MMed and DCH Lectures

Jaundice and liver disease in children

September 20, 2021

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Jaundice and liver disease in children

- Liver functional anatomy and physiology
- Tests of liver function
- Clinical signs of liver disease
- Neonatal jaundice
  - Physiological (normal) and pathological states
  - Thresholds for treatment
- Jaundice and liver disease in older children

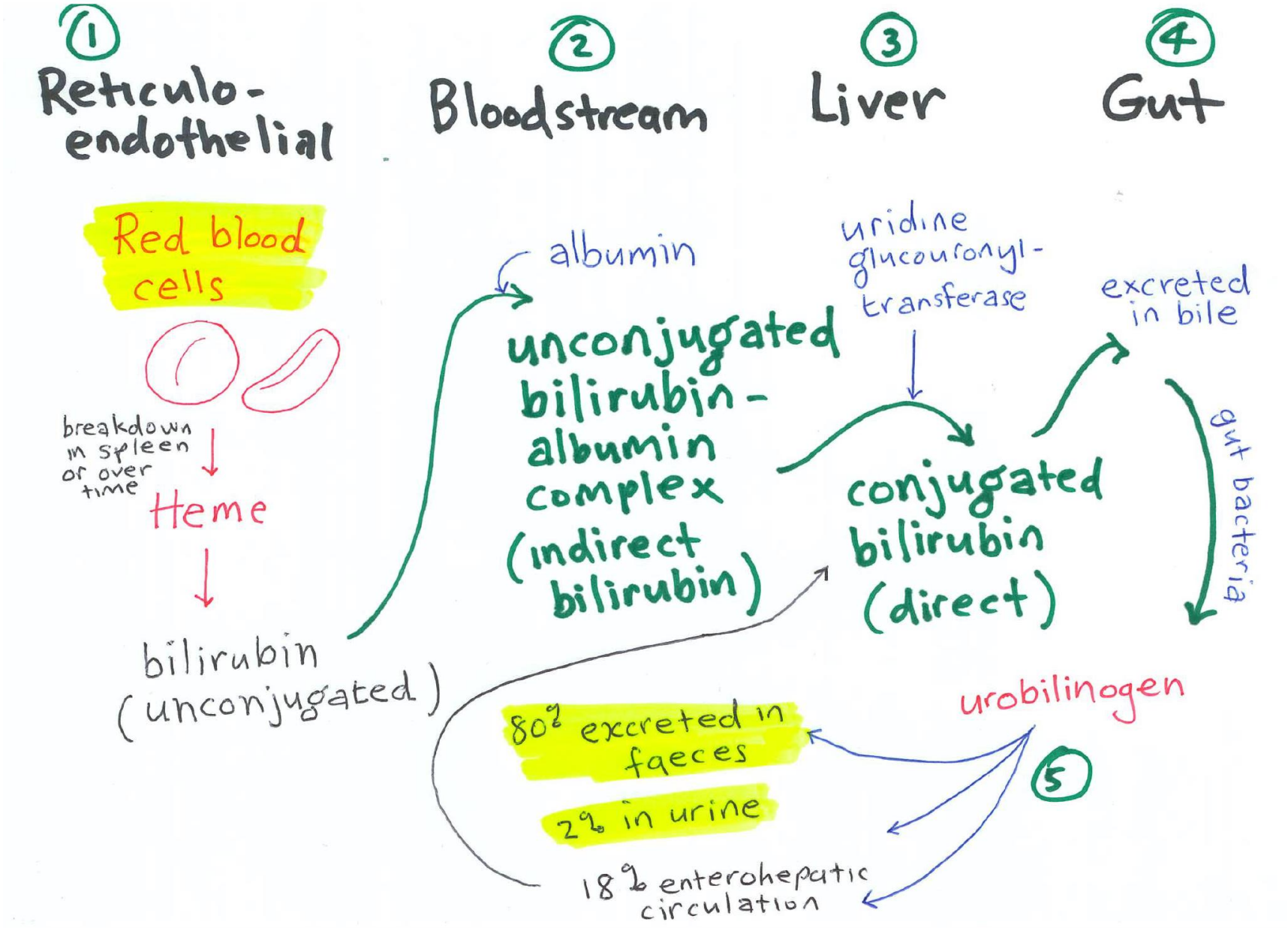
Functional anatomy

1. Liver parenchyma
   - Hepatocytes (gluconeogenesis, glycolysis, protein synthesis)
   - Stellate cells (fibrous tissue producing)
   - Kupffer cells – macrophage-like immune cells which process antigens that enter the liver from portal vein
2. Bile ducts and bile canaliculi
3. Blood flow
   - To liver
     - 70% portal vein (intestinal nutrients)
     - 30% hepatic artery (oxygen)
   - From liver: hepatic vein to IVC

