NICU Thrive Guide

Montreal Children's Hospital

Version – June 2024

Disclaimer:

This handbook is intended for trainees rotating through the Neonatal Intensive Care Unit at the Montreal Children's Hospital. It is not meant to replace official orientation documents. The authors and the NICU team do not take responsibility for any errors or omissions. This document is a consolidated "thrive" book to prepare for the NICU rotation at the Montreal Children's Hospital.

Official information from the orientation material has been included in this document with some pearls developed by the residents. However, remember that official documentation given by the NICU division has always precedence on the content of this thrive book. The hope is that the information contained here and centralized will promote efficient work, in a mindful spirit of appreciating the incredible learning opportunities during your NICU rotations.

Last Update:

June 2024

Acknowledgements:

We would like to mention that the official orientation guide was created by Dr. Thérèse Perreault. A large part of the orientation guide is included in the Thrive Book and we would like to acknowledge the huge work that was put in place prior to the creation of this repository. A lot of the material included in this "Thrive Book" was created by health care professionals who worked countless of hours to ensure that these protocols were well thought out and supported by evidence-based medicine. These are internal guidelines and regulations, not to be used outside of the MCH institution. The authors of some of the guidelines were not included in the document but should be acknowledged. Amongst them, various neonatologists, NNPs, fellows, consultant physicians, social workers, nurses, respiratory therapists, occupational therapists, administrative agents, pharmacists, nutritionists, residents, family members and others. This document is created by residents for residents.

Updated by Drs. Emilie Filion Ouellet and Bayane Sabsabi

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Resuscitation/Delivery Room

Delivery room Attendance

As part of your rotation in the NICU, you are expected to attend a delivery as part of the Resuscitation team. It is essential to have the knowledge of neonatal Resuscitation program prior to attending deliveries. The neonatal Resuscitation team is composed of respiratory therapist, NICU Resuscitation nurse and NICU on call personnel (nurse practitioner, NICU resident or clinical assistant. There is a staff neonatologist who is always assigned to the Resus team. The staff neonatologist accompanies the Resus team depending on the indication for the attendance.

The spectralink for the Resuscitation team is as follows:

- Neonatologist- 25643
- NICU on call personnel- 25645
- Respiratory therapist- 25646
- NICU Resuscitation nurse- 25647
- *NICU fellow may be called at 25644 depending on the availability.

The NICU on call personnel calls the Resuscitation team members for a huddle every morning between 8:45-9:00 AM and 21:00-22:00 in the evening. The Resus nurse is expected to touch base with the OB team to get latest update prior to the huddle. The goal of the huddle is to make the team familiar with each other, to discuss any potential deliveries that will require attendance by the Resus team and also assign team members for the different roles for neonatal Resuscitation.

If a situation is identified prior to labor, during labor, at delivery or after birth that will require the presence of Resuscitation team, the nurse taking care of the mother should call the NICU team member at “25645”. The nurse should be able to pass on the information regarding the situation, background information on the pregnancy and the presence of any complication, mode of delivery and level of urgency and the delivery room number to the NICU on-call person. This team member will announce on the spectralink the room number and the indication to the Resus team.

In the event of an emergency that arises that will require urgent Resuscitation of the newborn, the OB team members should press the “code pink button” in the labor room or D-6. The code pink button is linked to the spectralink numbers of all Resuscitation team members. If Resuscitation is required in the delivery room, the Resuscitation record form needs to be filled out and entered in the baby’s chart. The on-call NICU person is responsible to document indication, action taken, APGAR and plan of disposition for the baby in Centricity.

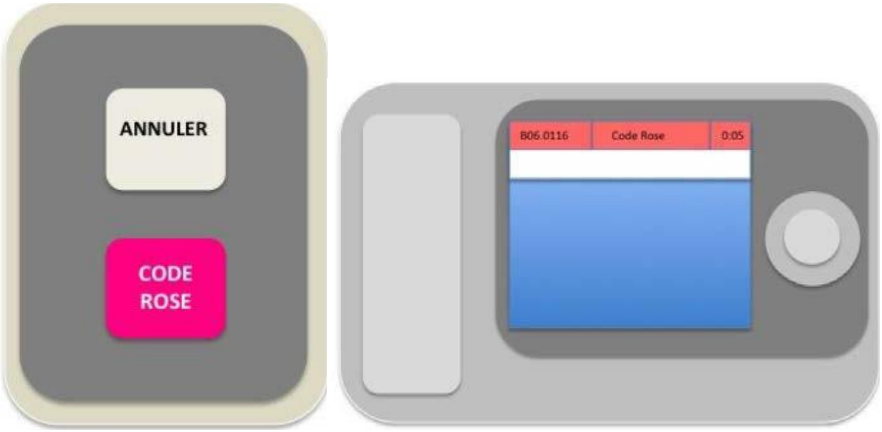
Extra Pearls Regarding delivery room:

Activating the resuscitation team:

Note that Code Pink Spectralink phones are equipped with a Push-to-Talk (PTT) function (ie. as a walkie-talkie). When you receive a call from the birthing center, push the PTT button and hold, wait 2 seconds for the “bip” to finish (indicating that it is transmitting to all the other Spectralink) and you state “resus team to room ___ (example: OR 1; OR2; Main OR; Delivery room 3) for ___

(example: meconium, urgent delivery, maternal fever, etc.)". Include gestational age if preterm, or simply "term baby" and the reason for the resus team activation. Examples include "meconium" and "fetal decels". If you are not comfortable with the case, ask for a backup trainee/NNP or staff to join you for the resus. A RT and RN will be joining at each resuscitation. Make sure to specify if it is the MAIN-OR (as it is on a different floor). Usually, deliveries will happen in the operating room 1 and 2, which are connected to the stabilisation room of the NICU. It may happen that a mother requires more advanced anesthesia care and that the newborn is delivered in a C-Section occurring the Main-OR (usually room 5) on the 3rd floor. Extremely rare, the delivery may happen in the adult ICU.

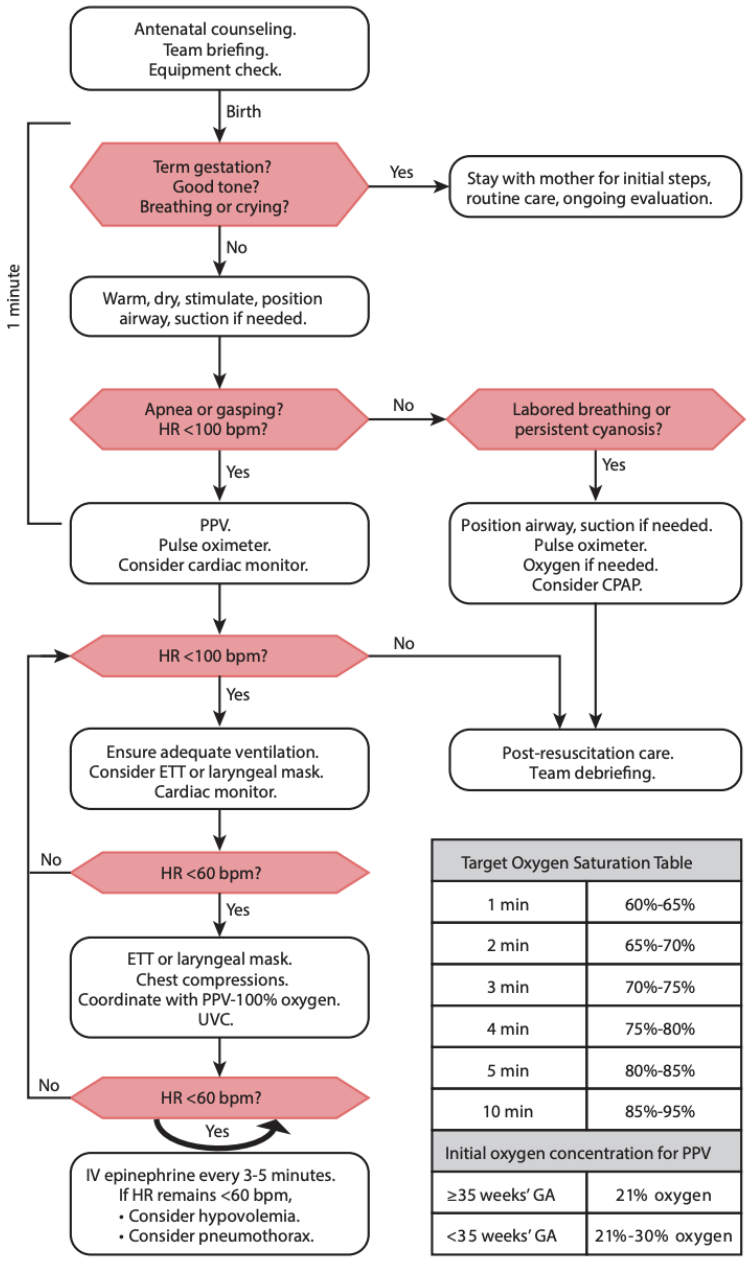
Code Pink Button



- Present in the delivery room
- Also present in every single patient room (sometimes hidden behind the isolette)
- Should flash with location on the resuscitation phones (25643-Staff; 25645-Resident/NNP; Resuscitation nurse and resuscitation RT). It should also flash at central stations on the central code monitor (picture above).

NRP Review (Refer to Textbook of NRP, 8th Edition)

Neonatal Resuscitation Program® 8th Edition Algorithm



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

1. Preparation:
    a. Team and equipment preparation: the Brief
        i. 4 pre-birth questions
            1. Expected gestational Age
            2. Is the AF clear
            3. Any additional risk factors
            4. Umbilical cord management plan
2. Delayed cord clamping: should be performed for at least 30 seconds in stable infants (aiming usually 60 to 90 seconds)

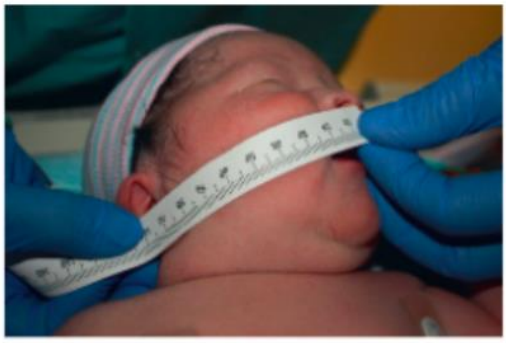
a. DCC for 30-60 seconds is reasonable for both term and preterm infants who do not require resuscitation at birth.
b. If PPV is required, cord should be cut and infant transferred to overbed warmer for resuscitation

3. Initial Steps:
   - Assessment: term, tone, crying?
   - Warmth
   - Dry and stimulate
   - Position airway
   - Suction if needed
4. **Temperature** should be maintained between 36.5 – 37.5 degrees Celsius (hat for all babies, plastic wrap/bag and thermal mattress for infants < 32 weeks)
5. **Oxygenation targets:** Starting resuscitation FiO2 for term babies should be 21%, for infants < 32 weeks should be 30%
   - Monitor saturation using preductal monitor
6. **PPV:** to be used if HR < 100 bpm (by auscultation) or apnea or grasping
   - Initial PIP 20-25cm H20
   - Initial PEEP 5 cm H2O
   - Consider electronic cardiac monitor when resuscitation is required. Should be applied in high risk deliveries and preterm deliveries.
   - After PPV is started, reassess in 15 seconds – if no response, perform MR SOPA corrective measures
   - If no response to MR SOP, will need an alternative airway: (intubation or LMA). LMA can be placed in newborns > 2 kg (indication of the company). The size is 1.0. Consider obstruction and suction via ETT.

Ventilation Corrective Steps	
M	Mask adjustment
R	Reposition airway
S	Suction
O	Open mouth
P	Pressure increase
A	Alternative airway

7. CPAP
   a. Consider CPAP if labored breathing or persistent cyanosis
      i. Position airway and suction if needed
      ii. Place pulse oximeter
8. Advanced Airway (Refer to Intubation section as well)

- Intubation is recommended before chest compressions (you cannot guarantee an effective ventilation if you do not have a secured airway)
- If intubation is not successful or feasible, laryngeal mask (LMA) should be used
- Depth of insertion using table or by measuring nasal-tragus length (NTL) + 1 cm. (Old NRPs use the rule 6+weight for oral position and 7+weight for nasal intubation in term babies – this overshoots often in smaller babies, hence was abandoned by NRP).



Weiner, G. M., & Zaichkin, J. (2016). Textbook of neonatal resuscitation. Elk Grove Village, IL: American Academy of Pediatrics

  - CO2 detectors (pedicap – there are specific ones for premature newborns), auscultation, steam in ETT or LMA, increase in heart rate (most sensitive sign) and direct visualisation are the classical ways to ensure securing your airway.
  - Make sure that the ETT or LMA are secured and that the air entry is symmetric (avoiding endobronchial intubation – or pneumothorax).

Insertion depth of ETT:

Initial endotracheal tube insertion depth ("tip to lip") for orotracheal intubation		
Gestation (weeks)	ETT insertion depth (at lips, in cm)	Weight (grams)
23-24	5.5	500-600
25-26	6.0	700-800
27-29	6.5	900-1000
30-32	7.0	1100-1400
33-34	7.5	1500-1800
35-37	8.0	1900-2400
38-40	8.5	2500-3100
41-43	9.0	3200-4200

Choosing your ETT size and blade size:

Patient Weight	ETT Size
<1 kg, <28 wk EGA	2.5
1–2 kg, 28–34 wk EGA	3.0
2–3 kg, 34–38 wk EGA	3.5
3–4 kg, >38 wk EGA	3.5–4.0

Table 1: Choosing blade size	
Blade size	**Weight**
No. 00	<1000g
No. 0	1000g-3000g
No. 1	>3000 g

Sudden deterioration after intubation: "DOPE-G"

- Displaced ETT

- Obstructed ETT
- Pneumothorax
- Equipment failure
- Gastric decompression (especially in those that have been ventilated for a prolonged period of time).

9. **Chest Compressions – begin if HR < 60 in spite of 30 seconds of effective PPV (with a secured airway)**
    - Make sure the FiO2 is at 100%
    - 2-thumb technique is recommended (you should adjust your position to be close to the head to allow securing UVL, but continuing the 2 hands technique). The thumb technique has been shown to be less efficient in recoil and is not recommended by NRP.
    - Electronic cardiac monitor is preferred for assessment of heart rate (but make sure to confirm with auscultation – avoiding electrical pulseless activity).
    - Continue chest compressions for 60 seconds before rechecking

If Heart Rate doesn't increase with Chest compressions: "CARDIO"

- Chest moving with each breath
- Airway secured
- Rate of compressions to ventilation 3:1
- Depth of compressions 1/3 of the AP diameter
- IO: Inspired Oxygen being delivered at 100%

10. **Epinephrine – indicated if HR < 60 after 30 seconds of effective PPV and 60 seconds of chest compressions using 100% oxygen.**

Epinephrine dosing [0.1mg/mL]
0.1mg/kg by ETT
0.02mg/kg via IV

    - There is 20 cycles of 1-2-3-Breath (3 chest compressions and 1 breath administered) for a 1 minute period. Hence, one trick is to synchronize between the one administrating the ventilation and the one doing the chest compressions: 1-and-2-and-3 – AND 1; 1-and-2-and-3 – AND 2; 1-and-2-and-3 – AND 3; etc. Until reaching 20 and re-evaluation.
    - Epinephrine should be administered by intravenous route. Hence, when you start chest compressions, one should be preparing to install the low-line umbilical venous line. If by the time of EPI administration, the intravenous access is not ready - one dose may be given via ETT, but the absorption is extremely erratic (especially in the context of post-natal birth with high pulmonary vascular resistances).
    - IV Epi may be given by emergency UVC (or intra-osseous if UVL not able to install). IO material can be found in the unit in the "Pediatric Crash Cart" and are available in the delivery room.
    - Flush with 3 ml of Normal Saline
    - Repeat every 3-5 minutes (consider increasing subsequent doses)
11. **Other Medications**

- Use NS0.9% (Saline = 154 meq/L of Na) or pRBC (O negative blood is available in the delivery room specifically for the baby). 10 mL/kg may be given if there is a history of blood loss (previa, abruption, suspicion of fetal-maternal hemorrhage, uterine rupture) and should be given over 5 minutes (not faster).
- UVC is preferred route of emergency vascular access but IO can be used as an alternative
- DO NOT USE NaHCO3 and/or Naloxone

12. Considerations for preterm infants
    - Temperature control: room temperature 23-25 deg., thermal mattress & plastic wrap for infants < 32 weeks, hat for all babies (normal temperature is 36.5-37.5)
    - 3-lead EKG monitor for rapid and reliable HR assessment
    - If resuscitation is required, PEEP 5 is recommended
    - CPAP can be used if stable but increased WOB (PEEP 5-8 cm H2O)
    - All babies less than 32 weeks should be placed on Bubble CPAP before arriving in the NICU. Refer to the CPAP protocol.
13. Reasonable time frame for considering cessation of resuscitation efforts is around 20 minutes after birth.
    a. It should be individualized based on patient and contextual factors.
        i. Optimal resuscitation
        ii. Availability of advanced NICU care
        iii. Specific circumstances before delivery
        iv. Wishes expressed by the family

Delivery Room attendance:

The goal is to anticipate any identifiable situation that may require pediatric presence prior to the delivery of the newborn in a timely fashion.

Clear communication / Written report on Centricity:

Identification	Identify yourself
Situation	Why is Neonatology being called? Briefly state the problem, what it is, when it started or happened, and how severe
Background	Gestational age Prenatal complications Presence/absence of major anomalies Membranes: intact/ruptured Fluid: clear/cloudy/meconium
Assessment	Level of risk to baby Plan for delivery: vaginal/c-section Level of urgency
Recommendation	Categorize level of priority anticipated, inform the neonatal team and initiate the group call if required

Delayed/Deferred Cord Clamping (DCC):

Please document each time in centricity and on admission note if admitted to the NICU – duration of the DCC.

*** Refer to Clinical practice guideline for Delayed Cord Clamping**

Eligibility

All babies who are vigorous at birth will be eligible for delayed cord clamping unless there are contraindications such as:

1. Cases with interruption of the placental blood flow and oxygenation due to abruption, maternal hemorrhage (bleeding placenta previa), fetal hemorrhage (vasa previa), active maternal seizure
2. Cord related issues- cord avulsion, cord prolapse or tight nuchal cord
3. A requirement for immediate newborn resuscitation – hydrops, congenital heart disease with anticipation need for immediate intubation, congenital diaphragmatic hernia
4. IUGR with certain abnormal umbilical cord Doppler evaluation
5. Multiple gestation involving monochorionic twins regardless of the presence or absence of twin to twin transfusion syndrome. The clinical trials involving DCC did not include multiple gestations and there is little information regarding its safety or efficacy in this group. There is theoretical risk of placental vessel anastomosis that may result in unfavorable hemodynamic changes during DCC.

DCC Procedure for preterm infant < 32 weeks of gestation:

- Staff neonatologist or fellow is present at delivery to supervise the transition of these infants to extrauterine life. One of these NICU members may scrub in for the delivery of < 29 week of gestation.
- Discuss with OB team if there is any contraindication for DCC prior to delivery.
- Ensure required supply such as Neo-HeLP (sterile polyethylene occlusive suit to prevent hypothermia) is provided to the OB delivering team by the attending NICU team.
- Assigned time-keeper (NICU resus RN) starts the APGAR timer as soon as the infant is delivered and thereafter announces the time in 15 second intervals.
- Immediately after birth, infant is covered with NeoHelp and stimulated with gentle tactile stimulation (rubbing of the back). Secretions can be suctioned if they are copious. During the first 20-30 seconds, the newborn's tone and respiratory effort should be evaluated to determine if the infant is vigorous or non-vigorous. If the preterm is vigorous, clamping of the cord should be delayed for at least 60 seconds. If

the infant is assessed to be non-vigorous, the cord needs to be clamped immediately and subsequent steps of resuscitation should be initiated per the NRP algorithm.

- Documentation of duration of DCC should be included in Centricity. Reason for early clamping if DCC was not offered needs to be documented as well.

DCC Procedure for preterm infant < 32 weeks of gestation:

- NICU resus team to attend the delivery of preterm infants of 32-37 weeks of gestation.
- NICU team (if present) to discuss with OB if there is any contraindication for DCC prior to delivery.
- Ensure required supply such as NEO HELP (for less than 32 weeks) or 2 sterile towels are available for the OB delivering team (circulating nurse to provide)
- Assigned time-keeper (NICU resus RN if present) or peds nurse starts the APGAR timer as soon as the infant is delivered and there after announces the time in 15 second interval.
- Immediately after birth, the infant is covered with Neo-Help or sterile towels depending on the gestational age and stimulated gently. Suction only if there are copious secretions. Assess if the infant is vigorous or not by evaluating breathing effort and tone. If the infant is vigorous, delaying of the cord should be delayed for at least 1-2 minutes or until cord pulsation stops. Clamp the cord immediately if the newborn is non-vigorous and hand-over to the NICU team (if present). Press code pink if the infant is non-vigorous and NICU team is not present.
- Documentation of duration of DCC should be included in Centricity. Reason for early clamping if DCC was not offered needs to be documented as well.

Examining the Newborn

Every patient on the unit must be examined at least once per day. Babies who are unstable or for whom there is an acute clinical concern should be examined multiple times per day, especially when there are changes made to management such as changes in ventilatory settings, or if the nurse notifies you of any acute concern. Physical exams are similar to assessments done in the Newborn Nursery, but with special considerations (ie. small size, prematurity, need for ventilatory support). Review the admission note template to better understand the physical examination that is required at the time of admission. Thereafter, physical exams should be timed with patient care times. If possible, visit each bedside nurse at the start of your shift to determine the care times for each of your assigned patients and ask them to call your Spectralink when he/she is starting the care. Cares are usually performed q3h, q4h or q6h. At discharge: make **sure** to document the hips exam (Barlow+Ortolani), the red reflex and the femoral pulses.

Newborn physical examination checklist (derived from OSCE checklist):

General appearance	☐ ☐ ☐	1. Posturing (flexed, limp, etc) 2. Color (cyanosis, mottling, etc) 3. Degree of distress if any
Head	☐ ☐ ☐ ☐	1. Fontanelles (size, bulge) 2. Sutures (split, overriding) 3. Shape (molding) 4. Swellings (cephalohematoma, caput succedaneum)
Oropharynx and neck	☐ ☐ ☐ ☐	1. Visualize: Palate (cleft, Epstein' pearls, gums 2. Palpate 3. Neck evaluation (masses, abnormalities, range of motion) 4. Clavicle
Eyes	☐ ☐	1. Red reflex 2. Presence of discharge
Lungs	☐ ☐	1. Auscultates bilaterally, anterior and posterior 2. Work of breathing (retractions, nasal flaring, respiratory rate, head bobbing, accessory muscle use)
CV	☐ ☐ ☐ ☐	1. Auscultates 4 points on chest (LLSB, LUSB, RUSB, Apex) 2. Auscultates back 3. Femoral pulses 4. Peripheral pulses
Abdomen	☐ ☐ ☐ ☐	1. Liver and spleen size 2. Umbilical cord 3. Masses 4. Auscultation of abdomen
GU male	☐ ☐ ☐	1. Scrotum (testes present, hydrocele, hernia) 2. Penis: size, location of meatus 3. Anus: patency and location
GU female	☐ ☐ ☐	1. Hymen and labia (hymenal tags and discharge) 2. Clitoris and urethra (clitoromegaly) 3. Anus: patency and location
Extremities incl. hips	☐ ☐ ☐	1. Barlow and Ortolani: (done correctly) 2. Examines feet (clubfeet) 3. Obvious deformities
Back and spine	☐ ☐	1. Sacral dimple or hair tuft 2. Scoliosis
Skin	☐ ☐ ☐ ☐ ☐	1. Cyanosis vs. acrocyanosis 2. Vernix, lanugo 3. Perfusion (mottling, capillary refill time) 4. Rashes, petechiae 5. Birthmarks

Neuro	☐ ☐ ☐ ☐	1. Level of alertness 2. Tone 3. 3 newborn reflexes (root, Moro, grasp) 4. Moves 4 extremities
Dysmorphic features	☐ ☐	1. Facial dysmorphic features (eye shape and position, philtrum, etc) 2. Distal extremities: (number of digits, clinodactyly, palmar creases, clubfeet)

Ballard Score/Assessment of Gestational Age

MATURATIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballard Score)

NAME _____ SEX _____
HOSPITAL NO. _____ BIRTH WEIGHT _____
RACE _____ LENGTH _____
DATE/TIME OF BIRTH _____ HEAD CIRC. _____
DATE/TIME OF EXAM _____ EXAMINER _____
AGE WHEN EXAMINED _____
APGAR SCORE: 1 MINUTE _____ 5 MINUTES _____ 10 MINUTES _____

NEUROMUSCULAR MATURITY

NEUROMUSCULAR MATURITY SIGN	SCORE -1	0	1	2	3	4	5	RECORD SCORE HERE
POSTURE								
SQUARE WINDOW (Wrist)	 >90°	 90°	 60°	 45°	 30°	 0°		
ARM RECOIL		 180°	 140–180°	 110–140°	 90–110°	 <90°		
POPLITEAL ANGLE	 180°	 160°	 140°	 120°	 100°	 90°	 <90°	
SCARF SIGN								
HEEL TO EAR								
							TOTAL NEUROMUSCULAR MATURITY SCORE	

PHYSICAL MATURITY

PHYSICAL MATURITY SIGN	SCORE -1	0	1	2	3	4	5	RECORD SCORE HERE
SKIN	sticky friable transparent	gelatinous red translucent	smooth pink visible veins	superficial peeling & / or rash, few veins	cracking pale areas rare veins	parchment deep cracking no vessels	leathery cracked wrinkled	
LANUGO	none	sparse	abundant	thinning	bald areas	mostly bald		
PLANTAR SURFACE	heel-toe 40–50 mm: -1 < 40 mm: -2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
BREAST	imperceptible	barely perceptible	flat areola no bud	stippled areola 1–2 mm bud	raised areola 3–4 mm bud	full areola 5–10 mm bud		
EYE / EAR	lids fused loosely: -1 tightly: -2	lids open pinna flat stays folded	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear stiff		
GENITALS (Male)	scrotum flat, smooth	scrotum empty faint rugae	testes in upper canal rare rugae	testes descending few rugae	testes down good rugae	testes pendulous deep rugae		
GENITALS (Female)	clitoris prominent & labia flat	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large minora small	majora cover clitoris & minora		
							TOTAL PHYSICAL MATURITY SCORE	

SCORE
Neuromuscular _____
Physical _____
Total _____

MATURITY RATING

SCORE	WEEKS
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

GESTATIONAL AGE (weeks)
By dates _____
By ultrasound _____
By exam _____

Reference
Ballard JL, Khoury JC, Wedig K, et al: New Ballard Score, expanded to include extremely premature infants. J Pediatr 1991; 119:417–423. Reprinted by permission of Dr Ballard and Mosby—Year Book, Inc.

Understanding babies' cues:

-Developmental Care-

A guide for understanding babies' cues

System	Green Light	Yellow Light	Red light
Autonomic	• Good even color • Smooth breathing • No tremors or startles	• Mild color changes (paling, mottling, acrocyanosis) • Grunting or rapid, shallow breathing • Few startles or tremors • Bowel movements	• Substantial color change • Chest wall retractions • Labored breathing or shallow breathing with pauses • Vigorous hiccups • Gagging or spitting up • Many startles or tremors
Motor	• Relaxed tone • Good range of motion • Hand-to-mouth movement • Sucking • Hand grasping • Smooth movements • Postural change • Body kept calm	• Jerky movements • Flaccidity or hypertonia • Uneven tone • Body held tensely	• Stiffening and arching away • Disorganized activity • Flailing and frantic movements • Limpness
State and social-interaction	• Bright-eyed alert state • Readiness for interaction • Visual/auditory locking • Self-quieting behavior • Robust sleep, alert and crying states	• Shutting out by moving into drowsy or sleep states • Irritability and difficulty being consoled • Gaze aversion • Hyperalert state	• Inconsolable crying • Extreme irritability • Saccadic (twitching) eye movement • Setting sun eyes • Panicked alertness • Constant eye averting • Inability to be aroused
Examiner's response to infant cues	• Continue exam	• Pause and observe: • Which direction is this baby going to go? • What do I have to do to facilitate?	• Allow resting period until color, tone and respirations return to normal. If the baby continues to look stressed and does not recover easily, end the exam.

Admission to NICU / and or D6 of late preterm/low birth weight babies

Criteria of Admission

Proposed criteria for admission of late preterm and/or LBW infants to D6:

1. Minimum 35+0 weeks gestation (strict)
   AND
2. Minimum birth weight 2000g (strict)

Proposed criteria for transfer of late preterm/LBW infants from D6 to NICU:

1. Refractory **hypoglycemia** (confirmed by CBG), despite appropriate feeding and or supplementation, as defined in the Hypoglycemia Protocol:

   - Any symptomatic hypoglycemia
   - 2 x consecutive glucose less than 1.5 in first 4 hours of life,
   - 2 x consecutive glucose less than 2.2 OR
   - 3 x glucose less than 2.6

2. Severe or persistent **hypothermia** (rectal temperature below 36.3 °C) not respondingto first-line measures (e.g.skin-to-skin, wearing a hat, proper feeding as described in the Late Preterm Feeding Protocol):
   - Axillary temperatures of hypothermic babies should be confirmed with a rectal temperature and re-checked every hour.
   - Transfer to NICU is appropriate if the rectal temperature is below 35°C on a single reading.
   - Transfer to NICU is appropriate if the rectal temperature remains between 35°C - 36.3°C after 4 - 6 hours.
3. Weight loss of **15%** or more.*

4. **Failure to gain weight** after 5 days, that is concerning enough to preclude discharge and outpatient follow-up.*

   Note* Consider a transfer to the MCH wards instead of NICU

Saturation Targets

"OWL"= OXYGEN WITH LOVE

	Alarm limits	
ALL BABIES (preterm, term, PPHN) except cardiac babies		
	Oxygen	**Room Air**
HIGH Saturation Limit	**95**	**100**
LOW Saturation Limit	**88**	**91**

Babies with congenital heart defects	
HIGH Saturation Limit	To be determined by the Cardiology Team + ordered.
LOW Saturation Limit	Please write limits on care plan.

Updated January 2017

Recommended isolette humidity levels

Less than or equal to 1000g **OR** **Between 23 weeks to 28+6 gestation**	DOL 0-7	Start isolette humidity level at 75-85% (the higher value is reserved for the 23-25 week neonate and the lower value reserved for the neonate above 26 weeks gestation)
	DOL 8+	Gradually reduce isolette humidity level to achieve final goal of 50%. Proceed to wean over 20 hours by reducing humidity level by 5% every 4 hours. To ensure tolerance to changing humidity levels, measure and document temperature every 3-4 hours. If axillary temperature is unstable, check temperature every 2 hours. Maintain 50% humidity until neonate attains 32 weeks corrected gestational age, then stop.
1001-1500g **OR** **29 weeks to 31 weeks gestation (inclusive)**	DOL 0-7	Start isolette humidity level at 70%.
	DOL 8	Gradually reduce isolette humidity level to achieve final goal of 50%. Proceed to wean over 20 hours by reducing humidity level by 5% every 4 hours. To ensure tolerance to changing humidity levels, measure and document temperature every 3-4 hours. If axillary temperature is unstable, check temperature every 2 hours. Maintain 50% humidity until neonate attains 32 weeks corrected gestational age, then stop.

Vitamin K Administration

Refer to: "Collective Order – MUHC: Vitamin K Administration to Newborns"

All newborns have precariously low vitamin K1 (hereafter referred to as vitamin K) stores and essentially undetectable plasma concentrations. Furthermore, if babies are born prematurely, with hepatic disease, with delayed micro floral gut colonization or if they received antibiotics and anticonvulsants, vitamin K synthesis/availability will be reduced. The 2013 Canadian Pediatric Society position statement recommends giving vitamin K by intramuscular route to prevent vitamin K deficiency bleeding (VKDB), also referred to as hemorrhagic disease of the newborn. In the event where parents refuse intramuscular route, repeated oral doses of vitamin K can be administered as a risk reduction strategy. In the less than 1000 g preterm newborn, the intravenous (IV) route can be used and appears to provide sufficient vitamin K, provided that multivitamin formulation in total parenteral nutrition combined with intralipids is administered. This provides more than 10 micrograms/kg/day of vitamin K.

Administration route:

- The recommended route of administration is IM
- For an unstable newborn of any weight, the IV route may be used if the IM route is judged to be detrimental to the patient. In that case, an individual order is required.
- For newborns with a birthweight < 1000g the IV route should be use

- Newborns of parents who refuse the IM route can receive vitamin K oral doses. Parents must be informed that the IM route remains the preferred route as the oral route has not been shown to be as effective.

Targeted time of administration:

- Newborn must receive their Vitamin K IM/IV dose within 6 hours from birth
- Newborn must receive their Vitamin K PO dose within 5 hours from birth
- Newborns who do not receive Vitamin K within the recommended time frame should receive their dose as soon as possible. The newborn treating physician must be notified and the newborn assessed.

Risk reduction strategy for newborns whose parents refuse the recommended IM route of administration:

Dose	Timing
1st	With first feeding or by 5 hours from time of birth: Vitamin K 2mg PO
2nd	At 2-4 weeks of age: Vitamin K 2mg PO
3rd	At 6-8 weeks of age: Vitamin K 2mg PO

Administration of Hepatitis B Vaccine/HBIg

Refer to (French only): https://msss.gouv.qc.ca/professionnels/vaccination/piq-immunoglobulines/hbig-immunoglobulines-contre-l-hepatite-b

Indications for HBIg in the newborn (province of Quebec):

- Mother has an acute hepatitis B infection in the 3rd trimester
- Mother is confirmed to be HBsAg positive
- Mother presents with an acute hepatitis B infection after delivery and it cannot be excluded that she may have been infectious at the time of delivery (independent of prenatal testing)
- Newborns < 2000g if mother's HBsAg status is unknown, unless her status can be determined within 12 hours from birth

* For newborns equal or greater than 2000g, if mother's HBsAg status is unknown – check for the presence of HBsAg in the mother. Immediately administer the HB vaccine, unless the mother proves HBsAg negative within 12 hours of birth. If the mother is HBsAg positive, administer HBIg.

HB vaccine at birth:

- Indicated for all neonates, regardless of weight, born to either HBsAg-positive mother or mother with unknown status
- Administer first dose within 12 hours of birth

* Other babies should follow the routine Quebec vaccination schedule (see section 32)

Admission of <29 weeks or <1000g

Please refer to NICU weebly for most up to date guidelines

Prescription and usage of Caffeine in Preterm Infants (Quick ReferenceGuide)

The Prescription and Usage of Caffeine in Preterm Infants at the Montreal Children's Hospital
Quick Reference Guide

This document is to be used as a quick reference guide to the protocol "The prescription and usage of caffeine in preterm infants at the Montreal Children's Hospital".

For the purposes of the protocol, the following terminology is used:

- **Clinically significant events** refer to any event that fulfills ALL of the following criteria:
  - Apneas, bradycardias (<100 beats per minute), and/or desaturations (SpO_2<85%)
  - Requiring stimulation, oxygen supplementation, and/or bag-mask ventilation
  - Not associated with oral feeding, reflux, or invasive procedures.

1. INDICATIONS AND TIMING OF CAFFEINE INITIATION

Caffeine initiation in infants born at	
< 29 weeks gestation	**≥ 29 weeks gestation**
On mechanical ventilation ❖ Weaning to extubate within 24h ❖ Insufficient respiratory drive and/or clinically significant events ***On non-invasive respiratory support*** ❖ Clinically significant events ❖ Infants not manifesting apneas should be considered candidates for caffeine therapy between 24 and 72h of life	❖ Prophylactic caffeine is NOT indicated ❖ Start caffeine if observed or documented clinically significant events ❖ Caffeine may be considered for infants on mechanical ventilation that are weaning to extubate within 24h

2. DOSING AND MAINTENANCE OF CAFFEINE

Caffeine prescription

- ❖ **Use caffeine citrate formulation**
- Loading: 20 mg/kg of caffeine citrate
- Maintenance: 10 mg/kg/day IV/PO Q24h, started 24h after the loading dose
- Do not stagger unless ordered by medical team; if possible, administer in the morning

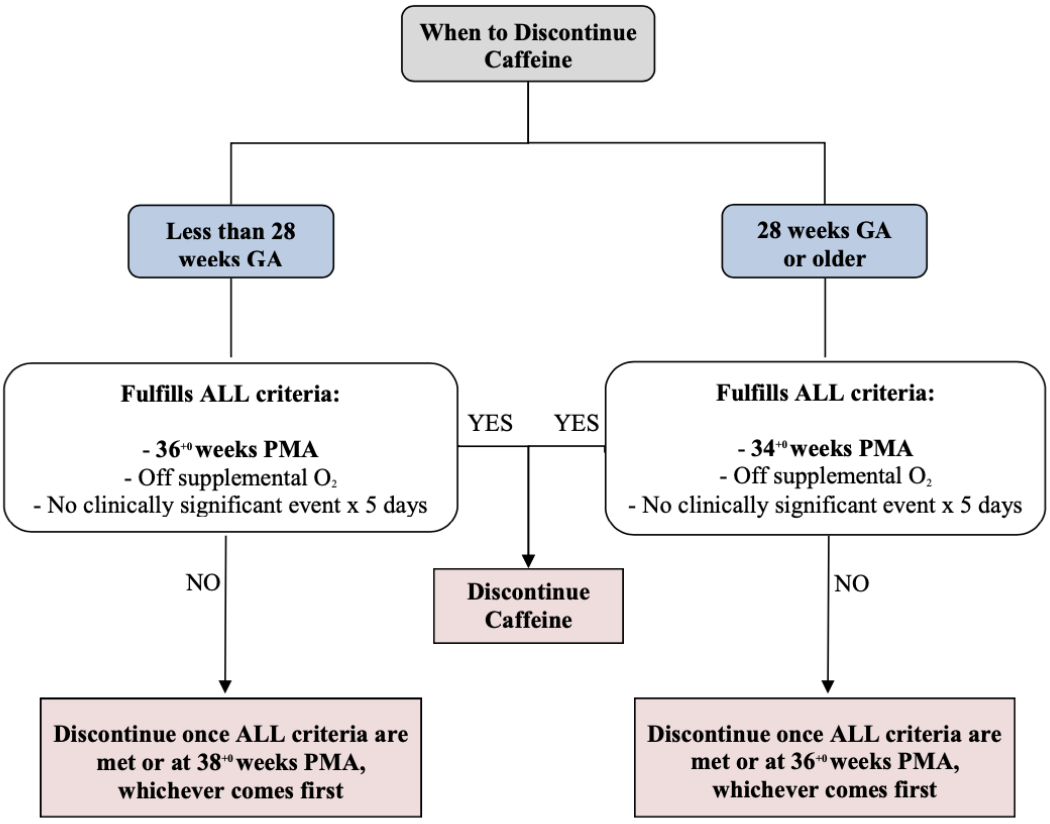
Route of administration

- Use IV caffeine until the infant can tolerate 60-80 mL/kg/day of enteral feeds

Monitoring and dose changes

- In exceptional circumstances where the infant has persistent clinically significant apneas AND other causes have been ruled out, then caffeine may be increased by a 5 mg/kg/dose increment up to a maximum of 15 mg/kg/dose of caffeine citrate once daily.
- If side effects (e.g. tachycardia, reflux, feeding intolerance) are difficult to manage, consider decreasing the dose by 5 mg/kg decrements to a minimum of 5 mg/kg/dose of caffeine citrate once daily.

3. *TIMING OF CAFFEINE DISCONTINUATION*



Notes:
Discontinue Caffeine as early as 34+0 weeks PMA if significant side effects persist despite using lowest dose (5mg/kg/day caffeine citrate).

Criteria for Caffeine Reinitiation: (any of the following)

- Frequently observed respiratory pauses with bradycardias/desaturations
- Frequent brief dips in SpO_2 despite a normal SpO_2 in room air*

* An overnight oximetry study documenting abnormal desaturation index (with central apneas/periodic breathing) may be helpful, in consultation with Respiratory Medicine.

Feeding & Fluids

Fluids

Recommended Fluids for Newborns

DOL	TFI	Fluid
0	65	D10W
1	80	D10W + 20 mEq Na
2	100	D10W + 40 mEq Na + 20 mEq K
3	100	
4	120	
5	150	

Initial total fluid intake

<29 weeks and/or <1000g in the first 72 hours after delivery:

- Birth weight ≤ 750 gm: 100 ml/kg/day
- Birth weight > 750 gm: 80 ml/kg/day
- Consider increasing total fluid intake by 10-20 ml/kg if
    - Significant weight loss
    - Urine output exceeds hourly rate for more than 4-6 hours o Serum sodium is increasing.
- Aim for serum Na 135-145 mmol/L. Avoid serum Na > 150
- Adjusting Fluids should consider: D5W as in Y. Avoid increasing TPN if there are a lot of protein and electrolytes, as this may become excessive. Often premature newborns are loosing free water (tubulopathy of prematurity).
- Avoid Na in IV fluids (except for UAC) for the first 24 hours.
- Avoid using too much volume when flushing lines.

Usually:

- 34 weeks to term : start on day 1 with 65 mL/kg/day
- 29 weeks to 34 weeks: start with 80 mL/kg/day

Progress of 20 mL/kg/day every day (based on clinical status and progression; urine output and weight; Na levels). Usually reaching a maximum of 150 to 160 mL/kg/day.

Solutions available within NICU

a) DW10% - standard amino acid 4% with 5 mmol/L of calcium and with heparin of 0.5 units/ml (no electrolytes) (This solution can also be given via a peripheral catheter; 810mosm/L) – reserved for extreme premature newborns (28 weeks and less) to give protein on day 1 of life. Usually the TPN will be prescribed the next day. Often will start SMOF lipid at 0.5 to 1 g/kg/day at the same day on arrival in the NICU.

b) D10W for most newborns on day 1 of life (usually started at 65 mL/kg/day in most newborns, except: Hypoglycemia (80 mL/kg/day), HIE on cooling (typically 50 mL/kg/day

because they have decreased insensible losses, as well as decreased renal water clearance – AKI and eventually, SiADH).

c) D10W + LYTES: Most newborns starting at 24 hours of life, onward.

d) SMOF lipids (soybean oil, medium-chain triglycerides, olive oil, and fish oil): usually the source of fat administered to newborns intravenously. To calculate infusion rate, it is a 20% solution. Hence: WEIGHT x 5 x X g/kg/day = Total over 24 hours in mL of SMOF to be infused. Sometimes needs to be given over less hours if there are incompatible medications (example: Tazocin). Other lipids are: Intralipid (same concentration 20%) and Omegaven (which is only Omega 3, sometimes used in severe direct hyperbilirubinemia by the Gastroenterology service recommendation). Omegaven has a different concentration (usually 10%, not 20%). Hence, the Rate is usually at 1g/kg/day.
   i. 1g/kg/day of SMOF or Intra-lipid for a 3 kg newborn = 3kg x 1g/kg/day x 5 = 15 mL per day = 0.624 mL/hr x 24 hours of infusion.
   ii. 1 g/kg/day of Omegaven for a 3 kg newborn = 3kg x 1g/kg/day x 10 = 30 mL for 24 hours = 1.25 mL/hr x 24 hours of infusion.
   iii. Also, it may happen that intralipid is prescribed in the first days of a newborn with HIE undergoing cooling because there are more essential fatty acids and we often do not progress their lipids during the cooling if they have Tg accumulation.
   iv. You will often be asked to prescribe the TPN labs: Triglycerides, Magnesium, Phosphorus, cBG (with normalized Calcium to pH).
   v. SMOF is not compatible with prostaglandins (but usually you have a double lumen and you can run each of them in a separate lumen – otherwise need to put intralipid). SMOF is also incompatible with Fentanyl 50 mcg/mL (so we usually run the Fentanyl 12.5 mcg/mL, or rarely run it with intralipid instead).

The maximal osmolarity that can run in a peripheral line is 850 mOsm/L. The maximal osmolarity that can run in a central line is 1800 mOsm/L.

Enteral Feeding

Refer to NICU Initiation of Feeding Protocol (May 2014)

Summary table (feeding protocol 2020):

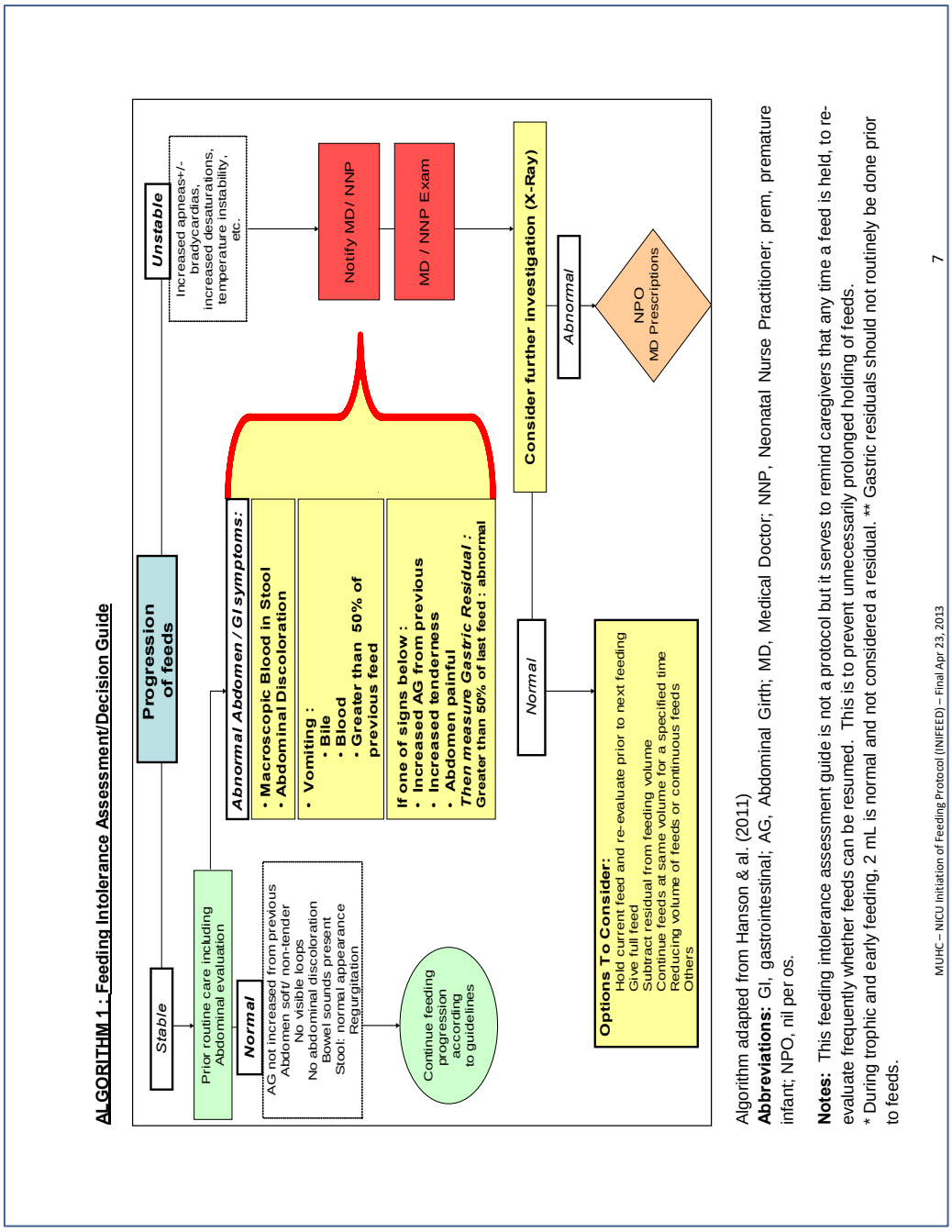
BIRTH WEIGHT (g)	TROPHIC FEEDS	INCREMENTS OF FEEDS	CONSIDERATION FOR MILK FORTIFICATION Volume at 100 mL/kg/day [a]	CONSIDERATION REMOVAL of CVL Volume at 120 mL/kg/day [b]
< 499	**Day 1 - 2:** 0.5 mL every 2h (~ 12 mL/kg/day)*	**Day 3:** 0.5 mL every 24h (< 12 mL/kg/day)	**Less than 540 g:** 4 mL every 2h **540 - 599 g:** 4.5 mL every 2h **600 - 659 g:** 5 mL every 2h **660 - 719 g:** 5.5 mL every 2h **720 - 779 g:** 6 mL every 2h **780 - 839 g:** 6.5 mL every 2h **840 - 899 g:** 7 mL every 2h **900 - 959 g:** 7.5 mL every 2h **960 - 1019 g:** 8 mL every 2h **1020 - 1139 g:** 8.5 mL every 2h **1140 - 1199 g:** 9.5 mL every 2h **1200 - 1249 g:** 10 mL every 2h	**Less than 550 g:** 5 mL every 2h **550 - 559 g:** 5.5 mL every 2h **560 - 649 g:** 6 mL every 2h **650 - 699 g:** 6.5 mL every 2h **700 - 749 g:** 7 mL every 2h **750 - 799 g:** 7.5 mL every 2h **800 - 849 g:** 8 mL every 2h **850 - 899 g:** 8.5 mL every 2h **900 - 949 g**: 9 mL every 2h **950 - 999 g:** 9.5 mL every 2h **1000 - 1099 g:** 10 mL every 2h **1100 - 1199 g:** 11 mL every 2h **1200 - 1249 g:** 12 mL every 2h
500 - 599	**Day 1 - 2:** 1 mL every 2 h (20-24 mL/kg/day)	**Day 3:** 0.5 mL every 12h (15-18 ml/kg/day)		
600 - 649	**Day 1 - 2**: 1 mL every 2 h (18-20 ml/kg/day)	**Day 3:** 0,5 mL every 8h (18-20 mL/kg/day)		
650 - 749	**Day 1 - 2:** 1 mL every 2h (16-18.5 ml/kg/day)	**Day 3:** 0.5 mL every 6h (20-23mL/kg/day)		
750 - 849	**Day 1 - 2**: 1.5 mL every 2h (21-24 ml/kg/day)	**Day 3:** 1 mL every 12h (21-24 ml/kg/day)		
850 - 999	**Day 1 - 2** 1.5 mL every 2h (18-21 ml/kg/day)	**Day 3:** 1 mL every 12h (18-21 mL/kg/day)		
1000 - 1199	**Day 1:** 2 mL every 2h (20-24 ml/kg/day)	**Day 2:** 1 mL every 6h (25-30 mL/kg/day)		
1200 - 1249	**Day 1:** 2 mL every 2h (19-20 ml/kg/day)	**Day 2:** 2 mL every 8h (28-30 mL/kg/day)		
1250 - 1500	**Day 1:** 3 mL every 3h (16-19 ml/kg/day)	**Day 2:** 2 mL every 6h (26-32 ml/kg/day)	**1250 g:** 16 mL every 3h **1300 g:** 17 mL every 3h **1400 g:** 18 mL every 3h **1500 g:** 19 mL every 3h	**1250 g:** 19 mL every 3h **1300 g:** 20 mL every 3h **1400 g:** 21 mL every 3h **1500 g:** 23 mL every 3h

Birth Weight	Less than 750g	750g – 999g	1 000g – 1 249g	1 250g – 1 499g	1 500g – 1 799g	Greater than 1 799g
TROPHIC FEEDS						
Initiate (hours of age)	Within 12			Within 12	Usually not necessary Only if ordered by medical team	Usually not necessary Only if ordered by medical team
Maximum wait time for EBM (hours of age)	· AS SOON AS POSSIBLE · Feeds with EBM or Donor milk should be initiated within maximum 24 hours, if the infants is hemodynamically stable · If patient NPO, Oral Immune Therapy (OIT) can be administer (0,1 mL in each cheek with care)					
NUTRITIONAL FEEDS						
Initiate (hours of age)	↓	↓	↓	↓	Within 6	Within 2
Maximum wait time for EBM (hours of age)					If mother wishes to give breast milk and infant is receiving IV fluids 12	12
Progression (mL/kg/day)	20	25-30	25-30	25-30	30-35	Clinically stable and as per order
Frequency of feeds	q. 2h	q. 2h	q. 2h	q. 3h	q. 3h	q. 3h
Goal to achieve full enteral feeds (days)	10-14	7-10	7	5-6	3-5	Straight to full enteral feed to over 1-3 days
Fortification to 81 cal/100 mL [a]	When feeds are at 100 mL/kg/day [a]					Fortify on a prn basis [a]
TOTAL FLUID INTAKE (TFI): *Need daily MD order during progression*						
End goal enteral TFI (mL/kg/day) [b]	150 -160	150 -160	150 -160	150 -160	130 or higher, as ordered	120 or higher, as ordered

Fortification and supplements:

- Multivitamins 1 mL PO daily in infants less than 2 kg
- Above 2kg: Vit D 400 PO daily (this might be adjusted by the nutritionist based on consumption of formula and if the newborn is from northern communities).
- After 14 days of age, premature infants less than 1.5 kg or those born at less than 32 weeks should receive Iron supplementation once fully fed enterally: 2 mg/kg PO twice a day (total of 4 mg/kg/day; this can be increased up to 6 mg/kg/day divided in 2 dosages).
    - Iron supplementation should be continued until the age of 6 months (or until significant intake of cereals with high iron content).

