Pediatrics I

New – 2018

General pediatrics

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Values (normal ranges) that you may need to use or memorize in your OSCE or final exam.

Electrolytes:
Na^{+}: 136-145
K^{+} : 3.5-4.5
Cl^{-} : 98-107
Ca^{+2} : 8.5-10.5

Acid-Base values:
PH: 7.35-7.45
HCO3-: 22-28
PCO2: 35-45 mmHg
PO2:80-100mmHg
Serum anion gap: 10-14
Base excess: -3 to +3

Respiratory rate:

<1 year: 30-40
1-2 years: 25-35
2-5 years: 25-30
5-12years: 20-25
>12 years : 12-20

Heart rate:

Newborn: 120-160
Infant: 70-100
Toddler: 80-110
Preschool: 80-110
School age: 80-120
Adolescent: 110-120

It is very important to memorize the values of CSF in normal and pathological conditions.

Good luck ☺

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NORMAL CSF VALUES

Color	**Clear**	
Glucose	*Neonate*	*>60%*
	Infants	*>50*
	Child/adult	*>60%*
Protein	**Neonate**	**<150 mg/dl**
	Infants	**<40 mg/dl**
	Child/adult	**20-45 mg/dl**
WBC	*Neonate*	*20-30 WBC/ml* *<10% neutrophils* *75% lymphocyte*
	Child/adult	*<5 WBC/ml* *Zero neutrophils* *<4 lymphocytes*
Pressure	**Neonate**	**50-180 mmH2O**
	Child/adult	**100-200 mmH2O**

NOTE:

→ CSF latex agglutination test

- Detects antigens
- Rarely used now
- Indication: Suspected bacterial meningitis with negative test (cause: partially treated meningitis). Usually for encapsulated bacteria

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NOTES

- **Bacterial meningitis**
  - Color: clear
  - Glucose: decreased <50 mg/dl
  - Protein: increased >45 mg/dl
  - WBC: increased PMN (neutrophils)
  - Pressure: increased >200

- **Viral meningitis**
  - Color: clear-cloudy
  - Glucose: normal
  - Protein: increased >45 mg/dl
  - WBC: increased PMN (mononuclear)
  - Pressure: normal or increased
  - RBC increase in CSF (crenated): you should differentiate it from traumatic cause (in trauma; RBCs in CSF analysis are fresh RBC)

- **Partially treated bacterial meningitis**
  - Glucose: decreased or normal
  - Protein: increased >100
  - WBC: increased (neutrophils)
  - Pressure: normal or increased

- **TB meningitis** (proteins are very high in TB)
  - Glucose: decreased <50 mg/dl
  - Protein: increased 100-500 mg/dl
  - WBC: 10-500 (lymphocytes)
  - Pressure: increased

- **Abscess** (parameningeal)
  - Glucose: normal
  - Protein: 20-2000
  - WBC: 0-100 (neutrophils)
  - Pressure: normal or increased

- **General look:**
  - Color (cyanosis, jaundice, pale).
  - Signs of respiratory distress.
  - Cognitive function.
  - Ill looking/ well looking.
  - Thin/ fat.
  - Mental status.
- **Vital signs:**
  - HR, RR, BP, temperature (these 5 vital signs are the most important).
  - Pulse oximetry/ pain score.
  - Pain score in infants assessed by face chart.
- **Growth parameters:**
  - Wight, height, head circumference and MBI.
  - We have blue growth charts for males and pink for girls.
  - We have growth charts for (birth- 36 months) age group: length/ weight/ head circumference/ weight for length.
  - We have growth charts for (2-20 years) age group: weight/ height/ BMI.
- **Head and neck:**
  - Eye: eye movement/ red reflex/ fundoscopy.
  - Dental caries.
  - Neck: stiffness/ masses/ lymph nodes.
  - Central cyanosis under the tongue.
  - Ears and nose.
  - Fontanelles:
    - ✓ The best situation to examine them is sitting position/ post feeding/ relaxed baby.
    - ✓ Febrile + bulging fontanelle: think of meningitis.
    - ✓ Brain imaging is contraindicated while fontanelle is open.
- **Hands:** clubbing/ widening of the wrist (rickets)/ nail changes/ capillary refill (normally 2 seconds/ normal delay in cold hands)
- Chest exam (cardiorespiratory): auscultation is done while baby is relaxed.
- Abdominal examination.
- Rectal examination is very rare to be done.
- MSS
- Neurological examination: primitive reflexes/ cerebellar signs.
- Skin: dehydration/ rashes.

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Growth and Development

Growth charts:

- ✓ The height, weight, and head circumference of a child can be compared to the expected parameters of children of the same age and sex to determine whether the child is growing appropriately. Growth charts can also be used to predict the expected adult height and weight of a child because.
- ✓ Also called as “road-to-health" chart.
- ✓ Growth charts are not intended to be used as a sole diagnostic instrument.

- **Uses of Growth charts :**

- ✓ Diagnostic tool to identify high risk children.
- ✓ Planning and policy making
- ✓ Education tool for educating mothers
- ✓ Tool for action helps in type of intervention that is needed Evaluation of effectiveness of corrective measure and impact of a program of special interventions for improving Childs growth and development.

- **Notes :**

- ✓ Growth assessment is the single measurement that best defines the health and nutritional status of children.
- ✓ The designation of a child as having impaired growth implies some means of comparison with a “reference” child of the same age and sex.

Length vs Height

Length of children less than 2 years old is measured lying down, while standing height is measured for children age 2 years or older.

- **Measurments**:

- ✓ Weight-for-age
- ✓ Height (Length)-for-age
- ✓ Weight-for-height
- ✓ BMI (more than two years old) :The body mass index is defined as body weight kilograms divided by height in meters squared
- ✓ Head circumference-for-age

- **Interpretation of different indicators**

Indicator	Acute Malnutrition	Chronic Malnutrition
Wt-for-age	⇩	⇩
Ht-for-Age	**Normal**	⇩
Wt-for-Ht	⇩	**Normal**

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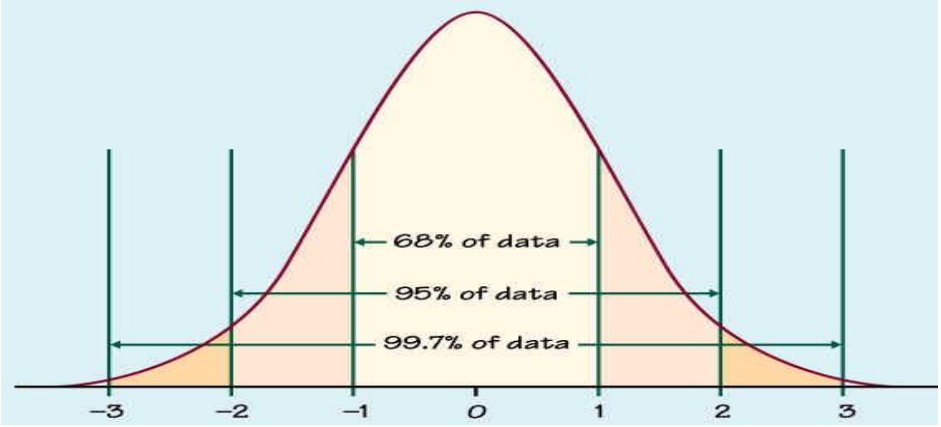
- **Scales of measurement :**

✓ Z scores
✓ Percentiles
✓ Percent of median
✓ The deviation of the value for an individual from the median value of the reference population, divided by the standard Deviation for the reference population

- **Z- Score or standard deviation score:**

$$\text{Z- Score} = \frac{\text{(Observed value) - (Median reference value)}}{\text{Standard deviation of reference population}}$$

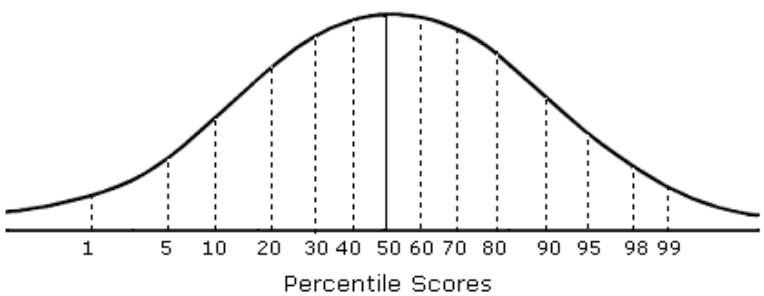


- **Percentile**

✓ The rank position of an individual on a given reference distribution, stated in terms of what percentage of the group the individual equals or exceeds .
Eg. A child of a given age whose weight falls in the 10th percentile weighs the same or more than 10% of the reference population of children of same age

✓ Towards the extremes of the reference distribution there is little change in percentile values, when there is in fact substantial change in weight or height.

✓



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Z score	Exact percentile	Rounded percentile
0	50	50
-1	15.9	15
-2	2.3	3
-3	0.1	1
1	84.1	85
2	97.7	97
3	99.9	99

Z score	Height for age	Weight for age	BMI for age
>3	May be abnormal	May be abnormal	obese
>2	Normal	Use BMI	Overweight

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>1	Normal	Use BMI	Risk of overweight
0	normal	Use BMI	normal
<-1	normal	normal	normal
<-2	stunted	underweight	wasted
<-3	Severely stunted	Severely underweight	Severe wasted

- **Compare the WHO Growth Standards and the CDC Growth Reference**

Comparison	WHO Growth Chart	CDC Growth Chart
Studied population	**Breastfed infants and toddlers**	**Breastfed and formula fed infants and toddlers**
Growth pattern	**How healthy children SHOULD GROW in ideal conditions**	**How certain groups of children HAVE GROWN in the past**
Concept of growth	**A STANDARD by which all children should be compared**	**A REFERENCE does not imply that pattern of growth is optimal**

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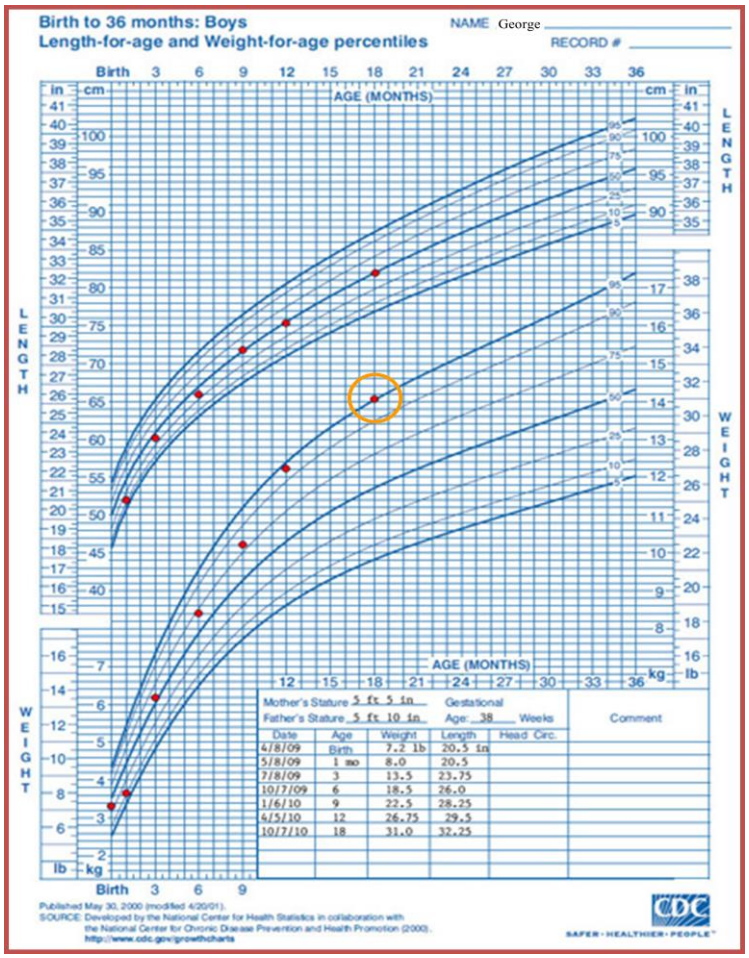
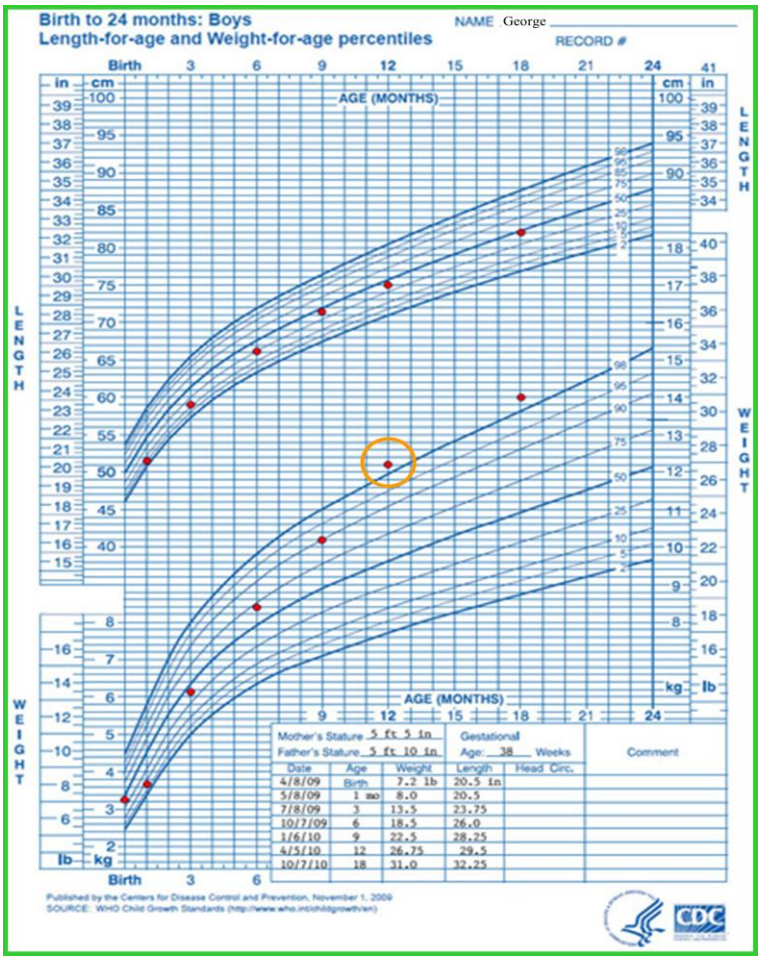
CDC Weight for age



WHO Weight for age



Look at the Length- and Weight-for-Age sides of growth charts side by side for a patient named George.

- ✓ Weight-for-age is important in early infancy for monitoring weight and helping explain changes in weight-for-length.
- ✓ Weight-for-age is not used to classify infants and children as under- or overweight. It reflects body weight relative to age and is influenced by recent changes in health or nutrition status.
- ✓ When George's measurements are plotted on the **CDC weight-for-age growth chart**, his weight-for-age crosses upward in percentiles and crosses above the 95th percentile at 18 months of age. His length-for-age tracks along the 50th percentile.
- ✓ When George's weight is plotted on the **WHO weight-for-age growth chart**, his weight is below the 50th percentile for the first three months of age. At six months, his weight-for-age begins moving upward across centiles and at 12 months is above the 98th percentile indicating that his weight is high for his age.

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Note that the **WHO weight-for-age chart** identified high weight-for-age at an earlier age than the **CDC weight-for-age chart** (12 months versus 18 months). See circles.

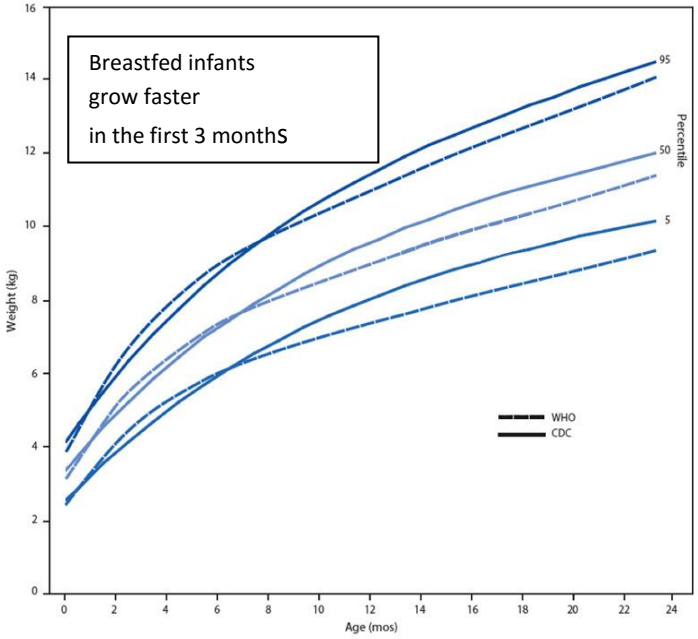
- **CDC recommends that health care providers:**

✓ Use the **WHO growth charts** for infants and children 0 to 2 years of age
✓ Use the **CDC growth charts** for children ages 2 to 20 years

- **Note :**
  - ✓ in JUH we still use CDC growth charts for all ages.
  - ✓ It is very important for you when you are in the pediatrics clinic to apply in the growth charts for both genders and for different ages.

- **Mode of feeding can influence infant growth rate**

Mode of feeding	Growth in the first 3 months	Growth after 3 months
Breastfeeding	Faster	Slower
Formula	Slower	Faster



Growth Disorders & their effect on growth charts

✓ Normal growth is the final common pathway of many factors, including endocrine, environmental, nutritional, and genetic influences.
✓ Maintenance of a normal linear growth pattern is good evidence of overall health and can be considered a "bioassay" for the well-being of the whole child

- **Growth Parameters**

➔ **Wight** :

- Weight is one of the best criteria for assessment of growth and a good indicator of health and nutritional status of child.
  - 1. Weight loss in first few days: 5%-10% of birth weight
  - 2. Return to birth weight: 7-10 days of age
    - Double birth weight: 4-5 mo

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- Triple birth weight: 1 yr
- Quadruple birth weight: 2 yr

- 3. Average weights: 3.5 kg at birth , 10 kg at 1 yr , 20 kg at 5 yr , 30 kg at 10 yr
- 4. Daily weight gain: 20-30 g for first 3-4 mo , 15-20 g for rest of the first yr
- 5. Average annual weight gain: 5 lb between 2 yr and puberty

→Height:

- Average length: 51 cm at birth, 77 cm at 1 yr
- At age 3 yr, the average child is 91 cm
- At age 4 yr, the average child is 102 cm in tall (double birth length)

Mid-parental height:

- 95% follow this range.
- In males: MPH = (father's height + mother's height + 13 cm)/ 2
- Range of MPH in males: ± 10 cm.
- In females: MPH = (father's height – 13 + mother's height)/ 2
- Range of MPH in females: ± 8.5 cm

{It is very important to apply this rule in the growth chart as it appeared in the OSCE}.

Note: Related object that you have to study is Short stature in endocrine section of your dossier.

➔ Head circumference

✓ It is related to brain growth and development of intracranial volume. Average head circumference measured about **35 cm** at birth.
- At **3 months** it is about **40 cm**, at **6 month 43 cm,** at **one year 45cm**, at **2 years 48 cm**, at **7 year 50 cm** and at **12 years** of age it is about **52 cm**, almost same a adult.

➔ Body mass index

- It is an important criteria which helps to assess the normal growth or its deviations i.e. malnutrition or obesity.
  - BMI > 95th percentile considered obese
  - BMI>85th percentile considered overweight
  - **Note** :
    The following criteria is for Adults and <u>is not</u> used in pediatrics : Underweight = <18.5 Normal weight = 18.5–24.9 Overweight = 25–29.9 Obesity = BMI of 30 or greater.

- **Percentile curves**

✓ Major percentile curves lie at the 5, 10, 25, 50, 75, 90, 95th percentiles
✓ Normal growth should fall between the 5th percentile and the 95th percentile

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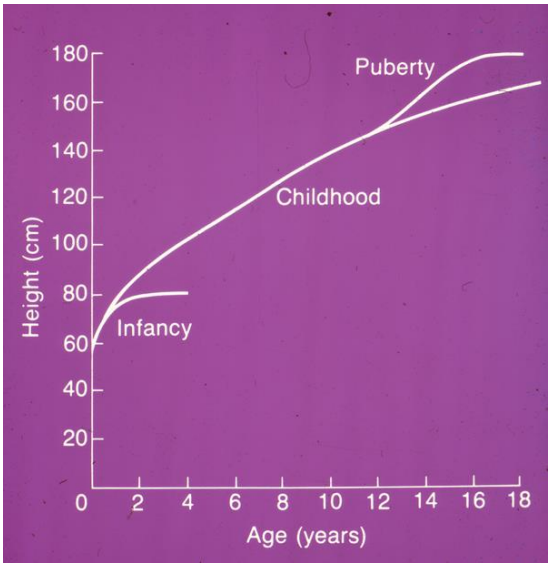
✓ Infants and children with a **length-for-age** <5th percentile have short stature.
✓ Infants and children with a **weight-for-age** <5th percentile are underweight.
✓ Main concern in infancy is poor growth
- underweight/malnutrition, short stature/stunting



- **Human linear growth**
Human linear growth can be divided into three: phases :
✓ Growth in infancy
✓ Growth in childhood
✓ Growth during puberty

Growth in infancy

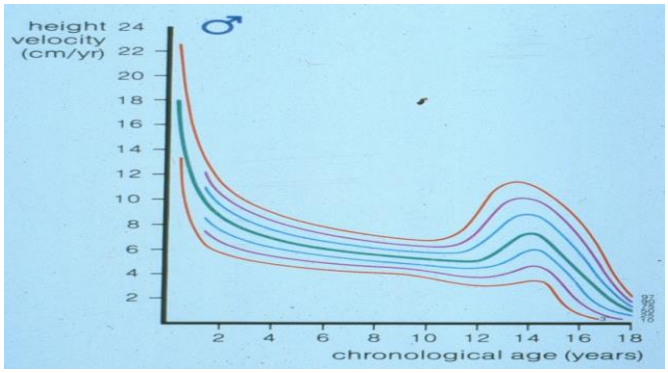
- linear growth is initially **rapid**
  - 1st year of life, the growth velocity about 25cm at 50th centile
  - in 2nd year of life, the growth velocity about 12cm at 50th centile

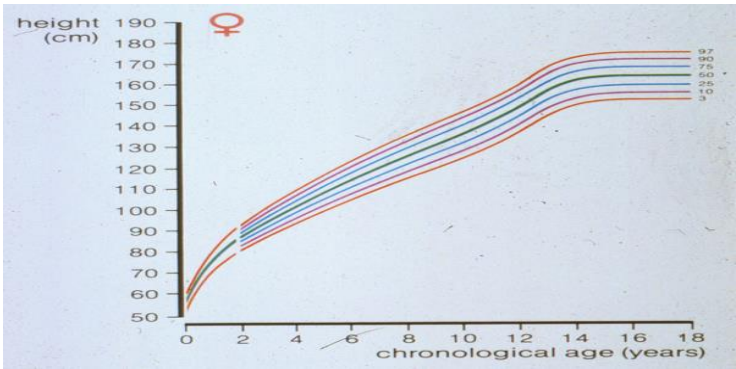
Note:
The major regulating influence of growth, in this phase, is the **nutritional status.(Growth hormone: effect after age of 1 year){This information appears many times in exams}**
In pre-term infant, the growth velocity may be higher than full-term due to high catch-up growth.

-Small for gestational age: > 90% will catch up with normal parameters during first 2 years
-Crossing centiles in the first 2 years of life in order to match genetics is normal

Growth in childhood

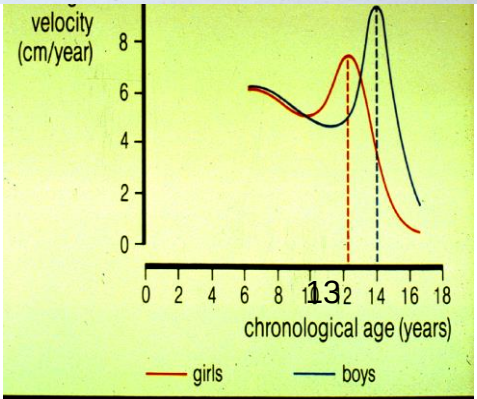
- Nutrition becomes less important
- Hormonal influences
  - ✓ Growth hormone (GH)
  - ✓ Insulin-like growth factor (IGF) axis,
  - ✓ Thyroid status is also a requisite for normal growth.
- Height velocity ranges between 4 and 8 cm/year





Growth in puberty

Growth changes dramatically
- Adolescent growth spurt (AGS)



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- ✓ caused by↑ androgen and estrogen, Which result in ↑↑ GH secretion
- ✓ During this stage can observe the difference of Growth velocity between male and female
- ✓ Average difference in height between males and females: 12 – 14 cm.
- ✓ Growth spurt hormones: estrogen and testosterone.
- ✓ Aromatase enzyme converts testosterone to estrogen. Its deficiency results in tall stature. The taller than expected height occurs because estrogen normally causes fusion of the epiphyseal growth plates in the bones, and in its absence, the girl will keep growing longer.

Tanner staging:

Definition of puberty is a time of physiological development between childhood and adult life which characterized by the beginning of **gametogenesis**, **secretion of gonadal hormones**, **development of secondary sexual characters**, and **reproductive functions**

- Puberty is divided into **five stages**, called Tanner Stages
- Represents the development of breast and pubic hair growth in <u>female</u> OR the development of genitalia and pubic hair growth in <u>males.</u>

Breast development in females

- Stage I : no breast enlargement
- Stage II: Beginning of puberty, Breast bud form with, small area of surrounding glandular tissue; areola begins to widen
- Stage III: Breast begins to become more elevated, and extends beyond the borders of the areola, which continues to widen but remains in contour with surrounding breast**. (mid puberty)**
- Stage IV:increased breast size and elevation; areola and papilla form a secondary mound projecting from the contour of the surrounding breast.(Advanced puberty)
- Stage V: full-pubertal , breast reaches final adult size

Pubic hair Growth in females

- Stage I: Prepubertal, No pubic hair at all
- Stage II: Beginning of puberty, small amount of long, downy hair with slight pigmentation along labia majora
- Stage III: Hair becomes more coarse and curly, and begins to extend laterally and across pubis
- Stage IV: extending across pubis but sparing medial thighs
- Stage V: adult hair quality, with extension to medial surface of the thighs.

Gonads growth in males

- Stage I:Prepubertal, testes smaller than 4 ml or long axis <2.5 cm
- Stage II: Beginning of puberty, testes size < 4 ml or long axis 2.5 to 3.2 cm
- Stage III: Testes size 12 ml or long axis 3.6 cm and further increased length (mainly) of penis
- Stage IV: Testes length 4.1 to 4.5 cm, further increased breadth (mainly) of penis, scrotum enlarges further and darkens.

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- Stage V: Full-puberty, mature genital size, testes size 25 ml or long axis >4.5 cm

Pubic hair growth in males

- Stage I: Prepubertal, No pubic hair at all.
- Stage II: Beginning of puberty, small amount of long, downy hair with slight pigmentation at the base of penis and scrotal.
- Stage III: Hair becomes more coarse and curly, and begins to extend laterally and across pubis.
- Stage IV: adult-like hair quality, extending across pubis but sparing medial thighs
- Stage V: adult hair quality, with extension to medial surface of the thighs

Notes:

- ✓ Age to start puberty in females is 11 years. If before 8 years it is a warning!
- ✓ If no signs of puberty in females (breast budding) at age of 13: delay.
- ✓ Age to start puberty in males is 11.5 years. If before age of 10 years it is a warning.
- ✓ If no signs of puberty in males (testicular enlargement) at age of 14: delay.
- ✓ 1st signs of puberty: breast enlargement in females and testicle enlargement in males.
  Orchidometer: is a medical instrument used to measure the volume of the testicles.
- ✓ Testicular enlargement starts at volume of 4 ml.
- ✓ For bone age assessment we use X-ray of left wrist and hand.

Done by: Mohannad abohamad

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Developmental milestones

GROSS MOTOR by: Rema Jundi

1) HEAD LAG

- 3 m → head lag partially compensated with bobbing
- 4 m → no head lag

2) SITTING

- 4-5 m → sits with trunkal support
- 7m → sits with pelvic support
- 8 m → sits without support , rounded back
- 9 m → sits without support, straight back

3) VERTICAL SUSPENSION

- Normal
- Or hypotonic (slips)
- Or Hypertonic (scissoring of legs)

4) VENTRAL SUSPENSION

- 1 m → head below plane of the body
- 6wk – 2m → head with plane of the body
- 3 m → head above plane of the body

C-shaped → truncal hypotonia

5) PRONE

- At birth → head side to side, flexed body
- 1 m → lifts chin up , lefts head momentarily , legs more extended
- 2 m → lifts head 15°
- 3 m → lifts head & chest with arms extended & outstretched , head above body plane
- 4 m → .....head vertical
- 5-6 m → rolls over from prone to supine
- 6-7 m → rolls over from supine to prone
- 8 m → creeps
- 9 m → crawls

6) SUPINE

- At birth → flexed
- 1,2,3 m → tonic neck posture
- 4 m → symmetric posture , hands in midline
- 6-7 m → rolls over ,lifts head

7) STANDING & WALKING

- 4 m → supports some weight , pushes with feet
- 7 m → supports most of the weight, bounces
- 9 m → pulls to stand
- 10m → cruises
- 1 yr → stands alone, walks with hand held or alone unsteadily
- 15 m → walks alone well , crawls upstairs
- 1.5yr→ runs stiffly , climbs upstairs with one hand held , sits on small chair
- 2 yr → runs well , goes upstairs & downstairs one step at a time , jumps
- 2.5yr → upstairs alternating
- 3 yr → pedals a tricycle , stands momentarily on one foot
- 4 yr → hops , stands on one foot for a longer time
- 5 yr → skips

FINE MOTOR

- < 3 m → hands closed
- 3 m → opens hands spontaneously (hands open >90% of time) , reaches & misses
- 4 m →hands in midline, reaches & grasps , brings objects to mouth
- 5 m → brings objects to mouth
- 6 m → transfers from hand to hand
- 9 m → pincer grasp
- 1 yr → releases objects on command, drinks from a cup, turns pages of a book
- 1.5yr→ eats with spoon with missing
- 2 yr → eats with spoon without missing

Cubes

- 15 m → 3
- 18 m → 4
- 2 yr → 6
- 2.5yr→9
- 3 yr → 10

Drawing

- 15 m → scribbling , vertical lines
- 2 yr → circular scribbling , horizontal lines
- 3 yr → copies a circle
- 4 yr → copies square , cross
- 5 yr → copies triangle

5 <u>yrs → Ties shoes</u>

LANGUAGE

- 3 m → coos
- 4 m →laughs
- 6 m → Babbles (ba,ma,da)
- 9 m → mama , dada (not specifically)
- 1 yr → mama, dada (specifically) PLUS 3 words
- 15 m → 6 words, responds to name , follows a simple command, jargons
- 1.5 yr → 10 words, tells body parts when pointed to
- 20 m → 20 words
- 2 yrs → (2-3)-word sentence
- 2.5 yr → refers to self using "I", knows full name , listens to a story
- 3 yr → knows age & sex , counts 3 objects, repeats 6-word sentence or 3 numbers
- 4 yr → counts to 4 , tells s story
- 5 yr → names 4 colors, repeats 10-word sentence, prints name

SOCIAL

- 1 m → prefers human face
- 2 m → social smile to anyone, listens to voice
- 3 m → social smile to known ppl , listens to music
- 4 m →laughs outloud, excited at sight of food
- 6 m → laughs to strangers
- 7 m → shows likes & dislikes, prefers mother, enjoys mirror
- 9 m → plays peek-a-poo & pat-a-cake
- 10 m → waves bye-bye
- 1 yr → plays simple ball game, adjusts to dressing
- 15 m → hugs parents, shows needs by pointing ,
- 1.5 yr → kisses parents , seeks help , complains when wet , plays alone symbolically
- 2 yr → listens to stories, helps undress , plays with clay
- 2.5 yr → pretends in play, helps putting things away
- 3 yr → plays with others , helps in dressing (unbuttons clothing, puts on shoes), washes hands
- 4 yr → goes to toilet alone, brushes teeth
- 5 yr →Understands rules, dresses & undresses , asks qs about meaning of words, engages in domestic-role playing

Table 10-2	Emerging Patterns of Behavior During the 1st Yr of Life*
NEONATAL PERIOD (1ST 4 WK)	
Prone:	Lies in flexed attitude; turns head from side to side; head sags on ventral suspension
Supine:	Generally flexed and a little stiff
Visual:	May fixate face on light in line of vision; "doll's-eye" movement of eyes on turning of the body
Reflex:	Moro response active; stepping and placing reflexes; grasp reflex active
Social:	Visual preference for human face
AT 1 MO	
Prone:	Legs more extended; holds chin up; turns head; head lifted momentarily to plane of body on ventral suspension
Supine:	Tonic neck posture predominates; supple and relaxed; head lags when pulled to sitting position
Visual:	Watches person; follows moving object
Social:	Body movements in cadence with voice of other in social contact; beginning to smile
AT 2 MO	
Prone:	Raises head slightly farther; head sustained in plane of body on ventral suspension
Supine:	Tonic neck posture predominates; head lags when pulled to sitting position
Visual:	Follows moving object 180 degrees
Social:	Smiles on social contact; listens to voice and coos
AT 3 MO	
Prone:	Lifts head and chest with arms extended; head above plane of body on ventral suspension
Supine:	Tonic neck posture predominates; reaches toward and misses objects; waves at toy
Sitting:	Head lag partially compensated when pulled to sitting position; early head control with bobbing motion; back rounded
Reflex:	Typical Moro response has not persisted; makes defensive movements or selective withdrawal reactions
Social:	Sustained social contact; listens to music; says "aah, ngah"

AT 4 MO	
Prone:	Lifts head and chest, with head in approximately vertical axis; legs extended
Supine:	Symmetric posture predominates, hands in midline; reaches and grasps objects and brings them to mouth
Sitting:	No head lag when pulled to sitting position; head steady, tipped forward; enjoys sitting with full truncal support
Standing:	When held erect, pushes with feet
Adaptive:	Sees raisin, but makes no move to reach for it
Social:	Laughs out loud; may show displeasure if social contact is broken; excited at sight of food
AT 7 MO	
Prone:	Rolls over; pivots; crawls or creep-crawls (Knobloch)
Supine:	Lifts head; rolls over; squirms
Sitting:	Sits briefly, with support of pelvis; leans forward on hands; back rounded
Standing:	May support most of weight; bounces actively
Adaptive:	Reaches out for and grasps large object; transfers objects from hand to hand; grasp uses radial palm; rakes at raisin
Language:	Forms polysyllabic vowel sounds
Social:	Prefers mother; babbles; enjoys mirror; responds to changes in emotional content of social contact
AT 10 MO	
Sitting:	Sits up alone and indefinitely without support, with back straight
Standing:	Pulls to standing position; “cruises” or walks holding on to furniture
Motor:	Creeps or crawls
Adaptive:	Grasps objects with thumb and forefinger; pokes at things with forefinger; picks up pellet with assisted pincer movement; uncovers hidden toy; attempts to retrieve dropped object; releases object grasped by other person
Language:	Repetitive consonant sounds (“mama,” “dada”)
Social:	Responds to sound of name; plays peek-a-boo or pat-a-cake; waves bye-bye
AT 1 YR	
Motor:	Walks with one hand held; rises independently, takes several steps (Knobloch)
Adaptive:	Picks up raisin with unassisted pincer movement of forefinger and thumb; releases object to other person on request or gesture
Language:	Says a few words besides “mama,” “dada”
Social:	Plays simple ball game; makes postural adjustment to dressing

15 MO	
Motor:	Walks alone; crawls up stairs
Adaptive:	Makes tower of 3 cubes; makes a line with crayon; inserts raisin in bottle
Language:	Jargon; follows simple commands; may name a familiar object (e.g., ball); responds to his/her name
Social:	Indicates some desires or needs by pointing; hugs parents
18 MO	
Motor:	Runs stiffly; sits on small chair; walks up stairs with 1 hand held; explores drawers and wastebaskets
Adaptive:	Makes tower of 4 cubes; imitates scribbling; imitates vertical stroke; dumps raisin from bottle
Language:	10 words (average); names pictures; identifies 1 or more parts of body
Social:	Feeds self; seeks help when in trouble; may complain when wet or soiled; kisses parent with pucker
24 MO	
Motor:	Runs well, walks up and down stairs, 1 step at a time; opens doors; climbs on furniture; jumps
Adaptive:	Makes tower of 7 cubes (6 at 21 mo); scribbles in circular pattern; imitates horizontal stroke; folds paper once imitatively
Language:	Puts 3 words together (subject, verb, object)
Social:	Handles spoon well; often tells about immediate experiences; helps to undress; listens to stories when shown pictures

30 MO	
Motor:	Goes up stairs alternating feet
Adaptive:	Makes tower of 9 cubes; makes vertical and horizontal strokes, but generally will not join them to make cross; imitates circular stroke, forming closed figure
Language:	Refers to self by pronoun "I"; knows full name
Social:	Helps put things away; pretends in play
36 MO	
Motor:	Rides tricycle; stands momentarily on 1 foot
Adaptive:	Makes tower of 10 cubes; imitates construction of "bridge" of 3 cubes; copies circle; imitates cross
Language:	Knows age and sex; counts 3 objects correctly; repeats 3 numbers or a sentence of 6 syllables; most of speech intelligible to strangers
Social:	Plays simple games (in "parallel" with other children); helps in dressing (unbuttons clothing and puts on shoes); washes hands
48 MO	
Motor:	Hops on 1 foot; throws ball overhand; uses scissors to cut out pictures; climbs well
Adaptive:	Copies bridge from model; imitates construction of "gate" of 5 cubes; copies cross and square; draws man with 2-4 parts besides head; identifies longer of 2 lines
Language:	Counts 4 pennies accurately; tells story
Social:	Plays with several children, with beginning of social interaction and role-playing; goes to toilet alone

60 MO	
Motor:	Skips
Adaptive:	Draws triangle from copy; names heavier of 2 weights
Language:	Names 4 colors; repeats sentence of 10 syllables; counts 10 pennies correctly
Social:	Dresses and undresses; asks questions about meaning of words; engages in domestic role-playing

*Data derived from those of Gesell (as revised by Knobloch), Shirley, Provence, Wolf, Bailey, and others. After 6 yr, the Wechsler Intelligence Scales for Children (WISC-IV) and other scales offer the most precise estimates of developmental level. To have their greatest value, they should be administered only by an experienced and qualified person.

Fluid management

Our journey today is in fluid management and how to deal with this subject in emergency room or in the floor, so consider yourself today a resident in JUH, It is also a very good idea to do the calculations with your residents for the patients, it is an easy subject but needs some practice.

We start with this equation :

$$\text{Calculated serum osmolarity}$$
$$2 \times [Na^+](meq/L) + \frac{\text{Glucose}\,(mg/dL)}{18} + \frac{\text{BUN}\,(mg/dL)}{2.8}$$

From this equation Note that Sodium is the main determinant of plasma osmolarity .

In The emergency room:

If patient is shocked or in severe dehydration → give **0.9% normal saline** in a dose **((20ml/Kg)) push** over 10 minutes.

You can repeat the push for 3 times then if failed give inotropes

If inotrope also fails you have to think in adrenal crisis and you can give corticosteroids

In hypoglycemic patients we give 10% dextrose water in dose (2ml/kg) push over 10 minutes

Before we go to the floor and calculate the maintenance and deficit for the patient you have first to know about the types of fluid that are available in our hospital ☺
In maintenance and deficit we give Glucose saline solution (Remember : we use 0.9% normal saline in the emergency room)

Types of fluids

0.9% G.S (Glucose saline) → have 154 meq/L of sodium
0.45 % G.S → have 77 meq/L of sodium
0.18% G.S → have 30 meq/L of sodium

Please notice that we do not use ringer lactate in any situation for Pediatrics

Now how to calculate Maintenance?

For fluids: First 10 Kg → 100 ml/Kg
Second 10 Kg → 50 ml/Kg
The rest Kg → 20 ml/Kg

For Sodium : 2-3 meq/Kg

For potassium : 1-2 meq/Kg

e.g.: a 25 Kg child, Calculate the maintenance for him?

Fluids: first 10 Kg → 1000 ml
second 10 Kg → 500 ml
the last 5 Kg → 100 ml (5*20)

Total Fluid: 1600 ml

Sodium: 3*25 = 75 meq

Potassium: 2*25= 50 meq

Now which fluid type to choose?

We look for the calculated sodium (75 meq) because the sodium is the main determinant of osmolarity as we said earlier , Then we think the closest fluid for this value is 0.45% Glucose saline as it contains 77 meq.

Rule if you want to choose fluid for maintenance without deficit
if the patient is < 14 Kg → Give 0.18% G.S
If the patient is > 14 Kg → Give 0.45% G.S

Now, as a resident in the hospital, How to write the order for the nurse in patient's sheet ?

Give 800 ml (Half of the 1600) of 0.45% G.S in the first 8 hours then repeat another 800 ml of 0.45% G.S over the next 16 Hours.
And give 50 ml KCl if the patient is passing urine.

Exercise: Patient, 18 Kg, Calculate the maintenance and write the proper order for the nurse.

Now we want to move to the deficit, but before that we have to remember that
In mild dehydration → patient lost 5%
In moderate dehydration → patient lost 7%
In severe dehydration → Patient lost 10%

How to calculate the deficit?

Fluids = Weight *the percentage of dehydration (5/7/10)*10

Sodium = Weight * the percentage of dehydration (5/7/10)

e.g : 3 year old male, 20Kg , came to the ER with acute gastroenteritis, on physical examination the patient have altered level of consciousness and he is hypotensive.
After you have dealt with patient in the ER and give him the proper, please write to your nurse the proper order for maintenance and deficit.

First notice that the patient is in severe dehydration → he lost 10% of his Weight

Maintenance:

Fluid: First 10 Kg → 1000 ml
second 10 Kg → 500 ml

Sodium: 3*20= 60 meq

Potassium:2*20= 40 meq

Deficit:

Fluid: 10*20*10 = 2000ml

Sodium = 20*10 = 200 meq

Total need:

Fluid = 1500+2000 = 3500 ml

Sodium 200+60=260 meq

Potassium = 40 meq

*هذا الجزء من حل السؤال على الاغلب كافي جدا لحل أسئلة الامتحان المتعلقة بهذا الموضوع وما تبقى استزادة لمن أحب قراءتها .

نكمل موضوعنا ..
يوجد هنا مشكلة دائماً في حسابات Maintenance & deficit في اختيار المحلول المناسب لانه لا يوجد محلول من المحاليل الثلاث الذي ذكرناها سابقا (0.45%,0.9%,0.18%) يستطيع أن يغطي الحاجة الكاملة للمريض وهي (260meq) في سؤالنا هذا وبالتالي نلجأ بهذه الحالة لصنع محلول خاص مكون من سكر وملح بالتراكيز المطلوبة .. كيف يتم ذلك ؟؟

1- نحضر محلول (Hypertonic saline 3%) وهذا المحلول تركيزه ((1000ml contains 512meq Na))
2- نحسب حاجتنا منه (260 meq) عن طريق الضرب التبادلي :

1000 ml ⟶ 512 meq
X ⟶ 260 meq
X= 508 ml (we need 508 ml of hypertonic saline 3% to cover the 260 meq of sodium)

3- هكذا نكون قد انهينا تحضير جزء الملح من المحلول وبقي جزء السكر منه ، وبالتالي نحتاج ل 5% dextrose لكن كم نحتاج منه ؟
نحن بالأساس نحتاج ل 3500 كسائل ككل واخذنا منهم 508 كملح وبالتالي الباقي سيكون هو السكر وبالتالي نحتاج من السكر 2992 مل .
4- بقي الخطوة الأخيرة وهو ماذا سنكتب للممرضة ؟

Give 254ml (half of the 508) 3% hypertonic saline and 1496ml (half of the 2992) 5%dextrose in the first 8 hours , then repeat in the next 16 hours
And give 40 ml KCl if the patient is passing urine .

Done by: Mohannad abohamad

Management of acute Gastroenteritis

- ✓ In Gastroenteritis we worry about dehydration.
- ✓ Dehydration means negative fluid balance.
- ✓ Dehydration causes major complications in CVS and neurological system
- ✓ Other complications are metabolic acidosis and electrolyte imbalance
- ✓ Hypokalemia → most dangerous consequence is diaphragmatic paralysis
- ✓ It may cause cardiac arrhythmia.
- ✓ Hypo and hypernatremia correction may cause cerebral edema.
- ✓ Chronic gastroenteritis is more dangerous than acute gastroenteritis because it leads to more malnutrition → more immune deficiency → Infections → Vicious cycle.
- ✓ Mild dehydration: Loss of 5% of body weight or NO clinical dehydration.
- ✓ Moderate dehydration: Loss of 7% of body weight or 2 signs of dehydration.
- ✓ Severe dehydration: Loss of 10% of body weight or 2 signs of dehydration + circulatory compromise.
- ✓ The most reliable sign of dehydration is the **general condition of the patient.**
  -Moderate dehydration → Irritable
  -Severe dehydration → Lethargic, comatose

Management of dehydration:

- ✓ In mild dehydration
  NO fluids given, just extra fluid and extra food
- ✓ In moderate dehydration
  -we give the **patient Oral rehydration solution (ORS)**
  -ORS contains of Anions : 80 Cl^- ,30 HCO_3^-
  Cations : 90 Na^+, 20 K^+
  Non Ionized : 110 Glucose
  } Per 1 L
  -The glucose is put for active transport of Ions rather than a nutrition source.
  -In a 10 Kg child with moderate dehydration we give 3 cups (each one is 250 ml) within 4 hours (The child has lost 750 ml of his weight (7% * 10Kg)) then tell the mom to feed him normally and give him/her 50 ml of ORS when passing stool.
- ✓ Dehydration should be corrected in **4 hours**
- ✓ Severe dehydration: ICU admission and IV fluids (to know the details of fluids please refer to the Fluids management sheet).
- ✓ Normally we do not do any investigation and do not give any antibiotics unless the patient passed bloody stool or the patient is very sick.

Remember Signs of dehydration :
Dry mucus membranes.
Pallor
Skin turgor at sternum
Capillary refill
Sunken eyes
Anterior fontanel depression
Crying without tears
Decrease urine output

Notes by Dr. محمد الرواشدة:

- ✓ **Baby should be put in the breast immediately after delivery**
- ✓ **On 17th week in utero the baby starts sucking**
- ✓ **Weaning starts when we put any type of food rather than breast milk**
- ✓ **Baby should be exclusively in breastfeeding in the first 6 months**
- ✓ **Majority of women can do breast feeding but just 26% of them continue until 6 months**
- ✓ **Contraindications for breastfeeding are:**
  Drugs (Radiations, Ergot, antiepileptics, Lithium)
  Active TB
  Hepatitis B

    - ✓ **AIDS is NOT contraindication of breastfeeding**

    - ✓ **After the first 6 months start give the baby (رز مطحون وفواكه وخضروات),but just give the baby one type of food every 3-4 days to know if there is any food allergy**

Done by: Mohannad abohamad

Poisoning in children

Introduction

Most poisonings are dose-related. Dose is determined by concentration over time. Toxicity may result from exposure to excess amounts of normally nontoxic substances. Some poisonings result from exposure to substances that are poisonous at all doses. Poisoning is distinguished from hypersensitivity and idiosyncratic reactions, which are unpredictable and not dose-related, and from intolerance, which is a toxic reaction to a usually nontoxic dose of a substance. Poisoning is commonly due to ingestion but can result from injection, inhalation, or exposure of body surfaces (e.g., skin, eye, mucous membranes). Many commonly ingested nonfood substances are generally nontoxic however; almost any substance can be toxic if ingested in excessive amounts. The majority of poisonings are accidental, especially in the under-5 age group, although intentional overdoses and substance abuse are seen in older children. Rarely, children present with symptoms as a result of deliberate administration of compounds by adults. Deaths in children from poisoning are becoming increasingly rare with only two deaths reported in 2006 and a decline in mortality rates of ~85% since 1976. Factors responsible for this decline include the introduction of child-resistant containers, reducing the pack sizes of aspirin and acetaminophen, and more effective management and the support provided by the National Poisons Information Service (NPIS).

Developmental consideration

Pediatric patients may be particularly vulnerable to certain toxins at specific stages of childhood. Breast fed infants may be exposed to drugs or toxins excreted in breast milk; neonates have immature metabolic capabilities, and toddlers, as they develop exploratory hand-to-mouth activity, may be exposed to a wide range of potential hazards.

Physical consideration

As physiology evolves from infancy to adulthood, there are many age-related changes in vital signs. Infants have a limited ability to increase stroke volume and therefore their cardiac output is primarily dependent on heart rate. They also have a limited ability to recruit alveoli and rely heavily on ventilatory frequency to vary their minute ventilation

Initial Assessment and Management

The initial priority in treating poisoned children is the standard ABC (airway, breathing, and circulation) resuscitation approach.

A: Assess airway patency by looking, listening, and feeling for air movement. If there is no air movement, try to open the airway with simple maneuvers such as the jaw thrust or the use of airway adjuncts. Certain ingested agents may predispose to airway oedema and obstruction, including caustic agents, angiotensin-converting enzyme inhibitors, and plants containing calcium oxalate crystals (e.g. *Dieffenbachia* and*Philodendron* houseplants).

B: Assess the adequacy of breathing by observing ventilatory frequency, use of accessory muscles, breath sounds, and oxygen saturations. Reduced respiratory effort may require bag-valve-mask ventilation until a definitive airway can be secured. It is important to remember that succinylcholine may cause prolonged block in children who have a reduced cholinesterase concentration due to exposure to cocaine or organophosphate compounds: prolonged apnoeas of up to 7 h have been described.[4]

C: Assess the circulation in terms of cardiovascular status (heart rate, arterial pressure, and capillary refill) and the effect of circulatory inadequacy on other organs (mental state, urine output, skin temperature, and colour). Hypotension should initially be treated with a 20 ml kg^{-1} crystalloid bolus, remembering that if it is caused by specific toxins such as β-blockers, the specific antidote should also be given, for example, glucagon. If the arterial pressure remains resistant to therapy, adequate filling must be ensured in conjunction with the judicious use of inotropic or vasopressor support. However, the use of inotropes may worsen cardiovascular toxicity and should first be discussed with a clinical toxicologist.Arrhythmias associated with poisoning are best treated by correcting precipitating factors (e.g. hyperkalaemia and acidosis) and by administering the appropriate antidote; antiarrhythmics may be pro-arrhythmic and negatively inotropic and make the situation worse.Children in cardiac arrest should be treated according to standard guidelines (e.g. The Advanced Cardiac Life Support protocol), although it is important to address the need for a specific antidote, for example, sodium bicarbonate for tricyclic antidepressant (TCA) poisoning.

D: Assess neurological function in terms of:

- level of consciousness using the Alert-Voice-Pain-Unconscious score or the Glasgow coma scale;
- pupillary size and reaction;
- posture and the presence of any seizure activity;

- bedside blood glucose concentration

Diagnostic Testing

All children with features of toxicity should have measurement of serum electrolytes, renal and hepatic function, blood glucose, and an assessment of acid-base balance from venous or arterial blood gas analysis.

Plasma drug concentrations are not routinely helpful with the exception of acetaminophen, salicylate, iron, lithium, digoxin, theophylline, ethylene glycol, methanol, carboxyhaemoglobin (COHb), methaemoglobin, and the anticonvulsants.

Pharmacological Manipulation

Gastric decontamination

In asymptomatic children with non-toxic ingestions, no decontamination is necessary. However, if the ingestion is recent, the child is symptomatic, or the toxin may cause delayed toxicity, then gastrointestinal (GI) decontamination is recommended.

Activated charcoal (AC) is the safest mode and is probably effective at reducing the amount of drug absorbed into the bloodstream.

Gastric lavage is usually reserved for children who present within 1 h of ingesting a potentially life-threatening poison. It is often difficult to remove the toxic agent from the GI tract because of the small size of lavage tube needed in paediatric patients, and the child will often need to be intubated to facilitate this technique. It is contraindicated in poisonings by most hydrocarbons, acids, and alkalis.

Antidote

An antidote is an agent used to neutralize or counteract the effects of a poison. They should not be used indiscriminately in patients with unknown poisonings because this complicates the clinical situation, and there may be adverse reactions to their administration.

Enhanced Elimination

Several methods exist to increase the elimination of toxins and their metabolites. Urinary alkalinization by the administration of sodium bicarbonate effectively increases the elimination of drugs with a low pKa such as salicylates and

chlorpropamide. Alkalinization increases the ionized fraction of the drug in the tubular lumen, preventing its reabsorption.

In nelson essential there are several tables about the symptoms of specific poisons and the antidotes, in addition, you will study poisoning in details in toxicology.

Sources: Merck manual and medscape.

Mohannad Abohamad

Iron Poisoning	

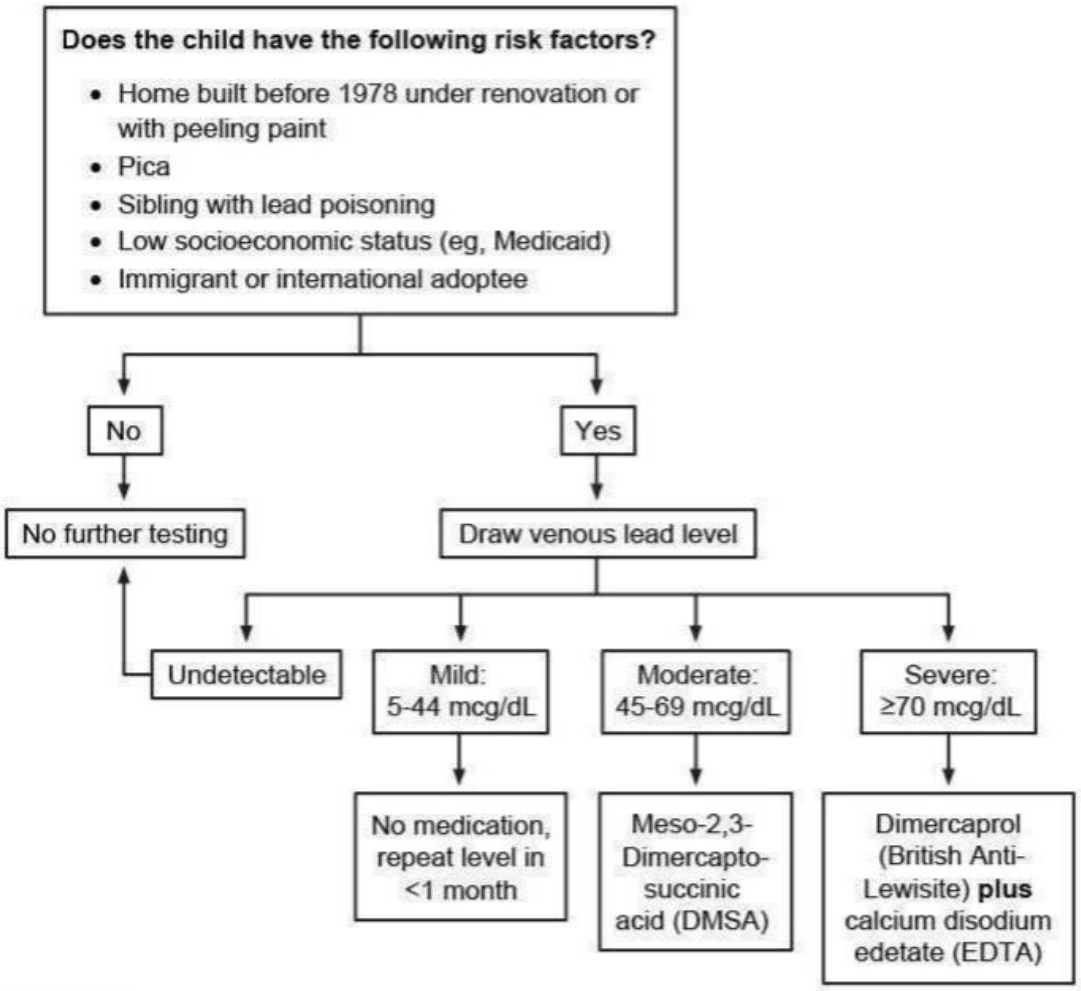
Clinical features	• Within 30 minutes to 4 days:
	  • Abdominal pain
	  • Vomiting (eg, hematemesis)
	  • Diarrhea (eg, melena)
	  • Hypotensive shock
	  • Metabolic acidosis
	• Within 2 days: hepatic necrosis
	• Within 2-8 weeks: pyloric stenosis

Diagnostic findings	• Anion gap metabolic acidosis • Radiopaque pills
Treatment	• Whole bowel irrigation • Deferoxamine • Supportive care for circulation, airway and breathing

Stages of Iron Poisoning

Stage	Time Postingestion	Description
1	Within 6 h	Vomiting, hematemesis, explosive diarrhea, irritability, abdominal pain, lethargy If toxicity is severe, tachypnea, tachycardia, hypotension, coma, metabolic acidosis
2	Within 6–48 h	Up to 24 h of apparent improvement (latent period)
3	12–48 h	Shock, seizures, fever, coagulopathy, metabolic acidosis
4	2–5 days	Liver failure, jaundice, coagulopathy, hypoglycemia
5	2–5 wk	Gastric outlet or duodenal obstruction secondary to scarring

Approach to childhood lead poisoning



Anatomy and physiology of the respiratory system

ANATOMY

Air enters the **nose** and passes over the large surface area of the **nasal turbinates**, which warm, humidify, and filter the inspired air. Secretions draining from the paranasal sinuses are carried to the **pharynx** by the mucociliary action of the ciliated respiratory epithelium. Lymphoid tissue can obstruct airflow through the nasopharynx (adenoids) or the posterior pharynx (tonsils).

The **epiglottis** protects the larynx during swallowing by deflecting material toward the esophagus. The **arytenoid cartilages**, which assist in opening and closing the glottis, are less prominent in children than in adults. The opening formed by the vocal cords (the **glottis**) is V-shaped, with the apex of the V being anterior. Below the vocal cords, the walls of the **subglottic space** converge toward the **cricoid** portion of the trachea.

In children under 3 years of age, the cricoid ring is the narrowest portion of the airway, whereas in older children and adults it is the glottis. C-shaped cartilage, extending approximately 320° around the airway circumference, supports the **trachea** and mainstem **bronchi**. The posterior wall of the trachea is membranous. Beyond the lobar bronchi, the cartilaginous support for the airways becomes discontinuous. The right lung has three lobes (upper, middle, lower) and comprises approximately 55% of the total lung volume. The left lung has two lobes (upper, lower). The inferior division of the left upper lobe, the lingula, is analogous to the right middle lobe.

The pediatric lung has tremendous capacity for growth. A full-term infant has approximately 25 million alveoli; an adult nearly 300 million alveoli. The growth of new alveoli occurs during the first 2 years of life and is complete by 8 years of age. After this time, lung volume increases primarily by increase in alveolar dimensions, with new alveoli rarely formed.

PULMONARY PHYSIOLOGY

Pulmonary Mechanics

The major function of the lungs is to **exchange oxygen** (O_2) and **carbon dioxide** (CO_2) between the atmosphere and the blood. The anatomy of the airways, mechanics of the respiratory muscles and rib cage, nature of the alveolar-capillary interface, pulmonary circulation, tissue metabolism, and neuromuscular control of ventilation all influence gas exchange.

Air enters the lungs when intrathoracic pressure is less than atmospheric pressure. During inspiration, negative intrathoracic pressure is generated by contraction and lowering of the **diaphragm**. The accessory muscles of inspiration (**external intercostal**, **scalene**, and **sternocleidomastoid muscles**) are not used during quiet breathing but are recruited during exercise or in disease states to raise and enlarge

the rib cage. Exhalation is normally passive, but with active exhalation, the **abdominal** and **internal intercostal muscles** are recruited.
During normal breathing at rest, lung volumes are usually in the mid-range of inflation.

Tidal volume (TV) is the amount of air inspired with each *relaxed* breath.
The volume of gas retained in the lung at the end of a *relaxed* exhalation is the **functional residual capacity (FRC)**. This gas volume maintains exchange of O2 during exhalation. **Total lung capacity (TLC)** is the volume of gas in the lungs at the end of *maximal* inhalation and **residual volume (RV)** is the volume of gas left in the lungs at the end of a *maximal* exhalation.

Vital capacity (VC) is the maximal amount of air that can be expelled from the lungs and is the difference between TLC and RV. **Airway resistance** is influenced by the diameter and length of the conducting airways, the viscosity of gas, and the nature of the airflow. During quiet breathing, airflow in the smaller airways may be laminar (streamlined), and resistance is inversely proportional to the fourth power of the radius of the airway. At higher flow rates, turbulent flow, especially in the larger airways, increases resistance. Relatively small changes in airway diameter can result in large changes in airway resistance.

Excessive airway secretions, bronchospasm, mucosal edema and inflammation, airway stenosis, foreign bodies, loss of airway wall integrity (as with bronchiectasis), and airway compression may all produce symptomatic increases in airway resistance. In pediatrics, laryngomalacia and croup are very common causes of increased upper airway resistance; whereas asthma, bronchiolitis and cystic fibrosis (CF) are among the most common causes of increased lower airway resistance.

Lung compliance (change in volume for a given change in Pressure) is a measure of the ease with which the lung can be inflated. Processes that decrease lung compliance (surfactant deficiency, pulmonary fibrosis, and pulmonary edema) may lead to decreases in measured lung volumes. Restrictive lung diseases are characterized by normal to low FRC and RV, low TLC and VC, decreased lung compliance, and relatively normal flow rates. Restrictive lung disease can result from neuromuscular weakness, an alveolar filling process (lobar pneumonia, pulmonary edema), pleural disease (pleural effusion, inflammation, or mass), thoracic narrowing/stiffness (scoliosis, severe pectus excavatum), and abdominal distention.

Respiratory Gas Exchange

Alveolar ventilation is defined as the exchange of carbon dioxide between the alveoli and external environment. Normally, about 30% of each tidal breath fills the conducting (non–gas-exchanging) airways (**anatomic dead space**). Because the anatomic dead space is relatively constant, increasing the tidal volume may increase the efficacy of ventilation.

Conversely, if tidal volume decreases, then the dead space/tidal volume ratio increases, and alveolar ventilation decreases.
Gas exchange depends on **alveolar ventilation**, **pulmonary capillary blood flow**, and the **diffusion** of gases across the alveolar-capillary membrane. Exchange of CO2 is determined by alveolar ventilation, whereas the exchange of O2 is influenced primarily by the regional matching of ventilation (V) with pulmonary blood flow (Q) (V/Q matching). V/Q matching is maintained, in part, by **hypoxic pulmonary vasoconstriction** (local constriction of the pulmonary vessels in areas that are hypoventilated). There are five causes of **hypoxemia**. Disorders resulting in **V/Q mismatching** (such as pneumonia and atelectasis) are the most common causes of hypoxemia.

Lung Defense Mechanisms

The lungs are constantly exposed to particles and infectious agents. The **nose** is the primary filter for large particles. The **ciliated epithelium** of the paranasal sinuses and nasal turbinates move filtered particles toward the pharynx. Particles less than 10 µm in diameter may reach the trachea and bronchi and deposit on the mucosa. Particles less than 1 µm may reach the alveoli. Ciliated cells lining the airways from the larynx to the bronchioles continuously propel a thin layer of mucus toward the mouth. **Alveolar macrophages** and **polymorphonuclear cells** engulf particles and pathogens that have been opsonized by locally secreted IgA antibodies or transudated serum antibodies.

Cough, important in protecting the lungs, is a forceful expiration that can clear the airways of debris and secretions. Cough may be voluntary or generated by reflex irritation of the nose, sinus, pharynx, larynx, trachea, bronchi, or bronchioles. Effective cough requires the ability to (1) inhale to near total lung capacity, (2) close and open the glottis, and (3) contract abdominal muscles to forcibly exhale. Loss of the ability to cough, as with neuromuscular weakness, results in poor secretion clearance and predisposes to atelectasis and pneumonia.

Source: Nelson essential

Table 133-1 Causes of Hypoxemia

CAUSE	EXAMPLE(S)	Pao_2	$Paco_2$	Pao_2 IMPROVES WITH SUPPLEMENTAL OXYGEN
Ventilation-perfusion mismatch	Asthma Bronchopulmonary dysplasia Pneumonia Atelectasis	↓	Normal, ↓, or ↑	Yes
Hypoventilation	Apnea Narcotic overdose Neuromuscular disease	↓	↑	Yes
Extrapulmonary shunt	Cyanotic heart disease	↓	Normal or ↑	No
Intrapulmonary shunt	Pulmonary arteriovenous malformation Pulmonary edema	↓	Normal or ↑	No
Low FIO_2	High altitude	↓	↓	Yes
Diffusion defect	Scleroderma Hepatopulmonary syndrome Pulmonary fibrosis	↓	Normal	Yes

RESPIRATORY FAILURE

ETIOLOGY

Acute respiratory failure occurs when the pulmonary system is unable to maintain adequate gas exchange to meet metabolic demands. The resulting failure can be classified as hypercarbic
(Paco2 >50 mm Hg in previously healthy children), hypoxemic (Pao2 <60 mm Hg in previously healthy children without an intracardiac shunt), or both. **Hypoxemic respiratory failure** is frequently caused by ventilation-perfusion mismatch (perfusion of lung that is not adequately ventilated) and shunting (deoxygenated blood bypasses ventilated alveoli).

Hypercarbic respiratory failure results from inadequate alveolar ventilation secondary to decreased minute ventilation (tidal volume × respiratory rate) or an increase in dead space ventilation (ventilation of areas receiving no perfusion). Respiratory failure may occur with **acute lung injury (ALI)** or **acute respiratory distress syndrome (ARDS)**. The definitions of these are in the process of revision; however, currently ALI is defined as having the following four clinical features: acute onset, bilateral pulmonary edema, no clinical evidence of elevated left atrial pressure, and a ratio of Pao2 to Fio2 ≤ 300 mm Hg regardless of the level of positive end-expiratory pressure (PEEP). ARDS is a subset of ALI with more severe hypoxemia (Pao2/Fio2 of ≤ 200 mm Hg). These syndromes can be triggered by a variety of insults, including sepsis, pneumonia, shock, burns, or traumatic injury, all resulting in inflammation and increased vascular permeability leading to pulmonary edema. Numerous mediators of inflammation (tumor necrosis factor, interferon-γ, nuclear factor κB, and adhesion molecules) may be involved in the development of ARDS. Surfactant action also may be affected.

EPIDEMIOLOGY

Respiratory failure is frequently caused by bronchiolitis (often caused by respiratory syncytial virus), asthma, pneumonia, upper airway obstruction, and sepsis/ARDS. Respiratory failure requiring mechanical ventilation develops in 7% to 21% of patients hospitalized for respiratory syncytial virus. Asthma is increasing in prevalence and is the most common reason for unplanned hospital admissions in children 3 to 12 years of age in the United States.

Environmental factors (exposure to cigarette smoke) and prior disease characteristics (severity of asthma, exercise intolerance, delayed start of therapy, and previous intensive care unit admissions) affect hospitalization and near-fatal episodes. The mortality rate of asthma for children younger than 19 years of age has increased by nearly 80% since 1980. Deaths are more common in African-American children.

Chronic respiratory failure (with acute exacerbations) is often due to chronic lung disease (bronchopulmonary dysplasia, cystic fibrosis), neurologic or neuromuscular abnormalities, and congenital anomalies.

CLINICAL MANIFESTATIONS

Early signs of hypoxic respiratory failure include **tachypnea and tachycardia** in attempt to improve minute ventilation and cardiac output and to maintain delivery of oxygenated blood to the tissues. Further progression of disease may result in dyspnea, nasal flaring, grunting, use of accessory muscles of respiration, and diaphoresis. Late signs of inadequate oxygen delivery include **cyanosis** and **altered mental status** (initially confusion and agitation).

Signs and symptoms of hypercarbic respiratory failure include attempts to increase minute ventilation (tachypnea and increased depth of breathing) and altered mental status (somnolence).

LABORATORY AND IMAGING STUDIES

A chest radiograph may show evidence of the etiology of respiratory failure. The detection of atelectasis, hyperinflation,infiltrates, or pneumothoraces assists with ongoing management. Diffuse infiltrates or pulmonary edema may suggest ARDS. The chest radiograph may be normal when upper airway obstruction or impaired respiratory controls are the etiology. In patients presenting with stridor or other evidence of upper airway obstruction, a lateral neck film or computed tomography (CT) may delineate anatomic defects.

Direct visualization through flexible bronchoscopy allows identification of dynamic abnormalities of the anatomic airway. Helical CT helps diagnose a pulmonary embolus. **Pulse oximetry** allows noninvasive, continuous assessment of oxygenation but is unable to provide information about ventilation abnormalities. Determination of CO2 levels requires a blood gas measurement (arterial, venous, or capillary). An **arterial blood gas** allows measurement of CO2 levels and analysis of the severity of oxygenation defect through calculation of an alveolar-arterial oxygen difference. A normal Pco2 in a patient who is hyperventilating should heighten concern about the risk of further deterioration.

DIFFERENTIAL DIAGNOSIS

Hypoxic respiratory failure resulting from impairment of alveolar- capillary function is seen in ARDS; cardiogenic pulmonary edema; interstitial lung disease; aspiration pneumonia; bronchiolitis; bacterial, fungal, or viral pneumonia; and sepsis. It also can be due to intracardiac or intrapulmonary shunting seen with atelectasis and embolism. Hypercarbic respiratory failure can occur when the respiratory center fails as a result of drug use (opioids, barbiturates, and anesthetic agents), neurologic or neuromuscular junction abnormalities (cervical spine trauma, demyelinating diseases, anterior horn cell disease, botulism), chest wall injuries, or diseases that

cause increased resistance to airflow (croup, vocal cord paralysis, post-extubation edema). Maintenance of ventilation requires adequate function of the chest wall and diaphragm.

Disorders of the neuromuscular pathways, such as muscular dystrophy, myasthenia gravis, and botulism, result in inadequate chest wall movement, development of atelectasis, and respiratory failure. Scoliosis rarely results in significant chest deformity that leads to restrictive pulmonary function. Similar impairments of air exchange may result from distention of the abdomen (postoperatively or due to ascites, obstruction, or a mass) and thoracic trauma (flail chest).

Mixed forms of respiratory failure are common and occur when disease processes result in more than one pathophysiologic change. Increased secretions seen in asthma often lead to atelectasis and hypoxia, whereas restrictions of expiratory airflow may lead to hypercarbia. Progression to respiratory failure results from peripheral airway obstruction, extensive atelectasis,
and resultant hypoxemia and retention of CO_2.

TREATMENT

Initial treatment of patients in respiratory distress includes addressing the ABCs (see Chapter 38). **Bag/mask ventilation** must be initiated for patients with apnea. In other patients, oxygen therapy is administered using appropriate methods (e.g., simple mask). Administration of oxygen by nasal cannula allows the patient to entrain room air and oxygen, making it an insufficient delivery method for most children in respiratory failure. Delivery methods, including intubation and mechanical ventilation, should be escalated if there is inability to increase oxygen saturation appropriately.

Patients presenting with hypercarbic respiratory failure are often hypoxic as well. When oxygenation is established, measures should be taken to address the underlying cause of hypercarbia (reversal of drug action, control of fever, or seizures). Patients who are hypercarbic without signs of respiratory fatigue or somnolence may not require intubation based on the P_{CO_2} alone; however, patients with marked increase in the work of breathing or inadequate respiratory effort may require assistance with ventilation.

After identification of the etiology of respiratory failure, specific interventions and treatments are tailored to the needs of the patient. External support of oxygenation and ventilation may be provided by **noninvasive ventilation** methods (heated humidified high-flow nasal cannula, continuous positive airway pressure, biphasic positive airway pressure, or negative pressure ventilation) or through invasive methods (traditional **mechanical ventilation,** high-frequency oscillatory ventilation, or extracorporeal membrane oxygenation). Elimination of CO_2 is achieved through manipulation of minute ventilation (tidal volume and respiratory rate).

Oxygenation is improved by altering variables that affect oxygen delivery (fraction of inspired oxygen) or mean airway pressure (PEEP, peak inspiratory pressure, inspiratory time, gas flow).

COMPLICATIONS

The major complication of hypoxic respiratory failure is the development of organ dysfunction. **Multiple organ dysfunction** includes the development of two or more of the following: respiratory failure, cardiac failure, renal insufficiency/ failure, gastrointestinal or hepatic insufficiency, disseminated intravascular coagulation, and hypoxic-ischemic brain injury. Mortality rates increase with increasing numbers of involved organs.

Complications associated with mechanical ventilation include pressure-related and volume-related lung injury. Both overdistention and insufficient lung distention (loss of functional residual capacity) are associated with lung injury. Pneumomediastinum and pneumothorax are potential complications of the disease process and overdistention. Inflammatory mediators may play a role in the development of chronic fibrotic lung diseases in ventilated patients.

PROGNOSIS

Prognosis varies with the etiology of respiratory failure. Less than 1% of previously healthy children with bronchiolitis die. Asthma mortality rates, although still low, have increased.
Despite advances in support and understanding of the pathophysiology of ARDS, the mortality rate remains approximately 30%.

PREVENTION

Prevention strategies are explicit to the etiology of respiratory failure. Some infectious causes can be prevented through active immunization against organisms causing primary respiratory disease (pertussis, pneumococcus, *Haemophilus influenzae* type b) and sepsis (pneumococcus, *H. influenzae* type b). Passive immunization with respiratory syncytial virus immunoglobulins prevents severe illness in highly susceptible patients (prematurity, bronchopulmonary dysplasia). Primary prevention of traumatic injuries may decrease the incidence of ARDS. Compliance with appropriate therapies for asthma may decrease the number of episodes of respiratory failure.

Source: Nelson essential

Bag-Mask Ventilation

Bag-mask ventilation is used to help apneic patients and those with inadequate spontaneous ventilation.