Liver functions

- Bile production and excretion
- Detoxification of toxins and metabolism of drugs
- Processing nutrients
  - storage of glucose as glycogen
  - mobilisation of glucose (glycogenolysis)
  - storage of fats
- Protein synthesis
  - Clotting factors, albumin
- Immune function
- Regulation of growth and endocrine functions
  - insulin-like growth factors, angiotensinogen

Bile production and excretion



Liver tests

1. Markers of hepatocyte dysfunction
2. Markers of biliary dysfunction or cholestasis
3. Markers of synthetic dysfunction
4. Markers of impaired hepatic detoxification

Tests of hepatocyte dysfunction

- Hepatocyte cellular enzymes – “transaminases”
  - **ALT (more liver specific)**
  - AST (muscle: skeletal and cardiac, red blood cells - haemolysis)
- Elevated ALT in hepatocyte damage
  - drugs, toxins, infections, immunological injury, ischaemia
- ALT may not be elevated in very severe liver disease, if necrosis of liver advanced or fibrosis extensive

Markers of biliary dysfunction or cholestasis

- Alkaline phosphatase
  - made by bile duct epithelium, and increases in production when bile ducts are blocked (after a few days)
  - ALP also in bone, intestine and kidney (not specific to liver disease)
- ɣ-Glutamyl-transferase (ɣ-GT, or GGT)
  - More sensitive and specific test for biliary disease (although also seen in pancreas, kidney, intestine)
  - Increase GGT with bile duct obstruction and inflammation
  - (Can be induced by some medications – phenobarbitone, phenytoin)
- Cholestasis: ↑*conjugated* bilirubin (>20%), ↑ALP, ↑GGT, plus bile in urine

Markers of synthetic function

- Albumin
  - Half-life of 3 weeks, so liver has to be dysfunctional for that time for albumin levels to be ↓↓
  - Other causes of hypo-albuminaemia (nephrotic, protein losing enteropathy), “negative acute phase reactant” (albumin levels fall in acute systemic inflammation)
- INR / Prothrombin time
  - Liver produces most clotting factors, especially vitamin K dependent (II, VII, IX, X)
  - High INR that is due to vitamin K deficiency should correct within 6 hours of giving vitamin K, but if not likely liver disease

