# NICU Handbook 2022

UWHealthKids | School of Medicine and Public Health, University of Wisconsin-Madison | UnityPoint Health Meriter Foundation

*The guidelines in this handbook are suggestions and a starting point for management of newborns in NICU supervised by neonatology providers. They are not intended, nor should they ever be used, as a substitute for careful evaluation of our patients and thoughtful diagnostic and therapeutic plans. Direct in-depth discussion with a member of neonatal supervisory team must occur for individualized patient care. Please consult a textbook of neonatology for more in-depth pathophysiology, differential diagnoses and management issues.*

*Nina Menda, MD*

**Table of Contents**

# Chapter 1: Definitions and Outcomes

*Nina Menda, MD*

## Vital Statistics: Definitions

- Perinatal Period — From 28 weeks to 7th day of life
- Preterm birth — Birth prior to 37 completed weeks
- Late preterm birth — Birth between 34 and 36 6/7 weeks
- Term birth — Birth from 37 to <42 weeks
- Post term birth — Birth from 42 weeks or greater
- Low birth weight — Less than 2500 grams
- Very low birth wt (VLBW) — Less than 1500 grams
- Extremely low birth wt (ELBW) — Less than 1000 grams
- SGA/LGA — <10%/<90th%
- IUGR — Intrauterine fetal growth <10% for GA
- Fetal death — Death after 20 weeks of gestation
- Neonatal death — Death prior to 28 days of age
- Infant death — Death up to one year of age

## 2019 US Births Statistics

- Total births — 3,747,540
- Total Preterm Births (<37 wks) — 10.2%
- Early Preterm Births (<34 wks) — 2.8%
- Low birthweights — 8.3%

## Meriter Survival Data

**Statistics collected from Meriter NICU from 2015-2020**

| Gestational Age at Birth | Percent Survival |
|---|---|
| 23 weeks | 60% |
| 24 weeks | 76% |
| 25 weeks | 94% |
| 26 weeks | 80% |
| 27 weeks | 93% |
| 28 weeks | 96% |
| 29 weeks | 94% |
| 30 weeks | 99% |
| 31 weeks | 97% |
| 32 weeks | 99% |

Reference: National Center for Health Statistics, CDC 2019.

*FastStats - Births and Natality (cdc.gov)*

*Vermont Oxford Network-Nightingale Database*

# Chapter: 2 NICU EPIC Survival Kit

(UPH-Meriter Epic)

*Adam Bauer, MD; Ann Ebert, PharmD; Kate Hirsch, NNP*

**1. Dot phrases for notes:**

a. Progress note: .NICUPROGRESS
b. History and Physical: .NICUADMISSION
c. Neonatal Encephalopathy Exam: .HIEEXAM
d. Delivery: .NICUDELIVERY
e. Transport: .NICUTRANSPORT, .NICUTRANSPORTBRIEF
f. Interim Summary: .NICUINTERIM
g. Inpatient Consult: .NICUCONSULT
h. Substance Abuse Counseling: .NICUMARIJUANABF, .NNNCONSULTMETHADONE
i. Procedures: .NICUINTUBATION,.NICUUMBILICAL,.NICULUMBAR,.NICUPICC, .NICUCHESTTUBE, .NICUPAL, .NICUARTERIALPUNCTURE, .NICUTHORACENTESIS, .NEWBORNCIRCUMCISION
j. Discharge Summary: .NICUDISCHARGE

**2. Dot phrases for labs:**

| | | |
|---|---|---|
| .NICUCBC | .NICUBILI | .NICUNUTRITION |
| .NICUDEXI | .NICUWBLYTES | .NICUBMP |
| .NICUCBG | .NICUCULTURES | .NICUABG |
| .NICUVBG | .NICUCORDBLOOD | .NICUCRP |
| .NICUHISTOGRAM | .NICUWBHGBHCT | .NICUABGTEMPCORRECTED |

**3. Deliveries**

a. Fill in APGARS and resuscitation information under the **Delivery Summary** tab located on the left side in mother's chart. The two sections that should be filled out by the Neonatal Provider attending the delivery include **Resuscitation** and **Assessment.**

b. Write a delivery attendance note (.NICUDELIVERY)for any baby that is not admitted to the NICU. If you attend the delivery and admit the baby, the NICU admission note will contain that information and a separate delivery attendance note is not required.

**4. Admission**

a. Use the **Neo Admission Navigator** (tab on left of screen) to do admission orders

b. Go to the **Dosing Weight** tab and enter the birth weight in the Drug Calculation Weight section

c. Go to the **Med Reconciliation** tab

d. Click on **Problem List** to enter problems for a patient

e. Click on **New Orders for Floor**

f. Under **Order Sets**, you can set as Favorites the following Order Sets that can be helpful orders:

MHM NICU Admission

NICU Feeding Panel NICU Intubation Meds

MHM NICU Lumbar Puncture

MHM NICU Mechanical Ventilation

MHM NICU Non-Invasive Mechanical Ventilation

MHM NICU Cooling

MHM NICU Prepare and Transfuse Blood Products

MHM NICU Discharge

MHM Newborn Admission

MHM Neonatal Circumcision

MHM Newborn Withdrawal

g. Update information in the **NICU Signout** (under Shared Patient Lists)

**5. Order Entry**

a. Use **Manage Orders** (tab on left screen) to enter orders during Rounds

b. For IV fluid orders: use the pseudonym "NICUIV" – this will give you an abbreviated list of IV solutions built for NICU patients (Under the **Facility** List tab).

c. Use the pseudonym “NICU MOR” for morphine options (both PO and IV) that are specific to NICU patients.

d. Orders for starter TPN can be entered and modified by providers

e. The unit pharmacist will enter orders for fat emulsion when started and will order and modify all custom TPN orders when needed.

f. Contact the unit pharmacist for any questions relating to order entry and for guidance with finding the correct product.

**6. Transfer**

a. Use the **Neo Transfer Navigator** to transfer patients from the Newborn Nursery to the NICU and vice versa. Select Med Reconciliation to reconcile transfer orders

**7. Discharge**

a. Use the **Neo Discharge Navigator** (tab on left of screen) and select **Med Reconciliation** to reconcile discharge orders

b. Order the follow up appointments through the Neo Discharge Navigator

**8. Important Reminders:**

a. To access the mother’s chart, go to the **Summary** tab on the left of the screen and then click the mother’s name

b. Labs should either be entered as “Routine” or “STAT”

# Chapter 3: Common NICU Guidelines

*Elizabeth B. McBride, MD*

## A. Admissions

- All babies born <35 wks GA or <2000 g must be admitted to NICU
- Admissions should be staffed with the neonatal provider (APP, hospitalist, fellow, neonatologist)

## B. Wisconsin Newborn Screen

**All Infants:**

– Collect an initial specimen at 24-48 hr of life
– Collect another specimen at 48-72 hr of life on infants initially tested at <24 hr of age
– Always try to collect the initial specimen prior to a blood product transfusion

**Infants with a birth weight <2,200 g**

– Collect a repeat specimen at 14 days of age
– Collect another specimen at 30 days of life or discharge, whichever comes first, and monthly there after until3monthsofageoruntil discharge.

**Infants with a birth weight ≥ 2,200 g and GAB ≥ 34 weeks**

– Collect a repeat specimen at 30 days or just before discharge or at one month of age, if hospital stay is longer than one month

**Transfused infants**

– Collect initial specimen before transfusion, if possible
– If specimen is collected before transfusion and less than 24 hours of age, repeat testing at 48-72hrs of life and another at 60 days of life (at least >14 days from previous transfusion)
– If initial specimen was collected post-transfusion, testing should be done at 60 days of life (at least>14daysfromprevioustransfusion)
– Always list date of most recent transfusion on specimen collection card

**At discharge:**

– Always collect a specimen at discharge unless the previous specimen was collected within 7 days of discharge.

**Before transfer**

– Collect a specimen before transfer, if possible
– Inform receiving hospital of specimen collection status

## C. Immunizations

All immunizations require parental permission

- Hepatitis B vaccine
  - <2 kg at birth–give at one month of age or prior to discharge, whichever comes first
  - ≥2 kg at birth – administer as soon as medically feasible after birth
- Other standard immunizations are given when baby is 2 months old and relatively stable. (Hib, Prevnar, Hep B, Polio, DTaP)
- During RSV season (November thru April) Palivizumab (Synagis®) prophylaxis should be given prior to discharge to:
  - All babies ≤ 28 6/7 weeks
  - Chronic lung disease of prematurity, < 1 yo, and birth < 32 weeks 0 days' gestation and required supplemental oxygen for at least 28 days after birth
  - Chronic lung disease of prematurity, between 1 yo and 2 yo who required at least 28 days of supplement oxygen after birth and who continues to require supplemental oxygen, chronic diuretic therapy, or chronic systemic steroid therapy
  - Infants <1yo with congenital heart disease with any of the following:
    - Congestive heart failure on medication
    - Moderate to severe pulmonary hypertension
    - Cyanotic heart disease in consultation with cardiologist
    - Infants undergoing cardiopulmonary bypass
    - Infants who receive cardiac transplantation
  - Infants with congenital abnormalities of the airway or neuromuscular disease that compromises handling of respiratory secretions.
  - Profoundly immunocompromised infants
  - Infants with Cystic Fibrosis < 24 months at beginning of RSV season
  - Infants with interstitial lung disease < 24 months at beginning of RSV season

**D. Hearing Screen: Perform within 90 days. Must be prior to discharge. Should also be done after completing phototherapy.**

- If refers on repeat testing & baby is < 7 days old
  - Send salivary CMV PCR
  - Request Meriter Family Liaison or Postpartum HUC to schedule repeat hearing screen in Meriter outpatient lactation clinic
- If refers on repeat testing & baby is > 7 days old
  - Ensure salivary CMV PCR sent
  - Enter referral either to:
- Audiology for an appointment in 2 weeks (1-3 hrs, may require sedation)

- UW Speech & Hearing Free Clinic with Amy Hartman; (608) 262-3951

**E. Updating parents, Primary Care Provider (PCP) and Obstetrician**

- Use NICU phone number 608-417-6215. Call through paging 608-262-2122, provide parents phone number to operator and ask operator to call
- For UW or Meriter PCPs, consider Healthlink or Meriter Epic inbox message
- Parents: Parents of NICU patients should be updated either in person or by phone.
  - On admission
  - Any major change in patient's status: Immediately.
  - Critical status: Daily.
  - During convalescence: Twice per week.
  - Prior to discharge: To assess that parents are fully prepared to take care of their infant
  - Phone etiquette: When calling a parent on phone, do not leave any medical information on voicemail or with a relative. Advise parents to call immediately if emergency or when available for routine update.
- PCP:
  - Once identified, notify PCP about NICU admission of the patient
  - Update at least every 2 weeks during NICU stay (unless PCP requests differently)
  - Call prior to discharge with summary of hospital course
  - Call in the event of patient's death
- Obstetrician: Notify the obstetrician if the infant dies and give brief summary. They will follow the mother post-partum and they should know about this event

**F. Discharge Management**

Discharging a high-risk infant requires significant preparation by the family and the NICU team. The goal is to prepare the family with education and training during infant's hospital stay such that they are ready to take care of their infant when infant is physiologically stable and ready for discharge.

**1. Discharge Planning**

- Hearing Screen
- Car seat challenge w/in 72 hrs of discharge for infants with any of the following criteria:
  - born <37 weeks gestation
  - birth weight <2500 g
  - discharging on home oxygen
  - hypotonia (T21, congenital neuromuscular disorder, etc.)

- Congenital heart disease screen
- Circumcision if requested
- CPR for parents
- Head circumference and length measured on the day of discharge
- When applicable, add “Home going Nutrition Plan” formulated by Sally Norlin and print hospital growth chart for PCP and the family

## 2. Evidence of Physiologic Stability and Medical Readiness for Discharge

- **Minimum Requirements in Each Category**

| | GA <30 weeks | GA 30-35 weeks | GA >35 weeks >7 days of age* |
|---|---|---|---|
| **Thermoregulation** | | | |
| Number of days in open crib | 2 days | 2 days | 1 day |
| **Feedings** | | | |
| Number of days on home nutrition with adequate weight gain and/or taking acceptable | 3 days | 2 days | 2 days |
| What is adequate weight gain? | 10 gm/kg/day OR Maintaining growth percentile | 10 gm/kg/day OR Maintaining growth percentile | |
| **Cardiorespiratory Stability** | | | |
| Breathing room air without any device | 3 | 3 | 2 |
| Days off caffeine without significant cardiopulmonary events | 7 | 7 | 5 |
| Days free of non-feeding related cardiorespiratory events requiring stimulation | 5 days | 3-5 days | 2-3 days |

*Not applicable for infants >35 weeks and ≤7 days old

**3. Follow-up Appointments**

Patient must have all followup appointments scheduled and recorded in the discharge summary.

- PCP: 1-3 days after discharge
- All subspecialty clinics (ask subspecialist about timing)
- Developmental follow-up:
  - Waisman Center Newborn Follow-up Clinic
    - All neonates <28 weeks and/or birth weight <1500gm.
    - Any infant with significant developmental concerns and all infants with NGT feed.
    - Neurologic abnormalities, HIE, multiple congenital anomalies
    - Schedule as soon as possible (typically multi-week wait)
  - Meriter Developmental Assessment Clinic:
    - Infants 28-32 weeks or at risk for developmental delays
    - Evaluation is done by RN, speech therapist, and OT
    - Seen at corrected age of 6, 18 and 30 months
  - Great Results After Discharge "GRAD" Program
    - Provide nutritional recommendations to the PCP and family during the transition from hospital to home
    - Criteria for referral to the program include infants born<326/7weeks or with a birth weight <1500 grams
    - 1st appointment within 2 weeks following discharge. (up to 3 appts)
    - Evaluation by nutritionist and lactation consultant

**4. Discharge of Infant with Bridled Nasogastric Tube (NGT) Feedings**

- Bridle is inserted & attached to NGT to reduce risk of tube dislodgement, but does not eliminate
  - If tube dislodgement occurs during business hours, replace in peds GI clinic
  - If tube dislodged overnight, contact peds GI on-call but may have to go to UW ED
- Infants may be candidates if PMA $\geq$ 40 weeks & $\geq$ 40% PO intake for at least 5-7 days
- Order "bridle order bundle" & enter "NG tube fed newborn" on problem list
  - Charge RN or NICU CNS place bridle bedside (AMT Microbridle Pro 5- 6 clip fits 6.5F NG)
  - XR to confirm NGT position

- Consultation with SLP & pediatric GI required
  - Weekly weight checks with PCP or GRAD Clinic
  - out-patient follow-up w/ SLP 1-2 weeks after discharge
  - peds GI 4 weeks after discharge
- Consult with Case Management for ENFit syringes & other home supplies
- Enter **.bridledischarge** & home-going feeding plan from NICU nutritionist in discharge summary
- Monitor for 48 hours after bridle placement
  - PO intake may decline in 1st 24 hrs post-placement
  - Duoderm on columella & Aquaphor to nares can help reduce risk, but monitor for septal irritation
  - parents to perform independent care session

# Chapter 4: NICU Procedures

**Must write a procedure note in the patient's chart after completing a procedure. A template is available for each of the NICU procedures.**

## A. Intubation

- Tube for tracheal aspirate gram stain and culture

**Equipment**

- Suction catheter: Use 6-10 F catheter
- Sterile gloves
- Bag and mask, check mask size
- Blow-by Oxygen(5-10 L)
- Laryngoscope and blade
  - –Term = "1" blade
  - –Pre-term = "0" blade
  - –Extreme prematurity = "00" blade
- Endotracheal tube

**ETT size based on weight and gestational age**

| Tube Size | Weight | Gestational Age |
|---|---|---|
| 2.5 | < 1000 g | < 28 wks. |
| 3.0 | 1000-2000 g | 28-34 wks. |
| 3.5 | 2000-3000 g | 34-38 wks. |
| 4.0 | > 3000 g | > 38 wks. |

**ETT position at the lip = Nasal-tragal length + 1**

- ETT bone and tapes (prepared by nursing)
  - –CO2 detector
  - –Stylet (optional)

**Medications for Non-Emergency Intubation in the NICU**

**A. Infants with IV access**

| Medication | Dose | Route | Pharmaco-dynamics | Notes |
|---|---|---|---|---|
| Morphine | 0.05-0.1 mg/kg | IV | Onset: 1-5 min<br>Duration: 3-5 hours | • Longer duration than Fentanyl<br>• Use with caution for in-out surfactant (INSURE) |
| Midazolam | 0.1 mg/kg | IV | Onset: 1-5 min<br>Duration: 20-30 min | • May use when considering In-Out Surfactant (INSURE) |
| Atropine | 0.02 mg/kg | IV | Onset: 1-2 min<br>Duration: 15-60 min | • No minimum dose is required |
| **Optional Agents** | | | | |
| Rocuronium | 0.6 mg/kg | IV | Onset: 1-5 min<br>Duration: 30-60 min | • Use only if needed<br>• Attending Neonatologist must be "in-house" |

**B. Infants with No IV access**

| Medication | Dose | Route | Pharmaco-dynamics | Notes |
|---|---|---|---|---|
| Morphine | 0.1 mg/kg | IM | Onset: 15-30 min<br>Duration: 3-5 hours | • Longer duration than Fentanyl<br>• Use with caution for in-out surfactant |
| | 0.3 mg/kg | NG/ PO | Onset: 30-60 min<br>Duration: 3-5 hours | |
| Midazolam | 0.1 mg/kg | IM | Onset: 1-5 min<br>Duration: 2 hours | • Use for in-out surfactant (INSURE) |
| | 0.2 mg/kg | Intra-nasal | Onset: 1-5 min<br>Duration: 30-60 min | • Use with intranasal atomization device |

Surfactant when indicated

– 2.5 ml/kg via ETT (Curosurf® first dose; subsequent doses 1.25 ml/kg every 12 hrs)

– Give in one aliquot via ETT catheter followed by bagged or ventilator breaths

**Complications**

- Acute
  - Tracheal/hypopharyngeal perforation
  - Hemorrhage
  - Laryngeal edema
  - Vocal cord injury
- Chronic
  - Glottic/subglottic stenosis
  - Subglottic granuloma/cyst

**B. Umbilical Catheters Indications**

a). Umbilical Arterial Catheter

1. Frequent measurements of blood gases
2. Continuous measurement of arterial blood pressure
3. Infusion of maintenance fluids
4. Access for exchange transfusion
5. Resuscitation (UVC preferred)

b). Umbilical Venous Catheter

1. Resuscitation
2. Exchange transfusion
3. Intravenous fluids and nutrition (≥ $D_{15}$)
4. IV medication infusions. e.g. Dopamine, Morphine

**Contraindications**

1. Evidence of vascular compromise of legs or buttocks (For UAC)
2. Peritonitis
3. NEC
4. Omphalitis
5. Omphalocele/gastroschisis
6. Acute abdomen

**Duration**

1. UAC/UVC should be removed after DOL 7-10 due to increased risk of infection

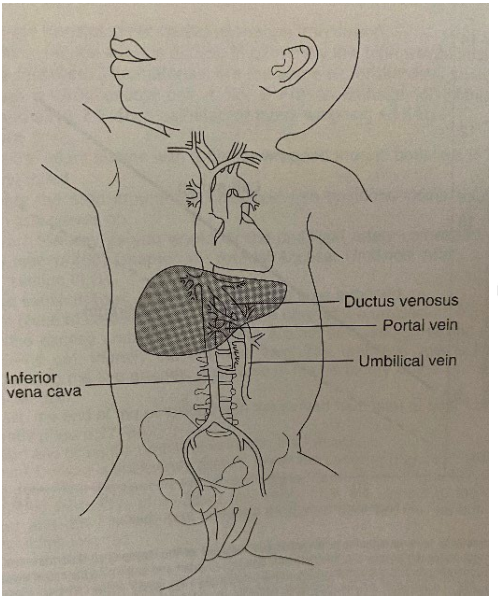
**Equipment**

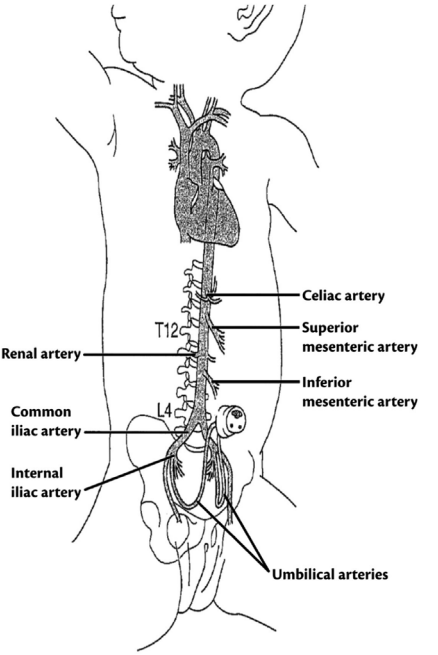
- Procedure cart
  - One located in each wing of NICU behind nurses' desk
- Soft infant restraints for wrists and ankles per nursing
- Hat, mask, sterile gown and gloves
- Sterile drapes
- Sterile umbilical catheter tray
  - Contains forceps, scalpel, umbilical cord tie, dilators, needle driver, scissors, hemostats
- Use surgical forceps for ELBW
- One three-way stopcock for each line being placed
- One sterile 10 mL syringe for each line being placed
- Red syringe connector to transfer saline from unsterile syringe to sterile syringe
- Chlorhexidine swabs
- Tubes/culture bottle for labs
- Umbilical venous catheters size
  - 3.5 French for infants < 1200 gm.
  - 5.0 French for infants > 1200 gm.
- Umbilical arterial catheter size
  - 3.5 French for infants > 500 grams
  - May use 2.5 French for infants < 500 grams

Determine catheter insertion length

- UAC length
  1. 3 x Birth Wt. (kg) + 9
  2. 1.5 times length of shoulder to umbilicus measurement
  3. Catheter tip should be between T6-T9
  4. On x-ray UAC goes caudally into the iliac arteries before heading cranially in the aorta
- UVC length
  1. 1.5 x Birth Wt. (kg) + 6
  2. 2/3 length of shoulder to umbilicus measurement
  3. Catheter tip should be 0.5-1 cm above the diaphragm, T8-T9

Path of umbilical artery
and important landmarks




**Complications**

Umbilical Artery Catheter

- Malposition: Vessel perforation, peritoneal perforation, false aneurysm, misdirection into internal or external iliac arteries
- Vascular accident: thrombosis, embolism/infarction, vasospasm, hypertension, air embolism, loss of extremity
- Equipment related: Transection of catheter, break in catheter
- Other: hemorrhage (including disconnection of UAC), infection, NEC
- b). Umbilical Vein Catheter
- Malposition in heart or great vessels: Cardiac arrhythmia, pericardial effusion, thrombotic endocarditis, hemorrhagic infarction of lung
- Malposition in portal system: NEC, hepatic necrosis (thrombosis of hepatic vein or infusion of hypertonic solution into liver
- Infection
- Thromboembolism
- Other: Perforation of peritoneum, portal hypertension, pneumo-pericardium

**C. Lumbar Puncture Equipment**

- Procedure cart
- Sterile gloves, mask, hat, gown
- Neonatal Lumbar Puncture Tray
  - Contains 1 spinal needle, 4 CSF collection tubes, drapes, syringe, needle, lidocaine, gauze and band-aid
- Chlorhexidine Swabs
- Extra spinal needles: 22 gauge, 1 inch needles
- Patient labels to place on specimen tubes after CSF collection
- Label each tube following the procedure with a patient label and number tubes in order they were collected
  - Tube 1 = CSF PCR BioFire Film Array
  - Tube 2 = CSF gram stain and culture
  - Tube 3 = CSF Glucose, protein
  - Tube 4 = CSF cell count and differential
  - Heel stick or venous tube for serum glucose

**Complications**

- Hypoxemia from knee-chest positioning
- Infection
- Bleeding: Spinal hematoma (consider platelet count)
- Spinal cord injury/spinal nerve injury
- Intraspinal epidermoid tumor from epithelial tissue introduced into spinal canal herniation

**D. Thoracentesis Equipment:**

- Sterile gloves
- Chlorhexidine or betadine swabs
- 25 g butterfly or 18-22 angiocath
- 3-way Stopcock
- 20 ml syringe

**Complications**

- Pulmonary laceration
- Pneumothorax
- Hemothorax
- Wrong location – due time out to confirm Right vs left
- Puncture diaphragm/spleen/liver

# Chapter 5: Neonatal Resuscitation

**Apgars**:

- Given at 1 and 5 minutes
  - Repeat every 5 minutes until 20 minutes of life if the score is less than 7 at five minutes.

| SIGN | 0 | 1 | 2 |
|---|---|---|---|
| Color | Blue or Pale | Acrocyanotic | Completely Pink |
| Heart Rate | Absent | <100 bpm | >100 bpm |
| Reflex irritability | No Response | Grimace | Cry or Active Withdrawal |
| Muscle Tone | Limp | Some Flexion | Active Motion |
| Respiration | Absent | Weak Cry; Hypoventilation | Good, Crying |

- Infants <35 weeks
  - Initiate resuscitation with 30% blended oxygen and adjust as needed
- Infants ≥35 weeks
  - Initiate resuscitation with 21% and adjust as needed
- All infants requiring prolonged PPV or if you're considering intubation (or LMA) should have EKG leads placed
- All infants should have pulse oximetry with probe on right upper extremity (wrist/hand) if:
  - Evidence of cyanosis
  - Needs oxygen, CPAP, or PPV

**CPAP/PEEP**

- Use T piece from Panda warmer or Neopuff
- Start at 5 mmHg

**PPV Positive Pressure ventilation**

- Give 40-60 breaths per minute
- Start with PIP at 20
- Consider placing OG if PPV for more than few minutes

**Chest Compressions**

- Thumbs between the nipple line and the xiphoid process

- Compress to a depth of 1/3 of the anterior-posterior diameter of the chest
- 90 compressions + 30 breaths in one minute
  - "One–and Two–and Three–and–Breathe–and"

**Endotracheal Intubation**

- Tube depth (cm at the lip) = Nasal-tragal length + 1
- Tube size
  - <1 kg/<28 weeks = 2.5 mm
  - 1-2 kg/28-34 weeks = 3.0 mm
  - >2 kg/>34 weeks = 3.5 mm
- Use $CO_2$ detector to determine if intubation is successful. It will change from purple to yellow (note: If there's no cardiac output, the color will not change. Also, contamination from esophageal fluids may cause color change).

**LMA**

- Use size 1 for neonates > 2kg
- Inflate cuff after placement with 2-4 ml of air

**Medications**

- Normal saline 10 mL/kg over 5-10 minutes,
- Epinephrine 0.1 mg/mL (flush with 3mL normal saline)
  - Via ETT 1 mL/kg (0.1mg/kg)
  - Via UVC/IV 0.2mL/kg (0.02mg/kg)

**Delayed Cord Clamping**

- Cord clamping should be delayed for 60 seconds for most term and preterm infants. Exclusions include abruption, bleeding placenta previa, cord avulsion.

**Special Circumstances**

- Infants <29 weeks (see Micropremie Section)
- Pneumothorax
  - 18-20 gauge needle (angiocath or butterfly) into fourth intercostal space at the anterior axillary line or the second intercostal space at the mid-clavicular line

**Cord Gases**

- Consider obtaining if prolonged/significant resuscitation, abnormal tone,

peripartum abnormalities

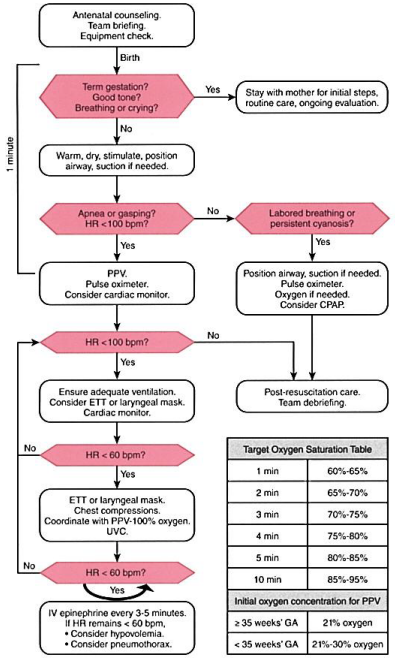
- Normal pH >7.2 (7.15-7.38), $pCO_2$ <60 mmHg (35-70), $pO_2$ > 20, base excess < -10 (-2 to -9)
- Abnormal: pH <7.0 or base excess ≥12 at risk for neonatal encephalopathy and may qualify for whole body cooling (see HIE Section)

**References:**

1. AAP Textbook of Neonatal Resuscitation 8th Edition

# Neonatal Resuscitation Program®, 8th Edition - Reference Chart

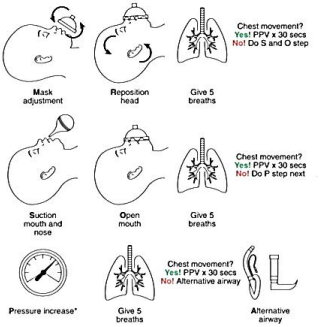
**The most important and effective step in neonatal resuscitation is ventilation of the baby's lungs.**




| Target Oxygen Saturation Table | |
|---|---|
| 1 min | 60%-65% |
| 2 min | 65%-70% |
| 3 min | 70%-75% |
| 4 min | 75%-80% |
| 5 min | 80%-85% |
| 10 min | 85%-95% |
| Initial oxygen concentration for PPV | |
| ≥ 35 weeks' GA | 21% oxygen |
| < 35 weeks' GA | 21%-30% oxygen |

## Ventilation Corrective Steps (MR. SOPA)

**When a MR. SOPA step results in chest movement, ventilate for 30 seconds and reassess heart rate.**




*Increase pressure incrementally by 5 to 10 cm $H_2O$. The maximum recommended pressure is 40 cm $H_2O$ in a term baby.

