

Transition to Extra Uterine Life

John J Moore MD

Physiological Changes at Birth

- Breathing
- Changes in Blood Flow
- Glucose homeostasis
- Temperature Control
- Detoxification
- Eating
- Integration into family

Physiological Changes at Birth

- Breathing Seconds
- Changes in Blood Flow Seconds
- Glucose homeostasis Minutes
- Temperature Control Minutes
- Detoxification Hours - Days
- Eating Hours – Days
- Integration into family Days - Years

How does baby know it is born?

Placental Blood Flow Terminated with clamping of umbilical cord



300 cc/min Extra Blood Shunted to Systemic Circulation



Stretch Receptors Activated



Catecholamines Released

Changes necessary for Breathing

BEFORE BIRTH

- No Gas exchange in lungs
- Lungs receive little blood flow (23% cardiac output)
- Lungs produce fluid – 100cc/kg of baby/day
- Lungs fluid filled

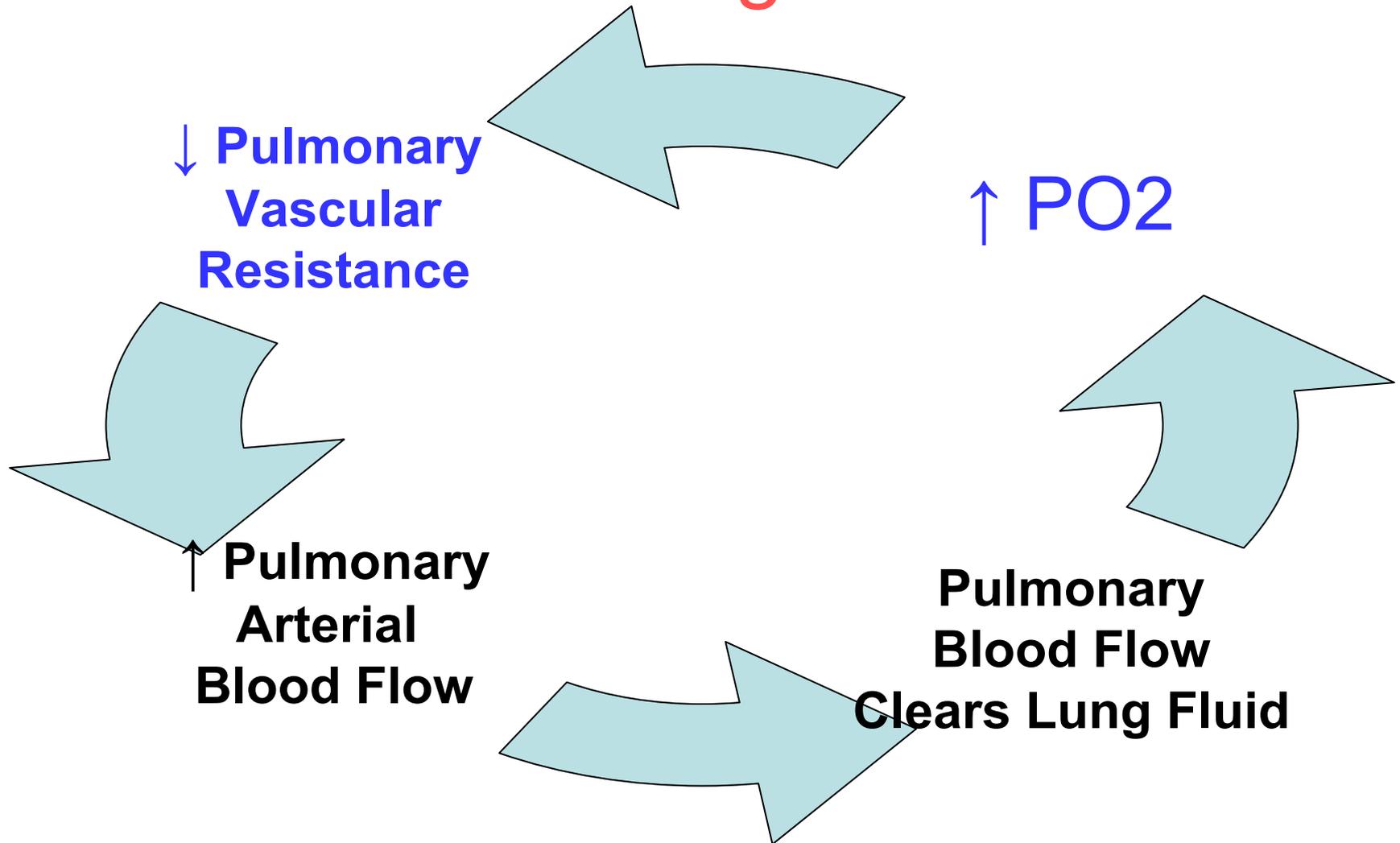
AFTER BIRTH

- All Gas exchange in lungs
- Lungs receive 100% cardiac output
- Lungs produce minimal fluid
- Lungs must clear 250 ml fluid

Catecholamines Trigger Breathing initiation & CV changes

- Catecholamines increase breathing movements
 - Breathing increases PO_2
 - Breathing directly reduces Pulmonary vascular resistance
 - Pulls open vessels
 - Reduces intra thoracic pressure
- Catecholamines decrease alveolar fluid production

