Fifth-year medical students
Neonatal Jaundice case-based education

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Introduction

will explore various scenarios that illustrate the complexity of neonatal jaundice, focusing on diagnosis, management, and the underlying knowledge required.

Learning Objectives

- Understand factors increasing bilirubin production, such as red cell lifespan, enzyme defects, and structural abnormalities.
- Recognize factors decreasing neonatal serum bilirubin excretion, especially those affecting enterohepatic circulation.
- Grasp bilirubin physiology, including synthesis, transport, and metabolism in the fetus and neonate.

Case Scenarios

Scenario 1: Physiological Jaundice

Description: A full-term, healthy newborn at 39 weeks gestation develops mild jaundice on the second day of life.
Diagnosis and Management:
Assess clinical condition, vital signs, feeding pattern, and bilirubin levels.
Educate parents about physiological jaundice and encourage frequent breastfeeding.
Monitor bilirubin levels and intervene based on age-specific treatment thresholds.

Scenario 2: Hemolytic Disease of the Newborn (HDN)

Description: A full-term newborn shows jaundice within 24 hours, with the mother having blood type O and the baby blood type A. and another case with Rh incompatibility
Diagnosis and Management:
Understand ABO and Rh incompatibility risks and conduct a direct Coombs test to confirm hemolysis.
Measure total and direct bilirubin levels and administer phototherapy or exchange transfusion as needed.
Regularly assess bilirubin levels and the baby's clinical condition.

Scenario 3: Inspissated Bile Syndrome due to HDN

Details of this scenario would include specific diagnostic and management strategies for newborns with conjugated hyperbilirubinemia including inspissated bile duct syndrome in the context of HDN.

Scenario 4: Breast Milk Jaundice (BMJ)

Description: A breastfed infant with appropriate weight gain develops prolonged jaundice at 3 weeks of age.
Diagnosis and Management:
Confirm breastfeeding status and growth trajectory.
Rule out other jaundice causes and educate parents about BMJ's benign nature.
Monitor growth and bilirubin levels to ensure they remain within safe limits.

Conclusion

Each scenario provides insight into the different aspects of neonatal jaundice, highlighting the importance of tailored diagnosis and management strategies to optimize outcomes and educate parents effectively**.**

Cas STUDY 1

A 36-weeks gestation, otherwise healthy infant aged 72 hours was being discussed on rounds in the regular newborn nursery.

Jaundice started on the second day

baby looks well and breast fed and pass urine 5-6 times/day, and pass stool 3 times per days

the baby's clinical condition, including vital signs and feeding were normal

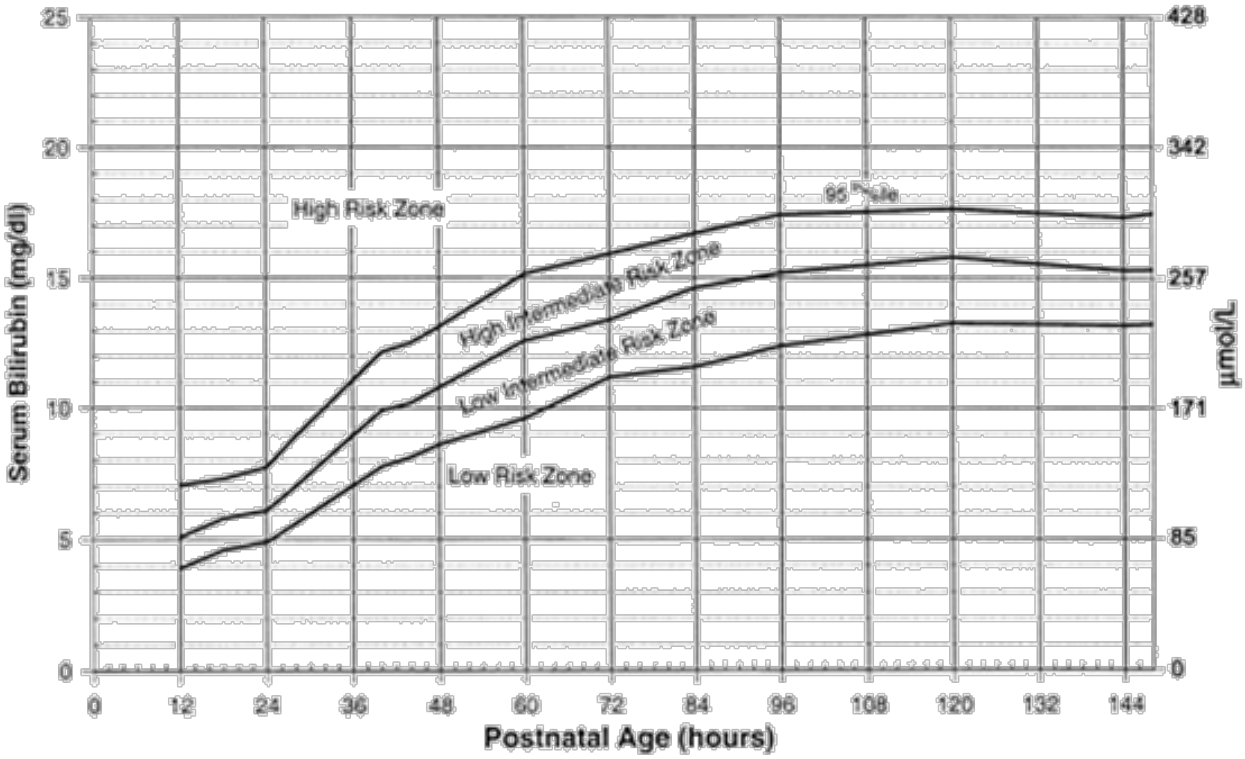
physical examination was normal

1. what is the required test

The STB was 16.0mq/dL. (MBG and BBG are A+ve) , DCT negative,

2. Which answer do you think is correct?

a. The resident plotted the result on the hour-specific bilirubin nomogram. Because the value was greater than the 95th percentile, this resident concluded that increased hemolysis was present.



b. The second resident related to the late prematurity of this infant. The bilirubin-conjugating system is immature, resulting in the increased STB.

