Neonatology Protocol of EHA

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Egyptian Clinical Practice Protocol

in

Neonatology

for

Egypt Healthcare Authority

First Edition

2024

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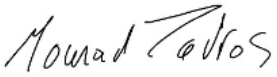

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PREFACE

Recently, there is an increasing need to provide programs with accurate competency-based assessments to ensure the delivery of high-quality healthcare. The aim of developing these Egyptian Clinical Practice Protocols in Neonatology is to unify and standardize the delivery of healthcare to all newborns at all health facilities.

The current state of healthcare in which avoidable failures are abound. “We train longer, specialize more, use ever-advancing technologies, and still we fail.” Part of the problem, is that the ever-increasing complexity of medicine makes uniform care delivery impractical or impossible. That is, unless there are protocols, checklists, or care paths that are readily available to providers.

Standard textbooks, journals, and online resources currently available create excellent repositories of detailed information about the etiology, pathogenesis, clinical picture, diagnosis, and treatment of a condition. However, for a busy clinician looking for the best way to manage a sick patient, a standardized path for effective management of the patient may be impossible to discern. So, it would be a lot easier if we all managed simple things in a uniform way using the best available evidence and resources.

In neonatology, busy clinicians have all felt the need for a concise, easy-to-use resource at the bedside for evidence-based protocols, or consensus-driven care paths where high-grade evidence is not available.

In this protocol, we offer comprehensive reviews of selected topics and comprehensive advice about management approaches and procedures based on the highest level of evidence available in each case. Our goal is to provide an authoritative practical medical resource for neonatologists, pediatricians, and other healthcare providers dealing with newborns after birth. This protocol is the product of contributions from numerous neonatologists from all over Egypt.

We hope that such an approach will encourage clinicians to apply available evidence to their practice and also track compliance with desired practices. We hope that practicing neonatologists, fellows, nurse practitioners, and other NICU personnel will find this protocol useful in delivering high-quality clinical care to their patients. We remain open to feedback and suggestions about how to improve this resource and how to make it maximally useful to those delivering care at the bedside in the NICU.

Members of the Working Group

For Development of the Egyptian Clinical Practice Protocol

In Neonatology

Table of Contents

Criteria of Admission & Discharge in NICU

There should be good clinical reasons for admission to NICU

Avoid unnecessary separation of mother and baby as it affects maternal bonding.

Ensure that all babies born have newborn infant physical examination and check the saturation between 6-72 hour of birth.

Criteria for Admission from Labour Ward or Postnatal Ward:

- Clinical condition requiring constant monitoring, <34 week's gestation or birth weight <1700 grams**.**
- Unwell baby:
  - Poor condition at birth requiring prolonged resuscitation for >10 min and/or cord pH <7.0 (a low cord pH may not in itself necessitate admission to NICU).
  - Respiratory distress or cyanosis.
  - Apnoeic or cyanotic attacks.
  - Signs of encephalopathy.
  - Jaundice needing intensive phototherapy or exchange transfusion.
  - Major congenital abnormality likely to threaten immediate survival.
  - Seizures.
  - Inability to tolerate enteral feeds with vomiting and/or abdominal distension and/or hypoglycaemia (blood glucose <36 mg/L for 37 weeks/< 46.8 mg/L for <37 weeks gestation).
  - Symptomatic hypoglycaemia or hypoglycaemia not responding to treatment.
  - Neonatal abstinence syndrome requiring treatment.
  - Short-term care while mother admitted to ITU.
  - Pre-& post-operative care of major surgical procedures case.

Procedure:

- Manage immediate life-threatening clinical problems (e.g. airway, breathing, circulation and seizures).
- Show baby to parents and explain reason for admission to NICU.
- Inform NICU nursing staff that you wish to admit a baby, reason for admission and clinical condition of baby.
- Ensure baby name labels present.
- Document relevant history and examination.
- Complete any local problem sheets and investigation charts.
- Measure and plot birth weight and head circumference on growth chart.
- Measure admission temperature.
- Measure blood pressure using non-invasive cuff.
- Institute appropriate monitoring and treatment in conjunction with nursing and senior medical colleagues.

Investigations:

For babies admitted to the NICU, Obtain 1 bloodspot on:

- Newborn bloodspot screening (Guthrie) card (TSH&PKU) on (Saturday and Tuesday).
- Babies <32 weeks/1500 grams weight/unwell/ventilated:
  - Full Blood Count.
  - Blood glucose.
  - Blood gases.
  - Clotting screen if clinically indicated.
  - Routine clotting screen in all babies <30 weeks' gestation is not recommended.
  - If respiratory symptoms or support given, chest X-ray.
  - If umbilical lines in place, abdominal X-ray.
  - If suspicion of sepsis, blood culture and CRP before starting antibiotics and consider lumbar puncture.
  - Additional investigations depend on initial assessment and suspected clinical problem (e.g. infection, jaundice, etc.).

Immediate Management:

- Evaluation of baby, including full clinical examination.
- Define appropriate management plan and procedures with Consultant and perform as efficiently as possible to ensure baby is not disturbed unnecessarily.
- Aim for examination and procedures to be completed ≤1hr of admission.
- If no contraindications, give vitamin K IM.
- If antibiotics indicated, give within an hour.
- Senior clinician to update parents as soon as possible (certainly within 24hr) and document discussion in notes.

Respiratory Support:

- If required, this takes priority over other procedures.
- Including; incubator oxygen, nasal oxygen, continuous positive airway pressure (CPAP) or mechanical ventilation.

Intravenous Access:

- If required, IV cannulation and/or umbilical venous catheterization (UVC).

Monitoring:

- Use minimal handling
- Cardiorespiratory monitoring through skin electrodes.
- Pulse oximetry. Maintain SpO2 not less than 95%.
- Temperature.
- Blood glucose.
- If ventilated, monitoring blood pressure and blood gases.

Criteria for Admission to Transitional Care:

The following are common indications for admitting babies to transitional care:

- Preterm 34–36 weeks' gestation and no other clinical concerns.
- Minor congenital abnormalities likely to affect feeding, e.g. cleft lip and palate.
- Requiring support with feeding.
- Babies of substance abusing mothers.
- Receiving IV antibiotics.
- Unknown babies.

Neonatal Levels of Care

TABLE 1 Definitions, Capabilities, and Provider Types: Neonatal Levels of Care

Level of Care	Capabilities	Provider Types[a]
Level I Well newborn nursery	• Provide neonatal resuscitation at every delivery • Evaluate and provide postnatal care to stable term newborn infants • Stabilize and provide care for infants born 35–37 wk gestation who remain physiologically stable • Stabilize newborn infants who are ill and those born at <35 wk gestation until transfer to a higher level of care	Pediatricians, family physicians, nurse practitioners, and other advanced practice registered nurses
Level II Special care nursery	Level I capabilities plus: • Provide care for infants born ≥32 wk gestation and weighing ≥1500 g who have physiologic immaturity or who are moderately ill with problems that are expected to resolve rapidly and are not anticipated to need subspecialty services on an urgent basis • Provide care for infants convalescing after intensive care • Provide mechanical ventilation for brief duration (<24 h) or continuous positive airway pressure or both • Stabilize infants born before 32 wk gestation and weighing less than 1500 g until transfer to a neonatal intensive care facility	Level I health care providers plus: Pediatric hospitalists, neonatologist, and neonatal nurse practitioners.
Level III NICU	Level II capabilities plus: • Provide sustained life support • Provide comprehensive care for infants born <32 wks gestation and weighing <1500 g and infants born at all gestational ages and birth weights with critical illness • Provide prompt and readily available access to a full range of pediatric medical subspecialists, pediatric surgical specialists, pediatric anesthesiologists, and pediatric opthalmologists • Provide a full range of respiratory support that may include conventional and/or high-frequency ventilation and inhaled nitric oxide • Perform advanced imaging, with interpretation on an urgent basis, including computed tomography, MRI, and echocardiography	Level II health care providers plus: Pediatric medical subspecialists[b], pediatric anesthesiologists[b], pediatric surgeons, and pediatric opthalmologists[b].
Level IV Regional NICU	Level III capabilities plus: • Located within an institution with the capability to provide surgical repair of complex congenital or acquired conditions • Maintain a full range of pediatric medical subspecialists, pediatric surgical subspecialists, and pediatric anesthesiologists at the site • Facilitate transport and provide outreach education	Level III health care providers plus: Pediatric surgical subspecialists

[a] Includes all providers with relevant experience, training, and demonstrated competence.
[b] At the site or at a closely related institution by prearranged consultative agreement.

Discharge from Neonatal Unit:

Decision to Discharge:

- Only consultant or specialist may discharge.
- Medical and nursing staff to agree discharge date with parents or persons with parental responsibility.
- Nursing team perform majority of discharge requirements.

Discharge Checklist:

Where appropriate, the following must be achieved before discharge:

Parental Competencies:

- Administration of medications when required.
- Baby cares (e.g. nappy changes, bathing etc.)
- Feeding.
- Nasogastric tube feeding where necessary.
- Stoma care (surgical babies).

Parent education:

In addition to above, it is best practice to offer parents education on:

- Basic neonatal resuscitation.
- Common infectious illnesses.
- Immunizations, if not already received (give national leaflet).

