

Zaporizhzhya State Medical University  
Department of hospital pediatrics

The collection of lectures on neonatology  
for the fifth year English-speaking medical students of  
international faculty  
delivered at the department of Hospital pediatrics

2016

The collection of lectures on neonatology which are delivering at the department of Hospital pediatrics for 5th year English-speaking students was prepared in accordance to the 5<sup>th</sup> year curriculum on Pediatrics. The specified illustrated collection is published for the first time and includes 5 lectures on basic problems of neonatology. The collection designed for the effective preparation of teachers for lectures delivered at the department of hospital pediatrics of Zaporizhzhya State Medical University,

#### TEMATIC PLAN OF LECTURES ON NEONATOLOGY

#	Topic	Amount od hours
1	Perinatal asphyxia.	2
2	Birth trauma of newborns.	2
3	RDS in newborns.	2
4	Origin, differential diagnosis and therapy of jaundices in newborns	2
5	TORCH - infections in newborns.	2

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Zaporizhzhya State Medical University

The collection of lectures ratified on the meeting of Central Methodical Council of Zaporizhzhya Sate Medical University/

Protocol # \_\_\_\_\_ from \_\_\_\_\_

УДК: 616-053.31(042)=111

ББК: 57.3Я73

Т-44

**Г.О. Леженко, Ю.Г. Резниченко, А.В.Каменщик, С.В. Врублевська, О.М.Лебединець, К.В. Гладун.** Збірник лекцій з неонатології, що читаються студентам 5 курсу міжнародного факультету англomовної форми навчання на кафедрі госпітальної педіатрії. –Запоріжжя , 2016- 140 с.- англ.м.

**Заклад-розробник:**

Запорізький державний медичний університет

Збірник лекцій затверджено на засіданні Центральної методичної Ради Запорізького державного медичного університету

Протокол №\_\_ від \_\_\_\_\_

**Content:**

<b>1. Perinatal Asphyxia.....</b>	<b>5</b>
<b>2. Birth trauma .....</b>	<b>37</b>
<b>3. Respiratory distress in newborns .....</b>	<b>50</b>
<b>4. Origin, differential diagnosis and therapy of jaundices in newborns.....</b>	<b>90</b>
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# *Neonatology:* *Perinatal Asphyxia*



## **Lecture Points**

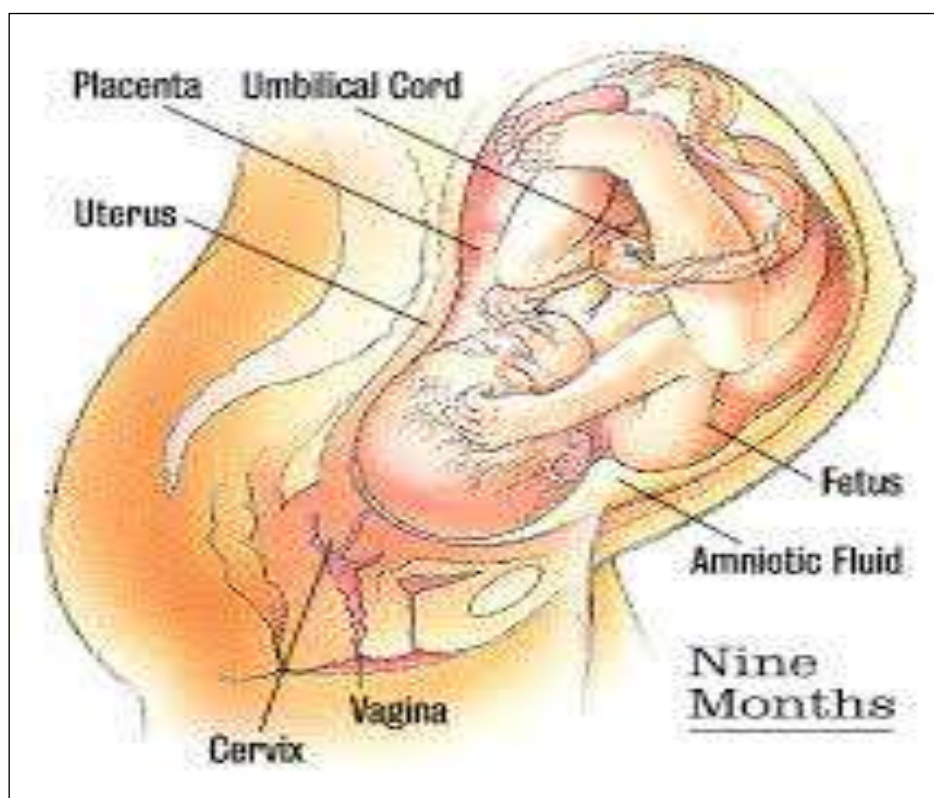
- **Clinical definition and Epidemiology:  
incidence/mortality**
- **Etiology and Pathophysiology**
- **Apgar's score  
significance of clinical use  
reevaluation of the score**
- **Resuscitation**
- **Complication and prognosis**

- Clinical definition and Epidemiology: incidence/mortality
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## Asphyxia neonatorum

**WHO:** Asphyxia is incapacity of newborn to begin or to support of spontaneous respiration after delivery due to breaching of oxygenation during labor and delivery

Asphyxia is incapacity of newborn to begin or to support of spontaneous respiration after delivery due to breaching of oxygenation during labor and delivery

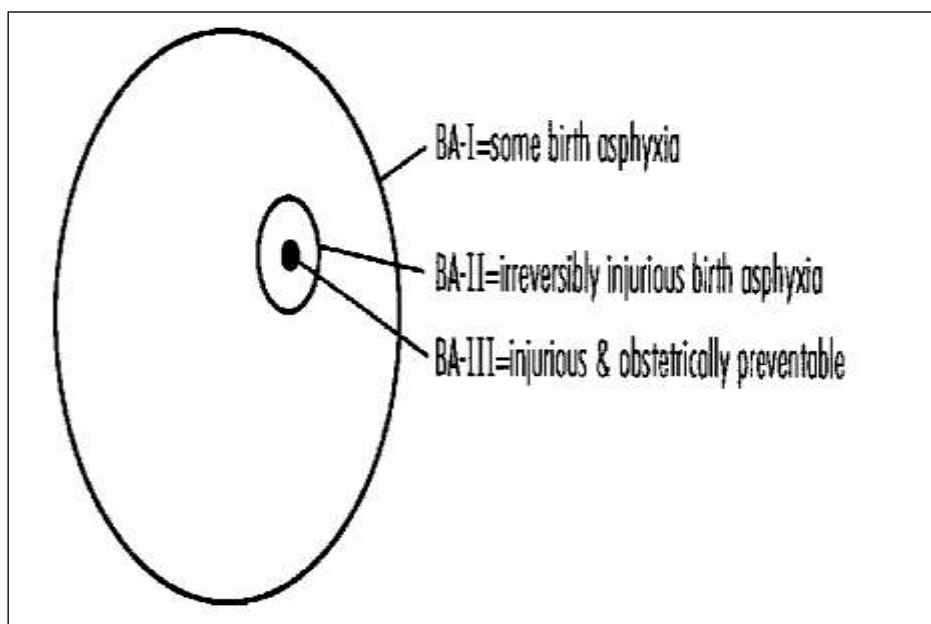


'Perinatal asphyxia' as a condition in the neonate where there is the following combination:

- An event or condition during the perinatal period that is likely to severely reduce oxygen delivery and lead to acidosis,
- A failure of

<http://www.abclawcenters.com/>

function of at least two organs consistent with the effects of acute asphyxia



There are two main types of neonatal asphyxia:

- Acute asphyxia – neonatal asphyxia, which was caused by intranatal factors only.

- Asphyxia, which was

<https://www.nichd.nih.gov/>

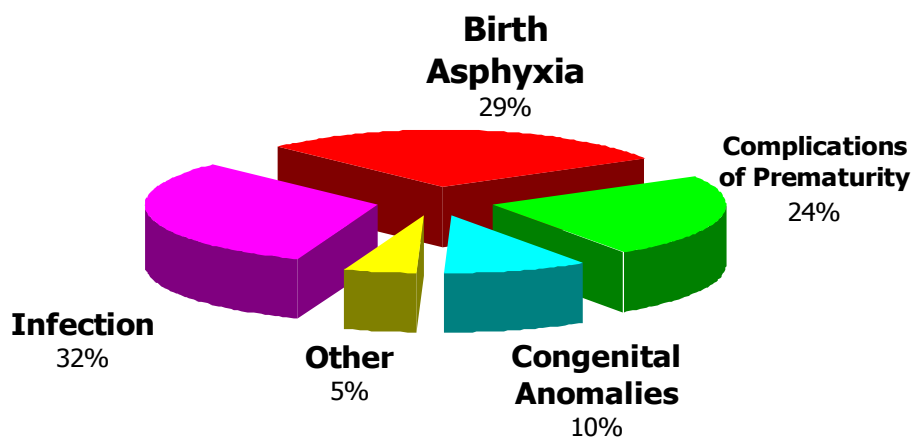
developed on the background of prolonged fetal hypoxia associated with placental insufficiency.



Of the 130 million babies born each year, about 4 million die in the first 4 weeks of life. About 30% of these deaths are due to asphyxia

<http://www.michigancerebralpalsyattorneys.com/>

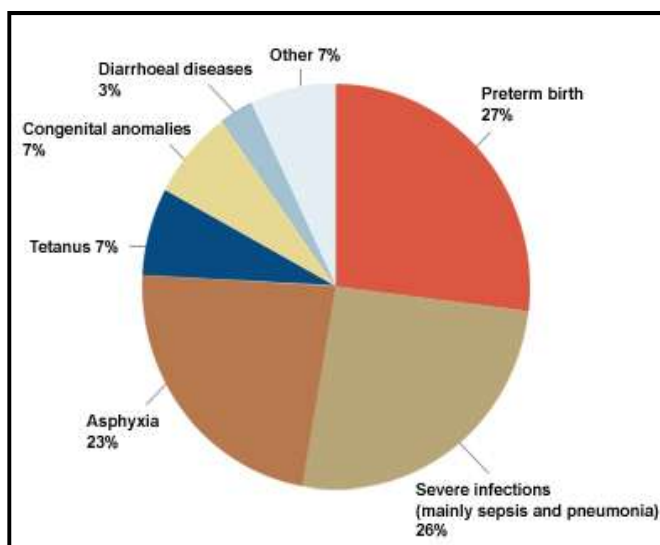
## *Causes of Neonatal Mortality*



Source: WHO 2001 estimates (based on data collected around 1999)

The causes of neonatal death globally also remind us that infection and prematurity, play major roles in addition to asphyxia.

## **Global Causes of Neonatal Death**



UNICEF 2007

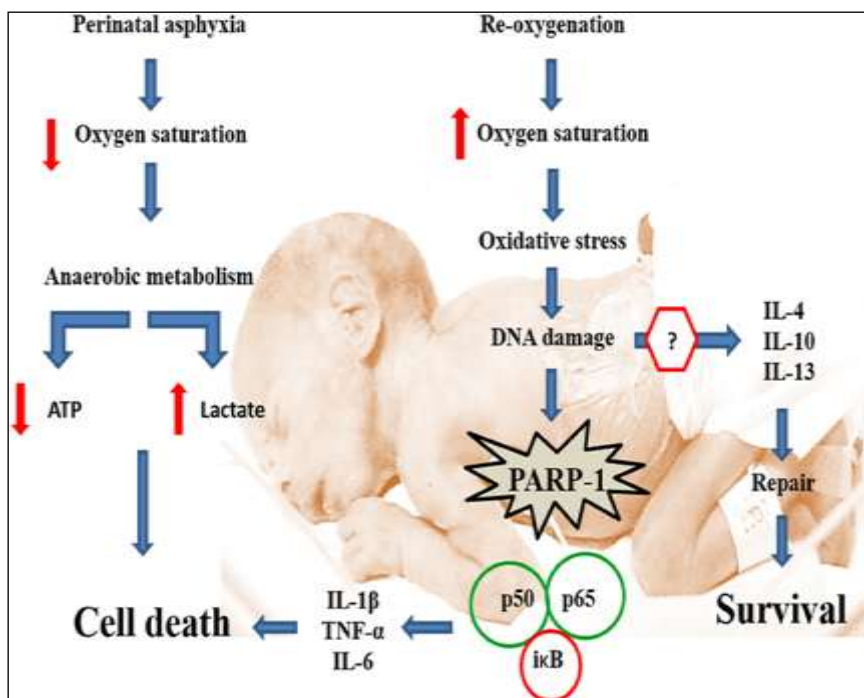
Lee, Wall, Cousens et al. *Int J Epidemiol* (in press)

Any intervention must address not only asphyxia, but also cleanliness and hygiene as well as warmth and early nutrition for small babies.

A forthcoming meta-analysis of in-facility resuscitation training concluded that death from

asphyxia, or intrapartum-related events, could be reduced by 30% in term infants and preterm mortality reduced by 5-10% through neonatal resuscitation.





Acute complications associated with Asphyxia

- hypotension
- hypoxic encephalopathy
- seizures
- persistent pulmonary hypertension
- hypoxic cardiomyopathy

<http://dx.doi.org/10.3389/fnins.2014.00047>

- ileum and necrotizing enterocolitis
  - acute tubular necrosis
- adrenal hemorrhage and necrosis
  - hypoglycemia
  - polycythemia
- disseminated intravascular coagulation

### **Critical transition from fetal to extra-uterine life**

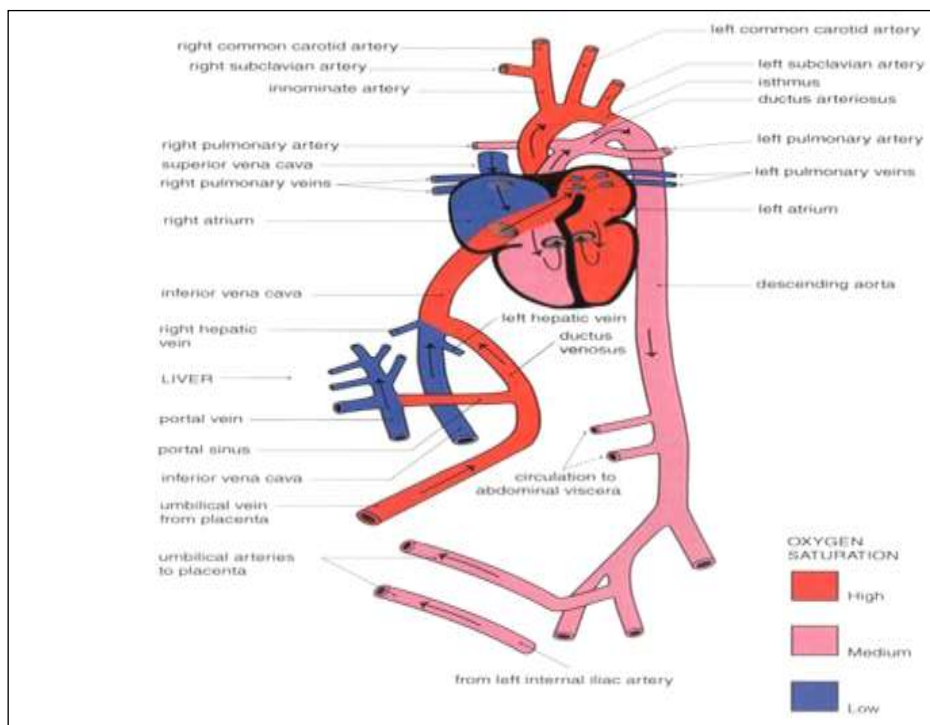
- Birth is a stressful process
- Changes in circulatory system closure of R-> L shunt, Ductus venosus, PFO, PDA
- Onset of breathing in AIR and adaptation of respiratory system
- Any cause of maladaptation may lead to persistent fetal circulation and hypoxaemia
- Adaptative capacity is lower in preterm infants

The transition from a fetus to a newborn is the most complex adaptation that occurs in human experience.

## Newborn lungs are different

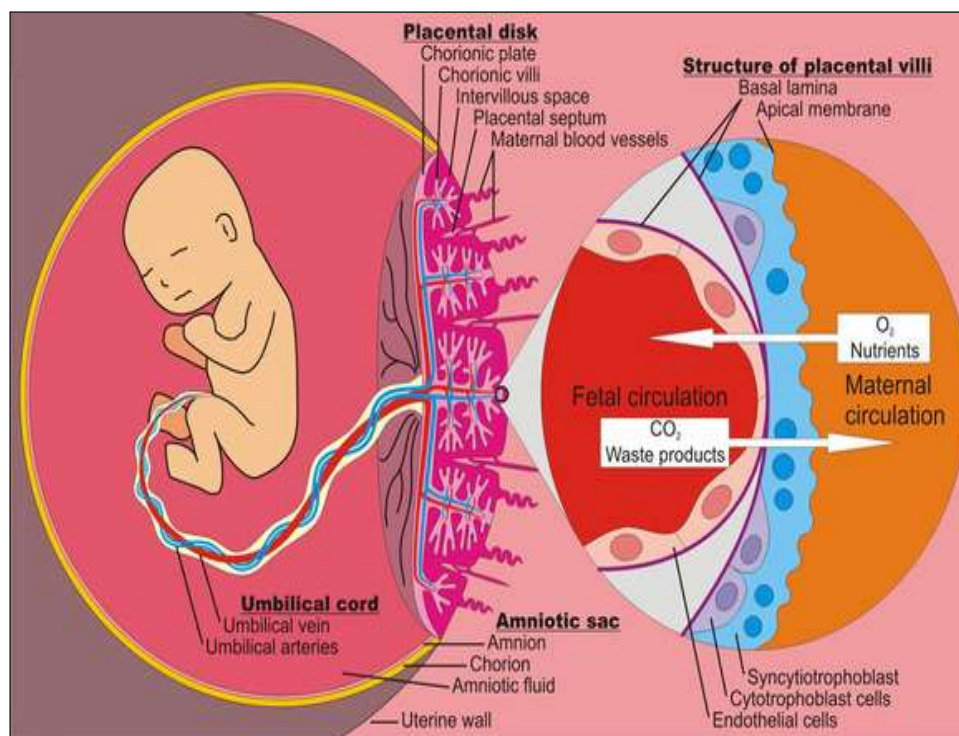
- Fluid filled at birth (35 mL/kg)
- Large proportion may be unaerated at birth
- Transition of high pulmonary pressure
- Limited absorptive surface
- Existence of R to L shunts

Lung adaptation requires the coordinated clearance of fetal lung fluid, surfactant secretion, and the onset of consistent breathing.



With the removal of the low-pressure placenta, the cardiovascular response requires striking changes in blood flow, pressures and pulmonary vasodilation.

<http://www.slideshare.net/bhagirathsn/physiology-of-transition-period-with-regard-to-cardio>



Risk factors of fetal hypoxia development are:

1. Maternal age of less than 16 years old or over 40 years old.

<http://www.abclawcenters.com/practice-areas/diagnostic-tests/hypoxic-ischemic-encephalopathy-and-umbilical-cord-blood-gases/>

Maternal age of less than 16 years old or over 40 years old.

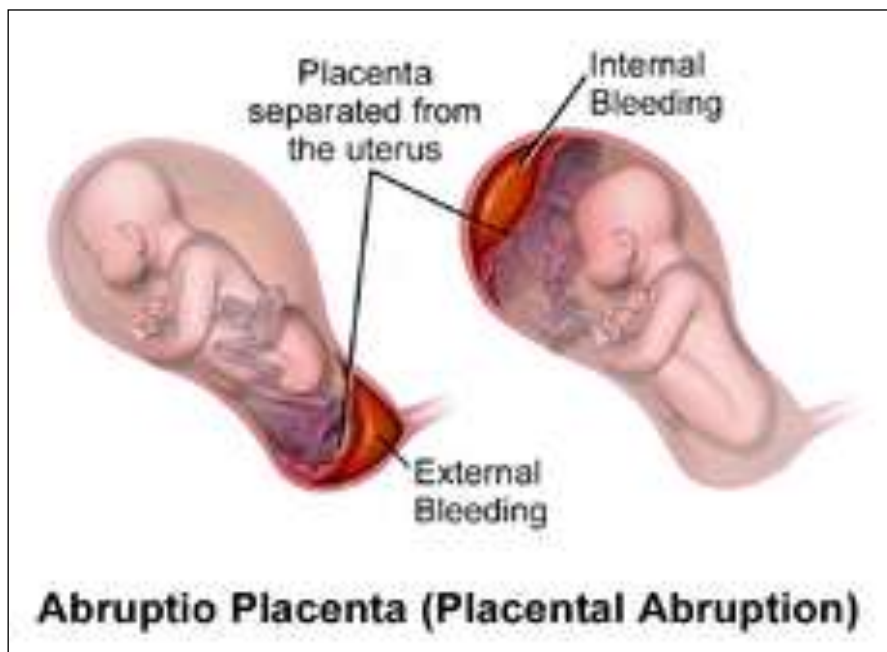
2. Postmaturity.
3. Prolonged (>4 weeks) gestosis of pregnancy.
4. Multiple pregnancy.
5. Threatened preterm labor.
6. Diabetes mellitus in pregnant women.
8. Severe somatic diseases in pregnant women.
9. Smoking or drug addiction in pregnant women.
10. Intrauterine growth restriction or another diseases revealed in fetus in ultrasound examination.



[https://en.wikipedia.org/wiki/Caesarean\\_section](https://en.wikipedia.org/wiki/Caesarean_section)

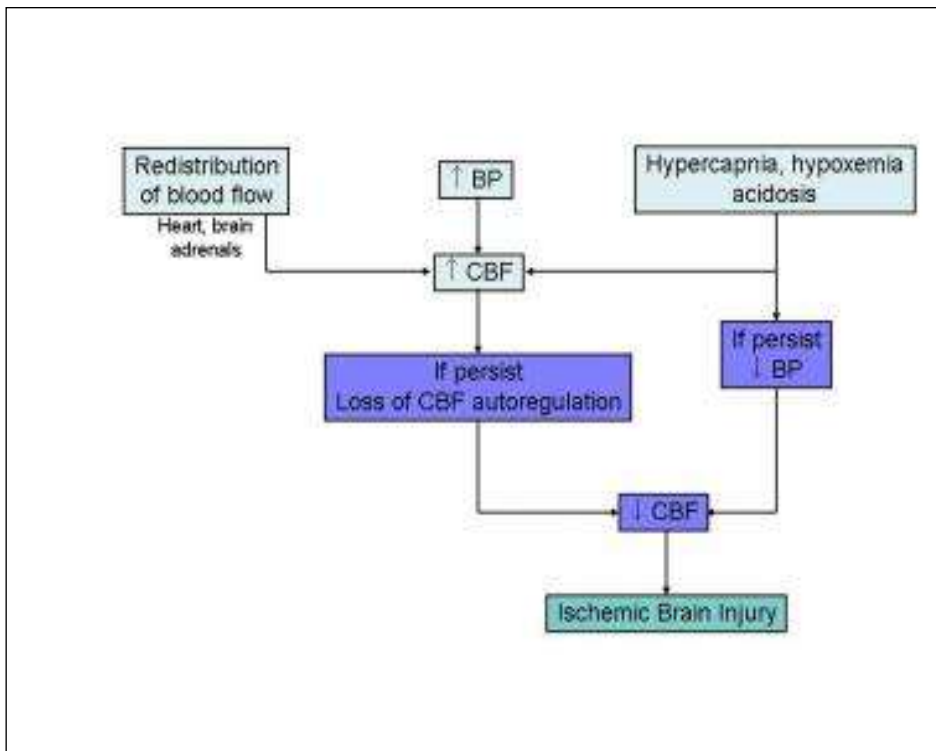
The high risk factors of acute (intranatal) asphyxia development

1. Cesarean operation (planned or urgent).
2. Malpresentation
3. Premature or retarded birth.
4. Waterless period > 24 or < 6 hours, accelerated labor - < 4 hours in primipara or < 2 hours in secundipara.



[https://en.wikipedia.org/wiki/Placental\\_abruption](https://en.wikipedia.org/wiki/Placental_abruption)

5. Placental abruption
7. Birth trauma.
8. Congenital malformations of fetus.
9. Acute labor hypoxia in mother.
10. Maternal anesthesia.



There are 5 basic pathogenetic mechanisms which lead to the development of the acute asphyxia neonatorum:

1) Blood flow interruption through the umbilical cord

<http://emedicine.medscape.com/article/973501-overview>



2) Disturbances of gaseous exchange through the placenta

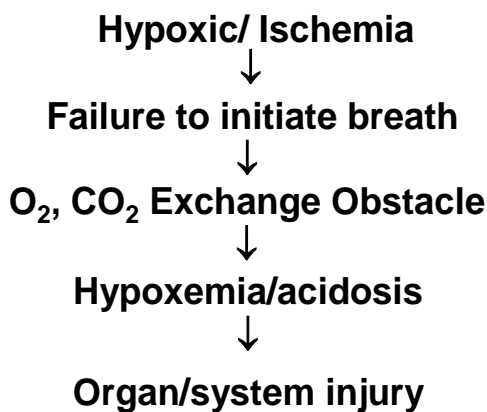
3) Unequal blood supply of the maternal part of placenta

4) Worsening of blood oxygenation in mother

5) Failure of respiratory efforts of the newborn

<http://www.nhs.uk/Conditions/cyanosis/Pages/Introduction.aspx>

## Pathophysiology



Let's talk about the pathogenesis of asphyxia. On the slide you can see the main links of it.

<http://www.slideshare.net/taialakawy/perinatal-asphyxia-44600846>

## Effects of Asphyxia

- Central nervous system
  - infarction, intracranial hemorrhage, cerebral edema, seizure, hypoxic-ischemic encephalopathy
- Cardiovascular
  - bradycardia, ventricular hypertrophy, arrhythmia, hypotension, myocardial ischemia

On the next slide you can see the main effects of asphyxia. It's a damage of the central nervous system, cardiovascular problems...

<http://www.slideshare.net/taialakawy/perinatal-asphyxia-44600846>

## Effects of Asphyxia

- Respiratory system
  - apnea, respiratory distress syndrome
  - cyanosis
- KUB
  - acute tubular necrosis, bladder paralysis
- Gastrointestinal tract
  - necrotizing enterocolitis , stress ulcer

Damage of:

- Respiratory system
- kidneys
- Gastrointestinal tract

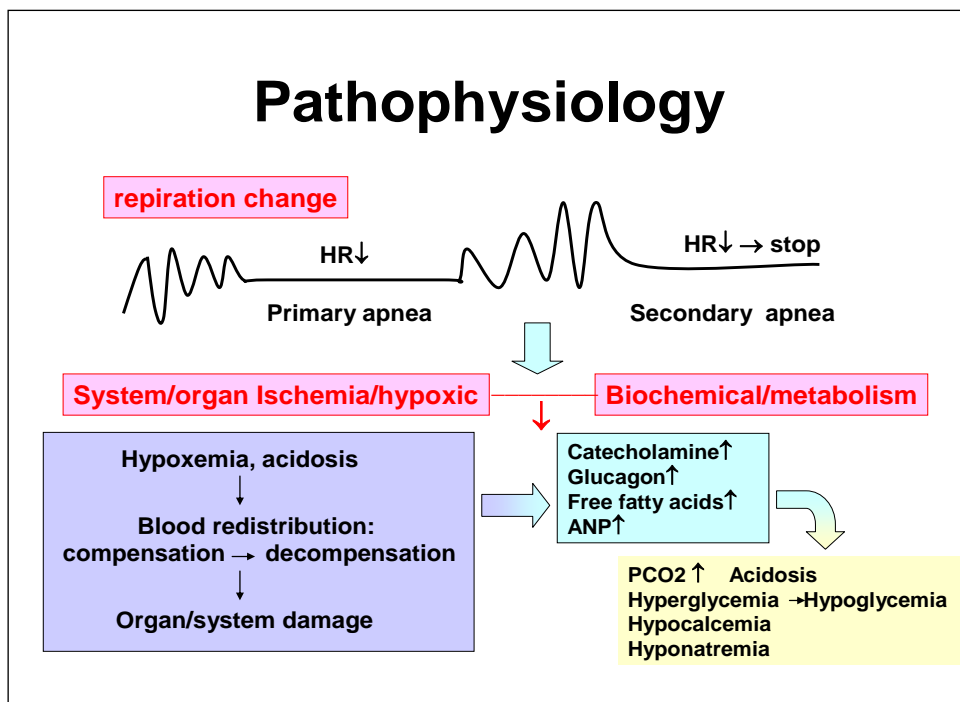
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## Effects of Asphyxia

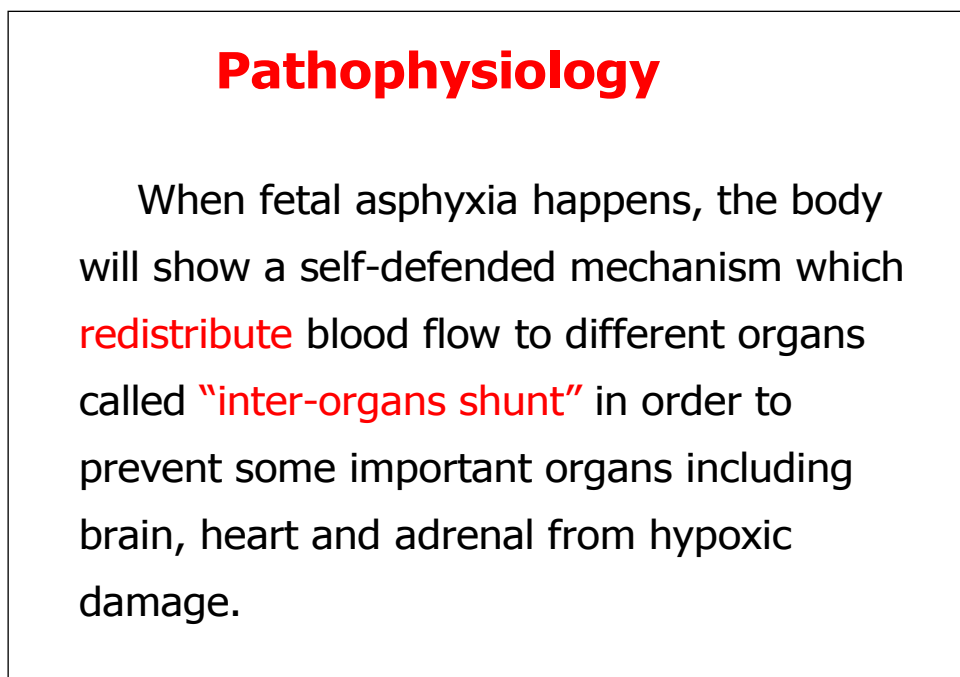
- Hematology
  - Disseminated intravascular coagulation
- Metabolic
  - hypoglycemia, hyperglycemia, hypocalcemia, hyponatremia
- Integument
  - subcutaneous fat necrosis

- Hematology
- Metabolic
  - Integument problems

<http://www.slideshare.net/taialakawy/perinatal-asphyxia-44600846>



<http://www.slideshare.net/taialakawy/perinatal-asphyxia-44600846>

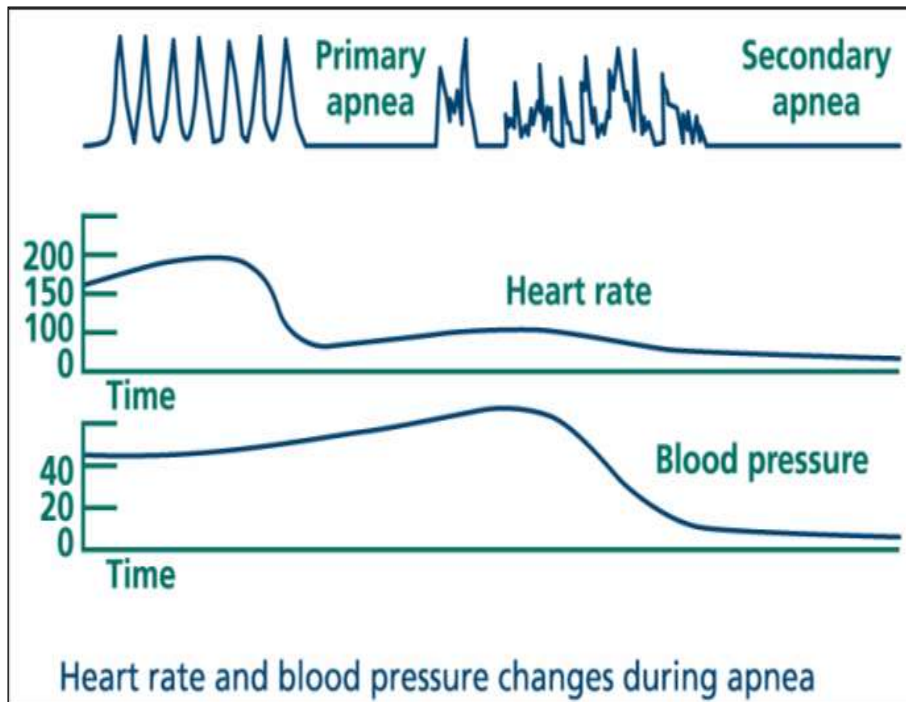


When fetal asphyxia happens, the body will show a self-defended mechanism which redistribute blood flow to different organs called “inter-organs shunt” in

[http://www.slid](http://www.slideshare.net/taialakawy/perinatal-asphyxia-44600846)

order to prevent some important organs including brain, heart and adrenal from hypoxic damage.



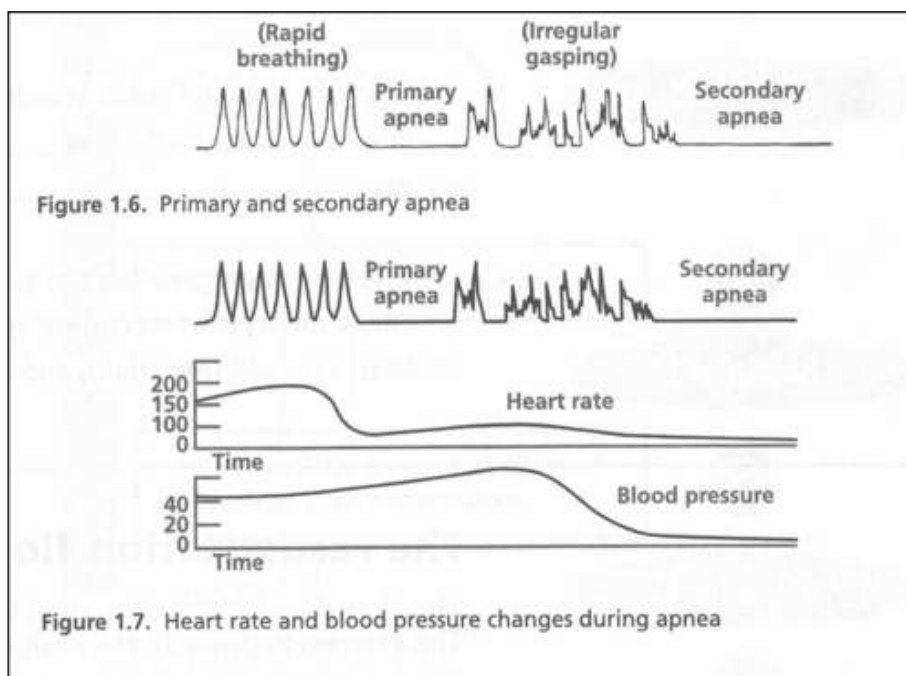


So, what happens at the beginning. Hypoxia may decrease the production of ATP, and result in the cellular functions. But these change can be reversible if hypoxia is reversed in short time.

If hypoxia exist in long time enough,

<http://www.fac.org.ar/scvc/lave/epi/niermeyer/niermei.htm>

the cellular damage will become unreversible that means even if hypoxia disappear but the cellular damages are not recovers. In other words, the complications will happen.



When a newborn first becomes deprived of oxygen, an initial period of attempted rapid breathing is followed by **primary apnea** and dropping heart rate that will improve with tactile stimulation. If oxygen deprivation

continues, secondary

<http://www.fac.org.ar/scvc/lave/epi/niermeyer/niermei.htm>

apnea ensues, accompanied by a continued fall in heart rate and blood pressure. **Secondary apnea** cannot be reversed with stimulation; assisted ventilation must be provided.

## Management at birth

1. Wipe dry
2. Keep warm
3. Position
4. Oral/nasal suction
5. Examine for gross congenital anomaly
6. If HR > 80/min, observe



Main links of management at birth are:

1. Wipe dry
2. Keep warm
3. Position
4. Oral/nasal suction
5. Examine for gross congenital anomaly
6. If HR > 80/min, observe

<http://www.fac.org.ar/scvc/llave/epi/niermeyer/niermei.htm>

## Neonatal Evaluation

### *APGAR Scoring*

- A** Appearance
- P** Pulse
- G** Grimace
- A** Activity
- R** Respirations



Virginia Apgar

Virginia Apgar invented the Apgar score in 1952 as a method to quickly summarize the health of newborn children. The five criteria are summarized using words chosen to form a backronym (Appearance, Pulse, Grimace, Activity, Respiration).

## Apgar Scoring System

SCORE	0	1	2
Heart rate	Absent	<100/min	> 100/min
Respirations	Absent	Slow, irregular	Good, crying
Muscle tone	Limp	Some motion	Active motion
Reflex irritability	No response	Grimace	Cough, sneeze, cry
Color	Blue, pale	Body pink, blue limbs	Completely pink

The Apgar scale is determined by evaluating the newborn baby on five simple criteria on a scale from zero to two, then summing up the five values thus obtained. The resulting Apgar score ranges from zero to 10.

<http://pediatrics.aappublications.org/content/117/4/1444>

## Apgar Score



Total Score = 10

score 7-10

normal

score 5-6

mild birth asphyxia

score 3-4

moderate birth asphyxia

score 0-2

severe birth asphyxia

A low score on the one-minute test may show that the neonate requires medical attention[3] but does not necessarily indicate a long-term problem, particularly if the score improves at the five-minute test. An Apgar score that remains below 3 at later times—such as 10, 15, or 30 minutes—may

<http://pediatrics.aappublications.org/content/117/4/1444>

indicate longer-term neurological damage, including a small but significant increase in the risk of cerebral palsy. However, the Apgar test's purpose is to determine quickly whether a newborn needs immediate medical care. It is not designed to predict long term health issues.

Apgar Score				Gestational age _____ weeks				
Sign	0	1	2	1 minute	5 minute	10 minute	15 minute	20 minute
Color	Blue or Pale	Acrocyanotic	Completely Pink					
Heart rate	Absent	<100 minute	>100 minute					
Reflex irritability	No Response	Grimace	Cry or Active Withdrawal					
Muscle tone	Limp	Some Flexion	Active Motion					
Respiration	Absent	Weak Cry; Hypoventilation	Good, Crying					
Total								
Comments:	Resuscitation							
	Minutes	1	5	10	15	20		
	Oxygen							
	PPV/NCPAP							
	ETT							
	Chest Compressions							
	Epinephrine							

If Apgar score is 0-3 at the first minute – neonatal mortality is 5,6%. Nelson and Ellenberg examined Apgar

<http://www.fac.org.ar/scvc/lave/epi/niermeyer/niermei.htm>

scores in 49000 infants. Of infants with an Apgar score 0-3 at 20 minutes, 59% of survivors died before 1 year, and 57% of the survivors had cerebral palsy. If Apgar score is 0-3 at the first minute and becomes 4 and more in the 5-th minute – possibility of cerebral palsy is 1%.

## Reevaluation of Apgar Score

**Apgar Score reflects:**

- Accuracy of Predict the death
- The severity of perinatal hypoxic
- The process and severity of intrauterine fetal hypoxic

**Facts:**

- The subjectivity of the scoring and experience based
- Low scoring always for prematures

*American Academy of Pediatrics, American College of Obstetricians and Gynecologists. Pediatrics 1996,98:141-2*

The test is generally done at one and five minutes after birth, and may be repeated later if the score is and remains low.

