In addition to Apgar scoring, neonates should be evaluated for the need immediate resuscitation:

- Low Apgar score (ego. < 7)<p></p>
- Prolonged (> 10 min) low Apgar score
- Fetal heart rate obtained by palpating umbilical stump (at level of insertion of catheter, N.B. infants cannot breath through nose, nasopharynx, esophagus) into stomach; – palpate tube tip in esophagus or auscultate for bubbling in esophagus when air is blown through tube;<p></p>
- Aspirate gastric contents (esp. in premature or delivered by section) to prevent aspiration; – detectable anomalies – posthierochial atresia*, esophageal atresia**
- Hemorrhage – antepartum and postpartum hemorrhage (PPH-VIH)
- Neonatal intraventricular hemorrhage (IVH)
- Seizures: vomiting, convulsions, limp, absence of reflex response to painful stimuli</p>

### EVALUATION

**Appar score at 1 and 5 min is used to evaluate all newborns immediately after birth (assessment of oxygenation):**

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>MENONIC</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) color</td>
<td>Appearance</td>
<td>all blue, pale</td>
</tr>
<tr>
<td>2) heart rate</td>
<td>Pulse</td>
<td>absent</td>
</tr>
<tr>
<td>3) reflex response to nasal catheter/tactile stimulation</td>
<td>Grimec</td>
<td>none</td>
</tr>
<tr>
<td>4) muscle tone</td>
<td>Activity</td>
<td>limp</td>
</tr>
<tr>
<td>5) respiration</td>
<td>Respiration</td>
<td>absent</td>
</tr>
</tbody>
</table>

at 1 min: 8-10 – no need for vigorous resuscitation. 5-7 – stimulation and supplemental O₂ 1-3 – assisted ventilation, possible cardiac support<br>

at 5 min (reflects adequacy of resuscitation and degree of perinatal asphyxia): 7-10 – normal 4-6 – intermediate 0-3 – low

- *heart rate obtained by palpatbing umbilical stump (at level of insertion of infant’s abdomen) or by direct auscultation of precordium.
- **many normal newborns have transient cyanosis that clears by 5-min Appar score! low Appar score is not per se indicator of perinatal asphyxia - components of score depend on physiologic maturity, fetal cardiorespiratory and neurologic conditions, and maternal perinatal therapy.
- *alternatively may be tested by holding infant’s mouth closed and occluding each nostril alternately (N.B. infants cannot breath through mouth! Obstruct nasal breathers – punch both nostrils will cause significant distress!*)
- **suggested by large amount of saliva in mouth.

In addition to Appar scoring, neonates should be evaluated within 24 hours:

- evaluation should ideally be performed under radiant warmer with family close by.

  for details of examination further see p. Exam11

1. Gross deformities (e.g. clubfoot, pterygium, birth trauma and other important abnormalities (such as heart murmur)*)
- *murmur heard in first 24 h is most commonly patent ductus arteriosus (murmur usually disappears within 3 days).
- 9% infants have abnormalities (mainly orthopelles), but many congenital abnormalities cannot be identified during first examination - inform parents that not all abnormalities are evident at birth (record this in writing).

2. Gestational age (primary determinant of organ maturity*) – when gestational age is uncertain or if infant seems large or small for age, can be determined in days immediately after birth using new Ballard score (typically accurate to ± 2 wks; each neonate is classified as preterm, full-term, postmature, see p. Exam11)

### DELIVERY ROOM
3. Body measurements - length, weight, head circumference are plotted against gestational age

- influenced by genetic factors and intrauterine conditions.
- also see p. 2735
- through plotting of weight vs gestational age, each infant is classified:
  a) SMALL for gestational age (SGA) see below
  b) APPROPRIATE for gestational age (AGA) (growth parameters are between 10th and 90th percentiles for specific time of gestation)
  c) LARGE for gestational age (LGA) see below

N.B. if head circumference > 90th percentile (regardless of other parameters), specific cerebral pathology should be investigated!

POSTDELIVERY CARE

- term infants with clear amniotic fluid, adequate respiratory effort, and good muscle tone.
  1) clearing of airway (if needed) see below (transfusion) >>
  2) drying see below (rennunciation) >>
  3) provision of warmth see above (rennunciation) >>
  4) assessing Apgar score

- low-risk delivery team consists of 2 persons: team leader to assess newborn and institute any necessary resuscitation; one assistant to aid in basic newborn resuscitation.
- neonate is bathed, wrapped, and brought to family.
- infants should remain with their mothers during and after routine care.
- head should be covered with cap to prevent heat loss.
- rooming-in and early breastfeeding should be encouraged.
- neonates are bathed once their temperature has stabilized at 37 C for 2 h.
- umbilical cord clamp can be removed when cord appears dry (usually at 24 h).
  - keep umbilical stump clean and dry to prevent infection - some centers apply THROMCAP.
  - cleanse, several times day or single dose of bacteriostatic trunke.
  - cord is observed daily for redness or drainage (cord is entry portal for infection!!!).
- neonates EXCHANGE within 48 h should be evaluated within 2-3 days to assess feeding success (breast feed, hentley hydration, and balance for those assumed risk).
- term neonates lose 5-8% of birth weight in first 3 days (urinary and insensible fluid losses, passage of meconium, loss of vernix caseosa, drying of umbilical cord, suboptimal colic intake).

URINATION

- most neonates void within 24 h after birth (average time of 1st void is 7-9 h after birth).
- most void at least 2 times in 24 h of life.
- in 1st 2 days, urine may stain diaper orange / pink (normal urine).
- delay in voiding -- light foreskin, posterior urethra, valves.
- normal well hydrated newborns void 6-8 diapers per day.

CIRCUMCISION

- can be performed (using local anesthetha) within 1st few days of life.
- decision regarding circumcision is ultimately made by personal choice, not medical indication.
- if abnormality of glans / penis is present -- delay circumcision (prepuce may be used later in plastic surgical repair).
- Circumcision must be delayed until at least first void!
- circumcision should not be performed if there is risk of bleeding disorders.
- benefits: circumcision prevents inflammation of glans and prepuce, decreases incidence of penis cancer, UTD.
- complications: local infection and bleeding.

DEFECATION

- if meconium has not been passed within 24 h after birth -- evaluate for anatomic abnormalities (imperforate anus, Hirschsprung's disease, cystic fibrosis).
- normal well hydrated newborns defece after every feeding = once every 4-5 days.
- breast-fed babies have loose stools with small curds, and bowel movements may be explosive.

PREVENTIVE INTERVENTIONS

- see p. 2700

SCREENING

- see p. 2856

PREMATURITY

- infant born before 37 wk gestation. - see p. 2458

EPIDEMIOLOGY

- 10% pregnancies in USA (17.9% for black infants).
- one of chief causes of neonatal morbidity and mortality (incidence of complications and mortality is roughly proportional to degree of prematurity).

PATHOPHYSIOLOGY

Organ maturation - structural & functional development.

- maturation is measured by comparison with adult level of organ function.
- variations in organ systems mature at different rates and at different times during gestation.

TERM INFANT

- has sufficient function of most organs to allow independent function.

PRETERM INFANT

- has inadequate function of some vital organs (e.g. lung) at birth, but within short period of time these organs will have accelerated development -- independent function of preterm infant at gestationally young age.

- *i.e. PREMATURE BIRTH alters normal sequence of organ maturation.