## Endotracheal Intubation

| Gestation | ET Insertion Depth at Lips (cm) | Approximate Weight (kg) | ET size (ID, mm) |
|---|---|---|---|
| 23–24 weeks | 5.5 | 0.5–0.6 | 2.5 |
| 25–26 weeks | 6.0 | 0.7–0.8 | 2.5 |
| 27–29 weeks | 6.5 | 0.9–1.0 | 2.5–3.0 |
| 30–32 weeks | 7.0 | 1.1–1.4 | 3.0 |
| 33–34 weeks | 7.5 | 1.5–1.8 | 3.0 |
| 35–37 weeks | 8.0 | 1.9–2.4 | 3.5 |
| 38–40 weeks | 8.5 | 2.5–3.1 | 3.5 |
| 41–43 weeks | 9.0 | 3.2–4.2 | 3.5–4.0 |

Shaded table adapted from Kempley ST, Moreiras JW, Petrone FL. Endoracheal tube length for neonatal intubation. *Resuscitation*. 2008;77(3):369–373.

## Neonatal Code Medications

| Drug | Dose* | 0.5 kg | 1 kg | 2 kg | 3 kg | 4 kg | Administration |
|---|---|---|---|---|---|---|---|
| Epinephrine IV/IO<br><br>Concentration:<br>0.1 mg/mL<br>1 mg/10 mL | 0.02 mg/kg<br><br>Equal to<br>0.2 mL/kg | IV Dose:<br>0.01 mg<br><br>Volume:<br>0.1 mL | IV Dose:<br>0.02 mg<br><br>Volume:<br>0.2 mL | IV Dose:<br>0.04 mg<br><br>Volume:<br>0.4 mL | IV Dose:<br>0.06 mg<br><br>Volume:<br>0.6 mL | IV Dose:<br>0.08 mg<br><br>Volume:<br>0.8 mL | IV/IO rapid push.<br>Flush with 3 mL NS.<br>Repeat every 3-5 minutes if heart rate less than 60 bpm. |
| Epinephrine ETT<br><br>Concentration:<br>0.1 mg/mL<br>1 mg/10 mL | 0.1 mg/kg<br><br>Equal to<br>1 mL/kg | ET Dose:<br>0.05 mg<br><br>Volume:<br>0.5 mL | ET Dose:<br>0.1 mg<br><br>Volume:<br>1 mL | ET Dose:<br>0.2 mg<br><br>Volume:<br>2 mL | ET Dose:<br>0.3 mg<br><br>Volume:<br>3 mL | ET Dose:<br>0.4 mg<br><br>Volume:<br>4 mL | May administer while vascular access is being established.<br>ETT rapid push.<br>No need for flush. Provide PPV breaths to distribute into lungs. |
| Normal Saline IV 0.9% NaCl | 10 mL/kg | 5 mL IV | 10 mL IV | 20 mL IV | 30 mL IV | 40 mL IV | Give over 5-10 min. |

*The recommended dose range for intravenous or intraosseous administration is 0.01 to 0.03 mg/kg (equal to 0.1 to 0.3 mL/kg).
The recommended dose range for endotracheal administration is 0.05 to 0.1 mg/kg (equal to 0.5 to 1 mL/kg).

These suggested epinephrine doses are based on a desire to simplify dosing for educational efficiency and do not endorse any particular dose within the recommended dosing range. Additional research is needed to ascertain the ideal epinephrine dose.

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NRP340

# Chapter 6: Micropremie Care Manual
# Infants < 29 weeks Gestational Age (GA)

*Nina Menda, MD & Claudette Adegboro, MD*

**Goal: To increase survival without morbidity for infants born < 29 wks GA.**

**A. Pre-Delivery**

i. Set up for double lumen UVC and single lumen UAC in the NICU admission room Use NS for flush, but do not use heparin flush
ii. Pre-order IVF with heparin for both umbilical lines. RN may set up D10W for PIV
iii. Set IVF rates for total of 80 ml/kg/day
iv. T-piece (TP) resuscitator settings: FiO2 0.3 and 20/5
v. Team assignments: NICU provider (APP, fellow), neonatologist, charge nurse, resident, respiratory therapist, admitting RN

**B. Delivery Room**

a. Delayed cord clamping
   i. Discuss and plan delayed cord clamping for 30–60 seconds with OB provider
b. Airway management by fellow, APP or neonatologist
   i. Resuscitation to follow NRP & Meriter Algorithm
   ii. Start with NCPAP+5, stabilize with appropriate-sized mask and TP
   iii. Recommend Intubation and surfactant for all infants < 25 wks GA OR < 500gms
   iv. For all micropremies, if intubated in DR, obtain CXR in NICU prior to surfactant administration
c. Respiratory Therapist
   i. Apply F&P Flexitrunk, and connect to BCPAP or NIPPV with ventilator
   ii. For intubated infants: start volume ventilation following surfactant administration
d. Charge nurse:
   i. Thermal mattress, plastic wrap & hat for thermoregulation; follow algorithm
   ii. Apply cardiac leads and SpO2 monitors
   iii. Prior to intubation: measure length from nose to tragus +1cm for depth of ETT
   iv. Weigh the infant, measure head circumference and apply tortle
      • If 22-23 weeks, do NOT use Tortle due to skin fragility

**C. NICU Admission**

a. Admitting RN
   i. Obtain weight if not done in DR
   ii. Check temperature
   iii. Ensure proper head placement
   iv. Place cardiorespiratory monitor

b. Providers
   i. Prioritize Lungs over Lines
   ii. Intubate and give surfactant to:
      - Infants < 25 wks GA OR infants < 500 gms at birth
      - For all micropremies requiring ≥ 30% oxygen on admission, consider placing PIV to infuse D10 W at 80 ml/kg/d before surfactant administration
   iii. Umbilical lines efficiently placed by a skilled NICU provider
      - UVC: Obtain blood glucose and start IVF immediately, prior to X-ray confirmation; the second lumen must be heparin locked
      - Draw all admission labs from UAC or UVC during umbilical line placement
      - **If lines are not placed within 30 minutes of starting, must call neonatologist for assistance**

**Participate in Delivery room brief and post golden-hour debrief**

**D. Open Lung Policy**

a. Load with caffeine and start maintenance caffeine on admission
b. First week: avoid hypocapnea and hypercapnia with goal $pCO_2$ = 45-55
c. After first week: Permissive hypercapnia; Goal $pCO_2$ 50-60
d. Surfactant administration:
   i. All infants < 25 wks GA OR < 500 gms: intubated in DR & CXR and surfactant in NICU
   ii. All infants requiring ≥ 30% oxygen at admission or for ≥ 30 minutes
   iii. For infants ≥25 wks, consider INSURE

iv. Give 2nd dose if: >12 hr from first AND < 48-72 hr of age AND > 30% oxygen

e. Ventilator Strategies: Initial Settings

i. Volume targeted ventilator: TV 6-7 ml/kg, R 40, PEEP 5-6, IT 0.35

ii. High Frequency Jet Ventilation:

| PATIENT POPULATION | JET RATE | JET PIP | JET INSPIRATORY TIME | PEEP |
|---|---|---|---|---|
| 22 - 23 weeks GA | 300 bpm | 24 - 26 | 0.02 seconds | 5 |
| 24 - 25 weeks GA | 360 bpm | 22 - 24 | 0.02 seconds | 5 |

- Obtain blood gas 30 min after converting to HFJV
- Obtain CXR 45-60 min after converting to HFJV
- See High Frequency Jet Ventilation Guideline for further details

iii. Non-Invasive: Provide support with BCPAP (PEEP 5-6 cm H2O) or NIPPV

f. Extubation readiness:

i. Ventilator settings:

Volume ventilation: FiO2 ≤ 0.3, VT ≤ 6ml/kg, PEEP ≤ 8

OR HFJV: FiO2 ≤ 0.3, MAP ≤ 9, rate 240

OR SIMV: FiO2 ≤ 0.3, rate ≤ 25, PIP ≤ 18, PEEP ≤ 8

ii. pH ≥ 7.25, pCO2 ≤ 55

iii. Successful 3 min ET-CPAP trial

## E. Brain Care

a. For infants < 25 wks GA, do not extubate for first 72 hrs

b. To consider **treatment of hypotension** with fluid bolus and/or inotrope during first 72 hrs, infant must have two or more of the following:

i. Persistent HR > 160/min

ii. Metabolic deficit > 8

iii. Lactate >4

iv. Capillary refill > 4 sec

v. Urine output < 1 ml/kg/hr for infants > 24 hr of age

c. Feeds every 2 hrs until on full feeds and 29 weeks PMA OR by two weeks of age, whichever is later

d. Limit to 2 full assessments per care session and ask for help with containment during assessment

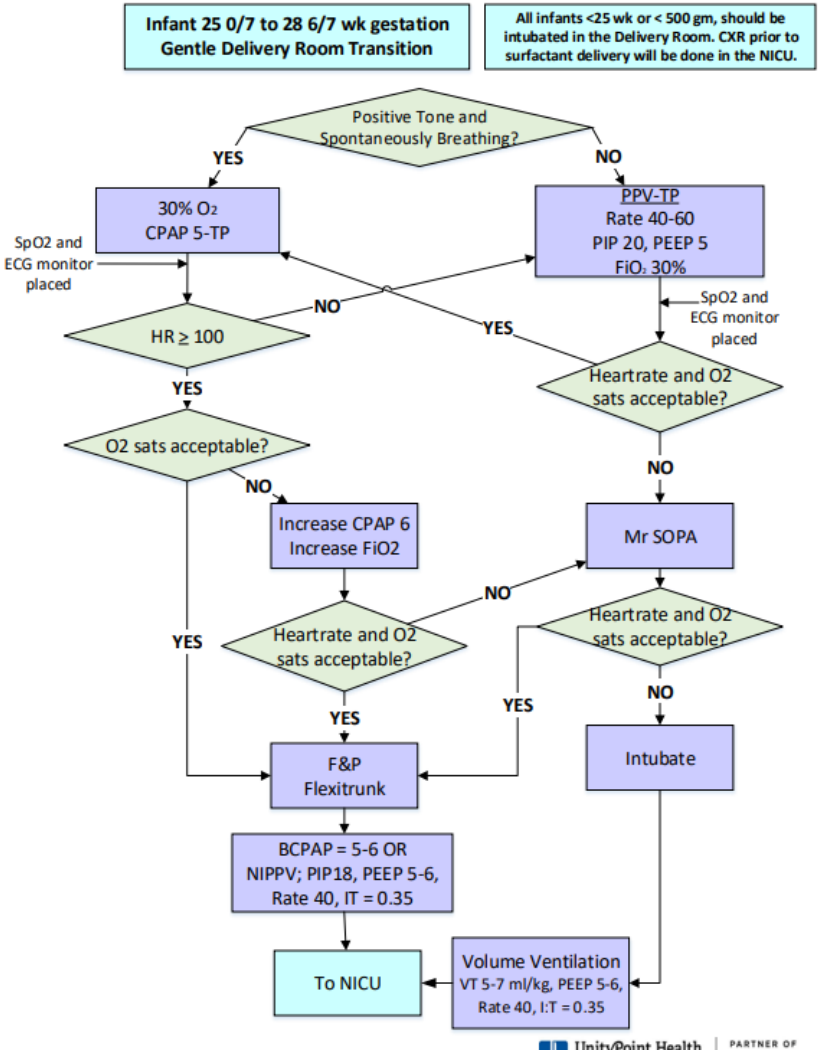
e. Maintain head in midline position for 72 hrs; no prone positioning for 72 hrs

**F. Nutrition Support**

a. Initiate colostrum feeds as soon as available
b. Remove central line when feeds ≥ 120 ml/kg/day

**G. Family Integration**

a. Integrate parents in infant's care
b. Encourage parents to participate in daily rounds
c. Discuss timing of kangaroo care on rounds

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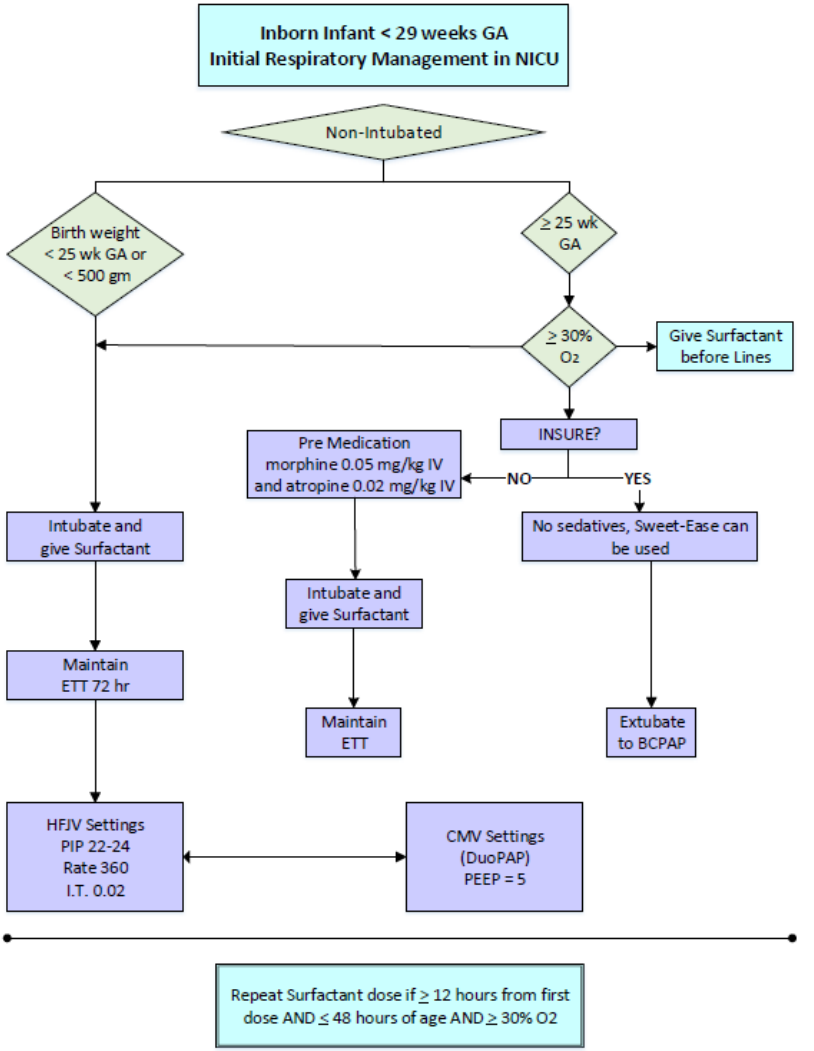

Inborn Infant < 29 weeks GA
Initial Respiratory Management in NICU
Non-Intubated
Birth weight < 25 wk GA or < 500 gm
≥ 25 wk GA
≥ 30% O2
Give Surfactant before Lines
INSURE?
Pre Medication morphine 0.05 mg/kg IV and atropine 0.02 mg/kg IV
NO
YES
Intubate and give Surfactant
No sedatives, Sweet-Ease can be used
Intubate and give Surfactant
Maintain ETT 72 hr
Maintain ETT
Extubate to BCPAP
HFJV Settings PIP 22-24 Rate 360 I.T. 0.02
CMV Settings (DuoPAP) PEEP = 5
Repeat Surfactant dose if ≥ 12 hours from first dose AND ≤ 48 hours of age AND ≥ 30% O2

## Chapter 7: Screening for Hypoglycemia in Newborn Nursery

Transient hypoglycemia after birth is normal in full term, healthy newborns. However, hypoglycemia has been associated with poor developmental outcomes. Because hypoglycemia is typically asymptomatic in newborns, babies at high risk for hypoglycemia are screened in the first 12-24 hours of life.

Management of Hypoglycemia in the Newborn Nursery

Screen per Patient Care Policy #34: Hypoglycemia in Birthing Center Infants

**Babies with symptomatic hypoglycemia require immediate evaluation.**

| Symptoms of Hypoglycemia | | |
|---|---|---|
| Lethargy | Vital sign instability | Apnea |
| High pitched cry | Cyanosis /Pallor | Seizures |
| Irritability | Sweating | Hypotonia |
| Jitteriness | Poor feeding | Respiratory distress |

Asymptomatic babies who require screening for hypoglycemia

- Screen IDM and LGA infants for first 12 hours of life
- Screen SGA infants, infants < 2500 gm and infants < 37 weeks for first 24 hours of life
- One time screen if Apgars <4 at 1 minutes or, <7 at 5 minutes of life, temperature < 97.4, maternal beta blocker, IUGR or exposure to steroids within 2 weeks of delivery

Low blood sugars (<40 in first 4 hours of life and <45 4-24 hours of life) are treated with the hypoglycemia treatment bundle which includes warming, feeding, and dextrose gel

Hypoglycemia can be treated with 4 total hypoglycemia treatment bundles in the newborn nursery. If baby has a low blood sugar after 4 hypoglycemia bundles the baby should be transferred to the NICU for further management.

Plasma glucose homeostasis requires glucogenesis and ketogenesis to maintain normal rates of fuel use. Neonatalhypoglycemiaoccurswithimpairedglucogenesisandketogenesis. As glucose is an essential source of cerebral energy, prolonged hypoglycemia can result in adverse neurologic sequelae.

## Etiology

A. Causes of transient hypoglycemia
   - Perinatal stress, asphyxia, hypothermia
   - LGA and/or IDM, polycythemia
   - Sepsis, shock
   - Maternal meds: terbutaline, chlorothiazide, labetalol, propranolol
   - Exchange transfusion

B. Decreased glycogen storage
   - IUGR/SGA: **Must monitor pre-feed blood sugar when infant coming off IVF and with any change of feeds to lower calories.**
   - Premature and post mature infants

C. Causes of persistent hypoglycemia
   - Hyperinsulinism: Beckwith-Wiedemann Syndrome, Islet cell adenoma, beta cell hyperplasia, Nesidioblastosis
   - Hormone Deficiencies: GH, Glucagon, cortisol, thyroid hormone
   - Defects of CHO metabolism: Glycogen storage disease type I, Galactosemia, Fructose intolerance, Fructose 1, 6 diphosphate deficiency
   - Defects in amino acid metabolism: MSUD, Tyrosinosis, Propionic acidemia, Methylmalonic acidemia
   - Defects in fatty acid metabolism: Medium and long chain fatty acid deficiency

## Treatment

A. Asymptomatic hypoglycemia
   - Early and frequent feeds
   - Follow hypoglycemia management guidelines for starting IVF

B. Symptomatic and persistent hypoglycemia
   - Monitor glucose level closely
   - Start IVF: D10W 60-80 ml/kg/d (GIR = 4-6 mg/kg/min)
   - **Maintain blood glucose >50-60 mg/dl**
   - Consider bolus of D10W 2 ml/kg (200 mg/kg) if persistently **<40 mg/dl** followed by infusion
   - Monitor GIR(mg/kg/min) = $\frac{\text{Dextrose concentration (gm/100 ml) x rate(ml/hr)}}{\text{6 x weight (kg)}}$

     D10W has 10 gm/100 ml
   - Need central line if dextrose concentration >12.5%
   - If stable, start enteral feeds and increase calories as tolerated
   - Once three preprandial blood glucoses > 60 mg/dl, begin weaning IVF. Suggested weaning protocol: wean IVF by 2 ml/hr if blood glucose > 70 mg/dl; wean IVF by 1 ml/hr for blood glucoses 60-69 mg/dl; hold current rate of IVF for blood glucoses 50-59 mg/dl; Notify provider for blood glucoses < 50 mg/dl.
   - If no improvement, endocrine and metabolic consults and w/u
   - Pharmacologic: For persistent hyperinsulinemic hypoglycemia: cornstarch, diazoxide and octreotide have been used.

**Work up for persistent hypoglycemia, in order of priority:**
   - Blood sugar, Insulin, Growth hormone, Cortisol
   - Serum ketones, CBG, Lactate, Ammonia
   - Glucagon, T4, TSH
   - Consider metabolic work up: Free fatty acids, alanine, amino acids, uric acid

# Initial Management of Newborn Hypoglycemia

## Birthing Center

**Screening Criteria:**

**Symptomatic** (e.g., jittery, Temp < 97.4°F any time, low tone) – check blood sugar (BS); if less than target range for age, initiate Hypoglycemia Treatment (HG Tx) Bundle

**Asymptomatic:**

- Check for 12 hours if LGA, IDM (infant of diabetic mother)
- Check for 24 hours if SGA, late preterm or <2500 gms
- Check once if: Apgar < 3 @ 1 min or < 6 @ 5 min; prenatal dx IUGR; maternal beta blockers; prenatal steroids w/in 2wks of delivery

| Birth to 4 hours of life | After 4 hours of life |
|---|---|
| • Place infant skin to skin<br>• Feed by 1 hour of life<br>• First blood sugar between 90-120 min of life (unless symptomatic); goal is 30 min after feeding completed<br>• Goal temperature ≥ 98°F | • Feed on demand (at least every 2-3hrs)<br>• Check blood sugar before feeding<br>• Goal temperature ≥ 98°F |

| **Blood Sugar <40 (HG Tx Bundle)** | **Target Blood Sugar ≥40** | **Blood Sugar <45 (HG Tx Bundle)** | **Target Blood Sugar ≥45** |
|---|---|---|---|
| 1. Warm blanket<br>2. Feed minimum 10-15ml*<br>3. Glucose gel<br>4. Skin to skin (STS)<br>5. Recheck 1 hour after gel | • Feed at least every 2-3 hours<br>• Check blood sugar before feeding<br>• Goal temp ≥ 98°F | 1. Warm blanket<br>2. Feed minimum 10-15ml*<br>3. Glucose gel<br>4. Skin to skin (STS)<br>5. Recheck 1 hour after gel | • Feed at least every 2-3 hours<br>• Check blood sugar before feeding<br>• Goal temp ≥ 98°F |

**Notify provider when:** POC BS < 25 mg/dL or if 2 BS in a row < 40mg/dL (whether screening due to symptoms or to presence of risk factors)

**Feeding, then Glucose Gel (Symptomatic and Asymptomatic):**
*Feed EBM, DHM or Formula per parental choice. RN actively assists with feeding (e.g., spoon, tube at breast, finger feeding, paced bottle feeding). Feeding time not to exceed 20 minutes. Give glucose gel directly after.

**Transfer to NICU for intermediate care when:** BS still low after 4 Treatment Bundles (feeding + glucose gel + STS/warm per bundle)

## NICU

Standard NICU Care.
Recheck blood sugar on admission to NICU.
Recommended feeding is EBM, DHM, or 20 calorie formula.
Criteria for transfer back to the Birthing Center: Stable blood sugars x 3. Transition Feeding Plan/Lactation Consult. Normal feeding volume for day of life with EBM, DHM or 20 cal formula. Stable temperature.

# Chapter 8: Respiratory System

*Contribution: Dinushan Kaluarachchi, MD, Heather Becker, RRT-NPS*

## A. Respiratory Distress in Newborn

- **Etiology**

**Pulmonary Causes**

- Transient tachypnea of newborn
- Hyaline membrane disease
- Meconium aspiration
- Air leak syndromes: Pneumomediastinum, pneumothorax, PIE, pneumopericardium, pneumoperitoneum
- Neonatal pneumonia
- Pulmonary hypoplasia: Idiopathic, agenesis of lung. Secondary to CDH, oligohydramnios, renal agenesis
- Congenital pulmonary lymphangiectasia

**Extrapulmonary causes**

- Sepsis
- Cardiovascular disorders: Congenital heart disease, PPHN, Hypotension
- Metabolic disorders: Hypoglycemia, Hyperthermia, Metabolic acidosis
- Neuromuscular disorders
  - Brain: Asphyxia, hemorrhage, infection
  - Spinal cord: trauma, Werdnig-Hoffmann disease
  - Nerves: injury (Phrenic nerve)
  - Myasthenia gravis
- Mechanical-restrictive problems
  - Airway obstruction: Choanal atresia, micrognathia, laryngeal web, tracheomalacia, vascular ring, cystic hygroma, mediastinal masses
  - Rib cage anomalies: Thoracic dystrophies, generalized bone disease, skeletal dysplasia's
  - Diaphragmatic disorders: Phrenic nerve injury, CDH, abdominal distension
  - Pleural effusion or chylothorax
- Hematologic disorders: Polycythemia, anemia

**B. Surfactant**

**Indication**

- Respiratory Distress Syndrome
- Meconium Aspiration Syndrome
- Congenital Pneumonia

**Mechanism of Action**

- Reduces alveolar surface tension
- Decreases opening pressure
- Provides alveolar stability
- Enhances alveolar fluid clearance

**Criteria**

- Infants requiring > 30% oxygen delivered by positive pressure using either nasal CPAP or an ET tube.
- Diagnosis of RDS on CXR
- If you have a baby meeting these criteria at 6 hours, you should give surf within an hour meeting the criteria.

**Dosage (Curosurf)**

- 2.5 ml/kg/dose intratracheally for first dose. Subsequent doses 1.25 ml/kg q 12 hrs (maximum dosage 5 ml/kg)
- Repeat surfactant dose if ≥ 12 hours from first dose AND ≤ 48 hours of age AND 30% $FiO_2$

**Initial management of Respiratory Distress in Delivery Room**

| <29 wks. Starting $FiO_{2_2}$= 21-30% | 29-34 6/7 wks. Starting $FiO_{2_2}$= 21-30% | ≥ 35 wks. Starting $FiO_{2_2}$= 21% |
|---|---|---|
| Follow Micro preemie DR guidelines | Apply CPAP ± rate in DR | Apply CPAP ± rate in DR Interface: Mask |
| Give surfactant if Intubated | Give surfactant if Intubated and concerns for RDS | Give surfactant if Intubated and concerns for RDS |

**Meriter NICU: Oxygen Saturation Parameter**

| Patient Status | Oxygen Saturations Goals | Oxygen Saturation Alarm |
|---|---|---|
| Preterm <37 Wks. | 90-94% | 88-95% |
| Preterm ≥37 Wks. | ≥95% | 92-98% |
| All infants in room air | ≥95% | 92-100% |

**C. Ventilation Support**

**Ventilation types**

- **High Flow Nasal Cannula**
  - Delivers heated and humidified gas such as oxygen, air, or nitric oxide for infants requiring support with low positive airway pressure.
  - Infants weaned from CPAP are typically started on heated humidified high flow cannula at 2 LPM and later weaned to room temperature humidified cannula when on ≤1 LPM
  - Recommended flowrates should be initiated between 2-6 Lpm. The flowrate can be titrated to provide a variable level of positive distending pressures.
  - Infants can PO feed on 2LPM and lower respiratory support
  - Indications: Bronchopulmonary Dysplasia, Respiratory Distress Syndrome, Transient Tachypnea of the Newborn, Apnea of prematurity, Failure to wean from NIV support (CPAP and/or NIPPV), Nasal and/or upper airway congestion/anomalies
- **Nasal Continuous Positive Airway Pressure (NCPAP)**
  - Recommended intervention in delivery room for all infants <29 wks.
  - For older infants, this is the first intervention for worsening respiratory distress despite nasal cannula oxygen.
  - Start at 5-8 cm H2O and adjust as needed
- **NIPPV (Nasal Intermittent Positive Pressure Ventilation)**
  - Nasal ventilation with higher level of support
  - Recommend in premature infants with apnea
  - Initial settings: Rate 40, PIP 18-20, PEEP 5-8, IT 0.35
- **NAVA and NIV NAVA (Neurally Adjusted Ventilatory Assist)**
  - NAVA delivers assist in proportion to and in synchrony with the baby's respiratory efforts, specifically depolarization of the diaphragm. These efforts are reflected by the Edi (electrical activity of the diaphragm) signal.
  - A low or absent Edi signal may be due to hyperventilation, sedation, muscle relaxants, neural disorders or the catheter being too deep
  - Edi max=force of the diaphragm contraction during inspiration
  - Edi min=force required to maintain FRC at the end of exhalation
  - Peak Pressure = NAVA level x (Edi peak – Edi Min) + PEEP
  - Initial NAVA settings
    - Initial NAVA level of 1.5-2 $cmH_2O/uV$ – Optimize the NAVA level according to Edi Max which is targeted between 5-15 uV. Max NAVA level 4 cmH2O/μV.