Positioning the patient appropriately is an essential first step. Maintaining a jaw thrust by positioning the last 3 fingers of one hand under the bony part of the mandible will facilitate ventilation. Keep these fingers off the soft tissue below the mandible to avoid occluding the airway. It may be necessary to move the patient's head and neck gently through a variety of positions to determine the optimum position for airway patency and effective ventilation. A neutral sniffing position without hyperextension is appropriate for infants and toddlers.

The 3 keys to providing adequate ventilation are:

- *Maintain an open airway.*
- *Establish a seal between the patient's face and the mask.*
- *Deliver optimal minute ventilation from the resuscitation bag to distal lung units.*

To assess the adequacy of bag-mask ventilation:

- *Evaluate chest rise and presence of bilateral breath sounds.*
- *Evaluate clinical response, including improved heart rate and return of good color.*
- *Monitor oxygen saturation.*

Ventilation Bags

There are 2 types of ventilation bags: self-inflating and flow inflating. Ventilation bags used for resuscitation should be self-inflating and a suitable size for the child. Neonatal bags (250 mL) hold only enough volume to be used with neonates. Pediatric bags (450-500 mL) are adequate for infants and children.

Many self-inflating bags are equipped with pressure-limited pop-off valves set at 35 to 40 cm H_2O. In patients with significant pulmonary disease or anatomic obstruction of the airway, these valves may need to be inactivated to achieve adequate chest rise. Flow-inflating bags require additional expertise.

The technique for bag-mask ventilation

The hand position is called the ***E-C clamp technique.*** The thumb and forefinger form a C shape and exert downward pressure on the mask while the remaining fingers of the same hand, forming an E, lift the jaw and pull the face toward the mask. This should create a tight seal. Once the mask is correctly applied, the other hand is used to compress the bag until the chest rises. Ventilation should synchronize with the patient's respiratory effort if the patient is spontaneously breathing; this will prevent gagging. It is better to lift the patient's face into the mask than to push the mask onto the patient's face.

. Ventilation provided by 2 rescuers can be more effective when there is significant airway obstruction or poor lung compliance. In this technique, 1 rescuer uses both hands to open the airway by placing 3 fingers of each hand on both posterior rami of the patient's mandible and maintains a tight mask-to-face seal while the other rescuer compresses the ventilation bag. Again, the rescuer holding the face mask should concentrate on lifting the jaw and face into the mask in preference to pushing the mask onto the face.

The 2-rescuer technique may be essential in children with difficult airways (e.g., epiglottitis or foreign body aspiration with complete obstruction). If a patient has any respiratory effort at all, rescuer ventilations should be timed with them. Allowing expiration to occur fully prior to providing another breath avoids hyperinflation with consequent hemodynamic and oxygenation problems. Use only the force and tidal volume necessary to make the chest rise. Excessive volumes may compromise cardiac output, distend the stomach, increase the risk of vomiting and aspiration, and add to the risk of barotrauma.

Troubleshooting

When adequate chest rise does not occur:

- Reposition the head. Make sure the head and neck are not hyperextended and thus causing airway obstruction.
- Ensure that the mask is the appropriate size and applied snugly on the patient's face.
- Make sure that you are lifting the child's jaw to the mask, not pushing the mask onto the child's face.
- Suction the airway if excessive secretions are noted.
- Place an OP airway.
- Disable the pop-off feature of the ventilator bag.
- Use the Sellick maneuver to decrease abdominal distension.
- Assess the need for a nasogastric tube to decompress the stomach and protect against aspiration.
- Check for the presence of a foreign body.

When chest rise is appropriate, but oxygen saturation remains low:

- Check if the bag is connected to an appropriate oxygen source.
- Assess the need for higher pressures and the need to disable the pop-off valve.
- Consider using a positive end-expiratory pressure valve. Patients with lung disease might require additional pressure for improved oxygenation.
- In children with partial airway obstruction, application of 5 to 10 cm H_2O of continuous positive airway pressure may maintain adequate airway patency

Pediatric Shock

Amirah Daher Malkawi M.D, MPH, FAAP

Bilasan notes for annual lecture were added in *italic font*

OBJECTIVES

Definition

Pathophysiology

Types

Management concepts

Definition

Inability to meet the cellular demand for oxygen

Oxygen delivery **<** Oxygen Consumption

Important concepts

CO= HR X SV

Know acceptable HR for age

Children can't modify stroke volume well *due to decreased controll of heart contractility.*

SV determined by Preload, Contractility, Afterload

Important concepts

Oxygen Delivery DO2= CO X CaO2

Oxygen Consumption=CO X CvO2 -CaO2

CaO2

Clinically more significant

CaO2 = Hb bound O2+ Plasma Dissolved O2

Hb X SaO2 X 1.34 + PaO2 X FiO2 X 0.003

(12 X 0.95 X 1.34) + (80 X 0.21 X 0.003)

15.28 + 0.05 = 15.33 ml/dl

Critical Concepts

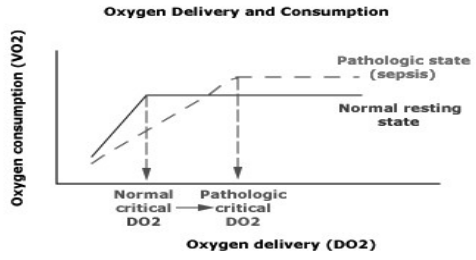
Normal CaO2 :17-20 ml/dl

Normal DO2: 500 ml/min/m2

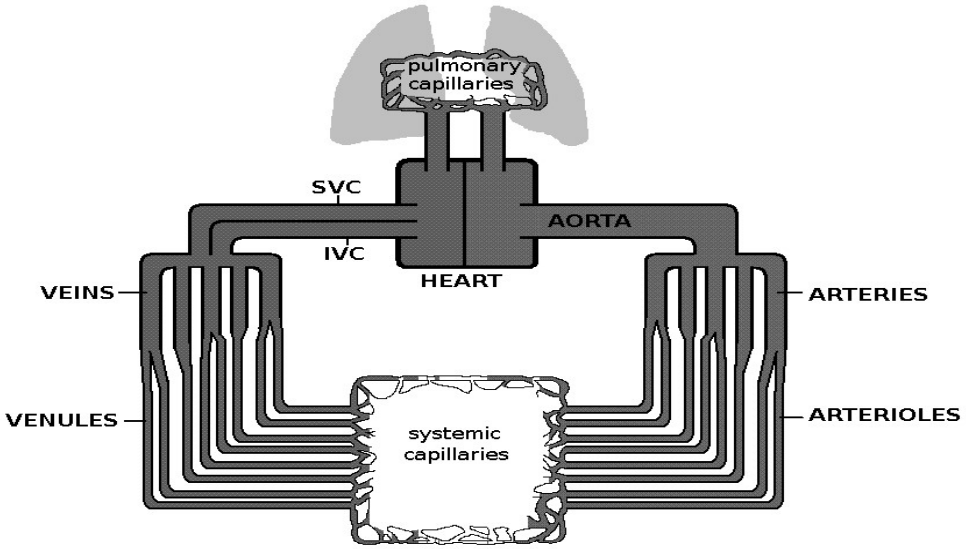
Normal oxygen extraction : 25-30%

Normal oxygen consumption in an adult is 250 ml/min

Oxygen delivery (DO2) and consumption (VO2)



In the normal state (blue line), oxygen consumption is constant over a range of DO2, and decreases only when DO2 falls below a critical level (critical DO2). Pathologic changes caused by sepsis or systemic inflammatory responses (red line) cause increased VO2 and impaired peripheral oxygen utilization, resulting in an elevation in critical DO2.



Types of Shock

Cardiogenic

Hypovolemic

Distributive

Obstructive

Dissociative

Cardiogenic

Congenital heart disease: Ductal dependent lesions such as HLHS, AS, Coarc or interrupted aortic arch

Cardiomyopathies : Dilated, restrictive , hypertrophic

Myocarditis: Infectious (Coxsackie B),Toxins(Cocaine), autoimmune

Abnormal rate or rythm: Extreme bradycardia, SVT, VT

Decreased driving force.
Decreased capillary perfusion is not part of cardiogenic shock.
Signs: enlarged liver, JVP elevated, oliguria, edema, gallop rhythm

Hypovolemic *(most common)*

Hemorrhagic : (Think of hidden blood loss like femoral Fracture, *intraventricular hemorrhage, spleen, liver, retroperitoneum*)

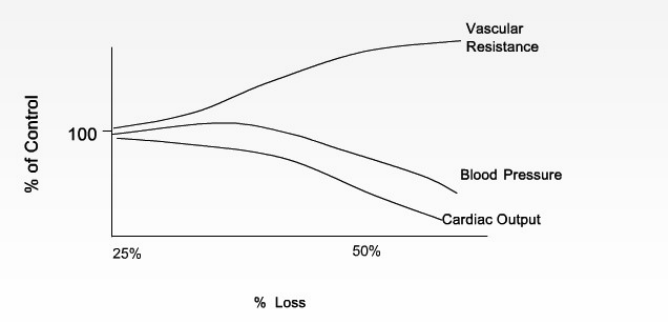
Plasma loss (Burns, Steven Johnson syndrome, Epidermolysis Bullosa)

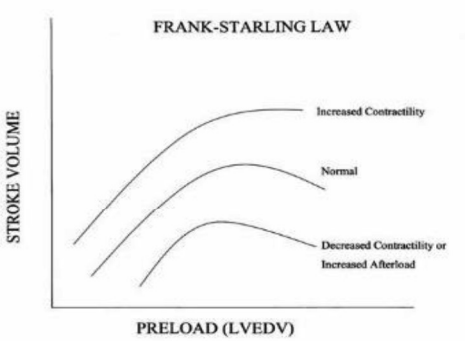
Loss of water *(m.c)* (Gastroenteritis, extreme diuresis in DKA, DI)

Relative hypovolemia (loss of fluid by third spacing, *e.g nephrotic syndrome)*

Signs of dehydration/ no signs of heart failure

Hemodynamic Response to Hemorrhage





Distributive shock *(hypotension & generalized tissue hypoxia)*

Septic (m.c): *↓ preload due to ↑ capillary permeability, ↑ cellular apoptosis, ↓ O2 consumption, ↓ contractility. Pulse increases in early stage (warm shock), vasoconstriction in later stage.*

SIRS

Anaphylactic: *release of histamine, vasodilation, ↓ SVR*

Neurogenic: *↓ alpha receptor activity*

Obstructive *(associated with physical obstruction of the great vessels or the heart itself).*

Tension Pneumothorax: *positive pressure in potential space, obstructs VR & CO*

Cardiac Tamponade: *positive pressure in pericordium*

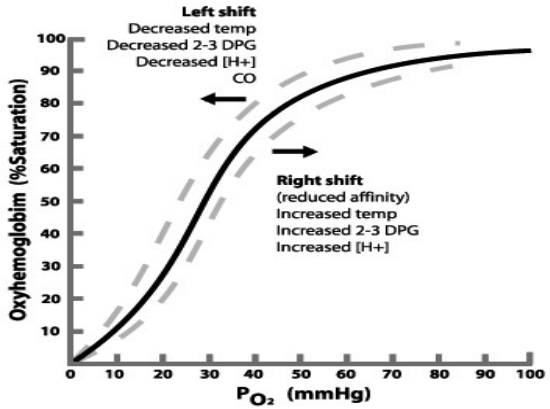
Pulmonary embolism

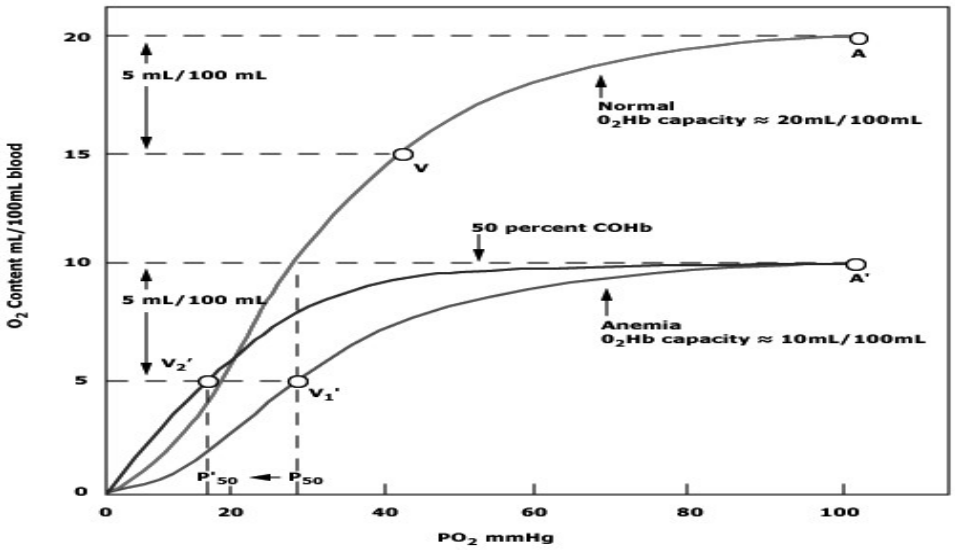
Dissociative

Cyanide poisoning: Blocks oxidative phosphorylation in the mitochondria with resulting switch to anaerobic metabolism. *Hyperdynamic cardiac system. ↑HR, normal BP, good pulse.*

Carbon monoxide: Increased affinity of CO to Hb, perfusion is good but no O2 to deliver. *Failure of uptake due to ↓ ATP*

Heat stroke





Hemodynamic profiles of the types of shock in children

Physiologic variable	Preload	Pump function	Afterload	Tissue perfusion	Tissue perfusion
Clinical measurement	Clinical signs* or central venous pressure (if measured)	Cardiac output or index¶	Systemic vascular resistance	Capillary refill time$^{\Delta}$	Mixed venous oxygen saturation$^{\diamond}$
Hypovolemic	↓	↓	↑	↑	Low
Cardiogenic	↑	↓	↑	↑	Low
Distributive	↓ or ↔	↑	↓	↓ (initial)	High
Obstructive	↑	↓	↑	↑	Low

* Clinical signs of decreased preload include tachycardia, tachypnea, decreased or absent peripheral pulses; normal or weak central pulses; capillary refill time >2 seconds; skin that is pale, mottled, cold or diaphoretic; dusky or pale extremities, altered mental status, decreased urine output, and flat jugular veins. Clinical signs of increased preload include jugular venous distension, pulmonary edema, and hepatomegaly. These patients are also typically tachycardic and poorly perfused. Refer to topics on evaluation of shock in children.

¶ Cardiac index (cardiac output per body surface area) is typically what is measured during clinical care.

Δ In patients with shock, capillary refill time >2 seconds is associated with low mixed venous oxygen saturation while flash capillary refill suggests increased mixed venous oxygen saturation.

◇ A low mixed oxygen saturation is <70 percent when measured through a triple lumen catheter and <65 percent when measured through a pulmonary artery catheter.

	CO	SVR	MAP	Wedge	CVP
Hypovolemic	↑	↑	↔ Or ↓	↓↓↓	↓↓↓
Cardiogenic	↓↓	↑↑↑	↔ Or ↓	↑↑	↑↑
Obstructive	↓	↑	↔ Or ↓	↑↑	↑↑
Distributive	↑↑	↓↓↓	↔ Or ↓	↔ Or ↓	↔ Or ↓
Septic: Early	↑↑↑	↓↓↓	↔ Or ↓	↓	↓
Septic: Late	↓↓	↑↑	↓↓	↑	↑ or ↔

MANAGEMENT PRINCIPLES

Decrease O2 consumption

- Minimize work of breathing
- Treat Fever
- Treat pain and anxiety
- Treat Seizures
- Treat Infection

MANAGEMENT PRINCIPLES

Increase O2 Delivery

- Normalize Contractility
- Normalize Systemic Vascular Resistance
- Normalize Pulmonary Vascular Resistance
- Normalize Preload

Management

Administer FiO2

Intubate If Airway is compromised or patient in impending Respiratory Failure

Establish Vascular Access

Management

Start fluid resuscitation with 20 ml/kg of isotonic crystalloid as a push

In patients with suspected cardiogenic shock give only 10 ml/kg

Reasses following each bolus (HR,CRT, Pulses,BP)

May repeat if some improvement noted up to 4-5 boluses *(100 cc/kg)*

Management

Check blood sugar *(usually hypoglycemic)* and serum electrolytes including Ca & Mg

If anaphylaxis suspected give epinephrine, diphenhydramine and hydrocortisone. Conside H2 blocker.

Continnous monitoring of HR, RR, BP, SaO2 & Urine output

Management

If cardiovascular exam not back to normal consider starting Inotropic support

Start Emperic Antimicrobial Therapy for suspected Septic Shock

In Infants with suspected ductus dependant lessions start Prostaglandin E1 drip to reopen the ductus

For Heamorhagic Shock give PRBC's

Management

In Refractory shock consider Adrenal Insufficiency and possible dissociative shock

Give steroids in adrenal insufficiency

Asses End Point Organ perfussion

- Level of Concioussnes
- BP, Pulses
- Urine Output

Vasoactive medication receptor activity and clinical effects

Drug	Receptor activity				Predominant clinical effects
	Alpha-1	Beta-1	Beta-2	Dopaminergic	
Phenylephrine	+++	0	0	0	SVR ↑↑, CO ↔/↑
Norepinephrine	+++	++	0	0	SVR ↑↑, CO ↔/↑
Epinephrine	+++	+++	++	0	CO ↑↑, SVR ↓ (low dose) SVR/↑ (higher dose)
Dopamine (mcg/kg/min)*					
0.5 to 2.	0	+	0	++	CO
5. to 10.	+	++	0	++	CO ↑, SVR ↑
10. to 20.	++	++	0	++	SVR ↑↑
Dobutamine	0/+	+++	++	0	CO ↑, SVR ↓
Isoproterenol	0	+++	+++	0	CO ↑, SVR ↓

+++: Very strong effect; ++: Moderate effect; +: Weak effect; 0: No effect.
* Doses between 2. and 5. mcg/kg/min have variable effects.

Management

If shock not responding consider stat Echo to assess function and volume status

To Improve contractility consider Milrinone *(phosphodiesterase inhibitor)* Or Dobutamine *(beta 2 agonist, for cardiogenic shock)*

If Contactility poor despite inotropic support consider afterlod reduction with vasodilators such as Nitroprusside

Management

Refractory Shock

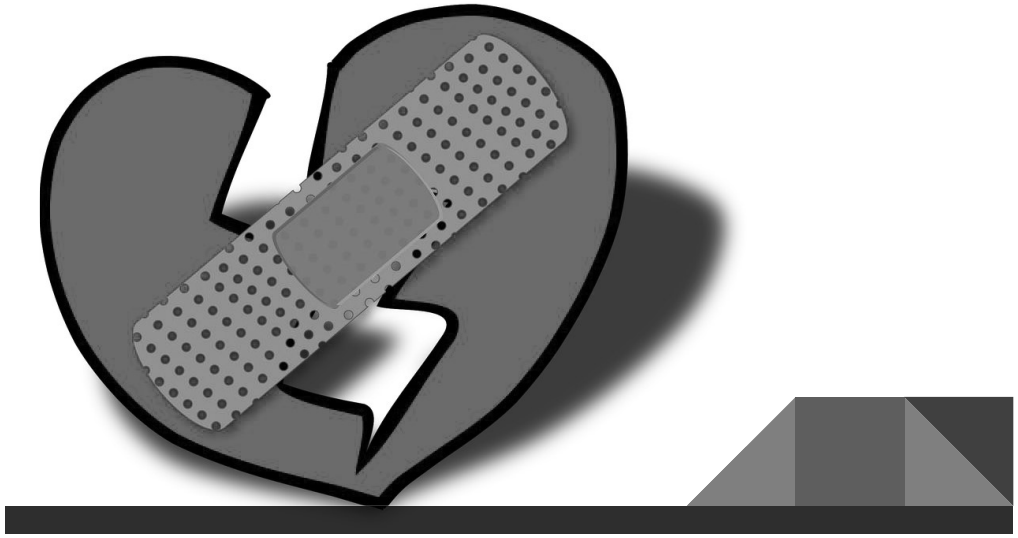
In Refractory shock send cortisol levels and start stress dose Hydrocortisone

Vasopresin may be use if patient not responding to multiple therapy *(used as last resort)*

Outcomes

Depends on cause

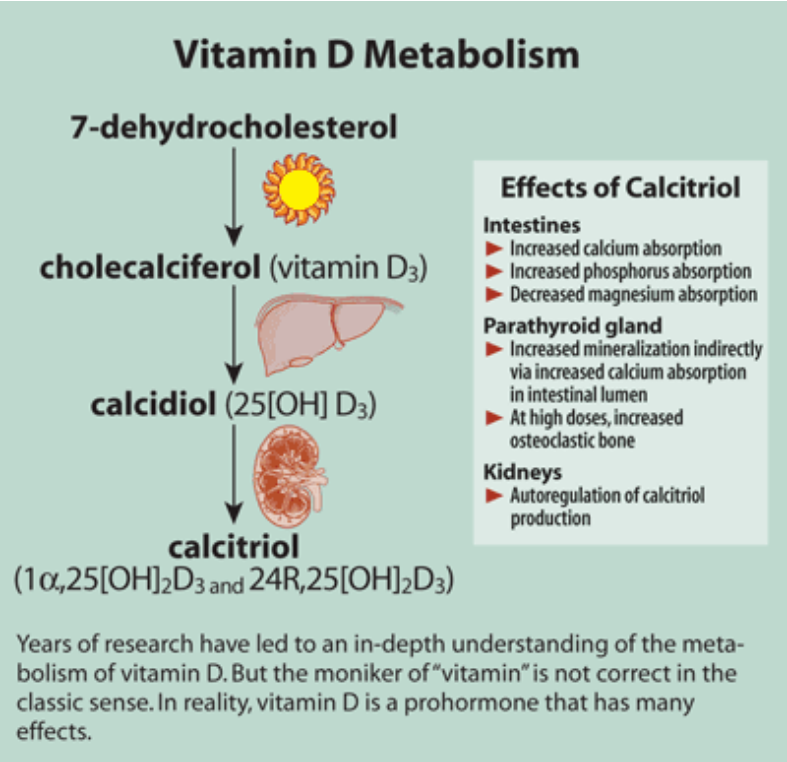
The sooner you make the diagnosis and start therapy the better the outcome



Rickets

Definition: Failure or delay in mineralization of growing skeleton caused by calcium, Vitamin D, or phosphorus deficiency in children (By definition, rickets occurs in children whose growth plates have not fused.).
Osteomalacia describes similar condition in adolescents whose growth
Plates have already closed.

Physiology:



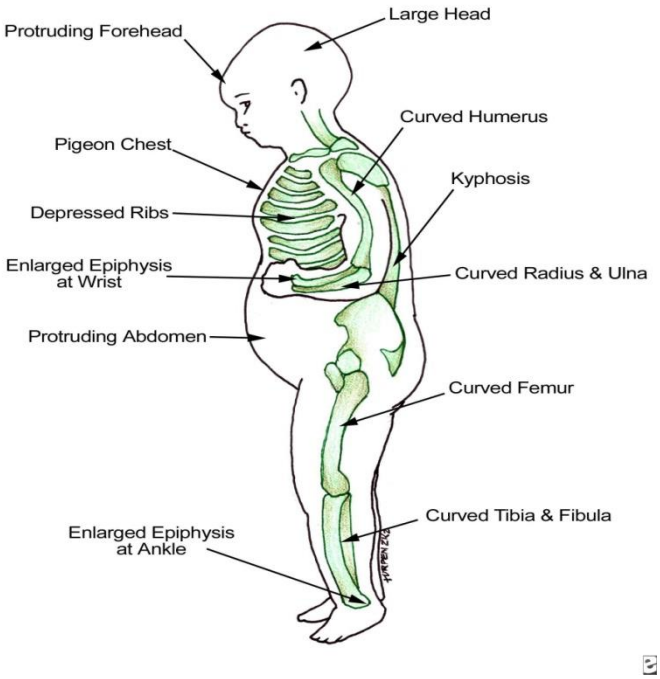
Vitamin D-3 (cholecalciferol) is formed in the skin when a cholesterol precursor, 7-dehydroxycholesterol, is exposed to ultraviolet light. Activation occurs when the substance undergoes 25-hydroxylation in the liver and 1-hydroxylation in the kidney.

The primary action of 1,25-$(OH)_2$ D3 is to promote gut absorption of calcium by stimulating formation of calcium-binding protein within the intestinal epithelial cells. Vitamin D also promotes intestinal absorption of phosphate ion, although the exact mechanism is unclear. Negatively charged phosphate ion may passively flow through the intestinal cell because of flux of the positively charged calcium ion. In bone, vitamin D may play a synergistic role with parathyroid hormone (PTH) in stimulating osteoclast proliferation and bone resorption. Compared to parathyroid hormone (PTH), vitamin D exerts a much slower regulatory effect on calcium balance.

Presentation:

In history : Elicit any history of frequent fractures, delayed dentition, weakness, poor

weight gain, seizures, and developmental delay.



In physical examination: look at the findings in the picture

Rickets causes:

Most common cause of rickets is Vitamin D deficiency *(treated by* Vitamin D supplementation, although sunlight and ultraviolet irradiation are therapeutic*)*.

Other causes are:

Vitamin D dependant Rickets type 1

- ✓ Autosomal recessive disorder
- ✓ Mutations in the gene encoding renal 1alpha hydroxylase
- ✓ Occur in first 2 years of life
- ✓ Classic features of rickets with symptomatic hypocalcemia
- ✓ Normal levels of 25-vitamin D but low or normal levels of 1,25-vitamin D
- ✓ Treatment : 1,25 vitamin D (Calcitriol)

Vitamin D dependant Rickets type 2

- ✓ Autosomal recessive disorder
- ✓ Mutations in gene encoding vitamin D receptor
- ✓ Levels of 1,25- vitamin D are extremely elevated
- ✓ Present during infancy,might not be diagnosed until adulthood
- ✓ 50-70% of children have alopecia,range from alopecia areata to akopcia totalis

Vitamin D resistant rickets (X linked Hypophospatemic Rickets)

- ✓ X-linked dominant disorder
- ✓ Ingestion of vitamin D is relatively ineffective.
- ✓ Abnormality is decreased proximal renal tubular resorption of phosphate, resulting in renal phosphate wasting and hypophosphatemia. This defect is due to circulating factors called phosphatonins. The principle phosphatonin in hereditary hypophosphatemic rickets is FGF-23. Decreased intestinal calcium and phosphate absorption also occurs.
- ✓ Oral phosphate and calcitriol prevent secondary hyperparathyroidism

Fanconi syndrome

Consists of multiple defects in renal proximal tubular reabsorption, causing glucosuria, phosphaturia, generalized aminoaciduria, and bicarbonate wasting.most common cause of Fanconi syndrome is Cystinosis.

Lab findings:

Patient with rickets should have calcium, phosphorus, PTH, and alkaline phosphatase concentrations measured, Renal function tests and 25-0H vitamin D and 1,25-0H vitamin D levels should also be obtained.

BIOCHEMICAL PROFILE

	Ca	P	PTH	ALP	25(OH) Vit D	
Vit D Defficiency	N/Low	N/Low	Increased	Increased	Low	Ur P-low
Vit D Dependant	Low	Low	Increased	Increased	Normal	
Vit D resistant	N/Low	Low	Normal	Increased		D3 –N Ur P-High
Renal Osteodystrophy	N/Low	Increased	Increased	Increased	Normal	D3- low

Sources: Step up to pediatrics, Medscape, Merck manual

Done by: Mohannad abohamad

Neonatology

NEONATAL EXAMINATION

P/E

GENERAL

Comment on the general look:

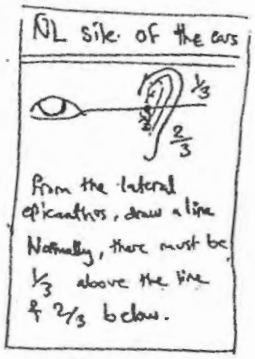
- Well looking
- Active / Crying / Calm / Moving his limbs
- Jaundiced / Cyanosed / Pale
- Distressed ? (Nasal Flaring / Grunting / Visible retractions)
- Dysmorphic features.

GROWTH PARAMETERS

- Wt
- Length — measured by putting one end of the meter on the heel & Align it along the side of the leg, the side of the trunk, till the level of the vertex of Skull.
- Head circumference — see next

HEAD EXAMINATION

- Head Circumference — By wrapping the meter around head Passing btw. the occiput & the farthest Point of the forehead.
- Comment on cephalohematoma or Caput Secreedaneum
- FEEL the head contour — Comment if smooth / molding
  - Comment on ant. & Post. fontanelles. (Present vs. Absent, Size, Depressed vs. Bulging)



- EYES : Hypertelorism / up or down slanting / ...
- NOSE - Depressed nasal bridge / ...
- EARS : Bat ears / Abnormally shaped / low set ears / ...
- MOUTH - Cleft lip / small mouth / look inside for Cleft palate.

(1)

NECK EXAMINATION

If Short — look also for excessive skin folds (esp. on the Post. aspect of the neck) → might be a sign of down syndrome.

CHEST

- Comment if gross chest deformity / Marked breast engorgement.
- As the baby becomes calm — examine the chest.
  - Start feeling the apex beat on BOTH sides (may have NL: Left 5th intercostal space, Midclavicular line. Dextrocardia)
- Measure RR — For 1 minute (because it's irregular)
  HR — for 6 seconds & multiply it by 10 (coz it's regular unlike RR)
- FEEL breast engorgement.
- Auscultate the Precordium — comment if murmer is present.

ABDOMEN

- Comment on shape (Bulging / Flat / Scaphoid) or if visible distended veins are seen.
- Catch the umbilical cord & look for umbilical vein (only one & larger) & umbilical artery (2 in no. smaller)
- Comment on UMBILICUS (Redness / Discharge / Tenderness / Distressing when you palpate)
- Feel the LIVER — NL (Palpable liver till the age of 2 yrs 2 fingers below costal margin)
  SPLEEN — NL (NOT felt in neonates.)

INGUINAL & HIP

- Feel femoral PULSES (felt when hips are flexed Not extended)
- Examine for DDH (Developmental Dislocation of the Hip) / ortolani \ Barlow

(2)

GENETALIA

♀: NL labia majora is totally covering minora

Comment ~~on~~ if discharge (may normally be Present)

Anus: Bring thermometer & put in rectum to make sure of the canalization of the rectum.

BACK

- Feel vertebral spines (comment if any is absent)
- Look for any skin dimple / tuft of hair / Depigmentation / fat Pad — which may indicate spina bifida

PRIMITIVE REFLEXES

- Moro Reflex — the most important!
- Red Reflex (v.imp.)
- Rooting Reflex

(3)

Care of newborn

At delivery room

Each delivery should be attended by a person who knows how to do neonatal resuscitation.

In the delivery room:

- Take prenatal history including problems during pregnancy, delivery mode, gestational age…
- Prepare equipment and team
- Communication with obstetric team, mother of family
- NICU preparation, if needed

- Neonatal period: birth to 28 days of life
- Transition period: phases of instability during the 1st 6-8 hours after birth

Initial assessment (3 questions)

- Full term?
- Is baby breathing, crying?
- Does baby have good muscle tone?

If any of the answers is no, then proceed to resuscitation guidelines
If all answers are yes, then continue with routine care:

1. Provide warmth
   - Deliver in a warm room
   - Dry and wrap newborn
   - Place in a war surface
   - Give to mother as soon as possible (for skin-to-skin contact in first few hours, advantage; enables early breastfeeding and remote bonding
2. Clear airway if necessary
3. Assessment of APGAR score

The physical appearance of the newborn:

- Babies are often coated with vernix which is; thick, greasy substance, that protect skin from irritating effect of amniotic fluid, and smoothens the passage through birth canal
- Baby's eyelid may be swollen and puffy from accumulation of liquids during birth

- Acrocyanosis my be normal in newborn

APGAR score

It's a rapid scoring system based on physiologic responses to the birth process and is a good method for assessing the need for resuscitation

Sign	0	1	2
Color Appearance	Blue	Pale, pink body, with blue extremity	Pink all over
HR Pulse	0	<100	>100
Reflex irritability Grimace	None	Some motion, fascial grimace	Active withdrawal
Muscle tone Activity	none	Weak, passive, some extremities flexion	Active, extremities well flexed
Respiration	none	Weak cry	Vigorous cry

- It's assessed at 1 minute and at 5 minute, every 5 minute there after as long as resuscitation is continuing (usually we don't wait 1 minute, we start immediately)

Normal score

Minimum of 7 at 1 min, and 9 at 5

Moderate asphyxia: 4-6, need close attention if 5 minute score is <7, repeat every 5 minute for 20 minutes.

Note:

Score can be misleading, why?

- Don't work well with preterm infants.
- Primarily, it measures brainstem function.

Requirement at delivery room

- 1 mg **vitamin K** IM injection, to prevent hemorrhagic disease of the newborn. Vitamin K is important for complete synthesis of certain proteins that are perquisites for blood coagulation.
  - Vitamin K passes the placenta poorly, and the levels of vitamin K in breast mild are low
  - If deficiency, increase risk of bleeding usually between day 3-7 of life.
  - The most common sites of bleeding; umbilicus, mucous membrane, GI tract, circumcision and venipuncture
- **Erythromycin** ointment or **silver nitrate** 1% to prevent ophthalmia neonatorum, which is conjunctivitis with discharge during the first two weeks of life (most common appear at day 2-5), it may cause corneal damage, blindness and systemic progression if untreated.
  - Pathogen: N. gonorrhea or C. trachomatis

Notes

- N. gonorrhea is worse and more sever than C. trachomatis
- N. gonorrhea; 30-50% transmission rate from mother
- Silver nitrate is not effective for chlamydia
- 2.5% provide iodine solution or 1% tetracycline ointment can be used
- Tetracycline is not effective in some N. gonorrhea strains

- **Triple antibiotic ointment** or **bacitracin**, may be applied to umbilical cord to decrease its colonization with gram positive bacteria

→ To continue assessment of the newborn, we conduct physical assessment which include:

1. **Transitional assessment**

· Transitional period: a period of instability during 6-8 hours after birth
· All healthy newborn go through predictable periods of alertness and sleep that should be assessed and taken into consideration when performing the comprehensive physical examination

Two periods of reactivity

→ <u>First period</u>

– Begins within 30 minute and last for 6-8 hours
– Child is alert, vigorous, crying, has his eyes open and is very interested in environment, and also has very vigorous suckling which makes it a good opportunity to begin breast feeding.

Then there is a state of sleep and relative calmness lasting 2-4 hours, undressing or bathing should be avoided during this state

→ <u>Second period</u>

– Start after sleep, last 2-5 hours
– The infant is alert and responsive
– This is an excellent opportunity for infant and family to interact with each other and to begin some teaching to the parents

2. Assessment of gestational age

- It's conducted during the first 24 hours
- *Expanded New Ballard Score* include physical and neurological criteria
- Physical criteria mature with advancing fetal age while neurological criteria mature with gestational age

- <u>Neuromuscular maturity</u>

- Posture
- Square window: an angle of wrist between the hypothenar prominence and forearm
- Arm recoil
- Popliteal angle
- Scarf sign
- Heel to ear

→ <u>Physical maturity</u>

- Skin
- Lanugo
- Plantar surface
- Breast
- Eye, ear
- Genitalia

- Apnea: no berating for a period >15 seconds
- Breathing period is abnormal if <30 or >60

<u>Gestational assessment:</u>

Assessing a baby's physical maturity is an important part of care. Maturity assessment is helpful in meeting a baby's needs if the dates of a pregnancy are uncertain. For example, a very small baby may actually be more mature than it appears by size, and may need different care than a premature baby.

An examination called **The Dubowitz/Ballard Exam** for Gestational Age is often used. A baby's gestational age often can be closely estimated using this exam. **The Dubowitz/Ballard Exam evaluates a baby's appearance, skin texture, motor function and reflexes**. The physical maturity part of the exam

is done in the first two hours of birth. The neuromuscular maturity examination is completed within 24 hours after delivery. Information often used to help estimate babies physical and neuromuscular maturity are shown below.

Physical maturity:

The physical assessment part of the Dubowitz/Ballard Exam looks at physical characteristics that look different at different stages of a baby's gestational maturity. Babies who are physically mature usually have higher scores than premature babies.

Points are given for each area of assessment, with a low of -1 or -2 for extreme immaturity to as much as 4 or 5 for post-maturity.

- Skin - ranges from sticky and red to smooth to cracking or peeling.
- Lanugo (the soft downy hair on a baby's body) is absent in immature babies then appears with maturity and then disappears again with post-maturity.
- Plantar creases - these creases on the sole of the feet range from absent to covering the entire foot depending on the maturity.
- Breast - the thickness and size of breast tissue and areola (the darkened nipple area) are assessed.
- Eyes and ears - eyes fused or open and amount of cartilage and stiffness of the ear tissue are assessed.
- Genitals, male - presence of testes and appearance of scrotum, from smooth to wrinkled.
- Genitals, female - appearance and size of the clitoris and the labia.

Neuromuscular maturity:

Six evaluations of the baby's neuromuscular system are performed. These include:

- Posture - how does the baby hold his or her arms and legs.
- Square window - how much the baby's hand can be flexed toward the wrist.

- Arm recoil - how much the baby's arms "spring back" to a flexed position.
- Popliteal angle - how much the baby's knee extends.
- Scarf sign - how far the elbow can be moved across the baby's chest.
- Heel to ear - how close the baby's foot can be moved to the ear.
  A score is assigned to each assessment area. Typically, the more neurologically mature the baby, the higher the score.

  When the physical assessment score and the neuromuscular score are added together, the gestational age can be estimated. Scores range from very low for immature babies (less than 26 to 28 weeks) to very high scores for mature and post-mature babies.

3. Systemic physical assessment

This is usually done in the nursery after a stable delivery room course

<u>In nursery bedside assessment</u>

There must be:

- ***Proper identification***
- **Maintenance of body temperature**
  - 6-12 hour still baby achieves stabilization of temperature
  - Heating production is predominantly by non-shivering thermogenesis in specialized area of tissue containing brown adipose tissue
  - Brown fat is highly vascular, contains many mitochondria per cell and is situated around large blood vessels, resulting in rapid heat release into circulation
  - These tissues are innervated by sympathetic nervous system that serves as primary stimulus for these cells to produce heat.

- Heat loss can be via

→ Evaporation: cutaneous and respiratory loss when wet
→ Radiation: loss to nearby not on direct contact, cold solid surface
→ Conduction: loss of heat to object in direct contact with infant
→ Conversion: loss of air current

- Shivering doesn't occur in newborn

→ Common location for brown fat:
· Neck
· Thorax
· Inter-scapular region

→ Thermal protection is needed because you have:
– Wet baby
– Large surface area
– Poor thermal insulation (no insulating subcutaneous fat)
– Small baby mass, unable to produce heat

- Early bathing may also cause hypothermia; hence, bathing should be delayed till stabilization temperature

○ ***Protection from infection and injury***
– Prevent infection by hand washing and keeping away from ill individuals

○ ***Genital care***
– Male infant, in uncircumcised, then don't retract foreskin
– Female infant wipe from front to back
– If smegma has accumulated in labial folds, it can be carefully removed
– Circumcision is an elective procedure with use of anesthesia, delayed 12-24 hours until infant is stable
– For the procedure don't feed for 1 hour prior to procedure and get consent from parents
– It is contraindicated in hypospadias

- Advantages:
- It may decrease phimosis
- Decrease UTI in infancy
- Decrease penile cancer
- Decrease STD (including HIV)

Smegma: is a thick sebaceous secretion that collects beneath the foreskin or around the clitoris

- ***Screening***

For PKU, galactosemia, hypothyroid

- Usually after 24 hours of life, but more reliable after 48 hours of oral feeding
- TSH if measured 1st days, it can be a reflection of maternal TSH, it takes 3-5 days for maternal TSH to decrease so it's preferred to do TSH at end of 1st week

	Phenylketonuria (PKU)	Classic galactosemia
Defect	Phenylalanine hydroxylase, accumulation of PHE in body fluids and CNS1	Gal-1-P uridyltransferse deficiency, accumulation of gal-1-P with injury of kidney, liver and brain
Presentation	Mental retardation, vomiting, growth retardation, hyperactive, purposeless movements, athetosis and seizure	Jaundice(often direct), hepatomegaly, vomiting, hypoglycemia, cataract, seizure, poor feeding, poor weight gain and mental retardation
Association	Fair hair, fair skin, blue eyes, rash, teeth abnormalities, microcephaly	Predisposition to E.coli sepsis, developmental delay, speech disorder, learning disabilities
Other comments	Normal at birth, gradual mental retardation over first few months	May begin prenatally, trans placental galactose from mother
Treatments	Low phenylalanine (PHE) diet	No lactose, this can reverse growth failure, kidney and liver abnormalities, and also cataract, but not neurodevelopmental problems

- ***Immunization***

  - If mother is Hep. B +ve, then give Hep B Ig and start Hep B vaccine series (active and passive immunization)
  - Hep B vaccination as soon as possible in places where perinatal infections are common

  - If mother is Rh –ve, then blood group and do direct combs test
  - BCG vaccination at all populations with high risk for TB

- ***Early and exclusive breast feeding***

  - First breast feed should be given within first hour of life
  - Teach proper technique and positioning to mother

- Pay special attention to jaundice development
- Hearing should be screened using AABR (Auditory brainstem response test), OAE (Otoacoustic emission) or both

Notes:

- It's normal for neonate to lose 5-10% of weight in the first 5-10 days
- Normal RBC ($4.8\text{-}7.1X10^6$), Hb (14-23), Hct (44-64) and WBC (18K at birth, and up to 25K at first day) are higher than adults
- Coagulation factor dependent on vitamin K are depleted
- Abdomen is easily distended after eating
- Initial fecal material is meconium
- Limited immunity after birth; passive IgG from mother, breastfeeding IgA
- 90% of all healthy infant void urine within 24 hours and it's usually cloudy, scant uric acid crystals
- Full term infants have stores of iron that last 4-6 months, preterm infant have less iron stores

- RBC: $4.8\text{-}7.1X10^6$
- Hemoglobin: 14-23
- Hematocrit: 44-64
- WBC: 18K-25K
- Platelets: 150K-350K

Levels of neonatal care

i. Level one

- Basic neonatal care; that is minimum for any facility providing maternal in-patient care
- Provide care for healthy newborn infants and can stabilize ill patients until transfer

ii. Level two

- Provides care to infants who are moderately ill

iii. Level three

- NICU
- Provide care for infants with extreme prematurity or critically ill require surgical intervention

The end

Neonatal resuscitation

- 10% of all newborn in USA requires some intervention at birth
- <1% of all newborn in USA requires resuscitation

Normal physiology changes at birth

a. Initial breath and cry leads to aeration and expansion of lungs
b. Oxygenated alveoli cause pulmonary arteriole dilatation and decrease Pulmonary vascular resistance
c. Umbilical cord clamping and stimulation of sympathetic nervous system Lead to increased systemic vascular resistance
d. Pressure gradient leads to transition from fetal to adult circulation
e. Ductus and foramen ovale close over minutes to hours after birth

Causes are numerous, but most involve asphyxia or respiratory depression (Respiratory problems more than cardiac). Incidence rises significantly if birth weight is < 1500 g.

Preparation for resuscitation

1. Communication between obstetricians and pediatricians is key.
2. Estimation of gestational age or weight allows preparation of endotracheal tube size , catheter sizes, and drug doses before delivery
3. Completion of the Neonatal resuscitation program should be considered by all hospital personnel who may be involved in the stabilization and resuscitation of neonates in the delivery room, and for all deliveries, at least 1 person should be present who is skilled in neonatal resuscitation and is responsible only for the infant.

Escalating Resuscitation:
Drying
Warming
Positioning
Suctioning
Tactile stimulation
Oxygen
Bagging
Intubate
Chest compressions
Medications

Rapid assessment

Newborn infants who need extensive resuscitation should be rapidly identified. **Term infants with clear amniotic fluid, adequate respiratory effort, and good muscle tone** (all three criteria must meet) should receive routine care, which includes provision of warmth, clearing of the airway (if needed, because Suctioning has not proved beneficial in infants without obvious obstruction, even if amniotic fluid was stained with meconium (suctioning was previously recommended in such infants)), drying of the infant, and assessment of the infant's color. These infants should remain with their mothers during and after routine care.

Infants who do not meet the criteria for routine care need additional steps in their resuscitation. For such infants, resuscitation may include not only initial stabilization (providing warmth, positioning, clearing the airway, drying, stimulating, and repositioning) but also ventilation, chest compressions, and medications.

Note that Apgar scores are not used for resuscitation because resuscitation should be assessed before the 1·minute Apgar is assigned.

When to intubate?

-Direct tracheal suctioning is required
- Effective bag-mask ventilation cannot be provided
-chest compressions are performed
- endotracheal (ET) administration of medications is desired
- Congenital diaphragmatic hernia is suspected
- Prolonged need for assisted ventilation exists.

Resuscitation

If spontaneous respirations are absent, the infant is gasping, or heart rate is < 100 beats/min (An assessment of the heart rate can be obtained through palpation of the umbilical stump at the level of insertion of the infant's abdomen or through direct auscultation of the precordium.), respirations are assisted with PPV via mask, or sometimes laryngeal mask airway or endotracheal tube. Note that infants with a sunken, convex (scaphoid) abdomen may have a congenital diaphragmatic hernia, in which case ventilation using a mask can be dangerous; if such infants require ventilatory assistance, they should undergo endotracheal intubation. O_2 saturation is monitored using a pulse oximeter placed to measure preductal saturation (typically on the right hand or wrist). Resuscitation should be started with room air or a blend of O_2 and air and titrated to achieve O_2 saturations within the target range, which increases over the first 10 min of life. Inspiratory and end-expiratory pressures should be monitored and kept at the lowest level necessary to maintain heart rate > 100 beats/min. It is particularly important to keep pressures low in extremely premature and/or extremely low-birth-weight infants, whose lungs are easily injured by PPV. *Bradycardia (heart rate < 60) in a distressed child is a sign of impending cardiac arrest; neonates tend to develop bradycardia with hypoxemia.* If bradycardia persists > 90 sec, O_2 concentration is increased to 100% until recovery. If heart rate is < 60 despite adequate ventilation for 30 sec, begin chest compressions using a 3:1 compression:ventilation ratio. Chest compressions may be performed either by circling the chest with both hands and using a thumb to compress the sternum or by supporting the infant's back with one hand and using the tips of the middle and index finger to compress the sternum. The thumb technique is **preferred** because it allows better depth control during compressions.

When to do chest compression?

Chest compressions should be initiated after only 30 seconds of effective PPV if the heart rate remains below 60 beats/min.

Neonatal resuscitation drugs should be stocked in any area where neonates are resuscitated.

Drugs currently recommended include epinephrine and isotonic sodium chloride solution (0.9%) as an intravascular volume expansion agent.
Epinephrine should be considered only when the heart rate is below 60 beats/min and ventilation has been established and provided for at least 30 seconds.

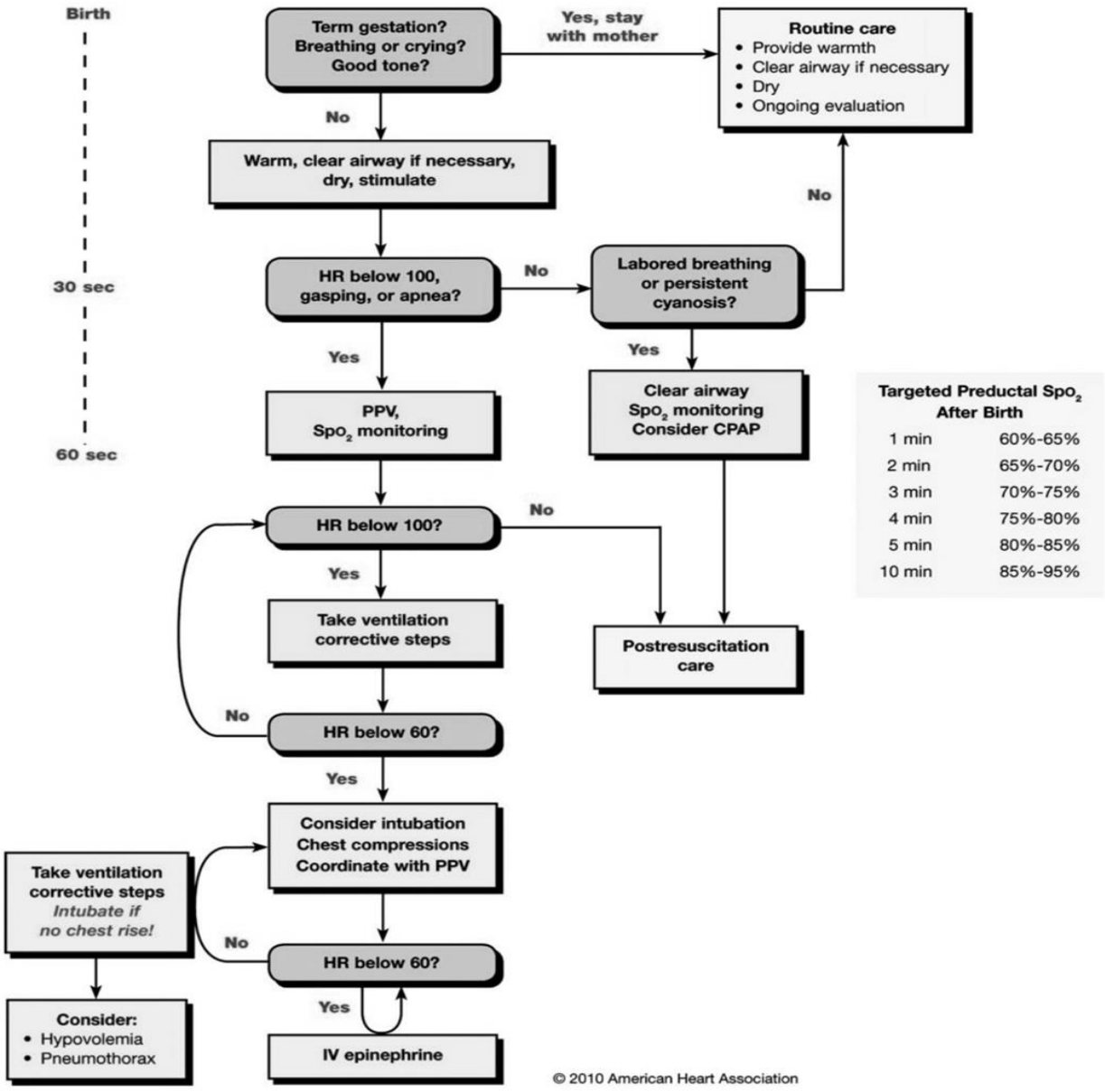
When to Use Epinephrine?

When the heart rate is below 60 beats/min and ventilation has been established and provided for at least 30 seconds

The only exception to this rule may be in infants born without a detectable pulse or heart rate.
Epinephrine is given Preferably IV but if vascular access cannot be obtained, epinephrine may be given via the ET tube, but in such cases, the dose should be increased to 3 times the IV dose.

Study this algorithm well since Dr.Manar spends the majority of the lecture in illustrating it .

Newborn Resuscitation Algorithm.



John Kattwinkel et al. Pediatrics 2010;126:e1400-e1413

Sources: Medscape, Merck manual, Step up to Pediatrics

Done by: Mohannad abo hamad

Preterm baby

Definition: preterm birth is the delivery of live born baby before 37 weeks of gestation (259 days) from the first day of last menstrual period. Preterm labor is defined as uterine contractions before 37 weeks.

Epidemiology

- Prematurity is the leading cause of neonatal mortality in Jordan. But in western countries, congenital anomalies are on the top of the list.
- Incidence of preterm is 8 – 12 %
- Causes of increased number of preterm: Increased number of multiple pregnancies / Increased pregnancy in old females (and also <20 years).

Terminology

- Extreme prematurity: less than 28 weeks of gestation.
- Late-preterm infants: 34^{+0} to 36^{+6} weeks of gestation.
- Early term infants: 37^{+0} to 38^{+6}
- Full term: 39^{+0} to 40^{+6}
- Late term: 41^{+0} to 41^{+6}
- Post-term: > 42 weeks

- Large for gestational age: > 90^{th} percentile.
- Small for gestational age: < 10^{th} percentile.

- Low birth weight: < 2.5 kg
- Very low birth weight: < 1.5 kg
- Extreme low birth weight: < 1.0 kg

Low birth weight infant could be small for gestational age, preterm, or both.

Of the preemies, majority are born between 32 and 36weeks of gestation.

The majority of preemies whom gestational age ≥ 32 weeks can survive with basic essential newborn care plus breathing support, continuous skin to skin contact and infection prevention and management.

Characteristics of prematurity

- Small baby, often weighing less than 2,500 grams.
- The skin is thin, gelatinous, pink or red, shiny, able to see veins.
- Little body fat.
- Little scalp hair (wooly and fuzzy), but may have lots of lanugo.

- Weak cry and body tone (extended posture), reflexes are weak (Moro, suckling, grasp).
- Genitals may be small and underdeveloped (undescended testis, scrotum poorly developed, widely separated labia majora).
- Breast nodule small or absent.
- Few wrinkles on soles.
- Ear cartilages are poorly developed, soft and poor recoil.

Risk factors:

50 % of cases are idiopathic.

1. **Maternal factors:**
    - Infection (such as group B streptococcus, urinary tract infections, vaginal infections, infections of the fetal or placental tissues).
    - Drug abuse (such as cocaine).
    - Abnormal structure of the uterus.
    - Cervical incompetence (inability of the cervix to stay closed during pregnancy).
    - Previous preterm birth.
    - Extreme of age.
    - Weight < 50 kg.
    - Smoking, alcohol.
2. **Factors involving the pregnancy:**
    - Abnormal or decreased function of the placenta.
    - Placenta previa.
    - Placental abruption.
    - Premature rupture of membranes.
    - Polyhydramnios.
3. **Factors involving the fetus:**
    - When fetal behavior indicates the intrauterine environment is not healthy.
    - Multiple gestations.
    - Macrosomia.

Prevention

- Smoking cessation.
- Treatment of infection.
- Family planning and avoid implantation of multiple embryos.
- Folic acid supplement.

- Cerclage: in these women with prior PTB, if the transvaginal ultrasound CL shortens to < 25 mm at < 24 weeks.
- Steroids.
- 17-a-hydroxyprogesterone: It's synthetic form of progesterone given by injection in gluteus muscle and anterior thigh starting at 16-20 weeks until 36 weeks. Advantages: decrease risk of recurrent preterm births by 33%. Don't use it if no history of preterm birth. Not beneficial in case of multiple gestation.
- Progestogens have not been associated with prevention of PTB in women who have in the current pregnancy multiple gestations, preterm labor, or preterm PROM.
- Transfer the mother prior to delivery to perinatal center with trained staff.
- Expectant neonatal resuscitation at delivery.

Management of preterm labor:

- Tocolytics to slow down labor.
- Antenatal corticosteroids.
- Antibiotics for PROM. In high income countries, it is standard practice to give antibiotics to women with preterm, pre-labor rupture of membranes to delay birth and reduce the risk of infection.

Management at delivery room

- Keep premature babies warm (24˚C): increase delivery room temperature, use warming pad, consider polyethylene bag for babies < 28 weeks.
- Transfer to pre-heated incubator.
- Delay cord clamp by 30 – 60 seconds to maintain normal BP.
- CPAP with pressure not more than 7 mmHg (not Ambu bag because it gives constant pressure (40 mmHg)).
- It needs 10 min for SaO2 to be normal (85 – 95%).
- ECG to determine HR/ pulse oximetry for pulse rate.

Acute Complications:

1. **Hypothermia**
   - Causes of increased susceptibility in preterm:
     - ✓ High surface area to volume ratio.
     - ✓ Thin non-keratinized skin (porous skin).
     - ✓ Lack of insulating subcutaneous fat.
     - ✓ Lack of thermogenic brown fat.
     - ✓ Born wet at cold environment.
     - ✓ Inability to shiver.

- ✓ Poor vasomotor response

- Adverse consequences:
  - ✓ High O2 consumption → hypoxia, bradycardia.
  - ✓ High glucose usage → hypoglycemia / decreased glycogen stores.
  - ✓ High energy expenditure → reduced growth rate, lethargy, hypotonia, poor suck/cry.
  - ✓ Decease surfactant production → RDS.
  - ✓ Vasoconstriction → poor perfusion → metabolic acidosis.
  - ✓ Delayed transition from fetal to newborn circulation.
  - ✓ Thermal shock → DIC → death.

Normally (in term), response to cold stress relies on oxidation of brown fat, so if cold temperature, sensors on posterior hypothalamus induce pituitary to produce T4 and induce adrenals to produce NE>> lipolysis induced>> energy production in form of heat in mitochondria.

Note: brown fat contains increased number of mitochondria.

2. Complications of respiratory system:

- **Hyaline membrane disease (RDS):**
  - ✓ A condition in which the air sacs cannot stay open due to lack of surfactant in the lungs.
  - ✓ Pathophysiology: surfactant deficiency (due to immaturity of surfactant producing type II alveolar cells), Decreased compliance and decreased functional residual capacity.
  - ✓ Treatment: IV fluids, O2, mechanical ventilation, antenatal steroids.
  - ✓ Role of antenatal steroids: reduce RDS, NEC, IVH and neonatal death by inducing structural maturation, increase in lung volume, and epithelial barrier function.
  - ✓ Definitive treatment: exogenous surfactant
- Immature alveoli and vascularization of the Lungs.
- Immature musculature and insufficient calcification of bony matrix.
- Air leak (pneumothorax).
- **Apnea of prematurity:**
  - ✓ Pauses in breathing (15-20) seconds, associated often with bradycardia.
  - ✓ 3 types: central (idiopathic), obstructive, mixed (m.c)
  - ✓ Causes: mother's medication/ sepsis/ respiratory distress/ asphyxia/ intraventricular hemorrhage/ hypoglycemia/ electrolyte disturbances/ pneumonia/ diaphragmatic hernia.
  - ✓ Occurs in about half of babies born at or before 30 weeks.

- ✓ Treatment: treat the cause/ O2/ Mechanical ventilation/ Stimulation (tactile)/ CPAP: to relieve obstruction/ Methyl-xanthine (ex. Caffeine)/ aminophylline.
- ✓ Mechanism of action of methyl xanthine: Adenosine inhibits the respiratory drive and methyl-xanthine inhibits adenosine, so this results in enhancing the minute ventilation.

- **Pulmonary hemorrhage**: Rare/ Bleeding into the lungs/ Increases the need for ventilatory support/ Occurs mainly 2-4 days after birth/ Predisposing factors include mechanical ventilation, immaturity and PDA.

Most neonatologists say it is best to aim for a saturation of at least 85% - 88% and probably lower than 95% to avoid wide swings in oxygen levels.

"Several recent multi-centered randomized trials have sought to further clarify the relationship between oxygen exposure and development of ROP. One of the gold standard studies, the Surfactant, Positive Airway Pressure, Pulse Oximetry Randomized Trial (SUPPORT), compared oxygen target ranges of 85-89% with 91-95% as measured by pulse oximetry in 1,316 infants born between 24-28 weeks gestation. Severe ROP occurred less frequently in the lower oxygen saturation group (85-89%) However, these data also demonstrated significantly increased mortality in the lower oxygen saturation group".

3. **Cardiovascular complications**
    - Patent ductus arteriosus PDA:
        - ✓ Mechanism: PDA shunts blood so increase flow through pulmonary circulation and decrease systemic circulation.
        - ✓ Premature infants at risk AT 24-48 hours.
        - ✓ Echo will confirm the diagnosis.
        - ✓ Clinical picture: Apnea, Tachypnea, Heart failure, Failure to thrive.
        - ✓ Treatment: indomethacin, IV ibuprofen, surgical ligation.
    - Too low (due to cardiac dysfunction, hypovolemia or sepsis) or too high blood pressure.
4. **Metabolic complications:**
    - Dehydration: Causes of increased susceptibility in premature
        - ✓ Increase insensible losses (trans-epidermal): less keratinization of epidermis, increased surface area to volume ratio.
        - ✓ Increased urinary losses: immature renal function that cannot concentrate urine, decreased ability to reabsorb water and sodium.

- ✓ Management: prevention of dehydration/ Humidified air for neutral thermal environment and ventilation/ IV fluids (if needed).
- Electrolyte imbalances.
- Hyper or hypoglycemia. Usually hypoglycemia. Blood glucose should be monitored routinely starting within 1-2 hours post-birth until feeding is well-established.

Use hydrogel blasters for skin care.

5. **Infections:**
   - Due to immature immunity.
   - Increased risk of neurodevelopmental outcome and growth.
   - Give amino acids in 1st day (PTN)
   - Give intravenous lipids in 2nd day (PTN)
6. **GI complications:**
   - Difficulty in self feeding.
     - ✓ No coordination between sucking and swallowing before 34 weeks.
     - ✓ Poor digestion
   - Decrease enzymes, decrease motility >> increase GERD
   - NEC (necrotizing entero-colitis)
   - Abdominal distension.
   - Immature liver: cannot detoxify and Less bilirubin conjugation.
7. **Neurological complications:**
   - Intraventricular hemorrhage: It's rupture of germinal matrix due to hypoxia, hypotension, trauma…
     - ✓ Why? Fragile germinal matrix (especially <34 weeks)
     - ✓ Leading to hydrocephaly, disability (diaplegic cerebral palsy)

Later problems when the baby is stabilized:

Retinopathy of prematurity (ROP)

- It's developmental vascular proliferative disorder that occurs in the incompletely vascularized retina.
- Incomplete retinal vascularization. Mature vessels extend to nasal ora at 36 weeks. Vessels extend to temporal ora at 39-41 weeks.
- Increased risk with weight <1.5 kg and GA <32 weeks.
- International Classification of Retinopathy of Prematurity (ICROP) describes ROP according to -Zone, Extent and Stage. Staging:
  - ✓ Stage 1: Demarcation line.
  - ✓ Stage 2: Ridge.

- ✓ Stage 3: Extaretinal Fibrovascular Proliferation.
- ✓ Stage 4: Partial Retinal Detachment.
- ✓ Stage 5: Total Retinal Detachment.

- Standard method of treatment: lazer.

Osteopenia of prematurity (OOP)

- Is a Metabolic Bone Disease of PT infants, in which decreased bone mineral content occurs mainly as a result of lack of adequate Ca & P intake in extra uterine life.
- It is a common problem in babies of <1000gr who have low intakes of Ca & P.

Anemia of prematurity

- In 6-8 weeks postnatal
- Causes:
  - ✓ Blood loss due to ↑ blood tests.
  - ✓ Shortened RBC lifespan (40-60 days).
  - ✓ ↓ RBC production due to ↓ erythropoietin.

Chronic lung disease (bronchopulmonary dysplasia)

- Diagnosis: Need additional oxygen after reaching 36 weeks gestational age for at least 28 days with chest x-ray changes.
- Caused by mechanical ventilation use and long term use of oxygen.
- lungs not fully developed in prematurity
- Decrease surfactant (decrease alveolzation>> decrease surface area for gas exchange)

Ventilator induced lung injury

- Barotrauma: high pressures damage walls.
- Volutrauma: high volumes → over-inflation.
- Atelectrauma: Cyclic closing and reopening of alveoli.
- Biotrauma.

Periventricular leukomalacia

- Softening of tissues of brain around ventricles
- Most common in premature infant
- Ischemic brain injury
- Risk to develop: CP, intellectual impairment and visual disturbance

Other risks in prematurity:

- Sudden infantile death syndrome SIDS
- Autism.
- High risk of re-admission.
- Dental problems.
- Sleep problems.
- Behavioral problems.

When can a premature baby go home?

- Serious illnesses are resolved.
- Stable temperature -able to stay warm in an open crib.
- Taking all feedings by breast or bottle.
- No recent apnea or low heart rate.
- Parents are able to provide care including medications and feedings.
- > 35 weeks

Note: vaccination as term baby except for Hep B

IUGR:

- Process that limit fetus from achieving its full growth potential, may or may not be SGA
- Same complications as prematurity
- Symmetrical vs asymmetrical

- **Symmetrical**
- Occurs early in utero
- Affects all growth parameters
- Usually fetal factors
- Continue to be small in later childhood

- **Asymmetrical**
- Occurs late in utero
- Head is spared
- Usually due to uteroplacental insufficiency
- Associated with oligohydraminous

Sources: Dr. Iman Badran slides and annual lecture notes, in addition to some notes from the old lecture.

Asphyxia

- 58% of fetuses are born normal and 15% are born with problems and need resuscitation
- Asphyxia clinically is 6/10 or less APGAR score
- Brain damage usually occurs at 8 minutes.

Rule of APGAR score to assess neurological outcome and brain damage:

- APGAR =<6 / asphyxia
- APGAR <3 / sever asphyxia (damage already happened)

CAUSES

→ **INTRA-UTERINE**

- Utero-placental insufficiency (chronic HTN/ PET/ DM)
- Cord prolapse
- Abruptio placenta
- Maternal hypotension (bleeding/ epidural anesthesia)

→ **INTRA-PARTUM**

- Birth trauma (ex. Breech presentation)
- Depressant medications (to relieve pain during labor)
- Airway obstruction by meconium or amniotic fluid
- Umbilical cord compression

→ **POST-PARTUM**

- CNS (trauma/ drugs)
- Pulmonary disease (hypoplasia/ diaphragmatic hernia/ pleural effusion)
- Infection (pneumonia/ sepsis)
- Airway disorder (choanal atresia/ laryngeal webs)
- Neuromuscular disease (myopathy/ congenital myasthenia gravis)
- Renal disorders

NOTES:

If the baby asphyxiated the he will go in the following sequence: Rapid breathing>> **Primary Apnea** (1-2 minutes)>> irregular gasping (2 minutes)>> **Secondary Apnea**

- Primary Apnea: he will start breathing again after rubbing/ massaging or slapping of foot
- Secondary Apnea: will not improve unless you support him with O_2/ ventilation
  - Should always be considered

ABGs/ very important to assess the degree of acidosis and hypoxia

COMPLICATIONS

CNS
- Interventricular hemorrhage
- Seizures
- Cerebral edema

HEART
- Arrhythmia
- Ischemia

HEMATOLOGY
- DIC

ELECTROLYTE IMBALANCE
- Hypocalcemia
- Hyponatremia
- Hypoglycemia

LUNGS
- RDS
- Persistent pulmonary HTN

GIT
- Necrotizing enterocolitis

KIDNEYS
- ARF>> due to acute tubular necrosis (ATN)
- Adrenal hemorrhage

Hypoglycemia

The end

Respiratory distress in newborn

Definition: any deviation from normal breathing pattern.

Signs:

1. Tachypnea- Increased respiratory rate (>60): indirect assessment of lung function/ patients can't increase tidal volume except by increasing RR.
2. Retractions: (intercostal, subcostal, suprasternal)/ more retractions → stiffer lung.
3. Use of accessory muscles.
4. Nasal flaring: to decrease nasal resistance.
5. Grunting: abnormal breathing sounds; premature closure of epiglottis to allow some air inside. Continuous grunting indicates respiratory failure, treat with CPAP.
6. Cyanosis: mainly central. Acrocyanosis (peripheral cyanosis) is normal in the newborn if everything else is normal. Cyanosis might be absent in the presence of anemia.

Causes	
Pulmonary	**Extra-pulmonary**
RDS Meconium aspiration Transient tachypnea of newborn TTN Air leak Neonatal pneumonia	Diaphragmatic hernia Abdominal distension Anemia Polycythemia Metabolic acidosis Neuromuscular disorders Cardiovascular Narcotics

Respiratory distress syndrome (RDS)

- AKA "hyaline membrane disease".
- Surfactant deficiency (lung underdevelopment) >> unopposed surface tension >> collapse of alveoli.
- Most important sign: retractions followed by grunting.
- Onset shortly after birth up to 6 hours. Beyond 6 hours, look for other causes of respiratory distress.
- Risk factors:
  - ✓ Prematurity (most important).
  - ✓ Male.
  - ✓ Low birth weight.

    - ✓ Maternal diabetes.
    - ✓ Asphyxia.
- Chest X-ray: (the best initial test).
    - ✓ Ground glass appearance (homogenous infiltrate, white lungs).
    - ✓ Decreased volume in lungs.
    - ✓ Airbronchogram.
- Macroscopic appearance of lungs: ruddy and airless resembling hepatic tissue.
- Microscopic: diffuse atelectasis, eosinophilic.
- L/S ratio (lecithin/sphingomyelin) is the most accurate diagnostic test.
- Complications:
    - ✓ Hypoxemia.
    - ✓ Acidosis.
    - ✓ Air leak.
    - ✓ Infections.
    - ✓ PDA (due to hypoxemia).
    - ✓ Hintraventricular hemorrhage.
    - ✓ Chronic lung disease (bronchopulmonary dysplasia).
    - ✓ Neurodevelopment delay.
- Prevention:
    - ✓ Antenatal steroids.
    - ✓ Prevention of asphyxia.
    - ✓ Avoid prematurity (tocolysis).
- Treatment: GSG
    - ✓ G: general supportive measures.
    - ✓ S: surfactant administration (depends on severity). You can't give unless you intubate (given slowly through endotracheal tube 100 mg/kg).

Meconium aspiration syndrome

- Meconium passed (as a result of hypoxia and fetal distress) may be aspirated in utero or with first postnatal breath.
- Commonly seen in term and post-term infants.
- This will lead to lung irritation and obstruction.
- Chemical pneumonitis in utero.
- Chest X-ray: hyper-inflated lungs, flattening of diaphragm.
- Not homogenous disease.
- Complications: Pulmonary hypertension of newborn, air leak, aspiration pneumonia.
- Treatment: Resuscitate/ O2/ Mechanical ventilation/ Exogenous surfactant.

- Meconium is sterile but locally irritative and obstructive; it's also a medium for bacterial culture.
- Similar symptoms of MAS are seen in aspiration of blood or non-stained amniotic fluid.
- Amnio-infusion: is instillation of fluid into the amniotic cavity; a method of thinning the meconium that has passed into amniotic fluid>> it's useless; doesn't decrease incidence of MAS.
- Suction is waste of time; because most of meconium is probably aspirated in utero.

Transient tachypnea of newborn TTN

- Most common cause of respiratory distress.
- Mostly in term babies.
- Short course (24 – 72 hours).
- Residual pulmonary fluid stays in fetal lung tissue after delivery. Remember, one of the first changes after baby is born is resorption of lung fluid, so TTN occurs if this doesn't happen fast enough.
- Normally, PG (prostaglandins) released after delivery dilate lymphatic vessels to remove lung fluid as pulmonary circulation induced with first breath (if fluid persists despite this >> TTN).
- Risk factors: C/S delivery, Rapid second stage of labor, Maternal DM, asthma, Male, Macrosomia.
- Chest X-ray: Diffuse parenchymal infiltrates (wet silhouette around heart)/ intra-lobar fluid accumulation.
- Tachypnea immediately after birth or within two hours + sings of distress (often no hypoxia or cyanosis).
- Symptoms can last from few hours to two days.
- Treatment:
  - ✓ Usually rapid improvement.
  - ✓ Supportive.
  - ✓ O2, if hypoxic.
  - ✓ Prevention.
  - ✓ Prenatal corticosteroids before C/S delivery between (37-39) weeks.

Persistent pulmonary hypertension

- Soon after birth.
- Occurs when pulmonary vascular resistance fails to decrease after birth.
- Idiopathic or secondary to meconium aspiration, sepsis, pneumonia.

Source: Dr. Manar annual lecture notes and old lecture

Sudden infant death syndrome (SIDS)

DEFINITION

Sudden death of an infant, not explained by history, not explained by thorough postmortem examination, including autopsy, investigation of death scene and review of medical history

PATHOLOGY

No findings are pathognomonic and none are diagnostic (markers for pre-existing, chronic, low-grade asphyxia

- Petechial hemorrhage
- Pulmonary edema

Differential diagnosis

- Explained at autopsy
  - Infection
  - Congenital anomalies
  - Unintentional injury
  - Traumatic natural causes
- Not explained
  - SIDS
  - Intentional suffocation

ENVIRONMENTAL RISK FACTORS

NON MODIFIABLE

- Low socioeconomic status
- African American and Native American
- Highest at 2-4 months of age; most by 6 months
- Highest in winter, midnight to 9 a.m.
- Male> female

MODIFIABLE

- Shorter inter-pregnancy interval
- Less prenatal care
- Low birth weight/ preterm/ IUGR
- Maternal smoking, postnatal smoking

SLEEP ENVIRONMENT

- Higher incidence related to prone position
- Supine position now better than side-lying
- Higher incidence with soft bedding/ surface
- Higher incidence with over-heating
- Pacifiers shown to consistently decrease risk

OTHER RISK FACTORS

- Episode of an apparent life-threatening event
- Subsequent siblings of SIDS victim
- Prematurity inverse with GA and birth weight

REDUCING RISK

** ABC: The ABC's of Safe Sleep to prevent SIDS

- **A**: sleep **A**lone
- **B**: sleep on **B**ack
- **C**: sleep is in a **C**rib or bassinet; flat surface; open place; no soft surfaces like sofas or water beds; no bed sharing; no toys or heavy blankets.

· Avoid over heating or over bundling
· Use prone position only while infant is awake and observed.
· No smoking.
· Stay away from crowded areas.

The end

Neonatal sepsis

Sepsis neonatorum: Disease of neonates (< 28 days) who are clinically ill and have positive blood culture.

Sources:

1. Maternal (transplacental)
2. Nursery environment.
3. At delivery room (most common).

Timing and etiology:

Early onset sepsis (birth-72 hours of age)

- GBS
- Gram negative (E. coli): most common in Jordan.
- Listeria

Late onset sepsis (72 hours- 28 days)

- Coagulase negative staphylococcus (CONS)
- Gram negative (E. coli)
- Listeria
- Fungal
- GBS (can be a cause of sepsis up to 2 months).