Breathing Initiation and Circulation Changes

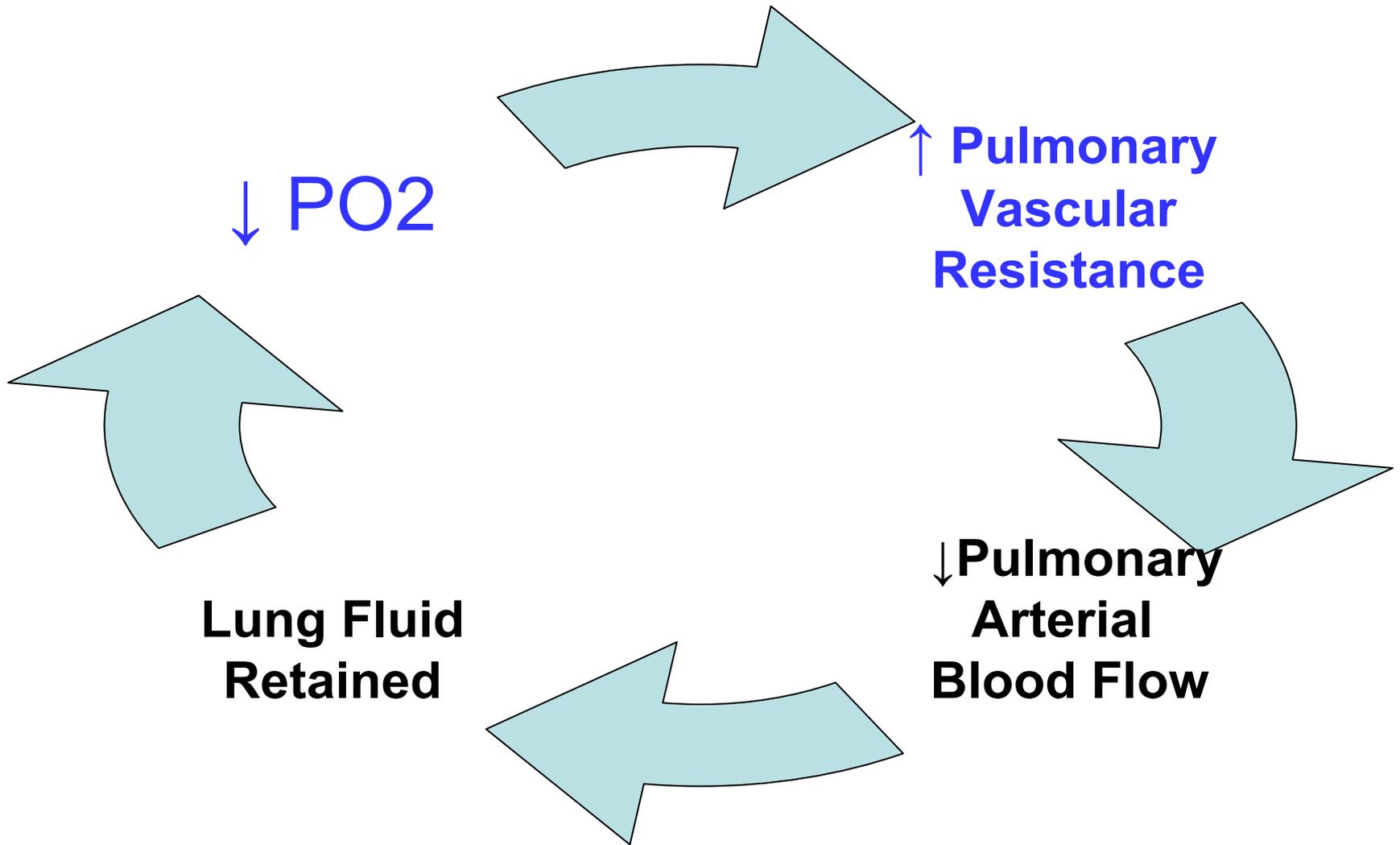


If Respiratory Transition does
not go smoothly

Symptoms of Breathing Difficulty in Newborns

- Tachypnea
- Grunting
- Flaring
- Retractions
- Cyanosis

The Paradigm in Reverse



Problems with Respiratory Transition

Minimal Respiratory Disease

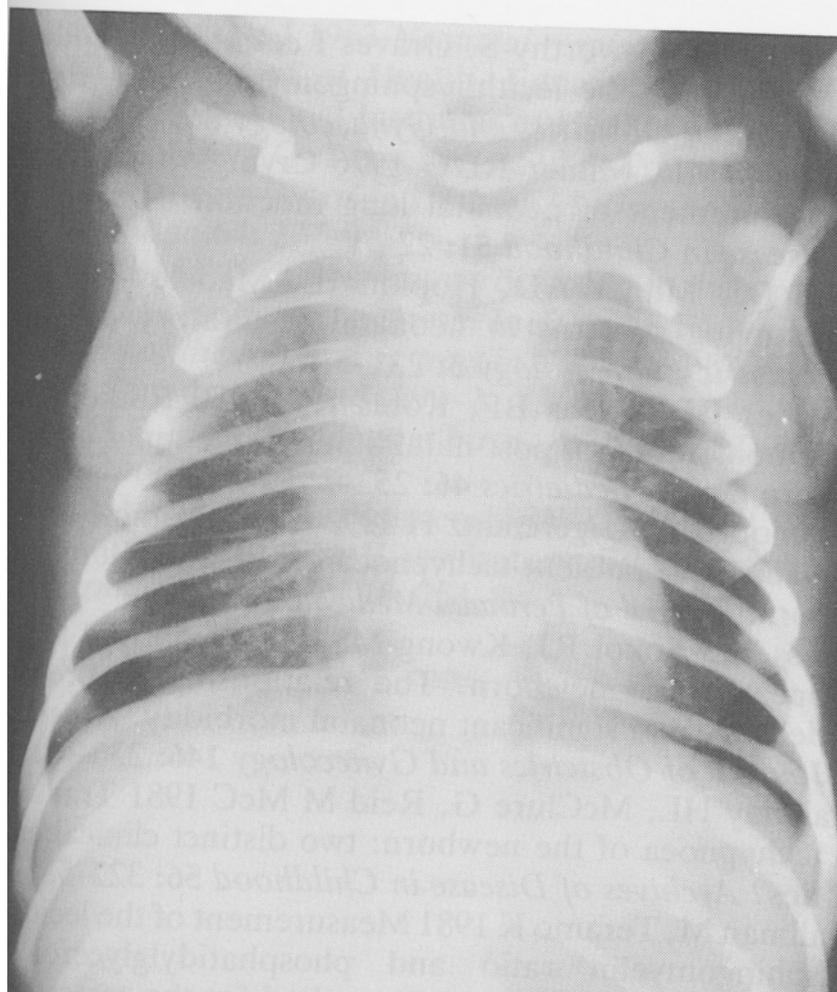
- Mild respiratory symptoms at birth, usually with minimal cyanosis
- No CXR findings or oxygen requirement
- Duration less than 4 hr
- 25% - 30% of infants may experience this

Problems with Respiratory Transition

Transient Tachypnea of the Newborn

- Etiology - immaturity of the fluid removal pathway or failure of signal to terminate fluid production
- Symptoms – generally lasts approximately 48h
 - Respiratory Distress
 - CXR shows fluid seen in fissures as well as picture of edema.
 - Oxygen Requirement
- Most frequently seen after repeat C-section without preceding labor.