- Management of Infants on NAVA
  - If Edi max is < 5 uV, decrease the NAVA level
  - If Edi max is >15 uV, increase the NAVA level
  - If Edi min is > 2 uV, increase PEEP
  - Initially set the same PEEP as the previous ventilator settings.
  - Initial apnea time is set for 5 seconds. If baby is apneic or desaturating, decrease the apnea time to 2-3 seconds.
  - Initial Backup settings: PC 10 above PEEP, PEEP 6-8, Rate 40, It 0.35s
- NIV NAVA: Consider increasing the PEEP when transitioning from invasive to NIV NAVA to maintain adequate MAP.
- Contraindications: insufficient/absent respiratory effort, anomaly (atresia, severe CDH), phrenic nerve injury, congenital myopathy, MRI scanning (remove catheter before scan)

- **Conventional Ventilation**

  **Indications**
  - Persistent respiratory acidosis with pH ≤ 7.10 and $PaCO_2$ >60
  - Severe hypoxemia (arterial $PaO_2$ < 50-60) despite a high $FiO_2$ (40-70%)
  - Significant apnea or increasing work of breathing

**Volume Ventilation mode: APV/CMV (Adaptive Pressure Ventilation/Controlled Mandatory Ventilation)**

Initial Ventilator Settings

| Volume | 4-6 ml/kg |
|---|---|
| PEEP | 5-6 |
| I-time | 0.35 |
| RR | 30-50 |

- APV should be combined with CMV because this mode supports all spontaneous breaths. APV/CMV is associated with more stable expired VT, better oxygenation and reduced tachypnea when compared with synchronized intermittent mandatory ventilation APV/SIMV.
- If ETT leak > 50% consider larger ETT
- APV mode not recommended if ETT leak > 40%. Consider changing to Pressure ventilation mode.
- May set upper PIP limit

- As the infant improves the PIP will gradually go down while the targeted tidal volume stays the same. Thus, infant weans naturally. When PIP is low (14-16), consider extubation.
- A trial of extubation may be considered when the patient is consistently over breathing the set ventilator rate without increased work of breathing and both MAP & $FiO_2$ have dropped to acceptable levels. MAP 8-10 & $FiO_2$ < 35%.

**Pressure Ventilation Mode: P-SIMV (Pressure-Synchronized Intermittent Mandatory Ventilation)**

Initial Ventilator Settings

| | RDS | Normal Lung |
|---|---|---|
| PIP | 18-20 | 12-16 |
| PEEP | 5-6 | 4-5 |
| I-time | 0.35 | 0.3 |
| RR | 30-40 | 20-40 |
| Pressure Support (PS) | 8-10 | 6-8 |

Evaluate chest rise and increase PIP if chest rise is inadequate

**Ventilation Goals Based on Disease Process**

| | pH | $pCO_2$ |
|---|---|---|
| RDS | ≥ 7.25 | 45-55 (60) |
| BPD/Air leak | ≥ 7.25 | 50-65 (<7d)<br>55-70 (≥7d) |
| PPHN | ≥ 7.40-7.55 | 35-50 |

**Management for infants on ventilator:**

To Improve Ventilation ($\downarrow PaCO_2$)

| Action | Effect | Risk |
|---|---|---|
| ↑RR | ↑Minute ventilation, ↑MAP | $\downarrow PaO_2$ |
| ↑PIP or ↑Volume | ↑FRC, ↑TV , ↑MAP, | Air leaks, BPD |
| ↓IT | ↑ET | $\downarrow PaO_2$ |

To Improve Oxygenation (increase $PaO_2$)

| Action | Effect | Risk |
|---|---|---|
| ↑$FiO_2$ | ↑$PaO_2$ | BPD with prolonged exposure, ROP |
| ↑PEEP or ↑CPAP | ↑Intrapulmonary shunt, ↑FRC, ↑MAP | Hyperinflation with ↑$CO_2$<br>Air leaks<br>↓Venous return and cardiac output |
| ↑PIP or ↑Volume | ↑FRC, ↑MAP, ↑PIP | Air leaks; BPD |
| ↑IT | ↑MAP | Air leaks; BPD<br>↓Venous return and cardiac output<br>↑$CO_2$ retention 2° to ↓E time |

**Pulmonary functions and equations**

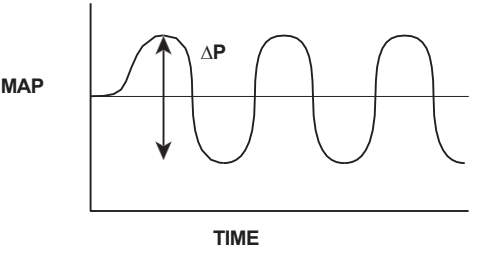
- Tidal Volume (TV): Amount of gas inspired n a single spontaneous breath or delivered through an endotracheal tube during a single cycle of the ventilator.
- Minute Ventilation = Rate (IMV) x Tidal Volume (TV)
- Rate is affected by IT and ET
- Tidal Volume is influenced by PIP, PEEP, pulmonary resistance and pulmonary compliance
- Oxygenation Index (OI) = (MAP x ($FiO_2$ x 100))/$PaO_2$
- MAP = $\frac{(IT \times PIP) + (ET \times PEEP)}{IT + ET}$

ET = Expiratory time IT = Inspiratory time

**High Frequency Oscillatory Ventilation (HFOV)**

- Uses small tidal volumes (usually less than anatomic dead space) and rapid respiratory rates at frequencies between 400 to 2400 breaths/min
- High frequency oscillators are air vibrators with piston pumps or vibrating diaphragms with active inspiration and expiration phase.
- Pressure oscillations within airway produce tiny tidal volumes around a constant mean airway pressure, maintaining lung volume.
- Advantages-delivers lower proximal airway pressures and possibly reduces ventilator related lung injury
- TV is determined by the amplitude(ΔP) of the airway oscillations, which in turn is determined by stroke of the device producing oscillations.

- Hz=number of oscillations/min, 1 Hz = 60 bpm
- Decreasing Hz prolongs inspiratory time, thereby increasing TV
- Oxygenation is controlled by MAP, $FiO_2$
- Ventilation is controlled by ΔP, Hz




**Indications**

- Respiratory failure unresponsive to conventional ventilation
  1. Inadequate oxygenation despite high $FiO_2$ and MAP
  2. Inadequate ventilation despite high PIP
- Air Leak Syndromes: pneumothorax, pulmonary interstitial emphysema
- Atelectasis

| Improve oxygenation | Improve ventilation |
|---|---|
| ↑$FiO_2$ | ↑Amplitude |
| ↑MAP (in increments of 1-2) | ↓Hertz |

**Complications of HFOV**

- Hyperinflation and barotraumas
- ↓venous return →↓cardiac output → hypotension →↓renal perfusion (↓UOP)
- Edema
- ↑need for sedation
- Difficult to perform physical exam

**High Frequency Jet Ventilation (HFJV)**

- HFJV is pressure-limited, and time cycled with adjustable PIP and Rate
- Inspiratory Time (IT) is kept as short as possible (0.02 sec.)
- Exhalation is passive

- Delivers small tidal volumes (Vt) (1-2 ml/kg) at rapid rates (240-600 bpm) via special Et tube adaptor (Life port adaptor) with built-in nozzle.
- Connecting the Life port adaptor to a patients ET tube enables tandem use of conventional mechanical ventilation (CMV) (Hamilton G5 vent)
- Monitored Servo-controlled driving pressure (Servo Pressure) is used to detect changes in lung compliance and resistance.
- Jet rate changes are made in increments of 60 bpm and is independent of the Jet Vt. Lowering Jet rate allows for a longer expiratory time and helps avoid gas trapping.
- Jet PIP primarily regulates $PaCO_2$
- CMV vent PEEP is the main contributor t mean airway pressure (MAP).
- CMV vent rate (sigh breaths) reverse atelectasis.

**Indications**

- Preventative lung protection strategy in infants < 25 weeks or < 500 grams.
- Strongly consider Jet ventilation for infants < 26 weeks or < 750 grams.
- Rescue therapy for air leak syndromes such as pulmonary interstitial emphysema, pneumothorax, lung hyperinflation, & air trapping.

**Recommended Initial HFJV Settings**

| Pt Population | Jet Rate | Jet PIP | Jet I.T. | PEEP |
|---|---|---|---|---|
| 22-23 wk GA | 300 bpm | 24-26 | 0.02 seconds | 5 |
| 24-25 wk GA | 360 bpm | 22-24 | 0.02 seconds | 5 |

**Management Strategies**

- HFJV delta P (PIP-PEEP) is the primary determinant of $PaCO_2$. HFJV I-time and Rate are secondary.
- Resting lung volume (FRC supported by set PEEP) and mean airway pressure (MAP) are crucial determinants of $PaO_2$

| Settings | When to Raise | When to Lower |
|---|---|---|
| HFJV PIP | To decrease $PaCO_2$ | To increase $PaCO_2$ |
| HFJV Rate | To decrease $PaCO_2$ | To eliminate inadvertent PEEP or hyperinflation |
| PEEP | To improve oxygenation | When oxygenation is adequate |

**Complication of HFJV**

- Atelectasis → Add sigh breaths or increase PEEP
- Hypotension → Decrease PEEP and PIP to decrease MAP
- Hyperinflation → Decrease PEEP and PIP or decrease Jet rate

**Complications of ALL Assisted Ventilation**

- Air leak: Pneumomediastinum, pneumothorax, PIE, pneumopericardium, pneumoperitoneum
- ETT complications: displacement, dislodgement, obstruction, atelectasis, palatal groves, subglottic stenosis
- Tracheal lesions: erosion, granuloma, perforation, necrotizing tracheobronchitis
- Infection: pneumonia, septicemia
- Impaired cardiac function
- CLD/BPD
- Oxygen toxicity
- Miscellaneous: Intracranial hemorrhage, PDA, ROP, delay in enteral feedings, complications of parenteral nutrition

**Inhaled Nitric Oxide (iNO):**

- Pulmonary vasodilator that facilitates perfusion of alveoli and can improve gas exchange and oxygenation.
- Indications: hypoxic respiratory failure despite optimal ventilator management, PPHN, meconium aspiration syndrome, pneumonia, and idiopathic pulmonary hypertension, differential pre and post $SpO_2$
- Inhaled nitric oxide can be given in conjunction with any oxygen system having 2 liters of oxygen or greater including: high flow nasal cannula, CPAP, NIPPV, conventional ventilation, and HFOV.

- Initial setting: 20 ppm of iNO
- Weaning: Can decrease nitric oxide by 5 ppm when $FiO_2$ is within a desired range. Once weaned to 5 ppm, then wean by 1 ppm.
- Due to the short half-life, nitric oxide should never be abruptly stopped. Wean slowly and be aware of a rebound effect.
- Consider monitoring methemoglobin levels daily while on iNO

**Extubation Checklist:**

**Infants must meet following criteria**

- Minimum Ventilator settings:
  Volume: $FiO_2 \leq 0.3$, Rate $\leq 25$, VT $\leq 6$ ml/kg, PEEP $\leq 6$
  Pressure: $FiO_2 \leq 0.3$, Rate $\leq 25$, PIP $\leq 18$, PEEP $\leq 6$
  NAVA level <0.5, $FiO_2 \leq 0.3$, PEEP $\leq 6$
  HFJV: Jet PIP $\leq 20$, Jet Rate 240-300, Jet MAP 7-8, $FiO_2$ 0.03
- Safe airway
- pH $\geq 7.25$, $pCO_2 \leq 55$

**Peri-Extubation Dexamethasone for Neonates**

- To assist in success of extubation for infants at high risk for airway edema and obstruction and prevent reintubation
- Recommended regimen:
  - 0.1 -0.25 mg/kg/dose IV q8h x 3 doses - begin 4 hr prior to extubation
  - Infant must be $\geq 7$ days of age
- Data not supportive of use for:
  - Low risk for airway edema and obstruction
  - Subglottic stenosis
  - Post-extubation atelectasis
- Use with caution in patients with respiratory or systemic infection

**Management of Bronchopulmonary Dysplasia (BPD)**

- Permissive hypercapnia (pH $\geq 7.25$ and $pCO_2$ 55-70)
- Ensure adequate caloric intake for weight gain-infants with BPD have increased basal metabolic rates: May need 130-150 kcal/kg/day
- Fluid restriction:130-150 ml/kg/day
- Diuretics

- Bronchodilators
- Systemic steroid: DART protocol
  - Use to facilitate extubation in vent-dependent infants
  - Do not use in infants less than 2 weeks of age
  - Dosing regimen: (IV or PO)
    - 0.075 mg/kg/dose q12h x 6 doses, THEN
    - 0.05 mg/kg/dose q12h x 6 doses, THEN
    - 0.025 mg/kg/dose q12h x 4 doses, THEN
    - 0.01 mg/kg/dose q12h x 4 doses, THEN STOP
  - Inhaled steroid options:
    - Budesonide 0.25-0.5 mg BID by nebulization
    - Fluticasone 110 mcg BID by inhalation
- Possible adverse effects: hyperglycemia, hypertension, hypokalemia, hypocalcemia, cessation of linear growth

**Pulmonary Hypertension Screening Guidelines for Preterm Infants**
(see Cardiology section for algorithm)

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# Chapter 9: Acid Base Balance

*Ashleigh N. Rushing, MD and C. Lydia Wraight, MD*

## A. Blood Gases

- pH, $pCO_2$, $pO_2$ are measured directly
- $HCO_3$-, $O_2$ saturation are calculated

| Normal Blood Gas Values | |
|---|---|
| pH | 7.35-7.45 |
| $pCO_2$ | 35-45* |
| $HCO_3$ | 22-26 |
| Base Excess | -1 to -3 |

* For infants ventilated > 7 days, permissive hypercapnea ($pCO_2$ 45-60) is accepted to decrease barotrauma.

- Acid-base balance is maintained with buffers

$$HCO_3^- + H^+ \longleftrightarrow H_2CO_3 \longleftrightarrow H_2O + CO_2$$

## B. Interpretation of blood gases

- **Step 1:** Is the pH acidic or basic?

| | |
|---|---|
| pH < 7.35 | Acidosis |
| pH > 7.45 | Alkalosis |

- **Step 2:** Is the disturbance respiratory or metabolic? Look at $pCO_2$.
  - Respiratory = pH and $pCO_2$ change in **opposite** directions
  - Metabolic = pH and $pCO_2$ change in the **same** direction

| | Acidosis | | Alkalosis | |
|---|---|---|---|---|
| | *pH* | *$pCO_2$* | *pH* | *$pCO_2$* |
| Respiratory | ↓ | ↑ | ↑ | ↓ |
| Metabolic | ↓ | ↓ | ↑ | ↑ |

- **Step 3:** Is there compensation?
  - Compensation occurs to bring the pH closer to normal when the derangement is chronic, it will not correct the pH to normal.

| | Acute | | Compensation | |
|---|---|---|---|---|
| | $pCO_2$ | $HCO_3$ | $pCO_2$ | $HCO_3$ |
| Respiratory Alkalosis | < 40 | normal | < 40 | low |
| Respiratory Acidosis | > 40 | normal | > 40 | high |
| Metabolic Alkalosis | normal | > 26 | > 40 | > 26 |
| Metabolic Acidosis | normal | < 22 | < 40 | < 22 |

- **Step 4:** Is there an anion gap?

$$\text{Anion Gap} = [Na+] - ([Cl-] + [HCO_3])$$

– Normal anion gap < 15 mEq/L

**C. Respiratory Acidosis**

- Most common cause of acidosis
- Poor ventilation results in $CO_2$ retention ($CO_2$ is high)

**D. Respiratory Alkalosis**

- Often iatrogenic, resulting from hyperventilation (ie we are giving the baby more support than they need)

**E. Metabolic Acidosis**

- Results from excess acid production or increased loss of base.
- **Normal anion gap:**
  - Renal: Immaturity, Renal Tubular Acidosis, Obstruction, Dysplasia
  - GI: Diarrhea, Short Gut
  - Endo: Congenital Adrenal Hyperplasia
  - High Protein Formula
  - Administration of Cl- containing compounds:

– TPN, $NH_4Cl$, $CaCl_2$ especially in ELBW

- Compensation of respiratory alkalosis

- **Increased anion gap:**
  - Lactic acidosis: Shock with poor tissue perfusion and oxygenation
  - Acute renal failure
  - Inborn errors of metabolism: Organic acidemias, mitochondrial disorders, glycogen storage disease (type 1), galactosemia
  - Toxins
- **Systemic effects of Metabolic Acidosis:**
  - Pulmonary vasoconstriction (Pulmonary hypertension)
  - Decreased myocardial contractility
  - Respiratory compensation: Increased work of breathing
  - CNS damage with severe acidosis
- **Management**
  - Treat the underlying cause when possible
  - TPN associated mild acidosis may be treated with decreasing chloride and increasing acetate for a few days.
  - Volume expansion if signs of hypovolemia
    - Excessive volume expansion is poorly tolerated in presence of decreased myocardial contractility
    - May use normal saline, packed RBCs or FFP as appropriate
  - Pharmacologic options
    - $NaHCO_3$
      - Only use when infant has excellent ventilation
      - <u>Risks of $NaHCO_3$ administration</u>
        - Acute expansion of intravascular volume with risk of IVH
        - Shift of Hgb dissociation curve to left (↑ binding of $O_2$ to Hgb)

- Increased Na load and increased $CO_2$

- THAM – an organic buffer
  - Can consider with severe acidosis with Na overload and high $CO_2$/poor ventilation
  - Associated with risk of apnea and hypoglycemia and is not as effective

**F. Metabolic Alkalosis**

- Commonly iatrogenic, resulting from diuretic use (ex: furosemide)
- Other etiologies:
  - Loss of gastric fluid: large gastric aspirates, emesis or diarrhea with $Cl^-$ loss
  - Compensation for chronic respiratory acidosis
  - Excessive administration of alkali (acetate in TPN)
- **Management**
  - Replace Cl- deficit, remove any acetate in TPN
  - Replace ongoing fluid and electrolyte losses
  - Adjust ventilator if respiratory acidosis

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# Chapter 10: Fluids, Electrolytes and Parenteral Nutrition (PN)

*Ann Ebert, Pharm D*

**General Information**

The overall goal for infant nutrition is to mimic in-utero growth rate

- Fetal Growth

| | |
|---|---|
| 24-28 weeks | 18 gm/kg/d |
| ≥ 28weeks | 16 gm/kg/d |

- From 24 weeks to term; as total body percentage
  - water decreases from 87 to 71%
  - protein increases from 8.8 to 12%
  - fat increases from 1 to 13.1%
- Growth goal for preemie: 15-20 gm/kg/day

Calculation of Fluid Requirements

- Three principals
  1. Maintenance
  2. Replacement of deficit
  3. Replacement of ongoing water loss
- Ongoing water loss
  - Insensible water loss (IWL)
  - Urinary loss
  - Stool loss
  - Gastric losses
  - Chest tube/ wound loss
- Insensible Water Loss
  - Mostly from skin and respiratory tract.
  - Gestational age is inversely proportional to insensible water loss.
  - Elevated body temperature, radiant warmer
  - Gastroschisis, omphalocele, myelomeningocele and phototherapy may increase IWL

Total caloric requirement:

- Enteral feeds ~110-130 kcal/kg/day
- Parenteral nutrition ~90-100kcal/kg/day

- Combined parenteral and enteral nutrition ~100-120 kcal/kg/day
- Need a minimum of 60 kcal/kg/day + 2.5-3.5gm/kg/d of protein for positive nitrogen balance

**Parenteral Fluids and Nutrition**

**1. Fluid volume:**

- Fluid requirement on first day of life
  - Goal is to prevent dehydration, fluid overload and hypoglycemia

| Components | Term (ml/kg/d) | Preterm (ml/kg/d) |
|---|---|---|
| Maintenance | 20 | ±25 |
| IWL | 15 | ±30 |
| Urine | 20 | ±20 |
| Stool | 10 | ±20 |
| **Total** | **65** | **±80** |

  - Suggested total fluid intake on Day 1 of life

| Weight (gm) | < 750 | 750-1000 | 1000-2500 | >2500 |
|---|---|---|---|---|
| Fluid (ml/kg/d) | 80-100 | 80 | 60-80 | 60 |

- Determining the amount of fluid to be administered as TPN
  - Decide the total daily fluid needed (ml/kg/day)
  - Subtract other drips and IV fluids
  - Subtract enteral feeding volume (if applicable)
  - Example: 1.2kg infant

| | |
|---|---|
| Total daily fluid = 120 ml/kg/day | rate = 6 ml/hr |
| UAC present | rate = 1 ml/hr (subtract) |
| Dopamine drip | rate = 0.5 ml/hr (subtract) |
| Remaining amount for TPN + fat | rate = 4.5 ml/hr (90 ml/kg/day) |

Key points for infants born < 2000 gm:

- For IV fluids
  - Initiate starter PN (D10W + 3% amino acids + heparin) ASAP after birth
  - Starting at 80-100 ml/kg/day will give 2.4-3 gm/kg/day of protein

- Add fat emulsion within the first 36 hours of life (consult with pharmacist)
- Transition to custom PN when clinically appropriate (consult with pharmacist)

- Total fluids after first day
  - If normal homeostasis, increase total fluid intake by 20 ml/kg/day until goal of 130-150 ml/kg/d is reached
  - Decrease total fluids if: Signs of CHF, poor urine output, hyponatremia
  - Increase total intake if: Increased urine output, high IWL, hypernatremia
  - Monitor hydration status: body weight, urine output (I/O's), HR, BP, Labs: Electrolytes, urine specific gravity

**2. Macronutrients**

A. Protein

- Supplied as crystalline amino acids
- Contains 40-50% of essential amino acids (cysteine, taurine, tyrosine, methionine)
  - Goal intake equals:
    - 4 gm/kg/day – infants less than 35 weeks' gestation
    - 3.5 gm/kg/day – infants 35-37 weeks' gestation
    - 3 gm/kg/day – infants greater than 37 weeks' gestation
- Calories = 4 kcal/gm
- Management of metabolic acidosis coincident with TPN
  - Do not exceed 3.5-4 g/kg/day amino acids
  - May need to add acetate 2-3 mEq/kg/day to TPN

B. Fat

- 20% lipid emulsion issued to supply calories from fat
  - Intralipid® consists of soybean oil (with glycerin and egg lecithin)
  - SMOF lipid® consists of soy, MCT, olive and fish oils and is used for infants at increased risk for developing cholestasis
- Calories = 9 kcal/gm (or 2 kcal/ml with 20% fat emulsion)
- Usual maximum is 3 g/kg/day
- Maintain lipid calories ≤ 50%-60% of total calories
- Very small premature infants develop evidence of essential fatty acid deficiency (EFAD) in less than a week
- It is safe to administer in a peripheral IV line

- Areas of concern with the infusion of fat emulsions include:
  - Hyperlipidemia
  - Consider checking TG levels with advancement, particularly in VLBW
  - Cholestasis (increasing direct bili with minimal PO intake): change infant to SMOF lipid product if not already on it.

C. Carbohydrate

- The balance of non-protein calories is provided as IV dextrose
- Calories = 3.4 kcal/gm
- Hepatic glycogen mobilization has been estimated at 4-8 mg/kg/min
- Most neonates requiring PN will tolerate an initial glucose infusion rate (GIR)* of 6-8 mg/kg/min (Dextrose 8.6-11.5g/kg/d)
- ELBW infants may need lower infusion rates (2-6 mg/kg/min) due to hyperglycemia
- Monitor for hyperglycemia and glucosuria
- Increase dextrose infusion in 1-3 gm/kg/day increments to a goal of 15-18 gm/kg/day (if needing full parenteral nutrition)
- GIR*(mg/kg/min) = $\frac{\text{Dextrose concentration x rate(ml/hr)}}{6 \times \text{weight (kg)}}$
  - D10W has 10gm/100ml
  - Conversion: mg/kg/min x 1.44 = gm/kg/day

**3. Electrolytes and Minerals**

A. Sodium

- Normal serum level 135-145 mEq/L
- Maintenance sodium requirement = 2-4 mEq/kg/day
- Hypernatremia(Na > 145)
  - Increase total fluid intake by 10-30 ml/kg/d
  - Remove or decrease Na in IVFs
- Hyponatremia (Na < 130)
  - Decrease total fluid intake
  - Increase Na supplement
- Growing preemie may need 5-8 mEq/kg/d Na supplements

B. Chloride
- Normal level 96-110 mEq/L
- Supplement 2-3 mEq/kg/d (balanced with other anions- P and acetate)

C. Potassium
- Normal serum level: 3.5-5.5 mEq/L (higher with hemolyzed specimen)
- Begin supplementing when good urine output and the serum potassium is within normal limits
- Maintenance potassium requirements = 1-2 mEq/kg/day
- Hyperkalemia
  - Tall, peaked T waves, prolonged PR interval, wide QRS
  - Acute treatment-calcium gluconate, + hyperventilation, sodium bicarbonate (1 mEq/kg)
  - Chronic treatment-albuterol, furosemide, insulin + glucose

D. Calcium
- Normal serum level: 6-11 mg/dl
- Ionized Ca: - 0.9-1.5 mmol/L in preemie (3.7-6 mg/dl)
  -1.15-1.4 mmol/L in term infant (4.5- 5.5 mg/dl)
- Ca accretion in fetus 25 wk-term is 90-120 mg/kg/d
- It is presently impossible to safely provide sufficient calcium in PN solutions to approximate in-utero accretion
- Parenteral supplementation is 2-3 mEq/kg/d
- Limit calcium in peripheral lines (Extravasations can cause tissue necrosis)
- High concentrations of calcium and phosphate in PN may lead to precipitation
- For acute, symptomatic hypocalcemia:
  – 10% calcium gluconate 50-100 mg/kg –

E. Phosphorus
- Normal serum level: 4.5-9 mg/dl
- Parenteral supplement 1- 2 mmol/kg/day
- SGA infants may be severely hypophosphatemic and may need additional supplement

F. Magnesium
- Normal serum level: 1.6-2.2 mg/dl

- A maintenance magnesium requirement is not known but is reported to be 0.2-0.5 mEq/kg/d
- Delay adding from mom was on $MgSO_4$ – assure normal infant Mg level before adding
- May need to remove if infant is anuric.

G. Acetate

- Acetate is rapidly metabolized to bicarbonate and is added to PN solutions when the infant has evidence of metabolic acidosis
- Requirement varies between 0-3 mEq/kg/day
- The amount that can be added to the PN solution is dependent on the amounts of Na+, K+, and phosphorus

**4. Vitamins**

- Exact intravenous vitamin requirement is not known for premature infants.
- Give 2 ml/kg for babies < 2.5 kg and 5 ml/day for infants ≥ 2.5kg

**5. Trace Elements**

- Trace elements are provided in the PN solution based on infant need and discretion of the pharmacist ordering the solution
- For short term PN patients, zinc is the only essential agent dosed at 400 mcg/kg/day
- Infants who remain on TPN for > 2 weeks with little enteral intake
- should have selenium 2 mcg/kg/day added to the TPN solution.

**Other Considerations:**

A. Peripheral Vein PN
   - Limit calcium
   - Glucose concentrations should not exceed 12.5%
   - Osmolarity should be < 900-1000 mOsm/L

B. Cessation of PN
   - PN infusion is gradually replaced by enteral feedings by decreasing the rate of PN infusion as feedings increase and modifying the composition based on enteral intake
   - Fat emulsion is discontinued when infant is tolerating 80-100 ml/kg/day of

enteral feeds and complete cessation of PN when tolerating 100-120 ml/kg/day of enteral feeds. – Refer to feeding guidelines

C. The NICU pharmacist will enter the PN order and a progress note into EPIC daily after consultation with the medical team.