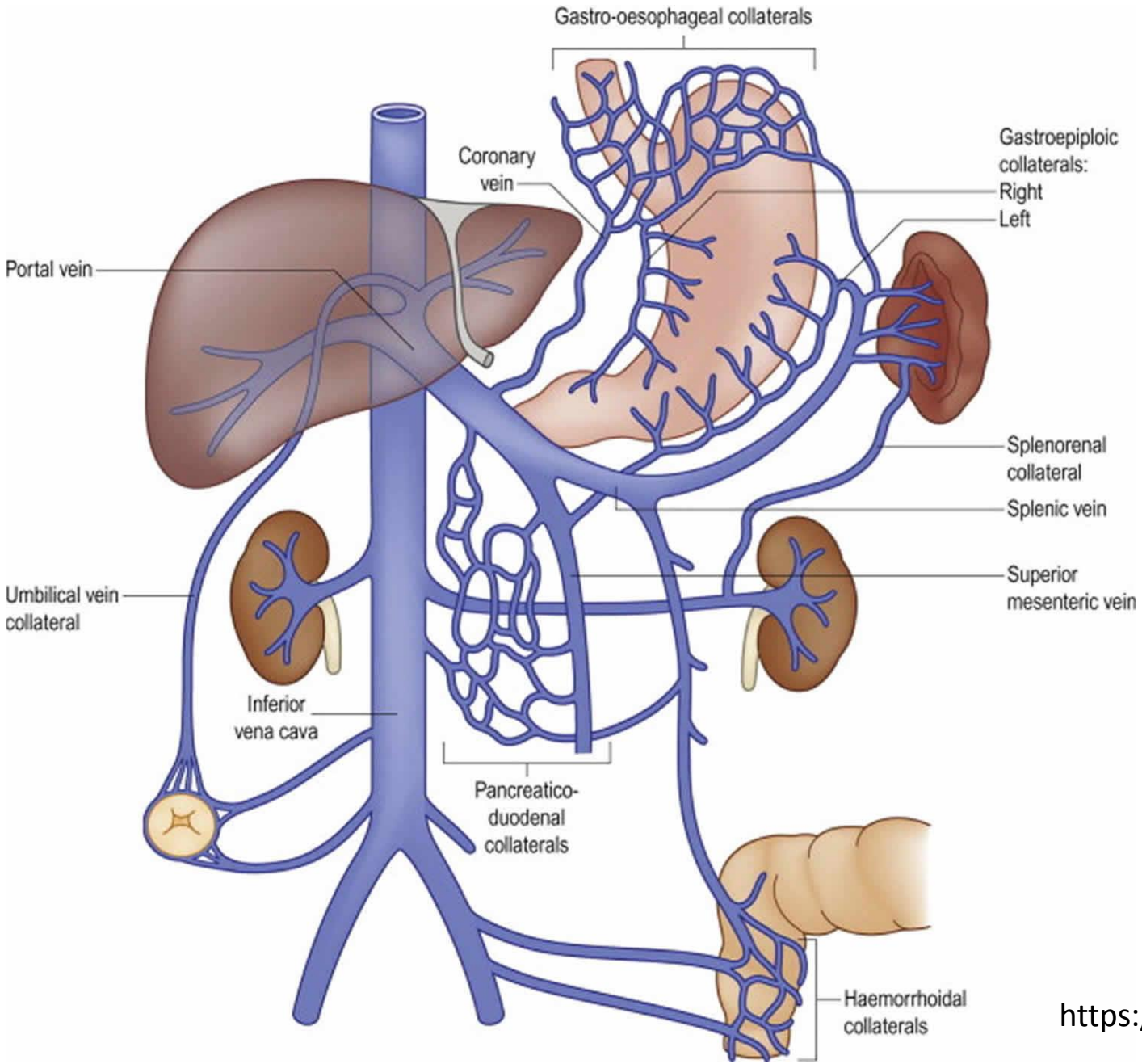
Markers of impaired detoxification

- Ammonia
  - A byproduct of protein catabolism
  - Liver normally metabolises ammonia
  - Neurotoxic – hepatic encephalopathy
- Lactate
  - Usually oxidised in citric acid cycle, or used for gluconeogenesis in liver
- Acute or severe liver failure leads to high ammonia and lactate

	Haemolytic	Hepatic	Cholestatic
Unconjugated Bilirubin	↑	↑	Normal
Conjugated Bilirubin	Normal	↑	↑
Urine Urobilinogen	↑	↑	↓
ALT / AST	Normal	↑	Normal / Mild ↑
ALP / GGT	Normal	Normal / Mild ↑	↑

Clinical signs of liver disease

- Jaundice
  - Dark urine, pale stools (+/-), steatorrhoea (lack of bile salts to break down fats), pruritis
- Hepatomegaly
  - Inflammation (tender), congestion (venous obstruction), infiltration, blockage of biliary flow
  - Tender, smooth, firm, hard, irregular, mass…
- Splenomegaly
  - Infectious hepatitis (e.g. EBV, hepatitis A)
  - Portal hypertension
- Encephalopathy, sleepiness
- Skin changes
  - Chronic changes – palmer erythema, dilated abdominal veins, clubbing
- Portal hypertension



https://healthjade.net/portal-vein/

Neonatal jaundice: mostly *not* liver disease

- 50-60% of newborns
- Physiological – onset *after* day 1, not too high, not beyond 2 weeks
  - Breakdown of HbF
- Breast milk jaundice
  - Incidence 30%+
  - Presents in first 2-3 weeks, can persist for 12 weeks
  - Diagnosis of exclusion – well baby, afebrile, thriving, bile pigment in stool
  - ? Cause: breast milk enhances entero-hepatic circulation of bilirubin (contains epidermal growth factor and β-glucuronidase which deconjugates intestinal bilirubin
  - No treatment, do not withdraw breast feeding
  - Weekly bilirubin levels

