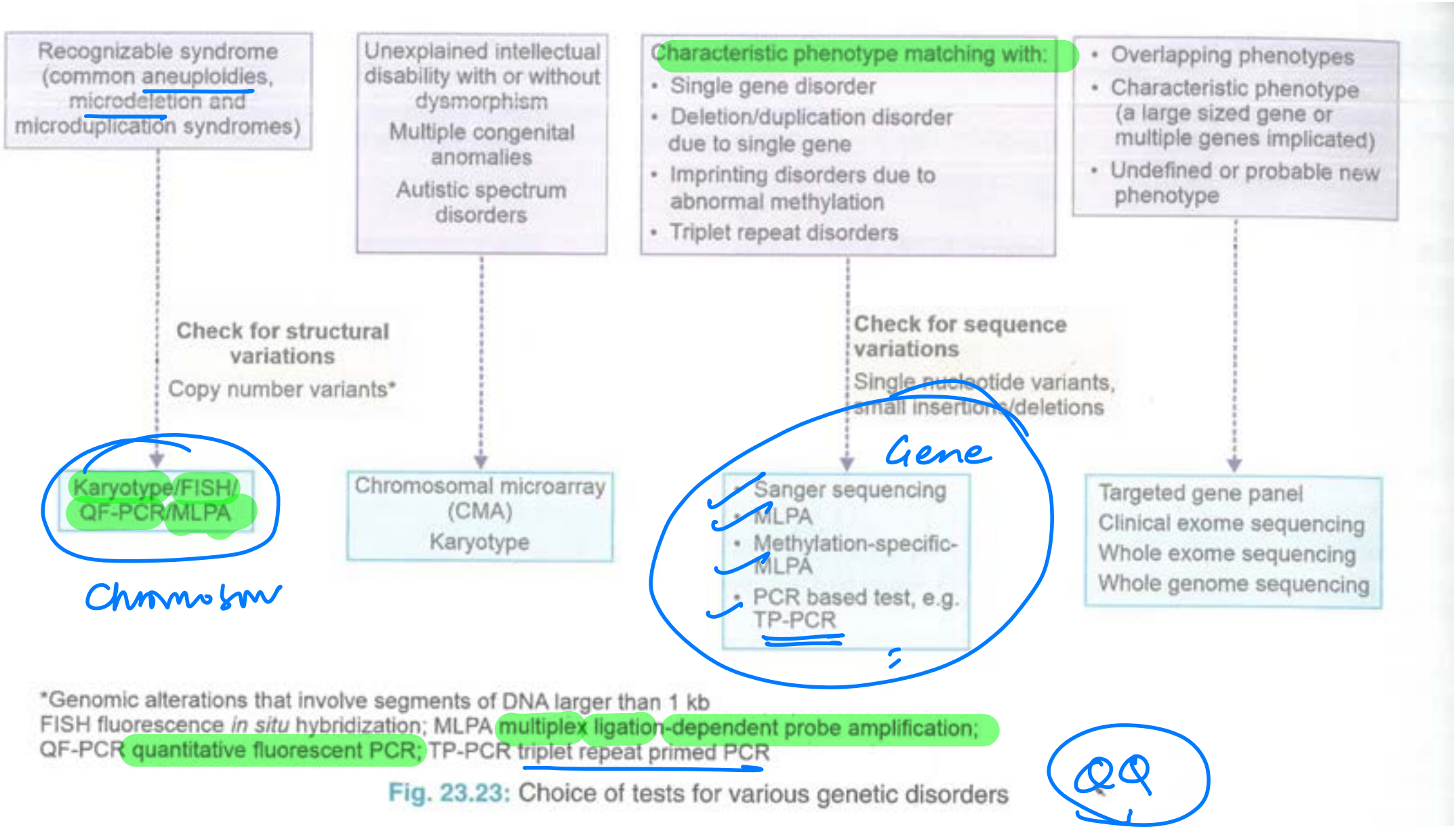


Fig. 23.23: Choice of tests for various genetic disorders

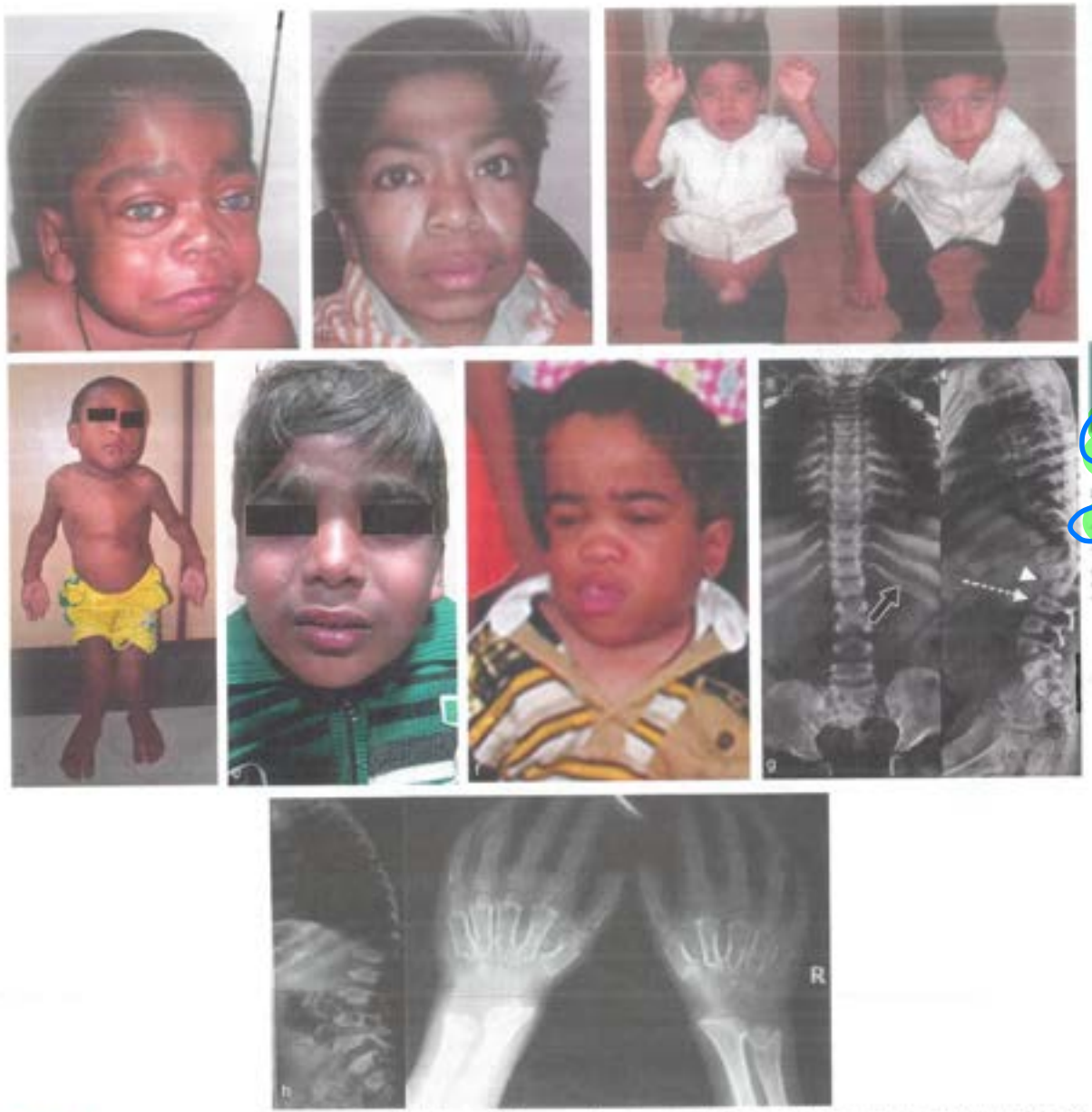


Fig. 24.11: Mucopolysaccharidoses: (a) Patient with type IH disease showing corneal clouding and coarse facial features; (b) MPS type II without corneal clouding but with facial coarseness; (c) MPS IHS (milder phenotype) with restriction of joint movements; (d) Short trunk with barrel-shaped chest, pectus carinatum and genu valgum in MPS IV (Morquio disease); (e) Mild facial coarseness in a child with MPS III; (f) MPS VI (Maroteaux-Lamy) with abnormal skull and facial coarseness; (g) Oar-shaped ribs (black arrow), localized gibbus deformity (dotted arrow), beaking of the inferior margins of vertebrae (dotted arrow) and proximal pointing of metacarpals in MPS type IV; (h) Central beaking of the lumbar vertebrae with proximally pointed metacarpals and short ulnae in MPS IV