D. Monitoring Parameters

- Baseline assessments should include serum electrolytes and blood glucose
- Serum triglyceride should be monitored more closely in extremely low birth weight infant.
- Infants who are expected to remain on parenteral nutrition≥1 week, or who are severely SGA should have a baseline nutritional panel checked (T/D bilirubin, LFT's (AST, ALT, GGT), Ca+, P, Mg, alkaline phosphatase, triglyceride, albumin, BUN, and creatinine) and repeated at 1-2 week intervals while continuing to receive parenteral nutrition.

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# Chapter: 11 Enteral Nutrition

*Sally Norlin, MS,RD,CLC*

**General Guidelines**

- Follow feeding protocols appropriate for infant's birth wt.
- Standardized feeding practices have been associated with earlier attainment of full enteral feeding, reduced rates of morbidities, including NEC, and optimized feeding practices can improve growth and neurodevelopmental outcomes.
- Early introduction of small volume or "trophic" feedings, ranging from 10-20 mL/kg/day, should be considered for all VLBW infants, even when critically ill or labile following birth. Not harmful and no increased incidence of NEC.
- Maternal breast milk is the preferred source of nutrition. Colostrum is administered in the order it was pumped as oral immune therapy (OIT), 0.05 mL- 0.5 mL to the buccal cavity every few hours, and is used as available for the earliest enteral feedings.
- When own mother's breast milk (EBM) is not available, donor breast milk (DBM) should be used for infants born < 2000 g or < 34 weeks. Furthermore, any infant whose parent/caregiver/s intend to provide human milk may receive DBM.
- Nutritional needs of the preterm infant exceed those amounts in human milk, particularly for protein, calcium and phosphorus. Human milk fortifiers are used to correct these nutritional inadequacies.
- Soy formulas are not recommended for preemies due to poor availability of calcium and phosphates.
- Feeding intolerance can present with frequent episodes of emesis or green bilious emesis. Any infant demonstrating these symptoms should have an immediate abdominal exam. An abdominal X-ray should be obtained if any abnormal findings are found on exam.

**Benefits of Colostrum**

- Colostrum is secreted during the early days post-birth when paracellular pathways between the mammary epithelium are open and permit transfer of high molecular weight components.
- Compared to mature milk colostrum has high content of lactoferrin, Oligosaccharides, secretory IgA, anti-inflammatory cytokines, growth factors, soluble CD14, antioxidants and other protective components

- Initial feedings of colostrum stimulate rapid growth in the intestinal mucosal surface area, facilitate the endocytosis of protein and induce many digestive enzymes.
- OIT has been associated with reduced rates of sepsis, transfers IgA and lactoferrin to the infant, and may contribute to the infant's microbiome.

**Growth Goals**

- The overall goal for preterm infant nutrition is to mimic in –utero growth.
- Preterm growth charts in EMR: Fenton (boys and girls) – 2013
    - Weight, length and Head circumference for age
    - Hover plot point for exact % and Z score
- First goal: regain birth weight after initial diuretic phase within 7-14 days of life.
- Growth phase goal: once infant is gaining after initial diuresis, goal is to at least maintain wt for age % / Z score. The average grams /day wt gain required to at least maintain metrics in growth phase will vary depending on age and gender. Additional wt gain or "catch up growth" may or may not be prescribed. Overall growth goals should be individualized based on medical course and nutritional history.
- Contact NICU RD for individualized goals if growth concerns.

**Recommended enteral energy and protein intakes**

| Infant age (wk.) | Energy goals (kcal/kg/d) | Protein goals (g/kg/d) |
|---|---|---|
| Preterm < 34 0/7 | 110-150 | 3.5-4.5 |
| Late preterm<br>34 0/7-36 6/7 | 120-135 | 3-3.2 |
| Term > 37 0/7 | 105-120 | 2-2.5 |

**NICU Feeding Protocol**

1. Provide colostrum as soon as it is available, ideally within 2 hours of birth.
2. Initiate trophic feeds on day of life 1-2 in infants without GI anomalies
3. If sufficient colostrum is not available after a minimum of 24 hours, consider using Donor EBM.
4. Calculate feeding volume with birth weight until infant surpasses birth weight after initial diuretic phase.
5. Use HMF to fortify human milk.
6. Schedule every 3 hour feeds.

**Advance feedings per the birth weight based tables below:**

**≤ 500 g BW Infants**

| Feeding Day | Total Daily Feeding Volume | Comments |
|---|---|---|
| 1 | 10 mL/ kg/day | |
| 2 | 10 mL/kg/day | |
| 3 | 20 mL /kg/day | |
| 4 | 20 mL/ kg/day | |
| 5 | 40 mL/ kg/day | |
| 6 | 60 mL /kg/day | |
| 7 | 80 mL/ kg/day | |
| 8 | 100 mL/kg/day | |
| 9 | 100 mL /kg/day | Fortify to 24 cal/oz |
| 10 | 120 mL/kg/day | Consider removing IV access |
| 11 | 140 mL/kg/day | |
| 12 | 150-160 mL/kg/day | |

**501- 1000 g BW INFANTS**

| Feeding Day | Total Daily Feeding Volume | Comments |
|---|---|---|
| 1 | 10 ml/kg/day | |
| 2 | 20 ml/kg/day | |
| 3 | 40 ml/kg/day | |
| 4 | 60 ml/kg/day | |
| 5 | 80 ml/kg/day | |
| 6 | 100 ml/kg/day | |
| 7 | 100 ml/kg/day | Fortify to 24 cal/oz |
| 8 | 120 ml/kg/day | Consider removing IV access |
| 9 | 140 ml/kg/day | |
| 10 | 140-160 ml/kg/day = GOAL | |

**1001 - 2000 g BW INFANTS**

| Type | Volume | Comments |
|---|---|---|
| **Trophic feeds** | 20 ml / kg/day x 1-2 days | |
| **Post trophic feeding progression** | Increase by 30 -40 ml / kg/day | -If cueing, may nipple above |
| **Fortification** | Fortify to 24 cal/ oz once tolerating 100-120 ml /kg/day | -Do not increase feeds on fortification day<br>-May consider d/c IV fluids/nutrition when feeds at least 100 ml / kg/day |
| **Goal feeds** | 140 -160 ml / kg/day | |

**Donor Human Milk:**

- Criteria for use:
  - All infants born < 34 weeks, < 2000 g bw or with provider concern for gut perfusion.
  - ANY infant outside of criteria if their parent/s intend to provide breastmilk
- If sufficient colostrum is not available after 24 hours, consider using DBM.
- Signed consent is required.
- Criteria for considering discussion with parents about discontinuation of DBM
  - Infant is 34 weeks or 1 week old, whichever comes later
  - At provider's discretion in the setting of poor growth
  - Parent/Caregiver's feeding plans for post – discharge should be considered.

**Liquid Protein Fortifier (LPF)**

- Extensively hydrolyzed liquid protein (1 g protein = 6 ml or 0.167 gm/ml)
- Purpose is to achieve goal protein intake and used primarily in VLBW, fluid restricted or donor human milk fed infant.
- LPF is part of feeding order dosed @ 0.5 ml / 25 ml (standard dose) or 1 ml/ 25 ml. This will add 0.5-1.0 gm. of protein /150ml of feeds

**Feeding Practice: Special Considerations**

**Transfusions:** PRBCs transfusion when patient has stable hemodynamics.

- Stop feeds 2-3 hours before starting transfusion
- Transfuse over 3 hours, maintain NPO
- Hold feeds for 2-3 hours after end of transfusion
- Restart at same feeding volume
- Patient **should not miss > 2 feeds** due to transfusion

**During pharmacotherapy for treatment of PDA**

- No need to reduce or withhold advancing feeds

**How to restart feeds** (Stopped for any reason)

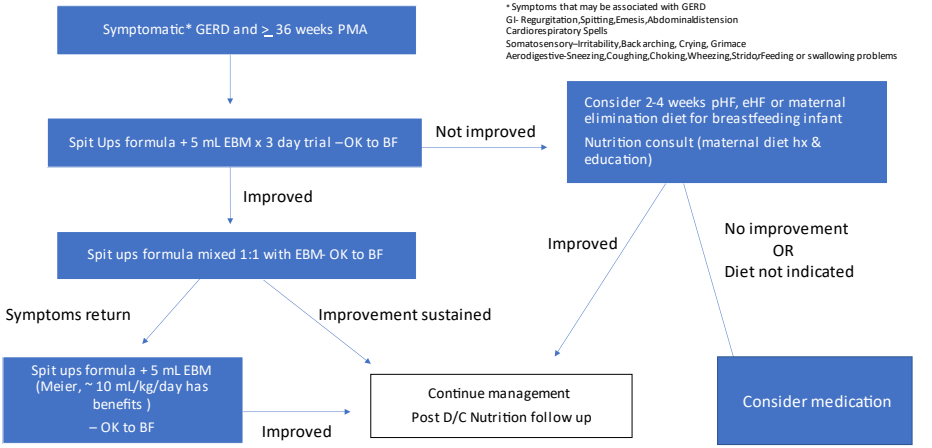
| Duration of NPO | Starting Volume of Feeds | Fortification | Feeding Advance |
|---|---|---|---|
| <24 hr. | Same as last feed | Same as last feed | Continue per protocol |
| 24-72 hr. | 50% of last feed | Same as last feed | To full previous volume in 24-48 hr.* Continue per protocol |
| 4-7 days | 50% of last feed | Unfortified | Feeding protocol using current wt. |
| >7 days | Beginning of feeding protocol using **current** weight | Unfortified | Per feeding protocol |

*Fortification may be delayed if necessary

**Transitioning to homegoing nutrition plan**

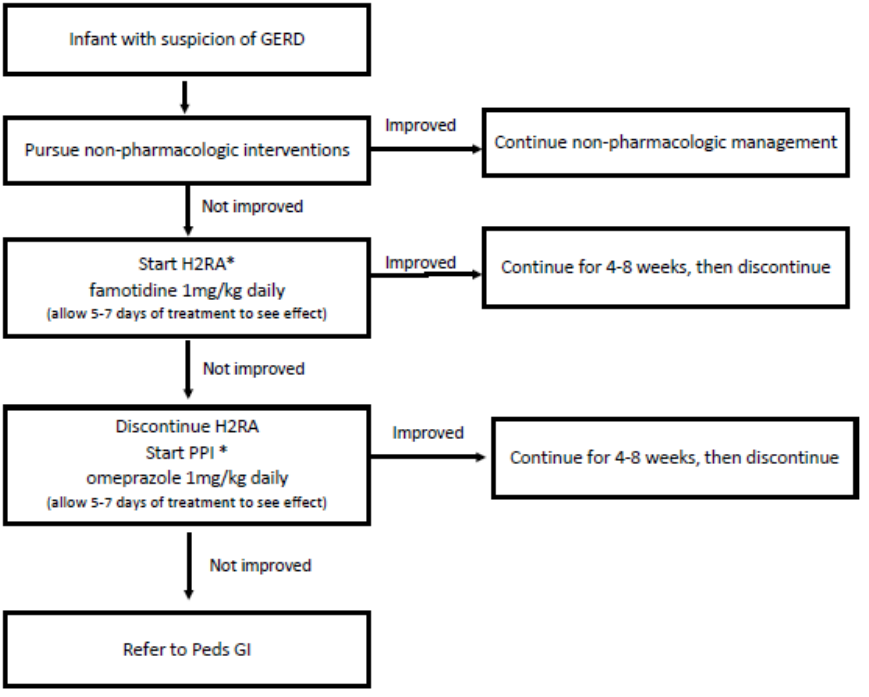
- Consider transitioning to homegoing nutrition plan once infant is taking > 50% orally with no other significant barriers to discharge.
- NICU RD may assist with involving parents in decision making about homegoing nutrition plan that involves fortification of breastmilk or formula.
- Parent/Caregiver/s who plan on breast feeding should be encouraged to offer the breast as often as they are available and infant is cueing.
- When available, a homegoing nutrition plan should be copied and pasted from NICU clinical nutrition note into D/C summary for the pediatrician.

# NON- SURGICAL GERD GUIDELINE



## Algorithm for acid suppression in Non-Surgical Infants

July 2020




*Medication should be prescribed at the lowest effective dose for the shortest amount of time possible.

H2RA – histamine receptor antagonist

PPI – proton pump inhibitor

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## Vitamins and Iron Supplements

*Ann Ebert, Pharm D and Sally Norlin, MS,RD*

### Vitamin D

- Start on term and preterm infants when tolerating enteral feeds.
- Dose is according to the total daily intake volume.

| | 400 units* | 200 units* | D/C when |
|---|---|---|---|
| EBM + HMF 24 | <200 ml/day | >200 ml/day | >400 ml/day |
| EBM + HMF 22 | <350 ml/day | >350 ml/day | >700 ml/day |
| Similac Special Care 24 | <200 ml/day | >200 ml/day | >400 ml/day |
| Neosure | <400ml/day | >400 ml/day | >800 ml/day |
| Term formula | <500 ml/day | >500 ml/day | >1000 ml/day |
| EBM (Exclusively or partially) | Daily | If less than half the feeds are EBM. | Never |

* Concentration is 400 units/ml

### Iron

- Term infants do not need routine iron supplement
- For infants < 37 weeks at birth or term SGA .
  - Start when on at least 60 mL/kg/day of feeds and approximately 2 weeks of age.
  - Standard dosing of iron for inpatients = 3 mg/ 0.2 ml. (Give 3 mg dose 1-3 times per day based on patient need)
  - If on erythropoietin = 6 mg /kg/day
  - Iron fortified formulas (@ ~ 150 ml/ kg/ day) provide ~ 2 mg/kg/day

### Multivitamin with Fe

- Each 1 ml provides 11 mg iron and 400 IU Vit D
- Can be used in lieu of separate Vit D and Fe supplements in the premature or SGA infant
- Give 1 ml/day or 0.5 ml 1-2 times/ day based on patient need

| Formula Analysis | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Nutrient | AAP-per kg/d | MBM Preterm | MBM Term | MBM w/HMF - CL- HP | Similac Special Care-24, HP | Similac Special Care -30 | MBM w/ Neosure | Similac Neosure | Similac Term formula |
| Kcal/oz | | 20 | 20 | 24 | 24 | 30 | 24 | 22 | 20 |
| | Preterm | 100 ml/kg | 100 ml/kg | 100 ml/kg | 100 ml/kg | 100 ml/kg | 100 ml/kg | 100 ml/kg | 100 ml/kg |
| Kcal/kg | 110-130 | 67 | 68 | 80 | 80 | 100 | 80 | 73 | 68 |
| Protein(g) | 3.4-4.4 | 1.4 | 1.0 | 2.44 | 2.68 | 3.0 | 1.5 | 2.08 | 1.4 |
| CHO (g) | 7-20 | 6.6 | 7.2 | 8.0 | 8.1 | 7.8 | 8.7 | 7.5 | 7.6 |
| Fat (g) | 5.3-8.4 | 3.9 | 3.9 | 4.0 | 4.4 | 6.7 | 4.7 | 4.1 | 3.7 |
| Calcium (mg) | 100-220 | 25 | 28 | 121 | 146 | 183 | 44 | 78 | 53 |
| Phosphorus (mg) | 60-140 | 13 | 14 | 67 | 81 | 101 | 24 | 46 | 28 |
| Iron (mg) | 2-4 | 0.12 | 0.03 | 0.47 | 1.46 | 1.83 | 0.32 | 1.34 | 1.2 |
| Zinc (mg) | 1.4-2.5 | 0.34 | 0.12 | 1.31 | 1.22 | 1.52 | 0.31 | 0.89 | 0.51 |
| Sodium (mEq) | 3-5 | 1.1 | 0.8 | 1.6 | 1.5 | 1.9 | 1 | 1.07 | 0.7 |
| Potassium (mEq) | 2-3 | 1.5 | 1.4 | 2.9 | 2.7 | 3.4 | 1.9 | 2.7 | 1.8 |
| Osmolality | | 290 | 286 | 450 | 280 | 325 | 340 | 250 | 310 |

*Pediatric Nutrition Handbook, 8th Edition. American Academy of Pediatrics, 2019

*Neofax, accessed on line 3/2022

# Chapter 12: Necrotizing Entercolitis

*Henry Zapata Galarza, MD; and Eileen Cowan, MD*

- Inflammation of the bowel wall leading to necrosis
- Most common GI emergency in preterm infants
- Affects 1-3 per 1000 live births
  - >90% of cases occur in infants ≤ 1500 grams
  - Occurs in 1-7% of infants ≤ 1500 grams
  - Affected term infants may have experienced asphyxia or have congenital heart disease including PDA (due to impaired intestinal perfusion)
- High risk until 35-36 weeks postmenstrual age
- Most commonly affects the distal ileum and proximal colon

**Pathophysiology**

- Unknown but hypothesized to be multifactorial
  - Mucosal intestinal injury (hypoxia/ischemia) + enteral nutrition + abnormal bacterial colonization → activation of inflammatory cascade → further bowel injury, invasion of bacteria into bowel wall → bowel necrosis
- Risk Factors
  - Prematurity
  - Enteral feeds
  - Intestinal ischemia: Clinically significant PDA, IUGR, birth asphyxia, CHD, exchange transfusion, indomethacin, maternal cocaine abuse
  - Absence of maternal antenatal steroid treatment
  - Recent blood transfusion, particularly of cells that are not type specific. Some evidence to suggest the anemia itself predisposes to NEC, not the actual transfusion
  - Prolonged antibiotic usage – impacts on microbiome of GI tract
  - Abdominal wall defects
  - Use of H2 blockers

**Measures to Prevent NEC**

- Feedings
  - Use human milk (EBM or DBM for high-risk patients)
  - Disciplined approach with NICU feeding protocols
- Limit use of antibiotic therapy
- Hold feedings 3 hours before and 3 hours after blood transfusion
- Do not use H2 blockers or PPIs until ≥ 35 weeks CGA

**Clinical Presentation**

- Temperature instability, lethargy, increased apnea/bradycardia/desaturation episodes
- Abdominal distension/tenderness/firmness, feeding intolerance with emesis (usually bilious), bloody stools, abdominal wall discoloration
- Laboratory: neutropenia, thrombocytopenia, coagulation abnormalities (platelet consumption), metabolic acidosis, electrolyte abnormalities, glucose instability
- Radiographic: ileus, dilation and thickening of bowel loops, fixed and/or dilated loop(s) of bowel, pneumatosis intestinalis, portal venous gas, free air

**Modified Bell Staging Criteria for NEC**

| Stage | Systemic signs | Abdominal signs | Radiographic signs |
|---|---|---|---|
| I (Suspected NEC) | Temperature instability, apnea, bradycardia, lethargy | Gastric residuals, mild abdominal distention, occult blood in stool | Normal or mild ileus |
| IIA (Mild NEC) | Same as above | Prominent abdominal distension + tenderness, absent bowel sounds, grossly bloody stools | Ileus, dilated bowel loops, focal pneumatosis intestinalis |
| IIB (Moderate NEC) | Mild metabolic acidosis and thrombocytopenia | Abdominal wall edema & tenderness + palpable mass | Extensive pneumatosis intestinalis, early ascites, + portal venous gas |
| IIIA (Advanced NEC) | Hypotension, respiratory & metabolic acidosis, oliguria, DIC, mechanical ventilation | Worsening wall edema & erythema with induration | Prominent ascites, fixed bowel loops |
| IIIB (Advanced NEC) | Shock | Evidence of perforation (tense abdomen, bluish discoloration) | Free Air |

**Differential Diagnosis**

- Spontaneous intestinal perforation (SIP): usually in terminal ileum or colon
  - Mostly in VLBW infants
  - Distinguished from NEC by absence of pneumatosis, hypotension and abdominal distention; can occur in the first week of life (earlier than NEC); independent of feeding
- Cow's milk protein allergy: rare in preterm; rarely occurs before 6 wks of age
- Infectious enteritis
- Anal fissures resulting in rectal bleeding

**Management***

- NPO, replogle to low intermittent suction
  - After 7-14 days* feeds should be started gradually
- Serial abdominal circumferences and serial abdominal examinations (both imaging and physical exam)
- Maintenance IVFs until TPN can be started
- Labs: CBC with differential, CRP, blood gas, electrolytes, glucose, blood culture, consider coagulation studies
  - Repeat labs every 6-12 hours (except blood culture) until infant clinically stable
  - Cultures positive in only 20-30% of cases
- Radiographs: APKUB & left lateral decubitus (for free air)
  - Repeat every 6-12 hours for first 24-48 hours
  - Abdominal US: to assess for pneumatosis, fluid collections, bowel wall thickness and peristalsis
- Broad-spectrum antibiotics to include anaerobic coverage*
  - Usually ampicillin or vancomycin, cefotaxime or gentamicin, and metronidazole
  - Treat for 7-14 days
- Monitor and manage homeostasis, DIC, and respiratory status as needed
- Pediatric Surgery Consult especially with x-ray or US diagnosis of NEC

(*See "Wisconsin State Guideline for Staging and Management of NEC)

**Prognosis**

- 27-63% of cases need surgical intervention (laparotomy with resection or peritoneal drain)

- Mortality: Overall 20-30%; Increases after perforation to 35-55%
- Survivors have a high prevalence of adverse GI sequelae (9-36% have strictures, short gut, TPN cholestasis)
  – Also increases risk of adverse neurodevelopmental outcomes

**Reference**


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   *http://www.uptodate.com/contents/prevention-of-necrotizing-enterocolitis-in-newborns*

   https://www.dynamed.com/condition/necrotizing-enterocolitis-19

# Wisconsin State Guideline for Staging and Management of NEC

Table 1: Guidelines for Staging and Management of Necrotizing Enterocolitis*

Babies may progress during first 48-72 hours and stage may need to be modified

| STAGE | ILLNESS SEVERITY | SYSTEMIC SIGNS | INTESTINAL SIGNS | RADIOLOGIC SIGNS | SURGERY CONSULT | XRAY FREQ. | ANTIBIOTICs | Course Length | Transfer to center that is able to do complex surgical procedures |
|---|---|---|---|---|---|---|---|---|---|
| **I. Suspected – No radiographic evidence. Differential includes ileus, other system infections and cows milk protein allergy** | | | | | | | | | |
| Ia. | Suspicious, mildly ill | Temperature instability, apnea, bradycardia, feeding intolerance | Residuals,mild distension,occult blood | Normal or mild ileus | No | Q6-8 hrs x 24-48 hours | Ampicillin Gentamicin | 48 hours | no |
| Ib. | Suspicious, mildly ill | Same as IA | Same as IA – gross blood | Same as IA | No | Same as IA | Ampicillin Gentamicin | 5 days | no |
| **II. Definite – Must have radiographic/ultrasound diagnosis** | | | | | | | | | |
| IIa. | Mildly ill | Same as IA, mild lab changes | Same as I, plus abdominal tenderness | Pneumatosis Intestinalis +/- fixed dilated loops | Yes | Q 6 hrs x 48 hours | Ampicillin Gentamicin | 7 days | If sentinel loops persists transfer to surgical center |
| IIb. | Moderately ill | Same as IA with more lab changes, needs more support | Same as IIA, plus abdominal cellulitis | IIA ± portal venous gas ± ascites | Yes | Q 6 hrs x 48 hours | Ampicillin Gentamicin Flagyl | 10 days | Presence of portal gas and/or abdominal cellulitis should prompt transfer to surgical center |
| **III. Advanced: Infants are severely ill with radiographic evidence (without or without evidence of perforation)** | | | | | | | | | |
| IIIa. | Severely ill, bowel intact [1] | *Severe* metabolic and/or resp acidosis, electrolyte & CBC abnormalities, shock | As above plus peritonitis, marked tenderness and distension | Same as IIB May see persistent ileus, abdominal distension, absent bowel gas | Yes | Q6 x 48 hours | Ampicillin Gentamicin Flagyl | At least 14 days | Transfer |
| IIIb. | Severely ill, perforated (not SIPs)[2] | Same as IIIA | Same as IIIA | Pneumoperitoneum | Yes | X-rays prn | Ampicillin Gentamicin Flagyl | At least 14 days | Transfer |

NOTES

1. Surgical intervention may be warranted if no clinical improvement after 48-72 hours and abdominal exam/x-rays remain concerning. Consider drain or paracentesis/ultrasound as a diagnostic study if NEC diagnosis unclear
2. *Spontaneous intestinal perforation (SIP) is not included in this guideline.
3. NPO Duration For non-surgical NEC—Feed on the day after antibiotic completion.

Arca, Garland, Uhing,

# Chapter 13: Hyperbilirubinemia

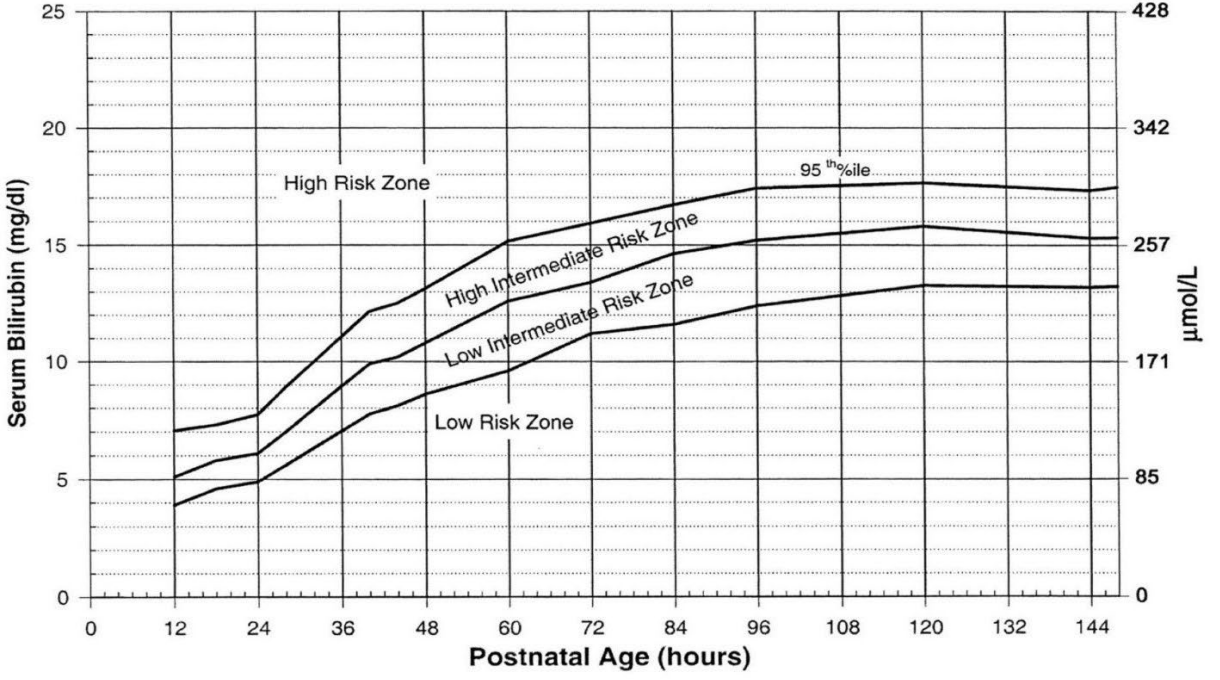
Neonatal hyperbilirubinemia is common and occurs in up to 80% of all newborns. Approximately 5-10% of newborns will require phototherapy, while a much smaller percentage will require more intensive therapies such as exchange transfusion. It is important to understand the risk factors for developing severe hyperbilirubinemia and the treatment guidelines based on these risk factors.