## Reevaluation of Apgar Score

### Inconsistent of the Apgar score with brain damage

- If lower score at 5 min., >4 at 10 min.
- Brain Damage only 1% in children at 7 years old
- In brain damaged children 75% were normal for Apgar score.

*American Academy of Pediatrics, American College of Obstetricians and Gynecologists. Pediatrics 1996,98:141-2*

On another hand,  
in brain  
damaged  
children 75%  
were normal for  
Apgar score.

## ABC resuscitation

- **A** - Airways (maintenance of passability of airway)
- **B** - breathing (stimulation of breathing)
- **C** - circulation (to support of circulation)
- **D** - drug

So, what does  
mean ABC  
resuscitation.


## The golden minute

- <30 seconds: complete initial steps
  - Warmth
  - Drying
  - Clear airway if necessary
  - Stimulate
- 30-60 seconds: assess 2 vital characteristics
  - Respiration (apnea/gasping/labored/unlabored)
  - Heart rate (<100/>100bpm)

During the golden minute we can achieve maximum benefit in resuscitation. We should complete initial steps during the 30 seconds. And during the other 30 seconds we should assess respiration and heart rate.

[http://www.wjpcch.com/article.asp?article\\_id=214](http://www.wjpcch.com/article.asp?article_id=214)

## <60 seconds of birth

- If gasping/apnea  
If heart rate <100 beats per minute
- 
- PPV( positive pressure ventilation)  
Spo2 monitoring by pulse oximeter
- Simultaneous evaluation of 3 vitals
    - Heart Rate,
    - Respiration,
    - oxygenation status

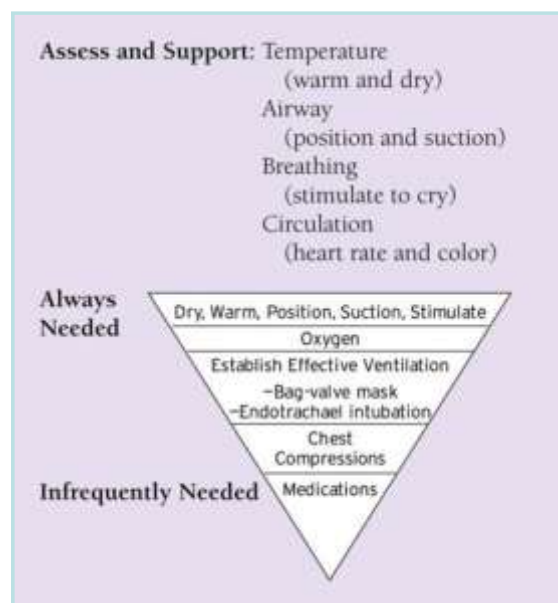
If the patient have gasping/apnea or heart rate <100 beats per minute, we should provide ventilation with positive pressure.

[http://www.wjpcch.com/article.asp?article\\_id=214](http://www.wjpcch.com/article.asp?article_id=214)

**Increase in heart rate is the most sensitive indicator of a successful response to each step practiced**

Increase in heart rate is the most sensitive indicator of a successful response to each step practiced

## Neonatal Resuscitation



Administer blow-by oxygen if the newborn displays:

- Cyanosis of the skin
- Spontaneous and adequate breathing
- Heart rate above 100 beats per minute
- Ventilation with the Bag Mask
- Provide ventilations with the bag mask at a

[http://www.wjpch.com/article.asp?article\\_id=214](http://www.wjpch.com/article.asp?article_id=214)

rate of 30 to 60 breaths per minute if:

The newborn's breathing is slow or otherwise inadequate.

- The newborn's heart rate is less than 100 beats per minute.
- The newborn's trunk remains cyanotic despite the administration of blow-by oxygen.
- Reassess the infant's color, respiratory effort, and heart rate after 30 seconds of ventilation.

Cardiopulmonary Resuscitation (CPR)

Provide CPR if:

- The newborn's heart rate is less than 60 beats per minute.
- Reassess the infant's color, respiratory effort, and heart rate after 30 seconds of CPR and treat according to findings.

Advanced Providers: See protocols for medications/dosages

## Keep me warm.....

- **What determines body temperature?**
  - Heat production vs Heat loss
- **How do neonate loose Heat?**
  - Radiation
  - Convection
  - Evaporation
  - Conduction
- **Who looses too much heat / does not produce enough heat?**
  - Preterm
  - IUGR
  - Wet babies
  - Cold atmosphere
  - Infection / hypoxia
- **Consequences ?**
- **Thermoneutral environment**



Temperature control

Drying the infant with prewarmed towels will help minimise heat loss in addition to use of a radiant warmer.

Infants less than 28 weeks gestation should be placed immediately after birth in a polyethylene bag or wrap

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/item/203](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/item/203)

(appropriate size, food grade, heat resistant) with their head out and the body completely covered.

Drying the infant's body prior to covering is not recommended. Aim for normothermia (36,5 to 37,5 C) in all

newborn infants and avoid iatrogenic hyperthermia.

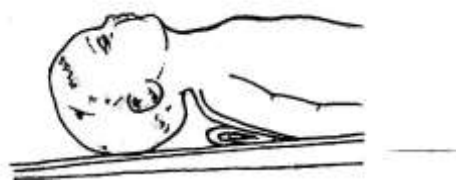
Airway

The head should be in a neutral or slightly extended 'sniffing' position.

Suction is rarely required and should not exceed -100 mmHg. It should be limited in depth to

## ABC resuscitation

- **Step A** - immediately after delivery the infant's head should be placed in a neutral or slightly extended position
- Rolled towel under the shoulders



5 cm below the lips.

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/item/203](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/item/203)



And airway established by clearing the mouth, then the nose by rubber bag



And airway established by clearing the mouth, then the nose by rubber bag

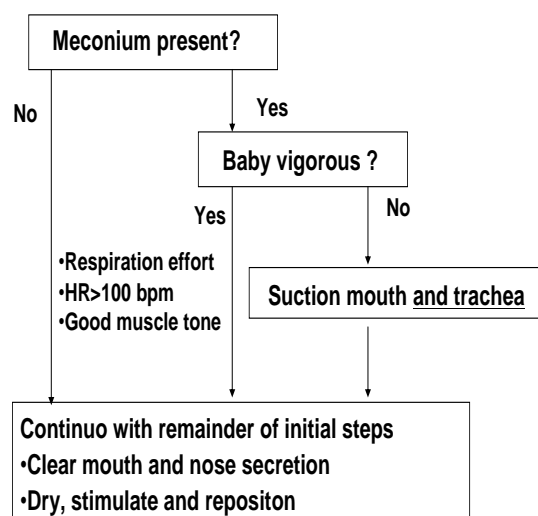
[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/item/203](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/item/203)

## Meconium-stained fluid



<http://pregnantpills.com/>

## Suction when Meconium present



<http://emedicine.medscape.com/>

## Suctioning Meconium



<http://pregnantpills.com/>

oxygenation can be harmful to the newborn during and after resuscitation.

Regardless of gestation, aim for oxygen saturations of 91-95%.

Wean supplemental oxygen once the saturations reach 90%.

## Stimulation

Drying with a soft towel will stimulate most newborns to breathe. If meconium is present in a non-vigorous infant, immediate suction below the vocal cords under direct vision may be appropriate. Delay tactile stimulation to avoid gasping in the infant with an oropharynx full of particulate meconium. Repeated suctioning of the trachea is not recommended and may unnecessarily delay commencement of active resuscitation.

## Guidelines for breathing include:

Attend to adequate inflation and ventilation before oxygenation

The rate for assisted ventilation is 60 inflations per minute.

Positive pressure ventilation should be commenced in air (21% oxygen) initially.

Supplemental oxygen administration should be guided by pulse oximetry.

Hyperoxia should be avoided as even brief exposure to excessive

## Targeted SPO<sub>2</sub> after birth

1 minute	60-65%
2 minutes	65-70%
3 minutes	70-75%
4 minutes	75-80%
5 minutes	80-85%
10 minutes	85-90%

If a longer inspiratory time is used, it may be possible to deliver the tidal volume at low pressure to minimize gastric inflation.

Cricoid pressure can compress the esophagus and reduce gastric inflation:

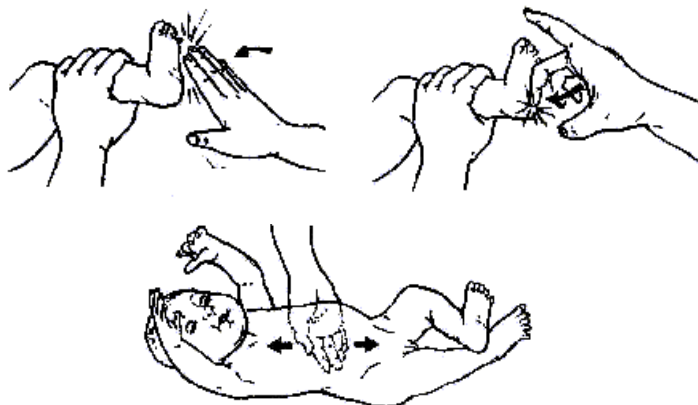
Cricoid pressure should be used only if the victim is unconscious with no cough

<http://emedicine.medscape.com/>

or gag reflex and an extra rescuer is available.

Avoid excessive pressure that will compress the trachea and occlude the airway.

If it is inadequate we must use **step B**.  
At first the tactile stimulation should be given to newborn, for example- gentle flicking of the feet or heel



Effective ventilation is confirmed by observing these three signs:

- Increase in the heart rate to about 100/min.
- A slight rise in the chest and upper abdomen with each positive pressure inflation.

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/item/203](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/item/203)

If these measures are inadequate, mechanical ventilation should be initiated, using mask and bag ventilation

## Bag & mask ventilation



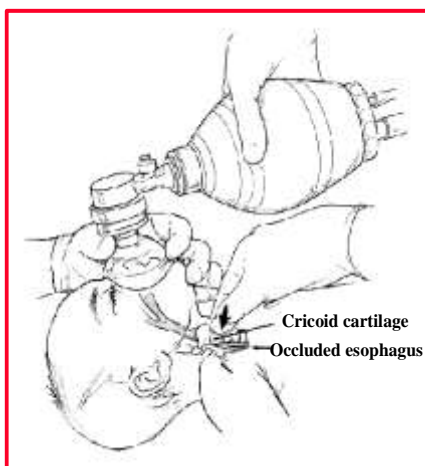
<http://pregnantpills.com/>

Few infants require immediate intubation. The majority of infants can be managed with positive pressure ventilation via a face mask. With improvement in the infant's condition, the inflation pressures and breath

rate can be progressively reduced.

## Effective Bag-Mask Ventilation

- Use only the amount of force and tidal volume needed to make the chest rise
- Avoid excessive volume or pressure
- Increased inspiratory time may reduce gastric inflation
- Cricoid pressure may reduce gastric inflation



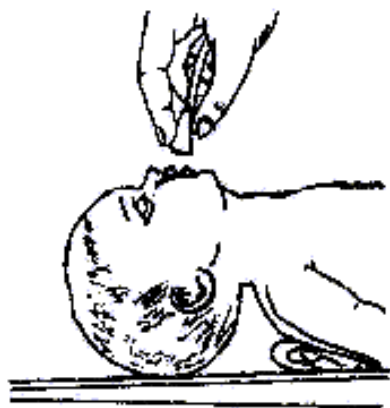
Bag-mask ventilation is now a required part of the BLS for Healthcare Providers Course and must be mastered by all healthcare providers.

Gastric inflation may develop during rescue breathing and is more likely to develop if excessive

[http://www.glowm.com/section\\_view/](http://www.glowm.com/section_view/)

force or volume is used. The rescuer should use only the amount of force and tidal volume necessary to cause the chest to rise.

If ventilation is adequate supplemental oxygen may be given to improve heart rate or skin colour

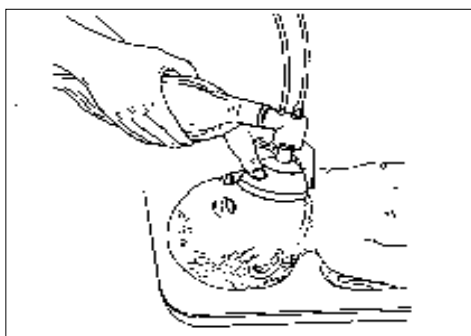


Use a bag with a minimum volume of 450 to 500 mL and be sure the chest rises.

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/item/203](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/item/203)

## Resuscitation technology

- O<sub>2</sub> supply via PPV bag



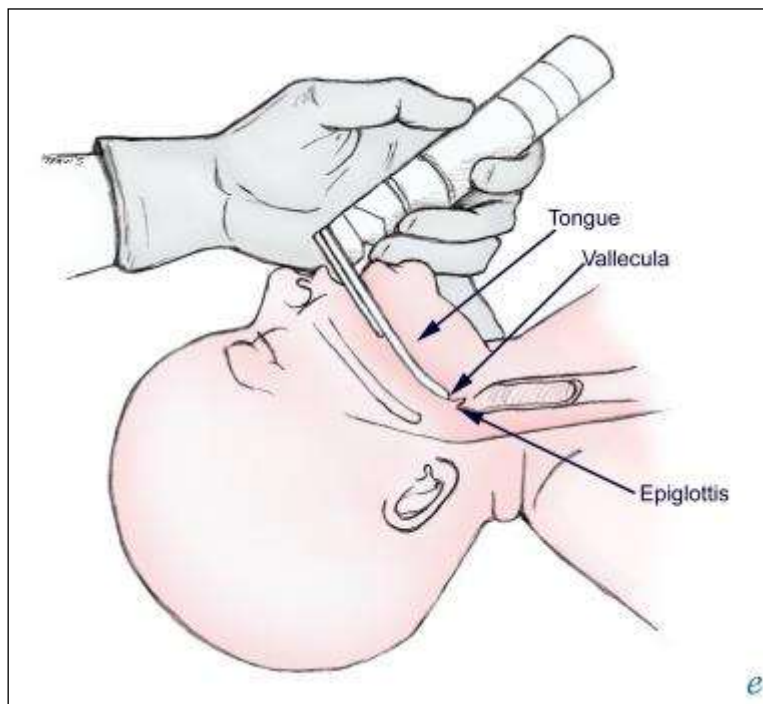
Effective ventilation is confirmed by observing these three signs:

- Increase in the heart rate to about 100/min.
- A slight

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/)

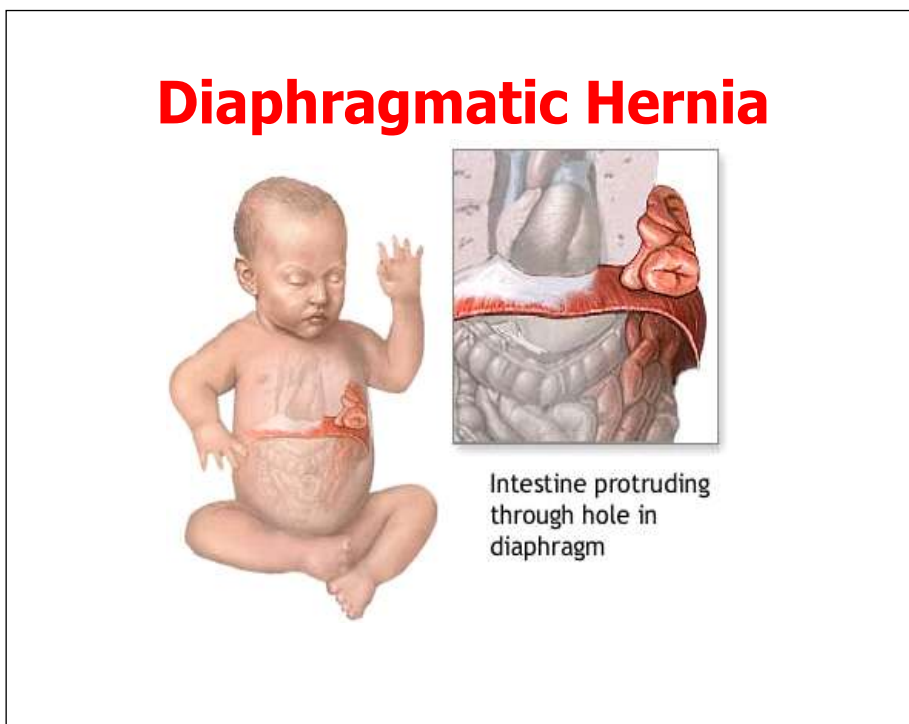
rise in the chest and upper abdomen with each positive pressure inflation.

- Oxygenation improves.



Few infants require immediate intubation. The majority of infants can be managed with positive pressure ventilation via a face mask. With improvement in the infant's condition, the inflation pressures and breath rate can be progressively reduced.

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/)



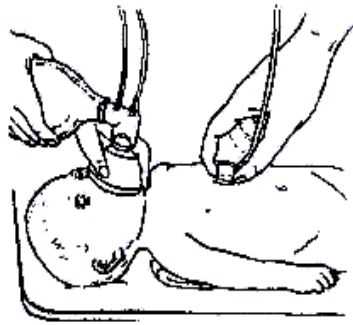
Protrusion of a part of the stomach through an opening in the diaphragm

- Risk factors  
Bag and mask ventilation can worsen condition

- Pathophysiology  
Abdominal contents are displaced into the thorax

Fanaroff and Martin's perinatal medicine: diseases of the fetus and infant. 18 edition. – Philadelphia: Elsevier Mosby, 2006. – Chapter 42.

If mechanical ventilation does not improve the respiration, heart rate or colour skin, the following step is "C"-circulation. At first the assessment of heart rate is necessary



– Heart may be displaced

– Respiratory compromise

If mechanical ventilation does not improve the respiration, heart rate or colour skin, the following step is "C"-circulation. At first the assessment of heart rate is necessary

Circulation

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/)

## Chest compressions

- Started when HR < 60 per minute despite adequate ventilation with 100% oxygen for 30 sec
- Delivered at lower third of sternum, to depth 1/3 of AP diameter of chest
- 2 techniques:
  - 2 thumb-encircling hands technique
  - Compression with 2 fingers, second hand supporting the back
  - 3:1 ratio:: [ 90 comp:30 ventilations]

In the majority of infants establishment of adequate ventilation will restore circulation.

Begin chest compressions for;

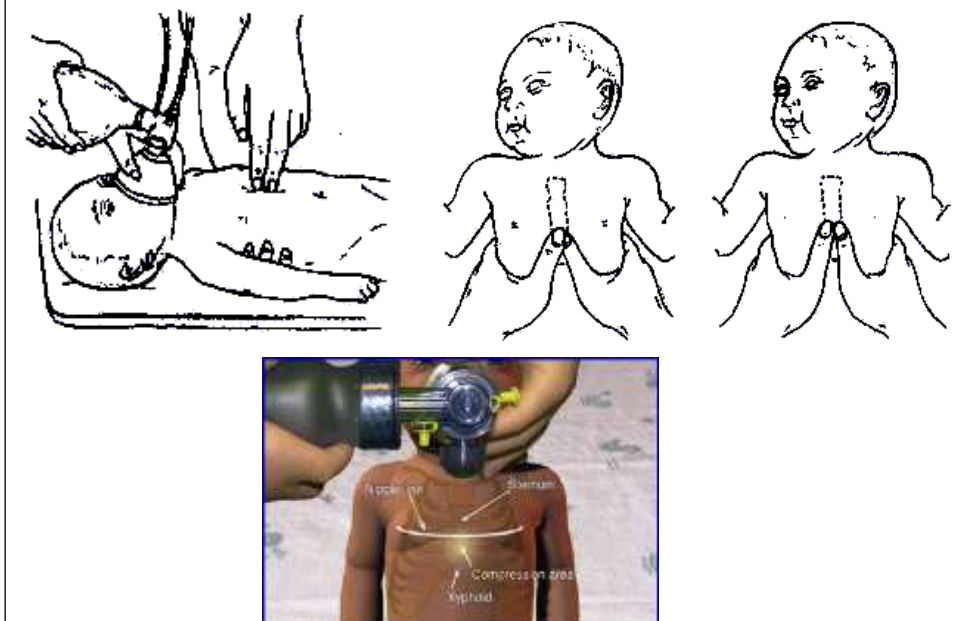
HR < 60 despite effective positive pressure ventilation for at least 30 seconds.

Aim for approximately a ratio

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/)

of 90 chest compressions to 30 breaths per minute (3:1). (120 events per minute) count one-and-two-and-three-and-breath etc.

## Chest compressions with two fingers



Supplemental oxygen should be increased to 100% when compressions are commenced and titrated with guidance of pulse oximetry.

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/)

The «two thumb» technique is preferred. Both thumbs meet over the sternum with fingers around the chest wall. The sternum should be compressed to one third of the antero-posterior chest dimension.

If heart rate is less than 80 beats per minute the cardiac compression should be continued. If heart rate is 80 beats per minute or more the cardiac compression should be stop .



If heart rate is less than 80 beats per minute the cardiac compression should be continued. If heart rate is 80 beats per minute or more the cardiac compression should be stop .

[http://www.glowm.com/section\\_view/heading/Neonatal%20Resuscitation/](http://www.glowm.com/section_view/heading/Neonatal%20Resuscitation/)





Drugs are rarely indicated in resuscitation of the newly born infant. Bradycardia in the newborn infant is usually the result of inadequate lung inflation or profound hypoxemia, and establishing adequate ventilation is the most important step toward

correcting it.

<http://pregnantpills.com/>

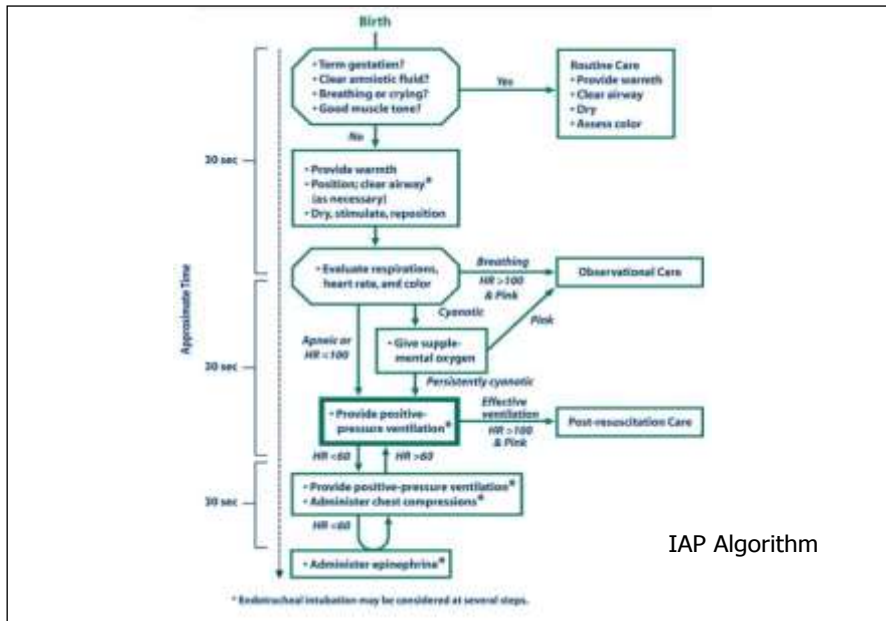
## Epinephrine for Bradycardia

- **Intravenous administration of epinephrine 0,01 – 0,03 mg/kg/dose is the preferred route (Class IIa).**
- **While access is being obtained, administration of a higher dose (up to 0,1 mg/kg) through the endotracheal tube may be considered.**

However, if the heart rate remains  $<60$  per minute despite adequate ventilation (usually with endotracheal intubation) with 100% oxygen and chest compressions, administration of epinephrine or volume expansion, or both, may be indicated. Rarely, buffers, a narcotic antagonist, or

<http://emedicine.medscape.com/article/973501-overview>

vasopressors may be useful after resuscitation, but these are not recommended in the delivery room.



On the figure you can see Newborn Resuscitation Algorithm.

<http://emedicine.medscape.com/article/973501-overview>



Babies who require resuscitation are at risk for deterioration after their vital signs have returned to normal. Once adequate ventilation and circulation have been established, the

Fanaroff and Martin's perinatal medicine: diseases of the fetus and infant. 18 edition. – Philadelphia: Elsevier Mosby, 2006. – Chapter 42.

infant should be maintained in, or transferred to an environment where close monitoring and anticipatory care can be provided.

Indications of poor outcome or CNS damage:

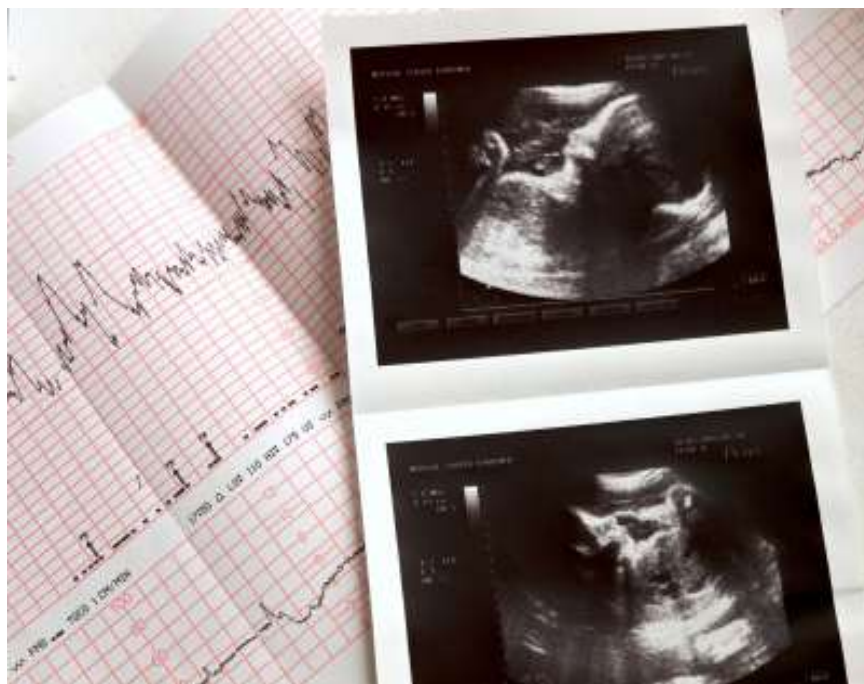
### Indications of poor outcome or CNS damage

- **Umbilical artery showed severe acidosis (PH <7.00)**
- **Apgar score 0-3 persists over 5 min.**
- **Manifesting signs of acute CNS damage (convulsion)**
- **multiple-organ dysfunction syndrome >3**

*American Academy of Pediatrics, American College of Obstetricians and Gynecologists. Pediatrics 1996,98:141-2*

- severe acidosis (PH <7.00)
- Apgar score 0-3 persists over 5 min.
- Convulsion
  - multiple-organ dysfunction

syndrome >3

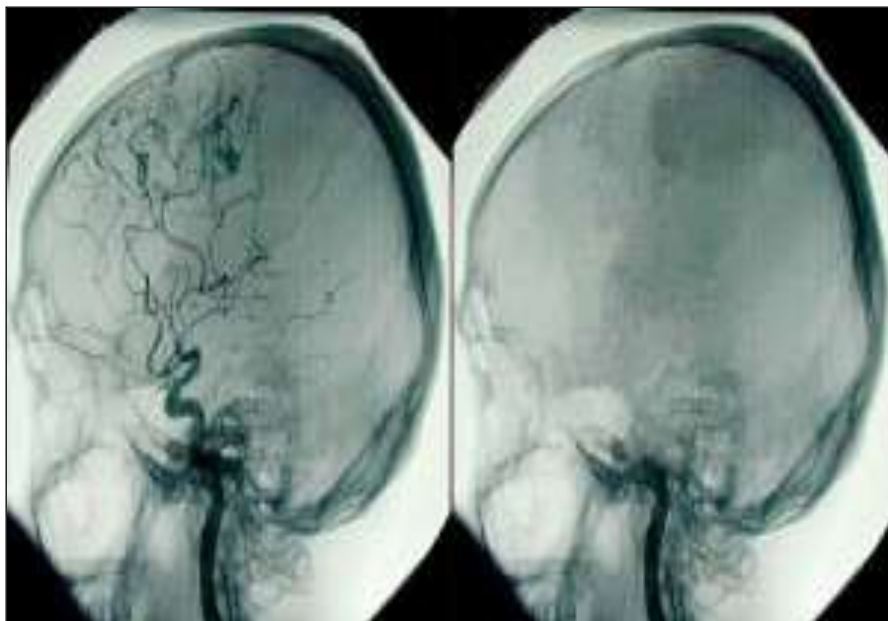


How we can prevent Asphyxia:

- **Antenatal care**
- **To avoid premature delivering and obstetric procedure (forceps)**
- **Monitoring high risk pregnant**
- **Pre and post born**

<http://pregnantpills.com/>

preparations and adequate care



And the next slide shows signs of brain death.

The clinical diagnosis of brain death is made on the basis of

- coma manifested by lack of response to pain, light, or auditory stimulation;

Fanaroff and Martin's perinatal medicine: diseases of the fetus and infant. 18 edition. – Philadelphia: Elsevier Mosby, 2006. – Chapter 42.

- - apnea confirmed by documentation of failure to breathe when  $p\text{CO}_2$  is greater than 60 mm Hg tested by 3 minutes;
- - absent bulbar movements and brainstem reflexes (including midposition or fully dilated pupils with no response to light or pain and with absent oculocephalic, caloric, corneal, gag, cough, rooting and sucking reflexes, flaccid tone and absence of spontaneous or induced movements (excluding activity mediated at the spinal cord level))

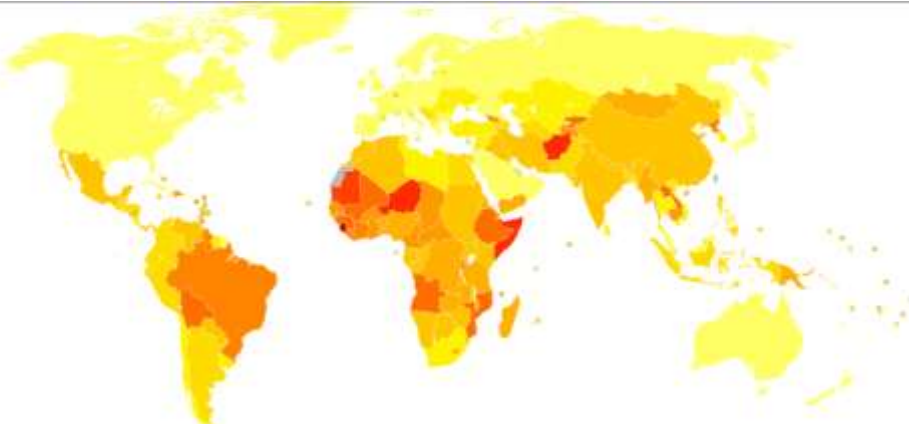


**The most important is to get air into the lungs**

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# Birth Trauma

The term "**Birth trauma**" is used to denote mechanical and anoxic trauma incurred by the infant during labor and delivery.



Disability-adjusted life year for birth asphyxia and birth trauma per 100,000 inhabitants in 2002.

The term "**Birth trauma**" is used to denote mechanical and anoxic trauma incurred by the infant during labor and delivery.

<https://en.m.wikipedia.org>

## The risk of birth injury

- Primiparity
- Small maternal stature
- Maternal pelvic anomalies
- Extremely rapid
- Prolonged labor
- Deep transverse arrest of descent of presenting part of fetus
- Oligohydramnions
- Abnormal presentation (i.e. breech)
- Use of mid-forceps or vacuum extraction
- Cesarean section
- Versions and extraction
- Very low birth weight infant or extreme premature
- Postmature infant (> 42 week of gestation)
- Fetal macrosomia
- Large fetal head
- Fetal anomalies

Risk factors for birth trauma include the following:

- Primiparity
- Small maternal stature
- Maternal pelvic anomalies
- Extremely

[www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

y rapid

- Prolonged labor
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- Abnormal presentation (i.e. breech)
- Use of mid-forceps or vacuum extraction
- Cesarean section
- Versions and extraction
- Very low birth weight infant or extreme premature
- Postmature infant

## **Classification of birth injuries**

### **I. Soft-tissue injuries**

caput succedaneum  
subcutaneous and retinal hemorrhage, petechia  
ecchymoses and subcutaneous fat necrosis

### **II. Cranial injuries**

cephalohematoma  
fractures of the skull

### **III. Intracranial hemorrhage**

subdural hemorrhage  
subarachnoid hemorrhage  
intra- and peryventricular hemorrhage  
parenchyma hemorrhage

[www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

## **Classification of birth injuries**

### **IV. Spine and spinal cord**

- fractures of vertebra
- Erb-Duchenne paralysis
- Klumpke paralyses
- Phrenic nerve paralyses
- Facial nerves palsy

### **V. Peripheral nerve injuries**

### **VI. Visceral (rupture of liver, spleen and adrenal hemorrhage)**

### **VII. Fractures of bones.**

[www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

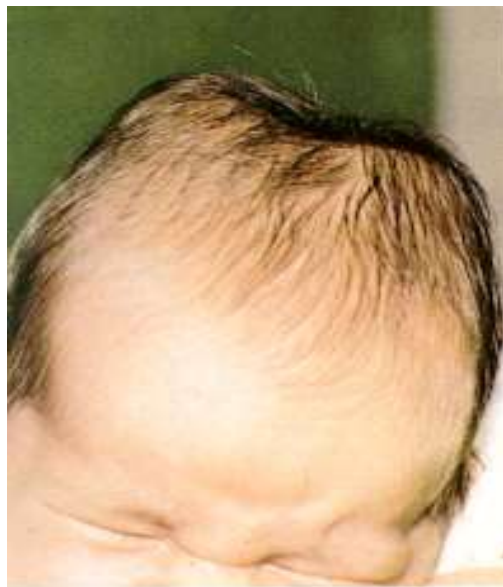
## Caput succedaneum



**Caput succedaneum** is oedema of the presenting part caused by pressure during a vaginal delivery. This is a serosanguineous, subcutaneous, extraperiosteal fluid collection with poorly defined margins, non fluctuating.

[www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

## Cephalhematoma



**Cephalhematoma** is a subperiosteal collection of blood between the skull and the periosteum. It may be unilateral or bilateral, and appears within hours of delivery

[www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

as a soft, fluctuant swelling on the side of the head. A cephalhaematoma never extends beyond the edges of the bone.



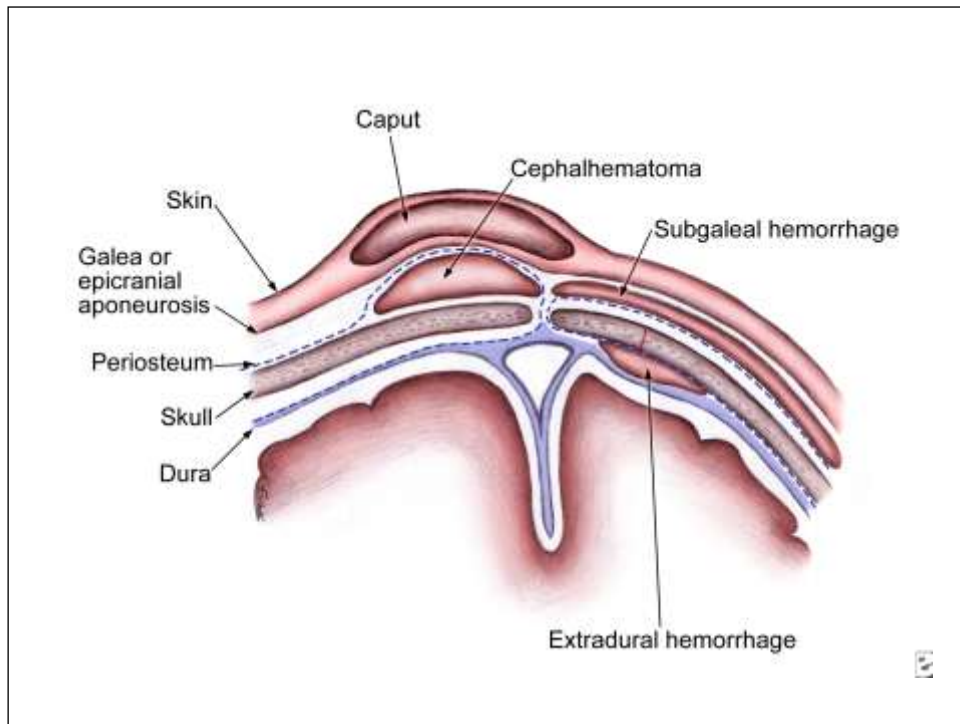
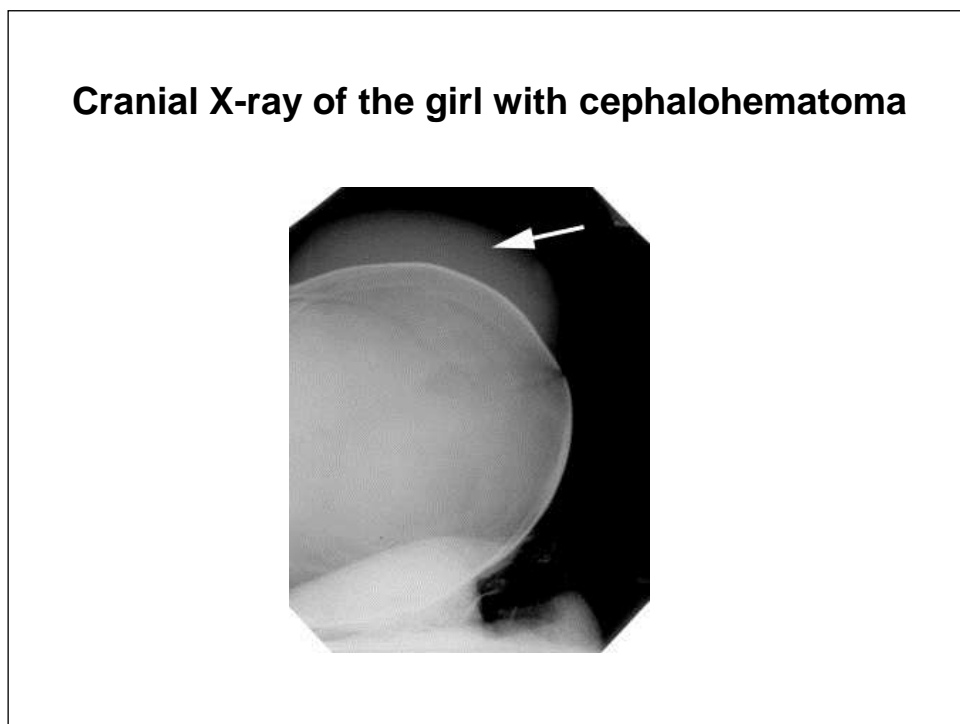


Figure shows different types of **Soft-tissue injuries and Cranial injuries in newborns.**

<http://nursingcrib.com>



Picture of the cranial X-ray of the girl with cephalohematoma

[www.radiopaedia.com](http://www.radiopaedia.com)



This is also Picture of the patient with cephalohematoma.