Risk factors:

- Prematurity
- Prolonged rupture of membrane
- Chorioretinitis
- Intra-partum fever, maternal UTI
- Maternal colonization with GBS (group B streptococcus)
- IV lines or invasive procedures

Clinical presentation:

Can present with anything!

- Temperature instability
- Apnea/ tachypnea
- Cyanosis
- Lethargy
- Poor feeding
- Hypoactivity
- GI symptoms: Vomiting, diarrhea, abdominal distension

- Metabolic acidosis (unexplained), hyperglycemia
  - Late manifestations
    - Hepatosplenomegaly
    - Jaundice
    - Petechia

Usually if well-looking baby and low grade fever, think of viral etiology. If toxic-looking baby and high grade fever, think of bacterial etiology.

Diagnosis:

- CBC (with differentials and platelets): not very helpful!
- I: T ratio (immature segmental cell: total segmental cells): elevated ratio means left shift. It is the most important and specific investigation.
- U/A
- Urine culture (not part of early septic work-up).
- Blood culture
- Chest x-ray (only in presence of respiratory symptoms).
- Lumbar puncture (LP): normal CSF values; WBCs (up to 25 cells/HPF), RBC (nil), neutrophils (>50%).
- CRP: to rule out sepsis; if normal >> unlikely to be sepsis.
- Urea, Cr, electrolytes.

Meningitis is similar to sepsis so it should part of septic work-up (lumbar puncture). Don't depend on meningeal signs because they are not reliable till the age of 18 months.

Treatment

→ Supportive.

→ Empirical antibiotics: ampicillin for GBS, ampicillin and aminoglycosides for gram (-) infections.

Usually we give meningitis dose (higher dose than usual).

Complications

- Death
- Feeding issues
- Necrotizing enterocolitis
- DIC
- Osteomyelitis (Staph is usually the cause)
- Hydrocephalus

- Poor neurological outcomes- especially in gram (-) due to increased cytokines and thus increased brain injury.

Prevention

- Screen pregnant ladies for GBS (done at 35 – 36 weeks; vaginal and rectal cultures); give intrapartum maternal antibodies if culture was positive (only for EARLY-onset GBS).
- Good hygiene.
- Antibiotics guideline.
- IV guidelines.
- Good nursery care.

Notes

- The presence of clinical manifestations differentiates sepsis from transient bacteremia (observed in some healthy neonates)
- Infections cause significant mortality and morbidity in neonates
- The outcome will be improved if illness recognized early

Source: Dr. Manar annual lecture notes and old sheet.

Neonatal jaundice

Definition

Neonatal jaundice: yellowish discoloration of the skin, sclera and mucus membrane (total bilirubin > 5mg/dl)

Hyperbilirubinemia: increase in the serum bilirubin above normal (>1.5-2 mg/dl)

Pathophysiology

- Increase production of bilirubin from breakdown of fetal RBCs plus immaturity of hepatic conjugation of bilirubin
- Concern is for rapidly increasing unconjugated (indirect) bilirubin, as it can cross the blood brain barrier (BBB) and lead to kernicterus

Kernicterus

Collection of unconjugated bilirubin in the basal ganglia and brain stem nuclei

Manifestation

1. Hypotonia
2. Seizures
3. Opisthotonos
4. Delayed motor skills
5. Choreoathetosis
6. Sensorineural hearing

Types

- Physiologic jaundice
- Pathologic jaundice

Work up for possible pathologic hyperbilirubinemia when:

- Appears on first day of life
- Rise > 5 mg/dl/day
- Bilirubin >13 mg/dl in term infant
- Direct bilirubin > 2 mg/dl at any time

Physiologic	Pathologic
· Appears in 2nd to 3rd day of life (term) · Disappear by 5th day of life · Clinical jaundice resolved in tem by 2 weeks, in preterm by 3-4 weeks · Peak bilirubin <12 mg/dl (in term), and <15 mg/dl (in preterm) · Rate of bilirubin rise <5 mg/dl/day · Dose not appear after it has resolved	· May appear in the first 24 hours of life · Clinical jaundice isn't resolved by 2 weeks in term, or by 3-4 weeks in preterm · Peak bilirubin >12 mg/dl in term, or >15 mg/dl in preterm · Usually > 5 mg/dl/day (or >0.5mg/dl/hour) · Clinical jaundice appear after it has been resolved

Remember

- Acute bilirubin encephalopathy is clinical nervous system toxicity caused by bilirubin toxicity
- Kernicterus: chronic, permanent clinical sequel of bilirubin toxicity

<table>
<tr><td colspan="4">Jaundice</td></tr>
<tr><td rowspan="4">Physiologic (direct)</td><td colspan="3">Pathologic</td></tr>
<tr><td colspan="2">Indirect</td><td>Direct</td></tr>
<tr><td>Coombs +</td><td colspan="2">Coombs -ve</td><td rowspan="3">· Sepsis
· TORCH
· Total parental nutrition (TPN)
· Hypothyroid
· Galactosemia
· Tyrosinemia
· Cystic fibrosis
· Choledochal cyst
· Biliary atresia (clay stool, yellowish to greenish discoloration).</td></tr>
<tr><td rowspan="2">Rh/ABO incompatibility</td><td>↑/Hb</td><td>NL/↓ Hb</td></tr>
<tr><td>· Polycythemia
· Twin-twin transfusion syndrome
· Maternal fetal transmission
· IUGR
· Infant of diabetic mother</td><td>Spherocytosis
Elliptocytosis
G6PD deficiency (ask in history if mother has eaten fava beans).
Pyruvate kinase</td></tr>
</table>

Bilirubin metabolism

Hb:

- Globin
  - protein that is conserved and utilized>> amino acid
- Heme
  - Can't be used, degraded and excreted
  - Fe^{+2}
  - Biliverdin>> Bilirubin unconjugated

(Travels in plasma, bound to albumin)

Hypoxia and hypothermia compromises bilirubin conjugation

Stercobilin gives the characteristic color to feces

Note

<u>Prolonged jaundice:</u>

>2 weeks in term

>3 weeks in preterm

90% of them are not pathological, breast milk jaundice is most likely the cause, but always rule out pathological by work up

PHYSIOLOGIC JAUNDICE

- Increase in bilirubin by the 2nd day of life
- It has pattern, peaks 3-4 day in term, 5-7 days in preterm
- Decline by the 5th day of life
- Clinically baby is well in general

Note:
Physiologic jaundice may be higher in breast milk fed infants than formula fed infants

Causes

- *Hepatic immaturity*
  - Defective uptake from plasma
  - Defective conjugation
  - Decreased excretion
  - Increased enterohepatic circulation

- *Increase β-glucorinidase*

- *Other factors contributing to physiologic jaundice*
  - Drugs: antibiotics (penicillin, ceftriaxone), valium
  - Bruises, cephalohematoma (ask about history of vacuum use)
  - Hypoxia, asphyxia
  - Hypothermia
  - Hypoglycemia
  - Dehydration
  - Lipolysis (increase FFA so decrease binding of albumen to bilirubin)

Good feeding;
every two hours

BREAST FEEDING JAUNDICE VS BREAST MILK JAUNDICE

- **Breast feeding jaundice:**

· Means that a baby is not nursing well and so not getting many calories
· This is frequent in first time breast feeding mothers
· The infant may in fact become dehydrated (but it's the lack of calories that causes the jaundice)
· Management: counselling and rehydrate the baby

- **Breast milk jaundice:**

· Occurs due to glucuronidase present n some breast milk
· Prolonged around 2-3 months
· Diagnosis and also treatment: stop breast feeding and give formula for 1-2 days, so when the bilirubin checked again, it will have fallen significantly, this diagnostic
· The baby may then be safely breast fed
· Despite the increase risk, exclusive breast feeding is still the recommended feeding choice

Pathologic jaundice

· Clinical jaundice appears in first 24 hours of age
· Total bilirubin rise >5 mg/dl/day
· Total bilirubin >12 mg/dl in term
· >15 mg/dl in preterm
· Direct bilirubin >1.5 mg/dl

Work up for pathological jaundice

- CBC, retics, blood film
- TSH, T4
- G6PD enzyme
- Urine
  - Culture
  - Reducing substance (to rule out galactosemia)

CAUSES OF UNCONJUGATED HYPERBILIRUBINEMIA

→ **Synthesis**
- Overload
  - Polycythemia
  - Organ hemorrhage
  - Swallowed maternal blood
- Hemolysis
  - Rh/ABO incompatibility
  - Abnormal RBC morphology
  - RBC enzyme deficiency
  - Sepsis
  - Galactosemia (in early stage only, then direct)

→ **Abnormal hepatic conjugation and secretion**
- Conjugation
  - type I and II Criglar-Najjar syndrome
  - Gilbert syndrome
- Secretion
  - Hypothyroidism
  - Galactosemia

→ **Increase enterohepatic circulation**
- Pyloric stenosis
- Small/ large bowel obstruction

CAUSES OF CONJUGATED HYPERBILIRUBINEMIA

Cholestasis jaundice>>75% due to
1. Biliary atresia
2. Neonatal hepatitis

3. α-1-antitrypsin deficiency

	Disease	Pathogenesis	Signs/ symptoms	Diagnosis/ treatment
Familial non hemolytic unconjugated hyperbilirubinemia	Criglar-Najjar type I	Type I glucuronyl transferase deficiency (autosomal recessive)	rapid increase of unconjugated bilirubin in 1st days of life persistence of bilirubin >20 mg/dl almost all infants have kernicterus	Diagnosis Closed liver biopsy (measure glucuronyl transferase) Treatment Intensive phototherapy and exchange transfusion
	Criglar-Najjar type II	Partial enzymatic deficiency (autosomal dominant)	May be similar to type I or milder with delayed onset Kernicterus is not common	Diagnosis and treatment is different from type I It will respond to oral phenobarbital
	Gilbert syndrome	Decrease Clucuronyl transferase levels with unconjugated hyperbilirubine-mia	Benign	No treatment necessary
Inherited conjugated hyperbilirubinemia	Dubin-Johnson syndrome (black pigmentation of liver cells) Rotor syndrome (liver cells are not pigmented)	Transfer of bilirubin and other organic anions from liver to the bile is defective (autosomal recessive)	Chronic, mild conjugated hyperbilirubinemia	Diagnosis: usually detected in adolescence

General treatment of hyperbilirubinemia

Goals of treatment

- Prevention of kernicterus
- Treatment of underlying condition
- Maintenance of hydration and nutrition

– PHOTOTHERAPY

Complications

- Loose stools
- Erythematous macular rash
- Overheating, leading to dehydration
- Bronze baby syndrome.

** In phototherapy Blue light (visible light) is used. It converts bilirubin into soluble form that is secreted with urine.

- EXCHANGE TRANSFUSION

  If bilirubin continues to increase despite intensive phototherapy or kernicterus is concern

- IVIG

  Significantly decrease need for transfusion in patients with isoimmune hemolytic disease

How to manage infants released within the first 48 hours of life?

In the era of early discharge in recent years, a number of infants have developed kernicterus, so

Know the risk for sever kernicterus which are

- Jaundice in the first 24 hours of life
- Visible jaundice before discharge
- Previous jaundice siblings with phototherapy (family history)
- 35-38 weeks gestation (prematurity)
- Exclusive breast feeding
- East Asian race/ male
- Cephalohematoma, bruising

Indication for phototherapy

- Bile rise > 5 mg/dl/day
- Persistent sever metabolic or respiratory acidosis
- Sepsis
- Sick very low birth weight

Factors that increase risk of kernicterus

- Prematurity
- Acidosis
- Hypoalbuminemia
- Rapidly increase serum bilirubin

- Use of hour-specific bilirubin nomogram may assist (do it as universal screen if no close follow up)

Added notes from Dr. Iman Badran seminar

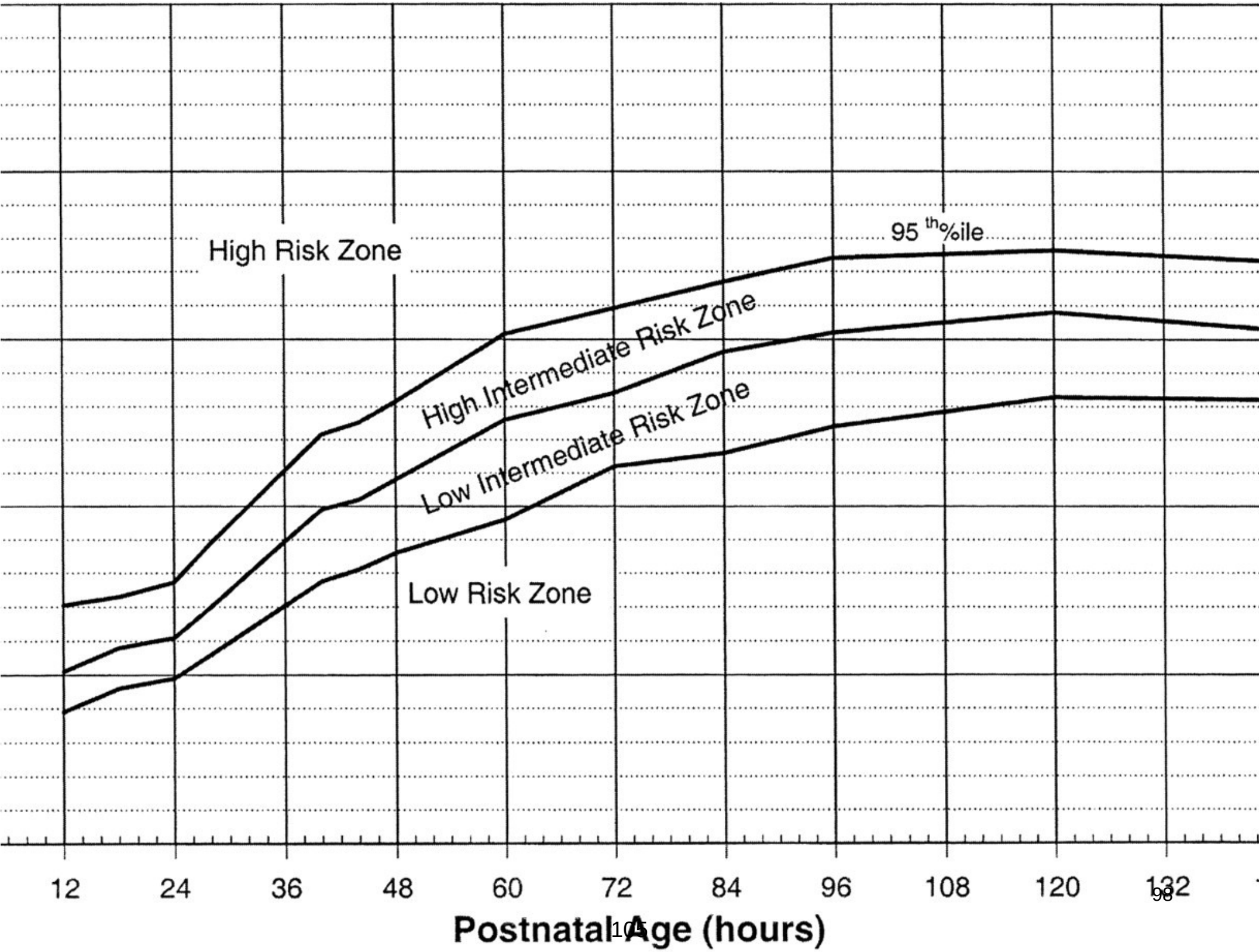
History of jaundice:

- Vomiting: think of UTI, sepsis, galactosemia, hepatitis.
- Stool color.
- Abdominal distension
- Diarrhea/ constipation.
- Constitutional symptoms: fever/ activity/ appetite/ feeding/ weight loss/ excessive crying.
- CNS: seizures/ LOC/ behavioral changes/ abnormal movements.
- HLS: bruises (biliary atresia)/ skin rashes.
- UGS: urine color and smell/ diapers (normally 4-6 per day)/ pain (crying) during urination/ black urine (alkaptonuria).
- Prenatal: maternal illness/ drugs/ blood group.
- Natal: method of delivery/ GA
- Acute bilirubin encephalopathy – acute toxicity: fever and lethargy.
- Family history: G6PD/ hemolysis/ spherocytosis (ask about splenectomy)

** Breast milk jaundice: mainly genetic cause.

risk factors for severe hyperbilirubinemia

Major Risks	Minor Risks	Decreased Risk
Predischarge TcB or TSB in high-risk zone	Predischarge TcB or TSB in high intermediate-risk zone	TSB or TcB in low-risk zone
Jaundice in first 24 hr.	Gestation age 37-38 wk	Gestation age ≥41 wk.
Blood group incompatibility with positive DAT, other known hemolytic disease, elevated $ETCO_2$	Jaundice observed before discharge	Exclusive bottle feeding
Gestation age 35-36 wk	Sibling with jaundice	Black race
Sibling received phototherapy	Macrosomic infant of diabetic mother	Discharge from hospital after 72 hr.
Exclusive breastfeeding, particularly with excessive weight loss	Maternal age ≥25 yr.	
East Asian race	Male gender	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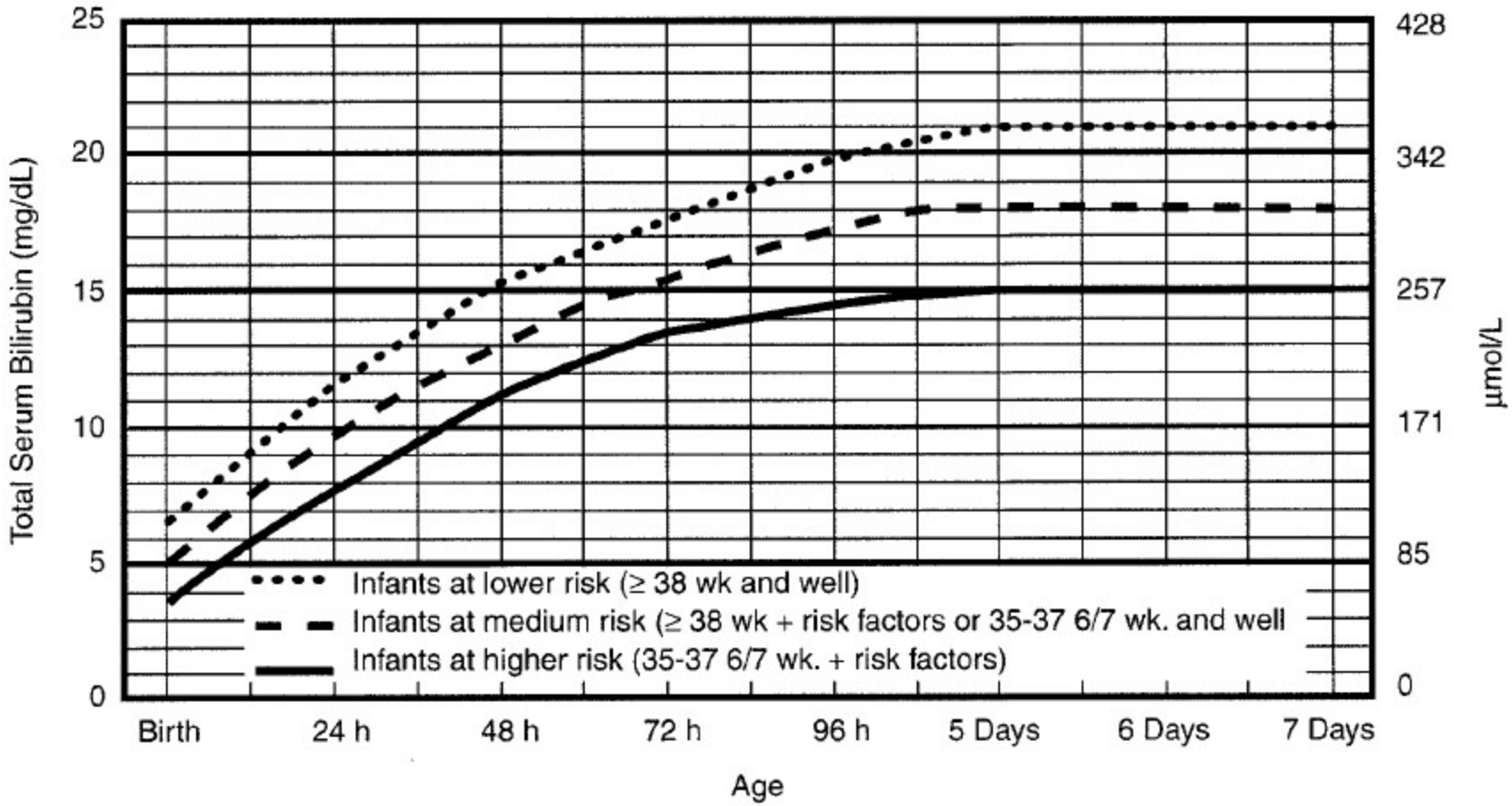
Postnatal Age (hours)



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

Breast milk feeding

- Human milk is the optimal feeding; it's beneficial for both mother and infant

DURATION OF EXCLUSIVE BREAST FEEDING

- Breast feeding for the first 6 months (only breast-feeding)

INITIATION AND MAINTENANCE

- Mothers need to establish and maintain milk production
- In terms, no barriers for initiation
- Sick baby and preterm expression either by hand or by use of pump

EARLY INITIATING

- With first 30-60 minutes after delivery, why?
  - Psychological bonding by skin contact is maximal
  - Rooting and suckling reflexes are maximal
  - Suckling stimulates milk secretion or let-down reflex
  - Colostrum has nutritious anti-infective characters

Prenatal education program is the most effective intervention to promote initiation of breast feeding

MAINTENANCE

- Should be continued, with the addition of solid foods, for at least 12 months
- Best for 18-24 months (1.5-2 years)

STEPS FOR SUCCESSFUL BREAST FEEDING

- Inform all pregnant women about the benefit (prenatal counselling)
- Help mothers initiate Brest-feeding within the first half-hour of birth
- Show mothers how to breast-feed and how to maintain lactation
- Don't give babies milk or food other than breast milk (unless medically indicated)
- Encourage breast feeding on demand

ADVANTAGES OF BREAST FEEDING

→ <u>ADVANTAGES TO THE MOTHER</u>

- Infant sucking promote involution of the uterus after parturition and weight loss
- It saves time and available all the time
- Cost-effective and less strain on family budget than buying milk formula
- Decrease risk of breast cancer in mother
- Psychological well-being and enhancement of the bonding between mother and baby
- Fulfills the feminine role of mother attitude
-

→ <u>ADVANTAGES TO THE INFANT</u>

- Human milk is warm, ready, sterile, perfectly balanced and doesn't cost anything
- More easily digested than cow's milk
- It has greater immunity (antimicrobial and anti allergic effects)
- Available all the time
- Less likely to have GI disorders, anemia and vitamins deficiency
- Less likely to acquire infection
- Psychological well-being and enhancing bonding with his mother

LONG-TERM

- Decrease risk of obesity
- Decrease risk of DM I and II
- Decrease risk of cardiovascular disease (HTN, dyslipidemia)
- Decrease overall risk of childhood CA (like leukemia and lymphoma)
- Higher IQ and better cognitive development

Several components of human milk stimulate GI maturity

- Growth factors; due to presence of GF, hormones and anti-inflammatory agents
- Motility increase (increase gastric empting)
- Decrease risk of necrotizing enterocolitis
- IgA and IgG
- Beneficial microbes (colonization of beneficial microbes of bifidobacteria and lactobacillus)

Note

- Premature infants immune system is particularly immature so high susceptibility to infection>> that's why premature should be breastfed because it also provide strong protection

DISADVANTAGES OF BREAST FEEDING

- Vitamins K deficiency
- Breast milk jaundice
- Transmission of infection (ex. HIV)
- Transmission of drugs

Breast milk composition differences

- GA at birth (preterm and term)
- Stage of lactation (colostrum and mature milk)
- During a feed (foremilk and hind-milk)

CONTRAINDICATIONS OF BREAST-FEEDING

→ <u>MATERNAL FACTORS</u>

- Infections
  - Maternal HIV infection (**Breast feeding with HIV is contraindicated in developed countries, while it's not in developing countries).
  - Active HSV on the breast
  - Active TB infection
  - Active varicella zoster (peripartum)
- Drugs (REAL)
  - R: Radioactive isotopes
  - E: ergotamines
  - A: Antimetabolite
  - L: lithium
  - CA chemotherapy
  - Substance abuse
  - Alcohol/ nicotine

Hepatitis A, B and C are not contraindicated

Mothers with HBV infection are free to breastfeed their infants after the neonate has received the appropriate recommended vaccination against HBV

Breast-feeding is not contraindicated in mastitis

→ <u>INFANT FACTORS</u>

- Congenital metabolic defect
  - Galactosemia (the only contraindication in metabolic diseases)

BREAST FEEDING POSITIONS

MADONNA OR CRADLE HOLD

- Sitting positing
- C-hold
- Tummy to tummy
- Baby's head in bend of mother's elbow and his arm around mother's waist

FOOTBALL HOLD

- Sitting position
- Baby cradled under arm and his head in palm of mother's hand
- Commonly used by mothers
  - Concerned about latch-on
  - Have a premature baby
  - Have large breasts
  - Have sore abdomen

CROSS-CRADLE HOLD

- Sitting position
- Baby held across mother's body with arm opposite of feeding breast
- In mothers
  - Having trouble with latch-on
  - Feeding premature baby

LYING-DOWN POSITION

- Side laying position
- Pillow under mother's head and back, mother's arm bent under baby's head
- C-hold
- Comfortable, alternative position especially at night

SINGS OF EFFICIENT BREAST-FEEDING

1. Audible rhythmic swallowing during nursing
2. Breast fullness relieved by breast-feeding
3. Absence of sore nipples and lack of persistent pain during breast-feeding sessions
4. Infant is calm and satisfied after feeds
5. Infant sleeps well 3-4 hours after feeds
6. At least 2-3 wet diapers/ day for the first 2 days of life, 4-6 wet diapers/ day after the third day of life
7. At least 3-4 bowel movements/ day
8. Weight gain

BREAST VS FORMULA FEED

→ Breast milk
  - 70% whey
  - 30% casein

→ Formula (cow's milk)
  - 20% whey
  - 80% casein

- Whey and casein are defined by their solubility in acid
- Whey is soluble protein but casein is insoluble

COMPOSITION OF BREAST MILK

- **COLOSTRUM** (only in first 5-7 days)
  - Bright lemon yellow, alkaline, viscous fluid, secreted during first 5-7 days
  - Colostrum vs mature milk
  - Colostrum is richer in protein but less carbohydrates and fat
  - Colostrum is contains antibodies to protect the newborn against disease (IgA)
  - After this, breast milk will become mature milk

- **ENERGY** (~70Kcal/100 ml)

- **PROTEIN**

- Protein content is highest at birth and declines over the next 2-4 weeks to a steady level
- Provides 8% of caloric needs
- Two fractions of proteins
  - Casein>> insoluble protein (30%)
  - Whey>> soluble protein (70%)
    - Compared to casein, whey is more easily digested and is associated with more rapid gastric emptying
    - When protein provides lower concentrations pf potentially deleterious amino acid (phenylalanine/ tyrosine/ methionine)
    - These amino acids, in high concentration may interfere with brain development

- Human milk has higher amounts of cysteine and taurine (less amount of methionine) which are important for bile conjugation and brain development

- Human Whey Protein
  - Lysozyme
  - Lactoferrin
  - Secretory IgA
  - Lactoalbumin: major human whey protein

- The major whey protein in cow's milk is lactoglobin not lactoalbumen

- **FAT** (triglycerides are the main fat constituent)
  - It's an essential nutrient for good health
  - Not affected by maternal diet
  - But differs with
    1. GA (more MCT if premature)
    2. Lipid varies over the course of one day
    3. Lactation patterns (foremilk and hind-milk)

- Breast milk contains DHA which is important for baby's visceral and brain development

- The hind-milk has the highest fat and caloric content

- **CARBOHYDRATES**
  - Lactose (7g/dl)
  - Oligosaccharides/galactose/ fructose
  - The main carbohydrate is lactose
  - Significance of lactose
    - Softer stool consistency
    - Nonpathogenic bacterial fecal flora
    - Improved absorption of minerals (mainly calcium)
  - Significance of oligosaccharides
    - Important in the host defense of the infant (as their structures mimic specific bacterial antigen receptors)

- **MINERALS AND TRACE ELEMENTS**
  - Ex. Iron, calcium, phosphorus, zinc, copper
  - Lower concentrations but better bioavailability
  - Although concentrations of iron, zinc and copper decrease lactation, the needs for these nutrients are usually adequately met through the first 6 months
  - Beyond 6 months of age, iron and other micronutrient containing complementary foods should be introduced to prevent deficiencies in full-term infants
  - Ca: PO_4^{-2} in human milk is 2:1, while in cow' milk it's 1:1, so the bioavailability of Ca^{+2} in human milk is more

- **VITAMINS**
  - Maternal vitamins status affects the content of vitamins in human milk
  - Vitamin K is present in low amounts in human milk
  - Also vitamin d is low, so daily supplements of vitamin D are recommended for exclusively breastfed infants to decrease risk of rickets
  - High risk infants are
    - Babies who are not adequately exposed to sun
    - Babies whose mothers don't consume adequate nutrients
  - Vitamin B12 deficiency may develop in babies whose mothers are vegetarian
  - Although vitamin D is low in breast milk but it's more biologically active

FORMULA FEEDING

- Infant formula is used as a substitute for or to support breast milk
- Most are cow-milk-based with modifications to approximate breast milk
- It contains ~ 70 kcal/10 ml
- Don’t give infants cow-milk before the age of one year.

To sum up

Component	Human milk	Cow milk
Water/solid	Same	
Calories	~70 kcal/100 ml	
Protein	1-1.5 (whey dominant)	3.3 (casein dominant)
Carbohydrates	6.5-7% lactose more	4.5% lactose less
Fat	High in LCFAs	High in MCFA
Minerals	Iron better absorbed	↓ iron and copper
Vitamins	Diet-dependent Low in vitamin K	Low in vitamin C and D
Bacterial content	Uncontaminated	Harmless bacteria
Digestibility	Faster emptying	Same after 45 days
Renal solute load	Low (Aids in renal function)	Higher

Some notes from Dr. Rawashdeh seminar:

- Strong indications for breast feeding: mastitis/ cleft lip and palate.
- Breast milk jaundice is not a contraindication.
- Breast milk contains 88% water.
- Weaning: 1 item at a time for 3 – 4 days to detect allergies.
- At age of 1 year, infant should be able to eat 90% of food.
- Breast milk in the 2nd year has little nutritional benefit but good for immunological benefit.

The end

TORCH

- Toxoplasmosis
- Others (syphilis, varicella, HIV and parvovirus B19)
- Rubella
- CMV (cytomegalovirus)
- HSV (herpes simplex virus)

Definition

Congenital neonatal infections occurring during pregnancy or the peri-partum period

- Most infant have IUGR
- They cause devastating long-term consequences

TOXOPLASMOSIS

- Caused by parasite toxoplasma Gondi
- The primary host is the domestic cat

Transmission
Most common: in 3rd trimester
Most lethal: in 1st trimester

Transmission:

- Ingestion of water/food with oocytes that have been excreted by infected cats (fecal contamination), most common in U.S
- Ingestion of undercooked/raw meat containing tissue cysts, most common world-wild

Clinical picture

- *MOTHER:*
  - Most infected females have no symptoms
  - If symptomatic (15%); flu-like symptoms with lymphadenopathy
- *INFANT:*
  - 70-90% are asymptomatic at birth
  - Up to 80% of affected infant develop learning or visual disabilities

Findings:

- Chorioretinitis
- Seizures
- Intra-cranial calcifications
- Microcephaly,
- Hydrocephaly
- Non-immune hydrops
- Symmetrical IUGR
- Hepatosplenomegaly and thrombocytopenia

The more sever forms can be fatal shortly after birth

Antenatal diagnosis

- PCR for parasite DNA detection in amniotic fluid/ fetal blood
- Serology;
  - IgG antibodies are detectable 1-2 months post-infection
  - IgM testing often yields false positive/negative results and IgM antibodies can persist for 6-24 months
  - IgA and IgE (T. Gondi specific) testing is preferred to IgM because their concentrations drop sooner than those of IgM
  - Serology should be repeated after 10 days because placental leak can cause false positive results

Prevention

- Education and serologic testing

Treatment

- Treatment during pregnancy reduces the likelihood of admission significantly
- Maternal treatment with Spiramycin
- Infant are treated with sulfonamide, pyrimethamine and folinic acid, for up to one year

Follow up

- Ongoing ophthalmologic and developmental follow up is warranted for infants with congenital toxoplasmosis

RUBELLA (German measles)

- RNA virus
- Highly contagious
- 85% of pregnant are IgG positive

Transmission

- Respiratory droplets
- Transmission is most commonly in the 1st 8 weeks of gestation
- Zero transmission after 20 weeks of gestation

Finding of congenital rubella

- Cataract
- Deafness
- Congenital heart disease (PDA, pulmonary hypoplasia)
- Blueberry muffin appearance (due to extra-medullary hematopoiesis)
- Hepatosplenomegaly and thrombocytopenia
- Microcephaly
- Mental retardation

Clinical picture

- Clinical rubella infection in the mother
- 1-5 day prodrome of low grade fever, headache, arthralgia or arthritis

Serology

- Increased IgM; indicates primary infection
- Increased IgG (4X); indicates reinfection

Diagnosis in neonates

- Clinical manifestations
- Cord blood rubella specific IgM
- PCR of amniotic fluid
- IgM in serum

Prevention

- Vaccination
- Screening

Treatment and prognosis

- No specific treatment for congenital rubella, only supportive
- Outcome depends on the severity of problems present
- Heart defects mat be corrected surgically, but damage to nervous system is permanent

Complications/ outcome

- Hearing loss
- Persistent growth retardation
- Mental and motor retardation
- Microcephaly

<u>CMV</u>

- The most common congenital viral infection
- The most common cause of non-hereditary sensorineural hearing loss in children
- Primary infection (higher risk of sever disease) or reactivation
- The most likely sources of infection for pregnant women are: young children at child care center, infected sexual partner

Transmission

- Prenatal: (congenital/ placental)
- Natal: 50% of exposed infants become infected
- Postnatal: human milk in preterm infant, blood transfusion, transplant

- Transmission is more common in a primary maternal infection, which results in fetal infection in 30-40% of cases
- Pre-existing maternal immunity decrease incidence of maternal to fetal transmission to about 1%

Clinical picture

- 10% are symptomatic at birth
- Hepatosplenomegaly and thrombocytopenia with petechial, pupura and blueberry muffin
- Small for gestational age
- Microcephaly
- Chorioretinitis
- Congenital hyper-bilirubinemia
- Calcifications

Diagnosis

PRENATAL DIAGNOSIS

- Viral culture of amniotic fluid
  - 100% specific
  - Not sensitive (high false positive)
- PCR of amniotic fluid: both specific and sensitive

POSTNATAL DIAGNOSIS

- Isolation of CMV from urine or saliva before 3 weeks of age
- PCR
-

Why before 3 weeks? To differentiate prenatal from natal and postnatal

Treatment

- Ganciclovir

Prevention

- Hygiene behavior changes
- Administration of CMV hyper-immune globin (HIG)
- Vaccine development

Remember
Calcifications of toxoplasmosis: diffuse intracranial
While
CMV: periventricular

Complications:

- Hearing loss
- Mental retardation
- Neuromuscular abnormalities

HSV

- Neonatal herpes is the result of HSV-2 infection (genital HSV)
- Prevalence differs from country to country
- Many genital herpes remain asymptomatic for long periods with no history of infection despite shedding virus
- In most cases of neonatal infection, mothers do not give a history of active genital herpes at the time of delivery
- The chance of a women (who has a past history of genital HSV) shedding virus at the time of delivery is around 1%

Transmission

- Intra-uterine <2%
- Intra-partum ~90%
- Post-partum 5-10%

Clinical picture

Usually appears within 1-3 weeks of birth, but should be considered thereafter

Risk of neonatal infection

- 50% risk>> for infants born to mothers with primary first episode
- 25%>> when mothers have antibodies to HSV-1 only
- <2%>> in cases of recurrent infections in seropositive mothers

Type	Findings	C/P	Diagnosis	Treatment
Disseminated	Pneumonia, shock, hepatitis	5-7 days	PCR, Tzanck smear culture	Acyclovir
Skin, eyes, mouth (localized)	Keratoconjuctivitis, Skin lesion	5-14 days	PCR, Tzanck smear culture	Acyclovir
CNS	Meningitis, lethargy, seizures	3-4 weeks	PCR, Tzanck smear culture	Acyclovir

- Usually it manifest as localized disease (present as vesicles or zoster-like eruptions on skin, eyes or mouth, if left untreated>> 70% progress to disseminated disease
- 40% of patients who have disseminated disease do not develop skin lesions
- 1/3 of patients with CNS manifestations present without skin findings

Always monitor neutrophil count during treatment due to risk of neutropenia

Treatment

- *Acyclovir:*
  - If localized, treat for 14 days
  - If disseminated, for 21 days
  - If HSV encephalitis, treat until CSF and PCR become negative

Clinical manifestations associated with poor prognosis

- Meningoencephalitis
- Sever coagulopathy
- Pneumonitis
- Liver failure

Prevention

- Elective C/S when active disease or visible lesions are identified, however it's not 100% effective in prevention

Complications

- Microcephaly
- Deafness
- Blindness
- Seizure disorder, spasticity
- Psychomotor retardation

Prognosis

- Disseminated disease is associated with high mortality rate
- 60%>> HSV-2
- 70%>> HSV-1

OTHERS

VARICELLA

- Neonatal
  - Seen when delivery occurs <1 week before/after maternal infection
  - Treatment with VZIG (varicella zoster Ig), if mother develop varicella 5 days before to 2 days after delivery
- Congenital
  - Associated with limb hypoplasia, cutaneous scars, cataract, chorioretinitis, microcephaly and cortical atrophy
  - Congenital varicella is associated with infection during 1st or 2nd trimester

CONGENITAL SYPHILIS

- Trans-placental transmission usually during 2nd half of gestation
- All infants must undergo serologic testing at the time of delivery

Findings

→ *Early (<2 years)*

- Fever, anemia, failure to thrive, snuffles, maculopapular rash, jaundice, periostitis

→ *Late (>2 years)*

- Hutchinson teeth, saber shins, saddle nose, osteochondritis

Diagnosis

- Characteristic radiographic bone changes
- Treponema in scrapings from any lesion or fluid
- Serologic tests

- Most helpful specific test is IgM-FTA-Abs

- Patients with positive VDRL and pathognomonic signs might help in diagnosis

Treatment

- Penicillin

SUMMARY

TOXOPLASMOSIS: hydrocephaly with generalized calcifications and chorioretinitis
RUBELLA: the classic findings of cataracts, deafness and heart defects
CMV: microcephaly with periventricular calcifications, petechia with thrombocytopenia
HSV: skin vesicles, keratoconjunctivitis, acute meningoencephalitis
SYPHILIS: osteochondritis and periostitis, skin rash involving palms and soles and is desquamating, snuffles (mucopurulent rhinitis)

Diagnosing TORCH infections

- General: elevated total blood IgM
- Urine CMV culture: if negative, exclude CMV
- Toxoplasmosis: need IgM against toxoplasmosis
- Maternal rubella immune status before pregnancy, positive exclude disease, but if negative or unknown, need IgM against rubella
- Herpes: negative culture dose not totally exclude, need PCR for definitive diagnosis

The end

Gastroenterology

Source: GI modules that you can find on the website:

radtf.iuhealth.org

☺

User ID: mfeist password: student

In addition to seminar and annual lecture notes

Organized by: Rafeef Qawasmeh, Rawan Shams & تسنيم سهيل

Nutrition

Infant formulas

- There are many different choices of infant formulas, and you will undoubtedly be asked for advice about infant formulas from the parents of your patients. Probably the most practical way to classify these formulas is based on their protein content because most formula allergies or intolerances are related to the protein content of the formulas. There are certain clinical situations, however, in which the carbohydrate or fat content of the formula is important.

Protein source	Examples	Indications	Price	Carbohydrate content	Fat content
Cow's milk	Similac S26 Sahha NAN Babelac Enfamil AR	-Normal GI tract -Enfamil AR used for gastroesophageal reflux	$	Lactose -Not indicated for galactosemia patients.	Long chain triglycerides (LTCs)
Soy	Prosobee Isomil Alsoy	Cow's milk protein allergy. Lactose malabsorption, or Galactosemia. Lactose intolerance.	$	Lactose-free and thus the formula of choice for infants with galactosemia. Prosobee: glucose polymers; others: combination of glucose polymers and sucrose.	Long chain triglycerides (LTCs)
Casein hydrolysate	Nutramigen Alimentum Pregestimil Babelac HA NAN HA	Cow's milk and/or soy allergy; Alimentum and Pregestimil are also used for malabsorption	$$	Glucose polymers -Alimentum: sucrose and glucose polymers which may make it taste sweeter.	Nutramigen: LTCs Alimentum & pregestimil: blend of LCTs & MCTs
Amino Acids	Neocate* Elecare	Severe protein allergy not responsive to casein hydrolysate formula	$$$$	Glucose polymers	Neocate: LCTs Elecare: blend of LCTs & MCTs

- As you move down this table, the formulas become less antigenic; formulas within a class are similarly antigenic to one another. When choosing a formula to treat milk protein allergy, you should progress down the table.

It is not beneficial to change to a different formula within the same class or to change to a formula in a class higher on the table that is more antigenic.

- In case of severe protein allergy, we give neocate for 6 months >> we give trial of regular milk >> if still allergic we give neocate for 1 year >> another trial of regular milk.

Types of carbohydrate content:

- Lactose - milk sugar; found in breastmilk.
- Sucrose - table sugar.
- Glucose polymers - chains of glucose molecules of various lengths which do not require lactase for digestion; may also be called: corn syrup solids, maltodextrins, modified corn starch, or modified tapioca starch. They do not require lactase for digestion and are indicated in patients with impaired lactase activity

Types of fat content:

- **Long chain triglycerides (LCTs)** - require normal fat digestion and absorption including the formation of micelles by bile salts which are taken into the lymphatic system and transported into the circulation via the thoracic duct.
- **Medium chain triglycerides (MCTs)** - do not require bile salts for absorption; are taken up directly into the portal circulation.

  MCTs: Important fat source in patients who have either impaired fat absorption (CF/ celiac disease/ biliary atresia) or abnormalities of the lymphatic system such as obstruction or chylothorax.

<u>Preterm infant formulas</u>

- The main differences between premature formulas and term infant formulas are in the sources of carbohydrates and fats and in the amounts of protein, calcium, and phosphorus.
- **Carbohydrate content**: a blend of lactose and glucose polymers which are thought to be easier for the premature gut to digest.
- **Fat content**: a blend of LCTs and MCTs, allowing for easier digestion by the premature gut.
- **Protein content**: cow's milk based, but protein makes up a higher percentage of calories in order to meet the higher protein requirements.
- **Calcium & phosphorus content**: higher levels in order to promote better bone mineralization which occurs mainly during end of the third trimester.
- Examples: Enfamil EnfaCare and Similac NeoSure.

<u>Formulas for older children:</u>

- PediaSure: cow's milk based/ 100 ml = 100 Kcal
- NIDO: cow's milk based
- Peptamen Junior: protein hydrolysate
- Neocate Junior, Pediatric Vivonex: amino acid based.

Cow's milk protein allergy

- Symptoms: increased regurgitation, irritability, and heme positive stools.
- Patients have also has both atopic dermatitis and a family history of atopy.
- It can cause frank colitis with grossly bloody stools, but the presentation may be more subtle.
- The treatment is dietary exclusion of cow's milk proteins. The treatment of choice is Nutramigen.
- 50% of patients have cross allergy with soya bean.
- It is possible to see some improvement in symptoms within 48 hours of initiating dietary therapy, but it may take 2-3 days before significant improvement is evident.

Caloric requirements:

As a general rule, normal infants need around 120 kcal/kg/day for the first 3 months of life and then around 100 kcal/kg/day until 2 years of age. Thereafter, caloric requirements decrease each year until the end of puberty to the adult requirement of 30-40 kcal/kg/day. After age 2, boys require slightly more calories on average than girls, probably because of increased activity levels.

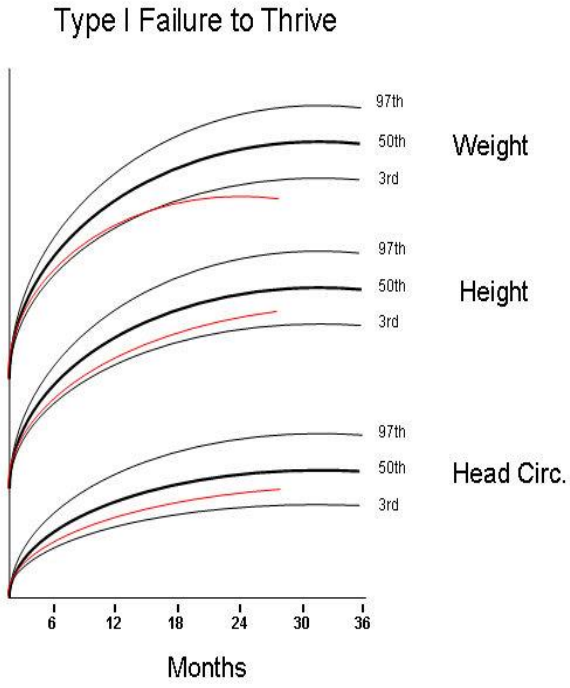
Failure to thrive FTT

- It is defined as the inability to maintain the expected rate of growth over time.
- 25% of normal children shift down by more than 25 percentile points in weight or height in the first 2 years of life.
- Symmetric IUGR usually results from intrauterine infections, chromosomal abnormalities, or prenatal exposure to toxins. These patients have a poor prognosis for catch-up growth and often continue to be symmetrically small for age.
- Asymmetric IUGR (weight much more decreased than length or head circumference) usually results from placental insufficiency late in pregnancy and has a good prognosis for catch-up growth with provision of adequate calories postnatally.
- There are two classifications of FTT; one is based on the cause, and the other is based on the growth patterns of weight, height, and head circumference.

Based on the growth patterns of wt, ht, and hc it is subdivided into 3 types:

Type I:

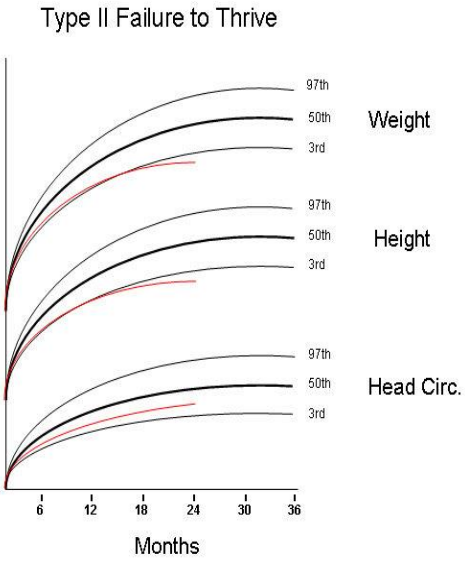
- Only weight for age is below 5th percentile on growth chart(growth rate significantly reduced or even weight loss). Height has normal or slightly decreased rate of growth. And head circumference has normal rate of growth.
- The most common type.
- Imbalance between the availability of calories and the caloric requirements of the patient. This can occur for three reasons:
    1. Inadequate intake of calories.
    2. Excess losses of calories (vomiting or diarrhea/malabsorption).
    3. Increased caloric requirements (for example, with hyperthyroidism or diencephalic tumor).



- Inadequate caloric intake and/or excessive losses (usually secondary to GE reflux) are by far the most common causes of type I failure to thrive (and failure to thrive in general).
- Patients are referred to as being "wasted", meaning that they are underweight for their height (evidenced by a low weight: length ratio or low BMI). This is in contrast to patients with type II failure to thrive who are characteristically "stunted".
- Nutritional rehabilitation may be beneficial because it is due to low calories.

Type II:

- Both weight and height growth rates are significantly reduced (< 5th percentile). But head circumference growth rate is normal.
- You should think about an endocrine etiology, as these patients actually have short stature.
- The most common causes are:
    1. Familial short stature.
    2. Constitutional growth delay.
    3. Hypothyroidism, growth hormone deficiency, hypopituitarism.

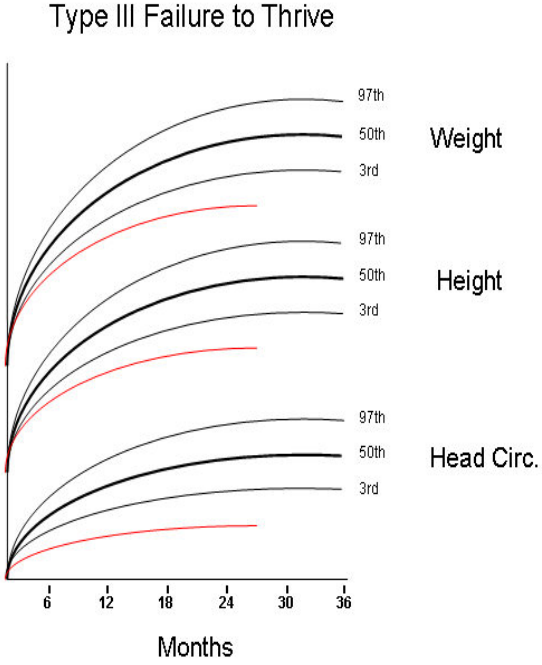


Patients with constitutional growth delay or familial short stature typically resume a normal growth velocity after crossing the 3rd percentile. This results in growth curves that are parallel to the 3rd percentile. Patients with hypothyroidism, growth hormone deficiency, or hypopituitarism typically continue to grow at a suboptimal rate, with growth curves that continue to fall further below the 3rd percentile.

- Patients with type II failure to thrive are referred to as being "stunted" meaning that their height for age is decreased, often in proportion to weight. Therefore, these patients have a normal weight: length ratio or BMI.
- Because this type of failure to thrive is usually not a result of insufficient caloric intake, nutritional rehabilitation is typically not beneficial. The exception to this is when stunting is secondary to chronic malnutrition. Chronic malnutrition can result in stunting, but this usually only occurs after months of malnutrition. In these patients, the decrease in weight velocity precedes the decrease in height velocity (they begin with wasting and progress to stunting). Provision of adequate calories can result in increased weight velocity followed by increased height velocity with catch-up growth.

Type III:

- Growth rate is significantly decreased for all 3 growth parameters.
- This growth pattern often begins at birth (symmetric IUGR) and usually results from:
    1. Intrauterine infections.
    2. Chromosomal abnormalities.
    3. Prenatal exposure to toxins.
- These patients often appear dysmorphic or have CNS abnormalities.
- These patients, like those with type II failure to thrive, are typically stunted with a normal weight: length ratio or BMI.



- Because this type of failure to thrive is usually not a result of insufficient caloric intake, nutritional rehabilitation is not beneficial unless wasting is present.

Causes of FTT are subdivided into organic and non-organic causes.

Non-organic causes: (80% of cases)

- **Lack of food:** poverty/ wars/ poor understanding of feeding techniques/ improperly prepared formula (over-diluting, may lead to hyponatremia)/ inadequate supply of breast milk.
- **Stimulus deprivation:** maternal depression/ anxiety/ poor parenting skills.

Organic causes:

- **Decreased nutritional intake**: cleft palate/ GERD/ CNS disorder (cerebral palsy).
- **Malabsorption**: cystic fibrosis/ celiac disease/ IBD in older children.
- **Impaired metabolism**: inborn errors of metabolism (galactosemia)/ chromosomal abnormality.
- **Increased energy requirements**: bronchopulmonary dysplasia/ CHF/ CF/ HIV (hypercatabolic state)/ hyperthyroidism.

Diagnosis:

- It is important to ask about following in history: Dietary history/ Assessment of elimination pattern (urine, stool, vomiting)/ Medical history/ Birth history (IUGR, prematurity)/ Family history/ Social history/ Chronic infections (HIV).
- Frequent weight monitoring is the most important thing in diagnosis.
- Lab testing is the least important in diagnosis. Delay extensive lab evaluations until after dietary management has been attempted for one week and has failed.
- Dietary management is feeding under supervision (may need hospitalization).
- Lab tests that used when organic causes are suspected:
    - CBC: anemia/ chronic kidney infection.
    - ESR/ CRP: inflammatory process.
    - Urinalysis: infections.
    - Sweat test: CF.
    - Stool for PH, fat: malabsorption.
    - Lead levels: anemia + mental retardation.
    - Serum protein, LFT.
- In the first 2 weeks of life, neonatal screening can detect CF.
- **Clinical picture of FTT patient:**
    - Thin extremities, narrow face, prominent ribs, and wasted buttocks.
    - Feeding aversion (refusal).
    - **Red flags for non-organic causes**: diaper rash/ unwashed skin/ dirty fingernails/ hypotonia/ loss of expression/ neglected hygiene/ loss of eye contact/ absence of cuddling response.
- Careful observation of the mother (may need video tape).

- Dehydration is one of jaundice risk factors if patient is not gaining enough weight.

Management:

- All cases caused by underfeeding from maternal neglect must be reported to child protective services.
- Infants discharged to natural home require intensive and long term intervention.
- Feeding in dietary management usually requires greater calories (almost triple; 150% of their recommended intake).
- In severe cases, may need NG tube or even gastrostomy.
- 1st line management should remain in the outpatient clinic.

Consequences of FTT:

- Underweight/ short stature.
- Behavioral problems.
- Cognitive delay.

Warning signals in patients with FTT:

- Diarrhea or fatty stools: may indicate malabsorption syndrome. Stools studies should be sent to rule out carbohydrate (pH, reducing substances) or fat (Sudan stain for fecal fat) malabsorption.
- Feeding refusal: do feeding evaluation, beginning with the observation. A swallowing study to evaluate for oro-motor dysfunction or frank aspiration should be done. Other organic causes of feeding refusal include anatomic abnormalities of the upper GI tract and esophagitis. These can be evaluated using barium upper GI series and upper endoscopy, respectively.
- Poor growth despite adequate caloric intake: inpatient admission with strict documentation of caloric intake.

**Cystic fibrosis is one of important organic causes of FTT. Fat soluble vitamins deficiencies are common to occur. Deficiencies of the different fat soluble vitamins result in:

- Vitamin A deficiency- night blindness, dry eyes.
- Vitamin D deficiency- rickets and osteoporosis.
- Vitamin E deficiency- peripheral neuropathy (decreased DTRs initially), cerebellar ataxia.
- Vitamin K deficiency- coagulopathy.

Because fat soluble vitamins can be stored by the body, there is potential for toxicity syndromes. The fat soluble vitamins most likely to cause toxicities are vitamin A and vitamin D. Manifestations are:

- Vitamin A toxicity- pseudotumor cerebri (headache, irritability, diplopia, papilledema).
- Vitamin D toxicity- hypercalcemia, hypercalciuria (which can result in stone formation).

Clinical case:

History: A 6-month-old male infant presents to your clinic for a routine health maintenance visit. You notice that his weight is only up 6 ounces since his 4 month visit. Upon questioning, the mother states that he is now taking less formula since she began feeding him rice cereal about one month ago. Prior to that time he was taking in approximately 30-32 ounces per day, but now he is only taking about 18-20 ounces per day. He does spit up small volumes occasionally, but not more than a few times per week. He has one to two soft mushy stools per day, without blood noted. The stools have not appeared to be "watery" or "greasy" to the mother. The mother denies cough, frequent infections, irritability, or any other symptoms at this time.

Past Medical History: The patient was born at 39 weeks gestation and weighed 7 lbs. 15 oz. (50%). He has not had any major health problems and has never been hospitalized. He has had one "cold" with nasal congestion and rhinorrhea that lasted a few days, but he has never required antibiotic therapy for any reason. He has met his expected developmental milestones, rolling over at about 4 months of age and beginning to sit up now with some support.

FHx: The mother and father are both healthy. The mother is 5' 7" tall and weighs approximately 130 pounds, and the father is 6' 1" tall and weighs approximately 200 pounds. The paternal grandmother has hypertension and the maternal grandfather has coronary artery disease. There is no family history of cystic fibrosis or other malabsorptive disorders. There are no known gastrointestinal or liver disorders in the family.

Social history: The patient lives in an apartment with his mother who is 18 years old and his father who is 19 years old. The mother recently finished high school and is now a stay-at-home mom, and the dad works at a local supermarket. They lived with the maternal grandparents for the first two months of his life, but they have been living in their current apartment for the past four months. Mom denies any stressors in the home and states that she does not feel overwhelmed in caring for the patient.

The diet history: The patient takes rice cereal from a spoon 2 times per day, usually in the morning and at dinner time. He is taking Enfamil formula 6 ounces, three times per day. The formula is being prepared correctly, with 3 scoops of formula to 6 ounces of water (20 cals/oz.). He usually takes a bottle around noon, at mid-afternoon, and before bedtime. He does not usually get formula whenever he eats cereal, but mom states that if he is fussy after eating the cereal, she will offer him a few ounces.

Physical Exam

VS: T 98.4 F, HR 146, BP 104/66, RR 34, Lt. 65 cm (25th%), **Wt. 6.4 kg (3rd%),** OFC 43 cm (25th%), weight:length ratio is 3rd%
General: awake and alert, thin with decreased subcutaneous fat stores, well hydrated
HEENT: pupils equal, red reflex present bilaterally, TMs clear bilaterally, nares clear, oropharynx clear, mucous membranes moist
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses, capillary refill <2 seconds
Resp: lungs are clear bilaterally, no respiratory distress noted
Abd: soft , non-distended, no hepatosplenomegaly, no palpable masses
GU: normal external male genitalia
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: good strength and tone of all extremities
Neuro: no gross deficits noted
Skin: clear without rashes or lesions
Rectal: no perianal disease, soft stool present in the rectal vault which tests hemoccult negative

Q1: The most likely cause of this patient's poor weight gain is
A celiac disease
B carbohydrate malabsorption
C inadequate caloric intake
D hyperthyroidism
Explanation:

A. No. This patient is not taking gluten in his diet so celiac disease could not be the cause of this patient's failure to thrive.
B. No. The most common cause of carbohydrate malabsorption in this age group would be a temporary lactase deficiency following an acute gastrointestinal infection, and there is no history of that in this patient. Adult onset hypolactasia, in which lactase levels decrease over time after weaning, would be very unusual in this age group. Regardless of the cause, carbohydrate malabsorption usually presents with watery diarrhea with or without abdominal cramping or distension.
C. Yes. This patient's dietary history reveals that he has inadequate caloric intake. By history, this patient is only taking in about 400 calories per day of formula which is only about 63 calories/kg/day. Although spoon feeding is important from a developmental standpoint, rice cereal and baby foods generally contain very few calories and should therefore not replace the more calorically dense formula feedings in a child this age. Instead, spoon feedings should be given in addition to an adequate volume of formula. This situation, in which the infant is simply not taking in (or being offered) enough calories, is often referred to as "psychosocial" or "non-organic" failure to thrive and is the most common cause of failure to thrive. The term "non-organic" is being used less often now because studies have shown that a significant portion of patients with psychosocial failure to thrive may have subtle oromotor dysfunction which makes the etiology multi-factorial.
D. No. Hyperthyroidism can cause poor weight gain because of increased metabolic rate and thus increased caloric needs. It is usually seen in older patients who may present with tachycardia, tremors, and/or heat intolerance.

Q2: Management of this patient at this time should include
A parental education with modification of the feeding regimen
B CBC, CMP, UA, and stool studies (pH, reducing substances, and fat)
C inpatient admission to monitor intake and growth
D both a and b
E all of the above
Explanation:

A. Correct. Nutritional counseling to the family about age-appropriate feeding strategies, provision of adequate calories, and close monitoring of weight gain is the treatment of choice for most patients with failure to thrive. In some cases this means writing out a feeding schedule so that the patient is fed appropriate volumes at appropriate intervals. Concentrating the formula to a higher caloric density is necessary in some patients who can not meet their caloric goals on standard 20 kcal/oz. formula. For the vast majority of patients with failure to thrive, these interventions will result in adequate weight gain. If this does not result in adequate weight gain or if there are warning signals in the history or physical exam, you should proceed with further diagnostic evaluation and/or consider an inpatient admission. You will learn about warning signals later on in the module.
B. Sorry. Laboratory tests are not indicated at this time in this patient with psychosocial failure to thrive. In fact, laboratory investigations in patients with

failure to thrive are of very limited value. A large study of hospitalized patients with failure to thrive showed that only about 1% of over 2600 lab tests ordered in these patients helped identify an organic etiology for the FTT. If this patient still fails to thrive despite the provision of adequate calories, then laboratory evaluation should be considered.

C. Sorry. Inpatient admission is not indicated at this time. Outpatient monitoring of weight gain while the patient is receiving adequate calories should be the first line treatment of this patient.

Q3: Caloric goals for this patient should be approximately:
A 80 kcal/kg/day
B 90 kcal/kg/day
C 100 kcal/kg/day
D 120 kcal/kg/day
Explanation:
Based on published data regarding caloric intake for patients of different ages, the average 6 months old male takes in about 100 kcal/kg/day. This patient will require more than the average caloric intake in order to have "catch-up" growth, and there is a calculation to determine calories needed in order for catch-up growth to occur. You must remember that these published charts and calculations for catch-up growth are simply reference points from which to start. When managing these patients, a caloric goal should be set and the patient must be followed very closely with weight checks every 1-2 weeks. Caloric goals may need to be reset depending on whether or not the patient is growing as expected.

When calculating caloric requirements for catch-up growth the following formula can be used:
(median weight for age/current weight) X average caloric intake for age
Using the child from the vignette as an example, the 50th percentile weight for a 6 month old male is 7.8 kg, his current weight is 6.4 kg, and the average caloric requirement for a 6 month old male is 100 kcal/kg/day:
Caloric requirements = (7.8 kg/6.4 kg) X 100 kcal/kg/day
= 1.22 X 100 kcal/kg/day
= 122 kcal/kg/day

Q4: Please respond to the following with TRUE or FALSE.

1- A shift down by more than 25 percentile points in the first 2 years of life is diagnostic of failure to thrive.
2- Patients with symmetric IUGR (weight, length, and head circumference all decreased) have a good prognosis for catch-up growth.
3- Caloric intake in toddler's and older children is most accurately assessed by 24-hour dietary recall.

Answers:

1- False. Actually 25% of normal children shift down by more than 25 percentile points in weight or height in the first 2 years of life. Birth size is more related to the size of the mother and intrauterine conditions than to the size of the father. Over the first 18-24 months of life, children converge to their genetic mean and then growth usually continues along that percentile. It is therefore important to determine the height and weight of the parents of infants who cross growth percentiles, as these patients may be simply adjusting to their genetic potential.
2- False. Symmetric IUGR usually results from intrauterine infections, chromosomal abnormalities, or prenatal exposure to toxins. These patients have a poor prognosis for catch-up growth and often continue to be symmetrically small for age. Asymmetric IUGR (weight much more decreased than length or head circumference) usually results from placental insufficiency late in pregnancy and has a good prognosis for catch-up growth with provision of adequate calories postnatally.

3- False. Although a 24-hour recall of caloric intake by the parent may be beneficial in determining the eating pattern and the type of foods eaten, it is not a reliable way to determine caloric intake because recall bias and under- or over reporting is common. A prospective 3-day food diary, where the family writes down and quantifies all intake during a 72-hour period, is probably the most reliable and valid clinical tool to assess caloric intake after the first year of life. Consultation with a registered dietician is helpful when evaluating a prospective 3-day diet record.

Clinical case

Hx: A 15-month-old female presents to your office because of poor growth. The mother is concerned because she is still wearing 6-9 month clothing and seems to be losing weight. She is having 3-4 mushy, foul-smelling stools per day, and upon questioning mom reports seeing what appears to be oil droplets mixed in the stool. She eats table foods and drinks whole milk, and the mother reports that her appetite is good. She is not having any emesis.
PMHx: She was born full term after an uneventful pregnancy and was discharged after 2 days in the newborn nursery. Her birth weight was 6 lbs, 5 oz (25th %). During the first six months of life, her weight was between the 10th and 25th percentiles. She was last seen in your office at 9 months of age when her weight was 7 kg (5th %). Her length has always been between the 10th and 25th percentiles.
Mom reports that she has been seen in the ER multiple times over the past 6 months and has been on antibiotics "all the time". On at least one occasion, she was diagnosed with pneumonia.
FHx: The father is 5'10" and weighs 165 pounds and the mother is 5'4" and weighs 150 pounds. Both parents are both healthy, and there is no family history of gastrointestinal disease or liver disease. Specifically there is no history of celiac disease or cystic fibrosis in the family.
Social Hx: The patient lives with her parents and her 4 years old brother. Dad is a high school coach and mom is a school counselor. There has not been any recent travel or unusual exposures.
Diet Hx: The patient eats a variety of table foods including meats, pastas, fruits, and vegetables and drinks whole milk with most meals. The mother estimates that the patient takes about 24 ounces of milk per day. The mother states that the patient has a good appetite, stating that she eats almost as much as her older brother. There have been no unusual food exposures.

Physical Exam
VS: T 99 F, HR 126, BP 108/72, RR 28, Lt. 74 cm (10th%), Wt. 7.6 kg (<3rd%), OFC 45 cm (10th%), weight:length ratio is <3rd%
General: awake and alert, significantly decreased subcutaneous fat stores, well hydrated
HEENT: pupils equal, TMs clear bilaterally, nares clear, oropharynx clear, mucous membranes moist
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses, capillary refill <2 seconds
Resp: lungs are clear bilaterally, no respiratory distress noted
Abd: soft , non-distended, no hepatosplenomegaly, no palpable masses
GU: normal external female genitalia
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: good strength and tone of all extremities

Neuro: no gross deficits noted
Skin: clear without rashes or lesions
Rectal: no perianal disease, soft stool present in the rectal vault which tests hemoccult negative.

Q1: The most likely cause of this patient's poor growth is

A. inadequate caloric intake
B. excessive loss of calories
C. increased metabolic requirements
D. familial short stature
E. constitutional growth delay

Explanation:

A. From the limited dietary information provided in the vignette, we do not have evidence to suggest inadequate caloric intake as a cause for this patient's poor weight gain. Milk intake of 24 ounces per day, in addition to table foods, would likely provide adequate calories to this patient; however, a 3-day prospective food diary would be a more reliable way to determine the adequacy of calories in this patient's diet.

B. Yes. This patient's poor weight gain is most likely being caused by a loss of calories secondary to fat malabsorption. The history of oil droplets in the stool is a warning signal that should prompt further evaluation in this patient with failure to thrive.

C. Although this patient's underlying disease process may lead to increased caloric requirements particularly as she gets older, this is unlikely to be the main cause of her poor growth at this time.

D. Familial short stature, a.k.a. genetic short stature, typically causes type II failure to thrive with a normal weight:length ratio or BMI. This patient is clearly a type I failure to thrive with a weight:length ratio of < 3rd percentile. Familial short stature occurs when an infant readjusts to their genetic potential which happens to be less than the 3rd percentile. This patient's parents are both of average height; therefore, her genetic potential would not fall below the 3rd percentile. Genetic potential can be approximated using the calculation for mid-parental height.

Boys: (Father's Height in cm + Mother's Height in cm +13 cm) / 2
Girls: (Father's Height in cm + Mother's Height in cm -13 cm) / 2

E. Constitutional growth delay typically causes a type II failure to thrive. Sometimes these patients will be thin with a weight:length ratio or BMI in the low-normal range, but they typically do not have a weight:length ratio less than the 3rd percentile like the patient in this vignette. Constitutional growth delay is thought to be a normal variant of growth where there is a deceleration of growth in the first two years of life with normal growth velocity thereafter. These patients are smaller than there peers until puberty, which occurs later, when they have a "growth spurt" and attain normal adult height. There is often a family history of so-called "late bloomers".

Q2: This patient most likely has

A. celiac disease
B. cystic fibrosis
C. Shwachman-Diamond syndrome
D. end stage liver disease with cholestasis

Explanation:

A. Celiac disease should definitely be in the differential diagnosis in a patient this age with failure to thrive and diarrhea, but the fatty stools and frequent infections make another cause more likely.

B. Correct. This patient's symptoms of failure to thrive and fatty stools are most likely caused by pancreatic insufficiency secondary to cystic fibrosis. Pancreatic insufficiency can cause severe fat malabsorption resulting in a significant decrease in calories available for utilization. This is the main cause of failure to thrive in patients with CF. More than 95% of all patients with CF are pancreatic insufficient and require treatment with oral pancreatic enzyme replacement therapy. If it is unclear whether the patient is pancreatic sufficient or insufficient, a 72-hour fecal fat balance study or a spot fecal elastase level can be done to determine the pancreatic phenotype. Although the 72-hour fecal fat balance study is considered the "gold standard", it is cumbersome and sometimes difficult to obtain accurately. The fecal elastase can be done on a single stool sample, which is much easier to obtain, and has good correlation with the 72-hour fecal fat study.

C. Shwachman-Diamond syndrome is the second most common cause of pancreatic insufficiency in childhood but is far less common than cystic fibrosis. Patients with pancreatic insufficiency should be presumed to have cystic fibrosis until proven otherwise. If they indeed do not have cystic fibrosis, then Shwachman-Diamond syndrome should be high in the differential diagnosis. Patients with Shwachman-Diamond syndrome have pancreatic insufficiency that is associated with hematologic abnormalities and occasionally skeletal abnormalities. There is now a genetic test for Shwachman-Diamond syndrome.

D. ESLD with cholestasis can indeed cause fat malabsorption, but this patient does not have a history of liver disease or physical exam findings that would support a diagnosis of ESLD.

Oral Enzyme Replacement Therapy

Patients who are pancreatic insufficient can be treated medically with oral pancreatic enzyme supplementation. These enzymes come in various forms and strengths. Some examples of the brands of pancreatic enzymes that can be used are:

- Pancrease
- Ultrase
- Viokase
- Pancreacarb
- Creon

All of these enzyme preparations contain lipase, amylase, and proteases. The dosage given is based on lipase units, and response to therapy manifests as improved absorption of fat. Enzymes are taken with each meal or snack (with few exceptions). Adequate oral enzyme replacement therapy can result in significant weight gain and a marked improvement in stooling frequency and consistency.

Q3: This patient is most at risk for

A vitamin K deficiency
B vitamin B-12 deficiency
C vitamin C deficiency
D iron deficiency

Explanation:

A. Correct. Vitamin K is a fat-soluble vitamin whose absorption is dependent on the absorption of fat. Vitamin K is important in the production of coagulation factors, and patients with vitamin K deficiency usually present with a tendency to bruise or bleed excessively. This patient with pancreatic insufficiency and fat malabsorption is at risk for vitamin K and other fat-soluble vitamin deficiencies.

B. This patient has no risk factors for vitamin B-12 deficiency. Since vitamin B-12 is found in meats, eggs, and dairy products, strict vegans are at risk for vitamin B-12 deficiency. This patient's diet should supply an adequate amount of vitamin B-12 and makes a deficiency state unlikely. Because vitamin B-12 is absorbed in the terminal ileum, patients with ileal disease (such as Crohn's disease) or patients with ileal resection (such as patients with necrotizing enterocolitis) are also at risk for vitamin B-12 deficiency. Vitamin B-12 deficiency manifests as megaloblastic anemia.

C. This patient has no risk factors for vitamin C deficiency. Vitamin C deficiency is usually related in inadequate dietary intake of vitamin C. Since vitamin C is found in many different fruits and vegetables, this patient's dietary intake makes vitamin C deficiency unlikely. The classic description of vitamin C deficiency is that of scurvy (bleeding gums, loosening of the teeth) but this presentation is rare. Vitamin C deficiency most often manifests as poor wound healing and altered immune function resulting in increased susceptibility to infection.

D. This patient has no risk factors for iron deficiency. Iron deficiency is usually related to inadequate dietary intake of iron. Iron is found mainly in meats, legumes, and green leafy vegetables. This patient's dietary intake makes iron deficiency unlikely. Patients this age whose diet consists almost exclusively of whole milk (remember that whole milk is not iron fortified like infant formulas) with low intake of meats or legumes are at risk for iron deficiency. Iron deficiency results in microcytic anemia.

Q4: Please respond to the following with TRUE or FALSE.

A. The patient in this clinical vignette is suffering from malnutrition.

B. Severely malnourished patients should receive aggressive nutritional therapy, starting with full caloric requirements for age plus calories for catch-up growth.

Explanation:

A. True. The patient is wasted (she has a weight:length ratio that is below the 3rd percentile), and wasting is indicative of acute malnutrition. This patient would be classified as having mild or mild-to-moderate malnutrition. Weight:length ratio and BMI are more sensitive and specific for acute malnutrition than the weight percentile alone. (**To learn more about assessing nutritional status see next page)**

B. False. Patient with severe malnutrition are at risk for the refeeding syndrome. Aggressive nutritional supplementation (either enteral or parenteral) provided to these malnourished patients can cause phosphorus, potassium, and magnesium to move intracellularly resulting in decreased levels in the plasma. This results in hypophosphatemia, hypokalemia, and hypomagnesemia and can be life-threatening. Patients who are at risk for developing the refeeding syndrome should have nutritional rehabilitation initiated slowly and work up to the caloric goal over 5-7 days. Careful monitoring of these electrolytes and aggressive supplementation with correction of any abnormalities is imperative.

Assessing Nutritional Status

When a patient presents to your practice with poor growth, it is important to perform a nutritional assessment. Assessing a patient's nutritional status in the clinical setting can be done relatively quickly and easily using the following data:

History

- dietary intake
- current symptoms that affect nutritional status
- chronic illnesses that affect nutritional status
- past growth data
- parental heights and family growth patterns

Anthropometric Measurements

- length (<2 years) or height (>2 years)
- weight
- weight:length ratio or BMI
- skinfold thickness* - triceps and subscapular skin folds can be measured using calipers and serve as a proxy for total body fat
- mid-upper arm circumference* - serves as a proxy for lean body mass

* Skinfold thickness and mid-upper arm circumference are not necessary in all patients but should be considered in patients with moderate to severe malnutrition as they can be followed over time and be used to assess response to nutritional support.

