Age group terminology

Premature	**Birth before 37 completed weeks gestation**
Neonate	**0-4 weeks**
Infant	**1month-1 year**
Child/children	**1-12 years**
Adolescent	**13-18 years**
Adult	**>18 years**

Neonatology

Hyperbilirubinemia in the Newbornb (Neonatal Jaundice)

- Bilirubin is derived primarily **from the breakdown of heme in the reticuloendothelial system**. Nonpolar and water-insoluble unconjugated bilirubin is conjugated inside liver cells to form Water-soluble conjugated bilirubin.
- Most conjugated bilirubin is excreted through the bile into the small intestine and eliminated in the stool. Some bilirubin may undergo hydrolysis back to the unconjugated fraction by intestinal glucuronidase, and may be reabsorbed (**enterohepatic recirculation**)
- Nearly all newborns develop transient hyperbilirubinemia (serum bilirubin >2 mg/dL) and nearly 65% (two third) are clinically jaundiced (serum bilirubin>5 mg/dL).
- Onset of jaundice in the **first 24 hours of life is always pathological** .
- Kernicterus **(Bilirubin Encephalopathy)** results when indirect (**unconjugated)** bilirubin is deposited in brain cells and disrupts neuronal function. Kernicterus usually does not develop in term infants when bilirubin levels are less than 20 to 25 mg/dL. **The incidence of kernicterus increases as serum bilirubin levels increase to greater than 25 mg/dL**
- Kernicterus may be noted at bilirubin levels less than 20 mg/dL in the presence of some conditions like **sepsis**, **meningitis**, and prematurity .

Unconjugated hyperbilirubinemia

1-Nonpathologic unconjugated hyperbilirubinemia

A-Physiologic Jaundice

- Physiologic jaundice is **an unconjugated hyperbilirubinemia that occurs after the first postnatal day and can last up to 1 week**. Total serum bilirubin (TSB) concentrations peak in the first 3 to 5 postnatal days and decline to adult values over the next several weeks.

- The underlying mechanisms for physiologic jaundice in newborn are related to:

  (a) **Increased bilirubin production** because of elevated red blood cell volume per body weight and a shorter life span.

  (b) **Infants have immature hepatic glucuronosyl transferase**, a key enzyme involved in the conjugation of bilirubin.

  (c) **Increased enterohepatic circulation** in newborn.

B-Breast milk jaundice

- 1-It occurs in some breast-fed infants because **breast milk may contain an inhibitor of bilirubin conjugation or may increase the enterohepatic recirculation of bilirubin because of breast milk glucuronidase**.
- Jaundice appears in the **seventh** day and it **gradually increased in severity** till it reaches its peak during third week. It may persists for several weeks.
- **Interruption of breast feeding and use of formula feeding for 1–3 days causes a prompt decline in bilirubin** (which do not increase significantly after breastfeeding resumes) but is only recommended for infants with serum bilirubin concentrations that put them at risk for kernicterus.

C-Breast feeding jaundice

1-Breastfeeding jaundice occur when a breastfeeding baby **is not getting enough breast milk** , which leads to infrequent bowel movements and increased enterohepatic circulation of bilirubin. It occurs during the first week of life) .

2-**Water and dextrose solutions should not be used** to supplement breastfeeding because they do not prevent hyperbilirubinemia and may lead to hyponatremia.

D-Prematurity.

1-Although preterm infants develop hyperbilirubinemia by the same mechanisms as term infants, **it is more common and more severe in preterm infants and lasts longer** (due to the relative immaturity of the red blood cells, hepatic cells, and gastrointestinal tract).

2-Kernicterus is extremely uncommon. However, kernicterus in preterm infants can occur at lower TSB concentrations .

2-Pathologic Unconjugated Hyperbilirubinemia.

A-Acute Hemolysis:

In this condition, jaundice appears at birth or during the ***first day*** and it is commonly severe. Serum bilirubin level may rise rapidly to reach serious levels where kernicterus may occur.

Kernicterus is a real risk and it may occur when serum bilirubin exceeds the critical level, which depends on the birth weight and the condition of the baby. The cause of haemolysis can be identified by clinical and laboratory evaluation.

1-Rh incompatibility:

- It is the ***commonest*** cause of hemolysis. **It occurs in some Rh positive babies born to Rh negative mothers**. Hemolysis occurs due to placental passage of maternal antibodies active against the fetal red cells. The ***first baby*** is usually not affected as maternal sensitization usually occurs during delivery of the first baby.

- Rh incompatibility can be prevented by injection of ***Rh immune globulin to the mother within 72 hours after delivery*** which prevents her from forming antibodies which might affect subsequent babies.

2-ABO incompatibility:

ABO incompatibility may occur if the **mother's blood type is O** and **the infant's blood type is A or B** . The ***first baby*** may be affected. ***Jaundice*** is not severe. ***kernicterus*** is rare.