Feeding Intolerance Algorithm:



Algorithm adapted from Hanson & al. (2011)

Abbreviations: GI, gastrointestinal; AG, Abdominal Girth; MD, Medical Doctor; NNP, Neonatal Nurse Practitioner; prem, premature infant; NPO, nil per os.

Notes: This feeding intolerance assessment guide is not a protocol but it serves to remind caregivers that any time a feed is held, to re-evaluate frequently whether feeds can be resumed. This is to prevent unnecessarily prolonged holding of feeds.
* During trophic and early feeding, 2 mL is normal and not considered a residual. ** Gastric residuals should not routinely be done prior to feeds.

Similac Human Milk Fortifier Extensively Hydrolyzed Protein "Liquid HMF"

Criteria of use:

1. Premature baby (<35wks OR <1.8kg @ birth) **with suspected CMPI or severe feeding intolerance** until weight of 2.5kg reached (then switch to Nutramigen >2.5kg)

a. Blood in the stools that can't be explained by the presence of diaper rash or anal fissures.
b. Persistent significant vomiting despite changes in fluid management and feeding schedule.
c. Unable to wean off TPN to promote or sustain growth despite changes in fluid management and feeding schedule and fortification.
d. Severe abdominal distension requiring holding feeds in absence of other reasons (ventilation, constipation, edema, etc)

2. Premature baby (<35wks OR <1.8kg @ birth) with history of NEC at high risk of feeding intolerance until weight of 2.5kg reached (then switch to Nutramigen >2.5kg)

Indication of use:

1. In replacement of semi-elemental formula (ie: Nutramigen powder) added to Mother's own milk or donor human milk
2. Can only be added to Mother's own milk or donor human milk (cannot be mixed with water or formula, no equivalent infant formula available)
3. Concentration of 81 kcal/100mL only (to increase concentration to 91 kcal/100mL or 100 kcal/100mL, Nutramigen powder should be added)

Prescribing on Milk Sheet:

1. Specify liquid next to Human Milk Fortifier and circle the word
2. Order 20 mL liquid HMF to be added to 100mL EBM or PHM. Cross out the packets to be added.

Formula to enrich the milk (breast milk fortification):

BREAST MILK FORTIFICATION (NICU)

	81	91	100
Baby less than 35 weeks at birth **OR** **Less than or equal to 1800 g at birth**	**100 mL EBM** **and** **4 packs HMF**	**100 mL EBM and** **4 packs HMF and** 2.5 g Enfacare	**100 mL EBM and** **4 packs HMF and** 5 g Enfacare
Baby *was* : **Less than 35 weeks at birth OR less than or equal to 1800 g at birth** 1. **NOW 40 weeks AND 3000 g and above OR** 2. **GOING HOME**	**100 mL EBM** **and** 2.5 g Enfacare	**100 mL EBM** **and** 5 g Enfacare	**100 mL EBM** **and** 7.5 g Enfacare
Baby greater than or equal to 35 weeks at birth **AND** **Greater than 1800 g at birth**	**100 mL EBM** **and** 2.5 g Enfamil A+	**100 mL EBM** **and** 5 g Enfamil A+	**100 mL EBM** **and** 7.5 g Enfamil A+
Baby greater than or equal to 35 weeks at birth and hypoglycemic	**100 mL EBM** **and** 4 g Polycose	**100 mL EBM** **and** 8 g Polycose	**SEE NUTRITIONIST**
Any neonate with suspected cow's milk protein intolerance	**100 mL EBM** **and** 2.5 g Nutramigen	**100 mL EBM** **and** 5 g Nutramigen	**100 mL EBM** **and** 7.5 g Nutramigen
Any neonate with suspected or diagnosed chylothorax	**See formula table**		

FORMULA FORTIFICATION (NICU) (If breast milk not available)

	67	74	81	91	100
Baby less than 35 weeks at birth OR 1800g or less at birth	Rare: on special request SEE NUTRITIONIST	Rare: on special request SEE NUTRITIONIST	Enfamil Premature 81 HP "Ready to feed"	Enfamil Premature 91 Formula Room	Enfamil Premature 100 Formula room
Baby was : Less than 35 weeks at birth OR 1800g or less at birth 1. Now 40 weeks AND 3000g or above OR 2. Going home	Not available	Enfacare 74 "Ready to feed"	Enfacare 81 Formula room	Enfacare 91 Formula room	Enfacare 100 Formula room
Baby greater than or 35 weeks at birth AND Greater than 1800g at birth	Enfamil A+ 67 "Ready to feed"	Rare: on special request SEE NUTRITIONIST	Enfamil A+ 81 "Ready to feed"	Enfamil A+ 91 Formula Room	Enfamil A+100 Formula Room
Any neonate with a suspected cow's milk protein intolerance	Nutramigen A+ 67 "Ready to feed"	Rare: on special request SEE NUTRITIONIST	Nutramigen A+ 81 Formula room	Nutramigen A+ 91 Formula room	Nutramigen A+ 100 Formula room
Any neonate with suspected or confirmed chylothorax	Vivonex Plus (formula room) → Pregestimil A+ → EBM or regular formula Progression requires approval of CVT				
Any neonate with intestinal failure	CONSULT INTESTINAL FAILURE AND NUTRITION TEAM (INFANT)				

NB. "Ready to feed" formulas are available on the unit

Management of Breast Milk Errors:

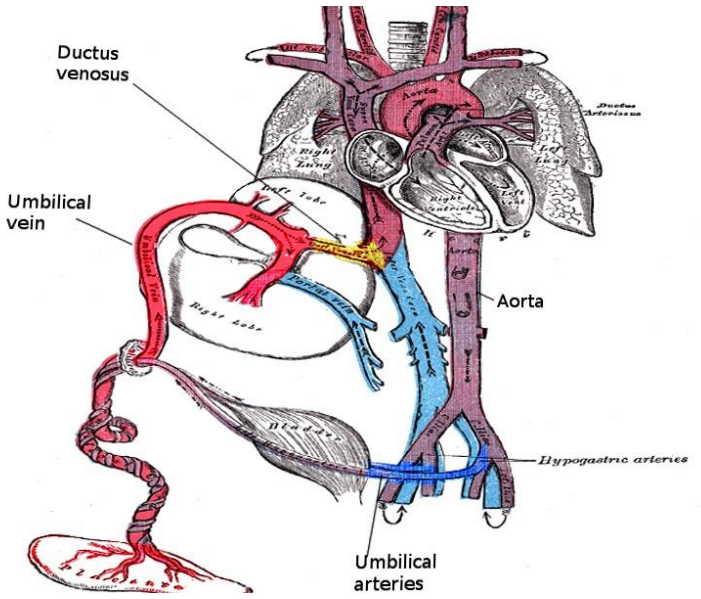
Please refer to NICU weebly

Common Procedures

UVL/UAL insertion

Materials:

- Chlorexidine swabs
- Drapes
- Long clamp
- Tie
- Scalpel
- Tweezers
- NS flushes
- Syringes
- Catheter
- Needle driver
- Sewing needle



Lewis K, Spirnak PW. Umbilical Vein Catheterization. [Updated 2020 Feb 21]. In: StatPearls [Internet]

Double lumen UVL for HIE newborns undergoing cooling, newborns on inotropic support (sepsis, PPHN) or cardiac newborns (since they will need Prostaglandins). Avoid double lumen in extreme premature newborns, since will need to run at least at 1.5 mL/hr to be kept open [KVO] (no heparin lock or NS lock of central lines in the NICU, since it increases the risk of infection). In babies more than 28 weeks, the KVO is at 2 mL/hr. UAL need to run with 0.5NS with heparin, NS with heparin or Na-Acetate (which gives more base to the baby – used often in the premature newborns since they lose bicarbonate in their urine from tubular immaturity). NaAcetate corresponds to about 70 mEq/L of Sodium. In extreme premature newborns UAL will run at 0.3 mL/hr and in babies above 28 weeks: 0.5 mL/hr. Usually the UVL is 5FR and the UAL is 3.5FR. Double lumen UVL is 4FR.

UVL/UAL Position calculation (MCH Protocol)

Procedure	Catheter Size	Depth Calculation	Anatomical target for tip of catheter
UVL Insertion	< 1kg = 3.5F > 1kg = 5F	5.5cm + (1.5 x weight)	At diaphragm
UAL insertion	<1kg = 2.5F Premature = 3.5F Term = 5F	9cm + (3 x weight)	Between T6 & T12

Hôpital de Montréal pour enfants
Centre universitaire de santé McGill
Montreal Children's Hospital
McGill University Health Centre

MUHC MCH-NICU Central Line Radiography Guideline

Calculating umbilical line insertion depth[a]

Catheter insertion depth	Insertion depth (cm)
Umbilical venous catheter (UVC)	(Birth weight [kg] x 1.5) + 5 + cord stump
Umbilical arterial catheter (UAC)	(Birth weight [kg] x 3) + 9 + cord stump

Central line imaging required after initial insertion[b]

		AP (Chest and abdomen)	Lateral shoot through (Chest and abdomen)
UAC	At initial insertion or on admission	x	x
	Follow up	x	
UVC	At initial insertion or on admission	x	x
	Follow up	x	
Arm NICU PICC	At initial insertion or on admission	x Both shoulders abducted 30°	x Both arms at patient's side
	Follow up	x	
Arm IGT PICC	At end of procedure, done in IGT suite	x Both shoulders abducted 30°	
Leg NICU PICC	At initial insertion or on admission	x Frog leg position	x Frog leg position
	Follow up	x	

Central line position guide:

Central line position guide[a]

	Target[b]	Avoid	Most important view	Guidelines for x-ray after catheter adjustment
UAC	T6-9 (preferred) L3-4 (acceptable)	T10-L2 Below L4 (bifurcation of aorta)	AP	Use only the most important view to assess catheter position after adjustment **** Repeat x-ray for ALL catheters pulled by ≥ 1 cm EXCEPT for UVCs pulled back below the liver (see below)** **An x-ray is NOT required for a UVC pulled back to below the liver if:** • Gestational age ≥ 35 wk **OR** ≥ 2.5 kg and UVC pulled to ≤ 4 cm marking at umbilicus • Gestational age < 35 wk **AND** < 2.5 kg and UVC pulled to ≤ 3 cm marking at umbilicus If UVC marking at umbilicus is deeper than these values, an x-ray is required to ensure that the catheter tip is not in the liver
UVC	~T8-9 Junction of IVC and right atrium	Right atrium ~ T7 Portal vein ~ T11	AP	
Right Arm PICC	T4-5 1 vertebral body below carina	Right atrium about below T5	AP	
Left Arm PICC	T4-5 1-2 vertebral bodies below carina	Right atrium about below T5	AP	
Leg PICC	T9-T11 (preferred) Above L4 (acceptable)	Right atrium ~ T7 Renal veins ~ L1 Below L4 (bifurcation of IVC)	AP	

(High and Low in context of UAL) – Risk for low catheters include thrombosis of an iliac artery or descending aorta branching artery, as well as dislodgement. Avoid low line.

UAL graph

Use Weight-based Formula as MCH protocol; Consider use of the graph for cases of Hydrops, abdominal mass, severe IUGR or situations in which weight may not be accurate.

UVL Graph

Use Weight-based Formula as MCH protocol; Consider use of the graph for cases of Hydrops, abdominal mass, severe IUGR or situations in which weight may not be accurate.

Usual infusion via UAL:

- Term & Preterm > 1.5 kg : 1⁄2 Normal Saline with 1 unit/ml of heparin to run at 0.5 ml/h
- Preterm < 1.5 kg : 1⁄2 Normal Saline with 0.5 unit/ml of heparin to run at 0.3 ml/h

Indwelling volumes for extension / UVL

Important in the context of extreme premature newborns with small circulatory volumes (usually 85-90 mL/kg is their total blood volume). Hence, even small dead space in their intravenous line make a difference when administrating fluids and medications (such as intravenous bolus). Often, if there are needs of an urgent medication (such as inotropes), may need to consider the dead space in the tubules.

Extravasation – Intravenous infiltration:

See NICU weebly for most up to date guideline

Hyaluronidase:

In case of severe extravasation, Hyaluronidase should be considered for preventing further tissue necrosis. The CHU-SJ protocol is below:

- Primary dilution: 1500 units/vial + 1 mL of water = 1500 units/mL
- Re-dilute for administration: dilute 1 mL of the 1500/mL in 9 mL of NaCl 0.9% (for total volume), giving a final concentration of 150 units/mL.
- Prepare 5 syringes of 0.2mL each using 25 gage needles or the tuberculin needles.
- Neonatologist or plastic surgeon will administer 5 injection around the area. DO NOT administer in infected or inflamed tissues.

Intubation

Medications for intubation

Nurses have pre-printed orders for intubation, with a chart by weight to prepare the medications of intubation. Here are the dosages that they prepare.

Medication	Suggested dosage
Atropine	20 µg/kg intravenously (avoids parasympathic activation and bradycardiac during intubation).
Fentanyl	3 µg/kg intravenous (premature newborns) - to 5 µg/kg intravenously (term newborns) Fentanyl should be given slowly to avoid chest rigidity (over 3-5 minutes), when not coupled with paralyzing agent. Provides analgesia.
Succinylcholine	2 mg/kg intravenously Provides paralysis for 1-3 minutes. Beware in HyperKalemia – can cause toxicity.

Sudden deterioration after intubation: DOPE-G

- Displaced ETT
- Obstructed ETT
- Pneumothorax
- Equipment failure
- Gastric Over-Distension

Lumbar puncture

Consider the use of EMLA or Maxilene Lidocaine Topical Anesthetic Cream to be placed 30 minutes on the skin before lumbar puncture in neonates greater than *30 weeks*. Tubes need to be sent usually for: bacterial culture, glucose and protein content (please compare to recent glucose from a cBG), viral culture (+/- HSV PCR), cell count (usually the last tube, as it tends to be the "clearest"). DO NOT DO a lumbar puncture without a CBC with adequate platelets level. Also, be careful in situation at risk of coagulopathy.

Selection of Antiseptic products

Infection Control recommendations for antiseptic skin preparation for intravascular access and for site care in children

PLEASE REFER TO PROTOCOL FOR CLEAR INSTRUCTIONS REGARDING THE APPLICATION OF EACH PREPARATION.

- **Neonates of < 1000 g birth weight OR < 28 wk gestational age AND who are < 4 wk old:**

2% aqueous CHG supplied in a single use format should be used [1,2]

Alcohol can cause severe burns and should not be used on the skin of these neonates.

Therefore 0.5% Chlorhexidine (CHG) in 70% alcohol SHOULD NO LONGER BE USED.

Refer to some specifics in protocol

- **Neonates of < 1000 g birth weight OR < 28 wk gestational age AND who are ≥ 4 wk old and < 4 wk corrected age**
- **Any premature infant of < 4 wk corrected age**
- **Term neonates < 4 wk old**
- **Any patient in a neonatal unit**

0.5% CHG in 70% alcohol supplied in a single use format should be used [2]

2% aqueous CHG is also acceptable but is theoretically less potent as a skin antiseptic as it does not have the immediate effect of the alcohol. In addition, the required drying time makes this product less convenient to use [3].
If future data shows 2% CHG in 70% alcohol to be safe in these infants, recommendations will be adjusted.

- **Term infants ≥ 4 weeks old and not in a neonatal unit**
- **Premature infants of ≥ 4 weeks corrected age and not in a neonatal unit**
- **All older infants and children**

2% CHG in 70% alcohol supplied in a single use format should be used. [2]
(This product should not be stocked in Neonatal Units, to prevent potential inadvertent use of 2% CHG in 70% alcohol instead of 2% aqueous CHG).

1. May contain small amounts of alcohol (<5%) as a preservative. This is not a significant amount of alcohol and does not influence the antiseptic property.
2. Chlorhexidine products in multi-use bottles may become contaminated with bacteria, especially if in use for any extended period of time after opening.
3. These infants make up the majority of the NICU population and account for the largest numbers of catheter related bloodstream infections; preventive efforts should be maximized

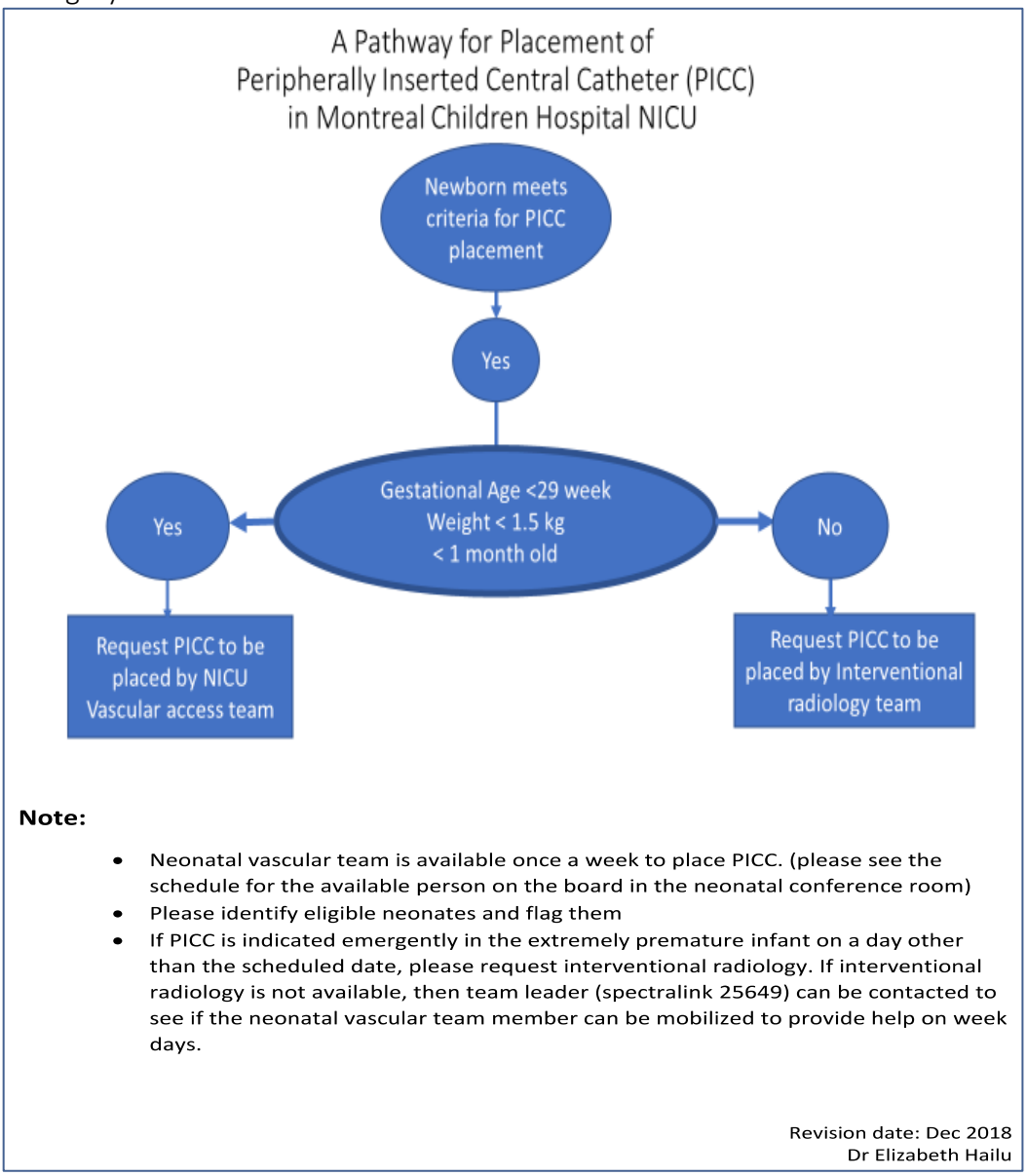
PICC Line:

Pathway and Requests

Please make sure to **request DOUBLE LUMEN PICC** in the context of newborns with:

- Congenital heart defect with anticipated neonatal cardiac surgery
- HIE undergoing therapeutic hypothermia
- Newborns requiring inotropic support (such as: sepsis, PPHN).
- Newborns particularly ill requiring multiple infusions.

Avoid double lumen PICC in premature newborns. Please refer to Umbilical Line section for KVO rates by category of newborn. NEVER NS-lock or HEP-lock a central-line or PICC line in the NICU.



MCH Neonatal Vascular Team guideline for PICC placement in the NICU

The NICU vascular team is responsible for placement of PICC in premature infants who are less than 29 weeks and/or < 1.5 kg as well less than a month old.
The interventional radiology at MCH is responsible for placement of PICC lines in all full-term infants and older premature infants. They are also available to help out in placing lines in extreme premature infants if a need arises.

Removal of PICC line

See NICU weebly for up to date guidelines

PICC lines check:

1. PICCs placement in lower extremities is favored as a first line in premature babies but if upper extremity is used it should be placed at T5-T6 in upper extremities.
2. If PICC tip is beyond T6 it should be pulled by max 0.5cm and x-ray repeated.
3. PICC line position should be followed up every 2 weeks or earlier if chest x-ray is done for other reasons.
4. When an x-ray is done for other reasons and PICC is present, please ensure proper positioning of extremities while the film is being taken so as to maximize proper position of PICC tip.

Teams should review the following once a week on Tuesdays: 1. Check for date of last x-ray
2. Look for the proper positioning of the PICC
3. Document its position in V-Sign

Growth Charts

Use www.growthcalculator.org

Fenton Growth Chart for Preterm Infants

Useful online resource: https://peditools.org/fenton2013/

Complications of Prematurity

Intraventricular hemorrhage (IVH): MCH NICU Guidelines for Brain Ultrasound Screening in Preterm Infants

Group A	Low risk for ultrasound-detected brain injury * Well infants born between 29 $^{0/7}$ and 31 $^{6/7}$ weeks gestation (GA)
US Timing	ONE STUDY At 5 weeks postnatal age, or 36 weeks corrected GA (CGA), or prior to discharge from MCH (whichever comes first)
Group B	Intermediate risk for ultrasound-detected brain injury * Well infants born at <29 weeks GA ** Sick infants born between 29 $^{0/7}$ and 31 $^{6/7}$ weeks GA
US Timing	TWO STUDIES 1. First study at 10 to 14 days of age 2. Second study at 5 weeks postnatal age, or prior to discharge from MCH (whichever comes first)
Group C	High risk for ultrasound-detected brain injury ** Sick infants born at <29 weeks GA
US Timing	THREE STUDIES 1. First study at 3 to 5 days of age 2. Second study at 10 to 14 days of age 3. Third study at 5 weeks postnatal age, or prior to discharge from MCH (whichever comes first)

* Well infants = No inotropic support, mechanical ventilation or CPAP with FiO_2<50%, no evidence of major organ failure in first 7 days

** Sick infants = Delivery room intubation, inotropic support, repeated volume expansion, mechanical ventilation or CPAP with FiO_2 > 50%, early onset sepsis, evidence of major organ failure in the first 7 days

NOTE 1. If a head ultrasound reveals abnormal findings, the frequency of follow-up exams is left to clinical judgement. See post-hemorrhagic ventricular dilatation guidelines for further recommendations.

NOTE 2. A normal head ultrasound does not guarantee normal long term neurodevelopment, follow up recommendations and referral to neonatal follow clinic should also be based on clinical risk factors and physical exam

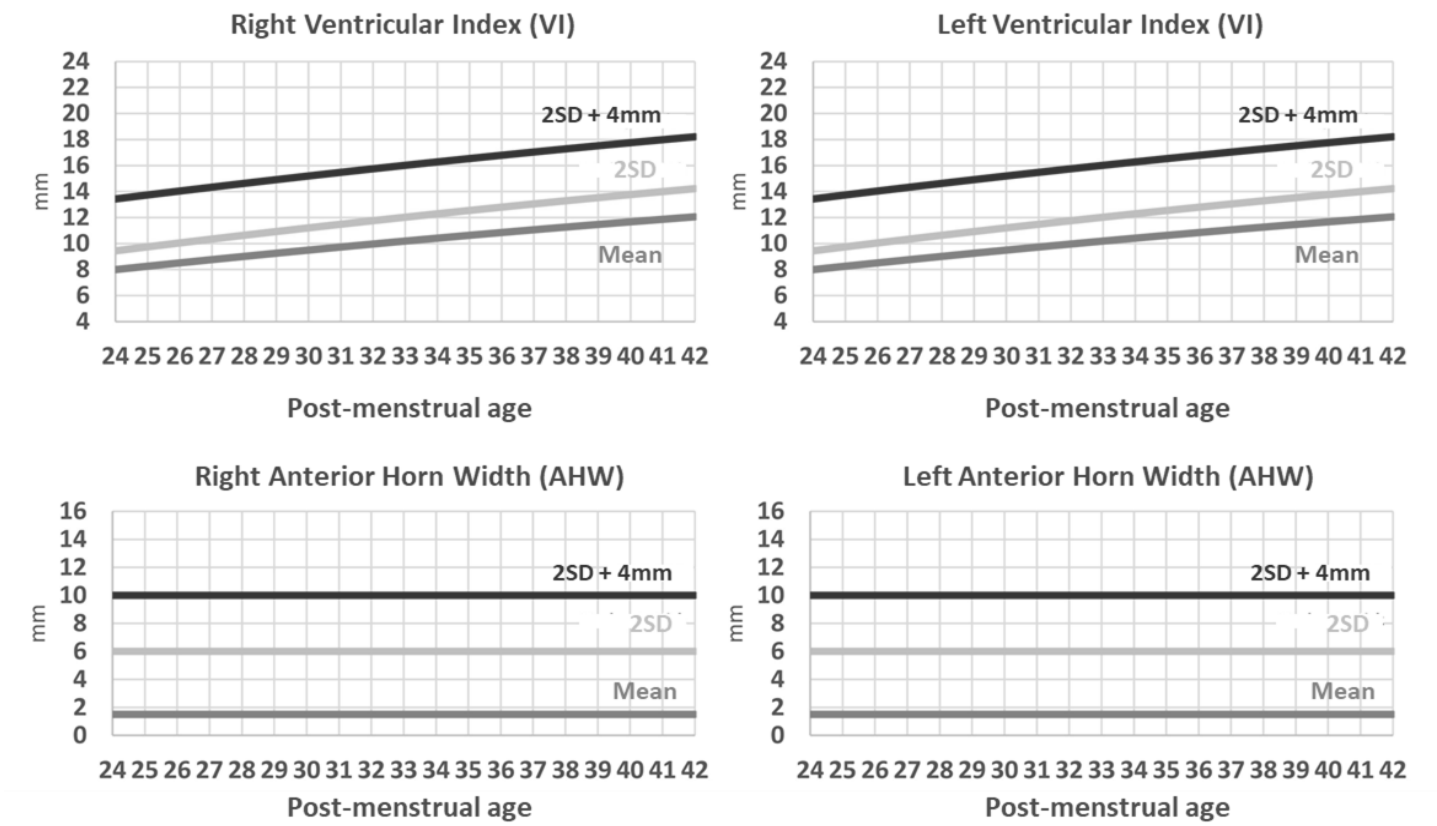
NOTE 3. If patient develops severe illness following the last imaging study (e.g., culture proven sepsis or NEC with instability), consider repeat imaging 4-6 weeks after the event

Post-hemorrhagic ventricular dilatation documentation

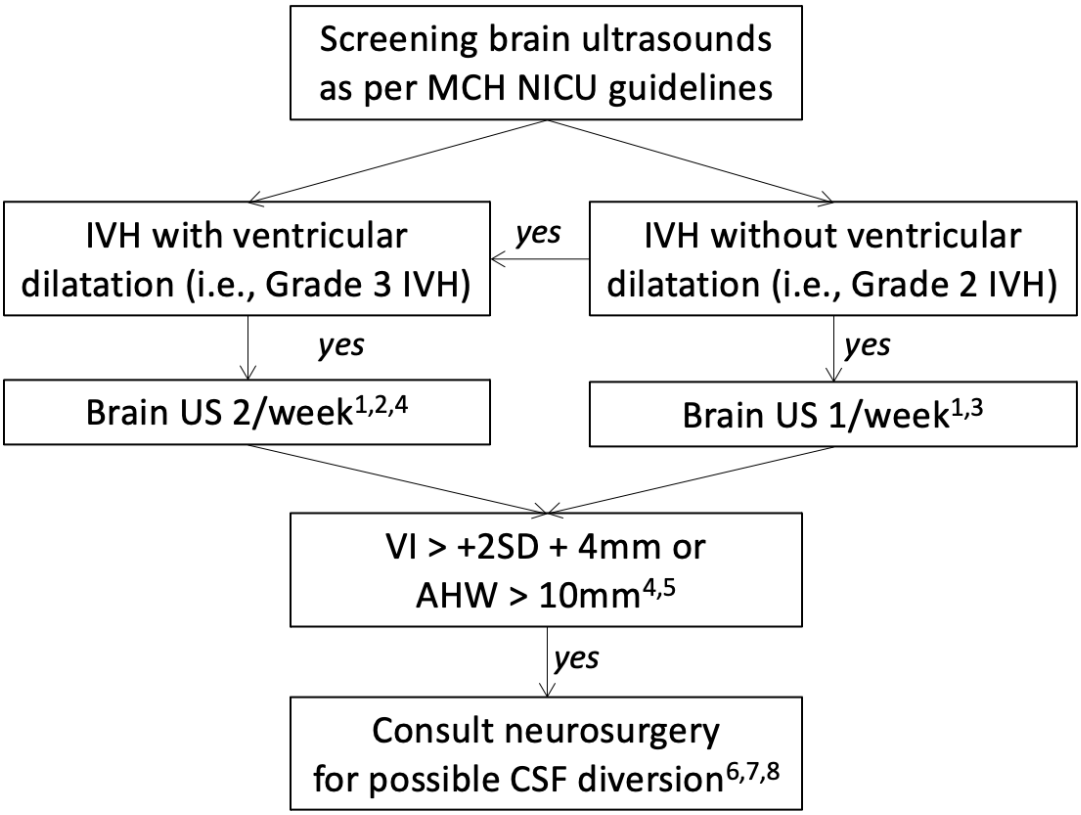
A compléter avec chaque échographie transfontanellaire en cas d'hémorragie intraventriculaire et dilatation / To be completed with each head ultrasound when there is intraventricular hemorrhage with dilatation

Date (yyyy/mm/dd)	**PMA (ww+d)**	**Droite /** Right **VI**	**Gauche /** Left **VI**	**Droite /** Right **AHW**	**Gauche /** Left **AHW**	**MD/NNP Signature**

Légende / Legend:
PMA: Age post-menstruel / Post-menstrual age **VI:** Indice ventriculaire / Ventricular index
AHW : Largeur corne antérieure / Anterior horn width **MD/NNP:** Neonatologist or Neonatal-Nurse Practitioner



Post-Hemorrhagic Ventricular Dilation (PHVD) Clinical Guideline



[1] In the brain US requisition, please request in the Comment box measurements of the ventricular index (VI) and anterior horn width (AHW) bilaterally.

[2] If after 2 weeks of identification of IVH with ventricular dilatation there is stabilization or resolution of the dilatation, the frequency can gradually be reduced to 1 week x 2 weeks, and then to 1x every 2-4 weeks.

[3] If after 2 weeks of identification of IVH without ventricular dilatation there is no dilatation, the frequency can gradually be reduced to 1x every 2-4 weeks.

[4] See guideline for measurement of ventricles. Each time a brain US of a newborn with IVH with ventricular dilatation is performed, the clinician (MD/NNP) should measure (if not done by the radiologist), document, and plot the newborn's VI and AHW.

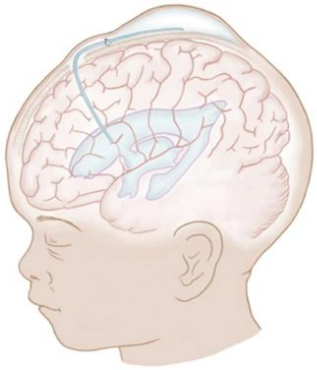
[5] Referring centers may choose to consult neurosurgery when the VI > +2SD or the AHW > 6mm.

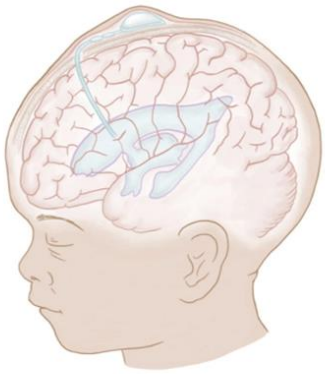
[6] Strategies for CSF diversion include ventricular reservoir or subgaleal shunt and will be determined on a case-by-case basis by discussion with the neurosurgical team.

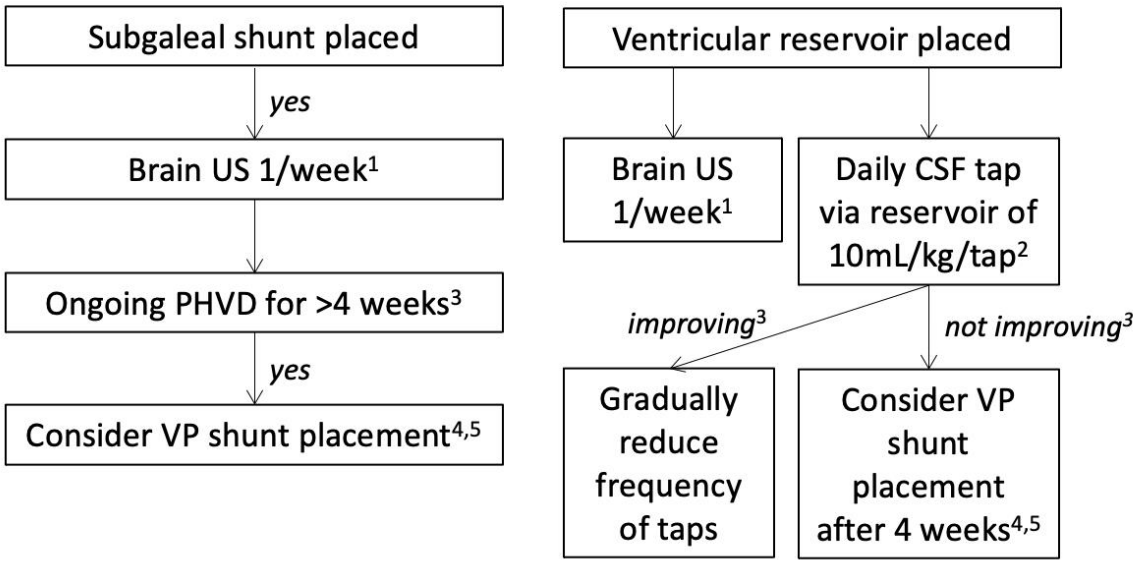
[7] Serial lumbar punctures should be considered if a neurosurgical CSF diversion is delayed or not feasible (e.g., less than 700g, high risk for surgical morbidity) as a temporizing measure.

[8] Repeat Brain US 2x/week while awaiting possible intervention.

Management after placement of subgaleal shunt or ventricular reservoir







[1] Brain US may be requested more than 1/week until size of the ventricles has stabilized.

[2] Rate of CSF aspiration of 1mL/kg/min is recommended, and not to exceed 2mL/min. A separate guideline for aspiration of the ventricular reservoir will be developed for specific technical guidance.

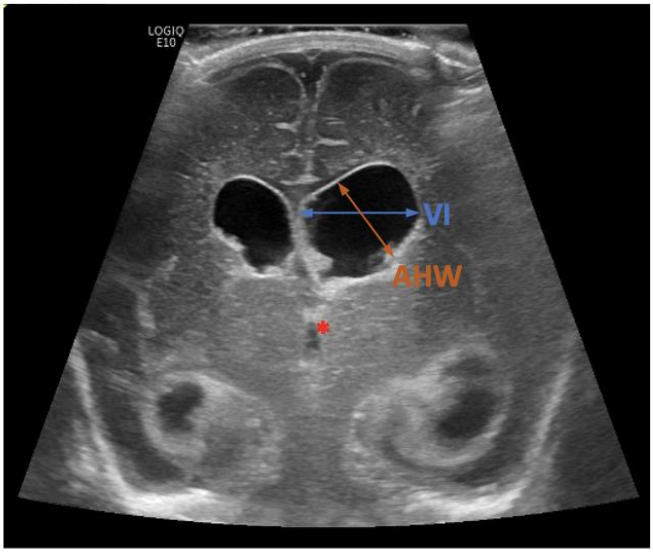
[3] Goal of subgaleal shunt is to achieve VI < +2 SD and AHW < 6mm with minimal subgaleal pocket of fluid.

[3] Goal of ventricular reservoir is to achieve VI < +2 SD and AHW < 6mm with no need for tapping of reservoir.

[4] A minimum weight of 2kg is desirable prior to ventriculoperitoneal shunt (VP shunt) placement

[5] Endoscopic third ventriculostomy with or without choroid plexus cauterization may be considered in lieu of VP shunt in selected infants.

Figures from Sandoval PV et al., Childs Nerv Syst 2020

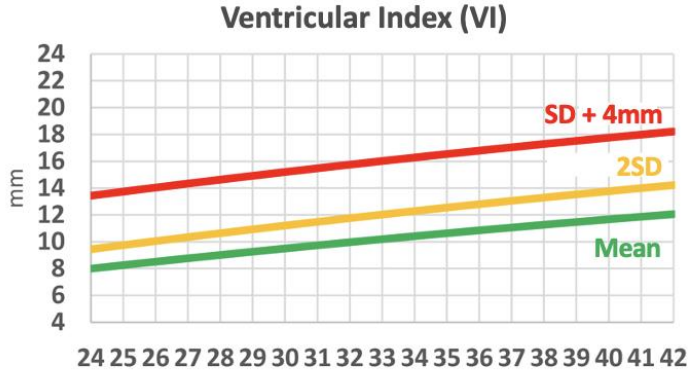


Choose a coronal section where the 3rd ventricle (*) is visible

Measure:

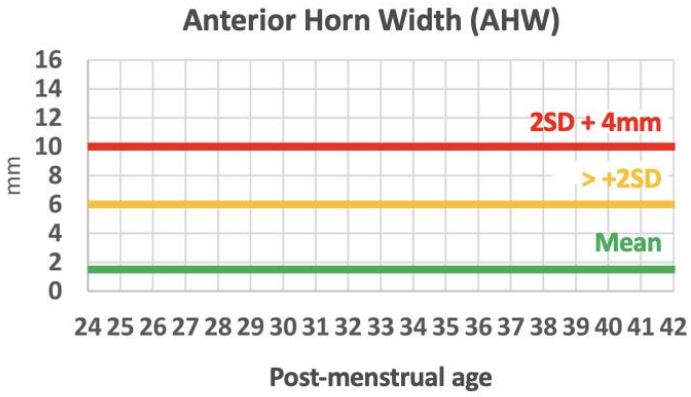
The **Ventricular Index (VI)** is the distance between the midline (falx) and the most lateral border of the lateral ventricle.

The **Anterior Horn Width (AHW)** is measured as the largest diagonal width between the walls of the frontal horns of the lateral ventricles at approximately a 45-degree angle.



Always record and plot measurements for both left and right.

In case of midline shift: Start the VI measurement from the shifted, 'new' midline.



Graphs modified from El-Dib M et al., J Ped 2020.

Retinopathy of prematurity

Screening at MCH: **New criteria: babies < 30 weeks GA or BW < 1200 g.**

Timing of first-time examination based on gestational age at birth:

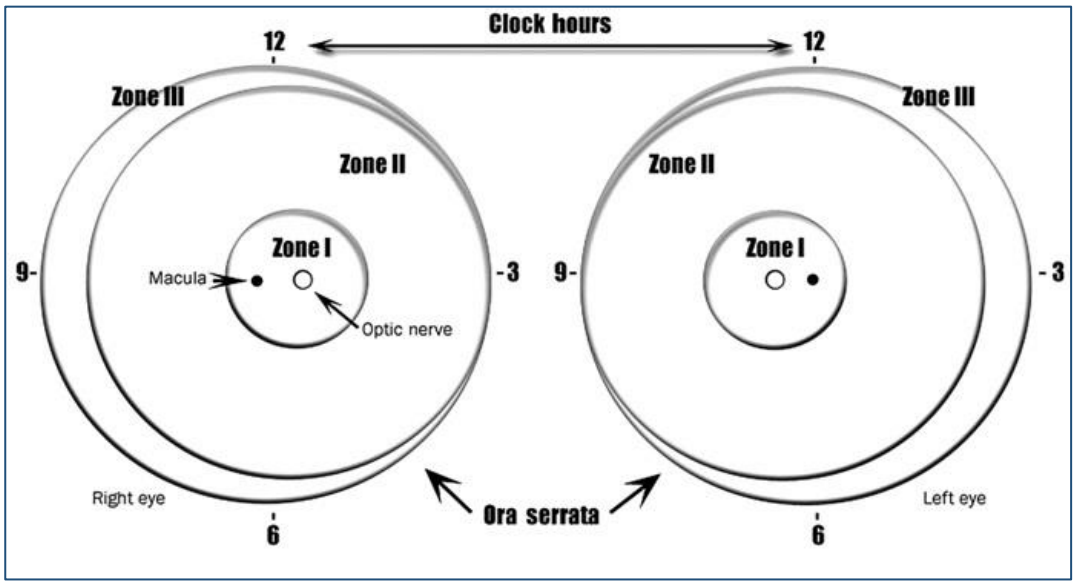
Gestational age at birth (weeks)	Postnatal age at initial examination (weeks)	Chronological age at initial examination (weeks)
22	31	9
23	31	8
24	31	7
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4

Follow up examination: should be recommended by the examining ophthalmologist on the bases of retinal findings classified according to the international classifications.

Timing of ROP follow-up:
1 week or less follow: - Stage 1 or 2 in zone 1 - Stage 3 in Zone 2
1-2 weeks follow up in: - Stage 2 ROP in Zone 2 - Regressing Zone 1 ROP - Immature vascularization in Zone 1 no ROP
2 weeks follow up in: - Stage 1 ROP in Zone 2 - Regressing ROP in zone 2
2-3 weeks follow up in: - Immature vascularization in zone 2, no ROP - Stage 1 or 2 ROP in zone 3 - Regressing ROP in zone 3

Treatment by laser ablation

- Zone 1: any stage with plus disease
- Zone 1: stage 3 without plus disease.
- Zone 2: stage 2 or 3 with plus disease.
- Plus disease: a degree of dilation and tortuosity of the posterior retinal blood vessel



Treatment may also be by bevacizumab (Avastin) intra-vitreal injection (Anti-VEGF)

Apnea of prematurity

Definition: Apnea of prematurity is a developmental disorder in preterm infants that occurs as a direct consequence of immature respiratory control.

Apnea in a preterm has a broad differential including sepsis, don't always assume it's only AOP.

How to treat AOP?

- Caffeine base IV loading dose of 10 mg/kg one dose then maintenance dose of 5 mg/kg/day orally to be started after 24 hours of loading dose.
- Caffeine can be increased up to 7.5 mg/kg/day at NICU MCH if the apnea is not controlled.

Anemia of prematurity

Preterm infants are susceptible to develop anemia secondary to decrease total body iron, reduced erythropoiesis, decreased red blood cell life span, blood sampling and rapid growth.

When to supplement with iron?

Supplement iron to all preterm infants with any birth weight at 1 month of age or when patient reach 100ml/kg/day of enteral feeds and continue until 6 to 12 months of corrected age.

What are the doses of prophylactic iron supplementation?

For preterm infants of all birth weights:
Elemental iron (20 mg/ml ferrous fumarate): 2-4 mg/kg/day, daily or divided in 2 doses.

For infants with malabsorption problems, use ferrous sulfate because it gets absorbed easily through the gut (but it has to be approved!)

What is the therapeutic dosing?

Elemental iron (20 mg/ml ferrous fumarate): 2-6 mg/kg/day, daily or divided in 2 doses

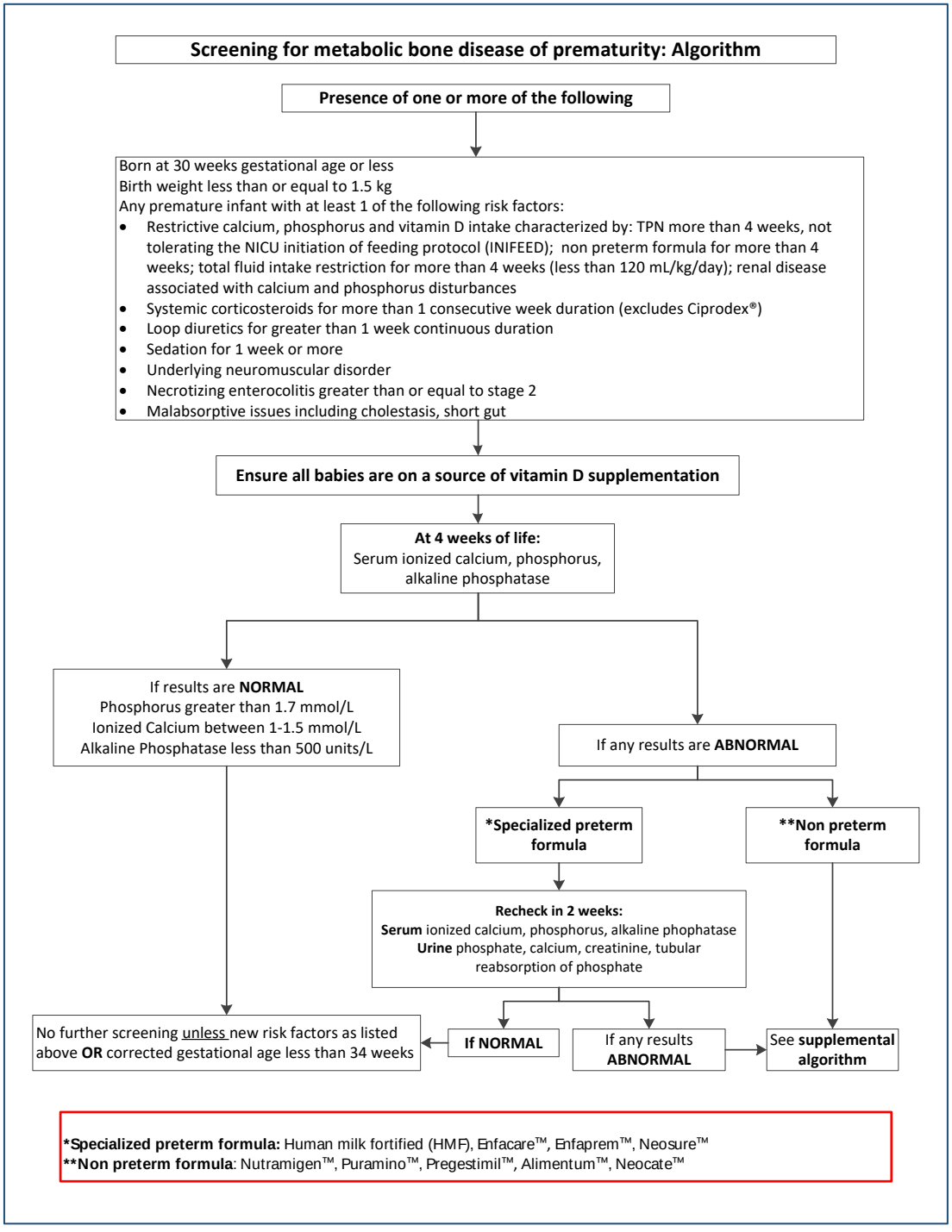
Suggested hemoglobin levels and hematocrit thresholds for transfusing infants with anemia of prematurity

Postnatal age	Respiratory support*	No respiratory support
Week 1	115 (35)	100 (30)
Week 2	100 (30)	85 (25)
Week 3 and older	85 (25)	75 (23)

Data presented as hemoglobin, g/L (hematocrit, %).
*Respiratory support is defined as an inspired oxygen requirement in excess of 25% or the need for mechanical increase in airway pressure (Adapted from

Pint Trial – CPS Statement

Metabolic Bone Disease



Cardiovascular System

Hypertension in neonates

Reference: Flynn, J. T. (2000). Neonatal hypertension: diagnosis and management. *Pediatr Nephrol, 14*(4), 332-341. doi:10.1007/s004670050771

What are the normal BP values for term and preterm neonates?
BP in neonates (preterm and term) admitted to NICU varies with:

- Gestational age
- Chronological age.
- post-conceptual age (corrected gestation).
- Birth weight. Hence it is difficult to define normal BP and hypertension in neonates.

On day 1 to 2 weeks of life, systolic and diastolic BP correlates strongly with gestational age and birth weight.

* Mean BP can be estimated as gestational age +/- 5. For example, for a 26 weeks preterm, the normal range of SBP should be 26 to 31.

> 2 weeks of life

- BP continues to rise rapidly in the first 1 or 2 weeks before the rate of rise slows down (see below).
- The primary determinant of BP is the post-conceptual age.
  Refer to table below for BP values from beyond 2 weeks of age in infants from 26 to 44 weeks postconceptional age.