Parent communication:

- Instructions about immunizations given and dates and care of other immunizations.
- Give parents copy of discharge summary and time to ask questions after they have read it. (Clarify red flags for seeking medical advice).
- Ensure parents have information regarding breastfeeding.
- Ensure parents have up-to-date safety information.
- If transporting in a car, use suitable car seat.
- If transferring to another unit, ensure parents understand reason for transfer. Provide information about receiving unit.

Procedures/investigations:

- Complete audiology screening and hearing test.
- All babies receiving CPAP or M.V or treated with O2 should have a fundus examination by an ophthalmologist to screen for retinopathy of prematurity (ROP).

Medical team:

- Complete discharge summary by date of discharge
- Complete neonatal dataset by date of discharge follow-up

Appointments:

- Ensure these are written on discharge summary Likely appointments could include any of the following depending on the clinical condition:
  - Neonatal/ Paediatric consultant outpatient clinic.
  - Ophthalmology screening.
  - Audiology referral.
  - Cranial ultrasound.
  - Brain US/MRI scan.
  - Physiotherapy.
  - Hip or renal ultrasound.
  - Dietitian.
  - Community paediatrician.
  - Child development center.
  - BCG immunization.

SOURCES:

1. **National institute for health and care excellence (NICE)**
2. **Bedside clinical guidelines partnership in association with Partners in pediatrics**

Neonatal Jaundice

Recognition and Assessment:

Risk Factors for Hyperbilirubinaemia:

- <38 weeks' gestation
- Previous sibling required treatment for jaundice
- Mother intends to exclusively breastfeed
- Visible jaundice in baby aged <24 hour

Risk Factors for Kernicterus:

- High bilirubin level (>20 mg/dl in term baby)
- Rapidly rising bilirubin level (>0.5 mg/dl /hour)
- Clinical features of bilirubin encephalopathy

Symptoms and Signs:

- When looking for jaundice (visual inspection):
- Check naked baby in bright and preferably natural light
- Examine the sclerae and gums, and press lightly on skin to check for signs of jaundice in 'blanched' skin

Assess:

- Pallor (haemolysis)
- Poor feeding, drowsiness (neurotoxicity)
- Hepatosplenomegaly (blood group incompatibility or cytomegalovirus)
- Splenomegaly (spherocytosis)

Causes:

- Physiological
- Prematurity
- Increased bilirubin load:
- Blood group incompatibility (rhesus or abo)
- G6pd deficiency and other red cell enzyme deficiencies
- Congenital spherocytosis
- Cephalhaematoma, bruising
- Rarely infection (e.g. UTI, congenital infection)
- Metabolic disorder

Persistent Jaundice After 14 Days of Age (see Liver dysfunction guideline):

- Breast milk jaundice
- Hypothyroidism
- Liver disease (e.g. extra hepatic biliary atresia and neonatal hepatitis)
- Alpha-1-antitrypsin deficiency
- Galactosaemia
- TPN-induced cholestasis

Investigations:

Assessment of Jaundice:

- Babies aged <72 hour, at every opportunity (risk factors and visual inspection)
- Babies with suspected or obvious jaundice, measure and record bilirubin level urgently
- <24 hour: within 2 hour
- ≥24 hour: within 6 hour
- If serum bilirubin >5.8 mg/dl in first 24 hour
- Repeat measurement in 6–12 hour
- Urgent medical review as soon as possible (and within 6 hour)
- Interpret bilirubin results in accordance with baby's gestational and postnatal age according to Table

Jaundice Approaching Treatment Level:

- If baby well, ≥38 weeks, aged >24 hour and
- Serum bilirubin ≤3 mg/dl below treatment threshold, repeat measurement in 18 hour if risk factors and 24 hour if no risk factors
- Serum bilirubin >3 mg/dl below treatment threshold, no further routine measurements required

Jaundice Requiring Treatment:

- Total bilirubin
- Baby's blood group and direct Coombs test (interpret result taking into account strength of reaction and whether mother received prophylactic anti-D immunoglobulin during pregnancy)
- Mother's blood group and antibody status (should be available from maternal healthcare record)
- PCV

Plus (if clinically indicated):

- Full infection screen (in an ill baby)
- G6PD level and activity (if indicated by ethnic origin: Mediterranean, Middle Eastern, South East Asian)
- Full blood count and film

Persistent Jaundice >14 days in term baby; OR >21 days in preterm baby (see Liver dysfunction guideline), Check:

- Total and conjugated bilirubin
- Examine stool colour
- Full blood count
- Baby's blood group and direct Coombs test (interpret result taking into account strength of reaction and whether mother received prophylactic anti-D immunoglobulin during pregnancy)
- Ensure routine metabolic screening performed (including screening for hypothyroidism)
- Urine culture

Baby with Conjugated Bilirubin >25 mg/dl,

Refer Urgently to A Specialized Center.

Second Line Investigations (not in NICE guideline):

- Liver function tests (ALT, AST, albumin, GGT)
- Coagulation profile
- G6PD screen in African, Asian or Mediterranean babies
- Thyroid function tests: ask for free T4 priority and then TSH'
- Congenital infection screen
- Urine for CMV PCR, toxoplasma ISAGA-IgM and throat swab for HSV culture/PCR
- Metabolic investigations e.g:
  - Blood galactose-1-phosphate
  - Urine for reducing substances
  - Alpha-1-antitrypsin

Treatment of hyperbilirubinemia with duration <7 days:

Do Not Start Treatment if Serum Bilirubin is Below Treatment Threshold

Babies ≥38 weeks' gestation:

- Use conventional blue light phototherapy (not fibre optic) as treatment of choice
- Use continuous multiple phototherapy for babies who:
  - Fail to respond to conventional phototherapy (bilirubin does not fall within 6 hour of starting treatment)
  - Have a rapid rise in bilirubin (>0.5 mg/dl /hour)
  - Have a bilirubin level within 3 mg/dl of exchange transfusion threshold
- When level falls to >3 mg/dl below threshold reduce intensity of phototherapy

Babies <38 weeks' gestation:

- Use fibre optic or conventional blue light as first line treatment
- based on gestational age and postnatal age, use Threshold graphs (**http://www.nice.org.uk/guidance/CG98** under 'Tools and resources' then 'CG98 Neonatal Jaundice: treatment threshold graphs') to determine threshold for phototherapy
- Indications for multiple phototherapy as term babies

Management During Phototherapy:

- Offer parents information on procedure
(www.nice.org.uk/guidance/cg98/resources/jaundice-in-newborn- babies-318006690757)
- Unless other clinical conditions prevent, place baby in supine position turn frequently
- Ensure treatment applied to maximum area of skin
- Monitor baby's temperature
- Monitor hydration by weighing baby daily and assessing wet nappies
- Use eye protection and give routine eye care
- Provided bilirubin not significantly elevated, encourage breaks of up to 30 min for breastfeeding, nappy change and cuddles
- Do not give additional fluids routinely
- During multiple phototherapy:
  - Do not interrupt for feeds
  - Continue lactation/feeding support so that breastfeeding can recommence when treatment stops

Monitoring During Phototherapy:

- Repeat serum bilirubin 4–6 hour after starting treatment
- Repeat serum bilirubin 6–12 hourly when bilirubin stable or falling
- Stop phototherapy once serum bilirubin has fallen to at least 3 mg/dl below threshold
- Check for rebound jaundice with repeat serum bilirubin 12–18 hour after stopping phototherapy. Babies do not necessarily need to remain in hospital for this to be done

Discharge and Follow-Up:

- GP follow-up with routine examination at 6–8 weeks
- If exchange transfusion necessary or considered, request developmental follow-up and hearing test
- In babies with positive Coombs test who require phototherapy:
  - Check haemoglobin at aged 2 and 4 weeks due to risk of continuing haemolysis
  - Give folic acid 1 mg daily

Table: Limits for Phototherapy and Exchange Transfusion For Babies ≥38 Weeks' Gestation

Age (hours)	Serum Bilirubin (micromol/L)	Serum Bilirubin (micromol/L)	Serum Bilirubin (micromol/L)	Serum Bilirubin (micromol/L)
0	–	–	>100	>100
6	>100	>112	>125	>150
12	>100	>125	>150	>200
18	>100	>137	>175	>250
24	>100	>150	>200	>300
30	>112	>162	>212	>350
36	>125	>175	>225	>400
42	>137	>187	>237	>450
48	>150	>200	>250	>450
54	>162	>212	>262	>450
60	>175	>225	>275	>450
66	>187	>237	>287	>450
72	>200	>250	>300	>450
78	–	>262	>312	>450
84	–	>275	>325	>450
90	–	>287	>337	>450
96+	–	>300	>350	>450
Action	Repeat transcutaneous bilirubin/serum bilirubin (6–12 hour)	Consider phototherapy (repeat transcutaneous bilirubin/serum bilirubin in 6 hour)	Start phototherapy	Perform exchange transfusion

NB: To Convert from (Mmol/L) to (mg / dl) divided by 17

SOURCE:

- **http://www.nice.org.uk/guidance/CG98**
- **Treatment graphs giving the phototherapy and exchange transfusion limits for each gestational age can be printed from http://www.nice.org.uk/guidance/CG98 under 'Tools and resources' then 'CG98 Neonatal Jaundice: treatment threshold graphs'**

Bind Score

Bilirubin-Induced Neurologic Dysfunction

Clinical Signs	BIND Score	Date: Time:	Date: Time:
Mental Status			
Normal	0		
Sleepy but arousable; decreased feeding	1		
Lethargy, poor suck and/or irritable/jittery with strong suck	2		
Semi-coma, apnoea, unable to feed, seizures, coma	3		
Muscle Tone			
Normal	0		
Persistent mild to moderate hypotonia	1		
Mild to moderate hypertonia alternating with hypotonia, beginning arching of neck and trunk on stimulation	2		
Persistent retrocollis and opisthotonus - bicycling or twitching of hands and feet	3		
Cry Pattern			
Normal	0		
High pitched when aroused	1		
Shrill, difficult to console	2		
Inconsolable crying or cry weak or absent	3		
TOTAL BIND SCORE			

Advanced ABE (score 7 - 9): urgent bilirubin reduction intervention is needed to prevent further brain damage and reduce the severity of sequelae
Moderate ABE (score 4 - 6): urgent bilirubin reduction intervention is likely to reverse this acute damage
Mild ABE (score 1 - 3): subtle signs of ABE

Note: An abnormal or 'referred' Auditory Brainstem Response (ABR) is indicative of moderate ABE. Serial ABR may be used to monitor progression and reversal of acute auditory damage and could be indicative of the effectiveness of bilirubin reduction strategy.

