* M.C time of Jaundice → 2-3 day
* M.C cause of Pathological Jaundice is hemolysis
* M.C cause of hemdysis is ABO incompetability
* Rh incompetability is the most common cause of kernicterus = most serious
* 1st day jaundice always Pathological

→ This because Rh has: [1] increased antigenicity [2] Low molecular weight

Hyperbilirubinaemia

تم التقريل بواسطة: عبادة العايد

تبييض : عامر العجالين

Hyperbilirubinaemia

The most common cause of direct hyperbilirubinemia in neonates is biliary atresia (after 8 weeks its irreversible (leads to liver cirrhosis) so the diagnosis is top emergency)

We treat it by Kasai procedure

The leading cause of kernicterus is indirect hyperbilirubinemia so in neonates its more Important than direct hyperbili.
Because conjugated bilirubin Can'nt Cross BBB.

The most common cause of indirect hyperbili. Is physiological jaundice.
And the most common pathological cause is ABO incompatibility . So the most important question to mother is blood group

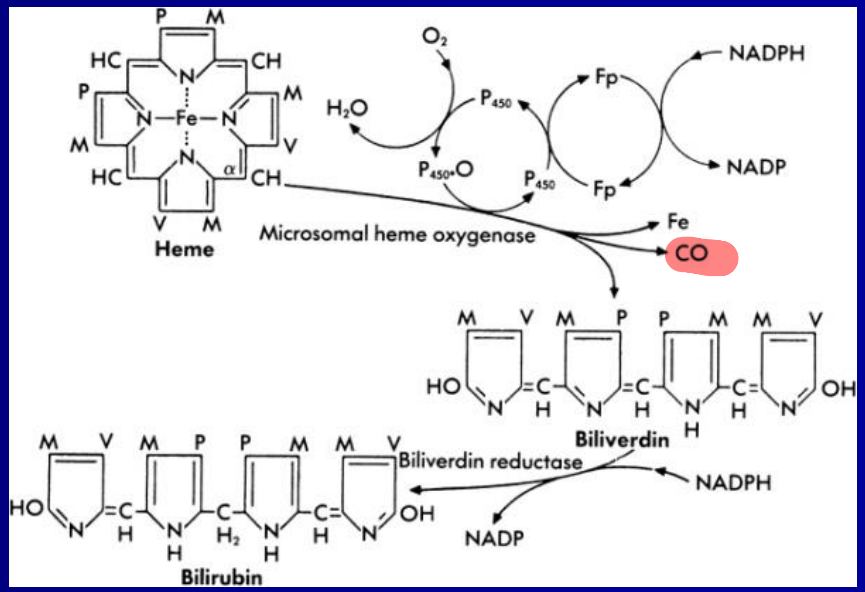
Background

- Jaundice is the most common condition that requires **medical attention** in newborns.
  - Jaundice is observed during the 1st wk
    - 60% of term infants
    - 80% of preterm infants
- The yellow coloration of the skin and sclera (***icterus)*** is the result of accumulation of **unconjugated bilirubin.**
- In most infants:
  - unconjugated hyperbilirubinemia reflects a **normal transitional** phenomenon.
- unconjugated bilirubin is neurotoxic (kernicterus).

BILIRUBIN METABOLISM

Bilirubin Production

- Lysis of red blood cells (RBCs) releases heme from hemoglobin
- heme is then converted to biliverdin by Heme oxygenase-1 (HO-1)
- This rate-limiting step produces free iron and carbon monoxide (CO)
- biliverdin is converted to bilirubin by biliverdin reductase



Catabolism of heme to bilirubin by mirosomal *heme oxygenase* and biliverdin *reductase*.

1 g of hemoglobin forms 34 micromole of bilirubin

In neonates there is high Hemoglobin level and short life span of RBCs so they will have high level of bilirubin.

* to distinguish of the infant who come with jaundice in 2-3day is Physiobgical or Pathological, you have to measure TSB & Hemoglobin
* Pathological → For each 1g drop of Hb, bilirubin has to increase up to 2mg = 34 mmol

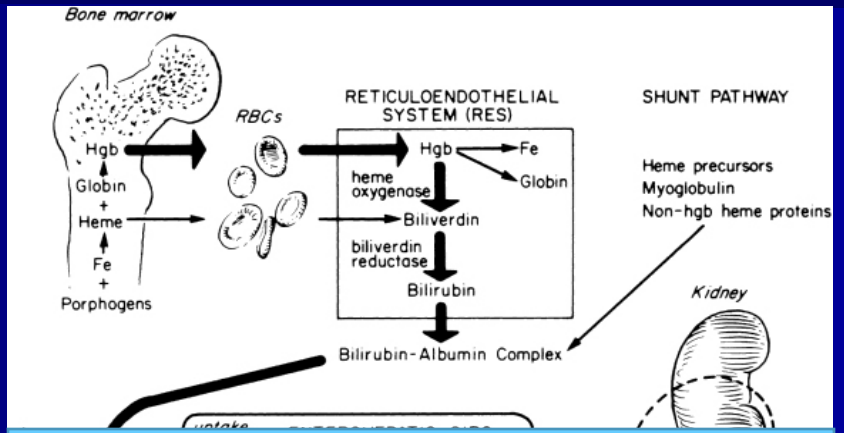
Physiological → not meet this rule

- 1 gram decrease in hemoglobin should produce 2 gram increase in TSB(total serum bilirubin)
- Pt hemoglobin level is 16 and TSB = 10.. after 4 hours hemo.level decreased to 15 and TSB increased to 12 so this is typical hemolysis (ABO or Rh incompatibility)
- Another pt .. Hemo.level was 16 and TSB =10 after 4 hours Hemo.level decreased to 15 and TSB increased to 11 … in this case the cause is not hemolysis (mostly its physiological jaundice)

BILIRUBIN METABOLISM

Transport of Bilirubin in Plasma

- Unconjugated bilirubin released into the circulation by the reticuloendothelial cells is rapidly bound to *albumin*
  - *7 to 8 mg/dL of unconjugated bilirubin can be bound to each 1 gram of albumin.*
- Binding of bilirubin to albumin increases postnatally with age and is reduced in infants who are ill.
- The presence of endogenous and exogenous binding competitors, such as certain drugs, and high level of fatty acid which is present in breast milk (although that, breast feeding is not contraindicated in hyperbilirubinemia)… also decreases the binding affinity of albumin for bilirubin



Breast milk doesn't lead to Kernicterus although TSB can reach high levels.