Physical Exam - There are many physical exam findings that are associated with various deficiency states. Below are some of the findings that you may see when examining patients with protein-energy malnutrition:

- decreased subcutaneous fat
- muscle wasting
- edema or ascites (secondary to hypoalbuminemia)
- rash (seen with zinc deficiency** and essential fatty acid deficiency)
- hair may become thin

** Zinc deficiency is often seen in patients with chronic diarrhea because zinc is lost in the stool. Zinc deficiency can result in decreased sense of taste, poor wound healing, and a characteristic rash that affects the perineum, face, and extremities. Alkaline phosphatase levels are often low in patients with zinc deficiency because alkaline phosphatase is a zinc-dependent enzyme.

Laboratory Data - Laboratory investigation is not necessary in all patients who present with poor growth as previously mentioned; however, some laboratory markers of nutritional status that may be of benefit are:

- visceral protein levels - circulating levels of albumin, prealbumin, transferrin, and/or IGF-1 can be used as markers of nutrition status. Prealbumin has the shortest half

life (about 2 days) and is probably the best marker of acute nutritional status. Albumin has the longest half-life (around 3 weeks) of the visceral proteins.

- lymphocyte count - malnourished patients are at increased risk of infection, and CBC with differential often shows lymphopenia in patients who are malnourished; however, sensitivity and specificity of lymphopenia are both low.

Nutritional support

- The goal of nutritional therapy is to provide the calories, protein, vitamins, and minerals that are necessary to restore or maintain normal nutritional status.
- Types of nutritional support are enteral and parenteral nutrition.
- Parenteral nutrition should be used when, and only when, enteral support is not possible or not adequate to meet the nutritional needs of the patient.
- Enteral feeding is generally preferred to parenteral nutrition because it is:
    1. More physiologic (provides stimulation of the gut).
    2. More economical.
    3. Safer (decreased risk of electrolyte disturbances, infection, and liver dysfunction).
- Occasionally a combination of enteral and parenteral support is necessary to meet the nutritional needs of the patient. In this situation, the maximal amount of enteral support possible should be used, with the remainder of nutritional support provided parenterally.
- The main symptoms of feeding intolerance which limit the ability to feed enterally are: vomiting, diarrhea, and abdominal distension or discomfort.
- When providing enteral support, one should use the most physiologic method tolerable to the patient. The feeding regimen should resemble a normal eating pattern as much as possible.
- Methods of enteral support from most physiologic to least physiologic:
    1. Increased-calorie foods or increased caloric density of infant formula.
    2. Supplementing the diet with oral nutritional drinks like Pediasure.
    3. Gastric bolus feedings (through NG tubes).
    4. Gastric continuous feedings (when volumes required for bolus are not tolerated).
    5. Jejunal continuous feedings (for patients with severely delayed gastric emptying, severe GER, and patients at risk for aspiration. must be given as a continuous drip, as the reservoir function of the stomach is bypassed).
- Patients who have a feeding tube in place often receive a portion of their nutrition orally and a portion of their nutrition through the tube. Typically the patient is allowed to feed orally first, and the remainder of the volume goal is given via the tube. This may be referred to as "nipple-gavage" feeding. Over time, the goal is to transition the patient completely back to oral feedings if possible.
- NG or NJ tubes should be used when the course of therapy is not expected to exceed 1-3 months. Surgical placement of feeding tubes should be strongly considered in patients who are expected to require long term tube feeding.
- **Complications of enteral nutrition:**
    1. Tube malposition; the most serious. For example, an NG tube may be misplaced and go into the airway. This can result in the infusion of formula into the lungs, which of course can be disastrous. Another example of tube malpositioning is an NG tube that traverses the pylorus and delivers bolus feedings to the small intestine. This can result in dumping syndrome and/or abdominal discomfort

Confirmation of tube position should be done prior to using any newly placed feeding tube or if clinical symptoms suggest tube malposition. This can be done by auscultation, pH testing for gastric acid, or radiographically.

2. Irritation of the tube site. (can be seen with nasal tubes or surgically placed tubes)
3. Infection of the tube site. (most often seen with surgically placed tubes)

- **Complications of parenteral nutrition:**
    1. Infectious: catheter-related sepsis is a significant risk and can be life-threatening.
    2. Metabolic: electrolyte abnormalities, hypo- or hyperglycemia, cholestasis.
    3. Mechanical: complications with line insertion; occluded or misplaced lines.

Complication can be seen with either enteral or parenteral therapy:
1-Refeeding syndrome is a serious complication of nutritional rehabilitation. 2- Electrolyte abnormalities: Slow progression to the caloric goal and careful monitoring for and treatment of electrolyte abnormalities can prevent life-threatening events.

Key points:

- Most formula intolerance is a result of the protein content of the formula.
- The most common cause of failure to thrive is "psychosocial" failure to thrive, and it should be treated by the provision of adequate calories and parental education.
- Failure to thrive can be divided into three types based on trends in weight, height, and head circumference.
- The differential diagnosis is vastly different between the different types of failure to thrive.
- A patient's genetic potential for growth must be taken into account when considering a diagnosis of failure to thrive.
- A weight: length ratio or BMI that is less than the 3rd percentile is indicative of acute malnutrition.
- Nutritional rehabilitation is the key component in the treatment of malnourished patients, but it is not without complications.

constipation

- **We need 2 of 6 criteria to diagnose constipation:**
  1. Frequency < = 2 stools per week.
  2. > = 3 months.
  3. Passage of lumpy or hard stools.
  4. Sensation of anorectal obstruction in rectal examination.
  5. Fecal impaction; can be defined as a hard mass of stool in the lower abdomen identified on physical exam, a dilated rectum filled with a large amount of stool on rectal exam, or excessive stool in the colon (particularly the rectum) on abdominal radiography.
  6. Abnormal posture trying to withhold stool.

- **Causes of constipation:**
  - ✓ Functional or idiopathic constipation.
  - ✓ Hirschsprung disease.
  - ✓ Hypothyroidism.
  - ✓ Spastic cerebral palsy: Patients have decreased intestinal motility which results in abnormal peristalsis.
  - ✓ Medications: baclofen and phenytoin / Antacids/ Anticholinergics/ Anticonvulsants/ Antidepressants/ Antihypertensives/ Bismuth/ Opiate analgesics/ Sympathomimetics.

Functional or idiopathic constipation:

- It is the most common cause of constipation in pediatrics.
- Defined as passage of big, hard stools at infrequent intervals, days or weeks apart; and by the child trying to avoid having a bowel movement by stiffening and straightening his or her legs and buttocks.
- It is a result of painful bowel movements with resultant withholding of stool which creates a vicious cycle.
- Although withholding does not totally exclude the possibility of an organic cause of constipation, it does make it extremely unlikely.
- Prolonged stretching of the rectal walls in chronic constipation often results in decreased rectal sensation and poor tone. As a result, larger volumes of stool in the rectal vault are necessary to initiate the urge to stool.
- Factors that can lead to unpleasant defecation or fear of defecation: a change in diet, illness, psychological stressors, toilet training, avoiding defecation in public restrooms or at school, and postponing defecation because the child is "too busy" to go to the toilet.

- Anal fissures often result from the trauma of passing large, hard stools. It is usually reported as bright red blood on the toilet paper or even in the toilet after passing a large stool.
- It is common for these patients to become impacted. The fecal impaction must be cleared before starting maintenance therapy to prevent inadequate response to treatment or worsening of the overflow encopresis*. It can be cleared by:

✓ Phosphate enemas; but excessive administration may result in systemic absorption and electrolyte imbalances, particularly hyperphosphatemia and hypocalcemia. Patients with Hirschsprung's disease, in which the enemas are retained, and very young infants are particularly at risk for this complication. Deaths from this complication have been reported.

- ✓ Saline enemas.
- ✓ Mineral oil followed by a phosphate enema. Mineral oil is generally not recommended in patients under 1 year of age because there is an increased risk of aspiration of the mineral oil. Likewise, it should be avoided in patients who have swallowing dysfunction or difficulty protecting their airway.
- ✓ High doses of oral medications such as mineral oil and polyethylene glycol solutions.

- Enemas are generally not recommended for use in patients under 2 years of age because of the risk of mechanical trauma to the rectal wall. If rectal medications are to be used, glycerin suppositories are recommended.
- Encopresis: developmentally inappropriate release of stool. It is the involuntary passage of stool not resulting from organic disease or illness. It is most likely to occur in School-aged children (6-12 years old).
- Maintenance therapy is usually required for many months in patients with chronic constipation so that stools remain and the patient does not associate stooling with pain. Only then will the patient stop withholding stool, and the cycle can be broken.
- Mineral oil or osmotic laxatives such as Miralax, magnesium hydroxide, lactulose, or sorbitol should be used as the 1st line in maintenance therapy.
- Dietary and behavioral modifications are important in treatment to prevent recurrence:
  - ✓ Adequate fiber intake is important in the long term management. *A simple equation can be used to determine adequate fiber intake. This equation is: age + 5 = # of grams of fiber recommended per day with a maximum of 25-30 grams per day (which is the adult dose).
  - ✓ Increasing intake of fluids, especially water and fruit juices, is advisable.
  - ✓ Apple, pear, and prune juices all contain sorbitol, a non-absorbable sugar which promotes softer stools.
  - ✓ Scheduled time on the toilet, usually after meals, is recommended in order to promote a normal bowel habit.

Hirschsprung disease:

- It is the most common cause of lower intestinal obstruction in neonates.
- It is caused by an absence of ganglion cells in the nerve plexuses, which causes sustained contraction. In 75% of cases it is limited to the rectosigmoid area.
- Red flags that suggest this disease:
  Hx:
  - ✓ Trisomy 21. Up to 10% have Hirschsprung disease.
  - ✓ Infrequent bowel movements with associated abdominal distension.
  - ✓ Delay in passage of meconium. > 90% fail to pass meconium in the first 24 hours of life. (90% of normal neonates pass meconium in the first 24 hours of life, so passage of meconium in the first 24 hours of life does NOT rule out Hirschsprung's disease.)
  - ✓ Onset in neonatal period.

  P/E:

  - ✓ Distended, hyperresonnant abdomen- indicative of retained gas and stool.
  - ✓ Empty rectal vault.
  - ✓ Expulsion of gas and stool after rectal exam.

- When you suspect HD you should do barium enema to both aid in diagnosis and identify the "transition zone" where normal bowel meets the aganglionic segment. Barium enema is a good screening tool and can be falsely normal, especially in very young infants simply because there has not been enough time to distend the normal portion of the colon with stool. Also, a recent therapeutic enema or rectal exam which results in passage of a large stool could make the transition zone difficult or impossible to see. Even if the barium enema is abnormal, histologic proof for Hirschsprung's disease should be obtained. Rectal biopsy is the gold standard. Also, anorectal manometry study is used in diagnosis; a normal study reliably rules out the disease.
- Enterocolitis associated with Hirschsprung disease occurs most often in the second and third months of life. It has a mortality rate of 20%, so it is a diagnosis that must not be missed. You suspect it if the patient has bloody diarrhea and fever.
- 8-20% of patients go undiagnosed until after the age of 3 years. Mostly due to short segment disease which affects only the distal few centimeters of rectum. Therefore it is important to keep HD in the differential diagnosis of patients with constipation who are refractory to treatment.

Red flags suggesting an organic cause of constipation	
History	Physical exam
Delayed passage of meconium. Stooling difficulties which began in the neonatal period. Fever, bloody diarrhea in a patient with difficulty stooling. report of abdominal distension Small caliber stools or "pencil-like" stools. Poor growth/failure to thrive. Cold intolerance, decreased energy. Anorexia/nausea/vomiting. Lower extremity weakness. Persistent constipation despite adequate treatment regimen.	Abnormal growth parameters. Abdominal distension. Midline lumbosacral abnormalities. Abnormal position of the anus. Decreased perianal sensation. Absence of anal wink or cremasteric reflex. Tight anal canal. Tight empty rectum in presence of palpable abdominal fecal mass. Mass palpable on rectal exam that is not a fecal mass. Gush of liquid stool and air upon withdrawal of finger. Occult blood in stool. Abnormal deep tendon reflexes. Decreased lower extremity strength or tone.

Evaluation for organic causes:

- A neonate with constipation who does not have HD should have a sweat chloride test done to rule out cystic fibrosis.
- In a patient who is compliant with adequate doses of osmotic laxatives and is not improving clinically, an organic cause should be considered. Screen for the common ones: hypothyroidism/ hypercalcemia/ lead toxicity/ celiac disease in some cases.
- Spinal cord abnormalities such as tethered cord, syringomyelia, or spinal cord tumor can present with constipation which doesn't respond to medical therapy. An MRI of the lumbosacral spine is used to rule out these conditions.
- Full colonic manometry to rule out colonic dysmotility.

Clinical case:

History: You see a new patient in your office who is a 6-year-old male with a long history of difficulty passing stools. The mother states that he began to pass hard stools at around 1 year of age and would often cry with bowel movements. She has noticed small amounts of bright red blood on the toilet paper intermittently after passing a bowel movement. He now has a bowel movement about once per week on the toilet, although the mother states that he often has accidents of loose stool in his underwear. The mother comments on the large caliber of his stools, stating that the toilet often becomes clogged after he has a bowel movement. She states that occasionally he will become really quiet and stand with an unusual posture; after a few minutes, he will resume playing or whatever he was doing.

PMHx: The patient was born at 39 weeks gestation after an uncomplicated pregnancy. He passed meconium on the first day of life. He stooled normally until about one year of age, and his stooling difficulties have gotten progressively worse. He was treated with mineral oil about 6 months ago for a few days but mom says that "it didn't work so I stopped it". He has no other chronic medical conditions and currently is on no medications. There have been no concerns about his growth parameters or his developmental milestones, and he is a very active child.

FHx: There is no family history of constipation, other gastrointestinal diseases, or endocrine disorders.

Social Hx: The patient lives with his parents and his 3-year-old sister. Mom denies any stressors at home, but she does report that some boys at school were teasing him about his soiling. The patient's father has become frustrated because his younger sister is fully potty trained, but he is still having accidents.

Diet Hx: Mom reports that he is a picky eater. His favorite foods are pizza and macaroni and cheese. He loves milk and drinks 3-4 glasses per day. There are hardly any vegetables that he will eat. Mom says that because both she and his father work, they eat fast food about 3-4 nights per week.

Physical Exam

VS: Afebrile, HR 102, RR 18, BP 95/60, Ht. 113 cm (25th%), Wt. 21 kg (50th%), BMI 16.4 kg/m2 (75th%)

General: well nourished, no acute distress

HEENT: pupils equal, TMs clear bilaterally, nares clear, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses

Resp: clear breath sounds bilaterally, no distress

Abd: soft, non-tender, no hepatosplenomegaly, **palpable mass in suprapubic area as well as in the LLQ**

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: good strength and tone, no spinal abnormalities

Neuro: CN II-XII intact, DTRs noted to be normal and symmetrical, cremasteric reflex intact

Skin: no rashes or lesions noted

Rectal: **visible stool on perineum**, anus in normal position, no fissures noted, normal sphincter tone, **large amount of hard stool in rectal vault** (about the diameter of a baseball), hemoccult negative.

Q1: This patient's stooling difficulties are most likely being caused by

A. Hirschsprung's disease
B. psychological problems
C. functional constipation
D. an abnormality of the spinal cord

Explanation:

A. Hirschsprung's disease is unlikely in this patient because of the age of onset and because he is having fecal soiling, which is unusual in Hirschsprung's.

B. The fecal impaction makes this diagnosis less likely and there are no other indications that he is willfully soiling.

C. Correct! Functional or idiopathic constipation is the most common cause of constipation in pediatrics. Other causes of constipation can usually be excluded by a good history and physical exam which should include inspection of the perianal area and a digital rectal exam.

D. Although this can be a rare cause of constipation, it is not the most likely cause in this patient; however, it should be considered in patients who are resistent to conventional therapy for functional constipation.

Q2: Blood on the toilet paper in this patient is most likely the result of

A. anal fissures
B. infectious colitis
C. enterocolitis associated with Hirschsprung's disease
D. a juvenile polyp

Explanation:

A. Correct. although no fissures were noted on physical exam today, it is still very likely that he has them intermittently after passing large stools.

B. usually manifests as bloody diarrhea.

C. This most feared complication of Hirschsprung's disease usually presents with fever, abdominal distension, and bloody diarrhea. The mortality of this condition is about 20%!

D. juvenile polyps are a common cause of rectal bleeding in this age group, however the vignette points to another cause for this patient's bleeding.

Q3: Please answer the following with TRUE or FALSE

1-This patient does not meet criteria to be diagnosed with constipation because he is having loose stools.
2-This patient demostrates withholding behavior.
3-Stool withholding is often indicative of an organic cause of constipation.
4-Functional constipation is most often caused by painful bowel movements which results in voluntary withholding of stool.
5-This patient has a fecal impaction.
6-Patients with functional constipation rarely become impacted.
7-This patient should first be disimpacted before beginning maintanence therapy.
8-Following disimpaction, maintenance oral therapy will probably be required for about 1 month.
9-Stimulant laxatives are the first-line choice in the treatment of functional constipation.

10-Dietary and behavioral modifications are important in the treatment of functional constipation.

11-Encopresis is the involuntary passage of stool not resulting from organic disease or illness.

12-Encopresis is most likely to be found in the toddler age group.

Answers :

1-False. This patient definitely meets criteria to be diagnosed with constipation. Constipation can be defined in a number of ways: infrequent stools (<3 stools per week), hard stools, large stools, or even painful stools. This patient has loose stools whenever he has accidents because of overflow encopresis.

2-True. The description of becoming quiet and assuming an unusual posture is very characteristic of a child who is trying to withhold stool. Other descriptions might be rising on their toes and rocking back and forth while stiffening their buttocks and legs or crying while straightening their legs, especially in infants. These actions are often misinterpreted by parents as being attempts to pass stool when in fact, they are contracting their anal sphincter and gluteal muscles in an attempt NOT to pass stool. Usually after a few minutes, the rectum accommodates the increasing stool burden and the urge to defecate passes.

3-False. Although withholding does not totally exclude the possibility of an organic cause of constipation, it does make it extremely unlikely.

4-True. The withholding of stool because of painful defecation or fear of defecation creates a vicious cycle. The rectum is able to accommodate the increasing stool mass which becomes larger and harder until finally it must be passed. This causes pain which results in the child withholding stool.

5-True. Remember the criteria of constipation at the first page.

6-False. It is actually quite common

7-True. The fecal impaction must be cleared before starting maintenance therapy.

8-False. Maintenance therapy is usually required for many months in patients with chronic constipation. The stools must remain soft so that the patient does not associate stooling with pain. Only then will the patient stop withholding stool, and the cycle can be broken. Also, many of these patients have decreased rectal sensation because of the chronic stretching of sensory nerve fibers. Regaining adequate rectal sensation needed to feel the urge to defecate probably takes months. Weaning should be done slowly and relapse is common.

9-False. Although stimulant laxatives may be necessary in certain situations for short periods of time, they are not first-line therapy. Mineral oil (a lubricant) or osmotic laxatives such as Miralax, magnesium hydroxide, lactulose, or sorbitol should be used alone or in combination for the treatment of functional constipation.

*If you want you can check the website to see recommended dosages.

10-True. These are both important to prevent recurrence. A balanced diet, which includes whole grains, fruits, and vegetables, is recommended in order to get sufficient fiber intake. Althought some clinicians do not push fiber in the early stages of treating patients with withholding behavior, adequate fiber intake is important in the long term management of these patients. family keep a diary of the stool frequency, and this may be combined with a reward system in order to provide positive reinforcement to the child.

11-True. Large volumes of stool in the rectal vault stretch the rectum and cause the internal anal sphincter to relax. The anal canal is also shortened and eventually the external anal sphincter is unable to function adequately as the fecal mass pushes against it. Unformed stool escapes around the impaction and leaks into the undergarments without warning to the patient. Families should be educated that this is not willful soiling by the child. Fecal incontinence due to organic disorders such as spinal cord lesions or anatomic lesions of the anorectum is not encopresis.
12-False. School-aged children (6-12 years old) are most likely to have encopresis. In fact, it is uncommon under the age of 3 years.

Clinical Case

History: You see a new patient who is a 3-month-old male infant with Trisomy 21 for a rountine health check up. The mother reports that he has been relatively healthy and states that she is very relieved that he wasn't born with any cardiac defects. She does report however that he has been having infrequent bowel movements and that she has been giving him glycerin suppositories about every 2-3 days as instructed by her mother-in-law. She states that this sometimes helps him have a bowel movement, but often he'll go 4-5 days without stooling. She also has noticed that his abdomen becomes distended, especially when he hasn't stooled in a few days.

PMHx: the patient was born at term via a vaginal delivery. The mother had an abnormal triple screen suggestive of Trisomy 21 and confirmed by amniocentesis. He has had no other health problems except for the previously mentioned stooling problems. The mother is unsure of when he passed meconium but she thinks it was when he was 2 days old, just prior to being discharged from the newborn nursery. He has not received his 2 month immunizations as this was the first available appointment for his 2 month visit.

FHx: There is no family history of Trisomy 21. There is no family history of any gastrointestinal disorders, including constipation. When asked about Hirschsprung's disease, the mother says that she has never heard of it.

Social Hx: The patient lives with his parents and the paternal grandparents. He is an only child. There are smokers who live in the home, but mom states that they only smoke outside.

Diet Hx: He is currently formula fed only. Mom reports that he takes 3-4 oz. every 3 hours during the daytime and that he wakes up once to feed during the night.

Physical Exam

VS: Afebrile, HR 136, RR 28, BP 84/56, Lt. 57 cm (3rd%), Wt. 4.8 kg (5th%), weight:length ratio is 10-25th percentile, OFC 37 cm (3rd%)

General: physical characteristics consistent with Trisomy 21, no acute distress

HEENT: Down facies, pupils equal, red reflex present bilaterally, nares clear, oropharynx clear, unable to visualize TMs

Neck: supple no palpable thyroid, no lymphadenopathy

CV: regular rate and rhythm, no audible murmur, good distal pulses

Resp: clear to auscultation bilaterally

Abd: soft, mildly distended, hyperresonnant to percussion, no organomegaly

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: mildly decreased tone, moves all extremeties well, no spinal abnormalities

Neuro: normal DTR's

Skin: clear without rash

Rectal: no perianal disease, normal position of the anus, no palpable stool in the rectal vault, **large amount of air and liquid stool expelled with removal of examining finger**

Q1: This patient's stooling pattern is most likely a result of

A. withholding behavior

B. Hirschsprung's disease

C. an abnormality of the spinal cord

D. a normal stooling pattern for a child this age

Explanation:

A. In this age group is extremely unlikely, some would say nonexistent.

B. True. There were a number of "red flags" in the history and physical.

C. There is nothing to indicate a spinal cord defect.

D. It is true that some babies this age may go for a few days without stooling, especially breast fed infants. However, there are "red flags" in this scenario that should make you think of something organic causing the stooling difficulties.

Q2: The next step in the management of this child would be to

A. continue the glycerin suppositories and reassure the mother

B. obtain an upper GI barium study

C. obtain a barium enema

D. obtain a CT of the abdomen with IV contrast

Explanation:

B. This would be helpful in a child with persistent or bilious vomiting but probably wouldn't be helpful in this case.

C. Excellent! This would be the best choice to evaluate for Hirschsprung's disease. see the results of the study that you ordered.

D. A CT with rectal contrast which included the pelvis might show dilated bowel proximal to the "transition zone", but this is not the preferred method to image this child.

Q3: Bloody diarrhea and fever in a patient like this should make you think of

A. milk protein intolerance

B. salmonella infection

C. duodenal atresia

D. enterocolitis

Explanation:

A. Milk and soy protein intolerance is a common cause of bloody stools in this age group, but this patient has a condition that points to something else.

B. S almonella can be a cause of bloody stools, but probably not in this case.

C. Duodenal atresia is associated with Trisomy 21, but presents with vomiting in the neonatal period.

D.Correct. Enterocolitis associated with Hirschsprung's disease.

Q4: Please answer the following with TRUE or FALSE

1-Hirschsprung's disease is the most common cause of lower intestinal obstruction in neonates.

2-Hirschsprung's disease is caused by too many ganglion cells in the submucosal and myenteric plexuses which causes sustained contraction.

3-Barium enema is the gold standard to diagnose Hirschsprung's disease.

4-Most cases of Hirschsprung's disease affect the entire colon.

5-It is possible for a 6 year old child to be diagnosed with Hirschsprung's disease.

6-A normal anorectal manometry study reliably rules out Hirschsprung's disease.

Answers & Explanation:

1-True. The incidence is about 1 in 5,000 live births.

2-False. It is caused by an absence of ganglion cells in the nerve plexuses, which causes sustained contraction.

3-Fasle. barium enema is a good screening tool for Hirschsprung's disease.

4-False. Although total colonic aganglionosis does occur, in 75% of cases disease is limited to the rectosigmoid area.

5-True.

6-True. Anorectal manometry evaluates the response of the internal anal sphincter to inflation of a balloon in the rectum. In normal patients, there is a reflex relaxation of the internal anal sphincter in response to rectal distention. In patients with Hirschsprung's disease, this relaxation is absent. Anorectal manometry is abnormal even in patients with short segment or ultra-short segment Hirschsprung's disease (a.k.a. anal achalasia) which may be missed with barium enema or rectal biopsy.

Clinical case

History: You see a patient who is an 11-year-old female with a history of cerebral palsy, mental retardation, developmental delay, and seizure disorder who presents with a history of hard, infrequent stools. Mom states that she has had trouble with constipation for many years but it seems to have gotten worse over the past few months. She has a bowel movement about once every 4-5 days and it is usually very hard. She often gets fussy when she hasn't stooled in a few days and seems to be uncomfortable. She is otherwise at her baseline with no other new complaints.

PMHx: She was born at 27 weeks gestation via a vaginal delivery after premature rupture of membranes and preterm labor. She spent about 10 weeks in the NICU and had a complicated neonatal course. She was on the ventilator for about 3-4 weeks and then required CPAP for another 2 weeks. She was weaned off oxygen just prior to her discharge from the NICU. She had a patent ductus arteriosus which had to be ligated surgically. She had bilateral intraventricular hemorrhage and subsequently developed seizures. She had feeding intolerance during the first two months of life, during which time she was on parenteral nutrition but was able to take adequate formula by mouth by the time she was discharged home. However, she didn't gain weight well during the first year of life and eventually had a surgical gastrostomy placed for feeding just prior to her first birthday. This was changed to a gastrostomy button at about 2 years of age. She has a seizure disorder and is treated with phenytoin. She has spastic cerebral palsy and is treated with baclofen. Her neurologist increased her dose about 6 months ago and mom says that her spasticity has greatly improved since that time.

FHx: The family history is negative for any gastrointestinal or liver disease with the exception of a grandfather who was recently diagnosed with colon cancer. There are no family members with endocrine disorders.

Social Hx: The patient lives with her mom and 2 older siblings. Mom does not work and stays home to take care of the patient. Mom smokes in the home and they have 2 outside dogs. The father is not involved in the care of the patient. There are no other social stressors except for the stress of caring for her medical problems.

Diet Hx: She takes most of her feeds through her gastrostomy button. She gets pediasure, 1 can (237 mls) four times per day as well as 600 ml as a continuous nighttime infusion. She can take some pureed foods by mouth, but mom states that she takes very little.

Developmental Hx: She was noted to have global developmental delay during the first year of life. She has mental retardation. She is non-verbal and is wheelchair-bound as a result of her cerebral palsy.

Physical Exam

VS: Afebrile, HR 88, RR 18, BP 98/64, Ht. 128cm (<3rd%), Wt. 26.2 kg (<3rd%), Body Mass Index 16.0 (25th%)

General: non-verbal, cerebral palsy, no acute distress

HEENT: Pupils equal, TMs clear bilaterally, nares clear, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses, normal capillary refill

Resp: clear breath sounds bilaterally

Abd: soft, non-tender, no hepatosplenomegaly, gastrostomy button in place

GU: Tanner III female genitalia

Extremities: contractures of all four extremeties

Musculoskeletal: increased muscle tone, mild scoliosis

Neuro: **hyperreflexic DTRs, clonus in lower extremities**

Skin: no rashes or lesions noted

Rectal: no perianal disease, normal sphincter tone, firm stool in the rectal vault, hemoccult negative

Q: Please answer the following with TRUE or FALSE

1-This patient most likely has abnormal intestinal motility.

2-Medications are unlikely to be a cause of this patient's constipation.

3-This patient is getting adequate fiber in her diet.

4-An osmotic laxative would be first-line treatment in this patient.

5-This patient will probably require treatment of her constipation for many years.

Explanation:

1-True. Patients with spastic cerebral palsy often have decreased intestinal motility which results in abnormal peristalsis. It is quite common for these patients to become constipated.

2-False. The increase in the baclofen dose is likely the cause of the recent worsening of her constipation, but it has made a large improvement in her overall condition.(Drugs known to cause constipation: Antacids, Anticholinergics,Anticonvulsants, Antidepressants, Antihypertensives, Bismuth, Opiate analgesics, Sympathomimetics, Many, many others)

3-False. Many patients who are tube fed become constipated because of lack of bulk in their diet. In this situation, using a formula with fiber added or adding an over-the-counter fiber supplement to her feedings would probably be beneficial.

4-True. Many patients with a history like this will end up requiring at least intermittent therapy with a stimulant laxative such as senna or bisacodyl, but an osmotic laxative should be tried first.

5-True. Her underlying pathology, dependence on tube feeding, and the need for medications that are likely to cause constipation all make it likely that this patient will require long-term treatment of her constipation.

Key points:

- Constipation is a very common complaint, and primary care providers must be able to successfully manage patients with this problem.
- Idiopathic constipation is by far the most common cause of constipation in children.
- Patient and parental education about the pathophysiology of constipation and encopresis is vital to a successful treatment regimen.
- Patients with a fecal impaction must first be disimpacted in order for maintenance therapy to be successful.
- Osmotic laxatives and/or mineral oil are first-line maintenance therapy for idiopathic constipation.
- Regular toileting, especially after meals to take advantage of the gastrocolic reflex, is an important part of treating idiopathic constipation. This helps establish a normal stooling pattern for the patient.
- Dietary modifications such as increasing the fiber content of the diet and increasing fluid intake are often helpful in treating these patients.
- Weaning of medication should only be considered after the patient is having regular bowel movements and when they no longer associate pain with defecation.
- Relapses are common, and therefore close follow-up and good communication are imperative for successful treatment of constipation.
- Patients who are not responding to an adequate treatment regimen should be evaluated for organic causes of constipation.
- Patients who present with difficulty stooling in the neonatal period should be evaluated for HD.
- Many drugs cause constipation as a side effect.

Abdominal pain

Irritable bowel syndrome IBS

- It is defined as abdominal pain or discomfort which is associated with the passage of stool or a change in bowel habit. The abdominal pain often precedes the passage of stool and is then relieved with defecation.
- Different subtypes of IBS are: diarrhea predominant, constipation predominant, and a combination type.
- The typical history in patients with IBS is usually that of intermittent periumbilical abdominal pain with altered bowel habit.
- Simple education, reassurance, and dietary modifications as a first line therapy for functional gastrointestinal disorders.
- The major outcome variable in management is the resumption of a normal lifestyle. This includes regular school attendance and participation in their normal extracurricular activities.
- Two commonly prescribed medications for IBS in children are dicyclomine (Bentyl) and hyoscyamine (Levsin). They are "antispasmodic" agents. Their principle side effects are anticholinergic.
- For patients with constipation predominant IBS, an osmotic laxative such as mineral oil could be a valuable adjunctive therapy. Because lactulose can cause gassiness and bloating, it is probably not the best choice. The principal side effect of these medications is diarrhea.

Functional abdominal pain:

- The presentation of functional abdominal pain syndrome is similar to that of IBS, but there is no history of abnormal stooling pattern.
- This condition has also been called isolated paroxysmal abdominal pain.
- History: periumbilical abdominal pain/ absence of warning symptoms/ stressors at home or at school are often present/ family may place very high expectations on child (school work, athletics)/ may be described as a perfectionist/ may be described as a "sensitive" child whose feelings are easily hurt.
- Physical exam: patient may not complain of any pain upon palpation/ may complain of pain in the periumbilical area upon palpation/ may complain of pain throughout the abdomen but is distractible/ localized tenderness, particularly in the right upper or right lower quadrants, is absent/ other warning signs in the physical exam are absent.
- Treatment: reassurance/ education/ dietary modifications with or without the use of antispasmodic medications/ psychosocial stressors must be addressed.

Functional dyspepsia

- Pain or discomfort in the upper abdomen (above the umbilicus) and may be characterized by early satiety, bloating, and nausea.

- Mild nausea may be present/ absence of significant vomiting, nocturnal symptoms, or other warning signals/ normal growth parameters/ no focal tenderness on exam.
- Treatment: reassurance/ education/ modification of stressors/ trial of empiric medication therapy (A time-limited trial of an H2-receptor antagonist or proton pump inhibitor would be first-line medical therapy).
- Although organic disease (particularly inflammation of the upper GI tract) may be present in patients with dyspepsia, most have functional dyspepsia.

Warning signals that may suggest organic cause of abdominal pain:

- History: weight loss/ pain that awakens the patient from sleep/ significant vomiting (frequent, bilious, or in a cyclic pattern)/ significant diarrhea (increased frequency)/ gastrointestinal bleeding/ unexplained fever/ arthralgia or arthritis/ unusual rash or skin lesions/ family history of inflammatory bowel disease.
- Physical exam: weight loss or deceleration in linear growth/ localized tenderness that is not periumbilical/ organomegaly/ perianal skin tag, fissure, fistula, or abscess/ grossly bloody or hemoccult positive stool/ delayed puberty.

Diagnostic evaluation of recurrent abdominal pain:

- Basic screening labs include: CBC with differential and platelets/ complete metabolic panel/ ESR/ stool hemoccult testing/ some clinicians advocate adding a lipase to this list.

Acute pancreatitis

- Defined as the sudden onset of abdominal pain associated with a rise in pancreatic enzymes in the blood to at least three times the upper limit of normal.
- Premature activation of trypsinogen to trypsin with subsequent activation of the other proenzymes.
- Treatment consists of pancreatic rest, provision of adequate analgesia, and maintenance of adequate hydration. Pancreatic rest entails keeping the patient NPO, ideally until pain has resolved.
- Although morphine does increase sphincter of Oddi pressure, similar increases are seen with other narcotics including meperidine. Therefore the choice of narcotic is probably not important in treating patients with acute pancreatitis.
- Most patients have mild disease which resolves in a few days with supportive care.
- Lipase usually peaks 24-48 hours after presentation, but it is common for the lipase to remain elevated for 7-10 days with acute pancreatitis. Amylase usually peaks by 12-30 hours and returns to normal in 3-4 days. The degree of elevation of the enzymes alone is not prognostic of the disease course.

- Most patients with acute pancreatitis only have one episode. The chance of recurrence is only about 10%.
- The causes in order of frequency: idiopathic/ systemic illness like HUS/ trauma (blunt abdominal trauma)/ Structural abnormality (pancreas divisum)/ Medications (valproate most common)/ Infectious (viral)/ gallstones.

- The role of antibiotics is limited to cases of severe necrotizing pancreatitis and to cases of infected pancreatic pseudocyst or pancreatic abscess.
- **Recurrent pancreatitis** occurs in about 10% of patients after the first episode of acute pancreatitis. It manifests as repeated episodes of acute pancreatitis without evidence of pancreatic dysfunction or destruction of normal pancreatic architecture.

Chronic pancreatitis

- It is characterized by glandular destruction secondary to longstanding or repeated episodes of pancreatic inflammation.
- It begins with acute inflammation and progresses over time to pancreatic atrophy, fibrosis, calcification, and eventually exocrine and/or endocrine dysfunction.
- In adults, long-term ingestion of large amounts of alcohol is the most common cause of chronic pancreatitis. In children, it is most commonly seen in patients with genetic forms of pancreatitis, metabolic abnormalities, or structural abnormalities.
- Evaluation:
  - ✓ Screening for CFTR gene (typical or atypical cystic fibrosis) and the cationic trypsinogen gene (hereditary pancreatitis).
  - ✓ Screening for hypercalcemia and hyperlipidemia.
  - ✓ Structural abnormalities can be screened for with a combination of ultrasound, CT, MRCP, and/or ERCP.

Red flags in patient with abdominal pain:

- History: bilious emesis/ feculent (dark and foul smelling) emesis/ pain which migrates and becomes localized/ pain with jarring movements such as coughing, sneezing, or riding in a car/ significant abdominal distension/ history of previous surgery/ testicular pain in males/ severe lower abdominal pain in females.

- Physical exam: "toxic" appearance of the patient/ guarding which persists despite distraction/ abdominal wall rigidity/ rebound tenderness/ localized tenderness, particularly in the RLQ/ swelling, erythema, or tenderness in the inguinal area or scrotum/ localized tenderness on rectal exam.

- Not all patients who present with symptoms such as these will have a surgical abdomen, but any of these symptoms should alert you to look for surgical conditions and/or obtain surgical consultation.

** You can read about surgical causes of abdominal pain in GI modules.

Key points:

- Functional gastrointestinal disorders are characterized by recurrent abdominal pain and an absence of warning signals in the history or physical exam.
- Most patients with chronic abdominal pain have a functional gastrointestinal disorder.
- Treatment of functional gastrointestinal disorders consists of reassurance, education, and dietary modifications with or without medication therapy.
- Warning signals in the history or physical exam of patients with abdominal pain should prompt an evaluation for organic causes of the pain.
- Most cases of acute pancreatitis are mild and self-limited and are treated with pancreatic rest, IV hydration, and pain medication.
- Patients suspected of having acute appendicitis, small bowel obstruction, gonadal torsion, or generalized peritonitis should have an emergent surgical consultation.

Test yourself:

A 15-year-old female presents to your office because of recurrent abdominal pain. Her mother reports that she has been having abdominal pain intermittently over the past year, but it has become more intense during the past few months. The pain occurs in the periumbilical region, is described as "crampy" in character, and usually lasts from a few minutes to half an hour. She passes stool once per day and it is usually formed, but she reports loose stools a few times per week. She states that the loose stool is usually preceded by abdominal pain and an urgency to stool, and the pain resolves after stooling. She states that this usually occurs immediately after eating a meal. She has not noticed any blood in her stool. She has not had any vomiting, weight loss, fevers, joint pains, or pain that awakens her from sleep.

The patient was born at 38 weeks gestation via a repeat C-section. She has no other chronic health problems and has never been hospitalized; however, she has been seen in the emergency room twice in the past year because of abdominal pain. The mom reports that when she was seen last week in the ER her labs were all normal. She states that they even did a CT scan of her abdomen but were unable to figure out what was causing the pain. Mom also states that her previous doctor didn't know what was causing the pain.

You are able to review her ER records and find that a CBC, a complete metabolic panel, an ESR, an amylase and a lipase were all normal. The CT of her abdomen and pelvis showed no abnormalities.

Her father has mild intermittent asthma, and her mother suffers from depression. Her 18-year-old sister and 9-year-old brother are both healthy. There is no family history of gastrointestinal or liver diseases, particularly no history of inflammatory bowel disease or celiac disease.

he patient lives with her mother and younger brother. Her parents separated last school year and their divorce was final last month. The patient states that her dad already has another girlfriend. Her sister recently moved away to start college, and the patient reports that she misses her sister. She recently started the ninth grade, and she reports that she is a straight-A student. She has missed about two days of school per week over the past two months because of her abdominal pain.

She continues to have a good appetite, but states that she doesn't eat pizza anymore because it sometimes makes her stomach hurt. She doesn't know of any other foods that make her abdominal pain worse.

Physical Exam

VS: Afebrile, HR 66, BP 118/76, RR 12, Ht. 163 cm (50th%), Wt. 59 kg (75th%), BMI 22.2 kg/m2 (75th%)

General: awake and alert, no acute distress, well nourished

HEENT: pupils equal, TMs clear bilaterally, nares clear, oropharynx clear, mucous membranes moist

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses

Resp: lungs are clear bilaterally, no distress

Abd: soft, non-distended, no hepatosplenomegaly, no palpable masses, she complains of only minimal discomfort during palpation of the periumbilical area but points out that she has not had any abdominal pain today, no localized tenderness or rebound tenderness

GU: normal external female genitalia, Tanner stage IV

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: normal strength and muscle tone

Neuro: DTRs normal and symmetrical, no gross deficits

Skin: no rashes or lesions noted

Rectal: no perianal disease, sphincter tone normal, soft stool in the rectal vault which tests hemoccult negative

Questions:

The most likely cause of this patient's symptoms is

A inflammatory bowel disease
B irritable bowel syndrome
C peptic ulcer disease
D cholelithiasis (gall stones)
E chronic pancreatitis

The next step in the management of this patient would be to

A repeat her labs and include liver function tests
B schedule upper and lower endoscopy
C obtain an upper GI series and abdominal ultrasound
D provide education, reassurance, and dietary recommendations
E refer the patient to a pediatric gastroenterologist

The main goal of treatment for this patient should be

A complete resolution of loose stools
B complete resolution of pain
C return of normal functioning with regular school attendance
D both a and b
E none of the above

Solutions: 1) B 2) D 3)
1)) *This patient has the classic presentation of diarrhea predominant irritable bowel syndrome (IBS). IBS is defined as abdominal pain or discomfort which is associated with the passage of stool or a change in bowel habit. The abdominal pain often precedes the passage of stool and is then relieved with defecation. An exaggerated

gastro-colic reflex may be reported. Change of bowel habit can be defined as either a change in frequency or consistency of the stool. Different subtypes of IBS are: diarrhea predominant, constipation predominant, and a combination type in which both diarrhea and constipation are seen intermittently. The typical history in patients with IBS is usually that of intermittent periumbilical abdominal pain with altered bowel habit. Warning signals that suggest an organic cause of abdominal pain are absent in both the history and physical exam
*For sure, it's not inflammatory bowel diease, no warning signals such as weight loss, significant diarrhea, or blood in the stool and a normal physical exam makes IBD unlikely. This patient, however, should be monitored over time for warning signals such as these.
*Peptic ulcer disease usually presents with epigastric pain or nausea, and may even present with upper GI bleeding. There may be a history of nocturnal awakening because of the pain. Peptic ulcer disease is less common in children than in adults and is most commonly a result of either NSAID use or Helicobacter pylori infection.
*Gallstones are relatively uncommon in healthy children and, even when present, often cause no symptoms. Gall stones that become lodged in the cystic duct cause biliary colic, which is severe, right upper quadrant pain that usually lasts 20 minutes to 2 hours and is triggered by eating. The pain may radiate to the area of the right scapula.
*Cholelithiasis, particularly if causing biliary colic, is treated surgically with a cholecystectomy.
*Chronic pancreatitis is usually associated with recurrent episodes of acute pancreatitis which result in chronic inflammatory changes, fibrosis, and pancreatic insufficiency.

2)) In this patient with IBS, conservative therapy should be the first line of therapy. Often the patient and/or the parents fear that there is a serious medical problem and that the diagnosis is being missed. In some patients, simply making a diagnosis and reassuring them that the pain is likely functional (and benign) makes a significant difference is the complaints of abdominal pain. Studies have shown that pain resolves in 30-50% of patients with functional abdominal pain within 2-6 weeks after the diagnosis is made. This makes a strong case for simple education, reassurance, and dietary modifications as a first line therapy for functional gastrointestinal disorders.

3)) Goals of therapy should be clearly delineated early in the treatment of patients with IBS or other functional gastrointestinal disorders. The major outcome variable in managing these patients is the resumption of a normal lifestyle. This includes regular school attendance and participation in their normal extracurricular activities. The patient must understand that some symptoms may persist despite treatment, but the goal of therapy is to not allow the symptoms to affect normal functions of daily life. It is common for symptoms to wax and wane, and patients may experience more symptoms during times of emotional stress or with intake of trigger foods. If significant disruption of daily life persists despite conservative treatment, consideration should be given to pharmacological therapy and/or further evaluation.

History: An 11-year-old male presents with a one day history of increasing abdominal pain. The pain began the previous evening with mild epigastric discomfort and has progressed to severe epigastric abdominal pain and vomiting. The patient reports that he ate a burger and fries for lunch, and this made the pain much worse. He vomited after eating the meal and had another episode of vomiting when he tried to drink a bottle of Gatorade. He states that the pain is continuous, is located in the upper abdomen, and radiates to the middle of his back. He rates the pain a 9 out of 10. He says that the nausea is better now that he hasn't eaten or drank anything is the past few hours. The vomiting has been non-bilious and non-bloody, and he has not had any diarrhea or fever. Prior to yesterday he had not had any signs of illness.

The patient was born at 37 weeks gestation with a birth weight of 5# 2 oz. He suffers from no chronic medical problems, has never been hospitalized, and has never had surgery. He takes no prescriptions or over-the-counter medications.

His dad has a history of hypertension, and his mother suffers from irritable bowel syndrome. There are no other GI or liver diseases in the family.

The patient lives with his parents and his 3-year-old brother. They deny any stressors at home or at school. There have been no unusual food exposures and no sick contacts.

The patient eats a regular diet and has had a normal appetite prior to today.

Physical Exam
VS: Afebrile, HR 90, BP 114/82, RR 18, Ht. 143 cm (50th%), Wt. 36 kg (50th%), BMI 17.6 kg/m2 (50th%)
General: awake and alert, appears to be in significant abdominal discomfort
HEENT: pupils equal, TMs clear bilaterally, nares clear, oropharynx clear, mucous membranes moist
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, mildly tachycardic, good pulses
Resp: lungs are clear bilaterally, no distress
Abd: soft, no hepatosplenomegaly or masses, moderately tender to palpation in the epigastric region with some voluntary guarding, no rebound tenderness or other peritoneal signs, no CVA tenderness, bowel sounds hypoactive
GU: normal external male genitalia, Tanner stage I
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: normal strength and muscle tone
Neuro: DTRs normal and symmetrical, no gross deficits
Skin: no rashes or lesions noted
Rectal: no perianal disease, sphincter tone normal, formed stool in the rectal vault which tests hemoccult negative

The most likely cause of this patient's abdominal pain is

A acute gastroenteritis
B acute pancreatitis
C acute viral hepatitis
D Pyelonephritis
E right lower lobe pneumonia

The next step in the management of this patient would be to

A obtain an abdominal CT
B discharge the patient home on oral pain medication
C monitor the patient with serial exams, avoiding pain medication
D admit the patient for IV fluids, IV pain medication, and nothing per os

Laboratory results:
CBC: WBC 11.2, Hgb 14.4, Hct 43.2, Plts 390
CMP: Na 138, K 4.4, Cl 101, Bicarb 22, BUN 16, Cr 0.7, Glucose 98, Ca 9.4, Albumin 4.2, Alk Phos 220, ALT 28, AST 22, Total Bilirubin 0.8
Amylase 540 (normal 25-120)
Lipase 944 (normal 20-110)

Solutions: 1) B 2) D
1))acute pancreatitis, This patient with an acute onset of epigastric pain that radiates to the back and is exacerbated by eating is suggestive of acute pancreatitis. Acute pancreatitis is defined clinically as the sudden onset of abdominal pain associated with a rise in pancreatic enzymes in the blood to at least three times the upper limit of normal. The mechanism of pancreatic injury is thought to result from the premature activation of trypsinogen to trypsin with subsequent activation of the other proenzymes. This results in a vigorous inflammatory response and damage to the pancreatic parenchyma.

* Although acute gastroenteritis is one of the most common causes of acute abdominal pain in this age group, there are some findings that suggest another cause in this patient. Abdominal pain associated with acute gastroenteritis is usually mild and generalized, not localized to the epigastrium with radiation to the back. Also, bowel sounds are often hyperactive in acute gastroenteritis. Vomiting in patients with acute gastroenteritis is usually accompanied by diarrhea, and fever may be present.

* Acute viral hepatitis, most commonly caused by hepatitis A virus, usually presents with flu-like symptoms, jaundice, and right upper quadrant pain.

* Pyelonephritis usually presents with fever, costovertebral angle tenderness and dysuria. It is important to remember that all abdominal pain does not originate from the GI tract and to keep GU causes in the differential diagnosis. Other GU causes of abdominal pain are renal stones (may present with hematuria and colicky pain that may radiate down into the groin) and ureteropelvic junction obstruction (may present with episodic abdominal pain that is usually associated with vomiting).

* right lower lobe pneumonia; It is important to remember this non-abdominal cause of acute abdominal pain, but this patient has symptoms suggestive of another cause. Abdominal pain from right lower lobe pneumonia occurs as a result of referred pain from diaphragmatic irritation. Fever, tachypnea, abnormal breath sounds, and/or cough would be suggestive of pneumonia as a cause of abdominal pain.

2)) Treatment for acute pancreatitis consists of pancreatic rest, provision of adequate analgesia, and maintenance of adequate hydration. Pancreatic rest entails keeping the

patient NPO, ideally until pain has resolved. Adequate analgesia is usually maintained with any of a number of intravenous narcotics. Teaching for years was that morphine should be avoided in patients with pancreatitis because it causes contraction of the sphincter of Oddi. Further studies have shown that although morphine does increase sphincter of Oddi pressure, similar increases are seen with other narcotics including meperidine (Demerol). Therefore the choice of narcotic is probably not important in treating patients with acute pancreatitis. Careful attention must be given to fluid balance as patients with pancreatitis may get third spacing of fluid and become intravascularly volume depleted. It is therefore recommended to provide aggressive fluid therapy in patients with acute pancreatitis.

* One of the goals of treatment for acute pancreatitis is adequate pain control, so avoidance of pain medications is not good patient care. This approach may be useful in patients in which there is a concern for an acute surgical abdomen.

* Although imaging of the abdomen is generally recommended to support the diagnosis of pancreatitis and to evaluate for any abnormalities of the pancreatobiliary tract, it should not delay therapy with adequate IV fluids and analgesia. The two most common imaging modalities used in children are ultrasound and CT. Ultrasound is often preferred because it is less expensive, avoids radiation exposure, and may provide a better view of the biliary tree. CT of the abdomen is probably most helpful when ultrasound is equivocal or in severe acute pancreatitis (to rule out pancreatic necrosis). Imaging studies usually show pancreatic edema which supports the diagnosis of pancreatitis; however, imaging is also used to rule out abnormalities of the pancreatobiliary tract such as pseudocysts, gallstones, or dilatation of the common bile or pancreatic ducts.

Please respond to the following with TRUE or FALSE.

T or F The most likely course of illness for this patient with acute pancreatitis is resolution of pain over the next few days.

T or F A lipase that remains elevated 72 hours after the onset of acute pancreatitis is a bad prognostic indicator.

T or F The chance of this patient having recurrent pancreatitis is about 50%.

T or F The most common cause of acute pancreatitis in children is obstruction of the pancreatic duct by a gallstone at the Ampulla of Vater.

T or F Antibiotic therapy is rarely necessary in patients with acute pancreatitis.

1)) T, Most patients with acute pancreatitis have mild disease which resolves in a few days with supportive care. Studies have shown that the median length of hospitalization in patients with acute pancreatitis is around 4 days.
2)) F, Lipase usually peaks 24-48 hours after presentation, but it is common for the lipase to remain elevated for 7-10 days with acute pancreatitis. Amylase usually peaks by 12-30 hours and returns to normal in 3-4 days. The degree of elevation of the enzymes alone is not prognostic of the disease course. This is best determined by the condition of the patient and their response to supportive therapy.
3)) F, Most patients with acute pancreatitis only have one episode. The chance of recurrence is only about 10%.
4)) F, Although this is a more common cause of acute pancreatitis in adults, it is relatively rare in pediatrics. This should be higher in your differential diagnosis, however, if jaundice is present. When jaundice is present, it suggests obstruction to bile flow and should prompt an evaluation for obstruction of the common bile duct.

This can be accomplished with an abdominal ultrasound, which can visualize stones and dilatation of the common bile duct and/or the pancreatic duct.
5)) T, The role of antibiotics is limited in acute pancreatitis. Their use is limited to cases of severe necrotizing pancreatitis, in which the necrotic pancreatic tissue may become secondarily infected, and to cases of infected pancreatic pseudocyst or pancreatic abscess.

History: A 10-year-old male presents with abdominal pain and vomiting. The parents report that he woke up about 3:00 a.m. complaining of abdominal pain and has continued to complain of pain over the past 8 hours. The pain seems to be getting worse, and he began to vomit about 3 hours ago so he was brought to your office to be evaluated. The emesis has been non-bloody and non-bilious. The patient describes the pain as constant and severe and is associated with severe nausea. When asked where the pain is located, the patient motions over his entire abdomen. He has not had any diarrhea or fever. He was well last night when he went to bed.

He was born full term after an uncomplicated pregnancy. He was hospitalized once as an infant for dehydration secondary to rotavirus. He has complained of "stomach aches" over the past year, and these have occurred mainly at school. Mom also reports that he will complain of abdominal pain if he is nervous about something. She states that she assumed that he just had a "nervous stomach" like her. She does report that this pain seems to be more severe than his usual episodes and that they have never been associated with vomiting.

His father is healthy and his mother has irritable bowel syndrome. She states that she does not take any medications for her IBS but has to monitor her diet or she gets abdominal pain and diarrhea. The maternal grandmother also has IBS. The paternal grandfather has lung cancer. There are no other health problems in the family.

The patient lives with both parents, and they have two pet dogs. Both parents work as real estate agents. The patient denies stressors at school or at home. He has had no sick contacts and no recent travel or other unusual exposures.

He eats a normal diet for his age. His appetite was normal yesterday, but he reports that he has absolutely no appetite today. He has not eaten any undercooked meat or unusual foods.

Physical Exam
VS: T 100.2 F, HR 100, BP 126/86, RR 18, Ht. 134 cm (25th%), Wt. 28 kg (25th%), BMI 15.6 kg/m2 (25th%)
General: awake but ill-appearing, seems to be very uncomfortable and somewhat anxious
HEENT: pupils equal, TMs clear bilaterally, nares clear, oropharynx clear, mucous membranes moist
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, tachycardic, good pulses
Resp: lungs are clear bilaterally, no distress
Abd: no hepatosplenomegaly or masses noted but difficult to examine because of guarding, very tender to palpation throughout the abdomen but worse in the right

lower quadrant, rebound tenderness is present and he refuses to try to get off the table and hop up and down
GU: normal external male genitalia, Tanner stage I
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: difficult to examine because of poor cooperation but no gross deficits noted
Neuro: DTRs normal and symmetrical, no gross deficits
Skin: no rashes or lesions noted
Rectal: no perianal disease, sphincter tone normal, no stool in the rectal vault for hemoccult testing, patient does complain of localized tenderness along the right lateral rectal wall during digital rectal exam

This patient's abdominal pain is most likely a manifestation of

A malrotation with midgut volvulus
B intussusception
C acute constipation
D acute appendicitis
E an acute exacerbation of functional abdominal pain

The next step in the management of this patient would be

A to admit the patient overnight and provide adequate analgesia
B to admit the patient overnight but withhold pain medications
C surgical consultation
D consultation with a pediatric gastroenterologist

Solutions: 1) D 2) C
1)) This patient has a number of signs that suggest acute appendicitis. His abdominal pain seemed to first be periumbilical or generalized and now seems to be localizing to the right lower quadrant. Rebound tenderness and his unwillingness to move around suggest peritoneal irritation. Finally, localized tenderness of the right lateral rectal wall suggests irritation from an inflamed appendix. Many patients experience discomfort during rectal exam, but localized tenderness is not usually present.
* Malrotation with midgut volvulus usually presents with bilious emesis. Since the obstruction with midgut volvulus occurs distal to the Ampulla of Vater (where bile enters the duodenum) the emesis is bile stained. Midgut volvulus occurs when the gut twists around its mesentery, resulting in ischemia of the bowel. If not corrected in a timely manner, the bowel will become necrotic and non-viable; therefore, midgut volvulus is a surgical emergency.
* Intussusception occurs when one segment of bowel telescopes into an adjacent segment of bowel and is propelled distally via peristalsis. Intussusception is most common in children 3 months to 3 years of age but could present in a patient this age. Patients with intussusception present with intermittent colicky abdominal pain. They often have abdominal distension and/or tenderness, vomiting, and stools which contain mucus and blood known as "currant jelly stools". Plain films of the abdomen show distended loops of small bowel or air fluid levels suggesting distal small bowel obstruction (intussusception is most commonly ileo-colic). Also the intussusceptum may be seen as a soft tissue mass in the right upper quadrant with a paucity of bowel gas in the right lower quadrant. Ultrasound is very sensitive in diagnosing intussusception, but water soluble or air contrast enema can be both diagnostic and

therapeutic. 80-90% of cases can be reduced using water soluble or air contrast enema.
* Constipation is not likely to be the cause of abdominal pain in this patient who has rebound tenderness. Constipation can cause acute abdominal pain, particularly if the patient is impacted and the stool is acting as an obstruction; however, this patient has no history of constipation and no stool in the rectal vault. Often this diagnosis is made after plain films of the abdomen show what is described as a moderate or large amount of stool in the colon. This is a very non-specific finding as most people have a moderate or even a large amount of stool in their colon (we're supposed to have stool in the colon). Be careful of making this diagnosis in patients with acute abdominal pain when there is no history of constipation and a rectal exam that does not reveal a fecal impaction.
* It sounds as if this patient does indeed have functional abdominal pain, with his history of chronic intermittent abdominal pain that seems to be exacerbated by stressful situations. It is true that a significant percentage of these patients who present with acute abdominal pain are simply having an acute exacerbation of their chronic abdominal pain. This diagnosis would be supported by a history of functional abdominal pain and an absence of alarm signals in the history and physical exam. This patient has alarm signals in his physical exam (tenderness localized to the RLQ, rebound tenderness and rectal wall tenderness) that suggest an organic cause for his pain.

2)) This should be considered a surgical emergency, and prompt surgical consultation is warranted. The decision to perform imaging studies to support the diagnosis can be made with input from the surgeon. Some advocate the use of abdominal ultrasound or CT to support the diagnosis prior to surgery. Others use these imaging techniques only if there is uncertainty about the diagnosis. Regardless, surgical consultation should be requested sooner rather than later if acute appendicitis is suspected. In acute appendicitis, appendectomy is recommended on the day of diagnosis to decrease the risk of perforation. In children it is estimated that about 20% of cases perforate within 24 hours of the onset of symptoms, but 80% perforate within 48 hours.

Upper GI bleeding

- It refers to bleeding that occurs proximal to the ligament of Treitz (between jejunum and duodenum).

Common causes according to age		
1st month of life	Infant (1st month – 1st year)	Child or adolescent
Swallowed maternal blood - can either be from delivery (seen in first few days of life) or from fissured breast during breastfeeding. **Stress gastritis or stress ulcer** - the neonatal gut is highly susceptible to mucosal injury during times of stress or shock (in NICU). **Vitamin K deficiency-termed "hemorrhagic disease of the newborn"**, this is seen in patients who did not receive vitamin K after birth (born at home) or who have cholestasis or fat malabsorption and, as a result, don't absorb vitamin K.	**Swallowed maternal blood** - from fissured breast during breastfeeding and is not true GI bleeding. **Stress gastritis or stress ulcer.** **Acid-peptic disease.** - History of irritability or poor per-oral intake. **Mallory-Weiss tear**-history of severe vomiting or retching precedes hematemesis. **Vascular anomaly**-cutaneous lesions. **Varices**- although less common.	**Mallory-Weiss tear** **Acid-peptic disease -** heartburn, abdominal pain, nausea, poor appetite, or vomiting**.** **Swallowed blood** - epistaxis or post-oral surgery, not true GI bleeding. **Varices**- a history of liver disease or physical exam suggestive of portal hypertension should make esophageal or gastric varices high on your differential diagnosis. **Drugs – doxycycline** for acne >> difficult swallowing >> pill esophagitis.

- Esophageal varices can lead to cirrhosis and portal hypertension (splenomegaly/ leukopenia/ thrombocytopenia).

- APT test: used in infants with blood in the vomitus or stool to differentiate between fetal Hb and adult Hb (swallowed maternal blood). Blood from specimen is mixed with water and centrifuged. The pink supernatant is mixed with alkali solution of NaOH and monitored for 2 minutes. If it remains pink then it is fetal Hb since it is resistant to alkali denaturation. If turns yellowish brown then it is adult Hb.

Management:

- Initial brief assessment to determine whether or not the patient is hemodynamically stable, the extent of blood loss, and the possible etiology of bleeding.

- If the bleeding is severe and the patient is not stable, aggressive resuscitation with IV fluids should be initiated until blood is available for transfusion.

- Gastric lavage should be performed to determine if the patient has active bleeding. If the bleeding has resolved and the patient is able to be stabilized, screening labs should be sent and acid suppression should be initiated. GI consultation should be made so that endoscopy can be arranged. If the patient has active bleeding, acid suppression and octreotide should be initiated. Both GI and surgery consultation should be made so that emergent endoscopic and/or surgical intervention can be arranged.

- If the patient is stable, screening labs should be sent and gastric lavage should be performed; if the bleeding has resolved, the patient can be monitored and started on acid suppression therapy. Endoscopy can be performed in a controlled setting, but preferably within 24 hours. If the patient has active bleeding, acid suppression therapy and octreotide should be initiated, and emergent endoscopy is indicated.

Lower GI bleeding

Common causes according to age		
1st month of life	Infancy	Child or adolescent
Anal fissure- usually presents with streaks of bright red blood on the surface of the stool in the diapers; stool may be firm (firm balls of stool). **Milk protein allergy**- may present with blood on the surface and/or mixed throughout the stool and mucus may be present; stool may be normal or softer than normal for the patient. **Swallowed maternal blood**	**Anal fissure** – the leading cause in all age groups. **Milk protein allergy.** **Infectious colitis**- presents with acute bloody diarrhea; fever or other signs of systemic illness are often present. Dark blood. **Intussusception**- typically presents with colicky abdominal pain, vomiting, and the passage of "currant jelly stool" (blood, mucus, and stool); over time the infant may become very lethargic with intermittent irritability. **Meckel's diverticulum**- presents with painless rectal bleeding which can be quite significant; stools usually formed, but patient may present with bleeding per rectum not accompanied by stool.	**Anal fissure.** **Juvenile polyp**- presents with painless rectal bleeding, usually bright red and small in amount; stools are formed and may also be accompanied by mucus/ benign course/ <3 in number/ school age. **Infectious colitis**. **IBD** - usually presents with chronic bloody diarrhea but may present acutely; often accompanied by other symptoms such as abdominal pain, cramping, and weight loss. **Meckel's diverticulum**- although usually seen in patients under 2 years of age, bleeding from a Meckel's can be seen in older patients as well.

- Fresh blood indicates lower GI bleeding. Fresh blood from upper GI = very sick patient.
- **Red flags in infant with hematochezia** which can be associated with serious condition such as necrotizing enterocolitis, Hirschsprung enterocolitis, infectious enterocolitis, volvulus, or intussusception:
    1. Abdominal distension.
    2. Abdominal tenderness.

3. Fever.
4. Severe constipation.
5. Bilious emesis.
6. Excessive or episodic irritability.

Determining the source of bleeding:

Color of blood:

- **Bright red blood usually** indicates that the bleeding source is very close to the anus; most commonly it suggests an anal fissure or rectal polyp but could also suggest distal colitis/proctitis in the right clinical setting**.**
- **Darker red blood** usually indicates a bleeding source higher up in the colon; this may suggest a polyp proximal to the rectum or can also be seen with diffuse colitis**.**
- **Very dark red or maroon blood** usually indicates bleeding from the distal small bowel; this may suggest a Meckel's diverticulum.
- **Black tarry stools (melena)** usually suggest significant bleeding from the upper GI tract; this may suggest a variety of causes such as ulcers or varices.

Character of blood:

- **Firm stool or very large stool** usually indicates that the bleeding is a result of trauma from passing stool and stooling may be described as painful; this suggests anal fissure or possibly hemorrhoids in older pediatric patients.
- **Normal formed stool with blood on the surface** indicates a source of bleeding in the distal sigmoid or rectum because the stool was formed before blood was present; this may suggest a rectal or sigmoid polyp but could also be caused by anal fissure or hemorrhoids (not all patients with fissure or hemorrhoids pass large, painful stools).
- **Normal formed stool with blood mixed throughout** indicates that the source of bleeding is proximal to the rectum since the blood had to be present before the stool became formed; this could suggest a more proximal polyp.
- **Bloody diarrhea** indicates colitis; this suggests infection, allergy, or inflammatory bowel disease.

Key points:

- The first step in evaluating any patient with GI bleeding is to determine the amount of blood loss and to assess hemodynamic stability.
- Emergent endoscopy is indicated in patients with active upper GI bleeding.
- Swallowed maternal blood is the most common cause of hematemesis in breastfed infants.
- The most common causes of severe upper GI bleed in pediatric patients are peptic ulcer disease and esophageal varices.
- Anal fissure is a common cause of lower GI bleeding in all age groups.
- Cow's milk protein allergy is the most common cause of lower GI bleeding in infants less than 6 months of age.
- Juvenile polyps are the most common cause of significant lower GI bleeding in toddlers and school-aged children.
- Inflammatory bowel disease most commonly presents in older children and adolescents.

TEST YOURSELF:

A 10-year-old male presents with vomiting of blood. He reports that the vomiting began early this morning and reports a total of four episodes. About two hours ago he vomited what appeared to be clear gastric contents followed by bright red blood. He alerted his parents of this and therefore they rushed him to the ER. On the way to the ER, he had another episode of emesis which contained dark material that mom also thinks was blood. Prior to this morning he was asymptomatic, specifically with no nausea, vomiting, or abdominal pain. He now complains of nausea and anorexia but no abdominal pain. He had a loose stool earlier today without blood or mucus. He denies dizziness, weakness, shortness of breath or any other complaints.

He was born at 34 weeks gestation after preterm labor. He spent about 2 weeks in the NICU but had no major complications. He has been healthy and has no chronic medical problems. He does not have a history of liver disease, bleeding disorder, or previous episode of gastrointestinal bleeding. He is not taking any prescription or over-the-counter medications.

Prior to today he was eating a normal diet. He has not eaten much today because of the nausea and specifically denies ingesting anything red such as Jello or Gatorade that could be mistaken for blood.

Physical Exam
VS: T 100.2 F, HR 90, BP 105/70, RR 18, Ht. 138 cm (75th%), Wt. 29.6 kg (50th%), BMI 15.5 kg/m2 (25th-50th%)
General: awake and alert, well nourished, well hydrated

HEENT: pupils equal, TMs clear bilaterally, nares clear with no blood noted, oropharynx clear, mucous membranes moist
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses, capillary refill <2 seconds
Resp: lungs are clear bilaterally, no distress
Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses
GU: normal external male genitalia
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: normal strength and muscle tone
Neuro: DTRs noted to be normal and symmetrical, no gross deficits
Skin: no rashes or lesions noted
Rectal: no perianal disease, sphincter tone normal, loose stool in the vault which tests heme negative

The next step in the management of this patient would be to

A start two large bore IVs and push normal saline
B upper endoscopy
C admit the patient to the ICU for close monitoring
D administer fresh frozen plasma
E place an NG tube for gastric lavage and obtain screening labs

The most likely cause of bleeding in this patient is

A epistaxis with swallowed blood
B reflux esophagitis
C Mallory-Weiss tear
D gastric ulcer
E Helicobacter pylori infection

Please answer the following with TRUE or FALSE

T or F
Coffee ground emesis suggests a rapidly bleeding lesion.
T or F
Hematemesis in the first day of life is suggestive of swallowed maternal blood during delivery.
T or F
Vomiting of blood in a breastfed infant is usually indicative of allergy to breast milk.

Solutions and explanations:
1)) E, Hematemesis is defined as vomiting of blood and is a common presentation of acute upper GI bleeding. Upper GI bleeding refers to bleeding that occurs proximal to the ligament of Treitz. Gastric lavage is a quick way to determine if the patient is having an active upper GI bleed. Gastric lavage is performed by placing an NG tube, flushing with normal saline, and then drawing back the gastric contents. Bright red blood that does not clear with repeated lavage suggests ongoing, or active, bleeding. Active upper GI bleeding is an indication for emergent upper endoscopy. If

it is unclear whether or not the lavage contains blood, it can be sent for Gastroccult testing which is similar to Hemoccult testing of stool. Screening labs should include CBC with platelets, complete metabolic panel, coagulation profile, and blood type and cross
* This patient will likely have endoscopy performed at some point in the evaluation, but he doesn't meet the criteria for emergent endoscopy at this point. Emergent endoscopy is indicated if significant ongoing blood loss is occurring, but we do not know that to be the case with the current data. You should think of a way to determine if the patient has ongoing bleeding.
* (A) would be a great choice in a patient who is hemodynamically unstable because of massive blood loss, but probably not necessary in this patient who has a normal heart rate and blood pressure and doesn't appear to be volume depleted.
* also, This patient does not appear to warrant ICU admission with stable vital signs and apparent minor blood loss.
* Fresh frozen plasma can be used to replace clotting factors in patients who are coagulopathic, but are not indicated at this point.

2)) C, The history of one or more episodes of vomiting followed by vomiting of bright red blood is suggestive of a Mallory-Weiss tear. A Mallory-Weiss tear is a tear in the mucosa at or near the esophago-gastric junction caused by forceful vomiting or retching. Although the sight of bright red blood can be quite alarming to the patient and/or the parents, the bleeding almost always stops spontaneously without aggressive medical intervention. If the bleeding spontaneously stops, supportive care is usually all that is necessary with close monitoring for further bleeding. Acid suppression with an H2-blocker or proton pump inhibitor is often provided to decrease the acidity of gastric contents that can come into contact with the damaged mucosa. The empiric use of medications to suppress gastric acid is recommended in patients who present with hematemesis because acid related disorders (such as peptic ulcers, gastritis, or erosive esophagitis) are a common cause of upper GI bleeding.
* Although swallowed blood after a nosebleed can be a cause of hematemesis and mistaken for an upper GI bleed, this history is more suggestive of another cause. In a patient with swallowed blood from a nose bleed, it would be unusual to have clear emesis immediately followed by hematemesis. It would be more common to see either "coffee ground emesis" or frank hematemesis that is not preceded by clear emesis. It is important to try to elicit a history of current or previous epistaxis in patients who present with hematemesis so that unnecessary invasive procedures can be avoided in these patients. Similarly, hemoptysis or oropharyngeal bleeding (such as after tonsillectomy) can present with hematemesis and be mistaken for upper GI bleeding.
* Erosive esophagitis from acid reflux disease can cause esophageal ulceration with bleeding and hematemesis, but there is a more common cause in this age group. The lack of reflux symptoms also makes erosive esophagitis less likely.

* Peptic ulcer disease (PUD) can cause upper GI bleeding, but is relatively uncommon in the pediatric population. Non-steroidal anti-inflammatory drugs (NSAIDS) have been associated with the development of peptic ulcers, and NSAID use should be included in your history of patients with GI bleeding. PUD can cause large amounts of bleeding if the ulcer erodes into a blood vessel and should be high in the differential diagnosis in patients who present with a significant upper GI bleed. PUD is often associated with a history of abdominal pain or dyspepsia
*H pylori infection can cause gastric or duodenal ulcers with bleeding, but this is not a very common cause of GI bleeding in the pediatric population. In children, H. pylori infection more often results in gastritis and is associated with abdominal pain or dyspepsia.

3)) false, "Coffee ground emesis" refers to the vomiting of small dark brown or black clots of blood mixed with gastric secretions. When blood is exposed to gastric acid, it turns a dark color and coagulates into small clots. These small dark clots can resemble the appearance of coffee grounds. Coffee ground emesis is usually seen with slow, low-volume bleeding that doesn't require emergent intervention. In contrast, lesions with high volume bleeding (such as an ulcer that has eroded into a vessel) often present with emesis of bright red blood or very large amounts of blood.

* Hematemesis on the first day of life in an otherwise healthy-looking infant is highly suggestive of swallowed maternal blood during delivery. This may also present with blood per rectum because of the rapid transit through the neonatal GI tract. Often there is a history of a placental abruption or traumatic delivery, but that is not always the case. Maternal blood in either the emesis or stool can be differentiated from the infant's blood using the Apt test for fetal hemoglobin.

* Hematemesis in a breastfed infant is usually a result of swallowed blood from a cracked or irritated breast. The breast may be infected (mastitis) or simply fissured from the mechanical trauma of breastfeeding. Your history in the breastfed infant with hematemesis should include maternal discomfort during breastfeeding, bleeding from the nipple, or blood-tinged milk expressed during pumping. If there is any doubt, examination of the mother's breast to look for fissuring of the nipples or signs of mastitis is encouraged.

Q1: History: A 10-year-old female with a history of biliary atresia presents with vomiting of blood. Her parents report that yesterday she began to complain of nausea. This morning she was noted to be pale, and she complained of being light-headed. She then vomited a large amount of bright red blood, and she was taken to the ER. She has not had any fever, diarrhea, blood in her stool, or other episodes of vomiting.

She was diagnosed with biliary atresia at 6 weeks of age and underwent a Kasai portoenterostomy at 7 weeks of age. She has had multiple episodes of ascending cholangitis after her Kasai procedure. Mom reports that she had about 2 episodes of cholangitis per year during the first 3 years of life and has had four or five episodes since that time. She has chronic liver disease with cirrhosis secondary to biliary atresia and is followed by a pediatric gastroenterologist. She has never had gastrointestinal bleeding before.

Her father has a history of acid reflux and "ulcers". Her mother and siblings are healthy. There are no other GI, liver, or hematological disorders in the family.

The patient lives with her parents and two older brothers. The dad works at a grocery store and the mom stays at home. Both parents smoke but outside the home. They have no pets and there has been no recent travel.

Her appetite has decreased over the past few months and mom is concerned because of poor weight gain. She was instructed to drink a nutritional supplement to increase her caloric intake, but mom reports that she doesn't like the taste of any of the supplements that she has tried.