MPS

MPS type	Developmental delay/intellectual disability	Coarse facies	Viscero-megaly	Joint contracture	Dysostosis multiplex	Corneal clouding	Urine GACs
Hurler (IH)	+	+	+	+	+	+	Dermatan sulfate, keratan sulfate
Scheie (IS)	–	+	±	+	±	+	
Hunter (II)	+ (mild to severe)	+	+	+	+	–	
Sanfilipo (III)	+	+	±	–	±	–	Heparan sulfate
Morquio A and B (IV)	–	+	–	– (laxity)	++	±	Keratan sulfate, chondroitin sulfate
Maroteaux-Lamy (VI)	–	+	+	+	+	+	Dermatan sulfate
Sly (VII)	+ (severe)	+	+	+	+	±	All except keratan sulfate

– absent; + present; GAGs glycosaminoglycans

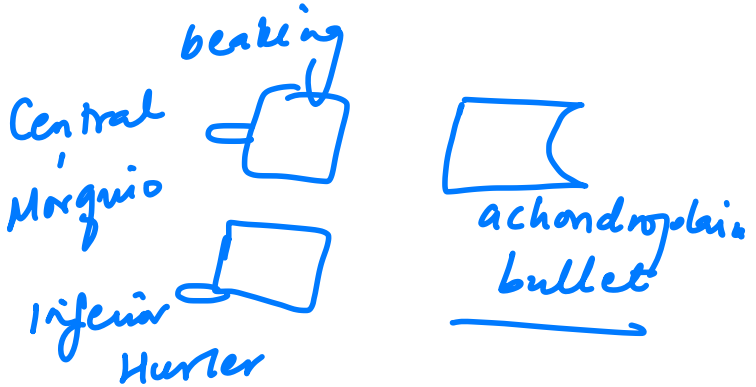


Table 21.26: Diagnostic criteria for HLH

HLH diagnosis established, if one of the two is fulfilled

A molecular diagnosis of HLH (e.g. *PERF, SAP, MUNC* mutations)
OR 5 of the following 8 criteria are fulfilled

- Fever
- Splenomegaly
- Cytopenias in at least two cell lines
  - Hemoglobin <90 g/L
  - Platelets <100 × 10^9/L
  - Neutrophils <1 × 10^9/L
- Hypertriglyceridemia and/or hypofibrinogenemia
  - Fasting triglycerides >3 mmol/L (>265 mg/dL)
  - Fibrinogen <1.5 g/L
- Hemophagocytosis in bone marrow or spleen or lymph nodes
- Low or absent activity of natural killer cells
- Ferritin >500 µg/L
- Soluble CD25 (soluble interleukin-2 receptor) >2400 units/mL