**Risk Factors for Severe Hyperbilirubinemia in Infants ≥ 35 Weeks' Gestation**

- Major risk factors
  - Pre-discharge TSB level in the high-risk zone (Fig 2)
  - Jaundice observed in the first 24 hours
  - Blood group incompatibility with positive direct Coombs test
  - Other known familial hemolytic disease (G6PD, spherocytosis, etc.)
  - Gestational age 35-36 wk.
  - Previous sibling received phototherapy
  - Cephalohematoma or significant bruising
  - Exclusive breastfeeding, particularly with poor feeding or excessive weight loss
  - Asian race
- Minor risk factors
  - Pre-discharge TSB or TcB level in the high intermediate-risk zone
  - Gestational age 37-38 weeks
  - Macrosomic infant
  - Male gender
- Low risk group
  - TSB or TcB level in the low-risk zone
  - Gestational age ≥ 41 wk.
  - Exclusive bottle feeding
  - Discharge from hospital after 72 hours

| Risk Zone as a Predictor of Hyperbilirubinemia | | |
|---|---|---|
| TSB<br>Before Discharge | Newborns Total<br>= 2840 n (%) | Newborns Who Subsequently Developed a TSB Level > 95th Percentile, n (%) |
| High-risk zone(>95th percentile) | 172 (6.0) | 68 (39.5) |
| High intermediate-risk zone | 356 (12.5) | 46 (12.9) |
| Low intermediate-risk zone | 556 (19. 6) | 12 (2.26) |
| Low-risk zone | 1756 (61.8) | 0 |

**Nomogram for designation of risk in 2840 well newborns at 36 or more weeks' gestational age with birth weight of 2000g or more or 35 or more weeks' gestational age and birth weight of 2500 g or more based on the hour-specific serum bilirubin values.**




**Subcommittee on Hyperbilirubinemia et al. Pediatrics 2004;114:297-316**



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**Ten Commandments for Preventing and Managing Hyperbilirubinemia:**

1. Promote and support successful breastfeeding
2. Measure TSB if clinical jaundice before 24 hours
3. If TcB is elevated, must confirm with TSB
4. Recognize that visual diagnosis of jaundice is unreliable
5. Interpret all TSB levels according to infant's age in hours
6. Do not treat late preterm as a term infant; they are at a much higher risk.
7. Determine the need for repeat bilirubin levels and safety for hospital discharge based on the 24 hour screening bilirubin level
8. Provide parents with information about newborn jaundice
9. Plan follow-up based on time of discharge and the risk assessment
10. When indicated, treat the newborn with phototherapy or exchange transfusion

**Indirect Hyperbilirubinemia**
**Etiology:**

- Concentration from dehydration
- Increased production
  - Blood group incompatibility: Rh, ABO, minor subgroup
  - RBC defects: spherocytosis, elliptocytosis, pyruvate kinase or G6PD deficiency, thalassemia
  - Extravascular blood: cephalohematoma, bruises
  - Polycythemia
  - Sepsis or UTI
- Increased enterohepatic circulation
  - Bowel obstruction, ileus
  - Breast milk jaundice
- Decreased excretion
  - Prematurity
  - Hypothyroidism
  - Hepatocellular dysfunction
  - Galactosemia, tyrosinemia
  - Drugs (aspirin, sulfa)
  - Crigler-Najjar syndrome
  - Gilbert syndrome

**Initial Work-up for bilirubin in high risk zone and/or requiring phototherapy:**

- Total and Direct bilirubin
- Document maternal antibody status and send cord blood for infant's Type and Coombs
- Hematocrit and reticulocyte count: evidence of hemolysis
- Smear: Spherocytosis, fragmented RBCs with hemolysis (heel stick will be a false positive)
- Consider screen for sepsis and/or UTI
- Consider G6PD, thalassemia and pyruvate kinase screen
- If hyperbilirubinemia occurs after two weeks of age, obtain results of newborn screen and consider testing for thyroid dysfunction (TSH, free T4)

**Management:**

- Consider supplementing feeds to decrease enterohepatic circulation or starting IVFs to improve urine output and increase bilirubin excretion

**Phototherapy**

- First line of treatment for management of hyperbilirubinemia in a newborn
- Can be a high-intensity bilirubin blanket (for babies in the newborn nursery) to multiple banks of overhead lights depending on the bilirubin level
- Use total bilirubin. Do not subtract direct bilirubin from the total.
- For infants > 35wks: Follow AAP guidelines and bilirubin charts (see pages 69 & 70)
- For infants < 35wks and <7 days:

| | Initiate Phototherapy | Exchange Transfusion for infants without neurologic findings |
|---|---|---|
| **Gestational Age (Week)** | **Total Serum Bilirubin (mg/dl)** | **Total Serum Bilirubin (mg/dl)** |
| <28 0/7 | 5-6 | 11-14 |
| 28 0/7-29 6/7 | 6-8 | 12-14 |
| 30 0/7-31 6/7 | 8-10 | 13-16 |
| 32 0/7-33 6/7 | 10-12 | 15-18 |
| 34 0/7-34 6/7 | 12-14 | 17-19 |

- Use postmenstrual age for phototherapy. For example, when a 29 0/7 week infant is 7 days old, use the TSB level for 30 0/7 weeks.
- Use lower range of listed TSB levels for infants at greater risk of bilirubin toxicity:
  - Lower gestational age
  - Rapidly rising TSB (rate of rise $\geq$0.2 mg/dL/hour)
  - Significant bruising
  - Clinically unstable

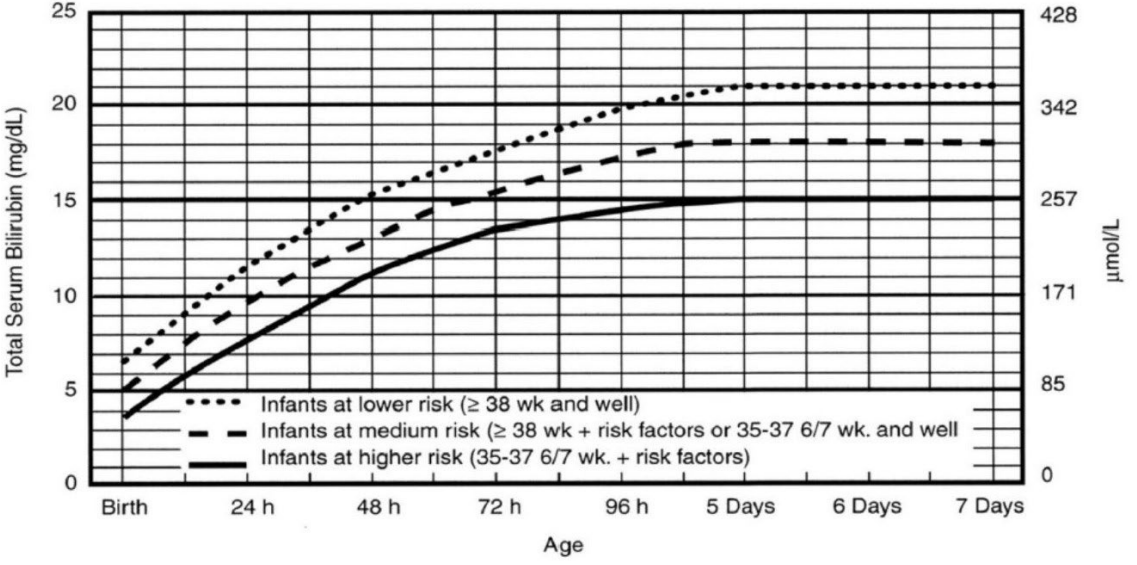
**IVIG & Albumin Infusions for Hypoalbuminemia:**

- IVIG: 1 gm/kg over 2-4 hours
  - May be useful for hyperbilirubinemia associated with hemolysis
- Albumin: 10-20 ml/kg of 5% Albumin
  - Studies have shown conflicting levels of efficacy but may be used on a case-by-case basis

**Exchange transfusion for Hyperbilirubinemia: Goal is to prevent kernicterus and bilirubin-induced neurologic dysfunction (BIND)**

- For infant ≥ 35 weeks GA, follow AAP guidelines
  - Also indicated when infant has signs of kernicterus or BIND regardless of TSB level
- For infants < 35 weeks and without neurologic findings, use table above

**Guidelines for phototherapy in infants of 35 or more weeks' gestation.**
**Note: levels shown are approximations.**




- 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 < 3.0g/dL (if measured)
- For well infants 35-37 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 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

**Subcommittee on Hyperbilirubinemia et al. Pediatrics 2004;114:297-316**



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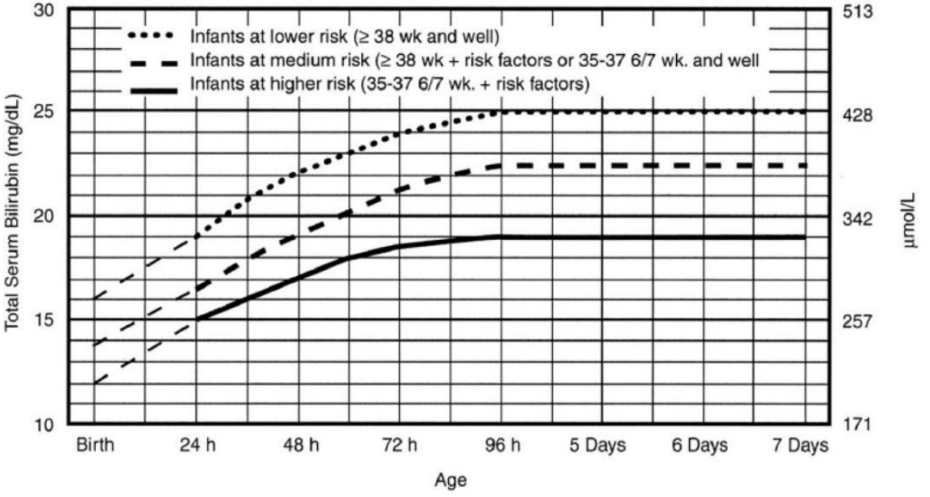
**Guidelines for exchange transfusion in infants of 35 or more weeks' gestation.**
**Note: levels shown are approximations.**




- 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 ≥5 mg/dL (85 µmol/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.

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**Exchange transfusion**

- Goal: To remove antibodies and bilirubin
  - Before exchange, send baby's blood for metabolic screen, G6PD screen, and Hgb electrophoresis
  - Request fresh blood (< 3 days)
  - Should be double volume (removes 87% of baby's RBCs, infants ≥35 weeks have blood volume of 85 mL/kg)
  - Aliquots should be no more than 5% of blood volume in a single pass
  - Length of exchange procedure would be about 2 hours
- Complications of exchange
  - Arrhythmia, cardiac arrest
  - Hypoglycemia, hypocalcemia, hyperkalemia
  - Necrotizing Enterocolitis
  - Portal vein thrombosis or other thromboembolic events
  - Thrombocytopenia
- Review detailed protocol for this procedure

**Direct Hyperbilirubinemia (if TsB <5, any direct bilirubin ≥1 mg/dL. If TsB ≥5, any direct bilirubin >20% of total)**

**Etiology**

- Prolonged TPN use
- Anatomic Obstruction
  - Biliary atresia and/or choledochal cyst
  - Alagille syndrome
  - Biliary sludge in preterm infants
  - Tumor/mass
- Infections
  - CMV
  - Enterovirus
  - HSV
  - Parvovirus
  - UTI
  - Sepsis
  - Toxoplasmosis
  - Congenital syphilis

- Genetic/Metabolic
  - Alpha-one antitrypsin deficiency
  - Cystic fibrosis
  - Galactosemia
  - Zellweger syndrome
  - GALD

**Diagnosis & Management:**

- Liver ultrasound
- LFTs, including GGT
- GI consult
- Consider HIDA scan
- Discuss with nutrition and pharmacy about reconstituting trace elements in TPN
- Consider ursodiol

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# Chapter 14: Cardiovascular System

*Megan Derrer, MD & Nathan Lepp, MD*

## A. Shock

### Definitions

- Insufficient organ perfusion to meet tissue metabolic needs, leading to tissue hypoxia, acidosis, metabolic derangements and cell death

Hypotension:

- BP lower than expected range for age
- Hypotension does not necessarily mean that an infant is in shock

- There is no BP threshold below which intervention to increase BP has been shown to improve outcomes
- A combination of low BP with clinical signs of poor perfusion appears to be more strongly correlated with poor outcomes

### Symptoms

- Tachycardia, poor perfusion/weak pulse, cold extremities, lethargy, apnea, tachypnea, metabolic acidosis

### Classification of Shock

- Hypovolemic Shock
  - From blood loss-antenatal or postnatal
  - Post-operative due to capillary leak and third spacing of intravascular volume
    - Can also be seen in sepsis
- Drug Induced Hypotension
  - Magnesium sulfate, beta blockers (Labetalol), nitroprusside, narcotics, barbiturates
- Cardiogenic Shock
  - Cardiac failure – impaired filling, ventricular emptying, and/or contractility
  - Birth asphyxia, CHD, metabolic abnormalities, arrhythmia, cardiomyopathy, obstruction to venous return

- Distributive shock (including septic shock)
  - Inadequate relative intravascular volume secondary to vasodilation
  - Septic shock due to release of endotoxins which lead to vasodilation
  - Also have capillary leak with third spacing due to endothelial injury
    - Anaphylaxis
    - Vasodilators
    - Adrenal insufficiency
- Neurogenic Shock
  - Birth asphyxia and IVH
- Shock in extreme prematurity
  - Due to hypovolemia, inability to regulate vascular tone, immature catecholamine response, IVH, adrenocortical insufficiency
  - Usually respond better to inotropes than to volume administration
  - PDA can cause transient hypotension

Stages of Shock

| Stage | Pathophysiology | Mechanisms | Change in vitals/lab values |
|---|---|---|---|
| Compensated | Heart, brain, lungs, kidney perfusion maintained, reduced flow to less vital organs | Vasoconstriction stimulated by acidosis/catecholamine release/decreased stimulation of baroreceptors à decreased urine output | Tachycardia<br>-Stable BP<br>-Normal HCO3 and lactate |
| Uncompensated Reversible | Decreased perfusion to all organs | Continuation of the above | - Increased tachycardia-BP begins to fall<br>-HCO3 - decreases<br>Lactate |

| | | | |
|---|---|---|---|
| Uncompensated Irreversible | Cellular dysfunction and acidosis secondary to ischemia à cellular death | Release of cellular mediators that lead to further reduced perfusion, injury to the endothelium, activation of coagulation cascade | Extreme tachycardia à bradycardia<br>-Severe decrease in BP<br>-Severe decrease in HCO3<br>-Severe increase in lactate |

**Diagnosis**

- CBC with differential
- Blood culture
- ABG, lactate
- Electrolytes, glucose, calcium
- Newborn transfusion work-up
- Chest x-ray, echocardiogram, and head ultrasound

**Treatment**

- Treat underlying abnormalities
- To improve hypotension:
  - Volume expansion
- Normal saline bolus 10 ml/kg over 10-30 minutes
- Consider blood products for volume expansion
  - Low hematocrit
  - Bleeding
  - Electrolyte abnormalities that may be sensitive to additional dextrose or sodium
- Colloids associated with increased mortality
- May worsen cardiogenic shock
- Medications for hypotension

| Medication | Dose | Mechanism | Adverse Effects | Notes |
|---|---|---|---|---|
| Dopamine | 1-5 mcg/kg/min | Dopamine receptor Increases renal blood flow | Tachycardia, arrhythmias, tissue ischemia (only use in central IV) | Preferred inotrope in neonates esp. for <1500 gm.<br>++Chronotrope<br>+Inotrope<br>SVR effect is dose dependent |
| | 5-15 mcg/kg/min | Dopamine and $\beta$1 and $\alpha$ receptors | | |
| | 15-20 mcg/kg/min | $\alpha$ receptors<br>Systemic vasoconstriction | | |
| Dobutamine | 2-20 mcg/kg/min | $\beta$1>>$\beta$2<br>Increase contractility, decreases SVR<br>+Chronotrope<br>+Inotrope | Tachycardia, hypotension with hypovolemia, cutaneous vasodilation, arrhythmia, tissue ischemia | Better than dopamine in presence of myocardial dysfunction<br>Less effect on heart rate |
| Epinephrine | 0.1-0.3 mcg/kg/min | $\beta$1 & $\beta$2<br>Vasodilation, Increases contractility | Hyperglycemia, tachycardia, increased lactate, arrhythmias, tissue ischemia, hypokalemia | Most potent vasopressor<br>++Chronotrope<br>+Inotrope |
| | 0.3-1 mcg/kg/min | $\alpha$ receptors<br>Vasoconstriction, increases HR | | |

| | | | | |
|---|---|---|---|---|
| Hydro-cortisone | Stress dosing:<br>1 mg/kg/ dose q8 hr.<br>Physiologic dosing = 1 mg/kg/day q8-12 hr. | Increases the expression of adrenergic receptors in the vascular wall enhancing vascular reactivity to other vasoactive substances | Hyperglycemia, GI perforation/ hemorrhage, infection, cardiac hypertrophy | Use for unresponsive hypotension<br>Do **not** use with indomethacin |
| Vasopressin | 0.01 hr – 0.04 units/kg/hr | Vascular effects via G protein coupled V1a (vasoconstriction via IP3 pathway) and V2 receptors (vasodilation via cAMP) in cardiovascular system | Hypertension, electrolyte abnormalities, fluid overload | Vasoconstrictive effects predominate in IV infusion<br>Minimal chronotropic and inotropic effects |
| Milrinone | Loading dose 50 mcg/kg over 15 minutes<br>Maintenance 0.3-0.75 mcg/kg/min | PDE-3 inhibitor → increased intracellular cAMP, increased myocardial intracellular calcium, and increased uptake of calcium after systole | Hypotension, arrhythmias | Dosing extrapolated from older infants and children<br>May potentiate diuretic effects<br>Does **not** increase myocardial oxygen consumption |

**B. Hypertension (see also Chapter 18, Neonatal Kidney) Definition**

- Systolic/diastolic BP >95th percentile in right upper extremity
  - Term infant >90/60
  - Preterm infant >80/50

**Etiologies**

- Renal artery or aortic thrombosis
- Primary renal disease
- Obstructive uropathy
- Coarctation of the aorta
- Endocrine disorders: hyperthyroidism, CAH (11-betaOH)
- Medications: theophylline, corticosteroids, pancuronium
- BPD
- Pain, agitation, drug withdrawal

**Diagnosis**

- Four extremity BPs-evaluate for coarctation
- Labs
  - UA, Urine culture
  - Urine Protein / Urine creatinine (Normal <1)
  - Electrolytes, creatinine, BUN
  - Plasma renin activity, aldosterone
  - TSH, free T4
- Imaging
  - Abdominal/Renal ultrasound with Doppler studies
  - Echocardiogram

**Treatment**

- Nephrology consult to determine appropriate medication
  - Usually start with a calcium channel blocker (isradipine)
  -

**C. Arrhythmias**

**Complete Heart Block**

- Seen with maternal connective tissue disorders (i.e. SLE) who have anti-SSA (Ro)

or anti-SSB (La) antibodies
  - Can lead to hydrops fetalis
- Treatment
  - Only necessary if symptomatic
  - Generally symptomatic if HR < 55 bpm
  - Atropine, isoproterenol, pacemaker

**Supraventricular Tachycardia**

- HR 230-330 bpm with decreased variability (fixed R-R interval)
- Increased risk with CHD (Ebstein's anomaly, L-TGA),WPW
- Acute Treatment
  - Unstable-synchronized cardioversion
    - Start with 0.5 J/kg, increasing by 0.5 J/kg to max 2 J/kg
  - Stable
    - Vagal maneuvers-gag reflex, ice to the face, knees to chest
    - Adenosine
      - 50 mcg/kg rapid IV push followed by rapid saline flush
        - Via PIV with 3 way stop cock for rapid flush
      - Increase by 50 mcg/kg every 2 minutes to max dose of 250 mcg/kg
      - Causes transient AV node block-have ECG running and defibrillator nearby

**D. Congenital Heart Disease (CHD)**

- VSD-most common CHD
- Transposition of the great arteries-most common CHD presenting in the first week of life
- HLHS-second most common in the first week of life and the most common cause of mortality in the first year of life
- Tetralogy of Fallot-most common CHD presenting after the first week of life

**Diagnosis**

- Four extremity blood pressures
- Pre- and post-ductal $O_2$ saturations (CHD screen)
- Chest x-ray-evaluate heart size and pulmonary vascular markings
- ECG
- ABG-evaluate for metabolic acidosis and hypoxemia
- Echocardiogram

**Clinical Presentation**

- Respiratory Distress: VSD, PDA, ASD, TAPVR, truncus arteriosus (TA)
- Murmurs
  - Systolic
    - Holosystolic – VSD
    - Ejection – aortic/pulmonic stenosis or obstructed outflow tract
    - Click – aortic/pulmonic stenosis or truncus arteriosus
  - Blowing
    - Valve regurgitation
  - Diastolic *always pathologic
    - Aortic/pulmonic regurgitation, tricuspid/mitral stenosis, increased flow across tricuspid/mitral valves
  - Continuous
    - PDA, AV fistula, venous hum, collateral vessels, truncus arteriosus, aortopulmonary window
  - Gallop
    - Decreased ventricular compliance and high-flow states
- Cyanosis – bluish discoloration of the tissues when deoxygenated hemoglobin in the capillary >3g/dL
  - Appearance of cyanosis depends upon the total amount of deoxygenated hemoglobin, not ratio of deoxygenated to oxygenated blood
  - Cyanosis with normal or increased pulmonary blood flow: TGA, TA, DORV
  - Cyanosis with decreased pulmonary blood flow: TOF, tricuspid atresia, pulmonary atresia/stenosis, Ebstein's anomaly
  - Differential Cyanosis - >10% difference in pre/post-ductal saturations
    - Lower body more cyanotic than upper body – R to L ductal shunting with increased PVR
    - Seen in coarctation of the aorta, pulmonary hypertension, interrupted aortic arch
  - Reverse differential cyanosis
    - Upper body more cyanotic than lower body
    - Seen with dTGA + coarctation of the aorta, pulmonary hypertension,

or interrupted aortic arch

- Shock: TAPVR with obstruction, HLHS, critical aortic stenosis, interrupted aortic arch, coarctation of the aorta

**Management**

- IV access; UAC, UVC, PICC line
- Prostaglandin E1
  - For ductal-dependent lesions
  - Dose: start at 0.01-0.02 mcg/kg/min for known ductal dependent lesions or lesions presenting soon after birth
    - If presenting several days after birth, consider starting at 0.5-1 mcg/kg/min
  - Side effects: apnea (may be treated with caffeine), fever, leukocytosis, cutaneous flushing, bradycardia, hypotension, hypoglycemia, hypocalcemia
  - Long-term causes reversible cortical proliferation of the long bones, and gastric outlet obstruction
- Generally, avoid supplemental oxygen as this causes pulmonary vasodilation and will increase pulmonary blood flow at the expense of systemic blood flow
  - Maintain oxygen saturations around 75-80% = Qp/Qs of 1
  - Qp/Qs = $(SaO_2\text{-}SvO_2)/SpvO_2\text{-}SpaO_2)$
    - Ratio of pulmonary to systemic blood flow
- Cranial ultrasound, renal ultrasound
- Genetic testing

**E. Patent Ductus Arteriosus in Preterm infants Clinical Presentation**

- Murmur-LUSB, systolic or continuous
- Hyperactive precordium, bounding pulses, palmar pulses
- Widened pulse pressure (> 30 mmHg)
- Worsening respiratory distress
- Hepatomegaly, cardiomegaly
  - Neither individual clinical trials nor meta-analyses have demonstrated that closing PDA results in improved long-term outcomes in preterm infants

– Trend toward a more conservative approach to PDA management

## PDA Guideline UnityPoint-Meriter and AFCH

### PDA Treatment Guideline

**Timing of Initial echocardiogram**

- 22 0/7- 25 6/7 weeks or <750g: Obtain a routine echocardiogram on day 3-5
- 26 0/7- 28 6/7 weeks: Obtain an echocardiogram on day 7 or after if clinical score is >=3
- Discuss with the Cardiology team about potential limited echo if the infant is critically ill

**Medical Treatment of PDA**

- Medical treatment is indicated if McNamara Echocardiographic score is >=3
- Decision for subsequent treatment courses based upon clinical judgement if echocardiographic score >=3
- Total of three courses of medical treatment is recommended
- Choice of medication based on provider preference and clinical status of the patient
- Medication and dosing
    - Ibuprofen: 10 mg/kg NG x 1, then 5 mg/kg q24h x 2 more doses NG
        - Do not use if evidence of renal dysfunction; SCr >1, AKI in past 7 days (rise of SCr by 0.3 or UOP < 0.5 mL/kg/d)
        - Do not use if GI bleeding or platelets < 100K
        - Do not use if hydrocortisone administration within 24 hours
    - Acetaminophen: 15 mg/kg NG q6h x 5 days
        - Do not use if evidence of liver injury/ cholestasis
    - Use IV ibuprofen or IV acetaminophen if on < 60 ml/kg/day of feeds
- Lab monitoring prior to each course:
    - Ibuprofen: BMP and platelets
    - Acetaminophen: nutrition panel
- No need to reduce or withhold advancing feeds while on medical treatment for PDA

**Definitive Closure of PDA (Transcatheter closure/ PDA Ligation)**

- If combined score is >=7 after three courses of medical treatment or if medical treatment is contraindicated, consult Pediatric Interventional Cardiology to discuss definitive PDA closure
- Preferred time for transcatheter closure of hemodynamically significant PDA is 21-35 days

**Table. Modified McNamara Scale**

| Points | Clinical Score | Echocardiographic Score |
|---|---|---|
| 1 | RSS < 1.5 | Continuous flow and increasing velocity flow into the branch PAs: <0.15 m/sec in diastole in LPA |
| 2 | RSS 1.5 – 1.8 | Small PDA, Continuous flow and increasing velocity flow into the branch PAs : >0.4 m/sec in diastole in LPA |
| 3 | RSS 1.8 – 3.0<br>OR hypotension requiring a single vasopressor | Moderate PDA, Diastolic flow reversal in the descending aorta below the level of the PDA |
| 4 | RSS >3.0 OR hypotension requiring more than 1 vasopressor | Large PDA, A dilated LA (typically 2 times larger the aorta in PLAX view) |
| 5 | | Large PDA, LV dilation |

RSS – Respiratory Severity Score (MAP x FiO2)

## F. Persistent Pulmonary Hypertension Diagnosis

- Pulmonary hypertension should be considered in a term/post-term infant with cyanosis
- Associated with fetal distress, RDS and meconium aspiration syndrome
- Pre-ductal and post-ductal saturations differ significantly (>10%)
- Desaturation with stimulation, crying
- S2 is loud with diminished split, murmur of tricuspid regurgitation
- Chest x-ray-decreased pulmonary vascular markings
- Echocardiogram
  - PDA with R $\rightarrow$ L shunting
  - Flattening of the interventricular septum
  - Bulging of the atrial septum
  - Pulmonary pressures determined using TR velocity

### Treatment

- Minimize handling
- Surfactant-for RDS or meconium aspiration
- Sedation/paralysis
- Supplemental oxygen as needed to maintain saturations within goal range:

Dilates pulmonary vasculature

- Correct acidosis: Acidosis leads to pulmonary vasoconstriction
- Inhaled Nitric oxide: See Respiratory Chapter
- Sildenafil
- Inotropic agents to increase systemic pressures (decreasing shunting)
- ECMO – consider if oxygenation index (OI) is > 35 for 5-6 hrs

$$OI = \frac{\text{mean airway pressure} \times FiO_2 \times 100}{PaO_2}$$

## G. Miscellaneous

### Electrocardiogram

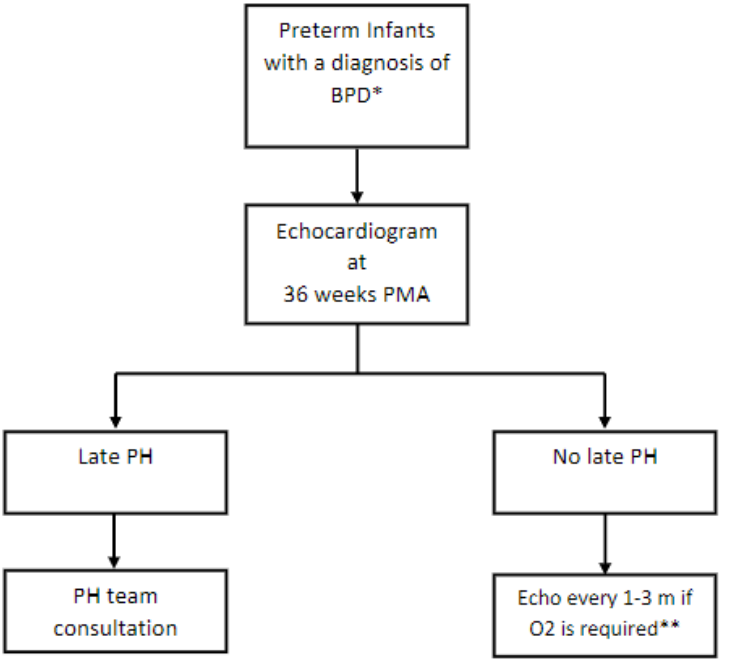
- Differs from the adult
- RV dominance with right axis deviation
- T wave inversion in V1-V4 after 48-72 hours of age is normal
  – If T wave inversion is not present consider RVH
- RSR' in right precordial leads is normal as long as QRS interval is <10 msec over normal intervals
- QTc interval
  – QT/square root of the previous R-R interval
  – <0.47 normal in first week of life
  – <0.45 normal from 1 week to 6 months of age

### Equations

- Shortening Fraction = $\frac{\text{LV diastolic diameter} - \text{LV systolic diameter} \times 100}{\text{LV diastolic diameter}}$
  - Normal is 28-40%
- Ejection Fraction = $\frac{\text{LV end-diastolic volume} - \text{LV end-systolic volume} \times 100}{\text{LV end-diastolic volume}}$

- Cardiac Output = Stroke volume x Heart rate
  - Stroke volume is affected by preload, afterload, and contractility
  - In the neonate the CO is more dependent on heart rate

## Pulmonary Hypertension Screening guideline for preterm infants




*BPD defined as need for respiratory support at 36 weeks PMA

**Every 1-2 months if inpatient, every 3 months if following up outpatient

**Indicate "Evaluate for pulmonary hypertension" on the echo request.**

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# Chapter 15: Hematology

*Pamela Kling, MD & Henry Zapata Galarza MD*

## A. Anemia

- Anemia-Blood Loss
  - Obstetrical-abruption, placenta previa, umbilical cord trauma
  - Immediate (vs. delayed) umbilical cord clamping
  - Feto-maternal hemorrhage
  - Twin-twin transfusion syndrome
  - Internal hemorrhage-IVH, subgaleal hemorrhage, cephalohematoma, adrenal hemorrhage, subcapsular hematoma of liver
  - Iatrogenic-lab tests
- Anemia-Increased RBC destruction
  - Hereditary RBC disorders-G6PD, hereditary spherocytosis, thalassemia
  - Immune hemolysis-Rh/ABO incompatibility
  - Acquired hemolysis-infection, drugs
- Anemia-Decreased RBC production
  - Anemia of prematurity
  - Aplastic or hypoplastic anemia
  - Bone marrow suppression-parvovirus, rubella
  - Nutritional anemia-iron deficiency
- Anemia-Physiologic
  - Normal nadir at 6-8 weeks in term infant
  - Delayed clamping or cord milking can minimize the Hgb at the nadir
  - Earlier for preterm infant (4-6 weeks)
  - Preterm infant nadir is lower than term infant (Hgb of 9 versus 11).