B-Neonatal septicemia:

1-Jaundice in septicemia, if present, usually appears between the ***fourth and seventh day*** or later and is usually moderate in severity.

2-The most important clinical signs are the markedly affected ***general condition(***The baby is not doing well with lethargy, poor suckling, fever or hypothermia, ...). Immediate hospitalization and combined parenteral antibiotic therapy are important .

Conjugated Hyperbilirubinemia

- 1-Conjugated (Direct-reacting) hyperbilirubinemia **is never physiologic** and should always be evaluated thoroughly.
- Direct-reacting bilirubin (composed mostly of conjugated bilirubin) **is not neurotoxic** to the infant, but **signifies a serious underlying disorder** involving cholestasis , hepatocellular injury or biliary atresia

Therapy of Indirect (unconjugated) Hyperbilirubinemia

The main concern is to prevent Kernicterus . Treatment options are:

A-Phototherapy. **B-Exchange transfusion**.

Table 2:bilirubin level at which phototherapy and exchange are indicated

	Phototherapy		**Exchange transfusion**	
	Healthy term baby	**Preterm or any risk factors***	**Healthy term baby**	**Preterm or any risk factors**
	Mg/dl µmol/l	**Mg/dl µmol/l**	**Mg/dl µmol/l**	**Mg/dl µmol/l**
Day 1	Any visible jaundice**		15 260	13 220
Day 2	15 260	13 220	25 425	15 260
Day 3	18 310	16 270	30 510	20 340
Day 4 and after	20 340	17 290	30 510	20 340

* Risk factors include small size (less than 2.5 kg or born before 37 weeks gestation), haemolysis, and sepsis. ** Visible jaundice anywhere on body on day 1.

A-Phototherapy

- Blue light (not ultraviolet) of wavelength 450 nm **converts the bilirubin in the skin and superficial capillaries into harmless water-soluble metabolites, which are excreted in urine and through the bowel** .
- The **eyes are covered to prevent discomfort** and additional fluids are given to counteract increased losses from skin.

B-Exchange transfusion

1-This is required if the bilirubin rises to levels considered dangerous despite phototherapy.

2- Twice the infant's blood volume (i.e. 2 x 80 mL/kg) is exchanged over about 2 hours (or 2 x 85 mL/kg).

3-The procedure is carried out **through umbilical vein catheter**.

Management of conjugated hyperbilirubinemia

Management depend on the treatment of the causative diseases (if treatable e.g. surgical correction of biliary atresia)

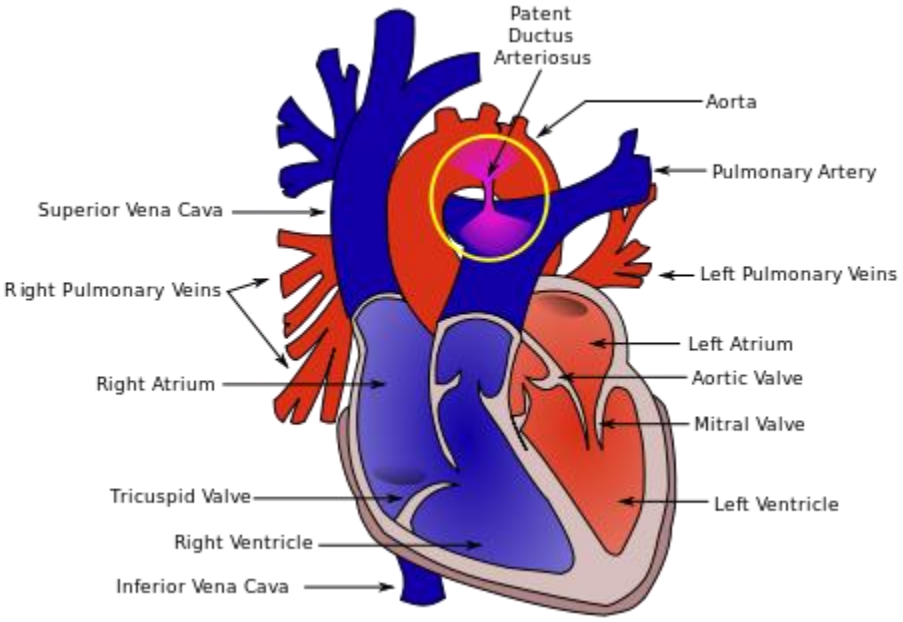
Patent ductus arteriosus

Failure of the DA to close after birth results in a condition called patent ductus arteriosus and the generation of a left-to-right shunt. If left uncorrected, patency leads to pulmonary hypertension and possibly congestive heart failure and cardiac arrhythmias. DA is a blood vessel connecting the main pulmonary artery to the

proximal descending aorta. It allows most of the blood from the right ventricle to bypass the fetus's fluid-filled non-functioning lungs.