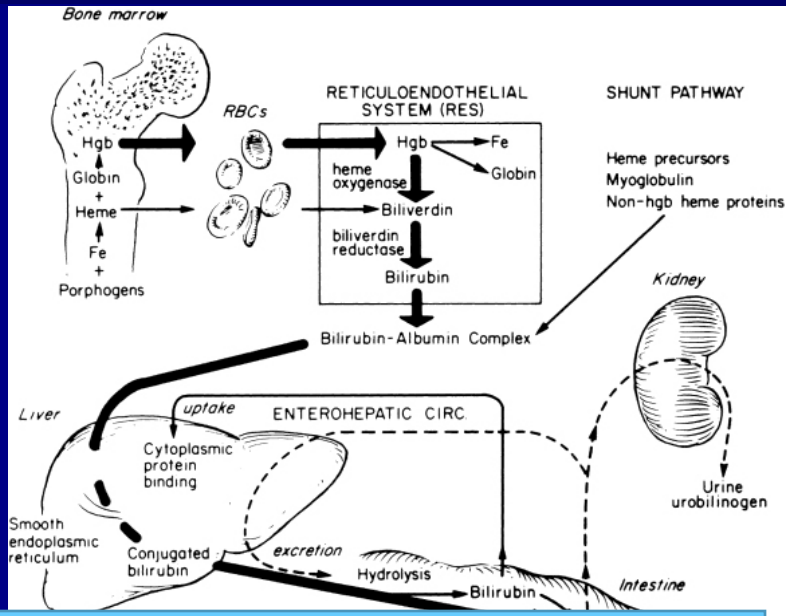
* albumin is the most important transporter of free bilirubin to hepatocytes, so → Low albumin = more Jaundice

BILIRUBIN METABOLISM

Hepatic Uptake of Bilirubin

* this is a carrier mediated diffusion = energy requiring, so hypoglycemia may lead to jaundice for this cause (Low energy)

- Bilirubin enters the liver cell by a process of carrier-mediated diffusion, with B-ligandin (Y protein) of the liver cell cytoplasm as the major intracellular transport protein.
  - Bilirubin dissociates from circulating albumin before its entry into the liver cell.
- Ligandin concentrations are low at birth but rapidly increase over the first few weeks of life (after 2 weeks).
- Uptake of bilirubin into hepatocytes increases with increasing ligandin concentrations
- Ligandin concentrations may be increased by the administration of pharmacologic agents such as phenobarbital.

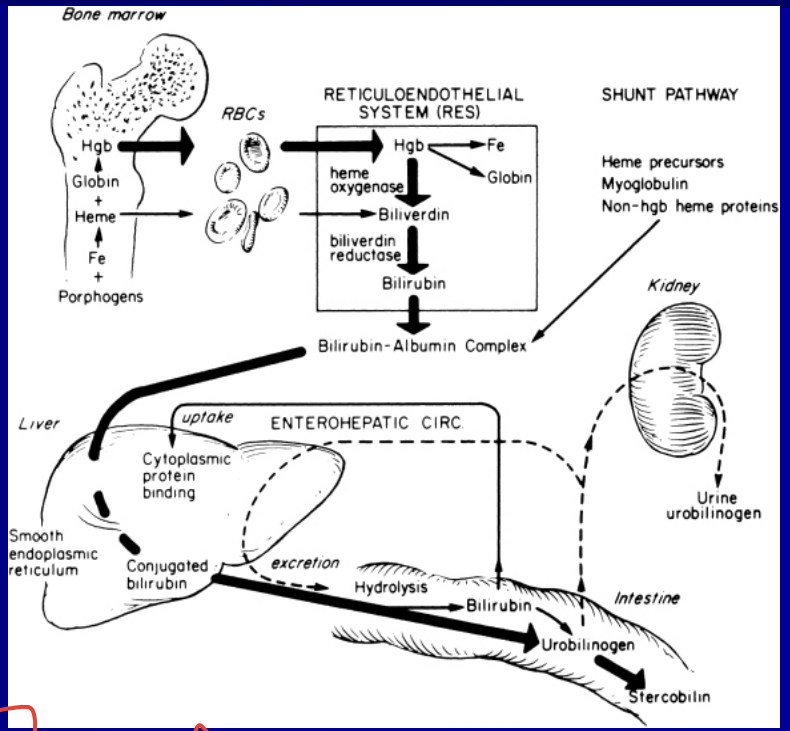


B-Ligandin need ATP so hypoglycemia can cause hyperbilirubinemia (in breast fed hyperbilli)

BILIRUBIN METABOLISM

Conjugation & Excretion of Bilirubin

- Bilirubin is bound to glucuronic acid (***conjugated***) in the hepatocyte endoplasmic reticulum in a reaction catalyzed by ***uridine diphosphoglucuronyltransferase (UDPGT).***
- Water-solubility allows conjugated bilirubin to be excreted into bile.



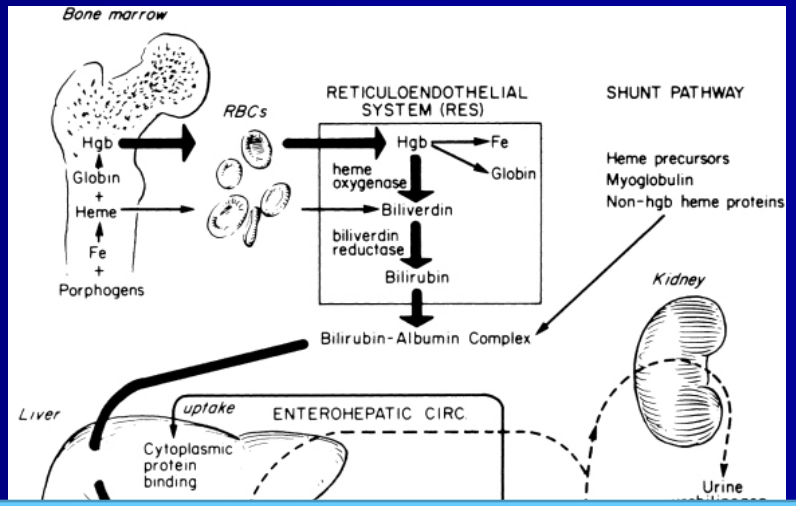
Low level of UDPGT is the main cause of physiological jaundice
Which reach normal level after 7-10 days in full term neonates
And after 2 weeks in preterm neonates

if Jaundice Persist up to this Period
↳ Delayed Jaundice

BILIRUBIN METABOLISM

Enterohepatic Absorption of Bilirubin

- Conjugated bilirubin is not absorbed from the intestine, whereas unconjugated bilirubin is absorbed
- Unconjugated bilirubin then may be reabsorbed across the intestinal mucosa to return to the liver via the portal circulation.



- There is 3 types of glucoronidation (mono , di and tri)
- Mono and di are unstable forms
- When it reaches the intestine its decoupled into unconjugated bilirubin by beta glucornidase enzyme and then reabsorbed again
- Breast milk contains high level of beta glucornidase enzyme
- In neonates transient time of the gut is long (6-8 hours while 2-4 hours in adults) so there is enough time for reabsorption of mono and di bilirubin
- And in some cases which delay gut transient time such as pyloric stenosis can lead to jaundice !