Classification of neonatal jaundice

	Too early (Day 1)	Too high	Prolonged (>2 weeks)
Indirect (Unconjugated)	Haemolysis Infection	Haemolysis Infection Malaria	Breast milk jaundice Hypothyroidism Malaria Haemolysis (G6PD, spherocytosis) Crigler-Najar, Glbert's disease
Direct (Conjugated)			Obstruction: Biliary atresia Hepatic inflammation / toxicity • Bacterial infection • Malaria • Viral hepatitis • Galactosaemia • Congenital infection: ToRCHES: toxoplasmoisis, rubella, CMV, herpes, EBV, syphilis

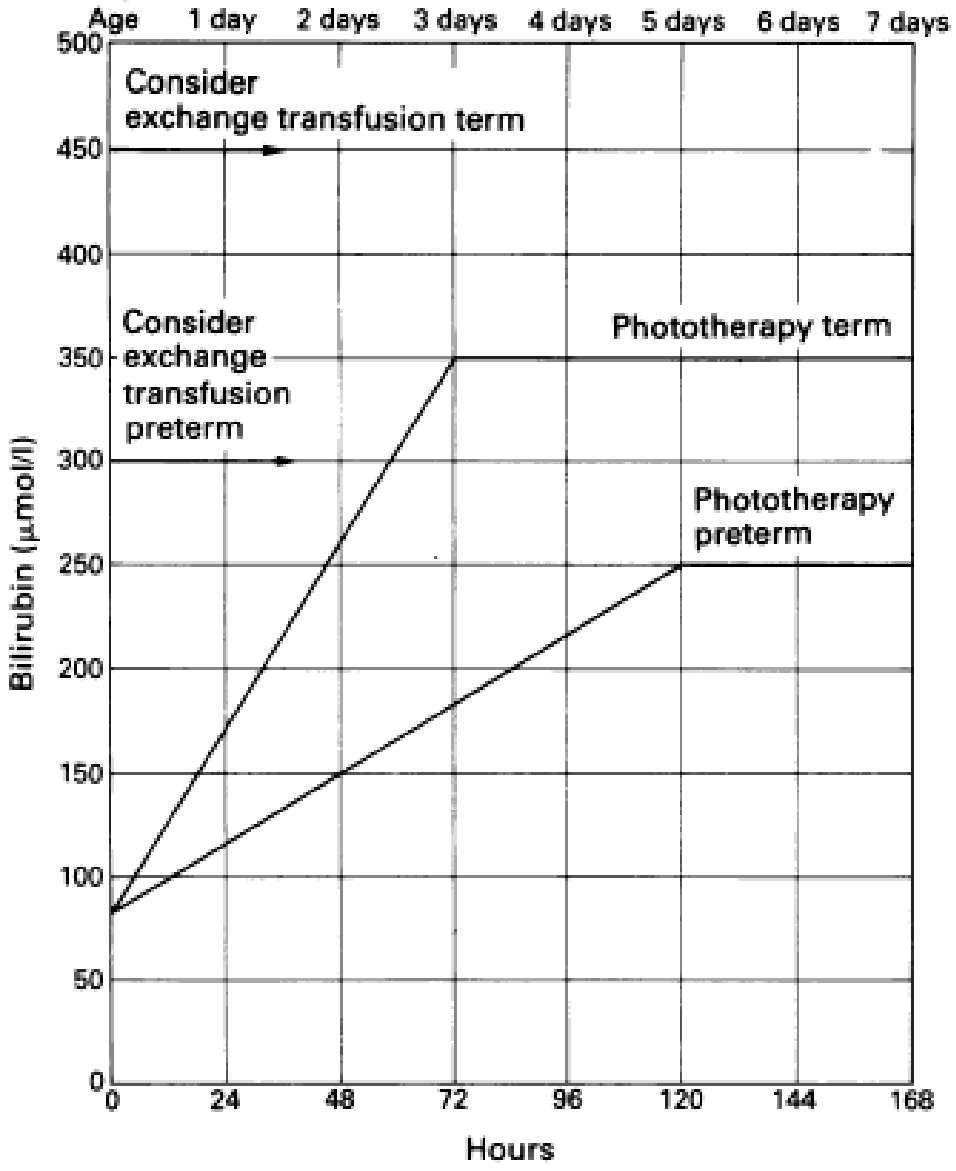
Clinical indications for phototherapy in a jaundiced newborn