N.B. neonates < 23-24 weeks' gestation do not have sufficient lung development (absent capillary network adjacent to immature ventilatory units) - cannot survive.

close correlation between somatic growth and maturation of vital organs, but various factors may accelerate or retard these processes, e.g. biochemical lung maturation.
accelerated by fetal malnutrition and betamethasone; delayed by maternal diabetes (→ fetal hyperinsulinemia).

**Clinical Features**

- correlate with gestational age:

1. Low birth weight (<2500 g)

2. Physical signs of immaturity

   1. thin, shiny, dark pink skin through which underlying veins are easily seen.
   2. little subcutaneous fat, hair (but abundant lanugo on back).
   3. ear pinnae are easily folded into various positions without ready recoil.
   4. absent plantar creases.
   5. palpable breast tissue < 1 cm in diameter.
   6. genitalia - scrotum has few rugae, testes may be undescended / labia majora do not yet cover labia minora (labia minora are prominent, prominent clitoris).
   7. "floppy" muscular tone - large range of motion:
      - spontaneous activity
      - no flexion of extremities with posture at rest (i.e. extremities are not held in flexed position typical of term infants).
      - "scarf" sign (elbow easily reaches midline up to anterior axillary line; vs. term infant - cannot reach midline of thorax).

   - heel-to-ear maneuver (heel reaches head while pelvis is held flat)

   - ventral suspension - infant assumes semicircular posture when suspended prone in air with chest resting on examiner's hand:

5) reflexes develop at different times: Moro reflex begins by 28-32 wk and is well established by 37 wk, palm reflex starts at 28 wk and is well established by 32 wk; tonic neck reflex starts at 35 wk and is most prominent at 1 mo post term.

3. Multisystem complications (determinate diagnosis) - relate to dysfunction of immature organ systems:

   1. inadequate surfactant production → respiratory distress syndrome (RDS) → bronchopulmonary dysplasia, see p. 2130 (5) → and p. 2157 (3)
   2. immaturity of respiratory center → apneic spells, see p. 2116 (2-3) →
   3. periventricular leucomalacia / hemorrhage, see below
   4. sepsis or meningitis are 4 times more likely! (due to indwelling intravascular catheters, endotracheal tubes, areas of skin breakdown, markedly reduced serum Ig levels).
   5. patent ductus arteriosus (incidence increases with increasing prematurity).
   6. exceptionally large body surface area to volume ratio → hyperthermia.
   7. small stomach and immature sucking and swallowing reflexes → aspiration.
   8. succedaneous enterocolitis (→ bowel perforation, strictures, short bowel syndrome) - most common surgical emergency in premature infant!
   9. retinopathy of prematurity; ↑incidence of myopia and strabismus.
   10. hyperglycemia / hyperuricemia, see p. 2750.
   11. hyperbilirubinemia occurs more commonly (inadequate hepatic excretion); kernicterus may occur at (bilirubin as low as 10 mg/dL, in small, sick, premature infants.
   12. immature kidneys' inability to excrete fixed acids (accumulate with high-protein formula feedings and as result of bone growth) → metabolic acidosis.
   13. anemia of prematurity, see p. 1559 (4)
   14. skin immaturity (poorly cornified epidermis, immature stratum corneum until 32-34 weeks' gestation) - little barrier function:
      - insensible water loss (transepidermal water loss is most important route for water depletion in extremely immature infant) with accompanying heat loss.
      - ↑insensible water loss -> increased fluid administration, place in humidified environment
   15. skin immaturity (poorly cornified epidermis, immature stratum corneum until 32-34 weeks' gestation) - little barrier function:
      - ↑risk for infection with organisms that colonize skin surface (e.g. staphylococcal species).
      - ↑risk for toxicity from topically applied substances.
      - skin integrity is easily disrupted with adhesives.

**Evaluation**

- routinely for all prematures; also see p. Exam11

1) pulse oximetry
2) serum Ca, electrolytes, bilirubin
3) CBC
4) blood culture
MANAGEMENT
best provided in neonatal ICU or special care nursery.
careful attention to thermal environment (servo-controlled humidified incubators, or at least plastic barriers if placed in open radiant warmers).
way suctioning must be not vigorous and not frequent (→ hypoxia, periventricular hemorrhage / leukomalacia).
RDS is not associated with mucous production in first 24 hours of life - suctioning must be minimal during this time.
ARTIFICIAL SUBSTRATES instillation effectively reduces death secondary to RDS.
– indications: all infants < 30 weeks' gestation, infants > 30 weeks' gestation with clinical signs of RDS.
– prophylactic dose is administered before first breath* or within 15 min following birth.
*more uniform and effective drug distribution when lungs are fluid-filled without air-fluid interfaces.
infants are continually monitored for apnea, bradycardia, and hypoxemia until they are 34.5-35 wk adjusted age.
infants < 34 wk gestation (inadequate coordination of sucking and swallowing reflexes) must be fed by NGT (throat milk or formula) intravenously (e.g. 10% glucose with maintenance electrolytes) → breastfeeding when > 34 weeks.
parents should be encouraged to visit and interact with infant.
scrapulous handwashing before and after all patient contact.
before discharge from hospital - car seat monitoring using pulse oximetry – if can maintain patent airway and good Os saturations while positioned in car seat?

FOLLOW-UP
Prematures are at risk for developmental and cognitive delays - careful neurodevelopmental follow-up during first year:
1) developmental milestones
2) muscle tone
3) language skills
4) growth (weight, length, head circumference weekly).
5) visual skills
6) auditory function

POSTDATING, POSTMATURITY
Postdation (post term pregnancy) - pregnancy of ≥ 42 weeks.
little fetal growth occurs after 40th week, growth plateaus after 42nd week.
Postmaturity - lasting placental function after 42nd wk → placental insufficiency syndrome.
1. soft tissue wasting
2. fetal hypoxia, oligohydramnios, meconium aspiration (may be unusually severe because post-term amniotic fluid volume is decreased and aspirated meconium is less diluted).
3. hypoglycemia (insufficient glycogen stores at birth → hypoglycemia / hypoglycemia during hypoxia).
infants are unusually alert and appear mature with fully developed primitive reflexes but have decreased amount of soft-tissue mass (particularly subcutaneous fat → thin parchment skin hangs loosely on extremities and is often dry and peeling with cracks); fingernails and toenails are long and may be stained with meconium passed in utero.
prognosis and treatment depend on complications.

SMALL-FOR-GESTATIONAL-AGE (SGA, DYSMATURITY, INTRAUTERINE GROWTH RESTRICTION, IUGR)
SGA / IUGR = fetal weight ≤ 10th percentile for gestational age.
At term, infant is low-birth-weight if < 2500 g if < 1500 g, very low-birth-weight.
– fetal growth rate is 5 gm/d at 14-15 weeks' gestation, 10 gm/d at 20 weeks, and 30 gm/d at 32-34 weeks; growth rate slows after 36 weeks' gestation.
– during 1st trimester, growth parameters (i.e. weight, length, head circumference) are fairly uniform in all fetuses!
Somatic growth occurs by two processes: hyperplasia and hypertrophy. Hyperplasia - increase in size of tissue / organ due to increase in cell number.
growth during 1st half of pregnancy is achieved by hyperplasia - problems that interfere with somatic growth early in pregnancy inhibit normal cell growth → symmetric growth retardation (weight, length, head circumference). 20% IUGR cases.
– factors that adversely affect hyperplastic growth of fetus:
1. Chromosomal abnormalities, nonchromosomal congenital syndromes
2. Congenital infection (e.g. CMV, Toxoplasma, rubella)
3. Cell toxins (e.g. alcohol, opioids, cocaine).
Hypertrophy - increase in size of tissue / organ due to increase in cell size.
growth during last trimester of pregnancy and postnatally is achieved primarily by hypertrophy – problems that interfere with somatic growth in last stage of pregnancy inhibit normal cell growth → asymmetric (head sparing) growth retardation (i.e. body weight is primarily affected, with preservation of brain, cranium, and long bones growth) → all measurements are normal, except abdominal circumference! 80% IUGR cases.
– factors that adversely affect hypertrophic growth of fetus - affect fetal nutrition:
1. Placental insufficiency (preeclampsia, primary hypertension, renal disease, long-standing diabetes)
2. Placental involution (in postmaturity)
3. Maternal malnutrition
4. Multiple gestation
5. Maternal use of cigarettes
best treatment – early delivery.
Placental infarction:
Placental infarction (necrotic chorionic villi):