C. The third resident suggested that the pathogenesis of the high STB value was multi-factorial and that both increased bilirubin production and hemolysis contributed to its development,

3. What is the risk factors for NJ

Look for
- Asphyxia
- Sepsis
- Lethargy
- Acidosis
- Low albumin <3g/dl
- Hemolysis
  - Isoimmune HD
  - G6PD

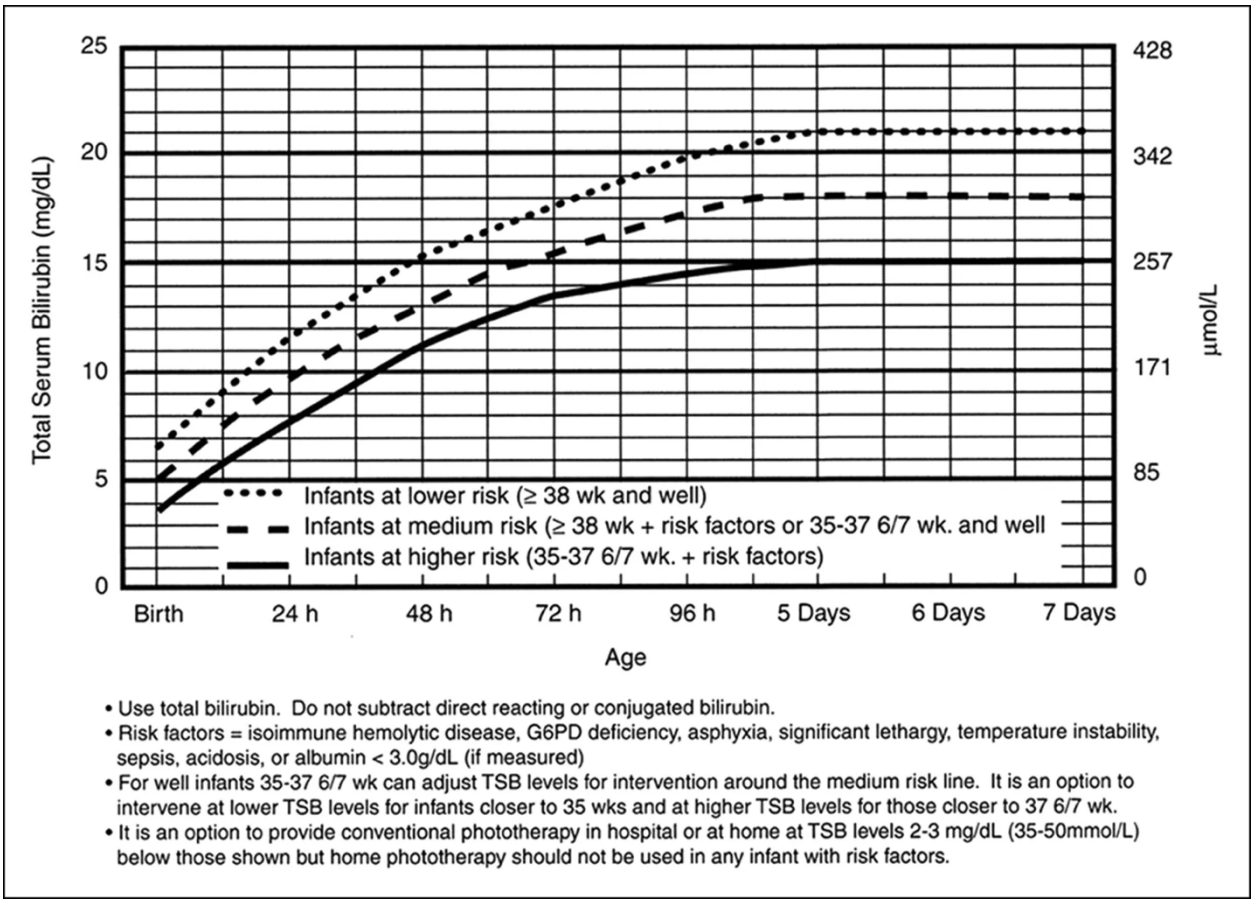
IDM (polycythemia)

4. What is The DDX of jaundice that appears on day 2 or 4

1. usually physiologic
2. mild hemolysis (ABO, G6PD etc)
3. early-onset breast-feeding jaundice. (BFJ)
4. Rare : metabolic , genetic (Familial non-hemolytic icterus (Crigler-Najjar syndrome)

5.When to start Phototherapy

Look at the Guidelines and use a chart



What is the most likely diagnosis

Physiologic

What are Other lines of management

- Encourage Breastfeeding every 2-3 hours
- Lactation consult (check and manage any problem)
- Encourage frequent breastfeeding to promote bilirubin excretion
- Monitor bilirubin levels and intervene if they reach treatment thresholds based on the baby's age and risk factors.
- Educate parents about the normal course of physiological jaundice.