Physical Exam

- VS: Afebrile, HR 120, BP 110/75, RR 20, Ht. 132 cm (25th%), Wt. 24.6 kg (5th%), BMI 14.1 kg/m2 (5th%)
- General: awake, cooperative but appears anxious, during exam patient has another episode of hematemesis (about 250 cc of bright red blood)
- HEENT: pupils equal and reactive, TMs clear bilaterally, nares clear with no blood noted, oropharynx clear, mucous membranes moist
- Neck: supple without lymphadenopathy or thyromegaly
- CV: tachycardic, good pulses, capillary refill 2 seconds
- Resp: lungs are clear bilaterally, no distress
- Abd: soft, non-tender, mildly distended with prominent superficial veins noted, hyperactive bowel sounds, liver is firm and down 6 cm below right costal margin and 8 cm below xiphoid process, spleen down 12 cm below left costal margin
- GU: Tanner stage I female genitalia
- Extremities: clubbing of her digits noted
- Musculoskeletal: normal strength, good movement of all extremities
- Neuro: DTRs noted to be normal and symmetrical, no gross deficits
- Skin: pallor noted
- Rectal: no perianal disease, sphincter tone normal, very dark stool in the rectal vault which tests heme positive

The next step in the management of this patient would be to

A start two large bore IVs, bolus with normal saline, and type & cross
B follow hemoglobin and hematocrit every 6 hours
C order screening labs and determine further treatment based on those results
D reassure patient and family that most GI bleeding in children is benign

E emergency surgery

The most likely cause of bleeding in this patient is

A esophageal varices
B peptic ulcer disease
C stress gastritis
D vascular malformation

Which of the following medications would be most beneficial for this patient with a significant acute upper GI bleed that has not spontaneously stopped?

A Propranolol
B Octreotide
C Nifedipine
D Vasopressin

Please answer the following with TRUE or FALSE

T or F Black stool that tests hemoccult positive is suggestive of an upper GI bleed.
T or F Melena suggests ongoing bleeding.

Solutions and explanations:

1)) A, Tachycardia is the initial manifestation of significant GI bleeding with hypotension being a late and ominous sign. This patient has tachycardia; therefore, you should assume that the patient has lost a significant amount of blood. Your first priority in this patient with significant GI bleeding is to stabilize the patient hemodynamically. This includes starting two large bore IVs and providing normal saline until blood type is determined. Consultation with a pediatric gastroenterologist should be done early so that endoscopic therapy can be arranged. Patients who have ongoing bleeding warrant emergent endoscopy, whereas those patients whose bleeding stops can have endoscopy done under more controlled conditions (but preferably within 24 hours). Screening labs should also be sent and include CBC with platelets, complete metabolic panel, and coags

* In this patient with a significant GI bleed, treatment needs to be initiated quickly. You are correct that screening labs will need to be ordered, but your immediate concern should be to correct volume loss and to have blood available if transfusion is necessary.

* Your first priority should be to stabilize the patient hemodynamically. Your surgical colleagues should be informed about this patient because she may indeed need surgical therapy, but emergency surgery is not indicated at this point. Endoscopic therapy is usually the first line therapy in patients with ongoing GI bleeding, with surgery being reserved for continued bleeding despite endoscopic therapy.

* if your answer was D, You are correct that most GI bleeding in children is benign, but that doesn't appear to be the case with this patient. This patient has risk factors for significant GI bleeding and signs of significant blood loss (tachycardia).

2)) A, This patient with cirrhosis and evidence of portal hypertension (massive

splenomegaly, leukopenia, thrombocytopenia) is at risk for esophageal varices and variceal bleeding. Increased pressure in the portal vein results in engorgement of blood in collateral vessels, such as the esophageal venous plexus in the distal esophagus. These vessels become dilated and can rupture resulting in significant upper GI bleeding. Variceal bleeding should be high in the differential diagnosis in patients with chronic liver disease and/or portal hypertension who present with upper GI bleeding.

* Stress gastritis (or even stress ulcers) occurs when the body endures a significant stressor such as burns, major trauma, severe systemic illness, etc. This can result in significant gastrointestinal bleeding but this patient has no risk factors for stress gastritis.

* Peptic ulcer disease can result in significant upper GI bleed, but this patient's liver disease puts her at risk for another cause of bleeding.

* Vascular malformations of the GI tract can cause bleeding but this patient's liver disease puts her at risk for another cause of bleeding. Symptomatic hemangiomas of the GI tract, although rare, may cause bleeding (usually during infancy). Hemangiomas of the GI tract are commonly associated with cutaneous hemangiomas; therefore careful inspection of the skin is important when faced with an infant with GI bleeding. Similar to skin hemangiomas, most GI lesions resolve spontaneously over the first 12-18 months of life and require no treatment. In some cases, treatment with steroids may be necessary to facilitate involution of the lesions.

3)) Octreotide decreases splanchnic blood flow and has been shown to be beneficial in the treatment of active upper GI bleeding. It is administered as a one-time bolus followed by a continuous drip. It has been studied more extensively in acute variceal bleeding but it has also been shown to be beneficial in non-variceal upper GI bleeding. Acid suppression is also indicated in this patient at this time, and blood transfusion will likely be required (particularly if the bleeding doesn't stop soon). Other treatment modalities that will improve the success of achieving initial hemostasis and reduce the risk of rebleeding in this patient are: fresh frozen plasma to correct the coagulopathy and platelets to correct thrombocytopenia.

4)) true, Melena is defined as very dark or black, tarry stool and is suggestive of an upper GI bleed. The dark black color is due to the effects of gastric secretions and/or intestinal bacteria upon heme. Lower GI bleeding, which is defined as bleeding distal to the ligament of Treitz, usually manifests as frank blood per rectum. The color of the blood can range from bright red to maroon, depending on the site of bleeding. The color of the blood in the stool can give you a clue as to where the bleeding originated. The further from the anus that the blood originates, the darker it will appear upon passage in the stool. Thus blood from the anus will look bright red, and bleeding from the upper GI tract manifests as melena. (This is a generalization and may not hold true in all circumstances, but it can be useful when developing a differential diagnosis.)

* false, melena simply indicates that there is blood in the stool that was once in the upper GI tract. It may persist for hours or days after the bleeding subsides and is not an indication of ongoing bleeding. Also, you should remember that not all dark stools are melena. Any dark stool that is thought to be melena should be Hemoccult tested to determine whether or not blood is present. Foods such as spinach or licorice and medications such as iron and Pepto-Bismol can all make the stool a very dark color and be mistaken for melena.

Q2: A 7-week-old male infant presents to your clinic because of blood in the stool. The parents report that two days prior to this visit, they noticed small streaks of blood in a few of his stools. This has progressed over the last two days, and they are now seeing gross blood in every stool. He is currently having 5-6 soft stools per day with blood mixed in with the stool. The parents report that, except for the presence of blood, the appearance of his stools hasn't really changed. The patient has not had any fever, abdominal distension, irritability, vomiting, or change in appetite. The parents report that the patient is acting normally and does not appear to be in any pain or distress.

The mother suffers from Type I diabetes, diagnosed at 10 years of age. The father suffers from asthma and allergic rhinitis. There are no family members with GI, liver, or hematologic diseases. Specifically there are no family members with a history of blood in the stool.

The patient is exclusively taking Enfamil Lipil, 3-4 ounces every 3 hours. The family uses bottled water to prepare the formula.

Physical Exam

VS: Afebrile, HR 140, RR 36, Lt. 60 cm (75th%), Wt. 6.5 kg (95th%), weight:length ratio is 90th percentile, OFC 42 cm (75th%)

General: well nourished, well hydrated, happy appearing infant

HEENT: pupils equal, red reflex present bilaterally, anicteric sclera, TMs clear bilaterally, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses, brisk capillary refill

Resp: clear breath sounds bilaterally, no distress

Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses

GU: normal external male genitalia

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: moves all extremities well, normal muscle tone

Neuro: DTRs noted to be normal and symmetrical

Skin: no rashes or lesions noted, no bruising or petechiae

Rectal: anus in normal position, perineum normal to inspection, stool present in the diaper that is soft and yellow-green in color with gross blood and mucus mixed throughout stool, stool tests heme positive

The most likely cause of blood in the stool in this patient is

A anal fissure
B cow's milk protein allergy
C hemorrhoids
D intussusception
E bacterial infection

The next step in the management of this patient would be to

A schedule outpatient colonoscopy
B continue current feedings and reassure the parents that the patient is otherwise asymptomatic
C change to Similac formula
D change to a soy or extensively hydrolyzed formula
E arrange for skin-prick allergy testing

The natural history of this condition is that it

A usually resolves within a few weeks
B usually resolves by 6-12 months of age
C usually resolves by 6-12 years of age
D usually persists throughout life

Solutions and explanations:

1)) A, Cow's milk protein allergy (CMPA) is the most likely cause of bleeding in this patient. CMPA usually presents in the first few months of life with blood per rectum in an otherwise asymptomatic patient. The blood may be accompanied by mucus, and the blood is often seen both on the surface of the stool as well as mixed within the stool. CMPA results in an allergic colitis characterized by eosinophilic inflammation of the colonic mucosa. There is often a family history of atopic diseases such as asthma, allergic rhinitis, or eczema. Often siblings or other family members have had a history of CMPA.

* Anal fissure, which is a superficial tear in the squamous epithelium of the anal canal, is a common cause of blood per rectum in this age group; however, this manifests as streaks of blood on the outside of the stool rather than mixed throughout the stool. Blood that is mixed throughout the stool suggests a more proximal site of bleeding or a diffuse colitis.

* Bacterial infection can cause bloody stools in patients of any age group and should be considered, but there is a more common cause of blood per rectum in this otherwise asymptomatic child. Fever or any other signs of illness would make infection more likely.

* Intussusception occurs when one segment of bowel telescopes into an adjacent segment of bowel and is propelled distally via peristalsis. Intussusception is most common in children 3 months to 3 years of age but could present in a patient this age. Patients with intussusception present with intermittent colicky abdominal pain. They often have abdominal distension and/or tenderness, vomiting, and stools which contain mucus and blood that have been termed "currant jelly stools". These "currant jelly stools" are secondary to ischemic injury to the intussuscepted bowel.

* Hemorrhoids are extremely uncommon in this age group.

2))D, The treatment of choice is an elimination diet which avoids intact cow's milk proteins. A soy protein formula may be beneficial in some patients, but up to 50% of patients who are allergic to cow's milk protein will also be allergic to soy protein. Therefore, many advocate t

2))D, The treatment of choice is an elimination diet which avoids intact cow's milk proteins. A soy protein formula may be beneficial in some patients, but up to 50% of patients who are allergic to cow's milk protein will also be allergic to soy protein. Therefore, many advocate the initial switch to a protein hydrolysate formula (Alimentum, Pregestimil, or Nutramigen). These formulas have been treated with an enzyme which hydrolyzes proteins in to smaller peptides that are less antigenic. Response to the dietary change is usually evident after 48-72 hours.

3)) B, Because cow's milk protein allergy usually resolves by 6-12 months of age, a strict cow's milk-free diet is recommended until at least 6 months of age. At that time, a challenge with a regular cow's milk formula can be performed. If the symptoms do not return, the patient may resume a regular diet. If the symptoms return with the challenge, the diet is continued for another 2-3 months and another challenge is performed

Q3: A 4-year-old female presents to your clinic with blood in the stool. Her mom reports that she first noticed a small amount of blood on the toilet paper after she passed stool a few weeks ago. She was not having any other symptoms at the time, and there was only a small amount of blood so the parents did not seek medical attention. She had another stool last evening which was accompanied by more blood. The stool was brown in color and normal in consistency. The blood was red and seemed to be on the outside of the stool. The mom reports that there was "so much blood that all of the water in the toilet turned red". Again the patient did not complain of any other symptoms at the time, but the parents decided to bring her in today because the amount of blood was alarming. The patient stools 1-2 times per day, and her stools are formed but soft. She does not strain or have pain when passing stools. She denies abdominal pain, nausea, anorexia, or lightheadedness. She has not had any fever or weight loss. She was born full term after an uncomplicated pregnancy. She has never been hospitalized and has never had surgery. She takes no medications. She has never had blood in her stool prior to 2 weeks ago and she has never had a problem with constipation. There is no family history of GI, liver, or hematologic problems in the family. The parents deny any history of GI bleeding in any family members. The patient lives with her parents and two older sisters. There are no smokers in the home, and they have an indoor cat. She has not been exposed to other animals or to anyone with diarrhea or blood in the stool. They have not traveled recently.

Physical Exam VS: Afebrile, HR 106, BP 95/65, RR 20,Ht. 98 cm (25th%), Wt. 15 kg (25th%), BMI 15.6 kg/m2 (50th%) General: well nourished, well hydrated, no acute distress HEENT: pupils equal, TMs clear bilaterally, nares clear, oropharynx clear Neck: supple without lymphadenopathy or thyromegaly CV: normal heart sounds, good pulses, brisk capillary refill Resp: clear breath sounds bilaterally, no distress Abd: soft, non-tender, no hepatosplenomegaly, no masses Extremities: no clubbing, cyanosis, or edema Musculoskeletal: good strength and tone Neuro: CN II-XII intact, DTRs noted to be normal and symmetrical Skin: no rashes or lesions noted Rectal: no anal fissures noted, normal sphincter tone, small amount of formed stool in rectal vault, small amount of gross blood on examining finger which tests hemoccult positive

The most likely cause of hematochezia in this patient is

A juvenile polyp
B anal fissure
C ulcerative colitis
D Henoch-Schönlein Purpura
E bacterial infection

The next step in the management of this patient would be

A barium enema
B radionuclide bleeding scan
C surgery
D colonoscopy
E capsule endoscopy

Please respond to the following with TRUE or FALSE.

T or F Anal fissure is the most common cause of hematochezia in the pediatric population.
T or F Most children with lower gastrointestinal bleeding require emergent endoscopy.
T or F Bleeding from a Meckel's diverticulum most commonly occurs during adolescence.

Solutions and explanations:

1)) Juvenile polyps are the most common cause of significant lower GI bleeding in toddlers and school-aged children. Bleeding from a juvenile polyp can occur because the surface of the polyp is very friable or if the polyp outgrows its blood supply, it can become ischemic and auto-amputate. Bleeding is usually bright red, painless, and small in amount (rarely do patients become anemic or require blood transfusions). The patient is otherwise asymptomatic with normal stools, except for the blood and/or mucus usually present on the surface of the stool. Most juvenile polyps are solitary and carry little, if any, malignant potential. They can occur in any portion of the colon, but most are found in the rectosigmoid area or left colon (thus the bleeding is usually bright red).

* Infection with organisms such as E. coli, Salmonella, Shigella, and Campylobacter usually presents with diarrhea, which may be bloody, rather than painless blood per rectum with otherwise normal stools.

* The fact that this patient is not having hard stools or difficulty passing stools makes anal fissure less likely. Also the amount of blood reported in this case is more than what is usually seen with an anal fissure.

* HSP is a systemic disease that can affect the skin (purpuric rash), kidneys (nephritis), joints (arthralgias), and gastrointestinal tract (abdominal pain, GI bleeding, or intussusception). The peak incidence is in children ages 3-7 years. The fact that this patient has no other symptoms makes HSP less likely; however, GI manifestation can precede other symptoms in a minority of cases.

* The fact that this patient is otherwise asymptomatic and has formed stool makes ulcerative colitis unlikely. Although ulcerative colitis can present in patients this young, it is usually seen in older children and adolescents.

2)) Colonoscopy is indicated in this patient with hematochezia and suspected juvenile polyp. Colonoscopy can be both diagnostic and therapeutic, as the treatment of choice for juvenile polyps is endoscopic removal. This is accomplished by snaring the polyp at the base of the stalk (juvenile polyps are pedunculated) and applying electrocautery

3)) true, Anal fissure, which is a superficial tear in the squamous epithelium of the anal

canal, is the most common cause of hematochezia in pediatric patients. It can occur at any age, from the newborn period through adolescence and into adulthood. It is usually the result of passage of hard or large stools, and the history is usually quite characteristic of this. Because anal fissures can be painful, children will often withhold stool to avoid painful defecation. This then results in more hard, large stools which perpetuates the cycle. The treatment of choice of anal fissures is softening of the stools and promoting a regular bowel habit.

* false, Most cases of lower GI bleeding in children are mild and self-limited and do not require emergent intervention. Your initial assessment in a patient with acute lower GI bleeding should be similar to that for a patient with upper GI bleeding. You should first assess the hemodynamic stability of the patient and make a rapid assessment of the degree of volume loss. If the bleeding is mild and the patient is hemodynamically stable, the child can undergo an outpatient workup under the guidance of a pediatric gastroenterologist. If the bleeding is severe and the patient is hemodynamically unstable, aggressive resuscitation with IV fluids should be initiated until blood is available for transfusion. Gastric lavage is recommended to determine if the patient has an upper GI source for the bleed and, if present, should be managed accordingly. Further evaluation and management should be undertaken under the guidance of a pediatric gastroenterologist. The most common cause of severe lower GI bleeding in children is Meckel's diverticulum.

* FALSE. Although bleeding from a Meckel's diverticulum can occur at any age, it is most common in patients under 2 years of age. Meckel's diverticulum is the most common congenital abnormality of the GI tract (found in about 2% of the population). Meckel's diverticula are located in the ileum and occur as a result of incomplete obliteration of the omphalomesenteric duct. Most cases of Meckel's diverticulum are asymptomatic and are found incidentally at autopsy or during abdominal surgery, but up to half of the diverticula contain ectopic gastric or pancreatic tissue. If the diverticulum contains acid-secreting gastric tissue, ulceration of the adjacent ileal tissue can occur and may result in GI bleeding. Bleeding from a Meckel's diverticulum usually presents with painless rectal bleeding in an otherwise asymptomatic patient, and the blood is typically described as dark red or maroon-colored (it arises from the mid-GI tract). The bleeding may be massive, requiring hospitalization and hemodynamic stabilization. Treatment is by surgical excision

- Large amount of diarrhea: think of small intestine pathology. Small amount: think of large intestine pathology.
- Acute diarrhea is almost always a result of infection.

Evaluation of acute diarrhea

When a patient presents with acute diarrhea, the evaluation depends on presenting symptoms:

- **Mild to moderate acute non-bloody diarrhea and no systemic signs of infection:** Perhaps no diagnostic evaluation is indicated. Some clinicians would order a rotavirus enzyme immunoassay (EIA), to look for the most common cause of this presentation. Although a positive rotavirus EIA does not alter therapy, it does define an etiology and may avoid further testing for other pathogens.
- **Severe acute non-bloody diarrhea with dehydration:** An evaluation should probably include a rotavirus EIA and, particularly if this is negative, a stool culture for enteric pathogens. If there is any history of recent antibiotic use, stool should be checked for C. diff toxin. You could consider checking stool for Giardia antigen or ova and parasites although the yield is probably very low in the setting of acute diarrhea. One could also consider an enteric viral culture of the stool to look for other pathogens, but these may be difficult to isolate.
- **Any acute diarrhea with signs of systemic illness such as persistent fever or significant abdominal pain or cramping:** A stool culture to rule out enteric pathogens is indicated in this situation, and you should also check for C. diff toxin. You can also check for viral causes and consider ova and parasites.
- **Dysentery:** A stool culture for enteric pathogens and C. diff toxin should be sent. You should consider sending stool for ova and parasites to look for Entamoeba histolytica, especially if the stool culture and C. diff studies are negative.
- Another test that may be used in the setting of acute diarrhea is a **Wright's stain** for fecal leukocytes. The presence of leukocytes in the stool suggests colonic inflammation and, in the setting of acute diarrhea, is suspicious for a bacterial enterocolitis. This should prompt a stool culture for enteric pathogens. Fecal leukocytes are not specific for bacterial infections as they are seen in other causes of colitis such as inflammatory bowel disease; however, the latter usually manifests as chronic diarrhea.

Evaluation of chronic diarrhea:

- **Grossly bloody stool:**
  - ✓ Hemoccult testing to verify that what looks like blood actually is blood.
  - ✓ Stool culture for enteric pathogens, C. diff toxin, +/- ova and parasites.
  - ✓ Labs: CBC with platelets, CMP, ESR and/or CRP.

- **Grossly non-bloody stool:**
  - ✓ Hemoccult testing to evaluate for presence of occult blood.
  - ✓ Wright's stain for fecal leukocytes.
  - ✓ Stool culture for enteric pathogens, C. diff toxin, ova and parasites (or antigen tests for giardia and/or cryptosporidium), Rotavirus +/-culture for other viral pathogens.
  - ✓ If poor growth, check for reducing substances in the stool and fecal fat, screening for malabsorption.
  - ✓ If poor growth, check sweat chloride to screen for cystic fibrosis.
  - ✓ If "red flags" are present in the history or physical exam, lab work-up.
  - ✓ Screening antibodies for celiac disease.

- **Toddler's diarrhea:**
  - ✓ Patients with a history and physical exam suggestive of toddler's diarrhea obviously do not need to undergo the above work-up.
  - ✓ It is a common cause of chronic diarrhea in children around 2 years old.
  - ✓ Typical presentation: loose stools in an otherwise healthy child.
  - ✓ The exact etiology is unknown, but many theories are present. One common theory is that it is caused by rapid transit of food through the GI tract. The history of seeing food particles in the stool may suggest rapid transit.
  - ✓ Other common theory is that it is caused by excess intake of high carbohydrate containing drinks like apple juice, other fruit drinks, or soft drinks. A patient should avoid ingestion of these juices.

Red flags in a child with chronic diarrhea:

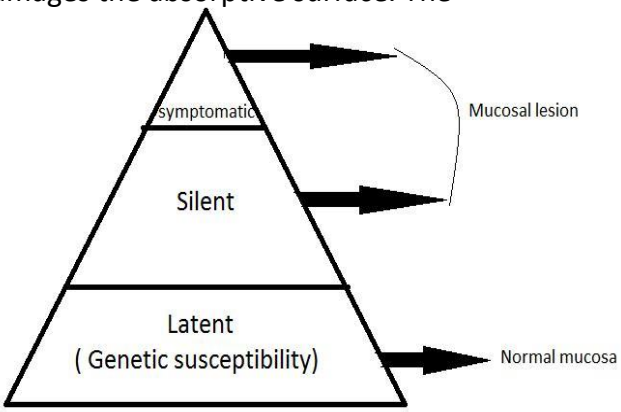
- **History:** gross blood in stool/ waking up at night to pass stool/ abdominal pain, particularly if it is localized/ vomiting/ anorexia/ weight loss/ persistent fevers/ rash/ arthralgia.
- **Physical exam:** grossly bloody or hemoccult positive stools/ pallor/ perianal disease (large anal skin tags, fissures, fistulae, abscesses)/ abdominal

tenderness that is localized/ malnutrition (weight: length ratio <3rd % or BMI <3rd %) / short stature/ dermatitis herpetiformis, erythema nodosum or pyoderma gangrenosum/ tenderness or swelling of joints.

** Two important causes of chronic non-bloody diarrhea are celiac disease and chron's disease.

Celiac disease

- It is an immune-mediated enteropathy characterized by permanent sensitivity to gluten in genetically susceptible individuals (HLA DQ2 and/or DQ8).
- Presentation is within a few months to years of starting a diet which contains gluten. So one can't get celiac disease before age of 4 months.
- Sources of gluten: wheat, rye, and barley / play dough / lipstick.
- **Pathogenesis:** gluten in the diet results in an inflammatory process of the small bowel mucosa which damages the absorptive surface. The inflammatory process is mediated by IL-15.



- **Risk factors:**
  1. Family history.
  2. Short stature/ anemia/ fatigue/ ↑ ALT, AST
  3. Down syndrome/ IgA deficiency/ autoimmune disorders/ infertility.
- The most common age of presentation is 6 – 24 months.
- **History:**
  - ✓ Classic: chronic or recurrent diarrhea, failure to thrive, abdominal distension, malnutrition.
  - ✓ More subtle presentations: mild diarrhea, abdominal pain, bloating, unexplained anemia, delayed puberty, or short stature.
- **Complications:**
  - ✓ Poor weight gain initially, but may progress to stunting of height.
  - ✓ Dermatitis herpetiformis: characteristic.
  - ✓ Dental enamel defects.
  - ✓ Aphthous ulcers (not common).
  - ✓ Delayed pubertal changes.
  - ✓ Occipital calcifications on CT (very rare).

- ✓ Risk of developing malignancies of the small bowel.
- ✓ Osteoporosis.

- **Diagnosis:**
  - ✓ **Serology:**
    - Anti-gliadin antibodies AGA (IgA and IgG) have poor sensitivity and specificity**.**
    - Anti-tissue transglutaminase antibody (tTG) and/or anti-endomysial antibody (EMA): screening antibodies of choice today with very high sensitivity and specificity, except in patients with IgA deficiency, in which they will be falsely negative as they are both IgA antibodies.
  - ✓ **Endoscopy:** may show scalloping/ nodularity or it may me normal.
  - ✓ **Biopsy:** the gold standard.
    - Villous atrophy: blunting/shortening of the villi.
    - Infiltrative → hyperplastic (hyperplasia of the crypts) → flat destructive.
    - Intraepithelial lymphocytes ↑ in number.

- Additional reading: Marsh classification of histologic findings.
- **Treatment:**
  - ✓ Adherence to a strict gluten-free diet results in resolution of symptoms and histologic abnormalities and is the recommended treatment.
  - ✓ Consultation with an experienced dietician is often beneficial to the family.
  - ✓ You have to screen siblings.

Chron's disease

- It is an immune-mediated inflammatory disorder that can affect any portion of the gastrointestinal tract. It is a major subtype of inflammatory bowel disease.
- Thought to be due to the body's immune response to exogenous or endogenous triggers in genetically susceptible individuals.
- Classic presentation is that of abdominal pain, weight loss, and diarrhea that may be either bloody or non-bloody depending on which part of the GI tract is affected.
- May have extra-intestinal manifestations such as fevers, arthralgia, arthritis, skin lesions, ocular manifestation, and/or liver disease.
- Physical exam:
  - ✓ Most common finding is abdominal tenderness.
  - ✓ Thickened loops of bowel may be palpable, most often in right lower quadrant (the terminal ileum).

- ✓ Weight loss may be significant enough to produce malnutrition.
- ✓ Pubertal changes may be delayed.
- ✓ Perianal disease.

- Most common lab findings are anemia (blood loss and/or anemia of chronic disease), thrombocytosis (acute phase reactant to inflammation), elevated ESR and CRP (acute phase reactants to inflammation), and hypoalbuminemia (malnutrition).
- Granulomas are characteristic collections of histiocytes sometimes seen on gastrointestinal biopsies from patients with Crohn's disease and are not present in ulcerative colitis.
- Treatment: varying combinations of corticosteroids, immunomodulators, topical 5-aminosalicylate preparations, antibiotics, and occasionally biologic agents.

Key points:

- Acute diarrhea is almost always a result of an infectious process.
- Acute non-bloody diarrhea is usually caused by a viral infection.
- Acute bloody diarrhea is usually caused by a bacterial infection.
- Chronic non-bloody diarrhea can result from many causes; some are benign and some are more serious.
- Chronic bloody diarrhea is often the result of inflammatory bowel disease and an evaluation to look for IBD is indicated.
- Perianal disease is highly suggestive of inflammatory bowel disease, particularly Crohn's disease.
- Empiric use of antibiotics and/or anti-diarrheal medications is not recommended in patients with diarrhea.
- Concomitant symptoms such as abdominal pain, anorexia, weight loss, poor growth, arthralgia, bloody stools, and nocturnal stools are all warning signals that should prompt a thorough evaluation and warrant consultation with a pediatric gastroenterologist.

Test yourself:

Q1: History: A 10-month-old male infant presents to your office with vomiting and diarrhea. The mother reports that the illness began 2 days ago with a few episodes of vomiting followed by 5 episodes yesterday; however, he has not had any vomiting today. The emesis has been non-bloody and non-bilious. Diarrhea began yesterday with about 10 episodes of watery diarrhea, and this has continued with 6 episodes this morning. The mother denies seeing any gross blood in the stools, but states that the stools have

been large in volume and often leak out of the diaper. The mother reports a fever up to 101 F on the first and second day of the illness but none today. The patient's oral intake was markedly decreased yesterday but mom reports the patient is breastfeeding well today. Urine output was decreased yesterday but seems to be improving today.

The patient was born at 41 weeks gestation after induction of labor without complications. His birth weight was 8 lb 10 oz, and he had a normal course in the newborn nursery. He has no other health problems, has never required antibiotics, has had all of his well child examinations, and his immunization status is up-to-date

The patient lives with both parents and his 3 year old sister. The father works in the insurance business, and the mother stays at home with the children. The mother reports that a child from their weekly playgroup had a few episodes of diarrhea last week. There have been no other sick contacts and the only animal exposure has been to the family's indoor cat.

The mom and dad are both healthy. The maternal grandmother had her gallbladder removed because of gall stones. There are no other gastrointestinal diseases in either side of the family.

The child is breastfed and also takes baby food and some table foods. Oral intake was slightly decreased over the previous two days, but the mom reports that the patient is currently breastfeeding well.

Physical Exam

VS: Afebrile, HR 168, RR 20, Lt. 75 cm (75th%), Wt. 10.2 kg (50-75th%), weight:length ratio is 75th percentile, OFC 47 cm (75th%)

General: alert, somewhat irritable but consolable, well nourished, appears mildly dehydrated

HEENT: pupils equal, red reflex present bilaterally, tears present, TMs clear bilaterally, oropharynx clear, mucous membranes are slightly tacky

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds but tachycardic, good pulses, capillary refill 2 seconds

Resp: clear breath sounds bilaterally, no distress

Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses

GU: normal external male genitalia

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: moves all extremities well, normal muscle tone

Neuro: DTRs noted to be normal and symmetrical

Skin: no rashes or lesions noted

Rectal: anus in normal position, mildly erythematous diaper rash present, stool from diaper is very watery and tests hemoccult negative

The most likely cause of this child's symptoms is

A Shigella
B enteric adenovirus
C "Norwalk-like" virus
D rotavirus
E Giardia lamblia

The next step in the management of this patient would be to

A continue breastfeeding and a regular diet
B avoid breastfeeding and substitute a lactose-free formula for 48 hours
C avoid breastfeeding and substitute pedialyte for 48 hours
D start IV fluids and make patient NPO in order to achieve "bowel rest"

Please answer the following with TRUE or FALSE

T or F Most cases of acute diarrhea require only supportive therapy.
T or F Drinks that contain large amounts of carbohydrates, such as apple juice, can result in worsening of diarrhea.
T or F Very young infants are usually not as severely affected as older patients with acute diarrhea.

Solutions and explanations:

1)) D

2)) A, Breastfeeding, or formula feeding, can be continued in almost all cases of rotavirus enteritis, and a balanced diet which provides adequate nutrition can aid in recovery. This is true for acute diarrheal illnesses in general, and only in severe cases with prolonged diarrhea should you consider interrupting the patient's regular diet. Although mucosal damage from enteritis can cause some degree of temporary lactase deficiency, it usually is short-lived and not clinically significant. It would be reasonable in this patient with mild dehydration to offer some pedialyte in addition to his regular diet, but cessation of breastfeeding is not necessary.

3)) true, More than 90% of acute diarrheal episodes are caused by an acute viral infection. Most of these cases do not result in dehydration and do not require any intervention other than maintenance of hydration status. This can usually be accomplished with the patient's regular diet, although supplementing the diet with an oral rehydration solution such as pedialyte is acceptable. In most patients who present with acute watery diarrhea, a diagnostic evaluation to determine the exact etiology of the diarrhea is not necessary as it does not change management and the diarrhea is self-limited. One setting where it is important to determine the etiology of diarrhea is in the neonatal period. Although infection is still the most likely cause, there are a number of rare congenital diarrheal disorders that must be included in the differential diagnosis.

* true, Because the absorption of glucose is coupled with the absorption of sodium by a specific cotransporter, solutions that contain excess glucose and inadequate sodium may result in a carbohydrate-induced diarrhea. Therefore these drinks should be limited or totally excluded from the diet in patients with diarrhea. Oral rehydration solutions which contain adequate amounts of sodium in addition to glucose are better suited for patients with acute diarrhea.
* false, Younger infants have a higher risk of severe, life-threatening dehydration as a result of acute diarrhea and require careful monitoring and aggressive rehydration. This is likely a result of limited renal capacity to concentrate urine and conserve total body water in very young children.

Q2: A 9-year-old male presents to your office with a 3-day history of crampy abdominal pain and diarrhea. Initially the diarrhea was watery but within 24 hours of the initial presentation it became grossly bloody. The patient reports having about one stool per hour while awake and waking up one to three times at night to pass stool. He comments that he often has the urge to defecate but when he attempts to pass stool, only a very small amount of bloody stool is produced. He reports that his abdominal pain is worse just prior to passing stool and is somewhat relieved with defecation. His parents report that the abdominal pain seems to be getting worse and often makes him cry. He has had no vomiting, no joint pains, no rash, and no weight loss.

The patient was born full term via a repeat C-section delivery. No complications with pregnancy or delivery. Birth weight was 7 lbs 2oz. He has no other medical problems and has never been hospitalized or had surgery.

He has a cousin who had GERD as an infant but is doing better now. His father also takes medications for GERD. His mother has seasonal allergies. There is no family history of inflammatory bowel disease or bleeding disorders. The parents are unaware of any family members with a history of blood in their stool.

The patient lives with his parents and two younger siblings. No one else in the family has been sick with abdominal pain or diarrhea. There have been no other exposures to anyone with diarrheal illnesses. They live on a farm just outside of a small community. They have many animals on the farm including an outside dog, many cats, sheep and cattle. They receive well water, but they use bottled water for drinking.

The patient eats a regular diet for his age. He has continued to have good oral intake of fluids but has had a decreased appetite for solid foods over the last few days. The parents can't recall any unusual food exposures, including any undercooked meat or poultry. The mother states that about one week ago the family had grilled chicken but that everyone in the family had the same meal and no one else became sick. He did however help prepare the meal and handled the raw chicken.

Physical Exam
VS: T 101.2 F, HR 105, RR 18, Ht. 130 cm (25th%), Wt. 25.6 kg (25th%), BMI 15.1 kg/m2 (25th%)
General: well nourished, well hydrated, appears to be in mild discomfort
HEENT: pupils equal, TMs clear bilaterally, oropharynx clear, mucous membranes moist
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses, brisk capillary refill
Resp: lungs are clear bilaterally, no distress
Abd: soft, non-distended, no hepatosplenomegaly, no palpable masses, complains of mild tenderness in the lower abdomen upon examination
GU: normal external male genitalia
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: normal strength and muscle tone
Neuro: DTRs noted to be normal and symmetrical, no gross deficits
Skin: no rashes or lesions noted
Rectal: no perianal disease, sphincter tone normal, grossly bloody stool on digital rectal exam which is heme positive

The most likely cause of this child's symptoms is

A Shigella
B Campylobacter jejuni
C Entamoeba histolytica
D ulcerative colitis
E Clostridium difficile

The next step in the management of this patient would be to

A colonoscopy with biopsies
B obtain a stool culture and begin empiric antibiotics while awaiting results
C obtain a stool culture and provide supportive care
D reassure the parents that this is likely an infection that no treatment is necessary

Please answer the following with TRUE or FALSE

T or F Isolation of E coli 0517:H7 from the stool of a patient with dysentery is an indication for prompt antibiotic therapy.
T or F E coli and Salmonella are the two most common enteric pathogens associated with hemolytic-uremic syndrome (HUS) in the United States.
T or F Antimotility agents should be avoided in patients with dysentery.

Solutions and explanations:

1)) B, Campylobacter is the most commonly isolated bacteria from patients with dysentery in industrialized countries. Both domestic and wild animals can be reservoir for Campylobacter. Most cases of Campylobacter enteritis are thought to be related to poultry, as the surface of raw poultry is commonly contaminated with Campylobacter. After an incubation period of 3-6 days, Campylobacter enteritis is characterized by diarrhea that often becomes bloody as well as crampy abdominal pain that may be so severe that it

mimics appendicitis. (Remember: "Campy is Crampy") Campylobacter is followed in frequency as a cause of acute bacterial enteritis by: Salmonella, E. coli, Shigella, and Yersinia. These "enteric pathogens" are the ones most often screened for by microbiology labs when a stool culture is sent, although some labs may not routinely screen for Yersinia. It is therefore important to know which pathogens are included in the stool culture at your lab.

2)) C, A stool culture should be obtained and further treatment based on the results of that culture. Because it is often difficult to determine the etiology of dysentery based on history and physical exam alone, a stool culture for enteric pathogens should be done on all patients with bloody diarrhea.

3)) FALSE, There is evidence that antibiotic therapy in patients with E. coli 0517:H7 does not improve outcomes and, in fact, may increase the risk of developing HUS and result in poorer outcomes compared to untreated patients. Therefore antibiotics are not recommended in these patients. The predominant mode of transmission is the ingestion of undercooked ground beef, but infection has also been associated with raw fruits and vegetables, contaminated water, and person-to-person via the fecal-oral route.

* FALSE, Enterohemorrhagic E. coli (such as E. coli 0157:H7) and Shigella are the two enteric pathogens most commonly associated with HUS in the U.S. HUS is characterized by hemolytic anemia, renal failure, and thrombocytopenia. It is the most common cause of acute renal failure in children. The association with E. coli 0157:H7 and Shigella is thought to be secondary to endotoxins produced by the bacteria that result in damage to endothelial cells in the kidneys. In addition to HUS, shigella infection may also be associated with seizures. It has been hypothesized that the endotoxin (Shiga-toxin) may play a role in the development of seizures; however, others have argued that these are simply febrile seizures.
* true, Antimotility agents are contraindicated in dysentery as they may actually exacerbate systemic symptoms and have been identified as a risk factor for the development of HUS.

Q3: A 21-month-old female presents to your office with diarrhea. Mom reports that she has been having 4-5 loose stools per day for the past few months. She describes the stools as being very soft to watery without gross blood. The mother states that sometimes she sees food particles in the stool. She has not had any vomiting or fever during this time period. She does not appear to have any abdominal pain and acts as if she feels well. She has a good energy level and a normal appetite. She continues to grow well. The mother is concerned because the diarrhea has been going on for months and does not seem to be improving.

The patient was born full term without complications. Her birth weight was 6 lbs 12 oz. She has been healthy without any hospitalizations or surgeries. She has not had any respiratory infections and has never required antibiotics. She has been growing along the 25th percentile for both height and weight.

The dad and a paternal uncle suffer from irritable bowel syndrome. The mother is healthy and no one else in the family suffers from any gastrointestinal or liver problems. Mom specifically denies any history of inflammatory bowel disease, celiac disease, cystic fibrosis, or any other family members with chronic diarrhea.

The patient lives with her parents and one pet dog. They have city water and there are no smokers in the home. The father owns his own business and the mother is a homemaker. The patient does not go to daycare and has not had any exposure to others with any diarrheal illnesses.

The mom reports that the patient eats a normal toddler diet, eating primarily table foods with the family. She only drinks about one serving of milk per day, as she prefers juice or soft drinks. Mom reports that she drinks about four 8-ounce cups of juice per day, primarily apple juice. She also drinks sodas, but mom says only once per day.

Physical Exam

VS: Afebrile, HR 105, RR 18, Lt. 82 cm (25th%), Wt. 10.8 kg (25th%), weight:length ratio is 50th percentile, OFC 47 cm (25th%)

General: appears well hydrated and well nourished

HEENT: sclera anicteric, pupils equal, round, and reactive bilaterally, TMs clear bilaterally, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses

Resp: clear breath sounds bilaterally, no respiratory distress

Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses

GU: normal external female genitalia

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: normal muscle strength and tone

Neuro: DTRs noted to be normal and symmetrical

Skin: no rashes, lesions, or jaundice noted

Rectal: perineum normal to inspection, digital rectal exam reveals very soft stool in the rectal vault that tests heme negative

The most likely cause of this child's symptoms is

A irritable bowel syndrome
B cystic fibrosis
C post-infectious enteropathy
D chronic non-specific diarrhea of childhood (toddler's diarrhea)
E hypolactasia (lactose intolerance)

The next step in the management of this patient would be to

A start the patient on an anti-diarrheal medication such as loperamide (Imodium)
B avoid ingestion of fruit juices and sodas and evaluate response
C start the patient on empiric antibiotics
D schedule upper and lower endoscopy
E place the patient on a lactose-free diet

Please answer the following with TRUE or FALSE

T or F Diarrhea that persists despite fasting is indicative of an osmotic diarrhea.
T or F Reducing substances present in the stool suggests secretory diarrhea.

Solutions and explanations:

1)) A, Toddler's diarrhea is a common cause of chronic diarrhea in this age group. The typical presentation of toddler's diarrhea is persistent loose stools in an otherwise healthy child with no signs of systemic illness. The exact etiology is debated and may have a variety of causes. Two common theories are that it is caused by rapid transit of food through the gastrointestinal tract or by excess intake of high-carbohydrate containing drinks like apple juice, other fruit drinks, or soft drinks. Excessive intake of these drinks exceeds the small intestine's ability to transport glucose and increases intraluminal osmolarity which results in an osmotic diarrhea. The history of seeing food particles in the stool may suggest rapid transit through the GI tract, and this patient is definitely ingesting excessive amounts of high-carbohydrate containing drinks.

* Cystic fibrosis is a disease that should be in the differential diagnosis of a child with persistent diarrhea, but there are no other warning signals in this patient. In patients with cystic fibrosis, the diarrhea is almost always accompanied by poor growth. Also, the absence of pulmonary symptoms or infections makes CF less likely in this patient.

* Post-infectious enteropathy can occur after acute enteritis and results in persistent diarrhea. The diarrhea is thought to be related to persistent damage to or delayed repair of the absorptive surface of the small intestine following the infectious process. Post-infectious enteropathy is a cause of persistent diarrhea in the pediatric population, but this patient does not have a history of an acute episode of enteritis prior to the onset of the chronic diarrhea.

* Hypolactasia refers to the decline in lactase activity that occurs in the majority of the world's population after weaning. The incidence of hypolactasia varies among different populations. It is very common in Latinos, African Americans, Asians, and Native Americans, occurring in more that 80% of adults in these populations. It probably occurs in about 10-20% of the adult caucasian population in the United States. Hypolactasia usually presents in late childhood or adolescence and should be in the differential diagnosis of patients in these age groups with chronic diarrhea and/or abdominal pain. It is very rare in patients under two years of age.

2)) B, This patient's history is highly suggestive of toddler's diarrhea and a trial of avoidance of high-carbohydrate drinks is indicated. If the diarrhea markedly improves or resolves, no other testing is needed. If dietary modifications do not result in improvement, then an evaluation that includes stool studies to look for bacteria, viruses, and parasites should be undertaken. If the diagnosis is still not evident, consultation with a pediatric gastroenterologist is warranted

3)) false, Osmotic diarrhea is caused by osmoles that are present in the intestinal lumen, such as malabsorbed carbohydrates, which draw water into the lumen resulting in diarrhea. The hallmark of osmotic diarrhea is that it resolves or markedly improves with fasting. This occurs because the amount of diarrhea is proportional to the osmotic load in the gut lumen and removing the malabsorbed substance from the diet eliminates the osmotic load. In contrast, secretory diarrhea results from secretion of fluid and electrolytes by the crypt epithelium of the gut and does not cease with fasting. Differentiating osmotic from secretory diarrhea can be helpful when evaluating patients with both acute and chronic diarrhea.

* false, Reducing substances are unabsorbed carbohydrates in the stool, and their presence in the intestinal lumen results in an osmotic diarrhea.

Stool Tests

Stool studies for infectious causes should be included in the evaluation of patients with persistent diarrhea. If infection if not the cause, other stool tests may need to be done. Some common tests that may be ordered are:

Fecal occult blood (hemoccult or guaiac testing): presence suggests mucosal damage with blood loss

Fecal leukocytes (Wright's stain): presence suggests colonic inflammation

Fecal reducing substances: presence suggests carbohydrate malabsorption

Fecal pH: an acidic fecal pH (<5.6) suggests carbohydrate malabsorption and results from fermentation of the unabsorbed carbohydrates by colonic bacteria

Fecal fat: presence suggests fat malabsorption which can result from a variety of conditions such as pancreatic insufficiency or cholestasis with poor bile flow

Fecal elastase: elastase is a protease produced by the pancreas and low levels of fecal elastase suggests pancreatic insufficiency

Fecal alpha-1 antitrypsin: elevated fecal alpha-1 antitrypsin suggests intestinal protein loss and is seen in protein-losing enteropathies

Q4: A 14-year old female presents to your office with diarrhea. She reports that the diarrhea began about 2 months ago with 2-3 loose stools per day. About 4 weeks ago she began to see blood on the toilet paper and in the toilet, and over the past few weeks she has been seeing an increasing amount of blood in her stool. She is currently having 4-5 bloody stools per day and waking up once per night to pass stool. She just recently brought this problem to the attention of her parents. Upon further questioning she states that she has a decreased appetite and has lost about 3 pounds. She has also been having abdominal pain in both lower quadrants, and some joint pains in her ankles. She denies fever, skin rash, or oral ulcerations.

The patient lives with her parents and two brothers. Both parents work outside the home. They receive city water and have no pets. She has not had any recent travel, unusual animal exposures, or contact with others with diarrhea or blood in the stool. She is a good student and participates in basketball.

The mom has been diagnosed with irritable bowel syndrome and specifically denies ever seeing blood in her stool. The dad is healthy. She has a brother who has asthma. The paternal grandfather had a colonic polyp removed recently. There is no family history of inflammatory bowel disease or bleeding disorders.

She denies any usual food exposures or eating undercooked meat. She reports that over the past 2 or 3 weeks her appetite has been decreased, and she states that eating often precipitates abdominal pain.

Physical Exam

VS: Afebrile, HR 82, RR 16, Ht. 165 cm (75th%), Wt. 50.5 kg (50th%), BMI 18.5 kg/m2 (25th-50th%)

General: well nourished, well hydrated, no acute distress

HEENT: anicteric sclera, pupils equal, round, and reactive bilaterally, TMs clear bilaterally with some scarring present, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: regular rate and rhythm, no murmurs, good pulses

Resp: clear breath sounds bilaterally, no distress

Abd: soft, non-distended, mildly tender to palpation in the lower abdomen, no palpable loops of bowel or other masses, no hepatosplenomegaly

GU: normal external female genitalia, Tanner stage IV

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: good muscle strength and tone

Neuro: no gross motor or sensory deficits, DTRs are normal and symmetrical

Skin: no rashes or lesions noted

Rectal: no perianal skin tags, fissures, or fistulas, loose grossly bloody stool present in rectal vault which tests hemoccult positive, patient expresses discomfort with palpation of the rectal walls during digital rectal exam

The most likely cause of this child's symptoms is

A Salmonella
B a juvenile polyp
C Entamoeba histolytica
D ulcerative colitis
E Clostridium difficile

The next step in the management of this patient would be to

A obtain stools studies and screening labs
B start the patient on an anti-diarrheal medication such as loperamide (Imodium)
C start the patient on empiric antibiotics
D perform upper and lower endoscopy
E start the patient on corticosteroid therapy

Please answer the following with TRUE or FALSE

T or F The incidence of ulcerative colitis is higher than Crohn's disease in the pediatric population.
T or F Patients with ulcerative colitis refractory to medical therapy can be treated with colectomy.

Solutions and explanations:

1)) The history in this patient is very suggestive of inflammatory bowel disease. The classic presentation of ulcerative colitis (UC) is that of bloody diarrhea and abdominal pain. This patient also has anorexia and mild weight loss which can be seen in UC, although usually to a lesser degree than that seen with Crohn's disease.

* Juvenile polyps can cause rectal bleeding but are not associated with diarrhea, abdominal pain, or weight loss. Juvenile polyps are usually seen in younger children and cause painless rectal bleeding.

2)) A, A diagnostic evaluation should be the initial step in the management of this patient. Stool studies should include culture for enteric pathogens, C. diff toxin, and perhaps ova and parasites. Laboratory studies should include CBC with platelets, complete metabolic panel, and inflammatory markers such as ESR and/or CRP. The results of stool and laboratory studies should guide further management. If infection is not the cause of the patient's symptoms, prompt consultation with a pediatric gastroenterologist is warranted so that endoscopy can be arranged.

3)) FALSE, Overall, the incidence of pediatric Crohn's disease exceeds that of pediatric ulcerative colitis. However, UC is more common among children diagnosed at a very young age (<5 years).

* true, The number of patient who come to colectomy is becoming smaller and smaller with advances in medical therapy. However, patients with UC who are refractory to all medical therapy or who are dependent on high dose steroids can be "cured" with colectomy. This is not the case with Crohn's disease as inflammation in Crohn's disease is not limited to the colon and often recurs in the more proximal bowel. Surgery can be performed on patients with refractory Crohn's or other complications such as intestinal strictures, but surgery does not "cure" Crohn's disease.

GER & GERD

- GER (gastro-esophageal reflux) is different from GERD. It is not a disease, it is rather a description.
  - ✓ Infantile GER is extremely common, occurring in up to 2/3 of 4 month old infants and usually resolves during the first year of life.
  - ✓ It manifests as effortless, painless "vomiting" in a well appearing infant. These patients are often referred to as "happy spitters".
  - ✓ It is defined as the passage of gastric contents into the esophagus. Regurgitation is defined as the passage of refluxed gastric contents into the oral pharynx. Vomiting can be defined in a number of ways: some define vomiting as the expulsion of regurgitated gastric contents out of the mouth; others consider vomiting a more complex behavior consisting of nausea, retching, and complete expulsion of stomach contents.
  - ✓ Some refer to the "vomiting" seen in infantile GER as "spitting up" or simply as "regurgitation" as the gastrointestinal correlates of vomiting do not occur, retching is rare, and the expulsion of stomach contents is neither forceful nor complete.
  - ✓ Transient lower esophageal sphincter relaxations (TLESRs) are believed to be the cause of most reflux episodes in infants as well as older children and adults. TLESRs are a normal physiologic process
  - ✓ A thorough history and physical examination with attention to warning signals is generally sufficient to diagnose uncomplicated infantile GER. A barium upper GI series is not necessary.
  - ✓ Parental education, anticipatory guidance, and reassurance, as well as institution of "conservative measures" should be used in treating infants with GER.
  - ✓ Referral to a pediatric gastroenterologist is warranted in infants with GER whose regurgitation is not improving by 12 months of age or resolved by 18-24 months of age.
- **Conservative measures for GER:**
  - ✓ Thickening of formula: Adding rice cereal to infant formula.
  - ✓ Avoid overfeeding.
  - ✓ Avoid provocative positioning: Supine, right-side down, and upright seated positioning have been shown to provoke GER. Prone positioning while awake is acceptable and could be considered in the postprandial period with adequate supervision, but not during sleep due to risk of SIDS.
  - ✓ Avoid exposure to tobacco smoke.

- ✓ Trial of hypoallergenic formula: A small subset of infants with GER suffers from a cow's milk protein intolerance. These infants will benefit from a change to a protein hydrolysate formula. This trial should be limited to 1-2 weeks, and if no improvement is seen the patient should be switched back to a regular cow's milk protein formula due to the financial burden of the hydrolysate formulas.

- There is evidence that obesity is associated with GER. It is probably a result of increased intra-abdominal pressure causing TLESRs; therefore weight loss should be a priority in these patients.
- Fatty meals slow gastric emptying and may make GER worse. There are a number of other foods that should also be avoided because they are thought to increase GER. They are caffeine, chocolate, spicy foods, peppermint, tomato based foods, and colas. For older children and adults, alcohol will also increase GER and should be avoided.
- **Infantile GERD** occurs when GER results in complications such as poor weight gain, irritability or other behaviors suggestive of esophagitis, or respiratory symptoms.
  - ✓ A barium upper GI series to detect anatomic abnormalities is warranted in infants with GERD. It is neither sensitive nor specific.
  - ✓ Referral to a pediatric gastroenterologist is warranted in infants with GERD who do not respond to conservative therapy with or without a brief period of pharmacotherapy.
  - ✓ Older children and adolescents who have symptoms of GERD should be tried on acid suppression therapy, and if they respond this can be continued for 2-4 months.
  - ✓ Referral to a pediatric gastroenterologist is warranted in older children with symptoms of GERD who do not respond to acid suppression therapy or who relapse when treatment is discontinued. Further evaluation is necessary to determine if there is an anatomic reason for the GERD (such as hiatal hernia) or if there is another etiology for the symptoms (such as eosinophilic esophagitis).

- **An upper GI series** is a good test to evaluate for anatomic abnormalities such as esophageal stricture, hiatal hernia, pyloric stenosis, annular pancreas, or malrotation.

- **Esophageal pH monitoring: A pH probe study** to measure esophageal acid exposure. Continuous 24-hour pH probe monitoring is a valid and reliable measure to quantitate acid exposure in the esophagus (frequency and duration of episodes). The percentage of time that the esophageal pH is <4 is called the reflux index. The upper limit of normal for the reflux index is 12%

in the first year of life and 6% thereafter. The limitations of a pH probe study are that it is unable to detect non-acidic reflux episodes and is unable to determine the volume of refluxed material.

- **Endoscopy with biopsy:** It can determine the presence, severity and etiology of esophagitis. It can establish the presence of strictures, webs, or inflammatory conditions of the GI tract.

- **Cintigraphy**: A nuclear scintiscan can be performed after the ingestion of technetium-labeled formula (liquid phase) or food (solid phase). One benefit of scintigraphy is that gastric emptying can be assessed which may affect treatment. The other benefit is that non-acid reflux can be detected; however a lack of age-specific normative data limits the value of this test.

Red flags in vomiting:

Poor weight gain / dehydration / forceful vomiting / excessive irritability / bilious emesis / GI bleeding / fever / diarrhea / lethargy / bulging fontanelle / hepatosplenomegaly/ abdominal tenderness or distension/ genetic disorders such as trisomy 21.

DDx of vomiting:

- GERD.
- Overfeeding.
- Pyloric stenosis.
- Intestinal obstruction.
- Inborn errors of metabolism.
- Milk or food allergy.
- Increased intracranial pressure.

Test yourself:

A 4-month-old white female returns to your office for her scheduled well child visit. As you take the history, you discover that the mother is very concerned about the number of times that her child is "spitting up". The mother reports that the infant has non-bilious, non-bloody emesis with almost every feeding and estimates the amount as "the entire feeding". This usually occurs either immediately after the feeding or up to 15 minutes later. This problem began at about the time of her 2 month well child visit and has gotten progressively worse. The infant does not seem to be bothered by these episodes. The mom denies excessive fussiness, respiratory distress, or a chronic cough. The mother states that "there's got to be something wrong with a baby who spits up this much".

The mother has a history of mild intermittent asthma. The father is healthy. There is no family history of gastrointestinal, liver, or metabolic diseases in the family.

The patient is taking Similac formula, and she usually eats 7-8 ounces six times per day. She is not yet taking infant cereal or baby food.

The patient lives with her parents, and they have one indoor cat. She has no siblings. They have city water, although they use bottled water to make the formula. The mother is an elementary school teacher and the father is a computer programmer. There are no social stressors with the exception of being new parents. The mother does state that the infant's spitting up is somewhat troubling to them because of the amount of laundry that is being dirtied and the fact that the infant often spits up on people when they hold her.

Physical Exam

VS: Afebrile, HR 132, RR 28, Lt. 60 cm (25th%), Wt. 5.8 kg (25th%), weight:length ratio is 50th percentile, weight at 2 month visit was 4.5 kg (25th%), OFC 40 cm (25th%)

General: well nourished, well hydrated, happy appearing infant

HEENT: pupils equal, red reflex present bilaterally, TMs clear bilaterally, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses, brisk capillary refill

Resp: clear breath sounds bilaterally, no distress

Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses

GU: normal external female genitalia

Extremities: no clubbing, cyanosis, or edema

Musculoskeletal: moves all extremities well, normal muscle tone

Neuro: DTRs noted to be normal and symmetrical

Skin: no rashes or lesions noted

Rectal: anus in normal position, perineum normal to inspection

The history and physical examination suggest that this patient has

A acute gastroenteritis
B uncomplicated gastroesophageal reflux
C gastroesophageal reflux disease
D a gastric outlet obstruction

Please answer the following with TRUE or FALSE

T or F Infantile GER is most prevalent in infants over 6 months of age.
T or F Infantile GER is primarily caused by the abnormally low resting tone of the lower esophageal sphincter (LES) during infancy.

The next step in the management of this patient would be to

A start the patient on ranitidine (zantac) at 3 mg/kg/day divided TID
B obtain a barium upper GI series
C perform a continuous 24-hour esophageal pH probe study
D reassure the parents

Which of the following in a infant with recurrent vomiting suggest GERD?

A poor weight gain
B feeding aversion or excessive irritability
C apnea or reactive airway disease
D a and b only
E all of the above

Solutions and explanations:

1)) B, This patient has a classic presentation for uncomplicated infantile gastroesophageal reflux (GER), which manifests as effortless, painless "vomiting" in a well appearing infant. These patients are often referred to as "happy spitters". GER is defined as the passage of gastric contents into the esophagus. Regurgitation is defined as the passage of refluxed gastric contents into the oral pharynx. Vomiting can be defined in a number of ways: some define vomiting as the expulsion of regurgitated gastric contents out of the mouth; others consider vomiting a more complex behavior consisting of nausea, retching, and complete expulsion of stomach contents. Therefore it is debated if the "vomiting" seen in infantile GER should be considered vomiting at all.

* Gastroesophageal reflux disease (GERD) is defined as GER which produces symptoms or complications. The only symptom that this patient is having is "vomiting" or "spitting up" which alone is usually not considered sufficient to diagnose GERD in an infant under 1 year of age.

* Acute gastroenteritis can cause vomiting but is usually accompanied by diarrhea with or without fever. Patients with acute gastroenteritis often present with anorexia, more frequent episodes of vomiting, and signs of dehydration. It is usually the result of a viral infection, rotavirus being a common etiology in this age group. The patient described in the vignette has a chronic problem with vomiting rather than an acute one.

* A gastric outlet obstruction can present with recurrent vomiting but there are no "red flags" such as poor weight gain or dehydration that would make you suspect that in this patient.

2)) false, Studies have shown that regurgitation at least one time per day occurs in about 50% of infants under 3 months of age. The prevalence peaks at 67% at 4 months of age, decreases to about 20% at 7 months of age and to about 5% at one year. Infants with at least 4 episodes of regurgitation per day showed a similar pattern. The prevalence was about 25% at 5 months, about 5% at 7 months, and about 1% at one year. Children whose vomiting is not improving by 12 months of age or is not resolved by 18-24 months of age should have a barium upper GI series to rule out an anatomic abnormality and be referred to a pediatric gastroenterologist for further work-up.

* False, This was long suspected to be the cause of infantile GER but this has not been supported by manometric studies that show LES pressures in infants to be similar to those in older children and adults. Transient lower esophageal sphincter relaxations (TLESRs) are believed to be the cause of most reflux episodes in infants as well as older children and adults. TLESRs are a normal physiologic process which allows the stomach to decompress (belching), but excessive or inappropriate TLESRs are seen infants with GER. Over distension of the stomach, among other things, induces TLESRs. The patient described in the vignette is being overfed and this is probably contributing to her reflux. There are also some anatomic variations in infants that may explain why they have "inappropriate" TLESRs. First the LES in infants is very short, perhaps less than 1 cm. In adults, the LES ranges from 3-6 cm. Also the LES in infants is located more superiorly than in adults and is subjected to negative intrathoracic pressure during inspiration. The pressure gradient of the abdomen (positive pressure) and the thoracic cavity (negative pressure) play a role in the reflux of gastric contents. The LES lengthens and moves more inferiorly during the first year of life. This probably influences the natural history of infantile GER.

3)) D, A thorough history and physical examination with attention to warning signals is generally sufficient to establish the diagonosis of uncomplicated GER. In a patient with uncomplicated infantile GER, parental education, reassurance, and anticipatory guidance is the recommended plan.* Also certain "conservative measures" can be instituted in order to decrease the volume of regurgitation. Click here to see these treatment strategies. *Parental education is accomplished by explaining the pathophysiology of GER as well as explaining the conservative treatment options. Reassurance can be accomplished by showing the parents their child's normal growth pattern and describing the warning signals that are absent in their child. Anticipatory guidance is given by explaining the natural history of infantile GER and sharing with them the decreasing prevalence which comes with increasing age.

* If there is concern for acid-related esophagitis, such as a patient with GER and excessive irritability or feeding aversion, continuous pH monitoring is a reasonable diagnostic choice.

* if there are signs of gastrointestinal obstruction or other "red flags" do upper GI series

4)) E, All of these are sufficient to change the diagnosis from GER to GERD. Some other symptoms seen in infants with GERD are back arching during feeds, disturbed sleep, hematemesis, chronic cough, and recurrent pneumonia. Patients with GERD should first be treated with the conservative strategies used for patients with uncomplicated GER. If symptoms persist, further work-up and/or therapy should be initiated. Patients with hematemesis should have a barium UGI and be referred to a pediatric gastroenterologist for further evaluation.

Q2: A 4-week-old male infant presents to your office with a 2 week history of vomiting. The parents report that the vomiting began at about 2 weeks of age when he would "spit up" after each meal. Initially the vomiting was effortless and didn't seem to bother him. However, over the next few days the vomiting became more forceful and the infant became very irritable. The parents report that the infant now has a large amount of emesis after each feeding and that sometimes he has multiple episodes of vomiting with each feeding. They report that often after he vomits he seems very hungry and will take another bottle, only to again vomit. Review of systems reveals that he is only having about 2 wet diapers per day. He was having about 8 wet diapers per day a few weeks ago.

The patient was born at 40 weeks gestation after an uncomplicated pregnancy and delivery. His birth weight was 8 pounds, 10 ounces (3.9 kg). He has no other health problems. He has not been hospitalized; however the parents did take him to the emergency room about 10 days ago because of the vomiting. They were told that his exam was normal and were instructed to avoid overfeeding. He has had no surgeries except for circumcision.

The parents are both healthy. The maternal grandmother had her gallbladder removed because of gall stones. Otherwise there is no family history of any GI, liver, or metabolic diseases.

The patient lives with his parents who are both college students. The father is working part-time as a waiter. They have a cat and a dog. They receive city water but they use bottled water to prepare the formula. The father occasionally smokes but only outside.

The patient is taking 3-4 ounces of Enfamil formula every 3 hours. As previously mentioned, occasionally after vomiting he will act as if he is hungry and another bottle is offered. He usually drinks this vigorously but then has emesis again.

Physical Exam

VS: Afebrile, HR 172, RR 38, Lt. 55 cm (50th%), Wt. 3.8 kg (25th%), weight:length ratio is 3rd percentile, OFC 38 cm (50th%)

General: thin, irritable infant, has a large non-bilious emesis within minutes of finishing bottle

HEENT: pupils equal, red reflex present bilaterally, TMs clear bilaterally, oropharynx clear, mucous membranes somewhat dry

Neck: supple without lymphadenopathy or thyromegaly
CV: tachycardic, no obvious murmur noted, good pulses, capillary refill 3 seconds
Resp: clear breath sounds bilaterally, no distress
Abd: soft, no hepatosplenomegaly, no obvious focal tenderness or palpable masses but patient crying during entire exam
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: moves all extremities well
Neuro: DTRs noted to be normal and symmetrical
Skin: no rashes or lesions noted
Rectal: anus in normal position, perineum normal to inspection

The next step in the management of this infant would be to

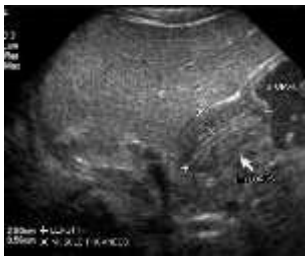
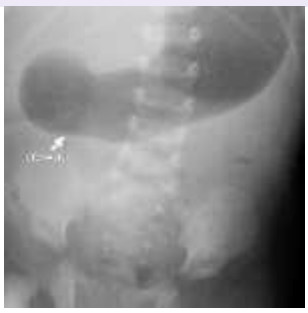
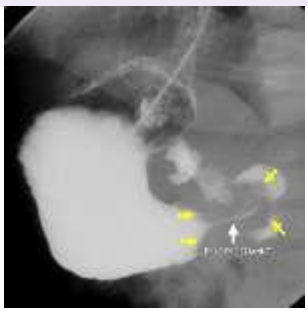
A admit the patient for IV hydration and further evaluation
B schedule an abdominal ultrasound for the following day
C schedule a barium upper GI series for the following day
D start the patient on pedialyte and reassure the parents

The most likely diagnosis in this patient is

A malrotation with volvulus
B pyloric stenosis
C acute gastroenteritits
D uncomplicated GER

Which imaging study can be used to establish the diagnosis?

A barium upper GI series
B ultrasound
C either a or b
D neither a nor b

Please answer the following with TRUE or FALSE

T or F Pyloric stenosis equally affects males and females.
T or F First degree relatives of someone with pyloric stenosis have increased risk of having pyloric stenosis.
T or F This patient should be taken to surgery immediately.

Labs:
CBC: WBC 11.2 , Hgb 12.3, Hct 37.9, Plts 335

BMP: Na 136, K 3.6, Cl 88, Bicarb 38, BUN 28, Cr 0.6, Glucose 78, Ca 9.2

UA: unremarkable for signs of infection, specific gravity 1.025

Solutions and explanations:

1)) A, The first step in managing this 4 week old infant who is dehydrated and below birth weight is rehydration. The history of decreased urine output suggests dehydration, and the physical exam findings of dry mucous membranes and tachycardia in the absence of fever further support this diagnosis. Screening labs such as a CBC to look for signs of infection and a basic metabolic panel to look for electrolyte imbalance would also be reasonable in this patient. A urinalysis should also be obtained to look for signs of urinary tract infection. A UTI can present with vomiting in an infant.

2)) B, This patient probably has pyloric stenosis. Pyloric stenosis usually presents with vomiting that begins in the second or third week of life. The vomiting is non-bilious, as the obstruction is a gastric outlet obstruction (proximal to the Ampulla of Vater). The vomiting is usually described as becoming more forceful to the point of being called "projectile vomiting". Parents often report that the patient is very hungry and this is because very little nutrition is able to pass the hypertrophied pyloris and the child is in a sense "starving". The physical exam finding of the "olive sign" is virtually diagnostic of pyloric stenosis. The "olive sign" is a small, firm, movable mass about the size and shape of an olive that can be palpated in the midline or just to the right of midline in the right upper quadrant. This "olive" is actually the hypertrophied pyloris muscle but is often difficult to palpate especially in an irritable child. Laboratory work often shows a hypochloremic metabolic alkalosis (remember you lose HCl, which is acid and chloride, from the stomach).

* Malrotation with volvulus is a surgical emergency that usually presents with bilious emesis, anorexia, and the passage of blood-tinged mucus per rectum. Bilious emesis occurs in conditions in which there is an obstruction distal to the Ampulla of Vater (where bile enters the intestinal tract).
* The two week history makes acute gastroenteritis less likely. Also patients with gastroenteritis often present with anorexia, and this patient acts as if he is very hungry.

3)) C, Both barium UGI series and a pyloric ultrasound are reliable tests to establish or rule out the diagnosis of pyloric stenosis. The pyloric ultrasound is probably used more often now because it is quick and easy to perform and there are objective parameters for making the diagnosis. A pyloric channel length of >16 mm or pyloric muscle thickness of >4 mm is highly suggestive of pyloric stenosis. Go on to the next page to see the results of these imaging studies.

4)) false, males are affected 5 times more

* true, Siblings and offspring of affected individuals are at increased risk. The highest risk is in a first-born male of a mother who herself had pyloric stenosis (about 20% risk).
* false, Pyloric stenosis is not a surgical emergency. If dehydration and metabolic alkalosis are present, they must be corrected first and surgery delayed for 24-48 hours. Pyloromyotomy is the operative procedure of choice.

Q3: History: A 12-year-old male presents to your office with a complaint of chest pain. He reports that for the past few weeks that he has been having daily episodes of discomfort in his chest and upper abdomen. He describes the discomfort as a burning pain that usually lasts for 10-20 minutes. He often wakes up in the night with pain, and he states that he has vomited on a few occasions during the night. He states that he also regurgitates sour-tasting material into his mouth. The mother states that she has given him over-the-counter antacids, and the child states that this sometimes makes him feel better. He passes stool once daily to once every other day without difficulty. He denies any other symptoms at this time.

The patient was born at 36 weeks gestation via a vaginal delivery. Birth weight was 6 lbs. He was hospitalized at 1 year of age for dehydration for one night. He had a tonsillectomy and adenoidectomy at 8 years of age for obstructive sleep apnea. He has had no other chronic health problems.

The mother states that there are many "stomach problems" in her family. The paternal grandfather has been diagnosed with GERD and told that he had an "ulcer" by his primary care doctor. An uncle also has GERD. The mother reports that she had "heartburn" when she was pregnant with all three of her children. Both the mother and the father are morbidly obese. There is a history of irritable bowel syndrome in the paternal grandmother and a paternal aunt.

The patient lives with his parents and two younger sisters. Mom and dad both smoke in the home. They receive city water and have 2 outside dogs. The mother denies any social stressors at home. The patient makes mainly As and Bs at school.

The mother reports that he has a very good appetite although it has been slightly decreased over the past two weeks. The patient reports that he eats three meals and one or two snacks per day, but the mother says that he snacks "all the time". He reports that his favorite food is "Taco Bell". He drinks about 3 or 4 sodas per day.

Physical Exam

VS: Afebrile, HR 85, RR 10, Ht. 155 cm (75th%), Wt. 65 kg (>97th%), BMI 27 kg/m2 (>97th%)

General: obese, no acute distress

HEENT: pupils equal, fundoscopic exam benign, TMs clear bilaterally, oropharynx clear

Neck: supple without lymphadenopathy or thyromegaly

CV: normal heart sounds, good pulses

Resp: clear breath sounds bilaterally, no distress

Abd: obese, non-tender, no hepatosplenomegaly, no palpable masses
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: good strength and muscle tone, no tenderness to chest wall or sternal palpation
Neuro: DTRs noted to be normal and symmetrical
Skin: no rashes or lesions noted
Rectal: no perianal disease, good sphincter tone, formed stool in rectal vault, hemoccult negative

This patient most likely has

A irritable bowel syndrome
B acute pancreatitis
C GERD
D costochondritis

This patient should initially be treated with

A Education and lifestyle changes
B H2 receptor antagonist or proton pump inhibitor for 2-4 weeks
C H2 receptor antagonist or proton pump inhibitor for 2-4 months
D a and b only
E a and c only

Please answer the following with TRUE or FALSE

T or F This patient should be instructed to lose weight.
T or F Fatty foods can increase GER.
T or F Evidence suggests that second hand tobacco smoke increases GER.
T or F Right side down positioning is thought to decrease GER.

Solutions and explanations:

1)) C, This patient's pain is most likely caused by gastroesophageal reflux. The symptoms presented here are classic for "heartburn" caused by GER. Older children and adolescents often present with similar symptoms to adults, whereas younger children may present with atypical symptoms such as abdominal pain, poor appetite, and frank vomiting.

* Costochondritis is a relatively common cause of chest pain in children and adolescents. It should be ruled out in any child who presents with chest pain. It presents with pain that is exacerbated by palpation of the chest wall and sternum. It is caused by inflammation of the joint between the ribs and sternal cartilage and is best treated with rest and anti-inflammatory medication such as NSAIDS.

2)) D, The treatment in a child such as this should include both lifestyle changes and a 2-4 week trial of empiric acid suppression therapy. If no improvement is seen, referral to a pediatric gastroenterologist is warranted for further evaluation.* If the child improves, the therapy can be continued for a finite period of time, usually 2-4 months. If symptoms recur as medical therapy is discontinued, a referral to a pediatric gastroenterologist is again warranted. If the patient does

not relapse upon discontinuation of the medical therapy, observation is all that is needed.

3)) true

* true, Fatty meals slow gastric emptying and may make GER worse. There are a number of other foods that should also be avoided because they are thought to increase GER. They are caffeine, chocolate, spicy foods, peppermint, tomato based foods, and colas. For older children and adults, alcohol will also increase GER and should be avoided.
* true, Tobacco smoke exposure is thought to increase TLESRs and as a result GER. Cigarette smoking should be discouraged in patients with GER and family members of patients with GER.
* false, Studies in adults have shown that reflux occurs less often in the left side down position than in the right side down position. It is also helpful to elevate the head of the bed 30 degrees when lying down. These positional advantages are probably because the esophago-gastric junction is located on the superior-medial aspect of the stomach. Finally it should be recommended that patients avoid eating 2-3 hours prior to going to bed so that the stomach has a chance to empty prior to lying down.

Pyloric stenosis

Epidemiology:

- Males are affected five times more frequently than girls.
- Siblings and offspring of affected individuals are at increased risk. The highest risk is in a first-born male of a mother who herself had pyloric stenosis (about 20% risk).

History & physical exam:

- It usually presents with vomiting that begins in the second or third week of life. The vomiting is non-bilious. The vomiting is usually described as becoming more forceful to the point of being called "projectile vomiting".
- Parents often report that the patient is very hungry and this is because very little nutrition is able to pass the hypertrophied pyloris.
- "Olive sign" is virtually diagnostic of pyloric stenosis. The "olive sign" is a small, firm, movable mass about the size and shape of an olive that can be palpated in the midline or just to the right of midline in the right upper quadrant. This "olive" is actually the hypertrophied pyloris muscle but is often difficult to palpate especially in an irritable child.

Diagnosis:

- Laboratory work often shows a hypochloremic metabolic alkalosis.
- Both barium upper GI series and a pyloric ultrasound are reliable tests to establish or rule out the diagnosis of pyloric stenosis.
- The pyloric ultrasound is probably used more often now because it is quick and easy to perform and there are objective parameters for making the diagnosis. A pyloric channel length of >16 mm or pyloric muscle thickness of >4 mm is highly suggestive.