TSB = 20 → High risk for kernicterus

The Bilirubin "Life Cycle"

Summary

- Bilirubin is the end product of haemoglobin breakdown
- Bilirubin is formed from non-toxic biliverdin
- Bilirubin is released into the circulation in the unconjugated form
- Unconjugated bilirubin binds with albumin and is transported to the liver
  - *Many medications compete with bilirubin for these albumin binding sites*

The Bilirubin "LifeCycle"

Summary

- Uptake of bilirubin by hepatocytes requires intracellular proteins known as "Ligandins"
- Bilirubin is converted to its conjugated form via glucuronidation
- The conjugated form is then excreted into the GI tract and eliminated from the body via the stool
- Reabsorption of stercobilin can occur from the GI tract via the enterohepatic circulation

Neonatal Risk Factors

- High initial haematocrit and decreased red blood cell survival
  - t1/2 of adult RBC's is 120 days, of HbF containing RBC's is 90 d.
- Frequent occurrence of haematomas (e.g. cephalhaematoma) and bruising
- The newborn liver Metabolism in utero occurs via the placenta and maternal liver

  ⇒ At birth there is a sudden increased bilirubin load
- **Decreased ligandin** concentration

Neonatal Risk Factors

- Decreased activity of the glucuronidation pathway
- Increased enterohepatic circulation
- Relative dehydration in the first few days concentrates the bilirubin
  - because of low experince of mother with lactation
- Relative calorie deprivation in the first few days decreases glucuronidation
  - To treat it, just establish the experince of mother & give formula milk only for 2 days
  - *These last 2 factors more marked in breast fed jaundice.*

In true breast milk jaundice the causes are : 1-high level of fatty acid in the milk
2-high beta glucoronidase content

Breast milk not contraindicated in neonatal jaundice

Neonatal Risk Factors

Binding Site Competitors مهم

- Sulfonamides
- Oxacillin
- Diazepam
- Cefonicid
- Cefotetan
- Ceftriaxone
- Cefmetazole
- Moxalactam

Avoid all these agents in the neonatal period, especially if jaundiced, they may *displace bilirubin from albumin binding sites* and precipitate **kernicterus**

Diagnosis of Hyperbilirubinaemia

History → mainly diagnosis by history

- Presentation and duration of neonatal jaundice
  - Typically, presentation is on the second or third day of life (physiological jaundice). → also it may occur in Pathological causes so it is Physiological after exclusion of other causes
  - Jaundice that is visible during the first 24 hours of life is likely to be pathological.
  - Infants who present with jaundice after 3-4 days of life may also require closer monitoring.(if it comes with diarrhea, vomiting and malnutrition signs is galctosemia until prove another diagnosis)
  - In infants with severe jaundice or jaundice that continues beyond the first 1-2 weeks of life:

⇒ the results of the newborn metabolic screen should be checked for galactosemia and congenital hypothyroidism (read about it) to prevent bad complications

شوفهم

Diagnosis of Hyperbilirubinaemia

History

- Family history

if there are history in siblings = baby is high risk group, and Rh incompetabili
increase with subsequent of next Pregnancy

  - Previous sibling with jaundice in the neonatal period, particularly if the jaundice required treatment
  - Other family members with jaundice or known family history of Gilbert syndrome
  - Anemia, splenectomy, or bile stones in family members or known heredity for hemolytic disorders
  - ممكن نستفيد من ال blood film حتى نقدر نحدد ال retic count (عمر 1 يوم الطبيعي يكون 7% ،، على عمر 7 ايام يصير 1% ،، اذا ارتفع معناته في (hemolysis
  - Liver disease
  - حكى كثير معلومات خارج الموضوع عن Gilbert syndrome, G6PD الدقيقة 52 من الريكورد ،،،، اوا قرا عنهم

(*) if Pt. commos with Jaundice, the cause incidince in order:-

1. Physiological jaundice, if not?? Do blood grouping to detect 2
2. ABo, Rh incompetability, if not? Do G6PD level to detect 3
3. G6PD, X-linked disease, if not?

↳ mainly affect male, but also may affect females by lionization theory
↳ deactivation of X^R in mother = affection for female

* There are 4 types of G6PD:

1. white american → A^+
2. Black american → A^-, more sever
3. Black African → B^+, more sever
4. meditirrian → B^- = absolute deficncy of enzyme

So any chemical (as Jaa oder) or stress condition (as delivery) may cause hemolysis so it may present in 1st or 2nd day.

4. Heriditary spherocytosis

● Note:

Thalassemia & sickle cell not Part of diffrential Dx in neonatal age group, it commos with older childs except of deletion of 3 alpha gens, it will has hydrops fetalis during fetal life & it will be incompetable of life

Diagnosis of Hyperbilirubinaemia

Direct hyper bilirubenemia, thrombocytopenia
Petechiae & Delayed of cord clamping
↳ plot of ... .- - — 39 weeks

History

- History of pregnancy and delivery
  - Maternal illness suggestive of viral or other infection ...
    *(**TORCH syndrome** is a cluster of symptoms caused by congenital infection with toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and other organisms including syphilis, parvovirus, and Varicella zoster.[1] Zika virus is considered the most recent member of TORCH infections)*
  - Maternal drug intake
  - Delayed cord clamping (cause polycythemia)
  - Birth trauma with bruising

* M.C cause of obstructed type → atresia
1. has to be Diagnosed & treated within 8 weeks
2. if not treated, it may cause irreversable type of liver cirrhosis

Diagnosis of Hyperbilirubinaemia

History

- Postnatal history
  - Loss of stool color
  - Breast feeding
  - Greater than average weight loss
  - Symptoms or signs of hypothyroidism
  - Symptoms or signs of metabolic disease (eg, galactosemia)
  - Exposure to total parental nutrition

Diagnosis of Hyperbilirubinaemia

Physical examination

- In most infants color is the only finding on physical examination.
- More intense jaundice may be associated with neurologic findings :→ Signs of kernicterus is very important to be examined
  - drowsiness
  - changes in muscle tone
  - seizures
  - altered cry characteristics

⇒ in a significantly jaundiced infant these are danger signs and require immediate attention to prevent kernicterus. Start exchange transfusion

↳ So it is very important to diagnose kernictirus because all management steps will be diffrent

Diagnosis of Hyperbilirubinaemia
Physical examination

- Neonatal jaundice with , Hepatosplenomegaly, petechiae, and microcephaly may be associated with :
  - *hemolytic anemia*
  - *sepsis*
  - *congenital infection*

- infant's weight curve should be evaluated

Diagnosis of Hyperbilirubinaemia

Bilirubin Screening

- Visible jaundice at about 5 mg/dl
- TCB Monitors (transcutaneous bilirubinometers)
  - Non invasive
  - Actual levels usually less than TCB
- Heelstick vs. venous serum levels
  - Correlate well with levels < 10 mg/dl
  - Heel sticks run about 1 mg higher when levels > 10 mg/dl
  - Heelstick is accurate when the level is below 10mg/dl ,, when the level is higher the reading is inaccuarte

Diagnosis of Hyperbilirubinaemia

When To Work Up مهم

- Conjugated hyperbilirubinaemia; any time
- Cord bilirubin (if obtained) > 70 µmol/l = hemolysis
- Total bilirubin > 170 µmol/l at or before 24 hours of life
- An increase of > 85 µmol/l/day or 0.5 per hour = hemolysis
- A total bilirubin > 250 µmol/l in any infant

Diagnosis of Hyperbilirubinaemia
The Initial Work Up

- A full history and physical exam , Attention to :
  - birth weight
  - discharge weight
  - weight on admission
  - feeding history
  - state of hydration

Diagnosis of Hype

The Initial

- Total and direct bilirubin
- CBC
- Blood type and Rh determination in mother and infant
- Direct antiglobulin test (DAT) in the infant (direct Coombs test) its needed to give IV/IG
- Hemoglobin and hematocrit value
- Serum albumin levels

Direct coombs test :
1-Rh strongly positive
2-mixed Rh and ABO incompatibility is moderately positive
3-ABO alone is slightly positive or negative
4-G6PD negative
Pure Rh is more antigenic than ABO or mixed incompatibility

Diagnosis of Hyperbilirubinaemia

Blood Group Incompatibility

- Blood group type and Coombs test on infant if :
  - There is a set up for blood group incompatibility : if the *mom O and baby A or B*
    - significant anaemia
    - Reticulocytosis

- The Direct Coombs test :
  - Reliable predictor of Rhesus (if the *mom –ve and baby +ve*) and minor blood group incompatibility
  - Poor test in ABO incompatibility due to the relative lack of type specific antigen on the surface of neonatal RBC's, therefore often negative.