TTN

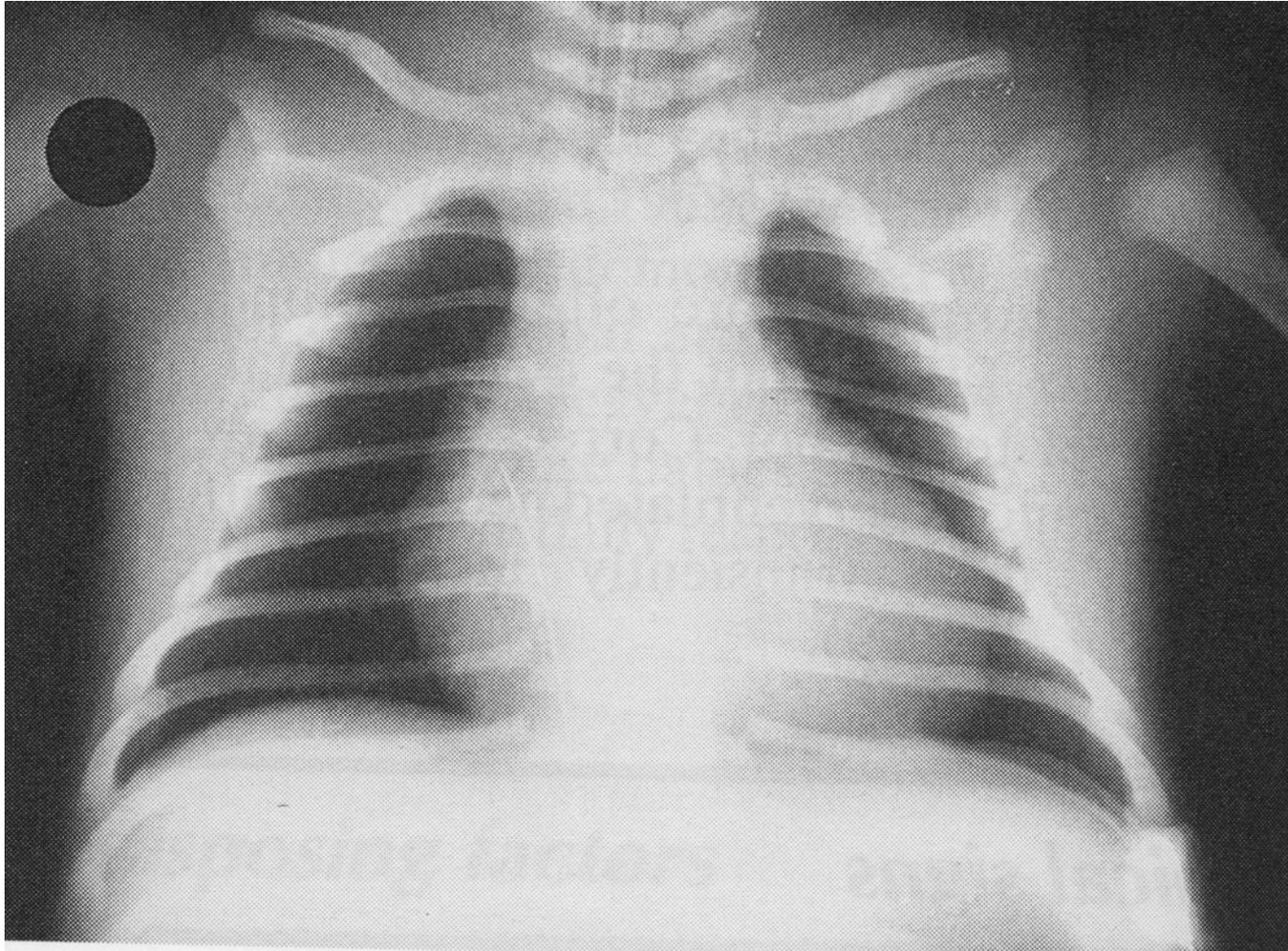


Problems with Respiratory Transition

Persistent Pulmonary Hypertension (PPHN)

- Pulmonary blood flow inadequate for gas exchange.
- Symptoms – may cause death; usually lasts 6-8 days
 - Severe Respiratory Distress – frequently with signs of shock
 - Responds only to high FiO_2 , ventilation and may require NO or ECMO.
- PPHN is most frequently seen with Meconium Aspiration Syndrome, Pneumonia or Severe Anomalies of the thorax (congenital diaphragmatic hernia).