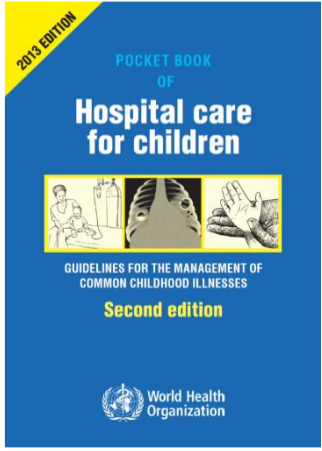
- Newborn where jaundice appears on day 1
- Preterm infants (< 35 weeks) with jaundice
- Palms and soles are yellow at any age
- Cephalhematoma or bruising and jaundice day 1 or 2
- Jaundice due to haemolysis

Clinical assessment and level of jaundice

- Jaundice first seen in the face and progresses caudally to the trunk and extremities
- *No jaundice below the nipple line*: = bilirubin concentration below 205 µmol/L (<12.0 mg/dL)
- However just because jaundice is below the nipple line does not mean the bilirubin level is over 205 µmol/L.

Arch Pediatr Adolesc Med. 2000;154(4):391-394

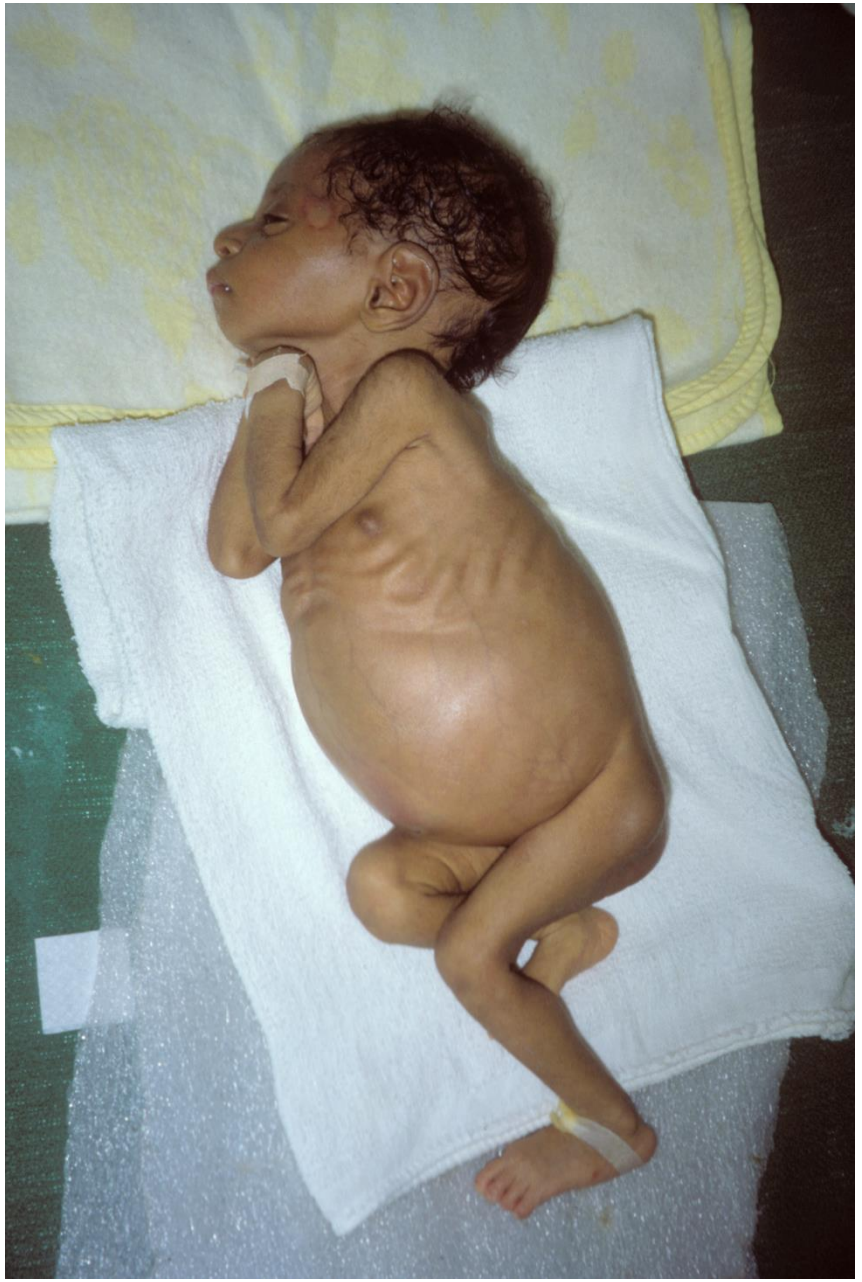




Age	Phototherapy		Exchange transfusion[1]	
	Healthy term infant ≥35 weeks	Preterm infant <35 weeks' gestation or other risk factors	Healthy term infant ≥ 35 weeks	Preterm infant < 35 weeks' gestation or other risk factors
Day 1	Any visible jaundice		260 µmol/l	220 µmol/l
Day 2	260 µmol/l	170 µmol/l	425 µmol/l	260 µmol/l
Day ≥ 3	310 µmol/l	250 µmol/l	425 µmol/l	340 µmol/l