.

Case 2

term newborn on the **first day** of life in the postpartum unit.

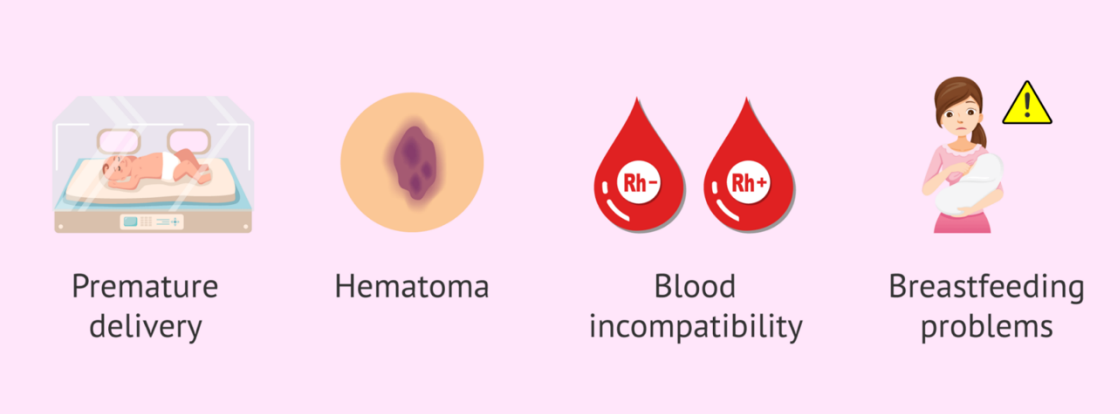
Name	Baby of SS				
BW	3,3kg	GA	39 weeks	Gender	female
Mother age	32	BBG	B+	MOD	S.NVD
MBG	O-ve	Apgar	7/9		
G2P1	Pregnancy	No complication (No HT,PET, GTT Normal)			
Breast feeding	Poor latch Frustrated Sore nipple				
History and physical					
General	Slightly lethargic, excusive crying with exam, flexed posture, visible jaundice				
Growth parameter	Head, length weight ($5o^{th}$)				
Vital signs	T 37.3C/, HR 144, RR 48 sat 96% (room air)				
HEENT	Normocephalic, fontanel are normal , eyes and ears normal set/shape, sclera yellow, palate intact, tongue with Epstein pearls, dry mucous membranes				
cardio	No murmur, pulses +2 bilaterally,			resp	breath sounds clear
GI/GU	Soft, non-distended, liver palpable, umbilical stump intact/clamped. passed 1 meconium stool, voided 1 time since birth				
Musculoskeletal	Hips stable bilaterally, back normal				
Skin					

1. List the 5 findings that need immediate follow-up to the chat box
    - Activity
    - Color
    - Fontanelles
    - Epstein pearls
    - Mucus membrane
    - Stooling
    - Urination
    - Vital signs
    - Sclera
    - Umbilical stump
    - Weight loss
    - Excessive crying
    - Flexed with exam

2.For each client finding click to indicate whether it is a risk factor or not a risk factor for jaundice. Item write in chat box risk or not risk

	Risk factor	Not a risk factor
Breastfeeding problems		
Maternal blood type		
Gestation age		
Second pregnancy		
Current stooling pattern		

Risk factors



Lab results		
	Level	Normal
TSB	16 mg/dL	<5.2 mg/dL within 24 hours of birth Link
Dirct bilirubin	0.5mg/dl	
Direct Coombs test	+ve	
Hematocrit	40%	< 65%
HB	11.5g/L	
Blood film	Peripheral smear demonstrated the presence of spherocytes (++) with features suggestive of hemolysis	

3.What is The DDX

Physiologic
Pathologic

4.what is DIFFERENTIAL DIAGNOSIS.Jaundice that is present at birth or appears within the 1st 24 hr of life.

1. Physiologic Jaundice
2. Breastfeeding Jaundice
3. Breast milk Jaundice
4. hemolysis
5. infection
    a. EOS
    b. congenital infections (including syphilis, cytomegalovirus, rubella, and toxoplasmosis)
6. concealed hemorrhage

5.what are/is A possible explanation is in this case

- Poor intake
- Impaired bilirubin excretion
- hemolysis

5.Explain your answer (hemolysis)

6.Select the plan of care. Each category may have one or more action(s).

Action for photo therapy	Yes	No
Monitor temperature.		
Phototherapy		
Monitor photo phototherapy level.		
Kangaroo care		
Eye shield		

Lactation care	Yes	No
Lactation consultants		
Encourage formula.		
Follow wet diaper		
Encourage feeding Q2-3 hours		

Medical care	yes	no
Input /out put chart		
Vital signs monitoring		
Frequent TSB monitoring		

7. specify if should implement the orders immediately, before the end of the shift, or by discharge. **Each row must have 1 selection**.