[www.medvisuals.com](http://www.medvisuals.com)



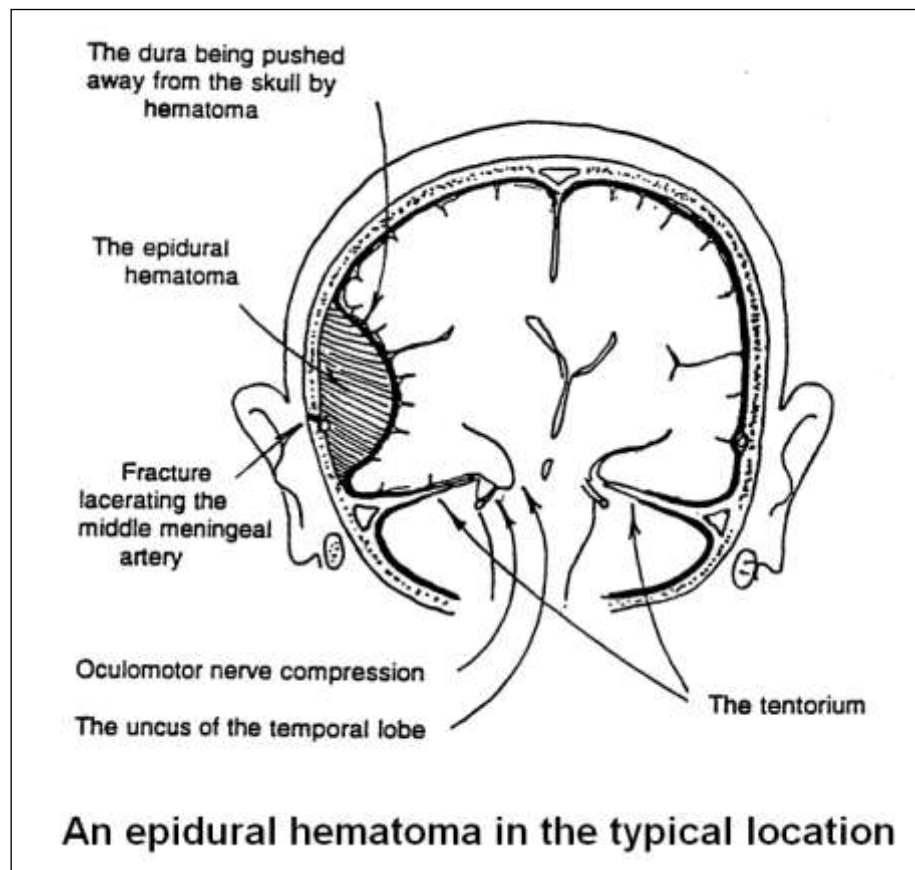
Subgaleal hematoma is bleeding in the potential space between the skull periosteum and the scalp galea aponeurosis. Clinical manifestations of it are:

Shock and pallor: tachycardia, a low blood pressure, within 30 minutes of the haemorrhage the

[www.medvisuals.com](http://www.medvisuals.com)

haemoglobin and packed cell volume start to fall rapidly.

Diffuse swelling of the head. Sutures usually are not palpable. The amount of blood under the scalp is far more than is estimated. Within 48 hours the blood tracks between the fibres of the occipital and frontal muscles causing bruising behind the ears, along the posterior hair line and around the eyes.



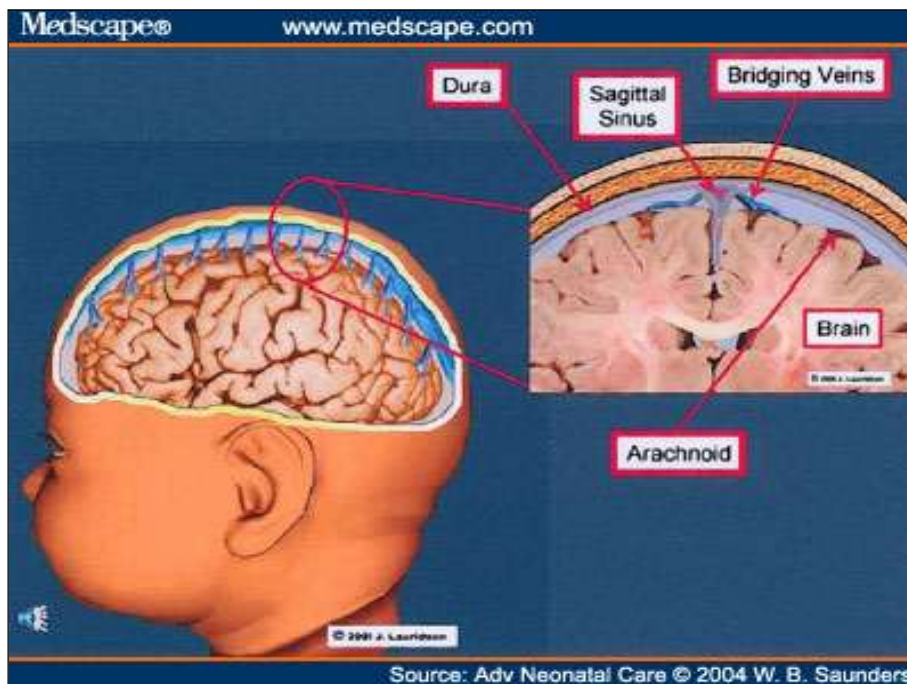
Clinical manifestations of **epidural hemorrhages** are:

Shock and/or anaemia due to blood loss.

Neurological signs due to brain compression, e.g. convulsions, apnoea, a dilated pupil or a depressed level

of consciousness ([www.medvisuals.com](http://www.medvisuals.com)).

A full fontanelle and splayed sutures due to raised intracranial pressure.

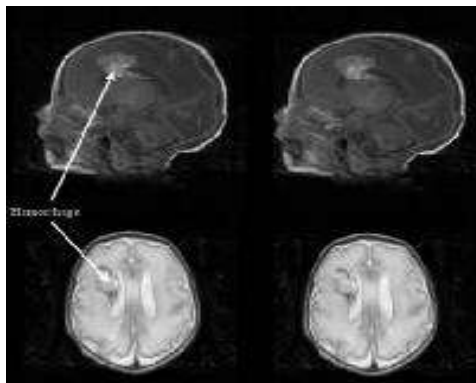


Of Subarachnoid hemorrhages (SAH)

Attacks of secondary asphyxia and apnoea, irregular breathing, bradycardia.

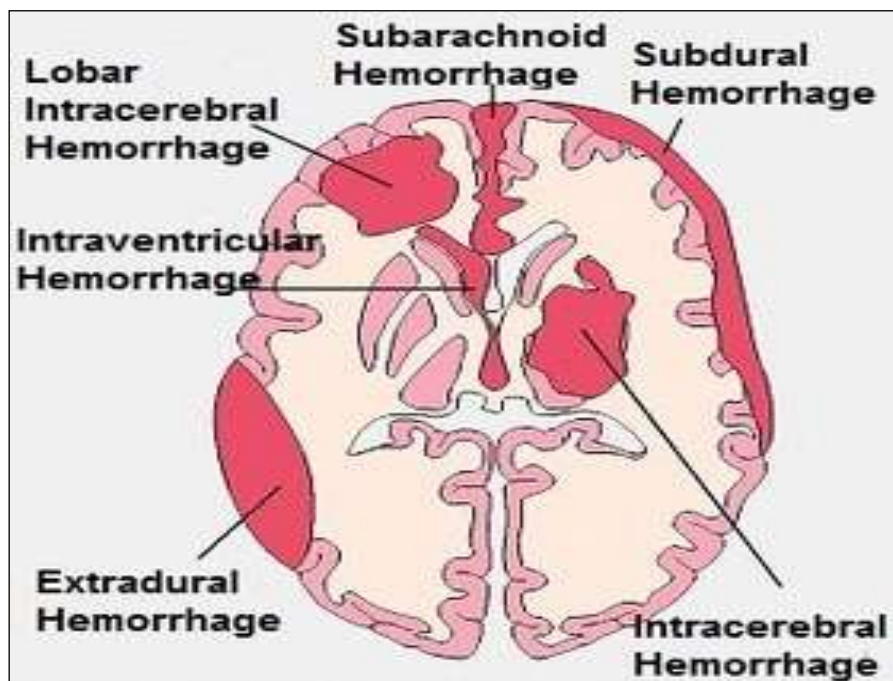
Hyperesthesia, tremor, seizures, bulging of fontanella. "Sunset" and Grefe symptoms are positive.

## Periventricular hemorrhagic infarction (PVHI) on MRI.



On the picture you can see periventricular hemorrhagic infarction (PVHI) on MRI.

[www.radiopaedia.com](http://www.radiopaedia.com)



[www.medvisuals.com](http://www.medvisuals.com)

## INTRACRANIAL HEMORRHAGE

occur in 20% to more than 40% of infants with birth weight under 1500 gm but is less common among more mature infants.

Intracranial hemorrhage may occur in the subdural, subarachnoid,

intraventricular or intracerebral regions. Subdural and subarachnoid hemorrhage follow head trauma e.g., in breech, difficult and prolonged labor and after forceps delivery. Other forms of intracranial bleeding are associated with immaturity and hypoxia. With better obstetric care intracranial bleeding has become rare.

## Clinical manifestation ICH

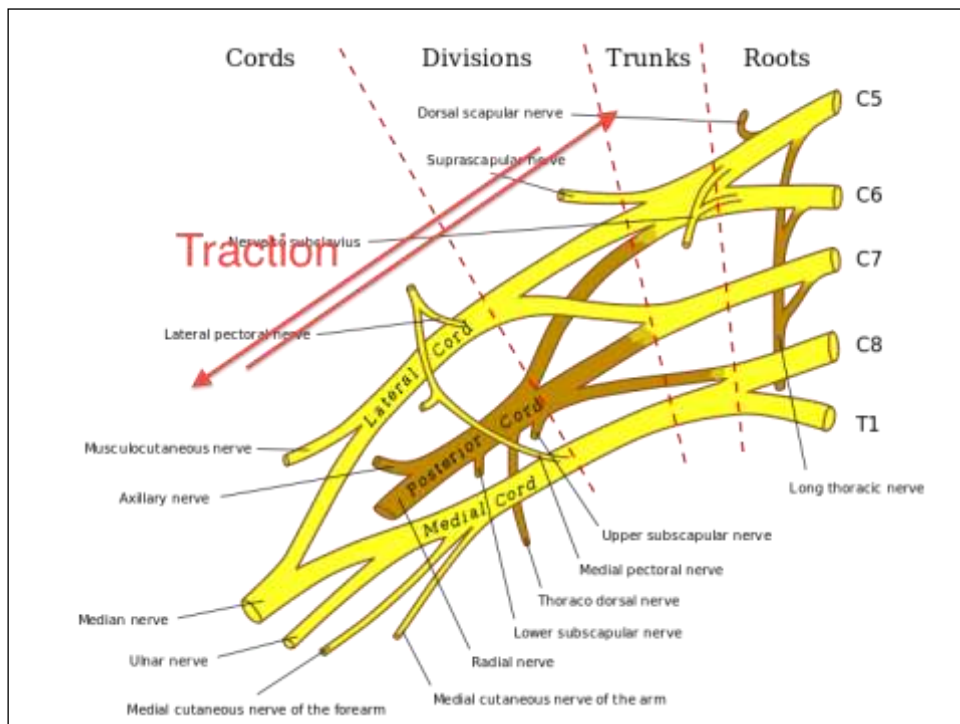
- Absent Moro reflex
- Poor muscle tone
- Lethargy
- excessive somnolence
- Pallor or cyanosis
- Respiratory distress
- DIC
- Jaundice
- Bulging anterior fontanel
- Hypotonia
- Weakness, seizures, muscular twitching
- Temperature instability
- Brain stem signs (apnea, lost extraocular movements, facial weakness, abnormal eye sing)

Clinically symptomatic cases with large hemorrhage and its complication may present with various degree of altered consciousness, cardiorespiratory deterioration, unexplained drop in hematocrit, acidosis, blood glucose alteration,

inappropriate antidiuretic hormone secretion, severe apnea or neonatal seizure, bulging fontanelles, abnormal eye movement or alignment, abnormal pupillary response, and abnormal neuromotor examination (hypotonia, decreased motility, tight popliteal angle).



Trauma usually occurs in breech deliveries after excess longitudinal traction to the spine. It can also be caused by cord compression due to epidural hemorrhage or hyperextension of the fetal neck in utero (the “flying fetus”). Injury usually affects the lower cervical region (C5 to C7).



Involvement of the entire plexus is less common and results in a flaccid upper extremity with little or no movement, absent reflexes, and usually sensory loss. Ipsilateral Horner

[www.medivisuals.com](http://www.medivisuals.com)

syndrome is present in the most severe cases. Ipsilateral pyramidal signs (eg, decreased movement, Babinski sign) indicate spinal cord trauma; an MRI should be done. The involved extremity's subsequent growth may be impaired. The prognosis for recovery is poor.



Erb palsy is the most common brachial plexus injury. It is an upper brachial plexus (C5 to C7) injury causing adduction and internal rotation of the shoulder with pronation of the forearm.

[www.medivisuals.com](http://www.medivisuals.com)

- This baby presents with an asymmetric posture of the arms.
- The left arm is not flexed and hangs limply.
- The baby demonstrates the findings of a left-sided **ERB PARALYSIS**.



Sometimes the biceps reflex is absent and the Moro reflex is asymmetric.

Ipsilateral paralysis of the diaphragm due to phrenic nerve injury also is common.

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Klumpke palsy is rare and is a lower plexus injury that causes weakness or paralysis of the hand and wrist. The grasp reflex is usually absent, but the biceps reflex is present. Often, the sympathetic fibers of T1 are involved causing an ipsilateral Horner syndrome (miosis, ptosis, facial anhidrosis).

[www.medivisuals.com](http://www.medivisuals.com)



The facial nerve is injured most often. Facial nerve injury usually occurs at or distal to its exit from the stylomastoid foramen and results in facial asymmetry, especially during crying. Identifying which side of the face is affected can be

[www.medivisuals.co](http://www.medivisuals.co)

m

confusing, but the facial muscles on the side of the nerve injury cannot move.



Facial paralysis can be caused by pressure on the facial nerves during birth or by the use of forceps during birth. The affected side of the face droops and the infant is unable to close the eye tightly on that side. When crying the mouth is pulled

[www.medivisuals.com](http://www.medivisuals.com)

across to the normal side.





[www.radiopaedia.com](http://www.radiopaedia.com)

Most phrenic nerve injuries (about 75%) are associated with brachial plexus injury. Injury is usually unilateral and caused by a traction injury of the head and neck. Infants have respiratory distress and decreased breath sounds on the affected side.



Common (general) regimen is administered for healthy child or convalescents

Hemostatics: 1% vit K 1mg/kg, dicinone 12.5 mg/kg

Hypovolemia: 5% albumine, plasma, 5% glucose – 1-10 ml/kg

Protect of nerve cells and anticonvulsants: 20% Natrium-oxybutirate 100 mg/kg, sibazone 0.3 ml/kg, Phenobarbital 20 mg/kg (5-10)

25% Magnesia 0.2 ml/kg.

[www.medivisuals.com](http://www.medivisuals.com)

**Treatment (underlying problems associated with BT):**

Hypoglycemia – 5% glucose i/v 1-10 ml/kg

Hypocalciemia–10% Ca-gluconate 2 ml/kg

Acidosis- 4.2% Sodium bicarbonate solution 2 meq/kg

# RESPIRATORY DISTRESS IN NEWBORNS

*Department of hospital pediatrics*

*Zaporizhzhya State Medical University  
(fifth year, English -speaking studying)*

2015

## RESPIRATORY DISTRESS IN NEWBORNS

- **1/13 newborns have breathing problems at birth (7.5%)**
- **1/6 newborns with breathing problems have infections**
- **GA < 31 uker: 1/2 have infections**
- **Boys 9.3%, Girls 5.9 %**
- **Mortality 0.4% (5% < 36 weeks GA)**

RDS occurs primarily in premature infants; its incidence is inversely related to gestational age and birthweight. It occurs in 60–80% of infants less than 28 wk of gestational age, in 15–30% of those between 32 and 36 wk, in about 5% beyond 37

wk, and rarely

at term. The risk of developing RDS increases with maternal diabetes, multiple births, cesarean section delivery, precipitous delivery, asphyxia, cold stress, and a history of previously affected infants.

This table presents the statistics on RDS

## **RESPIRATORY DISTRESS IN NEWBORNS**

**A wide variety of pathologic lesions may be responsible for respiratory disturbances, including**

- **hyaline membrane disease**
- **(aspiration (meconium or amniotic fluid) syndrome**
- **pneumonia**
- **sepsis**
- **congenital heart disease**
- **pulmonary hypertension**
- **choanal atresia**
- **hypoplasia of the mandible with posterior displacement of the tongue**

A wide variety of pathologic lesions may be responsible for respiratory disturbances.

## **RESPIRATORY DISTRESS IN NEWBORNS**

- malformation of the epiglottis
- malformation or injury of the larynx or chest
- pneumothorax, lobar emphysema
- pulmonary agenesis or hypoplasia
- congenital tracheoesophageal fistula
- avulsion of the phrenic nerve
- hernia or eventration of the diaphragm
- intracranial lesions
- neuromuscular disorders
- metabolic disturbances

## Fetal Lung Histology

- **STAGE 1: Pseudoglandular Period**  
(5-17 weeks) all the major elements of the lungs have formed except for those involved with gas exchange
- **STAGE 2: Canalicular Period**  
(16-25 weeks) bronchi and terminal bronchioles increase in lumen size and the lungs become vascularized

Respiratory disorders are the most frequent cause of admission for neonatal intensive care in both term and preterm infants. Signs and symptoms include cyanosis, grunting, nasal flaring, retractions, tachypnea, decreased breath sounds with rales and/or rhonchi, pallor, and apnea.

This table presents 4 stages of lung development.

The pseudoglandular period of lung

development from about the 7th to the 17th week is

characterized by 15 to 20 generations of airway branching to yield a fetal lung that is branched to the level of the future alveolar ducts

The canalicular stage between 16 and 25 weeks' gestation represents the transformation of the preivable lung to the potentially viable lung that can exchange gas. The bronchial tree has completely branched and respiratory bronchioles are forming. The three major events during this stage are the appearance of the acinus, epithelial differentiation with the development of the potential air-blood barrier, and the start of surfactant synthesis within recognizable type II cells.<sup>1</sup>

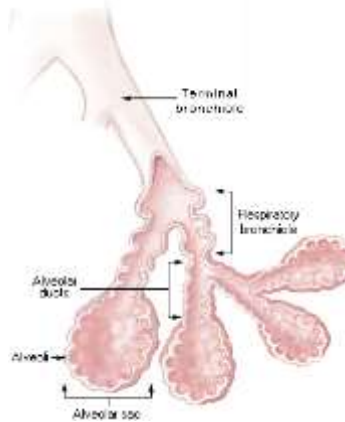
## Fetal Lung Histology

- **STAGE 3: Terminal Sac Period**  
(24 weeks to birth) more terminal sacs develop and interface with capillaries lined with Type I alveolar cells or pneumocytes  
--Also have Type II pneumocytes which secrete **surfactant** thereby decreasing the surface tension forces and aids in expansion of the terminal sacs

The saccular stage encompasses the period of lung development during the potentially viable stages of prematurity from about 25 weeks to term. The terminal sac or saccule is the distal airway structure that is elongating, branching, and widening until alveolarization is completed. Alveolarization is initiated from the terminal saccules by the appearance of septae in association with capillaries, elastin fibers, and collagen fibers.

## Fetal Lung Histology

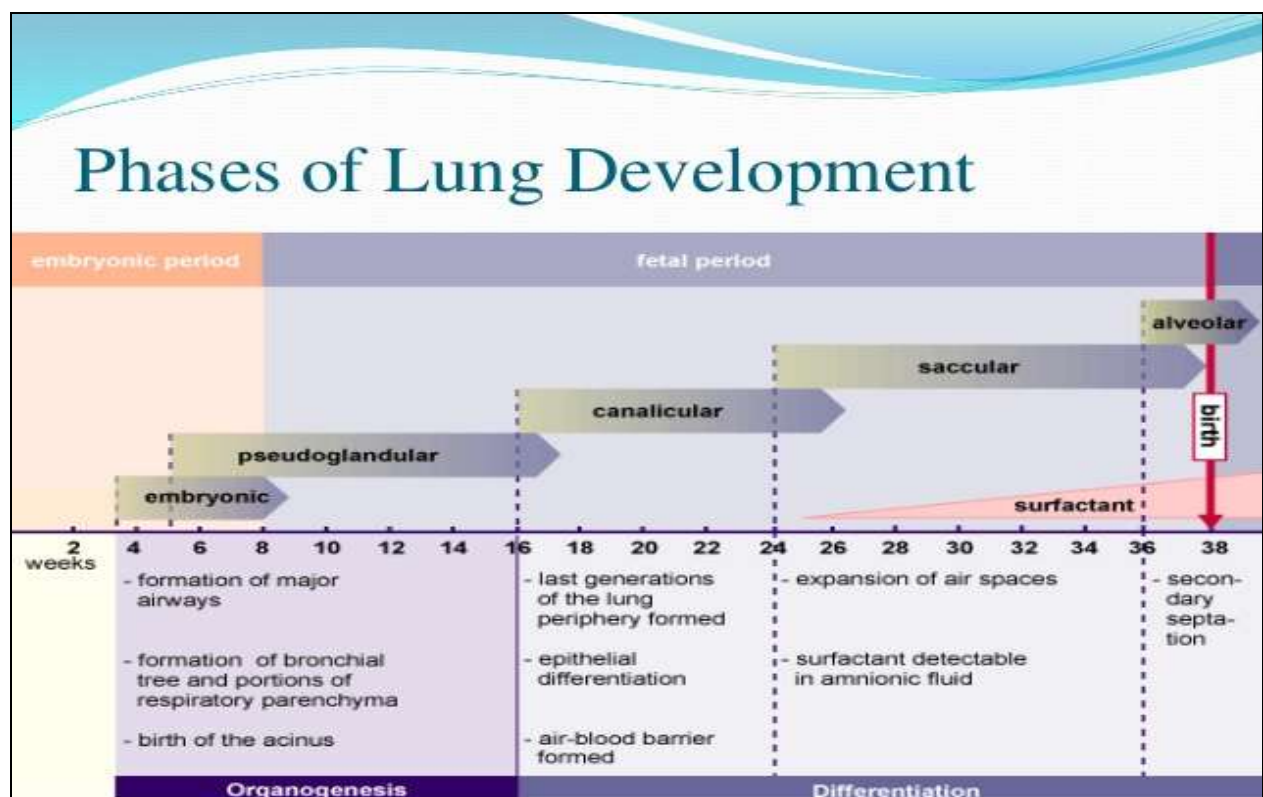
- STAGE 4: Alveolar Period** (late fetal period to 8 years)  
 95% of mature alveoli develop after birth. A newborn has only 1/6 to 1/8 of the adult number of alveoli and lungs appear denser on x-ray



Alveolarization progresses rapidly from late fetal to early neonatal life and may be complete by 1 to 2 years after birth.

Nelson textbook. 18<sup>th</sup> Edition / edited by R.M. Kliegman, R.E. Behrman, H.B. Jenson, B.F. Stanton. – Philadelphia : Saunders, 2007. – Chapter 101.

<http://www.picpara.com/nelson-textbook-of-pediatrics-18th-edition-free-download-medical-ebooks-pdf/>



[www.studyblue.com501 × 331](http://www.studyblue.com501x331) image screen\_shot\_2014-11-11\_at\_32308\_pm for definition side of card

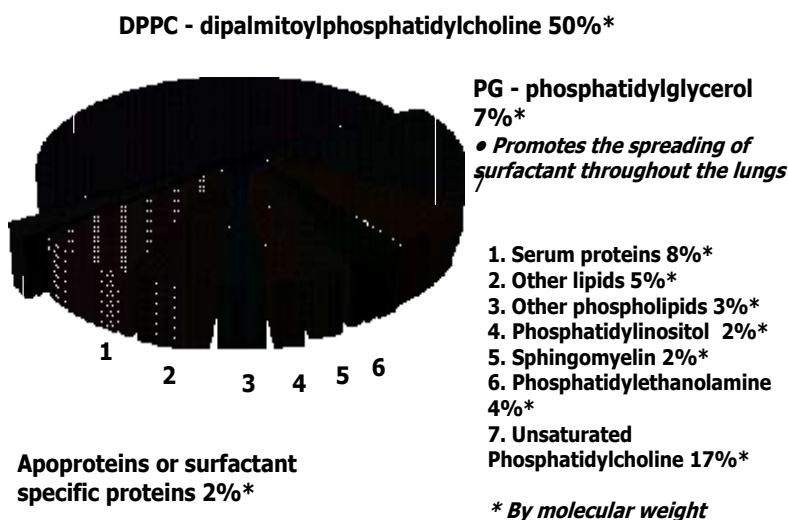
## Surfactant

- With advancing gestational age, increasing amounts of phospholipids are synthesized and stored in type II alveolar cells .
- Wk 20: start of surfactant production and storage. Does not reach lung surface until later
- Wk 28-32: maximal production of surfactant and appears in amniotic fluid
- Wk 34-35; mature levels of surfactant in lungs
- The amounts produced or released may be insufficient to meet postnatal demands because of immaturity.
- Surfactant inactivating states eg maternal DM may lead to surfactant of lower quality/ immature

**This tables presents 4 stages of lung development Surfactant detected in amniotic fluid from 22-24 w.**

These surface-active agents are released into the alveoli, where they reduce surface tension and help maintain alveolar stability by preventing the collapse of small air spaces at end-expiration

## Surfactant Composition



**This scheme presents Surfactant Composition**

The major constituents of surfactant are dipalmitoyl phosphatidylcholine (lecithin), phosphatidylglycerol, apoproteins (surfactant proteins SP-A, -B, -C, -D), and cholesterol. With advancing gestational age, increasing amounts of phospholipids are synthesized and stored in type II alveolar cells.

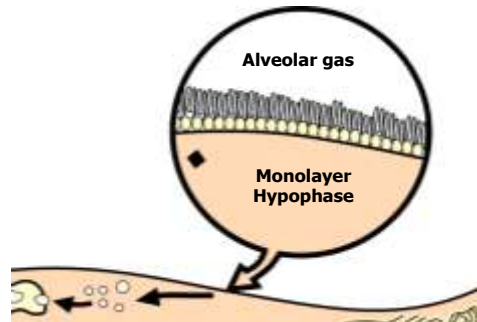
Nelson textbook. 18<sup>th</sup>

## Surfactant action

### Phospholipids

Polar heads  
Insoluble tails

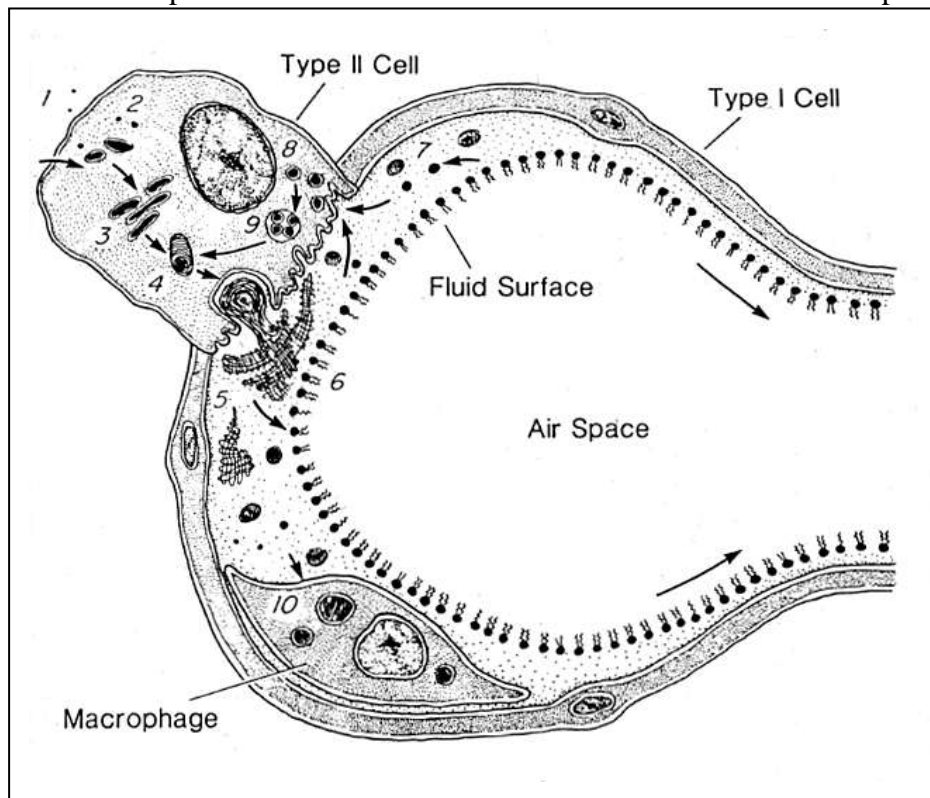
### Negative tails



This scheme presents Surfactant action

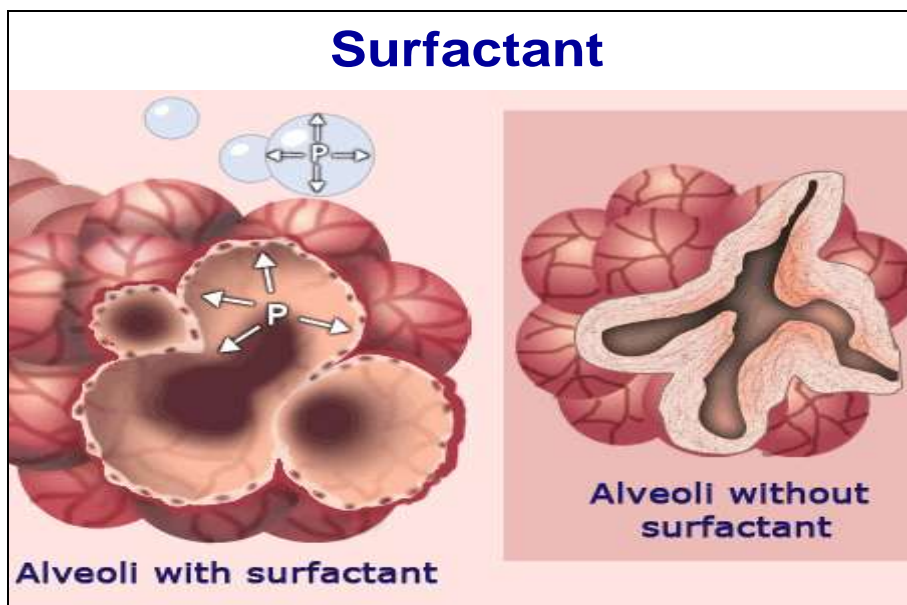
Surfactant deficiency (decreased production and secretion) is the primary cause of RDS.

Nelson textbook. 18<sup>th</sup> Edition / edited by R.M. Kliegman, R.E. Behrman, H.B. Jenson, B.F. Stanton. – Philadelphia : Saunders, 2007. – Chapter 101. <http://www.picpara.com/nelson-textbook-of-pediatrics-18th-edition-free-download-medical-ebooks-pdf/>



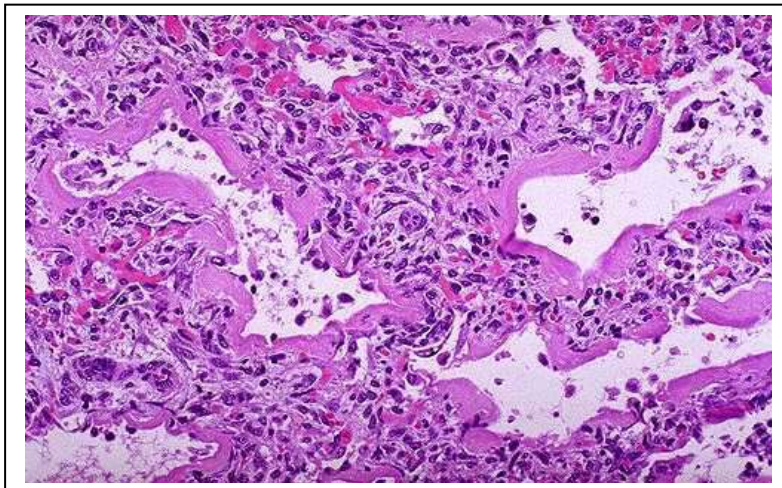
This scheme represents Surfactant production and action. Surfactant is present in high concentrations in fetal lung homogenates by 20 wk of gestation, but it does not reach the surface of the lungs until later. It appears in amniotic fluid between 28 and 32 wk. Mature levels of pulmonary surfactant are usually present after 35 wk.

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Synthesis of surfactant depends in part on normal pH, temperature, and perfusion. Asphyxia, hypoxemia, and pulmonary ischemia, particularly in association with hypovolemia, hypotension, and cold stress, may suppress surfactant synthesis. The epithelial lining of the lungs may also be injured by high oxygen concentrations and the effects of respirator management, thereby resulting in a further reduction in surfactant.



Alveolar atelectasis, hyaline membrane formation, and interstitial edema make the lungs less compliant, so greater pressure is required to expand the alveoli and small airways.

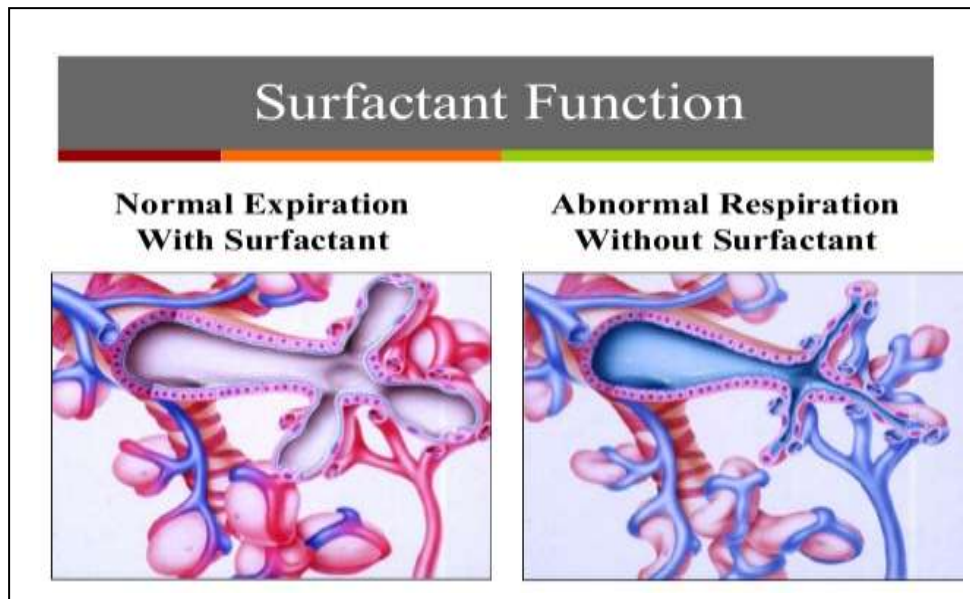
The lungs appear deep purplish red and are liver-like in consistency.

Microscopically, extensive atelectasis with engorgement of the interalveolar capillaries

<https://www.google.com.ua/search?q=Surfactant&biw>

and lymphatics can be observed. A number of the alveolar ducts, alveoli, and respiratory bronchioles are lined with acidophilic, homogeneous, or granular membranes. Amniotic debris, intra-alveolar hemorrhage, and interstitial emphysema are additional but inconstant findings; interstitial emphysema may be marked when an infant has been ventilated. The characteristic hyaline membranes are rarely seen in infants dying earlier than 6–8 hr after birth.





In affected infants, the lower part of the chest wall is pulled in as the diaphragm descends, and intrathoracic pressure becomes negative, thus limiting the amount of intrathoracic pressure that can be produced; the

<https://www.google.com.ua/search?q=Surfactant&biw>

result is the development of atelectasis. The highly compliant chest wall of preterm infants offers less resistance than that of mature infants to the natural tendency of the lungs to collapse. Thus, at end-expiration, the volume of the thorax and lungs tends to approach residual volume, and atelectasis may develop.

## **Neonatal Respiratory Distress**

### **Symptoms and signs**

- **Tachypnea (frequency > 60 per min)**
- **Cyanosis in room air**
- **Flare of the nostrils**
- **Chest retractions**
- **Grunting**
- **Nasal flaring**
- **Decreased breath sounds with rales and/or rhonchi**
- **Apnea**

Deficient synthesis or release of surfactant, together with small respiratory units and a compliant chest wall, produces atelectasis and results in perfused but not ventilated alveoli, which

causes **hypoxia**.

Decreased lung compliance, small tidal volumes, increased physiologic dead space, increased work of breathing, and insufficient alveolar ventilation eventually result in **hypercapnia**. The combination of hypercapnia, hypoxia, and acidosis produces pulmonary arterial vasoconstriction with increased right-to-left shunting through the foramen ovale and ductus arteriosus and within the lung itself. Pulmonary blood flow is reduced, and ischemic injury to the cells producing surfactant and to the vascular bed results in an effusion of proteinaceous material into the alveolar spaces

## CAUSES OF RESPIRATORY DISTRESS

Obstruction of the airway	Lung parenchymal disease
Choanal atresia Congenital stridor Tracheal or bronchial stenosis	Meconium aspiration Respiratory distress syndrome Pneumonia Transient tachypnea of the newborn (retained lung fluid) Pneumothorax Atelectasis Congenital lobar emphysema
Non-pulmonary causes	Miscellaneous
Heart failure Intracranial lesions Metabolic acidosis	Disorders of the diaphragm e.g. (diaphragmatic hernia) Pulmonary haemorrhage Pulmonary hypoplasia

Respiratory distress syndrome – differentials  
 The symptoms of respiratory distress can be caused by a wide diversity of pathophysiological states during neonatal life. In the differential diagnosis, nonrespiratory etiologies must always be considered.

Fanaroff and Martin's neonatal-perinatal medicine: diseases of the fetus and infant. 18<sup>th</sup> Edition / edited by R.J. Martin, A.A. Fanaroff, M.C. Walsh. – Philadelphia : Elsevier Mosby, 2006. – Chapter 42. /das/book/0/view/1349/1.html/top

## Neonatal Respiratory Distress Etiologies

### Pulmonary

- Transient tachypnea of the newborn (TTN)
- Respiratory distress syndrome (RDS)
- Pneumonia
- Meconium aspiration syndrome (MAS)
- Air leak syndromes
- Pulmonary hemorrhage

### Systemic

- **Metabolic** (e.g., hypoglycemia, hypothermia or hyperthermia)
- metabolic acidosis
- anemia, polycythemia
- **Cardiac**
  - Congenital heart disease; cyanotic or acyanotic
  - Congestive heart failure
  - Persistent pulmonary hypertension of the newborn (PPHN)
- **Neurological** (e.g., prenatal asphyxia, meningitis)

### Anatomic

- Upper airway obstruction
- Airway malformation
- Rib cage anomalies
- Diaphragmatic disorders (e.g., congenital diaphragmatic hernia, diaphragmatic paralysis)

Causes of neonatal RDS and Classification of neonatal RDS.  
 Some examples are thermal instability, circulatory problems, cardiac disease, sepsis, and anemia or polycythemia, all of which are addressed elsewhere.