Placental villi with increased pink collagen (fibrosis as consequence of fetal demise):

Marked involution of placental villi (because of prolonged fetal demise) – fibrosis, villi quite small (placenta is of 2nd trimester):

Clinical Features
- despite small size, SGA infants have physical characteristics (skin appearance, ear cartilage, sole creases) and behavior (alertness, spontaneous activity, zest for feeding) similar to those of normally sized infants of like gestational age.

Full-term SGA infants have increased risk of:
1. perinatal asphyxia → meconium aspiration**, neurologic deficiencies.
2. hypoglycemia (due to lack of adequate glycogen stores), hypocalcemia
3. polycythemia (due to chronic mild hypoxia caused by placental insufficiency).
4. sequelae of etiologic factors (e.g. malformations).

*if intranarterine growth restriction is caused by placental insufficiency, each uterine contraction slows / stops maternal placental perfusion by compressing spiral arteries; H: fetal heart rate monitoring during labor (fetal compromise → rapid cesarean section to avoid asphyxia).

**hypoxic (esp. postmature) infant passes meconium and begins deep gasping movements.

N.B. full-term SGA infants do not have complications related to organ system immaturity that premature infants of similar size have!

Diagnosis
- serial weight and fundal height measurements: lagging (> 4 cm) fundal height → ultrasound.
LARGE-FOR-GESTATIONAL-AGE (LGA)

LGA - fetal weight > 90th percentile for gestational age.

Prominent causes:
1) genetically determined size (i.e., maternal history of large infants)
2) maternal diabetics (→ high fetal insulin level → anabolic effect)
3) rare cause of macrosomia - Beckwith-Wiedemann syndrome - duplication of 11p with insulin and IGF-II genes → macrosomia, macrosomia, omphalocoele, hypoglycemia, predisposition to cancers (Wilms tumor, hepatoblastoma).
4) hydrops fetalis.

Clinically: large, obese, pellagoric.

- often listless and limp.
- may feed poorly.

Complications:
1. Delivery complications (e.g., shoulder dystocia, asphyxia), birth trauma (e.g., fractures of clavicles or limbs). H: cesarean section!
2. Infants of diabetic mothers:
   1) hypoglycemia (e.g. 1-2 h because of state of hyperinsulinism and sudden termination of maternal glucose).
   2) close prenatal control of mother's diabetes + prophylactic IV 10% dextrose for infant until early frequent feedings can be established.
   3) hypbilirubinemia - caused by intolerance for oral feedings in earliest days of life, high Hct.
3) delayed pulmonary maturation.

PERINATAL ASPHYXIA

- < 1/3 newborns (many of which are extremely premature infants) occur during first 24 hours following birth; number of these early deaths have component of asphyxia.
- for surviving infants, effective management of asphyxia in first few minutes of life may influence long-term outcome!

PERINATAL PHYSIOLOGY

- fetus / newborn subjected to asphyxia begins “diving” reflex (maintains perfusion and oxygen delivery to vital organs):
  1) pulmonary vascular resistance ↑ → pulmonary blood flow ↓, blood flow directly to left atrium.
  2) systemic cardiac output is redistributed - increased flow to heart, brain, and adrenal gland → decreased flow to rest of body.
  3) systemic BP↑ (due to increased release of epinephrine), with ongoing hypoxia and acidosis, myocardium fails and BP begins to decrease → tissue ischemia and hypoxia.

Respiratory pattern:
- rapid respirations → respiratory efforts eventually cease with continued asphyxia (primary apnea).
  H: infant responds to stimulation with reinstitution of breathing.
- if asphyxia continues, infant begins irregular gasping efforts, which slowly decrease in frequency and eventually cease (secondary apnea).
  H: secondary apnea require positive-pressure ventilation (PPV) to restore breathing (i.e. secondary apnea does not respond to stimulation); longer infant is asphyxiated, longer onset of spontaneous respirations is delayed following initiation of PPV
- N.B. primary and secondary apnea cannot be clinically distinguished - if infant does not readily respond to stimulation, PPV should be instituted.

Brain
- newborn BP range at which CBF autorregulation is maintained is quite narrow (10-20 mmHg, vs. 40-60 mmHg range in adults); autoregulatory zone is also set at lower level.
- as BP falls, CBF falls below critical levels.
- local GABA release reduces cerebral oxygen demand, transiently minimizing impact of asphyxia.
- 6-24 hours after initial asphyxial injury, new phase of neuronal damage may occur due to reperfusion (increases over first 24-48 hours and then resolve).
- mechanisms of neuronal damage - release of excitatory amino acids (→ intracellular calcium), release of free radicals (→ membrane lipid peroxidation).
- N.B. not all brain cells die at once following anoxia; rather, many cells go through reoxygenation and reperfusion period (with neuronal hyperexcitability and intracellular edema)

Sequence of events associated with perinatal asphyxia and recovery after institution of resuscitation:

CHRONOLOGICAL
- all must be present!
  1) persistence of Apgar score 0-3 for > 5 min
    - as asphyxia progresses changes occur in orderly fashion: color* → respiration → muscle tone → reflex response → heart rate.
    *acral (peripheral) cyanosis is first sign!
    - with efficient resuscitation, signs normalize in reverse order: heart rate → reflex response → color → inspiration → muscle tone.
  2) umbilical arterial blood pH < 7.00
  3) sustained neonatal neurologic sequelae (hypotonia, coma, seizures)
NOTIFY NEONATAL RESUSCITATION
Who should not be resuscitated

a) extremely premature (< 23 weeks’ gestation)
b) extremely low birth weight (< 400 g)
c) chromosomal anomalies inconsistent with life (e.g. trisomy 13)

Equipment for Neonatal Resuscitation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Respiratory Support</th>
<th>Suction</th>
<th>Fluids</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bag-ventilation</td>
<td>呼吸袋</td>
<td>吸痰器</td>
<td>液体</td>
<td>药物</td>
</tr>
<tr>
<td>Continuous positive airway pressure (CPAP)</td>
<td>CPAP</td>
<td>吸痰器</td>
<td>液体</td>
<td>药物</td>
</tr>
<tr>
<td>Oxygen therapy</td>
<td>氧气治疗</td>
<td>吸痰器</td>
<td>液体</td>
<td>药物</td>
</tr>
</tbody>
</table>

Birth may reveal conditions that posed no problem during intrauterine life - for all deliveries, at least one person should be present who is skilled in neonatal resuscitation and has responsibility for only infant!

If delivery is high risk - 4 skilled individuals (team leader and 3 assistants)

6-10% newborns require resuscitation at delivery. Incidence increases significantly if birth weight is < 1500 g.