Estimated BP values in well infants > 2 weeks from 26 - 44 weeks postconceptional age

Postconceptional age	50th percentile	95th percentile	99th percentile
44wks			
SBP	88	105	110
DBP	50	68	73
MAP	63	80	85
42wks			
SBP	85	98	102
DBP	50	65	70
MAP	62	76	81

40wks			
SBP	8o	95	100
DBP	50	65	70
MAP	60	75	80
38wks			
SBP	77	92	100
DBP	50	65	70
MAP	60	75	80
36wks			
SBP	72	87	92
DBP	50	65	70
MAP	59	72	71
34wks			
SBP	70	85	90
DBP	40	55	60
MAP	50	65	70
32wks			
SBP	68	83	88
DBP	40	55	60
MAP	48	62	69
30wks			
SBP	65	80	85
DBP	40	55	60
MAP	48	65	68
28wks			
SBP	60	75	80
DBP	38	50	54
MAP	45	58	63
26wks			
SBP	55	72	77
DBP	30	50	56
MAP	38	57	63

What are the causes of hypertension in neonates?Similar to the causes of hypertension in pediatric population with few additional differential specific for this age.

Renal

1. Renal artery thrombosis (particularly if a UAC has been in place)
2. Renal vein thrombosis
3. Renal artery stenosis or compression (e.g. from tumour, post tight abdominal wall closure)
4. Parenchymal renal disease – congenital (ARPKD and ADPKD) or acquired (ATN from inadequate perfusion e.g. sepsis, asphyxia)
5. Renal hypoplasia
6. Severely obstructed urinary tract
7. Idiopathic arterial calcification
8. Congenital rubella syndrome
9. Haemolytic uraemic syndrome
10. VLBW babies – low renal mass / impaired nephrogenesis / nephrocalcinosis

Cardiovascular

1. Coarctation of the aorta
2. Interrupted aortic arch
3. Distal aortic thrombosis (particularly if a UAC has been in place)
4. Fluid overload

Endocrine

1. Congenital Adrenal Hyperplasia
2. Hyperaldosteronism
3. Hyperthyroidism
4. Adrenal haemorrhage
5. Hypercalcaemia

Chronic Lung Disease

1. May manifest late after discharge from NICU

Medications

1. Dexamethasone
2. Adrenergic agents
3. Bronchodilators
4. Caffeine
5. Neonatal TPN through salt and water overload or hypercalcaemia

Neurological

1. Pain
2. Seizures
3. Intracranial hypertension
4. Drug Withdrawal
5. HIE

Miscellaneous / multifactorial

1. ECMO

MCH Quick reference summary for guideline and management of newborns with congenital heart defect in the early post-natal life

- See NICU weebly for up to date protocol

Septostomy protocol for d-Transposition of Great Arteries – MCH)

See NICU weebly for up to date protocol

Inotrope Support :

Inotropic support in Sepsis or NEC algorithm

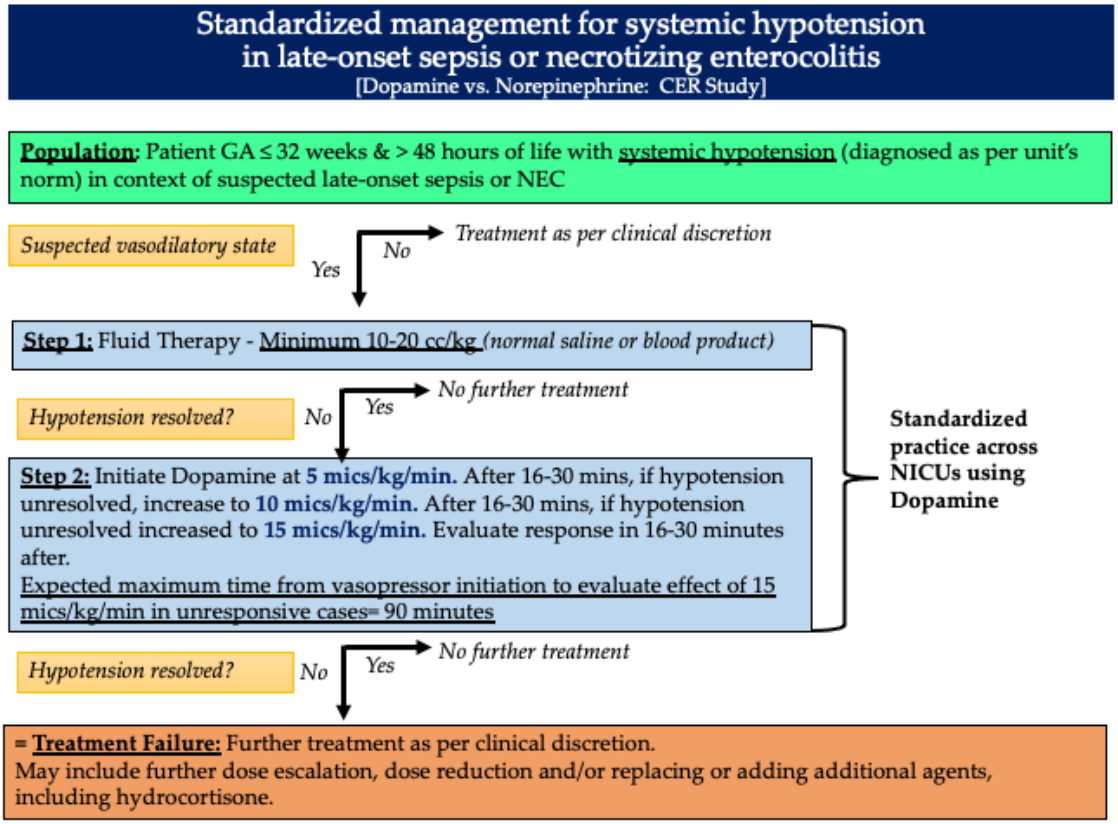


Table 1. **Mechanism of Action and Dosages of Inotropes**[a]

	Vascular			Cardiac		
	Peripheral Vasoconstriction		Peripheral Vasodilation	Contractility	Rate Contractility	
Drug Dosage	α_1	α_2	β_2	α_1	β_1	β_2
Dopamine, μg/kg/min						
0.5–2	0	0	0	0	+	0
2–6	0/+	0	++	0/+	++++	++
>6–10	++++	0	+	+++	++++	+
Dobutamine, μg/kg/min						
2–10	+	0	++	+	++++	++++
1–20	++	0	++++	+++	++++	++++
Epinephrine, μg/kg/min						
0.01–0.1	++	++	+++	+	++++	++++
>0.1	++++	++++	+	+++	++	++
Norepinephrine, μg/kg/min						
0.05–0.5	++++	++++	0/+	++	+++	++

[a]Specific dose responses are based on data in children and adults.

Theoretical concepts:

a) Adrenergic receptors (G-protein coupled)

- β1, β2 : Sinus and AV node ⇒ CHRONOTROPY
  Cardiac muscle ⇒ INOTROPY
- β2: Smooth muscle (vascular) ⇒ VASODILATATION
- α1, α2 : Smooth muscle (vascular) ⇒ VASOCONSTRICTION

b) Phosphodiesterase 3 (PDE3) inhibitors:

PDE3 inactivates cAMP. When inhibited, increase in cAMP, which activates protein kinase A leading to phosphyorylation of proteins → inotropic and lusitropic effect, but pro-arrhytmogenic effect.

c) Physiology reminder:

- BP= CO x SVR
- CO = SV x HR
- SV dependent on pre-Load, afterload and contractility
- SvO2 = SaO2 – (VO2/CO x Hb X 1.34)

d) Inotropes and cardiac support:

Review of Inotropes (by Dr. Altit)

Dopamine:

There is no neonatal data showing that different dosages have different cardiovascular impact in the newborn. Dopamine acts by DA1 receptors (theoretical vasodilation at renal, mesenteric, cerebral and coronary level), β1 (chronotropy, inotropy) and α1 (peripheral vasoconstriction). Adrenergic effect of dopamine works by degradation in norepinephrine and epinephrine (mostly in adrenal medulla – which may be immature or injured in hypoxic ischemia). No clear neonatal data on level of activity of Dopamine beta-hydroxylase (converts to norepinephrine) and Phenylethanolamine N-methyltransferase (converts norepinephrine to epinephrine). Potential impact on endogenous thyroid hormonal secretion. May increase pulmonary vascular resistance.
Initial dosage : 5-10 mcg/kg/min
Usual range: 1 à 20 mcg/kg/min

Dobutamine

Synthetic agonist of β1 (slightly β2): Inotropy and chronotropy (induces arrhythmias). Theoretical benefit in cardiogenic shock. However, increases cardiac O2 consumption. Can induce slight peripheral vasodilation. Can disturb diastolic function as heart rate increases (less filling time).
Initial dosage : 5-10 mcg/kg/min
Usual range: 1 à 20 mcg/kg/min

Epinephrine:

α1 and β1 (slight β2) - Vasoconstriction (α); Inotropy (β); adult data showing that it increases coronary perfusion during cardiac arrest.
Starting dose: 0,05 à 0,1 mcg/kg/min

Range of treatment: 0,01 à 1 mcg/kg/min
Side effects: In healthy volunteers, epinephrine induces hyperglycemia (insulin suppression, increase in hepatic glycogenolysis and in gluconeogenesi) and hyperlactatemia (increase in oxygen consumption).

Milrinone
PDE3 inhibitor, eventually leading to increased intra-cellular calcium. Inotropic, lusitropic, decrease in systemic and pulmonary vascular resistance. Renal excretion (beware in acute kidney injury, such as HIE – can cause intractable hypotension). Decreases afterload in the context of LV and/or RV dysfunction. May cause transient decrease in blood pressure by vasodilation (beware if hypotensive). Long half-life. Bolus rarely use in the context of neonatal indications. May also increase myocardial O2 consumption. In the same family (inamrinone – associated with thrombocytopenia). Can lead to V/Q mismatch (beware in meconium aspiration).
Usual initial dosage : 0,2 à 0,5 mcg/kg/min
Range : 0.2 à 0.75 mcg/kg/min

Norepinephrine
Mostly alpha effect leading to vasoconstriction with some beta-1 effect. Can induce mesenteric and cutaneous ischemia by vasoconstriction. Increases afterload (beware in conditions with poor LV function). Some animal and human data indicate that norepinephrine may have some advantageous effect in reducing pulmonary vasoconstriction (observational studies).
IV infusion usual initial dose: 0,05 à 0,1 mcg/kg/min
Range : 0,01 à 1 mcg/kg/min

Vasopressin
Vasopressin causes vasoconstriction by acting on vascular smooth muscle (skin, skeletal muscle, and splanchnic circulation, it produces potent vasoconstriction, while it seems to activate endothelial receptors potentially leading to NO pathways in the pulmonary vasculature (8). It may be beneficial in certain cases of neonatal pulmonary hypertension. Vasopressin has been associated with improved systemic hemodynamics in animal models. However, there is not enough safety data about its use in the context of HIE related to the impact on LV dysfunction (with its effect on increase of systemic afterload) and with the syndrome of inappropriate secretion of antidiuretic hormone, exacerbating the hyponatremia and water retention. Very limited data in the newborn population.
Usual range: 0.17 to 0.67 milliunits/kg/min (0.01 to 0.04 units/kg/hour). Dosing initiated at low end of range and titrated at 20 minute intervals in 0.01 units/kg/hour increments.

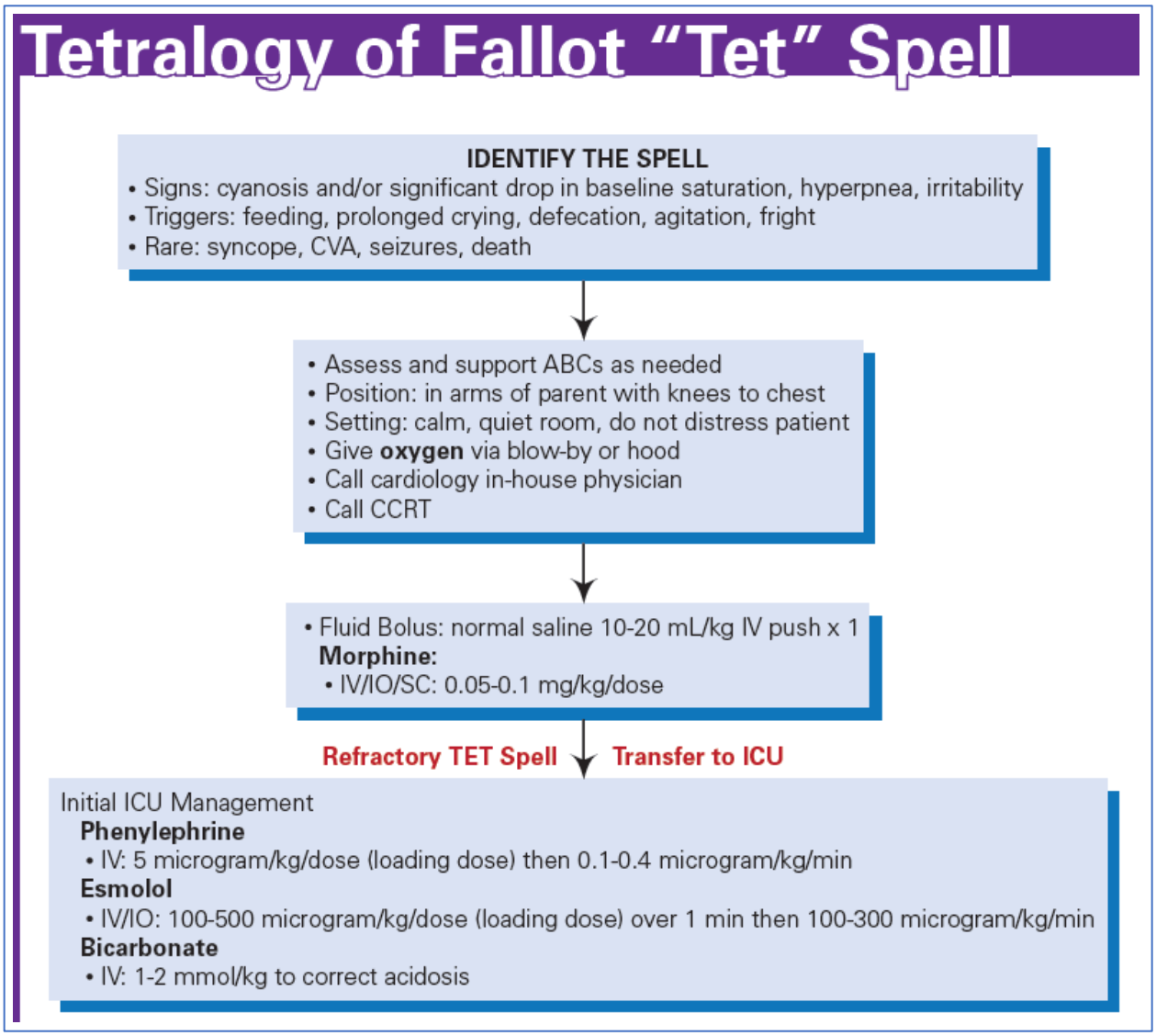
Hydrocortisone:
Appropriate response to stress by the hypothalamic-pituitary-adrenal (HPA) axis is essential for maintenance of hemodynamic stability. Glucocorticosteroids up-regulates the expression of adrenergic receptors in smooth muscles, inhibits nitric oxide synthase expression and decreases the reuptake of norepinephrine leading to an increase in vascular tone and support of myocardial function. Clinical studies have shown that hydrocortisone (HC) was effective in treating refractory hypotension of various causes in preterm infants and that it could decrease the need for inotropic

support. Only one small (n = 46) study prospectively evaluated HC in the context of neonatal sepsis and found no significant differences in outcomes between the groups treated with HC or conventional management. Currently, no study has demonstrated improved clinical outcomes with corticosteroids in acute critical illness related to shock in the newborn population.
Usual dose: 1 mg/kg IV q6h to q12 hr

Levosimandan

Levosimendan is another molecule that has been used to improve cardiac function in pediatric and adult patients with severe heart failure. It has been studied as a primary inotrope in the context of pediatric cardiac surgery. Authors in a study on 110 pediatric patients undergoing cardiac surgery found that: Levosimedan "offers optimized cardiac output with a well-controlled heart rate and a low incidence of arrhythmias in patients undergoing all categories of congenital heart surgeries". Levosimendan is a class III calcium sensitizers and act by increasing sensitivity of myocardial contractile system to intracellular calcium. It also acts as a vasodilating agent, decreasing the afterload and does not increase intracellular Ca and thus, does not impair diastolic relaxation. There is no current data in HIE population and the data in the newborn population at large is very sparse.

TOF – Tetralogy of Fallot – TET spells (hypoxic spells)



Hypoplastic left heart syndrome (HLHS)

Written by G. Altit.

Hypoplastic left heart syndrome (HLHS) have various type: Mitral atresia-Aortic atresia; Mitral Stenosis – Aortic Atresia; Mitral Stenosis-Aortic Stenosis and Mitral Atresia – VSD – Aortic Stenosis. Factors of poor prognostic includes: inter-atrial shunt restrictive or intact, lymphangiectasia, reverse flow in pulmonary veins and TR (which is, in this cardiac anomaly, the atrio-ventricular valve of the systemic ventricle). The Systemic output is fully dependent on ductal patency and these babies are at risk of pulmonary overcirculation and poor systemic perfusion in the post-natal life upon the progressive drop of the Pulmonary vascular resistances.

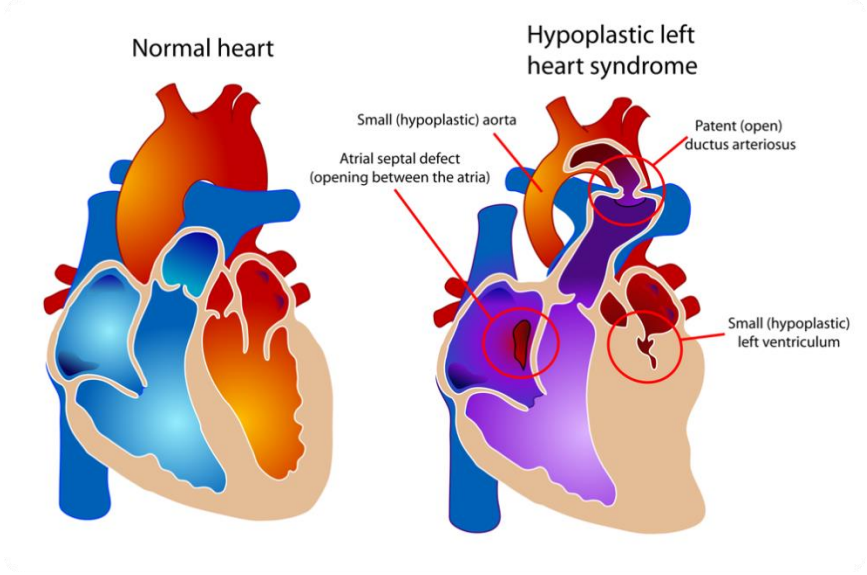
Hypoplastic left heart syndrome (HLHS) has implications in the immediate post-natal life (prostaglandins, neonatal intensive care hospitalization, surgical procedure, etc.), as well as pediatric consequences (further surgical steps) and life-long complications. This condition is associated with life-long challenges, involving: poor cardio-respiratory reserve, failing systemic right ventricle, arrhythmias, multiple procedures/surgeries/hospitalisations, possibility of strokes, bleeds, infections, important risks of severe neuro-developmental impairments, as well as more minor neurological challenges, plastic bronchitis, pulmonary hypertension, protein loosing enteropathy, etc. Many families opt for an approach that involves comfort care at home, with support from the PACT team. Other families opt for the options of palliative surgical procedures, understanding the risks that it entails. These surgeries will not correct the cardiac problem, but will really compensate by re-addressing the blood flow. The goal of these procedures are to achieve a single ventricular physiology. However, in the context of HLHS, there is the particularity that the systemic ventricle is of right ventricular conformation. There is also the added-complexity that these patients have had abnormal perfusion and oxygenation of their systemic organs, including the brain, throughout fetal growth and for years ahead after birth.

Initial Plan in HLHS:

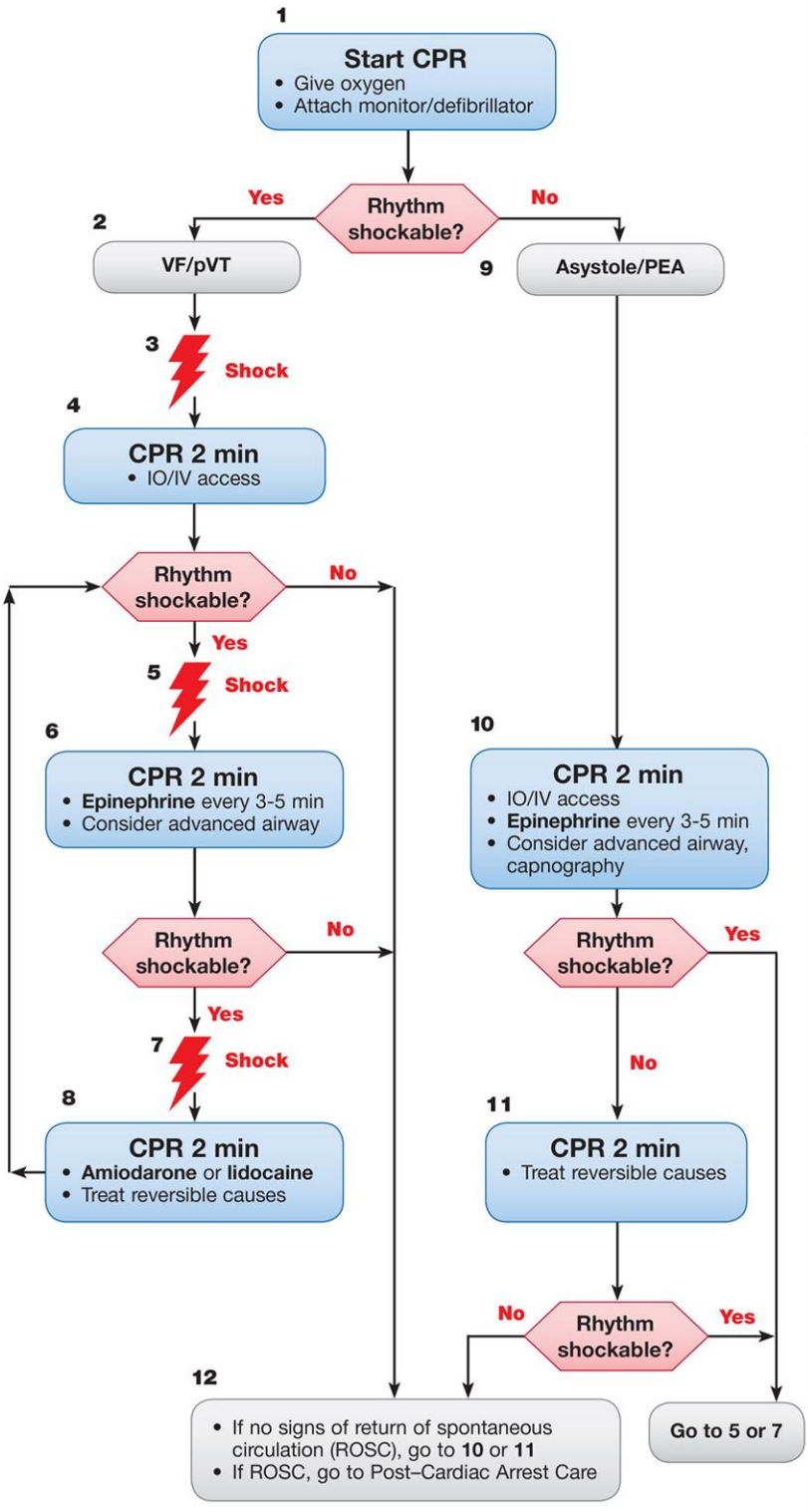
- No neonatal indication for c-section usually. Baby can usually undergo delayed cord clamping.
- Delivery should be done in the room connected to the stabilization room of the NICU and the patient needs to be transported to the NICU immediately after birth (no stay with parents).
- Initial stabilisation includes: rapid central UVL and UAL placement, with prostaglandins (PGE 0.03) started at birth. Will eventually need to plan for a PICC line. - Rapid involvement of cardiology and echocardiography.
- These baby should be kept NPO due to the risk of progressive under-perfusion of the GI tract.
- aBG should be done q6hours and weaned progressively to follow: lactate/CO2/pH (aim for hypercapnia to promote higher PVR). Baby will have a univentricular physiology and saturation more than 75% are adequate. Monitor urine output and perfusion, as at high risk of poor systemic output. Saturation above 90% are often a sign of increasing pulmonary blood flow at the expense of systemic blood flow (Qp above Qs). Oxygen, being a potent pulmonary vasodilator, should be avoided.
- Send cross-match, coombs, CBC, blood gaz initially. The baby will need to have a bilirubin, 61lbumin and baseline organ markers at 24 hours of life (urea creat, ALT, AST).
- Follow blood glucose considering maternal GDM
- Genetic work-up: genetic consultation (CGH normal but may need further testing such as for ciliary disorders), Brain MRI, abdominal ultrasound. No need for HUS if Brain MRI done.
- Will need Social Services consultation and Lactation consultant involvement. Nursing team of cardiology will be involved. Cardiac surgery team will need to meet the family in the post-natal life, in conjunction with cardiology.

Compassionate care at birth, staged palliation and heart transplantation are usually discussed by the cardiologist. The final decisions regarding the different options are taken with the family following birth and neonatal assessment. As such, it might be that these babies require palliative care team to be involved once the care plan is more precise and aligned with the family wishes.

If this is the wish of the family, and if the newborn requires a single-ventricular staged palliation surgery, the first stage palliation, the Norwood procedure, involves: an atrial septectomy, the creation of a sustained source of systemic output (via a BT shunt - between usually a right brachiocepahlic artery and a pulmonary artery - or a Sano Shunt - between RV and PA), as well as using the pulmonary artery as the neo-Aorta (Damus–Kaye–Stansel (DKS) procedure). The Norwood is usually performed in the first two weeks of life. The cardiologist explained to the family that the baby is likely to remain in hospital until the second operation called the Glenn operation, and then stay a few more weeks before being discharged. Mortality is high for the Norwood procedure and comorbidities are frequent. The overall survival is around 50-60% for the three stages. The neurological outcome is a prominent issue as many children will experience challenges but there are increasing survivors with this condition reaching adulthood.



PALS – Cardiac Arrest



CPR Quality

- Push hard (≥⅓ of anteroposterior diameter of chest) and fast (100-120/min) and allow complete chest recoil.
- Minimize interruptions in compressions.
- Avoid excessive ventilation.
- Change compressor every 2 minutes, or sooner if fatigued.
- If no advanced airway, 15:2 compression-ventilation ratio.

Shock Energy for Defibrillation

First shock 2 J/kg, second shock 4 J/kg, subsequent shocks ≥4 J/kg, maximum 10 J/kg or adult dose

Drug Therapy

- **Epinephrine IO/IV dose:** 0.01 mg/kg (0.1 mL/kg of the 0.1 mg/mL concentration). Repeat every 3-5 minutes. If no IO/IV access, may give endotracheal dose: 0.1 mg/kg (0.1 mL/kg of the 1 mg/mL concentration).
- **Amiodarone IO/IV dose:** 5 mg/kg bolus during cardiac arrest. May repeat up to 2 times for refractory VF/pulseless VT.

-OR-

Lidocaine IO/IV dose: Initial: 1 mg/kg loading dose. Maintenance: 20-50 mcg/kg per minute infusion (repeat bolus dose if infusion initiated >15 minutes after initial bolus therapy).

Advanced Airway

- Endotracheal intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm and monitor ET tube placement
- Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions

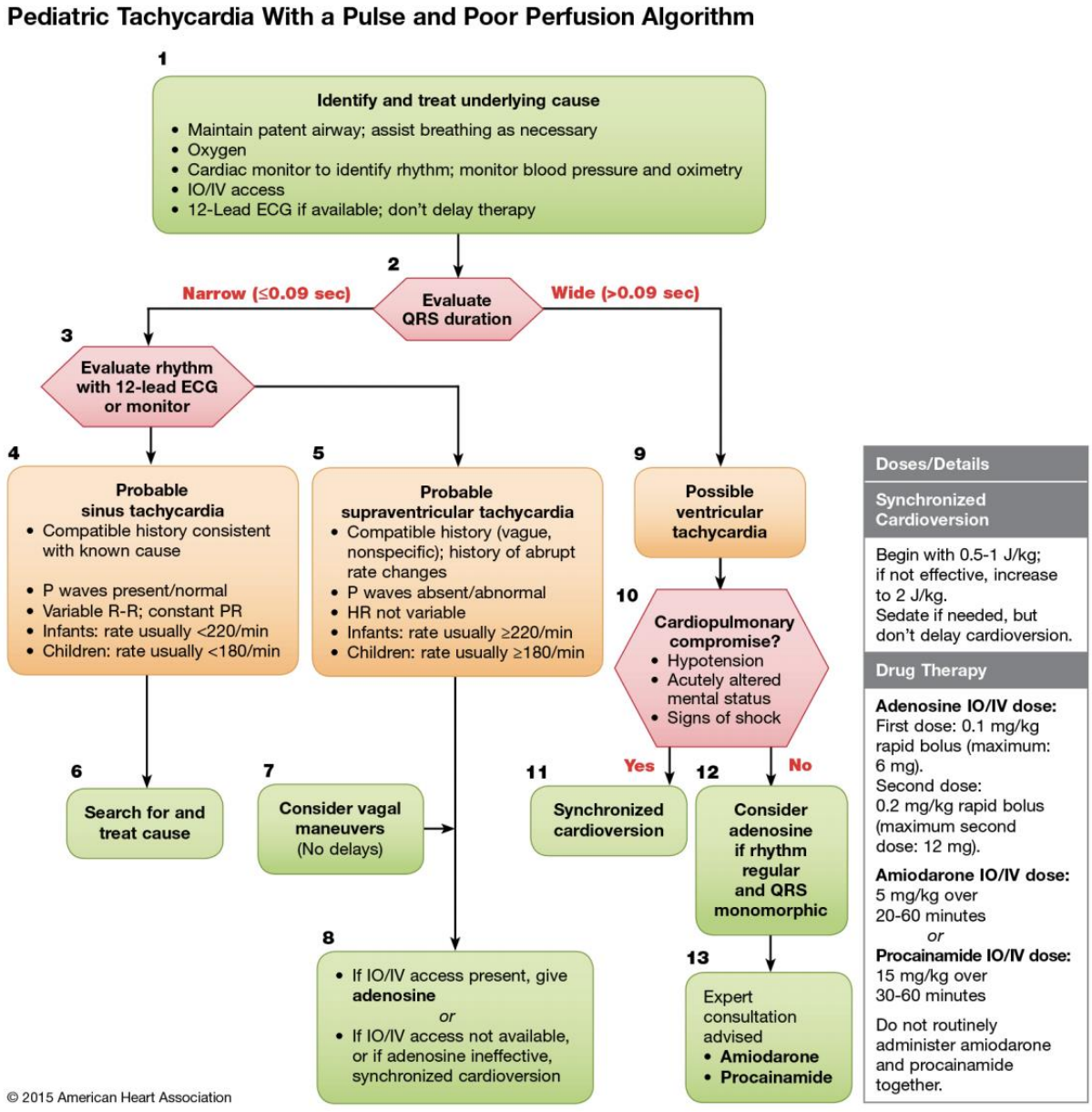
Return of Spontaneous Circulation (ROSC)

- Pulse and blood pressure
- Spontaneous arterial pressure waves with intra-arterial monitoring

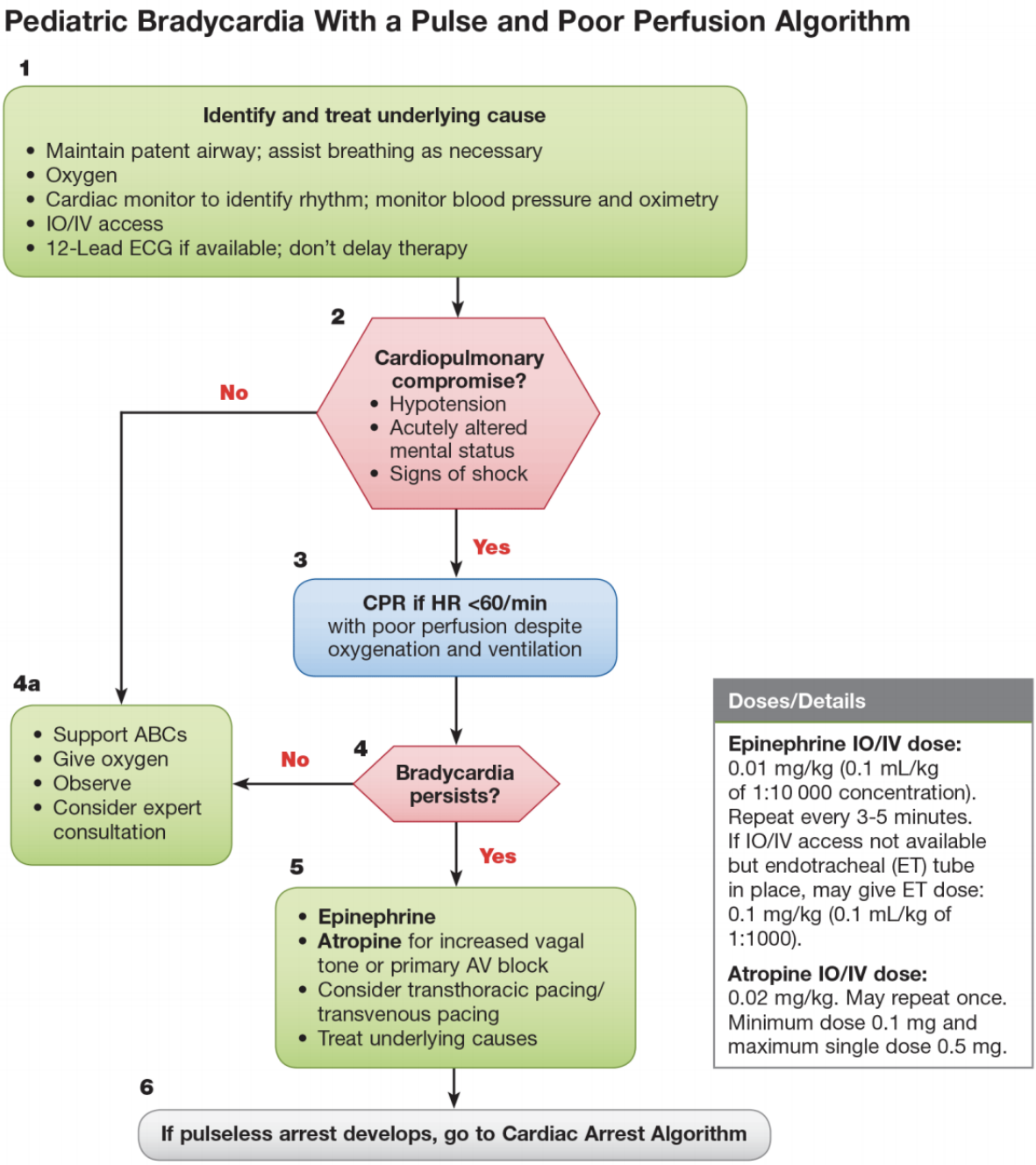
Reversible Causes

- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypoglycemia
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

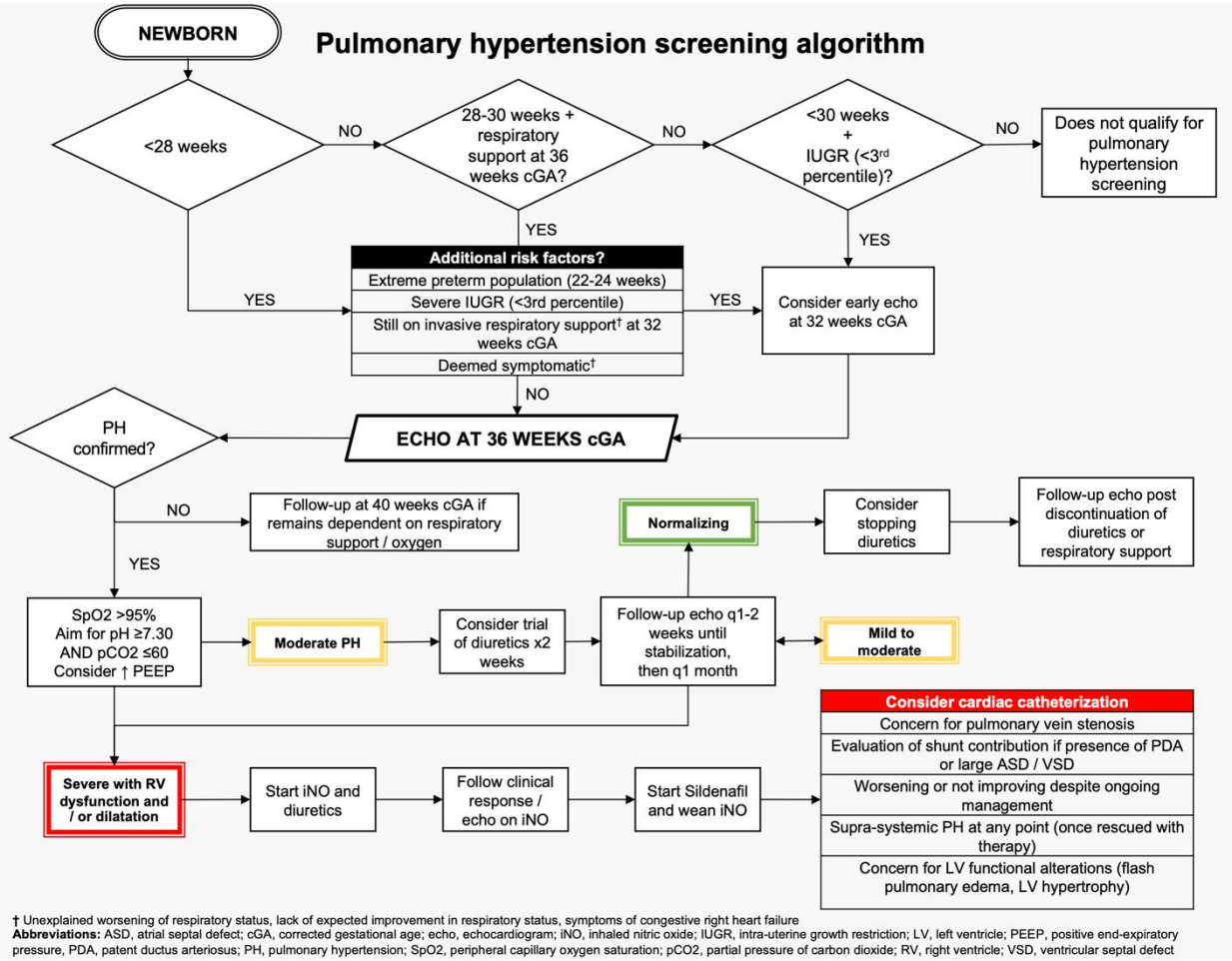
Tachycardia – PALS – SVT (Supra-ventricular tachycardia)



Bradycardia – PALS



Pulmonary hypertension screening guidelines:



PH severity (modified from Pediatric Pulmonary Hypertension Network)	
No PH	Right Ventricular systolic pressure <1/3 systemic pressure by tricuspid regurgitant jet (TRJ) or other metric (VSD, PDA); septal position round; LV eccentricity index <1.3; no RV hypertrophy; normal RV size and function
Concerns of echocardiographic signs of pulmonary hypertension mPAP > 20 (pulmonary insufficiency jet) sPAP > 40 (TRJ > 35 mmHg; VSD/PDA gradient) PAAT/RVET < 0.25 (RVET/PAAT > 4) Eccentricity index > 1.3 Septal flattening at peak systole D-RV / D-LV > 1.00 Inter-atrial or post-tricuspid shunt with a right-to-left directionality Signs of pulmonary venous stenosis	
Mild	RV systolic pressure 1/3-1/2 systemic pressure; septal flattening in systole, RV function normal
Moderate	RVSP ½-2/3 systemic pressure; septum flattening in systole, RVH or dilatation, RV with altered function (TAPSE 6.5 to 8 mm; FAC: 20-30%):

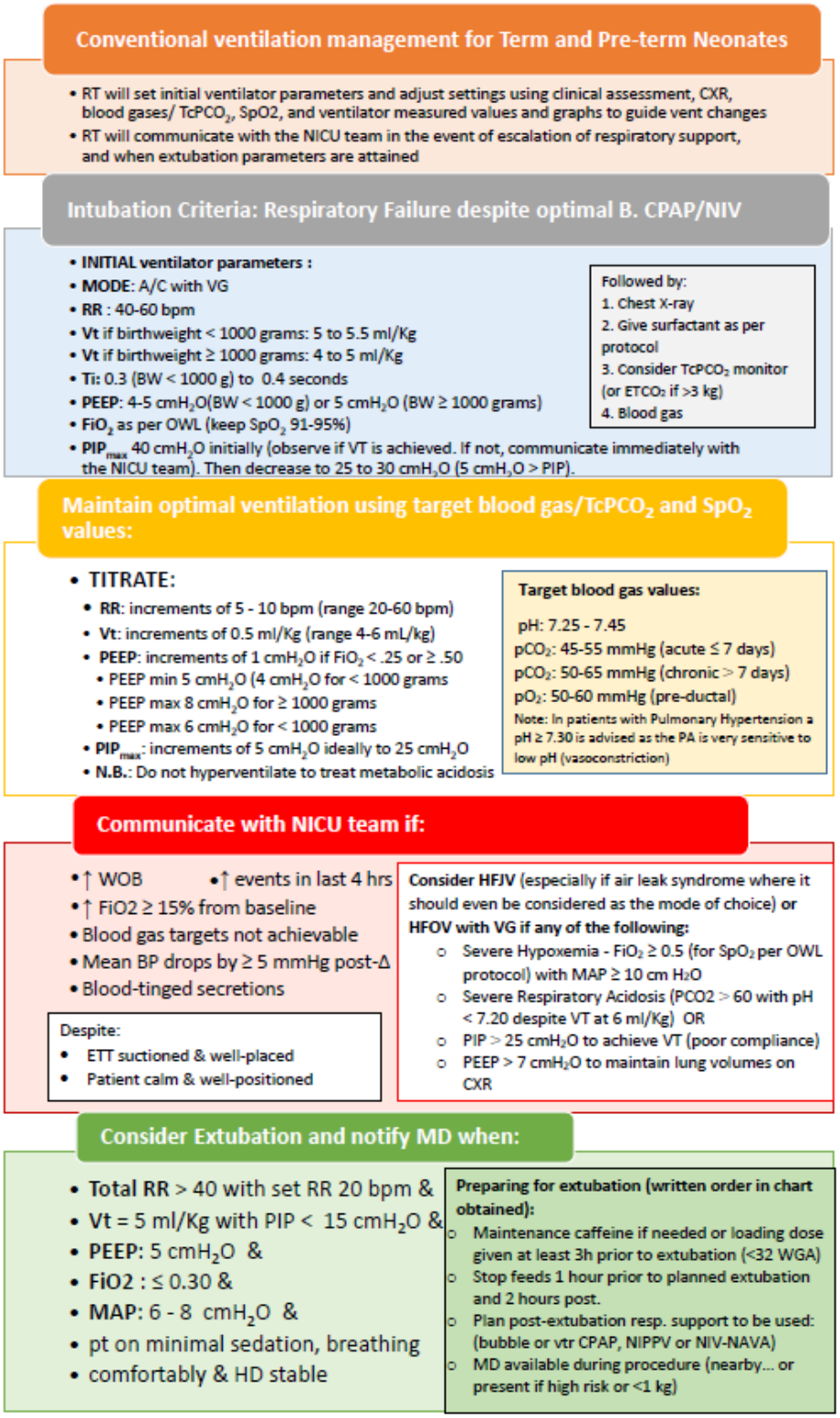
	- TAPSE (Normal > 8 mm; <Zscore -2 abnormal at 36 weeks would be 6.5 mm) o TAPSE Z-score: http://dev.parameterz.com/tapse - FAC: >30% normal (Ref Levy PT, Dioneda B, Holland MR, Sekarski TJ, Lee CK, Mathur A, et al. Right ventricular function in preterm and term neonates: reference values for right ventricle areas and fractional area of change. J Am Soc Echocardiogr. 2015;28:559–69)
Severe	RV systolic pressure >2/3 systemic pressure; If present, shunt (inter-atrial, post-tricuspid) with predominant R-L gradient, septal bowing, RVH, severe RV dysfunction, RV dilatation. Dilated right atrium, dilated inferior vena cava are also evidence of RA hypertension and RV diastolic dysfunction. Some concerning signs for severe alteration of RV function, • TAPSE <6.5 mm • Pericardial effusion • FAC < 20% *Clinical signs of concerns for severe RV dysfunction:* • Hypoxia secondary to R->L shunting to unload RA • Hepatomegaly • Hypotension • Growth failure

Respiratory System:

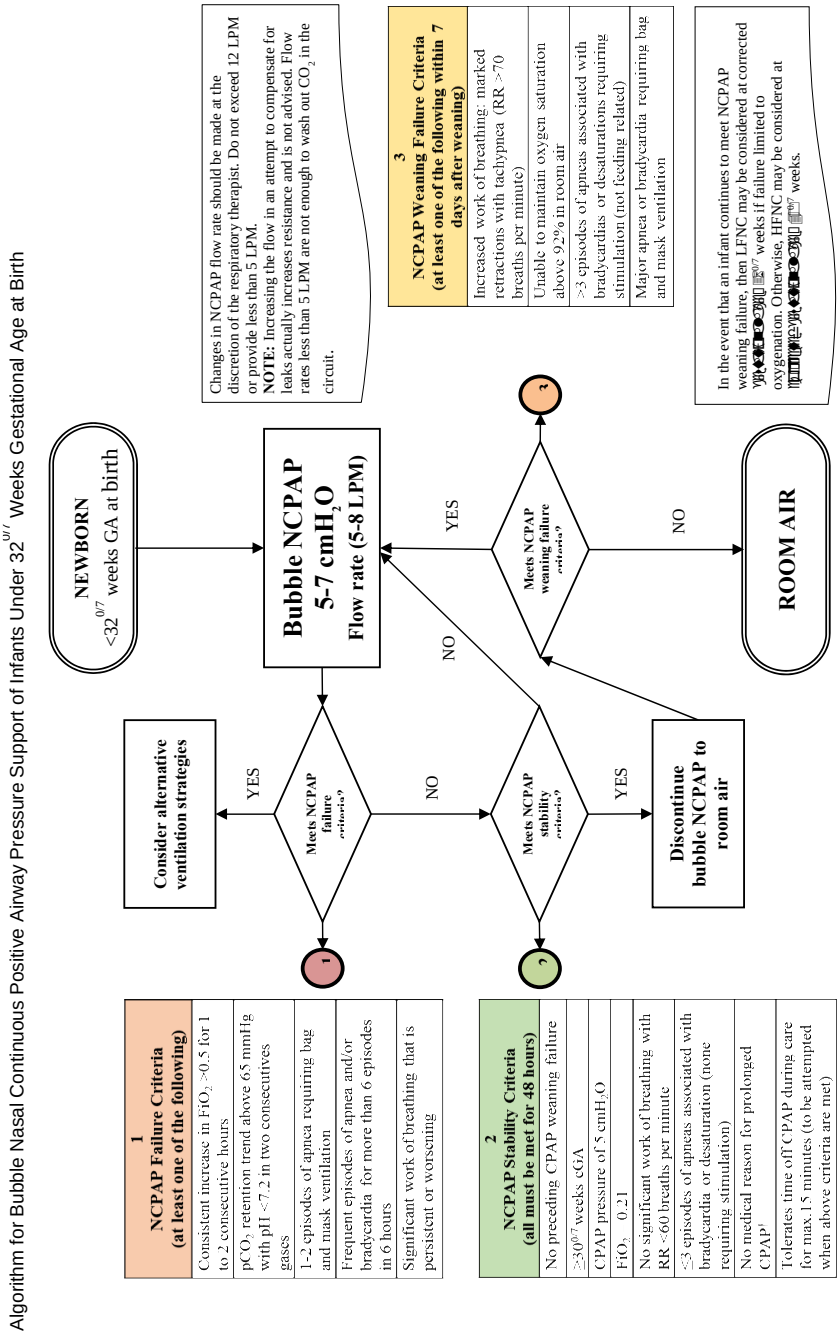
Ventilation

See Neumann and Sternberg, Pediatric Anesthesia 2013
See https://uihc.org/childrens/educational-resources/pulmonary-nicu-handbook

Weaning Ventilation Protocol:



BCPAP protocol and algorithm for discontinuation

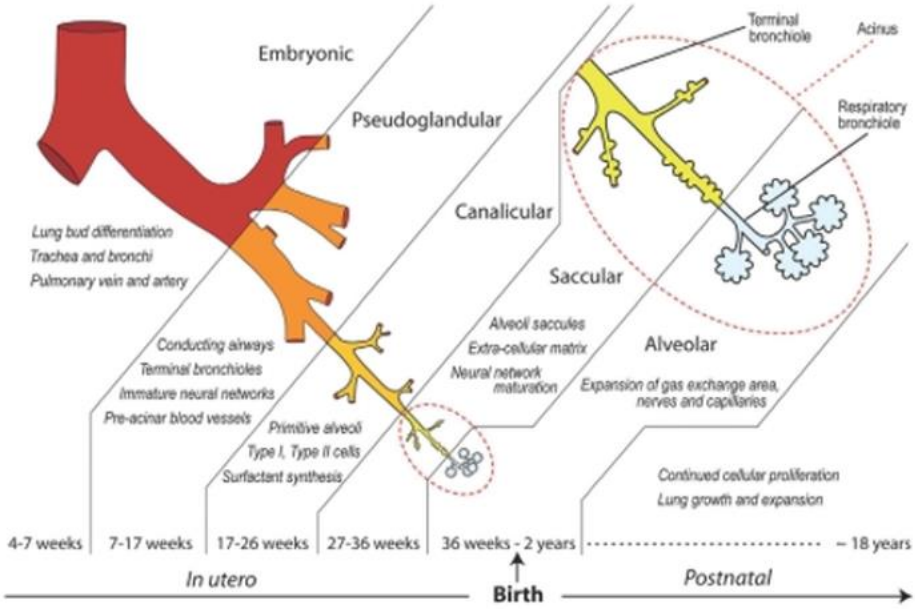


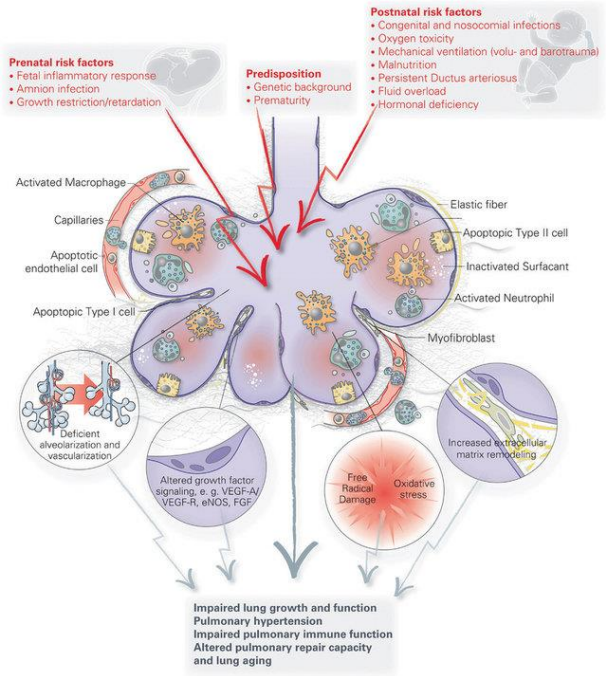
Bronchopulmonary Dysplasia:

Prepared by G. Altit

This is meant as a quick review.