→ Determine load of Ab, so if Rh incompatability was the cause it will be strongly +ve, in subsequent Pregncy also it is strongly +ve → it is very important to determine this because in this cased treatment directly by IVIG

(*) why we don't treat all cases by IVIG ??
1. it is very expensive (1 ampulla = 1000 JD)
2. has many side effects

Diagnosis of Hyperbilirubinaemia

- Peripheral blood film for erythrocyte morphology
- Reticulocyte count
- Conjugated bilirubin levels
- Liver function tests:
  - Aspartate aminotransferase (ASAT or SGOT) and alanine aminotransferase (ALAT or SGPT) levels are elevated in hepatocellular disease.
  - Alkaline phosphatase and γ -glutamyltransferase (GGT) levels are often elevated in cholestatic disease.
- Ultrasonography: Ultrasonography of the liver and bile ducts is warranted in infants with laboratory or clinical signs of cholestatic disease

Diagnosis of Hyperbilirubinaemia

- Tests for viral and/or parasitic infection: These may be indicated in infants with
  - Hepatosplenomegaly
  - petechiae
  - Thrombocytopenia
- Reducing substance in urine: This is a useful screening test for galactosemia
- Blood gas measurements: The risk of bilirubin CNS toxicity is increased in acidosis.
- Thyroid function tests

full term or Premature ??

Physiologic jaundice

(*) any jaundice in premature baby = should to be treated, why ??

1. immature BBB
2. 70% are complicated by sepsis → very high risk factor for Kernicterus
3. they has respiratory & metabolic acidosis → acidosis increase permiability of BBB
4. hypothermia

there are many risk factors for kernicterus in Preterm babies, so it is very important to ask about gestational age, which is very important in management because it determine if baby is [high, intermediate or low risk group]

Physiologic jaundice

- Neonatal physiologic jaundice results from simultaneous occurrence of the following 2 phenomena:
  - Bilirubin production is elevated because of increased breakdown of fetal erythrocytes. This is the result of the shortened lifespan of fetal erythrocytes
  - Hepatic excretory capacity is low both because of :
    - low concentrations of the binding protein ligandin in the hepatocytes
    - low activity of glucuronyl transferase, the enzyme responsible for binding bilirubin to glucuronic acid, thus making bilirubin water soluble (conjugation).

physiologic jaundice
TERM NEONATE

- characterized by a progressive rise in TSB concentration from approximately 2 mg/dL (34 µmol/L) in cord blood to a mean peak of :
  - 5 to 6 mg/dL (86 to 103 µmol/L) between 48 and 120 hours of age
  - most infants presenting at 72 to 96 hours of age
  - 10 to 14 mg/dL (171 to 239 µmol/L) between 72 and 120 hours of age.

2-5 days

activation to enzyme leads to this decline

- This is followed by a rapid decline to approximately 3 mg/dL (51 µmol/L) by the 5-7 day of life.

Physiological jaundice occur only one time.

Physiologic jaundice
TERM NEONATE

- results from :
  - Six fold increase in the load of bilirubin
  - marked deficiency in UGT activity
  - Hepatic uptake and excretion of bilirubin are also deficient during this period

Physiologic jaundice
PRETERM NEONATE

- in premature neonates is more severe than in full-term neonates
- mean peak TSB concentrations reaching 10 to 12 mg/dL (171 to 205 µmol/L) by the fifth day of life.
  - This delay in reaching the maximum concentration as compared with the full-term neonates primarily reflects the delay in maturation of hepatic UGT activity.

Physiologic jaundice
PRETERM NEONATE

- Because mean peak unconjugated bilirubin concentrations of 10 to 12 mg/dL (171 to 205 µmol/L) may be associated with ***acute bilirubin encephalopathy or kernicterus***

⇒ all degrees of visible jaundice in ***premature neonates*** should be monitored closely and investigated fully

PATHOLOGIC HYPERBILIRUBINEMIA

Conjugated Hyperbilirubinemia

- Direct fraction > 20% of the total bilirubin level
- Always pathologic
- Phototherapy ineffective, and in fact will stimulated melanin formation leading to the bronze baby syndrome

Phototherapy convert indirect billi to direct bilirubin

Exchange transfusion is ineffective too.

Conjugated Hyperbilirubinemia

Differential Diagnosis اعرف الى بالاصفر

Obstructed time is very dangerous

- Biliary atresia
- Choledochal cysts
- Choledocholithiasis
- Bile duct plugs, perforation, or compression
- Galactosemia
- Fructosemia
- Glycogen storage disease type IV
- Tyrosinemia
- Niemann-Pick
- Gaucher disease
- Wolmann Disease
- Cholesterol ester storage disease

Conjugated Hyperbilirubinemia
Differential Diagnosis

- Trisomy 18
- Down syndrome
- Alpha1 antitrypsin deficiency
- Hypopituitarism
- Cystic fibrosis
- Zellweger syndrome
- Familial hepatosteatosis
- Persistent intrahepatic cholestasis
- Drug induced cholestasis
- TPN hepatitis

Conjugated Hyperbilirubinemia
Differential Diagnosis

- **Infections**
  - Hepatitis B and C
  - Syphilis
  - Toxoplasmosis
  - Rubella
  - CMV
  - HSV
  - Varicella
  - Echovirus
  - Coxsackie
  - Leptospirosis
  - Tuberculosis
  - Bacterial sepsis

Unconjugated Hyperbilirubinemia

- By far more common
- Usually physiologic
- Pathologic etiology considered when:
  - Clinical jaundice in the first 24 hours
  - Rapid rise in level (> 85 μmol/L/day)
  - Prolonged jaundic
    - > 1 week term, > 2 weeks preterm : 1-hypothyroidism 2-breast milk jaundice , 3-pyloricstenosis
  - Approaching threshold for therapy