Perinatal asphyxia and extreme prematurity are states that most frequently require complex resuscitation and also 90% low birth weight infants require resuscitation and stabilization at delivery.

1-3 are considered routine care for most term infants:

1. Suctioning: of mouth and nose-pharynx should be done before thorax delivery (esp. if delivered through meconium-stained amniotic fluid) and then done intermittently, appropriately sized large-bore catheter using mechanical suction device with pressure limit. limit of 100 mm Hg (136 cm H2O)

2. Effective ventilation: bag – mask ventilation must be correct size and form tight seal on face.

3. Tactile stimulation: e.g. flicking soles, rubbing back – may be necessary to initiate and encourage regular, spontaneous breathing.

4. Heart rate > 100/min + adequate respiratory effort + cyanosis = O2 supplement at 8-10 L/min through face mask attached to self-inflatable or anesthesia bag.

5. Resuscitation: of mouth and nose-pharynx should be done before thorax delivery (esp. if delivered through meconium-stained amniotic fluid) and then done intermittently, appropriately sized large-bore catheter using mechanical suction device with pressure limit. limit of 100 mm Hg (136 cm H2O)

6. Oxygen therapy: bag – mask ventilation must be correct size and form tight seal on face.

7. Target saturations - 90-96% (85-92% in preterm infant)

Heart rate > 100/min OR respiratory distress OR cyanosis = O2supplement at 8-10 L/min through face mask attached to self-inflatable or anesthesia bag.

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- Target saturations - 90-96% (85-92% in preterm infant)
**ALGORITHM**

**Heart rate** < 60/min following 30 seconds of effective positive pressure ventilation → chest compressions (major difference from adult resuscitation!); see p. 3901

Neonates tend to develop bradycardia with hypoxemia:
- compress 90 times per minute.
- one ventilation is interposed after every 3 chest compressions (i.e. 30 breaths per minute).
- evaluate heart rate and color every 30 seconds.
- chest compressions are discontinued as soon as heart rate is > 60 BPM.

if after 30-60 sec HR remains < 60/min → intubation & mechanical ventilation:
- for medications use Millie size 0 blade, for term infants - size 1 blade.
- appropriate size of endotracheal tube (ETT) is based on weight of infant:

<table>
<thead>
<tr>
<th>Weight</th>
<th>ETT</th>
<th>ETT measurement at lip</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1000 g</td>
<td>2.5</td>
<td>7 cm at lip</td>
</tr>
<tr>
<td>1000-2000 g</td>
<td>2.5</td>
<td>8 cm at lip</td>
</tr>
<tr>
<td>2000-3000 g</td>
<td>3.5</td>
<td>9 cm at lip</td>
</tr>
<tr>
<td>&gt; 3000 g</td>
<td>3.5</td>
<td>1 cm at lip</td>
</tr>
</tbody>
</table>

- ventilation is provided via bag or ventilator after intubation.
- immediate increase in heart rate is excellent indicator of appropriate ETT placement.

if after 30-60 sec mechanical ventilation HR still remains < 60/min → EPINEPHRINE

- (1:1,000) 0.1-0.3 mg/kg IV via umbilical venous catheter is preferred route (if epinephrine is given via ETT, follow with 0.5-1 mL of saline flush to ensure that drug is delivered to lung).
- no need to wait if born without pulse

**BRADYCARDIA in distressed child is sign of impending cardiac arrest!!!**

- newborns, infants, and young children tend to develop bradycardia with hypoxemia, whereas older children tend initially to have tachycardia.

N.B. 5. Signs of bleeding, shock → *exsudation restoration* (0.9% SALINE, latched rangers, 5% albumin, Plasmanate, O-negative blood cross matched with mother); if necessary, add DOPAMINE.

- *is frequently used agent for volume expansion & rapid increase of lung compliance.
- dosage for volume expansion - 10 mL/kg IV over 5-10 min (inflame more cautiously in extremely preterm infants - risk of periventricular hemorrhage due to hypervolemia).
- neonatal cardiovascular system is very sensitive to preload, requiring adequate intravascular volume to maintain adequate cardiac output!!!
- cardiogenic shock → continued mechanical ventilation
- hypovolemia may be masked in newborn (significant peripheral vasoconstriction caused by elevated catecholamines following delivery).
- systolic BP may be falsely elevated with pain.

6. For prolonged resuscitation, use SODIUM BICARBONATE (0.5 mEq/mL) 2 mL/kg* IV to reverse metabolic acidosis.

- *if base deficit is known, more precise dose can be administered
- SODIUM BICARBONATE should not be used until adequate ventilation is obtained because of concomitant CO2 production following use of drug (if SODIUM BICARBONATE is used in face of respiratory acidosis and elevated PCO2, acidosis will not be corrected!)
- SODIUM BICARBONATE in delivery room has been associated with ↑risk of periventricular hemorrhage due to hypervolemia.
- N.B. recent studies show that 0.9% SALINE provides better cardiac & BP support to correct both acidosis and underlying etiology of metabolic acidosis.

Discontinuing resuscitation may be justified in infants who have not responded to continuous and appropriate resuscitation for full 10 minutes and who have no heart rate or respiratory effort (no signs of life).

**ALGORITHM** for resuscitation of neonates:

**At birth**
- Is gestation at term? Is dermoic fluid clear to the newborn breathing or coughing?

**If yes**
- Routine care: provide warmth, position the newborn, stedy airway, and try

**About 30 sec after birth**
- Evaluate: respiration, color, and rate.

**If the neonate is breathing and pulse with HR > 100**
- Routine care

**If the neonate is apneic/pulseless with HR < 100**
- Provide positive-pressure ventilation,

**After 30 sec of ventilation**
- If HR remains < 100:

**If HR > 100**
- If oxygen is not already provided

**Continued positive-pressure ventilation**
- Apple juice compression

**After 30 sec compression**

**If oxygen is already provided**
- If HR is < 100:

**If oxygen is not already provided**
- **(Optional)** Give supplemental O2 (1:1.0-0.3 mL/kg of 120,000,000% solution: X = mL/kg; X = mL/kg over 10 min)

**If HR will not rise**
- Continue measures

**Endotracheal intubation may be considered at any of several steps**
- Premature heart rate about 60 sec. Continued chest compressions until the spontaneous HR is > 60 beats/min.

**Ped9 (8)**

**N.B. primary importance is establishment of effective ventilation** - without ventilation, other therapies, including drugs, will not be effective in establishing adequate heart rate and perfusion.
Hypoxic-ischemic encephalopathy (HIE) - Subacute brain lesions due to systemic hypoxia or reduced cerebral blood flow - i.e., encephalopathy from asphyxia.
- Exact cause and exact time of brain injury often remain uncertain.
- E.g., acute perinatal/iatrogenic events are found in only 20% children with cerebral palsy
- Abnormal brain might be underlying risk factor
- Pathophysiology - see above (PERINATAL ASPHYXIA) >>

Brain Pathophysiology - depends on brain maturity at time of insult and duration of ischemia:
- Final brief (> 20-25 min) asphyxia results in deepfrozen lesions rarely compatible with life.
- Profound asphyxia lasting < 10 min in otherwise healthy newborn is not thought to cause any permanent brain damage.
- Partial asphyxia for minutes ÷ hours results in predominantly supratentorial lesions:
  - In preterm infants, damage is at GERMINAL MATRIX area - periventricular hemorrhages, leukomalacia (→)
  - After 36 weeks of gestation, lesions primarily involve:
    1. CEREBRAL CORTEX (laminar neuronal necrosis in depths of sulci (→) - ALEGGIA) - lesions are diffuse or localized watershed (e.g. in parasagittal location).
    2. BASAL GANGLIA (→ static manifestations) with choreoathetosis and related movement disorders.
    3. BRAIN STEM.
    4. CEREBELLAR PURINIC CELLS (→ cerebellar atrophy).
- Especially after fetal hypotension
- Unbearable disorientation due to patchy neuronal loss, gliosis, and hypomyelination (at > 6 months of age); full evolution of neuropathology may take months to years.