## Respiratory Distress Syndrome(RDS)

- (RDS) is a condition of increasing respiratory distress, commencing at, or shortly after, birth and increasing in severity until progressive resolution occurs among the survivors, usually around 2nd to 7th day

- Maybe primary or secondary

- Incidence and severity is inversely proportional to gestational age

- <28wks- 60-80%

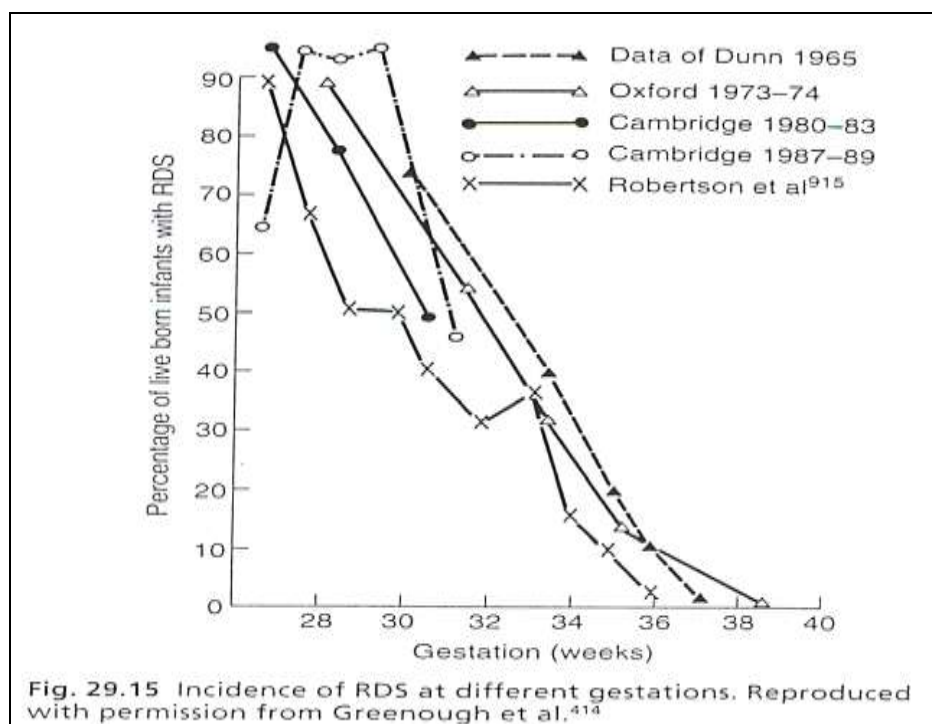
- 28-32wks- 25-50%

- 32-36wks- 15-30%

- >37 wks- 5%

- rare at term

Definition and incidence of neonatal RDS



In the preterm infant, respiratory distress syndrome (RDS) frequently dominates the clinical picture

Fanaroff and Martin's neonatal-perinatal medicine: diseases of the fetus and infant. 18<sup>th</sup> Edition / edited by R.J. Martin, A.A. Fanaroff, M.C. Walsh. – Philadelphia : Elsevier Mosby, 2006. – Chapter 42. [/das/book/0/view/1349/1.html/top](#)

## Respiratory Distress Syndrome(RDS)

### RISK FACTORS

- Neonates younger than 33-38 weeks
- Weight less than 2500g
- Maternal diabetes
- Cesarean delivery without preceding labor
- Precipitous labor
- Fetal asphyxia
- Second of twins
- Cold stress
- Previous history of RDS in sibling
- Males
- whites

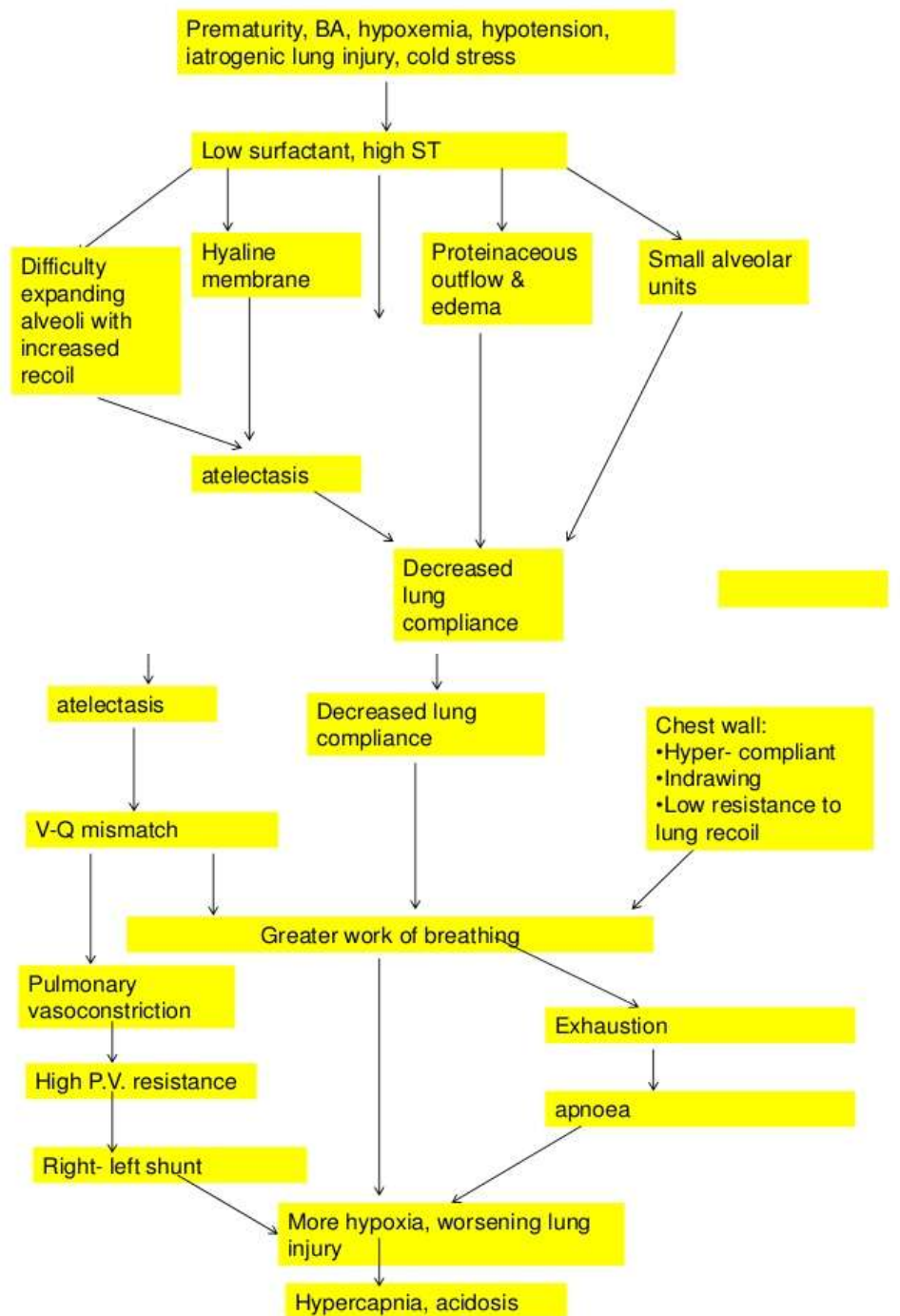
Neonatal RDS risk factors

## Respiratory Distress Syndrome(RDS)

### DECREASED RISK

- Use of antenatal steroids
- Pregnancy-induced or chronic maternal hypertension
- Prolonged rupture of membranes
- Maternal narcotic addiction
- Chronic intrauterine stress
- IUGR or SGA
- Thyroid hormones
- Tocolytic agents

Factors decreased risk of neonatal RDS



Fanaroff and Martin's neonatal-perinatal medicine: diseases of the fetus and infant. 18<sup>th</sup> Edition / edited by R.J. Martin, A.A. Fanaroff, M.C. Walsh. – Philadelphia : Elsevier Mosby, 2006. – Chapter 42. /das/book/0/view/1349/1.html/top

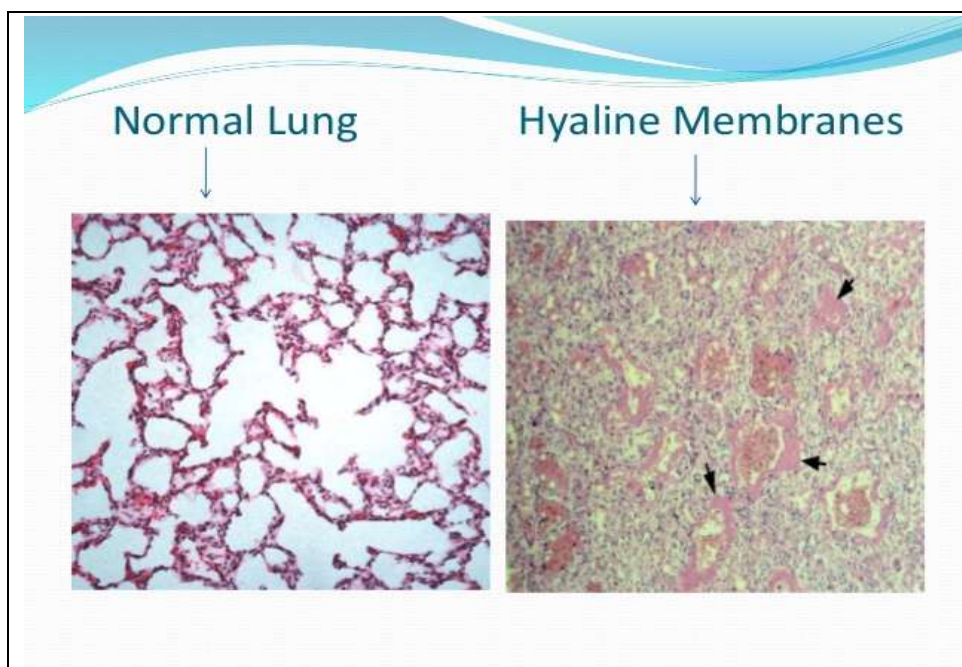
This scheme represents the pathogenesis of neonatal RDS

## **Neonatal Respiratory Distress**

### **Symptoms and signs**

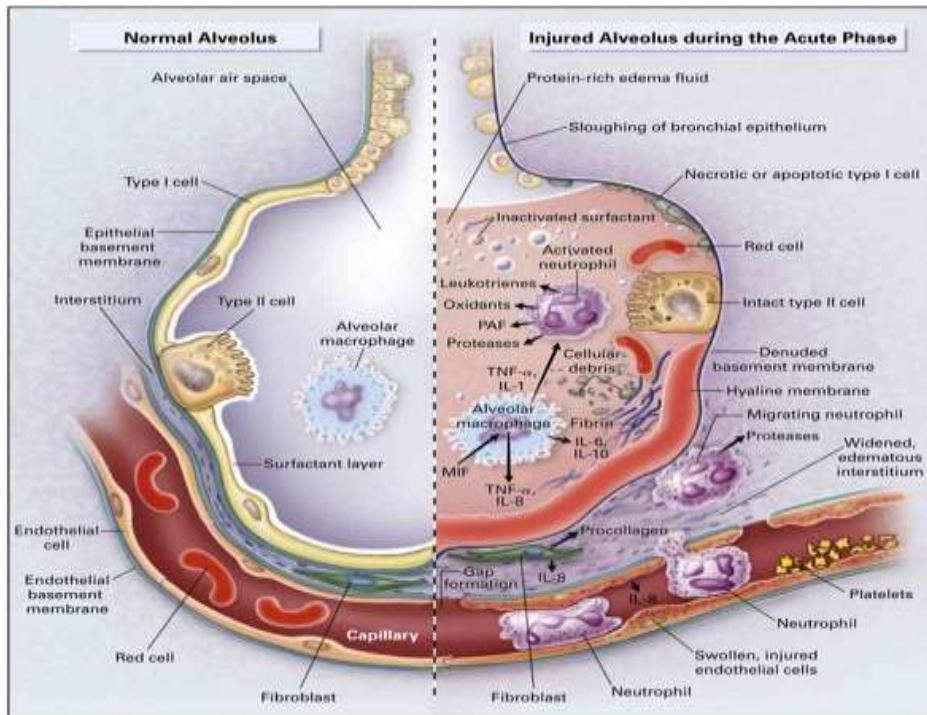
- **Tachypnea (frequency > 60 per min)**
- **Cyanosis in room air**
- **Flare of the nostrils**
- **Chest retractions**
- **Grunting**
- **Nasal flaring**
- **Decreased breath sounds with rales and/or rhonchi**
- **Apnea**

This scheme presents Symptoms and signs of Neonatal Respiratory Distress. Periodic breathing is a normal characteristic of neonatal respiration during sleep in the 1st months of life. Normal full-term infants may have infrequent episodes when regular breathing is interrupted by short pauses. This periodic breathing pattern which episodes of intermittent apnea, is more common in premature infants, who may have apneic pauses of 5–10 sec followed by a burst of rapid respirations at a rate of 50–60/min for 10–15 sec. Serious apnea is defined as cessation of breathing for longer than 20 sec, or any duration if accompanied by cyanosis and bradycardia



<https://www.google.com.ua/search?q=Surfactant&biw>

This micropreparation represents the morphological changes in the lung of patients with RDS (HMD)



<https://www.google.com.ua/search?q=Surfactant&biw>

This scheme represents the morphological changes in the lung of patients with RDS (HMD)

## Clinical manifestations

- Tachypnea
- Tachycardia
- Chest wall Retractions
- Fine crackles
- Expiratory grunting
- Nasal flaring
- Central cyanosis
- Ventilator failure (rising CO<sub>2</sub> in the blood)
- Extremities puffy or swollen
- apnea

<https://www.google.com.ua/search?q=Surfactant&biw=1360&bih>

Respiratory distress syndrome clinical manifestation

## Silverman Anderson Score for Premature Baby

Score	Upper Chest Retraction	Lower Chest Retraction	Xiphoid Retraction	Nasal Flaring	Grunting
0	Synchronous	None	None	None	None
1	Lag on Inspiration	Just visible	Just visible	Minimal	Stethoscope
2	See-Saw	Mark	Mark	Mark	Naked ear

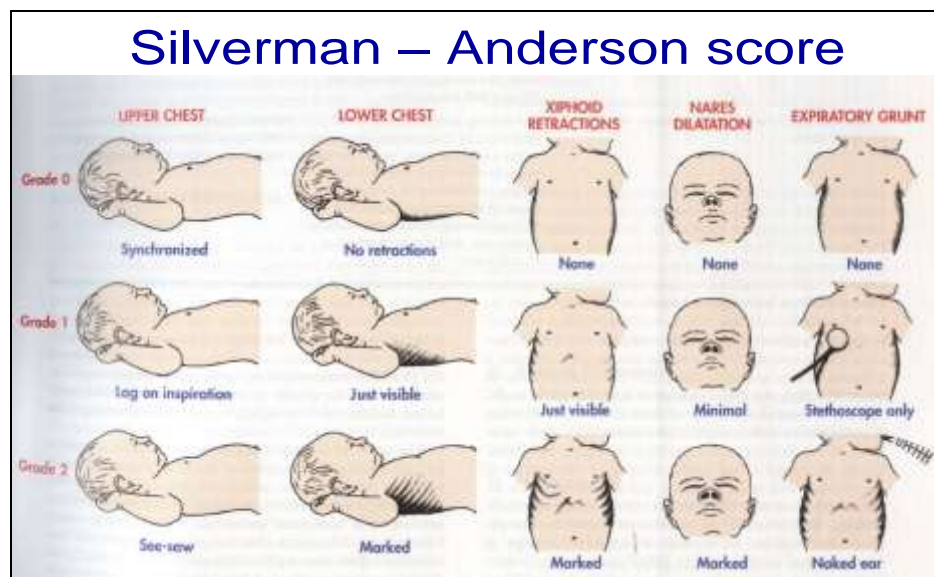
Score > 6 = impending Respiratory Failure

## Downe's Score for Term Baby

Score	Respiratory Rate	Cyanosis	Air entry	Retraction	Grunting
0	<60	None	Good	None	None
1	60-80	In air	Decrease	Minimal	Stethoscope
2	>80/ apnoea	In 40% O <sub>2</sub>	Barely audible	Moderate/severe	Naked ear

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Infants with RDS characteristically present immediately after delivery or within several hours of birth with a combination of tachypnea, nasal flaring, subcostal and intercostal retractions, cyanosis, and an expiratory grunt. Respiratory rate is usually regular and increased well above the normal range of 30 to 60 breaths per minute. These patients usually show progression of symptoms and require supplemental oxygen. The presence of apneic episodes at this early stage is an ominous sign that could reflect thermal instability or sepsis but more often is a sign of hypoxemia and respiratory failure.



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This scheme represents the Silverman – Anderson score

Retractions are prominent and are the result of the compliant rib cage collapse on inspiration, as the infant generates high intrathoracic pressures to expand the poorly compliant lungs. The typical expiratory grunt is an early feature of the clinical course and may subsequently disappear. It is believed to result from partial closure of the glottis during expiration and in this way acts as a means of trapping alveolar air and maintaining functional residual capacity



## Silverman – Anderson score

**Score 7 - 10 Severe RDS**

**Score 4 - 6 Moderate RDS**

**Score 1 - 3 Initial symptoms RDS**

**Score 0 = No respiratory distress**

**Score 5 and more –  
indications for mechanical ventilation**

This scheme represents the Silverman – Anderson score evaluation

## DOWNE'S SCORING OF RESPIRATORY DISTRESS

	0	1	2
<b>Cyanosis</b>	None	In room air	In 40% FIO <sub>2</sub>
<b>Retractions</b>	None	Mild	Severe
<b>Grunting</b>	None	Audible with stethoscope	Audible without stethoscope
<b>Air entry</b>	Clear	Decreased or delayed	Barely audible
<b>Respiratory rate</b>	Under 60	60-80	Over 80 or apnea

**Score:**

> 4 = Clinical respiratory distress; monitor arterial blood gases

> 8 = Impending respiratory failure

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This scheme represents the Downes Score

## Complications

- Metabolic disorders (acidosis, low blood sugar)
- Patent ductus arteriosus
- Low blood pressure
- chronic lung changes
- Intracranial hemorrhage



<https://www.google.com.ua/search?q=Surfactant+cycle&rlz>

This scheme represents the RDS complications

## Diagnostic evaluation

- Laboratory findings include an arterial  $pCO_2$  above 65mmof Hg and a pH of 7.15 .
- The foam stability or shake test is done .
- Radiographic examination of chest shows areas of atelectasis .
- **Prenatal Diagnosis**
- History of premature delivery
- Concentration of lecithin in amniotic fluids.
- Ratio of lecithin/sphingomyelin
- Lecithin indicate lung maturity
- Sphingomyelin remains constant during pregnancy
- L/S ratio 2:1 indicate lung maturity

This scheme represents the RDS diagnostic evaluation

A constant feature of RDS is the early onset of clinical signs of the disease. Most infants present with signs and symptoms either in the delivery room or within the first 6 hours after birth. Inadequate observation can lead to the impression of a symptom-free period of several hours. The uncomplicated clinical course is characterized by a progressive worsening of symptoms with a peak severity by days 2 to 3 and onset of recovery by 72 hours. Laboratory findings are initially characterized by hypoxemia and later by progressive hypoxemia, hypercapnia, and variable metabolic acidosis. The clinical course, x-ray of the chest, and blood gas and acid-base values help establish the clinical diagnosis.

## DIAGNOSIS

- CXR : fine reticular granularity of the parenchyma and air bronchograms : typical pattern developing at 6-12hr



This scheme represents the features of chest radiograph in patients with RDS (HMD). The diagnosis of RDS is based on a combination of the previously described clinical features, evidence of prematurity, exclusion of other causes of respiratory distress, and characteristic radiographic appearance.

## Diffused reticulogranular pattern



On x-ray, the lungs may have a characteristic, but not pathognomonic appearance that includes a fine reticular granularity of the parenchyma and air bronchograms, which are often more prominent early in the left lower lobe because of superimposition of the cardiac shadow.

Fanaroff and Martin's neonatal-perinatal medicine: diseases of the fetus and infant. 18<sup>th</sup> Edition / edited by R.J. Martin, A.A. Fanaroff, M.C. Walsh. – Philadelphia : Elsevier Mosby, 2006. – Chapter 42. [/das/book/0/view/1349/1.html/top](#)

## Ground glass opacity



Features of chest radiograph in patients with RDS (HMD)

## DIFFERENTIAL DIAGNOSIS

- Early-onset sepsis: group B streptococcus
- Pneumonia
- Cyanotic heart disease
- Persistent pulmonary HTN
- Transient tachypnea of newborn

The initial roentgenogram is occasionally normal, with the typical pattern developing at 6–12 hr. This scheme represents the RDS differential diagnosis.

In the **differential diagnosis**, early-onset sepsis may be indistinguishable from RDS. In pneumonia manifested at birth, the chest roentgenogram may be identical to that for RDS. Maternal group B streptococcal colonization, organisms on Gram stain of gastric or tracheal aspirates or a buffy coat smear, and/or the presence of marked neutropenia may suggest the diagnosis of early-onset sepsis. Cyanotic heart disease (total anomalous pulmonary venous return) can also mimic RDS both clinically and radiographically. Echocardiography with color flow imaging should be performed in infants who fail to respond to surfactant replacement to rule out cyanotic congenital heart disease as well as ascertain patency of the ductus arteriosus and assess pulmonary vascular resistance

## DIFFERENTIAL DIAGNOSIS

- Spontaneous pneumothorax
- Pleural effusion
- Diaphragmatic hernia
- Lobar emphysema

Persistent pulmonary hypertension, aspiration (meconium, amniotic fluid) syndromes, spontaneous pneumothorax, pleural effusions, and congenital anomalies such as cystic adenomatoid malformation, pulmonary lymphangiectasia, diaphragmatic hernia, and lobar emphysema must be considered, but can generally be differentiated from


RDS by

roentgenographic evaluation.

## THERAPEUTIC MANAGEMENT

### OXYGEN THERAPY

- **Indications**
  1. Clinical central cyanosis
  2. Hypoxemia (O<sub>2</sub> saturation < 87% and PaO<sub>2</sub> < 50 mmHg in room air)
  1. Neonates suspected RDS.
- **Commonly used O<sub>2</sub> delivery system in neonates:-**
  - Low flow system are commonly used in neonate. These system provide a variable FiO<sub>2</sub> depending upon the inspiratory flow rate generate by the neonate.




The basic defect requiring treatment is inadequate pulmonary exchange of oxygen and carbon dioxide; metabolic acidosis and circulatory insufficiency are secondary manifestations. Early supportive care of LBW infants, especially in the treatment of acidosis, hypoxia, hypotension, and hypothermia may lessen the severity of RDS.

Therapy requires careful and frequent monitoring of heart and respiratory rates, oxygen saturation, PaO<sub>2</sub>, PaCO<sub>2</sub>, pH, bicarbonate, electrolytes, blood glucose, hematocrit, blood pressure, and temperature. Arterial catheterization is frequently necessary. Because most cases of RDS are self-limited, the goal of treatment is to minimize abnormal physiologic variations and superimposed iatrogenic problems.

## Cont.

- **Precaution while administering O<sub>2</sub> :-**
  - i. humidify
  - ii. O<sub>2</sub> saturation should never cross 93% in preterm infant as – hyperoxia leads
  - iii. Use O<sub>2</sub> analyzer to check FiO<sub>2</sub>
- **following way of oxygen therapy-**
  - i. CPAP(continuous positive airway pressure)
  - ii. PEEP(positive end-expiratory pressure)
  - iii. SIMV(synchronized intermittent mandatory ventilation)
  - iv. HFV (high frequency ventilation)



This scheme represents the RDS Treatment. Warm humidified oxygen should be provided at a concentration initially sufficient to keep arterial levels between 50 and 70 mm Hg (85–95% saturation) to maintain normal tissue oxygenation while minimizing the risk of oxygen toxicity.

If the PaO<sub>2</sub> cannot be maintained above 50 mm Hg at inspired oxygen concentrations of 60% or greater, applying CPAP at a pressure of 5–10 cm H<sub>2</sub>O by nasal prongs is indicated and usually produces a sharp rise in PaO<sub>2</sub>. Early use of CPAP for stabilization of at-risk VLBW infants beginning in the delivery room is also common. CPAP prevents collapse of surfactant-deficient alveoli, improves FRC, and improves ventilation-perfusion matching. Another approach is to intubate the VLBW infant, administer intratracheal surfactant, and then extubate to CPAP. The amount of CPAP required usually decreases abruptly at about 72 hr of age, and infants can be weaned from CPAP shortly thereafter. If an infant managed by CPAP cannot maintain an arterial oxygen tension above 50 mm Hg while breathing 70–100% oxygen, assisted ventilation is required.



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This photo represents the CPAP-therapy

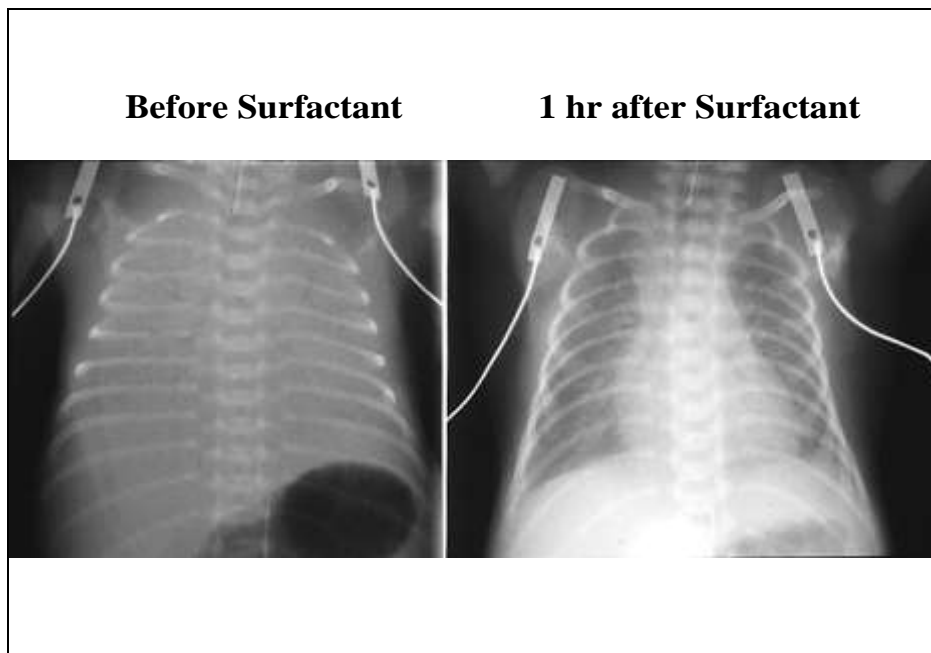
### Cont. SURFACTANT THERAPY

- **Indications:-**

- **Prophylactic:-**preterm infants of <28wks gestation. Administered within the initial 15-20min of life.
- **Early rescue:-**Administration is typical within the initial 2 hr of life.
- **Late rescue:-** Administration is typical within the beyond24 hr of life.

This scheme represents indications for Surfactant therapy  
Multidose endotracheal instillation of **exogenous surfactant** to VLBW infants requiring 30% oxygen and mechanical ventilation for the

treatment (**rescue therapy**) of RDS dramatically improves survival and reduces the incidence of pulmonary air leaks, but it has not consistently reduced the incidence of BPD. Immediate effects include improved alveolar-arterial oxygen gradients, reduced ventilator mean airway pressure, increased pulmonary compliance, and improved appearance of the chest roentgenogram. A number of surfactant preparations are available, including synthetic surfactants and natural surfactants derived from animal sources.



This photo represents the effect of Surfactant therapy

Fanaroff and Martin's neonatal-perinatal medicine: diseases of the fetus and infant. 18<sup>th</sup> Edition / edited by R.J. Martin, A.A. Fanaroff, M.C. Walsh. – Philadelphia : Elsevier Mosby, 2006. – Chapter 42. [/das/book/0/view/1349/1.html/top](#)

## Pulmonary diseases in the newborn period

### The natural course of Respiratory Distress Syndrome:

- **Maximum after 24 -36 hrs**
- **Spontaneous breathing in room air in uncomplicated cases**
- **Deterioration at 3-5 days due to an open ductus arteriosus**

This scheme represents the natural course of Respiratory Distress Syndrome  
Because of the difficulty of distinguishing **group B streptococcal** or other bacterial infections from RDS, empirical antibiotic therapy is indicated

## **Pulmonary diseases in the newborn period**

### **Respiratory Distress Syndrome - Therapy**

- Reduce prematurity rate
- Antenatal steroids 24 - 168 hrs before birth gives a 50% reduction in the incidens and 40% reduction in mortality
- Surfactant therapy reduces mortality/Chronic lung disease 30-40%
- General therapy: Oxygen, respirator, fluid-electrolytes, nutrition, antibiotics

This scheme represents the RDS Treatment

## ***RDS Prevention***

### **Lung maturity testing: lecithin/sphingomyelin (L/S) ratio**

- Tocolytics to inhibit premature labor.
- Antenatal corticosteroid therapy:
  - ▶ They induce surfactant production and accelerate fetal lung maturation.
  - ▶ Are indicated in pregnant women 24-34 weeks' gestation at high risk of preterm delivery within the next 7 days.
  - ▶ Optimal benefit begins 24 hrs after initiation of therapy and lasts seven days.

This scheme represents the RDS Prevention Administration of betamethasone to women 48 hr before the delivery of fetuses between 24 and 34 wk of gestation significantly reduces the incidence, mortality, and

morbidity of RDS. Corticosteroid administration is recommended for all women in preterm labor (24–34 wk gestation) who are likely to deliver a fetus within 1 wk. Repeated weekly doses of betamethasone until 32 wk may reduce neonatal morbidities and the duration of mechanical ventilation. Prenatal glucocorticoid therapy decreases the severity of RDS and reduces the incidence of other complications of prematurity, such as IVH, patent ductus arteriosus (PDA), pneumothorax, and necrotizing enterocolitis, without adversely affecting postnatal growth, lung mechanics or development, or the incidence of infection.



## **RDS Prevention**

- **Antenatal corticosteroid therapy** consists of either :
  - Betamethasone 12 mg/dose IM for 2 doses, 24 hrs apart, or
  - Dexamethasone 6 mg/dose IM for 4 doses, 12 hrs apart
- **Early surfactant therapy:** prophylactic use of surfactant in preterm newborn <27 weeks' gestation.
- **Early CPAP administration** in the delivery room.

This scheme represents the RDS Prevention Prenatal glucocorticoids may act synergistically with postnatal exogenous surfactant therapy. Administration of a 1st dose of surfactant into the trachea of symptomatic premature infants immediately after birth (prophylactic)

or during the 1st few hours of life (early rescue) reduces air leak and mortality from RDS, but does not alter the incidence of BPD.

## **Pulmonary diseases in the newborn period**

### **Pneumonia**

**Neonatal pneumonia may be an isolated focal infection but usually is a part of a general infection - sepsis.**

***Incidence of bacterial pneumonia:*  
3,7 per 1000 live born (Oxford)**

Neonatal pneumonia may be an isolated focal infection but usually is a part of a general infection – sepsis. Classification of neonatal pneumoniae – Congenital, Early onset (< 48 hrs), Late onset (> 48 hrs).

## Pulmonary diseases in the newborn period

### Early onset pneumonia

**1,8 per 1000 live newborn**

**Gr B streptococci (70% in UK)**

**H. Influenza**

**S. Pneumoniae**

**Listeria Monocytogenes**

**Gram negative enterobakterier**

**Fungi**

**Virus ( RS, Adeno, CMV, Coxsacki)**

Etiology of neonatal pneumonia. Congenital pneumonia may be caused by CMV, rubella virus, and *T. pallidum* and, less commonly, by the other agents producing transplacental infection. Microorganisms causing pneumonia acquired during labor and delivery

include GBS, gram-negative enteric aerobes, *Listeria monocytogenes*, genital *Mycoplasma*, *Chlamydia trachomatis*, CMV, HSV, and *Candida* species.

## Pulmonary diseases in the newborn period

### Late onset pneumonia

- Usual in preterm on artificial ventilation
- 10-35% of all on ventilator

#### **Gram positive**

**Staph aureus**

**Enterococci**

**Gr B streptococci**

**Fungi**

**Candida**

#### **Gram negative**

**Enterobakter**

**E. Coli**

**Klebsiella**

Etiology of neonatal pneumonia.

The bacteria responsible for most cases of nosocomial pneumonia typically include staphylococcal species, gram-negative enteric aerobes, and occasionally,

*Pseudomonas*. Fungi are responsible for an increasing number of systemic infections acquired during prolonged hospitalization of preterm neonates.

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## Pulmonary diseases in the newborn period

### Pneumonia - other agents

- *Ureaplasma urealyticum* (in vagina, -> pneumonia and lung fibrosis)
- *RS virus* (epidemics), more serious if chronic lung disease
- *Chlamydia* (early onset - may cross intact membranes). In term infants typical debut 3-4 weeks of age. Slow onset.  
Treated with erythromycin

Etiology of neonatal pneumonia  
Respiratory viruses cause isolated cases and outbreaks of nosocomial pneumonia. These viruses, usually endemic during the winter months and acquired from infected hospital staff or visitors to the nursery, include respiratory

syncytial virus, parainfluenza virus, influenza viruses, and adenovirus. Respiratory viruses are the single most important cause of community-acquired pneumonia and are usually contracted from infected household contacts.



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#### Clinical manifestations of neonatal pneumonia

- Respiratory distress (tachypnoe, apnoe, cyanosis, retractions)
- Vomiting, hypotension
- Poor weight gain, icterus, hypo/hyperthermia
- Pulmonary hypertension and hypoxemia R-->L shunting
- Reduced lungfunction (respirator patients)
- Increased tracheal aspirate

#### Therapy of neonatal pneumonia -

- Antibiotics
- General supportive therapy

## **Transient Tachypnea of the Newborn (TTN, wet lung)**

- **A mild respiratory disturbancy in newborn infants occasionally seen after birth**
- **Most common diagnosis of respiratory distress in the newborn**
- **Unknown etiology – increased lung water**
- **Ineffective clearance of amniotic fluid from lungs with delivery**
- **Most often seen at birth or shortly after.  
Duration max 5-6 days**

Transient Tachypnea of the Newborn definition  
Transient tachypnea usually follows uneventful normal preterm or term vaginal delivery or cesarean delivery. It may be characterized by the early onset of tachypnea, sometimes with retractions, or expiratory grunting and, occasionally,

cyanosis that is

relieved by minimal oxygen (<40%). Patients usually recover rapidly within 3 days.

## **Transient Tachypnea of the Newborn (TTN, wet lung)**

- **History**
  - Common with C-Section delivery
  - Maternal analgesia
  - Maternal anesthesia during labor
  - Maternal fluid administration
  - Maternal asthma, diabetes, bleeding
  - Perinatal asphyxia
  - Prolapsed cord

Transient Tachypnea of the Newborn Etiology

## Transient Tachypnea of the Newborn

- **X ray: perihilar streaking, patchy infiltrates**  
**Reduced air and/or reticular pattern**
- **Labs**
  - CBC within normal limits
  - ABG/CBG showing mild to moderate hypercapnia, hypoxemia with a respiratory acidosis

### *Therapy*

- **Observation in incubator**
- **Oxygen if needed**
- **Antibiotics until infection is excluded**

### Diagnostics and treatment of Transient Tachypnea of the Newborn

The lungs are generally clear without rales or rhonchi, and the chest x-ray shows prominent pulmonary vascular markings, fluid in the intralobar fissures, overaeration, flat diaphragms, and, rarely, pleural effusions. Hypercapnia and acidosis are uncommon. Distinguishing the disease from RDS may be difficult; the distinctive features of transient tachypnea are sudden recovery of the infant and the absence of x-ray findings of RDS (hypoaeration, diffuse reticulogranular pattern, air bronchograms). The syndrome is believed to be secondary to slow absorption of fetal lung fluid resulting in decreased pulmonary compliance and tidal volume and increased dead space. In severe cases, retained fetal fluid can interfere with the normal postnatal fall in pulmonary vascular resistance resulting in persistent pulmonary hypertension. Treatment is supportive. There is no evidence for the use of oral furosemide in this disorder.

## Pulmonary diseases in the newborn period

### Air leaks

- **Pneumothorax/mediastinum**
- **1% of all newborn but only 1/10 are symptomatic**
- **Increased risk in positive pressure ventilation**

Complications in newborns with bronchopulmonary diseases  
Complications related to RDS can occur spontaneously but are commonly the result of well-intended therapeutic interventions. Major complications include the consequences of mechanical ventilation, oxygen administration, and use of endotracheal tubes.

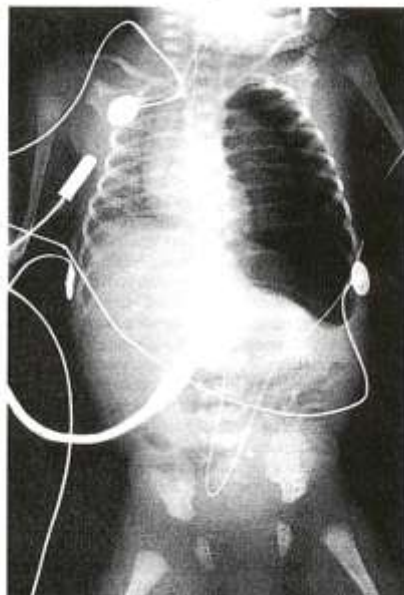


Fig. 29.43 Left tension pneumothorax, with displacement of left diaphragm downwards and mediastinum to the right. Note that the non-compliant left lung has only partially collapsed.

Complications in newborns with bronchopulmonary diseases

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### **Meconium Aspiration Syndrome (MAS)**

- **Frequency of Mec stained amniotic fluid = 10-25%**
- **OF MEC stained infants:**
  - 30 % depressed at birth
  - 10 % meconium aspiration syndrome (range 2-36 %)
- **OF infants with MEC aspiration syndrome**
  - 17 % deliver through thin meconium (range 7-35 %)
  - 35 % need mechanical ventilation (range 25-60 %)
  - 12 % die (range 5-37 %)

Meconium Aspiration Syndrome (MAS) definition and etiology  
Meconium-stained amniotic fluid is found in 10–15% of births and usually occurs in term or post-term infants. Meconium aspiration pneumonia develops in 5% of such infants; 30% of them require mechanical ventilation, and 3–

5% expire.

Usually, but not invariably, fetal distress and hypoxia occur before the passage of meconium into amniotic fluid. These infants are meconium stained and may be depressed and require resuscitation at birth. Meconium inactivates surfactant.

## Risk Factors for Meconium Passage

- **Postterm pregnancy**
- **Preeclampsia-eclampsia**
- **Maternal hypertension**
- **Maternal diabetes mellitus**
- **Abnormal fetal heart rate**
- **IUGR**
- **Abnormal biophysical profile**
- **Oligohydramnios**
- **Maternal heavy smoking**

Meconium Aspiration Syndrome (MAS) etiology

The risk of meconium aspiration may be decreased by rapid identification of fetal distress and initiating prompt delivery in the presence of fetal acidosis, late decelerations, or poor beat-to-beat variability. Despite initial enthusiasm for amnioinfusion, it does not reduce the risk of meconium aspiration syndrome, cesarean delivery, or other major indicators of maternal or neonatal morbidity. Nasopharyngeal suctioning of meconium-stained infants after delivery of the head was once considered a low-risk method of reducing the incidence of meconium aspiration syndrome (MAS).

## Meconium Aspiration Syndrome Pathophysiology

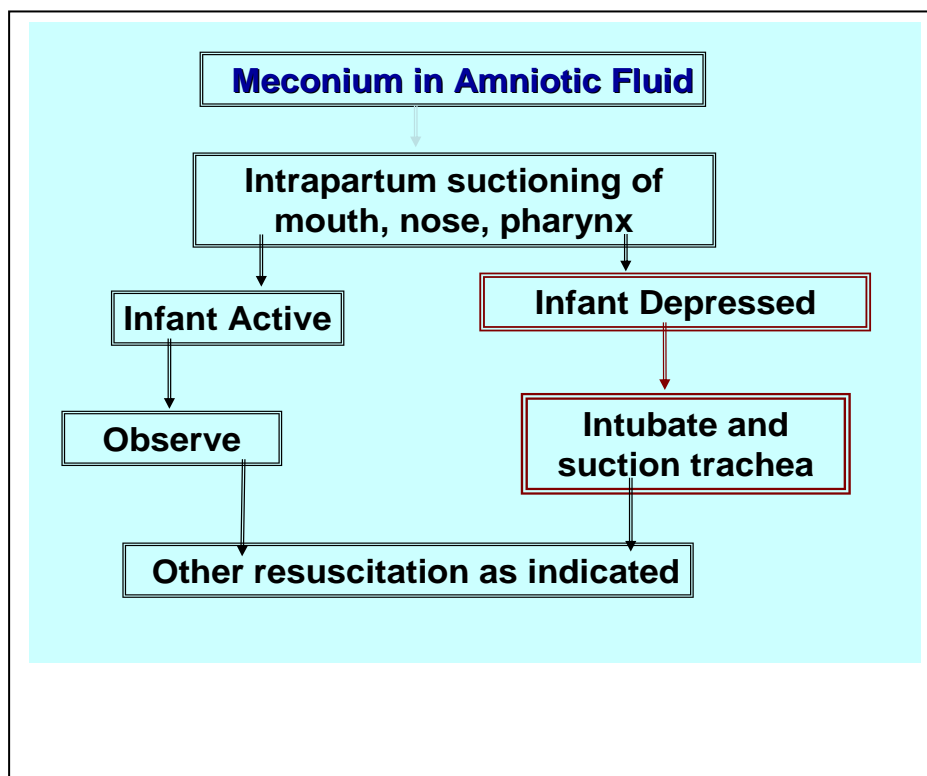
- **Airway obstruction of large and small airways**
- **Inflammation and edema**
  - **Protein leak**
  - **Inflammatory Mediators**
  - **Direct toxicity of meconium constituents = chemical pneumonitis**
- **Surfactant dysfunction or inactivation**
- **Effects of in utero hypoxemia and acidosis**
- **Altered pulmonary vasoreactivity (PPHN)**

The risk of meconium aspiration may be decreased by rapid identification of fetal distress and initiating prompt delivery in the presence of fetal acidosis, late decelerations, or poor beat-to-beat variability. Despite initial enthusiasm for amnioinfusion, it does not reduce the risk of meconium aspiration syndrome, cesarean delivery, or other major indicators of maternal or neonatal morbidity. Nasopharyngeal suctioning of meconium-stained infants after delivery of the head was once considered a low-risk method of reducing the incidence of meconium aspiration syndrome (MAS).