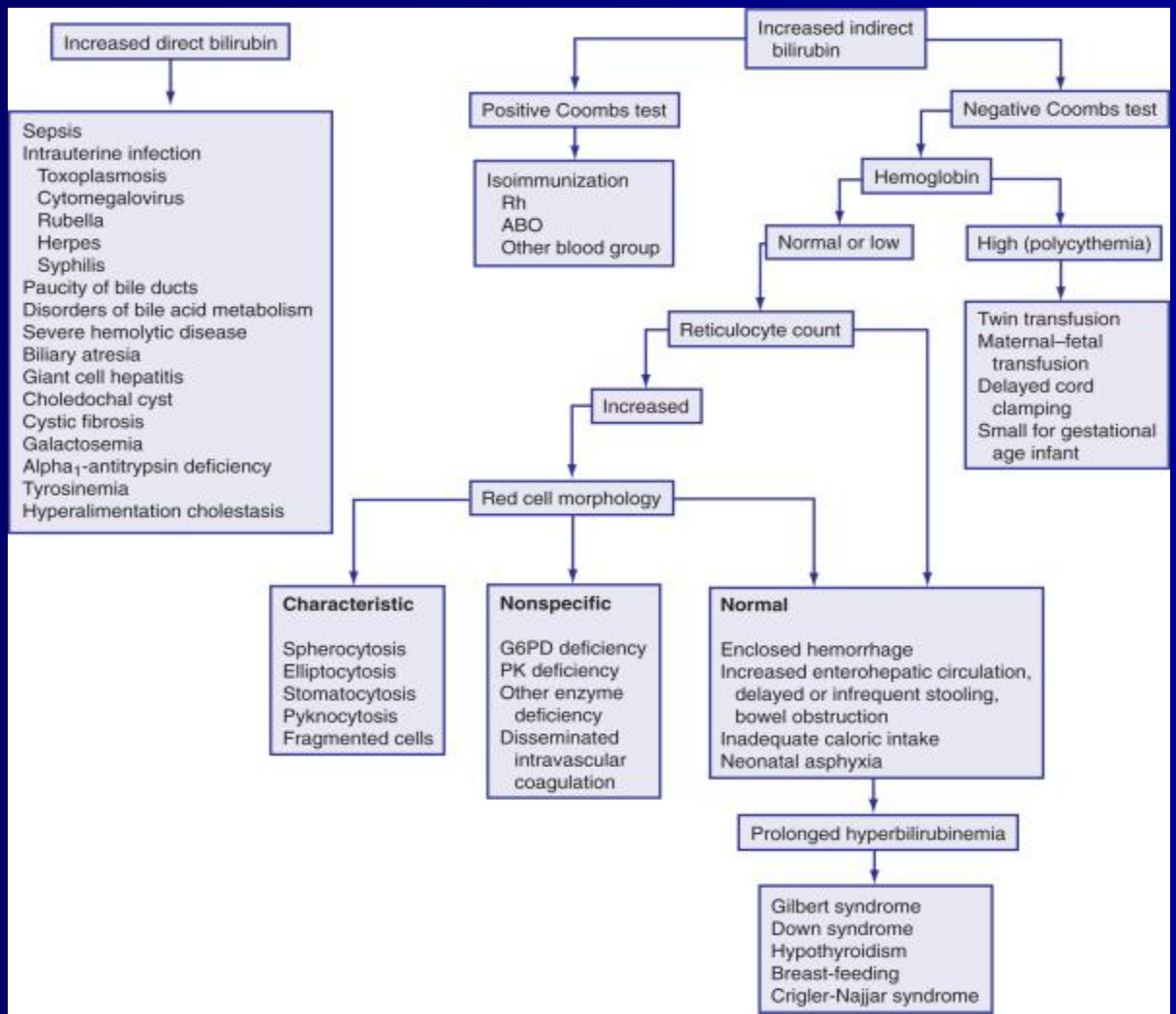
Unconjugated Hyperbilirubinemia
Differential Diagnosis

- Autoimmune hemolytic anemia
  - Rh, ABO, minor blood group incompatibility
    - ↳ sever hemolysis
- RBC defects
  - Spherocytosis, elliptocytosis, G-6-PD deficiency, thalassaemia
    - ↳ only with 3 alpha deletion
- Hemorrhage
  - Cephalhaematoma, birth trauma, clotting disorders

Unconjugated Hyperbilirubinemia
Differential Diagnosis

- Sepsis
- Maternal diabetes → always has Polycythemia
- Hypothyroidism
- Crigler- Najjar (types I & II)
- Gilberts → benign, doesn't cause kernicterus (5-7
- Upper GI obstruction

approach to the diagnosis of neonatal jaundice



→ True breast milk → composition of milk (high FA, high glucourindase enzyme)

→ Breast feed jaundice → Primigravida, low experince of mother with lactation

Breast Milk Jaundice

⊛ True breast milk jaundice:
- Rare
- baby will be mainly normal on examination
- commonly after 1 week
- Dx: *stop breast milk for 2 days, TSB has to be decreased dramatically
  *then go again to breast milk, if TSB increased = True breast milk jaundice

⊛ Breast feed jaundice:
- caused by low experince of mother with lactation.
- jaundice because of relative dehydration & calori depreviation
- Treated by: ① Start formula milk for 2 days.
  ② establish experince of mother with lactation.

Breast milk is not contraindicated in neonatal period

Breast Feeding Jaundice

- Decreased elimination and increased enterohepatic reabsorption
- associated with poor feeding practices and not with any change in milk composition.
  - *In contrast, the breast milk jaundice is apparently related to a change in the composition or physical structure of the milk*
- Poor initial feeding and lactation
- Relative dehydration and calorie deprivation
- Occurs within the first few days of life (1-3 days)
- Treatment should focus on establishing adequate lactation(and give formula)
- Usually occurs in prime gravida

True Breast Milk Jaundice

- Relatively uncommon
- β-glucuronidase may play a role by uncoupling bilirubin from its binding to glucuronic acid, thus making it available for reabsorption
- *fatty acids* in the breast milk interfere with *bilirubin uptake*
- Onset usually at about one week of age
- By definition, infant should be well nourished and gaining weight
- Brief cessation of BM will cause dramatic fall in levels

Isoimmunization

Rh Isoimmunization

- RH blood group proteins; are a highly antigenic causing severe isoimmunization with a high risk of fetal hydrops and death
- the D antigen may produce maternal sensitization with a fetomaternal hemorrhage as small as 0.1 mL.
- Rh hemolytic disease was the most common cause of kernicterus.
- maternal prophylaxis with high-titer anti-D immunoglobulin G (RhoGAM) combined with aggressive fetal surveillance and transfusion has greatly reduced the incidence and severity of this disease.

ABO Isoimmunization

Less sever than Rh

- Neonates with group A or B erythrocytes may have, hemolysis, and positive Coombs' tests
- because of transfer of maternal anti-A or anti-B antibody into the fetal circulation.
- **The disorder may occur in the first-born without prior sensitization of the mother and is generally milder and of shorter duration than Rh erythroblastosis
- may also cause severe hemolysis, jaundice, and kernicterus.

Kernicterus

Kernicterus

- Acute complication of Conj. Hyperbilirubinaemia

- Bilirubin stains and injures basal ganglia
  - High pitched cry
  - Neck retraction/ opisthotonus
  - Lethargy & coma
  - Seizures
  - Death
  - fever → although without infection or sepsis

Presence of any sign of Kernicterus change the management to exchange transfusion .
Neonates are more prone to Kernicterus because : 1-immature BBB (especially premature baby so any jaundice in those is alarming sign and need observation) ,2-premature babies have respiratory distress and metabolic acidosis ,3-hypothermia ,4-low albumin level
All these factors increase exchange across BBB

Kernicterus

phases of kernicterus ما ركز عليها

- **ACUTE FORM**
  - Phase 1 (1st 1–2 days):
    - poor sucking
    - stupor
    - hypotonia
    - seizures
  - Phase 2 (middle of 1st wk):
    - hypertonia of extensor muscles
    - opisthotonos
    - fever
  - Phase 3 (after the 1st wk):
    - hypertonia
- **CHRONIC FORM**
  - First year:
    - Hypotonia
    - active deep tendon reflexes
    - obligatory tonic neck reflexes
    - delayed motor skills
  - After 1st yr:
    - movement disorders (choreoathetosis, tremor), upward gaze, sensorineural hearing loss

Kernicterus

Outcome

- Long-term survivors often demonstrate :
  - choreoathetoid cerebral palsy → most dangerous
  - upward gaze palsy
  - sensorineural hearing loss
  - mental retardation
  - dental dysplasia during later infancy and childhood.