Treatment:

- It is not a surgical emergency.
- If dehydration and metabolic alkalosis are present, they must be corrected first.
- Surgery is delayed for 24-48 hours. Pyloromyotomy is the operative procedure of choice.

Liver diseases

Bilirubin measurements:

The most accurate way to measure bilirubin fractions is by measuring the total bilirubin, the unconjugated bilirubin (UB), and the conjugated bilirubin (CB). Often CB+UB does not equal the total bilirubin measured. This difference is referred to as delta bilirubin or the delta fraction [total – (CB+UB)]. Delta bilirubin is actually conjugated bilirubin that is covalently bound to albumin and is therefore not measured as conjugated bilirubin.

Unconjugated hyperbilirubinemia:

Red blood cells in the body are constantly being broken down. This results in a load of unconjugated bilirubin that must be conjugated by the liver in order to be excreted in bile. Unconjugated hyperbilirubinemia results when the body's bilirubin load exceeds the liver's conjugating ability. This may be caused by decreased conjugating ability, increased bilirubin load, or a combination of the two.

Most cases of jaundice are benign unconjugated hyperbilirubinemia. The followings are the main types:

- **Physiologic jaundice of infancy:** results from a physiologic decreased activity of the liver's conjugating enzyme, glucuronyl transferase. Jaundice begins after 24 hours of age, peaks by 3-5 days of life and 5-7 days in preterm. Usually resolves by 1-2 weeks of life and 3-4 weeks in preterm.
- **Breast feeding jaundice** (or breast milk jaundice type I): occurs in the first week of life and is thought to be related to the decreased fluid intake by the infant that occurs prior to adequate milk supply by the mother.
- **Breast milk jaundice** (or breast milk jaundice type II): occurs after the first week of life and the cause is unclear. It has been proposed that there is an unidentified component of breast milk that decreases glucuronyl transferase activity.
- **Hemolytic disease:** this may occur as early as the first day of life. There are a number of causes including ABO incompatibility, red cell membrane defects, and red cell enzyme defects. These conditions result in an increased bilirubin load.
- **Cephalohematoma:** breakdown of the red blood cells as a cephalohematoma resolves results in an increase in bilirubin load. This usually resolves by 1-2 weeks of age. This can also occur with large bruises.
- **Crigler-Najjar Syndrome (types I and II)**: This rare disorder results from a gene defect which causes either absent (type I) or severely decreased levels (type II) of glucuronyl transferase. Patients with type II Crigler-Najjar

syndrome do respond to treatment with phenobarbital. Type I is AR, and type II is AD.

- **Gilbert's Syndrome:** It is characterized by mild, intermittent elevations in unconjugated bilirubin. This often occurs at times of mild illness or fasting and is thought to be caused by decreased glucuronyl transferase activity. The total bilirubin level is usually less than 6 mg/dl and is all unconjugated. Transaminases and alkaline phosphatase are normal, although they can be mildly elevated because of the precipitating illness. The diagnosis can be made by the typical history, a normal physical exam, and laboratory findings described above. Reassurance is all that is necessary. Unlike above causes of unconjugated hyperbilirubinemia, Gilbert can present at any pediatric age.

Cholestasis:

- It is defined as reduction of bile formation or flow and normally manifests as conjugated hyperbilirubinemia. That is why it is important to obtain bilirubin fractions and not just a total bilirubin level.
- By laboratory criteria, it is defined as a direct (or conjugated) bilirubin that is greater than 20% of the total measured bilirubin.
- A urinalysis would show conjugated bilirubin present in the urine which is the cause of dark color of urine in these patients. It will be positive in most patients with a conjugated bilirubin > 1 and all patients with a conjugated bilirubin > 2. Patients with unconjugated hyperbilirubinemia will not have bilirubin detected on urinalysis.
- It is recommended that neonates noted to be jaundiced at 2 weeks of age be evaluated for cholestasis. The exception to this is the breast-fed neonate who has otherwise normal history and physical exam and has a family that can be relied upon for close follow-up. In this situation the infant can be reevaluated at 3 weeks of age and, if jaundice persists, be evaluated for cholestasis.

- Cholestatic jaundice is an uncommon cause of neonatal jaundice (1 in 2500 live births), but the serious consequences of misdiagnosis in these patients make ruling it out essential.
- All patients with neonatal cholestasis need supportive treatment: vitamins ADEK and formula containing MCTs.

Causes of neonatal cholestasis:

- Most common causes (75% of all cases):
    1. Biliary atresia (the most common).
    2. Idiopathic neonatal hepatitis
    3. Alpha 1-antitrypsin deficiency

- Causes treatable without surgery:

Cause	Treatment
Hypothyroidism/panhypopituitarism	Hormone supplementation
Galactosemia	Avoidance of lactose
Fructosemia	Avoidance of fructose & sucrose
Tyrosinemia (should be suspected in infants with severe coagulopathy or other signs of hepatic insufficiency).	A medication called NTBC
Bile acid synthesis defects	Bile acid supplementation
UTI & sepsis	Antibiotics
TPN associated cholestasis	Advancement of enteral feedings

- Causes which require surgical intervention: biliary atresia/ choledochal cyst/ choledocholithiasis/ spontaneous perforation of bile duct.
- Other causes: Alagille syndrome/ Cystic fibrosis.

Biliary atresia:

- Earlier diagnosis and surgical intervention, specifically before 2 months of age, are associated with better outcome.
- **Pathogenesis:** progressive fibrous obliteration of the bile ducts. Although there has been a fetal form described, most cases are thought to result from an insult that occurs either late in gestation or in the early post-natal period.
- **History:** usually born at term with normal birth weight/ usually feeding and growing well at time of presentation/ most patients are well-appearing except for jaundice/ may have dark urine and/or acholic (light-colored) stools.
- **Physical exam:** liver is usually enlarged (especially later in disease) and may be firm/ splenomegaly may be present as a result of portal hypertension/ hepatic insufficiency is usually late finding (after 3-6 month of age).
- **Labs:** ↑ total bilirubin (usually 6-12 mg/dl), ↑ conjugated bilirubin (50-80% of total bilirubin), ↑ alkaline phosphatase, ↑ GGT, ALT and AST may be normal or elevated.
- **Imaging:**
  - ✓ U/S: absent or small, atretic gallbladder is usually seen; however presence of normal appearing gallbladder does not totally exclude biliary atresia.
  - ✓ Nuclear scintigraphy (DISIDA scan): no excretion of radioisotope into the duodenum.
  - ✓ Intraoperative cholangiogram: obstruction to flow is seen. This is the gold standard.

- **Histology:** liver biopsy shows bile duct proliferation, inflammation, and evidence of bile stasis. If the liver biopsy and other data are suggestive of biliary atresia, laparotomy and intraoperative cholangiogram should be performed.

- **Surgical intervention:** Kasai procedure (hepatoportoenterostomy).
  - ✓ Kasai procedure is successful in establishing bile flow in about 80% of patients if done before 2 months of age, about 40% of patients 2-3 months of age, and about 20% of patients after 3 month of age so timely diagnosis is essential.
  - ✓ Even if it is successful, the majority of patients will require liver transplantation at some point in their lifetime.
  - ✓ Risk of ascending cholangitis.

Idiopathic neonatal hepatitis

- Accounts for about 20-30% of cases of neonatal cholestasis and is a diagnosis of exclusion**.**
- The most prominent histologic finding on liver biopsy is giant-cell transformation in which adjacent hepatocytes fuse together and form multinucleated giant cells with four or more nuclei. However, it is not specific to idiopathic neonatal hepatitis but simply represents a nonspecific response by the neonatal liver to injury.
- Bile duct proliferation is usually not seen. This can be helpful in distinguishing neonatal hepatitis from biliary atresia.

Alpha-1 antitrypsin deficiency

- It is the most common metabolic cause of neonatal cholestasis accounting for 5-15 % of cases.
- It is non-infectious cause of chronic liver disease.
- Most of patients present in infancy with neonatal cholestasis. However, it can present in late childhood or early adolescence with unexplained liver disease that may include chronic hepatitis, cirrhosis, and/or portal hypertension.
- Some of patients may have a history of unexplained prolonged jaundice in the neonatal period.
- Family history of emphysema in the third or fourth decade of life should raise your suspicion for alpha 1-antitrypsin deficiency.
- Physical examination in older children may show jaundice and hepatomegaly with or without splenomegaly. There are no characteristic exam findings.

- Labs: Older children who present with chronic hepatitis usually have elevated transaminases and may have mild elevations in bilirubin, alkaline phosphatase, or GGT. Screening labs that should be checked are serum alpha 1-antitrypsin level and alpha 1-antitrypsin phenotype. Phenotyping is recommended because alpha 1-antitrypsin is an acute phase reactant and may be falsely normal if infection or inflammation is present.

- Pathogenesis: Lung disease in alpha 1-antitrypsin deficiency is cause by decreased inhibition of neutrophil elastase with resultant panacinar emphysema. The pathophysiology of liver disease in these patients is not as clear. Alpha 1-antitrypsin is a protein that is primarily produced in hepatocytes. The genetic defect that causes alpha 1-antitrypsin deficiency results in an abnormal protein that is unable to be excreted from hepatocytes. Liver disease is thought to be caused by the hepatotoxic effects of the retained abnormal alpha 1-antitrypsin proteins.
- Treatment: it is mainly supportive as there is currently no medical therapy. These patients must be monitored closely for signs of portal hypertension and end-stage liver disease. Liver transplantation has been used successfully in patients with severe liver disease. All patients should be advised to avoid cigarette smoking because it greatly increases the risk of emphysema.

Alagille syndrome

- 3-5% of patients with neonatal cholestasis.
- It is characterized by paucity (decreased number) of bile ducts on liver biopsy, cardiac lesions (most commonly peripheral pulmonic stenosis), vertebral anomalies (butterfly vertebrae), and unusual facies - triangular faces- (broad forehead, deep-set eyes, hypertolerism and pointed chin).
- It is important to distinguish Alagille syndrome from biliary atresia because Kasai procedure in these patients is unnecessary and may actually increase mortality.

Galactosemia

- Only accounts for about 1% of patients with neonatal cholestasis, but should be ruled out since it is treatable.
- It is part of the newborn screen in Jordan and U.S
- Patients often appear ill with vomiting and diarrhea beginning shortly after the initiation of feeding of breast milk or lactose-containing formulas. On exam they have hepatomegaly and may have cataracts.
- It has been associated with E. coli sepsis.
- Labs: RBC galactose – 1 phosphate uridyltransferase.

Choledochal cyst

- It is a cystic dilation of the extrahepatic and/or intrahepatic biliary tree which can cause obstruction to bile flow. It can be diagnosed by U/S.

Evaluation of neonatal cholestasis

- The priority in evaluating any patient with neonatal cholestasis is to rule out biliary atresia in a timely manner. If biliary atresia can't be ruled out by lab work-up or the diagnosis is still unclear, a liver biopsy will be performed. If the histology suggests biliary atresia, a surgeon will perform an intraoperative cholangiogram. If the biliary tree is not patent, a Kasai procedure will be performed.
- If no diagnosis is made with lab work-up and biopsy, the patient will most likely be diagnosed with idiopathic neonatal cholestasis.

Red flags in jaundiced infant:

- History: dark urine/ acholic stools/ irritability/ vomiting/ poor intrauterine growth.
- Physical Exam: hepatomegaly/ splenomegaly/ acholic stools/ dark urine or bilirubin present on urinalysis/ heart murmur or other signs of cardiac disease/ abnormal facies/ microcephaly/ large anterior fontanelle/ cataracts.

Laboratory Tests in Patients with Liver Disease

ALT and AST: These enzymes, often called transaminases or aminotransferases, are markers for liver parenchymal disease. They actually do not tell you about liver function, but they are markers for hepatocellular injury or hepatocellular destruction. ALT is a more specific test for liver disease as AST can be elevated in a variety of other conditions besides liver disease.

Alkaline Phosphatase: An elevated alkaline phosphatase is usually indicative of biliary tract disease or obstruction. However, alkaline phosphatase is not specific for liver or biliary tract disease and may be elevated in a number of other conditions such as bone disease and intestinal ulceration or perforation. There is a condition called benign transient hyperphosphatasemia of childhood in which a marked elevation of alkaline phosphatase is seen (usually in the 1,000-10,000 range but can be even higher) without other evidence of bone or liver disease. This usually returns to baseline in 2-4 months without intervention.

Gamma Glutamyl Transpeptidase: GGT is similar to alkaline phosphatase in that elevation is usually indicative of biliary tract disease or obstruction. GGT is not found in bone and is a good test to differentiate liver disease from bone disease in patients with elevated alkaline phosphatase.

Bilirubin: The bilirubin is elevated in patients with cholestasis or biliary obstruction. The bilirubin level may also be increased in patients with hepatocellular destruction, such as a patient with acute hepatitis. In patients with end-stage liver disease or acute hepatic dysfunction, the bilirubin level can be used to assess the excretory function of the liver. A rising bilirubin in these patients is worrisome for impending hepatic failure.

Laboratory findings in patients with liver or biliary tract disease can be divided into two patterns:

hepatocellular injury: primarily manifests as elevations in ALT and AST with or without elevation in bilirubin
cholestatic or obstructive injury: primarily manifests as elevations in alkaline phosphatase, GGT, and bilirubin
In the real world, the two patterns are not always so clearly defined. Hepatocellular injury can result in reduced bile flow and, as a result, mild elevations in alkaline phosphatase and GGT. Also, obstructive injury often results in mild elevations in transaminases due to the noxious effect of bile on the hepatocyte. However, it is often possible to differentiate hepatocellular injury from obstructive injury by looking at the magnitude of elevation of the different enzymes.

Often people refer to transaminases as "liver function tests". These tests are measures of hepatocellular injury, not necessarily tests of hepatic function. Better tests to evaluate the function of the liver are albumin, PT, and ammonia.

Albumin: Serum albumin can be a marker for synthetic function of the liver. This can be affected by many other conditions such as malnutrition and conditions with protein loss like nephrotic syndrome. However in a patient with end-stage liver disease or acute hepatic dysfunction, the albumin can be indicative of the liver's ability to synthesize proteins.

Prothrombin Time: The PT, like serum albumin, can be used as a marker for the liver's ability to synthesize proteins (clotting factors). It can be prolonged in other conditions such as vitamin K deficiency or DIC.

Ammonia: Ammonia is normally converted to urea in the liver. Elevated serum ammonia can be indicative of significant liver dysfunction. It is thought to be the cause of (or at least one of the causes of) hepatic encephalopathy. The serum ammonia level can be falsely elevated if the specimen is not placed on ice immediately after it is drawn or if it is not processed within 30-60 minutes of being drawn.

TESTYOURSELF:
A 17-day-old female presents to your office for her scheduled two week check up. Mom reports that she has been doing well overall and has been taking her formula well. She has been producing an adequate number of wet diapers; however, mom states that her urine seems to be darker in color during the last week. Mom reports that the baby has been having 6-8 stools per day and describes the color as pale yellow. Mom also remarks that the baby still appears to be jaundiced. The only other complaint today is that the baby is sleeping most of the day and then is awake during the night. The mom reports that they are getting very little sleep.

She was born at 39 weeks gestation after an uncomplicated pregnancy and delivery which was by repeat C-section. Her birth weight was 7 lbs. 8 oz. She spent 2 days in the newborn nursery and her course was unremarkable. She was noticed to have some scleral icterus and jaundice to the face on the day of discharge. They have been using indirect sunlight exposure 2-3 times per day for the jaundice.
The mother has a history of gallstones and had her gall bladder removed 5 years ago. She also has a history of lactose intolerance. The father has a history of asthma and seasonal allergies. The maternal grandmother has a history of irritable bowel syndrome and the paternal grandfather has a history of acid reflux. There are no other gastrointestinal, liver, or metabolic diseases in the family.
The patient lives in a house with her parents and two older brothers aged 12 and The mother is 38 years old and is a homemaker and the father is 40 years old and works in real estate. They use city water and there are no smokers in the home. They have one outside dog.
The patient is taking 2-3 ounces of Similac formula every 2-4 hours. She does spit up on occasion but mother reports it to be no more than her other two kids and is not concerned.
Physical Exam
VS: Afebrile, HR 142, RR 38, Lt. 50 cm (25th%), Wt. 3.5 kg (50th%), weight:length ratio is 50th percentile, OFC 35 cm (50th%)
General: well nourished, well hydrated, happy appearing infant
HEENT: pupils equal, red reflex present bilaterally, icteric sclera, TMs clear bilaterally, oropharynx clear
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses, brisk capillary refill
Resp: clear breath sounds bilaterally, no distress
Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses
GU: normal external female genitalia
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: moves all extremities well, normal muscle tone

Neuro: DTRs noted to be normal and symmetrical
Skin: jaundice to face and chest, no rashes or lesions noted
Rectal: anus in normal position, perineum normal to inspection, small amount of stool in the diaper that is very light yellow in color

The next step in managing this child would be to

A obtain a total bilirubin level to see if the patient needs phototherapy
B have the child return in 2 weeks if the jaundice is still present
C obtain fractionated bilirubin levels
D reassure the mother

The dark color of the urine described in this patient is most likely caused by

A conjugated bilirubin in the urine
B unconjugated bilirubin in the urine
C blood in the urine
D dehydration

The most common cause of this patient's presentation is

A Hypothyroidism
B biliary atresia
C alpha 1-antitrypsin deficiency
D cystic fibrosis

Please answer the following with TRUE or FALSE

T or F Most infants with jaundice still present at two weeks of age have cholestasis.
T or F A urinary tract infection can cause cholestasis.
T or F A choledochal cyst can be diagnosed by ultrasound.

Cholestatic infants who do not have biliary atresia will most likely be diagnosed with

A Alagille syndrome
B galactosemia
C tyrosinemia
D idiopathic neonatal hepatitis

Bilirubin Measurements

The most accurate way to measure bilirubin fractions is by measuring the total bilirubin(TB), the unconjugated bilirubin(UB), and the conjugated bilirubin(CB). Often the unconjugated + conjugated bilirubin does not equal the total bilirubin measured. This difference is referred to as delta bilirubin or the delta fraction. Delta bilirubin is actually conjugated bilirubin that is covalently bound to albumin

and is therefore not measured as conjugated bilirubin. Now let's look at the results of the child in the vignette as an example:

TB = 9.0
UB = 3.2
CB = 4.8
The delta bilirubin, or delta fraction, in this example equals 1. This is calculated by the equation Delta = TB - (UB + CB) ; Delta = 9.0 - (3.2 + 4.

The other method of measuring bilirubin fractions is reporting the total bilirubin(TB) and the direct bilirubin(DB). This method is less accurate in measuring conjugated bilirubin in that the direct portion may contain conjugated as well as delta bilirubin.

Cholestasis by laboratory criteria has traditionally been defined as a direct (or conjugated) bilirubin that is greater than 20% of the total measured bilirubin. The child in the vignette does indeed have cholestatic jaundice as her conjugated bilirubin accounts for just over 50% of the total bilirubin. Once the diagnosis of cholestatic jaundice has been made, consultation with a pediatric gastroenterologist is indicated.

Solutions and explanations :
1)) C, it is recommended that infants noted to be jaundiced at 2 weeks of age be evaluated for cholestasis. The exception to this is the breast-fed infant who has a normal history and physical exam (except for jaundice) and has a family that can be relied upon for close follow-up. In this situation the infant can be reevaluated at 3 weeks of age and, if jaundice persists, be evaluated for cholestasis. Cholestatic jaundice is an uncommon cause of neonatal jaundice, but the serious consequences of misdiagnosis in these patients make ruling it out essential. The incidence of cholestatic jaundice is about 1 in 2500 live births. Cholestasis is defined as reduction of bile formation or flow and normally manifests as conjugated hyperbilirubinemia. That is why it important to obtain bilirubin fractions* and not just a total bilirubin level.
* With the amount of jaundice described, it is unlikely that this patient would require phototherapy. The clinical history of dark urine and light colored stools should make you want to evaluate this patient for cholestatic jaundice.
* it is recommended that infants noted to be jaundiced at 2 weeks of age be evaluated for cholestasis. The exception to this is the breast-fed infant who has a normal history and physical exam (except for jaundice) and has a family that can be relied upon for close follow-up. In this situation the infant can be reevaluated at 3 weeks of age and, if jaundice persists, be evaluated for cholestasis. This child is not breast-fed and, even if that were the case, there are warning signals that this patient has cholestatic jaundice.

2)) A, urinalysis obtained from this infant would show bilirubin present in the urine. Bilirubin detected on urinalysis is only detected in conjugated hyperbilirubinemia. It will be positive in most patients with a conjugated bilirubin > 1 and all patients with a conjugated bilirubin > 2. Patients with unconjugated hyperbilirubinemia will not have bilirubin detected on urinalysis. Therefore this finding should make you initiate a work-up for cholestatic jaundice.

3)) B, The most common cause of neonatal cholestasis is biliary atresia. It accounts for 25-40% of cases. Biliary atresia is the main reason that infants with persistent jaundice should be evaluated for cholestatic jaundice. There are many studies that show that earlier diagnosis and surgical intervention, specifically before 2 months of age, are associated with better outcome

4)) false, Most of these infants will have a benign condition which causes unconjugated hyperbilirubinemia.* Only a very small percentage of these patients (probably less than 1%) will have cholestasis (conjugated hyperbilirubinemia). However, the consequences of delaying the diagnosis of an infant with cholestasis make it imperative to obtain fractionated bilirubin levels.
* true, Urinary tract infections and sepsis are rare causes of neonatal cholestasis and thought to be related to bacterial endotoxin and its effect on bile flow. Therefore blood and urine cultures should be obtained in these patients. There is no data to support use of empiric antibiotics in infants with neonatal cholestasis and should probably be based on the clinical appearance of the child. In patients with a UTI or sepsis, treatment of the infection should result in resolution of the cholestasis.
* true, The main reason to obtain an ultrasound in a patient with cholestasis is to evaluate for obstructive lesions or anatomical defects of the biliary tree. Examples include a gall stone which obstructs bile flow and a choledochal cyst. A choledochal cyst is a cystic dilation of the extrahepatic and/or intrahepatic biliary tree. This can cause obstruction to bile flow and requires surgical management.

5)) d, idiopathic neonatal hepatitis accounts for about 20-30% of cases of neonatal cholestasis and is a diagnosis of exclusion. This diagnosis is made when other causes have been ruled out and characteristic findings on liver biopsy are seen. The most prominent histologic finding is giant-cell transformation in which adjacent hepatocytes fuse together and form multinucleated giant cells with four or more nuclei. However, giant cell transformation is not specific to idiopathic neonatal hepatitis but simply represents a nonspecific response by the neonatal liver to injury. Bile duct proliferation is usually not seen in idiopathic neonatal hepatitis. This can be helpful in distinguishing neonatal hepatitis from biliary atresia

Q2: History: A 13-year-old male presents to your office because of nausea, vomiting, mild abdominal pain, and jaundice. Mom reports that she first noticed the jaundice last night and it seems much more pronounced today. He was seen by you just three days prior to this visit for fever, headache, nausea, and malaise. He was diagnosed with a viral syndrome and treated with supportive care. His fever and headache have resolved

The patient was born full term after an uncomplicated pregnancy and delivery. He suffers from no chronic illnesses and takes no medications on a regular basis. He has taken Tylenol over the past 5 days because of headache and fever. He was taking one extra-strength tablet (500 mg) three to four times per day, but he has not had any in the last 24 hours.

The mother suffers from migraine headaches. The maternal grandmother had her gallbladder removed because of gallstones and also takes medication for depression. The maternal grandfather has hypertension and coronary artery disease. The paternal family history is unknown.

The patient lives with his mother and two younger half-siblings. His sister is 6 years old and his brother is 1 year old. The mom is 29 years old and works as a cashier at a grocery store. His younger brother attends daycare. There have been no sick contacts recently, although his brother was ill last month with vomiting and diarrhea. The patient's father is not involved in his life.

The mom reports that he is normally a very good eater. She states that he eats breakfast and lunch at school and that she cooks dinner at home most evenings. His appetite has been decreased over the past 4-5 days.

Physical Exam
VS: Afebrile, HR 86, RR 12, Ht. 151 cm (25th%), Wt. 46 kg (50th%), BMI 20 kg/m2 (75th%)
General: awake, alert, oriented, no acute distress
HEENT: scleral icterus present, pupils equal, fundoscopic exam benign, TMs clear bilaterally, oropharynx clear
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses
Resp: clear breath sounds bilaterally, no distress
Abd: soft, mildly tender to palpation in RUQ, liver edge palpable 3 cm below right costal margin, no splenomegaly, no palpable masses
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: good strength and muscle tone
Neuro: DTRs noted to be normal and symmetrical
Skin: jaundice noted, no rashes or other lesions

Rectal: no perianal disease, good sphincter tone, formed stool in rectal vault, hemoccult negative

CBC: unremarkable
Electrolytes: unremarkable
AST: 3100
ALT: 4400
Total bilirubin: 6.2
Conjugated bilirubin: 4.4
Alk Phos: 400
GGT: 60
Albumin: 3.9
PT: 12.8 (INR 1.0)

The above laboratory values are most consistent with

A hepatocellular injury
B bile duct perforation
C obstructive jaundice
D acute hepatic insufficiency

The test most likely to yield the diagnosis in this patient is

A an ammonia level
B a DISIDA scan
C a right upper quadrant ultrasound
D a hepatitis panel

Solutions and explanations:
1)) A, The marked elevation of the transaminases, elevation of bilirubin, normal alkaline phosphatase, and normal GGT suggest hepatocellular injury.

2)) D, This patient most likely has an acute viral hepatitis. Click here to see the results of this patient's hepatitis panel.
* right upper quadrant ultrasound is a reasonable test to order in a patient with hyperbilirubinemia in order to rule out obstructive lesions, but the hepatocellular pattern of injury in this patient make viral hepatitis more likely.
* DISIDA scan might show decreased uptake of contrast but this would not allow you to make the diagnosis.
* not ammonia level cos The patient has no mental status changes and normal hepatic function.

Acute Hepatitis

- It is a hepatocellular injury usually manifests as increased transaminases (usually 10 to 100 times the upper limit of normal) with some degree of hyperbilirubinemia. Alkaline phosphatase and GGT are both normal.
- Most cases of acute hepatitis are caused by viral infections; HAV, HBV, HCV, EBV, CMV, adenovirus, echovirus, Coxsackie virus, and herpes viruses.
- As most cases are caused by hepatitis A and B, a hepatitis screening panel should be obtained.
- EBV and CMV can be checked for using serologic tests. This can be done at the same time as the hepatitis panel or afterwards, if the hepatitis screen is negative.
- Hep A, CMV, EBV are self-limited.

Hepatitis A

- It usually affects older kids and adults more severely than young children. As young children are often anicteric, they may present with symptoms of a mild acute gastroenteritis.
- It is primarily spread via the fecal-oral route.
- It is usually a self-limited illness that resolves with only supportive therapy.
- Both passive and active immunizations are available.
- No chronic carrier state of hepatitis A has been identified.
- Fulminant hepatic failure may develop (give IV glucose).
- Infectivity period: about 2 weeks before to about 2 weeks after clinical symptoms appear.

Hepatitis B

- The risk of developing chronic infection depends on the age of 1ry infection (inversely related).
- About 90% of neonates with acute hepatitis B infection will go on to develop chronic hepatitis B. That is why maternal screening for hepatitis B is so important, and prophylaxis should be given to babies born to mothers with hepatitis B infection. Both HBIG and hepatitis B vaccine are recommended after delivery.
- All household members should take the vaccine and avoid patient's blood.
- Many patients with chronic infection are completely asymptomatic.
- Treatment of chronic hepatitis: INF-alpha and lamivudine.
- Increased risk of hepatocellular carcinoma in chronic infection. Screen with alpha-fetoprotein or ultrasound of liver.

- Hepatitis A vaccine is recommended for patients with chronic liver disease in order to prevent a second insult to the already affected liver.
- Serology:
  - ✓ HBsAg = acute or chronic infection.
  - ✓ Anti-HBs = protected (resolved infection or immunized).
  - ✓ Anti-HBc IgM = recent primary infection (4-6 months).
  - ✓ Anti-HBc IgG = remote primary infection (> 6 months).
  - ✓ HBeAg = replication or infectivity.

  To sum-up:
  - ✓ Acute infection = HBsAg and anti-HBc IgM
  - ✓ Chronic infection = HBsAg and anti-HBc IgG
  - ✓ Infection that has resolved = anti-HBs and anti-HBc IgG
  - ✓ Immunized = anti-HBs only

Hepatitis C

- The liver inflammation seen with an acute infection with hepatitis C is mild and most patients are asymptomatic.
- Vertical transmission is much less than that of hepatitis B. Only about 5-10% of infants born to mothers with hepatitis C become infected. Therefore no immunoprophylaxis is given.
- 60 to 80% of patients infected with hepatitis C develop chronic infection.
- Anti-HCV is not protective against HCV. It is just a screening test.
- No vaccine.
- Slowly progressive disease. Co-infection with hepatitis B, alcohol and obesity make disease progression worse.
- Association with hepatocellular carcinoma, but usually occurs after decades of infection.

Fulminant Hepatic Failure

Acute hepatic failure can result from a number of causes including infections, toxic ingestions, Wilson's disease, and a variety of metabolic disorders. Patients often present with encephalopathy and coagulopathy. Ammonia levels will be elevated and prothrombin time will be prolonged. Administration of parenteral vitamin K does not correct the coagulopathy (patients who have prolonged PT because of vitamin K deficiency will respond to parenteral vitamin K).

Remember that transaminases do not represent hepatic function. In hepatic failure the transaminases may be exceedingly high and trending even higher, or they may even be trending downward and falsely appear to be getting better. This downward trend is because of decreasing amounts of hepatic parenchyma to produce the enzymes. A lab pattern of transaminases that are "getting

better" (falling) and PT, bilirubin, and albumin that are getting worse is worrisome for hepatic failure.

There are a number of important things that must be done for a patient with hepatic failure.

Glucose must be provided to the patient in the IV fluids. This is important because mobilization of glucose from liver glycogen stores in the liver is affected in hepatic failure.
Attempts should be made to decrease ammonia levels. Lactulose is usually given to these patients at doses that produce 2-4 stools per day. Lactulose acts by acidifying the stools which then allows more ammonia to be bound and excreted in the stool.
If there are any signs of bleeding, attempts to correct the coagulopathy should be made. Often fresh frozen plasma is used to supply the patient with clotting factors.
The patient should be transferred as quickly as possible to a center that has the ability to perform liver transplantation .

Non-infectious causes of acute hepatitis:

1. Toxic ingestion (such as acetaminophen toxicity).
2. Medication induced (seizure meds, isoniazid, and antibiotics).
3. Ischemic (hypovolemic, septic or cardiogenic shock).
4. Autoimmune hepatitis.
5. Wilson's disease.
6. Alpha-1 antitrypsin deficiency. (it was discussed previously).

Acetaminophen toxicity

- It can be seen in both young children (usually accidental) and adolescents (usually non-accidental).
- It can progress to fulminant hepatic failure and death. Therefore it is very important to look at the medication list to see if any of the medications which they are taking are hepatotoxic.

Ischemic hepatopathy

- It is a relatively common situation seen in systemically ill patients.
- Hypotension, regardless of the cause, can cause decreased blood flow to the liver and result in hepatocyte damage.
- This usually manifests as increased transaminases shortly after the ischemic injury which rapidly decrease over the next few days following the event.
- The bilirubin level may also rise during the days following the ischemic event, and jaundice may be evident.
- The hyperbilirubinemia may take days to weeks to resolve. All of this occurs in the absence of other signs of liver dysfunction.
- No treatment is necessary.

Wilson disease

- It is a rare disorder of copper metabolism that occurs in about 1 in 30,000 individuals.
- It is caused by a genetic defect that results in the inability to excrete copper into bile. This results in excessive copper accumulation in the liver and, over time, in other organs in the body.
- It is an autosomal recessive disease. Screening is recommended so that presymptomatic patients can be identified and therapy can be initiated.
- It affects many organ systems in the body; the three most common are hepatic, central nervous system, and hematologic. Some patients present with involvement of just one organ system, and some present with more than one organ system involved.
- Hepatic system: asymptomatic hepatomegaly or elevated transaminases, acute hepatitis, chronic liver disease with portal hypertension, fulminant hepatic failure.
- CNS: poor school performance, behavioral or personality changes, decreased hand-eye coordination, tremor, depression, anxiety, psychosis.
- Hematologic: hemolytic anemia which is thought to be secondary to oxidative injury to red blood cells by excessive copper into the circulation.

- The "classic" presentation of cirrhosis, neurological manifestations, and Kayser-Fleischer rings is usually not seen in the pediatric population.
- Diagnosis: low ceruloplasmin and high urinary copper.
    - ✓ Ceruloplasmin acts as the major carrier of copper in blood, and patients with Wilson's disease can't incorporate copper into ceruloplasmin. This results in decreased levels of ceruloplasmin.
    - ✓ Normally copper is excreted from the body via bile and renal copper excretion is minimal. However patients with Wilson's disease are unable to excrete copper into bile. As a result, these patients have elevated urinary copper excretion.
- Kayser-Fleischer rings are not pathognomonic.
- Treatment:
    - ✓ First-line therapy is with chelators such as penicillamine or trientine. These drugs bind copper and allow it to be excreted from the body. Penicillamine was the first-line therapy for years, but many clinicians are now using trientine due to a better side effect profile.
    - ✓ Zinc for maintenance therapy. It works by blocking copper absorption from the GI tract.
    - ✓ Liver transplantation can be used but reserved for refractory cases or fulminant hepatic failure.
    - ✓ Treatment must be maintained lifelong. This point must be stressed to patients as non-compliance can result in hepatic decompensation and death.

Autoimmune hepatitis:

- Can present as acute hepatitis, chronic hepatitis, signs of portal hypertension or fulminant hepatic failure. Most patients present with either acute or chronic hepatitis. And the other presentations are seen only in a minority of patients.
- Patients with AIH who present as chronic hepatitis often present with intermittent jaundice and non-specific symptoms such as fatigue, anorexia, weight loss, and pruritus.
- Other autoimmune diseases are often present, either in the patient or in first degree relatives.
- Female to male ratio of about 3:1.
- The physical exam is often non-specific. They may present with jaundice, hepatomegaly, and vague right upper quadrant pain. Splenomegaly may also be noted if portal hypertension is present.
- Labs: elevated transaminases and bilirubin indicative of hepatocellular damage. The alkaline phosphatase and GGT are usually normal or only mildly

elevated. Screening labs that should be also checked include antinuclear antibody (ANA), smooth muscle antibody (SMA), liver/kidney microsomal type 1 antibody (LKM1) and total IgG.

- Pathogenesis: it is caused by autoimmune destruction of hepatic parenchyma by primarily T lymphocytes.
- Treatment: immunosuppressive agents like prednisone and/or azathioprine. Most patients require lifelong therapy.

Non-alcoholic steato-hepatitis NASH

- Risk factors: obesity and insulin resistance which is more important.
- Obesity, insulin resistance, hyperlipidemia and hypertension often cluster together and have been termed the "metabolic syndrome" or "syndrome X". Fatty infiltration of the liver is now often considered a part of this syndrome.
- Non-alcoholic fatty liver disease (NAFLD) is a term used to describe liver disease that resembles alcoholic steatohepatitis in patients who are not chronic alcohol users. It is characterized by fatty infiltration of the liver. When this fatty change is accompanied by inflammation, it is referred to (NASH).
- NASH is the most common hepatic disease in the United States.
- Most patients with NASH are asymptomatic with the exception of being obese.
- The ALT is usually higher than the AST at a ratio of 1.7:1.
- Weight loss is the mainstay of treatment. The weight reduction regimen should achieve gradual weight loss, and "starvation" diets should be avoided. In some pediatric patients, weight maintenance may be sufficient, as BMI will decrease as height increases.
- It can progress to cirrhosis and end-stage liver disease. Some patients with end-stage liver disease as a result of NASH require liver transplantation.

Drug-induced hepatitis:

- Many medications, even when used at normal doses, can cause hepatotoxixity.
- Although some may present with signs of acute toxicity such as abdominal pain and vomiting, often the only sign of hepatotoxicity is elevated liver enzymes.
- Anti-epileptics, antibiotics, anti-tuberculosis drugs, and chemotherapeutic agents are well known to cause hepatotoxicity.
- Discontinuation of the drug is recommended if a reasonable alternative drug is available.

Key points:

- Light stools or dark urine in an infant with jaundice are suggestive of cholestasis.
- Infants who are still jaundiced at two weeks of age should be screened for cholestasis. In breastfed infants, this can be delayed until three weeks of age.
- Screening for neonatal cholestasis can be accomplished by fractionating the bilirubin.
- Consultation with a pediatric gastroenterologist is warranted for infants with neonatal cholestasis.
- Biliary atresia, idiopathic neonatal hepatitis, and alpha 1-antitrypsin deficiency account for about 75% of all cases of neonatal cholestasis.
- Patients with biliary atresia have significantly better outcomes if diagnosed before two months of age.
- Acute hepatitis can result from a variety of causes including: infection, ischemia, toxic ingestion, medications, and metabolic disorders.
- When evaluating a patient with acute hepatitis, screening for infectious causes can be accomplished by sending a hepatitis panel as well as EBV and CMV serologies.
- Hepatitis A is a common cause of infectious hepatitis and may present with symptoms of an acute gastroenteritis or a flu-like illness.
- Supportive care is usually all that is needed for patients with hepatitis A infection.
- Patients with hepatic failure should receive adequate IV glucose and be transferred to a transplant center as quickly as possible.
- Chronic hepatitis can result from a variety of causes including: infection, medications, NASH, autoimmune disorders, and metabolic disorders.
- Hepatitis B and C are more prevalent in children adopted from other countries, and screening in these countries is often not done or is inaccurate.
- A presentation of liver disease, CNS or psychiatric disease, and/or hemolytic anemia should raise suspicion for Wilson's disease.
- Autoimmune hepatitis is seen more often in females, and they may have a personal or family history of other autoimmune disorders.
- Alpha 1-antitrypsin deficiency is the most common inherited metabolic liver disease and a family history of early onset emphysema should raise suspicion for this disease.
- NASH is the most common cause of liver disease in the U.S. and should be suspected in patients who are obese and have insulin resistance.

Please answer the following with TRUE or FALSE

T or F Young children infected with hepatitis A virus often show no signs of clinical jaundice.
T or F There is currently no specific therapy for acute hepatitis A infection.
T or F A chronic carrier state of hepatitis A develops in some patients.
T or F Fulminant hepatic failure develops in some patients with hepatitis A infection.
T or F By the time patients with hepatitis A present with clinical jaundice, the period of infectivity has already passed.

*true, Hepatitis A usually affects older kids and adults more severely than young children. As young children are often anicteric, they may present with symptoms of a mild acute gastroenteritis. It is very possible that the patient presented in the clinical vignette was infected by his younger brother who was sick the previous month with vomiting and diarrhea (the incubation period is about 30 days). Hepatitis A is primarily spread via the fecal-oral route. Therefore household contacts, especially if changing the diapers of an infected child, are at increased risk of becoming infected.

* true, Acute hepatitis A is usually a self-limited illness that resolves with only supportive therapy. However, both passive and active immunizations are available. Active immunization can be given for prevention of hepatitis A with one of the commercially available hepatitis A vaccines. As it is not clear exactly how long it takes to build up immunity, it is currently recommended that the immunization be given at least 2-4 weeks before exposure, such as travel to an endemic area. If travel to an endemic area will occur in less than 2-4 weeks, passive immunization can be provided by using serum immune globulin. Serum immune globulin can also be used for post-exposure prophylaxis, such as household contacts, if given within two weeks of exposure.

* false, No chronic carrier state of hepatitis A has been identified.

* true, Although this presentation is rare, especially in pediatric patients, it can occur. This is why it is important to check tests of liver function (PT, albumin) in patients with liver disease. It is also important to monitor mental status closely in patients with acute hepatitis, as hyperammonemia can occur with hepatic insufficiency.

* false

A 22-month-old female presents to your clinic for follow-up. One week prior to this visit, she was brought to your clinic for an initial evaluation by her adoptive parents after she was adopted from Russia. At that time you ordered some screening labs as recommended by the American Academy of Pediatrics. They are here today to discuss the lab results. Her labs showed that some of the serologic tests for hepatitis B are positive and her transaminases are mildly elevated. She is currently having no jaundice, pruritus, abdominal pain, vomiting, diarrhea, or any other symptoms.

Birth history is mostly unknown except that her birth weight was 5 lb. 15oz. They were told that she was healthy at birth and has been a healthy child. They were also told that she had been tested for HIV, hepatitis B, and hepatitis C in Russia and that they were all negative. The parents have no information about the medical history of her biological parents or their families
The patient lives with her adoptive parents and their two children ages 7 and 4. The dad works for a public relations firm and the mom stays at home with the kids. Everyone seems to be adjusting well to the adoption which occurred about three weeks ago. There are no smokers in the home, and they have two cats and a dog. There have been no sick contacts.
The parents report that the patient is eating table foods with the rest of the family and that she has a good appetite. She gets 2-3 servings of milk per day as well as fruit juices.

Physical Exam
VS: Afebrile, HR 102, RR 18, Lt. 83 cm (25th%), Wt. 10 kg (10th%), weight:length ratio is 10th percentile, OFC 47 cm (25th%)
General: thin but appears adequately nourished, well hydrated
HEENT: sclera anicteric, pupils equal, round, and reactive bilaterally, TMs clear bilaterally, oropharynx clear
Neck: supple without lymphadenopathy or thyromegaly
CV: normal heart sounds, good pulses
Resp: clear breath sounds bilaterally, no distress
Abd: soft, non-tender, non-distended, no hepatosplenomegaly, no palpable masses
GU: normal external female genitalia
Extremities: no clubbing, cyanosis, or edema
Musculoskeletal: good muscle strength and tone
Neuro: DTRs noted to be normal and symmetrical
Skin: no rashes, lesions, or jaundice noted
Rectal: anus in normal position, perineum normal to inspection

Below are some of the lab results obtained on this patient:

ALT	**105**
AST	**74**
Alk Phos	**222**
Total Bili	**0.8**
Albumin	**3.6**
Hep B surface antigen	**positive**
Hep B surface antibody	**negative**
Hep B core antibody	**positive**

Based on the above lab results, you plan to tell the parents that the patient

A was infected with hepatitis B in the past but has cleared the infection
B has been immunized against hepatitis B
C has hepatitis B infection
D is a hepatitis B carrier

Further serologic testing on this patient reveals that the hepatitis B core antibody is predominantly of the IgG subclass and the hepatitis B e antigen is positive. This indicates that the patient has

A acute hepatitis B with ongoing viral replication
B acute hepatitis B without ongoing viral replication
C chronic hepatitis B with ongoing viral replication
D chronic hepatitis B without ongoing viral replication

The household contacts of this patient should receive

A hepatitis B vaccine only
B hepatitis B Immune Globulin (HBIG) only
C both hepatitis B vaccine and HBIG
D none of the above; they are not at risk for acquiring hepatitis B from the patient

Which of the following patients with acute hepatitis B infection have the greatest risk of developing chronic hepatitis B?

A a neonate who acquired hepatitis B by vertical transmission (mother to infant)
B a 4 year old patient who acquired hepatitis B from repeated exposure to blood products
C an 18 year old patient who acquired hepatitis B through sexual contact
D none of the above. They all have the same (low) risk of developing chronic hepatitis B.
E none of the above. They all have the same (high) risk of developing chronic hepatitis B.

Please answer the following with TRUE or FALSE

T or F Patients with chronic hepatitis B are usually asymptomatic.
T or F There is currently no pharmacologic therapy approved for the treatment of chronic hepatitis B infection in the pediatric population.
T or F Chronic hepatitis B infection is associated with increased risk of hepatocellular carcinoma.
T or F Hepatitis A vaccine should be avoided in this patient.

Please answer the following with TRUE or FALSE

T or F Most infants born to mothers with hepatitis C become infected.
T or F Acute hepatitis C infection usually manifests with significant jaundice and markedly elevated transaminases.
T or F Most people who get infected with hepatitis C develop chronic hepatitis C infection.
T or F The antibody to hepatitis C virus (anti-HCV) is protective against hepatitis C.
T or F Chronic hepatitis C infection usually rapidly progresses to end-stage liver disease.

Solutions and explanations:
1)) These results indicate that this patient is currently infected with hepatitis B. These tests do not tell us if it is an acute infection or a chronic one, but this can be determined by ordering other serologic tests.

2)) C, This patient is chronically infected with hepatitis B and has evidence of ongoing viral replication. Hepatitis B e antigen is associated with ongoing viral replication, increased viral load, and increased infectivity.

3)) A, Hepatitis B vaccine is recommended for all household contacts of patients with hepatitis B infection. Families should also be instructed not to share household items that could be contaminated with the patient's blood such as nail clippers, razors, etc. They should also be instructed to use precautions when cleaning up blood from the infected individual (use of bleach solution and latex gloves).

4)) A

5)) TRUE, Many patients with chronic hepatitis B infection are completely asymptomatic. If the acute hepatitis B infection does not produce jaundice, many years may pass before the diagnosis is made. These patients are often diagnosed when mild elevations of the transaminases are discovered on lab work done for other reasons. Less often, they may present with signs of portal hypertension (such as enlarged spleen, thrombocytopenia, or variceal bleeding).
2* FALSE, Although treatment of an acute hepatitis B infection is purely supportive, there are medications approved for the treatment of chronic hepatitis B in children. Interferon-alpha is probably the most widely used therapy. Lamivudine, a nucleotide analogue, is also approved for treatment of chronic hepatitis B in children. Often these drugs are used simultaneously. Treatment of these patients should be initiated and managed by specialists who are experienced in the treatment of chronic hepatitis B.
3* true, Chronic hepatitis B infection is highly associated with hepatocellular carcinoma. Although this usually occurs after many years of infection, it can occur in children. Although no formal screening guidelines have been established, alpha-fetoprotein levels and/or ultrasonography of the liver are usually performed on an intermittent basis (yearly or biyearly).
4* false, Hepatitis A vaccine is actually recommended for patients with chronic liver disease in order to prevent a second insult to the already affected liver.

6)) FALSE, Although vertical transmission has clearly been documented, it is much lower than that seen with hepatitis B infection. Only about 5-

10% of infants born to mothers with hepatitis C become infected. Co-infection of the mother with HIV is thought to increase the risk of vertical transmission. Unlike hepatitis B, no immunoprophylaxis is given to infants born to mothers with hepatitis C infection.
2* FALSE, Only about 25% of patients with acute hepatitis C infection become jaundiced. Transaminase levels are usually only mildly elevated in the 100-500 range. Many patients may be either asymptomatic or just show mild nonspecific symptoms.
3* true, Studies have shown that about 60 to 80% of patients infected with hepatitis C develop chronic infection
4* FALSE, Anti-HCV is not protective against hepatitis C, and there is currently no passive or active immunization against hepatitis C. Anti-HCV is actually the screening test used for hepatitis C infection. A positive screen means that the patient has been infected with hepatitis C at some point in their life and further laboratory testing is indicated. This should be done under the guidance of a gastroenterologist.
5* false, HCV infection is usually a slowly progressive disease that often is present for years to decades before clinically significant liver disease becomes evident. Co-infection with hepatitis B, heavy alcohol intake, and obesity have all been shown to be associated with disease progression in patients with hepatitis C. Immunizations for hepatitis A and B are recommended, and counselling about alcohol intake and obesity should be provided. HCV infection does have an association with hepatocellular carcinoma, although it usually occurs after decades of infection.

Endocrinology

Type 1 diabetes in children

Written by : "Najla Laisa" Kasasbeh No need to refer to slides

*__Definition:__

Diabetes is a metabolic disorder characterized by the presence of hyperglycemia due to a defect either in the secretion of insulin or in its action (insulin resistance).

- Most common type of diabetes in children is type 1.
- Other types can affect children like type2 and Maturity onset diabetes of the young (MODY), which is a genetic disease.
- Diabetes can also be related to certain drugs like Steroids and some diseases like Cystic Fibrosis.

*__Epidemiology:__

- 285 million people worldwide have diabetes regardless of the cause.
- 10% of them have type1 diabetes and most of them are children under the age of 18.
- There are variable incidences among different ethnic groups.
- Males: females is 1:1.
- Incidence: 7 million/year.

__*Presentation:__

Patients might present at any age but there are 2 peaks for presentation:

- 1st Peak is at 5-7 years of age (school age) mostly triggered by infection or stress.
- 2nd peak is at puberty because sex hormones antagonize the action of insulin.

__*Diagnosis:__

1. Fasting blood glucose >126 mg/dL in addition to symptoms.
OR
2. Random blood glucose >200 (Random means 2 hours after eating) in addition to symptoms.
OR
3. Oral glucose tolerance test (OGTT) >200 mg/dL

*Etiology

There are *genetic* aspects that contribute to type 1 diabetes due to familial tendency to develop diabetes but the fact that not 100% of monozygotic twins are affected makes it known that there are *other factors* predisposing children to have the disease. These factors could be *environmental*, *viral* or other.

Incidence in monozygotic twins is 30-65% and in dizygotic twins and siblings it is around 6%.

The incidence of children having diabetes is higher if the *father* is affected; having a father with type1 diabetes raises the incidence of his offspring having diabetes to 7% and having a mother with type1 diabetes raises the risk to 2%.

The other thing that makes researchers and physicians believe that type1 diabetes is multifactorial and not purely genetic is the variation in incidence rate in the same ethnic group and the fact the there was increase in the incidence of diabetes over the past few years.

Monogenic Type 1 Diabetes Mellitus: Rare. E.g. IPEX syndrome and APS.

*Maturity onset diabetes of the youth (MODY)

- Genetic defect of beta cell function. A primary defect in insulin secretion.
- Incidence is between 9 and 25 years old.
- It is one of the ddx when a child presents with hyperglycemia.
- It's an autosomal dominant so there is always a strong family history.

Criteria for diagnosis:

- At least one family member diagnosed under the age of 25 years
- Diabetes in 3 generations.

*Signs and symptoms of diabetes:

The signs and symptoms appear when there is reduction in 80% of pancreatic β-cell mass.

When there is absolute deficiency in insulin the child will present with DKA.

- Weight loss.
- Fatiguability.
- Polydepsia, Polyuria and Polyphagia.
- DKA as first manifestation if parents did not notice the previous symptoms.
- Progression may be accelerated by intercurrent illness or stress.

***DKA**

DKA is 100% preventable except in three cases:

1. First presentation in type1 diabetes.
2. Noncompliance to insulin therapy.
3. Intercurrent illnesses not managed according to the sick day management guidelines. (Frequent blood glucose and ketone monitoring with adjustment of insulin doses).

Symptoms and signs

- Polyuria, polydipsia, weight loss.
- Abdominal pain, Vomiting.
- Confusion, Tiredness, Difficulty breathing.
- Kaussmaul breathing, lethargy, dehydration, signs of infection.

Diagnosis of DKA:

1. Glucose > 200 mg/dL
2. pH < 7.3
3. Ketonuria or ketonemia
4. Serum Bicarbonate < 18 mmol/L

Investigations

- Capillary glucose STAT.
- Venous blood – glucose, gases, electrolytes, urea, creatinine.
- Ketones in urine or blood

Case scenario #1

Patient came to the clinic with fever, stuffy nose and cough was diagnosed with URTI and was given Amoxicillin. 12 hours later, she was brought to the ER with increased respiratory distress and vomiting. History of increased voiding, increased fluid intake, weight loss recognized. Dry lips, RR 40/min. Glucometer blood sugar 490 mg/dL. PH 7.1 and Ketone +3

This patient has DKA

Management of DKA:

1. ABCs.
2. Rehydration: Normal saline 10 mL/kg to expand vascular space.
3. Decrease to 5-7 mL/kg/hr with KCl.

4. Observation and monitoring.
5. IV insulin infusion (not bolus) 0.1 units/kg/hr.
6. If acidosis is improving and BG < 270 mg/dL or falls > 90 mg/dL/hr → change IV to D5/Normal Saline with potassium and decrease insulin infusion rate.
7. Do not infuse NaHCO3 except in 3 circumstances:
    - Cardiac arrest
    - Inotrope resistant shock
    - Hyperkalemia

Complications of DKA:

1. Seizures, arrhythmias and cardiac arrest due to electrolyte disturbances.
2. Venous thrombosis
3. Acute renal failure
4. ARDS
5. Bowel ischemia.
6. Cerebral edema:

- Pathophysiology: Previous hypothesis assumed that fluid shifts caused by osmotic changes were central to DKA-related cerebral edema. This assumption has not been well supported by clinical data. Cerebral edema during DKA may be predominantly vasogenic and may result from activation of cell membrane ion transporters in the brain.
- Risk factors for cerebral edema:
    - ✓ Younger age (<5 years)
    - ✓ New-onset diabetes
    - ✓ High initial serum urea
    - ✓ Low initial partial pressure of arterial CO2
    - ✓ Rapid administration of hypotonic fluids
    - ✓ IV bolus of insulin
    - ✓ Early IV insulin infusion (within first hour of administration of fluids)
    - ✓ Use of bicarbonate

Strategies to prevent DKA

- To raise public awareness about symptoms and signs of diabetes.
- Beyond diagnosis:
    - ✓ Comprehensive diabetes education programs
    - ✓ Mental health intervention
    - ✓ Home monitoring of ketones or beta-hydroxybutyrate

Case#2:

Same as case number 1 except patient has no acidosis. This is not DKA!
We manage the hyperglycemia by giving 10-20% of the daily dose of rapid acting insulin.

Insulin dose: 0.5-1.2 unit/kg/day
If a patient came with DKA we start by giving the upper limit of insulin dose but if the patient came with hyperglycemia we start by giving them the lower dose and increase the dose gradually as needed.

*Insulin

Insulin is an anabolic hormone secreted by beta cells of pancreas. It antagonizes the action of Glucagon (Glucagon is given in unconscious patients with hypoglycemia).

Actions:

1. Inhibits glycogenolysis and gluconeogenesis in liver.
2. Stimulates protein synthesis and lipogenesis.
3. Inhibits lipolysis and proteinolysis

In the absence of insulin → Suppression of anabolic activities.

1. ↓ lipogenesis + ↑lipolysis (weight loss)
2. ↓protein synthesis + ↑proteinolysis
3. ↑ glycogenolysis + ↑gluconeogenesis

Counter regulatory hormones like epinephrine, cortisol, and glucagon blunt insulin action and elevate glucose levels.

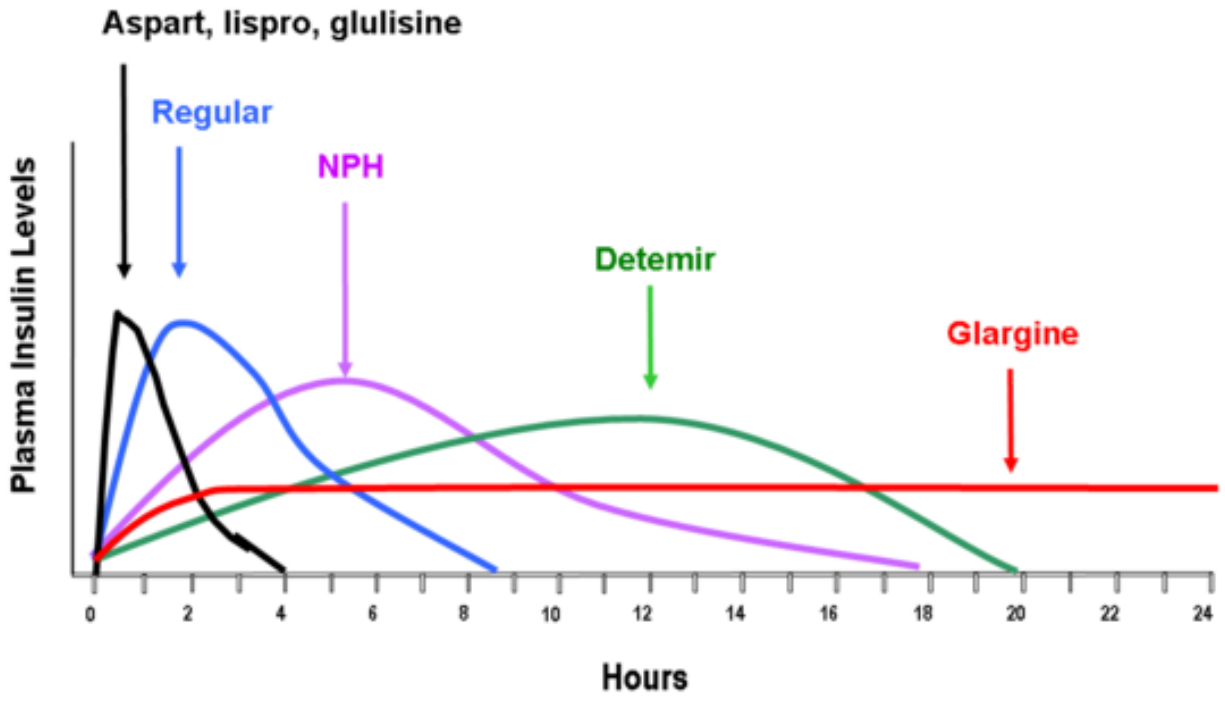
Counter-regulatory Hormones:						
	↓ insulin secretion	↓insulin action	↑Glycog-enolysis	↑Glucon-eogenesis	↑Lipolysis, ketogenesis	↓ glucose utilization
Epinephrine	+	+	+	+	+	+
Cortisol		+	+	+	+	+
GH		+	+	+	+	+
Glucagon			+	+	+	

Types of insulin:

1. Long acting:
- *Glargine*→ Given once a day and it's peakless.
It acts like pancreatic basal insulin (an amount of insulin that's secreted all day regardless of food intake). Given at any time, preferred at 9:00 pm.

-*Detemir* → Duration of action is 12 hours, given twice/day

2. Rapid acting:
- Given immediately before or after meals.
- Starts action within 5 minutes, peaks in 15-30 minutes and duration of action is 3 hours.
Examples: *Aspart, Lispro* and *glulisine*.



3. Regular: Actrapid.
The only use for it in pediatrics is in IV infusion in cases of DKA or NPO with IV fluids.

4. Intermediate acting: NPH

Best combination is Glargine with rapid acting; this mimics the action of pancreas.

An even better therapeutic technique is **Insulin Pump Therapy:**
It Provides a closer approximation of normal plasma insulin profiles and improved metabolic control and reduced risk of severe hypoglycemia.

Randomized trials comparing multiple daily insulin (MDI) regimen using glargine insulin and CSII in children with T1DM demonstrate similar metabolic control and frequency of hypoglycemic events.

NOTICE: 1 insulin syringe has 1 ml which is equivalent to 100 units

*HbA1C

- A reliable index of long-term glycemic control.
- The fraction of hemoglobin to which glucose has been non-enzymatically attached in the blood stream.
- HbA1c measurement reflects the average blood glucose concentration from the preceding 2-3 months.

Recommended glycemic targets for children and adolescents with type 1 diabetes

Age (years)	HbA1C (%)	Fasting/ preprandial PG (mg/dL)	2-hour postprandial PG (mg/dL)
<6	<8.5	110-220	
6–12	<8.0	72- 180	
13–18	≤7.0	72- 126	90-180

*Hypoglycemia

- Symptoms of Low Blood Sugar Include: Hunger, Trembling, Sweating, Extreme Mood changes, Extreme tiredness, Pale, Dizziness, Blurred Vision, Headaches.
- These symptoms will always preceede NEUROGLYCOPENIA except in long standing type 1 diabetes/hypoglycemia unawareness.
- Action: confirm blood sugar is less than 72 mg/dL and TREAT WITH CARBOHYDRATE.
- Make sure the family has GLUCAGON and knows how to use it.

*sick day management:

- Counter-regulatory hormones blunt insulin action and elevate glucose levels.
- Frequent blood glucose and ketone monitoring with adjustment of insulin doses.
- The overall goals are to maintain hydration, control glucose levels, and avoid ketoacidosis.
- DO NOT OMIT INSULIN.

Check ketones EARLY:

- Always test when nausea or vomiting.
- Urine keto diastix.
- Precision Xtra meter: Earlier detection, no need to collect urine.

*Comorbid Conditions:

1. Autoimmune thyroid disease: - 15-30% of individuals with type 1 diabetes.
-Annual TFT is required.

2.Celiac disease: - 4 to 9% of children with type 1 diabetes.
- 60 to 70% are asymptomatic.

3.Addison disease

*Complications of Diabetes

1. Nephropathy

2. Retinopathy: The risk after 15 yr duration of diabetes:
- 98% T1DM
- 78% T2DM.

Screening for retinopathy and nephropathy annually starting at the age of 11 or after 2 years of diagnosis. And at 9 if the patient was diagnosed 5 years prior to the age of 9.

3. Neuropathy: The risk after 20 yr duration of diabetes:
- 20-30% T1DM
- 15-20% T2DM

4. Dyslipidemia

5. Hypertension: Up to 16% of adolescents with type 1 diabetes

DKA management

Case discussion
A 5 year old patient presented to ER with tachypnea. Over the last one hour he developed shock.
How to approach him?

As usual we start with history and PE.
-History
It's important to ask about the following:

-If this is the 1st time or if there were any previous episodes.
-Is the patient medically free or not?
-If he has a history of previous episodes and he's not medically free, then think of medical diseases that can be associated with tachypnea (which is the patients' complaint here) like respiratory, cardiac or metabolic diseases.
If the patient is medically free and this is the 1st time to develop such thing then think of DKA.
- Ask if there's abdominal pain; ketoacidosis cause irritation to the peritoneum (chemical peritonitis).
- Ask about vomiting it may be one of the presenting symptoms.
-Other symptoms are loss of consciousness, Kussumal breathing (deep and rapid respiration to compensate for academia), Tachycardia, Tachypnea, fruity breath due to exhaled Acetone.
-Ask if he's having infection or not; it may be the trigger of DKA.
-Other triggers of DKA are pancreatitis, trauma, Drugs(Corticosteroids,Thiazide,Sympathomimetics)

It's really rare to develop DKA without having symptoms of DM like polydypsia and polyuria. So if the parents have basic knowledge of DM and its symptoms they will bring their child to the clinic once they notice these symptoms, he will be investigated and if he's really having DM he'll be on treatment and by this DKA can be prevented before its occurrence.

So Percentage of patients presented with DKA as the 1st symptom of DM depends on the society; good awareness within the society is surely associated with low % Of DKA as 1st symptom of DM.

- Physical examination
Assess vital signs and look for signs of dehydration
Also check mental status

Criteria for diagnosis of DKA:

1- Hyperglycemia >200mg/dl
2- Ketonuria or Ketonemia
3- PH <7.3 with Anion gap >12
4- HCO3 <18 (remember : Normal range 22-28)

Remember Signs of dehydration :
Dry mucus membranes.
Pallor
Skin turgor at sternum
Capillary refill
Sunken eyes
Anterior fontanel depression
Crying without tears
Decrease urine output

Electrolyte disturbances in DKA
Hyponatremia (Due to osmotic dieresis)

Note : sodium concentration should be corrected in the case of hyperglycemia → for each 100 mg/dl of glucose above the concentration of 100 mg /dL we add 1.6 meq/L for sodium .
e.g Sodium = 124 meq/L and glucose =600mg/dL correct sodium concentration . there is 500 mg/dL above the 100mg/dL → 5*1.6=8 → Corrected sodium = 124+8=132 meq/L

Hypokalemia
Initial serum potassium is typically normal or elevated because of the extracellular migration in potassium in response to acidosis

Management of DKA
The following points must be considered and closely monitored:
- Correction of fluid loss with intravenous fluids.
- Correction of hyperglycemia with insulin.
- Correction of electrolytes disturbances, particularly potassium.

It's important to pay attention to the correction of fluid and electrolyte loss during the first hour of treatment. Correction of fluid loss makes the clinical picture clearer and may be sufficient to correct acidosis.

Insulin should be started about an hour after IV fluid replacement; insulin infusion is started in the 2"d hour.

Fluid that should be given here is isotonic like NS or ringer lactate, we don't give hypotonic solutions.

The dose of fluid should be given is 20 *ml/* Kg over one hour (it's important to remember the dose).

The recommended schedule* for restoring fluid:
Administer 1-3 L during the 1st hour
Administer 1L during the 2"d hour
Administer 1 L during the following 2 hours
Administer 1 L every 4 hours, depending on the degree of dehydration.

*This is from Medscape, the Dr mentioned sth similar to it.
It's important to know that we give NS in the first 4-6 hours of treatment (until The patient becomes euvolemic), then we replace it by half NS.
As we said, we start insulin infusion after the 1st hour of treatment. We give it at rate of 0.1 unit/Kg/hr (it's important to know this number).
What is the type of insulin we give here?
We give regular insulin (act rapid)

Remember, insulin is an anabolic hormone; it decreases glucogenesis, glycogenolysis and lypolysis while it increases lypogenesis.
Function of insulin here:
- Reduce concentration of glucose.
- Treat acidosis (it shuts down lypolysis)

We don't stop insulin infusion unless there's improvement in acidosis and sugar level. And when this happen we should reduce insulin infusion slowly, BUT we should not reduce it to a level below 0.02 unit/ Kg/ hr because the normal insulin Level secreted from pancreas in **non** diabetic human is 0.02.

As you know, insulin cause potassium shift to the intracellular compartment, so you have to monitor its level and you should put any DKA patient on cardiac monitor.

If potassium concentration reaches a level below 5.5 we should start giving potassium; we can add KCl to the fluid.

In your follow up:
You have to check glucose level every hour.
You have to check vital signs every hour.
You have to check electrolytes every two hours.

Note :
-In most of hospitals we measure the acetoacetic acid as ketoacidosis NOT B-Hydroxybutyric acid.
-When there is a resolve of ketoacidosis , the B-hydroxybutyric acid converts to acetoacetic acid which is excreted in urine, so we cannot use our investigations for follow up because we might find the ketones is increasing while the patient is actually is improving
It's important to do neurological examination because of the risk of cerebral edema.

Acute cerebral edema is the most dangerous side effect of treatment of DKA .
Risk factors:
-High BUN
-Low PCO2
-Use of HCO3- in the treatment
-Hyponatremia

You can switch from insulin infusion IV to subcutaneous when you correct acidosis, patient can tolerate oral feeding, there's no vomiting and there's active bowel movement; no ileus.

Patient will be on subcutaneous insulin forever, and you have to teach the parents and give them the needed information about insulin; types, doses, when and how to give it to the child.

In DKA never treat acidosis by sodium bicarbonate; if you do so there's a risk of

cerebral edema. But there are special cases in DKA in which you can use sodium bicarbonate, which are :

- Life threatening hyperkalemia.
- Cardiac arrest.
- Ionotropic resistant shock.

Done by: Heba Alsmadi
Edited by: Mohannad abohamad

Common Adrenal Disorders in Children

#Introduction

The adrenal gland consists of ;
* **an outer cortex**, which is responsible for the synthesis :
MINERALOCORTICOIDS – regulate sodium retention and potassium loss and body fluid
GLUCOCORTICOIDS – act as anti-inflammatory agents; affect metabolism.
ANDROGENS – regulates growth and development of genetalia and puberty
***Adrenal Medulla**, which synthesizes :
ADRENALINE (EPINEPHRINE) – increases heart rate and blood pressure.
NORADRENALINE (NOREPINEPHRINE) – constricts arterioles.

Hypothalamic corticotropin-releasing hormone (CRH) stimulates the release of pituitary adrenocorticotropic hormone (ACTH /corticotropin), derived by selective processingfrom pro-opiomelanocortin.
ACTH governs the synthesis and release of cortisol and adrenal androgens.

Primary adrenal insufficiency or cortisol deficiency from any defect in the adrenal gland results in an oversecretion of ACTH; cortisol deficiency also may occur from **ACTH (secondary)** or **CRH (tertiary) deficiency**, causing low serum ACTH concentrations and low cortisol.
Endogenous (or exogenous) glucocorticoids feed back to inhibit ACTH and CRH secretion.
The renin-angiotensin system and potassium regulate aldosterone secretion; ACTH has little effect on aldosterone production except in excess, when it may increase aldosterone secretion.

-**Steroids that circulate in the free form (not bound to cortisol-binding protein [transcortin]) may cross the placenta from mother to fetus, but ACTH does not. The placenta plays an important role in steroid biosynthesis in utero, acting as a metabolic mediator between mother and child. Because the **fetal CRH-ACTH-adrenal axis** is operational in utero, deficiencies in cortisol synthesis lead to excessive ACTH secretion.

If a virilizing adrenal enzyme defect is present, such as 21-hydroxylase deficiency, the fetal adrenal gland secretes excess androgens, virilizing the fetus.
Normal variation of serum cortisol and ACTH levels leads to values that are high early in the morning and lower at night. This normal diurnal variation may take months to years to fully develop.

Adrenal Dysfunction

Decrease function

- Adrenal insufficiency (Low cortisol, aldestrone) Eg, Addison disease

inecrease function

- Cushing syndrome (High Cortisol)
- Hyperaldosteronism (High aldestrone)
- Pheochromocytoma (High catecholamine)

Table 178-1	Clinical Manifestations of Adrenal Insufficiency
Cortisol deficiency	
	Hypoglycemia
	Inability to withstand stress
	Vasomotor collapse
	Hyperpigmentation (in primary adrenal insufficiency with excess of adrenocorticotropic hormone)
	Apneic spells
	Muscle weakness, fatigue
Aldosterone deficiency	
	Hyponatremia
	Hyperkalemia
	Vomiting
	Urinary sodium wasting
	Salt craving
	Acidosis
	Failure to thrive
	Volume depletion
	Hypotension
	Dehydration
	Shock

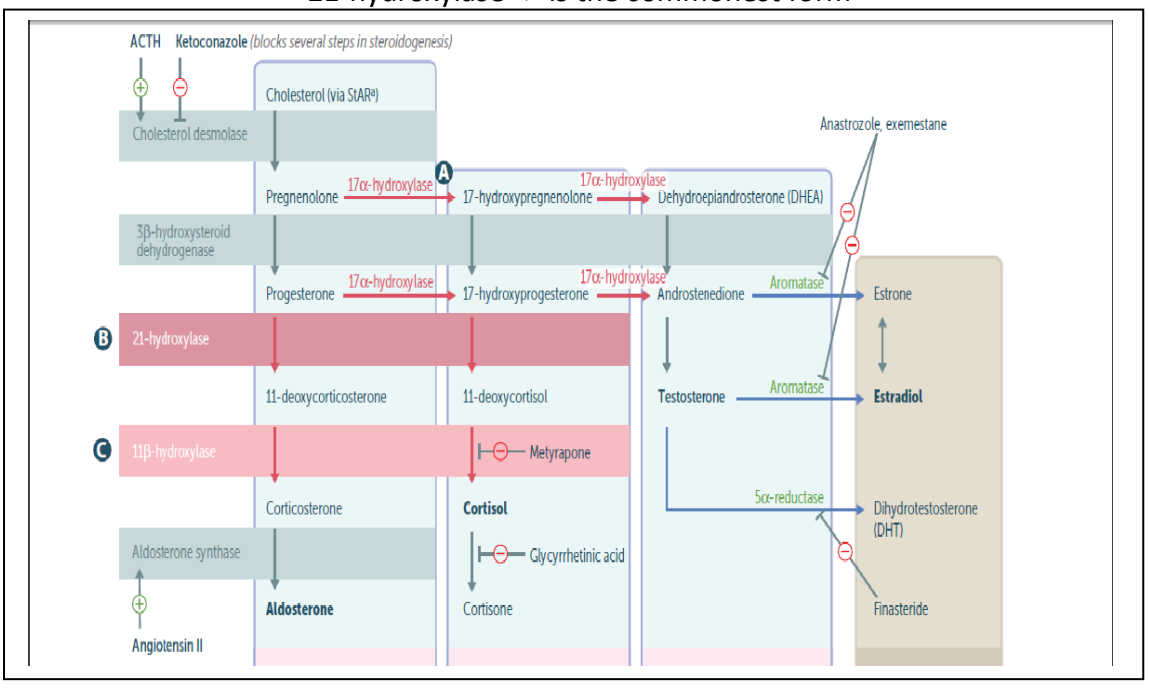
Adrenal insufficiency

Causes of Adrenal insufficiency :

- Congenital adrenal hyperplasia
- Addison disease
- Infection (TB, sepsis)
- Adrenoleukodystrophy

1) Congenital Adrenal Hyperplasia

- Family of inherited disorders of adrenal steroidogenesis
- Each disorder results from a deficiency of one of several enzymes necessary for steroid synthesis
- Autosomal Recessive (M=F)
- 21-hydroxylase ↓ is the commonest form



Steroid biosynthetic enzymes:

1) Cholesterol side chain cleavage=scc (20,22 desmolase)

2) 3β-Hydoxysteroid dehydrogenase

3) 17 α hydroxylase and 17,20 –lyase

4) **21β-Hydroxylase**

5) 11β-Hydroxylase

6) Aldosterone synthetase (11β,18 hydroxylase & 18 oxidase

ENZYME DEFICIENCY	MINERALOCORTICOIDS	CORTISOL	SEX HORMONES	BP	[K+]	LABS	PRESENTATION
A 17α-hydroxylase[a]	↑	↓	↓	↑	↓	↓ androstenedione	XY: ambiguous genitalia, undescended testes XX: lacks 2° sexual development
B 21-hydroxylase[a]	↓	↓	↑	↓	↑	↑ renin activity ↑ 17-hydroxy-progesterone	Most common Presents in infancy (salt wasting) or childhood (precocious puberty) XX: virilization
C 11β-hydroxylase[a]	↓ aldosterone ↑ 11-deoxycorti-costerone (results in ↑ BP)	↓	↑	↑	↓	↓ renin activity	XX: virilization

All congenital adrenal enzyme deficiencies are characterized by **skin hyperpigmentation** (due to ? MSH production, which is coproduced and secreted with ACTH) and **bilateral adrenal gland enlargement** (due to ? ACTH stimulation).