	Immediately	Before the end of the shift	By discharge
Start phototherapy			
Lactation consultant			
Parent education on use of phototherapy			
Parent education on follow-up labs			
Parent education Rh incompatibility			
Obtain transcutaneous bilirubin			

Educational mangment

orders	
Start phototherapy	◦ Start phototherapy. ◦ Obtain serum bilirubin every 6 hours.
Lactation care	◦ Lactation consultant ◦
hydration	○ Strict input out put ○ V/S every 1-2 hours
Educate	○ Parents

Educational:

ABO hemolytic disease of the newborn = **(HDN)** :

- arises due to the transplacental passage of immunoglobulin (Ig)-G antibodies of the mother with specificity for the ABO blood group system into the fetal circulation.
- high titer of IgG anti-A or anti-B in non O blood group mothers can even result in severe HDN
- This results in the hemolysis of fetal red blood cells, leading to fetal anemia and hyperbilirubinemia.
- Most commonly affected neonates are of A or B blood group with O blood group mother with immune anti-A and anti-B antibodies.
- The quantity and subclass of maternal IgG class anti-A or anti-B that cross the placenta affect the severity of ABO HDN as each has different biological properties affecting their lytic potential.
- The naturally occurring IgG isoagglutinin in group O mothers.
- Mostly, it is benign due
    - the wide distribution of A and B antigens.
    - the A and B antigens are weakly expressed over neonates RBC resulting in a mild form of the disease.

Case 4

Chief complaint: 3 days old Baby boy presented with yellowish discoloration of the body and eyes for a 1-day duration (started at age of 2 days)

Antenatal history

• This is the mother's second pregnancy with an uneventful antenatal period up to 34th week where the OGTT test has showed increased glucose levels but was controlled on diet.

Birth history

- The baby was delivered via a normal vaginal delivery at 37 weeks.
- Birth weight was 2.7Kg.
- APGAR 1 min- 9, 5 min- 10
- Blood sugars were monitored 4 hourly for 24 hrs and was above 46mg

History of presenting complaint

- The patient was last well 1 day ago and the mother noticed yellowish discoloration of the whole body and sclera.
- During the first two days stools were said to be dark in color which has turned vellowish by the 3rd day, but it was not pale

- **Constitution**

  Baby was said to be lethargic and the mother had to wake him up during the feeds. no fever

- **ROS**

  Renal

  Mother also mentioned of 1 episode of dark coloured urine on the 3rd day after birth. Pass urine 4-5 times per day

  CNS: no seizures,

  , **GI :** pass still 3-4 times per day after feed.no Vomiting or diarrhea

Family history:

no consanguinity

No family members with jaundice in the neonatal period. No history of anemia, splenectomy or Bile stones in family members or

known heredity for hemolytic disorders.

Nutrition: exclusive breast fed every 2-3 hours (pass urine every 4-5 hours and stool) every 6-8hours)

Social history

Baby is living with his mother, father, grandmother and the elder sibling who is 1 ½ years.

Mother is 36 years old and a housewife.

Father is a 36 years old unemployed.

She receives good family support(from grand parents).

The family is financially stable.
lives in -----
both are smokers.
no car, the house is rented, no insurance
Exam

General	Slightly lethargic, excusive crying with exam, normal posture, visible jaundice		
Growth parameter	Head, length weight ($5o^{th}$) Weight loss 4% (not significant		
Vital signs	T 37.3C/, HR 144, RR 48 sat 96% (room air)		
HEENT	Normocephalic, fontanelle is normal, eyes and ears normal set/shape, sclera yellow, +ve red reflex and no cataract, palate intact,		
cardio	No murmur, pulses +2 bilaterally,	resp	breath sounds clear
GI/GU	Soft, non-distended, liver palpable, umbilical stump intact/clamped. passed 1 meconium stool, voided 1 time since birth		
Musculoskeletal	Hips stable bilaterally, back normal		
Skin	Jaundice		

1.What tests are needed

Answer

blood was sent for CBC, CRP, SBR, retic ,film , DCT ,BBG, MBG

Results

MBG O : + ve

BBG B+ve

DCT – positive

FBC

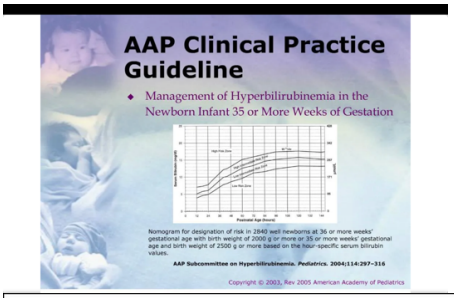
- Hb14.9 g/di
  - RBC 3.34 10^12/L
  - HCT 37%
  - WBC 14.53 10^9/L
  - N 38.1%
  - L 42.8%
  - PIT 343 10^9/L
- CRP - 1.4 mg/
- Retic 14%
- Total serum Bil - 26.46mg/dl Direct Bil - 1.21mg/d. Indirect Bil - 25.25mg/dl
- G6PD (deficient)
- **Blood film**

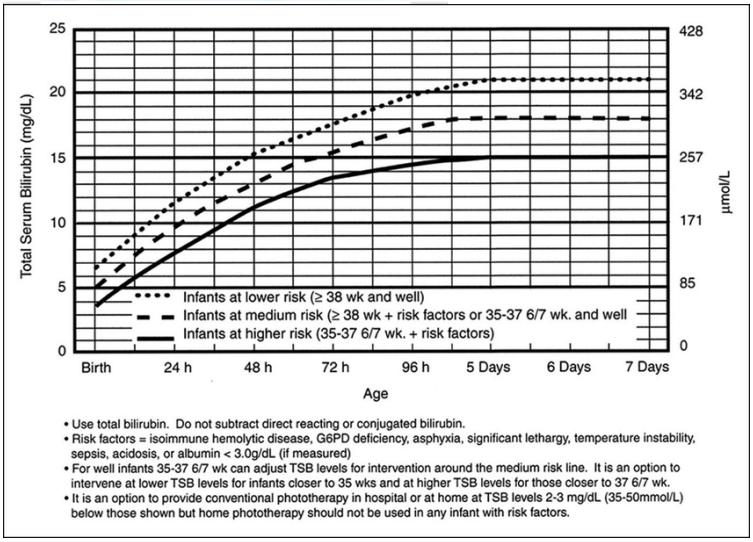
• Blood picture RBC - Normochromic Macrocytic red cells Occational sphyrocytes, .Polychromasia