- Death

* Kericterus incidince decreased in last years because of early detection and management of jaundice
↳ so screening is very important

Kernicterus

Vigintophobia (fear of 20 (mg/dl)

most dangerous factors for kernicterus
1. hemolysis
2. >20 mg/dl

- 1952 study of Rh incompatible infants
  - 50% with bilirubin levels > 500 μmol/l developed kernicterus
  - No cases in 200 consecutive infants with bilirubin levels < 340 μmol/l (20 mg/dl)

- 1959 study on 54 healthy full term infants without Rh or ABO disease
  - 19 infants > 425 μmol/l
  - 9 infants > 510 μmol/l
  - All with normal N/D exams at 6 months, 1, 2, and 4 years

- However kernicterus <u>can</u> occur in the absence of haemolysis

- مش مهم كثير ... يقول انه قبل كانوا يعتمدوا على رقم 20 اذا تخطاها تركيز البيلروبين رح يصير kernicterus ولكن هذا الكلام تم الغاءه

Kernicterus

The Dilemma المعضلة

- Not clear what level represents a risk to normal, healthy, term infants
- Infants with *Rhesus disease* clearly at risk > (20 mg/dl)
- ABO probably the same risks as those with Rhesus disease
- Premature infants can probably develop kernicterus at levels well below 340 μmol/l
- Sepsis increases risk for any infant
- Hyperosmolar states injure the blood brain barrier and make it more permeable to bilirubin

Hyperbilirubinemia
Treatment

- Conjugated
  - Treat underlying illness
  - *Phenobarbital*, has minor effect
  - Actigall (*Ursodeoxycholic acid* by mouth) appears moderately effective.
- Unconjugated
  - Benign neglect (With close follow up!)
  - Phototherapy
  - IVIG
  - Exchange transfusion

Only definitive treatment

given just to decrease TSB, Not the definitive treatment

1) Breast milk
2) Physiological

Hyperbilirubinemia

Treatment

- Breast feeding can be continued in the majority of infants
- If there is significant weight loss or poor breast feeding , you may supplement with formula
- If close to exchange level, *D/C feeding* as you may have to insert umbilical lines.

Conj. Hyperbilirubinemia Treatment

Phototherapy

↳ very safe & very effetive, it leads to reduce Blood exchange

- Induces a conformational change in the shape of the bilirubin molecule.
- Leads to 2 carboxyl groups becoming separated and thus ionized
- Therefore the bilirubin becomes water soluble.
- Known as photo-isomerization.

Conj. Hyperbilirubinemia Treatment

Phototherapy

- Start therapy at a bilirubin level which is 85 μmol/l
- The lights should cover the entire baby
- Increase in either intensity or body surface area covered will increase effectiveness.
- Double phototherapy is more effective, especially if all round illumination is provided

If you see bilirubin increased not decreased you have to check these factors.

ممكن مليشة الكاميرة أولي ومخزنة الexposure

Phototherapy to be effective should be :
1-blue light
2-wave length 420-450 nM
3- less than 40 cm far from baby
4-full exposure
5-lamp life not more than 10000 hour

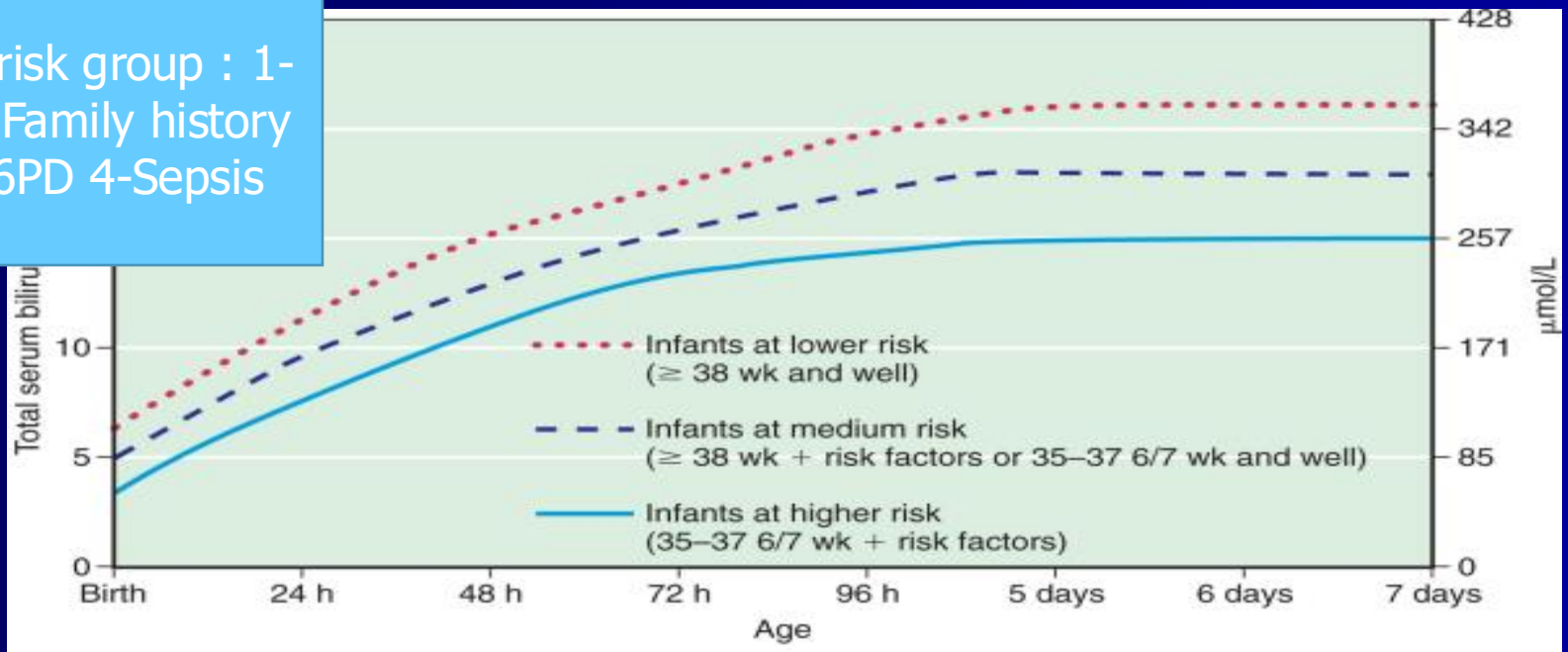
Conj. Hyperbilirubinemia Treatment
Phototherapy

- There are no known long term effects from phototherapy
- Animal studies have demonstrated a risk for *retinal damage*
  - All infants should have their eyes covered when being treated
- Minor adverse effects include :
  - abdominal distension
  - frequent green stools
  - decrease serum calcium
- Eye covers :
  - interfere with maternal-infant interaction
  - increase risk of conjunctivitis.