If deficient enzyme starts with **1**, it causes hypertension (increase in mineralocorticoid production only) ; if deficient enzyme ends with **1**, it causes virilization in females. (increase in sex hormone production only)

In **11b hydroxylase D** both are increase (BP , SEX hormone

The dominant clinical features of congenital adrenal mineralocorticoid deficiency are hyponatremia and hyperkalemia, usually developing by 5 to 7 days after birth but not immediately after birth. Vomiting, dehydration, and acidosis soon follow, as does hypotensive shock from glucocorticoid deficiency. Death may occur if the disorder remains undiagnosed and untreated.

In females the ambiguity of the external genitalia is an obvious clue that salt-losing congenital adrenal hyperplasia (CAH) or simple virilizing CAH must be ruled out. Because these forms cannot be distinguished clinically, all presentations of ambiguous genitalia should involve evaluation for mineralocorticoid deficiency.
In males the most common form of CAH, 21-hydroxylase deficiency, does not cause abnormal genitalia. There may be hyperpigmentation of the scrotal skin, but this is a subtle sign.

In all infants, the diagnosis of adrenal insufficiency may be overlooked or confused with pyloric stenosis. In pyloric stenosis, in contrast to salt-losing CAH, vomiting of stomach contents results in hypochloremia, serum potassium is normal or low, and alkalosis is present. This distinction may be lifesaving in preventing unnecessary investigations or inappropriate therapy.

Not all forms of adrenal hyperplasia present at birth; the spectrum of disorder ranges from severe (classic) to mild (late-onset) or nonclassic. Milder forms may manifest in childhood, adolescence, or even young adulthood (not as glucocorticoid or mineralocorticoid deficiencies, but as androgen excess).

In patients with **congenital adrenal hypoplasia or adrenal hemorrhage**, the secretion of all adrenal steroids is low. In contrast CAH leads to a diagnostic steroid pattern in blood and urine.

CAH due to 21-Hydroxylase Deficiency

90–95% of CAH cases are caused by 21- OHD ▪

Females affected with severe, classic 21- OHD are exposed to excess androgens prenatally and are born with virilized external genitalia ▪

Presentations of 21 HCAH : 1) ambiguous genitalaia in girl 2) dehydration 3) slat-loss presentations with electrolyte imbanlance (hyoNa hyperK) AND hypoglycemia 4) shock 5)Hyperpigementations

The treatment of 21-hydroxylase deficiency requires hydrocortisone and fludrocortisone in the case of the salt-losing Form
,,,, The goals of **treatment** are to achieve normal linear growth and bone age advancement. Long-term therapy consists of providing
glucocorticoids at a dose of approximately 10 to 15 mg/m2/24 hours in three divided doses of oral hydrocortisone or its equivalent.

Mineralocorticoid therapy for salt losers consists of fludrocortisone at a dose of 0.1 to 0.2 mg/24 hours, .

Surgical correction of ambiguous external genitalia may be considered.

The adequacy of glucocorticoid replacement therapy is monitored by determining serum concentrations of adrenal precursors, including androstenedione and 17-OHP for 21-hydroxylase deficiency. In addition, the assessment of linear growth and skeletal age, by bone age determination, is required as a reflection of appropriate therapy. To avoid adrenal insufficiency, threefold higher doses of glucocorticoids are given during **stressful states** such a s febrile illnesses and surgery. Intramuscular hydrocortisone isused in severe emergencies or with illnesses involving emesis.

Mineralocorticoid therapy is monitored with serum sodium, potassium, and plasma renin activity levels

*** Newborn screening for CAH Neonatal screening by filter paper on 3rd day of life and 17 Hydroxyprogestrone blood level (17 OHP)**

2) Addison disease

-Addison disease is a rare acquired disorder of childhood, usually associated with autoimmune destruction of the adrenal cortex.
-It is a form of primary adrenal insufficiency with absence of glucocorticoid and mineralocorticoid(Aldestrone & cortisol low, high ACTH, high renin
- Isolated or associated with other autoimmune disease
-Presents with tiredness, weight loss, skin pigmentation
Other clinical manifestations salt craving, postural hypotension, fasting hypoglycemia, anorexia, weakness, and episodes of shock during severe illness
-ACTH stimulation test
-Treatment : as mentioned in the above (10 to 15 mg/m2/24 hours of hydrocortisone, with supplementation during stress at three times the maintenance dosage or the use of intramuscular hydrocortisone. The dose is titrated to allow a normal growth rate. Mineralocorticoid replacement with fludrocortisones)

Adrenal crisis (Imp!!)
often occurs if the body is subjected to stress such as an accident , injury , surgery or severe infection.
DEATH MAY QUICKLY FOLLOW

Causes :
Rapthide wraipthydrawal of long-term steroid
Ketoconazole
Phenytoin
Ritampin
Mitotane
Septic shock
Trauma

DDx
Septic shock

Work up
-- Serum chemistry: abnormal in 56% of pts
Hyponatremia
Hyperkalemia
Metabolic acidosis
Hypoglycemia
-- Serum cortisol less than 20mg/dl in sever stress or after ACTH stimulation
--CBC:
Anemia (mild, nonspecific)
Lymphocytosis
Eosinphilia (highly suggestive)
--Serum thyroid levels
--Cultures: infection is a common cause
--ACTH test (diagnostic) **:**
Baseline serum cortisol level
Administer ACTH 250mcg intravenous push
Draw serum cortisol 30 and 60 min after ACTH administration
An increase of less than 9mcg/dl is considered diagnostic of adrenal insufficiency
--Imaging studies
Chest radiology : assess for TB , Histoplasmosis , malignant disease , sarcoid, and lymphoma
AbdCT scanning : visulaize adrenal glands for HMG , Atrophy , infiltrative disorders, and metastatic disease.
--Other tests
ECG

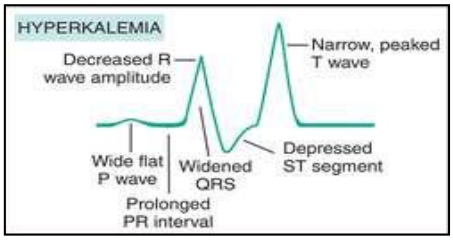
Treatment of hyperkalemia:

* *Stabilization of myocardial cell membrane*
(IV) calcium chloride or gluconat

* *Enhancement of cellular uptake of potassium*

- Sodium bicarbonate IV
- Regular insulin and glucose IV
- Beta-adrenergic agents, such as albuterol
-

**Enhancement of total body potassium elimination*
- Sodium polystyrene sulfonate (Kayexalate) orally (PO)/rectally (PR)
- Furosemide (only if renal function is maintained)
- Emergent hemodialysis



Histological findings
It depends on the cause of the adrenal insufficiency
In 1ry adrenocortical failure , histologic evidence of infection , infiltrative disease or other condition may be demonstrated
In 2ry adrenocortical failure , may cause atrophy of the adrenals or no histologic evidence at all , especially, if due to exogenous steroid ingestion
Apperance of bilateral adrenal HMG maybe striking , as if bags of blood are replacing the gland

Treatment
Its life threatening condition that requires emergency medical treatment
Immediately give an emergency injection of glucocorticoid(e.g. dexamethasone) in supraphysiologic or stress doses (the only definitive Treatment)
Aggressive fluid replacement with 5% ot 10% IV Dextrose and saline solutions and treatment of hyperkalemia is mandatory
flurocortisone, a mineralocorticoid,may also be given
look and treat any factors that may have triggered the crisis sush as infection (empiric antibiotics).
Reversal of coagulopathy with fresh frozen plasma
Pressors (eg, dopamine ,NE) maybe necessary to combat hypotention

Consultations
Endocrinologist//ID specialist//Critical care physician//Cardiologist//Surgeon//Other consultations as clinically indicated

Further inpatient care
Admit to ICU as clinically indicated
Perform fluid resuscitations and hemodynamic monitoring
Monitor serum electrolytes , mg and glucose every 4-6 until stable

Complications
Immunosuppression
HTN
Salt retention
Hypokalemia
Weight gain
Delayed wound healing
Hyperglycemia
Metabolic alkalosis

Prognosis
It's the same as for pts w/out adrenal insufficiency if the conditions is diagnosed and treated appropriately

Follow up
Treat any precipitating disorder
Carefully monitor the growth and development
Recommend medical tag or bracelet that alerts emergency personnel to adrenal gland insufficiency
If exposed to chickenpox prophylaxis with VZIG
If exposed to Measles prophylaxis with IG is indicated
Closely observed for reactivation of TB in pts with latent disease

Cushing's syndrome

Causes of crushing's syndrome :

- ACTH-secreting tumor of the pituitary (Cushing's disease)
- excess secretion of cortisol by a neoplasm within the adrenal cortex
- ectopic secretion of ACTH by a malignant growth outside the adrenal gland
- excessive or prolonged administration of steroids

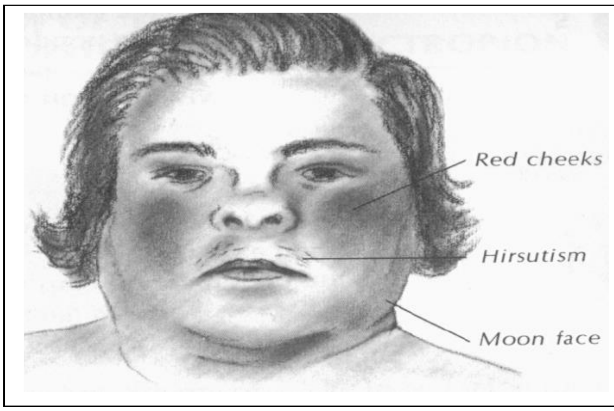
Characterized by:

- truncal obesity
- moon face
- buffalo hump
- acne, hirsutism

Differential Diagnosis of Cushing's Syndrome

Diagnosis	ACTH	Cortisol
Pituitary tumor	High	High
Ectopic ACTH	High	High
Adrenal tumor	Low	High
Exogenous cortisol	Low	High
Exogenous prednisone or dexamethasone	Low	Low

- abdominal striae
- hypertension
- psychiatric disturbances
- osteoporosis
- Amenorrhea
- Diabetes



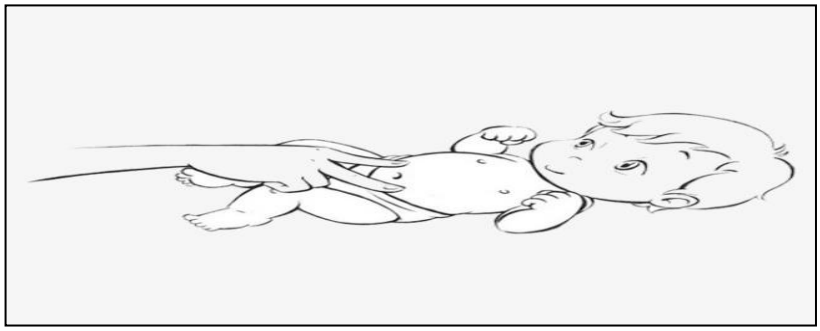
Diagnosis

low-dose dexamethasone suppression test // high-dose dexamethasone suppression test {20μg/kg orally every 6 hours for 48 hours }(helps distinguish Cushing syndrome from Cushing disease) //and late evening salivary cortisol sampling.

Treatment

is directed to the etiology and may include excision of autonomous adrenal, pituitary, or ectopic ACTH-secreting tumors. Rarely adrenalectomy is needed to control the symptoms.

Parenteral glucocorticoid therapy is necessary during and immediately after surgical treatment to avoid acute adrenal insufficiency.

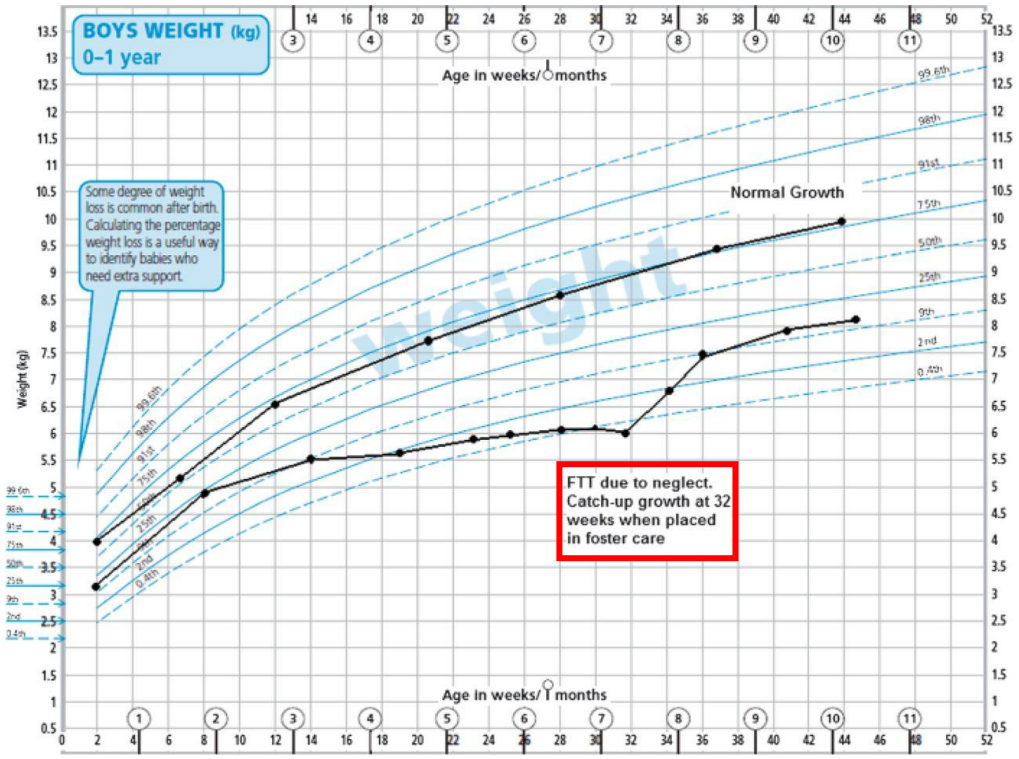


Short Stature

Short stature is defined as **<u>height</u> below the 2nd (3rd) percentile for age**. Most books define it as being below the 3rd percentile for age.

Failure to thrive/ weight faltering, is another term, that is usually applied to infants and pre-school children who fail to gain **<u>weight</u>** at an appropriate rate. So, it's a definition that relates to weight primarily but if the weight is severely affected, the child's height and head circumference can also be affected in the future.

Growth failure is the failure to maintain a height velocity that is appropriate for age and maturity. This means that the child is failing to sustain his height on the same centile, i.e. he is crossing centiles.



This is a growth chart for a child who is failing to gain weight due to neglect and not eating enough calories. Notice the catch-up growth represented by the increase in the rate of gaining weight, after the child being placed in foster care.

Causes of Short Stature -

- Normal variant (Genetic short stature and constitutional delay).
- IUGR, SGA.
- Dysmorphic syndromes.
- Skeletal dysplasias.
- Chronic diseases.
- Endocrine disorders.
- Dire social circumstances.

Now, each cause will be discussed briefly.

Genetic Short Stature –

Case scenario:
A Child who is short, looks normal, with normal physical examination. His/her bone age is not delayed.
Parent(s) is/are short and normal.
Looking at the growth chart of this child, he's growing on his own centile (below the 3rd centile by definition); his growth velocity is normal, he is growing the centimeters he's supposed to gain each year, his growth is within the range expected according to his mother and father's heights.

➔ The child is genetically destined to become a short adult.

Nothing can be done to this child.

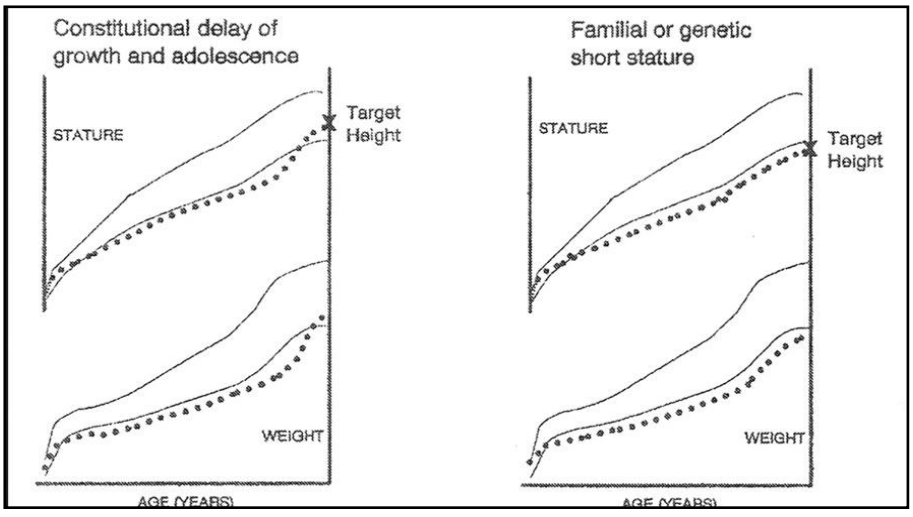
Constitutional Delay –

This is a normal variant of growth, seen a lot in clinics. Parents bring their children to the pediatrician, as they look different than their peers, thinking they have a problem but they actually don't.
This is more common in boys than in girls.

Case scenario:
A child who is short, normal but looks younger than his chronological age. Parent(s) is/are not short, but may have been so during their childhood.
(They had delayed puberty. In case of a short boy, ask about the father's puberty– when did he start shaving or when did he first notice his voice changing. If a girl ask about the mother's puberty and growth pattern– when was her first menarche).
The child's bone age is delayed.

➔ The child will most probably have late puberty and have his/her peak height velocity later on reaching a final normal height = (catch-up growth).

His/her final height will usually be in the lower half of the target range.



The small newborn –

Another reason for being short is being born small. Both IUGR and SGA are causes of short stature.
IUGR and SGA are not interchangeable terms.

SGA can be **symmetric** or **asymmetric**. An insult during the pregnancy is the cause of having a baby who is an SGA; If the insult was chronic, early on throughout the pregnancy, it will affect all the growth parameters and a symmetric SGA will result.
If the insult came at the end of the pregnancy, the head will be spared and asymmetric SGA will result.
Most symmetric SGAs catch up, and reach a normal weight and height by the age of 2 years, but some will continue to grow below what is expected for them.

Dysmorphic Syndromes –

Another reason for short stature is having a dysmorphic syndrome. Tens of syndromes are associated with short stature, like Williams syndrome and Down Syndrome.
The most important one to stress on and look for as a cause of being short is Turner syndrome.
Turner Syndrome is defined as loss or abnormality of the second X chromosome in at least one major cell line in a phenotypic female.

Clinical features of TS attributable to gene loss:

- Skeletal dysplasia.
  → Short stature, cubitus valgus.
- Ovarian failure.
- Lymphatic impairment.
  → Neck webbing, puffy feet and hands.
- Naevi.

Clinical features of TS NOT directly attributable to gene loss:

- Middle ear disease; like recurrent middle ear infections.
- Cardiac defects.
- Renal anomalies.
- Neuro-psychological features.
- Autoimmune diathesis.

Skeletal Dysplasia –

Dysplasia can be **frank**; affecting epiphyses (epiphyseal dysplasia), metaphyses (metaphyseal dysplasia), spine (spondyleal dysplasia) or in various combinations (like; spondylo-epiphyseal dysplasia).

Skeletal dysplasia results in **disproportionate short stature**; if the spine is affected, the child will have a short spine and normal limbs.
Another prototype is achondroplasia, in which the child will have short limbs and normal spine.

The real problem is when you're dealing with patients with **occult** skeletal dysplasia; since they have no identifiable abnormality on skeletal survey, their bone age is normal or advanced, and they have poor growth response to puberty. This kind of dysplasia becomes clear after the child becomes an adult.

Chronic systemic disease –

Any child who has a chronic systemic disease will stop growing; the body will be occupied fighting that disease, and the child may end up with malnutrition.

Any chronic condition, like GI, cardiac, respiratory, renal, metabolic or CNS disorders, can cause short stature and/or slow growth.
Chronic renal disease and GI disorders like coeliac disease, can be silent, and present with short stature.

Social and emotional circumstances –

Poor social and emotional circumstances is an underestimated yet very important cause of having a short stature and poor growth.
Children from poor communities tend to be shorter than those from affluent areas.

Severe short stature with growth failure may result from emotional abuse/neglect (psychosocial deprivation).

Endocrine disorders –

Having an endocrine disorder might be the cause of short stature and poor growth. However, it is not so common.

Some of endocrine disorders causing short stature:

- Growth hormone deficiency and resistance.
- Thyroxine deficiency.
- Cortisol excess.
- Idiopathic short stature.

▸ Growth hormone deficiency

GH deficiency can be classified according to **the cause**; it may be **congenital** or **acquired**, or according to **the nature**; it may be **true permanent deficiency** or **functional/temporary deficiency**, like living in poor social circumstances, or according to **the severity**; it may **partial** or **complete**.
GH deficiency can be isolated or part of multiple anterior pituitary hormone deficiencies (pan-hypopituitarism).

Causes of hypopituitarism:

Congenital Causes:

Idiopathic

Genetic Defects

- Isolated GH deficiency
- Multiple AP deficiencies*
- Prader Willi Syndrome

Midline Defects**

- Septo-optic dysplasia

Acquired Causes:

Surgery

Tumors

- Optic glioma
- Craniopharyngioma

Cranial Radiotherapy

- For medulloblastoma, for example.

Granulomatous diseases

- Langerhans cell histiocytosis

* Multiple AP hormone deficiencies result from mutations affecting the transcription factors that are responsible for differentiation of cells that produce the different hormones secreted by the anterior pituitary which are, TSH, GH, LH, FSH and prolactin.

** Since the pituitary gland is a midline structure, any structural midline anomaly/defect should raise the question of a possible pituitary hormone deficiency. Examples of midline anomalies are cleft palate, central incisor and septo-optic dysplasia.

Clinical presentation of hypopituitarism is variable, according to the cause and age of presentation.

Neonatal presentation of hypopituitarism:

- Hypoglycaemia (GH and cortisol deficiency).
- Prolonged jaundice (cortisol and T4 deficiency).
- Micropenis ± cryptorchidism (Gn deficiency).
- Nystagmus (suggestive of optic nerve hypoplasia).

Childhood and adolescent presentation of hypopituitarism:

- Growth failure (GH deficiency).
- Features of T4 deficiency (fatigue, weight gain, dry skin).
- Features of cortisol deficiency (fatigue, susceptibility to and difficulty shaking off intercurrent illnesses).
- Pubertal failure.
- Recognized related diagnosis (like a known lesion, irradiation or an affected family member).

If a tumor, like craniopharyngioma is the cause, in addition to the endocrine features of hypopituitarism, the child may also present with signs and symptoms resulting from the mass effect of the tumor; like visual **impairment from optic nerve/chiasm compression** presenting as visual field defects and/or decreased visual acuity, or **raised intracranial pressure** resulting from obstructive hydrocephalus.

Approach to a child with hypopituitarism:

Each hormonal axis should be investigated.

Keep in mind that most of the hormones of the pituitary gland are secreted in a pulsatile pattern, with variations in pulse characteristics that reflect specific physiologic states, so random serum levels are of little value.
A **stimulation test** is better to be done. Stimulation testing measures the response of certain glands within the endocrine system to different types of hormones.

Investigations of H-P axis –

Biochemical investigations:

GH axis –

- Growth hormone causes the body to make insulin-like growth factor (IGF1) and insulin-like growth factor binding protein 3 (IGFBP3). Tests can measure the level of these growth factors; reflecting the level of GH.

- Accurate growth hormone deficiency testing involves a stimulation test, which measures the level of GH in the blood after receiving a medication that triggers the release of GH, such as insulin, arginine, clonidine or glucagon.

Gonadal axis –
GnRH stimulation test is done to measure the pituitary response in terms of LH and FSH production.

Adrenal axis –
ACTH stimulation test is done; to assess the functioning of the adrenal glands stress response by measuring the adrenal response to ACTH.

Thyroid axis –
Thyroid axis is the only axis that you don't have to stimulate. You can just measure the level of TSH and T4, as the diurnal rhythm is not really well established.

Prolactin.

Imaging with MRI:

Possible findings on MRI:

- **Normal MRI.**
- **Small anterior pituitary gland.**
- **Interrupted pituitary stalk**, seen in cases of trauma or accidents.
- **Ectopic posterior pituitary.**
- **Absent septum pellucidum.**
- **Obvious tumor,** like intrasellar, craniopharyngioma or optic glioma.
- **Thickened stalk** in case of Histiocytosis.

Treatment of hypopituitarism –

Management depends on what hormones are deficient. Whatever is deficient should be replaced, keeping in mind that not necessarily all axes are involved.

- GH can be replaced by **subcutaneous injections,** given daily before bedtime until the child has his/her epiphyses closed.

- If the child fails to enter puberty s/he can be helped by **pubertal induction** with **testosterone** to the males, and **oestrogen** to the females; given in a certain protocol.

- If the child has adrenal insufficiency, **hydrocortisone** can be given in 3 daily doses, doubling or even tripling the dose with intercurrent illness trying to simulate the stressful conditions in normal individuals. These patients should also be advised to wear an ID card telling that they have adrenal insufficiency; as it is a life threatening condition. An IM injection might be needed in emergencies.

- **Thyroxine** should be given in case of thyroid hormone deficiency**.**

- If the patient has diabetes insipidus, **DDAVP nasal spray or Desmotabs** can be given, titrating the dose according to the patient's electrolytes, normalizing thirst as much as possible.

These patients must be followed up every 3-4 months; to make sure they are managed in a good manner. A growth pattern must be plotted to have an idea about the adequacy of GH replacement.
IGF-1 level can be measured to monitor compliance and titrate dosage.

Keep in mind that we're talking about secondary causes of hormone deficiencies, like for example, secondary hypothyroidism, or pituitary hypothyroidism, in which the pituitary is failing to produce TSH, in this case you don't follow the patient up by TSH, it will be low. You follow the patient up by measuring the level of T4 only.

There are many ways to measure the cortisol level, one of which is the salivary cortisol profile.

***

Thyroxine deficiency

Thyroxine is a very important hormone for normal growth. Its deficiency will affect the patient's height.

***

Cortisol excess

Any child who is **failing to grow** and at the same time, s/he is **gaining weight**, **thyroxine *deficiency*** and ***cortisol excess*** should be suspected; these are the two endocrine conditions that make the child both short and obese.

***

- **Idiopathic short stature**

Definitions vary according to different institutions. Basically, it is when there is no identifiable cause for short stature.
There are some schools that treat it and others that don't. The efficacy of treatment is not really well established.

Evaluation of a child with short stature –

History:
A detailed history should be obtained to try to figure out which of the causes discussed previously is responsible for the child being short.

- History of growth pattern and previous measurements.
- Parental heights (to calculate mid parental height) and parent's puberty time.
- Birth weight, postnatal hx.
- General health.
- Psychosocial situation.
- Educational status, to see if the child is getting all the attention needed.

Auxology:
Accurate measurements of both the child and his/her parents should be taken. Inaccurate measurements can lead to underdiagnosis and hence many cases being left unmanaged, and it also can result in overdiagnosis, and many unnecessary investigations being made.

Height and weight should be plotted accurately on the growth chart using nice clear dots. Mid parental height and target range should also be plotted.

Sometimes, in cases of disproportionate short stature, other measurements should be taken like, sitting height and arm span.

Bone age is an important tool to help in the diagnosis. Like in case of constitutional delay or GH deficiency, bone age will most probably be delayed, while in case of genetic short stature bone age will be normal.

Physical Examination:
- General appearance and nutrition.
- Body proportions.
- Dysmorphic features.
- Systemic examination, to look for any chronic illness that might be the cause of abnormal growth.
- BP measurement.
- Pubertal status, to tell if the patient has constitutional delay. It is also important to judge if it's too late to interfere.
- Fundi examination, to look for signs of increased intracranial pressure.

Investigations:
There is no specific work up to do in case of short stature. Basically every body system should be investigated to make sure the child is in good health.

CBC, **KFT** and **LFT** should be done to assess the child's general health.

Even if the child has no GI symptoms, a **coeliac screen** should be done; since coeliac disease can be silent and the patient can only present with short stature.

If the patient is a female, **karyotyping** must be done even if she has no dysmorphic features, as turner syndrome can present only with short stature in the early stages.

An endocrine work up is necessary.
A random sample of **IGF-1** is measured, which gives a reflection of GH level. It doesn't make any sense to measure a random GH level, since it is secreted in a pulsatile pattern during night.
An 8:00am-**cortisol** level is measured since it peeks in the morning.
A **TFT** and **prolactin** level are also necessary.
Upon these basic measurements, If only GH deficiency is suspected, only a **GH stimulation test** must be done. But if multiple hormone deficiencies are suspected, the other axes mentioned previously must also be stimulated.

Pituitary imaging might be needed.

Genetic evaluation might be needed if syndromes like Noonan and Williams are suspected.

A **skeletal survey** is done if the patient is disproportionate.

Management:
Management depends on the cause.

In case of genetic short stature, patients will not benefit from GH replacement.

In patients with constitutional delay, you reassure their parents, and follow the child up to make sure s/he is having a normal growth velocity. If the child is gaining the centimeters he is supposed to grow each year, this is reassuring. This is more sensitive and specific than doing a GH stimulation test.
Monitor these children till they enter puberty. If delayed puberty caused the child to suffer socially and psychologically, as they see their peers growing and they still look like kids, they can be helped by small doses of testosterone to kick in puberty.

If the patient has any kind of hormone deficiency, the deficient hormone can be replaced.

If the cause is a chronic systemic disease, it should be managed accordingly.

Good Luck :D
Esraa Arabiat

Table 173-3. Differential Diagnosis and Therapy of Short Stature

Diagnostic Feature	Hypopituitarism GH Deficiency*	Constitutional Delay	Familial Short Stature	Deprivational Dwarfism	Turner Syndrome	Hypothyroidism	Chronic Disease
Family history positive	Rare	Frequent	Always	No	No	Variable	Variable
Gender	Both	Males more often affected than females	Both	Both	Female	Both	Both
Facies	Immature or with midline defect (e.g., cleft palate or optic hypoplasias)	Immature	Normal	Normal	Turner facies or normal	Coarse (cretin if congenital)	Normal
Sexual development	Delayed	Delayed	Normal	May be delayed	Female prepubertal	Usually delayed, may be precocious if hypothyroidism is severe	Delayed
Bone age	Delayed	Delayed	Normal	Usually delayed; growth arrest lines present	Delayed	Delayed	Delayed
Dentition	Delayed	Normal; delay usual	Normal	Variable	Normal	Delayed	Normal or delayed
Hypoglycemia	Variable	No	No	No	No	No	No
Karyotype	Normal	Normal	Normal	Normal	45,X or partial deletion of X chromosome or mosaic	Normal	Normal
Free T_4	Low (with TRH deficiency) or normal	Normal	Normal	Normal or low	Normal: hypothyroidism may be acquired	Low	Normal
Stimulated GH	Low	Normal for bone age	Normal	Possibly low, or high if patient malnourished	Usually normal	Low	Usually normal
Insulin-like growth factor-1	Low	Normal or low for chronologic age	Normal	Low	Normal	Low	Low or normal (depending on nutritional status)
Therapy	Replace deficiencies	Reassurance; sex steroids to initiate secondary sexual development in selected patients	None	Change or improve environment	Sex hormone replacement, GH; oxandrolone may be useful	T_4	Treat malnutrition, organ failure (e.g., dialysis, transplant, cardiotonic drugs, insulin)

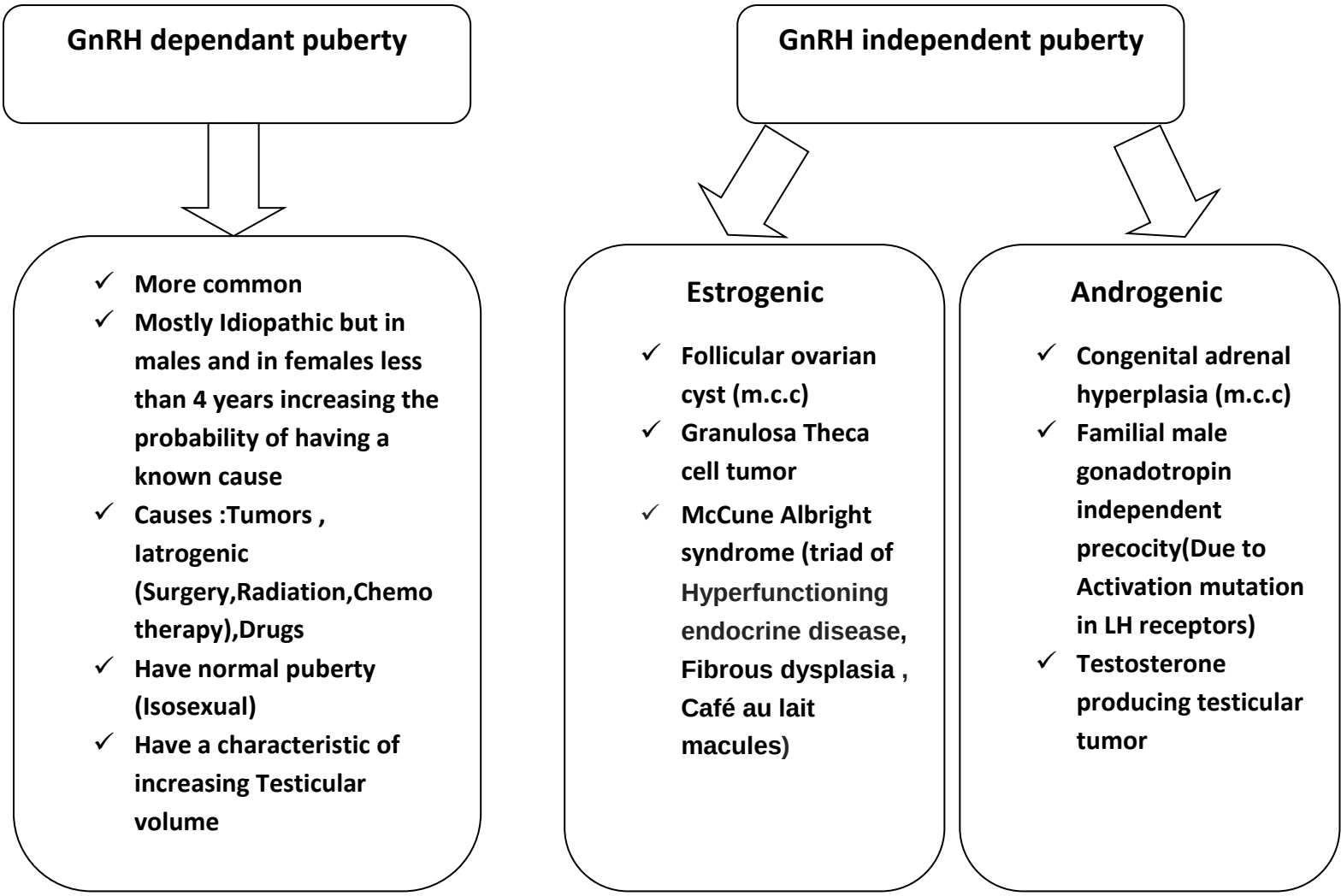
*Possibly with GnRH, CRH, or TRH deficiency.
ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; GH, growth hormone; GnRH, gonadotropin-releasing hormone; T_4, thyroxine; TRH, thyrotropin-releasing hormone.

Precocious puberty

Precocious puberty: Having secondary sexual characteristics (Breast buds in females and Testicular enlargement in males) <8 years in females and <9 years in males.

Notes:

- ✓ Delayed puberty: Having secondary sexual characteristics >13 years in females and >14 years in males.
- ✓ The first sign of puberty in males is Testicular enlargement.
- ✓ Testicular volume > 4 ml → beginning of puberty
  Testicular volume >25 ml → Adult
- ✓ Secondary sexual characteristics:
- ✓ Beast buds → Thelarche
  Pubic hair → Pubarche
  Secretion of DHEA from Adrenal gland → Adrenarche
- ✓ Most common cause of Pubarche is Adrenarche.
- ✓ Patient with normal testosterone level in blood but have Pubarche → Think of increase hypersensitivity in hair follicles.
- ✓ Central precocious puberty is always Isosexual (appearance of phenotypically **appropriate** secondary sexual characteristics).
- ✓ Peripheral precocious puberty could be heterosexual or isosexual.
- ✓ Please refer back to Growth and development lecture and study Tanner staging.
- ✓ If a patient has increasing in Testicular volume → the cause is always Central precocious puberty not peripheral.
- ✓ Premature thelarche : is Thelarche between age 6 month-2 years with normal pubic hair and bone age growth.
- ✓ Most common cause of delayed puberty is constitutional delay in growth and puberty.



Done by: Mohannad abohamad

Congenital Hypothyroidism

Congenital hypothyroidism is considered as neonatal emergency and it is very important to be diagnosed early because if left not diagnosed, by the age of 3-6 months it will result in overt deficiency with developmental delay or motor delay.

The problem is that it cannot be diagnosed at birth (asymptomatic) so here comes the importance of screening.

Epidemiology:

- Prevalence: 1/3500 in white infants.
- F:M ….2:1
- Only 25% of the annual birth population are born in countries with NB screening programs.
- Differ significantly among different ethnic groups.

Clinical manifestations

- Most are asymptomatic at birth.
- Birth weight and length are normal but head circumference may be increased.
- Prolongation of physiological jaundice, hypoactivity, constipation, feeding difficulties, subnormal temperature, slow pulse, and respiratory abnormalities.

If congenital hypothyroidism left undetected, there will be a progression over the following months leading to retardation of physical and mental development and by age of 3-6 months the clinical picture will be overt : short extremities, stunted growth, wide anterior fontanel and posterior fontanel (wide posterior fontanel is a clinical sign that raises the suspicion of congenital hypothyroidism), dry scaly skin, coarse brittle and scanty hair, protrusion of tongue (very late to appear), and hypotonia.

Actions of thyroid hormones:

- Increase the oxidative metabolism: ↑ oxygen consumption, ↑ basal metabolic rate, ↑ glucose and fat metabolism.
- Promote growth and development.
- Essential for normal myelination and development of CNS (by the age of two years **most** of the myelination is completed).
- Augmentation of cardiac function.
- Important for the reproductive function.

Causes:

Permanent causes:

A- The most common cause is **permanent primary** hypothyroidism (↓ T4 ,↑ TSH); particularly thyroid **dysgenesis** (ectopy (m.c), agenesis, hypoplasia, and hemiagenesis). So it is very important when you are suspecting congenital hypothyroidism to examine the mouth looking for lingual ectopic tissue.

Another cause of permanent primary hypothyroidism is **dyshormogenesis,** mostly you cannot find goiter in congenital hypothyroidism ***except*** in dyshormogenesis.

Another cause of permanent primary hypothyroidism is TSH receptor mutation (TSH resistance, rare).

B- Permanent central causes: low T4 and low TSH or

Low T4 with normal TSH (This is inappropriately normal TSH)

That's why we have to measure both TSH and T4 not only TSH.

1. Develpmental defect: pituitary or hypothalamic disorders. May have midline defect**.**
2. Inactivating mutations: TRH receptor, TSH beta subunit, Pituitary transcription factors**.**

C- Permanent peripheral hypothyroidism**:**

1. Abnormal thyroid hormone.
2. Defect in transport into the cell: X-linked/ severe mental retardation
3. Thyroid hormone resistance :mutations in TRB is most common/ ↑ T4, NL or ↑TSH.

Now the transient causes:

- Iodine deficiency.
- Iodine containing antiseptic (we recommend not to use antiseptic containing iodine when doing procedures to neonates involving large surface area because there will be absorption).
- Maternal drugs (clear in 3-4 days after birth).
- Transplacental transfer of TSH-receptor blocking antibodies (↓T4, ↑TSH).
- Hypothyroxemia of prematurity (↓ T4, ↓ T3, NL TSH), -adaptation to prematurity rather than true central hypothyroidism.

Normal thyroid physiology in the fetus:

Fetal bi-lobed shape	7 weeks of gestation
Thyroglobulin	4 weeks
Hypothalamic neurons contain TRH	6 – 8 weeks
Iodine trapping	8 – 10 weeks
The pituitary portal vascular system begins to develop	8 – 10 weeks
TSH secretion	12 weeks
Maturation of the H-P-T axis	2nd half of gestation

Maturation of the H-P-T axis occurs during the second half of gestation, but normal feedback relationships are 1 – 2 months of postnatal life.

The secretion of TSH and thyroid hormones begins at the end of first trimester.
The TSH values differ between neonates and children.

During the first trimester, T4 in circulation is of maternal origin. After that a rise in T4 due to ↑ in hepatic production of TBG, and ↑ in fetal thyroidal production stimulated by TSH.

The level of TSH at first hour of life ranges between (60-80), in the first day declines down to 20, in the first week declines down to 10, so it decreases gradually and if we have a neonate of 10 days age and a TSH value of 8, it is considered as normal.

Total and free T4 and T3 increase to peak at 24-36 hours, then gradually fall in the first 4 weeks of life. Leveling off at slightly higher values than are found in adults. After the 1st 4 weeks NL range for TSH is 0.9-7.7 mU/L.

In PRETERM infants total and free T4 at the time of neonatal screening are proportional to either birth Wt or GA. After birth, they undergo changes in TFT similar to those of term infants, but quantitatively smaller due the immaturity of the H-P-T axis.

Many screening programs recommend a routine second screening test in preterm infants. Infants with ↓free T4 and elevated TSH, should be considered to have congenital hypothyroidism → should be treated.
If normal free T4 but TSH remained ↑, they are considered to have "subclinical hypothyroidism" → should be treated and their TFT should be reassessed later (after 2 years of age).

Investigations:

- TFT
- Thyroid radionuclide uptake and scan:
  - Absent uptake: aplasia or TSH β gene or TSH R-inactivating mutations, iodide- trapping defects and maternal TSH R blocking AB's.
  - Large gland + increase uptake → dyshormogenesis beyond iodide trapping.
- Thyroid ultrasound: - Absent uptake should be followed by U/S to confirm thyroid aplasia. It is as accurate in detecting ectopic thyroid gland as radionuclide scan.
- Serum Thyroglobulin: - absent uptake + low serum Tg → thyroid aplasia.
  - absent uptake + increased Tg → TSH receptor-inactivating mutations, iodide-trapping defects, or maternal TRB-Ab.

Associated defects

- ☒ Major congenital anomalies occur in 3% of the normal population, but in up to 10% of newborns with CH.
- ☒ The most common associated defect is congenital heart anomaly.
- ☒ A hearing problem is reported in up to 20% of infants with CH → should undergo screening hearing tests.

Treatment

It is important to start the treatment early without delaying and waiting for thyroid scan because it needs time and the treatment would not change, the scan is to reassure the parents.
A study showed that infants diagnosed by age of 3 months had an IQ of 89 and infants diagnosed by age of 6 months had an IQ of 71 and more than that had IQ of 34.
Treatment: Levothyroxine (only tablets), there is no solution of levothyroxine has the same bioavailability of the tablet. We tell the mother to crush it and put it with milk or water directly before eating. Dose: 10-15 microgram.

Follow up:

Monitoring serum free T4 and TSH:

- At 2 and 4 weeks after initiation of L-T4 treatment.
- Every 1 to 2 months during the first 6 months of life.
- Every 2 to 3 months between 6 months and 3 yr of age.
- Every 6 to 12 months until growth is complete

Eman Droubi/ edited sheet to contain everything in the slides.

Nephrology

Acid-base disorders

$H_2O + CO_2 \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$
Normal blood PH is 7.35 – 7.45

- Acidemia: PH < 7.35
- Alkalemia: PH > 7.45
- Acidosis: pathologic process causing increase in [H+]
- Alkalosis: pathologic process causing decrease in [H+]

There are 2 ways to control serum PH:

1. Controlling $PaCO_2$ via controlling the respiratory rate and tidal volume (Respiratory compensation: quick, within 12-24 hours).
2. Regulation of kidney's reabsorption of HCO_3^- (Metabolic compensation: within 3-4 days).

Ratio of $PaCO_2$ to HCO_3^- is the determinant of PH, not the absolute level.

- Normal $[HCO_3^-]$ = (20 – 28) mEq/L
- Normal PCO_2 = (35 – 45) mmHg
- Serum anion gap = $[Na^+] – [Cl^-] – [HCO_3^-]$
    - ✓ It represents unmeasured anions.
    - ✓ It is normally 12 ± 4 mEq/L
    - ✓ Increased anion gap = increased unmeasured anions = increased unmeasured acids. So elevated anion gap means always metabolic acidosis.
- Urine anion gap = $[Na^+] + [K^+] – [Cl^-]$
    - ✓ It is normally close to zero.
    - ✓ Used to define the etiology in normal anion gap metabolic acidosis.
    - ✓ Positive urine anion gap means low urine $NH_4^+ \rightarrow$ renal tubular acidosis.
    - ✓ Negative urine anion gap means high urine $NH_4^+ \rightarrow$ diarrhea

Regulation of PH is necessary for metabolic processes. Disorders of PH are either respiratory or metabolic in origin.

1. Respiratory: the initial PH change is due to change in PaCO2 and the kidney slowly responses in an opposite direction.
2. Metabolic: the primary change is in HCO3- and the respiratory rate quickly decreases or increases.

Simple acid-base disorder = single primary disturbance. Mixed acid-base disorder = more than one primary disturbance.

Metabolic disorders

1. Metabolic acidosis
2. Metabolic alkalosis

Metabolic acidosis

Causes:

- Increased production of lactic acids or ketoacids (ischemia, DKA).
- HCO_3^- wasting (diarrhea, RTA type 2)
- Under-secretion of acids (renal failure).
- Ingestion of exogenous acids or compounds metabolized to acids or agents causing lactic acidosis or ketoacidosis.
- Failure to thrive suggests chronic metabolic acidosis.

Types:

1. **Normal anion gap metabolic acidosis**
   - ☒ The main cause is loss of HCO_3^- in diarrhea or RTA
   - ☒ Diarrhea is the most common cause of metabolic acidosis in children.
   - ☒ Mechanism in diarrhea: volume depletion and wasting of HCO_3^-
   - ☒ Other causes: increased organic acids (NH_4^+) in patients with total parenteral nutrition/ inability of the kidney to excrete endogenous acids.
   - ☒ Renal tubular acidosis (RTA): group of transport defects in nephron. We will talk about them later on.
2. **High anion gap metabolic acidosis**
   - ☒ Lactic acidosis.
   - ☒ Ketoacidosis.
   - ☒ Renal failure

Metabolic alkalosis

- It is usually due to activation of aldosterone and aldosterone mediated effect on distal tubules (Na^+/K^+ and Na^+/H^+ pumps) due to volume contraction state (vomiting).
- Hypokalemia contributes to maintenance of metabolic alkalosis by decreasing bicarbonate loss.

Types:

1. **Chloride responsive metabolic alkalosis**
   - ☒ Urine chloride < 15
   - ☒ Volume depletion.

- ☒ We give fluid in management.
- ☒ Causes: gastric loss/ pyloric stenosis/ loop thiazide diuretics/ chloride losing diarrhea.
- ☒ Chloride losing diarrhea: AR/ associated with cystic fibrosis/ post-hypercapnia.

2. **Chloride resistant metabolic acidosis**
   - ☒ Urine chloride > 20
   - ☒ Management: blocking the action of excess mineralocorticoids.
   - ☒ Causes:
     - ✓ High blood pressure: adrenal adenoma/ renovascular disease/ renin secreting tumor/ Liddle syndrome.
     - ✓ Normal blood pressure: Gitelman syndrome/ Bartter syndrome.
     - ✓ Gitelman/ Bartter/ Liddle syndromes: hyponatremia.
     - ✓ Hypokalemia + alkalosis: think of Gitelman and bartter syndromes.
     - ✓ Hypomagnesaemia found in Gitelman syndrome but not in Bartter syndrome.
     - ✓ Bartter: hypercalciuric stones/ sometimes deafness.
     - ✓ Gitelman: hypocalciuria/ cramps/ more common than Bartter/ late childhood.
   - ☒ Symptoms: tetany/ hypoxia/ arrhythmias.

Respiratory acidosis:

- Decrease in effectiveness of CO_2 removal.

Respiratory alkalosis:

- Inappropriate reduction of the blood CO_2 concentration.

Done by Zaina Almusa
Printed by: Rafeef Qawasmeh

Acid base balance

Normal values:

PH=7.35-7.45
HCO3-= 20-28
PCO2=35-45
Anion gap = 10-12

Metabolic acidosis:

Causes :

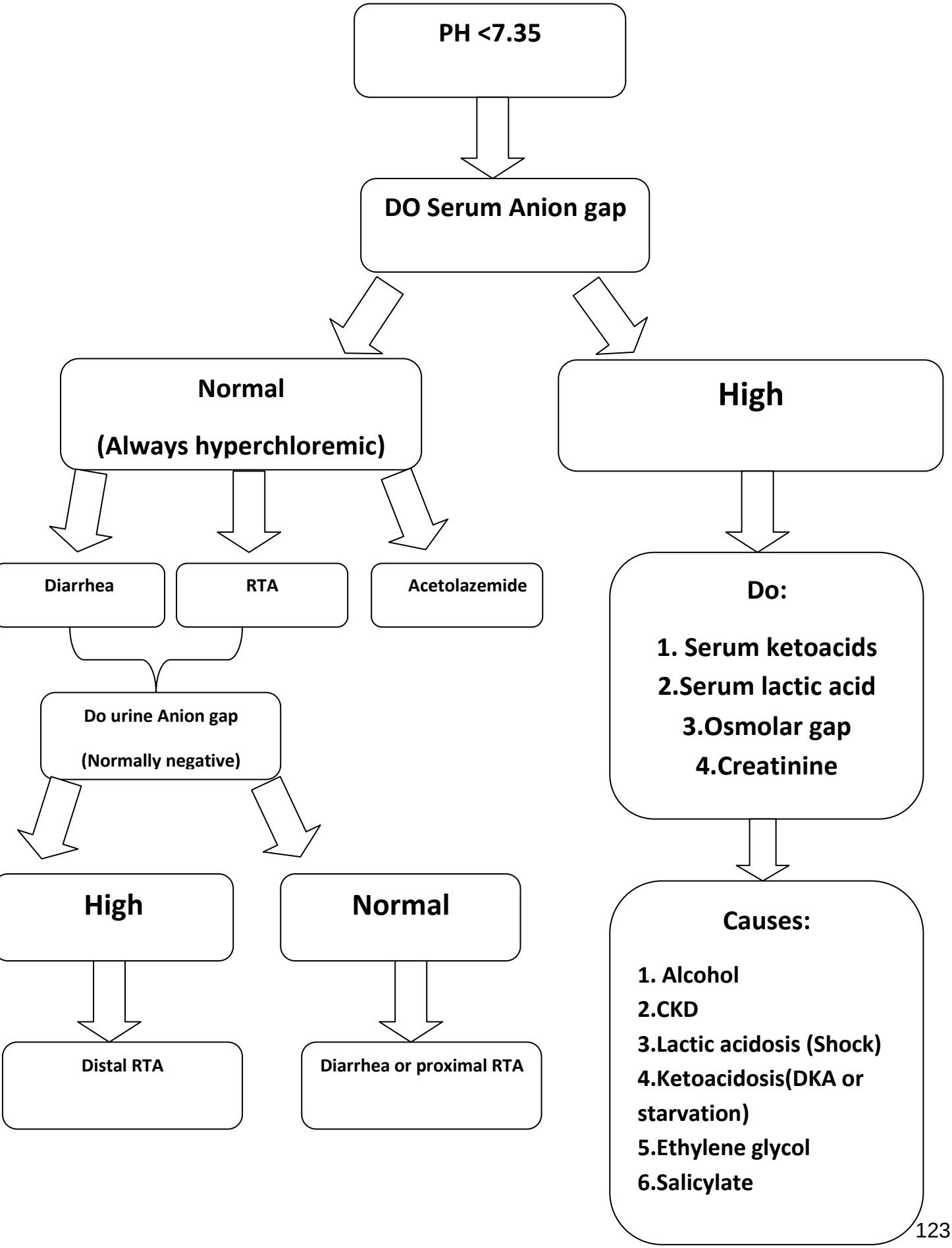
- ✓ Increase excretion of HCO3
- ✓ Decrease excretion of acids
- ✓ Increase production of acids
- ✓ Acidic drugs and poisons

Look at the diagram below but before you have to know that:

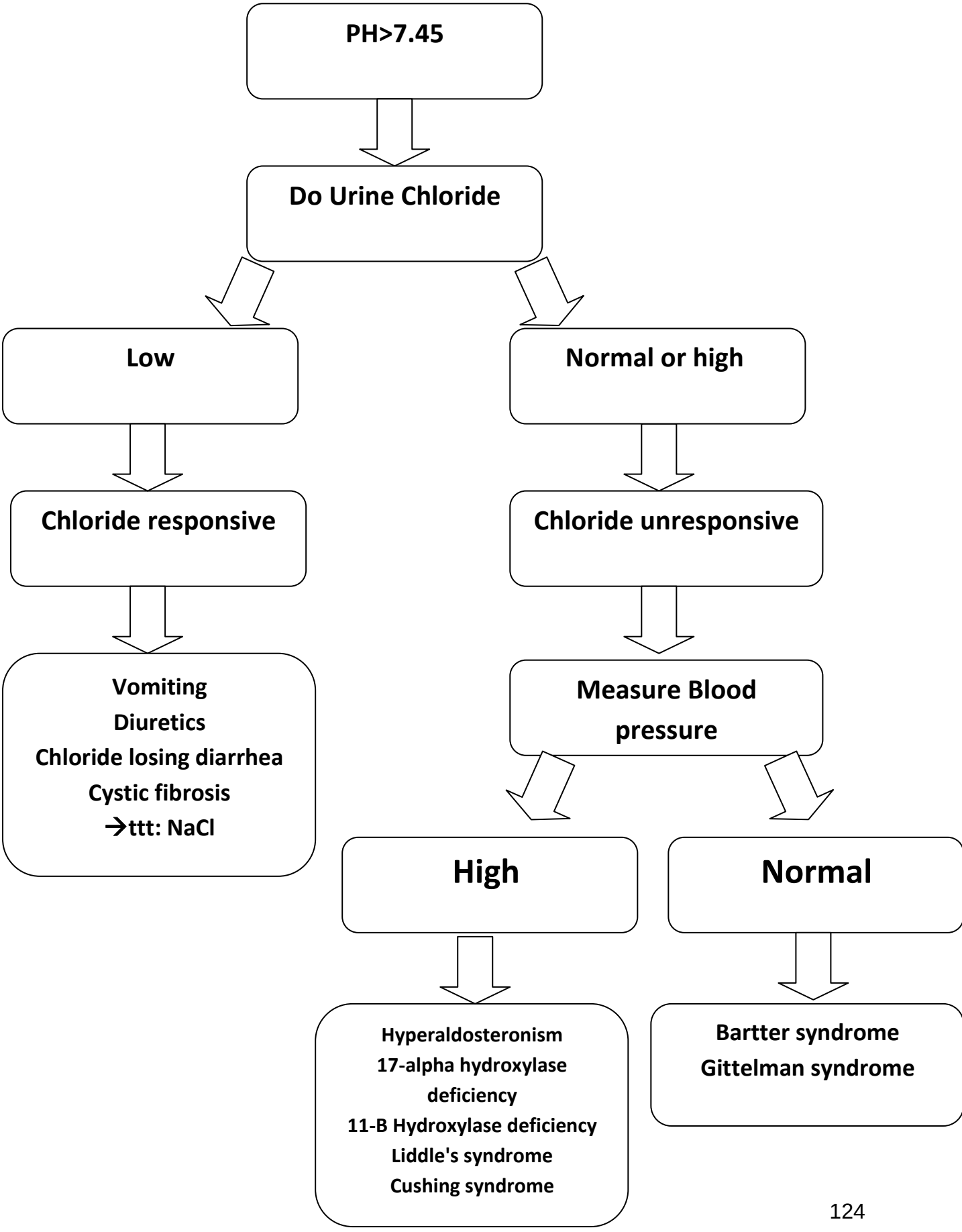
- ✓ Serum Anion gap =Na^+ -(Cl^- + $HCO3^-$)
  Urine Anion gap = Na^+ + K^+ - Cl^-
- ✓ Osmolar gap =Meausred Osmolarity – Calculated Osmolarity

Calculated serum osmolarity

$$2\times[Na^+](meq/L)+\frac{Glucose\,(mg/dL)}{18}+\frac{BUN\,(mg/dL)}{2.8}$$


PH <7.35
DO Serum Anion gap
Normal
(Always hyperchloremic)
High
Diarrhea
RTA
Acetolazemide
Do urine Anion gap
(Normally negative)
High
Normal
Distal RTA
Diarrhea or proximal RTA
Do:
1. Serum ketoacids
2.Serum lactic acid
3.Osmolar gap
4.Creatinine
Causes:
1. Alcohol
2.CKD
3.Lactic acidosis (Shock)
4.Ketoacidosis(DKA or starvation)
5.Ethylene glycol
6.Salicylate

Metabolic alkalosis:



Some Differences Between Bartter Syndrome and Gitelman Syndrome

Feature	Bartter Syndrome	Gitelman Syndrome
Location of kidney defect	Ascending loop of Henle (mimics effects of loop diuretics)	Distal tubule (mimics effects of thiazides)
Urinary calcium excretion	Normal or increased, commonly with nephrocalcinosis	Decreased
Serum magnesium level	Normal or decreased	Decreased, sometimes greatly
Renal prostaglandin E2 production	Increased	Normal
Usual age at presentation	Before birth to early childhood, often with intellectual disability and growth disturbance	Late childhood to adulthood
Neuromuscular symptoms (eg, muscle spasms, weakness)	Uncommon or mild	Common

Liddle syndrome

It is a rare autosomal dominant disorder of renal epithelial transport that clinically resembles primary aldosteronism, with hypertension and hypokalemic metabolic alkalosis and with low plasma renin and aldosterone levels. The syndrome results from an inherently increased activity of the epithelial sodium channels (ENaC), located on the luminal membrane in the collecting tubule, which accelerates sodium resorption and potassium secretion (underactivity of ENaC causes sodium excretion and potassium retention.

Diagnosis is suggested by the presence of hypertension in a young patient, particularly one with a positive family history. Low urine sodium (<20 mEq), low plasma renin and aldosterone levels, and response to empiric treatment usually are considered sufficient to confirm the diagnosis. Definitive diagnosis can be achieved through genetic testing.

Treatment: Triamterene 100 to 200 mg po bid and amiloride 5 to 20 mg po once/day are both effective because they close sodium channels. Spironolactone is ineffective.

Source: Merck manuals

Renal tubular acidosis (RTA)

It is a clinical-biochemical syndrome characterized by impaired renal acidification.

Type 1 (distal)	**Type 2 (proximal)**	**Type 4 (hyperkalemic)**
Impairment of hydrogen ion excretion in distal tubules (impaired distal acidification). Urine PH >5.5 always. Potassium reabsorption is impaired (hypokalemia). hyperchloremia Plasma HCO_3- <15 mEq/L Impaired excretion of NH_4^+ (positive urine anion gap) Hypercalciuria, nephrocalcinosis, decreased citrate excretion Urine to blood PCO_2 <15 It is almost always observed as a 1ry inherited entity (AD- mild or AR- severe with deafness)	Impairment of HCO_3 reabsorption in the proximal tubule (hypokalemia). Decreased renal bicarbonate threshold. Distal acidification remains intact. When plasma bicarbonate concentration decreases to a level below the renal threshold, patients may lower urine pH below 5.5 and excrete adequate amounts of NH_4. Negative urine anion gap. Most common in Fanconi syndrome (global proximal tubule dysfunction): glycosuria, phosphaturia, aminoaciduria, uricosuria, proteinuria, hypophosphatemia. May also occur as 1ry inherited disease. Urine to blood PCO_2 > 25 (normal; reflects normal H^+ secretion)	Involves an acidification defect that is primarily caused by impaired genesis of ammonia. Normal ability to acidify the urine after an acid load. However, net acid excretion remains subnormal due to a very low rate of NH_4 excretion. The decrease in NH3 production is largely caused by hyperkalemia. It is associated with low aldosterone states such as congenital adrenal hyperplasia, with aldosterone resistant states such as pseudohypoaldosteronism, and with medications such as spironolactone, ACE inhibitors, trimethoprim, and ARBs. Hyponatremia. Urine PH < 5.5 Negative urine anion gap. Urine to blood PCO2 <15 Most common type of RTA. Can occur in obstructive uropathy.

History:

- A pediatrician may suspect RTA during the workup of children with failure to thrive.
- Possible history of repetitive episodes of dehydration, with vomiting, or constipation.

Physical examination:

- May reveal only growth retardation, or signs of dehydration, or a secondary disease (cystine crystals in the cornea in patients with cystinosis).

Lab evaluation:

- The first step in the evaluation of children with metabolic acidosis is calculation of the plasma anion gap: Na-(Cl+HCO3) =12+-4 mEq/L.

Urine pH:

- This measurement has been used for diagnosis of distal RTA (type1), the only type of RTA in which the urine pH cannot decrease below 5.5-6 regardless of the severity of the acidosis.
- A urine pH of > 6 in the setting of metabolic acidosis suggests a defect in distal acidification. However, the urine pH may be misleading. Although urine pH of <5.5 rules out distal RTA (type 1), it does not ensure a normal distal acidification because it does not reflect the rate of NH4 excretion.
- It is important to assess the plasma potassium for characterization of RTA.

Other studies:

- FEof HCO3, Urine-Blood Pco2, renin & aldosterone for RTA type 4. Ulatrasound (to diagnose nephrocalcinosis & nephrolithiasis).

Management:

- The first goal in the treatment of both proximal and distal RTA is the correction of the metabolic acidosis with the use of daily alkali supplementation.
- Generally, patients with proximal RTA need a larger dose of alkali than patients with distal RTA.
- Potassium abnormalities should be corrected. Hypokalemia is treated with potassium supplementation; whereas hyperkalemia may need a potassium-restricted diet, diuretics, or potassium-binding exchange resin distal RTA.

Approach to metabolic acidosis

1. Look at the anion gap; if it is normal, think of diarrhea and RTA.
2. If no diarrhea; look for potassium. If high potassium, it is type 4 RTA.
3. If low potassium; look for urine PH. Increased in type 1 RTA.

How to differentiate distal and proximal RTA?

1. Urinalysis: glycosuria, uric acid and phosphate in urine; goes with proximal.
2. Ultrasound: if showing calcinosis; think of distal type.
3. Urine PH: in proximal it can be below 5.5 but not in distal.
4. Urine anion gap: positive in distal.

Case:

Patient admitted via ER with tachypnea, PH = 7.2, PCO_2 = 25, HCO_3^- = 8

- What is the metabolic disorder? Metabolic acidosis.
- What investigations to order? Sodium and chloride to measure the anion gap.
- If anion gap was 30, what is the next step? Blood sugar to check for DKA, urea and creatinine to rule out renal failure.
- If anion gap was 10, what investigation to order? Urinalysis.
- If patient came to you with failure to thrive and normal anion gap metabolic acidosis? Check potassium, if it is low (type 1 or 2 RTA)

Zaina Almusa & Rafeef Qawasmeh

Evaluation of renal function

A focused history and physical examination is of paramount importance.

Blood tests: serum creatinine, urea, serum electrolytes. Creatinine is better than urea. However, creatinine clearance is better than serum creatinine for assessing kidney function.

Serology: For new cases of hematuria, proteinuria, glomerulonephritis, and nephritic syndrome check ANA, Anti DNA for lupus, C3 and C4, hepatitis B and C serology.

Urinalysis: is like a living biopsy. Normal urinalysis: specific gravity 1.010-1.025. Dipstick : pH 4.6-8.0 , glucose negative , protein negative to trace , blood negative or trace , leukocyte esterase negative (positive if WBC) , nitrite negative(positive if UTI). Microscopy: RBC <3-5/HPF, WBC <2/HPF.

Casts: RBC casts → glomerular disease.
Hyaline casts → physiologic.
Granular casts (hyaline casts filled with granules→ proteinuria.
Crystals: significant according to the clinical situation.

Glomerular filtration rate (Creatinine clearance): a timed urine collection.

$$\frac{Ucr_{(umol/L)} \times Uvol_{(ml)} \times 1.73}{Scr_{(umol/l)} \times \text{time in hours} \times \text{surface area of child}} = ml/min/1.73m^2$$

For cases of CKD check:
Updated Schwartz formula: [Ht(cm)/serum creat(mg/dL)] x 0.413
For cases of metabolic acidosis first check serum anion gap.
Anion gap = (Na+)-(Cl+HCO3): normal 8-12.
Imaging: see UTI
Spiral CT: Gold standard for detecting stones. It is more sensitive than IVU and ultrasound.

Renal biopsy indications

Steroid resistant, atypical poststreptococcal glomerulonephritis, kidney transplant rejection, and before starting cyclosporin.

For renal biopsy to be useful; a specimen should be sent for light microscopy (in formali), immunoflorescence (in normal saline), and electron microscopy (in glutareydehyde).

proteinuria

- May be physiologic, orthostatic, or pathologic.
- History and physical examination is important. Initially spot morning urine is tested. May need 24 hour collection.

Urinary protein

- Spot $U_{protein}/U_{Creatinine}$ ratio (mg/L: mmol/L). Normal: < 50 mg/mmol/l in first few months, and <20 mg/mmol/L in older children. Nephrotic range : >250 mg/mmol/L.
- Microalbuminuria: 30-300
- 24 hour urine collection: Most accurate. Normal: < 4mg/m^2/h, Abnormal: 4-40 mg/m^2/h, and Nephrotic range: > 40 mg/m^2/h or > 50 mg/kg/day.
- Spot U_{ca}: U_{cr} ratio normal < 0.2. If more do 24 hour urine collection. Normal < 4 mg/kg/24 h.

Sources: Dr. Kamal Aqel handout

Approach to red urine (source: Dr. Jumana slides)

Causes of red urine

- Hemoglobinuria: G6PD deficiency
- Myoglobinuria: trauma, seizures, rhabdomyolysis
- Drugs (rifampicin),food
- Inborn errors of metabolism(porphyria)
- Urate crystals
- Hematuria: macroscopic

Analysis of hematuria

- Onset
- Color: Red if fresh (bladder), or brown color as Hb converted to acid haematin by urinary acids in renal causes
- Timing: Early hematuria (urethral cause) ,Terminal hematuria (bladder cause)
- Presence of clots : extra renal causes
- Painful/painless, symptomatic/asymptomatic
- gross/ microscopic
- Transient /persistent
- With or without proteinuria

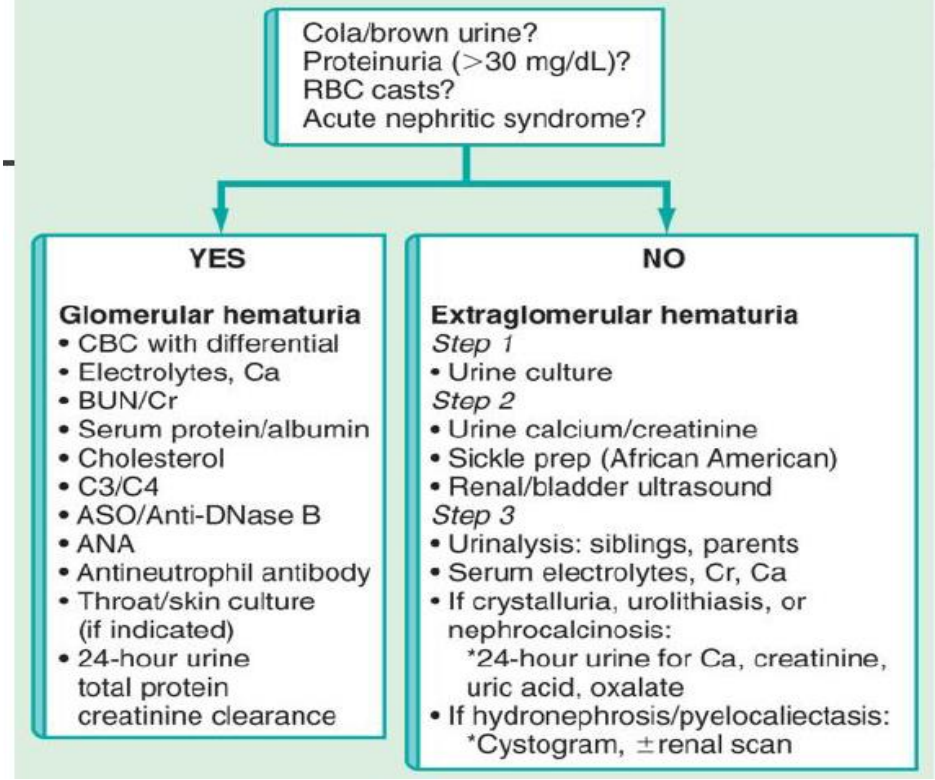
History and associated symptoms	Physical examination
• Fever, urinary symptoms ,dysuria, frequency, loin pain, supra-pubic pain. (looking for cystitis/ pyelonephritis/ stones) • Age/gender • Periorbital edema, lower limb edema, decreased urine output • Preceding URTI: PSGN, IgA nephropathy • History of previous attacks of red urine • Rash, arthritis …HSP, SLE • Coagulopathy, bleeding tendency • trauma • FH of hematuria, deafness, renal failure: Alport syndrome • FH of renal stones	• Vital signs: fever for UTI, hypertension for glomerulonephritis • Looking for edema: lower limbs, eyes • Abdomen exam: masses, (PCKD), tenderness • Genitalia exam

Investigations

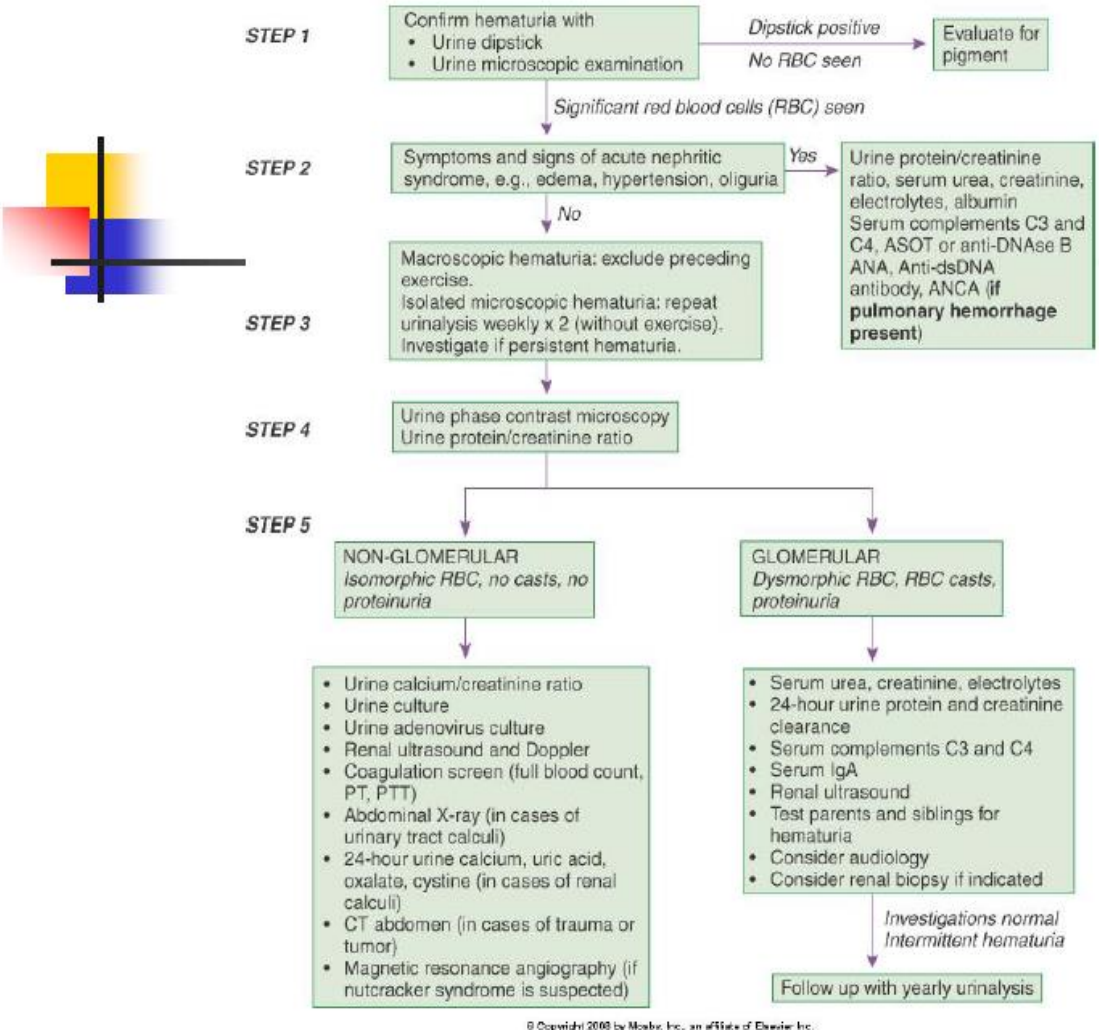
- Urine dipstick positive for hemoglobinuria, myoglobinuria (Positive heme, negative analysis), hematuria
- Microscopy: look for RBC, WBC, bacteria (UTI), high grade proteinuria (GN) ,crystals
- Dysmoprhic RBC by phase contrast microscopy, RBC cast: glomerular bleeding
- Urine protein/creat ratio, Electrolytes, albumin, KFT, ASOT, C3, C4, ANA for GN causes
- Urine culture if UTI
- CBC if infection, PT, PTT
- Urine calcium/creat ratio, 24 h urine collection
- U/S ,XRAY, spiral CT
- Later: Urine analysis for parents , cystoscopy, Renal biopsy

Distinguishing extraglomerular from glomerular hematuria

	Extraglomerular	Glomerular
Color (if macroscopic)	Red or pink	Red, smoky brown, or "Coca-Cola"
Clots	May be present	Absent
Proteinuria	Usually absent	May be present
RBC morphology	Normal	Dysmorphic
RBC casts	Absent	May be present



- Prevalence of microscopic hematuria is 0.5-2 %
- Definition of hematuria is the presence of more than 5 cells per high power field of centrifuged urine
- Transient hematuria seen with fever and exercise
- Persistent asymptomatic hematuria, weekly for three times, needs to be investigated
- Urethrorrhagia: urethral bleeding associated with blood spots after voiding, prepubertal



Macroscopic (gross) hematuria causes

- Most common cause is infection, then perineal irritation, trauma
- Viral infections, adenoviruses 11 and 12 may cause hemorrhagic cystitis
- Exercise induced hematuria not associated with renal disease.
- Recurrent gross hematuria as IgA nephropathy, Alport syndrome, nutcracker syndrome (thin patient/ loin pain/ compression of left renal vein between aorta and SMA)

Glomerular causes of hematuria	Non-glomerular causes of hematuria
✓ Familial benign hematuria ✓ Primary GN: postinfectious GN, MPGN, IgA nephropathy, ALport ✓ Secondary GN as SLE, HSP → (*Abdominal pain *Renal disease - hematuria *Palpable purpura-non-blanching) ✓ HUS, Acute tubular necrosis, interstitial nephritis, renal vein thrombosis, cystic renal disease ✓ Pyelonephritis, PCKD, Wilms tumor	✓ UTI ✓ Hypercalcuria, renal calculi, crystalluria ✓ Trauma, exercise ✓ Coagulopathy as sickle cell ✓ Vascular malformations ✓ Nutcracker syndrome ✓ Menarche ✓ Malignancy as nephroblastoma of the kidney or bladder tumors

Benign familial hematuria

- AD inheritance
- Present as microscopic hematuria, no proteinuria or renal failure
- EM: thinning of GBM
- Follow up for proteinuria, HTN

IgA nephropathy (Berger's disease)

- Recurrent macroscopic hematuria, loin pain 1-2 days following URTI, last < 3 days.
- Persistent microscopic hematuria ± proteinuria
- Mainly nephritic, nephrotic syndrome is rare
- Present in second decade, more in males
- Familial cases reported
- IgA high in 35-50%
- Diagnosis: LM (focal or diffuse mesangial cell proliferation, expansion of mesangial matrix)
- IM: IgA, C3 deposits
- Prognosis for children is better than for adults
- Young children without macroscopic hematuria have the best long term outcome
- Heavy proteinuria is a risk factor for progression to ESKD.
- Progression to ESRD is slow (25% need dialysis in 20y)
- ACEI are used to delay progression and decrease proteinuria

Alport syndrome

- 80% X-linked, 20% AR
- Renal failure, sensorineural deafness higher frequencies, ocular changes (anterior lenticonus, retinal changes)
- Present as micro and rarely macroscopic hematuria with URTI
- Proteinuria, HTN at later age
- Diagnosis by EM: Thinning of GBM, split and duplicated lamina densa, basket weave
- Males progress to ESRD, deafness by 30y
- ACEI may delay progression to ESRD
- Deficiency of α5 of type 4 collagen

Post streptococcal glomerulonephritis (PSGN)

- Follows GAS pharyngitis in winter, pyodrema in summer
- Certain nephritogenic M types, age 5-15 y, M:F 2:1
- Risk of PSGN following GABHS is 15%
- antibiotic treatment doesn't prevent PSGN
- Clinical features: latent period 10-14 days after pharyngitis, 3-6 wk after pyoderma
- Histopathology: exudative proliferative GN
- EM: deposits, humps on subepithelial side of GBM
- Clinical manifestations:
    - ✓ Nephritic syndrome: (edema, oliguria, HTN, hematuria, azotemia)
    - ✓ Gross hematuria 30-70% resolves in 1-2 wk, cola urine, relapses appear after infection and exercise
    - ✓ Microscopic hematuria, proteinuria
    - ✓ Edema due salt & water retention, oliguria
    - ✓ HTN 80% resolves in 4 wk
    - ✓ Malaise, lethargy, flank pain
- Complications:
    - ✓ pulmonary edema, HTN encephalopathy, CHF, ARF
    - ✓ Nephrotic syndrome, RPGN rare
    - ✓ Subclinical disease in 90% of cases
- Lab findings:
    - ✓ Urine shows dysmorphic RBC, casts
    - ✓ High K, acidosis, uremia, Throat culture
    - ✓ High ASOT, anti-DNAs after skin infections
    - ✓ 90% have low C3, normalize after 6-8 wk
- Treatment:
    - ✓ salt and water restriction
    - ✓ loop diuretics
    - ✓ anti-HTN drugs, calcium channel blockers
    - ✓ Pulse steriods in cresentic RPGN
    - ✓ Dialysis in ARF
- Prognosis:
    - ✓ Acute phase resolve in 6-8 weeks
    - ✓ Persistent proteinuria for 6 m
    - ✓ Persistent hematuria for 1-2 y
    - ✓ Excellent long term outcome
    - ✓ Rare recurrence, Mortality <1%

This lecture aims to differentiate between acute nephritis and nephrotic syndrome.