## Meconium Aspiration Syndrome Diagnosis

- **Known exposure to meconium stained amniotic fluid**
- **Respiratory symptoms not explained by other cause**
  - R/O pneumonia, RDS, spontaneous air leak
- **CXR changes - diffuse, patchy infiltrates, consolidation, atelectasis, air leaks, hyperinflation**

Meconium Aspiration Syndrome differential diagnosis



Depressed infants (those with hypotonia, bradycardia, fetal acidosis, or apnea) should undergo endotracheal intubation, and suction should be applied directly to the endotracheal tube to remove meconium from the airway. Treatment of meconium aspiration pneumonia includes supportive care and standard management for respiratory distress.



## Meconium Aspiration Syndrome Treatment

- **Ventilation strategies**
  - ❖ Avoid air leak, check CXR with acute deterioration
  - ❖ Prevent pulmonary hypertension - generous O<sub>2</sub>
  - ❖ HFOV if unable to maintain on conventional vent
- **Steroids** (no human data, controversial)
- **Antibiotics** (ampicillin, gentamicin)
- **Surfactant**
- Inhaled Nitric Oxide
- ECMO

Meconium Aspiration Syndrome treatment

The beneficial effect of mean airway pressure on oxygenation must be weighed against the risk of pneumothorax. Administration of exogenous surfactant to infants with MAS requiring mechanical ventilation decreases the need for ECMO support; the effect is greatest in those infants treated early. Severe meconium aspiration may be complicated by persistent pulmonary hypertension. Patients who are refractory to conventional mechanical ventilation may benefit from HFV, iNO, or ECMO

Meconium Aspiration Syndrome treatment

## Meconium Aspiration Syndrome Surfactant Treatment

### Results

- **No infant received more than 3 doses**
- **Significant improvement in OI, MAP, FiO<sub>2</sub> within 3-6 hours after 2nd dose of surfactant**
- **Significant improvement in a:A PO<sub>2</sub> within 1 hour of 1st dose of surfactant**

Meconium Aspiration Syndrome treatment

## **Meconium Aspiration Syndrome Outcome**

- High incidence **long term pulmonary problems**
  - ❖ At 6 months - 23% MAS with regular bronchodilator therapy\*
  - ❖ FRC was higher in symptomatic infants
  - ❖ IPPV and O2 were not predictors of problems
- Increased risk of poor **neurologic outcome** due to perinatal insult - seizures, CP, mental retardation

### Meconium Aspiration Syndrome outcome

The mortality rate of meconium-stained infants is considerably higher than that of non-stained infants. A decline in neonatal deaths due to meconium aspiration syndrome is related to improvements in obstetric and neonatal care. Residual lung problems are rare, but include symptomatic cough, wheezing, and persistent hyperinflation for up to 5–10 yr. The ultimate prognosis depends on the extent of CNS injury from asphyxia and the presence of associated problems such as pulmonary hypertension.

## **Pulmonary diseases in the newborn period**

### **Chronic Lung Disease**

### **(Bronchopulmonary Dysplasia)**

- **Preterm with RDS and artificial ventilation develop lung fibrosis and increased oxygen demand**
- **Typical chest X-ray (round woolen densities (fibrosis, emphysema, atelectasis), enlarged heart)**
- **The incidence has not changed after surfactant therapy was introduced but the course is milder. More immature infants survive but have to "pay" the prize with CLD**

Chronic Lung Disease (Bronchopulmonary Dysplasia) definition BPD or CLD occurs in a large fraction of infants surviving assisted ventilation. About 20% of infants with very low birthweight received oxygen supplementation at 36 weeks' corrected age

**Pulmonary diseases in the newborn period**  
**Chronic Lung Disease**  
**(Bronchopulmonary Dysplasia)**

- Preterm with RDS and artificial ventilation develop lung fibrosis and increased oxygen demand
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Chronic Lung Disease (Bronchopulmonary Dysplasia) definition

**Pulmonary diseases in the newborn period**  
**Chronic Lung Disease**  
**(Bronchopulmonary Dysplasia)**

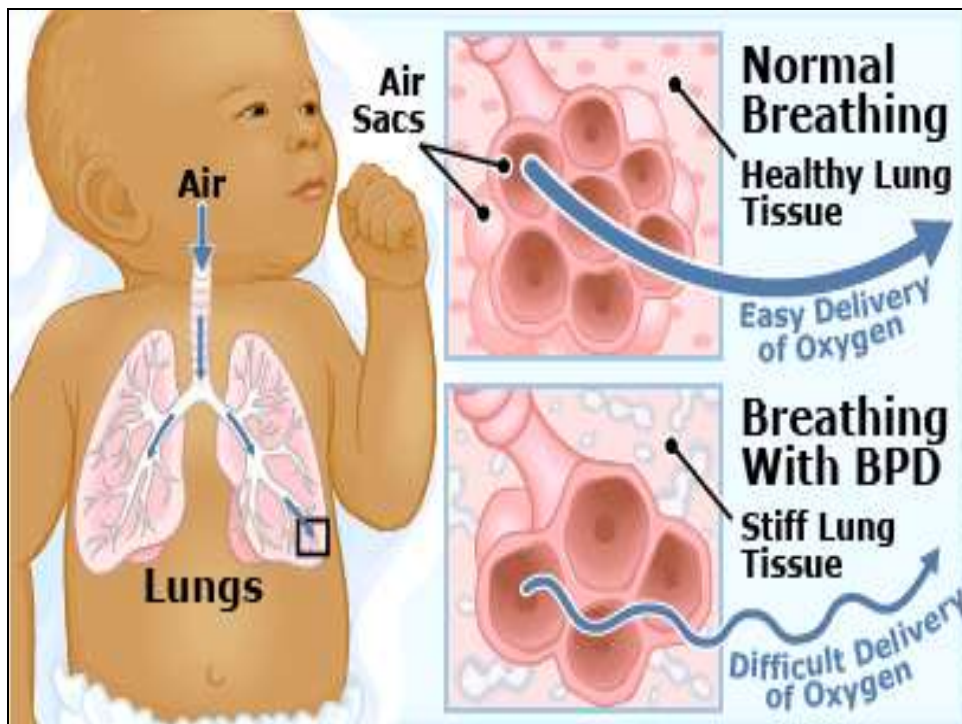
- Initially the child is better of its acute lung disease but then gradually needs more oxygen. Some are oxygen- and respirator dependent for months (years).
- 1/5 of children with RDS develop CLD

***Etiology***

- Inflammation (also prenatally)
- Oxygen toxicity /Free oxygen radicals
- Barotrauma- Volutrauma
- Chorioamnionitis reduces RDS but increases CLD

(The Watterberg paradox)

Chronic Lung Disease (Bronchopulmonary Dysplasia) etiology



[www.studyblue.com](http://www.studyblue.com)501 × 331 image screen\_shot\_2014-11-11\_at\_32308\_pm for definition

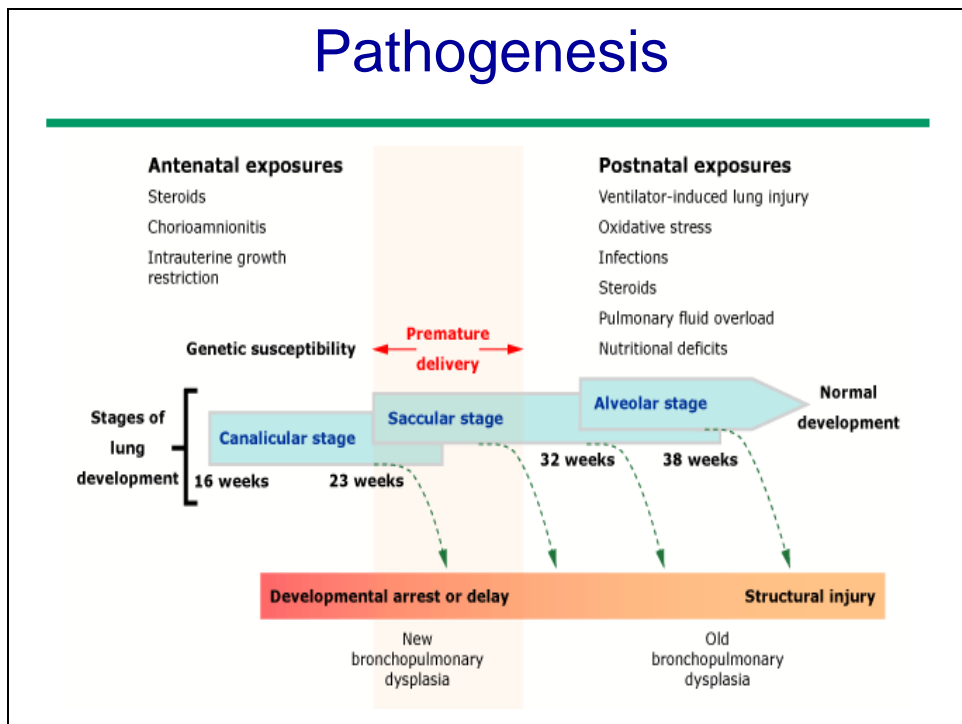
This scheme represents the morphological changes in the lung of patients with Chronic Lung Disease (Bronchopulmonary Dysplasia)

Bronchopulmonary Dysplasia		
	Gestational age	
	<32 week	≥32 week
Time point of assessment	36 weeks PMA or discharge to home, whichever comes first	>28 days but <56 days postnatal age or discharge to home, whichever comes first
	Treatment with oxygen >21 percent for at least 28 days plus	
Mild BPD	Breathing room air at 36 weeks PMA or discharge, whichever comes first	Breathing room air by 56 days postnatal age or discharge, whichever comes first
Moderate BPD	Need* for <30 percent oxygen at 36 weeks PMA or discharge, whichever comes first	Need* for <30 percent oxygen at 56 days postnatal age or discharge, whichever comes first
Severe BPD	Need* for ≥30 percent oxygen and/or positive pressure (PPV or NCPAP) at 36 weeks PMA or discharge, whichever comes first	Need* for ≥30 percent oxygen and/or positive pressure (PPV or NCPAP) at 56 days postnatal age or discharge, whichever comes first

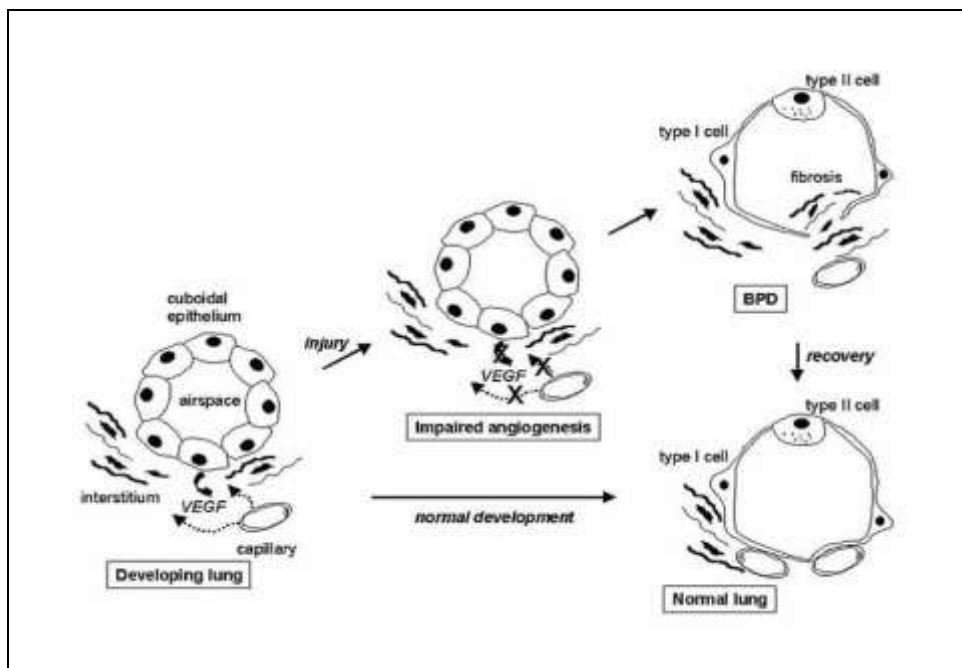
This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) severity definition. Prevention of lung injury has become more important with the marked increase in survival that has followed many recent respiratory and other therapeutic advances in

neonatology.

Various mechanisms could be involved in the development of lung injury in neonates



This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) pathogenesis

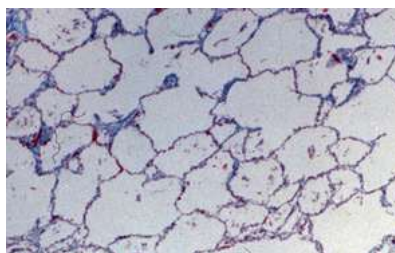
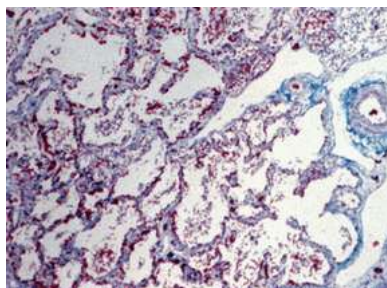


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This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) pathogenesis

## Pathophysiology

- **Old BPD:**
  - Airway injury, inflammation and parenchymal fibrosis due to mechanical ventilation and oxygen toxicity
- **New BPD:**
  - Decreased septation and alveolar hypoplasia leading to fewer and larger alveoli, so less surface area for gas exchange
  - Dysregulation of vascular development leading to abnormal distribution of alveolar capillaries and thickened muscular layer of pulmonary arterioles



<https://www.google.com.ua/search?q=Surfactant+cycle&rlz>

This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) pathophysiology

## Bronchopulmonary Dysplasia

- **“Old BPD” (before surfactant and steroids)**
  - Cystic changes, heterogeneous aeration
- **“New BPD” (after surfactant and steroids)**
  - More uniform inflation and less fibrosis, absence of small and large airway epithelial metaplasia and smooth muscle hypertrophy
  - Some parenchymal opacities, but more homogenous aeration and less cystic areas
  - **PATHOLOGIC HALLMARKS:** larger simplified alveoli and dysmorphic pulmonary vasculature



This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) pathophysiology

Fanaroff and Martin's neonatal-perinatal medicine: diseases of the fetus and infant. 18<sup>th</sup> Edition / edited by R.J. Martin, A.A. Fanaroff, M.C. Walsh. – Philadelphia : Elsevier Mosby, 2006. – Chapter 42. /das/book/0/view/1349/1.html/top

## Medical care in BPD

The following medications are used in the management of bronchopulmonary dysplasia:

- **Diuretics** (Furosemide, Thiazides)
- **Bronchodilators** (albuterol, caffeine citrate, theophylline, ipratropium bromide)
- **Corticosteroids** (systemic corticosteroids – dexamethasone, Inhaled steroids)
- **Vitamins** (vitamin A)

This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) treatment

## Prognosis

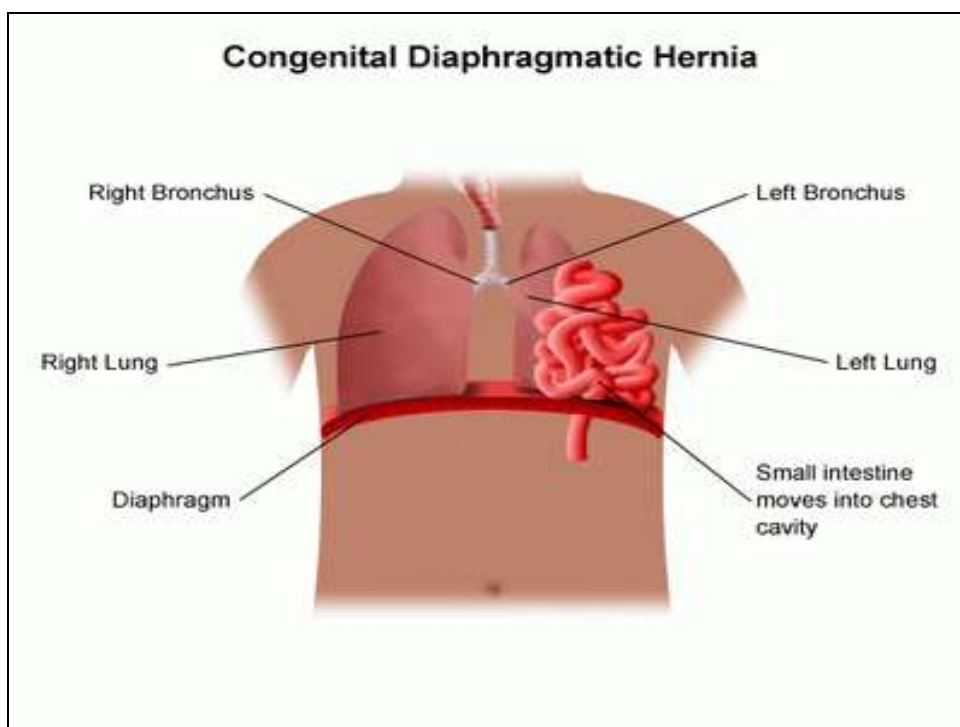
- **Morbidity:**
  - Higher rates of hospitalization in the first year of life e.g. resp infections
  - **Respiratory symptoms** may persist into adulthood
    - Abnormal pulmonary function
    - Asthma-like symptoms
  - Airway abnormalities e.g. tracheomalacia
  - Pulmonary artery hypertension
- BPD associated with worse **neurodevelopmental outcomes**

This scheme represents Chronic Lung Disease (Bronchopulmonary Dysplasia) prognosis. Because the etiology of lung injury in neonates is multifactorial, it should be expected that any individual intervention will only have limited and small effects on the incidence of BPD.

## Congenital Abnormalities of the Lung and Thorax

- Congenital Heart Disease (CHD)
- Congenital Diaphragmatic Hernia (CDH)
- Congenital Cystic Adenomatiod Malformation
- Tracheal Abnormalities
- Esophageal Atresia
- Pulmonary Hypoplasia

This scheme represents differential diagnosis in newborns with bronchopulmonary pathology



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This scheme represents differential diagnosis in newborns with bronchopulmonary pathology

CDH can be diagnosed on prenatal ultrasound (between 16 and 24 wk) in over 50% of cases. High-speed magnetic resonance imaging can further define the lesion. Findings on ultrasound may include polyhydramnios, chest mass, mediastinal shift, gastric bubble or a liver in the thoracic cavity, and fetal hydrops. Certain imaging features may predict outcome; these include lung size to head size ratio (LHR). Nonetheless, there is no definitive characteristic that reliably predicts outcome



## Congenital Diaphragmatic Hernia

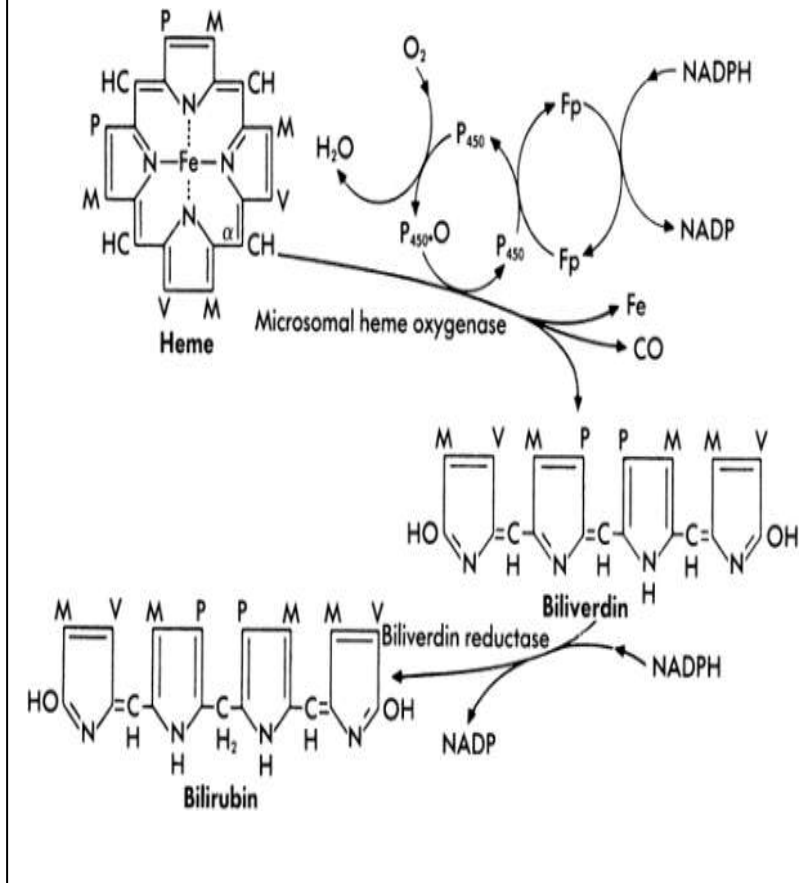
- Clinical Assessment
  - Scaphoid Abdomen- classic sign
  - Color
    - Cyanotic
  - Heart Rate
    - Fast, slow or normal
  - Perfusion
    - Depends upon the severity
  - X-Ray—Best diagnostic tool
    - Bowel, stomach, liver in chest
  - ABGs
    - Acidosis, hypoxemia and hypercarbia

This scheme represents differential diagnosis in newborns with bronchopulmonary pathology

After delivery, a chest radiograph is needed to confirm the. In some instances with an echogenic chest mass, further imaging is required. The **differential diagnosis** may include a cystic lung lesion (pulmonary sequestration, cystic adenomatoid malformation) requiring an upper gastrointestinal series to confirm the diagnosis.

## **Origin, differential diagnosis and therapy of jaundices in neonates**

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



Bilirubin occurs in plasma in four forms: (1) unconjugated bilirubin tightly bound to albumin; (2) free or unbound bilirubin (the form responsible for kernicterus, because it can cross cell membranes); (3) conjugated bilirubin (the only fraction to appear in urine); and (4)  $\delta$  fraction (bilirubin covalently bound to albumin), which appears in serum when hepatic excretion of conjugated bilirubin is impaired in patients with hepatobiliary disease. The  $\delta$  fraction permits conjugated bilirubin to persist in the circulation and delays resolution of jaundice.

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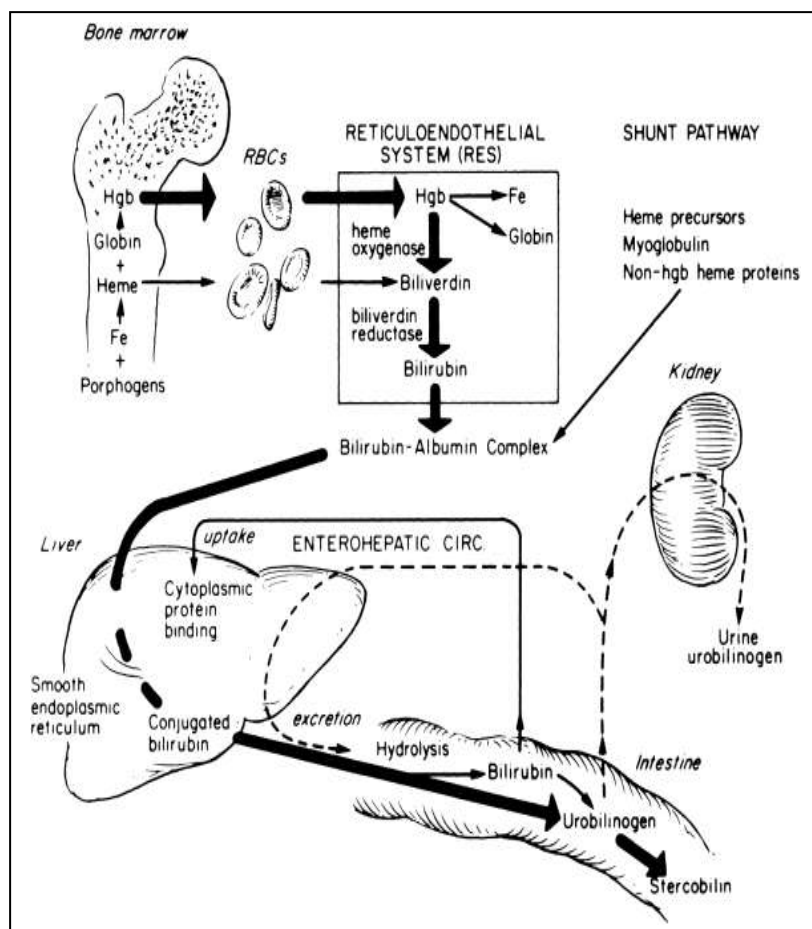
**Jaundice** is one of symptoms are observed in most of children of newborn period. According to the literature almost in 65% of children jaundice was observed in the first week of life. The necessity to be able differentiate jaundices in dependence of their etiopathogenesis is caused by possibilities for physical inability or even leads to death, having different levels of hyperbilirubinaemia.



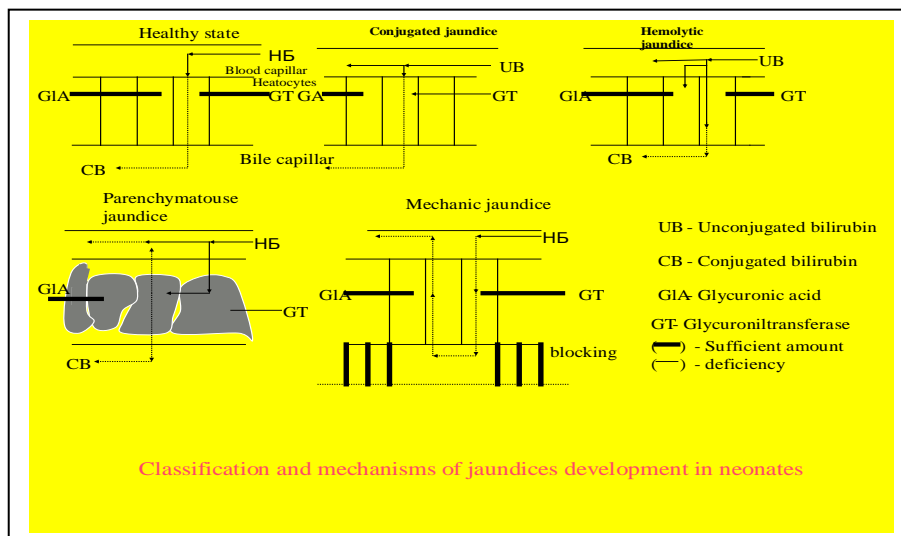
The physiological icterus develops in all newborns in the first days of life, whereas a skin yellowness only at 60-70 %. It appears for 2-5 day after birth, in the majority of children - not earlier than 36 hours of life. Firstly on the face, then on a trunk, extremities, conjunctives and mucous. The general state of term newborns remains unchanged.

<http://2.everyday-families.com/wp-content/uploads/2013/08/jaundice-in-newborns.jpg>

### The pathways of bilirubin synthesis, transport, and metabolism (Hgb, hemoglobin, RBCs, red blood cell)



In the normal adult, bilirubin is derived primarily from the degradation of heme contained in the circulating erythrocyte when senescence results in its lysis in the reticuloendothelial cells of the body. Erythrocyte precursors and other hemoproteins (mainly cytochromes, catalase) normally contribute about 20% of the bilirubin excreted into bile. Carbon monoxide excretion in humans and more direct measurements in animals have demonstrated that, in the first day of life, bilirubin production is increased to an estimated average of 8 to 10 mg/kg of body weight per day, an amount about two or three times greater than that of adults



Bilirubin exists in four different forms in serum:

- (1) unconjugated bilirubin reversibly bound to serum albumin, which makes up the major portion;
- (2) a relatively minute fraction of unconjugated bilirubin not bound to serum albumin (“free bilirubin”);
- (3) conjugated bilirubin

(mainly monoglucuronides and diglucuronides) readily excretable through the renal or biliary systems; and (4) conjugated bilirubin covalently bound to serum albumin (“ $\delta$ ” bilirubin), with a plasma disappearance rate similar to that of serum albumin. Conjugated bilirubin, but not  $\delta$ -bilirubin, gives a “direct” reaction with standard diazo reagents, whereas bound or unbound unconjugated bilirubin yields an “indirect” reaction.  $\delta$ -Bilirubin, virtually absent in the first 2 weeks of life, can be measured only with the newer techniques that do not first precipitate plasma proteins, such as in the Eastman Kodak (Ektachem) system.  $\delta$ -Bilirubin is found in detectable amounts in normal older neonates and children, and in significantly increased concentrations in those with prolonged conjugated hyperbilirubinemia resulting from various liver disorders.



In physiological jaundice the increasing of bilirubin level occurs for the unconjugated fraction (UB). Skin yellowness usually occurs in newborns in 2-3 day of life when UB concentration achieves of 51  $\mu\text{mol/l}$  in term newborns and 85  $\mu\text{mol/l}$  in preterms. Further, during the next some days continues the bilirubin increasing reaching it maximum to 3-4 days and after bilirubin gradually decreased, skin yellowness turn pale and disappears to the end of first or beginning of second week.

<http://www.wisegeek.org/what-is-jaundice.htm>



The signs of physiological jaundice:

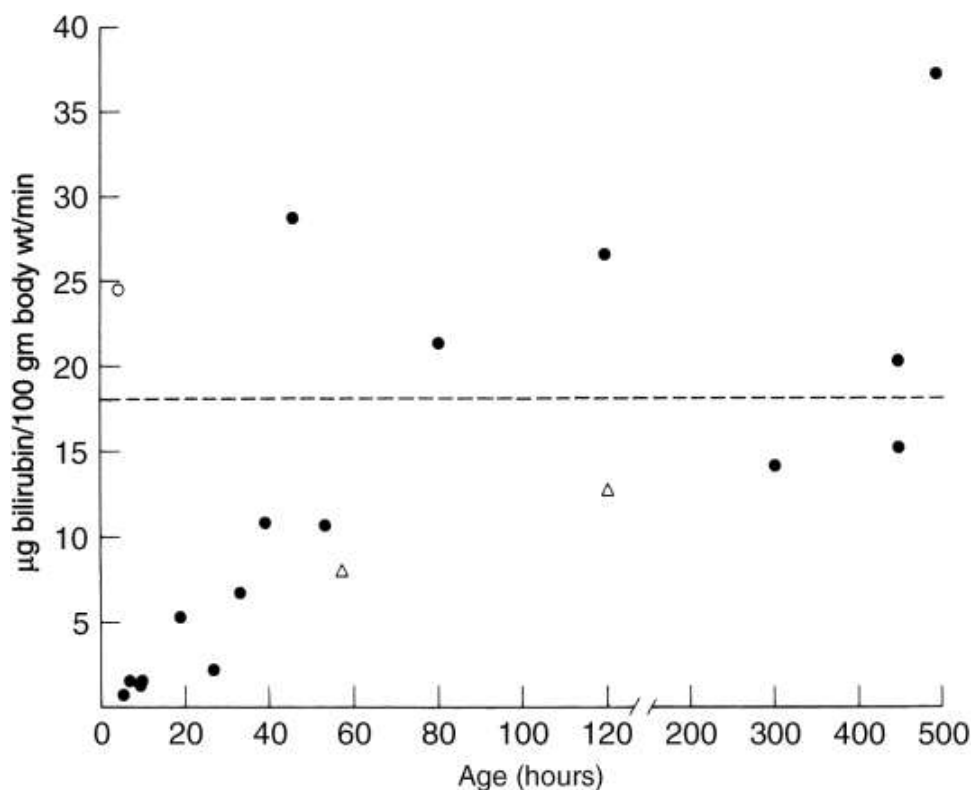
1. General state unchanged, no complaints.
2. Jaundice appears on 3-5 day after birth and stopped to 10 day.
3. Intensity is mild from the insignificant subicterity to more bright icterity.
4. There is no enlargement of liver and

<http://www.dreamstime.com/stock-photo-newborn-jaundice-baby-hospital-baby-acne-image35748010>

spleen (despite we can palpate it normally in newborns).

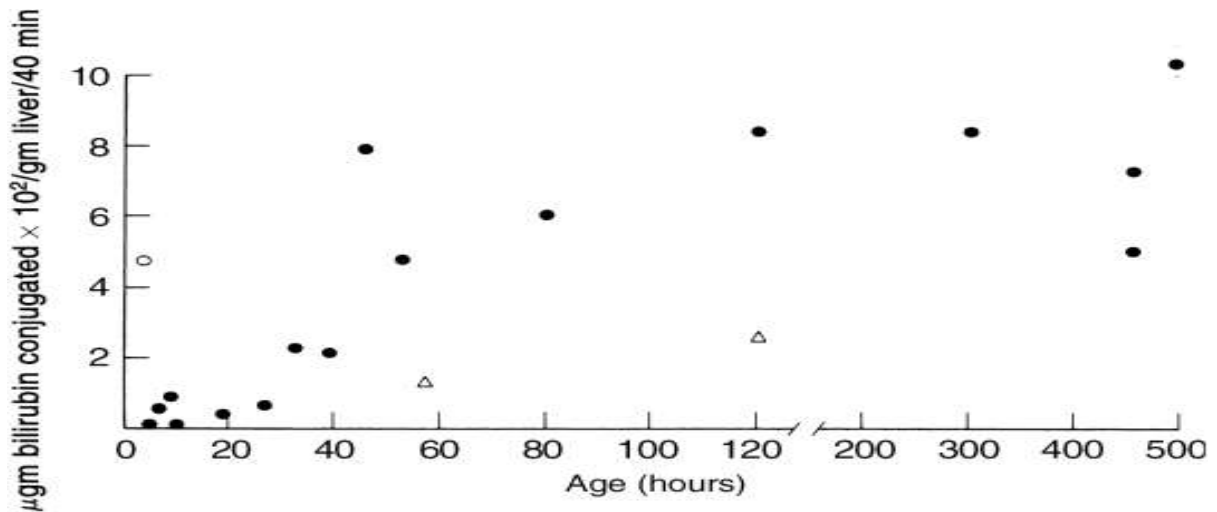
5. Bilirubin level is no exceeding 51-108  $\mu\text{m}/\text{l}$ . If level more than 35  $\mu\text{m}/\text{l}$  the jaundice become visible.

6. Blood test unchanged: hemoglobin 180-240  $\text{g}/\text{l}$ , RBC to  $6 \times 10^{12}$ .

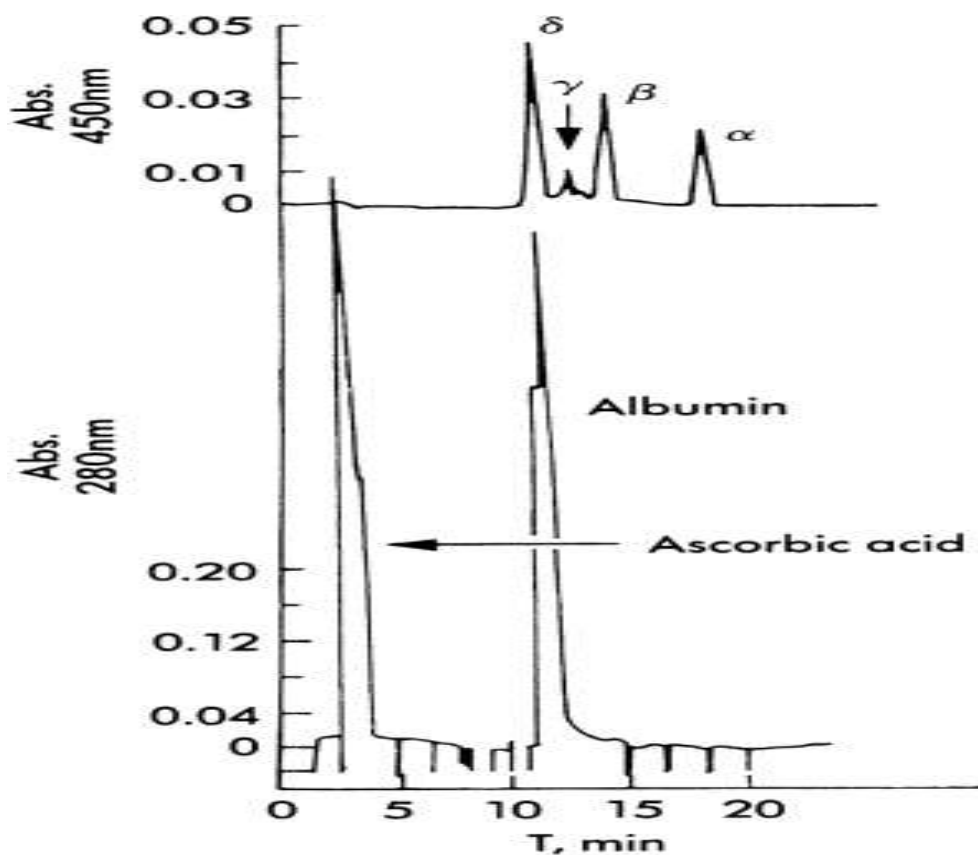


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Maximal hepatic bile bilirubin excretion in term (*filled circles*), premature (*triangles*), and postmature (*open circle*) newborn rhesus monkeys. The horizontal *dashed line* represents mean normal hepatic bile bilirubin excretion for nine adult rhesus monkeys ( $18.2 \pm 1.0$  SEM).

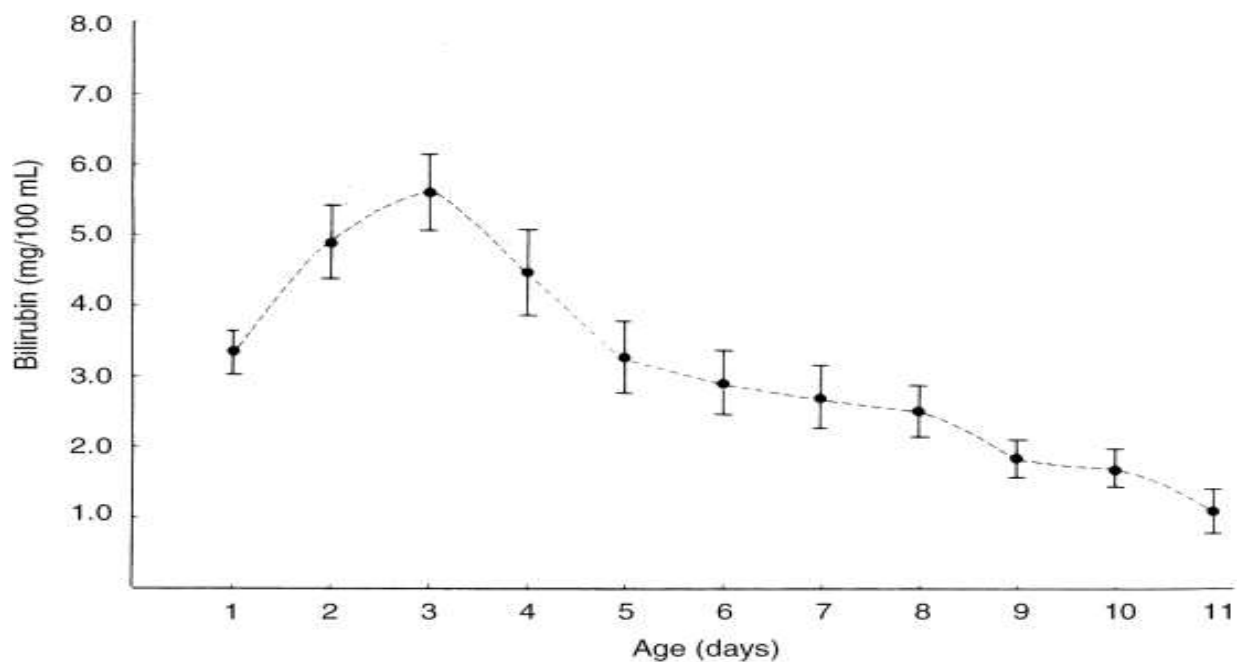


Hepatic bilirubin uridine diphosphoglucuronate glucuronosyltransferase (UGT) activity in term (*filled circles*), premature (*triangles*), and postmature (*open circle*) newborn rhesus monkeys.