Hemophago lympho histo cyt

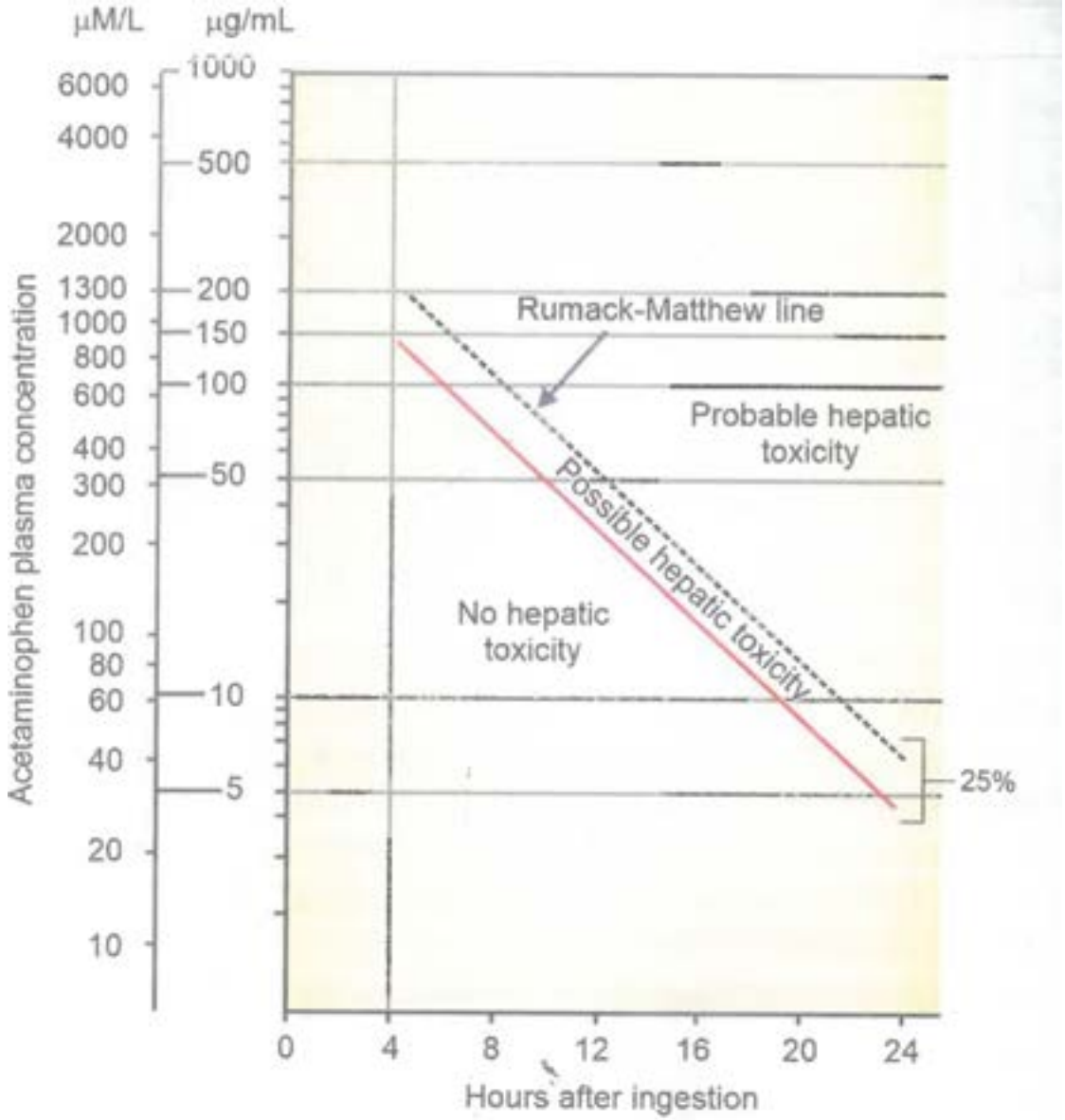
Table 22.3: Pattern of joint involvement with juvenile idiopathic arthritis (JIA)

JIA subtype	*Clinical presentation*	*Remarks*
Oligoarticular JIA	Young girls (3–5 years) ≤4 joints Lower limb predominance (usually knee)	ANA positivity High risk for chronic asymptomatic uveitis Need regular slit-lamp examinations
RF–ve polyarthritis	Young girls Symmetric or asymmetric polyarthritis	ANA positivity associated with high risk of chronic asymptomatic uveitis Genetic similarities to oligoarticular JIA
RF+ve polyarthritis	Adolescent girls Multiple small and large joints; often symmetric; deforming arthritis	Prognosis poor in comparison to RF –ve polyarthritis Phenotypic similarities to adult-onset rheumatoid arthritis Uveitis is not common
Systemic JIA	No age and sex predilection High grade fever, evanescent rash, generalized lymphadenopathy, hepatosplenomegaly, serositis	Fever is typically quotidian (touches baseline) Monoarthritis is uncommon; knee, wrist and ankle are involved usually Change in pattern of fever (continuous high-grade fever) along with rise in CRP and decline in ESR may herald the onset of macrophage activation syndrome
Enthesitis (HLA B27) related arthritis	Older boys (9–10 years) Lower limb large joint asymmetric arthritis Evidence of enthesitis	May present with acute symptomatic uveitis
Psoriatic arthritis	Bimodal age of presentation Usually start as lower limb monoarthritis Distal interphalangeal joint involvement	Dactylitis Family history of psoriasis Arthritis often precedes cutaneous manifestations DIP involvement is a characteristic feature; seen in approximately 30–50% patients

ANA antinuclear antibodies; DIP distal interphalangeal joint; RF rheumatoid factor

<16yrs
>6wks
uveitis

Still's D



ig. 28.5: Rumack-Matthew nomogram. The treatment-line is lotted 25% below the Rumack-Matthew line to allow for errors in lood assays and estimated time from ingestion of an overdose. -acetylcysteine is administered if acetaminophen levels are bove the solid line