<u>Lung development in the premature newborn:</u>





Extreme premature newborns have immature lungs with various degree of ongoing development of the parenchymal, airway and vascular structures. BPD develops at the inter-play between: acute and chronic inflammation, genetic predisposition, in-utero and post-natal environment, as well as exposure to post-natal insults (necrotizing enterocolitis, mechanical ventilation, oxygen supplementation, persistent fetal shunts, suboptimal nutrition, post-natal corticosteroids, bacterial colonization, etc.) nested within immature repair mechanisms and ongoing fibrosis.

In premature infants: Parenchyma damaged by reactive oxygen species, volu-trauma, baro-trauma, atelecta-trauma, excessive volume and pressure from PDA during systole and diastole. Also: Immature repair / defense mechanisms; Inflammation (NEC, infections, ventilation); Disturbed growth / sub-optimal nutrition; Post-natal steroids (alters vascular growth); Abnormal

vascular pruning and remodelling; Muscularisation of pulmonary vasculature (arteries, veins); Abnormal response to endogenous and exogenous substances regulating pulmonary vascular tone; V/Q mismatch. All this + Lung Fibrosis, Vascular remodelling leads to: Increase PVR, Heterogenous vascular tone, Decreased vascular territory, Abnormal venous drainage.

Risk factors for PH: extreme prematurity, IUGR (pre-eclampsia, gestational HTN), oligo, duration of ventilation, NEC and prolonged O2

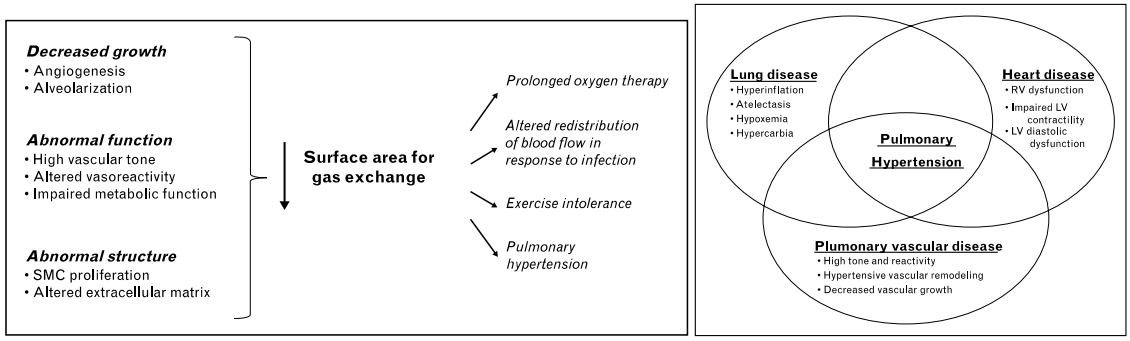


Table: Definition of bronchopulmonary dysplasia (BPD) - Diagnostic and Severity as per 2001 National Institute of Child Health and Human Development consensus workshop criteria and severity

TABLE 1. DEFINITION OF BRONCHOPULMONARY DYSPLASIA: DIAGNOSTIC CRITERIA

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

BPD definition with severity (Modified by Abman)

BPD severity	Definition (Modified from Jobe and Bancalari[4])
None	O_2 treatment <28 d and breathing room air at 36 wk PMA or discharge home, whichever comes first
Mild	O_2 treatment at least 28 d and breathing room air at 36 wk PMA or discharge home, whichever comes first
Moderate	O_2 treatment at least 28 d and receiving <30% O_2 at 36 wk PMA or discharge home, whichever comes first
Severe (type 1)	O_2 treatment at least 28 d and receiving ≥30% O_2 or nasal CPAP/HFNC at ≥36 wk PMA
Severe (type 2)	O_2 at least 28 d and receiving mechanical ventilation at ≥36 wk PMA.

New definitions explored for BPD and association with later outcomes:

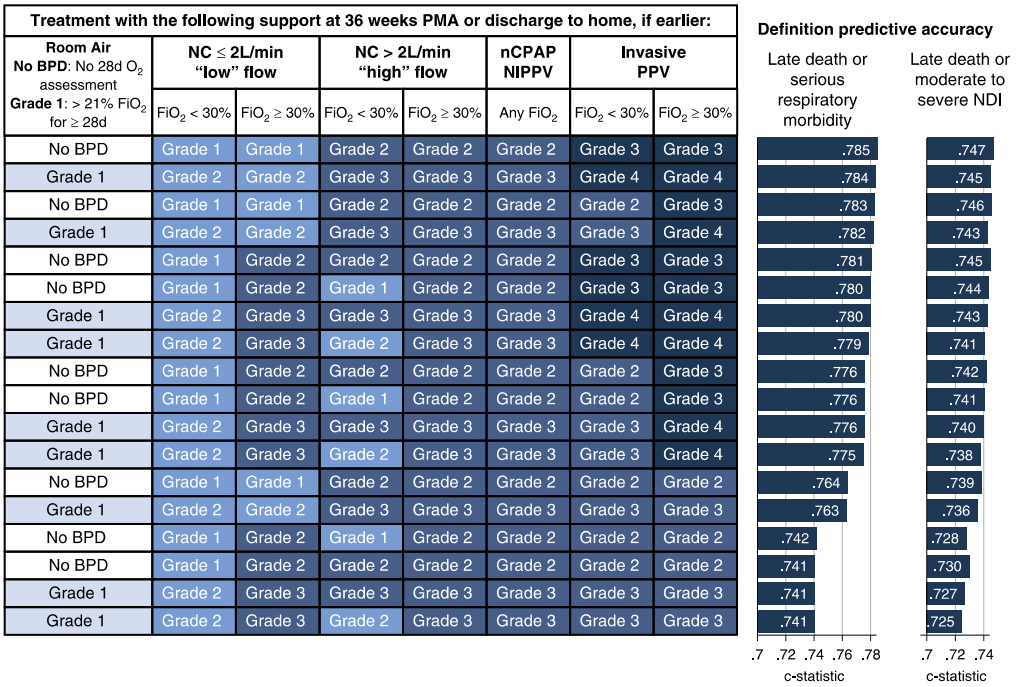


Figure 2. Rank order of the 18 evaluated definitions of bronchopulmonary dysplasia (BPD). The definitions are ordered from highest (top) to lowest (bottom) accuracy for predicting death between 36 weeks' postmenstrual age (PMA) and 18- to 26-month follow-up or serious respiratory morbidity. Concordance (c) statistic values were calculated using logistic regression, adjusting for gestational age, birth weight, sex, small for gestational age, race/ethnicity, treatment with antenatal corticosteroids, treatment with antenatal magnesium, maternal level of education, insurance type, primary caregiver marital status, and study center. NC = nasal cannula; nCPAP = nasal continuous positive airway pressure; NDI = neurodevelopmental impairment; NIPPV = nasal intermittent positive pressure ventilation; PPV = positive pressure ventilation.

Jensen, Dysart, Gantz, et al.: Defining Bronchopulmonary Dysplasia

The optimal definition (first one on Figure 2) categorized BPD severity according to the mode of respiratory support administered at 36 weeks' PMA, regardless of the prior duration or current level of oxygen therapy. On the basis of these diagnostic criteria, infants breathing in room air at 36 weeks' PMA did not have BPD. Disease severity among the remaining infants was classified according to treatment with the following support: grade 1, nasal cannula at flow rates <2 L/min; grade 2, nasal cannula at flow rates >2 L/min or noninvasive positive airway pressure; and grade 3, invasive mechanical ventilation. This definition produced the highest predictive accuracy.

Prevention of BPD:

- BCPAP to optimize lung growth (baby needs a PEEP to maintain FRC and support their breathing while they are growing). Too many trials of weaning of the BCPAP can lead to respiratory fatigue and calories are not invested in supporting brain and body growth/maturation. Refer to BCPAP protocol.
- If intubated: permissive hypercapnia (>45 CO2). The aim is really to maintain a pH that is adequate (>7.30), more than driving the CO2 down. Adjust PEEP to maintain appropriate expansion (avoid collapse or over-inflation). Consider JET ventilation if heterogeneous disease (such as in pulmonary interstitial emphysema). Consider HFOV if the generate PIP are excessive.
    - After 14 days of life, consider use of DART protocol with dexamethasone to promote extubation to non-invasive support (case by case basis).
- If patient is on 21% while on non-invasive support, and is weaned from CPAP but suddenly requires O2 support -> consider restarting CPAP (means that there are some collapse and V-Q mismatch and patient is probably not ready).
- AT MCH: Avoid HFNC in the population of extreme premature newborns.
- Caffeine starting after 24 hours of life.
    - May support diminish intermitted desaturations, apnea and bradycardia events.
    - Before 24 hours of life, A/B events can be the reflection of RDS and caffeine may mask these clinical events, preventing from benefiting the window for intubation and surfactant

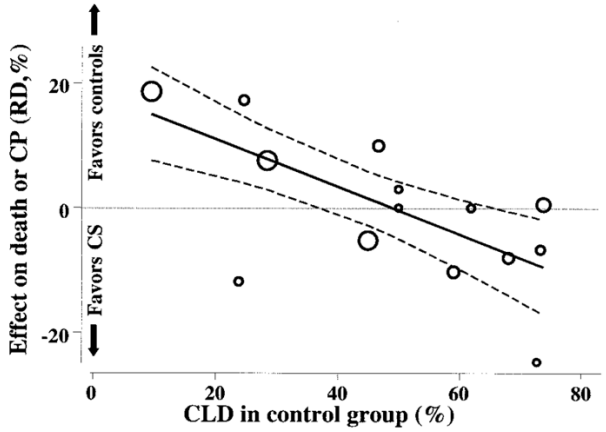


Fig 1. RD (%) for death or CP among all participants versus rate of CLD (%) in the control group. Each study is shown by a circle whose area is proportional to that study's weight. The control rates for CLD in the individual studies are given in Table 1, column 5. Regression line and its 95% CI are shown. Regression equation: $Y = 18.7 - 0.38X$; $P = .002$. CS, corticosteroids.

Impact of Postnatal Systemic Corticosteroids on Mortality and Cerebral Palsy in Preterm Infants: Effect Modification by Risk for Chronic Lung Disease;

The effect of postnatal corticosteroids on the combined outcome of death or CP varies with the level of risk for CLD. Hence, as the risk of BPD increases, the risk of poor outcomes increases.

Pediatrics 2005;115:655–661

Extubation (DART trial protocol)/ Bronchopulmonary dysplasia (IV/PO):

0.075 mg/kg/dose every 12 hours for 3 days
0.05 mg/kg/dose every 12 hours for 3 days
0.025 mg/kg/dose every 12 hours for 2 days
0.01 mg/kg/dose every 12 hours for 2 days

Randomized Trial of 42-Day Compared With 9-Day Courses of Dexamethasone for the Treatment of Evolving Bronchopulmonary Dysplasia in Extremely Preterm Infants
Bonnie L.Marr MD, Barbara B.Mettelman PhD, Michelle M.Bode MD, Steven J.Gross MD

In the study - infants eligible if 24-27 weeks; and at 10-21 postnatal days, met defined respiratory criteria: radiographic findings consistent with evolving BPD and ventilator support with sustained (≥18 hours) FiO_2 ≥60% and mean airway pressure ≥8 cm H_2O. Excluded if preexisting conditions with known increased risk for neurodevelopmental impairment : birthweight or head circumference <10th percentile, significant congenital malformations including chromosomal anomalies and congenital heart disease, grade IV intracranial hemorrhage, a 5-minute Apgar score <3, or a history of seizures or base deficit of >15. Infants with sepsis or significant patent ductus arteriosus became study eligible if these issues were treated before the end of the enrollment window.

Dexamethasone in the study:

- Dexamethasone 0.5 mg/kg/day first 3 days and 0.3 mg/kg/day for the next 3 days.
- Dexamethasone then reduced by 10% every 3 days until a dose of 0.1 mg/kg reached on day 34.
- Thereafter, dexamethasone is maintained for 3 days, alternated daily with saline placebo for 1 week, and then discontinued.

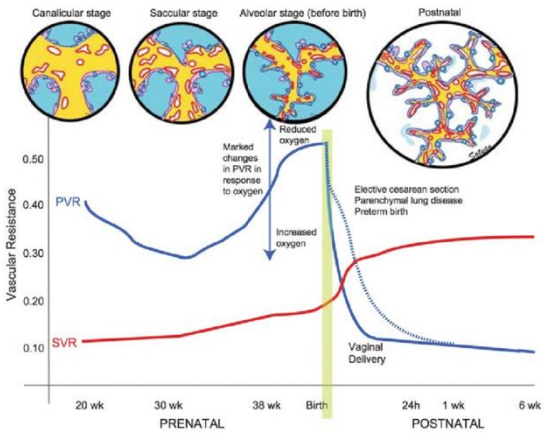
BPD - pulmonary Hypertension

Premature infants should have an echocardiogram performed to screen for PH in the following scenarios:

1. At the time of formal BPD diagnosis as per current practice (36 weeks postmenstrual age.
2. Severe hypoxemic respiratory failure shortly after birth attributed primarily to persistent pulmonary hypertension of the newborn (PPHN) physiology despite optimal management of underlying lung disease.
3. Continued need for ventilator support at postnatal day 7, as echocardiogram evidence of PH at day 7 suggests high risk for BPD and may alter therapy.
4. With sustained need for significant respiratory support at any age, especially with recurrent episodes of hypoxemia.

Normal Pulmonary artery (PA) pressure = 15/5 (mean of 10) after 3 months of age

- First 3 months: PVR dropping and should be < systemic.



<u>Abnormal PA pressure defined:</u>

- Mean PAP ≥ 20 mmHg (2018 definition, before 25 mmHg – measured by catheterization but can be estimated by echo), or
- Systolic PAP ≥ 40 mmHg (estimated by Echo), using:
    - TRJ ≥ 35 mmHg (assuming a Right Atrial pressure of 5)

PH is usually assumed by echocardiography if any of the following present:

- a mean pulmonary arterial pressure (mPAP) estimate ≥ 20 mmHg (using a pulmonary insufficiency jet) or
- an estimated systolic pulmonary arterial pressure (sPAP) ≥ 40 mmHg. sPAP estimated by echocardiography using either:
    1. tricuspid regurgitant jet (TRJ) ≥ 35 mmHg (plus expected right atrial pressure of 5 mmHg), when a full Doppler envelope is available,
    2. <u>Restrictive</u> ventricular septal defect (VSD) or patent ductus arteriosus (PDA) velocity gradient.
    3. A ratio of the estimated sPAP to the systemic systolic blood pressure (sBP) at the time of the echocardiography is important to compare the two compartments
- Flattening of the septum at the end of systole is a subjective surrogate of increased pulmonary pressure – indicating that there is relative iso-systemic pulmonary pressures (around 2/3 of systemic).
    1. Round LV simply tells you that the systolic RV pressure is less than systolic LV pressure (but the sPAP could still be higher than normal).
    2. Isosystemic = Flat Interventricular septum at peak of contraction. D-Shape LV (Type 2)
    3. Supra-systemic = Bowing septum into the LV cavity (Type 3)

<u>ATTENTION</u>: *It the setting of a large unrestrictive PDA – the PDA will expose the pulmonary circulation to systemic pressures in systole and diastole (like a window connecting the Aorta to the Pulmonary Artery). PDA is a Pressure lesion and a Flow lesion (excessive flow Qp>Qs; and excessive pressure in the pulmonary vascular compartment). As such, if the PDA is left to right – even if the TR is high – it could only represent this transmission of pressure and does not tell you a lot of information on underlying pulmonary vascular remodelling. Do not start pulmonary vasodilators because it will lead to further flow (while not changing the pressure since the PDA is a structural lesion). If the PDA is right to left – the PVR are higher than the SVR – in that setting there is supra-*

systemic pulmonary pressures. In the context of Bidirectional PDA – there is isosystemic pressures. A bidirectional PDA shunt at 36 weeks is worrisome for underlying pulmonary vascular disease. The same concepts apply to a large unrestrictive VSD (except that the VSD is a SYSTOLIC pressure and volume lesion, and only a DIASTOLIC volume lesion).

Markers of RV function by Echo:

- Subjective qualitative contraction
- PFO or ASD that is bidirectional or Right to Left informs you that the RV end-diastolic pressure are similar to the LV end-diastolic pressure or more. This could be a sign of RV diastolic dysfunction. A R->L shunt at the inter-atrial level explains the occasional desaturation spells that we see in PH.
- Fractional area change of RV (Aim > 30%).
- Tricuspid annular plane systolic excursion (TAPSE):

Table 1. Classification table for TAPSE values[1]

Week of gestation	TAPSE, cm							Birth weight, kg observed		
	observed				predicted			mean	min.	max.
	n	mean	−2 SD	+2 SD	mean	−2 SD	+2 SD			
26	14	0.44	0.30	0.59	0.45	0.32	0.58	0.66	0.53	0.80
27	12	0.48	0.36	0.61	0.48	0.35	0.61	0.88	0.68	1.00
28	15	0.52	0.37	0.68	0.52	0.39	0.65	0.97	0.73	1.20
29	14	0.57	0.41	0.73	0.56	0.43	0.69	1.10	0.85	1.45
30	14	0.60	0.48	0.71	0.59	0.46	0.72	1.14	0.86	1.50
31	20	0.63	0.53	0.74	0.63	0.50	0.76	1.38	0.98	1.70
32	14	0.68	0.51	0.85	0.66	0.53	0.80	1.54	1.15	1.95
33	15	0.70	0.58	0.83	0.70	0.57	0.83	1.69	1.25	2.09
34	24	0.73	0.60	0.87	0.74	0.61	0.87	1.81	1.41	2.70
35	14	0.74	0.61	0.88	0.77	0.64	0.90	1.95	1.55	2.30
36	18	0.78	0.65	0.92	0.81	0.68	0.94	2.13	1.62	3.04
37	14	0.82	0.68	0.96	0.84	0.71	0.98	2.31	1.78	3.20
38	13	0.86	0.75	0.97	0.88	0.75	1.01	2.50	1.96	3.25
39	19	0.90	0.77	1.02	0.92	0.79	1.05	2.73	2.12	3.14
40	20	0.95	0.81	1.10	0.95	0.82	1.08	3.32	2.66	3.83
41	18	1.03	0.85	1.21	0.99	0.86	1.12	3.64	2.85	4.20

Mean, minimum and maximum birth weight were calculated for several weeks of gestation.
[1] The observed and predicted means and the 95% confidence intervals are presented for each gestational week.

Table III. Echocardiogram findings of pulmonary hypertension and its severity

None: RVSP <1/3 systemic pressure by TR gradient; septal position rounded and committed to LV; no RVH; normal RV size and function; If present, large VSD or PDA gradients suggesting <1/3 systemic RV pressures (Ao pressure – gradient = PA pressure)
Mild: RVSP 1/3-1/2 systemic pressure; septal flattening in systole, mild RVH and RV dilatation, RV function may be normal.*
Moderate: RVSP ½-2/3 systemic pressure; septum flat or with late systolic posterior bowing, moderate RVH or dilatation, RV may have reduced function*.
Severe: RVSP >2/3 systemic pressure; If present, shunt with predominant R-L gradient, pansystolic posterior septal bowing, Severe RVH, RV dysfunction, RV dilatation, "low-velocity" shunting across PDA or VSD.*

Further evaluation:

Further evaluation and treatment of comorbidities that impact the severity of lung disease should be undertaken with the diagnosis of BPD-PH infants before the initiation of pulmonary arterial hypertension (PAH)-targeted therapy. Studies should include:

- *evaluation for intermittent or sustained hypoxemia (oxymetry),*
- *aspiration (evaluation by OT, consider videofluoroscopy, consider jejunal feeds trial)*
- *gastroesophageal reflux disease evaluation and treatment,*

- *structural airways disease with scope by ENT*
- *Have ECG and CXR baseline at diagnosis of pulmonary hypertension at 36 weeks.*
- *Consider NT-proBNP level for follow-up in patients with right ventricular dysfunction at diagnosis of pulmonary hypertension*
- *pulmonary artery and vein stenosis evaluation, left ventricular diastolic dysfunction, and aortopulmonary collaterals.*

<u>Management of BPD-PH:</u>

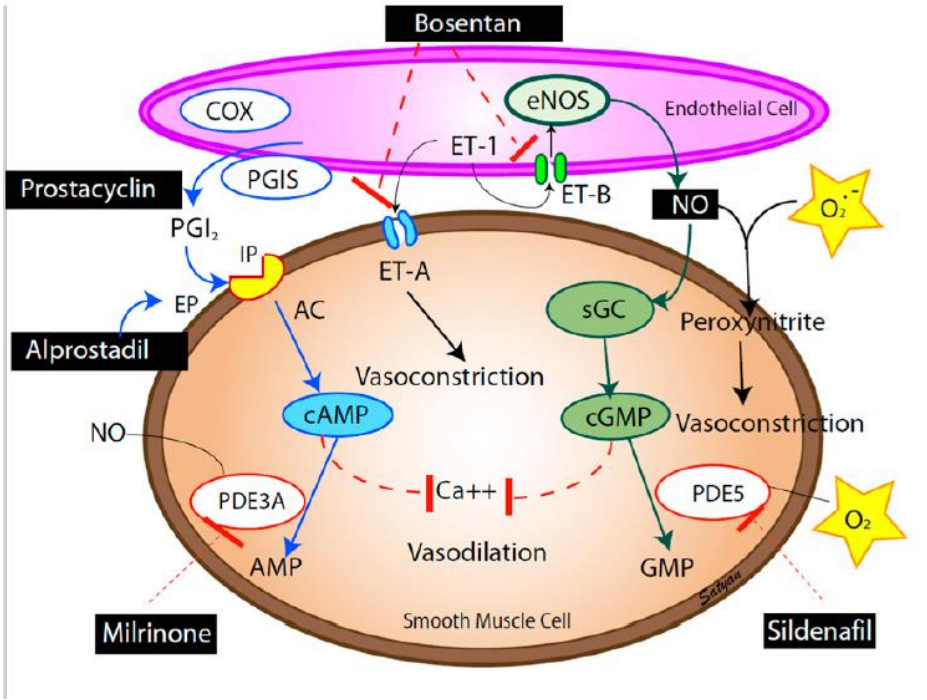
- Consider trial of Naso/Oro-jejunal feeds to avoid silent micro-aspiration
- Optimize respiratory care (suctioning, recruitment with maximal functional residual capacity to avoid V-Q mismatch)
- Consider diuretics (Hydro/Spiro) in the context of pulmonary hypertension in BPD
- Consider
- Aim saturations ≥ 92% for > than 95% of time. Supplemental oxygen therapy should be used to avoid episodic or sustained hypoxemia and with the goal of maintaining oxygen (O2) saturations between 92%- 95% in patients with established BPD and PH. Avoids vasculature vaso-spasm.
- Vaccination for avoidance of pulmonary infections
- Optimize nutrition (less volume more concentrate, aim normal weight/length ratio)
- Severe flare-up with viral / respiratory infections: require rigorous vaccination, avoidance of crowded areas (shopping center, kindergarten).
    - Prevnar 13, Synagis, Pneumovax (23 serotypes polysaccharide vaccine) at 2 years
- Influenza vaccine for the whole family and patient > 6 months
- Ensure with oximetry that baby has saturation ≥ 92 % for > 95% of the time
- Pulmonary vasodilators should be started with consultation of a pediatric cardiologist in the context of RV dysfunction and/or iso to supra-systemic pulmonary hypertension after optimization of everything above.

<u>If BPD with severe PH goes into PH crisis – Algorithm:</u>

- Patient in acute PH crises - Heterogeneous pulmonary vascular disease with V/Q mismatch
- Consider Re-intubation with sedation, aggressive chest physio and airway toilette + recruitment to minimize V/Q mismatch - Optimize ventilation with “BPD parameters” (long I-Time for CO2 release, lower rate, higher volumes). These lungs are fibrosed with airway disease that tend to collapse. They need usually a higher PEEP (8-10) in order to stent the airway.
- Optimize hemoglobin > 100
- iNO 20 ppm – will reach vessels of lung areas that are ventilated
- Milrinone – Lusitropic medication to promote RV function and filling
- If PH crisis, consider stress dose hydrocortisone 30 mg/m2/day
- Rule out concomitant infection +/- Abx (urine, viral, bacterial, pneumonia, etc.)
- Adjust nutrition, possibly induce diuresis with furosemide if oedema.

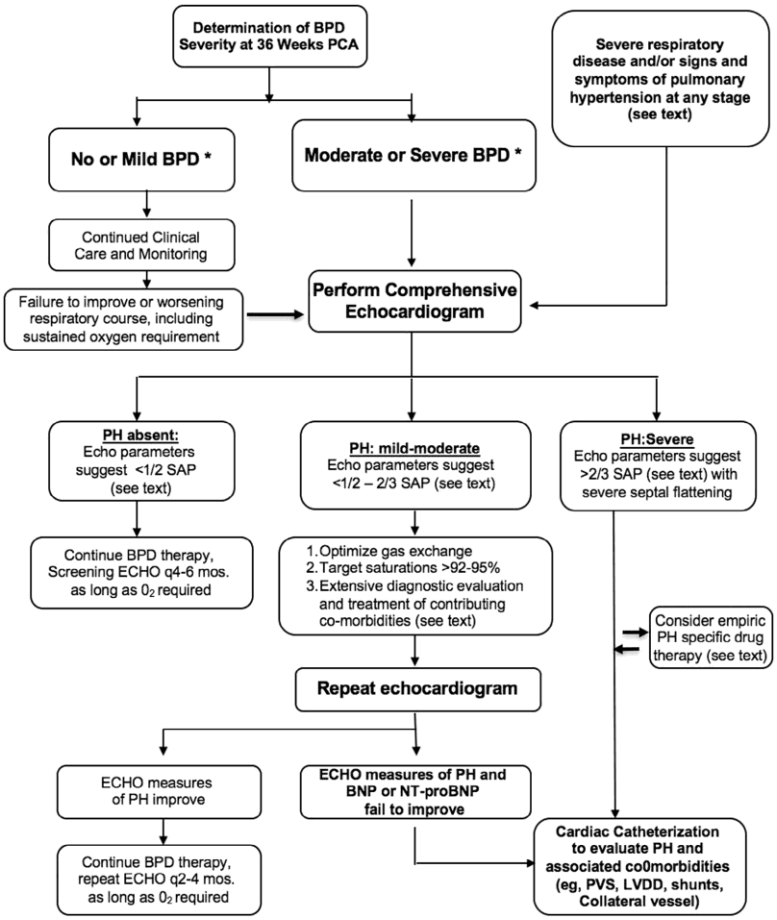
- BPD patients that are intubated and sedated do not need as much calories (the ventilator does much of the work and the sedation keeps them from activating metabolic rate). Need to avoid an increase in fat content and consider decreasing significantly calories and fluids.

Names	Dose/titration	Side effects	Comments
Sildenafil phiosphodiesterase-5 inhibitor	PO: 1 mg/kg 6-8 h; start with low dose (0.3-0.5 mg/kg/dose) and increase gradually to 1 mg/kg/dose as tolerated; slower as outpatient. Maximal dose of 10 mg q 8 h per EMA guidelines for infants. Intravenous:0.25-0.5 mg/kg/dose q 6-8 h (titrate slowly and administer over 60 min.	Hypotension, GER, irritability (headache), bronchospasm, nasal stuffiness, fever, rarely priapism	Monitor for adverse effects, lower the dose or switch to alternate therapy if not tolerated
Bosentan (Endothelin receptor antagonist)	1 mg/kg PO q 12 h as starting dose; may increase to 2 mg/kg BID in 2-4 wk, if tolerated and liver enzymes stable.	Liver dysfunction especially during viral infections, VQ mismatch, hypotension, anemia (edema and airway issues rare in infants)	Monitor LFTs monthly (earlier with respiratory infections); monitor CBC quarterly. Teratogenicity precautions for caregivers
Inhaled Iloprost	2.5-5 mcg every 2-4 h. Can be given as continuous inhalation during mechanical ventilation. Can titrate dose from 1-5 mcg and frequency from every 4 h to continuous.	Bronchospasm, hypotension, ventilator tube crystallization and clogging, pulmonary hemorrhage, prostanoid side effects (GI disturbances), may be teratogenic to caregivers	Need close monitoring for clogged tubing, may need further dilution. May need bronchodilators or inhaled steroid pretreatment with bronchospasm.
Intravenous Epoprostenol (Flolan)	Start at 1-2 ng/kg/min, titrate up slowly every 4-6 h to 20 ng/kg/min; need to increase dose at regular intervals because of tachyphylaxis. Further increases as guided by clinical targets and avoiding adverse effects.	Hypotension, VQ mismatch, GI disturbances. Needs dedicated line, very short half-life with high risk for rebound PH with brief interruption of therapy; line related complications include infection, clogging, breaks in line, thrombosis, arrhythmia)	Monitor closely if added to other vasodilator therapies, such as milrinone; careful attention to line care is essential.
Treprostinil (Remodulin) IV or Subcutaneous	Start at 2 ng/kg/min and titrate every 4-6 h up to 20 ng/kg/min, then slow increase dose as tolerated (dose often 1.5-2 times greater than equivalent epoprostenol dose, if switching medications)	SQ: local site pain; IV: similar risks as with epoprostenol, but treprostinil has a longer half- life, which reduces risk for severe PH with interruption of infusion	Site pain managed with local and systemic measures
Milrinone (IV) (phosphodiesterase-3 inhibitor)	0.15-0.5 mcg/kg/min –lower dosage range when used with other vasodilators	Arrhythmogenic; systemic hypotension and high risk for decreased myocardial perfusion; caution with renal dysfunction	May need to add a pressor, such as vasopressin, to mitigate effects of decrease in systemic pressures.



For home or follow-up (intra-hospital if still hospitalized):

- Home Oxygen needs to be organized for pulmonary hypertension patients
- Parents need to be informed that the whole family needs influenza vaccination
- The patient should not be in kindergarten while still on home oxygen. Avoid spaces with close contacts. Avoidance of viral infection (social distancing).
- Parents need to be trained to recognize signs of resp distress or RV failure: diaphoresis, retraction, work of breathing, cyanosis, abnormal neurological status
- Parents need basic CPR training
- Travelling by plane can be complicated by PH crises – needs assessment for fit to travelling with hypoxic challenge once PH infra-systemic and stable in room air.
- Sildenafil can accentuate GERD, ensure to manage reflux and follow growth: avoid abnormal Weight-Length Ratio. Energy needs can be up to 140 kcal/kg/d (Small volumes but high caloric enrichment).
- Follow Hgb (ensure no anemia), regular blood gaz and electrolytes (especially if on diuretics), +/- Brain Natriuretic peptide if RV failure (baseline and at follow-ups).
- Consider: Sweat test, occasional chest X-ray to rule out aspiration (especially if oral challenges) and CT scan of chest if progressive worsening of clinical status.

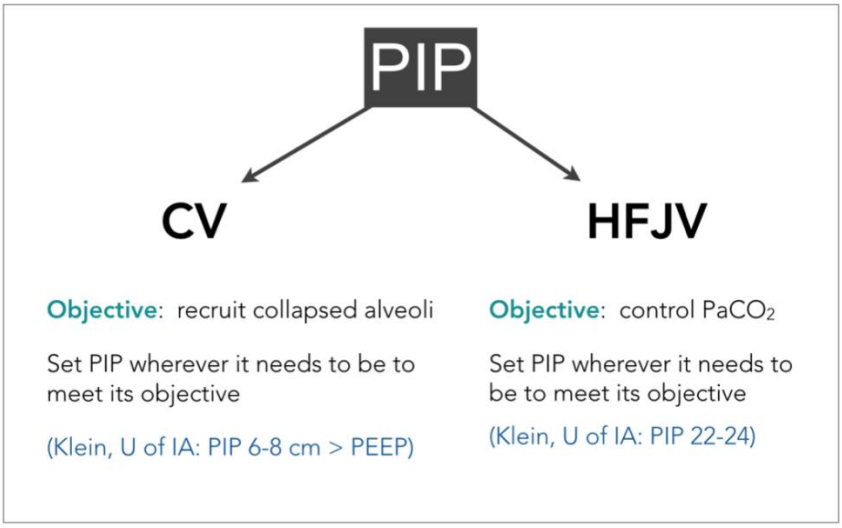


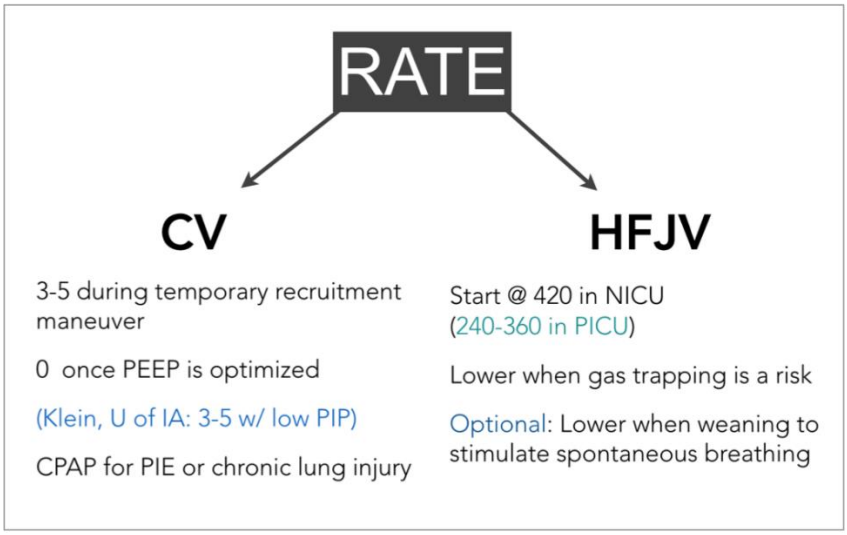
Algorithm proposed by PPHNET – BPD and Pulmonary Hypertension (JofPeds)

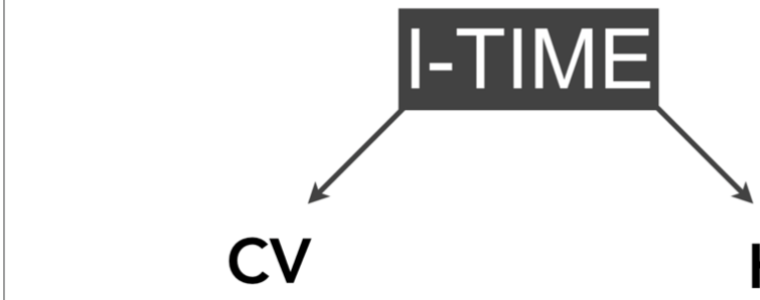
HFJV – High Frequency Jet Ventilation

Recommended Patient Management Strategies for HFJV

As described by MD and RRT HFJV Users







CV

Longer for poor compliance (e.g., RDS)

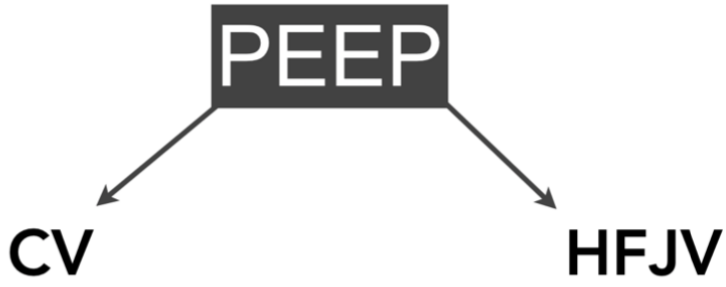
Shorter for pulmonary airleaks (e.g., PIE)

(Klein, U of IA: .4+ sec…with low PIP)

HFJV

Use the default setting of 0.02 seconds

Short I-time and small V_T are the secrets of HFJV



CV

~5-14+, depending upon the patient and the diagnosis

Optimize for each particular patient!

Increase PEEP to maintain MAP if patient desaturates when switching to HFJV

HFJV

Displays tracheal PEEP

Displayed HFJV PEEP ≧ set CV PEEP may indicate gas trapping

Lower HFJV Rate to correct

Stocking Your Bag of HFJV Tricks

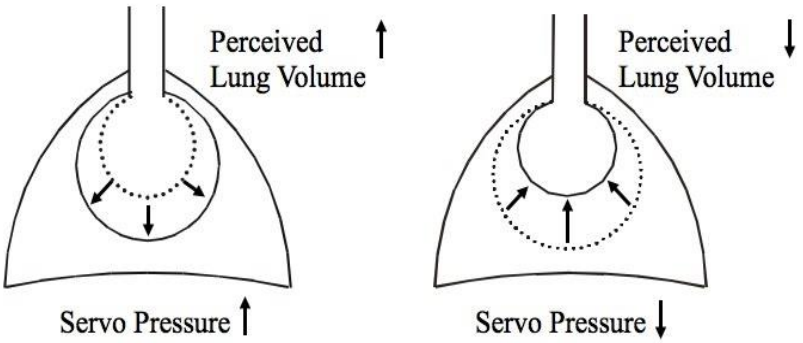
What to do when the recommended strategies are no longer effective

As described by MD and RRT HFJV Users

Long I-Time Low Pressure Recruitment	• As a temporary lung recruitment strategy, set CV PIP 4-5 cm H2O above PEEP • Set CV TI to 2-3 seconds • Apply strategy for 20-30 minutes while determining optimal PEEP
Optimizing PEEP The Easy Way	• When SaO2 is stable, switch CMV to CPAP • If SaO2 drops in less than 5 minutes, switch back to IMV • Raise PEEP by 1-2 cm H2O • Repeat until SaO2 is stable in CPAP mode
Increasing HFJV I-Time	• Raise HFJV TI if HFJV PIP is ineffective AND patient has pathophysiology suggesting long inspiratory time constants • Raise in increments of .004 - .006
Increasing PEEP for Inadvertent PEEP	• If patient is still exhibiting inadvertent PEEP despite adequate I:E Ratio (e.g., 1:7 - 1:12), gas may be trapped on distal side of collapsing airways • In this condition, raising PEEP can stabilize airways and allow gas to escape, thus reducing inadvertent PEEP
Lower HFJV Rate	3 reasons to lower HFJV rate: • To reduce gas trapping by extending expiratory time • When weaning the patient, to promote spontaneous breathing • When increasing HFJV TI
Monitoring Hand Bagging	• When oxygenation is poor despite adequate PEEP and FiO2, hand bag the patient with HFJV in Standby mode • When SaO2 is at a desired level, observe MAP on Life Pulse • Return patient to HFJV and adjust PEEP to achieve monitored value
LifePort Adapter Insights	• A leaking or obstructed tube in the LifePort adapter can cause pressure monitoring problems • Always position the pressure monitoring tube of the LifePort upward, at 12:00 • Replacing the LifePort is a good first option when troubleshooting • Always make sure you have the same or half-size larger LifePort in the ET tube
Troubleshooting Sequence	Two ways of expressing Troubleshooting Sequence 1. Begin with the baby and work your way back to the Life Pulse 2. Begin with the cheapest thing (LIfePort) and work your way back to the most expensive thing (Life Pulse) • Call the Hotline before replacing anything other than the LifePort
Weaning from HFJV to Nasal CPAP	• Wean PIP as patient improves • Begin to wean HFJV rate, if you haven't already • When ready, extubate to the level of the last recorded MAP

The Importance of Servo Pressure

- Servo Pressure = Automatically controlled driving pressure
- Servo Pressure changes as perceived lung volume changes



- Observing Servo Pressure can facilitate patient management

Servo Increases	**Servo Decreases**
• Improved compliance and/or resistance	• Worsening compliance and/ or resistance
• Airleak (in patient or circuit)	• Obstruction of ET Tube
• Disconnected Tubing	• Tension pneumothorax
	• Patient needs suctioning

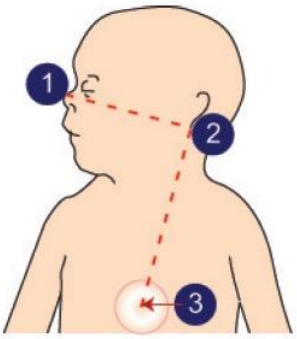
It is EXTREMELY RARE that we will adjust I-Time on HFJV at the MCH – Always validate with the neonatologists.

NAVA:

Neurally-adjusted ventilation assist:

NAVA invasive ventilation

Using NAVA:



- ☐ Get written medical order to start NAVA
- ☐ Connect Edi cable to module on left side of Servo i ventilator
- ☐ Connect the Edi cable on itself to perform module test
- ☐ Select catheter according to weight/height (tables above)
- ☐ Measure NEX
- ☐ Determine depth of insertion "Y" (refer to table); nasal insertion preferred
- ☐ Suction nasopharynx/oropharynx
- ☐ Dip catheter in sterile water to activate lubricant
- ☐ Insert catheter at determined length (as per table)
- ☐ Connect catheter to cable
- ☐ Confirm proper positioning on Servo i screen
  (Edi catheter positioning option under Accès cmd neuro)
  - Largest P waves in upper leads, minimal to absent in lower leads **AND**
  - Largest QRS complexes in upper leads, attenuation in lower leads **AND**
  - PINK signal present in the 2 middle leads (once other 2 criteria are met)
- ☐ Assure enough Edi signal present (2-3 ∝V)
  - Lower values may be due to over-sedation or excessive ventilation
  - Reduce one or the other in order to have acceptable Edi signals

OPTIMAL SIGNAL (will be pink)

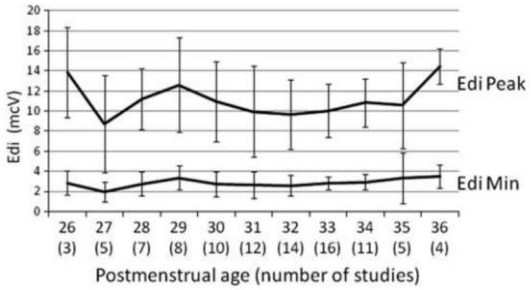
- ☐ Secure catheter as per protocol / document length on VTR flow sheet
- ☐ Select NAVA mode and set:
  - PEEP level (same as conventional)
  - FiO_2 as per OWL guidelines
  - Back up ventilation according to clinical criteria
  - Trigger Edi: leave at 0.5 ∝V
  - Flow/pressure trigger: -8 cmH_2O or less to assure Edi trigger is used
- ☐ Adjust NAVA level:
  - Set level to 1 cmH_2O/∝V
  - Observe Edi peak
    - If Edi ≥ 10-15 ∝V: ⇑ NAVA level by 0.2-0.3 increments until Edi approximates 10 ∝V
    - If Edi < 5 ∝V: ⇓ NAVA level by 0.2-0.3 increments until Edi approximates 10 ∝V
- ☐ **OR**
  - Go to NAVA preview window
  - Adjust NAVA level so that Edi curve is slightly lower than PIP while superimposed while in conventional ventilation
- ☐ Set alarms:
  - Max press limit (invasive ventilation): 10-15 cmH_2O above measured PIP (the pressure will cut off 5 cmH_2O below this value) – Notify the physician if ≥ 40 cmH_2O is required for invasive application
  - Max press limit (non-invasive support): 25 cmH_2O
  - Apnea time: 10-15 seconds (VTR will ring if pt has 3 episodes triggering apnea ventilation within 2 min)
  - High/low minute volume: 1.5-2.0 X MV / ½ MV
  - High/low respiratory rate: + 10-20 / - 10 intrinsic rate
  - High/low PEEP: + 3-5 / -2 set values

Note that:

Catheter is not MRI compatible

NAVA will deliver ventilation assist **proportional to patient's effort**

NAVA maintenance:



- Observe for first 15-20 minutes post initiation
- Edi should be 5-15 ∝V
- Document respiratory status
- Every 2 hours:
  - Trend screen – observe:
    - Edi peak, min, average (done over last 60 breaths)
    - VT (expect variability)
    - RR (may show increase due to improved capture)
  - Edi levels:
    - Peak should be 5-15 ∝V (average 10 ∝V)
    - Min should be < 1 ∝V
  - Increase NAVA level if:
    - Edi peak trending up **OR** > 15 ∝V
    - Clinical signs or ⇑ WOB (VT < 4 ml/kg, ⇑ RR) – discuss with medical team
  - Decrease NAVA level if:
    - Edi < 5 ∝V
- Causes for high Edi peak:
  - ⇑ resp. effort
  - Diaphragm weakness
  - Pain, anxiety
- Causes for low Edi peak:
  - Hyperventilation / over ventilation
  - Sedation
  - Neural disorder
  - Muscle relaxant
- Causes for high Edi min:
  - Inadequate PEEP, de-recruitment
  - If > 1∝V: ⇑ PEEP by 1 cmH_2O until Edi min ≤ 1 ∝V
  - **NOTE: a sudden significant ⇑ in Edi min can indicate a pneumothorax**

Edi catheter maintenance:

- Assure catheter patent and has good signal
- Change catheter Q 30 days + PRN
- Verify position Q 2H / document adjustments
- Document position Q shift if no change made

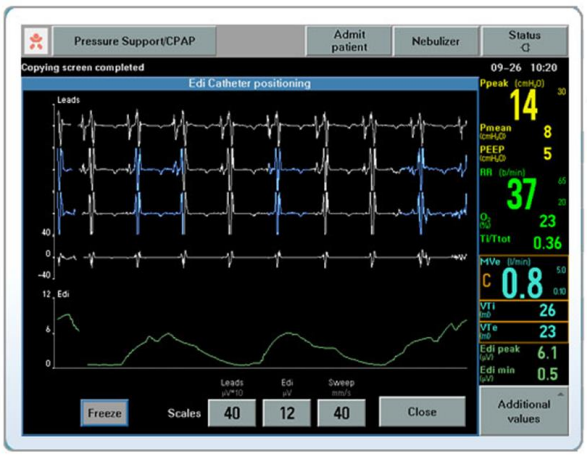
NAVA monitoring/documenting:

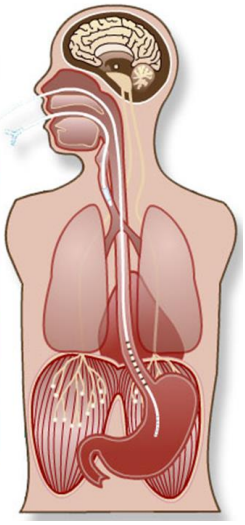
- On ventilator flow sheet Q2H + when changes being done:
  - Edi peak/min
  - NAVA level (notify MD after every change)
  - All other measured values as per protocol
  - Respiratory assessment
  - ETT position / if secure
  - SpO_2
  - Catheter position

NAVA weaning/discontinuing:

- Consider weaning when pt is stable with minimal WOB, FiO_2 < 0.30, PEEP 5, appropriate VT with average Edi peak 10 ∝V
- ⇓ NAVA level 0.2-0.3 $cmH_2O/\propto V$ increments Q 2-4 hours
- Observe Edi peak for no significant increase 15-20 min post change
- If ⇑ Edi peak, return to previous level
- Wean until extubation criteria met (as per NICU standards) **OR** medical order given to change mode
- Consider extubation when NAVA level ≤ 0.5 $cmH_2O/\mu V$ with Edi peak and VT in normal range
- Post extubation, keep catheter in place to observe WOB via Edi measurement trending for 2 hours

NAVA troubleshooting:

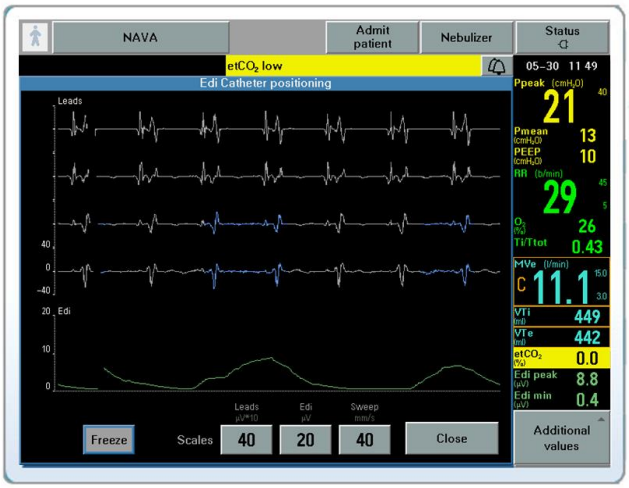


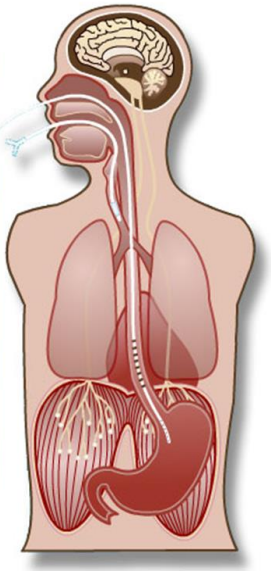


[Correct position](#)

[Signal will be pink](#)

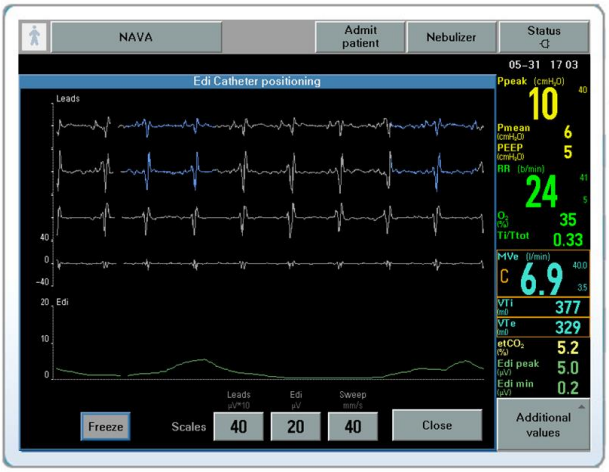
Edi Catheter too far up

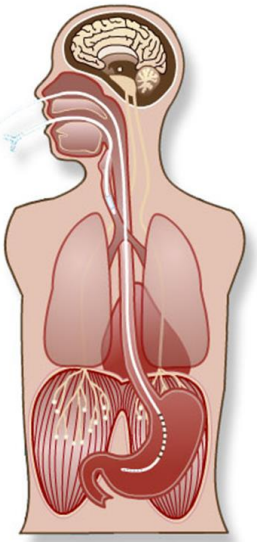




[Too high]

Edi Catheter too far down





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Inhaled Nitric Oxide (iNO)

Patient population: The following patient populations may be considered, however the indications listed below must apply:

1. Term and late preterm infants (greater than or equal to 34 weeks): In these patients, persistent pulmonary hypertension of the newborn (PPHN) is a frequent cause of hypoxemic respiratory failure, affecting 0.43 to 6.8 per 1000 live births. PPHN can be considered as a primary condition owing to difficulties in neonatal adaptation, or secondary to respiratory distress syndrome (RDS), meconium aspiration (MAS), sepsis or congenital lung malformations such as congenital diaphragmatic hernia (CDH). Current therapies for PPHN include mechanical ventilation, hemodynamic support and sedation. Inhaled Nitric Oxide (iNO) is a therapy that is very effective in improving oxygenation in patients with hypoxic respiratory failure that have not responded to other therapies. For the newborn with parenchymal lung disease, it is recommended that optimal alveolar recruitment should be established prior to initiation of iNO therapy. This alveolar recruitment is frequently achieved by the use of specific ventilatory strategies which includes high frequency ventilation (oscillatory or jet).