Adapted: Johnson L, Bhutani VK, Karp K, et al. Clinical report from the pilot USA Kernicterus Registry (1992 to 2004). J Perinatol. 2009 Feb;29 Suppl 1:S25-45

Exchange Transfusion:

- Exchange transfusion replaces withdrawn baby blood with an equal volume of donor blood

NB: Discuss all cases with "Neonatal consultant"

Indications:

Haemolyticanaemia:

- A newborn who has not had an in-utero transfusion (IUT) with a cord Hb <120 g/L and is haemolysing. May require urgent exchange transfusion to remove antibodies & correct anemia, if Hb < 100g/L: discuss urgently with consultant &proceed to exchange transfusion level, use intravenous immunoglobulin (IVIG).
- A newborn who has had IUTs & whose Kleihauer test (this test may not be available in your hospital) demonstrates a predominance of adult Hb, anemia can be managed using a top-up transfusion of irradiated, CMV-negative blood.

Hyperbilirubinaemia:

- Discuss promptly with consultant. If bilirubin values approaching guidance below; senior decision required: guidance as determined by exchange transfusion line on gestation-specific NICE jaundice chart.
- If bilirubin rises faster than 0.5mg/dl/hr. despite phototherapy, anticipate need for exchange transfusion.

Other Indications:

- Chronic feto-maternal transfusion.
- Disseminated intravenous coagulation (DIC).

Complications:

- Cardiac arrhythmia.
- Air embolism.
- Necrotizing enterocolitis.
- Coagulopathy.
- Apneas & bradycardia.
- Sepsis.
- Electrolyte disturbances.
- Acidosis owing to non-fresh blood.
- Thrombocytopenia.
- Late hyporegenerative anemia.

Procedure:

Prepare:

- Ensure full intensive care space & equipment available &ready.
- Allocate 1 doctor/practitioner & 1 other member of nursing staff, both experienced in exchange transfusion, to care for each baby during procedure; document their names in baby's notes.
- Obtain written consent & document in babies notes.
- Phototherapy to be continued during exchange.
- Calculate volume of blood to be exchanged: double volume exchange removes 90% of baby's red cells & 50% of available intravascular bilirubin.

Use:

- ***Term babies:*** *160ml/kg.*
- ***Preterm babies:*** *200ml/kg.*

- Order appropriate volume (usually 2 units) of blood from blood bank, stipulating that it must be:
  - Crossmatched against mother's blood group & antibody status, & (if requested by your blood bank) baby's blood group.
  - CMV negative,
  - Irradiated (shelf-life 24 hr.) for any baby who has had an in-utero blood transfusion.
  - As fresh as possible, & certainly <4 days old.
  - Plasma reduced red cells for exchange transfusion (haematocrit 0.5-0.6), not SAG-M blood & not packed cells.

Meconium Aspiration Syndrome

Most infants born to mothers with meconium-stained amniotic fluid are asymptomatic.

MAS occurs in term or post-term infants born through meconium-stained amniotic fluid.

Diagnosis:

- Meconium passage
- Respiratory distress
- Characteristic x-ray findings

Investigations:

CXR:

- May demonstrate a spectrum of disease from widespread patchy infiltration, +/- small pleural effusions, to diffuse homogenous opacification with severe disease a picture similar to CLD can be seen as the disease progresses.

Blood Tests:

- Full Blood Count.
- ABG.
- Blood cultures.
- CRP

Echocardiography:

- Where there is suspicion of PPHN, it is advisable to obtain an echocardiogram as early as possible to help guide further therapy.

Management:

General Measures:

- Nurse in a thermo-neutral environment.
- Minimal handling.
- Consider need for CFM +/- therapeutic hypothermia.
- Establish appropriate vascular access.
- Avoid/manage systemic hypotension.
- Antibiotics.
- Nutrition: consider early Parenteral Nutrition

Respiratory Care:

- **Assess degree of respiratory compromise:**
    - ➢ Infants should be managed with adequate respiratory support dependent upon their clinical condition as indicated by:
    - ➢ Effort of breathing.
    - ➢ Oxygen requirement: aim to keep pre-ductal oxygen saturations 95-98%.
    - ➢ Blood gas indices.

Mild Respiratory Distress:

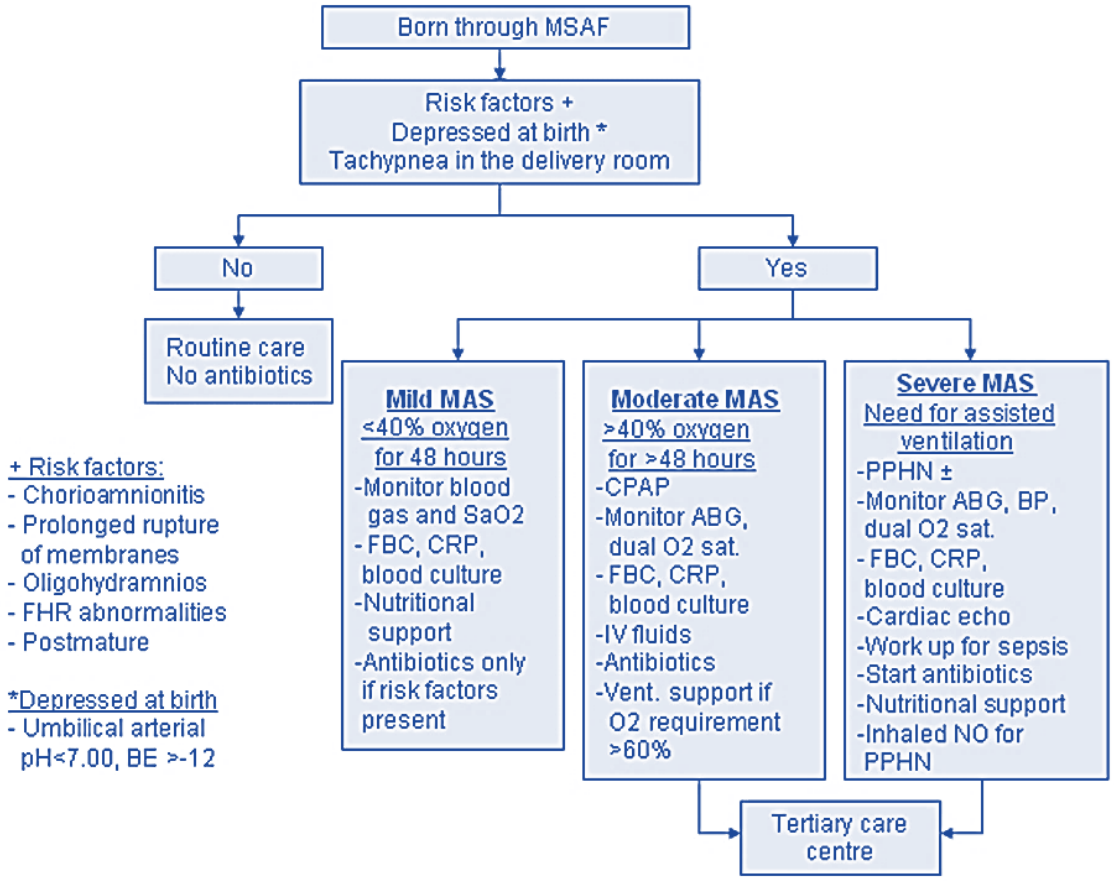
- Humidified oxygen.
- Consider High Flow Nasal Cannula oxygen.
- Pneumothorax
    - ➢ Non-tension may not need treatment.
    - ➢ Transilluminate +/- chest x-ray

Moderate-Severe Respiratory Distress:

- CXR
- Hyperexpanded
- Patchy infiltrations
- Small pleural effusions

Ventilation:

- Critical to maintain PaO2 >10kPa
- Aim for normal PaCO2 and pH
- Use conventional ventilation initially
- Avoid high PEEP where possible
- Sedation may be required
- Surfactant 200mg/kg
- Aim for early echocardiogram if PPHN is suspected
- Aim to maintain systemic BP ≥ normal values
- Consider inhaled Nitric Oxide [iNO]
- Consider ECMO



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Hypoxic Ischaemic Encephalopathy (HIE)

Immediate Treatment:

- Prompt and effective resuscitation
- Maintain body temperature, avoid hyperthermia
- IV access
- Isotonic glucose-containing IV fluids at 40 mL/kg/day (see Intravenous fluid therapy guideline)

Subsequent Management:

Continue with management below if baby not transferred to cooling center, or in cooling center without local guideline for active cooling. NOTE that some of the target values are different to those recommended if a baby is being actively cooled.