Primary PPHN



Respiratory Problems which Exacerbate Transition

- Lung Immaturity – Premature infants – Respiratory Distress Syndrome
- Infection – Pneumonia, Sepsis
- Asphyxia
- Meconium Aspiration Syndrome
- Anomalies of the Respiratory Tree and Thorax
- Problems with Temperature regulation, Metabolism

Glucose Homeostasis

Glucose

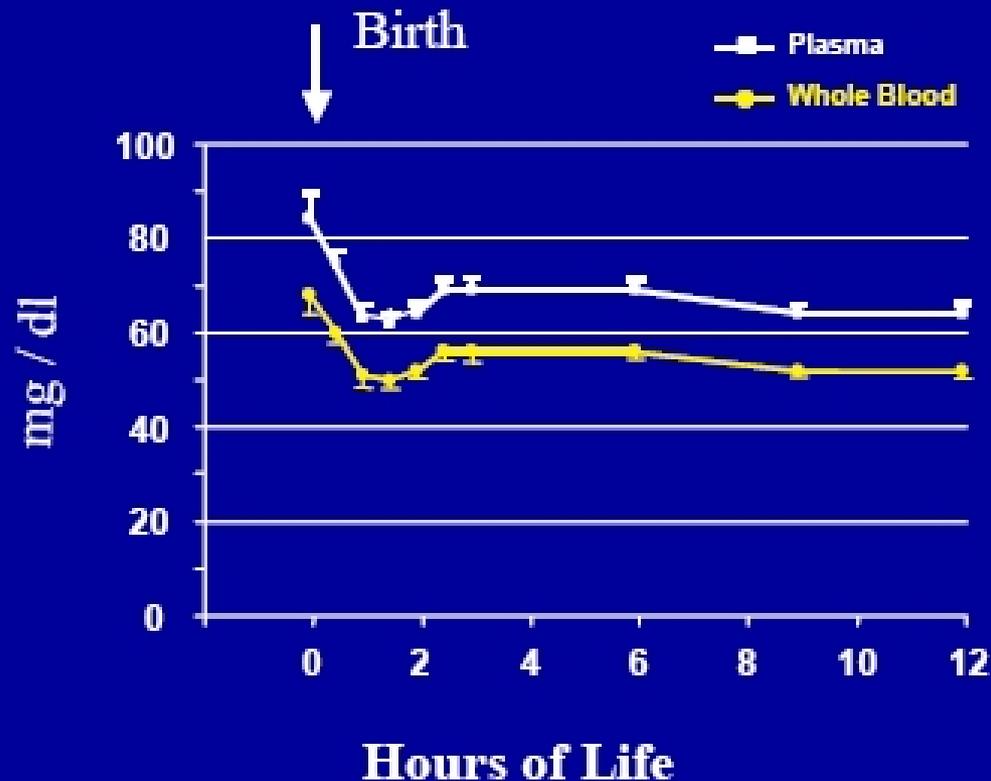
Before Birth

1. Major fuel – only fuel for brain
2. Fuel source – mother via placenta – continuous
3. Glycogen stored, available in emergency
4. No gluconeogenesis

After Birth

1. Glucose and fat utilized
2. Fuel source food – intermittent.
3. Glycogen stored, available in emergency
4. Active gluconeogenesis

Glucose Values in Normal Newborns



Issues with Glucose

- **Catecholamines** initiate neonatal glucose homeostasis by activating glycogen breakdown and gluconeogenesis.
- Glycogen and Fat are both laid down mostly in 3rd trimester. Limited in preterms and SGA (small for gestational age; intrauterine growth retarded).
- Gluconeogenesis starts at birth with induction of PECK enzyme. Limited in preterms.
- Infants of Diabetic Mothers (IDM) have high insulin levels – can not use glycogen stores or initiate gluconeogenesis

Glucose Transition Problems

- Symptoms
 - Lethargy
 - Respiratory Irregularities – usually apnea
 - Temperature Irregularities – usually hypothermia
 - Neurological Irregularities – sometimes jitteriness, seizures

Glucose Transition Problems

- Low Glycogen Group – preterm, SGA, IUGR, hard labor, maternal β agonists; sepsis also possible – provide IV glucose support until glycogen replete and gluconeogenesis established (usually OK by 2-3 days except very preterm).
- High Insulin Group – IDM, Obese mothers, Rh disease, Nesidioblastosis – carefully support with minimal glucose necessary to avoid symptoms (may require 5-10 days support).
- Congenital Metabolic Abnormalities – hundreds of rare problems. Support with IV glucose, make diagnosis and then give specific therapy if available.

Temperature Control

Heat Processing

- Three heat processing steps must be understood in order to understand temperature control.
 - Heat Generation – the process which heat is produced (generally in the body core)
 - Heat Conservation (Insulation) - the mechanisms by which heat is restricted from reaching the body surface (generally done at the periphery).
 - Heat Loss – physical processes of heat loss from the body surface.