**Anemia Initial Work-up**

- Must be completed before transfusion
- CBC with platelets
- Reticulocyte count
- Peripheral smear (spherocytes, ABO incompatibility; nRBC, Rh disease)
- Type/Coombs on mother and infant
- Kleihauer-Betke on mother (looking for fetal RBCs)

**Additional Tests**

- RBC enzyme studies: G6PD and pyruvatekinase
  - G6PD-may be falsely negative during acute process due to increased enzyme activity in reticulocytes
- Hemoglobin electrophoresis (newborn screen)
- Head or abdominal ultrasound

**Management**

- Consider transfusion guidelines from Iowa Study: Low Threshold vs. (High Threshold): Less IVH in High group, better long-term outcome in girls in Low.

| Hematocrit | Other Clinical/Lab data |
|---|---|
| <7-10 (<21-30) | Stable child > 1 wk old, asymptomatic, RA or NC, NCPAP with FiO2<40%, Room air, & retic <4% |
| <28 (<38) | Mild lung disease, NC/CPAP/NPSIMV with FiO2>40%, or major surgery >21% |
| <11-13 Hb (<33-39 Hct) | Critically ill, severe lung disease in first week or major surgery |
| Any Hct | Acute blood loss & signs of shock |

- Draw first newborn screen prior to transfusion
- Neonatal Transfusion workup (NTW; aka-Type and screen) only needs to be completed once during the admission, up to 4 months of age
- Transfuse with 15-20 ml/kg of CMV negative, irradiated, type specific pRBCs.
  - Irradiation inactivates donor lymphocytes reducing GVHD, but increases potassium concentration of packed cells and reduces the half-life of stored blood.
  - Some centers used leukocyte-reduced/filtered blood in place of CMV negative blood. This also reduces CMV transmission.
  - Transfusion of 15-20 ml/kg will raise the Hct about 10%
  - Transfusion of pRBCs causes bone marrow suppression
  - Hold feedings, before & during transfusion per guidelines in the feeding protocol chapter
  - Note: At UW AFCH pRBCs are not type-specific and have higher Hct., so transfuse up to 15 ml/kg/d in one installation.

**Special Transfusions**

- Double-Volume Exchange Transfusion
  - Indications-hemolytic disease of the newborn
- Volume to be exchanged = 2[infant's blood volume (ml/kg) x weight (kg)]
- Blood volume estimates: term = 80 ml/kg; preemie = 90 -100 ml/kg
- Partial Exchange Transfusion
  - Indications
- Polycythemia, Significant anemia with normal blood volume
  - Volume to be exchanged if wanting to lower

$$\text{Hct} = \frac{[(\text{Blood volume} \times \text{wt}) \times (\text{observed Hct} - \text{desired Hct})]}{\text{Observed Hct}}$$

  - Volume to be exchanged to increase Hct = $\frac{(\text{Blood volume} \times \text{wt}) \times (\text{desired Hct} - \text{observed Hct})}{\text{Hct of pRBCs}}$

**B. Anemia of Prematurity Etiology**

- Reduced erythrocyte half-life
- Iatrogenic losses from phlebotomy
- Hemo-dilution due to increasing body mass
- Relative deficiency of erythropoietin
  - Site of Epo production shifts from liver to kidney
  - Liver less sensitive to hypoxia, thus protection from polycythemia in fetus

**Prevention**

- Delayed umbilical cord clamping is indicated to prevent anemia/iron deficiency
- Possible Exceptions: abruption, cord avulsion, monochorionic twins, or extremely poorly controlled diabetes

**Management**

- Minimize phlebotomy losses (obtain only relevant lab tests that can change clinical care, use ABL point of care if possible).

**IV Iron Sucrose (*do not use IV Iron Dextran*) to prevent Anemia of Prematurity**

- Use with premature/SGA patients with prolonged NPO status (usu. surgical)
- Start at 14 days of life (3 mg/kg IV iron sucrose over 4 hrs once weekly)
- Monitor vital signs during transfusion, tachycardia, tachypnea, BP may fall
- If not tolerating, stop infusion & consider premedicating for next dose
- Monitor CBC, plus Ferritin or reticulocyte Hb after 2 wks
- Switch to oral iron 6 mg/kd/d when feeds are tolerated
- Target Ferritin 70-100 ng/mL (µg/L) or target reticulocyte Hb 29-35 pg
- If Ferritin <100: dose IV iron weekly. If 101-199: IV iron every other week
- If Ferritin 200-249: dose IV iron every 4 weeks. If >250: stop IV iron sucrose

**ESA (rEpo and Darbepoietin) to Prevent Transfusions**

- RBC-stimulating doses are neuroprotective in retrospective studies
- rEpo: 250-300 U/kg SQ or IV, 3 times weekly until 34-35 wks gestation or later if Hct <28 and on respiratory support
- Consider with premature/small surgical infants with prolonged NPO
- Begin either rEpo or Darbepoietin at approx. 2 weeks of life
- Consider dosing in some ELBW micropremie infants, esp. <850 g BW
- Begin either rEpo or Darbepoietin within 24-48 hours of life
- Darbepoietin: 10 mcg/kg SQ or IV once weekly until 34-35 wks gestation
- If Hb does not rise by 1 g/dL after 4 weeks, increase dose by 25%
- If Hb rises >1 g/dL after 4 wks, consider decreasing dose by 25%
- Stop ESA if Hb >15 g/dL or Hct >45%
- Do not stop ESA for transfusion or with infection work up
- Must give iron with ESA
- Start oral Iron 6 mg/kg/d if tolerating 60 mL/kg/day enteral feeding
- If NPO/unable to take oral iron in 1st wk, IV iron sucrose 3 mg/kg/wk
- Consider stopping oral or IV iron X 1-2 wks post transfusion.
- Target Ferritin 70-100 ng/mL (µg/L) or target reticulocyte Hb 29-35 pg
    - If Ferritin <100: dose weekly. If 101-199: every other week
    - If Ferritin 200-249: dose every 4 weeks. If >250: stop IV iron sucrose–Term infants (unless SGA, late preterm, or < 2500 g)
- No need for routine iron dosing until later in life
  - Iron fortified formulas (@150 ml/kg/day) provide ~2 mg/kg/day
  - Standard concentration of iron for inpatients = 3 mg/0.2 mL

- Give 3 mg dose 1-3 times per day based on patient need
  - Multivitamin drops with iron provide 10 mg iron/1 mL
  - Continue iron until 12 months of age.
  - Hold oral iron for 2 wks after transfusion, unless on ESA (hold for 1 wk)
- Blood transfusion (PRBC) may be needed (see Transfusion Guidelines).
- Check Ferritin at 28 days before immunizations: Should be ≥70ng/mL

***See IV Iron/Erythrocyte Stimulating Agents Clinical Guidelines***

**C. Thrombocytopenia**

**Etiology**

- Increased Platelet Destruction
  - Autoimmune – maternal ITP, maternal autoimmune disease (SLE)
  - Neonatal Alloimmune – due to human platelet antigen 1, 3, or 5
  - Placental insufficiency – ex. Preeclampsia or chronic hypertension
  - Sepsis/NEC/Perinatal asphyxia – DIC
  - Drug-induced – heparin, antibiotics
- Decreased Platelet Production
  - TORCH

**Platelet transfusions**

| Clinical Characteristics | Platelet Count |
|---|---|
| Stable term infant or premature >7 days | <25,000 |
| <28 wks, <7 days, risk for IVH | <50,000 |
| Prior significant hemorrhage/surgery | <50,000 |
| Hemorrhage | Transfuse |

- Transfuse at any level in presence of active bleeding
- Platelets short shelf life, may need to put on hold for some, delays up to 4-6 hrs.
- Transfuse 10-20 ml/kg of CMV negative, irradiated platelets over 2-3 hrs

**Other Blood Products**

- FFP transfusion:

- Indications – bleeding, DIC, vitamin K deficiency, Factor IX deficiency
- Components – All clotting factors, fibronectin, gamma-globulins, albumin, plasma proteins

• Cryoprecipitate
  - Indications – Factor VIII deficiency, von Willebrand disease
  - Components – Factor VIII, vWF, fibrinogen, factor XIII, fibronectin

**Statistics about Safety of Blood Supply; ARC 2004**

| | |
|---|---|
| HIV 1:2,000,000 | HBV 1:250,000–500,000 |
| HCV 1:2,000,000 | HTLV 1:640,000 |
| WNV 1.5/1000, 3/100,000 | HAV 1:1,000,000 |
| Malaria 1:1,000,000 | Bacterial RBC– 1:1:500,000; Platelet–1:1000-2000 |

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# Chapter: 16 Infectious Disease

*Nina Menda, MD*

**Neonatal Sepsis**

Risk Factors for early sepsis

- Prematurity and low birth weight
- Five minute Apgar<6, need for resuscitation at birth
- Premature ROM
- Prolonged ROM >18 hours prior to delivery
- Maternal peri-partum fever
  - post-epidural fevers do not increase risk for infection
- Chorioamnionitis
- Maternal GBS (especially GBS bacteriuria)
- Previous sibling with GBS sepsis
- Multiple gestation

**Early vs Late Onset**

- Early onset sepsis
  - Occurs in the first 7 days of life
  - Most common organisms GBS, E. coli, Listeria
  - Neonatal Sepsis Risk Score for infants ≥ 34 weeks gestational age
    - *https://neonatalsepsiscalculator.kaiserpermanente.org/*
    - Information needed: CDC incidence of Early-Onset Sepsis, Gestational age, Highest maternal antepartum temperature, ROM (hours), GBS status, Intrapartum antibiotic use
    - Risk stratified analysis based on physical exam of neonate
  - Antibiotic time out at 24-36 hours to discuss stopping antibiotics if all cultures negative
- Late onset sepsis occurs at 7-89 days of life
  - Increased risk with foreign bodies (central lines, ETT, etc.)
  - Most common organism is coagulase negative staph, but other common organisms are S. aureus, GBS, Klebsiella and Enterococcus

**Evaluation for infection**

- Obtain blood culture and a CBC with manual differential
- In healthy infants' neutrophil counts initially rise over first 6-12 hours, peak at 12-18 hours and then decrease over the next 24-48 hours.

$$\text{I:T ratio} = \frac{\text{Immature (bands+metas+myelos+promyelocytes)}}{\text{Immature neutrophils + mature neutrophils}}$$

  - Concerning if > 0.2-0.3
- For late onset – obtain a UA, urine culture and consider lumbar puncture
  - If blood culture is positive a lumbar puncture must be done
- Chest x-ray if respiratory symptoms present
  - CBC/D at 12 and 24 hours of age, or after onset of symptoms
- If concerns for HSV follow guidelines
- CMV is by salivary PCR, order for all SGA or head circumference < 3%

**Treatment**

- Ampicillin and gentamicin – most commonly used as empiric treatment for early onset sepsis and rule out sepsis coverage
  - Ampicillin: covers GBS, Listeria and some *E. coli*
    - Always start with meningitic dosing (100 mg/kg/dose)
  - Gentamicin: covers gram-negative organisms
    - May have synergistic effect with ampicillin
  - Cefotaxime (third generation): occasionally used in place of gentamicin
    - Covers some gram-positive and most gram-negative organisms
    - Better CSF penetrance than gentamicin
  - Vancomycin
    - Commonly used for late onset sepsis, especially if there is a central line.
    - Necessary for multi-drug resistant coagulase negative staphylococcus
  - Acyclovir: When HSV is suspected

**Treatment: Empiric Therapy**

- Early onset: < 7 days at time of presentation
  - Ampicillin AND Gentamicin if low suspicion for meningitis
  - Ampicillin AND Cefotaxime if high suspicion for meningitis, CSF Gram stain positive
- Late onset: > 7 days at time of presentation
  - Ampicillin and Gentamicin
  - If central line present, start Vancomycin and Gentamicin
- Duration of therapy at least 7 days after first negative blood culture

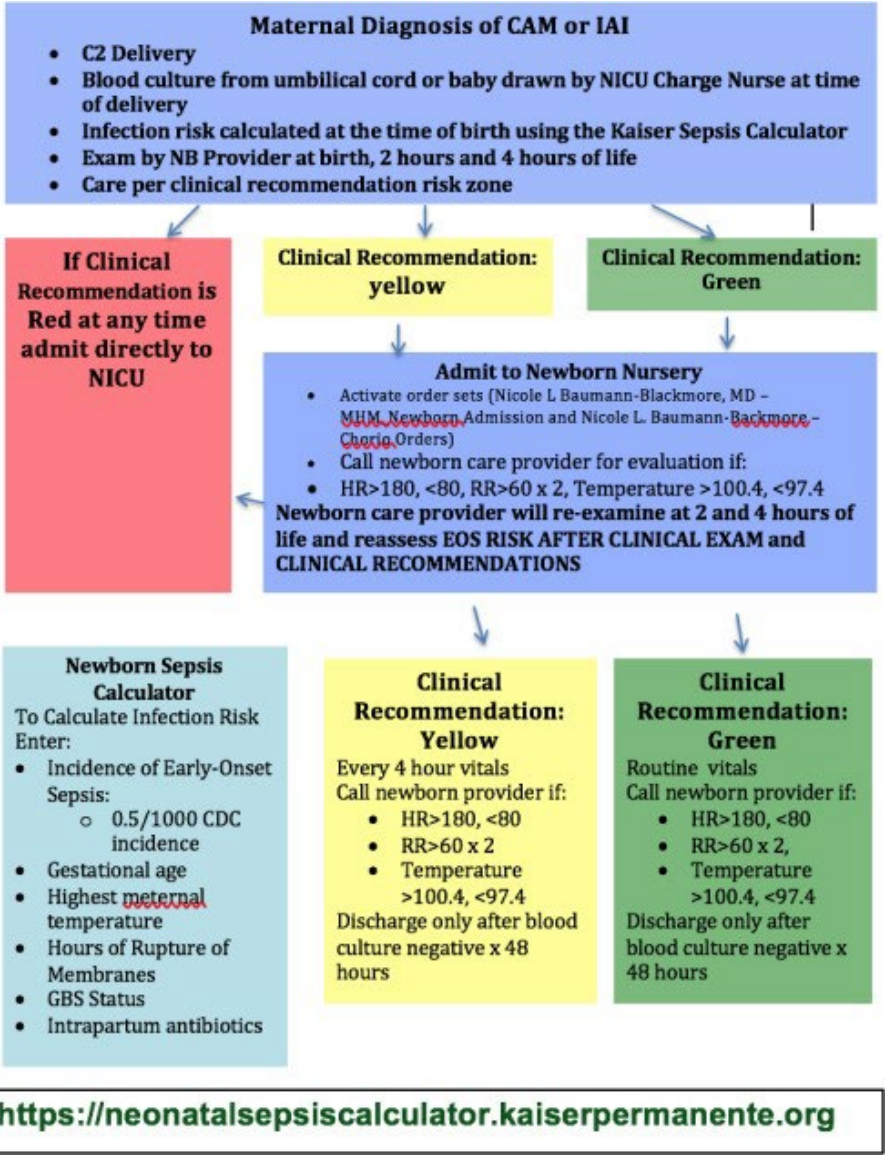
**Meningitis Diagnosis**

- Lab evaluation
  - Blood culture, CBC with differential
  - CSF culture/Gram stain
  - CSF Biofire PCR
- Increased CSF WBC
(> 20-30 WBC/microL with predominance of neutrophils)
- Elevated CSF protein concentration
(> 150 mg/dl in preterm and > 100 mg/dl in term)
- Decreased CSF glucose concentration
(< 20 mg/dl in preterm and < 30 mg/dl in term)

**Meningitis Treatment**

- GBS: Ampicillin or Penicillin, add Gentamicin until documented sterility; Complete 14 day course after negative repeat CSF culture
- Ecoli: Cefotaxime; Complete 21 day course after repeat negative CSF culture
- CONS: Vancomycin, Consider rifampin for synergy; Complete 14 day course after repeat negative CSF culture
  - Narrow antibiotic spectrum once susceptibilities known

Maternal Diagnosis of Chorioamnionitis (CAM) or Intrapartum Infection (IAI)




https://neonatalsepsiscalculator.kaiserpermanente.org

**Starting Dose Recommendations**

| | Ampicillin 100 mg/kg/dose Cefotaxime 50 mg/kg/dose | | Vancomycin 10-15 mg/kg/dose | |
|---|---|---|---|---|
| PMA (weeks) | Postnatal age (days) | Dosing interval (hr) | Postnatal age (days) | Dosing Interval (hr) |
| < 30 | 0-28 | 12 | 0-14 | 18 |
| | > 28 | 8 | > 14 | 12 |
| 30-36 | 0-14 | 12 | 0-14 | 12 |
| | > 14 | 8 | > 14 | 8 |
| 37-44 | 0-7 | 12 | 0-7 | 12 |
| | > 7 | 8 | >7 | 8 |
| > 44 | ALL | 6 | ALL | 6 |

| Gentamicin | | | |
|---|---|---|---|
| PMA (weeks) | Postnatal age (days) | Dose (mg/kg) | Dosing Interval (hr) |
| < 30 | 0-7 | 5 | 48 |
| | 8-28 | 4 | 36 |
| | > 28 | 4 | 24 |
| 30-34 | 0-7 | 4.5 | 36 |
| | > 7 | 4 | 24 |
| > 34 | ALL | 4 | 24 |

**Fungal Sepsis Prophylaxis**

- Prophylactic fluconazole for 22-23 wk GA infants
- Infants ≤ 1000 grams birth weight with central lines are ONLY given prophylactic fluconazole (3 mg/kg every 72 hours) if they are on systemic antibiotics for > 3 days

**Streptococcus agalactiae (GBS)**

- Gram positive diplococci in chains
- Acquired during passage through the vaginal canal, by ascending infection following rupture of membranes, person-to-person, and via breast milk.

- Causes early and late onset sepsis in infants
- Intrapartum antibiotic prophylaxis (IAP) of GBS positive mothers has dramatically reduced the incidence of early onset GBS sepsis
  - IAP does not prevent late-onset GBS sepsis
- Once GBS is confirmed antibiotic therapy should be narrowed to Penicillin G

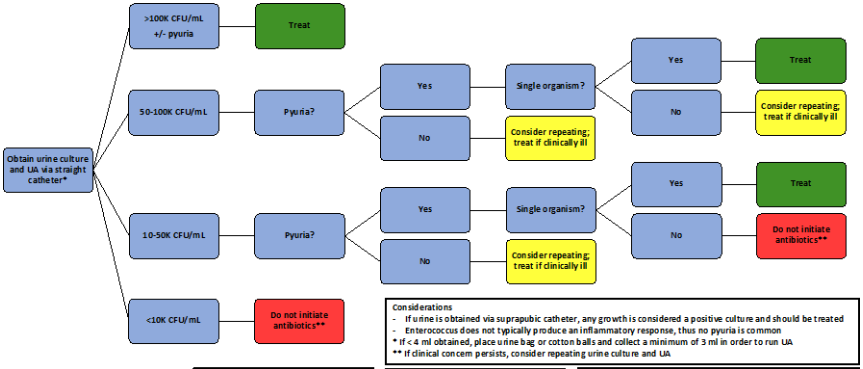
**Herpes Simplex Virus (HSV)**

- HSV infection of the neonate is fairly uncommon but with potentially devastating consequences.
- More than 75% of infants who contract HSV are born to mothers with no prior history of clinical signs of genital herpes.
- Transmission occurs in utero, intrapartum (85%) or postpartum.
- Risk factors: Maternal primary infection, prolonged rupture of membranes, mode of delivery (vaginal > C-section), disrupted integrity of mucocutaneous barriers (e.g. scalp electrode) and prematurity
- Three forms of disease in neonates: Disseminated, CNS disease (+/- skin lesions), Skin, Eye, Mouth (SEM) disease
- Disseminated disease presents earliest (DOL 4-10), SEM (DOL 6-9) and CNS disease presents latest (DOL 10-18)
- Consult AAP RedBook for most recent recommendations

**Hepatitis B**

- Infants born to Hepatitis B positive mothers should receive hepatitis B vaccine and HBIG within 12 hours after birth
- If maternal hepatitis B status is unknown infants should receive hepatitis B vaccine within 12 hours after birth
  - Infants < 2000 grams: HBIG should be given within 12 hours after birth if maternal status cannot be determined
  - For infants ≥ 2000 grams: HBIG can be given up to 7 days after birth
- For infants< 2000gramswith Hepatitis B positive or unknown mothers the vaccine dose given at birth does not count towards the 3 dose vaccination schedule.
- Infants< 2000gm at birth should receive hepatitis B vaccine prior to discharge from the hospital or at one month of age, whichever is earlier
- Infants≥ 2000gm at birth should receive hepatitis B in the first 24 hours of life

## A. **Neonatal Urinary Tract Infection:** Incidence dependent on GA




### Treatment of Positive Urine Cultures Diagnosed as UTI in the NICU

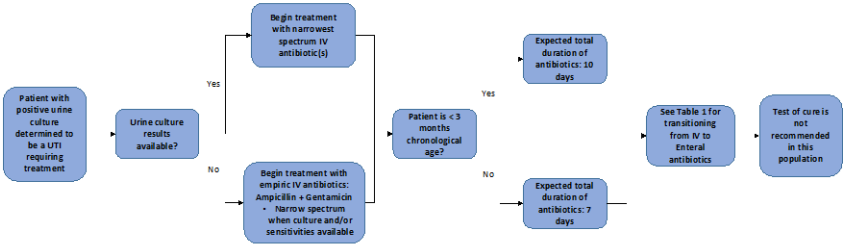



**Table 1: Transitioning from IV to Enteral Antibiotics**

May transition to Enteral antibiotic when:
- Patient has received ≥ 3 days of IV antibiotics*
- Clinically improving and asymptomatic for >24 hours
- Able to tolerate enteral medications and no concern for malabsorption

*Duration of IV antibiotics may be shorter based on clinical judgment if wishing to avoid central line placement and patient otherwise meets the above criteria. This should not impact total duration of antibiotic therapy as indicated in flowchart.

**Table 2: Enteral Antibiotic Options for Infants**

| Medication | Acceptable Ages for Use | Treatment Dose | Treatment Considerations |
|---|---|---|---|
| Amoxicillin | Any age | 25-45 mg/kg/day divided into 2 doses | Narrow spectrum, preferred if susceptible |
| Amoxicillin clavulanate | Any age | Same dose as above for the amoxicillin component | Increased GI adverse effects, broader spectrum |
| Cefdinir | Any age | 14 mg/kg/day divided into 1-2 doses | Broader spectrum |
| Cephalexin | Any age | 25-50 mg/kg/day divided into 2-4 doses | Narrow spectrum, preferred if susceptible |
| Trimethoprim sulfamethoxazole | >2 months of age | 8-10 mg/kg/day of the trimethoprim component divided every 6-12 hours | Relatively high rate of resistance in *E. coli*, *not* preferred |

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Created by: Luke Watts, PharmD; Anvit Sant, PharmD; Daniel Gorski, MD; Matthew Hare, MD.