2.What is the treatment?

started on triple phototherapy. And monitor TSB and HB

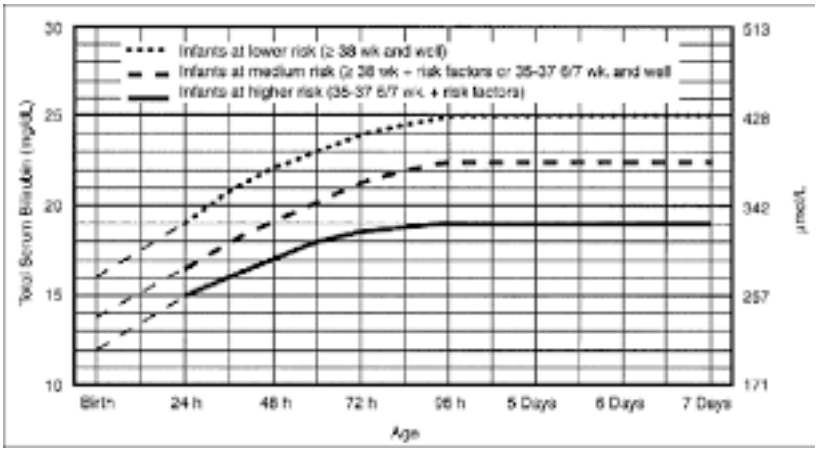
IV fluid
Feeding is allowed.





For phototherapy >35 weeks

Prepare exchange



Indication
when hyperbilirubinemia remains at high levels despite intensive phototherapy

Moderate-severe acute bilirubin encephalopathy (ABE), regardless of the bilirubin level at the time

3.Does he need further treatment modality

Indication of IVIG in neonates

In Rh or ABO hemolytic disease, if the total serum bilirubin is rising despite intensive phototherapy or the total serum bilirubin level is within 2 to 3 mg/dL

What is the diagnosis

Early Neonatal Jaundice

What is DDx
Hemolysis
- G6PD : deficient
- Infection

Case 5

scenario. Reference

Neoreviews (2019) 20 (8): e464–e467.
https://doi.org/10.1542/neo.20-8-e464

Case baby Doa

age	A 2-day-old,	BW	2.68-kg	GA	39 wk	Gender	male	MOD	VD
G4P3	1 ab 1 SB 1 term	$Rh_o(D)$ $Rh_o(D)$ $Rh_o(D)$	After 3 weeks After 2 weeks After 2 weeks		BF	Day 1 (3 times)	Day 2 (2 times)		

MBG	AB -ve	Pregnancy	Uncomplicated Father and sibling are healthy							
BBG	B+ve	DCT	+4	Mother Indirect coombs						
		Constitution	No fever	Poor feed	Decrease activity					
		Jaundice	Onset	7 hr	Progressive sclera, skin					
		GI symptoms	No V,D No bloody stool	Passed once No blood			feed	poor		
		Hematology	No pallor	No bruise						
		CNS	No seizure	Poor feed	No abn tone					
exam										
generla	Jaundice, t\lethargic		Poor cry							

Growth parameter	Head, length weight (5oth)
Vital signs	T 37.3C/, HR 144, RR 48 sat 96% (room air)
HEENT	Normocephalic, fontanelle slightly depressed, eyes and ears normal set/shape, sclera yellow, palate intact, tongue normal , dry mucous membranes Week cry
cardio	No murmur, pulses +2 bilaterally, resp breath sounds clear
GI/GU	Soft, non-distended, liver palpable, umbilical stump intact/clamped. passed 1 meconium stool, voided 3 time since birth dark brown urine
Musculoskeletal	Hips stable bilaterally, back normal
Skin	

Lab	TFT	Normal								
TSB	42.2 mg/dL	direct	28.2mg/dL	unconjugated bilirubin	12mg/dL					
Retic	23	hemoglobin	11.6 g/dL	AST	239 U/L		(ALT)	55 U/L		
PTT	Increased (30.7 seconds)							NBS	-ve	

Case progression	
A jaundice panel (genetic study) (ABCB11, ABCB4, ATP8B1, JAG1, and TJP2),	ruling out Alagille syndrome and progressive familial intrahepatic cholestasis as possible causes later was negative
Abdominal ultrasonography showed : a normal-appearing liver and gallbladder, no biliary ductal dilation, and patent vessels	