1. Oxygen:

- Avoid hypoxaemia. Maintain PaO2 10–12 kPa and SpO2 >94%
- Episodes of hypoxaemia (possibly associated with convulsions) are an indication for IPPV

2. Carbon Dioxide:

- Maintain PaCO2 5.0–7.0 kPa
- Hypoventilation leading to hypercapnia (>7.0 kPa) is an indication for IPPV
- Hyperventilation is contraindicated but, if baby spontaneously hyperventilating, mechanical ventilation, may be necessary to control PaCO2

3. Circulatory Support:

- Maintain mean arterial blood pressure at ≥40 mmHg for term babies
- If cardiac output poor (e.g. poor perfusion: blood pressure is a poor predictor of cardiac output) use inotropes
- Avoid volume replacement unless evidence of hypovolaemia، maintain fluid balance and monitor renal function
- Start fluids at 40 mL/kg/day (see Intravenous fluid therapy guideline)
- Some babies develop inappropriate ADH secretion at 3–4 days (suggested by hypo-osmolar serum with low serum sodium, associated with an inappropriately high urine sodium and osmolality)
- Further fluid restriction if serum sodium falls and weight gain/failure to lose weight
- If in renal failure, follow Renal failure guideline

4. Acidosis

- Will normally correct itself once adequate respiratory and circulatory support provided (correction occasionally required during initial resuscitation)
- Sodium bicarbonate correction is rarely required post resuscitation and it is better to allow spontaneous correction

5. Glucose

- Regular blood glucose monitoring
- Target >2.6 mmol/L (> 45 mg/dl)
- Fluid restriction may require use of higher concentrations of glucose to maintain satisfactory blood glucose
- Avoid hyperglycaemia (>8 mmol/L) (>140 mg/dL)

6. Calcium

- Asphyxiated babies are at increased risk of hypocalcaemia
- Treat with calcium gluconate when serum corrected calcium <1.7 mmol/L (7mg/dL) or if ionized calcium <0.8 (<3 mg/dL)

7. Seizures

- Prophylactic anticonvulsants not indicated
- In muscle-relaxed baby, abrupt changes in blood pressure, SpO2 and heart rate can indicate seizures
- Treat persistent (>3/hour) or prolonged seizures (>3 min, recur >3 times/hour) (see Seizures guideline)
- Give phenobarbital − if ineffective or contraindicated, give phenytoin. If no response, give clonazepam or midazolam (see Seizures guideline)
- Seizures associated with HIE can be notoriously difficult to control (preventing every twitch is unrealistic)
- Regular seizures causing respiratory insufficiency are an indication for IPPV
- Once baby stable for 2–3 days, anticonvulsants can usually be withdrawn, although phenobarbital can be continued for a little longer (duration can vary depending on individual practice and clinical severity of seizures)
- Avoid corticosteroids and mannitol

8. Thermal Control

- Maintain normal body temperature (36.5–37.2°C).
- Avoid hyperthermia

9. Gastrointestinal System

- Term babies who suffer a severe asphyxial insult are at risk of developing NEC [see Necrotising enterocolitis (NEC) guideline]
- In other babies, gastric motility can be reduced: introduce enteral feeds slowly

10. Cranial Ultrasound

- Generalised increase in echogenicity, indistinct sulci and narrow ventricles
- After aged 2–3 days, increased echogenicity of thalami and parenchymal echodensities
- After 1 week, parenchymal cysts, ventriculomegaly and cortical atrophy may develop
- Cerebral Doppler used early, but does not affect management
- Relative increase of end-diastolic blood flow velocity compared to peak systolic blood flow velocity (Resistive Index <0.55) in anterior cerebral artery predicts poor outcome (repeat after 24 hour)
- MRI scan of brain between days 5–14 of life for baby with moderate and severe encephalopathy and in baby with seizures due to encephalopathy
- Areas of altered signal in thalamus, basal ganglia and posterior limb of the internal capsule indicate poor outcome

SOURCES:

1. **Bedside clinical guidelines partnership in association with Partners in pediatrics**
2. **National Institute for Health and Care Excellence (NICE)**

Total Body Cooling Protocol for Infants with Hypoxic Ischemic Encephalopathy

Practice Statement:

Upon the order of the attending Senior Resident or Neonatal Consultant the nurse shall initiate, monitor and discontinue total body cooling therapy on infants with moderate to severe Hypoxic Ischemic Encephalopathy (HIE).

Purpose:

Total body cooling has been proven to decrease moderate and severe disability or death in infants born with moderate to severe asphyxia.

Current evidence indicates that moderate induced hypothermia (cooling) to a rectal temperature of 34C improves survival and neurological outcomes to 18 months of age in infants with moderate or severe perinatal asphyxial encephalopathy (BMJ. 2010 Feb 9;340:c363).

Equipment:

- Blanketrol II Model 222R
- Distilled Water
- Rectal/Esophageal Sterile Temperature Probe

Eligibility Criteria:

- 36 weeks or more gestation
- 1800 grams weight or more
- Within 1st 6 hrs. of life
- Diagnosis of neonatal depression, acute perinatal asphyxia or encephalopathy

Cooling is not appropriate if:

- The infant is likely to require surgery during the first 3 days after birth
- There are other abnormalities indicative of poor long-term outcome

Cooling may not be appropriate if the infant appears moriband or has persisting extremely severe encephalopathy such that further treatment is likely to be futile, for example if the AEEG/EEG is isoelectric beyond 12-24 hours of age.

Consider treatment with cooling in infants that meet the following criteria:

A. Infants ≥36 completed weeks gestation admitted to the neonatal unit with at least one of the following:

- Apgar score of ≤5 at 10 minutes after birth
- Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth
- Acidosis within 60 minutes of birth (defined as any occurrence of umbilical cord, arterial or capillary pH <7.00)
- Base Deficit ≥ 16 mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth

Infants that meet criteria A should be assessed for whether they meet the neurological abnormality entry criteria (B):

B. Seizures or moderate to severe encephalopathy, consisting of:

- Altered state of consciousness (reduced response to stimulation or absent response to stimulation) and
- Abnormal tone (focal or general hypotonia, or flaccid) and
- Abnormal primitive reflexes (weak or absent suck or Moro response)

Infants who meet criteria A and B may be considered for treatment with cooling.

If an infant meets these criteria, but cooling is Not offered, **the reasons for this should be clearly documented in the medical notes.** It is possible that this decision may need to be justified in the future.

The Criteria for Defining Moderate and Severe Encephalopathy are Listed in this Table "At Least 3 of the Following Should Be Present"

Parameter	Moderate Encephalopathy	Severe Encephalopathy
Level of Consciousness	Reduced response to stimulation	Absent response to stimulation
Spontaneous Activity	Decreased Activity	No activity
Posture	Distal flexion, complete extension	Decerebrate
Tone Reflexes	Hypotonia (focal or general)	Flaccid
Suck	Weak	Absent
Moro	Incomplete	Absent

Full neurological assessment should be done especially for signs of lateralization: pupils, tone, reflexes and cooling team should be notified.

AEEG assessment:

- The amplitude integrated EEG (AEEG) must be recorded in all infants treated with cooling but cooling need not be delayed until the AEEG is initiated.
- A normal AEEG record (confirmed by assessing the underlying EEG and excluding artefact distortion of AEEG indicates a high probability of normal outcome, and clinicians may consider that treatment with cooling is not required.

EEG/AEEG recording for at least 30 min within 5.5 hrs after birth, no anticonvulsants within 30 min before recording; recording may be performed from 1 hour of age:

1. Standard EEG:

- Burst suppression
- Continuous low voltage < 25 µV
- Seizures

2. AEEG:

- Burst suppression
- Lower amplitude < 5 µV
- Upper amplitude < 10 µV
- Seizures

Starting cooling and consent:

- Clinicians should discuss the option of treatment with the parents and seek parental consent for the baby to be transferred for treatment with cooling.
- Following parental consent, cooling should be initiated prior to and during the transfer to the cooling center.
- Cooling outside the treatment center is started by turning off heating equipment, and removing coverings from the baby. If necessary a fan can help induce cooling (see passive cooling protocol).
- The baby's age at the time heating equipment is turned off should be entered as the time cooling started on the data collection form.
- The baby should be monitored and observation data collected during this period. This includes continuous monitoring of rectal temperature, blood pressure and heart rate.
- If immediate transfer to a cooling treatment center is not possible, for example because of a lack of intensive care costs, passive cooling should be continued with guidance from the cooling center.

Seizures:

- The management of seizures will be guided by local protocols.
- In general, symptomatic seizures or frequent (>3/hour) subclinical (EEG) seizures will be treated with anticonvulsants.
- Cooling may affect the metabolism of several drugs, including anticonvulsants and sedatives, and toxic drug levels may occur even with normal doses.
- 1st line anticonvulsants may be phenobarbital or phenytoin. Phenytoin should be administered at a rate no faster than 1mg/minute.
- Benzodiazapines such as midazolam, or clonazapam are commonly used if seizures persist. The dose should be adjusted according to response

Ventilation:

- Almost all infants treated with cooling will initially require mechanical ventilation.
- Blood gases will guide ventilatory requirements; as a guide PaO2 should be maintained between 6-10 KPa and the PaCO2 between 5-7 KPa.
- Ventilator gases should be warmed and humidified in the normal way, according to local policy.