Less severe intrauterine anoxic episodes of undetermined duration may involve neurons DIFFUSELY or may preferentially affect HIPPOCAMPAL AREAS.

INCLINATION PHENOMENA - Most gauged by NARAB CLASSIFICATION (in conjunction with EEG, neuroimaging, and brain stem auditory and cortical evoked responses):

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>STAGE I (MILD)</th>
<th>STAGE II (MODERATE)</th>
<th>STAGE III (SEVERE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration*</td>
<td>&lt; 24 h</td>
<td>2-14 days</td>
<td>hours to weeks</td>
</tr>
<tr>
<td>Consciousness level</td>
<td>hyperalertness and irritability</td>
<td>lethargy</td>
<td>deep stupor or coma</td>
</tr>
<tr>
<td>Muscle tone</td>
<td>normal or slightly ↑</td>
<td>significant hypotonia or proximal limb weakness</td>
<td>Flaccidity</td>
</tr>
<tr>
<td>Posture</td>
<td>mild distal flexion</td>
<td>strong distal flexion</td>
<td>Intermittent decerebration</td>
</tr>
<tr>
<td>Moro reflexes</td>
<td>normal</td>
<td>exaggerated</td>
<td>Absent or ↓</td>
</tr>
<tr>
<td>Segmental myoclonus</td>
<td>present</td>
<td>present</td>
<td>Absent</td>
</tr>
<tr>
<td>Seizures</td>
<td>none</td>
<td>common (70%)</td>
<td>Infrequent (x 24- 48 hrs, then usually stop)</td>
</tr>
<tr>
<td>EEG</td>
<td>normal</td>
<td>low voltage, periodic or paroxysmal, epileptiform activity</td>
<td>Partial periodic pattern → isoelectric</td>
</tr>
<tr>
<td>Complex reflexes</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Autonomic Function:
- Pupils: Dilated, weak
- Respiratory: Variable in rate and depth, periodic
- Heart rate: Low or normal, occasional pauses
- GI Motility: Normal or ↓
- Risk of death: < 1% 14% (> 50%)
- Risk of severe handicap: 2-20% 60% + 70% 

*Maclang, depression → hyperalertness and hyperreflexia → coma.
- Hypoxic-ischemia: ≤ 1% cases per 1000 births.
- Symptoms of moderate/ severe HIE almost always manifest at birth or within few hours.
- Infants who sustain hypoxic / ischemic insults weeks > months before birth may seem normal at birth (but later show signs of static encephalopathy or seizures), others already exhibit signs of chronic cerebral disease at birth (with overt microcephaly and spasticity).
Multicystic encephalomalacia

Since there are already extensive changes at age 12 hours, insult occurred in utero, at least 24 hours before scan.

Resistive index (0.43).

Pulsed Doppler - diastolic velocities with reduced resistive index (< 0.50), sign of luxury perfusion; or decreased peak-systolic velocities, sign of low blood flow.

CT is best method to confirm cerebral edema, evolving zones of infarction (areas of reduced density)

MRI is valuable to confirm, preexisting involvement of multiple organs

EEG performed within few hours of birth can help evaluate severity of brain injury.

Multi-organ involvement is hallmark of HIE.

Mild to moderate: Reduced amplitude

Severe: Absense of normal peak–systolic velocities, sign of cerebral edema

CT - normal peak–systolic velocity (40 cm s⁻¹), but increased end-diastolic velocity (25 cm s⁻¹) and decreased resistive index (0.43).

SEMMERSTEDT

Severe partial hypoxia at birth

Prolonged aEEG may be used to confirm prenatally in heavily sedated or paralyzed infants.

Brain-stem auditory evoked responses (BAER) may imply poor prognosis.

In assisted ventilation, drugs for muscle paralysis and morphine (for sedation) can mask seizures!

Invasive methods include:

- Cranial ultrasound
- Pulsed Doppler
- EEG
- Brain-stem auditory evoked responses (BAER)
- Cortico-subcortical ischemic injury

Correlation between MRI and findings at school ages!

Sequela - microcephaly, mental retardation, epilepsy, cerebral palsy.

* even in absence of obvious neurologic deficits in newborn period, long-term functional impairments may be present (e.g. learning difficulties)- prognosis is always guarded - all children with moderate/severe HIE should be monitored well into their school ages!

**Multicystic encephalomalacia** of 18-month old girl who suffered severe partial hypoxia at birth (T2-MRI): most of cerebrum has undergone cystic destruction; mesencephalon and thalamus have normal appearance. Dilated lateral ventricles; head is small and hydrocephaly but this is not caused by hydrocephalus.
TREATMENT

- transfer to tertiary neonatal intensive care unit.
- most infants need ventilatory support during first week (avoid hyperventilation → severe hyperperfusion of brain).
- maintain mean BP > 35 mm Hg (for term infants); Dopamine (inotropic of choice) or Dobutamine can maintain adequate cardiac output.
- avoiding hyperthermia after hypoxic-ischemic event at birth is essential!!!
- current data are insufficient to recommend Brain Hypothermia for all infants with suspected asphyxia, but it is slowly emerging as useful therapy for mild-to-moderate cases!
  - cooling must begin within 1 hour of injury.
  - keep 3-4°C below baseline temperature for up to 48-72 hours.
  - two methods may be used:
    a) selective head cooling cap (Cool-Cap) – FDA approved for moderate to severe HIE!
    b) whole body hypothermia
      - rewarming is carried out gradually (over 6-8 hours).
- seizures should be treated early with Phenobarbital (drug of choice!!!) or Lorazepam (second drug of choice), Phenytion IV (third drug of choice) may be added.
  - drugs can be weaned and stopped during first month of life (unless persistent neurological abnormalities and clinical or EEG evidence of seizures → treatment is continued for several months to 1 year).
  - Even asymptomatic seizures (seen only on EEG) continue to injure brain!
- hypotonia and feeding difficulties often persist, requiring tube feeding for weeks/months.
- fluids 60-80 mL/kg for infant in humidified incubator (rates much higher for infant in dry radiant environment).
  - in first 2-4 days, restrict IV fluids to 2/3 of daily requirement (for gestational age and nursing environment) because of high frequency of acute tubular necrosis and IAH.
  - for those on high-frequency ventilators (venous return may be impaired), fluid volumes must be increased.
  - electrolytes (sodium, potassium, chloride) should not be added initially because fluid shifts from other body compartments allow for adequate electrolyte supply until adequate renal function is documented.
- hypoglycemia may occur rapidly in critically ill/premature infants - GLUCOSE 4-6 mg/kg/min IVI should be started for those who do not tolerate enteral feedings.
  - avoid dextrose boluses (→ transient hyperosmolarity and rebound hypoglycemia).
- Avoid hypoglycemia or hyperglycemia (both damage brain).
- the newborn may tolerate, but do not tolerate enteral feedings.
- severe hypoglycemia may be seen in a several months to 1 year).
- hypothermia is decreasing due to increasing use of premature labor and delivery occasionally cause physical injury to infant.
- factors for increased heat losses in newborns:
  1) large skin surface area to body weight ratio → heat and fluid evaporative loss!,
  2) thin skin with blood vessels near surface provides poor insulation
  3) newborn (especially if premature) has limited capacity to change body position for heat conservation (by decreasing exposed surface area in flexed position).
- very limited capacity for metabolic heat production: limited energy stores (subcutaneous fat and brown fat), esp. in premature and growth-retarded infants; infants do not shiver effectively.
- heat loss increases metabolic rate and uses more oxygen (dangerous if already in respiratory compromise) → rapidly used glucose and glycogen reserves → metabolic acidosis, hypoglycemia.
- hypothermia also may be caused by pathologic conditions that impair thermoregulation (e.g. sepsis, intracranial hemorrhage).