2. Congenital diaphragmatic hernia (CDH): In CDH patients, iNO should not be used routinely. Pulmonary hypertension in CDH patients is in part secondary to underdevelopment and anatomical changes of the pulmonary vasculature. In addition, left ventricular and surfactant dysfunction may contribute to hypoxemia. Two randomized studies failed to show improvement of infants with CDH with iNO. The lack of improvement in some patients may be due to the severe left ventricular systolic and diastolic dysfunction. In these patients, the use of iNO will decrease pulmonary vascular resistance increasing blood flow to the lungs and left ventricle preload. . This could be detrimental by worsening pulmonary venous hypertension. On the other hand, some CDH infants with persistence of pulmonary vascular hyperactivity in spite of parenchymal improvement may benefit from the use of iNO. The role of iNO is likely far more complicated than simply vasodilation alone, as the NO/cGMP pathway is also involved in alveolar growth and lung angiogenesis.

3. Preterm infants (less than 34 weeks) with severe respiratory failure: In very sick preterm infants who meet the criteria for poor oxygenation before day 3 of life, rescue therapy with iNO does not improve their survival, survival without bronchopulmonary dysplasia (BPD) or brain injury, even though oxygenation may improve in the short term. In addition, there is some evidence of an increase in severe intraventricular hemorrhage (IVH) and of the combined outcome of severe IVH or periventricular leukomalacia. In view of these findings, iNO should not be routinely used for preterm infants. Exception: Although iNO use cannot be recommended in preterm infants outside of clinical trials, the subgroup of infants with Preterm Premature Rupture of Membrane (PPROM) and oligohydramnios may theoretically derive greater benefit from the drug due to nitric oxide-sensitive pulmonary hypertension and beneficial effects of iNO on the parenchyma, conducting airways, and pulmonary vasculature.

4. Congenital heart disease (CHD): Some neonates with congenital heart disease can be considered for iNO. These cases should always be consulted with Pediatric Cardiology before initiation of the therapy.

5. Preterm infant with mild-moderate RDS and at risk for BPD (Prophylactic use/BPD prevention): It is not recommended at this time to use iNO prophylatically in this population. Results from ongoing randomized control trials may modify this recommendation.

Beneficial effects of iNO can be summarized as follows: 1. Improved ventilation / perfusion (V/Q) matching 2. Improved pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR) 3. Enhancement of pulmonary surfactant activity 4. Prevention of neo-muscularization 5. Decreased reperfusion injury 6. Decrease inflammation and vascular permeability 7. Nitric Oxide (NO) replacement

INDICATIONS for considering iNO:
1. Any term and late preterm infant greater than or equal to 34 weeks gestational age with hypoxic failure and diagnosis of primary PPHN or PPHN secondary to: a. RDS b. Perinatal Aspiration Syndromes (amniotic fluid or meconium) c. Pneumonia/ sepsis d. Pulmonary hypoplasia e. Asphyxia
2. Neonates with congenital heart disease and CDH may be considered for iNO however, a consultation with cardiology and an echocardiogram is recommended prior to initiation to assure for no severe left ventricular dysfunction or ductal-dependent lesion.
3. Pre-term infants less than 34 weeks with severe respiratory failure, with PPROM and oligohydramnios.

CONTRAINDICATIONS 1. In patients with ductal-dependent cardiovascular defect or severe left ventricular dysfunction, the use of iNO has the potential to be fatal. 2. Preterm infants less than 1000 grams with severe RDS and less than 3 days of life. If the physician responsible for a patient under this condition [where respiratory and cardiovascular are optimized, and sedation is adequate] needs iNO, it is recommended that he/she obtain a second opinion and if possible, a head US prior to initiation.

WARNINGS
Left to Right Shunting Treatment with iNO might aggravate cardiac insufficiency in a situation with left-to-right shunting. This is due to unwanted pulmonary vasodilation caused by iNO, resulting in a further increase of already existing pulmonary hyperperfusion. Therefore, it is recommended that prior to the administration of iNO, cardiology consultation and echocardiographic examination of central hemodynamics should be performed.

Initiation of iNO and Oxygenation Index:

The physician, nurse and respiratory therapist must optimize mechanical ventilation, cardiovascular stability, and patient comfort through sedation.

AND

It is highly suggested to obtain cardiology consultation and insert an indwelling arterial line in place.

Optimize mechanical ventilation: The goal of mechanical ventilation is to achieve optimal lung volume while minimizing the risks of lung injury. Suggested mechanical ventilation strategies include High Frequency Oscillation, High Frequency Jet Ventilation, and/or Surfactant administration (as per the protocol "Surfactant Administration to newborns – MUHC Interprofessional Protocol").

Optimize sedation: Minimal and gentle handling is mandatory as pulmonary vascular reactivity is high. The use of sedation and in certain situations, muscle paralysis, may be necessary. Note that opiate or benzodiazepine may cause systemic hypotension and worsening of the oxygenation.

Optimize cardiac output: Systemic blood pressure needs to be kept high enough to prevent, as much as possible, the right to left shunt. Use of adequate ventricular filling pressures and drugs to improve oxygen transport is mandatory.

After assuring for all the above, the impairment of gas exchange should be estimated by the calculation of the **oxygenation index (OI)**

$OI = 100 \times (FiO_2 \times MAP) / PaO_2$

MAP = mean airway pressure
FiO_2 = fraction of inspired oxygen
PaO_2 = arterial oxygen tension.

e. INDICATION FOR iNO INITIATION:

1. Patient with respiratory distress, after assuring that sedation, ventilation and cardiac output is optimized, plus one of the following:
   - OI is more than or equal to 20, with evidence of pulmonary hypertension (PH) by echocardiogram or a pre/post ductal oxygen saturation (SpO_2) difference more than or equal to 5%

     OR
   - Pre-ductal SpO_2 less than 92% on FiO_2 of 1

     OR
   - FiO_2 greater than or equal to 0.8 with pre/post ductal SpO_2 difference greater than or equal to 10%
2. If the first OI is more than or equal to 40

Complications

Methemoglobin

Methemoglobin Level	Action
Methemoglobin greater than 10%	Discontinue iNO
Methemoglobin 2.5 – 10 %	Decrease iNO by 50 % and repeat level
Methemoglobin les than 2.5%	Safe

Note: Laboratory reports from MCH/RVH of methemoglobin levels should be multiplied by 100 to obtain the %. For example, a methemoglobin level of 0.012 is = 1.2%.

Methemoglobin level will be documented on patient ventilator flowsheets.

Nitrogen Dioxide NO_2

Consistent Nitrogen Dioxide Level	Action
Nitrogen dioxide (NO_2) above 0.5 ppm	Check ventilator circuit Discontinue iNO
NO_2 0.3 – 0.5 ppm	Check ventilator circuit, wean iNO by half the set value every 15 minutes until NO_2 less than 0.3 ppm
NO_2 less than 0.3 ppm	Safe

Weaning of iNO – iNO protocol

See Weebly for Weaning of iNO protocol

Hematology System:

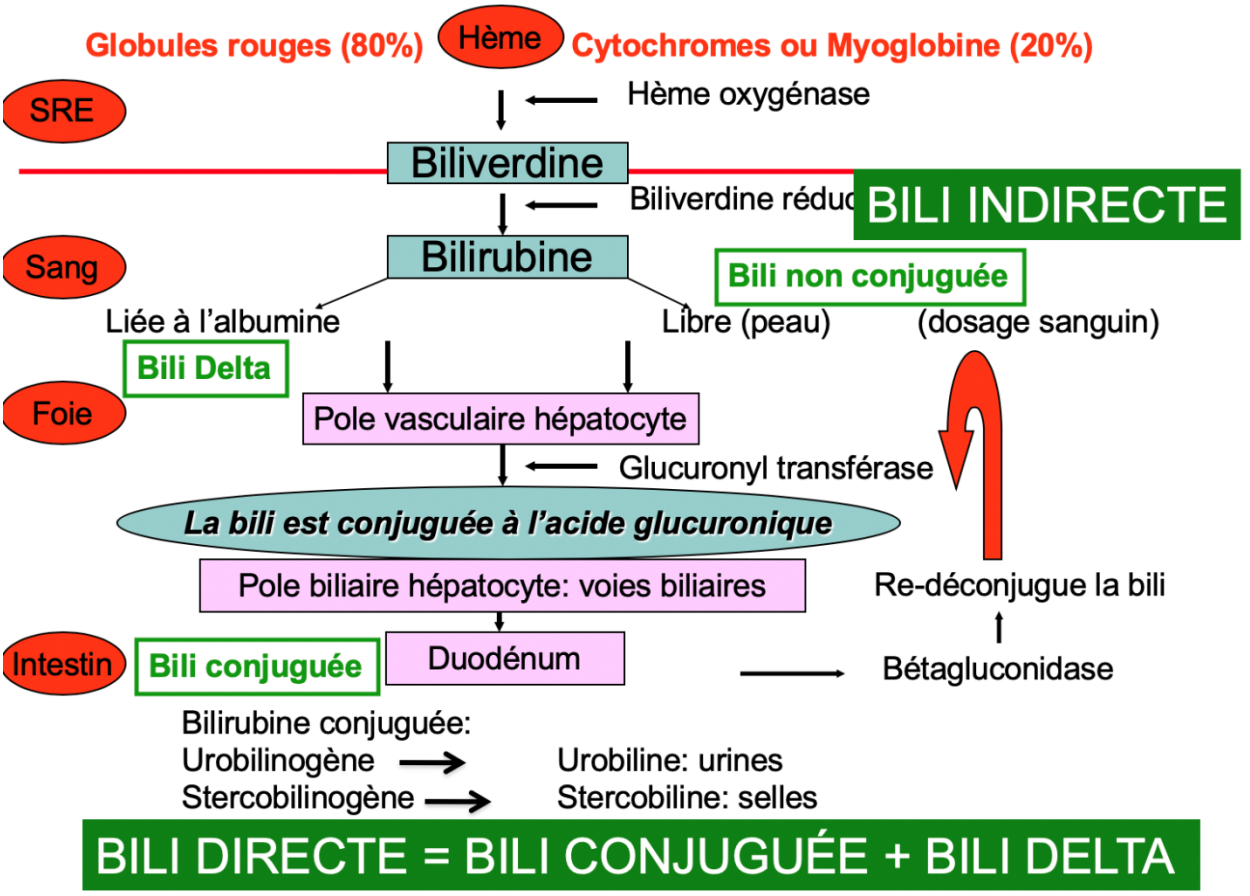
Neonatal Hyperbilirubinemia

Hyperbilirubinemia in neonate is very common and trainees will deal with it in term and preterm infants at NICU and normal newborn nursery rotation. Here is a simple guide on screening and interpretation of serum bilirubin levels and what are the modality of treatment.

Physiologic jaundice (non-pathologic unconjugated hyperbilirubinemia):

1. Term Infants: •50-60 % of all newborns are jaundiced in the first week of life. •Total serum bilirubin peaks at age 3–5 d (later in Asian infants). •Mean peak total serum bilirubin is 100 µmol/L (higher in Asian infants).
2. Preterm Infants: •Incidence of visible jaundice is much higher than in term infants. •Peak is later (5-7d). •Because of ↑ risk of bilibubin encephalopathy (see below), "physiologic" jaundice is more difficult to define and jaundice should be followed closely.

Bilirubin metabolism:



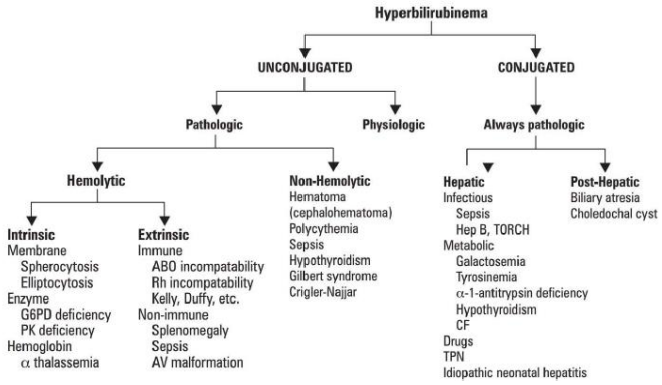
Definition of non-physiologic jaundice: •Jaundice in the first 24 hours •Bilirubin rising faster than 85 µmol/L in 24 hours (> 8/hours) •Clinical jaundice >1 week •Direct bilirubin >34 µmol/L •In

healthy term infants total serum bilirubin concentration >340 µmol/L during first week •Lower levels in preterm infants, "sick" infants, and hemolytic disease.

Bilirubin encephalopathy: The mildest form of bilirubin encephalopathy is sensorineural hearing loss due to damage to the cochlear nuclei. Severe encephalopathy causes kernicterus. Factors predisposing to neurotoxicity of unconjugated hyperbilirubinemia include: •When bilirubin concentration exceeds the binding capacity of serum albumin •Displacement of bilirubin from albumin by acidosis or certain drugs (e.g., sulfonamides, ceftriaxone) •Sepsis •Preterm infants due to↑ risk due lower serum albumin concentrations and ↑ risk for acidosis and sepsis.

Causes of indirect hyperbilirubinemia:
1. Increased lysis of RBCs (i.e., increased hemoglobin release) •Isoimmunization (blood group incompatibility: Rh, ABO and minor blood groups) •RBC enzyme defects (e.g., G6PD deficiency, pyruvate kinase deficiency) •RBC structural abnormalities (hereditary spherocytosis, elliptocytosis) •Infection (sepsis, urinary tract infections) •Sequestered blood (e.g., cephalohematoma, bruising, intracranial hemorrhage), Polycythemia •Shortened life span of fetal RBCs (80 vs. 120 d)
2. Decreased hepatic uptake and conjugation of bilirubin •Immature glucuronyl transferase activity in all newborns: term infants have 1% of adult activity, preterm infants have 0.1%. •Gilbert Syndrome •Crigler Najjar Syndrome (Non-hemolytic Unconjugated Hyperbilirubinemia): inherited conjugation defect (very rare) •Pyloric stenosis (mechanism is unknown) •Hypothyroidism •Infants of Diabetic Mothers (polycythemia is also common) •Breastmilk Jaundice (pregnanediol inhibits glucuronyl transferase activity)
3. Increased enterohepatic reabsorption •Breast feeding jaundice (due to dehydration from inadequate milk supply) •Bowel obstruction •No enteric feedings

Evaluation of Indirect hyperbilirubinemia
1. Initial evaluation: •Total and direct bilirubin •Blood type and Rh (infant & mother)
•Hematocrit •Direct Antiglobulin (Coombs) Test on infant
2. Later evaluation (as indicated): •RBC smear, reticulocyte count (if evidence or suspicion of hemolytic disease) •Blood culture, urinalysis, urine culture •Thyroid function tests, G6PD/PK assay, Hgb electrophoresis (done on newborn screen – obtain results).



Screening:

When do we screen/test for hyperbilirubinemia?

All infants should be screened

- Either TSB or TcB concentration should be measured in all infants during the first 72 h of life. If not required earlier because of clinical jaundice, a TSB measurement should be obtained at the same time as the metabolic screening test; alternatively, a TcB measurement should be obtained either at discharge or, if not yet discharged, at 72 h of life.
- Any infant discharged before 24 h of life should be reviewed within 24 h by an individual with experience in the care of the newborn who has access to testing and treatment facilities.
- All newborns who are visibly jaundiced in the first 24 h of life should have their bilirubin level determined.

What after obtaining the result if bilirubin level?

- If the TSB concentration does not require immediate intervention, the results should be plotted on the predictive nomogram. The result of the TSB measurement, the time at which it was obtained and the zone should be recorded, and a copy should be given to the parents. Follow-up of the infant should be individualized according to the risk assessment.
- There should be a systematic approach to the risk assessment of all infants before discharge and institution of follow-up care if the infant develops jaundice.

What additional tests we need to send in hyperbilirubinemia?

- Blood group evaluation and a DAT (Coombs test) should be performed in infants with early jaundice of mothers of blood group O.
- Selected at-risk infants (Mediterranean, Middle Eastern, African or Southeast Asian origin) should be screened for G6PD deficiency.
- A test for G6PD deficiency should be considered in all infants with severe hyperbilirubinemia.
- Infants with severe or prolonged hyperbilirubinemia should be further investigated, including measurement of the conjugated component of bilirubin.
- Transcutaneous bilirubinometry is an acceptable method, either as a routine procedure or in infants with visible jaundice. The result should be summed with the 95% CI of the device to estimate the maximum probable TSB concentration.
- TSB concentration may be estimated on either a capillary or a venous blood sample.

Modalities of hyperbilirubinemia management

1. Intensive phototherapy for infants with severe hyperbilirubinemia or those at greatly elevated risk of developing severe hyperbilirubinemia.
2. In addition, there is an option for conventional phototherapy for infants with a moderately elevated risk and a TSB concentration of 35 µmol/L to 50 µmol/L below the thresholds.
3. Breastfeeding should be continued during phototherapy.

4. Supplemental fluids should be administered, orally or by intravenous infusion, in infants receiving phototherapy who are at an elevated risk of progressing to exchange transfusion.
5. The bilirubin concentration should be checked within 2 h to 6 h of initiation of treatment to confirm response.
6. If phototherapy fails to control the rising bilirubin concentrations, exchange transfusion is indicated to lower TSB concentrations. For healthy term newborns without risk factors, exchange transfusion should be considered when the TSB concentration is between 375 µmol/L and 425 µmol/L (despite adequate intensive phototherapy).
7. An infant with clinical signs of acute bilirubin encephalopathy should have an immediate exchange transfusion.

Clinical notes:

- Neonates should receive phototherapy for at least 24 hours and then to be revaluated.
- Total serum bilirubin levels should be followed after starting phototherapy every 2 to 12 hours according to the severity of hyperbilirubinemia and how fast the progression.
- After stopping phototherapy, usually the TSB level should be measured in 24h.
- If the patient is not dehydrated and tolerate oral feeding, breast feeding shouldn't be stopped and IV fluid is not necessarily with phototherapy.

Reference charts for total serum bilirubin and phototherapy in term and late preterm infants:

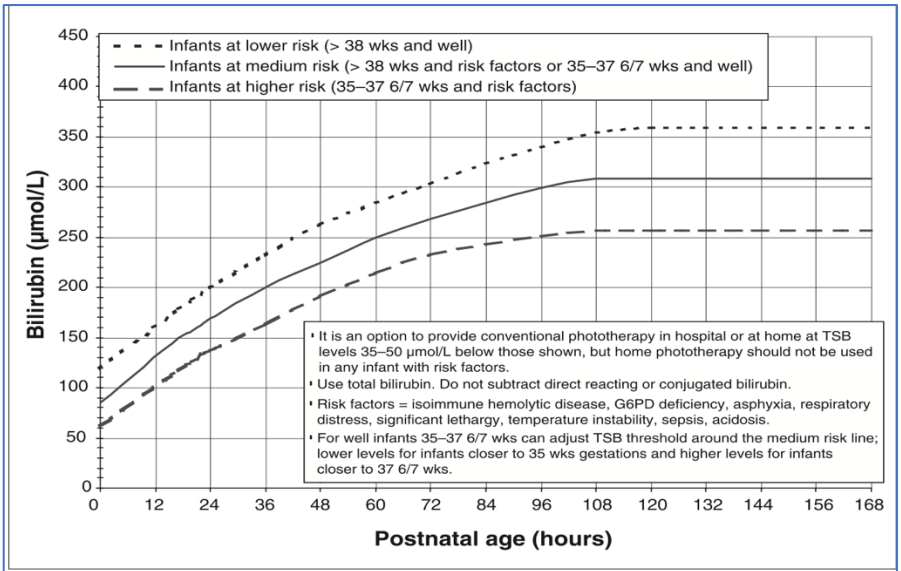


Figure 2) *Guidelines for intensive phototherapy in infants of 35 or more weeks' gestation. These guidelines are based on limited evidence and the levels shown are approximations. Intensive phototherapy should be used when the total serum bilirubin (TSB) concentration exceeds the line indicated for each category*

Phototherapy in preterm infants in use at the MCH:	
Gestational age (weeks)	Total serum bilirubin (umol/L)
< 28 0/7	85-102
28 0/7 – 29 6/7	102-136
30 0/7 – 31 6/7	136-170
32 0/7 – 33 6/7	170-204
34 0/7 -34 6/7	204-238

Reference charts for total serum bilirubin and exchange transfusion in term and preterm infants:

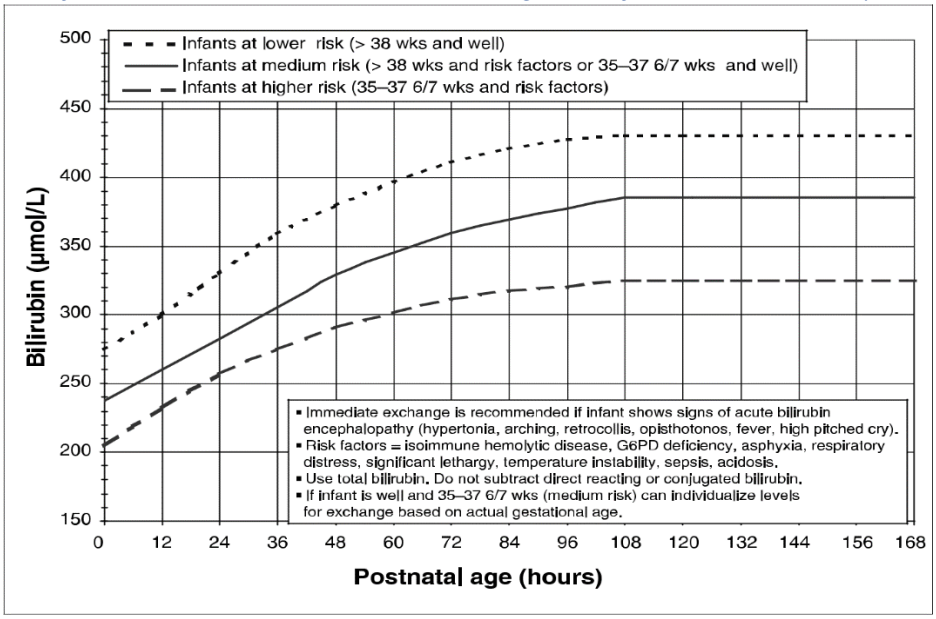
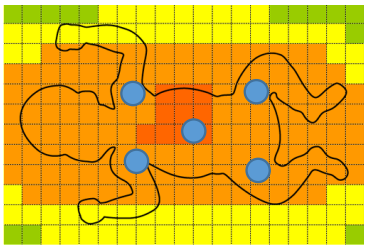


Figure 3) *Guidelines for exchange transfusion in infants of 35 or more weeks' gestation. These guidelines are based on limited evidence and the levels shown are approximations. Exchange transfusions should be used when the total serum bilirubin (TSB) concentration exceeds the line indicated for each category*

Radiance

- **RADIANCE**: The measure of "dose" of phototherapy – how many photons are reaching the baby. The goal is to reach a radiance of 30-60 mw/cm^2/nm. Exceeding this dose can mutate DNA, and has been suggested to linked to an increased risk of cancer in adulthood.
- Types of bilirubin:
  - ***Direct*** *(or conjugated) bilirubin. Direct bilirubin dissolves in water (it is soluble) and is made by the liver from indirect bilirubin.*
  - ***Total*** *bilirubin (combination of direct and indirect bilirubin)*
  - ***Indirect*** *(or unconjugated) bilirubin. This form of bilirubin does not dissolve in water (it is insoluble). Indirect bilirubin travels through the bloodstream to the liver, where it is changed into a soluble form*
  - Total and direct bilirubin levels are measured directly in the blood, whereas indirect bilirubin levels are derived from the total and direct bilirubin measurements

5. **Turn on** lamps and ensure baby positioned so that **entire body is under light**. Allow 10 minutes for lamps to "warm up".
6. **Measure radiance** of light to ensure dose of phototherapy is appropriate (after lamps have warmed up).
    - Follow instructions to **zero the unit** on the back of the Ohmeda Biliblanket Meter
        - *Extend HOLD /RUN button on side of unit*
        - *Install cap, then set ON/OFF switch to ON*
        - *Allow display to zero*
    - Position meter at **the 5 key points** of the baby and note 5 radiance measurements: both shoulders, belly button, and both thighs (see picture beside).



    - **Radiance should be measured once per shift, and each time lights are added or removed.** Measurements should be documented in the Nursing Flowsheet.
    - **Goal radiance** is between 30-60 mw/cm^2/nm. Exceeding this radiance has been shown to mutate DNA**. If radiance exceeded, discuss with MD. To decrease radiance, lamps can be placed further away from baby, or one can be turned off. Radiance should always be re-measured once lamp position has been changed.**

Exchange transfusion

An exchange transfusion involves removing aliquots of patient blood and replacing with donor blood in order to remove abnormal blood components and circulating toxins whilst maintaining adequate circulating blood volume. It is primarily performed to remove antibodies and excess bilirubin but can be used to remove other toxins like ammonia. A term baby's circulating blood volume is approximately 80-90 mL/kg. Aliquots used in exchange transfusion should be equal to approximately 10% (or slightly less) of the baby's total blood volume.

Exchanges may be either partial, single volume, or double volume.

- Partial – Baby's blood volume only partially exchanged. Usually used for polycythemia, with replacement as normal saline, albumin, or plasma.
- Single volume – 1 x circulating blood volume exchanged; replaces approximately 60% of the blood volume (because blood added as blood removed, so not all blood removed is old blood).
- Double volume – 2 x circulating blood volume; replaces approximately 85% of the blood volume and should cause a reduction of bilirubin by about 50%

In all cases, only very small volumes of blood (often 5-10 mL at a time) are removed and given over 1 minute periods, (i.e. 1 minute to remove, 1 minute to inject) to avoid significant pressure changes in the blood vessels.

Indications

▪ Alloimmune hemolytic disease of the newborn – to remove circulating bilirubin and replace antibody-covered red cells with antigen-negative red blood cells
▪ Significant unconjugated hyperbilirubinemia when intensive phototherapy unsuccessful
▪ Antibodies in maternal autoimmune disease
▪ Polycythemia – to reduce hematocrit, usually via partial exchange using NS, plasma, or albumin

Contraindications

▪ Hemodynamic instability, sepsis, or otherwise unable to tolerate fluid shifts (should be corrected first) ▪ Severe hypocalcemia (should be corrected first as exchange may worsen hypocalcemia)

Materials

- If umbilical line not in place already:
  - *Exchange transfusion sterile tray (for umbilical line insertion)*
  - *Umbilical line insertion kit (from intervention cart) – contains swabs, scalpel, bridge, etc.*
- Exchange transfusion kit (Vygon)
- Male-to-male luer lock adapter
- Blood transfusion tubing
- Medtronic EVD collection bag

  } Extra pieces needed to create new sterile dump bag. Found attached to exchange transfusion kits.

- Hotline Fluid Warmer
- Hotline Fluid Warmer Set (found on top of shelves at back of CSR)
- Blood products or solution that will be infused as replacement
- Masks & hairnets for all
- Sterile gloves (for sterile nurse, line inserter & helper)

Double Exchange transfusion:

From uptodate: The procedure involves umbilical catheter placement and removing and replacing blood in aliquots that are approximately 10 percent or less of the infant's blood volume. The infant's circulating blood volume is approximately 80 to 90 mL/kg. A double-volume exchange transfusion (160 to 180 mL/kg) replaces approximately 85 percent of the infant's circulating red blood cells (RBCs) with appropriately cross-matched reconstituted (from packed RBCs and fresh frozen plasma) blood. It is vital that reconstituted blood is used with a substantial albumin content to ensure bilirubin binding, as packed RBC is inadequate and may potentiate ongoing bilirubin toxicity due to its reduced intravascular bilirubin binding capacity. Irradiated blood products should be used to reduce the risk of graft versus host disease and cytomegalovirus (CMV)-safe blood products should be used to reduce the transmission of CMV in seronegative recipients.

Patial exchange transfusion (from UpToDate): Technique — PET can be performed in several ways. One approach is to remove blood from an umbilical venous or arterial catheter and infuse normal saline into a peripheral vein. The exchange volume (in mL) is calculated using the following formula:

Exchange volume = [(observed hct – desired hct) × blood volume] ÷ observed hct

Where hct = hematocrit and blood volume is calculated at 80 to 100 mL/kg body weight.

Higher volumes are associated with lower gestational ages and/or delayed cord clamping. The desired hct is usually set at 55 percent.

In general, the exchange volume is 15 to 20 mL/kg body weight. Blood can be removed and saline infused continuously (isovolumetric technique, the best approach in unstable infants) or the process can be accomplished using serial aliquots of 10 to 15 mL/kg.

See NICU Weebly for Procedure for Exchange Transfusion

Conjugated (direct) hyperbilirubinemia (cholestasis)

Definition : Direct Bilirubin >20% of Total Bilirubin OR >17.1 µmol/L absolute value.

CONJUGATED (DIRECT) HYPERBILIRUBINEMIA (CHOLESTASIS):

Clinically, jaundice is green compared to jaundice due to unconjugated hyperbilirubinemia (yellow).

1. **Hepatocellular diseases:**
   A. Hepatitis:
      •Neonatal idiopathic hepatitis
      •Viral (Hepatitis B, C, TORCH infections)
      •Bacterial (E. coli, urinary tract infections)
   B. Total parenteral nutrition
   C. Hepatic ischemia (post-ischemic damage)
   D. Erythroblastosis fetalis (late, "Inspissated Bile Syndrome")
   E. Metabolic disorders (partial list):
      •Alpha-1 antitrypsin deficiency
      •Glycogen storage disorders
      •Cystic fibrosis
      •Galactosemia, tyrosinemia, fructosemia
      •Cerebrohepatorenal disease (Zellweger)
      •Hypopituitarism
2. **Biliary tree abnormalities:**
   A. Extrahepatic biliary atresia: In first 2 weeks,, unconjugated bilirubin predominates; elevated conjugated bilirubin is late.
   B. Paucity of bile ducts (Alagille's vs. non-syndromic)
   C. Choledochal cyst
   D. Bile plug syndrome

EVALUATION and MANAGENMENT of CHOLESTASIS:

1. **Initial evaluation:**
   •Total and direct bilirubin
   •AST, ALT, GGT, urine reducing substances
   •Hepatic ultrasound
2. **Later evaluation (as indicated):**
   •Hepatitis B and C serology
   •Very long chain fatty acids
   •HIDA scan
   •α1-antitrypsin deficiency studies
   •Brain sonogram
   •Cholangiogram
3. **Management:**
   •Conjugated bilirubin is not toxic.
   •Management is treatment of cause.
   •Phototherapy will cause "bronzing" with conjugated hyperbilirubinemia.

Blood Transfusions/Blood Products

TABLE 1
Suggested hemoglobin levels and hematocrit thresholds for transfusing infants with anemia of prematurity

Postnatal age	Respiratory support*	No respiratory support
Week 1	115 (35)	100 (30)
Week 2	100 (30)	85 (25)
Week 3 and older	85 (25)	75 (23)

Data presented as hemoglobin, g/L (hematocrit, %).
*Respiratory support is defined as an inspired oxygen requirement in excess of 25% or the need for mechanical increase in airway pressure (Adapted from reference 6)

Reference: CPS Position Statement "Red blood cell transfusion in newborn infants"

pRBC Dosing

Conventional volume is 10-20mL/kg per transfusion. In the NICU we often order 15ml/kg. Before ordering pRBC see if patient was randomized in the WHEAT trial.

Irradiated Blood Products

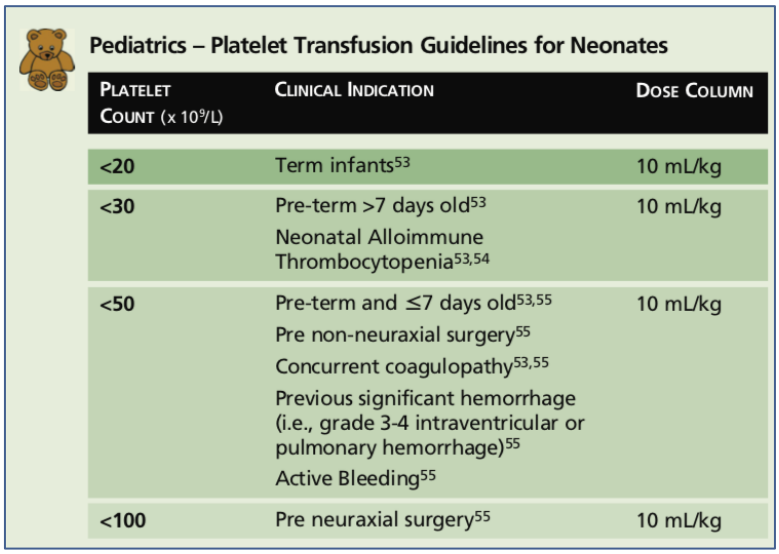
As of January, 2017, the Blood Bank no longer irradiates blood products for all neonates < 4 months. Irradiation is limited to:

- Neonates of birth weight < 1200g until they reach the age of 4 months
- Intrauterine transfusion
- Neonatal exchange transfusion

* Irradiation may be omitted in extreme emergencies to avoid delays
* Please enter the baby's weight in comments when ordering blood products to avoid extra phone calls

Reference: Bloody Easy 4

Platelet Transfusion:



Pediatrics – Platelet Transfusion Guidelines for Neonates

Platelet Count (x 10^9/L)	Clinical Indication	Dose Column
<20	Term infants[53]	10 mL/kg
<30	Pre-term >7 days old[53] Neonatal Alloimmune Thrombocytopenia[53,54]	10 mL/kg
<50	Pre-term and ≤7 days old[53,55] Pre non-neuraxial surgery[55] Concurrent coagulopathy[53,55] Previous significant hemorrhage (i.e., grade 3-4 intraventricular or pulmonary hemorrhage)[55] Active Bleeding[55]	10 mL/kg
<100	Pre neuraxial surgery[55]	10 mL/kg

Infectious Disease:

Infections during pregnancy:

Table 11. Infections During Pregnancy

Infection	Agent	Source of Transmission	Greatest Transmission Risk to Fetus	Effects on Fetus	Effects on Mother	Diagnosis	Management
Chicken Pox	Varicella zoster virus (herpes family)	To mom: direct, respiratory To baby: transplacental	13-30 wks GA, and 5 d pre- to 2 d post-delivery	Congenital varicella syndrome (limb aplasia, chorioretinitis, cataracts, cutaneous scars, cortical atrophy, IUGR, hydrops), preterm labour (prematurity)	Fever, malaise, vesicular pruritic lesions	Clinical, ± vesicle fluid culture, ± serology	VZIG for mother if exposed, decreases congenital varicella syndrome Note: Do not administer vaccine during pregnancy (live attenuated)
***CMV**	DNA virus (herpes family)	To mom: blood/organ transfusion, sexual contact To baby: transplacental, during delivery, breast milk	T1-T3	5-10% develop CNS involvement (mental retardation, cerebral calcification, hydrocephalus, microcephaly, deafness, chorioretinitis)	Asymptomatic or flu-like	Serologic screen; isolate virus from urine or secretion culture	No specific treatment; maintain good hygiene and avoid high risk situations
Erythema Infectiosum (Fifth Disease)	Parvovirus B19	To mom: respiratory, infected blood products To baby: transplacental	10-20 wks GA	Spontaneous abortion (SA), stillbirth, hydrops in utero	Flu-like, rash, arthritis; often asymptomatic	Serology, viral PCR, maternal AFP; if IgM present, follow fetus with U/S for hydrops	If hydrops occurs, consider fetal transfusion
Hepatitis B	DNA virus	To mom: blood, saliva, semen, vaginal secretions To baby: transplacental, breast milk	T3 10% vertical transmission if asymptomatic HBsAg +ve; 85-90% if HBsAg and HBeAg +ve	Prematurity, low birth weight, neonatal death	Fever, N/V, fatigue, jaundice, elevated liver enzymes	Serologic screening for all pregnancies	Rx neonate with HBIG and vaccine (at birth, 1, 6 months); 90% effective
***Herpes Simplex Virus**	DNA virus	To mom: intimate mucocutaneous contact, To baby: transplacental, during delivery	Delivery (if genital lesions present); less commonly in utero	Disseminated herpes (20%);CNS sequelae (35%); self-limited infection	Painful vesicular lesions	Clinical diagnosis	Acyclovir for symptomatic women, suppressive therapy at 36 wks controversial C/S if active genital lesions, even if remote from vulva
HIV	RNA retrovirus	To mom: blood, semen, vaginal secretions To baby: in utero, during delivery, breast milk	1/3 in utero, 1/3 at delivery, 1/3 breastfeeding	IUGR, preterm labour, premature rupture of membranes	See Infectious Diseases, ID29	Serology, viral PCR All pregnant women are offered screening	Triple antiretroviral therapy decreases transmission to <1% Elective C/S: no previous antiviral Rx or monotherapy only, viral load unknown or >500 RNA copies/ml, unknown prenatal care, patient request
***Rubella**	ssRNA togavirus	To mom: respiratory droplets (highly contagious) To baby: transplacental	T1	SA or congenital rubella syndrome (hearing loss, cataracts, CV lesions, MR, IUGR, hepatitis, CNS defects, osseous changes)	Rash (50%), fever, posterior auricular or occipital lymphadenopathy, arthralgia	Serologic testing; all pregnant women screened (immune if titre >1:16); infection if IgM present or >4x increase in IgG	No specific treatment; offer vaccine following pregnancy Do not administer during pregnancy (live attenuated)
Syphilis	Spirochete *(Treponema pallidum)*	To mom: sexual contact To baby: transplacental	T1-T3	Risk of PTL, multisystem involvement, fetal death	See Infectious Diseases, ID26	VDRL screening for all pregnancies; if positive, requires confirmatory testing	Pen G 2.4 M U IM 1 dose if early syphilis 3 doses if late syphilis, monitor VDRL monthly If Pen G allergic: consider desensitization before treatment
***Toxoplasmosis**	Protozoa *(Toxoplasma gondii)*	To mom: raw meat, unpasteurized goat's milk, cat feces/urine To baby: transplacental	T3 (but most severe if infected in T1); only concern if primary infection during pregnancy	Congenital toxoplasmosis (chorioretinitis, hydrocephaly, intracranial calcification, MR, microcephaly) NB: 75% initially asymptomatic at birth	Majority subclinical; may have flu-like symptoms	IgM and IgG serology; PCR of amniotic fluid	Self-limiting in mother; spiramycin decreases fetal morbidity but not rate of transmission

* Indicates TORCH infection

Empirical Antibiotic Guide – MCH

Please refer to the MCH formulary for detailed dosing guidelines in neonates (term, pre-term, low birth weight). This is only a portion of the Empirical Guide with information pertaining to the NICU.

HIV protocol:

See NICU weebly.

Ventilator-associated pneumonia (VAP)

<table>
<tr><td colspan="2">All of the following:
Patients mechanically ventilated for ≥ 48h

Radiological findings (present on 2 consecutive days)+ worsening gas exchange +

<u>3</u> other clinical/laboratory findings

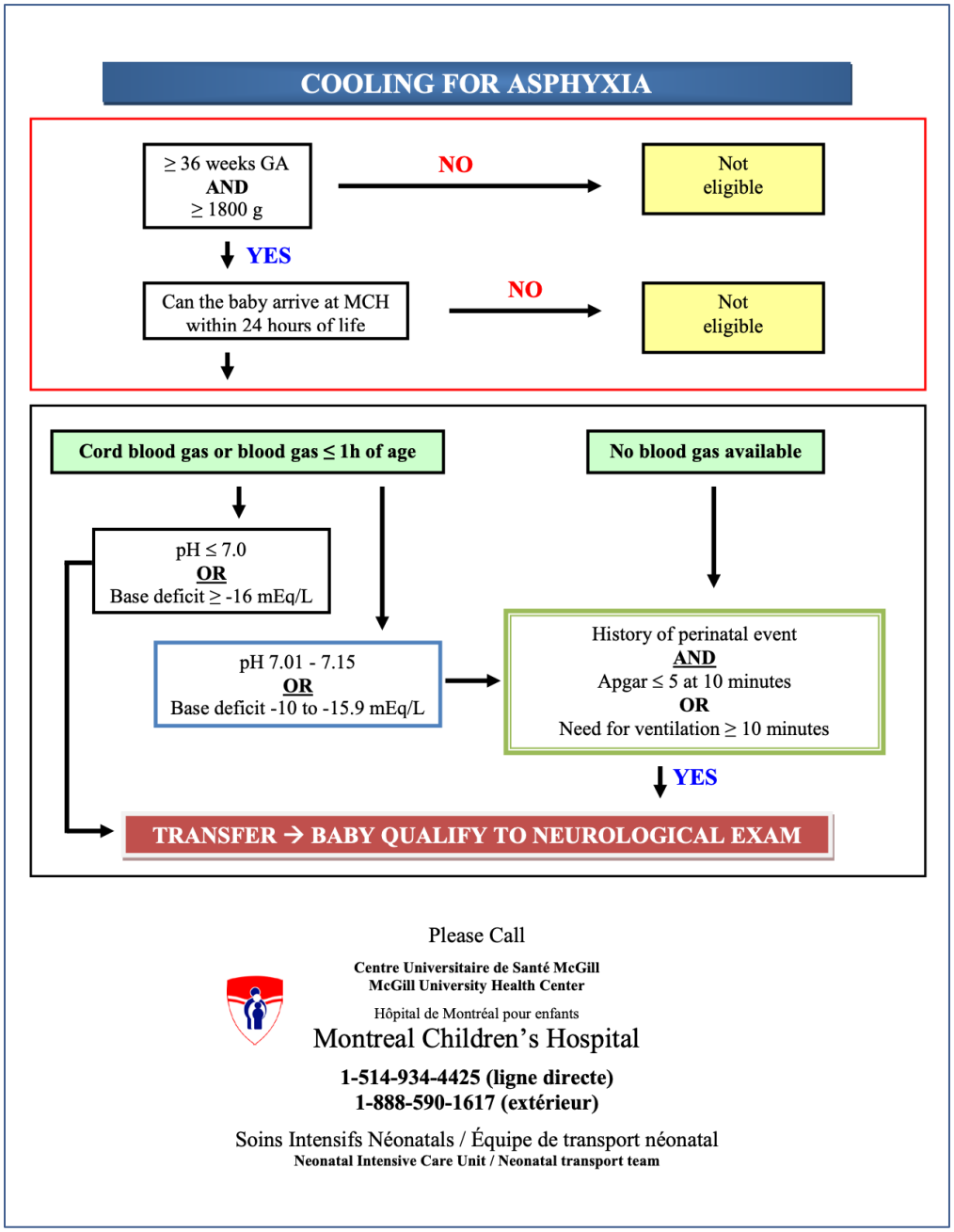
NB. Complete clinical criteria only after x-ray criteria are met.</td></tr>
<tr><td><u>Radiological</u>
(two or more abnormal chest x-rays with at least one of the following symptoms)</td><td>▪ New or progressive pulmonary infiltrate and persistent pulmonary infiltrate
▪ Consolidation or cavitation or pneumatoceles</td></tr>
<tr><td><u>Worsening gas exchange</u></td><td>▪ FiO_2 needs higher to maintain SpO_2 appropriate for gestational age
▪ Increased mean airway pressure
▪ Increased ventilation needs</td></tr>
<tr><td><u>Clinical</u></td><td>▪ Temperature instability with no other recognized cause (≥ 38.5ºC or < 36ºC)
▪ New onset of purulent sputum or change in character of sputum
▪ New onset of increased respiratory secretions or increase suctioning requirements
▪ New onset of apnea, tachypnea, nasal flaring with retractions of the chest wall, or grunting
▪ New wheezing, rales, or rhonchi
▪ Bradycardia (<100 bpm) or tachycardia (>170 bpm)</td></tr>
<tr><td><u>Laboratory</u></td><td>1. Leukopenia or leukocytosis
▪ 0 days – 1 wk: > 34 x 10^9 L
▪ 1wk – 1month: >19.5 or <5 x 10^9 L
▪ 1month – 1y: > 17.5 or < 5 x 10^9 L
2. Significant positive culture from respiratory secretions
3. Relevant positive culture from alternative site of infection</td></tr>
</table>

Other pro-inflammatory markers (such as: CRP), may be increased in the context of VAP.

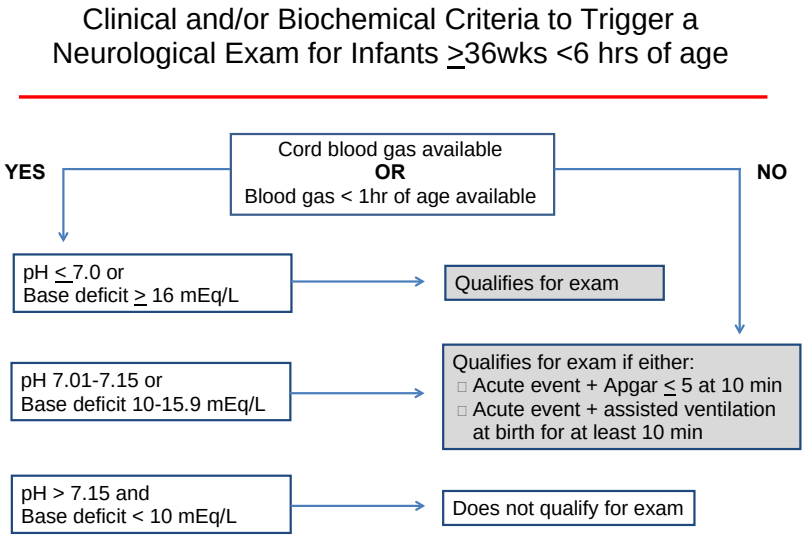
Neurodevelopment/ Central Nervous system:

Hypoxic ischemic encephalopathy (HIE)/ Therapeutic Hypothermia – Cooling

Algorithm for transfer of asphyxiated babies for cooling assessment:



You can access all transport protocols at https://sites.google.com/view/mch-transport/home
ID: mchneonataltransport@gmail.com
password: mchtransport



Rarely we would consider cooling for a newborn 35 weeks and more.

During NICU rotation at MCH, residents will be involved in evaluating/treating neonates with HIE either for babies inborn or outborn and transferred for evaluation in a tertiary center.

What are the criteria for treatment of HIE with therapeutic hypothermia?

Infants are candidates for hypothermia if they meet the following criteria:

Physiological criteria: Evidence of significant acidemia defined as **pH <7.00 or BE -16** on cord gas or first hour postnatal gas. In the absence of cord blood gas or if pH between **7.01 and 7.15, or BE between -12 and – 16** if a sentinel event is identified and Apgar score at 10 minutes ≤ 5 and need of assisted ventilation for ≥ 10 minutes

AND

Neurological criteria: Evidence of moderate or severe encephalopathy on neurological exam performed within the first 24 hours of age at the MCH NICU. Seizure in the setting of perinatal depression puts you in a category of at-least moderate HIE.

Hypothermia should be instituted ideally before the infant reaches 6 hours of life, therefore transfer of such infants should not be delayed. However, recent studies have shown that it is beneficial to offer therapeutic hypothermia up to 24 hours of age when there is evidence of encephalopathy and/or seizures. Please note that a thorough history is necessary before concluding an infant has an encephalopathy secondary to a hypoxic ischemic event.

Contraindications:

Absolute contraindications: For the following situations, there is evidence that hypothermia may be harmful. For these patients hypothermia is not recommended:

1. Prematurity: gestational age less than 36 weeks by best estimate
2. Weight less than 1800g

Relative contra-indications: For the following conditions, the effects of hypothermia are not known. These are usually rare circumstances, and there is very little evidence to guide us. Each case should be considered on an individual basis by the treating team:

1. Known major chromosomal anomalies or complex syndromes
2. Major life threatening cardiac or pulmonary malformations
3. Bleeding diathesis: low platelet count, disseminated intra-vascular coagulation, intra cranial hemorrhage or clinical bleeding. In the presence of unmanageable bleeding diathesis, hypothermia may be contra-indicated since it may aggravate bleeding. However, if the condition is manageable with blood products, it may still be advisable to cool the infant. The risks of further bleeding vs. sequelae of asphyxiated need to be weighed carefully.

INITIATION OF COOLING ON TRANSPORT:

Encephalopathy examination (SARNAT)

SARNAT exam needs to be done in the context of a newborn being un-stimulated. Leave the baby 15-20 minutes without external stimuli, and then go evaluate the newborn. The beginning of the exam should be by inspection, looking at the baby spontaneous movement, level of consciousness, posture. Then evaluate tone (scarf sign, vertical/horizontal suspension, angles, recoil), then primitive reflexes and ANS.

Neonatal Intensive Care Unit

Exam: Admission ❑ Day 1 ❑ 2 ❑ 3 ❑ ___ ❑

Date _____ Time _____ Hours of life _____
YYYY/MM/DD 00:00

Head circumference _____ cm Temperature _____R/ A/ E

When a category can be scored in two different columns, use the one where the Level of Consciousness is.