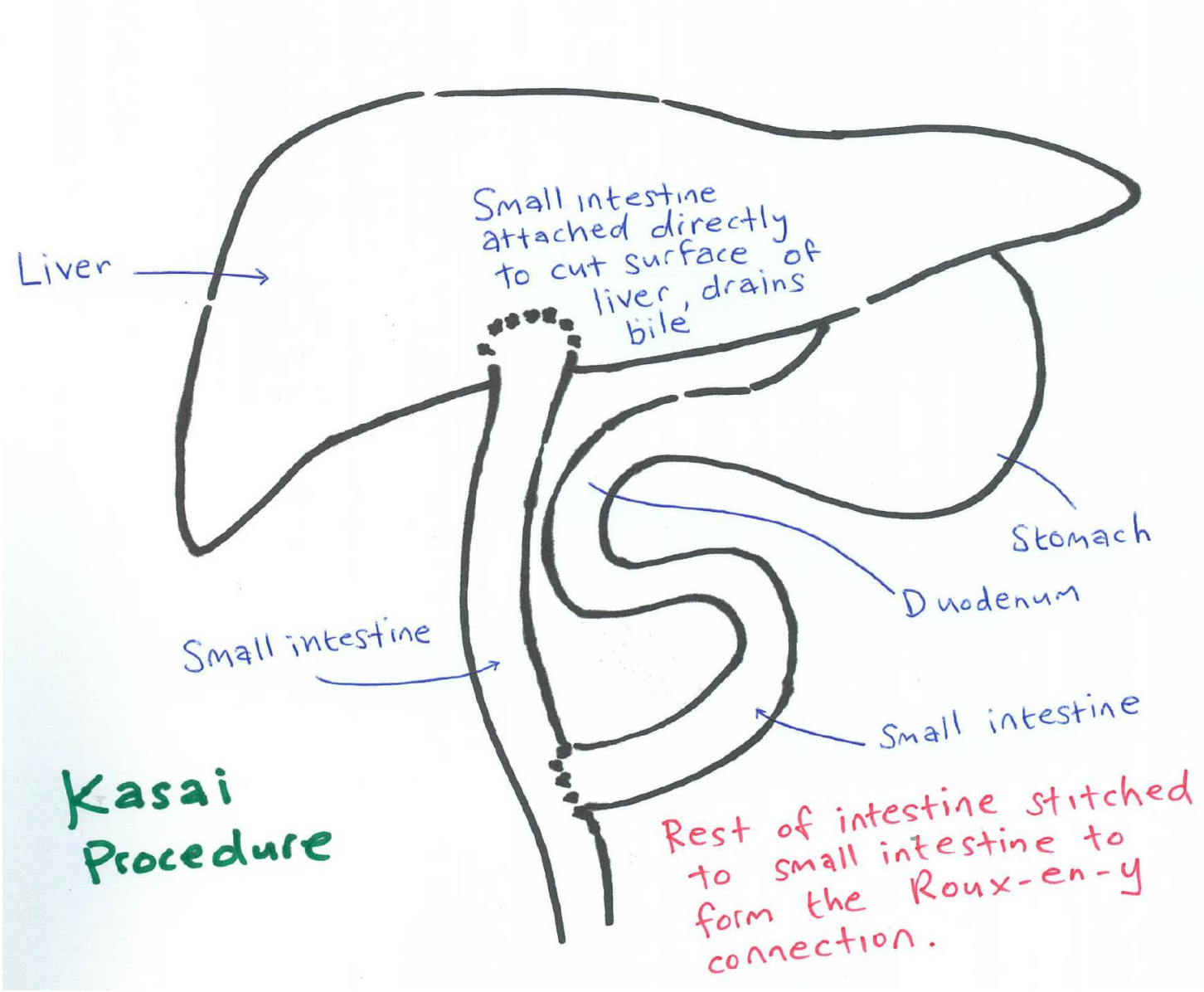
Biliary atresia

- Onset of jaundice 2-3 weeks of age
- Pale stools (no bile), dark urine (urobilinogen)
- Conjugated hyperbilirubinaemia
- High ALP, GGT
- Vitamin K deficient bleeding (fat soluble vitamin malabsorption, not liver cellular synthetic failure)
- ALT / AST more normal



Kasai procedure

- Kasai procedure – restores bile drainage by anastomosing a bowel loop (“Roux-en-y”) to the cut surface of the liver