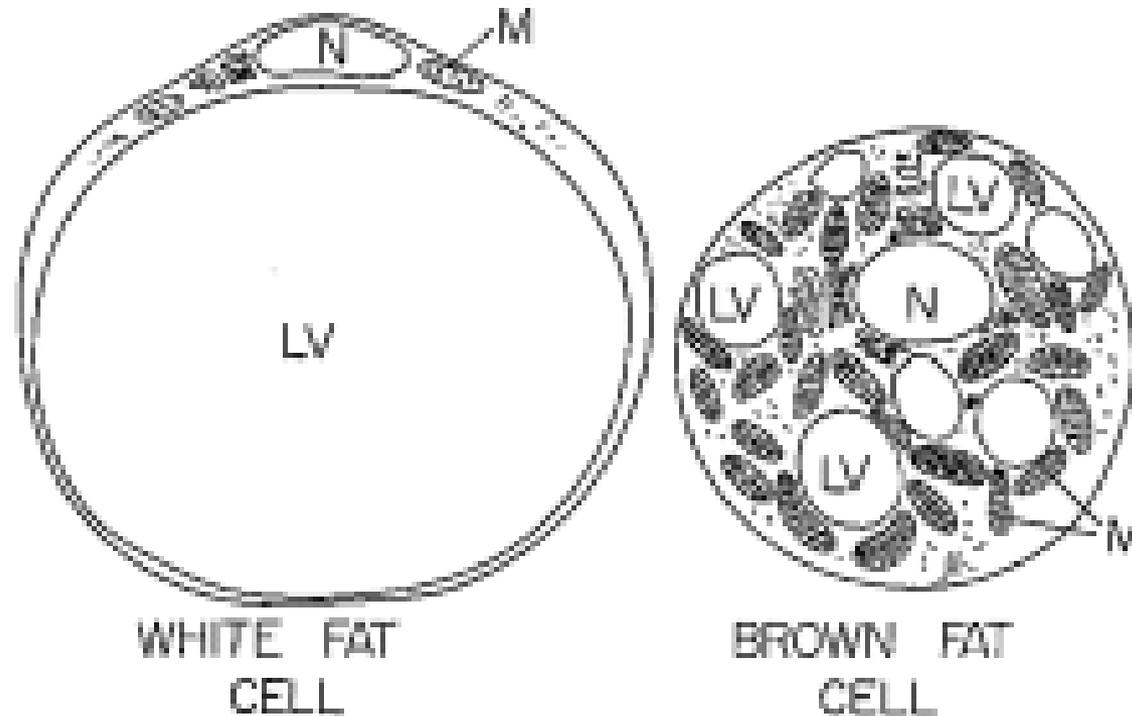
Mechanisms of Heat Generation

- Basal Metabolism – biochemistry is inefficient, the result is heat. **The heat generated by this mechanism is proportional to mass.**
- Shivering – not used by neonates
- Large body movements – minimally used by neonates
- Brown Fat – a neonatal organ

Brown Fat vs.. White Fat

- Brown Fat
 - A neonatal organ: It is not used in older humans to any degree.
 - Located in the core of the body – under scapula and in retro-peritoneal cavity.
 - An organ of heat generation
- White Fat
 - Present throughout life
 - Located subcutaneously in the periphery .
 - An organ of storage and insulation.

Brown Fat vs. White Fat



The White fat cell has single fat globule and only a few mitochondria.
The Brown Fat Cell has many fat globules and many mitochondria.

Brown Fat vs. White Fat

- Brown Fat
 - **Has many globules of fat** this allows incremental release of fat to feed its heat generation machinery
 - **The large number of mitochondria** are necessary as the metabolism of this fat occurs locally, in the brown fat cell.
 - **The mitochondria have a special protein – uncoupling protein 1** which allows the proton gradient of the external mitochondrial membrane to be dissipated without making ATP. **The result is heat production**
- White Fat
 - Has a **single globule** of fat that is released all at once – all or nothing.
 - The **small number of mitochondria** demonstrate that very little fat is metabolized here. The metabolism of the fat in these cells takes place in the liver after release.
 - **Uncoupling Protein 1 is not present** in these cells. Very little heat is generated.

Brown Fat Cells are activated by
Catecholamines

Prematures and Heat Generation

- Prematures have little mass – thus minimal generation of heat from these mechanisms.
- Prematures like all neonates do not shiver and do not have significant large body motion.
- Prematures do not have much brown fat as it is laid down mainly in the third trimester.

Mechanisms of Heat Conservation

- Insulation

- White Fat lines the dermis providing insulation.
- Neurological control of the blood vessels connecting the superficial and deep venous plexuses (on opposite sides of the fat) in the skin determine how much blood reaches the cool areas peripheral to the white fat.
 - In order to raise body temperature these vessels are closed and blood does not reach the periphery. (The body appears mottled, blue and feels cold.)
 - In order to lower the body temperature these vessels are opened and blood reaches the skin surface. (The body is flushed, red and feels warm)

Prematures and Insulation

- Prematures do not have much white fat as it is laid down mainly in the last trimester.
- Prematures can not control vasodilatation and vasoconstriction adequately to control flow from the deep and superficial venous plexuses.

Mechanisms of Heat Loss

-These are all physical processes

- **Conduction** – solid to solid contact transfer of heat.
 - This is dependent upon the surface area in contact.
 - Smaller newborns and prematures tend to have larger percentages of their total body surface area in contact with the mattress.
- **Convection** – solid to gas transfer.
 - The transfer of heat by convection increases with the radius of curvature of the surface. Prematures and neonates have more loss per square inch of surface than older children and adults due to their smaller body parts.
- **Radiation** – solid to solid at a distance transfer of heat.
 - Loss or gain of heat is related to the solid angle which is made to the surface to which radiation occurs. Thus we are colder when we are close to a window rather than further from it.
- **Evaporation** – Liquid to gas transfer. Babies are born wet and tiny prematures leak fluid through the skin making this more of a problem.

Temperature in the Neonate

- A very important concept is that temperature control becomes more problematic as the **mass to surface area ratio** decreases. Heat generation is proportional to mass. All heat loss mechanisms are proportional to body surface area.
 - This ratio shows the following:
 - **ADULT > Child >> Term Baby >>> Premature**

How do we assist Neonates with Temperature Control?

- We can only assist with heat loss control. We can do nothing for heat generation or insulation.
- Radiant Warmers and Isolettes are used.