Category	Normal	Stage 1 (Mild)	Stage 2 (Moderate)	Stage 3 (Severe)
1. Level of Consciousness	☐ 0 = Alert, responsive to external stimuli	☐ 1 = Hyper-alert, moving around and does not maintain a single posture	☐ 2 = Lethargic Delayed but complete response to external stimuli (start with mild stimuli first then proceed to more noxious	☐ 3 = Stupor/Coma Not arousable and non-responsive to external stimuli; may have delayed but incomplete response
Neuromuscular Control				
2. Spontaneous activity	☐ 0 = Normal, changes position when awake	☐ 1 = Normal or decreased activity	☐ 2 = Decreased activity	☐ 3 = No activity
3. Posture	☐ 0 = Predominately flexed when quiet	☐ 1 =Moving around and does not maintain one posture (mild distal flexion)	☐ 2 = strong distal flexion, or complete extension or frog leg position	☐ 3 = Decerebrate with or without stimulation
4. Tone	☐ 0 = Strong flexor tone in all extremities	☐ 1= Normal or slightly ↑resistance	☐ 2a = Hypotonia or floppy (focal or general) 2b = Hypertonia	☐ 3a = Flaccid (rag doll) 3b = Rigid (stiffness on inflexibility)
5. Primitive Reflexes				
Suck	☐ 0 = Strong, easily illicit	☐ 1 = Weak or incomplete	☐ 2 = Weak and/or bite	☐ 3 = Absent
Moro	☐ 0 = Complete	☐ 1 = Complete but with, low threshold to illicit	☐ 2 = Incomplete	☐ 3 = Absent
6. Autonomic System				
Pupils	☐ 0 = normal	☐ 1 = Mydriasis (dilated)	☐ 2 = Myosis (constricted and reactive to light)	☐ 3 = skew deviation of eyes, pupils dilated or non-reactive to light
Heart Rate *do not code if cooling initiated	☐ 0 = 100-160 bpm	☐ 1 = 100-160 bpm -or Tachycardia	☐ 2 = Bradycardia ≤ 100 bpm with occasional increase to 120 bpm	☐ 3 = Variable HR: varies from < 100 to ≥ 120 bpm
Respirations *intubated infant coded 3	☐ 0 = Regular respirations	☐ 1 = Hyperventilation	☐ 2 = Periodic breathing	☐ 3 = Apnea or requires ventilation a) Spontaneous breaths b) No spontaneous breath

Category

1. Level of consciousness _____
2. Spontaneous activity _____
3. Posture _____
4. Tone _____ _____ (note a or b)
5. Primitive reflexes _____
6. Autonomic system _____

aEEG ❑ Normal ❑ Depressed

Is the infant sedated/paralyzed?
❑ Yes ❑ No

Seizures? Anti-convulsant
❑ Yes ❑ No _____

Is a gag reflex present?
❑ Yes ❑ No

Clonus?
❑ Yes ❑ No

What is the level of encephalopathy? ❑ Normal ❑ Mild ❑ Moderate ❑ Severe

Name of examiner _____ Signature: _____

DEFINITIONS FOR NEUROLOGIC EXAMINATION

- Did the infant have documented seizures? Record "Y" if seizures have been diagnosed or if the infant's chart or verbal summary included the diagnosis of seizures. Seizures can be subtle such as ocular deviation, sucking and lip smacking movements, swimming or "rowing" or "bicycling" movements of limbs. They can be tonic, clonic, localized multifocal or generalized. **Seizures make the infant eligible for cooling – but still needs neurological exam**

- Points to consider for neurological exam;
  - Observation period first followed by exam
  - Score the awake state, start with observation (activity, posture, HR and respirations)
  - Do least noxious part first (tone) and most noxious part last (pupils)

- Does the infant have signs of moderate or severe encephalopathy in ≥ 3 categories (3 of the 6 categories) on the neurologic examination

1. **Level of Consciousness**: **extremely important as the code for LOC may be the deciding factor to assign stage of HIE.**
   Code "0" alert and responsive to external stimuli
   Code "1" hyper-alert; moving around and does not maintain a single posture
   Code "2" lethargic: delayed but complete response to external stimuli (start with mild stimuli then proceed to more noxious)
   Code "3" stupor/coma infant is not arousable and non-responsive to external stimuli; may have delayed or incomplete response

2. **Spontaneous activity**: Code "0" infant changes position when awake. Code "1" activity is normal or decreased Code "2" if activity is decreased. Code "3" if no activity. ***infant is sedated clinical judgment has to be used to decide whether the examination is reliable. If uncertain code the worst level.**

3. **Posture**: **Observe infant in wake state.** Code "0" predominately flexed when quiet. Code "1" infant is moving around and does not maintain only one posture or mild distal flexion. Code "2" strong distal flexion or complete extension, or "frog-legged" position. Code "3" decerebrated with or without stimulation (rare) ***if posture is abnormal but does not fit 2 or 3, code as 2.**

4. **Tone**: Code "0" strong flexor tone in all extremities. Code "1" if tone is normal (resistance to passive motion) or slightly increased. Code **"2a"** if hypotonic or floppy, either focal or generalized. Code **"2b"** is hypertonic or increased tone or tension of extremities or trunk upon passive movement. Code **"3a"** if infant lies like a rag doll with no tone at all (flaccid). Code **"3b"** if the infant is rigid with extreme stiffness of inflexibility of extremities or trunk upon passive movement.

5. **Primitive Reflexes: (remember: count only one sign in this category – the highest level of HIE)**

   - **Suck**: Code "0" if strong and easily elicit. Code "1" if weak or incomplete. Code "2" if suck is weak or infant has bite. Code "3" if suck is absent.

   - **Moro**: Code "0" if complete. Code "1" if intact with low threshold. Code "2" if incomplete. Code "3" if absent.

6. **Autonomic system : (remember: count only one sign in this category – the highest level of HIE)**

   - **Pupils**: Code "0" if normal size and reactive to light. Code "1" if mydriasis (dilated and reactive to light). Code "2" if constricted and reacting to light. Code "3" if variable and none reactive to light, skew deviation of eyes.

   - **Heart Rate**: Code "0" 100 to 160 BPM. Code "1" greater than 100 or tachycardia. Code "2" bradycardia (<100/minute) with only occasional increases to > 120/minute. Code "3" HR not constant and widely between less than 100 and greater than 120. ***do not code heart rate if cooling has been initiated. HR evaluation based on documented HR over previous minutes/hours.**

   - **Respiration**: Code "0" regular breaths: Code "1" hyperventilation: Code "2" periodic breathing: Code "3" if apnea or requiring ventilator: 3a) breath above ventilator: 3b) not breathing above ventilator. ***intubated infant with spontaneous breaths would still be coded as 3 as it cannot be ascertained if the spontaneous breaths can sustain respiration without ventilator support**

Legend	≤ less or equal to	< less than
	≥ more or equal to	> more than
	↑ slightly increases	

What is MUHC guideline to determine if the infant is needed to be cooled?

The algorithm attached will help you determine if an infant is to be cooled. Our criteria are modified from the NICHD trial entry criteria:

- To qualify for cooling, the patient MUST have a history compatible with asphyxia whether blood gas data or a history of resuscitation, AND evidence of encephalopathy whether clinical or electrographic.
- We realize that there are infants who will not fit the algorithm, or infants who will have incomplete data. In those cases clinical judgement should be used. We ask however that clinicians respect the spirit of the document. It was never the intent of the authors that a single event, blood test, exam or lab result be the sole determinant in the decision to cool.

The following is an explanation of the terms used in the algorithm:

History of event: History of an acute perinatal event such as, but not limited too, abruptio placenta, cord prolapse, shoulder dystocia, severe FHR abnormalities, late decelerations, etc... Please be very careful of histories where the infant is born "flat." This may or may not be evidence of an asphyxial event. Chrorioamnionitis is particularly problematic, since infants may be born infected, asphyxiated or both. Careful evaluation and clinical judgement should be used in these cases. Infants who have no history of an event can still be cooled, if clinical suspicion of asphyxia is high. Such cases MUST be discussed with staff neonatologist.

Blood gas: arterial cord blood gas is ideal. A postnatal gas, performed with proper technique, within l hour of life is an acceptable substitute as long as the acidosis is not purely respiratory. If the cord gas and postnatal gas are contradictory, clinical judgement should be used to ascertain the most accurate result. Healthy infants with bad gases should not be cooled. Conversely, c learly encephalopathic infants with a normal cord pH may be cooled if deemed appropriate.

Apgar score: Can often be over or under scored. Extreme caution must be taken when the decision to cool is based on the Apgar score.

Need for **PPV:** this may be due to true perinatal depression, or inadequate resuscitation, or both. It is up to the treating team to determine the relevance of this item.

Encephalopathy: the standard neuro admission exam sheet (MRC 0557) should be used. We realize that not all infants can be classified within 6 hours of life. The starred criteria, marked with a (*) are the most important. Not all infants can be neatly classified in to the staging system. Do the best that you can. If it is uncertain whether the infant is encephalopathic, aEEG may be of help.

Seizures: Early seizures with a history of asphyxia are strongly suggestive of encephalopathy. However, other causes of seizures should be carefully evaluated.

How to stage HIE to determine the need for treatment with TH?

At the NICU MCH there is a SARNAT scoring sheet. For every infant admitted for evaluation for HIE, SARNAT score should be calculated at the time of arrival and repeated at 6 hour of life if the score was 1 or less.

What are the contraindications for therapeutic hypothermia?

- Moribund infants.
- infants with major congenital or genetic abnormalities for whom no further aggressive treatment is planned (relative).
- infants with severe intrauterine growth restriction.
- infants with clinically significant coagulopathy (relative).
- Infants with evidence of severe head trauma or intracranial bleeding (relative).

What we should monitor for and what are the other clinical considerations during cooling?

- Keep the patient NPO on restricted TFI.
- Regular labs according to the clinical status and the complications (blood gas, LFT, renal function,etc).
- Continuous monitoring for seizure and the evolution of the neurological status.
- Monitoring for complications of HIE and side effects of cooling.

What are the side effects/complications we should be monitoring in patient with HIE being treated with therapeutic hypothermia?

Acute complications of HIE:

- Cardiac like Arrhythmias.
- Hematological like anemia, leukopenia and coagulopathy.
- Metabolic like hypoglycemia, hypokalemia.
- urinary retention or organ failures (AKI, liver failure).

Side effects of hypothermia:

- Sinus bradycardia (a heart rate of 80 to 100 beats per minute).
- Hypotension with possible need for inotropes
- Mild thrombocytopenia.
- Persistent pulmonary hypertension with impaired oxygenation.

When and how should the infants be rewarmed?

The infant should be warmed after 72h and over 6 to 12 hours (0.5°C every 1 to 2 hours). Most centres rewarm infants by 0.5°C every 1 to 2 hours.

Seizures and worsening of clinical encephalopathy upon rewarming have been reported [35]. In such circumstances, experts suggest recooling for 24 hours and resuming rewarming.

REWARMING

1 After 72 hours of cooling, the infant should be slowly rewarmed. If started cooling after 6 hours of life, the re-warming occurs at 96 hours of life (as per NICHD Late-Cooling Trial).

2 To re-warm: increase the set temperature by 0.5°C per hour until infant reaches 36.5°C. Consider slower re-warming in critically ill infant – discuss with team.
3 Vital signs q 30 minutes during re-warming.
4 aEEG monitoring during the rewarming is mandatory to assess for possible seizure.
5 After the infant reaches 36.5°C, remove the cooling blanket and return the infant to servo control warmer mode.

Once cooling is started – IT SHOULD NOT BE STOPPED.

1. It has been our experience that early discontinuation of hypothermia is rarely indicated, other than for withdrawal of care. Decision to terminate hypothermia before 72 hours should be carefully considered by the treating team.
2 If hypothermia terminated early for reasons other than palliation, follow procedure above.

What investigations and follow up we usually do after cooling?

- The patient neurological status is evaluated.
- 24hour EEG (usually during cooling and could be for longer depends on the clinical condition).
- Daily Sarnat Exam (including in the 24 hours following re-warming).
- Arrange MRI brain in day 10 of life for prognostic purposes.
- Arrange follow up with Neonatal follow up clinic to follow development milestones and the evolution of the neurological status +/- Neurology according to the severity of the clinical condition.

Monitoring / Management:

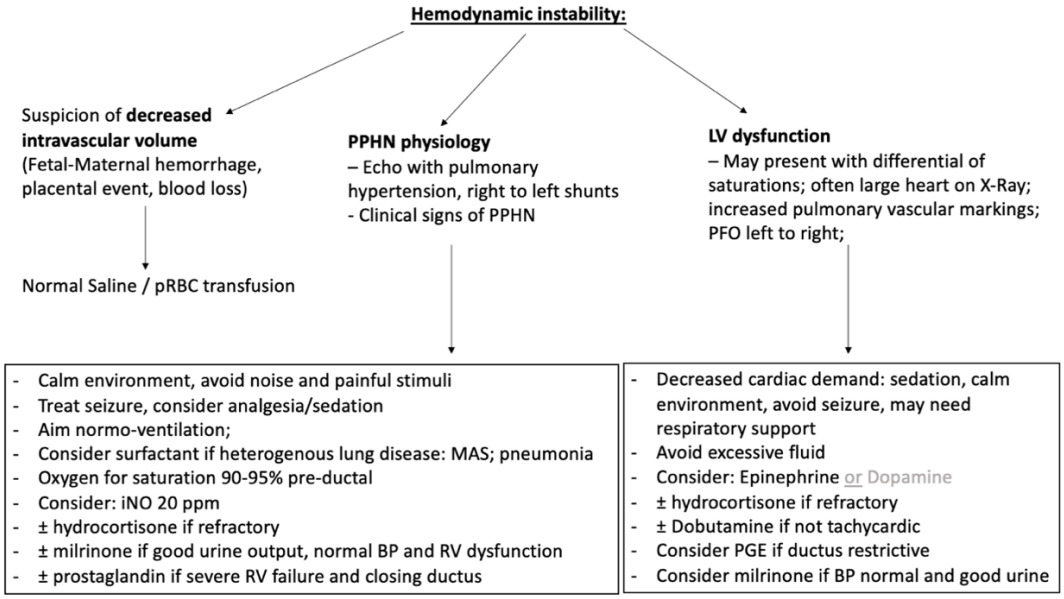
1. Blanket, skin and esophageal temperature will be monitored hourly for the first 12 hours than q2h thereafter.
2. Infant is placed on cardiac monitor and with oxygen saturation probe
3. Vital signs every 15 minutes for the first 4 hours followed by every 1h for the next 8 hours and every q2h until cooling period has ended
4. Continuous bedside aEEG monitoring
5. Glucose, BUN, creatinine, calcium, magnesium, ALT, AST and electrolytes at baseline then at 24 hrs. These patients are at high risk of developing hyponatremia secondary to fluid overload. Maintain fluid restriction and avoid adding sodium for the first 24 hours of age.
6. Blood gases at baseline then q4-6h for the first 24 hours. Reassess need of extra blood gases based on individual needs.
7. CBC at baseline and at 24 hours of age. After that, only if needed. A higher target platelet count (≥ 100.000) may be advisable in this population (rather than the usual 50.000).
8. PT/PTT at baseline then as needed if presence of bleeding - make sure to have the corrected (heparin absorb) before treatment is initiate.
9. Strict intake and output = remember to include all boluses and transfusion in total daily fluids. Remember that infants cooled and intubated have minimal insensible losses.
10. Total fluids are restricted to 30-50 ml/kg/day and should be re-adjusted every 6 to 12 hours based on fluid balance.
11. Record neurological exam (on proper sheets MRC 0557 and MRC 0546) at admission and daily for the first three days, and on day 4 post rewarming

12. Imaging: perform head ultrasound between 24-48 hours of age and brain MRI as per current protocol

Consults / discharge Planning:

1 Neurology consult for management and follow up
2 Occupational therapy consult for assessment and follow up
3 Head MRI at day of life 10
4 Full EEG to be done as per neurology recommendations
5 Cardiology consult MUST be done in cases of hemodynamic instability and/or need for inotropes – or suspected Persistent Pulmonary Hypertension of the Newborn. 6 Consult to Neonatal follow up clinic
On OACIS – Go to Orders, on the right side and click Full Catalogue, By Department – and Click: NICU – you will find the list of labels for therapeutic hypothermia. Will need a neurology consultation.

Cardiovascular management in HIE



- Clinical diagnosis of shock in neonates is difficult to establish and is mainly based on physical examination findings such as: a prolonged capillary refill time, cold extremities, decreased urinary output and metabolic acidosis with or without hypotension. The positive predictive value of these clinical signs has often been questioned.
- Catecholamine:
- Epinephrine or Dopamine when the hypotension is assumed to be secondary to vasomotor dysregulation.
- Dobutamine when underlying cause is assumed to be myocardial dysfunction.
- Extreme caution with Milrinone, as it is renally excreted. If good urine output and in the context of PPHN with RV failure, milrinone can be considered.

- Data on hydrocortisone for shock in is weak. Hydrocortisone should be considered for refractory shock, especially if suspected adrenal suppression (adrenal hemorrhage or adrenal hypoxia), with increasing use of inotropes or in the presence of severe PPHN.
- Consider to obtain ECHO to guide management of shock – echocardiography in the 24 hours after the start of inotropes.
- Consider iNO in newborns with PPHN in the context of prolonged rupture of membranes, once optimization of ventilation and clinical status achieve (calm environment, sedation optimized, acid-base status optimized). Please refer to iNO protocol.

Table III. Confounders of assessment of systemic hemodynamics in patients because of HIE* and/or TH†[39]

Variables	Change	Pathophysiology
Heart rate	Sinus bradycardia	↓ repolarization at SA node†
Blood pressure	↑ DAP	Systemic vasoconstriction†
	↓ SAP	↓ cardiac output†
Color	Pallor	↓ skin perfusion†
Capillary refill time	Prolongation	↓ skin perfusion†
Urinary output	Oliguria or anuria	Acute renal injury*
Blood gas	Metabolic acidosis	Residual perinatal acidosis*
Lactate	Lactic acidosis	Lactate washout after initial insult*, sequestering†

DAP, diastolic arterial pressure; *SA*, sinoatrial; *SAP*, systolic arterial pressure.
*HIE.
†TH.

Feeding during therapeutic hypothermia

General criteria for considering feeding during TH/rewarming:

Criteria should be assessed during morning rounds and reassessed each day thereafter.

Infants may be fed if they meet **all of the** following criteria:

- Over 24 hours old
- Respiratory status: FiO2 < 0.5, not ventilated with an oscillator, not receiving nitric oxide, no chest tubes
- Cardiovascular status: Not hemodynamically unstable, not receiving inotropes
- Neurological status: Sarnat 1 or 2, and no seizures in the past 24 hours

Criteria for Oral Feeding:

Evaluation criteria for initiation of **oral** feeding (by bottle):

- Breathing: Breathing comfortably in room air or low flow nasal cannulae
- Medical stability: Not on anti-seizure medication
- Protective oral reflexes: Must have gag and cough reflex
- Sucking: Able to achieve strong, rhythmic non-nutritive sucking pattern
- Positioning: Tolerates handling and able to achieve safe, functional positioning for feeding
- Behavioral state: Able to achieve quiet/alert state
- Hunger cues: Demonstrates interest in oral feeding (rooting, crying)

To initiate regular oral feeding in a neonate with encephalopathy treated with TH, he/she must fulfill the following criteria on clinical feeding evaluation with OT:

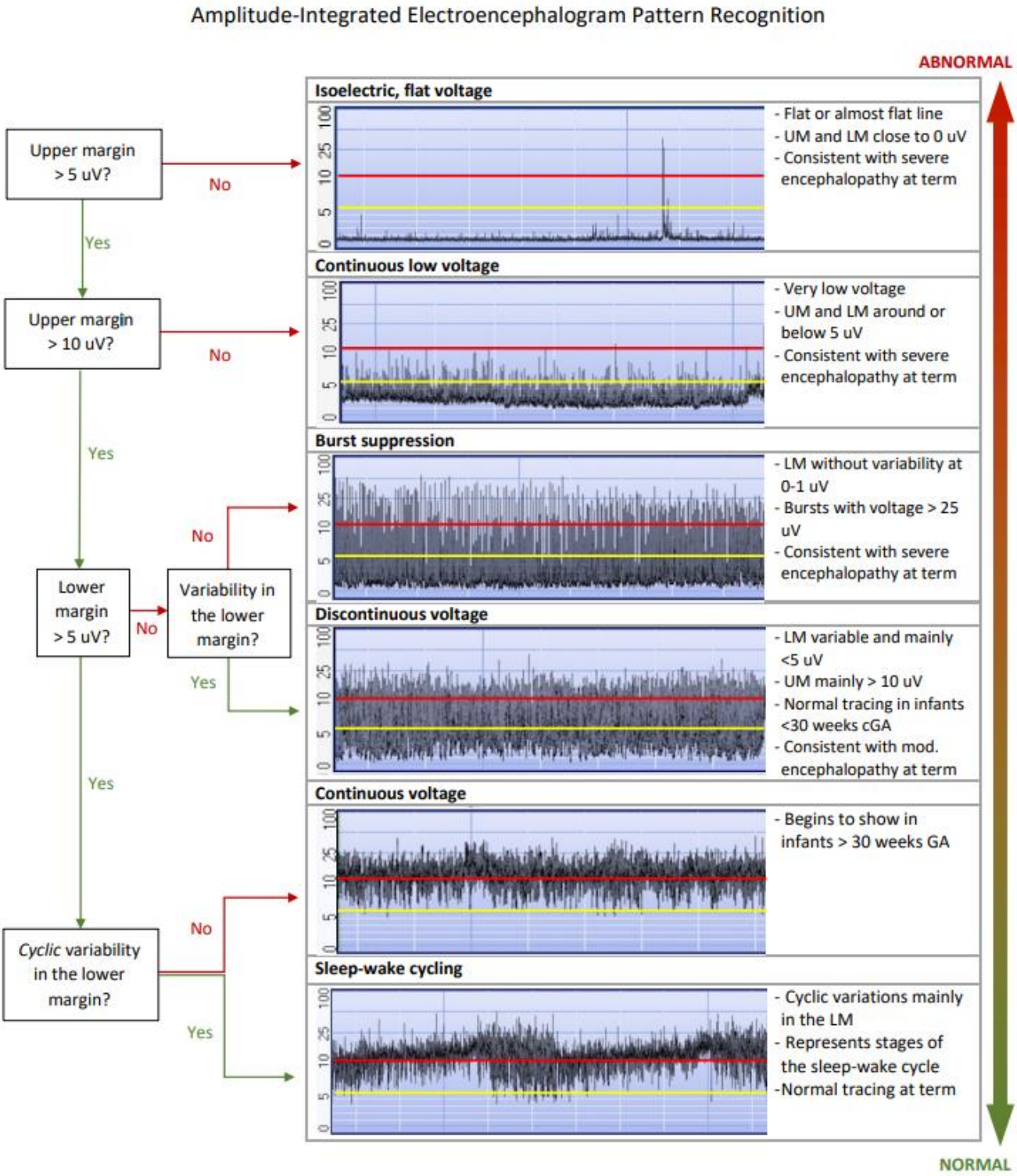
- Physiologic stability
- Functional behavioral state
- Functional coordination of suck-swallow-breathing
- Absence of clinical signs of aspiration

Note: *If patient meets criteria for feeding, but does not meet criteria for ORAL feeding, gavage feeding should be offered. See below for information regarding gavage feeding. If patient does not meet criteria for feeding during TH/rewarming, OIT should be offered.*

aEEG (Amplitude-integrated EEG)

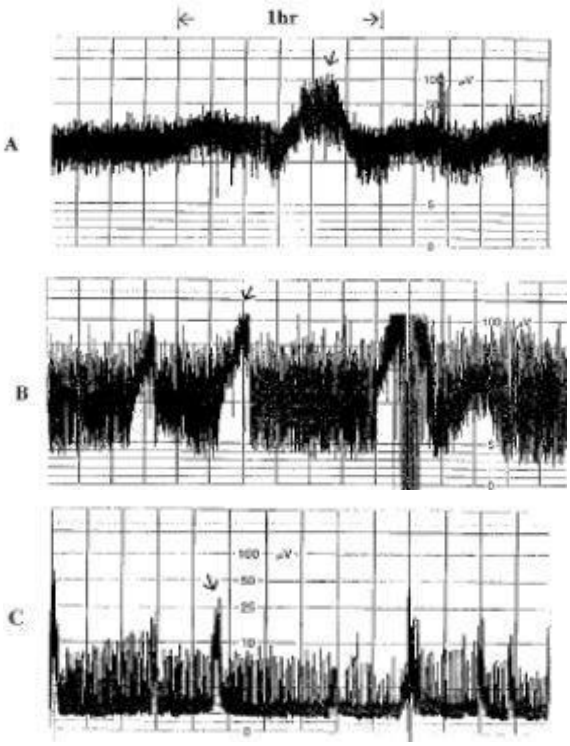
For aEEG examples go to www.neoweb.org.uk
Go to CFM training guide then CFM quiz

aEEG pattern recognition:



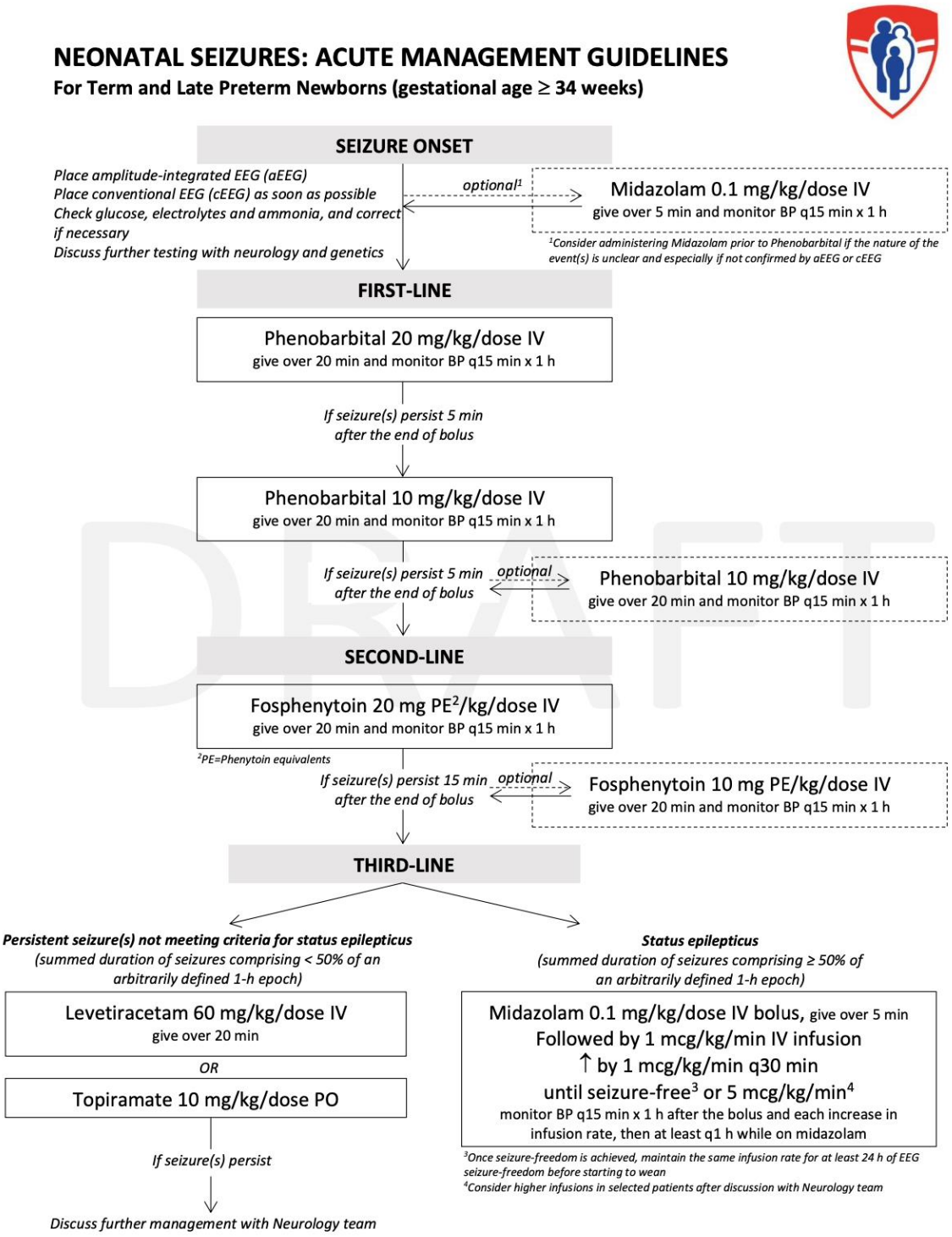
- Seizure activity on aEEG

- Sudden rise and narrowing pattern in the aEEG tracing (prolonged periods of sudden elevation in both the lower and upper margins)
  - *Suspicion of seizures (increase in EEG voltage?)*
  - *Look at EEG tracing in the gaps of the rising and narrowing:*
  - *if distinct repetitive spike and wave discharge pattern on EEG tracing:* ***seizures***
- The trace returns to the previous appearance when seizure activity stops
- Seizures may only be identified if sufficiently prolonged (more than 2-3 min)
  - *shorter lasting discharges may be missed since the aEEG is recorded at a very slow speed*
- Note: difficult to distinguish burst suppression from brief seizures in a severely abnormal trace
- Note: it may be difficult to comment on background aEEG amplitude if very frequent seizures



Neonatal Seizures:

See Protocol in NICU weebly



Pyridoxine trial (consider if persistent seizures despite use of first, second and third-line pharmacotherapy, after discussion with Neurology and Medical Genetics teams)

1. Tests to be collected prior to giving pyridoxine: alpha aminoadipic semialdehyde (urine) and pipecolic acid (blood and CSF) – CONFIRM with neurology and Metabolic genetic team
2. Pyridoxine 100 mg IV x 1 (while monitoring EEG response, oxygen saturation and other vital signs, given risk of apnea)

Hypotonia :

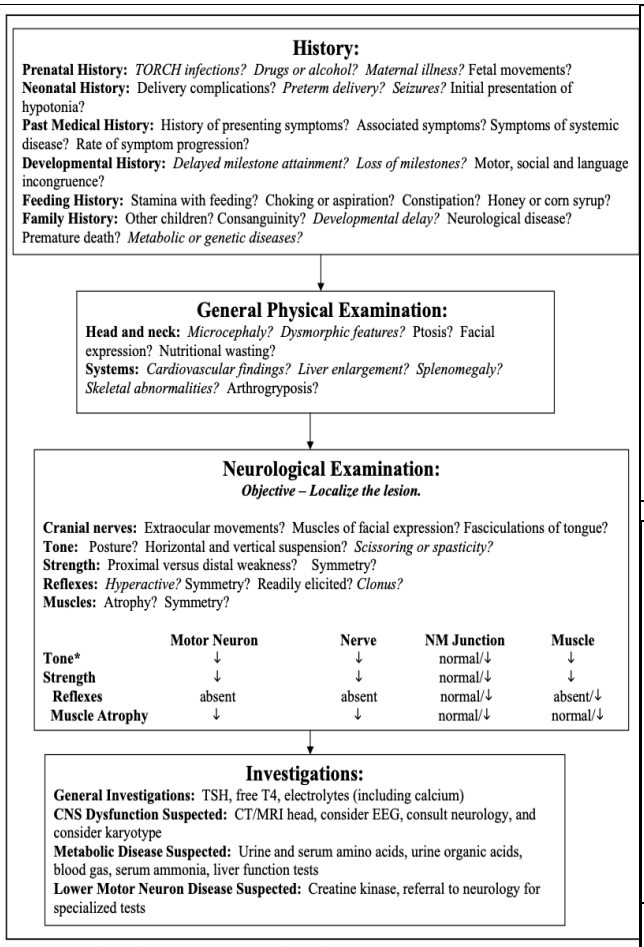
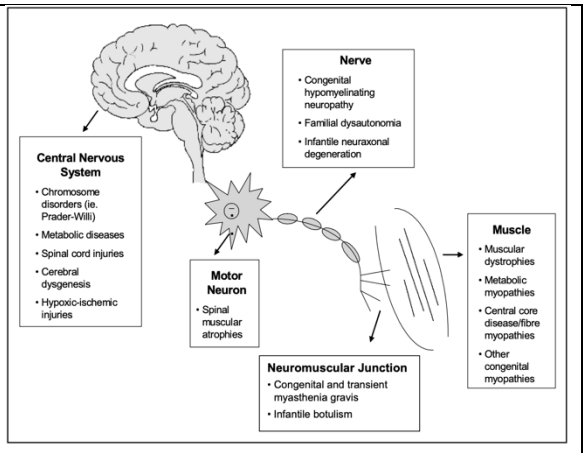


Figure 2) *Schematic approach to hypotonia in infancy. Pertinent posi tives, highlighted in italics, raise suspicion of central nervous system an metabolic diseases. ↑ Increased; ↓ Decreased; CNS Central nervou system; CT Computed tomography; EEG Electroencephalography MRI Magnetic resonance imaging; NM Neuromuscular; TORCH Toxoplasmosis, other infections, rubella, cytomegalovirus infection an herpes simplex; TSH Thyroid-stimulating hormone. *Adapted from ref erence 2*

A schematic approach to hypotonia in infancy
JoAnna Leyenaar MD MPH, Peter Camfield MD FRCPC, Carol Camfield MD FRCPC



Central (most common)	Hypoxic ischaemic encephalopathy Intracranial haemorrhage Cerebral malformations Chromosomal abnormalities (e.g.Trisomy 21, Prader-Willi syndrome) Congenital infections (TORCH) Acquired infections Peroxisomal disorders Drug effects (e.g. benzodiazepines)
Spinal cord	Birth trauma (especially Breech delivery) Syringomyelia
Anterior Horn Cell	Spinal Muscular Atrophy Pompe's disease (acid maltase deficiency)
Neuromuscular junction	Myasthenia gravis (transient/ congenital) Infantile botulism
Muscle	Muscular dystrophies (inc. congenital myotonic dystrophy) Congenital myopathies (e.g. central core disease)
Peripheral nerves	Hereditary motor and sensory neuropathies
Metabolic myopathies	Acid maltase deficiency Carnitine deficiency Cytochrome-*c*-oxidase deficiency

Weaning of opioids: MCH Clinical Guideline

1) Recommendations for the weaning of opioids and benzodiazepines

a) Duration of analgesia/sedation less or equal to 4 days

Usually, these patients do not need a step wise weaning due to the short duration of exposure (low risk for withdrawal).

Procedure:

- Weaning over 24 to 48 hours could be considered, depending on the dose and duration of the received analgesia/sedation. If the patient has been on a low dose of sedation for less than 24-48 hours, no wean is required, stop the infusion/medication.
- When regular opioid and/or benzodiazepine ends, keep an intermittent dose to be use if needed (PRN) for the next 24 hours, then discontinue.
    - Note: do not use a conversion table to prescribe the intermittent PRN dose. Order a regular dose of the opioid or benzodiazepine (the patient did not develop tolerance, there is a risk of overdose if converting the dose from the infusion).

b) Duration of analgesia/sedation 5 to 9 days

Usually, the weaning can be tolerated over a period of a few days (intermediate risk for withdrawal).

Procedure:

- Wean opioids and/or benzodiazepines over a period of 3 to 5 days.
    - Example: decrease by 10% of the initial dose every 12 hours or by 20% every 24 hours
- Remain on continuous infusion instead of switching to the equivalent intravenous boluses for the weaning of the opioid or benzodiazepine if the patient is nil per os (NPO) or receiving only a small amount of enteral feeds.
- If the patient is on two agents (an opioid and benzodiazepine), the wean can be done in an alternating fashion as long as it remains over 3 to 5 days.

- Convert the continuous infusion of opioid and/or benzodiazepine to an enteral agent to be given as regular boluses when ready to remove the intravenous line (if the only reason to keep the central line is the infusion of analgesia-sedation) to continue the step wise weaning.

c) Duration of analgesia/sedation 10 days or more

Usually, the weaning is performed over a period of 10 days (higher risk for withdrawal).

Procedure:

- Wean opioids and/or benzodiazepines over a period of 10 to 14 days.
    - Example: decrease by 10% of the initial dose every 24 hours
- Remain on continuous infusion instead of switching to the equivalent intravenous boluses for the weaning of the opioid or benzodiazepine if the patient is NPO or receiving only a small amount of enteral feeds.
- If the patient is on two agents (an opioid and benzodiazepine), the wean can be done in an alternating fashion as long as it remains over 10-14 days.
- Convert the continuous infusion of opioid and/or benzodiazepine to an enteral agent to be given as regular boluses when ready to remove the intravenous line (if the only reason to keep the central line is the infusion of analgesia-sedation) to continue the step wise weaning.
- Consider addition of clonidine if the weaning might be longer than planned or if there are recurrent signs of withdrawal.

Monitoring the response to the opioid and/or benzodiazepine weaning

- Sunscale[1] above 24
    - Use non-opioid analgesia.
    - Breakthrough dose of opioid if necessary.
- WAT score more than 3
    - Give a breakthrough dose of opioid or benzodiazepine.
    - If more than 3 episodes of WAT score above 3 within 24 hours:
        - Hold the weaning and consider going back to the previous dose.
- Sedation score equal or more than 2
    - Sedation score of 2
        - Hold opioid and/or benzodiazepine.
        - Resume at a decreased dose by 25%, when sedation score equal or less than 1
    - Sedation score of 3
        - Stimulate the patient, administer oxygen
        - Hold opioid and/or benzodiazepine
        - Resume at a decreased dose by 50%, when sedation score equal or less than 1

[1]Sunscale if applicable (to be monitor only if clinically indicated)

2) Recommendations for weaning of dexmedetomidine infusion

Usually, the wean of dexmedetomidine can be held while weaning first IV opioids/benzodiazapines. However, if the opioids/benzodiazepines are given enterally and IV access is used only for

dexmedetomidine, holding the wean of opioids/benzodiazepines to allow weaning of the dexmedetomidine is recommended to allow for IV access removal as soon as possible.

There is increasing documentation of withdrawal following abrupt or rapid discontinuation of dexmedetomidine after a prolonged use (more than 72 hours). Clinical presentation of dexmedetomidine withdrawal is related to sympathetic overactivity and include signs and symptoms as hypertension, tachycardia, agitation, insomnia, diaphoresis and tremor. After a prolong use of dexmedetomidine, a step wise weaning is recommended.

Procedure for weaning of dexmedetomidine:

1) Infusion duration less than 24 hours: no wean required, stop infusion
2) Infusion duration ranging from 24 to 72 hours: wean over 12 to 24 hours
3) Infusion duration more than 72 hours:
    a. Low dose (less than 0.6 mcg/kg/h): ↓ by 0.1 mcg/kg/h q8h until off
    If not tolerating wean: prolong interval between each dose decrease and consider switch to clonidine if enteral route is possible
    b. Intermediate dose (0.6 to 1.2 mcg/kg/h): ↓ by 0.15 mcg/kg/h q8-12h until off
    If not tolerating wean: prolong interval between each dose decrease and consider using clonidine if enteral route is possible
    c. High dose (more than 1.2 mcg/kg/h): ↓ by 0.2 mcg/kg/h q8-12h until off
    If not tolerating wean: prolong interval between each dose decrease and consider using clonidine if enteral route is possible

    Consider switching to clonidine for a more rapid transition to a non-intravenous formulation if the IV access is used only for dexmedetomidine continuous infusion or if patient is on enteral opioids/benzodiazepines and expected duration of wean is more than 3 days.

Procedure for switching to clonidine:

Once dexmedetomidine dose is 0.6 mcg/kg/h or less, start clonidine and further decrease dexmedetomidine infusion rate after each clonidine dose for an overlap time of 24 hours (decrease dexmedetomidine approximately by one third of initial infusion rate after each dose so that dexmedetomidine is stopped after the third dose of clonidine).

Dexmedetomidine dose at time of switch	Suggested initial clonidine dose
0.5 to 0.6 mcg/kg/h	10 mcg/kg/day divided q8h
0.3 to 0.49 mcg/kg/h	6 mcg/kg/day divided q8h
0.29 mcg/kg/h or less	3 mcg/kg/day divided q8h

Clonidine can be weaned after the switch or after the end of opioids/benzo wean if applicable. Clonidine must be weaned over a few days. For a clonidine dose of 10 mcg/kg/day, wean over 5 to 7 days and if the clonidine dose is of 3 to 6 mcg/kg/day, wean over 3 to 5 days.

Pain or withdrawal assessment:

Scale for Use in Newborns (SUN scale):

Used for pre-term and newborn infants in the NICU; Observation of central nervous system state, breathing, movement, tone, heart rate, blood pressure, oxygenation, temperature. Validated with procedural pain

NIPS	Comfort scale	SUN
Facial expression 0: Relaxed 1: Grimace Cry 0: No cry 1: Whimper 2: Vigorous Breathing problems 0: Relaxed 1: Change in breathing Arms 0: Relaxed 1: Flexed Legs 0: Relaxed 1: Flexed/extended State of arousal 0: Sleeping/awake 1: Fussy	Alertness 1: Deeply asleep 2: Lightly asleep 3: Drowsy 4: Fully awake and alert 5: Hyper-alert Calmness/agitation 1: Calm 2.:Slightly anxious 3: Anxious 4: Very anxious 5: Panicky Respiratory response 1: No coughing 2: Spontaneous respiration with little or no response to ventilation 3: Occasional cough or resistance to ventilator 4: Actively breathes against ventilator 5: Fights ventilator; coughing and choking Physical movement 1: No movement 2: Occasional, slight movement 3: Frequent, slight movement 4: Vigorous movements including torso and head Blood pressure (mean) 1: Blood pressure below baseline 2: Blood pressure consistently at baseline 3: Infrequent elevations of 15% or more (1–3) 4: Frequent elevations of 15% or more (>3) 5: Sustained elevation ≥15% Heart rate 1: Heart rate below baseline 2: Heart rate consistently at baseline 3: Infrequent elevations of ≥ 15% above baseline (1–3) 4: Frequent elevations of ≥ 15% above baseline 5: Sustained elevations of ≥ 15% Muscle tone 1: Muscles totally relaxed 2: Reduced muscle tone 3: Normal muscle tone 4: Increased muscle tone and flexion of fingers and toes 5: Extreme muscle rigidity and flexion of fingers/toes Facial tone 1: Facial muscles totally relaxed 2: Facial muscle tone normal; no facial muscle tension 3: Tension evident in some facial muscles 4: Tension evident throughout facial muscles 5: Facial muscles contorted and grimacing	CNS state 0: Deeply asleep 1: Drowsy, light sleep 2: Awake, quiet alert, calm 3: Anxious, fussy 4: Hyper-alert, panicked Breathing 0: No spontaneous breathing 1: Shallow, intermittent breathing 2: Quiet respiration, relaxed, usual pattern 3: Increased rate and work of breathing, change from baseline 4: Fights ventilator, coughs, chokes Movement 0: No movement or 1: Decreased activity, infrequent movements 2: Occasional activity, usual movements 3: Increased activity, flexion and extension of extremities 4: Vigorous movements of extremities, torso, head Tone 0: Flaccid, no tone 1: Decreased tone 2: Normal tone 3: Increased tone, some finger/toe flexion 4: Rigidity, limb extension, finger/toe flexion Face 0: Totally relaxed, no tone or expression 1: Reduced facial tone or expression 2: Normal, neutral, no tension 3: Increased tension, furrowed brow 4: Contortion, grimace, vigorous cry Heart rate 0: Depressions >15% below baseline 1: Depressions to 15% below baseline 2: Baseline 3: Elevations to 15% above baseline 4: Elevations >15% above baseline Mean blood pressure 0: Depressions >15% below baseline 1: Depressions to 15% below baseline 2: Baseline 3: Elevations to 15% above baseline 4: Elevations >15% above baseline

NIPS, Neonatal Infant Pain Scale; SUN, Scale for Use in Newborns.

THE CLINICAL JOURNAL OF PAIN

WITHDRAWAL ASSESSMENT TOOL (WAT):

WAT is also used for those with progressive weaning of sedation. Ideally, patients should have a WAT of 3 or less. If above 3, PRN medications should be administered or weaning should be postponed.

Information from patient record, previous 12 hours	
Any loose/watery stools	No = 0 Yes = 1
Any vomiting, retching, gagging	No = 0 Yes = 1
Temperature > 37.8 °C	No = 0 Yes = 1
2 minute pre-stimulus observation	
State	SBS[1] ≤ 0 or asleep/awake calm = 0 SBS[1] ≥ +1 or awake distressed = 1
Tremor	None/mild = 0 Moderate/severe = 1
Any sweating	No = 0 Yes = 1
Uncoordinated/repetitive movement	None/mild = 0 Moderate/severe = 1
Yawning or sneezing	None or 1 = 0 >2 = 1
1 minute stimulus observation	
Startle to touch	None/mild = 0 Moderate/severe = 1
Muscle tone	Normal = 0 Increased = 1
Post-stimulus recovery	
Time to gain calm state (SBS[1] ≤ 0)	< 2 minutes = 0 2 - 5 minutes = 1 > 5 minutes = 2
Total Score (0-12)	

Modified Finnegan scoring system

Used for Neonatal abstinence syndrome. Not validated in premature newborns.

SYSTEM	SIGNS AND SYMPTOMS	SCORE
CENTRAL NERVOUS SYSTEM DISTURBANCES	Excessive High Pitched (or other) Cry < 5 minutes	2
	Continuous High Pitched (or other) Cry > 5 minutes	3
	Sleeps < 1 Hour After Feeding	3
	Sleeps < 2 Hours After Feeding	2
	Sleeps < 3 Hours After Feeding	1
	Hyperactive Moro Reflex	2
	Markedly Hyperactive Moro Reflex	3
	Mild Tremors Disturbed	1
	Moderate-Severe Tremors Disturbed	2
	Mild Tremors Undisturbed	3
	Moderate-Severe Tremors Undisturbed	4
	Increased Muscle Tone	2
	Excoriation (Specific area)	1
	Myoclonic jerks	3
	Generalized convulsions	5

METABOLIC/VASOMOTOR/ RESPIRATORY DISTURBANCES	Sweating	1
	Fever 38°C to 38.3°C	1
	Fever > 38.3°C	2
	Frequent Yawning (> 3-4 times/interval)	1
	Mottling	1
	Nasal Stuffiness	1
	Sneezing (> 3-4 times/interval)	1
	Nasal Flaring	2
	Respiratory rate > 60/min	1
	Respiratory rate > 60/min with Retraction	2
GASTRO-INTESTINAL DISTURBANCES	Excessive Sucking	1
	Poor Feeding	2
	Regurgitation	2
	Projectile Vomiting	3
	Loose Stools	2
	Watery Stools	3
TOTAL SCORE		

Table 1. Medications to treat neonatal abstinence syndrome

Medication	Mechanism of action	Dose	Comments
Morphine	Natural m-receptor agonist	If score is ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations, start at 0.32 mg/kg/day, divided every 4 h–6 h, orally. If score persists ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations, increase by 0.16 mg/kg/day every 4 h–6 h, to a maximum of 1.0 mg/kg/day. Most tapering protocols decrease dose by 10% of the total daily dose, every 48 h–72 h, depending on NAS scores. http://pcmch.on.ca/ClinicalPracticeGuidelines/NeonatalAbstinenceSyndrome.aspx	Most commonly used as first-line treatment in Canada Does not contain alcohol Short half-life (9 h) When NAS scores are stable (< 8) for 48 h–72 h, consider weaning.
Methadone	Synthetic complete m-receptor agonist; N-methyl-D-aspartate receptor antagonist	0.05–0.1 mg/kg/dose every 6 h–12 h, orally Increase by 0.05 mg/kg every 48 h Maximum dose 1 mg/kg/day	Long half-life (26 h) Used in many countries as a first-line treatment (instead of morphine) when mother is on methadone. Available in Canada but requires special dispensing /prescriptive authority Contains 8% alcohol
Phenobarbital	Gamma aminobutyric acid (GABA) receptor agonist	May be used in addition to morphine, especially in poly-substance abuse cases. Loading dose: 10 mg/kg, orally, every 12 h for three doses Maintenance dose: 5 mg/kg/day, orally. Wean by 10% to 20% every day or every two days when symptoms are controlled.	Long half-life (45 h–100 h) Requires blood level monitoring May make GI symptoms worse Sedative effect Contains 15% alcohol
Clonidine	Alpha-2 adrenergic receptor agonist	Alternative therapeutic option in combination with morphine. Especially effective when autonomic symptoms of NAS are present. Start at 0.5 mcg/kg, divided every 4 h–6 h, orally. Wean by 25% of the total daily dose every other day (Q4h to Q6h × 48h, to Q8h × 48h, to Q12h × 48h to HS, then d/c)	Alcohol-free preparation available Long half-life (44 h–72 h) Abrupt discontinuation may cause rapid rise in blood pressure (BP) and heart rate (HR). Gradual weaning is therefore recommended.
Buprenorphine	Semi-synthetic partial m-receptor agonist, k-receptor antagonist	4–5 mcg/kg/dose every 8 h; sublingual route Maximum dose 60 mcg/kg/day	Half-life (24 h–60 h) Sublingual administration of a dilution of buprenorphine solution in ethanol and sucrose Contains 30% alcohol

Dexmedetomidine / Clonidine

ALPHA2-AGONISTS: DEXMEDETOMIDINE AND CLONIDINE

Dexmedetomidine

- Selective alpha2-adrenergic receptor agonist
  - specificity 1600:1 (α2 : α1)
- Used for sedative, anxiolytic and analgesic effects
- Half life: 3.2h term neonate (7.6h in preterm)

Clonidine

- Non selective alpha2-adrenergic receptor agonist
  - specificity 200:1 (α2 : α1)
- Used for analgesic and sedative effects, adjunctive treatment of opioid withdrawal
- Half life: neonates and infants 9-12h

Withdrawal : related to sympathetic overactivity, include hypertension, tachycardia, agitation, nervousness, insomnia, diaphoresis and tremor.

➜ well documented for clonidine following abrupt discontinuation
➜ increasing documentation for dexmedetomidine following abrupt or rapid discontinuation of prolonged duration (> 72 h)

1. Glaess et al. Clonidine as a strategy for discontinuing dexmedetomidine sedation in critically ill patients: A narrative review. Am J Health-Syst Pharm,. 2020; 77:515-522
2. Burbano et al. Discontinuation of prolonged infusions of dexmedetomidine in critically ill children with heart disease, Intensive Care Med. 2012 February; 38(2): 300-307

Using clonidine as a strategy for discontinuing dexmedetomidine

➜ Limited supportive data, but advantages include :

- Transition to a non-intravenous formulation
- Decrease cost and can facilitate transition of cares
- Clonidine is recognized as an adjunctive treatment for withdrawal to opioids/benzodiazepines

➜ Consider in patients :

- With prolonged used of dexmedetomidine (> 72 h)
- Having symptoms of withdrawal (hypertension, tachycardia, agitation) upon discontinuation/wean of dexmedetomidine
- Requiring weaning for other(s) sedatives(s) agents (morphine, benzodiazepine)

3. Haenecour A. et al. Prolonged dexmedetomidine infusion and drug withdrawal in critically ill children. J Pediatr Pharmacol Ther 2017; 22 (6) 453-460

- No clear evidence on the best way to wean dexmedetomidine when used for prolong duration
- No equivalent dosage exist between dexmedetomidine and clonidine

➜ Wean dexmedetomidine « slowly »

- 0.1 – 0.4 mcg/kg/h q8-24h
- need to adjust based on patient status, duration and dose
- effect of decrease or discontinuation will be evident rapidely due to the short half life

➜ Introduction of clonidine if required

- when able to wean to a lower dose if previously on high dose (> 0.7 mcg/kg/h)
- overlap time of dexmedetomidine and clonidine should be between 24 to 48 h to avoid side effects

Gastrointestinal System:

Gastroschisis

Delivery Room Interventions and Procedures:

See complete protocol in NICU weebly

Pre-delivery Huddle:

1. Review maternal antenatal history
    a. is there fetal growth restriction, polyhydramnios/oligohydramnios, known GI obstruction
2. Discuss with OB:
    a. Place of delivery – In OR (even if it is vaginal delivery)
    b. The importance of keeping long cord (clamp and cut the umbilical cord at least 30 cm to preserve the option of suture less umbilical closure
    c. To plan for delayed cord clamping unless there is contraindication
3. Inform pediatric surgery regarding the laboring mother with fetal gastroschisis and expected timing of delivery
4. NICU resuscitation team huddle should include:
    a. Discussion of plan of care and clear defined team member roles
    b. Gather equipment needed for abdominal wall defects
        i. Repogle-8 F for pre-term and LBW < 2.5 kg and 10F for full-term infants
        ii. Sterile bowel bag
    c. Advise NICU regarding the expected admission and anticipate expected procedures
        i. Securing IV in upper extremities and administration of IV fluids
            1. Replace Gastric losses:
                a. 1 for 1 with D5-1/2NS + 20 mEq/L KCl. If 5 mL or less of gastric drainage over 4 hours - do not replace
        ii. Administration of antibiotics post drawing blood culture
        iii. Discussion of plan for abdominal closure with peds surgery
        iv. Preparation of drugs for sedation
        v. Labs required post admission-CBC, CBG, blood culture, blood type and cross-match

Delivery Room Interventions:

- Delayed cord clamping x 60 seconds unless there is contraindications
- Clamp and cut the umbilical cord at least 30 cm.
- Initial resuscitation of the newborn per NRP
- If prolonged PPV needs to be provided, consider to intubate and ventilate to avoid gaseous distension of the bowel
- Apply cardiac leads (may need to put them on upper arms) and temperature probe.
- Care of the exposed bowel
    - Assess color, matting and dilation of the bowel
    - Utilize sterile gloves when manipulating bowel. Avoid excessive handling.