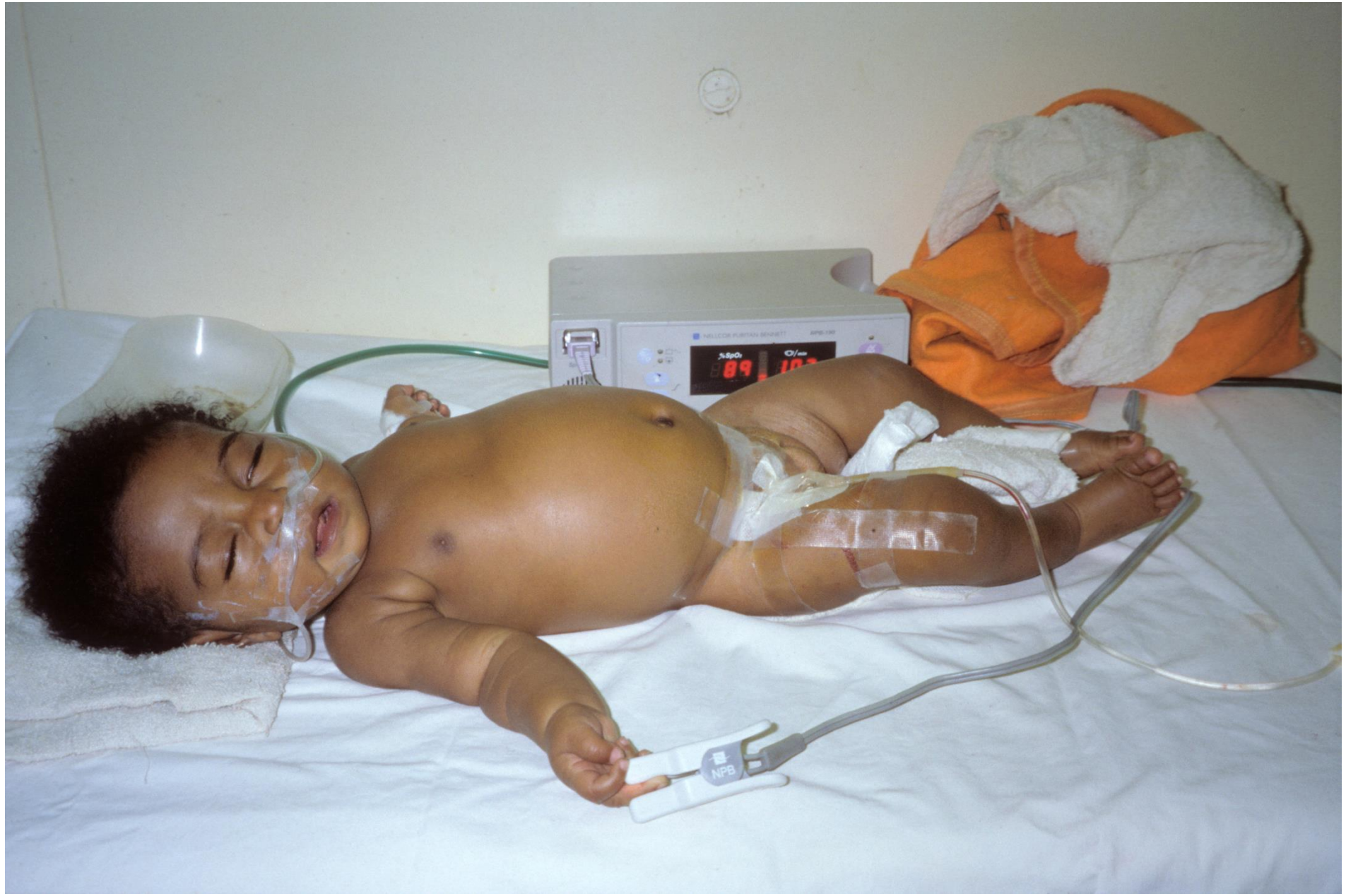


Galactoseamia

- Lactose in breast milk
- Lactose = glucose and galactose
- Lack of enzyme Gal-1-Ph uridyl-transferase leads to blockage of galactose breakdown → galactose-1-phosphate, after a few days of breast feeding
- galactose-1-phosphate is toxic to the liver
- 5-7 days – lethargy, jaundice, irritability, vomiting
- Treatment - withdrawal of lactose containing feeds (including breast milk)
- Cataracts, *E.coli* septicaemia

G6PD deficiency

- G-6-PD enzyme in all cells of the body, protects against oxidation damage to cells, red blood cells most susceptible
- Oxidation damage to cells by infection / foods / drugs
  - Virus infections
  - Broad beans
  - Primaquine
  - Sulphnamides
  - Aspirin
  - NSAIDS
- Haemolysis → release of haemoglobin →
  - Low Hb
  - Jaundice
  - Reticulocyte count ↑
  - No bile in urine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Jaundice and acute liver disease in older children

- Hepatitis A
  - Water and food borne, faecal-oral spread