The *E* series of prostaglandins are responsible for maintaining the patency of the DA (by dilation of vascular smooth muscle) throughout the fetal period. Prostaglandin E2 (PGE_2), produced by both the placenta and the DA itself, is the most potent of the E prostaglandins. Immediately after birth, the levels of both PGE_2 and the EP4 receptors reduce significantly, allowing for closure of the DA and establishment of normal postnatal circulation.

DA closure may be induced by administration of nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin production. The most common NSAID that is used to force DA closure is Indomethacin (a prostaglandin



synthetase inhibitor), which can be administered after birth (used in first week of life) . By inhibiting PGE_2formation, EP4 receptor activation will decrease and normal circulation can begin. NSAIDs taken late in pregnancy can cross the placenta and lead to premature closure of the DA in the fetus. In this case, exogenous PDE_2 can be administered to reverse the effects of the NSAIDs and maintain the patency of the DA for the remainder of the pregnancy.

Respiratory distress syndrome:

is a syndrome in premature infants caused by developmental insufficiency of pulmonary surfactant production and structural immaturity in the lungs. It can

also be a consequence of neonatal infection. It can also result from a genetic problem with the production of surfactant associated proteins. IRDS affects about 1% of newborn infants and is the leading cause of death in preterm infants.[5] The incidence decreases with advancing gestational age, from about 50% in babies born at 26–28 weeks, to about 25% at 30–31 weeks. The syndrome is more frequent in infants of diabetic mothers and in the second born of premature twins.

Symptoms:

IRDS begins shortly after birth and is manifest by fast breathing, more than 60 per minute, a fast heart rate, chest wall retractions (recession), expiratory grunting, nasal flaring and blue discoloration of the skin during breathing efforts.

As the disease progresses, the baby may develop ventilatory failure, and prolonged cessations of breathing ("apnea"). Whether treated or not, the clinical course for the acute disease lasts about 2 to 3 days. During the first day the patient worsens and requires more support. During the second day the baby may be remarkably stable on adequate support and resolution is noted during the third day.

Prevention:

Giving the mother glucocorticoids speeds the production of surfactant. For very premature deliveries, a glucocorticoid is given without testing the fetal lung maturity. The American College of Obstetricians and Gynecologists (ACOG), has recommended antenatal glucocorticoid treatment for women at risk for preterm delivery prior to 34 weeks of gestation.

Treatment:

1- **O2**
2- **IV fluid** to control BP , glucose level
3- **Endotracheal tube** is inserted if the symptoms worsened
4- **Exogenous surfactant** is admitted to the lungs

Febrile convulsion

1-A febrile convulsion is a fit occurring in a child (**generally between the ages of 6mths and 6yrs**), **precipitated by fever** (temp > 38 C) arising from infection outside the nervous system in a child who is otherwise neurologically normal [(1-3)] and in case of absence of acute electrolyte imbalance [(4)].

2-They occur in up to 4% of all children . The vast majority of febrile seizures are **harmless.**

3-Children prone to febrile seizures **are not considered to have epilepsy** (95–98% of children who have experienced febrile seizures do not go on to develop epilepsy).

Etiology

1-The **etiology is unknown**. Genetic predisposition appear to be a risk factor
2-Typically febrile seizure **occurs within the 1st 24 hour of a febrile episodes** and most commonly due to acute viral respiratory infections.

Types of febrile seizure

1-**Simple febrile seizures** last **less than 15 minutes**, and occur **only once in a 24-hour** period. The risk of subsequent epilepsy is not substantially greater than that for the general population.

2-If the seizure lasts **longer than 15 minutes** or **recurs within 24 hours** the seizure is referred to as a **complex or atypical febrile seizure**. It signify a greater risk of later epilepsy.

Diagnosis:

Diagnosis is made by **exclusion of other causes** of symptomatic seizures like meningitis or metabolic abnormalities.

Treatment

1-**Control fever** : Measures to reduce elevated temperature should be initiated. Acetaminophen (or ibuprofen) and tepid sponge baths usually are helpful. However, **administration of antipyretics during febrile illnesses does not prevent febrile seizures** .

2-Febrile seizures always are **outgrown**, so typically, **Long-term treatment or prophylaxis with antiepileptic drug (AED) for simple febrile seizures is not recommended**.

3-Oral diazepam (Valium) prophylaxis, **started at the onset of fever**, **prevents febrile seizure** (oral diazepam, 0.3 mg/kg q8h , is administered for the duration of the illness (usually 2-3 days). This strategy may be useful when parental anxiety associated with febrile seizures is severe.

4-Patients who have **prolonged febrile seizures** can benefit from **rectal diazepam gel** given soon after the onset of a febrile seizure to prevent additional prolonged seizures.