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Separation of serum bilirubin fractions by high-performance liquid chromatography, showing bilirubin profiles at 450 nm (*upper trace*) and 280 nm (*lower trace*).  $\alpha$ , unconjugated bilirubin;  $\beta$ , monoconjugated bilirubin;  $\delta$ , delta fraction bilirubin;  $\gamma$ , diconjugated bilirubin; Abs, absorption.



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Mean total serum bilirubin (TSB) concentrations in 22 full-term normal white and African-American infants during the first 11 days of life.



Pathologic factors  
aggravating physiologic  
jaundice:

- Prematurity
- Infections
- Inadequate calories
- Dehydration
- Hypoxia
- Meconium retention
- Hemolysis
- Hypoglycemia
- Intestinal obstruction
- Polycythemia
- Hypothyroidism

<http://www.mounnittany.org/articles/healthsheets/5475>



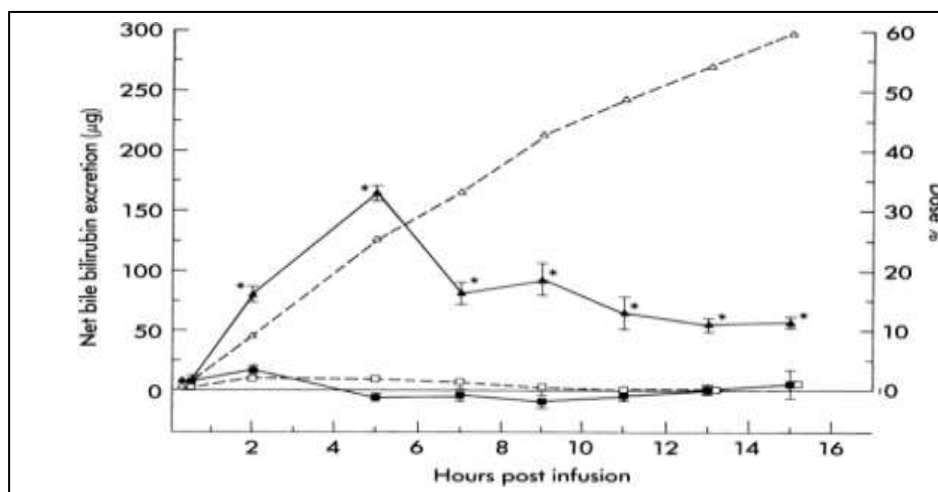


#### Causes of conjugated hyperbilirubinemia:

- Extrahepatic biliary disease
- Biliary atresia
- Choledochal cyst
- Bile duct stenosis
- Spontaneous perforation of the bile duct
- Cholelithiasis
- Neoplasms
- Intrahepatic biliary disease
- Intrahepatic bile duct paucity (syndromic or nonsyndromic)
- Progressive intrahepatic cholestasis
- Inspissated bile
- Hepatocellular disease

<http://reference.medscape.com/features/slideshow/strange-coloration>

- Metabolic and genetic defects
- $\alpha$ 1-antitrypsin deficiency, cystic fibrosis, Zellweger's syndrome,
- Dubin-Johnson and Rotor's syndromes, galactosemia
- Infections
- Total parenteral nutrition
- Idiopathic neonatal hepatitis
- Neonatal hemochromatosis
- 

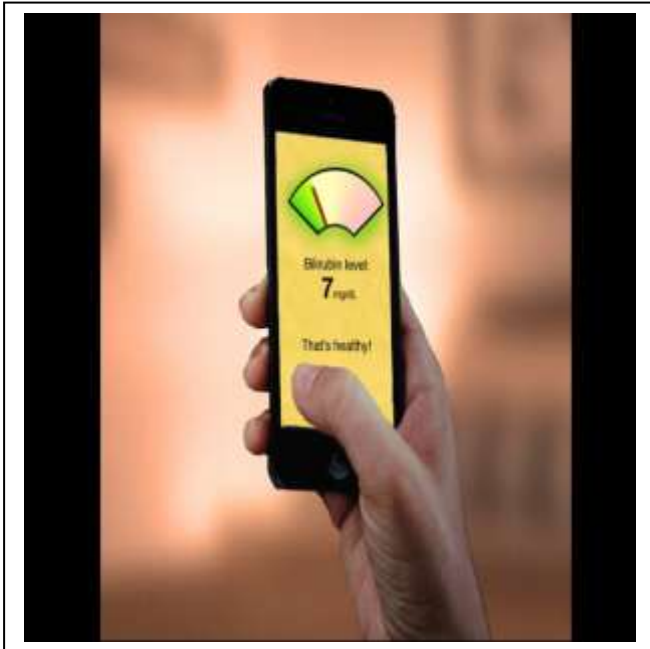


Net rate of bilirubin excretion in adult rat bile over 15 hours after intraduodenal administration of 1000  $\mu$ g unconjugated bilirubin in normal human milk at pH 8.6 (filled squares, mean  $\pm$  SEM;  $n = 5$ ) and human milk

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from mothers of infants with breast milk jaundice syndrome, pH 8.6 (filled triangles, mean  $\pm$  SEM;  $n = 5$ ). Cumulative net bilirubin excretion in bile for the same experiments expressed as a percentage of administered dose (open squares, bilirubin in normal human milk; open triangles, bilirubin in human milk from mothers of infants with breast milk jaundice syndrome). Asterisks indicate  $P < .$

01 for bilirubin in normal human milk versus bilirubin in human milk from mothers of infants with breast milk jaundice syndrome.



### **Causes of unconjugated hyperbilirubinemia**

#### **Physiologic jaundice Hemolytic anemia**

Congenital: red blood cell defects (hereditary spherocytosis, infantile pyknocytosis, pyruvate kinase deficiency, G6PD deficiency, and thalassemia)  
Acquired: blood group incompatibilities (ABO or Rh incompatibility), infection, and drug-induced hemolysis

#### **Polycythemia Blood extravasation**

<http://reference.medscape.com/features/slideshow/strange-coloration>



### **Defects of conjugation**

Congenital: Crigler-Najjar syndrome (types I and II), Gilbert syndrome

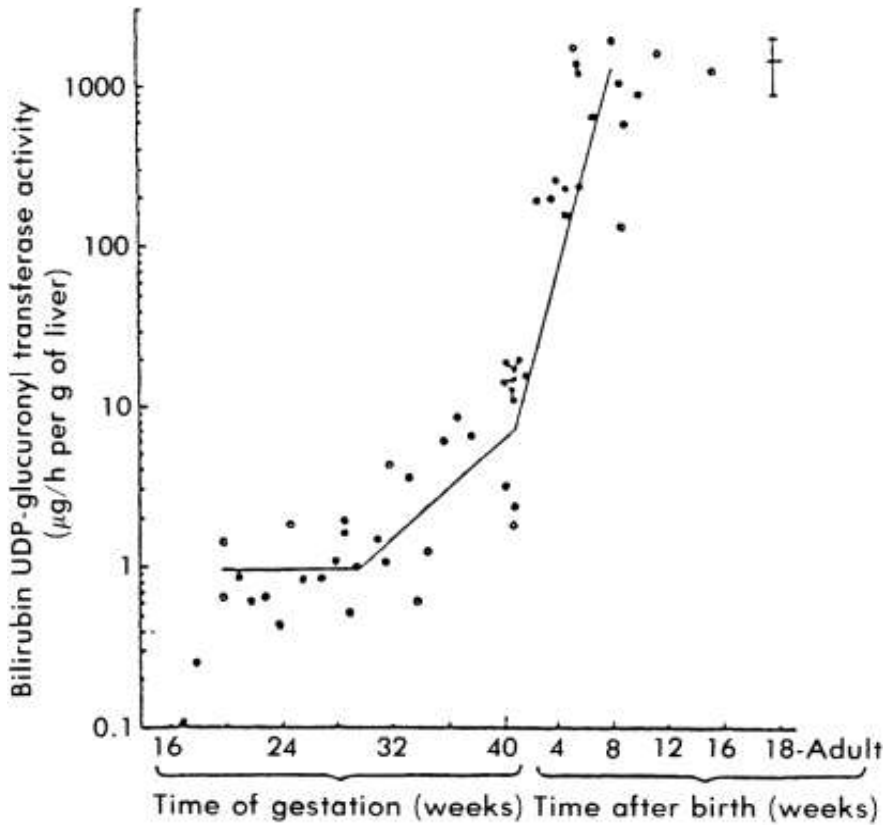
Acquired: Lucey-Driscoll syndrome

### **Breast-feeding and breast milk jaundice**

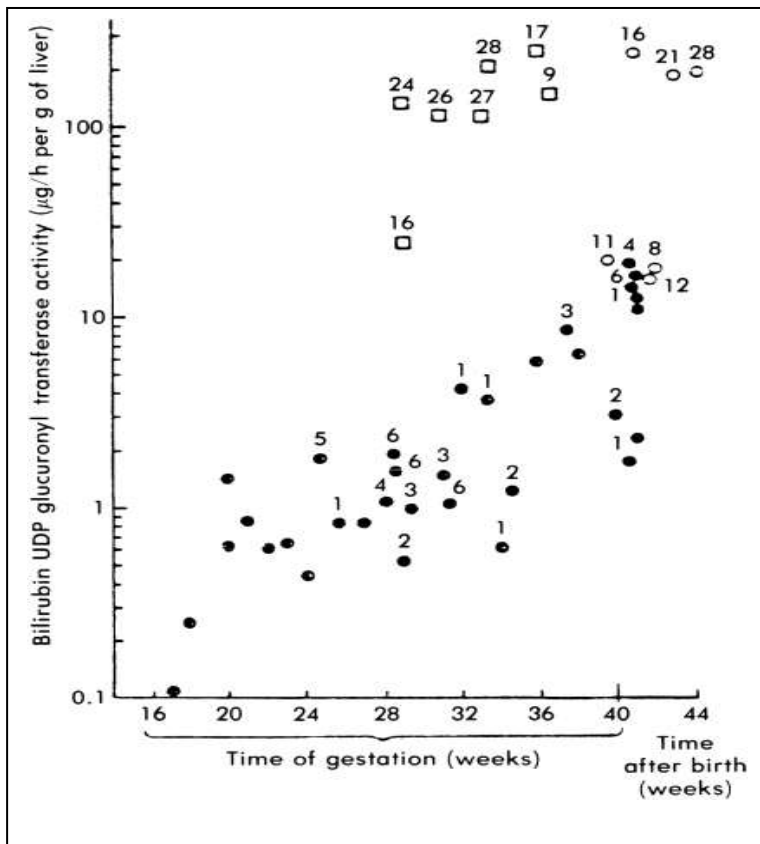
**Metabolic disorders:** galactosemia, hypothyroidism

**Increased enterohepatic circulation of bilirubin**  
**Substances/ disorders affecting binding of bilirubin to albumin:** drugs, fatty acids in nutritional products, asphyxia, acidosis, sepsis, hypothermia, hyperosmolality, hypoglycemia  
G6PD, glucose-6-phosphate dehydrogenase.

<https://www.netterimages.com/phototherapy-and-exchange-transfusion-in-hyperbilirubinemia-unlabeled-pediatrics-carlos-dragonfly-57>



Developmental pattern of hepatic bilirubin uridine diphosphoglucuronate glucuronosyltransferase (UGT) activity in humans



Effect of premature birth on development of hepatic bilirubin uridine diphosphoglucuronate glucuronosyltransferase (UGT) activity in humans. Numbers beside symbols represent age (days) at which activities were measured. Symbols represent enzyme activities for premature (*open squares*) and full-term (*open circles*) infants who lived more than 8 days after birth, and for fetuses and premature and full-term infants who died within 7 days of delivery (*filled circles*).

## Genetics of the ABO System

A person with at least one A gene will produce the A protein



Type A

A person with at least one B gene will produce the B protein



Type B

A person with one A gene and one B gene will produce both proteins

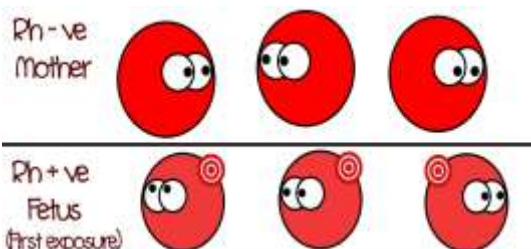


Type AB

A person with neither A nor B gene will not produce either protein



Type O



Mother's immune system recognizes the new antigen as non self.

That cell doesn't look familiar!



Looks like a trespasser.  
We better catch it next time!

Mother's white blood cells produce IgM antibodies.  
IgM does not cross the placenta.  
First baby is safe.


Immunology Insight

<http://www.rheumatologynetwork.com/articles/hemolytic-disease-newborn/page/0/2>

## Conditions associated with increased erythrocyte destruction

1. Isoimmunization
  - Rh incompatibility
  - ABO incompatibility
  - Other blood group incompatibilities
2. Erythrocyte biochemical defects
  - Glucose-6-phosphate deficiency
  - Pyruvate kinase deficiency
  - Hexokinase deficiency
  - Congenital erythropoietic porphyria
  - Other biochemical defects
3. Structural abnormalities of erythrocytes
  - Hereditary spherocytosis
  - Hereditary elliptocytosis
  - Infantile pyknocytosis
  - Other
4. Infection
  - Bacterial
  - Viral
  - Protozoal
5. Sequestered blood
  - Subdural hematoma and cephalohematoma
  - Ecchymoses
  - Hemangiomas

### Laboratory evaluation of the jaundiced infant with gestation $\geq 35$ weeks

INDICATIONS	ASSESSMENTS
Jaundice in first 24 hours	TcB and/or TSB
Jaundice appears excessive for infant's age	TcB and/or TSB
Infant receiving phototherapy, or TSB rising rapidly (i.e., crossing percentiles and unexplained by history and physical examination)   <small>wiseGEEK</small>	Blood type and Coombs' test, if not obtained with cord blood
	CBC and smear
	Direct or conjugated bilirubin
	Options: reticulocyte count, G6PD, and ETCoc if available
	Repeat TSB in 4 to 24 hours, depending on infant's age and TSB level
TSB concentration approaching exchange levels or not responding to phototherapy	Reticulocyte count, G6PD, albumin, ETCoc (if available)
Elevated direct (or conjugated) bilirubin level	Urinalysis and urine culture
	Evaluate for sepsis indicated by history and physical examination
Jaundice present at or beyond age 3 weeks, or sick infant	Total and direct (conjugated) bilirubin level
	If direct bilirubin elevated, evaluate for causes of cholestasis
	Check results of newborn thyroid and galactosemia screen, evaluate for signs and symptoms of hypothyroidism
CBC, complete blood count; ETCoc, end-tidal carbon monoxide, corrected for inhaled CO; G6PD, glucose-6-phosphate dehydrogenase; TcB, transcutaneous bilirubin; TSB, total serum bilirubin.	

### Risk factors for development of severe hyperbilirubinemia in Infants $\geq 35$ weeks of gestation



#### Major Risk Factors

- Predischarge TSB or TcB level in the high-risk zone
- Jaundice observed in the first 24 hours
- Blood group incompatibility with positive direct antiglobulin test, other known hemolytic disease (e.g., G6PD deficiency), elevated ETCOc
- Gestational age 35 to 36 weeks
- Previous sibling received phototherapy
- Cephalohematoma or significant bruising
- Exclusive breastfeeding, particularly if nursing poorly and weight loss is excessive
- East Asian race

#### Minor Risk Factors

- Predischarge TSB or TcB in the high-intermediate-risk zone
- Gestational age 37 to 38 weeks
- Jaundice observed before discharge
- Previous sibling with jaundice
- Macrosomic infant of diabetic mother
- Maternal age  $\geq 25$  years
- Male sex

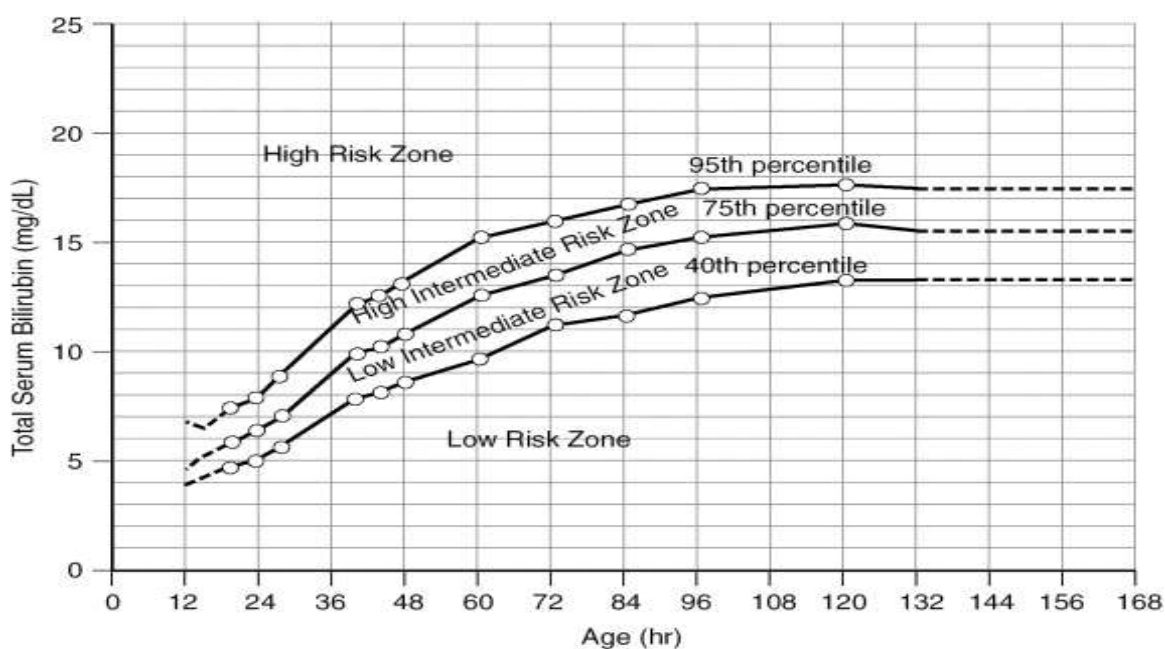
#### Decreased Risk Factors \*

- TSB or TcB in the low-risk zone
- Gestational age  $\geq 41$  weeks
- Exclusive bottle feeding
- Black race
- Discharge from hospital after 72 hours

BIRTHWEIGHT	Total Serum Bilirubin Level (mg/dL)			
	Healthy		Sick	
	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion
<1000 g	5–7	Variable	4–6	Variable
1001–1500 g	7–10	Variable	6–8	Variable
1501–2000 g	10–12	Variable	8–10	Variable
2001–2500 g	12–15	Variable	10–12	Variable

**Guidelines for the management of hyperbilirubinemia based on the birthweight and relative health of the newborn**

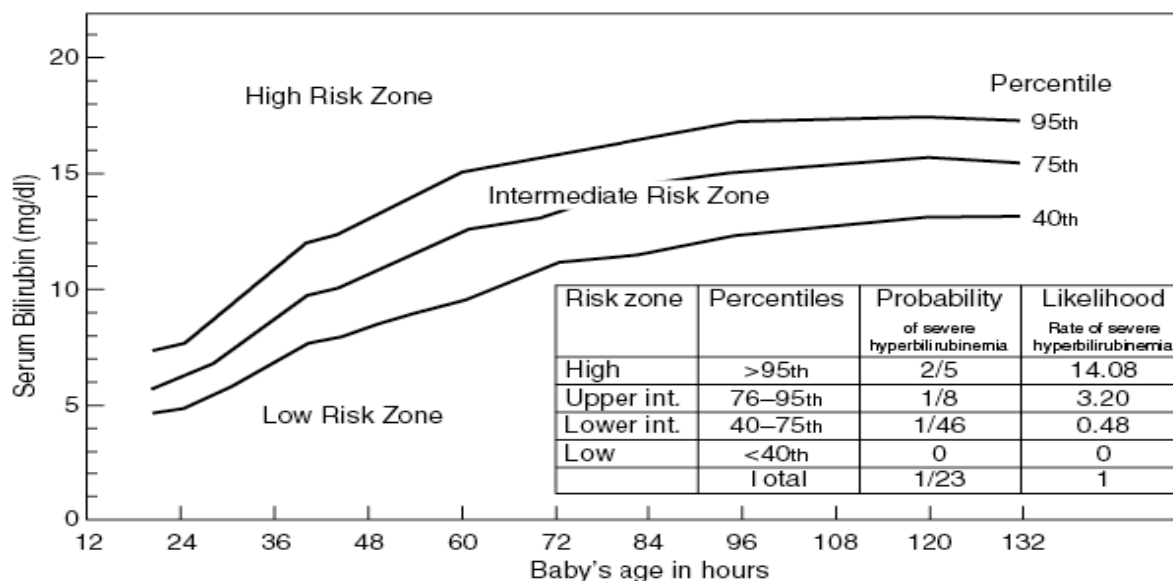
Total serum bilirubin levels rising at a rate greater than 0.5 mg/dL per hour (8.6  $\mu$ mol/L) indicate a state of active hemolysis; such patients should be considered as falling into the “sick” category. It is exceedingly important in these cases to institute and revise therapies on the basis not only of the current level of bilirubin but also of an estimate of the anticipated peak. Thus, early in the patient’s course, phototherapy or exchange transfusion may occur at a relatively lower bilirubin level than for a similar bilirubin level achieved at a later time



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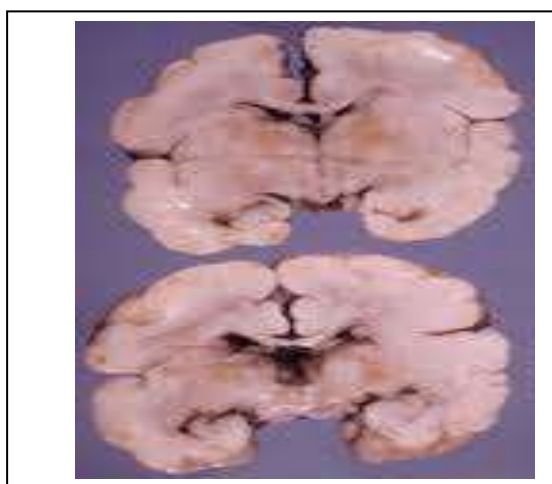
Outcome of newborns as defined by the percentage of newborns that remain or move up to the high-risk zone after their risk assessment with the predischarge bilirubin value (represented by the *shaded area*). A, Outcome for newborns designated in the high-risk zone ( $n = 172$ ). B, Outcome of newborns in upper-intermediate-risk zone ( $n = 356$ ). C, Outcome of newborns in the lower-intermediate-risk zone ( $n = 556$ ). D, Outcome of newborns in the low-risk zone ( $n = 1756$ ).

### Zones of risk for pathologic hyperbilirubinemia based on hour-specific serum bilirubin levels.



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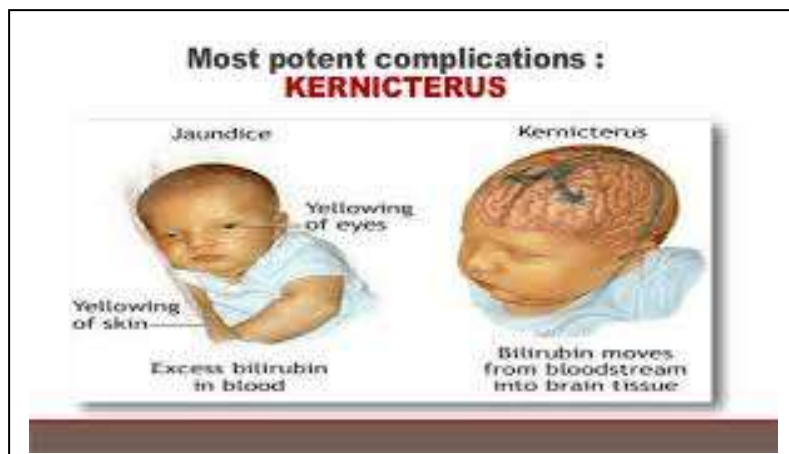
### Hour-specific bilirubin nomogram with the predictive ability of the predischarge bilirubin value for subsequent severe hyperbilirubinemia, >95th percentile tract.



#### Bilirubin encephalopathy

- If early acute bilirubin encephalopathy is unrecognized or untreated, it may progress to permanent neurologic impairment. The term kernicterus (German kern, kernel or nucleus, and ikteros, jaundice) has been traditionally used to describe the pathologic findings of bilirubin toxicity within the brain: staining and necrosis of neurons in the basal ganglia, hippocampal cortex, subthalamic nuclei, and cerebellum followed by gliosis of these areas should the patient survive.
- The cerebral cortex is generally spared. Approximately half of all infants with kernicterus observed at autopsy also have extraneural lesions of bilirubin toxicity. These include necrosis of renal tubular cells, intestinal mucosa, and pancreatic cells in association with intracellular crystals of bilirubin. Gastrointestinal hemorrhage may accompany these lesions.





### Kernicterus:

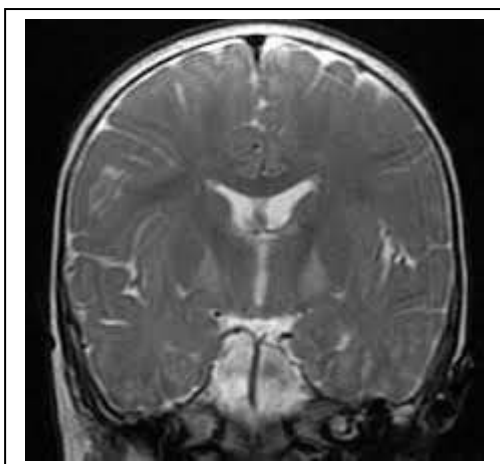
- Term kernicterus is also used to describe the clinical presentation of worsening encephalopathy. In the term newborn, several phases of kernicterus have been classically described.

<http://www.mumzone.com.au/newborns-with-yellow-skin-could-it-be-jaundice/>

- Phase 1 is marked by poor sucking, hypotonia, and depressed sensorium. Fever, retrocollis, and hypertonia that may progress to frank opisthotonos are seen
- Phase 2. The hypertonia becomes less pronounced
- Phase 3. High-pitched cry, hearing and visual abnormalities, poor feeding, and athetosis are manifest. Seizures may also occur.

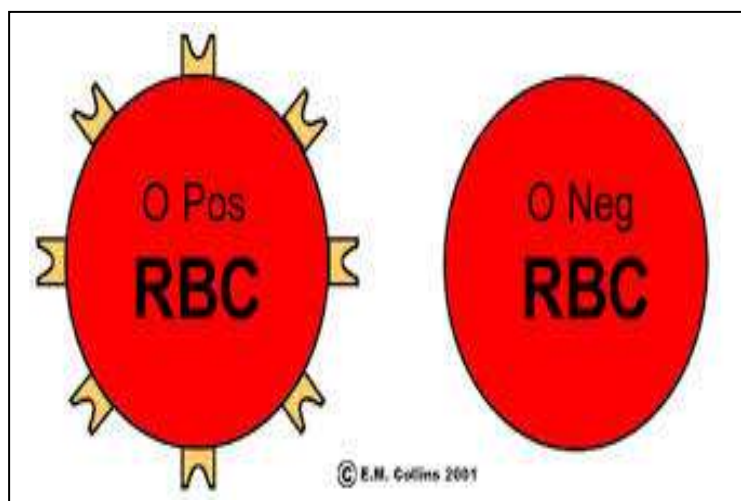


The usual time course for progression of the disease is approximately 24 hours. Long-term survivors often demonstrate choreoathetoid cerebral palsy, upward gaze palsy, sensorineural hearing loss, and, less often, mental retardation, and dental dysplasia during later infancy and childhood. Although these affected infants have severe physical handicaps and normal intellect, rehabilitation and education are difficult and



These sequelae of bilirubin toxicity may also develop in neonates who never manifested clinical signs of acute bilirubin encephalopathy during the newborn period. In addition, earlier epidemiologic studies suggest that some neonates may have sequelae of subclinical bilirubin encephalopathy characterized only by the later development of mild disorders of motor function or abnormal cognitive function, or both

<http://www.rheumatologynetwork.com/articles/hemolytic-disease-newborn/page/0/2>

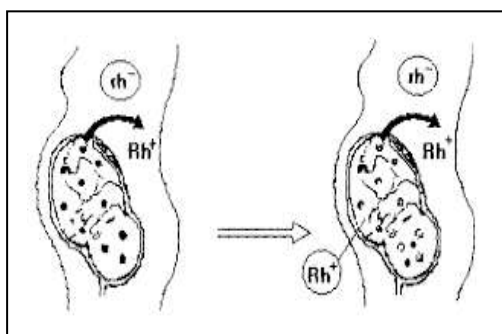


Clinical and serologic differences of hemolytic disease among ABO and Rh sensitization

1. a - и b –agglutinins normally exists in blood serum of mother and capable to penetrate fetus. Rh antibodies normally are absent both in mother and fetus.

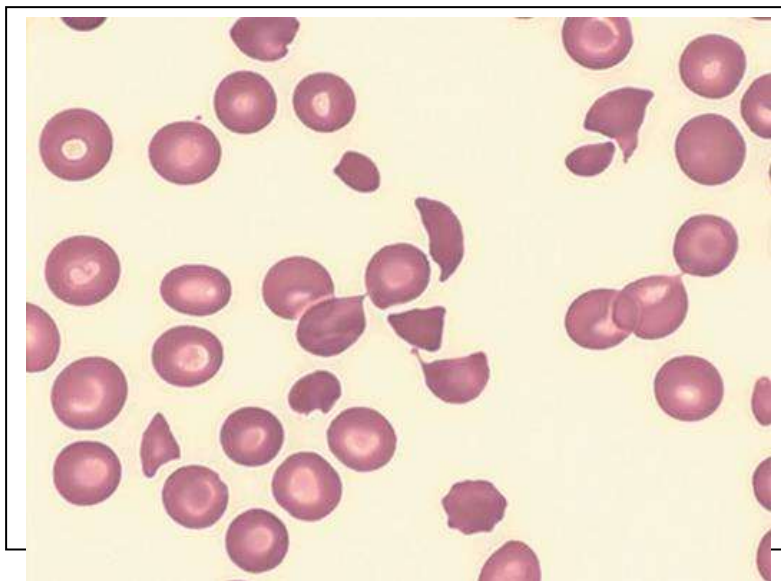
2. Anti-A and Anti-B being full agglutinins as other antibodies could penetrate placenta whereas full Rh antibodies couldn't penetrate it.

[http://intranet.tdmu.edu.ua/data/kafedra/internal/pediatria2/classes\\_stud/en/med/lik/ptn/pediatrics/5/theme\\_07.%20hemolytic%20dis](http://intranet.tdmu.edu.ua/data/kafedra/internal/pediatria2/classes_stud/en/med/lik/ptn/pediatrics/5/theme_07.%20hemolytic%20dis)



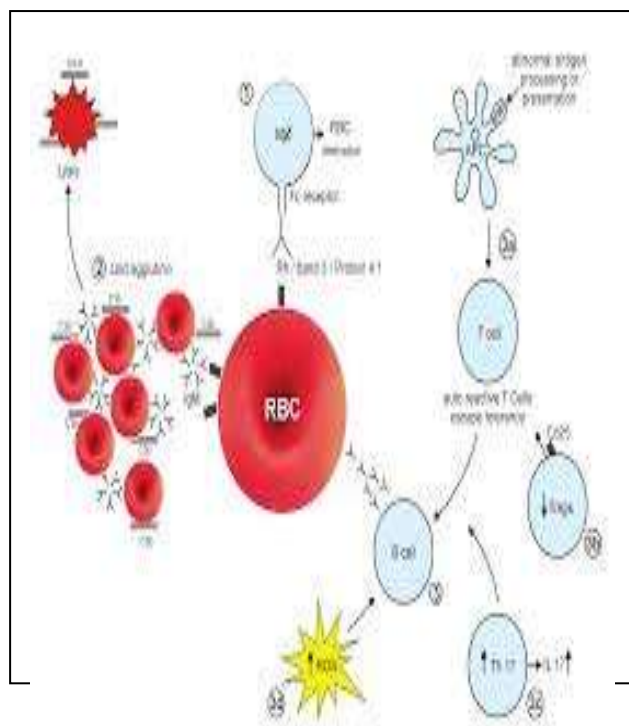
3. Fetus tissues in “extractors”( people who reveals A and B substances not only in blood but in humors as well) and in “non-extractors” contains both A and B substances which is usually neutralizes anti-A and anti-B antibodies. Rh –antibodies doesn't neutralizes by the tissue antibodies therefore their infiltration of Rh positive fetus causes hemolysis. This very characteristic differential feature of ABO antibodies leads to hemolytic disease development without

previous sensibilisation as mother blood already consists of a and b agglutinins.



Mild course of hemolytic disease is diagnosed in presence of moderate clinical, laboratory or only laboratory data. In this case in absence of any complications, underlying states or concomitant diseases only conservative therapy indicated. Level of Hb in umbilical blood in first hours more than 140 g/l and UB no less than 60 - 85,5  $\mu\text{mol/l}$ .

[http://intranet.tdmu.edu.ua/data/kafedra/internal/pediatria2/classes\\_stud/en/med/lik/ptn/pediatrics/5/theme\\_07.%20hemolytic%20dis](http://intranet.tdmu.edu.ua/data/kafedra/internal/pediatria2/classes_stud/en/med/lik/ptn/pediatrics/5/theme_07.%20hemolytic%20dis)



About mild severity of hemolytic disease testifies the hyperbilirubinemia is requires of change blood transfusion but not accompanied by brain bilirubin intoxication or by other complications development. In particular, for mild severity testifies the jaundice is appear in in the first 5 hours of life in case of Rh conflict or in first 11 hours of life in case of ABO conflict, Hb concentration in the first hour less than 140 g/l, presence of more than 3 risk factors of brain bilirubin intoxication. The UB level in the umbilical blood in mild severity of hemolytic disease consists of 85,6-136,8  $\mu\text{mol/l}$

<http://mahmrabeh.weebly.com/haematology---605-zoo.html>

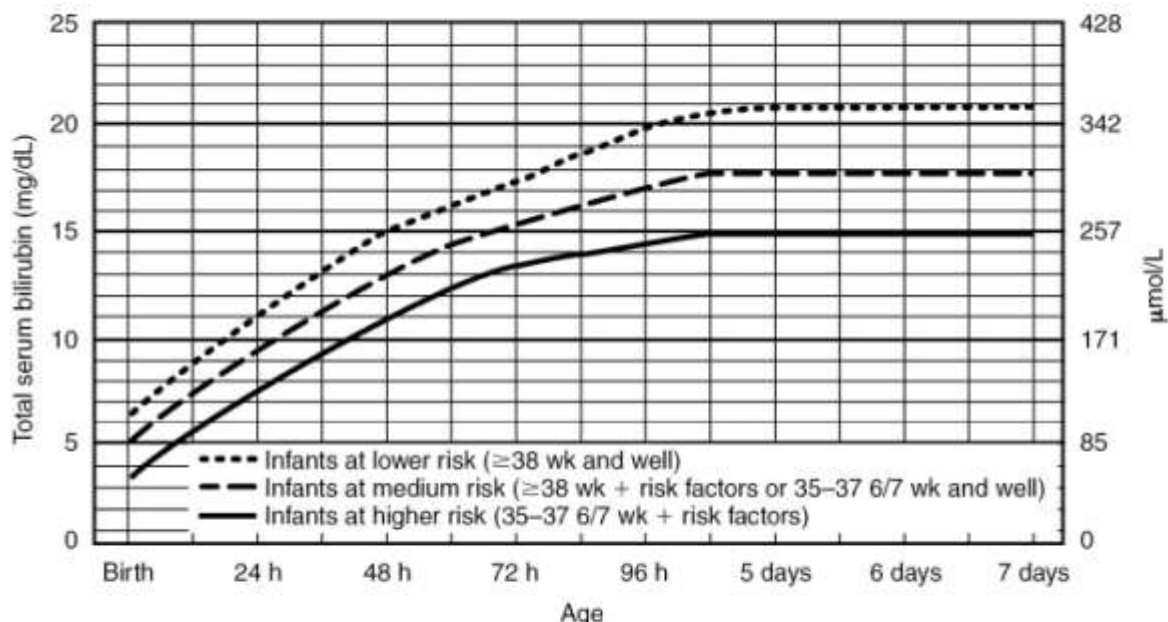


For severe course of hemolytic disease testifies severe anemia (Hb less than 100 g/l) or jaundice (hyperbilirubinemia more than 136,9  $\mu\text{mol/l}$  at birth), symptoms of bilirubin brain damage of any severity in all periods of disease, disturbances of breath and heart in absence any data of concomitant pneumo- or cardiopathy, necessity for more than 2 change blood transfusions, hydropic type of disease.

<http://www.bilicam.com>

### Guidelines for Phototherapy in Hospitalized infants $\geq 35$ Weeks

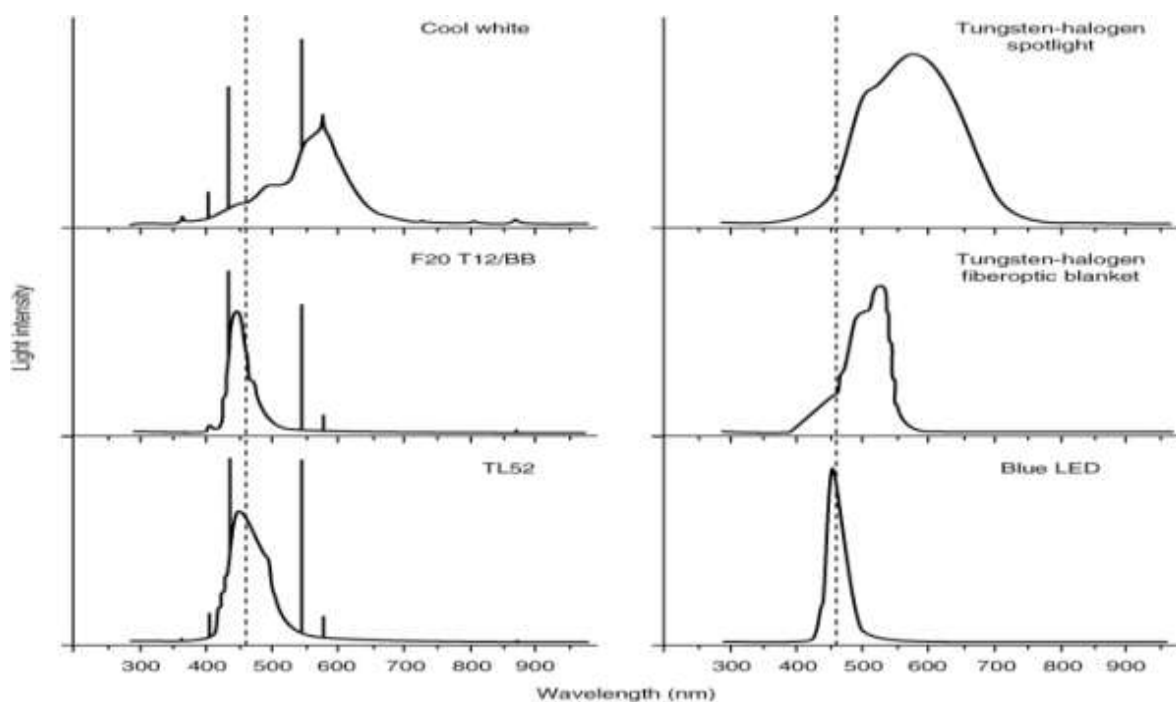
Note: These guidelines are based on limited evidence and the levels shown are approximations. The guidelines refer to the use of intensive phototherapy which should be used when the TSB exceeds the line indicated for each category.