Cardiovascular Support:

- Alterations in heart rate and blood pressure are common during cooling. In general, the heart rate is reduced and blood pressure increases with a reduction in body temperature.
- Most infants with a rectal temperature of 33-34°C (the target rectal temperature for whole body cooling) will have a heart rate around 100 bpm and a mean blood pressure greater than 40 mmHg.
- A rapid rise in body temperature may cause hypotension by inducing peripheral vasodilatation.
- Treatment with volume replacement and/or inotropes should be considered if the mean arterial blood pressure is less than 40 mmHg.
- Infants being treated with cooling should not be treated with steroids (other than for treatment of hypotension), or mannitol as brain dehydrating measures.

Fluid Management:

- Renal function is commonly impaired following severe perinatal asphyxia. The infant's weight, blood creatinine and electrolytes and urine output will guide fluid management.
- As a guide infant will require about 40-60 ml/kg/day. Infants in renal failure should receive a total of 30 ml/kg/24 hours plus any measured losses. Boluses of 0.9% saline may be required to avoid hypovolaemia if diuresis occurs in the infant or if vasodilatation occurs during rewarming.
- Enteral feeding can be cautiously introduced once the initial biochemical and metabolic disturbance are corrected, usually after about 24 hours.

Cooling Procedures:

Peripheral and Central Vascular access (umbilical venous catheter) should be secured before initiation.

1. Pre-cool the blanket:

A. Attach the hypothermia blankets to the hypothermia machine.

B. Fill the cooling unit reservoir with Distilled Water till the water is touching the strainer and visible from the water fill opening.

C. Plug in the system.

D. POWER ON - status light will come on which says "Check Set Point". Make sure the temperatures are reading in the Celsius mode. The switch is on the front of the unit beside the "On/Off Switch".

E. Push "TEMP SET" switch to pre-cool and lower temperature to 5°C by pushing the down arrow▼. (Do not go <5° or the blanket will alarm).

F. Press MANUAL CONTROL to start cooling blanket (the blanket's motor should come on).

2. Place the temperature rectal probe 5 cm into rectum.

3. Place the infant on the pre-cooled blanket. The blanket should be kept dry. The infant may be placed directly on the blanket or one thin sheet may be placed over the blanket, under the infant.

4. Make sure none of the hoses are kinked.

5. Turn the infant's incubator to manual mode and decrease heat output to 0. There should be no external heat source. Maintain temperature probe so the skin temperature reading is on.

6. Press "TEMP SET" on the blanket and adjust the temperature to 33.5oC with the ▲ arrow.

7. Goal temperature 33.5 degrees C with an acceptable temperature range of 32.5 – 34.5 º C.

8. Achieve target temperature by 60 minutes of commencing cooling If using manual mode, on reaching 34.5 degree increase temp by 5 degree for each 0.5-degree rectal temp to avoid further decrease in temp < 32.5c.

9. Record rectal and skin temperature continuously for 72 hours.

10. Record heart rate and blood pressure at baseline, hourly for 12 hours, then every 2 hours. If infant requires inotropic support record blood pressure at baseline, then hourly while on inotropic support. Anticipate bradycardia and hypotension (≥ 2SD below normal for age and sex).

11. Thompson score should be done daily and recorded

Score Sign	0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC (level of consciousness)	Normal	Hyperalert, stare	Lethargic	Comatose
Fits (seizures)	None	< 3/day	>2/day	
Posture	Normal	Fisting, cycling	Strong distal flexion	Decerebrate
Moro response	Normal	Partial	Absent	
Grasp reflex	Normal	Poor	Absent	
Suckling reflex	Normal	Poor	Absent ± bites	
Respiration	Normal	Hyperventilation	Brief apnea	IPPV (apnea)
Fontanelles	Normal	Full, not tense	Tense	

Total Score = sum of all 9 parameters interpretation:

- **Minimum total score=0**
- **Maximum total score=22**
- **Total score =15 or more correlated with poor neurodevelopmental outcome at 1 year**

REFERENCE:

- **Thompson CM, Puterman AS, Linley LL, Hann FM, van der Elst CW, Molteno CD, et al. The value of a scoring system for hypoxic ischaemic encephalopathy in predict ing neurodevelopmental outcome. Acta Paediatr. 1997;86:757–61**

12. obtain venous blood gases at baseline, 4, 8, 12, 24, 48 and 72 hrs of age. Record infant temperature on blood gas slip
13. Obtain serum electrolytes, BUN, and creatinine at baseline, 24, 48, and at 72 hours.
14. Follow up blood glucose and coagulation profile.
15. Check skin condition every 4 hours for areas of skin breakdown. Notify the consultant of areas of redness.
16. Use pulse oximetry cautiously, if at all Obtain Consultant orders to discontinue pulse oximetry during hypothermia if not functioning properly.
17. Notify attending if temperature drops below 32ºC.
18. A cranial US shall be performed within 24 hours as clinically indicated. Soon after decision of cooling especially if signs of lateralization
19. Echocardiography should be done before starting (as possible) and during cooling then during rewarming.
20. EEG should be done before rewarming (better AEEG).
21. Pain management should be considered.
22. The infant is to remain on the hypothermia blanket continuously for 72 hours.
23. After 72 hours rewarming orders will be initiated.

Stop Cooling If:

- Persistent hypoxemia in 100% oxygen
- Life threatening coagulopathy despite treatment
- Arrhythmia requiring medical treatment (not sinus bradycardia)

Re-warming procedures (at the end of 72 hours from commencement, should be done in Shift A with continuous EEG monitoring, unless cooling is mandatory to be stopped earlier)

Electrical / clinical seizures during re-warming is an indication for continuation of cooling until cessation of seizures (re-cooling policy to be revised):

1. Avoid rapid re-warming of the infant.

2. Increase the temperature on the cooling unit by 0.5ºC every hour until the set point temperature on the cooling unit is on 36.5 º C. Record rectal and skin temperature, heart rate, blood pressure and blanketrol readings continuously on the rewarming worksheet.

3. Once the set point on the cooling unit has been on 36.5 for one-hour switch the cooling unit to monitor only.

4. Switch the radiant warmer temperature mode from manual to servo and set the servo control temperature to 0.5ºC above infant's skin temperature.

5. Increase the servo control temperature by 0.5ºC each hour until the servo control reading is set 36.5ºC. Record rectal and skin temperature, heart rate and blood pressure readings continuously on the rewarming worksheet.

6. Once the infant's skin temperature reaches 36.5ºC remove cooling blanket and rectal probe.

The infant's temperature must be carefully monitored for 24 hours after normothermia has been achieved to prevent rebound hyperthermia, as this might be detrimental.

7. Obtain further vital sign per level of care and document on the NNICU flowsheet.

8. An MRI should be performed at discharged or at 44 weeks post conceptual age per standard of care.

Systemic Complications of Therapeutic Hypothermia in the NICU:

Cardiovascular and Pulmonary Complications of Hypothermia

1. Sinus bradycardia
2. Hypotension
3. Lower cardiac output and stroke volume (without hypotension)
4. Cardiac arrhythmia
5. Hyperviscosity
6. Pulmonary vasoconstriction with development of pulmonary hypertension

Hematological Adverse Effects

1. Coagulation abnormalities include platelet dysfunction, increased fibrinolytic activity, and inhibition of enzymatic reactions of the coagulation cascade with substantial prolongation of PT and PTT
2. Thrombocytopenia

Renal Impairment with Cooling

1. Antidiuretic hormone suppression
2. Decrease in renal perfusion and glomerular filtration rate.

Immunologic Adverse Effects of Cooling

1. Immunosuppressive and anti-inflammatory effects

Effects of Cooling on Laboratory Values During Hypothermia:

Ventilation, Blood Gases and Cooling

- With each degree Celsius decrease in core temperature, pH increases by 0.015, PCO2 and PO2 decrease by 4% and 7% respectively.

Serum Electrolytes and Cooling

- Hypothermia causes an intracellular shift of potassium. Aggressive correction of hypokalemia during hypothermia may result in hyperkalemia on rewarming.
- Hypocalcemia
- Hypomagnesemia
- Hypoglycemia

Serum Lactate

- Hypothermia reduces tissue perfusion and shifts the hemoglobin oxygen dissociation curve to the left reducing oxygen availability to tissues; both lead to metabolic acidosis. However, if perfusion is reduced proportionately with reduced demand, then there would be no increase in anerobic metabolism.

SEIZURES

Neonatal seizures are a manifestation of neurological dysfunction. Seizures occur in 1–3% of term newborn babies and in a greater proportion of preterm babies. They can be subtle, clonic, myoclonic or tonic.