HYPOTHERMIA

- core temperature < 35.35°C
- intracranial thermoregulation is passive - no use of calories or oxygen by fetus (allows for maximal intratradinal growth without fetal energy expenditure for thermal homeostasis).
- neonates respond to cooling by sympathetic nerve function is documented.
- do not shiver effectively
- may occur rapidly in critically ill / premature infants - GLUCOSE 4-6 mg/kg/min IVI should be started for those who do not tolerate enteral feedings.
  - avoid dextrose boluses (→ transient hyperosmolarity and rebound hypoglycemia).
- Avoid hypoglycemia or hyperglycemia (both damage brain).
- monitor weight, hydration status, urine output, serum [sodium]!

PROPYLHALS

- newborns should be dried with prewarmed blankets or towels.
- place on prewarmed heat source; open bed warmers, which use radiant heat, are used in most delivery rooms (convenient access to newborn)
  - sick neonates should be maintained in neutral thermal environment to minimize metabolic rate.
  - proper incubator temperature depends on birth weight and postnatal age (alternatively, servoheating can be set to maintain skin temperature at 36.5°C)
  - for those on high-frequency ventilators (venous return may be impaired), fluid volumes must be increased.
  - electrolytes (sodium, potassium, chloride) should not be added initially because fluid shifts from other body compartments allow for adequate electrolyte supply until adequate renal function is documented.
- hypothermia may be caused by pathologic conditions that impair thermoregulation (e.g. sepsis, intracranial hemorrhage).

BIRTH TRAUMA

- forces of labor and delivery occasionally cause physical injury to infant.
- incidence is decreasing due to increasing use of cesarean section (in place of difficult versions, vacuum extractions, or mid- or high-forceps deliveries).
- risk factors: small pelvic measurements, large for gestational age infant, breech or other abnormal presentation, primipara.

HEAD TRAUMA

- forces of labor and delivery occasionally cause physical injury to infant.
- incidence is decreasing due to increasing use of cesarean section (in place of difficult versions, vacuum extractions, or mid- or high-forceps deliveries).
- risk factors: small pelvic measurements, large for gestational age infant, breech or other abnormal presentation, primipara.
Most vaginal delivery elevation for cosmetic reasons). Forceps delivery slow deformational forces intracranial hemorrhage; presentation operative delivery risk factors: supratentorial subdural hemorrhage — exclusively full-term or large infants with difficult deliveries. supratentorial SAH of venous origin — full-term newborns who have focal seizures and benign clinical course; SAH may be found in premature infants, but there is no recognized clinical syndrome: periventricular hemorrhage — premature infants of ≤ 32 weeks gestation, see below >>.

hypoxia-ischemia usually precedes bleeding (hypoxia-ischemia damages endothelium, impairs cerebrovascular autoregulation, and can increase cerebral blood flow and venous pressure, all of which make hemorrhage more likely).

diagnosed by CT (ultrasound is not good method - extracerebral fluid collections over hemispheres and posterior fossa masses are very difficult to detect).

- evaluate for skin petechiae or hemorrhage from other sites (e.g. vit. K deficiency, hemophilia, DIC).

- be life threatening (esp. if born prematurely).

- prognosis: for SAH is generally good; prognoses for subdural hemorrhage is guarded (some infants do well);

- treatment is supportive;

- give vitamin K if it was not previously given;

- symptomatic subdural hematomas → daily subdural taps. see p. 79.3

- in posterior cranial fossa hematoma, surgical drainage may be lifesaving!

Slow deformational forces → tears in tentorium (less commonly, in falx, in junction between falx and tentorium) → subdural hematoma.

Forceps delivery → ‘ping-pong’ skull fractures — depressed fracture without fracture line (may require elevated cosmetic response, see p. 79.5)

- may be associated with subdural bleeding, SAH, or brain compression / laceration.

Vaginal delivery may result in:

1) MOLDING (bone overlapping at sutures) - disappears within 2-14 days after birth.

2) CAPUT SUCCESSIONUM — swelling in presenting portion of scalp (above peristrium) secondary to compression by cervix (due to vacuum effect after amniotic sac rupture); resolves within 2 weeks.

3) SUBGALEAL HEMATOMA — blood accumulation in sub-galeal loose areolar tissue.

- soft fluctuant swelling over entire scalp (i.e. not limited by perioral insertions).

- self-limiting condition.

- Needle / incisional drainage may result in infection!!!

4) CEPhALODemaTOMA — subperiosteal blood accumulation; may develop after instrumental delivery.

- not present at birth, appears within 24 hours.

- fluid-blood collection is limited by perioral insertion at suture lines, i.e. does not extend across suture (vs. caput succedaneum).

- initially soft, but may develop raised bony margin within 2-3 days (rapid Ca deposition at edges of raised peristrium).

- small percentage have associated linear fracture in underlying bone.

- commonly unilateral and partial.

- visible on plain radiograph as subperiosteal elevation.

- usually resolve spontaneously within few weeks (occasionally calcify and form bony protraction; self-correcting cosmetic deformity - calcified tissue is gradually absorbed by expanding calvarium and appearance becomes normal before age 1-2 years).

- Needle / incisional drainage may result in infection!!!

CRANIAL NERVE INJURY

Most often: FACIAL NERVE:

a) most injuries — pressure on nerve in utero (head lying against shoulder, saccral promontory, or uterine fibroid).

b) facecups pressure.

- injury usually occurs at or distal to exit from stylomastoid fossae.

- facial asymmetry is most apparent during crying (differentiate from mandibular asymmetry resulting from intrauterine pressure; maxillary and mandibular occlusal surfaces are not parallel, vs. facial nerve injury).

- testing of treatment is not needed for peripheral CN7 injuries or mandibular asymmetry - they usually resolve by age 2-3 months.

BRACHIAL Plexus INJURIES

- injury: stretching by shoulder dystocia, breech extraction, neck hyperabduction in cephalic presentations.

KN9 [12]
- pathophysiology – simple stretching, hemorrhage within nerve, tearing of nerve or root, avulsion of roots with accompanying cervical cord injury (spinalateral pyramidal signs).
- associated injuries – fractures of clavicle or humerus or subluxations of shoulder or cervical spine.
- clinical features – see p. P97.
- treatment – hand support, passive range-of-motion exercises.
  - usually improve rapidly:
    - if significant deficit persists > 3 mo → MRI to determine extent of injury to plexus, roots, and cervical cord; surgical repair may be helpful.
    - if entire brachial plexus is injured → neurosurgical exploration; prognosis for recovery is poor; extremity's growth may be impaired.