1.What is Treatment

Start Photo No start of photo

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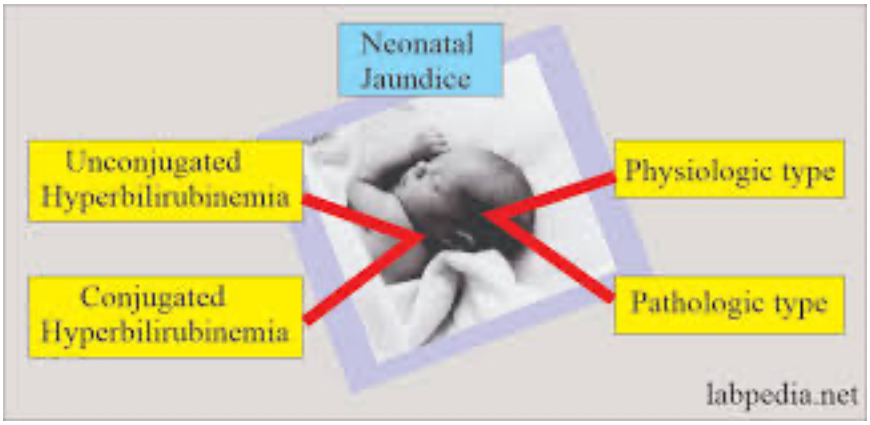
The 2004 American Academy of Pediatrics guidelines for the treatment of hyperbilirubinemia state that,

> “In unusual situations in which the direct bilirubin level is 50% or more of the TB, there are no good data to guide therapy.”(1)

2.What is the DDX



3.How the baby was Treated

Treatment included:

intensive phototherapy initial

intravenous fluids

double volume exchange transfusion,

intravenous immunoglobulin,

Antibiotics ampicillin, cefotaxime,

phenobarbital (for activation of the promotor sequence of hepatic UGT1A1).

Acyclovir: pending TORCH results

The Fig demonstrates the decline of bilirubin after each of these interventions. Enteral feeds were initiated after 2 days of hospitalization, which the infant tolerated well.

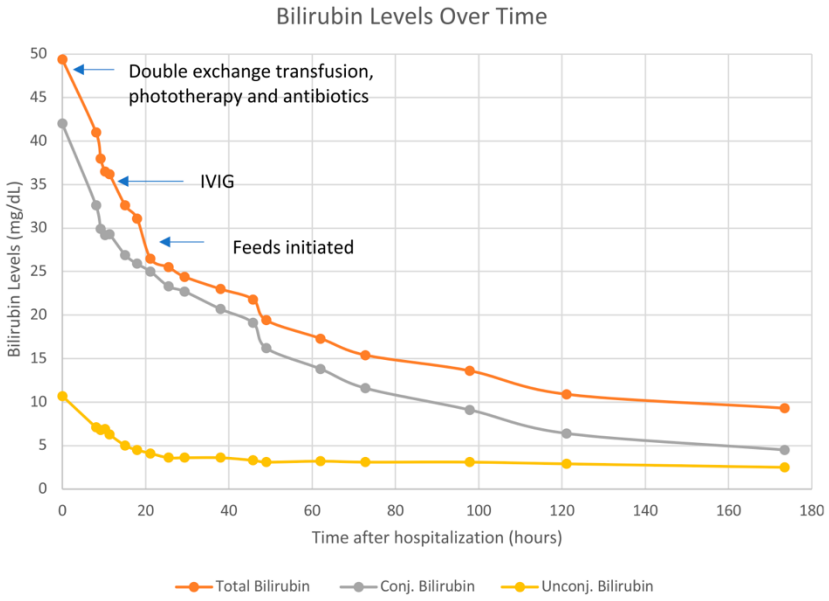


Figure. Bilirubin levels over time.

4.At discharge on hospital day 35,

laboratory findings were as follows:

TB 9.3 mg/dL (159 mmol/L),

conjugated bilirubin 4.5 mg/dL (77 mmol/L),

unconjugated bilirubin 2.5 mg/dL (42.8 mmol/L),

AST 81 U/L (1.3 mkat/L), ALT 36 U/L (0.6 mkat/L),

and alkaline phosphatase 82 U/L (1.4 mkat/L).

(HIDA scan)Hepatobiliary iminodiacetic acid scan was offered, but the parents declined because of the normal hepatic ultrasound scan with decreasing bilirubin levels.

Brain MRI: parents declined brain magnetic resonance imaging because the neurologic findings at discharge were reassuring.

5.What is DDX ie DDX if Jaundice that prolonged persists the 1st mo of life:

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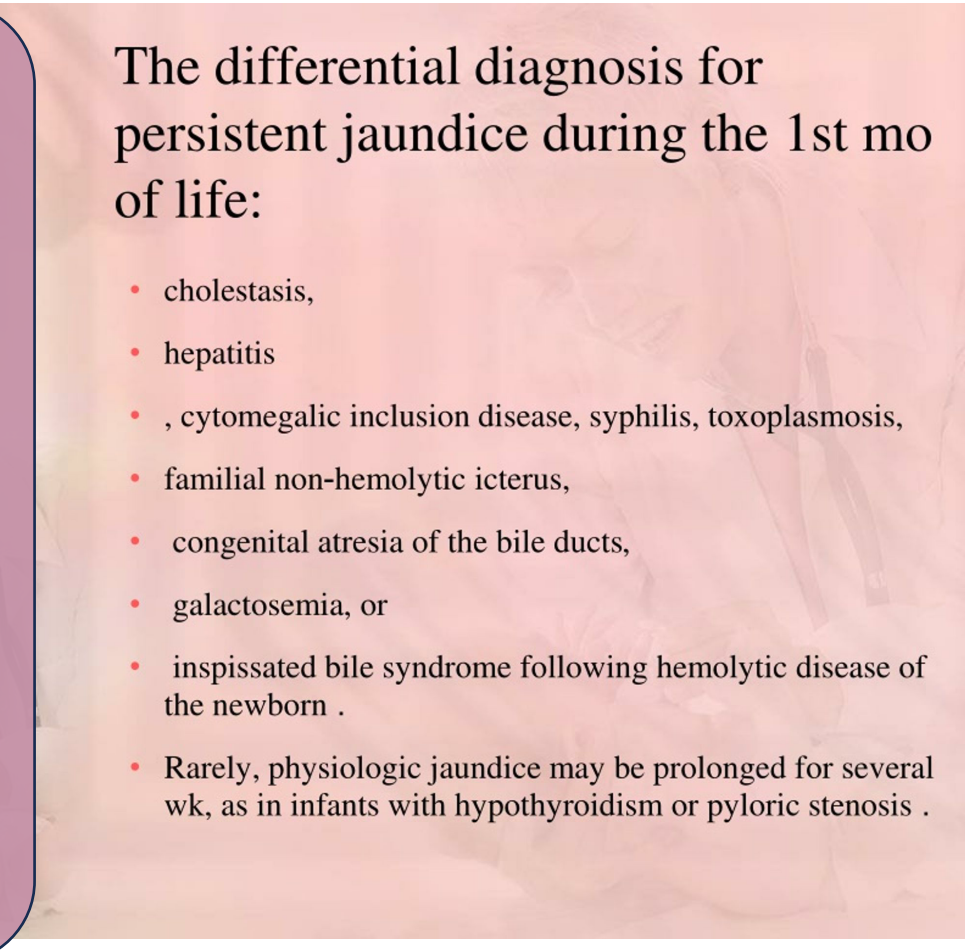
Prolonged jaundice:

- 2 weeks term
- 3 weeks preterm



FOLLOW-UP

At 2 months

The infant was evaluated in the developmental pediatrics clinic at 2 months, 19 days of age.

Growth was appropriate:

weight 5.88 kg (36th percentile), length 59.7cm (35th per- centile), and head circumference 38.5cm (9th percentile).

Jaundice had resolved.

TB concentration was 0.8 mg/dL (13.7 mmol/L) and direct bilirubin 0.0 mg/dL (0.0 mmol/L).

developmentally appropriate with normal findings on neurologic examination.

Take home massages

Jaundice in the first few days.

Common : after birth is a common neonatal problem, occurring in approximately two-thirds of newborns. (2)

Type

unconjugated hyperbilirubinemia:

Most cases are represented by unconjugated hyperbilirubinemia, which is usually treated with phototherapy.

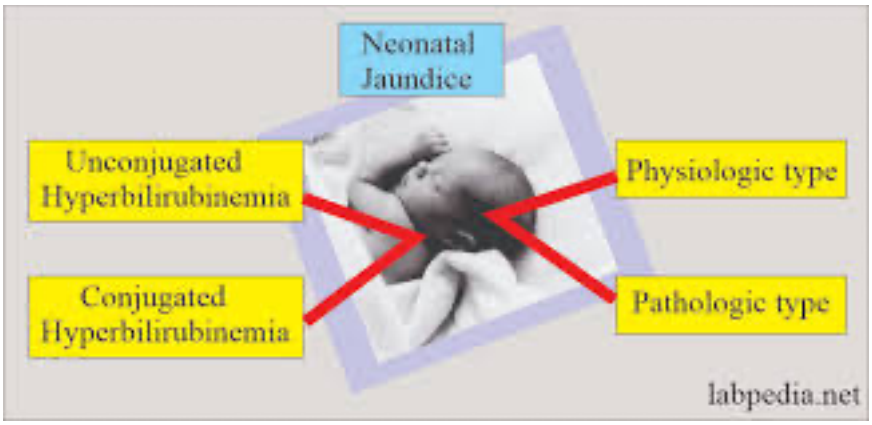
Conjugated hyperbilirubinemia

is much less common in the neonatal period, and is indicative of cholestasis.

Role of the physical exam

Neonatal jaundice caused by unconjugated versus conjugated hyperbilirubinemia cannot be differentiated with physical examination alone.

What is Direct hyperbilirubinemia?



Direct bilirubin concentration greater than 1.0 mg/dL (17.1 mmol/L) with TB less than 5 mg/dL (85.5 mmol/L),

Or a direct bilirubin greater than 20% of the TB (if TB >5 mg/dL) is diagnostic of conjugated hyperbilirubinemia.

What are the Causes of Conjugated hyperbilirubinemia and cholestasis

Infectious (sepsis, UTI)

metabolic,

hepatitis

genetic /metabolic

Direct hyperbilirubinemia? Is the most common marker of cholestasis

Common causes of obstructive cholestasis

- biliary atresia,
- choledochal cysts,
- bile duct paucity,
- neonatal sclerosing cholangitis,
- inspissated bile syndrome,
- gallstones/biliary sludge,
- cystic fibrosis,
- Caroli disease.

6.What is the diagnosis of the current patient

Repeat data

was born full-term,

had inadequate prenatal care,

demonstrated significant generalized jaundice within the first 7 hours after birth.

He presented with hemolytic anemia (likely because of Rh incompatibility) and conjugated hyperbilirubinemia (which was unusual given that Rh incompatibility usually results in unconjugated hyperbilirubinemia).

He has cholestasis

The most common causes of cholestasis had been excluded:

Alagille syndrome and pro-gressive familial intrahepatic cholestasis (negative jaundice pannel),

hypothyroidism and hypopituitarism (normal thyroid- stimulating hormone and free thyroxine),

congenital heart disease (normal chest radiograph and a patent foramen ovale on echocardiography).

Urinary tract infection with E coli could have been a contributory factor, but it is an unlikely main cause.