Ⓐ Baby 24 hrs & TSB = 10 mg/dl, what is the treatment?? Depend on risk group ① high ② moderate ③ sever

Guidelines for phototherapy in hospitalized infants of 35 or more G.A

High risk group : 1-Rh 2-Family history 3-G6PD 4-Sepsis



- 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 < 3.0 g/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.

في الرسمة بتشوف العمر والـ TSB وبترسم نقطة الالتقاء فإذا أصبحت عالخط تبع الـ gestational age أو فوقه = لازم Blood transfusion

Conj.Hyperbilirubinemia Treatment

IVIG

only with direct coombs test +ve

*Dose: 0.5 g/Kg given slowly over 4 hrs

- 1992 – Rubo J, et al prospective randomized trial:
  - 32 infants with Rh haemolytic disease
  - Study group treated with 500 mg/kg as a single dose
  - Both groups treated with phototherapy
    - 11/16 controls required exchange transfusions vs. 2/16 study patients
    - No adverse effects in treatment group.
- Alpay F, et al. Acta Paediatrica 1999;88(2):
  - Another randomized study, 58 patients per group which also showed benefit in haemolytic disease with less exchange transfusion required.

Conj.Hyperbilirubinemia Treatment

Done with:
1) bilirubin level ≥ 30mg/dl
2) any sign of kernicterus
other wise depend on guidlines

←Exchange Transfusions

we don't have enough studies that exclude kernicterus with benign causes with level more than 30mg/dl

- All infants with bilirubin ≥ 500 μmol/l
- All infants with haemolytic disease and bilirubin ≥ 340 μmol/l

- Implement exchange transfusion at lower levels when there is:
  - Rapid rise
  - Failed phototherapy
  - Prematurity

شوفو صور لل
anatomy of umbilical cord

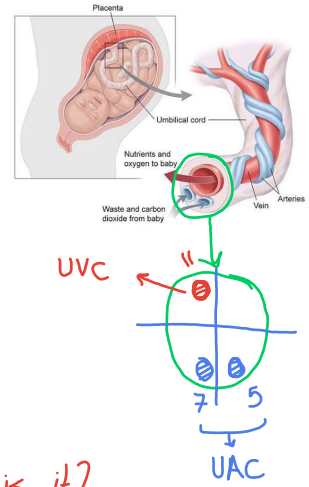
- لما نوصل جهاز الexchange transfusion ما نسحب اكثر من 20 مل في كل مرة حتى نمنع ال intraventricular hemorrhage due to pressure fluctuation.
- نحتاج نعطي المريض ضعف كمية الدم الموجودة عنده weight*85ml*2=
- طريقة اختيار نوعية الدم المناسبة للمريض :
- في حالة ال abo incompatibility نعطي blood group تبع الام وال Rh تبع الطفل
- في حالة Rh incompatibility نعطي blood group الطفل وال Rh تبع الام
- في حالة mixed Rh and ABO incompatibility نعطي blood group الام و Rh الام

* in transfusion with Polycythemia we use **Partial transfusion** → remove & give.
* But in cases of jaundice we use **double exchange transfusion** → Blood given is doubled

How to calculate? $2 \times B.w \times 80$ → each 1kg needs 80 cc
ex: 3kg baby → $2 \times 3 \times 80 \approx 500$ → so you order 500cc blood from blood bank

What To Do??

1. Sit 2 cath into umbilical arteries, How?
   Imagine that the umbilical cord is o'clock, you find that at levels of "5" & "7" o'clock umbilical arteries found, and at "11" you find umbilical vein.
   So, at "5" & "7" o'clock you sit UAC [umbilical Artery cath.], and on "11" o'clock you give UVC.
2. By these 2 cath., you will draw 10 cc from artery, then give 10 cc from vein.
   * this step continue untill all ordered blood transfused [ex. 500 cc].
   * often it takes about (60-90) minutes



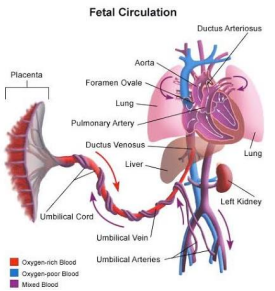
Because of these steps, there are alot of complications, what is it?

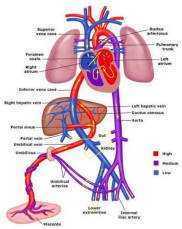
Blood complication

- whole fresh blood is Preffered, but often it is not offered, so it usually not fresh which leads to:
1. Hypocalcemia → so after each 100 cc we give 1 ml equivalent of Ca^{+2}
2. Hyperkalemia → because it is old blood
3. thrombocytopenia.
4. cross rejection.
5. infection → as Hepatitis
   ↳ decreased recently by screening

2 Cath. complication

* Because of connection between umbilical & mesentiric arteries, Liver, Rt atrium:
1. NEC → it may cause necrotizing enterocolitis, Umbilical cord transfusion is very important risk facto for NEC
2. Liver abcess → some times it cause kinking in liver & not follow the Pathway.
3. Rupture of Rt. atrium.
4. Arrythemia → Cath touch SA node
5. Rupture of artery → may occur at any Point of Artery