OTHER PERIPHERAL NERVE INJURIES
- usually not related to labor and delivery (i.e. usually secondary to local traumatic event, e.g. injection in or near sciatic nerve).
- treatment – placing muscles antagonistic to those paralyzed at rest until recovery; neurosurgical exploration is seldom indicated.
- recovery is complete.

FRACTURES
Most common – MIDCLAVICULAR FRACTURE.
- occurs with shoulder dystocia.
- neonate is irritable and does not move arm (either spontaneously or when Moro reflex is elicited).
- most clavicular fractures are greenstick - heal rapidly and uneventfully (large callus forms within week, and remodeling is completed within month).
- treatment – sling by pinning shirt sleeve of involved side to opposite side of infant's shirt.

HUMERUS AND FEMUR FRACTURES: difficult deliveries.
- most are greenstick, mid-shaft fractures → excellent remodeling, even if moderate angulation occurs initially.
- epiphysis fractures also bear excellent prognosis.

SOFT-TISSUE INJURIES
- if they are presenting part or fulcrum for forces of uterine contraction.
- periorbital and facial tissues in face presentations; scrotum or labia during breech deliveries.
- edema and ecchymosis.
- added burden of bilirubin may produce sufficient hyperbilirubinemia to require phototherapy, a exchange transfusion.

PERIVENTRICULAR / INTRAVENTRICULAR HEMORRHAGE (PVH-IVH)
- hemorrhage into germinal matrix seen exclusively in \textbf{INTRAUTERINE INFANTS after asphyxial insult}.
- Intraventricular hemorrhage in \textbf{TERM INFANTS} – from choroid plexus.

ETIOLOGYPATHOPHYSIOLOGY
- hemorrhage occurs into subependymal fragile, richly vascular germinal matrix (lies on lateral wall of lateral ventricles between thalaliumus and ventricle, near foramina of Monro; from lateral ventricle separated only by ependyma).
- germinal matrix is site of neuronal proliferation as neuroblasts divide and migrate into cerebral parenchyma:
  - by ≥ 20 weeks' gestation, neuronal proliferation is completed; however, glial cell proliferation is still ongoing;
  - germinal matrix supports division of glioblasts and glial differentiation until ≥ 32 weeks' gestation, at which time regression is nearly complete.
- N.B. germinal matrix is present only in fetus and premature < 32 weeks' gestation.
- metabolically active differentiating cells of germinal matrix are rich in mitochondria (quite sensitive to ischemia):
  - supplying this area is primitive and fragile retelike capillary network.
  - arterial supply – recurrent artery of Heuber and lateral striate arteries.
  - venous supply – thalamostriate veins.
  - as result of respiratory distress from immature lungs along with episodes of hypoxemia and fluctuations in cerebral perfusion, vessels in germinal matrix have tendency to rupture.

N.B. only sites in adult brain where neurons still being produced – olfactory bulb and hippocampus!

CRANIAL INJURIES:
- dense layer of small dark blue cells below ependyma of lateral ventricle:
  - lies on lateral wall of lateral ventricles, near foramina of Monro; from lateral ventricle separated only by ependyma.

- N.B. only sites in adult brain where neurons still being produced – olfactory bulb and hippocampus!

- two major pathophysiologic factors:
  1. (1) loss of cerebral autoregulation (autoregulatory abilities vary proportionally to gestational age – range of perfusion pressures over which premature neonate can control regional CBF is narrower and lower than that of infants born at term) → pressure-passive circulatory pattern.
  2. (2) abrupt alterations in cerebral blood flow and pressure (esp. hypotension followed by hypertension, increased venous pressure)

- two major pathophysiologic factors:
conditions that overwhelm autoregulatory abilities: asynchrony between spontaneous and mechanical breaths; birth (esp. vacuum-assisted delivery); frequent noxious procedures of care-giving; instillation of mydriatics; tracheal suctioning; rapid volume expansion; rapid colloid infusion (e.g. exchange transfusion); infusions of hypertonic solutions (e.g. sodium bicarbonate); seizures, changes in pH, PaCO₂, and PaO₂.

- source of bleeding – capillaries (possess neither tight junctions between endothelial cells nor strong basement membrane - increased flow and pressure may rupture delicate capillaries).

**CLINICAL FEATURES**

**Grades (worsening prognosis):**

- **Grade I** – confined to germinal matrix, i.e. subependymal (usually asymptomatic - most infants do well!)

- **Grade II** – small blood amount (< 40% of ventricular volume) in ventricles without ventricular enlargement (nonspecific irritability or lethargy - most infants do well!)

- **Grade III** – blood in ventricles, ventricular dilation (mortality < 10%); sequelae - static or reversible or progressive posthemorrhagic hydrocephalus → 30-40% incidence of cerebral palsy and mental retardation.

**Grade IV** (periventricular hemorrhagic venous infarction) – additional hemorrhage into parenchyma which involves periventricular motor tracts (poor prognosis – 27-80% mortality; 90% incidence of cerebral palsy and mental retardation); it is **secondary to lower grade** (I-III) hemorrhage which leads to congestion in periventricular white matter → venous infarction → secondary hemorrhage; almost always unilateral and anterior, clinically:

1. severe apnea, bradycardia, hypotension, altered mental status.
2. extensor posturing and opisthotonos; pupils fixed in midposition.

**Sequela:**

- Destruction of periventricular cerebral parenchyma (esp. motor tracts*) → cerebral palsy (!!!), mental retardation, seizures.
- tracts innervating lower extremities are nearest to ventricles, followed by those innervating arm, and, finally, face – greater degree of motor dysfunction of extremities as compared to face (spastic hemiplegia in unilateral lesions and spastic diplegia or quadriplegia in bilateral lesions)

- Posthemorrhagic hydrocephalus

Because PVH-IVH development is related to alterations in cerebral blood flow, injury to other portions of brain may occur:

1. **GLOBAL HYPOXIC-ISCHEMIC INJURY**
2. **PERIVENTRICULAR LEUKOMALACIA (PVL)** - nonhemorrhagic ischemic necrosis.

**DIAGNOSIS**

<table>
<thead>
<tr>
<th>Hematocrit fall (%)</th>
<th>Clinical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10%</td>
<td>1. Deterioration of periventricular cerebral parenchyma (esp. motor tracts*) — cerebral palsy (!!!), mental retardation, seizures.</td>
</tr>
</tbody>
</table>

*tracts innervating lower extremities are nearest to ventricles, followed by those innervating arm, trunk, and, finally, face — greater degree of motor dysfunction of extremities as compared to face (spastic hemiplegia in unilateral lesions and spastic diplegia or quadriplegia in bilateral lesions)
2) CSF bloody or normal → xanthochromic.
3) cornerstone of diagnosis - ultrasound - sensitivity 96%, specificity 94% (has replaced CT) - delineates site of blood in parenchyma and ventricles, ventricular size, and shifts of major structures.

**American Academy of Neurology recommendation:** all infants < 30 weeks gestational age must be screened* by cranial ultrasonography at 7-14 days postnatal life and at 36-40 weeks postmenstrual age.

- PPH can occur without clinical signs - serial weekly examinations are necessary for follow-up (progression of hemorrhage, development of posthemorrhagic hydrocephalus).
- **HYPERECHOGENIC area** on inferior wall of lateral ventricle, overlying caudate nucleus head.
- when it ruptures into ventricular lumen, it appears as intraventricular hemorrhage material (when it is small - must be distinguished from choroidal plexus - colour Doppler may help); later, intraventricular clot becomes less echogenic in its centre but is surrounded by echogenic line.
- parenchymal hemorrhage is seen as unilateral or asymmetric echodense area, radiating from external angle of ventricle, which evolves to anechoic cavitation (porencephalic cyst).