    - Position patient and bowel on right side to decrease tension on the mesenteric vessels.
    - Place legs, exposed bowel and viscera, lower body up to axilla into “bowel bag” and secure bag opening loosely across upper chest. Do not use saline-soaked gauze.
    - Insert Repogle and suction manually until transfer to NICU.
- Prevent hypothermia and reduce losses of fluid

Admission for Gastroschisis:

Admission Orders:

- Place on continuous cardio-respiratory monitor.
- Monitor temperature closely.
- Ensure repogle is placed on intermittent low-wall suction 30-40 mmHg.
- Document Vital signs every 15 minutes for the first 4 hours until abdominal closure is complete and vital signs are stable.(HR, Sat, BP and RR)
- Place peripheral IV In upper extremities.
- Run TFI of 100 ml/kg/day (D10W at 60 ml/kg/day and NS at 40 ml/kg/day)
- Perform specified blood tests (CBC, blood gas, blood culture, blood type and cross-match)
- Start antibiotics – Ampicillin and tobramycin are drugs of choice for 48 hours and reassess.
- Ensure the presence of pediatric surgical team at bedside and know the plans for closure of abdominal bowel defect i.e primary closure vs Silo placement. Regardless of the closure method, have the gastroschisis kit box at the bedside.

Nutritional support:

1. Consider initiation of TPN in 12-24 hours.
2. Consider placement of PICC in 24-48 hours

To avoid variation in the timing of feeding initiation and advancement to full enteral feeds, the following guideline is suggested.

1. Removal of repogle when out-put is non-bilious and is < 20 ml/kg/day post placement to gravity.
2. To initiate oral bolus feeds post no vomiting after placement of repogle to gravity x 24 hours
3. Recommend use of maternal breast milk for feeding initiation. If maternal expressed milk is not available, obtain consent for human donor milk.
4. Start with expressed breast milk at 20 ml/kg/day divided into q 3 hourly feeds.
5. If tolerated x 48 hours, advance by 20 ml/kg/day until a volume of 140 ml/kg.day is reached.
6. Recommend removal of PICC at TFI tolerance of 120 ml/kg/day
7. Avoid use of Gastroesophageal reflux medications prophylactically.

Necrotizing enterocolitis

Modified Bell staging criteria for necrotizing enterocolitis (NEC) in neonates

Stage	Classification of NEC	Systemic signs	Abdominal signs	Radiographic signs
IA	Suspected	Temperature instability, apnea, bradycardia, lethargy	Gastric retention, abdominal distention, emesis, heme-positive stool	Normal or mild intestinal dilation, mild ileus
IB	Suspected	Same as above	Grossly bloody stool	Same as above
IIA	Definite, mildly ill	Same as above	Same as above, plus absent bowel sounds with or without abdominal tenderness	Intestinal dilation, ileus, pneumatosis intestinalis
IIB	Definite, moderately ill	Same as above, plus mild metabolic acidosis and thrombocytopenia	Same as above, plus absent bowel sounds, definite tenderness, with or without abdominal cellulitis or right lower quadrant mass	Same as IIA, plus ascites
IIIA	Advanced, severely ill, intact bowel	Same as IIB, plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, DIC, and neutropenia	Same as above, plus signs of peritonitis, marked tenderness, and abdominal distention	Same as IIA, plus ascites
IIIB	Advanced, severely ill, perforated bowel	Same as IIIA	Same as IIIA	Same as above, plus pneumoperitoneum

From UpToDate

Gastro-Esophageal Reflux – GERD

Summary of Diagnosis and Management of Clinically Significant Gastroesophageal Reflux for Infants Born Prematurely

Please refer to the full guidelines for details

Diagnosis

Good **VIBEs** only for reflux!

The infant must have at least 2 of the following[1]:

V – **VOMITING** on average > 2 times in 24 hours for at least 1 week
I – **IRRITABILITY** that prevents age-appropriate activities for at least 1 week
B – Poor **BOTTLE/BREAST** feeding progression at 37 weeks corrected gestational age or later[1]
E – Requires **EXTENDED** gavage feed time for age-appropriate physiology (i.e. inability to compress feeds)

[1]Occupational therapy needs to be consulted to fulfill this criterion. Failure to remove CPAP by 37 weeks corrected gestationa agel does not automatically fulfill criterion.

Treatment Algorithm

Continue all previous steps if advancing through the algorithm

Step 1: Conservative Management

Step 1a: 1-week trial of extended feed time OR decreased TFI
Step 1b: 1-week trial of extended feed time AND decreased TFI
*Additional practices to include in Step 1: i) Encourage Kangaroo Care; ii) Prone positioning and elevation of the head-of-bed if not approaching discharge; iii) Use nasogastric tubes (not orogastric) if off respiratory support; iv) Use thickener or thickened formula if oral feeding and cGA ≥ 37 weeks[1]; v) Encourage oral stimulation and/or oral feeds

Step 2: CMPI Evaluation and Management

Step 2a:
- Evaluate likelihood of CMPI based on CBC and family history. If normal CBC and no family history of atopy, skip Step 2.
- If eosiniophilia or family history of atopy, 1-week trial of hydrolyzed fortifier (liquid HMF/Nutramigen)

Step 2b
- 1-week trial of hydrolyzed milk (base + fortifier) (Nutramigen +/- EBM with CMPI diet)

Step 3: Pharmacologic Management

Step 3a: One Pharmacologic Agent if cGA ≥ 37 weeks
- If primary symptom is irritability or poor oral feeding or inability to compress feed time, 1-week trial of acid-blocker (PPI or H2 blocker)
- If primary symptom is vomiting, 1-week trial of domperidone

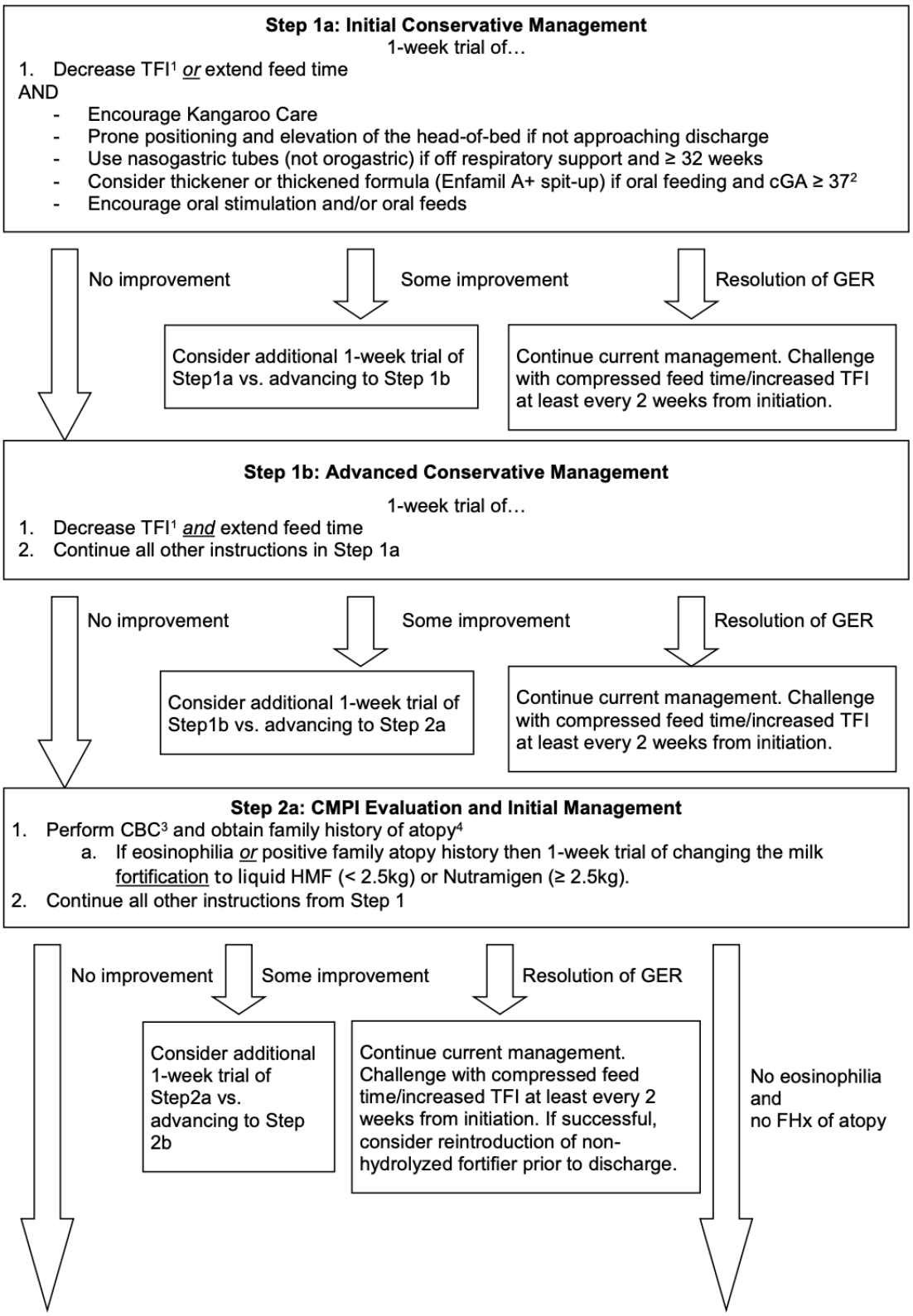
Step 3b: Two Pharmacologic Agents if cGA ≥ 37 weeks
- If already prescribed acid-blocker, 1-week trial of adding domperidone
- If already prescribed domperidone, 1-week of adding acid-blocker

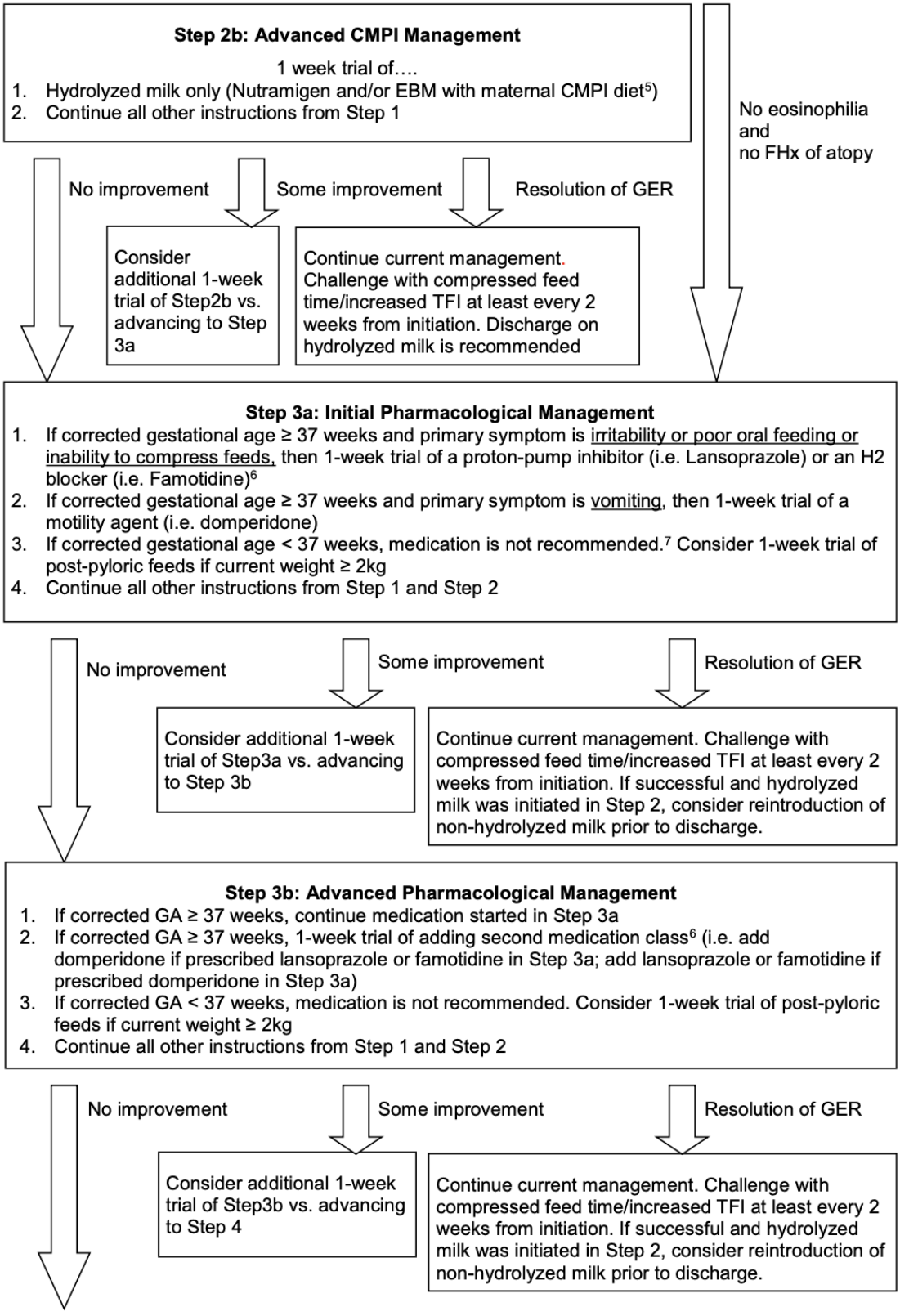
*If cGA < 37 weeks, medication is not recommended. Consider 1-week trial of post-pyloric feeds if current weight ≥ 2kg

Step 4: Refractory GER
- Consult GI for further investigations and management
- Consult Neonatal Follow-Up Bridge Team for long-term management plans

[1]Discuss thickener options with the nutritionist and occupational therapist

Treatment Algorithm for Clinically Significant GER in Infants Born Prematurely




Step 2b: Advanced CMPI Management
1 week trial of….
1. Hydrolyzed milk only (Nutramigen and/or EBM with maternal CMPI diet[5])
2. Continue all other instructions from Step 1
No eosinophilia and no FHx of atopy
No improvement
Some improvement
Resolution of GER
Consider additional 1-week trial of Step2b vs. advancing to Step 3a
Continue current management. Challenge with compressed feed time/increased TFI at least every 2 weeks from initiation. Discharge on hydrolyzed milk is recommended
Step 3a: Initial Pharmacological Management
1. If corrected gestational age ≥ 37 weeks and primary symptom is irritability or poor oral feeding or inability to compress feeds, then 1-week trial of a proton-pump inhibitor (i.e. Lansoprazole) or an H2 blocker (i.e. Famotidine)[6]
2. If corrected gestational age ≥ 37 weeks and primary symptom is vomiting, then 1-week trial of a motility agent (i.e. domperidone)
3. If corrected gestational age < 37 weeks, medication is not recommended.[7] Consider 1-week trial of post-pyloric feeds if current weight ≥ 2kg
4. Continue all other instructions from Step 1 and Step 2
No improvement
Some improvement
Resolution of GER
Consider additional 1-week trial of Step3a vs. advancing to Step 3b
Continue current management. Challenge with compressed feed time/increased TFI at least every 2 weeks from initiation. If successful and hydrolyzed milk was initiated in Step 2, consider reintroduction of non-hydrolyzed milk prior to discharge.
Step 3b: Advanced Pharmacological Management
1. If corrected GA ≥ 37 weeks, continue medication started in Step 3a
2. If corrected GA ≥ 37 weeks, 1-week trial of adding second medication class[6] (i.e. add domperidone if prescribed lansoprazole or famotidine in Step 3a; add lansoprazole or famotidine if prescribed domperidone in Step 3a)
3. If corrected GA < 37 weeks, medication is not recommended. Consider 1-week trial of post-pyloric feeds if current weight ≥ 2kg
4. Continue all other instructions from Step 1 and Step 2
No improvement
Some improvement
Resolution of GER
Consider additional 1-week trial of Step3b vs. advancing to Step 4
Continue current management. Challenge with compressed feed time/increased TFI at least every 2 weeks from initiation. If successful and hydrolyzed milk was initiated in Step 2, consider reintroduction of non-hydrolyzed milk prior to discharge.

Step 4: Refractory Gastroesophageal Reflux

1. Consult Pediatric Gastroenterology (GI) for further investigations and management.
2. Consult Neonatal Follow-Up (i.e. Bridge Team) to facilitate long-term management plans
3. Continue lansoprazole/famotidine and domperidone pending GI consult
4. Consider trial of post-pyloric feeds if > 2kg pending GI consult
5. Continue all other instructions from Step 1 and Step 2

Footnotes:

[1]Consult with nutritionist to ensure adequate caloric intake

[2]Discuss thickening options with occupational therapist and nutritionist

[3]Eosinophilia definition: mild: 0.70-0.99 x 10^9/L; moderate 1.00-2.99 x 10^9/L; severe ≥3.00 x 10^9/L

[4]Questions to ask for family atopy history:

- Sibling with CMPI?
- Siblings with allergies/asthma/eczema?
- Parents with allergies/asthma/eczema?

[5]Consult nutritionist and lactation consultant for details of maternal CMPI diet.

[6]Dosing as per Lexicomp guidelines and clinician discretion.

Esophageal Atresia

Checklist for Esophageal Atreasia – TEF Patients (for Discharge)

Checklist for Esophageal Atresia - TEF Patients

During the hospital stay

- ❑ Refer to post-operative pre-printed orders
  - Start Famotidine IV (1mg/kg/day ÷ BID) as soon as post op #1
  - Then Famotidine PO (1mg/kg/day ÷ BID) as soon as enteral feedings are started
- ❑ NICU team must:
  - Consult GI team on call after the initial surgery for "routine" cases
  - Notify Hélène Bacha extension 22657 (nurse of the MCH EA-TEF team) of the existence of the patient (call GI Secretariat at extension 23745 to leave message)
- ❑ Consultation to Social Services
- ❑ Please do CPR teaching **PRIOR** to discharge home
- ❑ If patient requires endoscopy for symptoms of cough/aspiration, Surgery should be made aware and present at endoscopy (bedside or OR)

When planning discharge from NICU OR transfer to wards

- ❑ Contact the GI Secretariat at extension 23745 to organize 1st appointment as an out-patient. If clinic appointment is too far ahead (> 5 weeks), arrange F/U in Surgery Residents' Clinic 2-3 weeks following discharge (extension 24489)
- ❑ If patient is transferred to Surgery floor: please consult Pediatric Service
- ❑ Complete the special letter to request Synagis
- ❑ Outpatient prescription for acid suppression medication.
  - Regular patient: Famotidine (1mg/kg/day ÷ BID)
  - If patient has an esophageal stricture: Prevacid 2 mg/kg/day BID, 30 minutes before breakfast and supper

- ❑ HEFP (Home Enteral Feeding Program) through GI: GI Nurse and Marie-Josée Trempe, Nutritionist, if needed

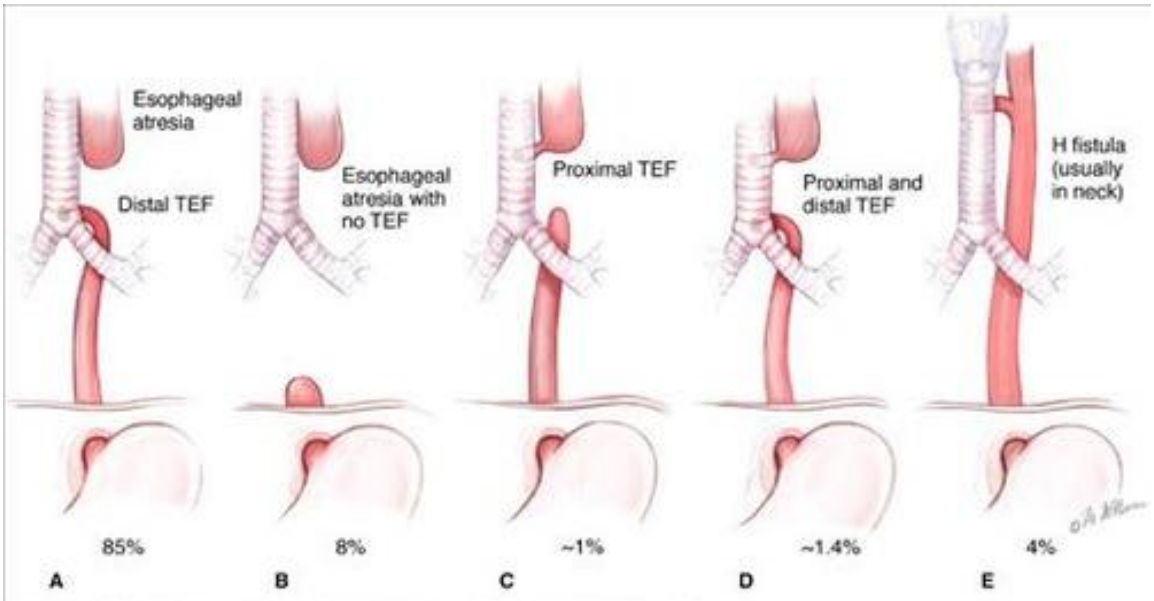
- ❑ Please make sure that the baby has a pediatrician upon discharge

SPECIAL CONSIDERATIONS for COMPLEX CASES

- **"Long Gap" Esophageal Atresia**
- **Delayed anastomosis**
- **Premature or significant associated malformations**
- **Prolonged hospitalisation (> 2-3 weeks)**

- ❑ Consult Occupational Therapy

- ❑ Discuss with Cardiology if further imaging is required to r/o vascular aberrancy



Source: Sugarbaker DJ, Bueno R, Krasna MJ, Mentzer SJ, Zellos L: *Adult Chest Surgery*: http://www.accesssurgery.com

Granuloma Treatment Protocol

See NICU weebly

Congenital Diaphragmatic Hernia/CDH

Prepared by G. Altit as an overall guide. Everything needs to be reviewed with Neonatologist on duty for corresponding patient.

CDH Delivery Room Management :

- Team by experienced personnel.
- Team composition well thought – avoid too many or too little
- In the delivery room: avoidance of high airway pressures and the adequate preductal arterial saturation
- Goal = Keeping preductal 70% and 95%.
- Progressive natural increase overall several minutes
- May consider delayed cord clamping – discuss on a case by case basis.
- No need for aggressive normalization due to slow transition
- Most recommendations align with: intubation immediately after birth by the most skilled intubator (usually neonatologist or fellow):
    - « Done to reduce a possible risk of pulmonary hypertension due to prolonged acidosis and hypoxia which might be caused by delayed intubation »
    - Some centres have started to do intubation during Delayed Cord Clamping (CHOP) – not something done yet at the MCH.
- Bag-and-mask ventilation avoided due to distension of GI tract
- Low peak pressures, (below 25 cmH2O)
    - FiO2 - NRP : recommends 21%
- Immediate placement of oro- or nasogastric tube with continuous suction to prevent bowel distension and kept until surgical repair + frequent aspirations to prevent blockage. In the delivery room, the replogle should be introduced and the air should be aspirated with a large syringe.
- Ensure temperature control from birth.
- Place electrodes in the delivery room.

CDH - On arrival in the NICU:

- A central venous (for fluids/medications) and an arterial line should be inserted for blood sampling and monitoring the arterial blood pressure.
- If liver in chest: Peripheral UV often, install PICC when stable.
- UAL placed due to rapid and secure access = but this reflects postductal PaO2.
- Preductal PaO2 measurements reflect cerebral oxygenation = arterial line should be into the right radial artery if possible when no UAL available.
- No specific evidence on sedation and analgesia. Most recommends : mild sedation and analgesia. Consider Fentanyl infusion 1 mcg/kg/hour in those with more severe CDH with oxygen needs and sign of pulmonary hypertension

- DO NOT TRITRATE oxygen based on post-ductal FiO2. Only pre-ductal.
- No routine neuromusc blockade.
- Spontaneous breathing is associated with better V/Q matching
- Adjust O2 for Preductal: 80 - 95%,
- In first 2h, preductal as low as 70% accepted if slowly improving and organ perfusion is acceptable (EuroConsensus: pH ≥ 7.2 and PaCO2 < 65 mmHg; most aim 7.30 and pCO2 < 55)
- After 2h: 80-85% acceptable if organs well perfused (pH >7.2, lactate < 5mmol/L and UO > 1 cc/kg/h).
- Patient needs quiet environment and avoidance of manipulation
- « Gentle » ventilation with permissive hypercapnia : Arterial CO2: 45–60 mm Hg (permissive hypercapnia)
- No evidence that HFOV superior to CMV (VICI trial)
    - Airway care of extreme importance
    - Most recommends PIPmax 25 cmH2O, PEEP of 3–5 cmH2O and target: PaCO2 45 – 55 mm Hg. (Ideally pre-ductal values, post-ductal can be associated with aggressive increase in ventilator support)
    - No good data on volume targeted ventilation in light of abnormal pulmonary architecture and bilateral pulmonary hypoplasia. However, some data showing that 4 to 5 mL/kg seems to be an acceptable alternative to pressure controlled ventilation.
- Indications for HFOV not clearly defined. Mostly a rescue therapy in severe and persisting hypoxemia and hypercapnia on conventional
    - If switched to HFOV (most if PIP more than 25): MAP adjusted for adequate expansion (contralateral lung expansion not more than 8 ribs)
    - HFOV: initial setting mean airway pressure 13–15 cm H2O, frequency 10 Hz, A 30–40 cm H2O depending on chest wall vibration
    - Possibility of HFO-Vg (no Data) ; No Data HFJV
- TFI = 65 ml/kg/day including medication for the first 24h, intake increases thereafter + replacements of gastric loss
- Diuretics considered if positive fluid balance, aim for diuresis of 1–2 ml/kg/h
- No need to increase BP to supranormal values if preductal sat are between 80 and 95%.
    - Maintain BP at normal levels for gestational age.
    - Transition from Fetal to Neonatal life perturbed in CDH patient. Prolonged transition up to 96 hours for the transition of pulmonary vascular bed. Patients need time for adaptation
    - If poor perfusion and BP considered below the normal AND associated preductal saturation below 80%, echocardiographic assessment for Hypovolemia VS cardiogenic cause
    - In case of possibility of hypovolemia, isotonic fluid therapy 10–20 ml/kg NaCl 0.9% up to 3 times during the first 2 h may be given and inotropics should be considered

    - Hydrocortisone may be used for treatment of hypotension **after** conventional treatment has failed
    - Consider Milrinone if signs of poor RV/LV function (baby needs to be voiding because it is renally excreted).
    - Consider iNO only if no signs of small left sided LV and pulmonary hypertension with good LV function. Refer to iNO protocol
- Perform echocardiography in post-natal life
- Consider Dopamine or Epinephrine if need for inotropy and some increase in perfusing pressure.

CDH - Before discharge – patient will need to be referred to the CDH Clinic

- Genetics should be involved and structural evaluation should be done: abdominal and head ultrasound.
- Head ultrasound should be obtained early, especially in the severe CDH that may need ECMO.
- Surgeons are involved since day 1 of life
- Consults should be placed for: Dr Adam Shapiro (Respiratory medicine); Dr Ana Sant'anna (Gastro-enterology), Dr Louise Koclas (neonatal follow-up)

Canadian CDH guidelines:

Recommendation
Prenatal diagnosis
Ultrasound measurement of O/E LHR should be used between 22 and 32 w of gestational age to predict the severity of pulmonary hypoplasia in isolated CDH.
In left-sided CDH, an O/E LHR < 25% predicts poor outcome. In right-sided CDH, an O/E LHR < 45% may predict poor outcome.
Fetal magnetic resonance imaging should be used (where available) for the assessment of lung volume and liver herniation in moderate and severe CDH.
Ventilation
Newborns with CDH and immediate respiratory distress should be preferentially intubated at birth. Bag-valve-mask ventilation should be avoided.
Sedation should be provided to all mechanically ventilated newborns with CDH. Deep sedation and neuromuscular blockade should be provided selectively to those with greater ventilation or oxygen requirements.
A T-piece should be used with the ventilator to avoid a peak inspiratory pressure > 25 cm H_2O.
An arterial pCO_2 between 45 and 60 mm Hg and a pH between 7.25 and 7.40 should be targeted in all newborns with CDH.
Supplemental oxygen should be titrated to achieve a preductal saturation of at least 85%, but not > 95%.
Gentle, intermittent mandatory ventilation should be the initial ventilation mode for newborns with CDH who require respiratory support. High-frequency oscillatory ventilation or high-frequency jet ventilation should be used when the peak inspiratory pressure required to control hypercapnia using intermittent mandatory ventilation exceeds 25 cm H_2O.
Hemodynamic support
Treatment of poor perfusion (capillary refill > 3 s, lactate > 3 mmol/L, urine output < 1 mL/kg/h) and blood pressure below norms for age should include: • judicious administration of crystalloid, generally not exceeding 20 mL/kg; • inotropic agents such as dopamine or epinephrine; and • hydrocortisone. If poor perfusion continues, assessment of cardiac function (i.e., echocardiogram, central venous saturation) should be performed
Echocardiography
Two standardized echocardiograms, one within 48 h of birth and one at 2–3 w of life, are needed to assess pulmonary vascular resistance, as well as left ventricular and right ventricular function. Additional studies may be conducted as clinically indicated.

Management of pulmonary hypertension

iNO is indicated for confirmed suprasystemic pulmonary arterial hypertension without left ventricular dysfunction, provided lung recruitment is adequate. In the absence of clinical or echocardiographic response, iNO should be stopped.

Sildenafil should be considered in patients with refractory pulmonary hypertension (i.e., unresponsive to iNO) or as an adjunct when weaning iNO.

Milrinone should be used to treat cardiac dysfunction, particularly if it is associated with pulmonary hypertension.

Prostaglandin E_1 can be used to maintain ductus arteriosus patency and reduce right ventricular afterload in patients with pulmonary hypertension with right ventricular failure, or in the presence of a closing ductus.

Extracorporeal life support

The possibility of extracorporeal life support should be discussed during prenatal counselling for CDH, and should disclose that available evidence does not suggest a survival benefit to its use.

Surgery

The following physiologic criteria should be met before surgery:
• urine output > 1 mL/kg/h
• FiO_2 < 0.5
• preductal oxygen saturation between 85% and 95%
• normal mean arterial pressure for gestational age
• lactate < 3 mmol/L
• estimated pulmonary artery pressures less than systemic pressure.
Failure to meet these criteria within 2 w should prompt consideration of either attempted repair or a palliative approach.

Patch repair: For diaphragmatic defects that are not amenable to primary repair, oversized, tension-free polytetrafluoroethylene/GORE-TEX patches should be used.

Open repair v. minimally invasive surgery: A minimally invasive surgical approach or technique should not be used in the repair of neonatal CDH because of the high rates of recurrence.

For patients on extracorporeal life support: Surgery should be avoided until after decannulation. If the patient cannot be weaned off extracorporeal life support, consideration should be given for either surgery or palliation, as appropriate.

Long-term follow-up

• We recommend standardized multidisciplinary follow-up for children with CDH to provide surveillance and screening, optimal and timely diagnosis and clinical care adjusted to the level of risk.

• We recommend identifying the subset of CDH survivors at high risk for long-term morbidity as comprising those infants and children who require extracorporeal life support, who have been repaired with a patch or who required respiratory support at 30 days of life.

Dumping Syndrome

Dumping syndrome is a reported complication of fundoplication, a surgical procedure to correct severe gastro-intestinal reflux disease (GERD) in children. Dumping syndrome occurs as a result of the rapid emptying of hyperosmolar carbohydrate containing solutions into the small bowel leading to reactive hypoglycemia. Postprandial hypoglycemia occurs 60 minutes to180 minutes post end of feeds. Symptoms may include shakiness, pallor, diaphoresis, headaches, fatigue, mood or behavior changes and/or general feeling of discomfort. Postprandial hypoglycemia occurs more commonly in children with fundoplication but can occur in any patient who has abnormal motility or gut anatomy. Children, including those with neurological impairment, may become hypoglycemic without additional symptoms or signs. Clinically relevant hypoglycemia associated with dumping syndrome is diagnosed when postprandial blood glucose (BG) level less than 3.5 mmol/L (confirmed in laboratory), is measured on one (1) occasion.

Time intervals for BG testing: Pre-feed, 60 minutes post end of feed, 90 minutes post end of feed, 120 minutes post end of feed, 180 minutes post end of feed (may coincide with the start of the following feed). If fasting greater than 180 minutes overnight, test 240 minutes post end of feed (may coincide with the start of the following feed) If at any time, point of care BG is less than 3.5 mmol/L, send a STAT capillary blood specimen to the laboratory for confirmation and initiate treatment as described below. Note: A BG result less than 3.5 mmol/L, confirmed in laboratory, is considered a hypoglycemic event even if the patient feels no symptoms ("hypoglycemia unawareness")

Patients admitted in the Neonatal Intensive Care Unit (NICU), recommendations are to, in conscious patients:

- Restart continuous feeds or go back to previous mode of feeding that achieved normal blood glucose.
- Retest BG 15 minutes later
- If the blood glucose remains less than 3.5 mmol/L, advise attending team

Unconscious or convulsing patient (All patients)

- Call "Code Pink", provide basic life support and prepare treatment as below :
- If IV in place:
    - D10W 2 mL/kg to a maximum of 125 mL. Maximum rate: 2 mL/kg over 1 minute
    - If no IV: Neonates less than 28 days: Glucagon 0.02-0.2 mg/kg SC or IM (maximum single dose 1mg). May repeat dose in 20 minutes if needed. Patients aged 28 days to 6 years old: Give Glucagon 0.5 mg SC or IM o Patients older than 6 years: Give Glucagon 1 mg SC or IM

ENT:

Critical Airway (Called CODE INDIGO):

Involves the presence of Anesthesia and, often, ENT for critical airways.

Neonatal Intensive Care Unit
Critical Airway
Patient Information

Date _____

If any of these diagnoses or symptoms is present, please consult ENT/Anesthesia for assessment of Critical Airway and post Team Indigo sign until Evaluation.

Diagnosis (es)

- Pierre Robin sequence
- Treacher Collins syndrome
- Goldenhar syndrome
- Apert or Crouzon syndrome
- Klippel-Feil syndrome

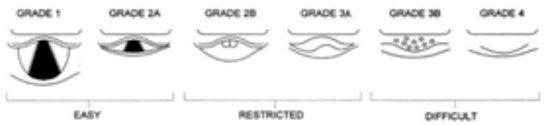
Symptoms

- Mandibular Hypoplasia/Micrognathia
- Cleft palate or high palatine arches
- Limited neck extension
- Limited temporomandibular joint mobility
- Macroglossia
- Severe subglottic/glottic stenosis (or suspected)
- Neck mass
- History of difficult intubation

NICU/ORL/Anesthesia Attending name: _____ Signature_____

Clinical Evaluation Date: _____

Bag mask possible? Yes No
Laryngeal mask possible? Yes No
Intubation possible? Yes No Grade:_____



NICU/ORL/Anesthesia Attending name: _____
Signature_____

Details of intubation:

Date: _____ Number of attempts:_____

Successful intubation done by whom: _____
Laryngoscope Blade type/size: _____ ETT /LMA size: _____ Cuff: Yes No
Cricoid pressure used: Yes No
Videolaryngoscope type: _____ blade type/size: _____
Rigid bronchoscope Size: _____ Length: _____
Fiberoptic bronchoscope Size: _____
Adjunctive equipment used: _____

NICU/ORL/Anesthesia Attending name: _____
Signature: _____

Details of intubation:
Date: _____ Number of attempts:_____
Successful intubation done by whom: _____
Laryngoscope Blade type/size: _____ ETT /LMA size: _____ Cuff: Yes No
Cricoid pressure used: Yes No
Videolaryngoscope type: _____ Blade type/size: _____
Rigid bronchoscope Size: _____ Length: _____
Fiberoptic bronchoscope Size: _____
Adjunctive equipment used: _____

NICU/ORL/Anesthesia Attending name: _____
Signature: _____

Details of Bronchoscopy:
Date: _____

Scope:_____
Findings: _____
_____
_____
_____

NICU/ORL/Anesthesia Attending name: _____
Signature_____

Recommendations:

Team Indigo: **Yes** **No**
Transport: _____
Sedation: _____
Who should intubate: _____
Type of scope: _____ Size: _____ Length: _____
Laryngoscope Blade type/size: _____ ETT /LMA size: _____
Tracheostomy set: Yes No (If yes): Size tracheostomy tube needed: _____
Other: _____

Date: _____
NICU/ORL/Anesthesia Attending name: _____
Signature: _____

Team Indigo Removal

Date: _____
NICU/ORL/Anesthesia Attending name: _____
Signature: _____

Particularities – Code Indigo

- When?

- Unexpected difficult intubation
- Patient known for difficult airway in need of an intubation

- How?

- Call 55555
- Code Indigo
- Site Glen
- Bloc B 6 South
- Room #
- Give your name and unit extension (22389)

TRACHEOSTOMY

After the first 10 days

Indications

- To assist in long-term mechanical ventilation due to pulmonary disease, congenital heart disease or neurological/neuromuscular disease
- To bypass chronic obstruction within the upper airway (tracheomalacia, tracheal stenosis, bilateral vocal cord paralysis, compression by large vessels)

Materials

- Required at bedside at ALL TIMES

- One tracheostomy tube same size as in current use
- One size smaller tracheostomy tube
- Emergency tracheostomy tray
- Tracheostomy dilator (curved mosquito forceps)
- Hemostats
- Removable obturator (size of current tracheostomy)
- Water-based lubricant (Muko)
- Scissors
- Tracheostomy ties
- Self-inflating bag with extension and face mask (ambubag)
- Sign: do not suction beyond ____cm
- NS
- Sterile water
- Suction catheter (appropriate size)

Procedure - Dressing and ties change

- When?

- Q DAY, usually with bath

- Materials

- 6 alcohol free chlorhexidine gluconate 2%
- 4 packs of 4x4 sterile gauze
- 1 Mepilex foam or type of dressing used by patient
- 1 clean trach ties

- How?

- Always done with **2 people**
- Tracheostomy must **always be held during the entire procedure**

1. **Suction** the tracheostomy as per protocol before starting

2. **Position** the patient supine, **place a small roll** under his/her shoulders
3. **Wash your hands** with solution and put on non-sterile gloves
4. Open material:
    - *6 alcohol free chlorhexidine gluconate 2% swabsticks*
    - *2 packs of sterile 4x4s*
    - *Have the clean trach ties close by*
5. **Remove gauze** or Mepilex from the trach, if there is one
6. Using one swab at a time, **clean the skin** starting from stoma towards the periphery 4 times
7. Dry the skin & under the flange with sterile gauzes
8. Change one side of the ties at a time, ensuring trach remains securely held in place:
    - *Remove the dirty tie on one side*
    - *Clean with alcohol free chlorhexidine gluconate 2% swabsticks one side of the neck*
    - *Dry the skin with sterile gauze*
    - *Insert the new trach ties and put the velcro*
    - *Do the same procedure for the other side*
9. **Verify if ties are tight enough and centered**: one little finger should be able to slip beneath the ties

Procedure – Cannula change

When?

- Q MONTH, by the RT
- Following resolution of any upper or lower respiratory tract infection to avoid airway reinfection or granulomas
- Every time the tracheostomy tube cannula appears partially obstructed with secretions to avoid tracheostomy tube occlusion

Materials

- One tracheostomy tube same size as in current use
- Smaller size tracheostomy tube
- Tracheostomy ties (Velcro or twill tape)
- Water based lubricant
- Scissors
- Hemostats (or blunt tipped tweezers)
- Suction supplies
- Mask & manual resuscitator connected to 100% oxygen
- Gauzes or tissues
- Sterile gloves

How?

1. Requires **2 trained persons** for routine changes with an **RT present**
2. Keep patient **NPO 3 hours prior** to the tracheostomy tube change to minimize the risk of aspiration
3. **Wash and dry hands**
4. Keep the tracheostomy tube cannula sterile
5. **Prepare ties & tie to flanges** of the new tracheostomy tube
    - *For Velcro ties, tie only one side of the tracheostomy tube*
    - *For twill tape ties, attach ties to both flanges prior to reinserting the tracheostomy tube*
6. **Suction** patient as per protocol
7. **Position** the patient supine, **place a small roll** under his/her shoulders
8. 1st person **removes the ties** while holding the tracheostomy in place
9. 2nd person put on **sterile gloves**
10. 2nd person **moistens the tip** of the tracheostomy tube with lubricant holding the obturator in place with thumb

11. **Preoxygenate** the child with 100% oxygen
12. **On exhalation**, 1st person **removes** the tracheostomy tube following the natural curve of the tube
13. 2nd person **inserts immediately** the tracheostomy tube **sideway** in the stoma to visualize adequately the tracheostoma **then turns** the tracheostomy tube gently, once in the stoma, in alignment with the trachea & continues the insertion of the tracheostomy tube in a smooth curving motion, directing the tip of the tracheostomy tube toward the back of the neck. **Never force** the tracheostomy tube into the stoma to avoid tracheal wall injuries
14. **Remove the obturator**, holding the tracheostomy tube securely in the tracheostoma
15. To **confirm that the tracheostomy tube is in place**, place your hand in front of the tracheostomy tube hub and feel for air movement or verify for secretions coming out of the tracheostomy tube
16. Insert a suction catheter & **suction**. The suction catheter should pass easily beyond the tracheostomy tube without resistance
17. **Remove shoulder roll** to relieve the hyperextension of the neck before tying the tracheostomy ties to ensure a correct fit
18. **Tie** the tracheostomy ties, allowing room for only one finger between neck & the ties
19. Perform a respiratory **assessment**
20. **Document** procedure & patient's tolerance in the chart

Accidental decannulation

After the first 10 days the stoma tract is more established at this time & should present little resistance to reinsertion but it should still be the professional at the bedside with the most experience related to tracheostomy tube insertion (RT, MD, NNP, ENT or RN) who reinsert the tracheostomy tube

- What to do?

1. **Reinsert the tracheostomy tube** into the stoma
2. **Call RT stat**
3. In the event of **respiratory distress or cyanosis**, call a **CODE PINK** if additional medical support is required

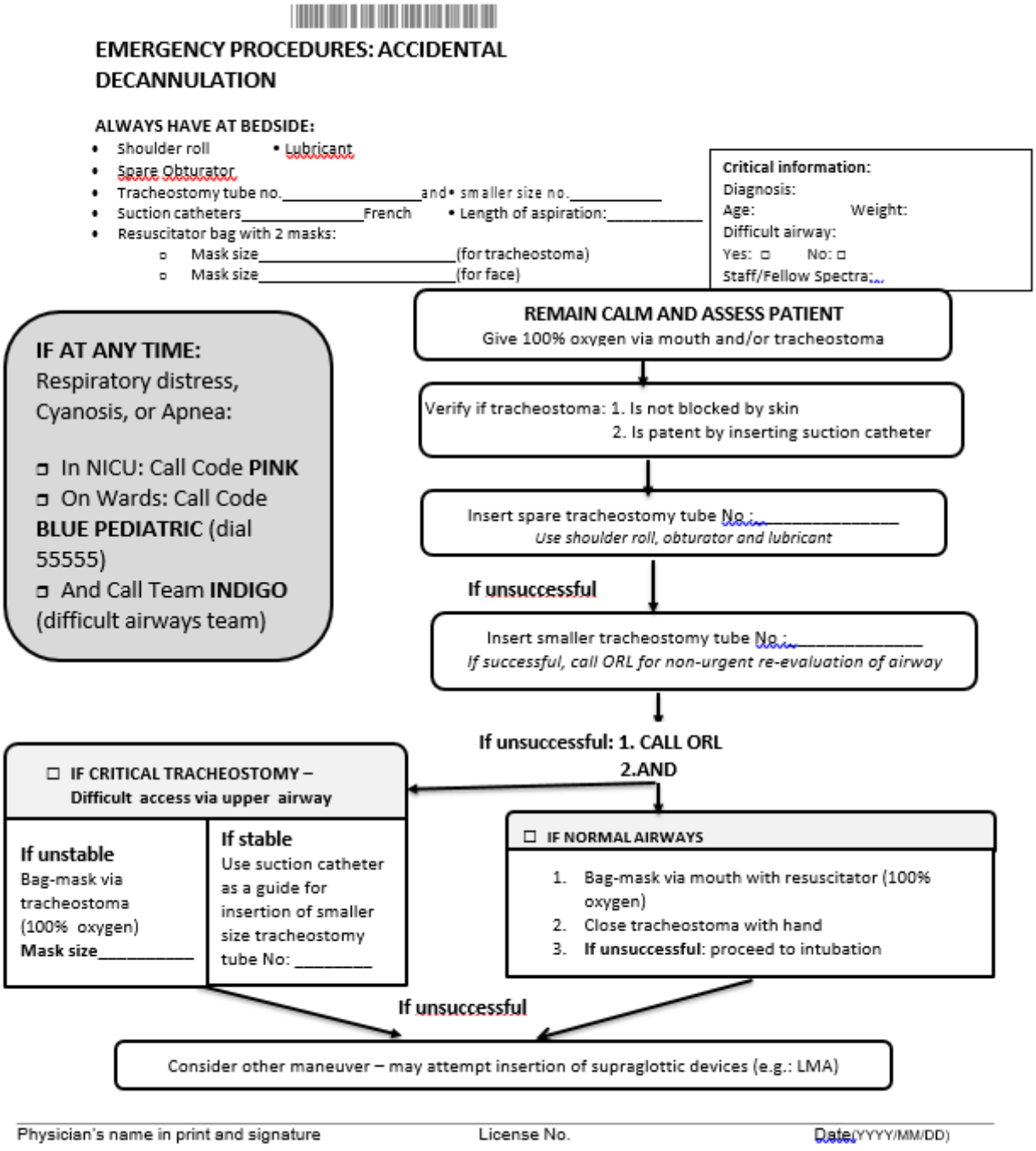
- If unable to replace the current size tracheostomy tube:

1. **Notify** physician & the ENT physician
2. **Ventilate** the patient using the **bag-and-mask** ventilation technique with 100% oxygen **occluding the tracheostoma** with a gloved finger or a piece of gauze
3. **Reposition** the patient so the head is back & the stoma is more visible using a roll under the patient's shoulders to hyperextend the neck & expose the tracheostoma
4. **Lubricate a smaller size** tracheostomy tube; **try to insert** it into the tracheostoma
5. In the event of **respiratory distress or cyanosis**, call a **CODE PINK** if additional medical support is required
6. The tracheostomy tube **should be changed later for a new one of the appropriate size** when the patient's respiratory status is stable.

- If unable to insert the smaller size tracheostomy tube:

1. Try inserting an **endotracheal tube a ½ size smaller** than the outer diameter of the tracheostomy tube
2. If endotracheal intubation is not feasible, **insert a suction catheter** through the smaller size tracheostomy tube
3. Guide the suction catheter tip into the stoma, then **slide the tracheostomy tube over** the suction catheter & into the stoma
4. Remove the suction catheter
5. Resume **ventilation**
6. Obtain a **chest x-ray** to verify the position of the tracheostomy tube
7. In the event of respiratory distress or cyanosis, call a CODE PINK if additional medical support is required
8. The tracheostomy tube **should be changed later for a new one of the appropriate size** when the patient's respiratory status is stable.

Decannulation protocol:



Immune system:

Immunoglobulins:

Please refer to the full protocol for IVIG infusion. IVIG are rarely used in the NICU. They are occasionally administered to newborns with (NAIT – neonatal alloimmune thrombocytopenia). Rarely, they are administered in the context of hyperbilirubinemia in the context of Rh incompatibility (although the data is weak in the literature and the practice surrounding their administration at the MCH is variable according to neonatologist).

Protocol mentions: "Gamimmune usually infused at the following rate or at MD's discretion: for Kawasaki disease, rates differ. Please refer to IVIG infusion specific to Kawasaki disease at the end of present protocol.

- 0.01 ml/kg/min for 15 minutes
- 0.02 ml/kg/min for 15 minutes
- 0.03 ml/kg/min for 15 minutes
- 0.04 ml/kg/min for 15 minutes
- 0.05 ml/kg/min for 15 minutes
- 0.06 ml/kg/min for 15 minutes
- Increase as per orders and tolerance (see precautions and complications section) until the end of the infusion. For small children and infants, may not be able to infuse higher volumes (such as > 60 cc/hr) due to fluid overload. The tubing used to infuse stable blood products must be changed every 24 hrs

To monitor vital signs: pre-infusion vital signs must be recorded to establish a baseline; check every 15 minutes or every time you increase the rate; check 15 minutes after it is completed. Patients with selective IgA deficiency may have true anaphylactic reactions due to the trace quantities of IgA in most intravenous gammaglobulin preparations. These patients frequently have anti IgA antibodies despite having never received blood or blood products previously. If an anaphylactic or anaphylactoid reaction occurs, the infusion is to be discontinued immediately, the treating physician notified and treatment with adrenaline, antihistamines Diphenhydramine (Benadryl), and/or steroids instituted. When symptoms subside it is usually possible to resume the infusion at a rate which is tolerated by the patient. IVIG preparations can on occasion cause a precipitous fall in BP and the clinical picture of anaphylaxis. If patient develops fever, chills, shortness of breath or urticaria, contact MD and slow rate to previous tolerated rate. These reactions are sometimes related to the rate of infusion. The patient's vital signs must therefore be monitored continuously and careful observation made for any symptoms throughout the entire infusion. If symptoms disappear, continue infusion at present rate. If reaction persists, then stop the infusion and notify physician again. If the reaction is severe (anaphylactic), stop the infusion, infuse Normal Saline TKVO and contact the physician. Adrenaline should always be available for treatment of any acute anaphylactoid reaction. Other reported complications include aseptic meningitis, renal dysfunction, acute renal failure and osmotic nephrosis. Patients predisposed to

acute renal failure include those with any degree of preexisting renal insufficiency, diabetes mellitus, volume depletion, sepsis, or those receiving nephrotic drugs.