- 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  $\frac{6}{7}$  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 wk and at higher TSB levels for those closer to 37  $\frac{6}{7}$  wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50  $\mu\text{mol/L}$ ) below those shown but home phototherapy should not be used in any infant with risk factors.

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Guidelines for phototherapy in hospitalized infants  $\geq 35$  weeks of gestation. Infants are designated as *higher risk* because of the potential negative effects of the conditions listed on albumin binding of bilirubin, the blood-brain barrier, and the susceptibility of the brain cells to damage by bilirubin.



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Emission spectra of phototherapy devices. The intensities are shown on a linear relative scale. The spectra of the three fluorescent lamps (cool white, and special blue [F20 T12/BB and TL52]), tungsten-halogen (spotlight [Olympic Medical Mini-BiliLite, Seattle, Wash., and fiberoptic blanket (BiliBlanket, Ohmeda, Columbia, Ohio)], and blue light-emitting diodes (LEDs) (neoBLUE, Natus Medical, Inc., San Carlos, Calif.) were measured under identical conditions on an S-2000 spectrophotometer (Ocean Optics, Inc., Dunedin, Fla.). *Dotted line* represents the peak absorption of bilirubin at approximately 460 nm.

**Bilirubin-to-albumin ratio as a determinant of the need for exchange transfusion**

RISK CATEGORY	<i>Ratio at Which Exchange Transfusion Should Be Considered</i>	
	TSB (mg/dL) to Albumin (g/dL)	TSB ( $\mu\text{mol/L}$ ) to Albumin ( $\mu\text{mol/L}$ )
Infants $\geq 38$ 0/7 weeks	8.0	0.94
Infant 35 0/7 to 37 6/7 weeks and well, or $\geq 38$ 0/7 weeks if higher risk or isoimmune hemolytic disease or G6PD deficiency	7.2	0.84
Infant 35 0/7 to 37 6/7 weeks if higher risk or isoimmune hemolytic disease or G6PD deficiency	6.8	0.80
If TSB is at or is approaching the exchange level, send blood for immediate type and cross-match. Blood for exchange transfusion is modified whole blood (red blood cells and plasma) cross-matched against the mother and compatible with the infant.		
G6PD, glucose-6-phosphate dehydrogenase; TSB, total serum bilirubin.		

Examples of a clinical pathway for the management of the newborn infant readmitted for phototherapy or exchange transfusion

## Treatment

Use intensive phototherapy and/or exchange



## Laboratory Tests

TSB and direct bilirubin level

Blood type (ABO, Rh)

Direct antibody test (Coombs' test)

Serum albumin

CBC with differential and peripheral blood smear for RBC morphology

Reticulocyte count

ETCO<sub>2</sub> (if technology is available)

G6PD screen, if indicated by ethnicity or geographic origin or if poor response to phototherapy

Urinalysis for reducing substances

If history or presentation suggests sepsis, perform blood culture, urine culture, and CSF examination for protein, glucose, cell count, and culture.

## Interventions

If TSB  $\geq 25$  mg/dL (428  $\mu\text{mol/L}$ ) or  $\geq 20$  mg/dL (342  $\mu\text{mol/L}$ ) in a sick infant or an infant  $< 38$  weeks' gestation, obtain a type and cross-match, and request blood in case an exchange transfusion becomes necessary.

In infants with isoimmune hemolytic disease and a TSB that is rising despite intensive phototherapy or rising to within 2 to 3 mg/dL (34 to 51  $\mu\text{mol/dL}$ ) of exchange level administer IVIG (500 to 1000 mg/kg) over 2 hours and repeat if necessary.

If infant's weight loss from birth is greater than 12% or there is clinical or biochemical evidence of dehydration, recommend formula or expressed breast milk. If oral intake is in question, give IV fluids.

## For Infants receiving intensive phototherapy



Breastfeed or bottle-feed (formula or expressed breast milk) every 2 to 3 hours.

If TSB  $\geq 25$  mg/dL (428  $\mu\text{mol/L}$ ), repeat TSB within 2 to 3 hours.

If TSB = 20 to 25 mg/dL (342 to 428  $\mu\text{mol/L}$ ), repeat TSB within 3 to 4 hours.

If TSB <20 mg/dL (342  $\mu\text{mol/L}$ ), repeat TSB in 4 to 6 hours.

If TSB continues to fall, repeat TSB in 8 to 12 hours.

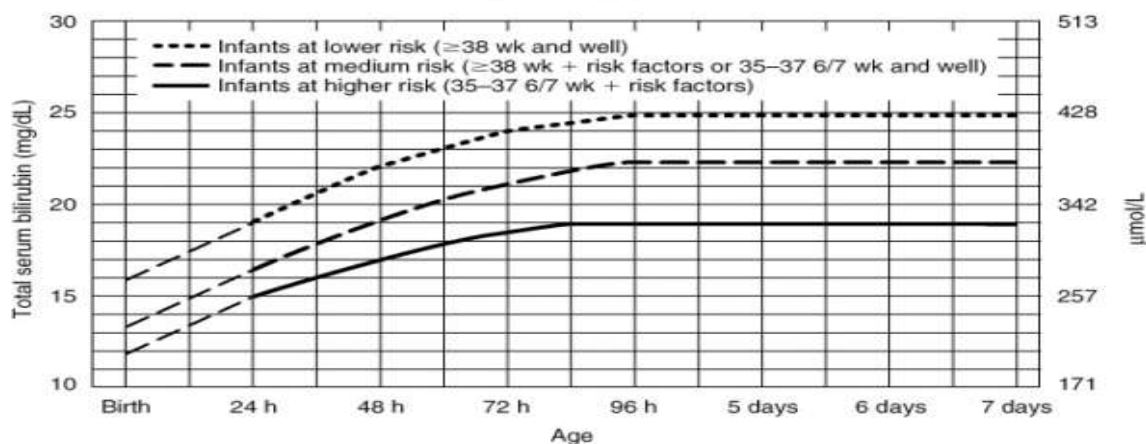
If TSB is not decreasing, or is moving closer to the level for exchange transfusion, or the TSB-to-albumin ratio exceeds levels shown in consider exchange transfusion.

When TSB is below 13 to 14 mg/dL (222 to 239  $\mu\text{mol/L}$ ), discontinue phototherapy.

Depending on the cause of the hyperbilirubinemia, it is an option to measure TSB 24 hours after discharge to check for rebound hyperbilirubinemia.

### Guidelines for Exchange Transfusion in Infants $\geq 35$ Weeks

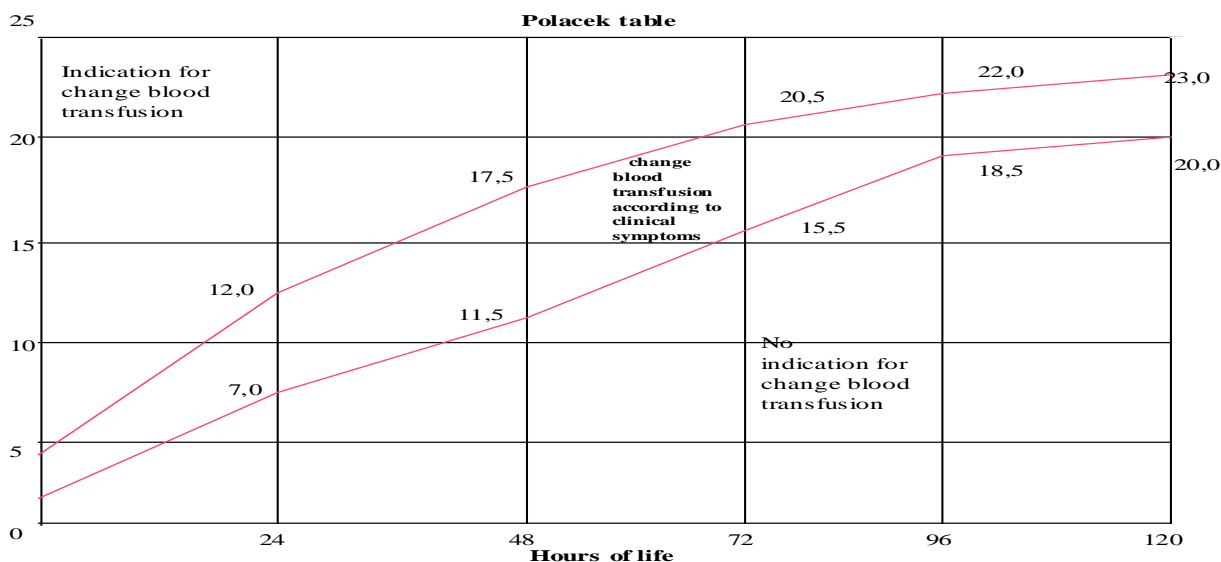
Note: These guidelines are based on limited evidence and the levels shown are approximations. During birth hospitalization, exchange transfusion is recommended if TSB rises to these levels despite intensive phototherapy. For readmitted infants, if TSB is above exchange level, repeat TSB every 2-3 hr and consider exchange if TSB remains above levels indicated after intensive phototherapy for 6 hours.



- 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 25mg/dL, (85 $\mu\text{mol/L}$ ) 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.

Guidelines for exchange transfusion in hospitalized infants  $\geq 35$  weeks of gestation. Note that these suggested levels represent a consensus of most of the committee but are based on limited evidence and the levels shown are approximations.

Bilirubin ratio per hour  
(mcmol/l)



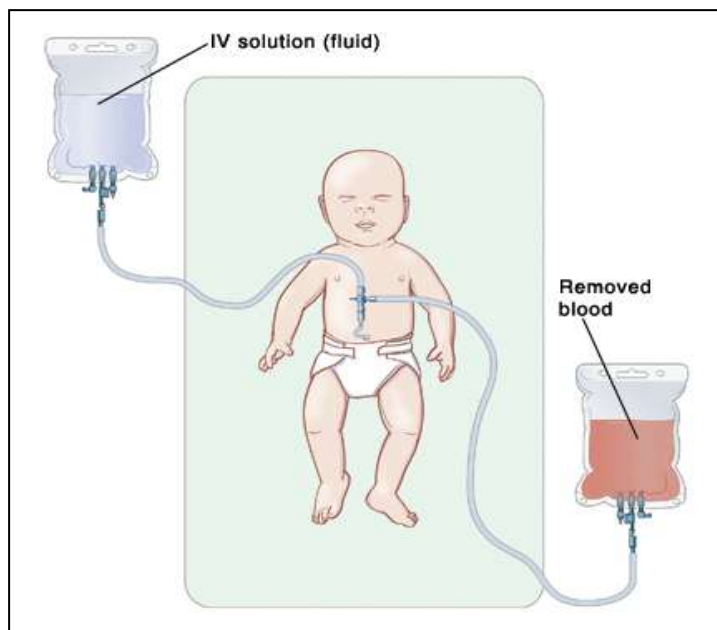
Polacek table for defining the indications for exchange blood transfusion based on per hour bilirubin ratio.



#### Potential 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, rebound metabolic alkalosis
  - Graft-versus-host disease
  - Human immunodeficiency virus, hepatitis B and C infections
  - All other potential complications of blood transfusions





The basic principles of exchange blood transfusion.

1. The tip of correctly fixed umbilical vein catheter must be placed into vena cava being situated between the diaphragm and left atrium.
2. The length of umbilical vein catheter from its end to the level of the umbilical ring is equal to the distance from the brachium to the belly-button – 5 cm; the procedure initiates with removing of 30 -40 ml of blood (20 ml in preterms).

<https://www.tesco-baby.com/baby/baby-health/jaundice-in-babies/>

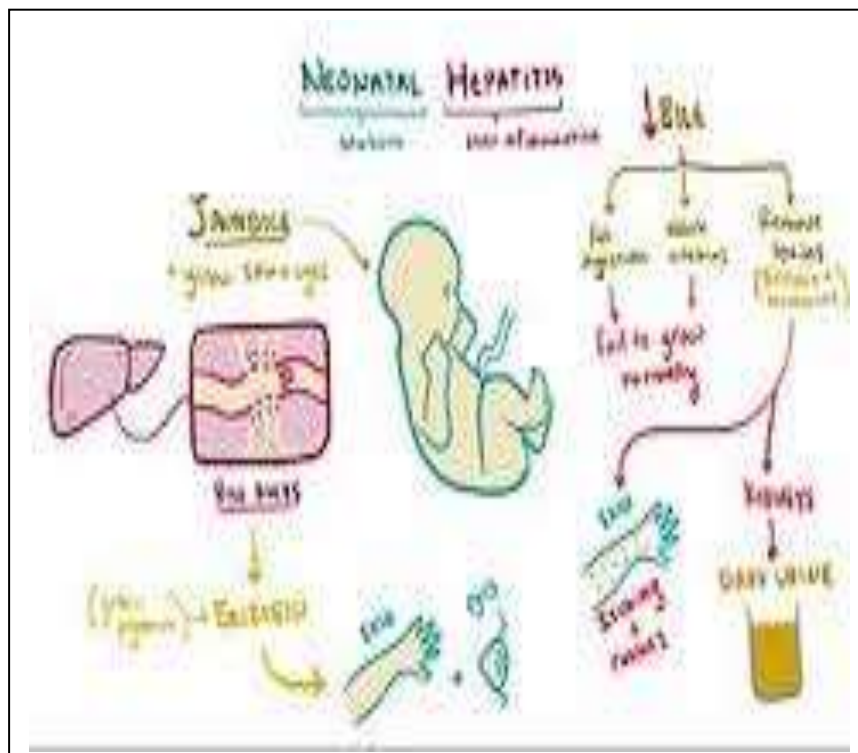
3. The total amount of injected blood must be 50 ml more than removed; operation must be carried slowly at 3-4 ml per minute alternating with injecting and rejecting of 20 ml blood (10 ml in preterms) with total duration no less than 2 hours; every 100 ml of entering blood need to administer 1 ml of 10 % calcium gluconate solution.

4. In the blood serum before change transfusion and just after the bilirubin level must be detected.

5. In congenital hydrops type of hemolytic disease is necessary urgently (during the 5-10 sec.) to press umbilical cord because delaying could stimulate the development of hypervolemia.

6. Thermal defence. Urgent start of change blood transfusion. There is no heart failure but it can be easily developed soon after birth, therefore, at first, red packed cells transfused only at volume of 10 ml, but at first time change transfusion total volume sometimes decreased to 75-80 ml per kg or in case of full transfusion volume the blood removed 50 ml more than injected.

7. In case of heart failure indicated digoxin administration (in sated dose of 0,03 mg/kg during the 2-3 days). At 2-3 day of life the furosemide administering. After change transfusion the liquid therapy begins according to the common principles.



## HEPATITIS

*Idiopathic neonatal hepatitis* is defined as prolonged conjugated hyperbilirubinemia without the apparent stigmata of a generalized viral illness, the evidence of identifiable infectious agents, or an etiologically specific metabolic abnormality. On liver biopsy, this group is characterized by extensive transformation of hepatocytes into multinucleated giant cells, and it is therefore sometimes referred to as neonatal giant cell

hepatitis. Giant cell transformation of hepatocytes does not reflect any specific etiology. It is caused by rupture of lateral cell membranes of adjacent hepatocytes, with consequent reduction in the number of bile canaliculi and retention of conjugated bilirubin. It is seen in various inherited metabolic disorders and some infections. Necrosis of hepatocytes and inflammation are usually present, although special stains (e.g., silver impregnation) may be necessary to demonstrate loss of hepatocytes. Necrosis and inflammation may be transient, with giant hepatocytes persisting for many months or even years

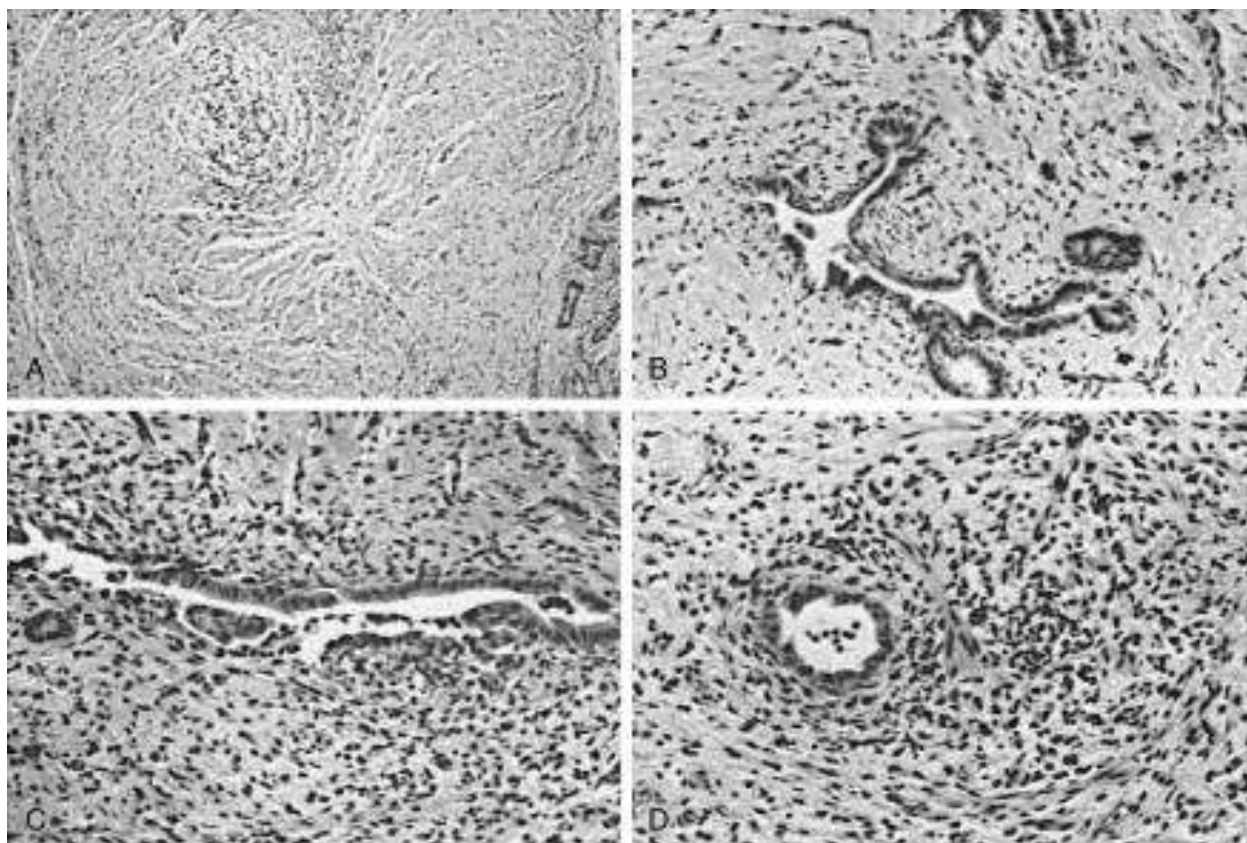
## Biliary Atresia

- ▶ Biliary atresia is the most common cause of end stage liver disease in infants and is a leading cause of liver transplantation in pediatrics.
- ▶ Incidence is estimated to be between 1:8000 and 1:12000 per live births and has a female preponderance.
- ▶ There is no excretion of bile from the liver into the duodenum leading to cholestasis, fibrosis and ultimately cirrhosis.

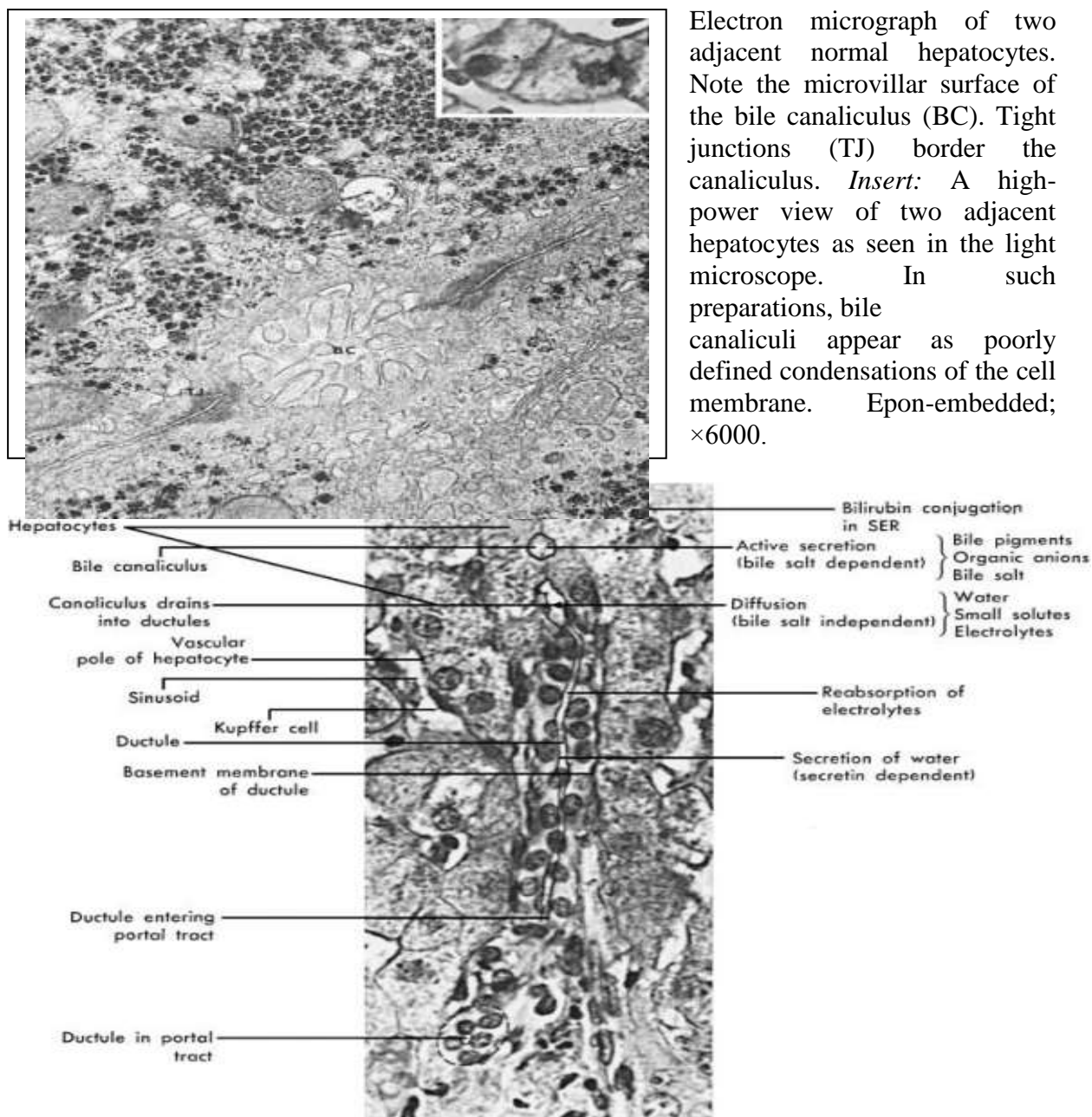


**Clinical findings associated with  
Extrahepatic biliary atresia (EHBA) and idiopathic  
neonatal hepatitis (INH)**

<b>Variable</b>	<b>EHBA</b>	<b>INH</b>
Jaundice at birth	Never	Rarely
Jaundice presentation	2-4 weeks	2-4 weeks
Dark yellow urine	Yes	Yes
Hepatomegaly	Yes	Yes
Splenomegaly		
Sometimes (signifies cirrhosis)		
More commonly than with EHBA		
Acholic stool	Yes	Transient/incomplete
Alpha-fetoprotein (serum, infant)	May be absent	Frequently (+)

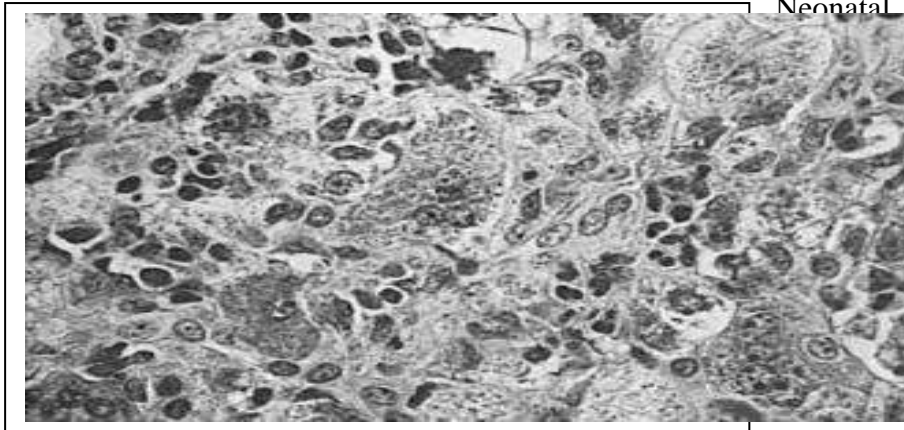


Microscopic preparations of “fibrous remnant” of extrahepatic biliary system resected during Kasai procedure for biliary atresia. A, Most distal portion of specimen, showing complete obliteration of lumen by fibrous tissue. B to D, More proximal segments, illustrating a spectrum of changes that includes necrosis of lining epithelium, acute and chronic inflammation, mural fibrosis with distortion of lumen, and great variation in size of ductlike structures. All micrographs  $\times 60$ .

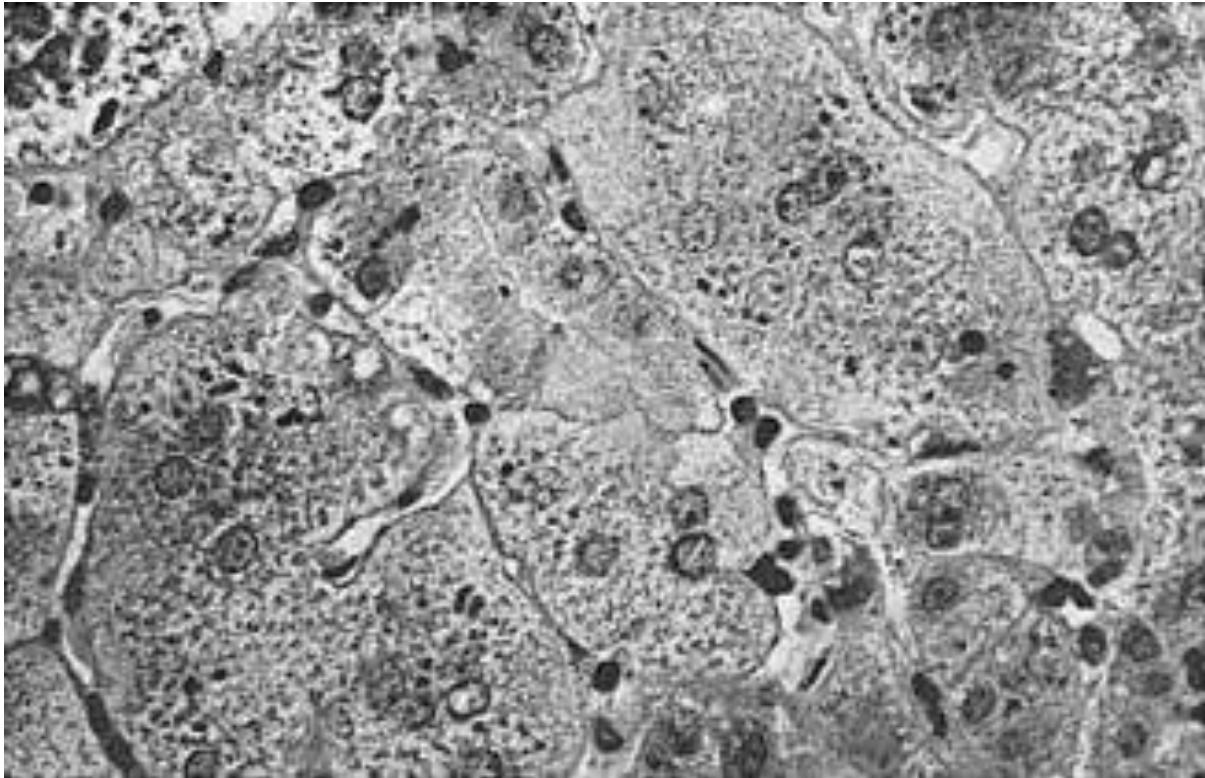


Microscopic section of normal liver depicting transition between bile canaliculus and bile ductule entering portal tract. Anatomic structures are identified to the left of the illustration, and the corresponding physiologic events are listed on the right. SER, smooth endoplasmic reticulum.

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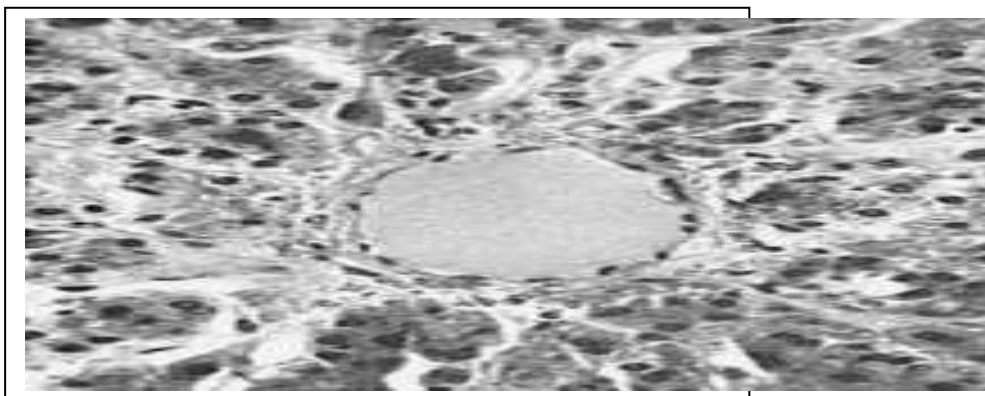


Neonatal hepatitis. Note the cellular irregularity and the normal orderly arrangement. Intrahepatic bile is present. Erythrocytes in sinusoids are present and elements of primary hematopoiesis. Paraffin embedding and hematoxylin-eosin staining;



High-power view of transformed giant hepatocytes. Most of the intracytoplasmic granules represent bile pigment. Paraffin embedding and hematoxylin-eosin staining;  $\times 200$ .

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biliary atresia. surrounded by acanalicular bile nt. In addition, contain bile pigment n embedding and n staining

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#### Differential diagnosis of jaundices.

Unconjugated bilirubin (UB) increasing		Increasing of direct (conjugated) bilirubin(CB)	
Conjugated jaundice	Hemolytic jaundice.	Panenchymatouse	Mechanic
1 UB prevails. 2. No anemia 3. No enlargement of liver and spleen. 4.Reticulocytes unchanged.	1.UB prevails 2. Anemia 3. Enlargement of liver and spleen. 4. Reticulocytes increased.	1.CB prevails 2. Enlargement of liver and spleen. 3.Urea periodically colored intensively. 4.Stool periodically decolorized. 5.Early hemorrhagic syndrome. 6. Syndrome of cytolysis (Increasing of liver enzymatic activity) 7.Monoglucuronide prevails.	1. CB prevails. 2. Enlargement of liver and spleen. 3.Urea colored constantly. 4 Stool decolorized constantly. 5. Late hemorrhagic syndrome. 6. Liver enzymatic activity at first weeks of disease unchanged. 7. Diglucuronide prevails.

## Intrauterine infections



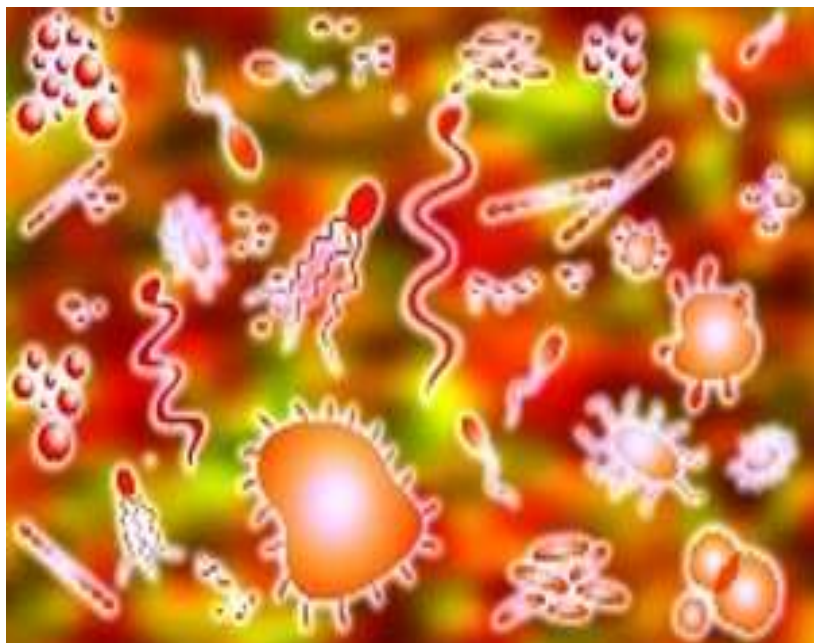
[http://www.utmb.edu/pedi\\_ed/CORE/Neonatology/page\\_40.htm](http://www.utmb.edu/pedi_ed/CORE/Neonatology/page_40.htm)

**Intrauterine infections** - infection of the fetus while still inside the womb.

The type and severity of symptoms is determined by the type of infection and at what stage of pregnancy it occurs. Some cases are mild enough to be asymptomatic and others are severe enough to cause a miscarriage.

Mothers with recurrent infection usually transfer significant antibody to the infant in utero. Even if this does not occur, the term infant who acquires infection after birth, denoted a perinatal infection, is usually asymptomatic.

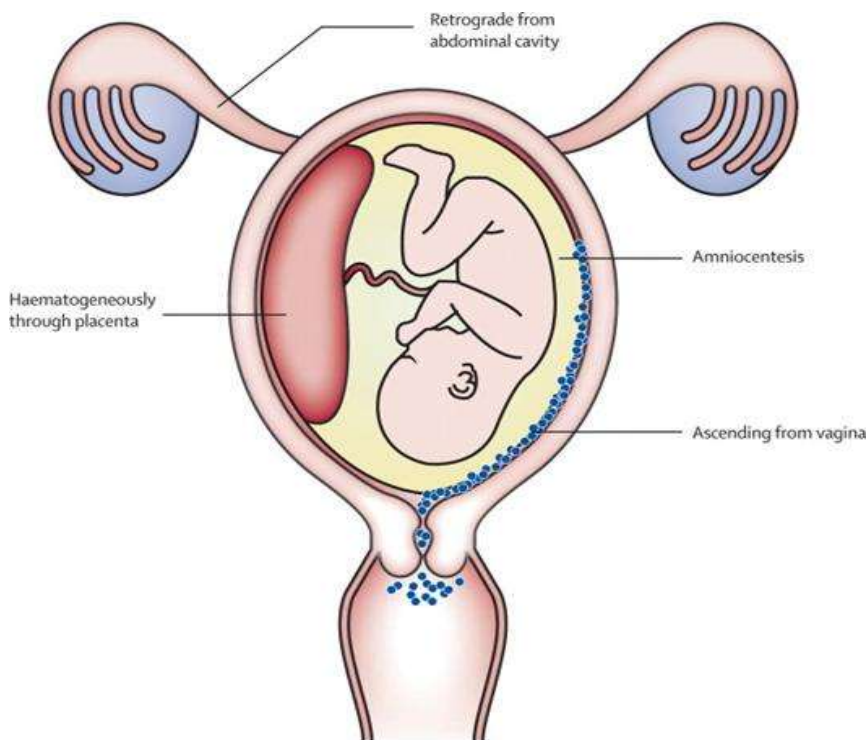
## PERINATAL INFECTION



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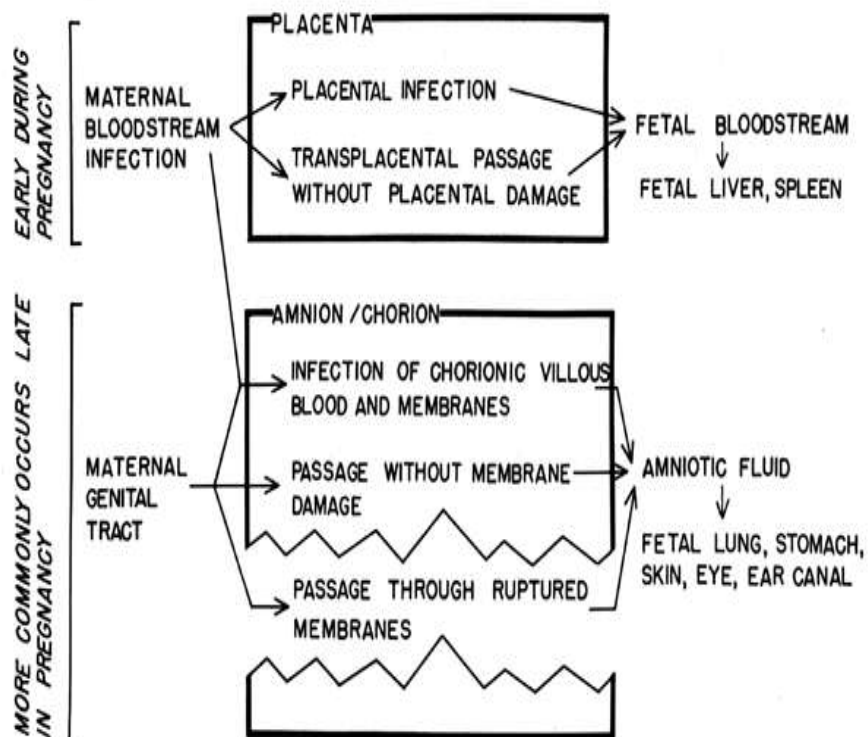
Intrauterine infection complicates 1% to 10% of pregnancies, leading to an increase in maternal morbidity and perinatal morbidity and mortality.

Transmission may occur in passage through the birth canal, through breast milk, or secondary to blood transfusion. Breast-feeding infants largely seroconvert. The incubation period ranges from 4 to 12 weeks.



In the uterus, bacterial infection may occur: 1) between maternal tissue and the fetal membranes, 2) within the fetal membranes (chorioamnionitis), 3) within the placenta, 4) within the amniotic fluid (intra-amniotic infection, amnionitis), or 5) within the umbilical cord (funitis) or the fetus 6) intra-amniotic infection correlates strongly with chorioamnionitis.

[http://www.medicinenet.com/image-collection/uterine\\_fibroids\\_picture/picture.htm](http://www.medicinenet.com/image-collection/uterine_fibroids_picture/picture.htm)



Term infants may acquire pneumonitis, which presents with cough, tachypnea, congestion, wheezing, and apnea.

They also may have pneumonitis, but with a picture of: overwhelming sepsis, hepatosplenomegaly, thrombocytopenia, neutropenia.

There may be an increased risk in these infants of neuromuscular handicaps, even though there does not appear to be a higher rate of sensorineural hearing loss, microcephaly, or chorioretinitis.

[http://www.utmb.edu/pedi\\_ed/CORE/Neonatology/page40.htm](http://www.utmb.edu/pedi_ed/CORE/Neonatology/page40.htm)



# TORCH

## Torch

**T: Toxoplasmosis**

**O: Other (i.e. syphilis)**

**R: Rubella**

**C: Cytomegalovirus**

**H: Herpes simplex virus**

*The most common bacteria in spontaneous preterm labor with intact membranes are: Ureaplasma urealyticum, Mycoplasma hominis, Gardnerella vaginalis, peptostreptococci, and bacteroides species.*

Ureaplasma urealyticum is the most common bacteria found both in PPRM (preterm PROM) and in preterm labor with intact membranes.