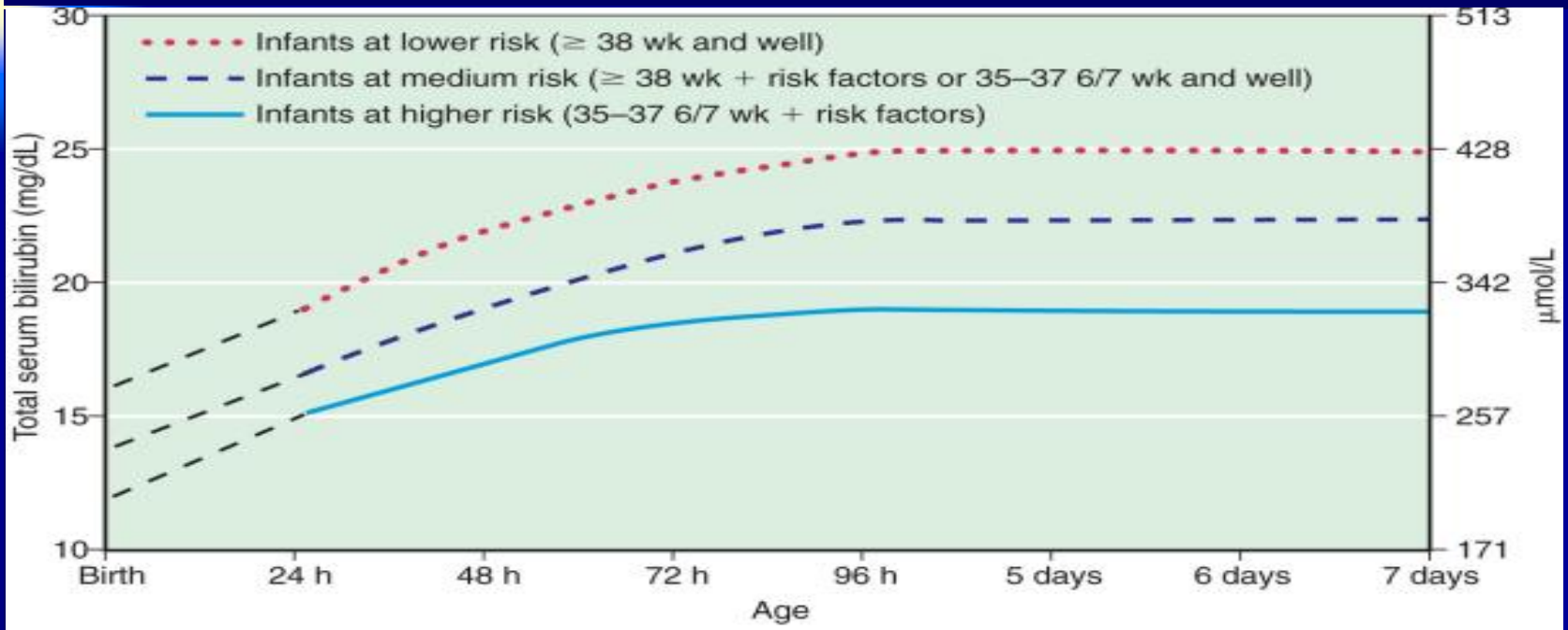
* So it Preffered to sit cath just above the diaphragm, How to determine? Calculate:
  1. for UAC → 3X weight + 9 [ex. 3x3 + 9 = 18]
  2. for UVC → UAC/2 + 1 [ex: 18/2 + 1 = 10]

Procesure complication

may cause infection

* Infection her is very it admitted via Umbilical vein which may cause Portal HTN & esophageal varices later on.

Guidelines for exchange transfusion in hospitalized infants of 35 or more G.A

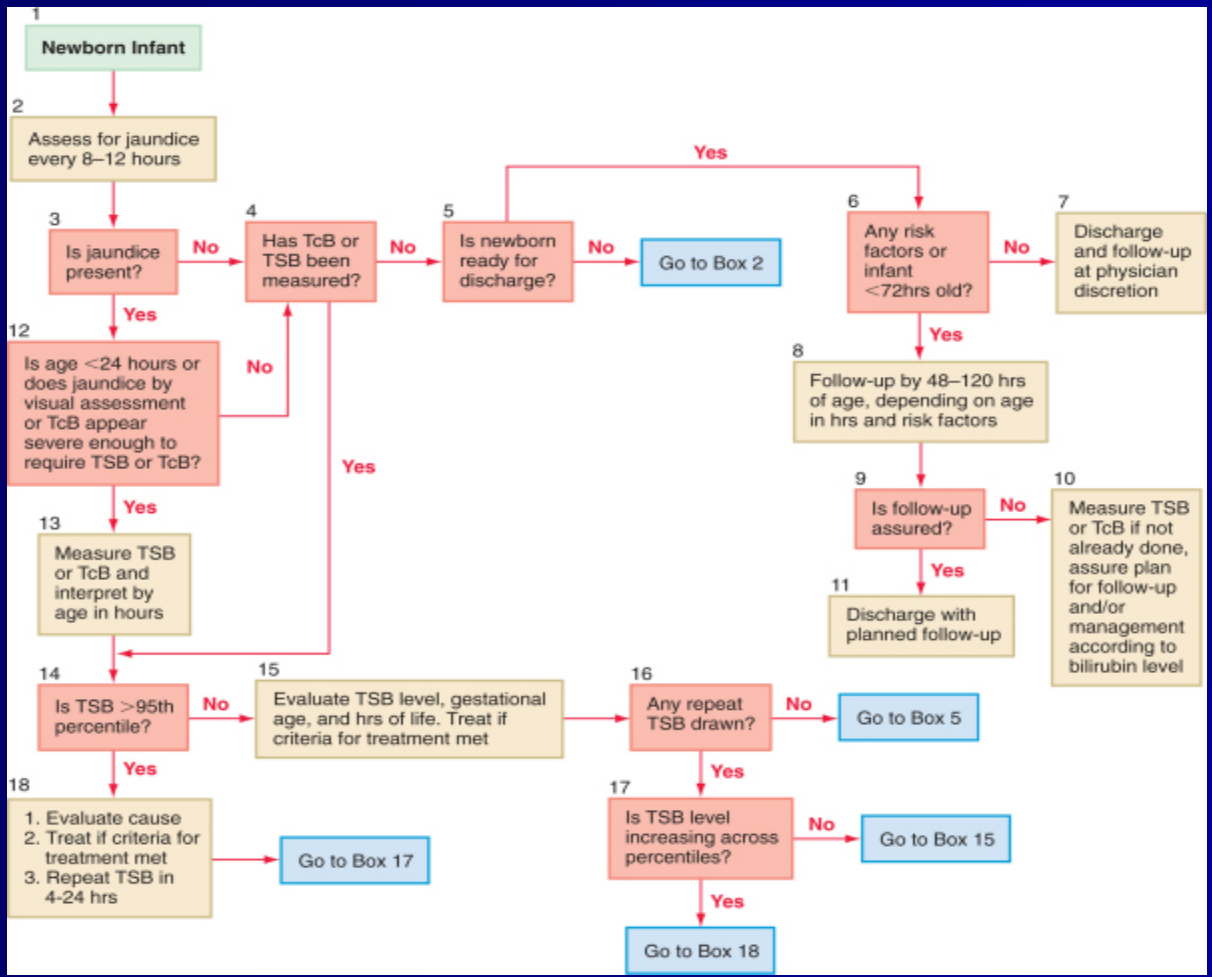


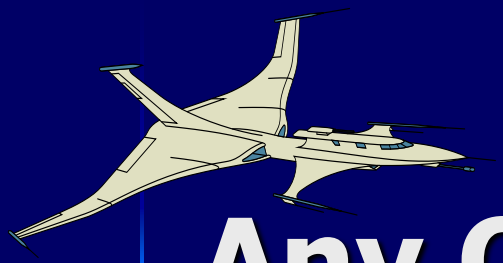
- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥ 5 mg/dL (85 µmol/L) above these lines.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend).
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- If infant is well and 35–37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

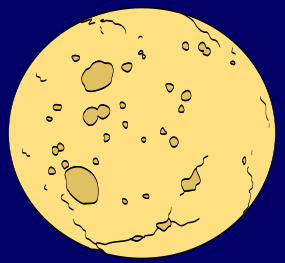
Complications of Exchange Transfusion

- Thrombocytopenia particularly with repeat transfusions
- Portal vein thrombosis or other thromboembolic complications
- Umbilical or portal vein perforation
- Acute necrotizing enterocolitis
- Arrhythmia, cardiac arrest
- Hypocalcemia, hypomagnesemia, hypoglycemia
- Respiratory and metabolic acidosis
- Graft-versus-host disease
- Human immunodeficiency virus, hepatitis B and C infections
- All other potential complications of blood transfusions

Algorithm for the management of jaundice in the newborn nursery







Any Questions?