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# Chapter 17: Central Nervous System

*Megan Berube, MD and Jamie Limjoco, MD*

## A. Neonatal Seizures

- Neonatal seizures more often present with subtle symptoms
  - Apnea, lip smacking, tongue thrusting, tonic eye deviation, leg pedaling, cyanotic spells, autonomic dysfunction
  - Focal rhythmic flexion of extremity or distal joint (wrist/hand, ankle/foot)
  - Generalized tonic-clonic seizures are rare
  - Electroclinical dissociation (subclinical seizures) is common

**Differential Diagnosis**

- Hypoxic-ischemic encephalopathy
  - Most common etiology of neonatal seizures
- Cerebral vascular
  - Intracranial hemorrhage
    - Intracerebral/parenchymal, intraventricular, subarachnoid, subdural
  - Arterio-venous malformation (AVM)
  - Stroke: arterial or venous
- Congenital CNS malformations
  - Agenesis of corpus callosum
  - Polymicrogyria
  - Lissencephaly
  - Schizencephaly
  - Hemimegancephaly
  - Focal cortical dysplasia
  - Holoprosencephaly
  - Subcortical band heterotopia (gray matter heterotopia)
- Metabolic
  - Hypoglycemia
  - Hypocalcemia/ Hypomagnesemia
  - Hypo/Hypernatremia
  - Pyridoxine dependency

- Inborn errors of metabolism – amino acidopathies, organic acidopathies
- Infection
  - Meningitis
  - TORCH
- Drug Toxicity
  - Withdrawal-barbiturates, benzodiazepines, opioids (heroin, methadone)
  - Maternal anesthetics-accidentally injected into fetal scalp during delivery
- Neurocutaneous Disorders
  - Tuberous Sclerosis (gene: TSC1, TSC2)
  - Incontinenta Pigmenti (gene: IBKKG)
  - Sturge-Weber (gene: GNAQ)
- Neonatal Onset Epilepsy Syndromes
  - Benign familial neonatal epilepsy (days 2-3, remission in 1 to 12 mo)
    - Autosomal dominant: KCNQ2, KCNQ3, SCN2A
  - Benign nonfamilial neonatal epilepsy ("fifth day fits")
  - Early myoclonic encephalopathy
  - Early infantile epileptic encephalopathy (Ohtahara's syndrome)
  - Malignant migrating partial seizures of infancy (rare)

**Work up for Seizures**

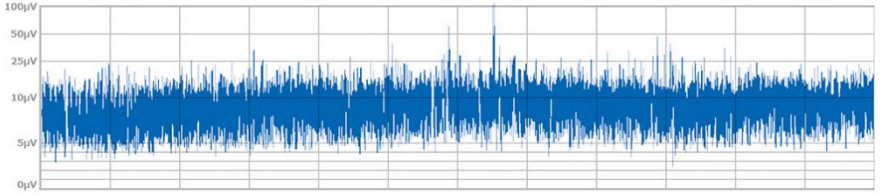
- History
  - Maternal history – drug use, IDM, infection
  - Delivery history – birth trauma, hypoxic events
- PE
  - Signs of trauma – bruising, petechiae
  - Dysmorphic features/congenital anomalies
  - Neurologic status
- Labs
  - Blood sugar
  - Electrolytes, calcium, magnesium
  - CBC with differential, blood culture
  - Blood gas, ammonia-if concerns for inborn error of metabolism
  - Consider UA/Urine Culture and CSF studies

- Continuous video EEG, aEEG*
- Imaging
  - Ultrasound – best for IVH in preemie, may miss intracranial bleed in term infants (subdural or subarachnoid hemorrhage)
  - CT scan – good for concerns of intracranial bleeding in term infants
  - MRI – best for structural anomalies and hypoxic-ischemic injury

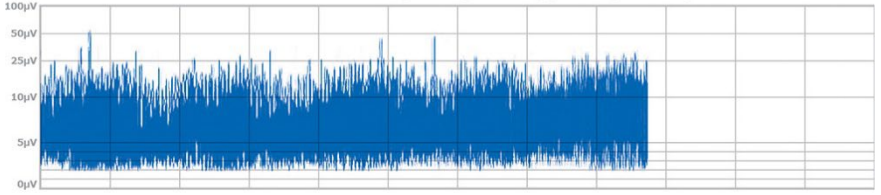
***Monitoring with Amplitude-Integrated EEG (aEEG)**

- aEEG is a bedside tool used to monitor brain function and identify seizure activity. Most common electrode placement includes biparietal (P3 and P4) and central leads (C3 and C4). Hydrogel, cups or needles can be applied to the scalp for monitoring.
- Classification
  - Continuous (lower margin >5μV and upper margin 10-25μV)
  - Discontinuous (lower margin<5μV and upper margin >10μV)
  - Burst Suppression (lower margin <5μV and upper margin >25μV)
  - Low Voltage (lower margin<5μV and upper margin <5μV, variability)
  - Flat (lower margin<5μV and upper margin <5μV, isoelectric)
- Seizures present as a sudden onset of rhythmic activity lasting >10sec
  - Lower and upper margins appear like continuous “humps”
  - Artifacts such as patting, oscillator use, hiccups, EKG can mimic seizure appearance on aEEG

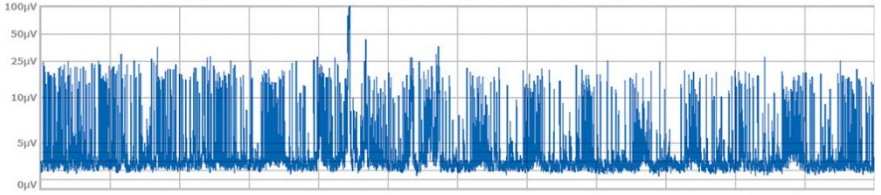
Pattern: **Continuous** Lower Margin: **>5μV** Upper Margin: **10-25μV**



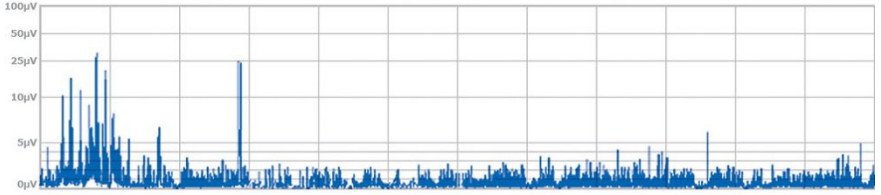

Pattern: **Discontinuous** Lower Margin: **<5μV** Upper Margin: **>10μV**



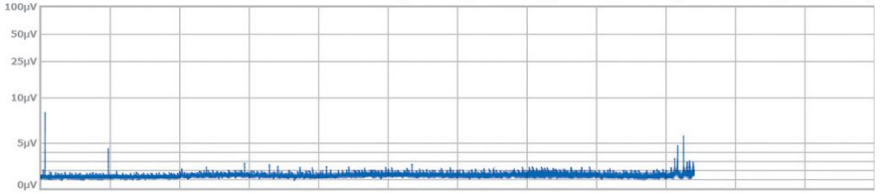

Pattern: **Burst Suppression** Lower Margin: **<5μV** Burst: **>25μV**




Pattern: **Low Voltage** Lower Margin: **<5μV** Upper Margin: **<5μV** with some variability




Pattern: **Flat** Lower Margin: **<5μV** Upper Margin: **<5μV** (Isoelectric)



**Seizure Treatment**

- Correct electrolyte disturbances
- Anticonvulsants

Levetiracetam (Keppra)

1st Loading dose: 50 mg/kg

2nd Loading dose if ongoing seizures: 50 mg/kg

Maintenance dose: 25 mg/kg BID

Desired blood levels: not established

Adverse effects: none known in neonates (reports of irritability, behavioral dysregulation in older children receiving high doses)

Phenobarbital

1st Loading dose: 20 mg/kg

2nd Loading dose if ongoing seizures: 10mg/kg

Maintenance dose: 2.5 mg/kg BID

Desired blood levels: 20-40 mcg/ml

Adverse effects: Can cause respiratory depression, hypotension

Vimpat (Lacosamide)

1st Loading dose: 10 mg/kg

2nd Loading dose if ongoing seizures: 5-10 mg/kg

Maintenance dose: 5 mg/kg BID, then increase to 10mg/kg BID

Desired blood levels: not established

Adverse effects: asymptomatic bradycardia and/or prolonged PR interval, can consider 12 lead EKG

Fosphenytoin

1st Loading dose: 20 PE/kg
(PE: phenytoin equivalents)

2nd Loading dose if ongoing seizures: 10 PE/kg

Maintenance dose: 4-8 PE/kg/day

Desired blood levels: 6-15 mcg/ml

Adverse effects: arrhythmias, bradycardia, hypotension

**B. Intraventricular Hemorrhage**

- Periventricular bleeding from the subependymal germinal matrix in preemie
  - Bleeds in term infants are from choroid plexus
- Germinal matrix involutes around 36 weeks gestation
- 90% of IVH occurs in the first 3 days of life
  - 50% in first 24 hours
  - May progress in the first 5-7 days

**Papile's classification:**

- Grade 1: Isolated germinal matrix hemorrhage
- Grade 2: Intraventricular hemorrhage without dilatation of the ventricle
- Grade 3: Intraventricular hemorrhage with ventricular dilatation
- PVHI: periventricular hemorrhagic infarction represented by intra-parenchymal echodensity (formerly known as Grade IV)

**Risk Factors:**

- Prematurity < 30 wks gestation
- Perinatal asphyxia, Birth Trauma
- Rapid fluctuations in blood pressure
- Shock
- PDA

- Antenatal steroids are protective

**Diagnosis:**

- Head Ultrasound (HUS)
  - Guidelines from American Academy of Neurology
- Screen all infants less than 30 weeks gestation
- First ultrasound at 7-14 days of age
- Repeat ultrasound at 36-40 weeks PMA or discharge
- Consider term equivalent age MRI for infants with history of abnormal HUS

**C. Periventricular Leukomalacia**

- Cystic lesions in corticospinal white matter adjacent to the lateral ventricles
  - Due to repeated hypoxic-ischemic events from cerebral hypoperfusion in the neonatal period
  - Hypoxic injury causes necrotic cell death
- Seen most commonly in premature infants
- Leads to long-term neurodevelopmental disability
  - Spastic diplegic cerebral palsy

**D. Apnea**

**Apnea:** Absence of breathing for >20 seconds or short pause (>10 sec) associated with oxygen desaturation or bradycardia

**Periodic Breathing:** Cyclic pauses in breathing for ≤ 10 secs followed by a series of rapid, shallow breaths

**Bradycardia:**

- For infants < 30 wk: HR <100/min for >10 sec
- For infants ≥ 30 wk: HR <80/min for >10 sec

**Practical tips:**

- Apnea of prematurity: Typical onset is 2-3 days in preemies <34 weeks' gestation
- Apnea in a full-term infant is never physiologic
- Apnea on first day of life is abnormal, search for causes other than prematurity

**Causes of Apnea and Bradycardia by Gestational Age**

| All ages | Premature Infant | Full term infant |
|---|---|---|
| Sepsis | Apnea of prematurity | Cerebral infarction |
| Meningitis | PDA | Polycythemia |
| Hypoxia | HMD | Drug Withdrawal |
| Aspiration | NEC | |
| GER | PV-IVH | |
| Pneumonia | Anemia of prematurity | |
| Cardiac disorder | Posthemorrhagic Hydrocephalus | |
| Post-extubation atelectasis | Polycythemia | |
| Seizures | | |
| Cold Stress | | |
| Metabolic imbalance | | |
| Airway malformations | | |
| CNS malformations | | |

**Approach to Apnea & Suspicion of Reflux**

- Most spells are not temporally linked to reflux
- Usually apnea precedes the reflux when temporally linked
    - Only 3% of spells preceded by reflux

**Interventions for Apnea:**

1. Positioning: Optimize left side down and prone.
2. Continue bolus feeds (every 3 hours). No strong evidence that continuous drip feeds will decrease apnea/bradycardia/desaturation spells.
3. Consider thickening feeds using commercial reflux formula (see Reflux Guideline)
4. No evidence to support changing/decreasing maintenance caffeine dose (no evidence to support caffeine worsening reflux)
5. Anti-reflux medications should be used with caution, and if no difference is observed in frequency or severity of spells after 5-7 days of therapy, consider discontinuation.

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**Hypoxic Ischemic Encephalopathy**

- Incidence = 3-5/1000 live births
- Mortality up to 60%
- Generally occurs after event of perinatal asphyxia
    - Event is not always easily recognized

**Perinatal Asphyxia**

- ACOG and AAP "Neonatal Encephalopathy and Neurologic Outcome, 2nd Edition" 2019
    - Asphyxia
        - Marked impairment of gas exchange leading, if prolonged, to progressive hypoxemia, hypercapnia, and significant metabolic acidosis.

    - Describes a process of varying severity and duration rather than an end point.
    - Should not be applied to birth events unless specific evidence of markedly impaired intrapartum or immediate postnatal gas exchange can be linked to neurologic illness in the neonate.
- Perinatal Asphyxia
    - Profound metabolic or mixed acidemia (pH <7.0 on umbilical arterial blood gas)
    - Persistence of an Apgar score of 0-3 for >5 minutes
    - Neurologic manifestation in the immediate neonatal period (seizures, encephalopathy)
    - Evidence of multi-organ dysfunction in the immediate neonatal period

## Neonatal Encephalopathy Exam (Modified Sarnat Score)

| | Level of Encephalopathy | | | |
|---|---|---|---|---|
| | **Normal/None** | **Mild** | **Moderate** | **Severe** |
| **1. Level of Consciousness** | 0 – Normal/ Alert | 1 – Hyperalert or irritable (responsive to minimal stimuli) | 2 – Lethargic | 3 – Stupor or coma |
| **2. Spontaneous Activity** | 0 – Normal | ----- | 2 – Decreased activity | 3 – No activity |
| **3. Posture** | 0 – Predominantly flexed | 1 – Mild flexion of distal joints (fingers, wrist) | 2 – Flexion of distal joints or complete extension | 3 – Decerebrate |
| **4. Tone** | 0 – Strong flexor tone in all extremities | 1 – Slightly increased tone in extremities | 2a – Hypotonia (focal or general)<br>2b – Hypertonia (focal or general) | 3a – Flaccid<br>3b – Rigid |
| **5. Primitive Reflexes[1]:**<br>**Suck** | 0 – Strong, coordinated, easy to elicit | 1 – Weak, coordinated | 2 – Weak and uncoordinated, and/or bite | 3 – Absent |
| **Moro** | 0 – Complete | 1 – Exaggerated | 2 – Incomplete | 3 – Absent |
| **6. Autonomic System[1]:**<br>**Pupils** | 0 – Normal | 1 – Mydriasis (dilated), reactive | 2 – Myosis (constricted), reactive | 3 Deviated/unequal, dilated, or fixed/ nonreactive to light |
| **Heart Rate** | 0 – Normal: 100 – 160 bpm | 1 – Tachycardia: >160 bpm | 2 – Bradycardia: <100 bpm | 3 – Variable |
| **Respiration** | 0 – Normal: regular respirations | 1 – Tachypnea, Hyperventilation | 2 – Periodic breathing | 3a – Apnea, requires on-going PPV or intubation, and has spontaneous breaths<br>3b – Apnea, requires on-going PPV or intubation, and does not have spontaneous breaths |

## Documenting the Neonatal Encephalopathy Exam (.HIEEXAM)

*Contribution: Megan Berube, MD*

1. **Level of consciousness:** 0- Normal/Alert; 1- Hyperalert or irritable, responsive to minimal stimuli; 2- Lethargic; 3- Stuporor coma
2. **Spontaneous activity:** 0- Normal; 2- Decreased activity; 3- No activity
3. **Posture:** 0- Predominantly flexed; 1- Mild flexion of distal joints (fingers, wrist); 2- Flexion of distal joints or complete extension; 3- Decerebrate
4. **Tone:** 0- Strong flexor tone in all extremities; 1 – Slightly increased tone in extremities 2a- Hypotonia (focal or general); 2b- Hypertonia (focal or general); 3a- Flaccid; 3b- Rigid
5. **Primitive reflexes:***
   - **Suck:** 0- Strong, coordinated, easy to elicit; 1- Weak, coordinated; 2- Weak and uncoordinated, and/or bite; 3- Absent
   - **Moro:** 0- Complete; 1- Exaggerated; 2- Incomplete; 3- Absent
6. **Autonomic system:***
   - **Pupils:** 0- Normal; 1 – Mydriasis (dilated), reactive; 2 – Myosis (constricted), reactive; 3- Deviated/unequal, dilated, or fixed/nonreactive to light
   - **Heart rate:** 0- Normal (100-160 bpm); 1- Tachycardia (>160 bpm); 2- Bradycardia (<100 bpm); 3- Variable
   - **Respiration:** 0- Normal; 1 – Tachypnea, hyperventilation; 2- Periodic breathing; 3a – Apnea, requires on-going PPV or intubation, and has spontaneous breaths; 3b – Apnea, requires on-going PPV or intubation, and does not have spontaneous breaths

*For Primitive Reflexes (Suck, Moro) and Autonomic System (Pupils, Heart Rate, Respirations), the item with the highest score determines the level of encephalopathy.

**Total categories with score of 0 = ____**

**Total categories with score of 1 = ____**

**Total categories with score of 2 = ____**

**Total categories with score of 3 = ____**

- Neonate has a normal encephalopathy exam if he/she has scores of 0 in all six categories.
- Neonate has mild encephalopathy if he/she has < three categories with a score of 2 or 3, but has a score of 1, 2, or 3 in at least one category.
- Neonate has moderate encephalopathy if he/she has a score of 2 in three or more categories.
- Neonate has severe encephalopathy if he/she has a score of 3 in three or more categories

**Neonatal Encephalopathy Exam Definitions**

1. **Level of consciousness:**
   a. **Hyperalert -** Full wakefulness with eyes open/staring but decreased frequency of blinking/tracking. Spontaneous motor activity normal or decreased with lowered threshold to all stimulus types.
   b. **Irritability –** Lowered threshold with excessive response to all stimulus types. Can be seen with varied states including hyperalert, lethargy, and obtundation.
   c. **Lethargy -** Slightly delayed but complete response to stimuli with slightly increased threshold for eliciting responses and decreased spontaneous movement
   d. **Obtundation -** Delayed and incomplete responses with markedly increased threshold to all sensory stimuli and little or no motor activity
   e. **Stupor -** No spontaneous eye opening and tactile stimulation elicits poorly sustained eye opening. Responds only to strong, noxious stimuli. Absent gag, corneal reflex.
   f. **Coma-** No eye opening with vigorous tactile stimulation.
2. **Spontaneous activity:**
   a. **Decreased spontaneous activity-** Decreased frequency or amplitude of spontaneous facial and extremity movements.
   b. **Absent spontaneous activity -** Movements absent.
3. **Posture:**
   a. **Distal flexion -** Fingers, toes in strong flexion; incomplete extension of fingers when stroked on dorsal surfaces. Thumbs flexed, adducted, opposed across palms (i.e."corticalthumbs").
   b. **Decerebrate posturing -** Head, neck, and back are arched in extension (opisthotonos), elbows are extended, wrists are pronated, and hips are adducted.
4. **Tone (remove positioning barriers for accurate examination of tone):**
   a. **Hypotonia -** Focal or generalized decreased resistance to passive movement. Associated with greater extension of the extremities than normal.
   b. **Hypertonia -** Focal or generalized increased resistance to passive movement. Associated with greater flexion of the extremities than normal.
   c. **Flaccid -** "Flat on the mat" appearance. May be associated with frog-leg posturing with arms and hips/legs lying in abduction.
   d. **Rigidity -** "Lead pipe" feel of extremities, severe hypertonia with extreme resistance to passive movement. Does not depend on imposed speed or threshold of movement. Unilateral contraction of antagonist or agonist muscle groups can occur with rigidity, but the limb does not tend to return to a fixed posture or extreme joint angle. May be associated with exaggerated deep tendon and tactile reflexes.

5. **Primitive Reflexes:**
   a. **Weak suck–** Some sucking noted, but it is not as vigorous or sustained as it should be. A pacifier or gloved finger can be easily pulled from the mouth.
   b. **Absent suck –** No sucking or root reflex elicited.
   c. **Bite-** Insertion of pacifier or gloved finger into mouth elicits neonate to "clampdown" or bite object. No sucking motion elicited.
   d. **Moro-** The Moro reflex is elicited by holding the baby's head and shoulders off the mat with arms held in flexion on chest. While supporting the head and neck, the examiner suddenly lets the head and shoulder drop while releasing the arms. The arms should fully abduct and extend, then return towards midline with the hand open and the thumb and index finger forming a "C" shape. An incomplete Moro is marked by absence of any component or any asymmetry in movements. Incomplete Moro reflex often extends irregularly but typically does not return to midline.
   e. **Absent Moro-** Absence of any reflexive activity (see above for method of eliciting Moro reflex).
6. **Autonomic System:**
   a. **Dilated pupils (mydriasis) -** Normal pupil size for term newborns is 3.9 mm +/- 0.8 mm. Dilated pupils are larger than this even in bright light.
   b. **Constricted pupils (miosis) -** Normal pupil size for term newborns is 3.9 mm +/- 0.8 mm. Constricted or pinpoint pupils are smaller than this even in dim light.
   c. **Unequal; Fixed; Dilated; Poor light reflex pupils -** Pupils that are not normally symmetrically aligned or symmetrically dilated, are fixed in position, or that do not accommodate (constrict) in the presence of light.
   d. **Tachycardia-** Resting heart rate > 160 beats per minute.
   e. **Bradycardia-** Resting heart rate of < 100 beats per minute, typically 80-90 beats per minute. Only occasional increases to 120+ beats per minute are noted.
   f. **Variable heart rate -** Resting heart rate varies considerably without a consistent baseline.
   g. **Periodic breathing-** Three or more respiratory pauses of three seconds or longer separated by normal breathing for less than 20 seconds. Often associated with shallow breathing pattern.
   h. **Apnea-** Absence of airflow and respiratory effort lasting 20 seconds or longer. Apnea may also be present if a respiratory pause is shorter than 20 seconds but is associated with heart rate change or oxygen desaturation.

# Therapeutic Hypothermia Protocol

UWHealth

## Hypoxic Ischemic Encephalopathy (HIE) – Neonatal – Inpatient Guideline Summary

**Target Population**: Neonatal infants with suspected or diagnosed HIE

**Link to Full Guideline**: Hypoxic Ischemic Encephalopathy - Neonatal - Inpatient

### Therapeutic Hypothermia Assessment Tool

***Infant must meet the following criteria to be considered for treatment:***

- Gestational age ≥ 35 and 0/7 weeks
- Birth weight ≥ 1800 grams
- ≤ 6 hours of life at time of initial evaluation

AND

I. Clinical and/or biochemical criteria
II. Demonstrate moderate or severe encephalopathy
III. Does not meet ANY listed exclusion criteria

**Step I: Clinical and biochemical criteria**

- History of acute perinatal event (e.g., uterine rupture, placental abruption, umbilical cord prolapse or avulsion, or severe fetal heart rate abnormality)
- APGAR score < 6 at 10 minutes of life
- Prolonged resuscitation, defined as positive pressure ventilation (via bag-mask or advanced airway) initiated at birth and continued for at least 10 minutes
- pH ≤ 7.0 on arterial cord blood gas or first postnatal hour blood gas
- Base deficit ≥ 12 mEq/L on arterial cord blood gas or first postnatal hour blood gas

**Infant meets clinical and biochemical inclusion criteria if A or B are met:**

A. pH ≤ 7.0 **or** base deficit ≥ 12 mEq/L
B. pH between 7.0 and 7.15 with history of an acute perinatal event **and** at least one of the following:
   i. Apgar score < 6 at 10 minutes
   ii. Prolonged resuscitation

**Step II: Neurologic evaluation using neonatal encephalopathy exam**

- Inborn evaluation should occur after 15 minutes of life using .HIEEXAM
- Outborn evaluation should be done with referring site under guidance of medical control, use of telemedicine (if able) is strongly encouraged

**Infant meets neonatal encephalopathy inclusion criteria if A or B are met:**

A. Seizures
B. Moderate or severe encephalopathy using neonatal encephalopathy exam (See Appendix1: Neonatal Encephalopathy Exam or EPIC smartphrase .HIEEXAM)

**Exclusion criteria:**

- Presence of major congenital anomalies
- GA < 35 and 0/7 wks
- Severe IUGR; BW < 1800 g
- Moribund infants for whom no additional intensive therapy will be offered, as determined by attending neonatologist

**Relative contraindications:**

- Infant > 6 hours old at time of initial evaluation
- Severe hemodynamic compromise
- Severe coagulopathy with active bleeding
- Confirmed venous sinus thrombosis

**Additional considerations:**

- Consult PICU for infants with critical congenital heart disease who require cooling
- If there is a question whether to initiate cooling, place aEEG, obtain STAT Pediatric Neurology consult, and begin passive cooling for up to 6 hours while decision is being made
- If infant is outborn, eligibility will be determined in conjunction with the referring clinician. An infant with a qualifying exam prior to transfer, will still be cooled per the guideline regardless of admission exam

**Cooling – Targeted esophageal temperature of 33.5-34.5°C**

- Therapeutic hypothermia (i.e., active or passive cooling) should be initiated within 6 hours of life
- Once targeted temperature is reached (i.e., first esophageal temperature), maintain for 72 hours

**Re-warming**

- Re-warm after 72 hours from first esophageal temperature
- Slow re-warming of patient preferred at rate of 0.5°C per hour to core body temperature of 36.5°C
- Maintain normothermia with the cooling blanket for 24 hours s/p rewarming to avoid rebound hyperthermia

For additional information on conducting cooling on transport, passive cooling and cooling in NICU, refer to Neonatal Whole Body Cooling Procedure

| Therapeutic Hypothermia – Patient Labs for Monitoring | |
|---|---|
| **Lab (Normal Range)** | **Suggested Frequency** |
| **Temperature corrected blood gas, lactate, ionized calcium (iCa)**<br>(4.5-5.3 mg/dL which equals: 1.12-1.32 mmol/L; 2.25-2.65 mEq/L) | Every 6 hours for first 24 hours then every 12-24 hours (minimum during cooling)<br>**Note:** Temperature corrected blood gases are available on the NICU ABL 90 and the main lab.<br>To get temperature corrected readings, do the following:<br>• On workstation order, clearly write patient's temperature at time of draw<br>• If processed in the NICU, notify respiratory therapy of the patient's current temperature and desire for temperature corrected blood gases.<br>The temperature corrected values that will appear in Health Link include:<br>• PH, TEMP CORRECTED • PCO2, TEMP CORRECTED • PO2, TEMP CORRECTED |
| **Glucose** | Every hour during initiation of cooling until temp 33.5-34.5°C is reached; thereafter, check every 6 hours during cooling.<br>During rewarming, check at start of rewarming, every 2 hours x 2, then PRN and with lab draws |
| **Chemistries**<br>(Ca 8.7-10.1 mg/dL)<br>(Mg 1.8-2.3 mg/dL) (K 4.0-6.0 mEq/L) | Check Electrolytes, Ca, Mg, Phos every 12-24 hours during cooling<br>Consider monitoring during rewarming |
| **CBC** | Check every 12-24 hours |
| **Cultures** | Obtain blood culture; consider sputum and cerebral spinal fluid culture |
| **PT/PTT/INR** | Check every 24 hours |
| **BUN/CR** | Check every 12-24 hours |
| **AST/ALT** | Check every 24 hours |

| Therapeutic Hypothermia – Medical Management by System | |
|---|---|
| **System** | **Considerations** |
| **Monitoring (including radiographic studies)** | • Babygram STAT on admission; confirm esophageal probe placement<br>• aEEG/cEEG on admission<br>• Cranial ultrasound on admission with Doppler*<br>• NIRS (i.e., cerebral and renal)<br>• Echocardiogram if hemodynamically unstable or concern for pulmonary hypertension<br>• Brain MRI*<br>- If severely encephalopathic and family is considering withdrawal of support, discuss early MRI with neuroradiologist and consider obtaining at 24-48 hours of life<br>- Routine MRI and MRS on DOL #4-5<br>- Consider follow-up MRI and MRS on DOL #10-14<br>***When ordering, must note "HIE Protocol" in comment section to ensure appropriate study*** |
| **Fluids, Electrolytes, Nutrition (FEN)** | • NPO through rewarming<br>• Initial total fluid goal of 50-60 mL/kg/day (D10W)<br>• Treat hypovolemia with volume (normal saline, PRBCs)<br>• If acidosis worsens base deficit > 10 mEq/L, consider:<br>- Normal Saline (NS) (10 mL/kg IV)<br>- Sodium bicarbonate (1-2 mEq/kg IV over 30 mins)<br>- Add sodium acetate to maintenance fluids |
| **Respiratory** | • Avoid hypocapnia (goal $PCO_2$ 45-50 mmHg)<br>• Avoid hyperoxia (goal $PaO_2$ 80-100 mmHg, $SpO_2$ < 98%)<br>• Persistent pulmonary hypertension (PPHN) may worsen in some cases, consider pre- and post-ductal monitoring |
| **Cardiovascular** | • Continuous BP monitoring with arterial line preferred<br>• Monitoring with 3-lead EKG<br>• Maintain BP in normal range (SBP 60-70 mmHg / DBP 40-50 mmHg and MAP 40-50 mmHg)<br>• If needed, support BP: 1st choice dopamine 2-5 mcg/kg/minute<br>• Heart Rate: Expect bradycardia < 100 bpm<br>• For deep bradycardia (< 80 bpm):<br>- May be tolerated if BP is stable within target range and perfusion is appropriate on physical exam<br>- If not tolerated, raising core temp to 34°C may be adequate; if symptomatic bradycardia persists, consider dopamine |

| | |
|---|---|
| **Infectious Disease (ID)** | • Initiate rule out sepsis evaluation with empiric antibiotics for all infants being treated with therapeutic hypothermia<br>• Start ampicillin 100 mg/kg/dose IV q12 hours and gentamicin 4 mg/kg/dose q24 hours (for patients with renal concerns, consider ceftazidime 50 mg/kg/dose IV q12 hr)<br>• Consider lumbar puncture to rule out meningitis |
| **Neurologic** | • Obtain Pediatric Neurology consult<br>• Document complete neuro exam and neonatal encephalopathy exam using .HIEEXAM Epic SmartPhrase<br>• Maintain adequate sedation; *NPASS score goal -1 – Do not allow patients to shiver!*<br>- Morphine is drug of choice<br>- **Day 1:** Morphine loading dose 0.05 mg/kg IV<br>- Start maintenance continuous infusion at 0.01 mg/kg/hr<br>- Escalate infusion rate by 0.005 mg/kg/hr as needed<br>- Provide bolus doses of morphine 0.02 mg/kg IV every 3-4 hours PRN<br>- If continuous infusion not available, schedule morphine 0.05 mg/kg every 6 hours<br>- **Day 2:** Wean continuous morphine infusion by half to avoid toxic accumulation; goal rate of 0.005 mg/kg/hr<br>- **2nd Line**: Consider starting dexmedetomidine 0.2 mcg/kg/hr if morphine infusion > 0.015 mg/kg/hr<br>- Do not administer dexmedetomidine as a loading dose or bolus due to the risk of bradycardia and hypotension<br>- When administering dexmedetomidine, wean morphine infusion to lowest rate tolerated (may discontinue)<br>- If on-going concerns for pain and normal liver function, consider acetaminophen 7.5-10 mg/kg IV every 6 hours PRN<br>• Treat seizures; load with levetiracetam 50mg/kg/dose (refer to Neonatal Seizures – Neonatal – Inpatient/Emergency Department Clinical Practice Guideline for ongoing management)<br>• Continue aEEG/EEG monitoring through re-warming process or until patient is seizure free for 24-72 hours based on Pediatric Neurology's recommendation |
| **Skin** | • Maintain pressure relieving device<br>• Reposition every 2 hours<br>• Monitor for fat necrosis, pressure ulcers |

## Patient Follow-Up

- Patients should follow up at 3 months of age after discharge with Waisman Center Newborn clinic or accessible neurodevelopment clinic
- May consider consult with Waisman Center prior to discharge for transition of care consultation
- Patients should follow up with Pediatric Neurology per service's recommendation

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# Initial Management of Newborns with Myelomeningocele

*Bermans Iskandar, MD Lisa McLennan, RN*

**Pre-Operative Care**

1. The attending neurosurgeon should be notified as soon as the ob/gyn has selected a delivery date/time. UW/AFCH Pediatric Neurosurgery: 608-263-9585.
2. On day of admission and once baby is delivered, the neurosurgery resident (AFCH or Meriter) or attending who performed prenatal visit should be notified.