  - Almost everyone is affected by 10 years of age (based on HAV antibodies), but young children rarely have symptoms
  - Incubation period 2-6 weeks, vomiting, fever, jaundice
  - Rarely causes acute fulminant hepatic failure
  - Always look for G-6-PD, as many children have both hemolysis (↑↑ reticulocyte count) *and* hepatitis
- Drugs
  - INH, pyrazinamide, rifampicin
  - Paracetamol – overdose leads to severe hepatocellular damage, severe synthetic dysfunction (INR)
  - Antibiotics – look for rash, arthralgia, eosinophilia
  - Sodium valproate

Jaundice and acute liver disease in older children

- Septicaemia – jaundice from hepatitis and haemolysis
- Pneumococcal pneumonia
- Malaria – always treat any jaundiced patient with anti-malarials

- Amoxycillin + gentamicin + metronidazole

- Do not use ceftriaxone or cloxacillin (cholestasis and liver dysfunction)

Amoebic liver abscess

- Painful hepatomegaly and ↑↑↑ WCC
- Chest x-ray – marked elevation of right hemi-diaphragm + pleural effusion
- Differential diagnosis
  - Pyogenic abscess
  - Tuberculoma
  - Hepatoma
- Ultrasound guided drainage
- Metronidazole + tinidazole