A patient with acute nephritis presents with hypertension, oliguria, hematuria, azotemia, decreased kidney function and edema, while in nephrotic syndrome, edema and proteinuria are always present, while the other disorders present in acute nephritis may not be present.

In acute nephritis, proteinuria is mild or moderate, while it's heavy in nephrotic.

PSGN (poststreptococcal glomerulonephritis) is the prototype of acute nephritis. Glomerular disease can be silent, it may as well present with mild symptoms like hematuria or proteinuria, or may present with acute nephritis and renal failure. RPGN is now called crescentic GN.

Infections other than streptococcal infections can cause glomerulonephritis, including chickenpox, EBV, mumps; any virus can potentially cause GN.

There are nephrogenic strains (as well as cardiac strains) of streptococcus, so it's unlikely for a patient to present with both PSGN and rheumatic fever simultaneously.

PSGN usually affects children between 3-12 years, and it's unlikely for a patient under the age of 3 to present with PSGN.

It's an immune complex disease with consumption of complement, there's a debate whether these immune complexes form in the circulation or inside the kidney.

PSGN (biopsy shows subepithelial humps) is proliferative in nature, deposition of complexes causes narrowing of bowman's space, causing oliguria→fluid retention, edema, hyperkalemia,,,etc.

There's a latent period after acute strep infection, 10-14 days after acute pharyngitis, and 2-3 weeks after impetigo. In tropical areas, it's more likely for impetigo than pharyngitis to cause PSGN.

Gross hematuria may be present, it may persist for a week or two until it resolves, for 1-2 years after that, each upper respiratory infection, triggers gross hematuria. A patient may present with the relapse of gross hematuria rather than the primary episode (all serologic parameters are normal by then),so you have to ask about prior episodes of hematuria preceded by respiratory tract infections.

Major causes of gross hematuria in Arab countries are: UTI, glomerular disease, crystals and stones. 30% each, and 10% for the rest (trauma, drugs, sickle cell).

Once edema is present in a patient with hematuria, you have to think of glomerular disease, and distinguish whether it's primary or secondary (ask about presence of

photosensitive skin rash and aphthous ulcers),a detailed history is very important in patients with gross hematuria.

RBC casts are classically found in patients with glomerular disease, dysmorphic RBCs (>25% dysmorphic RBCs are enough for the diagnosis of glomerular disease), but it requires phase contrast microscopy to be visualized, and it's not available here in Jordan.

Clinical presentation: Salt/water retention causing edema and hypertension, one injection of furosemide is sufficient to relieve salt and water retention.

70% of PSGN cases are subclinical (microscopic hematuria and low complement)

The hypertension in PSGN is usually biphasic, it goes up for 4-5 days, and returns back to normal, and then peaks again after 2 weeks.

Complications:

1**- Circulatory congestion**, resulting in edema, hypervolemia and hypertension (can lead to hypertensive emergency with end organ damage (retina, CNS, heart, kidney), severe blood pressure elevations can also result in hemolysis), these all can be treated by a single injection of furosemide.

In hypertensive encephalopathy, BP has to be dropped gradually (25% of the MAP in the first 2-3 hours), one subcategory of hypertensive encephalopathy is posterior reversible encephalopathy syndrome (PRES), patients suddenly become aphasic and lose their vision (it mainly affects occipital and parietal lobes, and sometimes temporal).it's usually reversible after 2 weeks if detected early.

2 -**Acute renal failure.**

What we mentioned, applies to 95% of patients with PSGN, 5% are atypical, presenting as nephrotic syndrome (it's called nephritic nephrotic syndrome).

Lab Findings in patients with PSGN:

Urinalysis: acidic urine pH, high specific gravity (due to concentrated urine), FE_{Na} is <1% (like prerenal , because tubules are normal) , RBC casts (the most important finding) , mild to moderate proteinuria, white cells.

Dilutional anemia(normochromic normocytic).

Hyperkalemia, acidosis.

Throat swab (patient should be treated if positive)

ASO titer (the rise may be attenuated by antibiotics)

Complement (C3) will be low, it usually gets back to normal after 8 weeks, test is repeated after 12 weeks, if it's still elevated, it's not PSGN.

Indications for biopsy in PSGN:

- Normal complement.
- If a patient presents 2-3 days after upper resp. tract infection (it's IgA nephropathy)
- If history suggests nephritic nephrotic syndrome (it might be membranoproliferative or lupus)
- If the complement doesn't come back to normal after 8-12 weeks.

Differential Diagnosis:

-IgA nephropathy (if patient presents within 3 days of respiratory infection)

- Alport syndrome

-benign recurrent hematuria (the new terminology is thin basement membrane nephropathy) ,it's a relative of alport.

Treatment:

Bed rest (for 2-3 days)

Fluid and salt restriction

Protein: 1g/kg/day (if decreased GFR).

Adequate calories: at least 300 calories/m2/day, to prevent catabolism (because catabolism causes hyperkalemia and acidosis)

Furosemide is given at a dose of 1mg/kg, higher doses are given in patients with pulmonary edema (furosemide can cause ototoxicity).

If hypertension doesn’t resolve, drugs like CCBs can be used.

For hypertensive emergencies, drugs of choice are labetolol (not used in patients with asthma) or nitroprusside.

Restrict potassium in patients with hyperkalemia, if potassium levels don’t drop, give calcium gluconate to protect the heart, then add kayexalate, if still no response, do dialysis.

PSGN is not like rheumatic fever, prophylactic antibiotics are not given.

Indications for dialysis:

- Severe hyperkalemia not responding to medical treatment
- Azotemia (relative indication)
- Metabolic acidosis not responding to medical treatment (sodium bicarbonate may increase the circulatory congestion, so we have to be careful)
- Uncontrolled hypertension (rare)
- CV insufficiency.
- Pulmonary edema not responding to diuretics.

PSGN is not always a benign condition; some patients may end up with renal insufficiency resulting from PSGN.

The most important risk factor for acute kidney injury is underlying chronic kidney disease.

SGA is a risk factor for developing CKD.

CHAPTER 164

Hemolytic Uremic Syndrome

Etiology and Epidemiology

Hemolytic uremic syndrome (HUS) is characterized by the triad of **microangiopathic hemolytic anemia, thrombocytopenia,** and **renal injury** and is an important cause of acute kidney injury in children. HUS typically occurs in children less than 5 years of age, but can occur in older children. The most common type of HUS is associated with a prodromal diarrheal illness (**D + HUS**). Contamination of meat, fruit, vegetables, or water with verotoxin (VT)-producing *Escherichia coli* (most commonly ***E. coli* O157:H7**) is responsible for many outbreaks. VT may be produced by other *E. coli* strains as well as other bacteria such as *Shigella*. VT causes hemorrhagic enterocolitis of variable severity and results in HUS in ~5-15% of affected children.

HUS presenting without a prodrome of diarrhea **(atypical HUS)** may occur at any age. The clinical course is usually more severe than D + HUS. Atypical HUS can be secondary to infection (*Streptococcus pneumonia*, human immunodeficiency virus), genetic and acquired defects in complement regulation, medications, malignancy, systemic lupus erythematosus, and pregnancy.

Clinical Manifestations

Classic D + HUS begins with enterocolitis, often with bloody stools, followed in 7-10 days by weakness, lethargy, and oliguria/anuria. Physical examination reveals irritability, pallor, and petechiae. Dehydration is frequent; however, some children have volume overload. Hypertension may be due to volume overload and/or renal injury. Central nervous system (CNS) involvement, including seizures, occurs in up to 25% of cases. Other potential organ involvement includes pancreatitis, cardiac dysfunction, and colonic perforation.

Children without evidence of diarrheal prodrome may have a similar microangiopathic syndrome, identified as **thrombotic thrombocytopenic purpura** (TTP). Children with TTP typically have predominant CNS symptoms but may also have significant renal disease. Recurrent episodes are common. Because CNS involvement is also seen in HUS, TTP can be difficult to distinguish from HUS in some cases. Deficiencies of ADAMTS13, a von Willebrand factor-cleaving protease, have been identified in children affected with TTP.

Diagnostic Studies

Common laboratory findings in HUS are listed in Table 164.1. Peripheral blood smear reveals evidence of microangiopathic hemolysis. Coombs test is negative. Diarrhea and presence of toxin-producing *E. coli* may have resolved by the time HUS is diagnosed.

TABLE 164.1

Common Laboratory Findings With Hemolytic Uremic Syndrome

EVIDENCE OF MICROANGIOPATHIC HEMOLYTIC ANEMIA
Anemia
Thrombocytopenia
Presence of schistocytes, helmet cells, and burr cells on peripheral blood smear
Increased LDH
Decreased haptoglobin
Increased indirect bilirubin
Increased AST
Elevated reticulocyte count
EVIDENCE OF RENAL INJURY
Elevated creatinine
Presence of hematuria, proteinuria, pyuria, casts on urinalysis
OTHER POTENTIAL FINDINGS
Leukocytosis
Positive stool culture for *E. coli* O157:H7
Positive stool test for shiga-toxin
Elevated amylase/lipase

AST, Aspartate aminotransferase; *E. coli*, *Escherichia coli; LDH,* lactate dehydrogenase.

Treatment and Prognosis

Therapy for HUS is supportive and includes volume repletion, hypertension control, and managing complications of renal insufficiency, including dialysis when indicated. Red blood cell transfusions are provided as needed. Platelet transfusions should be avoided because they may add to the thrombotic microangiopathy and are indicated only by active hemorrhage or prior to a procedure. Antibiotics and antidiarrheal agents may increase risk of developing HUS. Early hydration during the diarrheal phase may lessen the severity of renal insufficiency. Most children (>95%) with D + HUS survive the acute phase and recover normal renal function, although some may have evidence of long-term renal and other morbidity.

Nephrotic syndrome

- ☒ May be primary or secondary.
- ☒ **Minimal change nephrotic syndrome**: Most common in children.
- ☒ The nephrotic syndrome consists of heavy proteinuria, hypoalbuminemia, and hyperchlesterolemia. The proteinuria is > 50 mg/kg/day or >40 mg/m^2/hour.

Presentation

- ☒ The child presents with periorbital edema, usually in the morning, to subside during the day. Later on gets leg edema. Initially, often mistaken for allergy.
- ☒ There may be decreased urine output. When serum albumin drops below 2.5 and 1.5 gm/dL ascites edema and ascites appear respectively.

Complications

- ☒ The most common complications of nephrotic syndrome are infections, thrombosis, and hypovolemia. Other complications include acute renal failure (uncommon) and malnutrition. Infections include peritonitis, UTI, cellulites, and upper respiratory infections. Spontaneous bacterial peritonitis is most commonly caused by Strep pneumonia, but may also be due to E coli and Hemophilus influenzae. Thrombotic phenomena are due to loss of coagulation factors, and are exacerbated by overzealous use of diuretics. Hypovolemia usually occurs during relapse. One should be on the lookout for dehydration during diuresis.

Treatment

- ☒ Salt restriction.
- ☒ No need for fluid restriction except if there is acute renal failure or hyponatremia (Na < 125 mEq/L).
- ☒ The standard treatment consists of oral prednisolone at a dose of 2 mg/kg/day or 60 mg/m^2/day in 3 divided doses for 6 weeks, then 40 mg/m^2/day given every other day for another 6 weeks. Some like to give steroids for a longer period to avoid relapses. However, the side effects of steroids must be taken into consideration.
- ☒ Any child taking steroids for more than one month should be put on calcium and vitamin D .A DEXA scan may be done every 6-12 months.

- ☒ **Use of statins**: sometimes the lipid abnormalities persist when the child is in remission. Also in cases of steroid resistance or dependence, or frequent relapse use of statins may be indicated.

☒ **Use of albumin**: at a dose of 1 gm/kg is indicated if there is genital edema, respiratory distress from distended abdomen, and oliguria from hypoalbuminemia. A chest film should be done to assess if the patient is hypervolemic. In this case furosemide is given without albumin. In cases where the volume status is unclear, a small dose of albumin (0.2-0.5 gm/kg) is given with two doses of furosemide during and after the albumin infusion.

☒ **Immunization**: all nephrotics are encouraged to take pneumococcal, influenza, and chickenpox vaccines.

Source: Dr. Kamal Aqel handout.

Definition

- Nephrotic range proteinuria: Urinary protein excretion greater than (50 mg/kg/day)
  Or we can say it is (>40 mg/m^2/hour)
  Or (+3-4 on dipstick)
- first-morning urine protein/creatinine of 2 mg/mg creatinine or greater
  (If <0.2 it is negative, if 0.2-2 it is non-nephrotic ratio proteinuria)
- Hypoalbuminemia − Serum albumin concentration less than 2.5 g/dL
  (This will cause Edema)
- Hyperlipidemia
  (High cholesterol and TGA)
  The mechanism of Hyperlipidemia:
  1) Due to hypoalbuminemia the liver will try to compensate by increasing the albumin synthesis. This increased synthesis would be accompanied by increase in lipoproteins synthesis.
  2) Abnormalities in regulatory enzymes, such as lipoprotein lipase and lecithin-cholesterol acyltransferase.

Epidemiology

More common in males and usually < 6yrs.

Pathogenesis

3 Theories were discussed:
1) The most recent theory suggests that a genetic mutation in **Nephrin** (transmembrane protein that is a major structural element of the slit diaphragm) And **Podocin** (this is another podocyte protein that interacts with nephrin and is integral to the assembly of the slit diaphragm) will lead to disruption in the podocytes of the slit diaphragm which will cause a leakage across the glomerular membrane.

2) A circulating factor (cytokine VPF) which alters the slit diaphragm and increases the proteins permeability. (This factor explains the early recurrence after renal transplant for FSGS patients; the disease returned as fast as 1 hour after the surgery. This fast recurrence was the hint for searching for something with a rapid action such as a circulating factor)

3) Immune mediated disease.
Nephrotic syndrome has been reported in patients with Hodgkin lymphoma, a T-cell disease. In addition to T-cells, the recent studies show a role for B cells in the pathogenesis of nephrotic syndrome.

Pathophysiology

A mutation in the slit diaphragm or in the foot processes of the podocytes can lead to a disrupted leaky glomerular membrane and as a result proteins will be lost in the urinary space.

So a genetic mutation in Nephrin (in slit diaphragm) or in Podocin (in podocytes) can present as nephrotic syndrome.

The mechanism of Edema:

2 theories were presented: 1) underfill hypothesis 2) overfill hypothesis

Underfill hypothesis

- The kidneys lost proteins (mainly Albumin) in the urine, which lowered the plasma oncotic pressure. Thus, fluid will be shifted into the extravascular component (interstitium), depleting the intravascular volume with subsequent activation of renin/aldosterone and consequent renal sodium retention.
- Aldosterone and Renin works to increase sodium and water retention to compensate the intravascular fluid depletion and this causes a Low Urine Sodium in these patients.
- Also Sympathetic system and ADH are activated, all work to increase the salt and water retention which will eventually lead to edema.
- These patients improve when Albumin is given.
  Albumin increases oncotic pressure and this will shift the fluid from extra- to intra-vascular component. After that Diuretics are given to induce diuresis and relief of edema.

Overfill hypothesis:

- The nephrotic syndrome not only leads to urinary protein wasting, but also to primary sodium retention with consequent intravascular overfilling (increases blood volume) that leads to increase in Blood pressure.
  These changes lead to alteration in Starling forces which result in edema.
- Several mechanisms explain this primary sodium retention:
  -Distal tubular injury causes resistance to atrial natriuretic peptide (ANP) resulting in decrease in natriuresis.
  -Proteinuria includes plasma proteinases, such as plasmin, which activate the epithelial sodium channel (ENaC) in the collecting duct and this enhance Sodium and water reabsorption.
  (Further evidence for this hypothesis is being presented by confirming increased plasmin content in the urine of children with nephrotic syndrome and demonstrating ENaC activation).
- For these patients Albumin should NOT be given.

(Be cautious when a nephrotic patient with high blood volume and pressure is given Albumin, this might lead to pulmonary edema).

- Clinically it is difficult to differentiate between under- and over-fill hypotheses.
- Low Urine sodium could give a clue that this is underfill hypothesis.
- For any nephrotic patient when you give Albumin. Give it slowly over 4 hours with monitoring the blood pressure and respiratory status.

Histopathology

1) Minimal change disease (MCD)

- Normal under light microscope (LM)
- IF is negative
- Effacement of foot processes of podocytes under EM.
- Most common in Pediatrics.

2) Mesangial proliferative

- IgM mediated disease
- Mesangial proliferation and IgM deposits on biopsy.

3) Focal segmental glomerulosclerosis (FSGS)

- Focal sclerosis in some segments of the glomeruli on LM

Presentation

- Periorbital swelling, increase in weight, pleural effusion, sacral edema in infants, Abdominal pain either due to hypovolemia or secondary to peritonitis …etc.

Types

1) Primary

MCD, FSGS, Membranous, Mesangial proliferative and MPGN (very rare to be nephrotic)

2) Secondary

Secondary to: Infections (Malaria, HIV) or systemic diseases (HSP, lupus–stage 5 can present as nephrotic-)

3) Congenital

In the first 3 months of life either 2ry to an infection or as a part of a syndrome.

Laboratory investigations

- Low Albumin and Calcium (Total calcium is low)
- Hyponatremic (if fluid overload).
- ANA, complements, Hepatitis B & C (asked for older patients when thinking of 2ry nephrotic due to lupus or Hepatitis).
- High Haemoglobin and platelets.
- Urine Analysis: 30% of patients have microscopic haematuria; it is usually transient in MCD but more persistent in FSGS.

Course and outcome

- Majority of children with nephrotic syndrome respond by 4 weeks of therapy.
- 80-90% would relapse (very rare to have a single episode of the disease).
- Up to 50% would have frequent relapsing.
- Up to 80% would have complete remission at age of 8, but certain types like FSGS about 50% of them would continue in adolescents and progress to CKD and ESRD.

CLASSIFICATION	DEFINTION
REMISSION	Urine prot <4mg/m2/hour, urine prot/creat <.2 mg/mg, 0 on dipstick for 3 persistent days
STERIOD RESISTANCE	Failure to respond after initial 4-8 weeks of steroids
RELAPSE	Urine prot >40mg/m2/hour, urine prot/creat > 2 mg/mg, +3 prot on dipstick for 3 days or edema
INFREQUENT RELAPSE	1 relapse in 6 months,1 to 3 in 12 months
FREQUENT RELAPSE	2 or more relapse in 6 months,4 or more in 12 months
STERIOD DEPENDANT	Two consecutive relapses during steroid therapy or within 14 days of ceasing therapy

When a renal biopsy is done?

- Age less than 1. (when you think about congenital nephrotic syndrome)
- Fail to respond to steroid.
- Unusual features (Nephrotic is 2ry to a disease)
- Steroid dependent (to know the exact pathology)

Biopsy is sent to LM, IF and EM.

Treatment

First Episode Treatment:

- Steroids: 2mg/kg/day as a single daily dose for 4 weeks (some give it 4-6 weeks).
- In the first episode it is important to complete the treatment for the whole duration, usually these children will respond after 10 days-2 weeks but the treatment should be continued for 4 weeks then we could start tapering (the longer the duration of tapering the less likely to relapse).
- The tapering can continue up to 3-6 months.(at least 3months)

Treatment of relapses

- Same dose of Steroids: 2mg/kg/day till the child is in remission for 3 days.
- In relapses the tapering is not as long as in the first episode treatment. We can stop the steroid in 2-3 months.

- Steroid is the mainstay of therapy but other drugs and regimens were added:
- Immune modulators.
- Long-term alternate steroids (small alternative dose to prevent relapses)
- Cyclophosphamide (for frequent relapsing)
- Cyclosporine or Tacrolimus.
- Mycophenolate acetate

Side effects

- Steroids: growth, osteopenia, cataract, cushingoid, glaucoma..
- Cyclosporine: hirsuitism, gum hypertrophy, HTN, reduced GFR (on long term use so it shouldn't be given for long duration)
- Cyclophosphamide: infertility, alopecia, leukopenia, haemorrhagic cystitis.
- Mycophenolate acetate: abdominal pain, anemia, leukopenia.

Supportive treatment

- Salt restriction (salt increases thirst and eventually edema, Salt is not given unless severe hyponatremia)
- Albumin: 1-2g/kg/day over 4 hours with furosemide (in underfill hypothesis)
  -Albumin is useful especially in cases of severe ascetics with respiratory distress, severe scrotal swelling and in oligouria.
  -Usually we don't use diuretics alone. They are used in combination with albumin.

- If steroid resistant nephrotic syndrome (most probably :FSGS) we might use long term, low dose ACEI to decrease persistent edema and proteinuria.

Complications

1) Infections

- Due to: loss of Igs in urine, steroid use, immunosuppressant therapy, low factor B (C3 proactivator), and impaired opsonisation.
- Most Common organisms: Encapsulated bacteria
- Spontaneous -primary- bacterial peritonitis (nephrotic patient with abdominal pain, fever and tender abdomen be aware to exclude this peritonitis)
- More prone to Pneumococcus infection (Immunization should be given for protection against Pneumococcus, varicella and influenza)

2) Thromboembolism: Anticoagulants and AT3 are lost in urine, fibrinogen is high, platelets are high and hyper-viscosity state.
No need for anticoagulant treatment in most nephrotic patients.

3) Acute renal failure

Congenital Nephrotic syndromes:

CNS Finish type

- A Type of congenital nephrotic syndromes.
- Mutation in **Nephrin** gene (part of slit diaphragm).
- Usually High amniotic AFP (antenatally)
- Presents at birth with Edema, severe proteinuria and very low albumin.
- GFR is normal in the first year of life after that the disease progress into renal failure.

Diffuse Mesangial Sclerosis

- Also a type of congenital nephrotic syndromes.
- Mutations of WT1 gene.
- Presents Later (unlike Finish type)
- ESRD occurs very fast almost months after presentation (fast progression).

Treatment of congenital Nephrotic Syndromes

- No role of steroids
- The mainstay of treatment is supportive:
- Albumin infusions (every 1-2weeks)

- High protein diet
- They are prone to Hypothyroidism (check thyroid function test regularly)
- Indomethacin (decreases GFR)
- ACEI
- Diuretics (Lasix)
- Anticoagulants as prophylactic to thrombosis
- Prophylactic Penicillin (to protect them from infections)
- For Renal failure, transplantation might be needed.

SRNS

- Mostly FSGS.
- Usually we do testing for:
  NPHS1 gene (for nephrin) and NPHS2 gene (for podocin).
  If the results were positive, this indicates that this patient has a genetic mutation and we can start giving him ACEI and Steroids.
  If the genes were negative we can start on Immune mediated therapy or Cyclosporine (better than cyclophosphamide).
- If genetics are negative but it is an immune mediated disease, we should know that the disease can recur after transplantation.
- A newly introduced drug which is Rituximab (acts on B-cells depletion) could be used in these cases.

The End **Farah Amer**

RENAL FAILURE *(nelson essentials & Dr slides)*

- Acute kidney injury - *formerly termed Acute Renal Failure*
- Chronic kidney disease- *Chronic Renal Failure*

-Acute kidney injury

- **Definition-** an abrupt, reversible decrease in glomerular filtration rate(GFR) and tubular function.
- This may lead to decreased excretion of waste products (e.g., urea) and a disturbance in fluid and electrolyte homeostasis.
- Early recognition and management of AKI are **crucial**.

- **Types of ARF**
  - **RIFLE** classification based on Cr,urine output.(risk,injury,renal failure,renal loss,ESRD)
  - **Pre-renal, Renal, Post-renal**
  - **Oliguric, Non-oliguric**

- AKI may be
- **oliguric** or **non-oliguric**
  - **Oliguric** (<1 mL/kg/h in neonates and infants,<0.5 mL/kg/h in children)
  - **Nonoliguric**, *which is more difficult to recognize*, urine output in nonoliguric AKI is normal or polyuric.

- **Pre-renal** *renal hypoperfusion*, **Renal** *(tubular, glomerular, or vascular injury)*, **Post-renal** *urinary tract obstruction*.
  - Pre-renal azotemia is most commonly due to **dehydration** but may be secondary to other mechanisms of glomerular hypoperfusion.
  - **Tubular injury** encompasses the **most common** causes of **intrinsic Renal** AKI in children. ***Dr slides HUS most common cause of intrinsic Renal AKI***

    *Tubular injury may occur from hypoxia-ischemia (**acute tubular necrosis**), infection (**sepsis**), **nephrotoxic agents** (medications, contrast, myoglobin) and inflammation (**interstitial nephritis**).*
  - **Post-renal** may be due to either structural or functional **urinary tract obstruction**.

- **Causes-**

Table 165-1 Causes of Acute Kidney Injury
PRERENAL
Dehydration
Hemorrhage
Septic shock
Burns
Heart failure
Cirrhosis
POSTRENAL (OBSTRUCTION)
Urethral obstruction (stricture, posterior urethral valves)
Ureteral obstruction
Ureterocele
Extrinsic tumor compressing bladder outlet
Neurogenic bladder (myelomeningocele, spinal cord injury)

INTRINSIC
Acute tubular necrosis
Nephrotoxins (medications, contrast, myoglobin)
Infection (sepsis)
Interstitial nephritis
Glomerular injury (primary glomerulonephritis, vasculitis, hemolytic uremic syndrome)
Vascular (renal vein thrombosis, arterial emboli, malignant hypertension)

Pigment nephropathy: rhabdomyolysis myoglobinuria, result trauma, status epilepticus, hereditarytx with fluids,alkali,diuretics

Tumor lysis syndrome:high uric acid, phosphate, low calcium .Tx allopurinol, alkalinazation of urine ph 7

- Pre-renal Treatment: fluid management and restoration of effective circulatory volume.
- Post renal ARF
  - Obstruction at level of ureter till urethra
  - Elevated tubular pressure decrease GFR
  - Duration of obstruction affects recovery
  - Congenital (PUJ,PUV),acquired (stones)
  - Post obstructive diuresis: dilute urine with large Na losses, reduced excretion of H,K.

- **History, physical examination, and basic studies usually allow proper classification.** Important points in history:
  - Previous GE, previous throat infection
  - Fever, rash, joint pain
  - Urinary symptoms
  - Drug history
  - FH of renal disease
  - P/E: state of hydration, volume overload, hemodynamic status
  - **Prerenal azotemia** is characterized by precipitating factors and oliguria.
  - **Intrinsic tubular injury** is associated with **precipitating factors** but urine output may be low, normal, or high, depending on the severity of the injury.
  - **Glomerular and vascular disorders** may present with ***hematuria, edema, hypertension, and oliguria.***
  - The urine output with **postrenal AKI** may be low or normal and may be associated with **flank masses or a distended bladder** on examination.

Diagnostic Studies *(refer to the table)*

- **Urinalysis** (UA) should be obtained in all children with AKI.
- In **pre-renal azotemia**, the UA is unremarkable with a **high specific gravity** reflecting appropriate renal retention of water in the setting of renal hypoperfusion.
- With intrinsic **tubular injury and post-renal AKI**, the UA may show mild **hematuria** and/or **proteinuria** with a specific gravity of 1.015 or less.
- With **glomerular and vascular injury**, the amount of **hematuria and proteinuria** is usually moderate to severe.
- In **oliguric** states, differentiation between **pre-renal azotemia** and **acute tubular necrosis** may be aided by determining the **urine osmolality** and **fractional excretion of sodium**

FeNa=(Una X Pcr)/(Pna XUcr) X 100% , ***FeNa < 1% in Pre-renal, 2-3% Renal***
FeNa unreliable in diuretics, neonate High in bartter, CRD.

- **Renal U/S**
- Complements, ANA, antiDNAs, ANCA
- Electrolyte abnormalities hyperkalemia,metabolic acidosis,hypocalcemia,hyperphosphatemia.
- CBC should be obtained as anemia is frequently observed, Blood smear-schistocytes of HUS.

Table 165-2 Laboratory and Clinical Evaluation of Acute Kidney Injury

	PRERENAL		RENAL		POSTRENAL
LABORATORY/ CLINICAL FEATURE	CHILD	NEONATE	CHILD	NEONATE	
Urine output	Low		Low, normal, or high		Low or normal
Urinalysis	Normal		RBCs, WBCs, protein, casts		Variable
Urine Na^+ (mEq/L)	<15	<20–30	>40	>50	Variable, may be >40
FE_{Na}* (%)	<1	<2.5	>2	>2.5	Variable, may be >2
Urine osmolality (mOsm/L)	>500	>350	~300	~300	Variable, may be <300
Renal ultrasound	Normal		Increased echogenicity, decreased corticomedullary differentiation		Hydronephrosis

- **Renal ultrasound** is often helpful in determining AKI category,kidney size &echogenicity.
- Dilated PCS -> *Obstruction*
- Large, echogenic kidneys -> *AKI*
- Small kidneys or cysts->*CKD*
- *Renal biopsy is indicated in select cases only.*
- *New kidney markers of injury: KIM 1,cystatin C*

Management & Treatment

- **Monitoring: weight, input/output chart, B.P**
- In some cases the **underlying disorder can be treated**. Examples include volume repletion in dehydration, stopping an offending nephrotoxic medication, and relieving urinary tract obstruction.
- In all cases - **limit additional renal injury** (e.g., ensuring adequate renal perfusionand avoiding nephrotoxic medications).
- **Fluid therapy depends on the volume status and urine output.**
- If **hypovolemia** is present**, intravascular volume** should be expanded by intravenous administration of saline.
- If **hypervolemia** is present, 1 to 2 mg/kg of **furosemide and fluid restriction** may be attempted.
- If the patient is relatively **euvolemic,** then the total fluid input should be adjusted to meet the total output, which may be higher or lower than normal, depending on the urine output.

- **Manage complications** - Electrolyte disorders are treated as appropriate.

HYPERKALEMIA –imp.

- *Potassium intake and medications that increase potassium should be restricted.*
- *Intravenous calcium will lower risk of arrhythmia while measures are initiated to shift potassium into cells (bicarbonate, beta-agonists, insulin/dextrose) and hasten removal (diuretics, sodium-potassium exchange resins, dialysis).*

- **Hypocalcemia** - oral supplementation and calcitriol, IV is reserved for severe cases.
- **Hyponatremia**: dilutional, fluid restriction, Na<120, hypertonic saline= (125-measures) X 0.6 X wt over 2-4 h.

- **Hypertension** may be treated with diuretics, calcium channel blockers, and vasodilators. *ACE inhibitors are avoided in the setting of AKI.*
- Nutrition: catabolism result in high urea, K, need sufficient calories.

- Medical therapy may be attempted before initiating renal replacement therapy.
- **Renal replacement** options in children include **peritoneal dialysis, hemodialysis, and continuous renal replacement therapy.**

Indications for renal replacement therapy

- Persistent hyperkalemia
- Diuretic resistant volume overload and associated HTN & HF
- Refractory acidosis
- Severe uremia with risk of encephalopathy and /or pericarditis

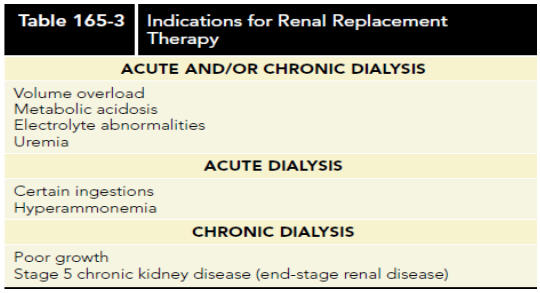


Table 165-3	Indications for Renal Replacement Therapy
ACUTE AND/OR CHRONIC DIALYSIS	
Volume overload Metabolic acidosis Electrolyte abnormalities Uremia	
ACUTE DIALYSIS	
Certain ingestions Hyperammonemia	
CHRONIC DIALYSIS	
Poor growth Stage 5 chronic kidney disease (end-stage renal disease)	

Choice of renal replacement therapy

1.acute peritoneal dialysis:

- Peritoneal membrane is a semipermeable membrane with a large surface area
- Needs tenkoff catheter (rigid,permnant)
- Use diffusion and convection by ultrafilteration
- PD fluids has electrolytes,glucose (1.5 %,4.25 %),acid buffer of biocarbonate
- Volume of 10-50 ml/kg
- Dwell time of 20-60 min
- Used for young infants, avoids sudden shifts of fluid and metabolites, minimal fluid and dietary restrictions

- **Complications :**
  -Infection

*Indwelling catheters used for peritoneal dialysis may develop **exit site infections**, **tunnel infections**, or lead to **peritonitis**. The usual route of infection is from the skin surface along the tunnel and into the peritoneum.*

-Blockage

Dialysis Solution (*Dialysate*)

- **DIFFUSION OF WASTE PRODUCTS**

•The movement of solid particles (across a semi permeable membrane) from an area of high concentration, to an area where the concentration is lower in order to achieve eventual equilibrium
•Small amount of solute removal by convection

PD Solution

Sodium - 132
Chloride = 98
Lactate = 40
Calcium = 1.2 - 1.75
Mg = o.5

- **Water Removal by Osmosis**

"The movement of water through a membrane from a higher to a lower water concentration area." This is achieved by adding **glucose** to the dialysis solution, however alternative osmotic agents are the future of PD.

2-Acute intermittent hemodialysis

- Needs vascular acsess and anticoagulation.
- Rapid correction so contraindicated in hemodynamic instability.

- Complication : hypotension, dialysis disequilibrium due to rapid correction of urea.
- Requires greater fluid restriction.
- **Continuous veno-venous hemofiltration** (CVVH)

Prognosis

- Recovery from AKI depends on the **etiology, severity, availability of specific treatments**, and other aspects of the patient's course.
- **Nonoliguric AKI** usually **recovers well**, whereas the outcome with **oliguric AKI is more variable**.
- *History of AKI may place the child at increased risk for future renal complications, including (CKD).*

CHRONIC KIDNEY DISEASE

Etiology and Epidemiology

- **Congenital anomalies** of the kidney and **urinary tract** (CAKUT) are the **most common causes of CKD** that present between birth and 10 years of age.
- After age 10 **acquired diseases**, such as focal segmental glomerulosclerosis and glomerulonephritis (GN), are more common causes of incident CKD.
- The risk of progression to end-stage renal disease (**ESRD**) is related to the **underlying cause and severity of CKD.**
- Plasma Cr does not rise until renal function has fallen to less than half normal levels.
- Cr affected by **muscle bulk**.
- The **GFR** can be estimated in children using **the Schwartz formula**

$$\text{GFR} = \frac{0.413 \times \text{Ht}}{\text{Cr}_{\text{serum}}}$$

-Height is measured in centimeters, Serum creatinine is measured in milligram per decilitre
-GFR - ml/min/1.73 m²

- CKD is **staged** to facilitate appropriate evaluation and monitoring.
- **Most complications** of CKD do not manifest until at **least stage 3 CKD**.
- Children with **stage 5 CKD** (ESRD) are typically treated with either **dialysis or renal transplantation.**

Table 165-4 Classification of the Stages of Chronic Kidney Disease

STAGE	GFR (ml/min/ 1.73 m²)*	DESCRIPTION
1	>90	Minimal kidney damage
2	60–89	Kidney damage with mild reduction of GFR
3	30–59	Moderate reduction of GFR
4	15–29	Severe reduction of GFR
5	<15 (or dialysis)	End-stage renal disease

From National Kidney Foundation Kidney Disease Outcomes Quality Initiative.
GFR, Glomerular filtration rate.
*GFR ranges apply for children 2 years of age and older.

Clinical Manifestations

- The clinical presentation of a child with CKD may be related to both the underlying diagnosis and complications of CKD.
- A child with CAKUT may have polyuria, polydipsia, and recurrent urinary tract infections.
- A child with glomerular disease may have hematuria, proteinuria, edema, and HTN.

Complications

- **Growth failure** include poor nutrition, **renal osteodystrophy (ROD)**, metabolic acidosis, hormonal abnormalities, and resistance to growth hormone.
- **Anemia** failure to produce adequate **erythropoietin** and iron deficiency.
- ROD is usually due to **secondary hyperparathyroidism** as a result of diminished 1,25-dihydroxyvitamin D production in the kidney, hypocalcemia, and hyperphosphatemia (from decreased renal excretion). If prolonged and/or severe, ROD may eventually lead to rickets and bone deformities.
- **Hypertension** and **left ventricular hypertrophy** are commonly seen.
- **Delayed puberty** results from altered gonadotropin secretion and feedback patterns.

Management & Investigations-

- CBC, iron studies
- Electrolytes Urea Creatinine *EUC*, biocarbonte,Ca,PO4,ALP,PTH
- Urine protein, lipid profile
- Attention: Nutrition, fluid, growth, anemia, HTN, renal osteodystrophy.

Treatment

- Measures taken to preserve kidney function or **slow down the progression** of CKD.
- **HTN and proteinuria** can be treated with **ACE inhibitors or ARBS.**
- **TREAT COMPLICATIONS** *refer to the table*
- The optimal treatment of **ESRD** is **renal transplantation.**
- Deceased and living donors used for renal transplantation, but living donors are preferred.
- **Maintenance dialysis** is effective for a child awaiting renal transplantation or for whom renal transplantation is not possible..
- **Peritoneal dialysis** is done at home by the family. **Hemodialysis** is typically done three times a week at a dialysis facility.

Table 165-5 Common Complications and Treatments of CKD

COMPLICATION	TREATMENT
1. Poor growth	Increased caloric intake, treat acidosis, treat renal osteodystrophy, recombinant GH
2. Anemia	Erythropoietin, iron supplementation
3. Renal osteodystrophy/ secondary hyperparathyroidism	1,25-Dihydroxyvitamin D supplementation, calcium supplementation, dietary phosphorous restriction, phosphate binders
4. Cardiovascular 4a. Hypertension 4b. Left ventricular hypertrophy	 Antihypertensive medications Volume control
5. Electrolyte abnormalities 5a. Hyperkalemia 5b. Hyponatremia 5c. Metabolic acidosis	 Low K diet, furosemide, sodium polystyrene sulfonate Sodium supplementation Alkali replacement

CKD, Chronic kidney disease; *GH*, growth hormone; *K*, potassium.

Prognosis

- Children with mild CKD **(stages 1 and 2)** may do well but need to be **monitored for progressive loss of kidney function.**
- Children with **stages 3 and 4 CKD** have a high likelihood of progressing to **ESRD**.
- Children with kidney transplants generally do well but have to take immunosuppressive medications associated with a variety of S/E infections, nephrotoxicity, CVS complications and increased risk for certain malignancies.
- Children on **maintenance dialysis** have the **highest morbidity and mortality**.

Complications *in more details – Dr Slides*

➢ BONE DISORDERS IN CKD

- PTH
- Mobilizes Calcium from bones ,
- Decrease renal tubular absorption of PO4,
- Increase renal tubular absorption of Calcium
- Promote 1 alpha hydroxylase

Disorders of Bone Mineral Metabolism in CKD

- Reduced 1,25 OH vit D impairs intestinal Calcium absorption leads to low Calcium and increase PTH stimulates 1hydroxylase increase Vit D,Ca.
- Calcemic response to PTH is reduced CKD
- Ca major regulator of parathyroid
- High PO4 increase FGF23 increase excretion
- High PO4 stimulates PTH, lowers Ca
- Acidosis impairs bone mineralization

Clinical Manifestations

- Bone pain , Myopathy due uremic toxins, carnitine deficiency.
- Skeletal deformities: bowing,genu valgum, ricket changes of widening of metaphyseal regions.
- Slipped epiphyses, proximal femur, presents as limping, waddling gait.
- Fractures.
- Vascular calcification (maintain PO4 X Ca <65 mg2/dl2).

Biochemistry

- Ca low or normal, high in low turnover, tertiary hyperparathyroidism.
- Tx with calcitriol,volume depletion
- PO4 high is age dependant
- PTH high, ALP high
- Xrays detect subperiostal resorption.

Treatment

- Optimal control of PO4 by diet ,phosphate binders (Ca carbonate 40%elemental Ca),dialysis not enough,to be taken with meals.
- Sevelamer HCL.:lower risk of hypercalcemia, lower lipids, same efficacy as CaCO3 in lowering PO4.
- maintain PO4 X Ca <55mg2/dl2 in adults, <65mg2/dl2 in children

- Vitamin D:1increase PO4,Ca,given daily or intermittent
- Calimimetic, Parathyroidectomy

➢ Anemia

• Erythropoietin Deficiency
• Blood loss (HD lines,GIT losses due to impaired platelet function)
• Decreased RBC survival
• Hyperparathyroidism decrease BM production.
• Aluminum toxicity
• Iron deficiency
• Vitamin B12,folate deficiency
• Inflammation,infection

- Systemic symptoms of fatigue, loss of appetite, decrease exercise tolerance
- Anemia increase mortality
- Evaluation: CBC, reticulocyte count ,ferritin, iron, TIBC
- TSAT:Iron/TIBC should be >20%
- Target Hb levels based on KDOQI guidelines is between 11-13
- Ferritin be above 100 in pre-dialysis patients

➢ Nutrition

- Protein intake 1.1 g/day 1-6 y.
- Higher protein in dialysis.
- Low phosphate, potassium diet.
- Vitamins, minerals as folic acid.
- Special formula low in K,PO4,increase energy by adding lipid, sugar.
- Salt supplements in tubular losses.

➢ Causes of growth failure in CKD

- Genetic factors: gender, parental height, syndromes
- Age of onset of CKD
- Residual renal function
- Treatment modality
- Energy malnutrition
- Water and electrolyte disturbances: renal dysplasia needs salt.
- Metabolic acidosis
- Anemia, renal osteodystrophy

➢ Gonadotropic hormone axis

- Growth hormone levels are normal to high
- **GH resistance** due to low GH receptor expression or post-receptor signalling defect.
- **IGF1 levels are high and there is resistance to its action**
- Treatment of growth failure

- Adequate caloric intake to 100% of RDA

- Treatment with alkali,salt
- Calcitriol
- Growth hormone: benefit more in pre end-stage CKD, than dialysis

Treatment of ESRD

- Peritoneal dialysis:
  - CAPD *continuous ambulatory peritoneal dialysis*
  - NIPD *nocturnal intermittent peritoneal dialysis*
  - CCPD *continuous cycling peritoneal dialysis* Uses an automated machine with 7 night cycles with a long day time dwell
- Acute intermittent hemodialysis: needs vascular access as AV fistula, permcath
  - Requires 3 X 5 hour sessions/week
- Transplantation
  - Complications :rejection, HTN, infection, obstruction, chronic allograft nephropathy
  - LRD *living related donor* 1 year graft survival of 91%,5 years of 74 %
  - CRD *cadaveric related donor* 1 year graft survival of 80%,5 years of 60 %

Esra'a Alkubaisi

Urinary tract infections

Urinary tract infections (UTIs) occur in 1% of boys and 1-3% of girls. The prevalence of UTIs varies with age.

In boys, most UTIs occur during the 1st year of life; especially in uncircumcised boys. In girls, the first UTI usually occurs by the age of 5 years, with peaks during infancy and toilet training.

Males are more or equally affected in infancy. But after the first year, females have a 10-fold risk.

Definition: UTI symptoms + positive culture. A positive culture without symptoms is called asymptomatic bacteriuria.

Causative agents:

- ☒ UTIs are caused primarily by colonic bacteria. Most commonly by Escherichia coli, followed by Klebsiella and Proteus.
- ☒ Staphylococcus saprophyticus and enterococcus.
- ☒ Adenovirus and other viral infections also can occur, especially as a cause of cystitis with gross hematuria.
- ☒ Atypical (TB, fungi, schistosomiasis).

Pathophysiology

- ☒ It is classified clinically to upper (pyelonephritis) and lower UTI (cystitis.)
- ☒ UTI is classified etiologically to ascending "which is the most common", and hematogenous "which occurs mostly at very young age secondary to sepsis."
- ☒ Any factor causing urinary obstruction or stasis will increase bacterial incubation time, thus predisposing to infection.

Clinical manifestations

Pyelonephritis:

- ☒ Abdominal, back, or flank pain.
- ☒ Fever; malaise; nausea; vomiting; and, occasionally, diarrhea. Fever may be the only manifestation.
- ☒ Newborns can show nonspecific symptoms such as poor feeding, irritability, jaundice, and weight loss.
- ☒ Pyelonephritis is the most common serious bacterial infection in infants younger than 24 months of age who have fever without an obvious focus.
- ☒ Involvement of the renal parenchyma is termed acute pyelonephritis, whereas if there is no parenchymal involvement, the condition may be termed pyelitis.

- ☒ Acute pyelonephritis can result in renal injury, termed pyelonephritic scarring.
- ☒ **Xanthogranulomatous pyelonephritis** is a rare type of renal infection characterized by granulomatous inflammation with giant cells and foamy histiocytes. It can manifest as a renal mass or an acute or chronic infection. Renal calculi, obstruction, and infection with Proteus spp. or E. coli contribute to the development of this lesion, which usually requires total or partial nephrectomy.

Cystitis

- ☒ Dysuria, urgency, frequency, suprapubic pain, incontinence, and malodorous urine. Malodorous urine is not specific for a UTI.
- ☒ Cystitis does not cause fever and does not result in renal injury.
- ☒ **Acute hemorrhagic cystitis** often is caused by E. coli; it also has been attributed to adenovirus types 11 and 21.
- ☒ **Adenovirus cystitis** is more common in boys; it is self-limiting, with hematuria lasting approximately 4 days.
- ☒ **Eosinophilic cystitis** is a rare form of cystitis of obscure origin that occasionally is found in children.
    - The usual symptoms are those of cystitis with hematuria.
    - On imaging, typically there are multiple solid bladder masses that consist histologically of inflammatory infiltrates with eosinophils.
    - Ureteral dilation with hydronephrosis also is common.
    - Patients may have been exposed to an allergen.
    - Bladder biopsy often is necessary to exclude a neoplastic process.
    - Treatment usually includes antihistamines and nonsteroidal anti-inflammatory agents.
- ☒ **Interstitial cystitis** is characterized by irritative voiding symptoms such as urgency, frequency, and dysuria, and bladder and pelvic pain relieved by voiding with a negative urine culture.
    - The disorder is most likely to affect adolescent girls and is idiopathic.
    - Diagnosis is made by cystoscopic observation of mucosal ulcers with bladder distention.
    - Treatments have included bladder hydrodistention and laser ablation of ulcerated areas, but no treatment provides sustained relief.

Risk factors

- ☒ Female gender.
- ☒ Uncircumcised male.
- ☒ Vesicoureteral reflux.
- ☒ Toilet training.
- ☒ Voiding dysfunction.

- ☒ Obstructive uropathy.
- ☒ Urethral instrumentation.
- ☒ Wiping from back to front in girls.
- ☒ Tight clothing (underwear).
- ☒ Pinworm infestation.
- ☒ Constipation.
- ☒ Anatomic abnormality (labial adhesion).
- ☒ Neuropathic bladder.
- ☒ Sexual activity.

Diagnosis

- ☒ Pyuria and at least 50,000 CFU/ml of a single pathogenic organism.
- ☒ Enhanced urinalysis: to evaluate the number of WBC/mm^3. Pyuria: >10 WBC/mm^3
- ☒ Urine culture is necessary for confirmation and appropriate therapy. It is the gold standard. Methods of collection "in order of sterility":
    - Suprapubic aspiration: it is usually done in infants <2 months.
    - Cathetheterization: for children before toilet-training (<2 years).
    - Mid-stream urine: In toilet-trained children
    - Suprapubic aspiration an catheterization are preferred in females and uncircumcised males.
- ☒ DMSA scan shows hypodensity >> repeat after 4 months, if still the same this indicates renal scarring from UTI.
- ☒ With acute renal infection, leukocytosis, neutrophilia, and elevated serum ESR, procalcitonin, and CRP are common.
- ☒ Renal sonogram plus voiding cystourethrogram; this approach will identify upper and lower urinary tract abnormalities.

Complications

- ☒ UTI itself doesn't cause renal failure. It may result from associated congenital anomalies.
- ☒ Acute lobar nephronia: a complication of pyelonephritis. It is a renal mass caused by acute focal infection without liquefaction. It may be an early stage in the development of a renal abscess. Manifestations are identical to pyelonephritis; renal imaging demonstrates the abnormality.
- ☒ Renal abscess can occur following a pyelonephritic infection caused by the usual uropathogens or may be secondary to hematogenous infection (Staphylococcus aureus).
- ☒ Perinephric abscess can occur secondary to contiguous infection in the -+

- ☒ perirenal area (e.g., vertebral osteomyelitis, psoas abscess) or pyelonephritis that dissects to the renal capsule.
- ☒ 6 – 7 % of gastroenteritis caused by UTI.

Treatment

- ☒ Don't treat asymptomatic bacteriuria.
- ☒ If the patient is symptomatic, treat even with negative culture.
- ☒ Acute cystitis should be treated promptly to prevent possible progression to pyelonephritis.
    - Trimethoprim-sulfamethoxazole: effective against many strains of E. coli.
    - Trimethoprime not for infants <6 weeks.
    - Nitrofurantoin also is effective and has the advantage of being active against Klebsiella and Enterobacter organisms.
    - Amoxicillin also is effective as initial treatment but has a high rate of bacterial resistance.
- ☒ In acute febrile infections suggesting clinical pyelonephritis, a 7-14 day course of broad-spectrum antibiotics capable of reaching significant tissue levels is preferable.
    - Parenteral treatment with ceftriaxone or cefotaxime, or ampicillin with an aminoglycoside such as gentamicin is preferable.
    - Treatment with aminoglycosides is particularly effective against Pseudomonas spp., and alkalinization of urine with sodium bicarbonate increases its effectiveness in the urinary tract.
    - Oral third-generation cephalosporins such as cefixime are as effective as parenteral ceftriaxone against a variety of Gram-negative organisms other than Pseudomonas, and these medications are considered by some authorities to be the treatment of choice for oral outpatient therapy.
    - Nitrofurantoin should not be used routinely in children with pyelonephritis because it does not achieve significant renal tissue levels.
- ☒ Children who are dehydrated, are vomiting, are unable to drink fluids, are 1 month of age or younger, have complicated infection, or in whom urosepsis is a possibility should be admitted to the hospital for IV rehydration and IV antibiotic therapy.
- ☒ Children with a renal or perirenal abscess or with infection in obstructed urinary tracts can require surgical or percutaneous drainage in addition to antibiotic therapy and other supportive measures.
- ☒ Norfloxacin and ciprofloxacin are not used in pediatrics except in necessary cases.

Vesicoureteral reflux (VUR)

It describes the retrograde flow of urine from the bladder to the ureter and kidney. The ureteral attachment to the bladder normally is oblique, between the bladder mucosa and detrusor muscle, creating a flap-valve mechanism that prevents VUR.

VUR occurs when the submucosal tunnel between the mucosa and detrusor muscle is short or absent.

VUR usually is congenital and often is familial.

VUR predisposes to kidney infection (pyelonephritis) by facilitating the transport of bacteria from the bladder to the upper urinary tract.

It affects 1-2% of children. VUR is present in approximately 30% of females who had a urinary tract infection and in 5-15% of infants with antenatal hydronephrosis.

Classification

- ☒ Primary: if urinary system is functionally normal. Mostly result from anomalies.
- ☒ Secondary: caused by obstruction (posterior urethral valve), or abnormal function (neurogenic bladder).

Grading

- ☒ VUR severity is graded using the International Reflux Study Classification of I-V and is based on the appearance of the urinary tract on a contrast voiding cystourethrogram (VCUG).
- ☒ The higher the VUR grade the greater the likelihood of renal injury. VUR severity is an indirect indication of the degree of abnormality of the ureterovesical junction.
- ☒ Grade I: VUR into a non-dilated ureter.
- ☒ Grade II: VUR into the upper collecting system without dilation.
- ☒ Grade III: VUR into dilated ureter and/or blunting of calyceal fornices.
- ☒ Grade IV: VUR into a grossly dilated ureter.
- ☒ Grade V: massive VUR, with significant ureteral dilation and tortuosity and loss of the papillary impression.

Clinical manifestations

- ☒ It usually is discovered during evaluation for a UTI (the most common presentation).
- ☒ Advanced presentations include HTN, uremia, and renal failure.
- ☒ Sterile reflux (without UTI) may manifest as:

1. Flank or abdominal pain before or daring voiding.
2. Double voiding: with VUR, urine will get trapped in the ureters with voiding. When it returns to the bladder, another urge to void is felt.

☒ Findings in examination are the same as UTI.

Diagnosis

☒ Children with grade 3 or beyond: do screening for siblings.
☒ A contrast VCUG or radionuclide cystogram.
☒ Radiation exposure during a radionuclide cystogram is significantly less than that from a contrast VCUG. However, the contrast VCUG provides more anatomic information.
☒ Radionuclide cystogram: can't detect urethral abnormalities.
☒ The bladder and upper urinary tracts are imaged during bladder filling and voiding.
☒ Indirect cystography is a technique of detecting VUR without catheterization that involves injecting an intravenous radiopharmaceutical that is excreted by the kidneys, waiting for it to be excreted into the bladder, and imaging the lower urinary tract while the patient voids. This technique detects only 75% of VUR cases.
☒ After VUR is diagnosed, assessment of the upper urinary tract is important. The goal of upper tract imaging is to assess whether renal scarring and associated urinary tract anomalies are present.
☒ The child should be evaluated for bladder–bowel dysfunction.

Treatment

☒ The goals of treatment are to prevent pyelonephritis, VUR-related renal injury, and other complications of VUR.
☒ Medical therapy is based on the principle that VUR often resolves over time and that if UTIs can be prevented, the morbidity or complications of VUR may be avoided without surgery.
☒ Medical therapy includes observation with behavioral modification and antimicrobial prophylaxis in some patients.
☒ The basis for surgical therapy is that in selected children, ongoing VUR has caused or has significant potential for causing renal injury or other VUR-related complications, and that elimination of VUR minimizes the risk of these problems.
☒ Therapy for VUR should be individualized based on a particular patient’s risk factors.

Prognosis

- ☒ Long-standing VUR will cause parenchymal scarring with resultant HTN, renal failure.
- ☒ Renal scarring before 1 year is mostly due to intra-uterine damage. Intrauterine reflux may cause hydronephrosis or renal dysplasia.

Sources: Nelson textbook, seminar notes, and the old lecture by Mohammad Sawaf

Rafeef Qawasmeh

Hypertension

Mild to moderate hypertension usually asymptomatic, Symptoms depend on duration and rate of rise of the BP.

In general < 10 years of age : > 80% are secondary to renal causes (renal scarring, do DMSA scan).

> 10 years of age: essential

For taking the blood pressure properly, we must refer to the age matched- cuff size as undersized cuff lead to falsely high reading and vice versa.
We mean by the cuff size, the rubbery or internal size not the external Fabric size.

First time we take blood pressure in 4 limbs, and then we take it from the right arm only. Elevated BP must be confirmed on repeated visits (usually 3) before characterizing a child as having hypertension.

- ☒ Children more than 3 years old who are seen in a medical setting should have their BP measured.
- ☒ In children < 3 years, when to check BP?
  - Bronchopulmonary aplasia.
  - CHD
  - Renal abnormalities/ UTI
  - NICU admission.
  - History of prematurity, very low birth weight.
  - Increased ICP
  - Malignancy or bone marrow transplant.
  - Family history of congenital renal disease.
- ☒ Blood pressure readings:
  - Normal BP < 90^{th}
  - Pre-HTN: 90^{th} – 95^{th} or if BP exceeds 120/80 in any child > 12 years.
  - stage I: 95^{th} – 99^{th}
  - stage II: > 99^{th}
- ☒ target organs in hypertension:
  - Eye: retinopathy.
  - Brain: decreased LOC
  - Heart: gallop
  - Renal: renal failure.
  - Lung: crepitations.
  - Blood: microangiopathic microcystic anemia
- ☒ **Transient HTN** causes: post infectious/ HUS/ HSP/steroids/ cyclosporine/ NSAIDs/ tacrolimus.

☒ **Functioning food** like grapefruit and licorice cause increased HTN and decreased potassium.

☒ **Resistant HTN**: uncontrolled HTN despite use of 3 drugs, one of them is diuretic. Possible causes:

- Drug induced: NSAIDs/ cyclosporine/ steroids.
- Increased Na intake.
- Ingestion of licorice.
- Non-compliance.
- Inadequate doses or inappropriate combinations.
- Herbal remedies.

☒ **Hypertensive crisis**: is not defined by magnitude of BP elevation but rather by the presence of associated end –organ dysfunction (usually neurologic eye, or cardiac).

☒ **Hypertensive emergency**: It is a clinical situation characterized by marked elevation of BP (> 99th percentile for age & sex) associated with progressive target organ damage that requires immediate reduction of BP.

- Admit to ICU
- Hypertension +/-tachycardia +/-tachypnea, headache, visual complaints, hypertensive retinopathy, LVH, cardiac failure, seizures, encephalopathy, hemiplegia, facial palsy, cranial bruit.
- Situations include: Hypertensive encephalopathy, Heart failure, subarachnoid or intracerebral bleed, malignant hypertension.

☒ **Hypertensive urgency:** Significant elevation of BP without associated end organ damage.

Causes of HTN in children

☒ Most common cause in children is renoparenchymal not renovascular.
☒ Renal causes: AKI, GN, HUS, CKD, PCKD, renal tumors, renal scarring and dysplasia, renal transplantation, renovascular mainly < 1 year of age.
☒ Endocrine causes: cushing, pheochromocytoma, mineralocorticoid dysregulation, Liddle syndrome.
☒ 1ry hypertension.
☒ Coarctation of aorta.
☒ A renal scar is not a renal scar if found in those less than 1 year, it is actually a renal dysplasia and is important cause in pediatric age group.

Renovascular hypertension

- ☒ Uncommon cause in children, mostly below 1 year.
- ☒ RAS (Renal artery stenosis) is commonest cause */* associated with fibromuscular dysplasia.
- ☒ We don't use angiography so much nowadays, instead, we use MRA = Magnetic Resonance angiography which is highly sensitive.

History:

- ☒ Symptoms of visual, cerebral, cardiac & renal dysfunction.
- ☒ Prior history of hypertension.

Physical examination:

- ☒ VS, GCS, neurologic exam, fundi. The most common affected cranial nerve in symptomatic hypertension is abducens nerve.
- ☒ CVS exam: apex, brachiofemoral pulse delay.
- ☒ State of hydration, edema (peripheral & pulmonary). When you check for peripheral edema you should put 1 finger, 1 place and 1 minute so as not to miss a mild edema.
- ☒ Bruits, abdominal masses.

Investigations:

- ☒ ABG, serum electrolytes, urea, cr, CBC, blood film, urine analysis.
- ☒ With congestive heart failure o ECG & ECHO.
- ☒ Chest X ray.
- ☒ Consider plasma rennin, urine catecholamines, TSH, T4.
- ☒ If neurologic abnormalities persist after control of BP do emergency CT.

Management

- ☒ Weight reduction/ decrease salt intake/ discontinue certain food items or drugs.
- ☒ Pharmacologic treatment: ACE inhibitors/ Angiotensin receptor blockers/ Alpha and beta blockers/ Beta blockers/ Calcium channel blockers/ Central alpha agonist/ Diuretics/ Peripheral alpha antagonist/ Vasodilator.
- ☒ Hypertension and migraine: beta blocker.
- ☒ Pheocytochroma: alpha blocker only then beta blocker.
- ☒ Do not drop BP acutely if elevated in response to Increased ICP (need increased MAP to sustain CPP).

Neurologic hypertensive emergencies

- ☒ **Hypertensive encephalopathy:** mental status changes without focal neurologic signs, papilledema
  - Rx Nitroprusside
- ☒ **Acute ischemic stroke:** focal neurologic signs , headache
  - Rx Nitroprusside (controversial)
- ☒ **Intracranial hemorrhage:** Headache, focal neurologic signs
  - Rx Nitroprusside (controversial)
- ☒ **Subarachnoid hemorrhage:** Headache
  - Rx Nimodipine
- ☒ **Acute head injury:** Headache, signs of external trauma
  - Rx Nitroprusside

CV hypertensive emergencies

- ☒ **Acute MI**: chest discomfort, dyspnea, anxiety
  - Rx : Nitroglycerin
- ☒ **Acute pulmonary edema**: dyspnea, pulmonary rales
  - Rx : Nitroprusside or nitroglycerin
- ☒ **Recent vascular surgery**: tense suture lines
  - Rx : Nitroprusside
- ☒ **Epistaxis unresponsive to packing**: uncontrolled blood from the nose
  - Rx : Nitroprusside

Renal hypertensive emergencies

- ☒ **Acute deterioration in renal function**: none that is characteristic of this condition.
  - Rx: Fenoldopam

Catecholamine-excess states

- ☒ **Pheochromocytoma:** headache, sweating attacks, orthostatic hypotension.
  - Rx: Phentolamine
- ☒ **Drug related:** headache, mental status change, tachycardia.
  - Rx: Phentolamine

Sources: Dr. Kamal Agel handout, the old sheet by Sameer Al-hadidi and lecture notes.

Rafeef Qawasmeh

Enuresis

Source: Dr. Kamal Akl slides

Milestones of urinary control

- Newborn: reflex voiding 20 times per day
- 6 months: frequency of voiding decreases and volume increases
- 1 - 2 years: child recognizes the sensation of bladder fullness
- 3 years: some conscious control over micturition, achieve daytime control but accidents can occur
- 4 years: bladder volume now adequate, central control and mostly dry nights
- Dry Daytime : by age of 4 years
- Dry Night : by the age of 5
- First, bowel control is established at night Followed by bowel control during the day.
- Bladder control is achieved during day usually after 24 months & before 4 yrs. Finally children remain dry at night

Definitions

- Incontinence is defined as the uncontrollable leakage of urine that may be intermittent or continuous and occurs after continence should have been achieved.
- Continuous incontinence: constant urine leakage (eg. Ectopic ureter, iatrogenic damage to external sphincter)
- Intermittent incontinence: urine leaking in discrete amounts during day, night, or both.
- Enuresis: any urinary wetting that occurs during the night
- Daytime incontinence: urinary leakage that occurs during the day (no longer called diurnal enuresis).
- Dysfunctional voiding: inappropriate muscle contraction during voiding that is usually associated with constipation and is referred to as dysfunctional elimination syndrome.

Nocturnal enuresis:

- Primary: Nocturnal wetting in a child who has never been dry on consecutive nights for longer than 6 months in children ages 6 and older.
- Secondary: New-onset nighttime wetting on consecutive nights after a 6-month or greater period of dryness.
  -Usually not due to an organic cause.

-In some cases, a stressful event, such as a birth of a sibling, a move or the death of a parent or grandparent, is the source.
-Should be evaluated and treated like primary without need for additional lab work or studies.

Pathophysiology:

- Nocturnal polyuria, decreased ADH
- Small bladder capacity
- Impaired arousal
- rarely- GU abnormality or neurologic

Epidemiology:

- AGE:
  - 7 years old: 10%-15 % prevalence
  - Each subsequent year, 15% of bed wetters become dry
  - By 15 years of age, only about 1% of adolescents remain enuretic
- 20% of 5 yr old children still wet at night
- Rate of spontaneous resolution of nocturnal enuresis is 15%/year
- Boys > girls
- 1% of adults wet at night
- Daytime wetting is 2-3 x more common in girls than in boys.
- Enuresis occurs more frequently in lower socioeconomic populations and in larger families.

Etiology of enuresis:

- Only 3% of nocturnal enuresis has an organic etiology.
- Organic causes:
  - Tethered spinal cord (neuropathic bladder): abnormal gait, back pain, abnormal spine, abnormal gluteal crease, abnormal neurologic examination.
  - Ectopic ureter: constant wetting without dry interval, no urgency or frequency.
  - PUV
  - Uretrocele: prolonged stream, distended bladder.
  - Diabetes insipidus, DM, isothenuria (sickle cell disease), habit polydipsia.
  - UTI, fecal impaction, lower urinary tract obstruction.
  - Sleep apnea (increased atrial natriuretic factor which inhibits the renin-angiotensin-aldosterone pathway leading to increased diuresis).

- Since only 3% of nocturnal enuresis is caused by an organic disease state, most nocturnal enuresis is caused by a multifactorial combination of the following:

1- Genetics:
   - If both parents were bedwetters-->77% chance offspring would have enuresis
   - If one parent was a bedwetter--> 45% chance
   - If neither parent--> 15% chance
   - Concordance for enuresis is 68% for identical twins vs 36% for fraternal twins
   - Thus, parental age of resolution often predicts when the child's enuresis should resolve.
2- Sleep arousal dysfunction
   - By age 5, most (85%) children can associate between the presence of a full bladder and the sensation in the brain from a full bladder.
   - Daytime urination control is achieved first followed by the ability to wake up in the night to the sensation of a full bladder.
   - Anecdotally, parents report that the bedwetting episodes occur with their children who are difficult to arouse from sleep. However sleep studies HAVE NOT found an association from sound sleep cycles and bedwetting.
3- Urodynamics
4- Nocturnal Polyuria
   - There are some children who may have an abnormal circadian release of ADH. Normally, based on circadian rhythms, nocturnal urine production is approximately 50% less than daytime urine production but this may be altered in some children who suffer from enuresis.
   - Nocturnal polyuria may also be exacerbated by caffeine, medications, irregular drink intake, staying up late or its most common cause - habit polydipsia.The patient must try to modify these factors.
   - Nocturnal polyuria > 130% of [(30ml x age+ (30ml] up to 12 years of age
5- Psychological Components
   - Children with ADHD have a 30% increased chance for enuresis.
   - Enuretic children have lower self-esteem than children with chronic, debilitating illnesses.
6- Maturational Delay
   - Children with enuresis have more fine and gross motor delays, Perceptual dysfunction, Speech defects.
   - However, most enuretic children eventually are cured with or without treatment.

Evaluation of nocturnal enuresis:

- Usually, enuresis at 5 years old concerns parents. It does not concern children usually until around age 7. So generally, at age 6, evaluation should start.
- History:
  - Primary or Secondary
  - Family history
  - Symptoms- Polyuria, Polydipsia, Urgency, Frequency, Dysuria، Abnormal Urine Stream, Constant wetness
  - PMHX- UTI, Bowel complaints (15 % with enuresis have encopresis), Sleep Apnea Symptoms, Sleep Disorders, Developmental delay, ADHD
- Physical Exam: most will have a normal exam
  - Genitalia: Ectopic ureter, labial adhesions, urethral abnormalities, traumatized urethra
  - Abdomen: Distended bladder vs. fecal impaction
  - Upper airway: Mouth breathing secondary to adenoidal hypertrophy
  - Neurologic: Lumbrosacral exam to r/o overlying midline defect (sacral dimples, hair patches, vascular birthmarks), Gait, muscle tone, strength, DTRs and cremasteric, anal, abdominal reflexes.
  - Direct observation of urinary stream if hx. Suggests abnormality.
- Laboratory Tests (for all workups)
  - Urinalysis : Usually the only test needed

  -/+glucosuria r/o diabetes mellitus

  <1.15 specific gravity--r/o diabetes insipidus
  - Urine Culture if screening UA shows signs of UTI
- Radiographic tests (only if has history of UTI)
  - Voiding Cystourethrogram and Renal Ultrasound--if symptoms or signs suggest urinary tract obstruction or neurogenic bladder or history of UTI
  - Bladder Ultrasonography (pre- and post- voiding)-- to rule out partial emptying
- Sleep studies (if indicated by history) To rule out sleep disorders or sleep apnea.

Management:

- Avoid punishment.
- Behavioral and motivational treatment
  - If the child does not want to do the treatment then wait til he/she is ready to be an active participant
  - The child must do three things: 1)wake up by himself, 2)find the toilet and 3)urinate there.
  - Make the toilet easy access.
  - Avoid excess fluids 2 hrs before sleep.

- Empty bladder prior to bed time.
- No diapers.
- Include child in morning cleanup.
- Use bedwetting chart - Reward the child for a dry night--including for waking up and going to the bathroom.
- If unsuccessful after 3 to 6 months, a different treatment program should be tried.

- If >7yo:
  - Enuresis alarm
  - Desmopressin- 0.2 - 0.6mg PO up to 1hr before bedtime
  - Combo +/- refer if not effective after 6-8wks
  - 2nd line: oxybutynin, imipramine
- If there is any other comorbid conditions that can lead to enuresis, they must be treated first:
  - constipation--stool softeners to have daily bowel movements
  - urinary tract infection---prophylactic antibiotics
  - sleep apnea - adenoidectomy and tonsillectomy

Pharmacologic therapy:

- Used to treat---not to cure while awaiting natural resolution from maturation.
- DDAVP (Desmopressin) is the FIRST LINE CHOICE
  - Synthetic analogue of ADH.
  - Decreases urine production by increasing distal tubule water resorption and urine concentration overnight.
  - Contraindications: habit polydipsia (hyponatremia), hypertension or heart disease.
  - General use: Increase dose every 2 weeks to minimal effective dose, use for 6 months. Then try off for 2 weeks to see if patient has outgrown the problem.
- Imipramine
  - Mechanism of action: anticholinergic effect increases bladder capacity and norardrenergic effect decreases bladder detrusor excitability.