Bilirubin Metabolism

Bilirubin

Before Birth

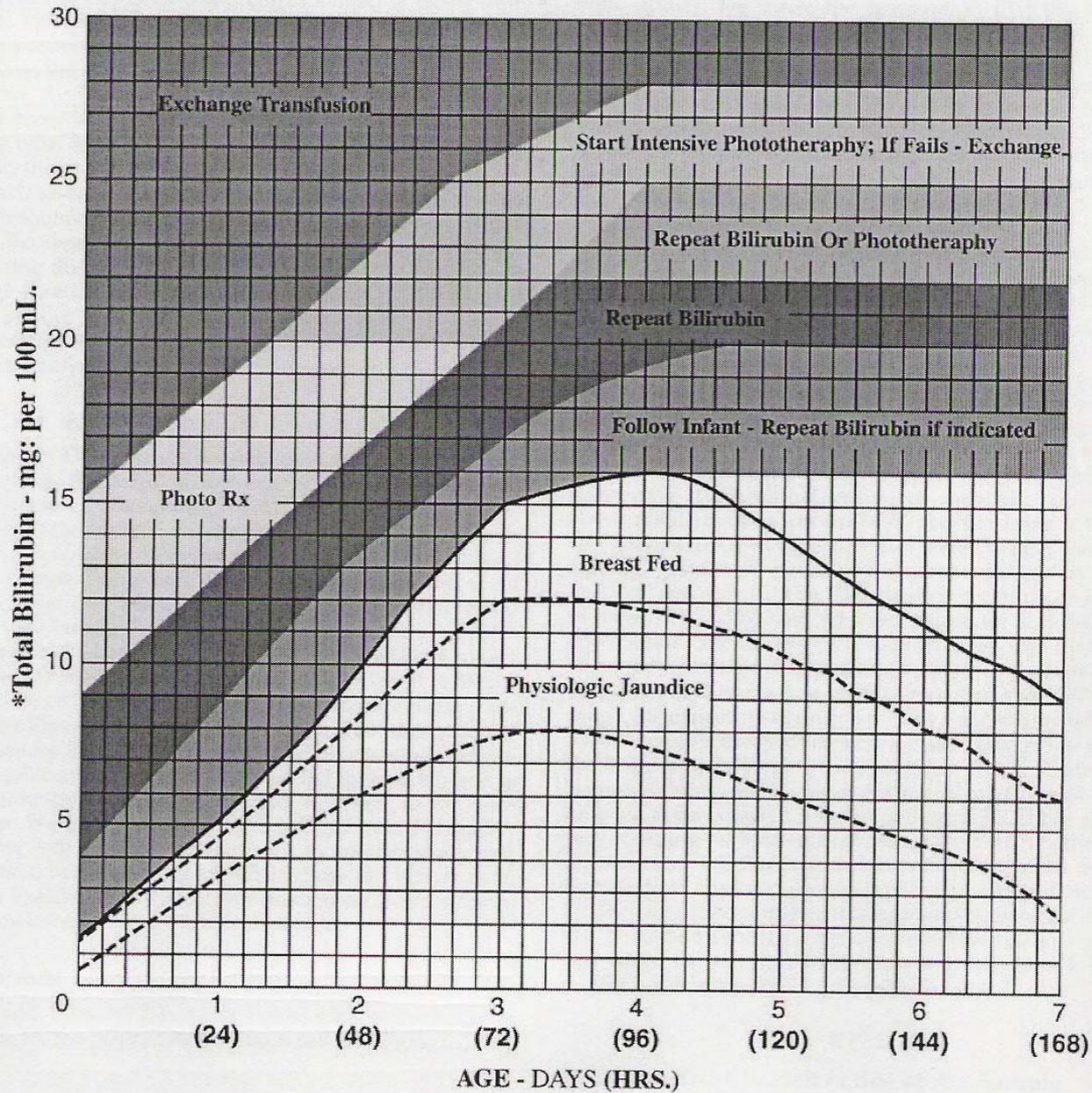
- Red cell mass increased in utero due to relative hypoxia
- Bilirubin transferred to mother for detoxification fetal liver and gut not involved

After Birth

- Red Cell mass decreases after birth due to relative hyperoxia
- Conjugation initiated by neonatal liver and then excreted by neonatal gut.

Physiological Bilirubin Elevation

- Increase in bilirubin production
 - Large Red Cell mass at birth
 - Breakdown increases due to bleeding at birth – cephalohematomas etc
 - Large number of infants with ABO
- Decrease in excretion
 - Need for induction of liver enzymes
 - Problems with gut functioning
 - Inadequate intake for hydration and carrying out the conjugated bilirubin



Neonatal Hyperbilirubinemia

Factors Complicating Physiologic Jaundice

– Increased bilirubin production

- Increased red cell mass - Polycythemia
- Hemolytic Disease of the Newborn
 - Isoimmunization
 - » ABO incompatibility.
 - » RH incompatibility.
 - Enzyme defect
 - » G-6-PD
 - » Pyruvate Kinase
 - Structural membrane defects
 - » Spherocytosis
 - » Elliptocytosis.

Neonatal Hyperbilirubinemia

More complicating factors

- Decreased Conjugation
 - UDPGT deficiency(Crigler-Najjar)
 - » Type I (AR) severe unconjugated.
 - » Type II (AD)
 - Gilbert Syndrome
- Extra vascular blood
 - Cephalohematoma
 - Intracranial bleeding
 - Renal vein thrombosis