PCM

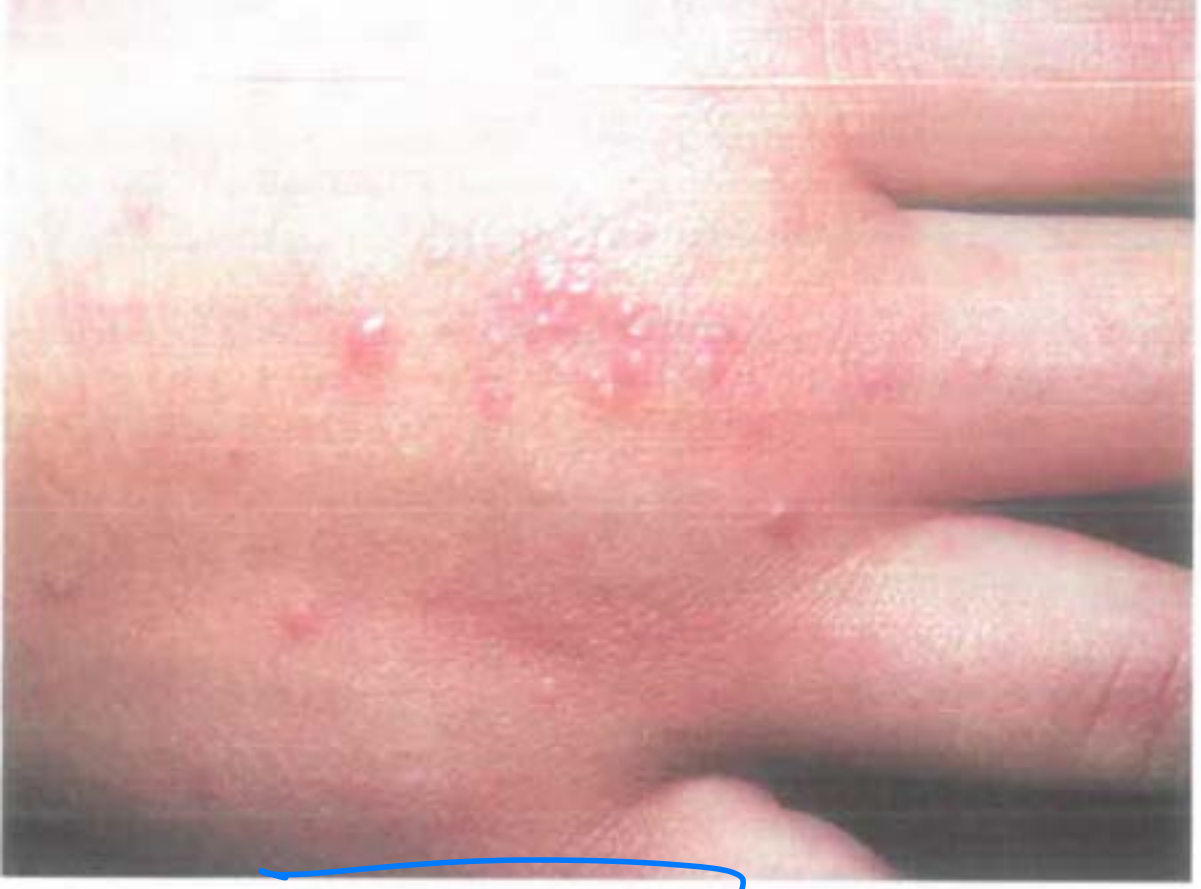


Fig. 27.72: Gianotti-Crosti syndrome: Multiple, monomorphic, flat/umbilicated erythematous papules present symmetrically over the dorsae of hands

Gianotti-Crosti Syndrome

Also known as papular acrodermatitis of childhood, the condition is associated with hepatitis B virus and Epstein-Barr virus.

It presents as characteristic lesions (Fig. 27.72) on the face, buttocks and limbs, associated with mild constitutional symptoms. The mucous membranes are not affected. The eruption fades with mild desquamation in 3–4 weeks.