Inborn error of metabolisms and Genetics:

IBEM:

From Neoreviews and Dr. Jocelyn Gravel:

Table 1. Initial Tests for Evaluation of Possible Inborn Error of Metabolism

General Laboratory Tests

- Blood gas
- Serum electrolytes
- Blood urea nitrogen and creatinine
- Blood glucose
- Liver function tests
- Creatine kinase
- Ammonia
- Serum uric acid
- Serum lactate
- Urine ketones
- Urinalysis

+/- LP (lactate…)
+/- cXR
+/- ECG
Urine PH

Metabolic Screening Tests

- Plasma amino acids
- Plasma acylcarnitine profile
- Urine organic acids

Table 2. Key Laboratory Findings for Neonates Who Have Inborn Errors of Metabolism

Tests	Key Finding	IEM Consideration
Complete blood count with differential count	Neutropenia Hemolytic anemia	OA, GSD I G6PD deficiency, pyruvate kinase deficiency
Blood gas	Metabolic acidosis Respiratory alkalosis	OA, Mito, PDH, PC, FAO UCD
Blood glucose	↓	FAO, GSD I, Galac, OA, HFI, Tyr 1
Blood urea nitrogen	↓	UCD
Serum lactate	↑	Mito, PDH, PC, FAO, GSD I
Blood ammonia	↑	UCD, OA, FAO, PDH, PC
Serum uric acid	↑ ↓	GSD I Molybdenum cofactor deficiency
Creatine kinase	↑	FAO
Ketones	↓ (with hypoglycemia) ↑	FAO OA
Plasma acylcarnitine profile		FAO, OA
Plasma (free and total) carnitine		FAO, OA
Plasma amino acids		UCD, OA
Urine organic acids		OA, FAO, Mito, PDH, PC
Urine reducing substances		Galac, HFI, Tyr 1
Very long-chain fatty acids		Peroxisomal disorders
Urine mucopolysaccharides		Lysosomal storage disorders
Urine oligosaccharides		Lysosomal storage disorders
7-dehydrocholesterol		Smith-Lemli-Opitz syndrome
Serum transferrin glycoforms		CDG

CDG=congenital disorder of glycosylation, FAO=fatty acid oxidation defect, Galac=galactosemia, GSD I=glycogen storage disease type I, G6PD=glucose-6-phosphate dehydrogenase, HFI=hereditary fructose intolerance, IEM=inborn error of metabolism, Mito=mitochondrial energy metabolism defects, OA=organic aciduria, PC=pyruvate carboxylase deficiency, PDH=pyruvate dehydrogenase deficiency, Tyr 1=tyrosinemia type 1, UCD=urea cycle defect

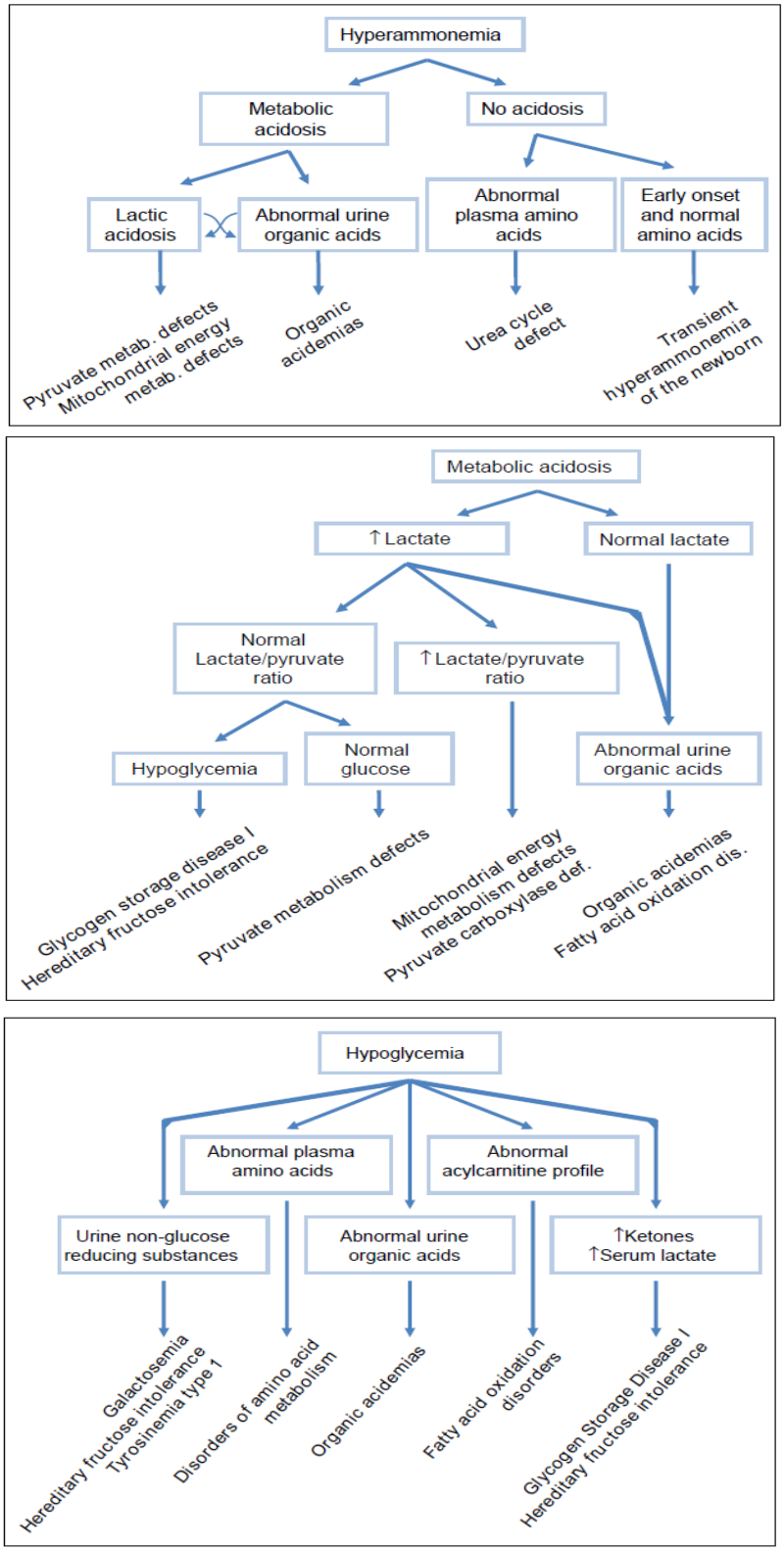
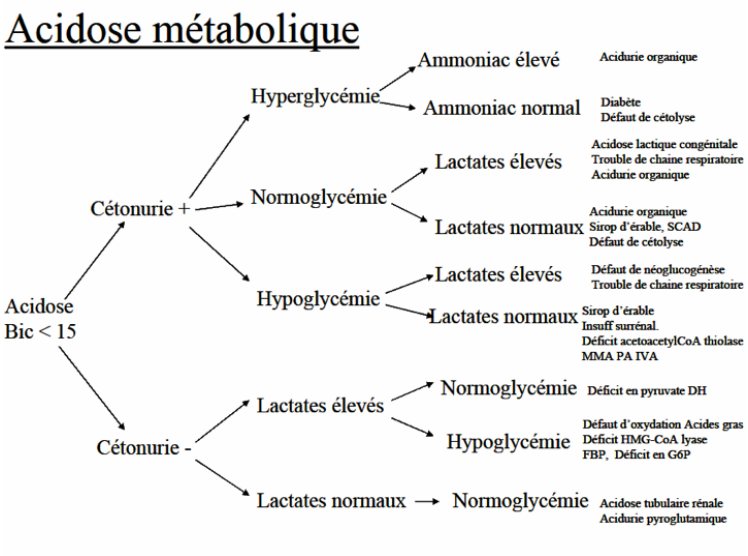
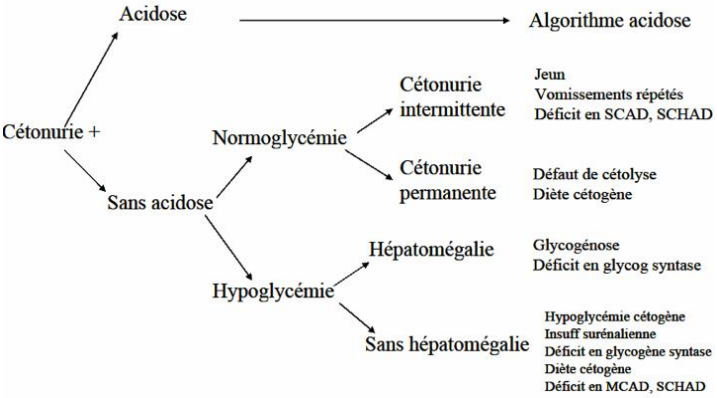


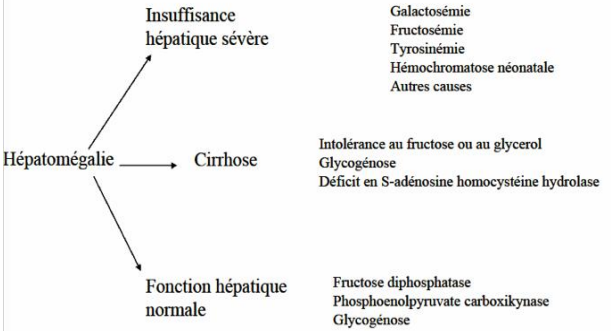
Figure 3. Algorithm for evaluation of hypoglycemia in a neonate who has a suspected inborn error of metabolism.

Acidose métabolique

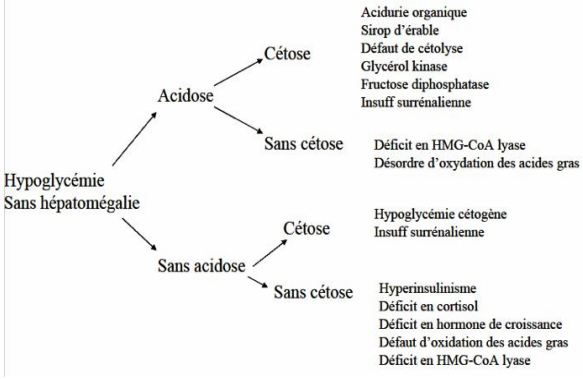




Hypoglycémie avec hépatomégalie



Hypoglycémie sans hépatomégalie



Commons Syndromes and Genetic disorders in the NICU

Cheat sheet by G. Altit

Screening of disease per ethnicity:

- Tay Sachs (Ashkenazi, French Canadian) = serum hexosaminadase A decreased in serum, DNA studies. A cherry-red spot is a finding in the macula of the eye in a variety of lipid storage disorders and in central retinal artery occlusion. Several conditions, classically Tay–Sachs disease, but also in Niemann–Pick disease, Sandhoff disease, and mucolipidosis.
- Ashkenazie Families: familial dysautonomia, Gaucher, Canavan, Bloom, Fanconni Anemia, Niemann Pick type A, Mucolipidosis.
- Sickle cell disease: African descent, Afro-Americans, Caribbean of African descent, Mediterranean, Arabic, Indian, Pakistanis

Turner: 45 X. newborn = lymphedema of feet and or hands (can present as hydrops). Primary amenorrhea due to ovarian dysplasia. Short stature often prompts initial workup. Most with normal mental development. Webbed neck with low hairline, broad chest with wide-spaced nipples. Risk of Coarctation: 1 in 8000. Shield chest. Spatial-perceptual difficulties. Streak ovaries with deficient follicles. Most common aneuploidy anomaly = 1.4%. Only monosomy to survive, 99% will be lost pregnancy.

Noonan: similar symptoms to Turner (can present as hydrops, cardiomyopathy). Rasopathy (same family as Costello Syndrome). Dorsal hand and pedal edema, low posterior hairline, web neck (pterygium colli), congenital elbow flexion (cubitus valgus), broad chest with wide spaced nipples, narrow, hyperconvex nails, prominent ears, short fourth metacarpal and or metatarsal.
Differences with Turner = Turner only women with chromosome d/o, near normal intelligence, Coarctation, amenorrhea and ovarian dysgenesis / Noonan will affect both sex, normal chromosome, AD, cognitive challenges, pulmonary stenosis, normal menstrual cycle.

47 XXX: Triple X syndrome. 1 in 2000. Associated with maternal age (as Klinefelter). Tall, normal phenotype. 90-110 IQ, behavioral prob. Normal ovaries.

47 XYY : 1 in 2000, tall severe acne, male normal phenotype. Behavioral and aggressive behaviour. Normal size testes and histology.

47 XXY : 1 in 2000, tall eunuchoid habitus, underdeveloped secondary sexual characteristics, gynecomastia. Behavioral problems. Reproductive function rare. Hypoplastic testes, leydic cell hyperplasia, Sertoli cell hypoplasia, seminiferous tubule dysgenesis, few spermatogenic precursors. Klinefelter = 47 XXY; Long legs, short arms, hypergonadotropique hypogonadisme (FSH et LH increased)

Fragile X : 1 in 1000 males and 1 in 2000 females. Most common inherited form of developmental delay. 2-6% males and 2 to 4 % female with unexplained developmental delay will have fragile X. Expansion triplet. Grow lymphocyte in folate-deficient medium = break near distal end of long arm

of X = fragile X mental retardation-1 gene (FMR1), repeat of CGG. Normal = 6 to 45 copies. In carriers 50 to 200 (premutation = carrier). Fully affected = 200 to 600. Related medical prob = flat feet 80%, macro-orchidism (80%), MV prolapse, recurrent OMA, strabismus, refractive errors, seizures and scoliosis. Heterozygous females have more behavioral and developmental prob (TDAH), cognitive difficulties (50% IQ in MR or borderline zone), physical differences (prominent ears, long and narrow face). Cytogenetics for every sister of fragile X. Present with elongated face, flattened nasal bridge, protruding ears.

Genetic "large" baby syndromes : Pradder Willi (later age obesity, neonatal hypotonia, small hands feet), Beckwith Wiedemann (macrosomia, omphalocele, macroglossia, ear creases, hypoglycemia), Sotos (macrosomia, macrocephaly, large hands and feet), infants of diabetic mother, Weaver (macrosomia, accelerated skeletal maturation, camptodactyly = fixed flexion deformity of the interphalangeal joints of the little finger), Bardet Biedl (retinal pigmentation, polydactyly).

Fanconi Anemia (not the same as syndrome): Risk of esophageal atresia, thumb anomalies, blood lineages anomalies. Classic features include abnormal thumbs, absent radii, short stature, skin hyperpigmentation, including café au lait spots, abnormal facial features (triangular face, microcephaly), abnormal kidneys, and decreased fertility. About 80% of FA will develop bone marrow failure by age 20. Chromosomal breakage study with Diepoxybutane (DEB) analysis. FA is the result of a genetic defect in a cluster of proteins responsible for DNA repair.

Fanconi Syndrome: Syndrome of inadequate reabsorption in the proximal renal tubules of the kidney. The syndrome can be caused by various underlying congenital or acquired diseases. Cystinosis is the most common cause of Fanconi syndrome in children. The clinical features of proximal renal tubular acidosis are: polyuria, polydipsia and dehydration. Hypophosphatemic rickets (in children), Growth failure, Acidosis, Hypokalemia, Hyperchloremia, Hypophosphatemia/hyperphosphaturia, Glycosuria, Proteinuria/aminoaciduria, Hyperuricosuria.

Pradder Willi : H3O = hyperphagia, hypotonia, hypopigmentation and obesity (later). Maternal uniparental disomy in 20% (receives the 2 maternal imprinted copies), 70% with deletion of one SNPRN gene on long arm of paternally imprinted chromosome 15.

Angelman : unprovoked outbursts of laughter ("puppet children"), Severe developmental delay, lack of speech, unsteady gait, microcephaly, seizures; maxillary hypoplasia, large mouth (protruding tongue), prognathism (large chin). 70 % = deletion de UBE3A imprinted (E6-associated protein ubiquitin protein ligase gene) on long arm of maternally derived chrom 15. 25% = UBE3A mutation; the rest = paternal disomy of chromosome 15 (2 paternal copies).

William Syndrome: Elfin facies; supravalvular aortic stenosis, small and abnormally shaped primary teeth, low muscle tone, joint laxity, increased calcium, frequent ear infections, hyperacusis (sensitivity to loud noises), failure to thrive, strong social orientation and music capacities (cocktail party syndrome), anxiety problems. Cause by elastin deletion on chromosome 7 (microdeletions).

Smith Lemli Opitz : Microcephaly, upturned nose, syndactyly of 2nd and 3rd toes, developmental delay. AR. Defect in cholesterol metabolism with deficiency in 7-dehydrocholesterol (7DHC) enzyme because mutation of DHCR7 on chrom 11, no conversion of 7-DHC in cholesterol. Cholesterol low. Grim prognosis with moderate to severe developmental delay.

Dwarfism: 2 most common identifiable at birth are thanatophoric dwarfism ("death loving" dwarfism) and achondroplasia. Thanatophoric is the most common but lethal chondrodysplasia – flattened, U-shaped vertebral bodies; telephone receiver-shaped femur; macrocephaly; redundant skinfolds (pug-like appearance) with incidence of 1/6400 births. Achondroplasia = most common viable skeletal dysplasia with 1/26000 births live. Small stature, microcephaly, depressed nasal bridge, Iordosis, trident hand (A trident hand is a description where the hands are short with stubby fingers, with a separation between the middle and ring fingers).

Cri-du-chat syndrome: deletion of material of 5p. Growth retardation, microcephaly, severe developmental delay. Cat-like cry in infancy. 85% de novo mutation; 15% mal-segregation of balanced parental translocation.

Marfan : Mutation of fibrillin – chrom 15. AD. Abnormal crosslinking between collagen and elastin. Degeneration of elastic elements in aortic root leading to dilation, and eventually risk of acute dissection or rupture. Tall, thin habitus, hypermobile joints, pectus excavatum/carinatum, kyphscoliosis, lens dislocation,etc. Revised Ghent nosology for diagnosis and molecular testing.

DiGeorge/velocardiofacial syndrome : CATCH22 (congenital heart, abnormal face, thymus hypophlasia or aplasia, cleft palate / cerebral – developmental delay, hypocalcaemia (hypoparathyroidism), deletion of 22q11. Heart = conotruncal (TOF, truncus arteriosus, interrupted aortic arch, right sided Aortic arch, DORV).

Congenital limb hemihypertrophy: Beckwith Wiedemann, Conradi Hunermann, Klippel-Trenaunay-Weber, Proteus syndrome, Neurofibromatosis, Hypomelanosis of Ito, CHILD syndrome (congenital hemidysplasia, ichtyosiform erythroderma, limb defects). All have increased risk (6%; 7.5 chez BW) for embryonal cell tumors (Wilms, adrenal, hepatoblastoma) and surveillance is abdominal ultrasound and alpha-fetoprotein q3months ad 5 years.

Beckwith Wiedemann: facial appearance round in childhood with prominent cheeks and narrowing of forehead with trend to normalization in adolescence. 7.5% risk of embryonal cell tumors. Overgrowth disorder usually present at birth. A minority (<15%) cases of BWS are familial. Hypoglycemia. Macrosomia, Macroglossia Hemihyperplasia (asymmetric overgrowth of one or more regions of the body), Omphalocele or umbilical hernia, Embryonal tumor (e.g., Wilms tumor, hepatoblastoma, neuroblastoma, rhabdomyosarcoma) in childhood, Visceromegaly involving one or more intra-abdominal organs including liver, spleen, kidneys, adrenal glands, and/or pancreas, Cytomegaly of the fetal adrenal cortex (pathognomonic), Renal abnormalities including structural abnormalities, nephromegaly, nephrocalcinosis, and/or later development of medullary sponge kidney, Anterior linear ear lobe creases and/or posterior helical ear pits. Placental mesenchymal dysplasia.

Klippel Trenaunay: hypertrophie of bones and soft tissues. Cutaneous angiomas, varicose veins. Usually limited to 1 limb. Sporadic or AD. Supportive treatment. Sometimes lymphedema.

Trisomy 18 (Edward syndrome) – most common autosomal trisomy after T21 in live born. 1 in 3000. IUGR, microcephaly, overlapping fingers, prominent occiput, micrognathia. Poor prognosis.

Down (T21): 1 in 800 lives births. Physical: up-slanted palpebral fissures with epicanthal folds, small lo set ears with overfolded upper helices, short neck with excess skinfolds, prominent tongue, flattened occiput, exaggerated gap btw 1st and 2nd toe, hypotonia. Brushfield spots are not pathognomonic, 75% have it (7% of normal newborns) = speckled areas in periphery of iris. Simian crease (single transverse palmar crease) is present in 5% normal when single and 1% when bilateral with boys 2x more. 45% of Down have single simian crease. A baby with a single simian crease has 1 in 60 chances of having Down (cause 45% down have it and incidence is 1/800). Need extensive cardiac evaluation cause 40-50% have congenital heart defects (60% being canal AV - AVSD), also VSD, PDA. Congenital hypothyroidism in 2% (0.025% in normal = 1/4000). Other conditions = GI malformation (duodenal atresia, Hirschsprung, T-E fistula), cryptorchidism, lens opacities and cataracts, strabismus, hearing loss (sensorineural and conductive). IQ = 25 to 50 with mean of 54 but deteriorates with advanced Alzheimer; age 40 = mean is 24 of IQ. Risk of leukemia: 50x in 0 to 4 years; 10x in 5 to 29 years, 20x lifetime risk. Transient myeloproliferative disease (marked leukocytosis, blast cells, thrombocytopenia, HSM = spontaneously resolve) and leukemoid reaction (increased WBC with myeloblasts without splenomegaly = resolve spont.) Full trisomy in 94%, mosaic in 2.4% and transolcation in 3.3%. Nondisjunction at Meiosis I cause lengthy stage of meiotic arrest (up to 40 yr); risk for down at 30yo (1:1000) at 35 (1:365), 40 (1:100), 45 (1:50). Babies with Down have mother over 35 yo in 20% cases (those women represent 5% of pregnancies in US); 10% of all T21 derive extra chrom 21 from father.

Leopard syndrome: Multiple Lentiggines syndrome = Lentigines, ECG abnormalities, Ocular hypertelorism (wideset eyes; other facial anomalies include broad nasal root, prognathism, low set ears), pulmonary stenosis, Abnormal genitalia (crypto or monorchidism, missing ovaries), Retarded growth (initial normal BW and length), Deafness (sensorineural). Lentigines = freckling reminiscent of large cat in large numbers 10000+ also inside mouth and sclera (small pigmented spot on skin with clear defined edge). AD (PTPN11 gene mutation). ECG = mostly bundle branch block. Dx if lentigines and 2 other criteria. If no lentigines need 3 other criteria and a 1st degree relative with disease.

Association: Non-random occurrence of multiple anomalies without a known sequence initiator or causal relationship but such a frequency that the malformations have a statistical connection.

CHARGE : **C**oloboma, **H**eart anomalies, Choanal **A**tresia, **r**etardation (mental developmental delay and growth), **G**enital anomalies (genito-renal-urinary), **E**ar anomalies (semi-circular canal classically). AD due to CHD7 gene in 70%. Most de novo mutations. Chromodomain helicase DNA binding protein 7.

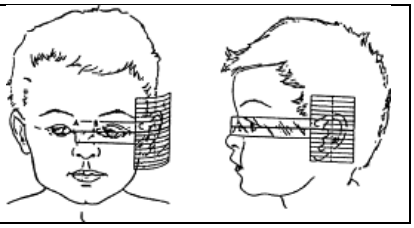
MURCS : Mullerian duct aplasia, renal aplasia, cervicothoraci somite dysplasia

VATER: Vertebral, anal imperforation, Tracheo-Esophageal fisutal with usually esophageal atresia, Renal or radial anomalies

VACTERL: VATER and cardiac + limb anomalies (radial)

Coloboma: abnormal ocular development and embryogenesis. Associated with trisomy 13; 4p-, 13q-, CHARGE, Goltz, Rieger. Should do chromosomal analysis. If Aniridia, think of WAGR (wilms) and possibly due to 11p-.

Low set ears:

Upper portion of ear (helix) meets head at level below horizontal line from lateral aspect of palpebral fissure. Align a straight edge btw 2 inner chanthi and determine if ears lie completely below plain. Normal individuals = 10% ear is above the plane.	

Prelingual hearing loss (loss detected before speech development) : most common mutation is GJB2 (gap junction beta-2 gene). Congenital non-syndromic deafness = 75% are due to mutations and this one is the most common, encodes for protein CONNEXIN 26 – critical for gap junctions btw cochlear cells, it is AR. Congenital hearing loss has prevalence of 1 in 500 newborn. Mutation 167delT found in Ashkenazi. Most common acquired hearing loss = CMV infection.

Cleft lip / palate : Most are polygenic or multifactorial pattern. Male to female = 3:2. Incidence = 1 in 1000. Recurrence is 3-4% if one affected child and 8-9% if 2 affected child.

Hypertelorism If imaginary 3rd eye btw 2 eyes = possible. Precise measure = inter-pupillary distance but difficult. Measure inner and outer canthal distances and chart on tables of norms.

Incontinenta Pigmenti: X-linked dominant genetic disorder that affects the skin, hair, teeth, nails and central nervous system. X-linked dominant genetic disorder that affects the skin, hair, teeth, nails and central nervoIncontinentia pigmenti is caused by a mutation in the IKBKG gene, which encodes the NEMO protein, which serves to protect cells against TNF-alpha-induced apoptosis. A lack of IKBKG therefore makes cells more prone to apoptosis. The skin lesions evolve through characteristic stages: blistering (from birth to about four months of age), a wart-like rash (for several months), swirling macular hyperpigmentation (from about six months of age into adulthood), followed by linear hypopigmentation. Many neurological issues.

RTA

Renal Tubular Acidosis (type 3 is usually excluded from modern classifications) - Wiki:

Type	Type 1	Type 2	Type 4
Location	Collecting Tubules, distal tubules	Proximal tubules	Adrenal
Acidemia	Yes (very severe)	Yes	Mild when present
Potassium	Hypokalemia	Hypokalemia	Hyperkalemia

Pathophysiology	Failure of α intercalated cells to secrete H^+ and reclaim K^+	Failure of proximal tubular cells to reabsorb bicarb.	Deficiency of aldosterone, or a resistance to its effects, (hypoaldosteronism or pseudohypoaldosteronism)

Urine anion gap: Na + K – Cl

The urine anion gap is an 'artificial' and calculated measure that is representative of the unmeasured ions in urine. Usually the most important unmeasured ion in urine is Ammonia since it is the most important form of acid excretion by the kidney. A negative urine anion gap can be used as evidence of increased NH_4^+ excretion. In a metabolic acidosis without a serum anion gap:

- A positive urine anion gap suggests a low urinary NH_4^+ (ex: RTA)
- A negative urine anion gap suggests a high urinary NH_4^+ (ex: Diarrhea, GI losses).

Endocrinology:

Neonatal hypoglycemia

Hypoglycemia is a frequent problem among neonates especially in the first few days of life. Residents should be able to recognize it, know the risks and have and approach for management. Here is a quick guide and a useful approach.

Who are the population of neonates at risk of hypoglycemia? / What is the differential diagnosis of hypoglycemia in neonates?

Infants at risk for hypoglycemia
- Weight <10th percentile (SGA) - Intrauterine growth restriction (IUGR) - Weight >90th percentile (LGA) - Infants of diabetic mothers (IDMs) - Preterm infants <37 weeks GA - Maternal labetalol use - Late preterm exposure to antenatal steroids - Perinatal asphyxia - Metabolic conditions (e.g., CPT-1 deficiency, particularly in Inuit infants) - Syndromes associated with hypoglycemia (e.g., Beckwith-Wiedemann)

When to screen asymptomatic infants for hypoglycemia?

- IDM or large for gestational age:

DM/LGA infants were the most likely to develop hypoglycemia in the first few hours post-birth. Therefore, screening is not required for this population after 12 hours of age if blood glucose levels remain ≥2.6 mmol/L.

- Preterm infants & IUGR infants.
  SGA and preterm infants may become hypoglycemic as late as the second day, although a decline in blood glucose levels may be prevented by establishing peroral intake. If there are no feeding concerns and the infant is well, screening may be discontinued at 24 hours of age. It is reasonable to screen once or twice on day 2 when there has been more than one glucose reading <2.6 mmol/L in the first 24 hours, to ensure levels remain at or above this level.

What is the threshold to investigate and treat hypoglycemia?

It is according to the infants age, the threshold to treat differ in clinical practice according each physician expertise but all around the same range and here is the threshold in the CPS statement which was updated in Nov 2019.

Thresholds for investigation and treatment of hypoglycaemia		
	Birth to 72 hours of age	≥72 hours of age
Therapeutic goal	2.6	3.3
Investigation threshold	2.6	2.8*

How to calculate glucose infusion rates (GIR) when the patient is on IVF Dextrose?

There are many online formula and app that can help with calculating GIR, this is one of the formulas:
The rate of the IVF infusion X the % of dextrose in the IVF
Divided by 6 X the weight of the infant.

How to monitor blood sugar after starting IV dextrose for hypoglycemia

See the algorithm and here is a quick clinical note.
Monitor blood sugar every 1/ 2/ 3/4/6/8 h according to the severity of hypoglycemia and the clinical condition.

If blood sugar starts to stabilize

- Wean IVF (after 12h of stabilization).
- Start enteral feeding gradually.
- Check BG Q3h pre- feeding/ when intervene check after 30 min.

If blood sugar still low

- Increase GIR by 1mg/kg/min
- Check Q 30 min, check lytes Q8h

- If GIR 8-10>> consider level 3 care
- If GIR> 10>> consider medications and investigation if more than 72h of life.

What are the initial investigations for persistent/severe hypoglycemia?

- Usually sent at the MCH: Critical sample (growth hormone, insulin and cortisol) during hypoglycemia episode that is confirmed by the blood gas (cBG). Bicarbonate, Lactate
- Other elements of a critical sample that can be considered depending on the case: Free fatty acids, Carnitine, Acylcarnitine profiling, Beta-HydroxyButirate, urine analysis. IT IS NEVER NORMAL TO FIND KETONES IN THE URINE OF A NEWBORN.
- Reference table with extend critical sample provided here for reference.

TABLE 2. Critical sample.

Blood
Chemistry panel with bicarbonate
Insulin, C-peptide
Cortisol, growth hormone
Free fatty acids, β-hydroxybutyrate, acetoacetate
Alanine
Lactate, ammonia
Total and free carnitine
Acylcarnitine profile
Serum amino acids
Extra serum tube
Urine
Dip for ketones
Urine-reducing substances
Organic acids

MCH Hypoglycemia Protocol

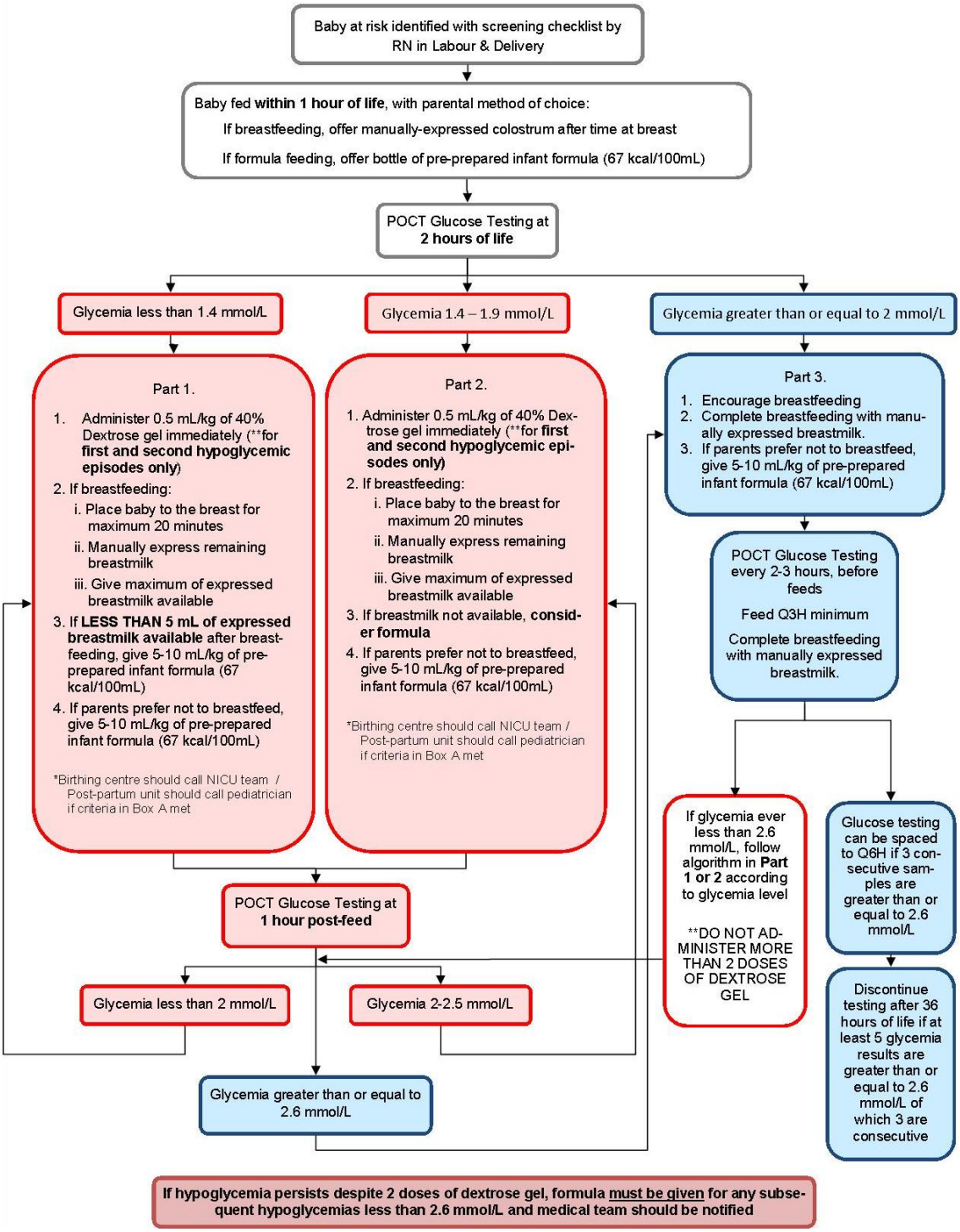


Table 1. *Risk Factors for Neonatal Hypoglycemia*

- Gestational age less than 37 weeks
- Small for gestational age (birth weight below 10th percentile) – see Table 2
- Identified as intrauterine growth restriction (IUGR) during the pregnancy, even if normal birth weight
- Large for gestational age (Birth weight above 90th percentile) – see Table 2
- APGAR score of less than 6 at five minutes
- Infant of diabetic mother (includes diabetes type 1 and 2, and gestational diabetes treated with diet, oral hypoglycemic agent or insulin)
- Beta-blockers administration to mother during the last week of pregnancy (ex: labetalol, propranolol, metoprolol)
- Betamethasone (Celestone ^{R}) administration to the mother during the last week of pregnancy

Table 2. *Weight for Gestational Age, 10th and 90th Percentiles by Sex*

Gestational Age (completed weeks)	Birthweight (g)			
	10th Percentile		90th Percentile	
	Male	Female	Male	Female
37	2552	2452	3665	3543
38	2766	2658	3877	3738
39	2942	2825	4049	3895
40	3079	2955	4200	4034
41	3179	3051	4328	4154
42	3233	3114	4433	4251

Table 3. *Signs and symptoms of Neonatal Hypoglycemia*

- Hypothermia (axillary temperature lower than 36.5 degrees Celsius) despite warming measures
- Jitteriness and/or tremors
- Seizures and/or eye-rolling
- Weak and/or high-pitched cry
- Limpness and/or lethargy
- Cyanosis, intermittent apneic spells, and/or tachypnea
- Feeding difficulty and/or poor suck
- Diaphoresis
- Sudden pallor

NOTE: Respiratory distress immediately after birth should receive proper assessment and care by NICU before patient is tested for hypoglycemia

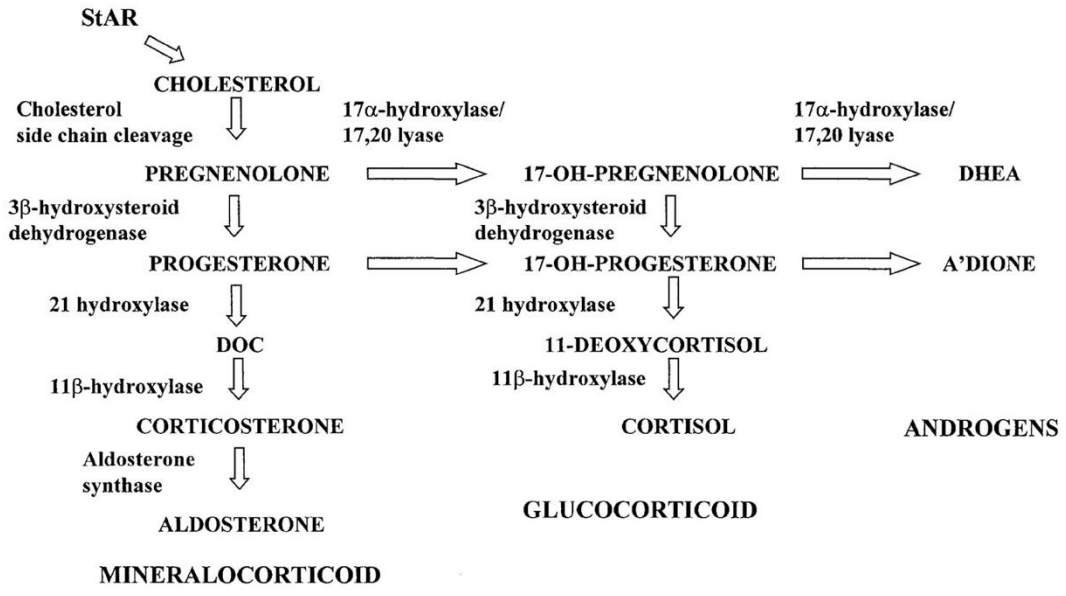
Adrenal Insufficiency :

TABLE 1. Etiology of primary adrenal insufficiency.

Congenital
Congential adrenal hyperplasia
Congenital adrenal hypoplasia
Familial glucocorticoid deficiency (ACTH unresponsiveness)
Allgrove syndrome (alachrima, achalasia, ACTH unresponsiveness)
Metabolic disease
Adrenoleukodystrophy
Smith-Lemli-Opitz syndrome
Wolman disease
Zellweger disease
Mitochondrial disease
Acquired
Autoimmune adrenalitis (Addison disease)
Isolated autoimmune adrenalitis
Autoimmune polyendocrine syndrome
Hemorrhage
Birth trauma
Trauma
Meningococcemia (Waterhouse-Friderichsen syndrome)
Medication
Ketoconazole
Etomidate
Infection
Cytomegalovirus
Human immunodeficiency virus
Fungal
Tuberculosis

TABLE 2. Etiology of secondary adrenal insufficiency.

Congenital
Septo-optic dysplasia
Maternal hypercortisolemia (hypothalamic suppression)
Corticotropin releasing hormone deficiency (hypothalamic dysfunction)
ACTH deficiency (pituitary dysfunction)
Pituitary aplasia/hypoplasia
Prader-Willi syndrome
Acquired
Chronic steroid use
Abrupt steroid withdrawal
Increased metabolic demand
Megesterol acetate (Megace) withdrawal
Tumor
Head trauma
Burn injury
Radiation
Infiltrative disease



Congenital Adrenal Hyperplasia (CAH)

- occurs in 1/15000 live births and is the most common cause of ambiguous genitalia
- autosomal recessive condition causing partial or total enzyme defect
- 21-hydroxylase deficiency causes 95% of CAH cases; this causes decreased cortisol and aldosterone with shunting toward overproduction of androgens
- cortisol deficiency leads to elevated ACTH, which causes adrenal hyperplasia
- clinical presentation depends on the specific deficiency and the cause – may present with shock, hyperkalemia if not suspected
- for steroid biosynthesis pathway, see Endocrinology, E29

Salt-Wasting 21-Hydroxylase Deficiency (2/3 of cases)

- infants present with shock, FTT, low Na^+, high K^+, low Cl^-, low glucose, adrenal insufficiency, high ACTH
- hyperpigmentation of genitals and areola and postnatal virilization

Late-Onset 21-Hydroxylase Deficiency

- allelic variant of classic 21-hydroxylase deficiency – mild enzymatic defect
- girls present with amenorrhea
- boys present with precocious puberty with early adrenarche, dehydration
- accelerated linear growth in early puberty but early fusion of epiphyses leading to decreased adult height
- diagnosis
  - increased plasma 17-OH-progesterone after ACTH stimulation test
- treatment
  - dexamethasone, spironolactone (anti-androgen)
  - mineralocorticoid replacement is not needed

Simple Virilizing 21-Hydroxylase Deficiency

- virilization in girls but not boys

11-Hydroxylase Deficiency

- sexual ambiguity in females
- may have insidious onset; may present with hirsutism, occasionally hypertension

17-Hydroxylase Deficiency

- sexual ambiguity in males, hypertension

Investigations

- low Na^+, high K^+, low cortisol, high ACTH if both glucocorticoid and mineralocorticoid deficiency
- increased serum 17-OH-progesterone (substrate for 21-hydroxylase)
- increased testosterone, DHEAS, urinary 17-ketosteroids
- advanced bone age

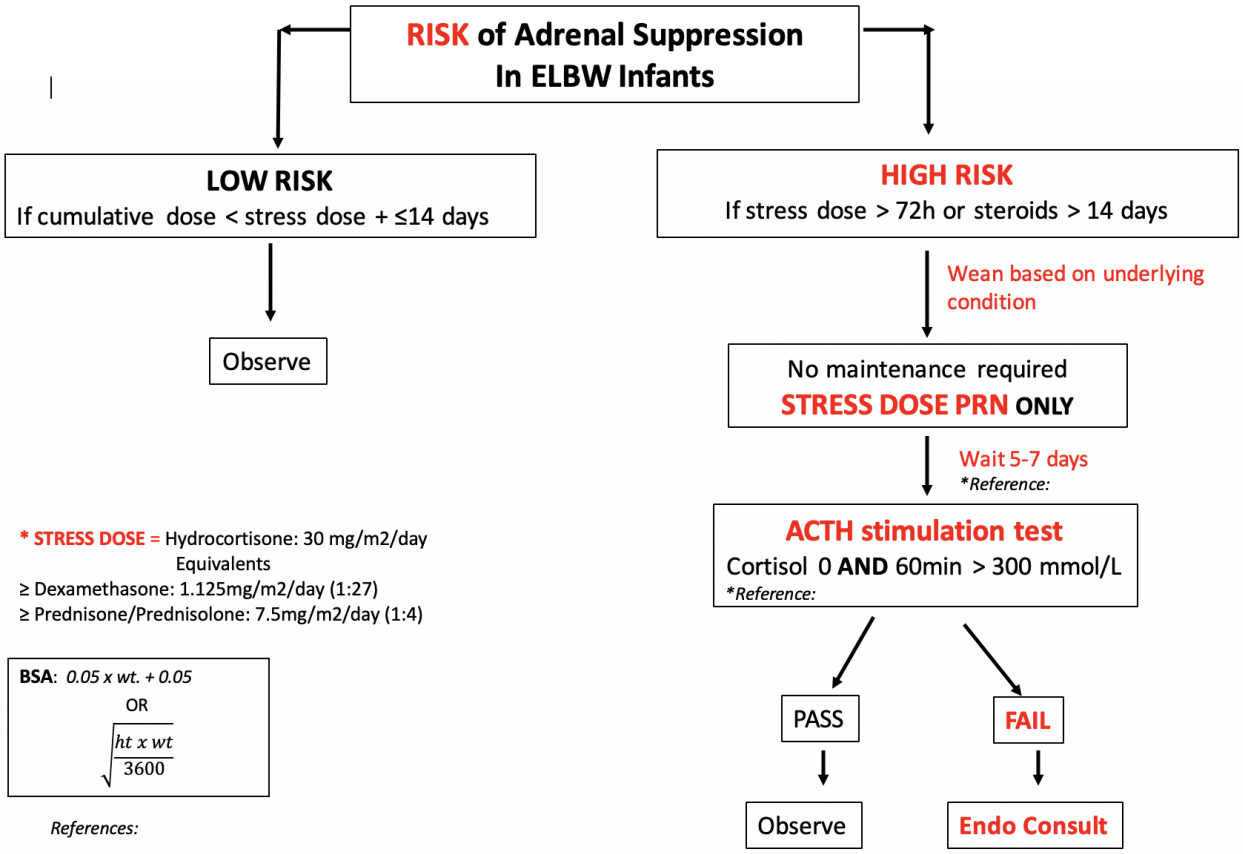
Treatment

- glucocorticoid replacement to lower ACTH
- in salt-wasting type mineralocorticoids given as well
- spironolactone is used in late-onset 21-hydroxylase deficiency as anti-androgen
- surgery to correct ambiguous genitalia

Table 15. Clinical Features of CAH Based on Enzyme Defect

Enzyme Defect	Sexual Ambiguity		Postnatal Virilization	Salt Wasting	Hypertension
	Female	Male			
21-hydroxylase					
salt-wasting	–	–	+	+	–
simple virilizing	+	–	+	–	–
late onset	–	–	+	–	–
11-hydroxylase	+	–	+	–	+
17-hydroxylase	–	+	–	–	+

Risk of Adrenal suppression in ELBW – MCH protocol



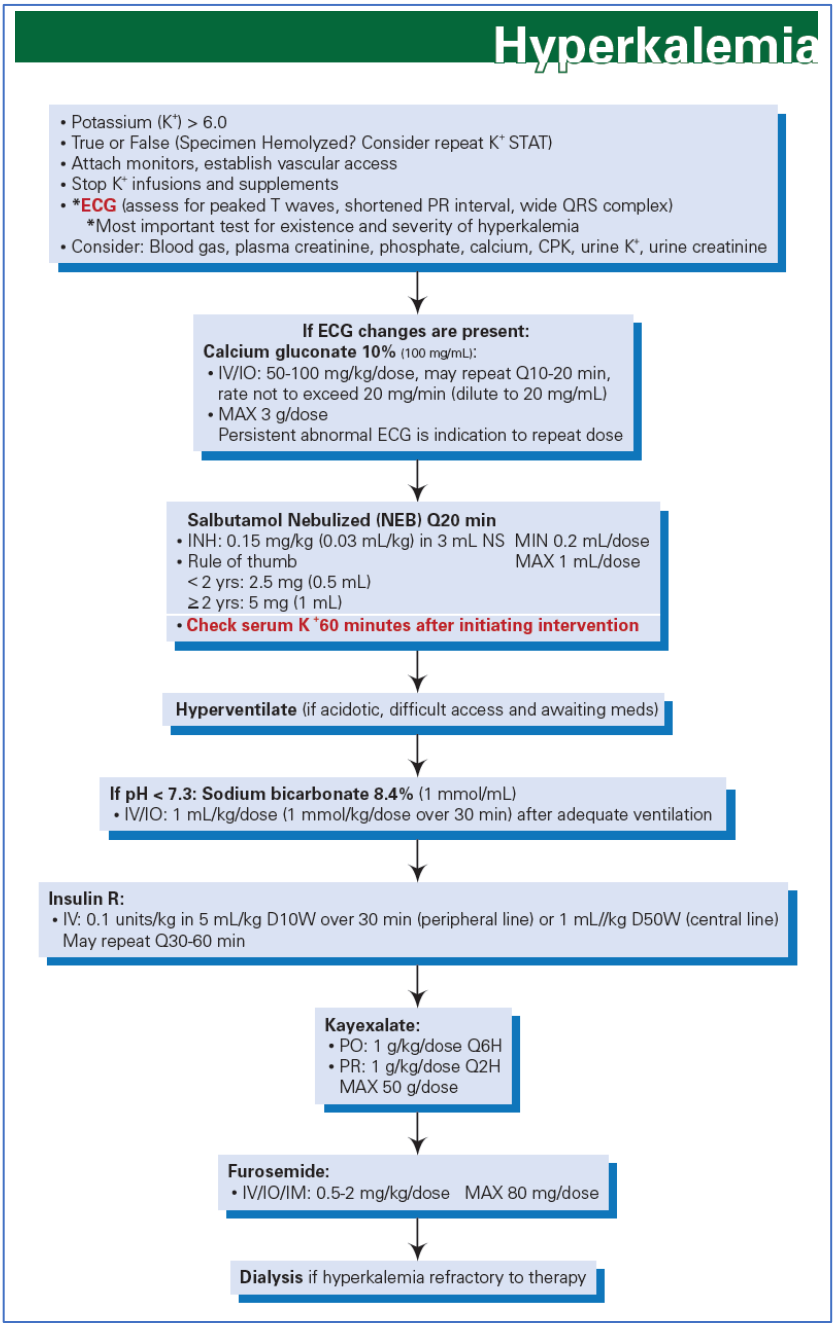
* STRESS DOSE = Hydrocortisone: 30 mg/m2/day Equivalents
≥ Dexamethasone: 1.125mg/m2/day (1:27)
≥ Prednisone/Prednisolone: 7.5mg/m2/day (1:4)

BSA: *0.05 x wt. + 0.05*
OR
$$\sqrt{\frac{ht \times wt}{3600}}$$

References:

Prepared by: L. Gervais NNP, Dr. J. Von Oettingen, Dr. W. Shalish
2018-07-25

Hyperkalemia:



MCH Statistics:

Extreme Premature Newborns:

Categories	GA < 29 weeks	29-32 weeks	33-36 weeks	> 37 weeks
Number of infants	68	80	178	362
Early onset sepsis, n (%)	2 (3%)	1 (1%)	9 (5%)	8 (2%)
Late onset sepsis, n (%)	24 (35%)	3 (4%)	9 (5%)	8 (2%)

Outcome		2022	2021	2020	2022	2021	2020
		< 29 weeks N=68	<29 weeks, n=67	<29 weeks, n=62	<33 weeks, n=148	<33 weeks, n=153	<33 weeks, n=137
Mortality	Rate (%)	17.7	11.9	9.7	9.5	6.5	5.1
IVH ¾ or PVL	Rate (%)	16.9	22.4	15.3	13.0	15.3	13.3
Late-onset sepsis	Rate (%)	35.3	20.9	25.8	18.2	13.1	13.9
NEC	Rate (%)	4.4	7.7	3.5	3.4	4.6	2.3
BPD	Rate (%)	45.6	47.5	45.5	25.9	25.0	26.4
ROP	Rate (%)	8.8	7.1	9.6	6.8	5.1	7.1
Mortality or any morbidity	Rate (%)	64.7	62.7	59.7	39.9	36.0	39.4

Suggested References

- CPS Statements → These are essential for the royal college exam (to know by heart).
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