**Immediately after birth:**

3. Initial care should be taken in keeping the myelomeningocele (MMC) defect clean and moist. Immediately after birth cover defect with sterile Telfa and then layer with wet 4x4 gauzes. Telfa should be left in place until surgery but wet sterile gauzes can be changed as needed to keep area moist. This non adherent dressing can be kept in place by covering with a steri-drape or loosely wrapping Kerlix around abdomen.
4. Care should be taken to prevent contamination or exposure of MMC area, protect from soiling with a plastic flap (steri drape).
5. Perform initial measurement of head circumference.
6. Prophylactic antibiotic coverage should be started with broad spectrum coverage (Ampicillin + Gentamicin recommended) which should be continued for 48 hr. post op.
7. Infant must be nursed and kept prone to prevent injury to the exposed neural tissue.
8. If infant has not voided within first hours of birth, bladder ultrasound/straight catheterization must be performed. Notify Urology
9. **Arrange for transfer to AFCH NICU in consultation with Neurosurgery and Neonatologist.**

For more information, go to: *https://workspaces.uconnect.wisc.edu/display/nicuunitres/Policies+and+Clinical+Practice+Guideline/MyelomeningoceleNeonatalProtocol*

# Chapter 18: Neonatal Kidney

*Matthew Harer, MD & Dan Gorski, MD*

## A. Neonatal Hypertension

- BP Measurement
  a. Technique- Optimal cuff size is 2/3 the length of limb segment and 75% of limb circumference
- **Protocol for BP measurement in hypertensive infants**
  a. Measure 1.5h after a feed or intervention
  b. Infant lying supine, taken on RIGHT upper arm
  c. Place cuff and wait 15 min before measures
  d. Optimal if infant is asleep
  e. 3 successive readings at ~ 2 min intervals, average of these values
- Incidence
  a. 0.3-3% of Neonatal patients
  b. Risk Factors: history of UAC, BPD, history of AKI, IVH, PDA
- What is abnormal?

  (>95th%tile) a. 26-32 weeks

  PMA – 83/55 b. 32-36 weeks

  PMA – 87/65 c. 36-44 weeks

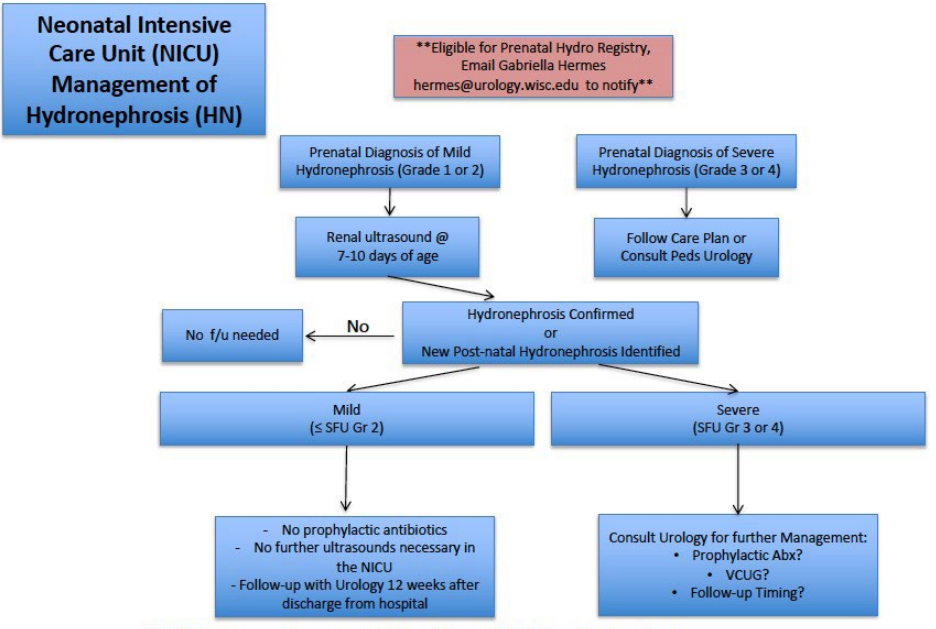
  PMA – 105/68

  d. For full table: HTN in infancy, Peds Nephro, 2012:27
- Initial Work-up
  a. Urine analysis(+/- culture)and Urine protein
  b. CBC,BMP, Calcium
  c. Renal ultrasound with Doppler
  d. Upper/Lower BPs
  e. Consider the following dependent on the situation
     – Thyroid studies
     – Echocardiography
     – Aldosterone, renin, cortisol
     – Abdominal ultrasound
     – VCUG

**B. Fetal hydronephrosis:** Most common prenatal abnormality

Definition - Prenatal identification of dilation of the upper urinary tract

| Causes | Grading |
|---|---|
| Ureteropelvic or ureterovesical junction obstruction | Mild < 10 mm dilation |
| Posterior urethral valves | Moderate > 10 mm dilation |
| Vesicoureteral reflux | Severe > 15 mm dilation |




**If hydronephrosis + UTI, obtain VCUG prior to discharge

**Exclusion Criteria: Bilateral grade 4 hydro, PUV, Spina Bifida, Prune belly, megacystis, imperforate anus, h/o oligohydramnios, and renal insufficiency

**C. Renal Tubular Acidosis:** The most encountered RTA in premature neonates is transient proximal RTA which resolves as the infant ages

| Test | Type I | Type II (Proximal) | Type IV |
|---|---|---|---|
| Urine pH | High > 6.5 | High > 7.0 | Low < 5.5 |
| Potassium | Low | Low | High |
| Nephrocalcinosis | Yes | | |
| Defect | Reduced H+ secretion | Impaired HCO3 reabsorption | Impaired cation exchange |
| Association | | Fanconi Syndrome | Pseudohypo-aldosteronism |
| Treatment | Bicarbonate | Bicarbonate | |

**E. Neonatal Acute Kidney Injury**

- Prevalence - 30% of all patients in the NICU have AKI(50% of <29weekpreterms)
- Etiology – Primarily prerenal, congenital anomalies like PUV can cause post-renal
- Definition – neonatal KDIGO definition – most commonly used

| Stage | Serum Creatinine (sCr) | UOP over 24 hours |
|---|---|---|
| 1 | sCr increase by 0.3 within 48 hours OR sCr increase by 1.5-1.9x baseline in 7 days | > 0.5 but < 1 mL/kg/hr |
| 2 | sCr increase by 2-2.9x baseline in 7 days | > 0.3 but < 0.5 mL/kg/hr |
| 3 | sCr above 2.5 OR sCr increase by >3x baseline in 7 days | < 0.3 mL/kg/hr |

- Work-up for AKI - Renal Ultrasound, BMP,UA, U Osm, U creatinine/sodium
- Treatment: Supportive care – Support BP, minimize fluid overload, avoid NTX meds
- Consult Peds Nephro for stage 2 or 3 injury, follow-up as outpatient

| Test | Prerenal AKI | Intrinsic AKI |
|---|---|---|
| BUN/Cr ratio | > 30 | < 20 |
| FENa (%) | < 2.5 | > 3.0 |
| Urinary Na | < 20 | > 50 |
| Urinary Osm | > 350 | < 300 |
| Specific Gravity | > 1.012 | < 1.014 |
| Response to Volume Challenge | Improved UOP | No change in UOP |

**F. Helpful formulas:**

a. FeNa (%) = (PCr x UrNa / PNa x UrCr) x 100
   i. Avoid single measurement
   ii. Very variable in the 1st week in preterm infants
b. Renal failure index(RFI) = (UrNa/UrCr) x 100
c. Hyponatremia correction:
   i. (desired Na – actual Na) x 0.6 (kg)

# Chapter 19:
# Neonatal Opioid Withdrawal Syndrome (NOWS)

*Ann Ebert, Pharm D*

**Definition:** Due to withdrawal from in-utero opioid exposure

- Occurs in infants with chronic exposure to opioids in utero-maternal. Opioid use is frequently accompanied by use of other substances such as nicotine, alcohol, benzodiazepine, and marijuana
- CNS irritability in infants can also occur following exposure to nicotine and SSRIs

**Clinical Presentation**

- Signs of abstinence occur in 60%-80% of infants exposed to opiates
- Symptoms can begin within 24 hours of birth for short acting opiates and within 3-7 days for longer acting drugs, like methadone.
- **Neurologic signs:** hypertonia, excessive suck, tremors, hyperreflexia, irritability, high-pitched cry, poor sleep, rarely seizures
- **Autonomic dysfunction signs:** yawning, sneezing, nasal stuffiness, low-grade fever, sweating, skin mottling
- **Gastrointestinal signs:** diarrhea, vomiting, poor feeding, poor weight gain

**Eat -Sleep-Console Assessment**

- Begin ESC assessment at 24 hours of life
- Assess after feeding/cares (~ every 3-4 hours)
- If infant experiences withdrawal symptoms, a caregiver huddle will be called to discuss
- Pharmacologic therapy may be indicated if enhanced sensitive care guidelines are not working to control symptoms

**Treatment**

- Non-pharmacologic (sensitive care) begin ASAP after birth
  - Gentle handling, quiet environment, swaddling, pacifier, skin to skin
- Pharmacologic: The goal of pharmacologic therapy is to have the baby feeding well without vomiting and diarrhea, gaining weight, decreased irritability, and sleeping between feeds as appropriate for age without undue sedation.
- Refer to ESC algorithm for treatment details

- Note: Breastfeeding is contraindicated when women continue to use illicit drugs such as cocaine, heroin, and marijuana

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## Eat, Sleep, Console Care Model

Provide Sensitive Care immediately following birth.
Using the Eat, Sleep, Console (ESC) model, assess infant for signs of withdrawal **starting at 24 hours** of life.
ESC Assessments are on-going. Minimally one ESC Assessment occurs each 8 hour shift or more often as indicated by the infant.
**Assess infant after feedings,** preferably while skin-to-skin or held swaddled by family or caregiver.

**ESC Assessment:**
- Is poor feeding due to NAS? **YES or NO**
- Is sleep <1 hour due to NAS? **YES or NO**
- Unable to console in 10 min? **YES or NO**

Review ESC behaviors which have occurred since last assessment, using **Newborn Care Diary** with family or caregiver.

If "**YES**" to any question in the ESC Assessment, perform huddle with caregiver and RN and increase Sensitive Care if possible.

**Optimize Sensitive Care**

Reassess after next feeding (e.g., every 3-4 hours

**"NO" to all questions** - Continue to provide Sensitive Care. Continue to assess after each feeding (e.g., every 3-4 hours)

Infant is ready for discharge after 5 days of observation and meeting ESC criteria for 24 hours.

If "**YES**" to any question in the ESC Assessment, perform team huddle with caregiver, RN, and Provider to evaluate Sensitive Care. Consider Morphine initiation. Exclude any non-NAS causes.

**Morphine Initiation:**
- Notify Provider infant meets criteria for PRN Morphine
- Give a one-time dose of oral Morphine 0.04 mg/kg (use birthweight for dosing)
- Monitor infant for 4 hours after dose given using portable pulse oximeter
- Notify Provider of any vital sign instability
- If a second dose is considered, wait minimum 3 hours from first dose

**NICU**

**Infant requires transfer to NICU for scheduled Morphine if infant needs >2 consecutive doses of Morphine or 4 PRN doses of Morphine in 24 hour period. Infant may require transfer to NICU for ongoing PRN doses if treatment has been needed for 7 days in Postpartum.**

Start morphine 0.04 mg/kg PO q3h
*YES
Increase morphine dose to 0.06 mg/kg PO q3h
*YES
Add clonidine 1 mcg/kg PO q6h
*YES
Increase clonidine to 1 mcg/kg PO q3h (confirm BP wnl)
*YES
Increase morphine by 0.02 mg/kg to maximum of 0.2 mg/kg/dose

NO

* If "**YES**" to any question in the ESC Assessment, huddle with caregiver and RN and increase Sensitive Care if possible.

**"NO" to all questions** - Continue to provide Sensitive Care. Continue to assess after each feeding (e.g., every 3-4 hours)

**Weaning morphine:**
- When infant is stable on medications for 24 hr, begin to wean morphine by 10% of the maximum dose daily if "NO" to ESC assessment
- Discontinue morphine when absolute dose is less than or equal to 0.04 mg

**Weaning clonidine:**
- When infant stable off morphine for 24 hr ("NO" to all ESC questions) – begin lengthening clonidine interval q3h-> q6h -> off every 24 hr if continues with "NO" to all ESC questions

**Failed weaning:**
- If infant has "YES" to any question in the ESC assessment despite optimal Sensitive Care after weaning or discontinuing morphine, give one-time dose of previously effective morphine – if infant continues with "YES" to any question – increase to previously effective dosing regimen and maintain for a minimum of 24 hrs

**Discharge criteria:**
- Monitor for minimum of 24 hr off morphine and/or clonidine prior to discharge

# Chapter 20: Retinopathy of Prematurity

*Nina Menda, MD*

- ROP is a multi-factorial condition of abnormal vascularization of developing etinal vessels occurring in premature infants due to incomplete vasculogenesis of the retina at the time of birth.
- Leads to retinal detachment and blindness if severe and untreated.

**Retinal Vasculature Embryology**

- Retinal vasculature begins to develop at 14-15 weeks gestation
- Growth of the vessels begins centrally at the optic disc and grows out peripherally to the ora serrata
- Retinal vessels develop initially by the process of vasculogenesis and later angiogenesis
- 70% of retinal vasculature present at 27 weeks
- Reaches nasal ora serrata by 36 weeks and the temporal ora serrata by 39-41 weeks
- Preterm birth leads to an avascular zone in the peripheral retina

**Epidemiology**

- Global health epidemic
- Leading cause of childhood blindness worldwide
- Overall prevalence is between 10-25% in premature infants, while incidence is about 50-70% in infants weighing ≤ 1500 grams at the time of birth.[Incidence of 18-40% in premature infants in developed countries]

**Pathogenesis of ROP**

- Phase 1 (Vaso-obliteration)
  - Characterized by cessation of normal new retinal vessel growth
  - Occurs shortly after birth, following hyperoxia exposure
  - Hyperoxia downregulates vascular endoethelial growth factor (VEGF) secretion
- Phase 2(Vaso-proliferation)
  - Characterized by retinal neovascularization, fibrosis and detachment
  - Four to six weeks after birth, the retina becomes hypoxic due to inadequate vasculature to nourish it
  - Hypoxia upregulates VEGF secretion, and excess VEGF leads to dysregulated angiogenesis
  - Vessels leave the retinal plane and grow into the vitreous leading to cicatrization, tugging of fibrous scars on the retina and eventual detachment

**Risk Factors**

- Prematurity (ROP incidence is inversely proportional to gestational age at birth)
- Prolonged hyperoxia or supplemental oxygen use
- Low birth weight
- Post-natal growth restriction
- Inadequate post-natal nutrition
- Sepsis
- RDS/BPD
- Shock
- Asphyxia
- Hypothermia
- Acidosis
- Vitamin E deficiency

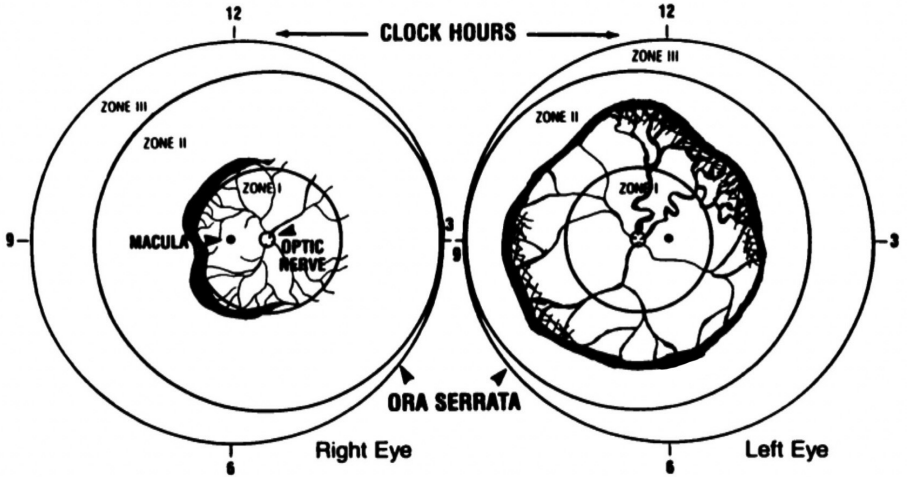
**Classification**

- Zone=Location of abnormal vascularization
- Clock Hour =Extent
- Stage = Severity

| Stage | Features of Disease |
|---|---|
| 1 | Demarcation line between the vascular and avascular portions of the retina |
| 2 | Ridge-like structure between avascular and vascular retina |
| 3 | Fragile new vessel proliferation from the ridge into the vitreous gel |
| 4A | Partial retinal detachment not involving the macula |
| 4B | Partial retinal detachment involving the macula |
| 5 | Total retinal detachment |

- Plus Disease is defined as a significant retinal vein dilation and arterial tortuosity
- Pre-threshold disease is defined as stage 3 ROP in Zone II or any ROP in Zone I

Example of what ophthalmologists document in chart




Right Eye = Stage 2 Zone I/II, 6 clock hours without plus disease

Left Eye = Stage 2/3 Zone II, 12 clock hours with plus disease in one quadrant

**Treatment**

*Most treatments for ROP are targeted for Phase 2 ROP*

A. Monitoring of pulse oximetry and judicious use of oxygen
   - Monitoring oxygenation using pulse oximetry has become the mainstay of ROP prevention.
   - Controversies surround target $SpO_2$ levels due to concerns of multi-centered randomized clinical trial (SUPPORT trial) showing increased mortality in low oxygen saturation target group (85-89%) compared to high (91-95%), despite reduction in severe ROP.
   - Oxygen saturation goals from birth to <37 weeks corrected age (90-94%), while infants >37 weeks corrected age(>95%)

B. Serial Monitoring : Dilated retinal exams using a binocular indirect ophthalmoloscope by an ophthalmologist to determine retinal maturity and early detection of ROP to facilitate early treatment.

C. Laser photocoagulation or cryosurgery
   - Current standard therapy for ROP
   - Ablates the avascular portion of the retina to reduce hypoxic stimulus from VEGF production, stopping abnormal vessel growth
   - Goal is to prevent retinal detachment
   - Patients will still lose some peripheral vision after treatment
   - Who should be treated?
     - Zone I any stage with Plus disease
     - Zone I Stage 3 without Plus disease
     - Zone II stage 2-3 with Plus disease

D. Intravitreal bevacizumab (avastin) monotherapy has shown significant benefit for Zone I stage 3 disease in a RCT. Bevacizumab is a monoclonal antibody against VEGF. It is an intravitreal injection, used in premature infants with severe ROP and has shown significant promise in the treatment of ROP.
   - There is concern for systemic absorption of Avastin, which may result in pan-VEGF blockade which may interfere with angiogenesis in other developing organs. There is insufficient long term data on efficacy and safety.

**Prognosis**
- Up to 80% of ROP will resolve spontaneously or regress
- Less than 6% require any treatment
- 3% or less will become blind from ROP

# Screening Eye Exams

*Nina Menda, MD*

AAP/Meriter Guidelines

- All infants with a birthweight ≤ 1500 grams, or gestational age at birth of≤ 30 weeks
- Select infants with birth weight 1500-2000 grams or gestational age at birth of
- 30 weeks with an unstable clinical course and at higher risk for ROP as determined by attending neonatologist
- In most cases, ROP exams will begin at a PMA of 31 weeks or a chronological age of 4 weeks, whichever is longer.
- **As an exception, infants born at < 25 weeks gestation should be considered for earlier initiation of ROP screening at 6 weeks chronological age based on severity of comorbidities to identify and treat posterior ROP (severe form that is aggressive with rapid progression)

**Timing of Initial ROP Exam**

| Gestational Age at Birth, Completed Weeks | Age at Initial Exam in Weeks | |
|---|---|---|
| | Postmenstrual | Chronological |
| 22** | 31 (28**) | 9 (6**) |
| 23** | 31 (29**) | 8 (6**) |
| 24** | 31 (30**) | 7 (6**) |
| 25 | 31 | 6 |
| 26 | 31 | 5 |
| 27 | 31 | 4 |
| 28 | 32 | 4 |
| 29 | 33 | 4 |
| 30 | 34 | 4 |
| Older gestational age, high-risk factors | | 4 |

- Discontinuation of examinations
    - PMA 45 weeks with no Pre-threshold disease
    - Progression of vascularization in zone III without previous ROP in zone I or II
    - Mild and regressing of ROP in zone III
    - Full retinal vascularization

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# Chapter 21: Metabolic Disorders in Newborn

*Sarah Trinh, MD and Lydia Wraight, MD*

## Overview

- Heterogenous group of disorders that typically present after 48 hours of life and after the initiation of feedings
- Often associated with hypoglycemia, hyperammonemia, and acidosis
- Presentation in the newborn period includes lethargy, emesis, poor feeding, hypotonia, tachypnea, temperature instability, seizures, coma, and apnea
- Always consider in a newborn who is being evaluated for sepsis
- May have family history of unexplained neonatal deaths
- Consanguineous matings (most are autosomal recessive)

## Diagnosis

- Initial labs
  - Blood glucose
  - Arterial blood gas
  - Lactate (arterial sample)
  - Electrolytes (look for acidosis and aniongap)
  - Ammonia (arterial sample, place immediately on ice)
  - Liver function tests
  - Urine ketones and reducing substances
  - Newborn screen
- Diagnostic labs
  - Plasma amino acids (amino acidopathies, urea cycle disorders)
  - Urine organic acids (fatty acid oxidation disorders, amino acidopathies)
  - Plasma acylcarnitine (fatty acid oxidation disorders, organic acidemias)
  - Serum carnitine (fatty acid oxidation disorders, organic acidemias, carnitine deficiency)

## Hyperammonemia

- Medical emergency
- Treatment:
  - Stop all feeds and discontinue all protein intake
  - Provide IV hydration with D10W

- Correct electrolyte disturbances
- Consult a metabolic specialist
- Promote an anabolic state with lipids
- IV arginine HCL, sodium benzoate, sodium phenylacetate
- Peritoneal or hemodialysis if above therapies are not effective
- Monitor for increased intracranial pressure

**Galactosemia**

- Presentation: Progressive vomiting and lethargy, jaundice, encephalopathy, hepatomegaly
- Associated with E. coli sepsis
- Diagnosis: NBS, urine reducing substances
- Treatment: soy formula, galactose free diet

*Table 1. Inborn Errors of Metabolism Associated With an **Acute Crisis***

| Diagnostic Clues | | |
|---|---|---|
| Primary | Secondary | Suggested Disorders |
| Acidosis | ± Hypoglycemia<br>± Lactic Acidosis<br>± Ketosis<br>± High ammonia<br>Increased Anion gap (AG) | Various Organic Acid Disorders |
| | Significant Lactic Acidosis<br>Normoglycemia | Mitochondrial disorders, Pyruvate dehydrogenase deficiency, Alpha-ketoglutarate dehydrogenase deficiency, Pyruvate carboxylase deficiency |
| | Sig. lactic acidosis<br>Hypoglycemia | Glycogen storage type I, Fructose-1, 6-bisphosphatase deficiency |
| | Normal AG<br>Normal lactate<br>No ketosis | Renal tubular acidosis |

| | | |
|---|---|---|
| Hyperammonemia | Alkalosis or normal pH<br>Normal lactate | Urea cycle disorders |
| | Reye-like illness (hypoglycemia, elevated LFTs, no ketones) | Fatty acid oxidation defects |
| | Acidosis<br>± Lactic acidosis<br>± Ketosis<br>± Hypoglycemia<br>Increased AG | Various organic acid disorders |
| Hypoglycemia | Acidosis<br>± Ketosis<br>± Lactic acidosis<br>± high ammonia<br>Increased AG | Various organic acid disorders |
| | Hepatomegaly<br>± Lactic acidosis | Glycogen storage disorders |
| | No acidosis or ketosis<br>No Lactic acidosis | Hyperinsulinemia<br>Fatty acid oxidation defects |
| | Hyponatremia<br>Hypotension | Adrenal insufficiency |
| | Signs of liver failure | Tyrosinemia<br>Glycogen storage disease type IV<br>Galactosemia<br>Niemann Pick type C |

*Table 2. Characteristic of common Inborn Errors of Metabolism*

| Disorder | Fatty Acid Oxidation Disorders (MCAD, LCHAD, SCAD) | Amino-acidopathies (MSUD, PKU, tyrosinemia) | Organic Acidemias (pro-pionic acidemia, methylmalonic acidemia) | Urea Cycle Disorders (OTC deficiency) |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Key Finding | Hypoketotic Hypoglycemia | No acidosis, Nml ammonia, elevations in specific AAs | Metabolic acidosis + AG, hypogly, hyperammonemia | Hyperamonemia, Resp alkalosis No acidosis |

| | | | | |
|---|---|---|---|---|
| Key Test | Acylcarnitine Profile | Plasma amino acids | Urine organic acids | Plasma amino acids |
| Supple-mental Tests | Carnitine Profile | Urine organic acids | Acylcarnitine profile | Urine organic acids |
| Signs/ Symptoms | Presents 6 mos-2 yr. VLCAD/LCHAD -rhabdomyolysis -cardiomyopathy -hypotonia, SIDS | MR, lethargy, coma, liver failure | Vomiting, lethargy, end organ dysfunction, be-gins with feeds | Lethargy, vomiting, coma |
| Acute Treatment | D10, early IVFs | Dextrose, special TPN, insulin | D10, early IVFs, no protein, +/- bicarbonate | D10, early IVFs, sodium benzoate, phenylacetate, arginine, insulin, dialysis |
| Chronic Treatment | Low fat diet, avoid prolonged fasts, nighttime feeds when sick, carnitine | Low protein diet, supplemental formula | Low protein diet, supplemental formula, carnitine, liver transplant | Low protein diet, supple- mental formula, phenyl acetate, arginine, liver transplant |

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| Disorder | Fatty Acid Oxidation Disorders (MCAD, LCHAD, SCAD) | Amino-acidopathies (MSUD, PKU, tyrosinemia) | Organic Acidemias (pro-pionic acidemia, methylmalonic acidemia) | Urea Cycle Disorders (OTC deficiency) |
|---|---|---|---|---|
| Key Finding | Hypoketotic Hypoglycemia | No acidosis or hyperam-monemia, elevations in specific amino acids | Metabolic acidosis with anion gap, hypoglycemia, hyperammonemia | Hyperam-monemia w/o acidosis, respiratory alkalosis |
| Key Test | Acylcarnitine Profile | Plasma amino acids | Urine organic acids | Plasma amino acids |
| Supple-mental Tests | Carnitine Profile | Urine organic acids | Acylcarnitine profile | Urine organic acids |
| Signs/ Symptoms | Presents 6 mos-2 yr. VLCAD/LCHAD -rhabdomyolysis -cardiomyopathy -hypotonia, SIDS | MR, lethargy, coma, liver failure | Vomiting, lethargy, end organ dysfunction, be-gins with feeds | Lethargy, vomiting, coma |
| Acute Treatment | D10, early IVFs | Dextrose, special TPN, insulin | D10, early IVFs, no protein, +/- bicarbonate | D10, early IVFs, sodium benzoate, phenylacetate, arginine, insulin, dialysis |
| Chronic Treatment | Low fat diet, avoid prolonged fasts, nighttime feeds when sick, carnitine | Low protein diet, supplemental formula | Low protein diet, supplemental formula, carnitine, liver transplant | Low protein diet, supple- mental formula, phenyl acetate, arginine, liver transplant |

***By taking care of a newborn we make a difference that lasts a lifetime!***

*–Neena Shah, MD*