Table 21.15 St Jude staging system for childhood non-Hodgkin lymphoma

Low risk (localized)	
I	Single tumor (extranodal), single anatomic area (nodal) excluding mediastinum or abdomen
II	• Single tumor (extranodal) with regional node involvement • Primary gastrointestinal tumor (completely resected with or without involvement of mesenteric nodes) • Two/more tumors/nodal areas on one side of the diaphragm
High risk (advanced)	
III	• All primary intrathoracic (mediastinal, pleural and thymic) tumors • All extensive primary intra-abdominal disease • All paraspinal or epidural tumors regardless of other tumor sites • Two/more nodal or extranodal areas on both sides of diaphragm
IV	Any of the above with CNS and or bone marrow involvement

HL

Ann Arbor

AML

Table 21.7: Risk stratification of acute myeloid leukemia by genetics

Risk category	*Genetic abnormality*
Favorable	• t(8;21)(q22;q22.1); *RUNX1-RUNX1T1* • inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11* • Mutated NPM1 without *FLT3-ITD* or with *FLT3-ITD*^{low} • Biallelic mutated *CEBPA*
Intermediate	• Mutated *NPM1* and *FLT3-ITD*^{high} • Wild-type *NPM1* without *FLT3-ITD* or with *FLT3-ITD*^{low} (without adverse-risk genetic lesions) • t(9;11)(p21.3;q23.3); *MLLT3-KMT2A* • Cytogenetic abnormalities not classified as favorable or adverse
Adverse	• t(6;9)(p23;q34.1); *DEK-NUP214* • t(v;11q23.3); *KMT2A* rearranged • t(9;22)(q34.1;q11.2); *BCR-ABL1* • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); variations in *GATA2, MECOM;* monosomy 5 or del(5q); monosomy 7; (17p) • Complex karyotype, monosomal karyotype • Wild-type *NPM1* and *FLT3-ITD*^{high} • Mutated *RUNX1* • Mutated *ASXL1* • Mutated *TP53*

Table 21.5: Genetic abnormalities in acute lymphoblastic leukemia (ALL)

Chromosomal abnormality, translocation, affected gene	*Subtype*	*Frequency (%)*	*Implication*
Hyperdiploidy (>50 chromosomes)	Pre-B	20–30	Excellent prognosis
t(12;21)(p13;q22) *ETV6-RUNX1* *TEL AML 1*	Pre-B	15–25	Excellent prognosis, needs minimal therapy
Trisomy 4 and 10	Pre-B	20–25	Excellent prognosis
t(1;19)(q23;p13) *TCF3-PBX1*	Pre-B	2–6	High risk, probable CNS relapse
t(4;11)(q21;q23) *MLL-AF4*	Pre-B	1–2	Infant ALL, poor prognosis
High tumor burden, drug resistant			
t(9;22)(q34;q11.2) *BCR-ABL1*			
Philadelphia chromosome	Pre-B	2–4	Very high risk; improved outcome with imatinib and chemotherapy
t(8;14)(q23;q32.3) *MYC IgL*	Mature B cell	2	Burkitt leukemia, need intensive therapy, favorable outcome
Hypodiploidy (<44 chromosomes)	Pre-B	1–2	Unsatisfactory outcome
HOX 11 rearrangement by t(5;14)(q35;q32)	T	7–8	Good prognosis
Early Tcell precursor	T	12	Poor prognosis

ALL

RB

Table 21.18: International Retinoblastoma Staging System (IRSS)

Stage	*Description*	
Stage 0	Eye has not been enucleated and no dissemination of disease Conservative treatment	
Stage I	Eye enucleated, completely resected histologically	
Stage II	Eye enucleated, microscopic residual tumor in form of i. Tumor invasion into extrascleral space ii. Tumor invasion into cut end of optic nerve	
Stage III	Regional extension	a. Overt orbital disease b. Preauricular or cervical lymph node extension
Stage IV	Metastatic disease	a. Hematogenous metastasis (without CNS involvement): single or multiple lesions b. CNS extension (with or without regional or metastatic disease)

Table 21.17: International classification of intraocular retinoblastoma

Group A Very low risk	No tumor greater than 3 mm in dimension; away from fovea and optic nerve
Group B Low risk	Any eye with tumor not in group A with no vitreous seeding, subretinal fluid <5 mm from base of tumor
Group C Moderate risk, focal seeds	Tumors with focal fine vitreous seeding or subretinal fluid (<1 quadrant)
Group D High risk	Massive/diffuse vitreous seeding, extensive subretinal masses
Group E Very high risk, extensive retinoblastoma	• **Unsalvageable eyes** • Tumor involving >50% globe, touching the lens, involves anterior segment • Diffuse infiltrating retinoblastoma, neovascular glaucoma • Opaque media from hemorrhage • Tumor necrosis, aseptic orbital cellulitis, phthisis bulbi