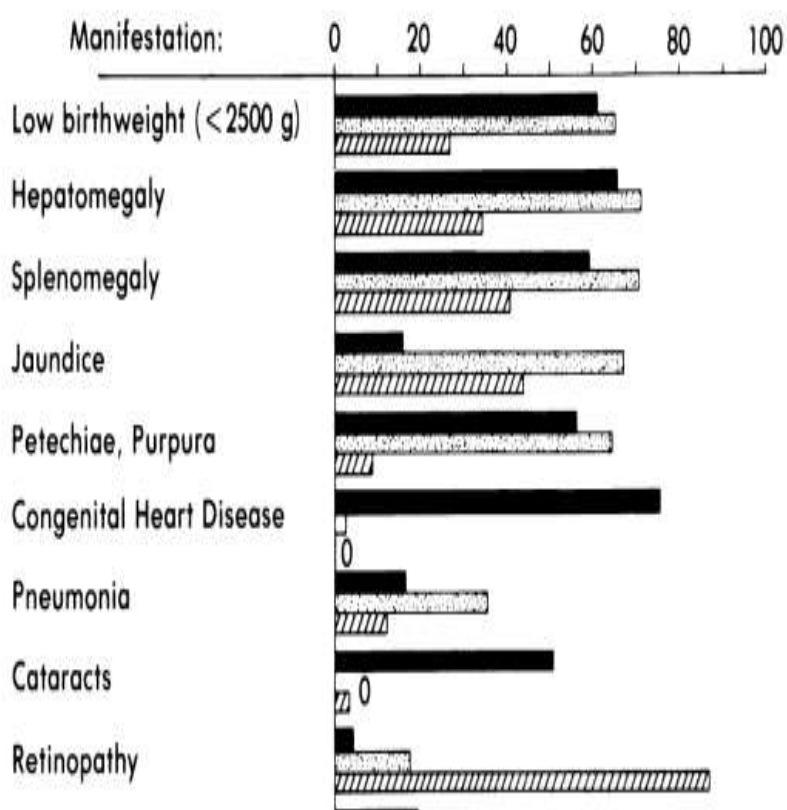
The most often found bacteria in chorioamnionitis and fetal infection after PROM are group B streptococci and Escherichia coli. Chronic chorioamnionitis occurs in at least 50% of pregnancies of less than 30 weeks' duration.



**Baby with IUGR (left) at term, compared to average sized baby at term**

### General Clinical symptoms of TORCH – infections:

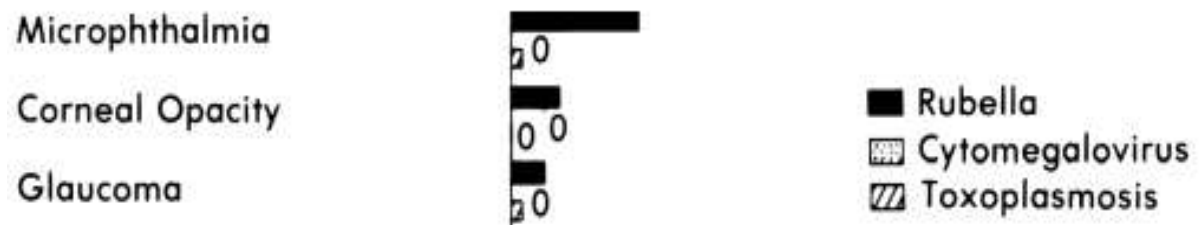
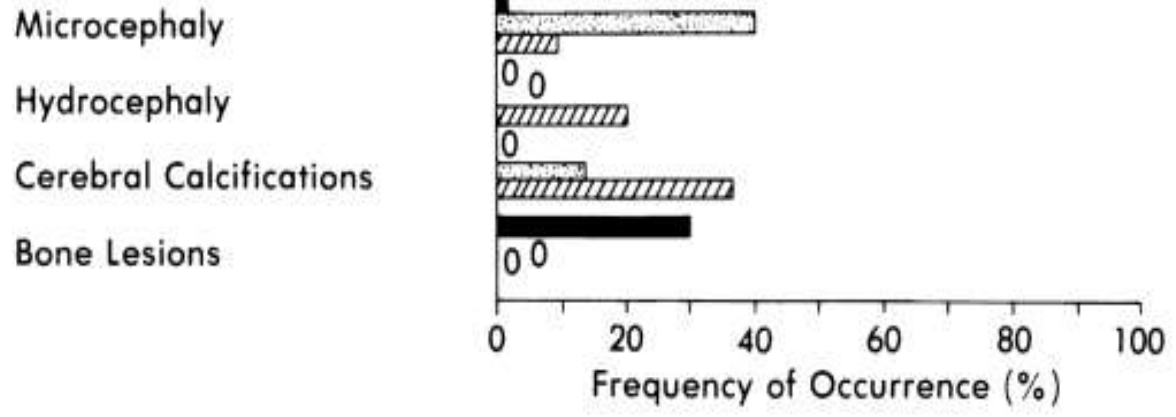
- Premature birth
- Brain damage
- Neurological problems
- Developmental delays
- Mental retardation
- Asymptomatic
- Behavioral problems
- Stillbirth
- Vision problems
- Hearing problems
- Miscarriage
- Low birth weight
- Physical abnormalities



<http://emedicine.medscape.com/article/235213-overview>

**Clinical**  
 chorioamnionitis is considered as an infection of the uterus and its contents during pregnancy. According to histological examination it is affected 20% of term as compared to 60% of the preterm deliveries.  
 The association between chorioamnionitis and cerebral palsy was demonstrated using meta-analysis. Also, an association between CA and both CP and cystic periventricular leukomalacia (cPVL). It was estimated that up to 12% of spastic CP could be due to intrauterine infection and inflammation.

**Manifestation of symptoms.**



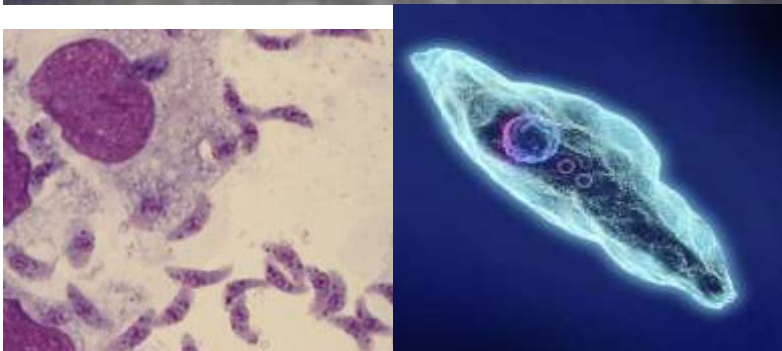
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## *Toxoplasmosis* INCIDENCE



**Congenital toxoplasmosis** - occurs almost exclusively as a result of primary maternal infection during pregnancy.

38% of pregnant women in the United States had Toxoplasma immunoglobulin (Ig) G antibodies. Three to 8 infants per 1000 live births worldwide are infected in utero. A higher incidence is seen in women born in Cambodia or Laos. An estimated 400 to 4000 cases of congenital toxoplasmosis occur in the United States each year.



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Toxoplasmosis is caused by *Toxoplasma gondii*, an obligate intracellular protozoan parasite.

*Toxoplasma* can be propagated in tissue cell cultures or by animal inoculation in research laboratory settings

## TRANSMISSION AND PATHOGENESIS



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This ubiquitous organism exists in three forms: an oocyst excreted by infected cats that produces sporozoites; a proliferative form (trophozoite or tachyzoite); and a cyst (cystozoite) found in tissues of infected animals.

The cat is the only definitive host, but other mammals can be infected incidentally. Farm animals (cattle, pigs, sheep) can acquire infection after ingestion of food or water contaminated with infected cat feces that contain oocysts.



[www.abc64.ru](http://www.abc64.ru)

Humans can acquire infection by ingestion of raw or poorly cooked meat containing the *Toxoplasma* cysts or by ingestion of food or water contaminated with oocysts.

Risk factors include any exposure to cat feces: changing cat litter boxes, playing in sandboxes, playing in gardening in areas used by cats. The general risk of transmission of acute infection from mother to fetus is estimated to be 40% and increases with increasing gestational age.

## CLINICAL MANIFESTATIONS



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The classic clinical presentation of congenital toxoplasmosis is the triad : *hydrocephalus, chorioretinitis, and intracranial calcifications.*

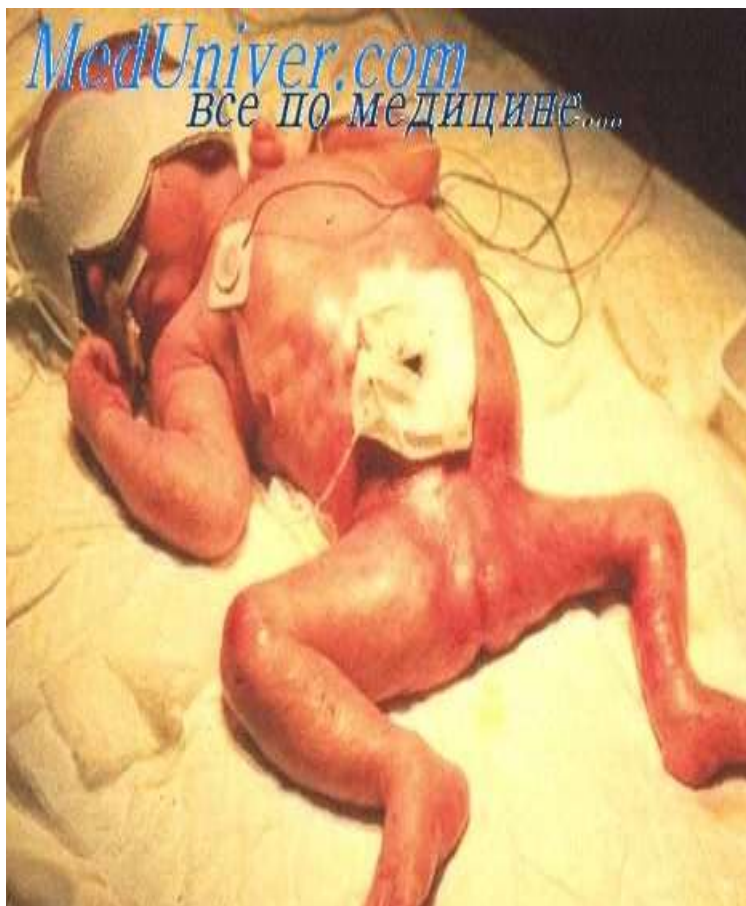
The classic clinical classification:

- 1) most maternal infections are **asymptomatic**
- 2) **mild illnesses**: fatigue and lymphadenopathy (only a single posterior cervical node), or generalized lymphadenopathy;
- 3) **acute maternal infection** can manifest as an infectious, mononucleosis-like syndrome with fever, nonsuppurative lymphadenopathy, headache, fatigue, sore throat, and myalgias.

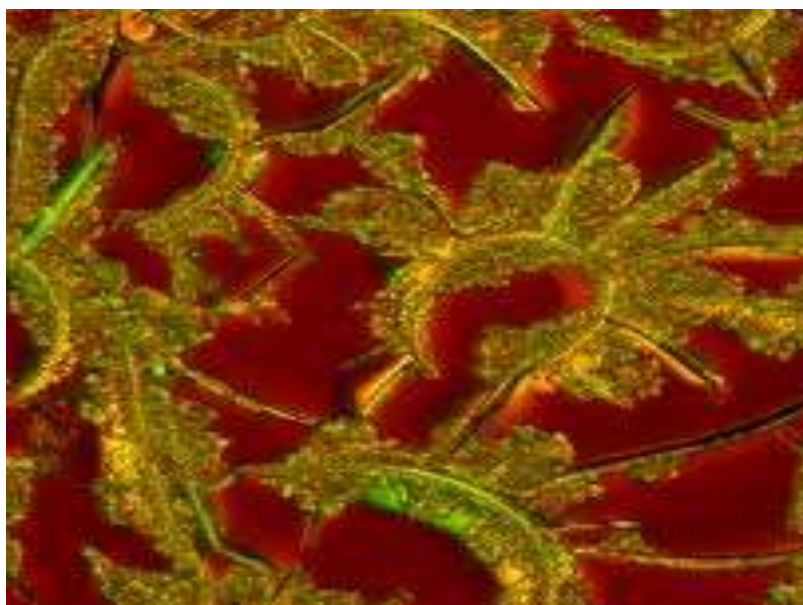


There is a wide spectrum of manifestations, and more than 75% of infected newborns are asymptomatic in early infancy.

They all have a DNA core and are enveloped in an icosahedral (20-sided) capsid. These viruses are also characterized by the development of latent states following the primary infection.



## DIAGNOSIS



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### The four most common presentations (McAuley):

- (1) the healthy-appearing term infant with **subclinical infection** in whom symptoms develop later in childhood;
- (2) the healthy-appearing term infant in whom clinical evidence of disease develops in the first few months of life;
- (3) the infant with **generalized** disease at birth;
- (4) the infant with predominantly neurologic involvement at birth.

Several tests are available to determine the duration of maternal infection when both IgG and IgM antibodies are positive. Fetal infection is best determined using amniotic fluid polymerase chain reaction amplification of the *Toxoplasma* gene B1.

Infants with suspected toxoplasmosis should undergo computed tomographic scanning of the brain, evaluation of cerebrospinal fluid, indirect ophthalmologic examination.

## HERPESVIRUS FAMILY

The herpesvirus family consists of :  
 herpes simplex virus (HSV) types 1  
 and 2, cytomegalovirus (CMV),  
 varicella-zoster virus (VZV),  
 Epstein-Barr virus (EBV),  
 human herpesvirus (HHV) types 6  
 and 7.

### *Herpes Simplex*



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They all have a DNA core and are enveloped in an icosahedral (20-sided) capsid. These viruses are also characterized by the development of latent states following the primary infection.

After viral DNA-replication, the virus is transported to the dorsal root ganglia, where at least some portion of the viral DNA persists for the lifetime of the individual, resulting in periodic recurrences at the site of skin or mucosa supplied by that nerve, often for undetermined reasons. The more severe the primary infection, the more likely are

The primary source of infection for the neonate is acquisition of the virus during delivery, yet far more women have infected genital tract secretions than there are neonatal infections.

Transplacental transmission, responsible for in utero infection, is inferred by the documentation of HSV skin lesions and viremia at birth and by elevated specific cord immunoglobulin (Ig) M levels.

Most HSV-1 infections occur in childhood and are usually asymptomatic, sometimes causing a gingivostomatitis or mononucleosis-like syndrome.

## EPIDEMIOLOGY AND TRANSMISSION



<http://emedicine.medscape.com/article/235213overview>

Transmission from mother to infant including transplacental, intrapartum, and postnatal acquisition.

Intrapartum transmission is responsible for 85% to 90% of neonatal infection. A high titer of viral particles (more than  $10^6/0.2$  mL inoculum) is excreted for 3 weeks with a primary maternal infection, which is more likely to involve cervical shedding than is a recurrent maternal infection, in which 10<sup>2</sup> to 10<sup>3</sup> viral particles per 0.2 mL inoculum are shed for only 2 - 5 days.

Ascending infection may also be possible, and symptomatic infection during pregnancy may be responsible for spontaneous abortion, but the actual risk of this is not clear



Maternal neutralizing antibodies may also be partially protective for the newborn in recurrent infections and may not yet be present (and available to cross the placenta) in a primary maternal infection.

Half of all neonatal HSV-2 infections occur secondary to recurrent maternal infection, even though transmission from mother to infant occurs in only 5% of the cases. In contrast, 50% of mothers transmit virus to their infants after a primary infection in the third trimester.



## NEONATAL INFECTION



Although asymptomatic HSV infections are common in adults. Of all neonatal infections, 30% are caused by HSV-1 rather than HSV-2. Half of the infants are born prematurely, usually between 30 and 37 weeks of gestation, and many have complications of prematurity, particularly respiratory distress syndrome. Two thirds of the term newborns have a normal neonatal course and are discharged before the onset of disease. They may also have simultaneous bacterial infections. As much as one fourth of the infants will present on the first day of life, and two thirds by the end of the first week.

**Approximately 22% of cases are disseminated, 34% are CNS, and 40% are localized to the skin, eyes, or mouth.**



**Clinically, neonatal infections are classified as**

- 1) disseminated, involving multiple organs, with or without central nervous system (CNS) involvement;**
- 2) encephalitis, with or without skin, eye, or mouth involvement**
- 3) localized to the skin, eyes, or mouth.**

**Approximately 22% of cases are disseminated, 34% are CNS, and 40% are localized to the skin, eyes, or mouth.**

**Disseminated infections predominantly involve the liver, adrenal glands, and lungs.**

**The infants usually present by 9 to 11 days of life with signs of bacterial sepsis or shock, but often had unrecognized symptoms several days earlier: cutaneous vesicles, vesicles.**

## DISSEMINATED INFECTION



The infants usually present by 9 to 11 days of life with signs of bacterial sepsis or shock, but often had unrecognized symptoms several days earlier: cutaneous vesicles, vesicles.

Disseminated intravascular coagulation (DIC) with decreased platelets and petechiae and purpura, and bleeding in the gastrointestinal tract.

Pneumatosis intestinalis.

Hepatomegaly or hepatitis with or without jaundice.

Respiratory distress, often with pneumonitis or pleural effusion .

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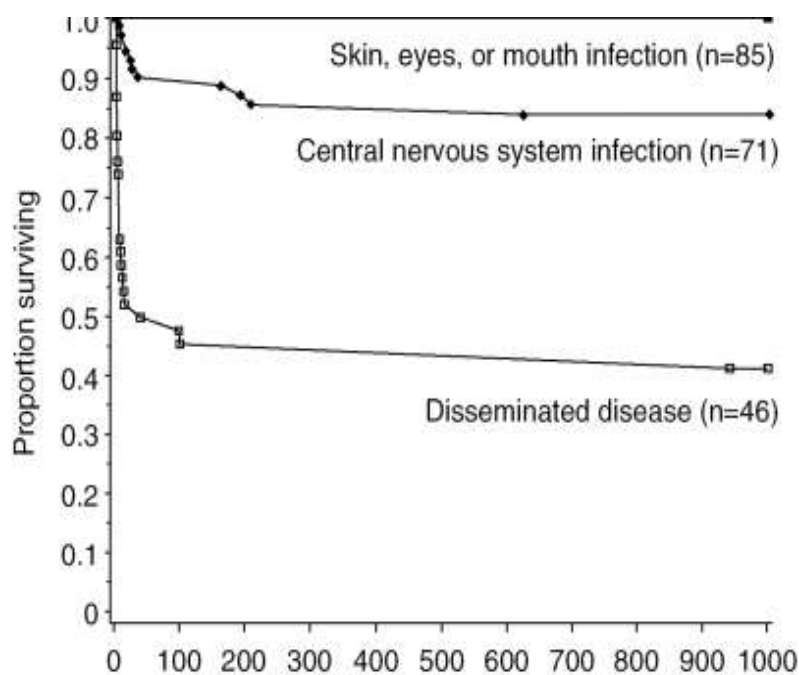


Symptoms of CNS: irritability, apnea, a bulging fontanelle, focal or generalized seizures, opisthotonos, posturing, or coma.

The cerebrospinal fluid (CSF) may be normal or may show evidence of hemorrhage. Virus can be isolated from the CSF of only one third of the infants with CNS symptoms.

The routine use of polymerase chain reaction (PCR) on CSF has therefore aided considerably in recognition of disease. Death usually occurs at approximately 2 weeks of age, roughly 1 week from the onset of symptoms, and often involves respiratory failure.

# ENCEPHALITIS



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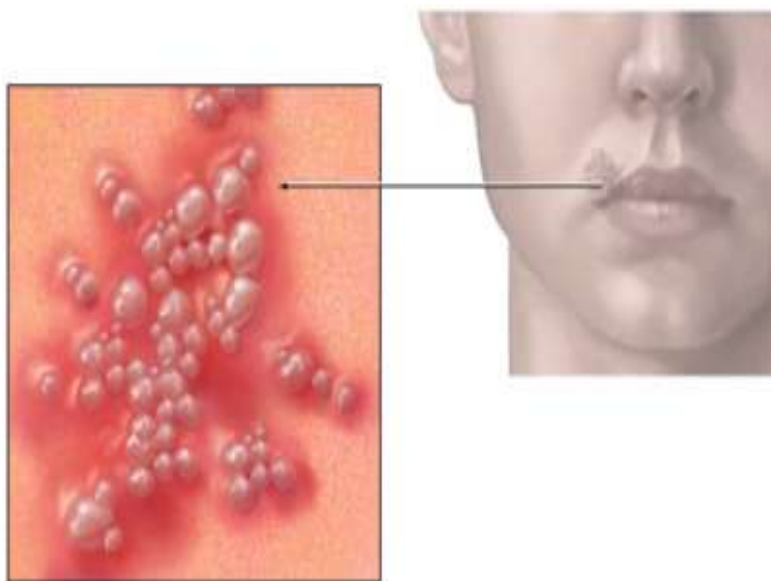
Encephalitis may occur as a component of disseminated disease, cortical hemorrhagic necrosis, usually at 15 to 17 days of life, or in association with oral, eye, or skin lesions, at 16 to 17 days of life, Regardless of the source of neurologic infection, only approximately 60% of the infants have skin vesicles and less than half have virus isolated from the CSF. Although the CSF is occasionally normal, it usually shows a mild pleocytosis, with a predominance of mononuclear cells, an elevated protein concentration, and a normal glucose concentration.

Lethargy, poor feeding, irritability, and localized or generalized seizures may be the presenting manifestations.

Nearly all the electroencephalograms show abnormalities, and computed tomography may be important in defining abnormalities.

Nearly half the untreated children die from neurologic deterioration as late as 6 months after onset, and virtually all survivors have severe sequelae (microcephaly and blindness or cataracts).

## SKIN, EYE, AND MOUTH INFECTIONS



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Infants with disease localized to the skin, eyes, or mouth usually present by 10 to 11 days of life. More than 90% of these infants have skin vesicles, usually over the presenting part at birth and appearing in clusters. Recurrences are common for at least 6 months.

Either HSV-1 or HSV-2 can cause keratoconjunctivitis, chorioretinitis, microphthalmos, and retinal dysplasia, later possibly leading to cataracts.

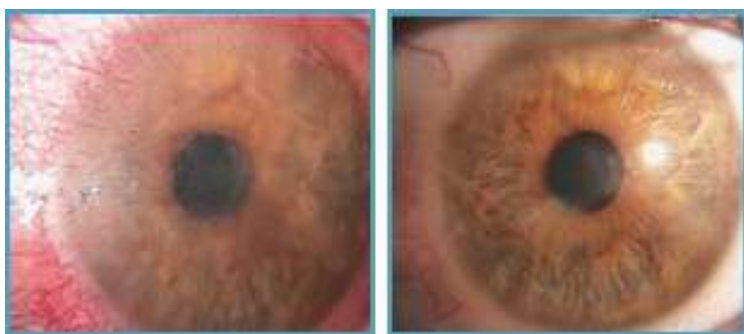
## DIAGNOSIS



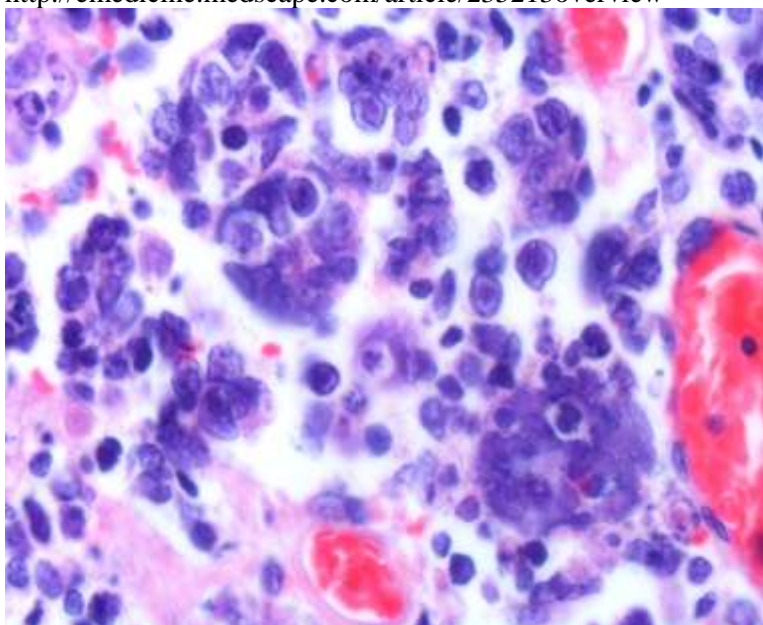
More rapid diagnosis is may be obtained by immunofluorescence antibody staining or enzyme immunoassay testing of mucocutaneous lesions.

Cultures of the newborn (mucocutaneous lesions, CSF, stool, urine, nasopharynx, and conjunctivae) should be delayed to 24 to 48 hours after birth to differentiate viral replication in the newborn from transient colonization of the newborn at birth. Acute and convalescent sera may also be tested for a rise in antibody titers to confirm a diagnosis later. HSV DNA identification by PCR in the CSF is the method of choice because the yield of CSF culture is so low.

## THERAPY AND PREVENTION



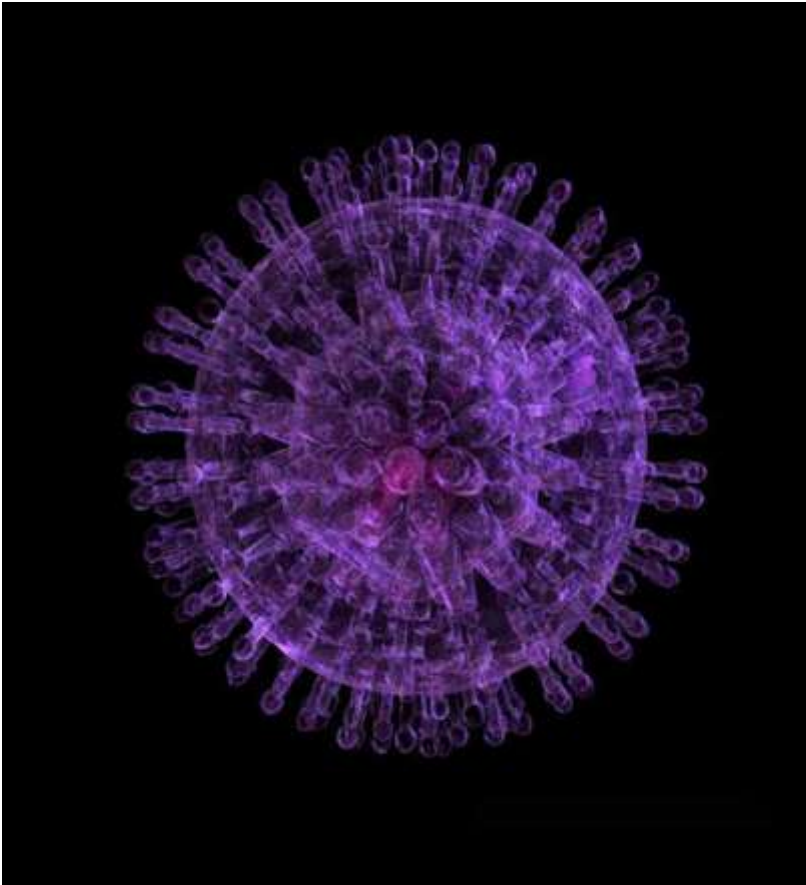
<http://emedicine.medscape.com/article/235213overview>



Cesarean delivery, is recommended for women with clinically apparent infection. These infants need immediate isolation and inspection of the eyes, mouth, and skin, with cultures obtained 24 to 48 hours after birth. A complete blood count and liver function tests should be obtained and followed. Treatment of an infant born vaginally to a mother with active lesions is controversial. Although some would treat the infant empirically, others would treat only if cultures are positive or the infant manifests symptoms. Breast feeding should not be allowed if herpetic lesions are

All women with either active labial or genital herpes or a history of herpes should be counseled to recognize herpetic lesions and to learn the precautions taken when touching the infant. Circumcision is delayed until the infant is discharged and cultures are known to be negative.

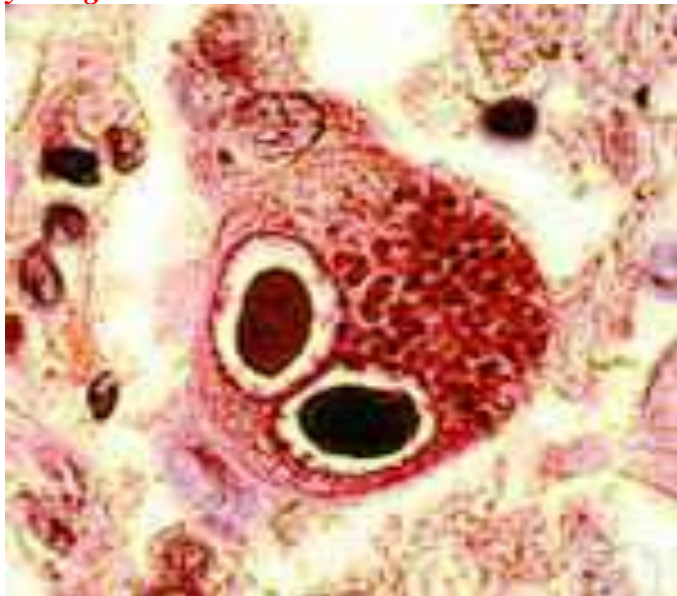
Acyclovir or vidarabine is a specific inhibitor of the viral DNA polymerase. The newer antiviral drugs have not been studied in neonates and are not licensed for use in these patients. Acyclovir is administered at a dosage of 20 mg/kg every 8 hours for 14 days for skin, eye, and mouth disease and for 21 days for either CNS or disseminated disease.



2) Topical ophthalmic antiviral drugs should be given to infants with ocular involvement in addition to parenteral therapy. This may include 1–2% trifluridine, 0.1% iododeoxyuridine, or 3% vidarabine. All other therapy is supportive.

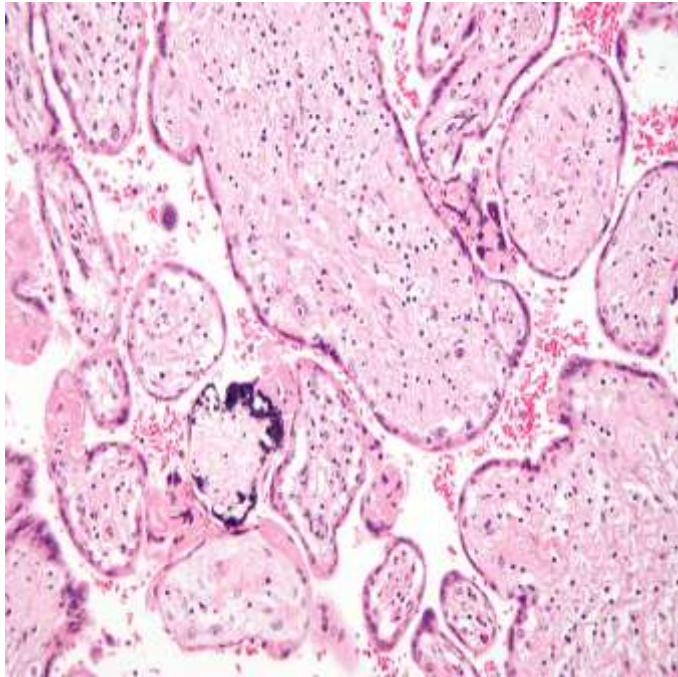
All infants with skin, eye, or mouth infections treated with acyclovir survived, and 98% of them had normal development at 1 year. Infants with encephalitis had an 86% survival rate, but only 29% had normal development at 1 year. Finally, the survival rate was only 43% for infants with disseminated disease treated with acyclovir, but 60% were developing normally at 1 year).

### *Cytomegalovirus*



[https://en.wikipedia.org/wiki/Congenital\\_cytomegalovirus\\_infection](https://en.wikipedia.org/wiki/Congenital_cytomegalovirus_infection)

The virus has a double-stranded DNA core surrounded by an icosahedral, or 20-sided, capsid. These inclusion bodies often yield an “owl’s eye” appearance to the cells. The virus does not code its own thymidine kinase or DNA polymerase, which is important when considering treatment. The virus is cultured in the laboratory only in human fibroblasts, although it replicates in vivo primarily in epithelial cells.



<http://emedicine.medscape.com/article/235213overview>

**Seropositivity also increases with age, with 50% to 60% of adult women of middle economic status seropositive compared with 90% of women of lower socioeconomic status. Seropositivity is also associated with ethnic groups, with nearly half of white women, three fourths of black women (African, Caribbean), and 90% of Asian women being seropositive. Among women, seropositivity is associated with increasing parity, older age, lower social class, and being single during antenatal care.**



**Periventricular calcifications can be found in half of infants with congenital CMV on computed tomography scans, and they are associated with moderate to profound mental retardation, cerebral palsy, hearing loss, and chorioretinitis.**

## PERINATAL INFECTION



[https://en.wikipedia.org/wiki/Congenital\\_cytomegalovirus\\_infection](https://en.wikipedia.org/wiki/Congenital_cytomegalovirus_infection)

**Chorioretinitis is nearly always indicative of significant mental impairment and often leads to optic atrophy. Hearing loss, either unilateral or bilateral, is progressive for years after birth in at least one third of the infants. Dental defects and caries in 40% of the primary dentition, as well as inguinal hernias in boys, are the only definite teratogenic effects.**



**Mothers with recurrent infection usually transfer significant antibody to the infant in utero. The incubation period ranges from 4 to 12 weeks.**

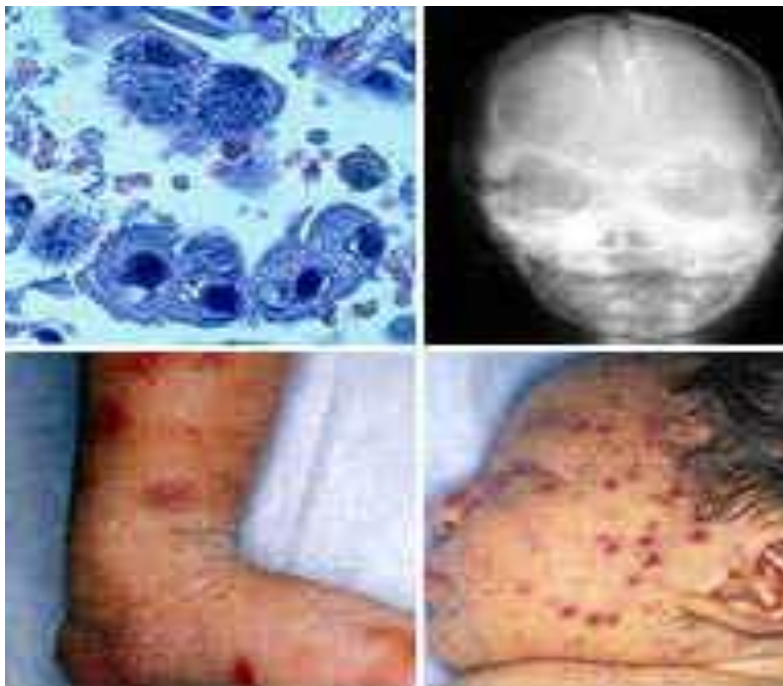


## Sequelae in Children with Congenital Cytomegalovirus Infection According to Type of Maternal Infection

[https://en.wikipedia.org/wiki/Congenital\\_cytomegalovirus\\_infection](https://en.wikipedia.org/wiki/Congenital_cytomegalovirus_infection)

<b>SEQUELAE</b>	<b>PRIMARY INFECTION</b>	<b>RECURRENT INFECTION</b>	<b>PVALUE</b>
<b>Sensorineural hearing loss</b>	<b>15 (18/120)</b>	<b>5 (3/56)</b>	<b>0.05</b>
<b>Bilateral hearing loss</b>	<b>8 (10/120)</b>	<b>0 (0/56)</b>	<b>0.02</b>
<b>Speech threshold <math>\geq 60</math> dB</b>	<b>8 (9/120)</b>	<b>0 (0/56)</b>	<b>0.03</b>
<b>IQ <math>\leq 70</math></b>	<b>13 (9/68)</b>	<b>0 (0/32)</b>	<b>0.03</b>
<b>Chorioretinitis</b>	<b>6 (7/112)</b>	<b>2 (1/54)</b>	<b>0.20</b>
<b>Other neurologic sequelae</b>	<b>6 (8/125)</b>	<b>2 (1/64)</b>	<b>0.13</b>
<b>Microcephaly</b>	<b>5 (6/125)</b>	<b>2 (1/64)</b>	<b>0.25</b>
<b>Seizures</b>	<b>5 (6/125)</b>	<b>0 (0/64)</b>	<b>0.08</b>
<b>Paresis or paralysis</b>	<b>1 (1/125)</b>	<b>0 (0/64)</b>	<b>0.66</b>
<b>Death</b>	<b>2 (3/125)</b>	<b>0 (0/64)</b>	<b>0.29</b>
<b>Any sequelae</b>	<b>25 (31/125)</b>	<b>8 (5/64)</b>	<b>0.003</b>

## PERINATAL INFECTION



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Breast-feeding infants largely seroconvert. The incubation period ranges from 4 to 12 weeks. Term infants may acquire pneumonitis secondary to CMV, which presents with cough, tachypnea, congestion, wheezing, and apnea. Although the mortality rate may be as high as 3%, few infants require hospitalization. In contrast, premature infants, often infected through blood transfusion, have a high rate of serious or fatal illness. They also may have pneumonitis, but with a picture of overwhelming sepsis, hepatosplenomegaly, thrombocytopenia, and neutropenia. There may be an increased risk in these infants of neuromuscular handicaps, even though there does not appear to be a higher rate of sensorineural hearing loss, microcephaly, or chorioretinitis.

## SYMPTOMATIC CONGENITAL INFECTION



Most commonly, premature infants or ones who are small for gestational age have hepatosplenomegaly and abnormalities on liver function tests. Hyperbilirubinemia is more likely to be persistent, with a gradual rise in the direct component. Petechiae, purpura, and thrombocytopenia (direct suppression of the megakaryocytes in the bone marrow) usually develop after birth and may persist for weeks. One third of infants with congenital infection are thrombocytopenic and one third of those have severe thrombocytopenia, with platelet counts less than 10,000/dL. There may also be a Coombs-negative hemolytic anemia. Diffuse interstitial or peribronchial pneumonitis is possible but less common than with perinatally acquired disease.

## **ASYMPTOMATIC CONGENITAL INFECTION**



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The most important sequela appears to be sensorineural hearing loss, which is often bilateral and may be moderate to profound. The presence of periventricular radiolucencies or calcifications on computed tomography are highly correlated with hearing loss. The hearing loss may be present at birth or appear only after the first year of life and it is frequently progressive, often presenting as late as 6 years of life, secondary to continued growth of the virus in the inner ear.

Likewise, although there is a very low risk of chorioretinitis, it may not be present at birth but may develop later. A further finding may be a defect of tooth enamel in the primary dentition, leading to increased caries. Neurologic handicap may occur, but is uncommon. Prematurely born infants are most at risk.

**Леженко Геннадій Олександрович  
Резніченко Юрій Григорович  
Каменщик Андрій Володимирович  
Врублевська Світлана Володимирівна  
Лебединець Олександра Миколаївна  
Гладун Катерина Валеріївна**

**Збірник лекцій з неонатології, що читаються студентам 5 курсу  
міжнародного факультету англomовної форми навчання на кафедрі  
госпітальної педіатрії  
(англійською мовою)**

The collection of lectures on neonatology  
for the fifth year English-speaking medical students of international faculty  
delivered at the department of Hospital pediatrics

Видруковано з готового оригінал-макету авторів.