7.What is the Work upp cholestasis

As above (LFT with ammonia and PT., TORCH, urine C@S, metabolic as AA, in blood and Mscreen, CF,TFT, Genetic panel VS WES, echo)

In cases of suspected cholestasis,

Imaging ultrasonography is the initial imaging modality of choice.

8.What is the most likely Diagnosis

After all test results returned, the exclusion diagnosis, in this case, remained Rh incompatibility with severe chronic hemolysis, complicated by inspissated bile syndrome.

Inspissated bile syndrome

- is a rare clinical entity, with an incidence of 1 in 175,000 live births as reported in UK studies England.
- Inspissated bile syndrome (IBS) is a rare but serious complication of HDN
- inspissated bile syndrome is a rare cause of cholestatic jaundice in infancy, occurring due to obstruction of the biliary ducts and gallbladder by biliary sludge
- Rare in high-income countries (due to preventive care)
- treatment for IBS ranges from hydration to ultrasound-guided percutaneous cholecystostomy drain catheter placement to physically drain the sludge

More on Take home massage for case 5

- Two-thirds of newborns will experience jaundice within the first few days after birth.

- Conjugated hyperbilirubinemia is less common than unconjugated hyperbilirubinemia
- and is indicative of cholestasis caused by infection, metabolism defects, or obstruction.

- Common causes of obstructive cholestasis include biliary atresia, choledochal cysts, bile duct paucity, neonatal sclerosing cholangitis, inspissated bile syndrome, gall- stones/biliary sludge, cystic fibrosis, and Caroli disease.

More take-home massage

- Evaluation for neonatal cholestasis includes blood, urine, and cerebrospinal fluid cultures, urinalysis, cerebrospinal fluid studies, complete blood cell count with differential, comprehensive metabolic panel, prothrombin time/international normalized ratio, and partial thromboplastin time.
- Newborn screening results should be reviewed for possible metabolic causes.

- Abdominal ultrasonography should be performed to assess for biliary atresia.
- A jaundice genetic panel chip is useful if Alagille syndrome or progressive familial intrahepatic cholestasis is suspected.

Case Number 6. (prolonged Jaundice)

demonstrate understanding of BMJ, and develop an appropriate management plan.

A 18-day-old infant is presented by the mother, who is concerned about the baby's persistent jaundice.

The baby is breastfed and formula

gaining weight normally, and has no signs of dehydration or illness.

Previous bilirubin levels were mildly elevated but not at the level requiring phototherapy.

What is the next step

1.Take a focused history to assess the feeding pattern, stool frequency, urine output, and any family history of jaundice or hemolytic diseases. (2 min)

2. Perform a focused physical examination, paying special attention to the skin and sclera for jaundice, and check for signs of liver enlargement or any other abnormalities.

What is the most likely diagnosis?

- Pathological Jaundice
- Physiologic
- BMJ
- BFJ

What workup is needed for this Baby who has prolonged Jaundice?

TFT, CBC, Retic, Blood film ,Uine C@S, urine RS, G6PD are normal

Has TSB 14

Theme	Detailed Explanation

Breast Milk Jaundice (BMJ) Impact	BMJ can lead to the interruption or early cessation of breastfeeding, which may have adverse effects on infant development and immune system maturation. The condition is characterized by prolonged jaundice in breastfed infants, typically appearing in the first week after birth and can last several weeks.
Intestinal Flora Role	The intestinal flora, or gut microbiota, plays a crucial role in the metabolism and excretion of bilirubin. An imbalance in these microbial populations, known as dysbacteriosis, can disrupt these processes. Specifically, healthy gut bacteria help transform bilirubin into stercobilin, which is excreted from the body. Dysbacteriosis can reduce this transformation, leading to increased bilirubin absorption and circulation.
SCFA and BMJ	Short-chain fatty acids (SCFA) are key metabolites produced by the fermentation of dietary fibers by the gut microbiota. They are critical in maintaining the integrity of the intestinal barrier and modulating the immune response. In BMJ, the levels of SCFA may decrease due to dysbacteriosis, impairing their protective role and contributing to increased bilirubin levels.
GPR41/43 Pathway	SCFAs exert their effects through specific receptors, notably G protein-coupled receptors 41 and 43 (GPR41/43), which are involved in regulating inflammation and intestinal motility. A decrease in SCFA levels can downregulate the GPR41/43 pathway, leading to enhanced intestinal inflammation and **reduced motility**. Consequently, this results in increased reabsorption of bilirubin into the bloodstream, exacerbating BMJ.
Therapeutic Targets	Understanding the interaction between gut microbiota, SCFAs, and bilirubin metabolism highlights potential therapeutic targets for managing BMJ. **Probiotics and prebiotics** that modulate the gut microbiota and increase SCFA production may offer new strategies for treating BMJ. These interventions could promote healthier bilirubin metabolism and reduce its enterohepatic circulation, thereby mitigating the severity of jaundice
Genetic	Associated with gilbert, TATAbox gene polymprphism (decses UGTA! Enzyme)

Explanation and Management Plan

1. Explain the likely diagnosis of Breast Milk Jaundice to the mother, including the pathophysiology related to intestinal flora and SCFA as per the document.

2. Discuss the typical course and prognosis of BMJ.

3. Outline your management plan, stressing the importance of continued breastfeeding, monitoring of bilirubin levels, and when to return for further evaluation.

4. Guide on the importance of frequent breastfeeding and signs to watch for that would necessitate a return to the clinic.

Thank you