Neonatal Hyperbilirubinemia

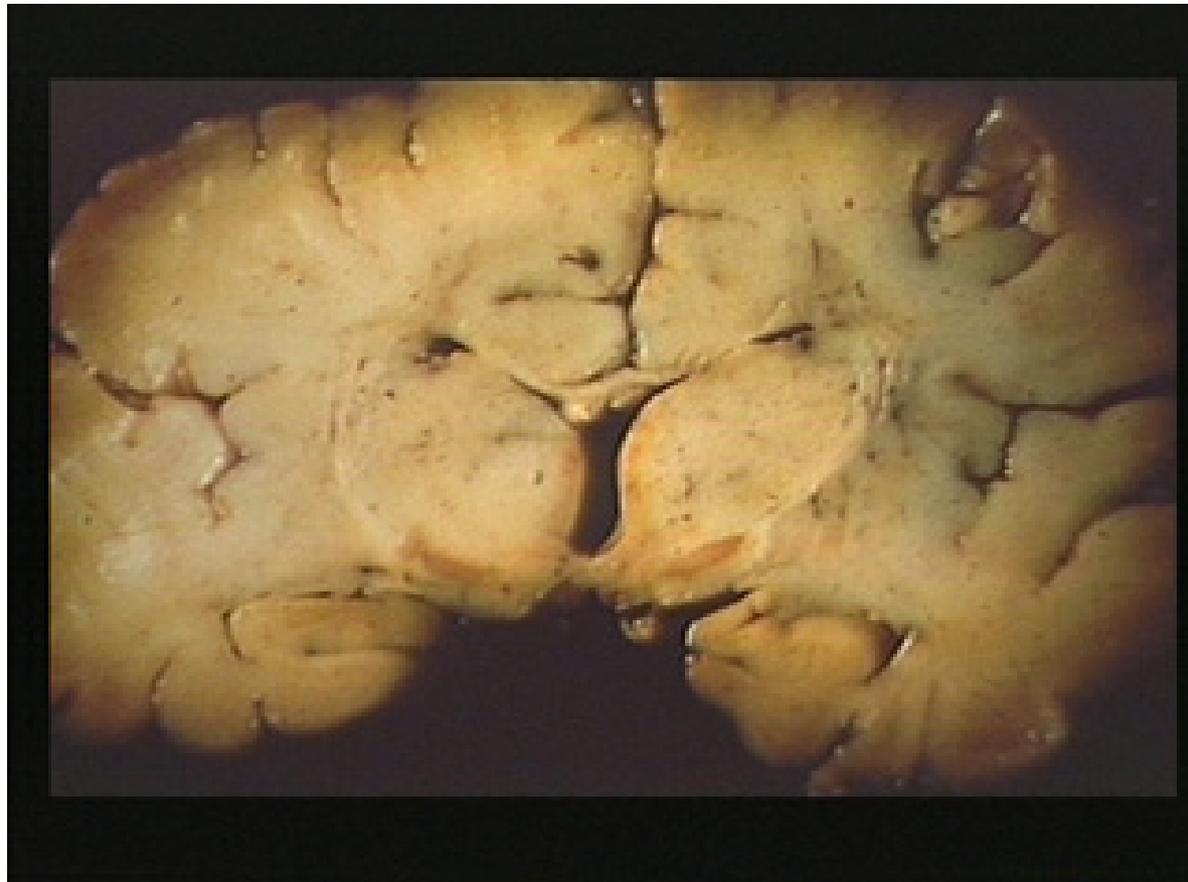
More complicating factors

- **Decreased Excretion**
 - Increased enterohepatic circulation
 - Bowel obstruction
 - Hypothyroidism.
 - Decreased Throughput
 - Poor feeding
 - Failed breast feeding

Kernicterus

- Clinical Syndrome
 - Acutely- Irritability, hyperreflexia, muscle rigidity, seizures
 - Progression - Paralysis of upward gaze, oculogyric crises, irregular respirations, pulmonary hemorrhage, death
 - Survivors - nerve deafness, choreoathetoid CP, mental retardation
- Pathology - staining of basal ganglia

Kernicterus



Kernicterus is clearly bad... but isn't Physiological Hyperbilirubinemia Benign?

0031-3998/01/5006-0701
PEDIATRIC RESEARCH
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Vol. 50, No. 6, 2001
Printed in U.S.A.

Are Moderate Degrees of Hyperbilirubinemia in Healthy Term Neonates Really Safe for the Brain?

INEKE SOORANI-LUNSING, HENK A. WOLTIL, AND MIJNA HADDERS-ALGRA

*Department Neurology, University of Groningen, NL-9713 GZ Groningen, The Netherlands [I.S.-L., M.H.-A.];
Department Paediatrics, Martini Hospital, NL-9700 MM Groningen, The Netherlands [H.A.W.]*

Data Suggests that Bilirubin in the Range of 15-25 can cause Sequellae

Table 1. Perinatal and neonatal condition and social status in study and control group

	Study group	Control group
Peak TSB in $\mu\text{mol/l}$ (mean \pm SD)	313 \pm 62	No data available (no jaundice)
No phototherapy (n = 10)	284 \pm 41	
With phototherapy (n = 10)	342 \pm 67*	
Sex (M:F)	15:5	15:5
Gestational age at birth in days (mean \pm SD)	272 \pm 12	278 \pm 12
Number of infants aged 36 wk at birth	4	2
Birthweight in g (mean \pm SD)	3480 \pm 403	3357 \pm 402
Rate of cesarean section	2/20	14/20†
Neonatal breast feeding	15/20	14/20
Social class‡		
Low	8 (40%)	4 (20%)
Middle	6 (30%)	13 (65%)
High	6 (30%)	3 (15%)

TSB = total serum bilirubin; wk = weeks.

* phototherapy - or +: *t*-test, *p* = 0.03.

† Study vs. control group: $\chi^2 = 12.6$, *p* < 0.001.

‡ Social class according to maternal education (low = primary education/junior vocational training; middle = secondary general education/senior vocational training; high = university education/vocational colleges (33).

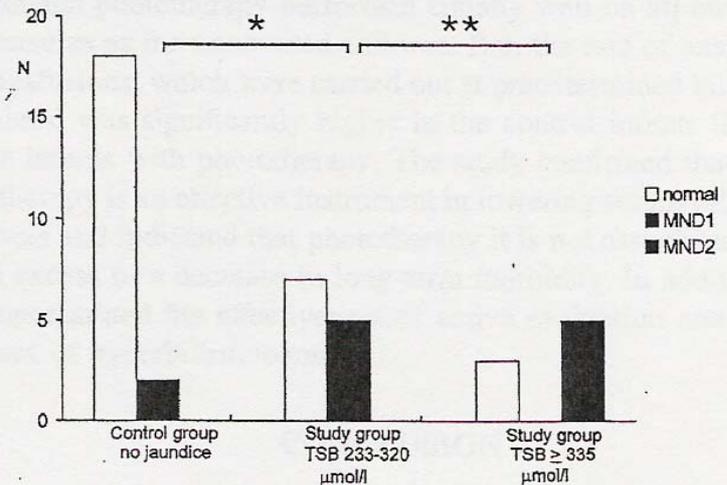


Figure 1. Neurologic condition at 12 mo of age in the control group, the study infants with a moderately high peak of the total serum bilirubin (233–320 $\mu\text{mol/L}$) and the study infants with a high peak of the total serum bilirubin (335–444 $\mu\text{mol/L}$). *Proportion of minor neurologic dysfunction (MND) type 1, Fisher: *p* = 0.04, **proportion of minor neurologic dysfunction type 2, Fisher: *p* < 0.01.