Sagittal sonogram (intraventricular hemorrhage): hyperechoic blood fills lumen of lateral ventricle.

Coronal sonogram - right intraventricular hemorrhage with parenchymal hemorrhagic infarction (straight arrows), mass effect on interhemispheric fissure (curved arrow), dilatation of left ventricle (frontal horn F, temporal horn T).

Grade III: hyperechoic areas represent hemorrhage in lateral ventricle; ventricles are markedly dilated.

Grade IV (periventricular hemorrhagic infarction):
A. Axial T2-MRI - anterior periventricular cavity contains residual blood clot.
B. Axial T1-MRI in 2-year-old girl with congenital right hemiplegia; she was born prematurely and had periventricular hemorrhagic infarction.

Grade II PVH-IVH:

Grade III PVH-IVH:

Grade II PVH-IVH:

Grade III PVH-IVH:
Grade IV PVH/IVH:

Grade IV with porencephalic cyst formation:

Periventricular hemorrhagic infarction (MRI):
PANCURONIUM

- Measures not proven clearly beneficial

- volume administered rapidly it

- then q24h for 2 d for total of 3 doses

INDOMETHACIN

- Greatest risk is first

- Avoidance of premature birth!

- Not recommended

- Grade

- No treatment

- Correction of anemia, acidosis, hypotension + ventilatory support.

PVL in children born at term is effect of intrauterine damage.

75% prematures have PVL on postmortem examination.

a) PHENOBARBITAL

- intermittent ventilatory support

- prophylaxis

- acetazolamide and

- furosemide in posthaemorrhagic

- hypotension

- decreases cerebral blood flow

- grade PVH

- death, shunt placement or both

Primary outcomes at 1 year

- Drug + Standard therapy

- Standard therapy alone

- p value

- Head, shunt placement or both

- 65%

- 85%

- 0.026

References:

Lancet 1998 ; 352 : 433

International randomised controlled trial of acetazolamide and furosemide in posthaemorrhagic ventricular dilatation in infancy .


Whitelaw A.

Mortality at 68 weeks' gestation and 1 year of life in infants with posthemorrhagic

ventricular dilatation.


Multi-centre randomized controlled trial, 177 patients.

Infants in the drug therapy group had a significantly increased risk (p = 0.012) of death, impairment or disability at 1 year. Risk ratio of 1.40 (1.12 – 1.76).

PREVENTION

- avoidance of premature birth!

- Greatest risk is first 72 hours of life (50% hemorrhages occur on 1st day) – reduce infant's systemic blood pressure fluctuations (may diminish incidence of hemorrhage and its spread):

1) PANCURONIUM paralysis while infant is ventilated (prevents asymmetry between spontaneous and mechanical breaths)

2) Not too rapid volume expansion following ischemia or hemorrhagic shock.

INDOMETHACIN prophylaxis must be administered within hours of birth: 0.1 mg/kg IV when aged 6 h, then q24h for 2 d for total of 3 doses) – accelerates maturation of germinal matrix vasculature; when administered rapidly it decreases cerebral blood flow, cerebral blood flow velocity, and cerebral blood volume → reduced incidence of high-grade PVH-IHV.

PHENOBARBITAL

- history of maternal chorioamnionitis is common

- bilateral white matter lesion of premature infants

- Clinically most significant destructive lesions in immature brain - strong relationship to subsequent handicap?

- 75% prematures have PVL on postmortem examination.

- PVL in children born at term is effect of intrauterine damage.

- selective loss of oligodendrocytes due to:

  a) hypoxia, ischemia → ischemic/reperfusion injury by free radicals.

  e.g. due to respiratory distress syndrome, pneumonia, mechanical ventilation → hypocarbia, maternal cocaine abuse

  N.B. mechanically ventilated premature infants are at greatest risk for PVL!

  b) controversial: maternal / fetal infection → cytokine-induced damage.

  *history of maternal choriosamnionitis is common.
• damage occurs in white matter adjacent to superolateral borders of lateral ventricles – it is watershed zone of deep penetrating arteries of middle cerebral artery.

• site of injury affects corticospinal tracts, visual radiations, and acoustic radiations.

• reactive increase of astrocytes.

• macroscopic - chalky yellow plaques (white matter necrosis and mineralization); extensive damage → multicystic encephalopathy.

Central focus of white matter necrosis with peripheral rim of mineralized axonal processes (staining blue):

Clinical features
Initially, asymptomatic or subtle symptoms:
1. Decreased tone in lower extremities
2. Increased tone in neck extensors
3. Apnea and bradycardia
4. Irritability
5. Pseudobulbar palsy with poor feeding
6. Clinical seizures (10-30%)

Sequela:
1) cerebral palsy (60-100%) – most commonly spastic diplegia or quadriplegia.
2) intellectual – developmental impairment.
3) visual disturbances (fixation difficulties, nystagmus, strabismus, blindness)

Diagnosis
• cranial ultrasonography (modality of choice): N.B. initial exam may be normal!
  1) periventricular edema - increased echotexture (echodensities) - greater than or equal to choroid plexus; disappears at 2-3 weeks.
  2) periventricular cysts (15% patients) appearing at 2-3 weeks after initial echodensities; severity of PVL is related to size and distribution of these cysts.
  3) cysts are transient and subsequently collapse → atrophy of damaged periventricular white matter → secondary ventricular dilatation with irregular ventricular margins (first detectable 4-8 weeks after injury; persists throughout life).

• CT - ventriculomegaly of lateral ventricles with irregular margins and loss of deep white matter.

• MRI (most helpful in monitoring) - loss of white matter, abnormal signal intensity of deep white matter (1-2 years after injury, when myelination process is complete); ventriculomegaly; in severe cases - thinning of posterior body and splenium of corpus callosum.

• volumetric MRI - extent of injury to corticospinal tracts.

Coronal ultrasound - normal periventricular echotexture:

Coronal ultrasound - increased periventricular echodensities:

Coronal and sagittal ultrasounds (5-week-old premature infant): multiple bilateral periventricular cysts.
Axial CT (5-week-old premature infant) – mild ventriculomegaly, irregular ventricular margins (incorporation of periventricular cysts), loss of periventricular white matter.

Axial CT (14-month-old premature infant) – ventriculomegaly limited to lateral ventricles secondary to diffuse loss of periventricular white matter.

T1-MRI (18-month-old premature infant) – lateral ventricles enlarged without hydrocephalus due to diminished periventricular white matter.
T1-MR1 (18-month-old premature infant) - hypoplasia of corpus callosum, most evident in body:

Posterior coronal ultrasound - multiple small echolucencies in periventricular white matter adjacent to trigones of lateral ventricles (arrows):

End-stage of PVL:

A. Significant reduction of periventricular white matter close to trigone of lateral ventricles bilaterally (arrows); cortical structures deep in Sylvian fissure abut lateral ventricle directly and appear to indent ventricular wall; and deep portions of Sylvian fissures are dilated; remaining white matter shows no abnormal signal.
B. Significant reduction in size of corpus callosum.
C. 8-year-old girl with severe visual cognitive impairment without cerebral palsy - significant dilatation of posterior horns of lateral ventricles (due to occipital white matter loss); remaining white matter anteriorly shows abnormal signal.
No medical treatment currently exists!
• close developmental follow-up.