Kernicterus in the Term Infant

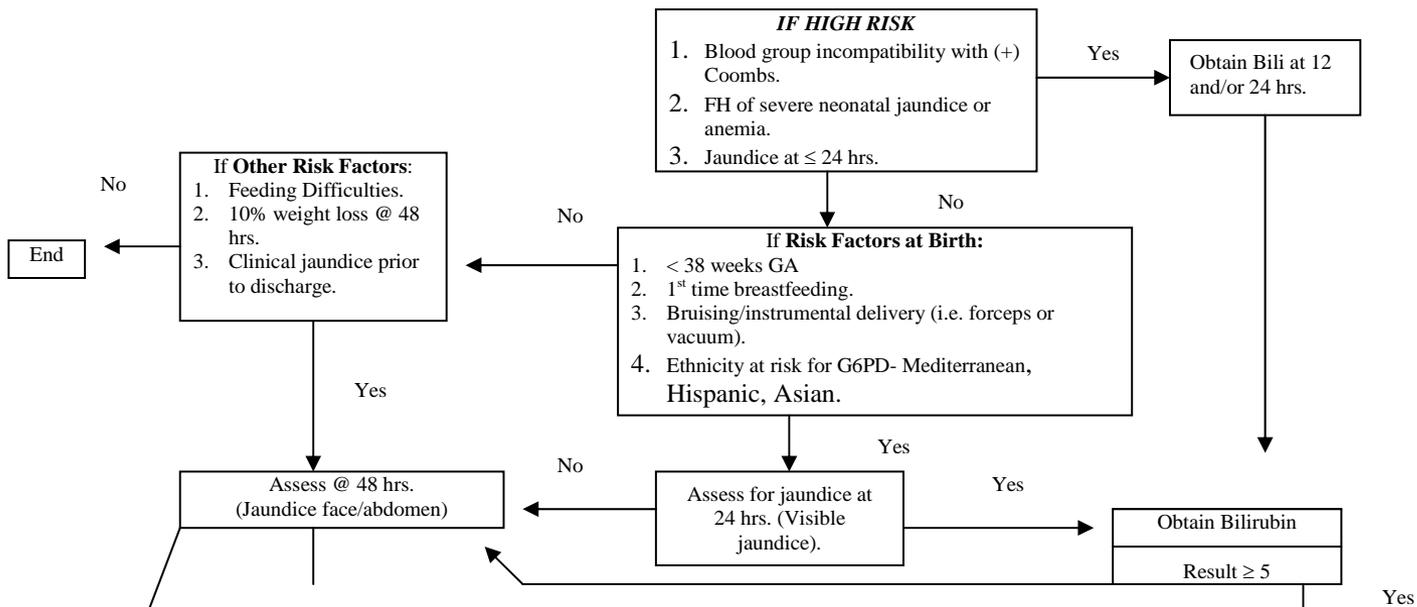
- Risk factors (usually combination)
 - First time Breastfeeding
 - ABO or other hemolytic disease
 - Lack of continuity of care
- Presentation
 - Incidence - 1/30,000 births ??, middle class/suburban parents
 - Complicating Issues
 - Physician attitude toward neonatal jaundice
 - Fears of interfering with breast feeding
 - Early discharge

Neonatal Network Roundtable Bilirubin Management Algorithm

Design Objectives

- Use risk factors to focus screening.
- Minimize invasiveness and disturbance of families.
- Support Breast Feeding
- Keep Total Serum Bilirubin under 20.
- Avoid Exchange Transfusion
- Prevent Kernicterus

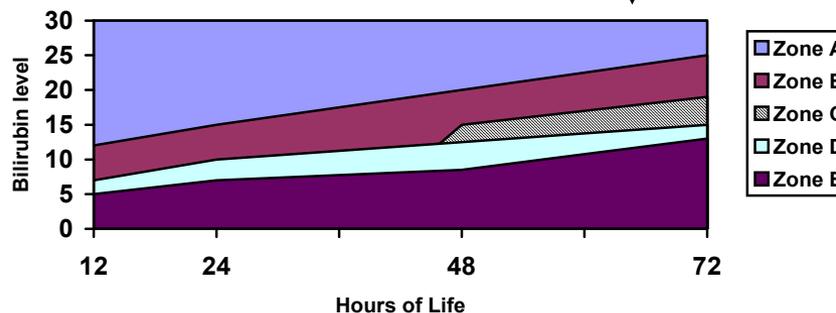
**Hyperbilirubinemia Guideline
(Infants > 34 wks. gestation)**



Note:

1. Total and Direct Bilirubin, CBC & blood smear, Retic. Count, Type & Coombs should be obtained if phototherapy or bili blanket started.
2. Supplement: offer 30-60 cc per feed of formula after breastfeeding. (Administration by any method acceptable). Bottle feeders should take at least 45-60 cc/feed.
3. Bili blanket—if not available, consider retention/admission for phototherapy.

Management of hyperbilirubinemia



	12 hours	24 hours	48 hours	72 hours
Zone A: Exchange transfusion	12	15	20	25
Zone B: Inpatient hydration and phototherapy			15	19
Zone C: Hydration and phototherapy	7	10	12.5	15
Zone D: Supplemental feedings and observation	5	7	8.5	13
Zone E: No intervention	< 5	< 7	< 8.5	< 13

Questions

- What major life processes are initiated at birth?
- What is the physiological signal of birth and what causes it to be sent?
- What physiological changes facilitate respiration?
- Explain the physiological paradigm that accomplishes these changes.
- Explain minimal respiratory disease, TTN and PPHN as problems in respiratory transition.
- What changes occur in glucose supply at birth?
- What process stabilizes the glucose levels?
- Explain the problems of preterm infants and infants of diabetic mothers in terms of problems of glucose transition.
- Explain the difference between brown and white fat.
- Explain the problems of premature infants in terms of temperature control transition.
- Why does bilirubin rise after birth and then fall?
- What issues aggravate this transition?