Recognition and Assessment:

Physical Signs

In addition to obvious convulsive movements, look for:

- Eyes: staring, blinking, horizontal deviation
- Oral: mouthing, chewing, sucking, tongue thrusting, lip smacking
- Limbs: boxing, cycling, pedaling
- Autonomic: apnoea, tachycardia, unstable blood pressure
- Focal (1 extremity) or multifocal (several body parts)
- Perform a detailed physical examination and neurological assessment

Differential Diagnosis

- Jitteriness: tremulous, jerky, stimulus-provoked and ceasing with passive flexion
- Benign sleep myoclonus: focal or generalized, myoclonic limb jerks that do not involve face, occurring when baby is going to or waking up from sleep; EEG normal; resolves by aged 4–6 months
- Differentiation between jitteriness and seizures

Table 1

Sign	Jitteriness	Seizure
Stimulus provoked	Yes	No
Predominant movement	Rapid, oscillatory, tremor	Clonic, tonic
Movements cease when limb is held	Yes	No
Conscious state	Awake or asleep	Altered
Eye deviation	No	Yes

Investigations:

First Line:

- Blood glucose
- Serum electrolytes including calcium, magnesium
- Full blood count coagulation (if stroke suspected, thrombophilia screen)
- Blood gas
- Blood culture
- CRP
- Liver Function Tests
- Serum ammonia, amino acids
- Urine toxicology, amino acids, organic acids
- Lumbar puncture – CSF microscopy and culture (bacterial and viral PCR for herpes simplex including enterovirus)
- Discuss CSF sample for further metabolic testing [e.g. glycine, lactate etc. (as guided by metabolic testing)] with consultant
- Cranial ultrasound scan (to exclude intracranial haemorrhage)
- EEG (to identify electrographic seizures and to monitor response to therapy). Consider cerebral function monitor (CFM–aEEG)

Second Line:

- Congenital infection screen (TORCH screen)
- MRI scan
- Screen for maternal substance abuse
- Serum acylcarnitine, biotinidase, VLCFA, uric acid, sulphocysteine, total and free homocysteine
- Trial of pyridoxine treatment, preferably during EEG monitoring, may be diagnostic as well as therapeutic
- If further advice required, contact metabolic team

Treatment:

- Ensure ABC
- Treat underlying cause (hypoglycaemia, electrolyte abnormalities, infection)
- Hypoglycaemia: give glucose 10% 2.5–5 mL/kg IV bolus, followed by maintenance infusion. Wherever possible, obtain 'hypoglycaemia screen' (see Hypoglycaemia guideline) before administration of glucose bolus
- Hypocalcaemia (total Ca <1.7 mmol/L (7 mg/dL) or ionized Ca <0.64 mmol/L (3mg/dL)): give calcium gluconate 10% 0.5 mL/kg IV over 5–10 min with ECG monitoring (risk of tissue damage if extravasation) (see Hypocalcaemia guideline)
- Hypomagnesaemia (<0.68 mmol/L): give magnesium sulphate 100 mg/kg IV or deep IM (also use for refractory hypocalcaemic seizure)
- Pyridoxine (50−100 mg IV) can be given to babies unresponsive to conventional anticonvulsants or seek neurologist opinion Initiation of anticonvulsants (for immediate management follow flowchart)
- Start anticonvulsant drugs when:
  - Prolonged: >2–3 min frequent: >2–3/hour
  - Associated with cardiorespiratory compromise (frequent apnoeas and bradycardia requiring intervention)

Administration:

- Slowly IV to achieve rapid onset of action and predictable blood levels
- To maximum dosage before introducing a second drug
- If no IV access and glucose and electrolyte abnormalities excluded, consideration can be given to buccal/intranasal midazolam

Maintenance and Duration of Treatment:

- Keep duration of treatment as short as possible. This will depend on diagnosis and likelihood of recurrence
- May not require maintenance therapy after loading dose
- If maintenance therapy is required: monitor serum levels develop emergency seizure management plan, including, if required, a plan for buccal/intranasal midazolam

Stopping Treatment:

- Consider seizures have ceased and neurological examination is normal or abnormal neurological examination with normal EEG

Anticonvulsant Drug Therapy Schedule

Drug	Loading dose	Maintenance dose
Phenobarbital	• 20 mg/kg IV – administer over 20 min • Optional additional doses of 10 mg/kg each until seizures cease or total dose of 40 mg/kg can be given	• 2.5–5 mg/kg IV or oral once daily beginning 12–24 hr after loading dose
Phenytoin	• 20 mg/kg IV – maximum infusion rate of 1 mg/kg/min • Monitor cardiac rate and rhythm and blood pressure for hypotension	• 2.5–5 mg/kg IV or oral 12-hrly • Measure trough levels 48 hr after IV loading dose
Midazolam (if no response to above drugs)	• Give 200 microgram/kg IV over 5 min followed by continuous infusion 60–300 microgram/kg/hr if required • Reconstitution and dilution: dilute 15 mg/kg of midazolam up to a total of 50 mL with sodium chloride 0.9%, glucose 5% or glucose 10% 0.1 mL/hr = 30 microgram/kg/hr may cause significant respiratory depression and hypotension if injected rapidly, or used in conjunction with narcotics • If no IV access, glucose and electrolyte abnormalities excluded, give 300 microgram/kg intranasal/buccal. (**Note:** can be repeated once; wait 10 min before repeating. Ensure cardiorespiratory status stable)	
Clonazepam (if midazolam not available)	• 100 microgram/kg IV push over 2 min repeat dose after 24 hr if necessary concurrent treatment with phenytoin reduces the half-life of clonazepam	
Lidocaine (if above medications ineffective)	• 2 mg/kg IV over 10 min, then commence infusion 6 mg/kg/hr for 6 hr, **then** 4 mg/kg/hr for 12 hr, **then** 2 mg/kg/hr for 12 hr	Exercise caution with phenytoin as concurrent IV infusion of both these drugs has a cardiac depressant action (refer to **Neonatal Formulary** for doses in preterm babies)
Levetiracetam (if not responding in any order)	• Loading dose: 20 mg/kg IV infusion over 15 min can be repeated if seizures persist (maximum 40 mg/kg)	• 10–15 mg/kg 12-hrly IV/oral **[Note:** ½ maintenance dose in infants with severe renal impairment (creatinine >150 micromol/L)]

Discharge and Follow-Up:

Discharge:

- Ensure parents are provided with appropriate discharge documentation
- Seizure emergency management plan
- Copy of discharge summary, including: types of seizures, medications/anticonvulsants administered

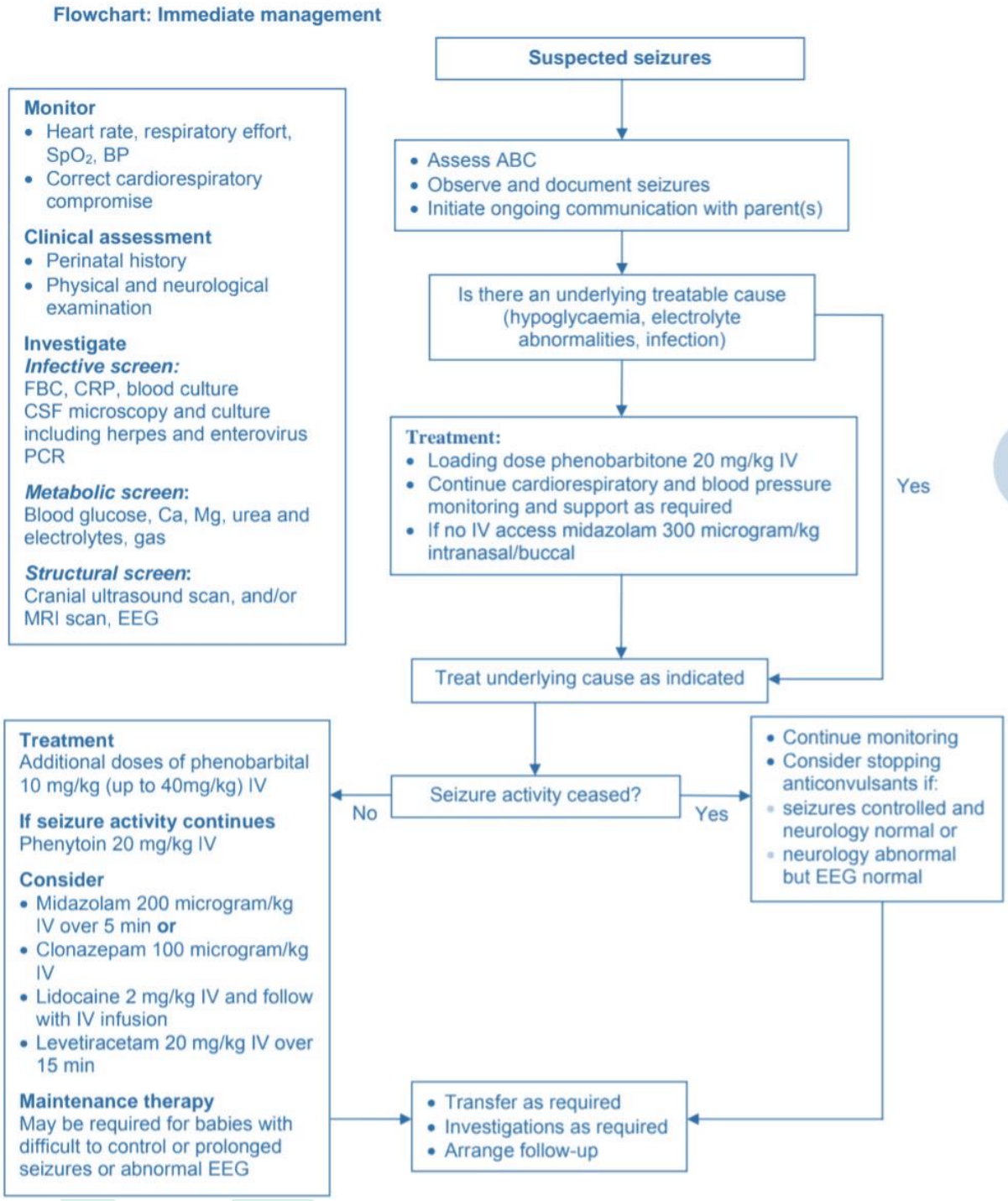
Follow-Up:

- Follow-up will depend on cause of seizures and response to treatment
- Consider: specialist follow-up for babies discharged on anticonvulsant drugs

Further Information for Parents:

- **www.bcmj.org/sites/default/files/HN_Seizures-newborns.pdf**

Flowchart: Immediate Management



HYPOCALCAEMIA

Recognition and Assessment:

- Term or preterm infants birth weight ≥1500 g, total serum calcium <2 mmol/L (8 mg/dL) or ionized fraction <1.1 mmo/L (4.4 mg/dL)
- Preterm infant, birth weight <1500 g, total serum calcium <1.75 mmol/L (7 mg/dL) or ionized fraction <1 mmol/L (4 mg/dL)

Symptoms and Signs:

- Early onset occurs in first 2−3 days of life and is usually asymptomatic
- Late onset develops after first 2−3 days of life and typically occurs at the end of the first week
- Most infants are asymptomatic and identified on screening
- Characteristic sign is increased neuromuscular irritability including:
- Jitteriness and irritability
- Generalized/focal seizures
- Non-Specific symptoms e.g.:
    - Poor feeding
    - Lethargy
    - Apnoea
- Prolonged QTc on ECG
- Rare presentations:
    - Stridor
    - Bronchospasm
    - Pylorospasm

Causes:

Early Onset	Late Onset
• Prematurity • Intrauterine Growth Restriction • Infants of Diabetic Mother • Hypoxic Ischaemic Encephalopathy • Hypomagnesaemia • Hypoparathyroidism • Syndromes e.g. Digeorge Syndrome • Maternal Hyperparathyroidism	• High Phosphate Load – Cow's Milk, Renal Failure • Hypomagnesaemia • Parenteral Nutrition • Exchange Transfusion • Alkalosis • Maternal Hypercalcemia • Maternal Vitamin D Deficiency • Transient Hypoparathyroidism • Syndromes and Genetic Mutations e.g. Digeorge and Kenny-Caffey Syndromes

Investigations:

- Serum calcium
- Only monitor if risk factors, most infants with hypocalcaemia are asymptomatic
- Well preterm infant with birth weight >1500 g and well term infants of diabetic mothers receiving milk feedings on day 1 of life do not need testing routinely
- Ionized calcium preferred
- If using total calcium, measure albumin and correct for hypoalbuminemia
- Phosphate
- Magnesium

- Persistent hypocalcaemia or severe hypocalcaemia despite adequate calcium therapy
  - 25-hydroxyvitamin D level
  - Renal function tests
  - Liver function test
  - Alkaline phosphatase
  - Parathyroid hormone level
  - Urinary calcium:creatinine ratio
  - ECG for prolonged QTc interval
  - If pseudohyperparathyroidism suspected, X-ray hand
  - Chest X-ray for thymic shadow
  - If hypoparathyroidism suspected, renal ultrasound
  - If DiGeorge syndrome suspected, echocardiography
  - Genetic test for gene mutations or suspected syndrome e.g. DiGeorge syndrome

Management:

Asymptomatic Infants	Symptomatic Hypocalcaemia
• Most infants with early onset hypocalcaemia recover with nutritional support; so early feeding provides adequate calcium • Infants requiring IV fluid: add calcium gluconate 10% 0.46 mmol/kg/day (= 2 mL/kg/day) to IV fluid and give as continuous infusion • Infant tolerating oral feeds: give 0.25 mmol/kg oral 6-hourly	• If seizures, prolonged QT interval, apnoea, unstable or poor feeding give IV calcium gluconate 10% 0.11 mmol/kg (= 0.5 mL/kg) over 5−10 min followed by maintenance • Dilute with sodium chloride 0.9% or glucose 5% 4 mL to each 1 mL calcium gluconate 10% to give a concentration of 45 micromol/mL. Can be given undiluted via central line in an emergency • Doses up to 0.46 mmol/kg (= 2 mL/kg calcium gluconate 10%) have been used • Maximum rate of administration 22 micromol/kg/hour

- Stable baby or following acute treatment:
  - Oral calcium dose 0.25 mmol/kg 6-hourly
  - If enteral feeds not tolerated add calcium gluconate 10% 0.46 mmol/kg/day to IV fluid as above
  - If symptomatic hypocalcaemia: hypomagnesaemia − magnesium sulphate 100 mg/kg IV/IM 12-hourly for 2−3 doses
- Vitamin D deficiency give 1000 units daily and adjust dose according to response
- Hyperphosphataemia
- High calcium, low phosphate diet
- Human milk is preferable, if not available, use formula with low phosphate 60/40 and oral calcium IV calcium precautions and considerations
- Extravasation can cause skin and subcutaneous tissue necrosis (see Extravasation guideline). Monitor IV site closely
- Continuous infusion preferred to bolus, but use bolus for initial management in symptomatic hypocalcaemia
- Bolus IV calcium can cause dysrhythmias − administer slowly over 5−10 min with cardiac monitoring
- Calcium can be given via UVC provided catheter tip is in vena cava
- Inadvertent administration into portal vein can cause hepatic necrosis
- Do not mix calcium solutions with those containing phosphorus or bicarbonate as this can cause precipitation

Subsequent Management:

- Monitor bone profile and phosphate levels according to clinical need
- If calcium normal after 48 hour treatment, halve maintenance dose
- If calcium fails to normalize investigate for underlying cause
- Hyperphosphataemia – calcium and phosphate normalize in 3−5 days. Stop calcium after 1 week and switch to normal formula in 2−4 weeks

INTRAVENOUS FLUID THERAPY

Hyponatraemia (<130 mmol/L):

Response to treatment should be proportionate to degree of hyponatraemia.

Causes:

Excessive Free Water:

- Reflection of maternal electrolyte status in first 24 hour
- Failure to excrete fetal extracellular fluid will lead to oedema without weight gain
- Water overload: diagnose clinically by oedema and weight gain
- Excessive IV fluids
- Inappropriate secretion of ADH in babies following major cerebral insults, or with severe lung disease
- Treatment with indometacin or ibuprofen

Excessive Losses:

- Prematurity (most common cause after aged 48 hour)
- Adrenal insufficiency
- GI losses
- Diuretic therapy (older babies)
- Inherited renal tubular disorders

Inadequate Intake:

- Preterm breastfed babies aged >7 days

"Management Depends on Cause"

Excessive IV fluids and failure to excrete fetal ECF:

Management:

- Reduce fluid intake to 75% of expected

Inappropriate ADH:

Clinical Features:

- Weight gain, oedema, poor urine output
- Serum osmolality low (<275 mOsm/kg) with urine not maximally dilute (osmolality >100 mOsm/kg)

Management:

- Reduce fluid intake to 75% of expected
- Consider sodium infusion only if serum sodium <120 mmol/L

"Risk of Accidental Hypernatraemia When Using Sodium Chloride 30%. Use with Caution and Always Dilute Before Use"

Acute Renal Failure:

Management:

- Reduce intake to match insensible losses + urine output
- Seek advice from middle grade doctor/consultant

Excessive renal sodium losses

Management:

"If Possible, Stop Medication (Diuretics, Caffeine) That Causes Excess Losses"

- Check urinary electrolytes
- Calculate fractional excretion of sodium (FE Na+ %):
- FE Na+ = [(urine Na ´ plasma creatinine)/(urine creatinine ´ plasma Na)] ´ 100
- Normally <1% but in sick preterm babies can be up to 10%
- Affected by sodium intake: increased intake leads to increased fractional clearance
- if >1%, give sodium supplements
- Calculate sodium deficit
- = (135 − plasma sodium) ´ 0.6 ´ weight in kg
- Replace over 24 hour unless sodium <120 mmol/L or symptomatic (apnoea, fits, irritability)
- Initial treatment should bring serum sodium up to approximately 125 mmol/L
- Use sodium chloride 30% (5 mmol/mL) diluted in maintenance fluids. Ensure bag is mixed well before administration

Adrenal Insufficiency:

Clinical Features:

- Hyperkalaemia
- Excessive weight loss
- Virilization of females
- Increased pigmentation of both sexes
- Ambiguous genitalia

Management:

- Seek consultant advice

Inadequate Intake:

Clinical features:

- Poor weight gain and decreased urinary sodium

Management:

- Give increased sodium supplementation
- If taking diuretics, stop or reduce dose

Excessive Sodium Intake Leading To Water Retention:

Clinical features:

- Inappropriate weight gain

Management:

- Reduce sodium intake

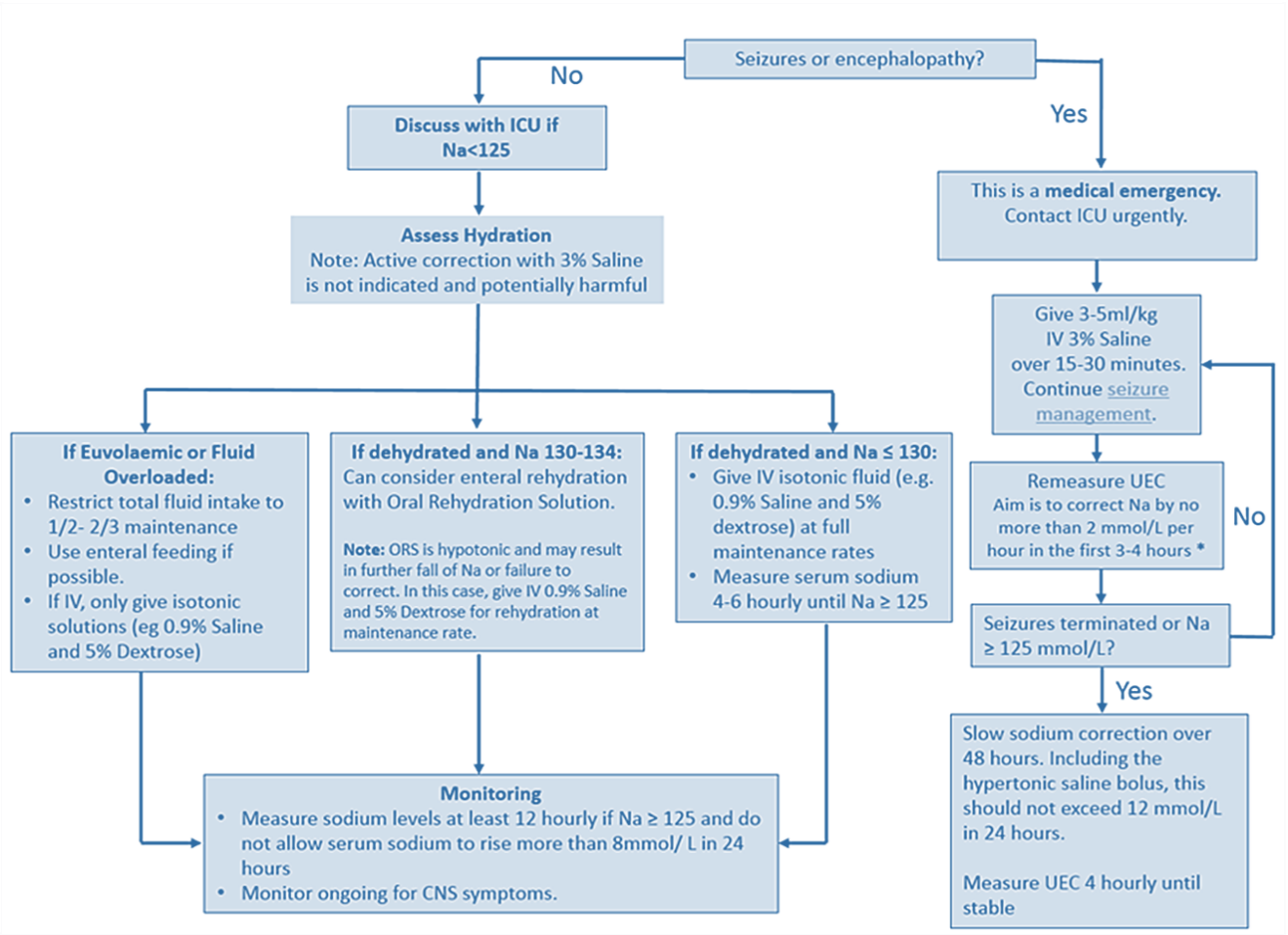
Treatment of Acute Symptomatic Hyponatraemia with Seizures:

- Do not manage hyponatraemic encephalopathy using fluid restriction alone
- Give sodium chloride 2.7% 2 mL/kg IV over 10-15 min
- If symptoms still present, repeat
- Measure serum sodium hourly until symptoms resolve
- When symptoms resolved, ensure serum sodium does not increase by >12 mmol/L/24 hour

Causes (common causes in bold)

Fluid Overloaded	Euvolemic	Dehydrated
• **IV fluid administration in excess of the child's needs** • Nephrotic syndrome • Cirrhosis • Heart Failure • Acute/ Chronic Renal Failure • Obstructive uropathy	• **Administration of enteral hypotonic fluids (including dilute formula, Oral Rehydration Solutions, excessive water intake)** • Psychogenic Polydipsia • **Increased ADH secretion** • **Pulmonary: pneumonia, bronchiolitis, mechanical ventilation** • **CNS: infections, injury, tumour** • Post-operative, trauma, pain • Endocrine: Hypothyroid, low cortisol • Medications • Chemotherapy (cyclophosphamide, vincristine, platinum based agents) • Antiepileptics (valproate, carbamazepine, oxcarbazepine) • Vasopressin	• **GI losses and rehydration with free water** • Gastroenteritis • Secretory/osmotic diarrhoeas • Ostomies • Skin losses (CF / burns) • Abdominal 3rd spacing • High rate fluid consumption post exercise • Hyperglycaemia • Renal Losses • Thiazide Diuretic • Cerebral salt wasting • Primary renal Tubular Disorders • Hypoaldosteronism • Metabolic alkalosis

The Royal Children's Hospital Melbourne



NEONATAL SEPSIS

A.Early Onset Neonatal Sepsis:

Risk factors for infections:

1. Invasive Group B streptococcal infection in a previous baby
2. Maternal Group B streptococcal colonization, bacteriuria or infection in the current pregnancy
3. Pre-labour rupture of membranes
4. Preterm birth (<37 weeks) following spontaneous labour
5. Suspected or confirmed rupture of membranes for >18 hour in a preterm birth
6. Intrapartum fever >38°C, or confirmed or suspected chorioamnionitis
7. Mother given parenteral antibiotics for confirmed or suspected invasive bacterial infection
8. Suspected or confirmed infection in a co-twin

Red Flag Signs and Clinical Indicators Suggestive of Neonatal Infection:

1. Systemic antibiotics given to mother for suspected bacterial infection during labour or within 24 hour either side of birth
2. Suspected or confirmed infection in a co-twin
3. Respiratory distress starting >4 hour after birth
4. Seizures
5. Signs of shock
6. Need for mechanical ventilation in a term baby

REFERENCE:

- **An online calculator interface which provided clinicians with guidance regarding the risk ofEOS and clinical action (*https://neonatalsepsiscalculator.kaiserpermanente.org/*)**

ACTIONS:

Any red flags or no red flags but 2 risk factors or clinical indicators perform investigations, including blood cultures, and start antibiotics.

Investigations before Starting Antibiotics:

1. Blood culture (in all)
2. Measure CRP at presentation and 18-24 hour after
3. If strong clinical suspicion of infection or signs/symptoms of meningitis, perform lumbar puncture (LP) and baby does not respond satisfactorily to antibiotics clinically &/or laboratory (CRP persistent or rising), if safe to do but if performing LP will delay antibiotics, give antibiotics first
4. Do not carry out routine urine MC&S
5. Take skin swabs only if clinical signs of localised infection
6. If purulent eye discharge: collect eye swabs for urgent MC&S and swabs in viral transport media for viral PCR, especially if looking for chlamydia or gonococcus start systemic antibiotics while awaiting results
7. If signs of umbilical infection, including purulent discharge or periumbilical cellulitis, perform blood culture, take swab for MC&S and start flucloxacillin and gentamicin IV if microbiology results indicate infection not due to Gram- negative infection stop gentamicin

Early Onset Sepsis Most Common Organisms:

- E. coli, Klebsiella species, and S. aureus
- The combination of IV benzylpenicillin and gentamicin is an appropriate choice for empirical therapy.

Early onset sepsis Meningitis:

CSF Gram Stain:

- Uninformative ⇨ treat with IV amoxicillin and cefotaxime
- Gram negative infection ⇨ stop amoxicillin and treat with cefotaxime alone
- Gram-positive infection ⇨ continue treatment with IV amoxicillin and cefotaxime while awaiting the CSF culture result

CSF Culture:

According to C/S after making sure it passes BBB

Usual duration of treatment:

- 5 days if blood culture negative and baby is well with no strong clinical suspicion of infection nor CRP >6
- 7days if blood culture +ve or strong clinical suspicion of infection or CRP >6
- >7days if baby is not fully recovered or advisable based on blood culture

B.Late Onset Neonatal Sepsis:

Definition:

Infection after first 72 hour of life

Presentation:

Can be vague and non-specific

Symptoms:

1. Respiratory distress **2. Apnoea/bradycardia** **3. Cyanosis or poor colour** **4. Poor perfusion (CRT >3 sec; toe-core temperature gap >2°C; mottling)** **5. Hypotension** **6. Tachycardia**	**7. Temperature instability (high or low)** **8. Glucose instability** **9. Hypotonia** **10. Irritability** **11. Lethargy/inactivity** **12. Poor feeding and poor suck**	**13.Jaundice** **14.Seizures** **15.Vomiting** **16. Abdominal distension** **17. Nursing staff may describe babies with a mixture of these symptoms as not doing well'**

Signs:

1. Systemic signs of sepsis such as tachycardia, poor perfusion, reduced tone, quiet, lethargy, unsettled and crying/moaning 2. Tachypnoea and intercostal and/or subcostal recession	3. Bulging of the fontanelle (rare in babies with neonatal meningitis) 4. Abdominal distension and tenderness, bowel sounds, Inspect stool for visible blood	5. Petechiae, bleeding diathesis 6. Septic spots in eyes, umbilicus, nails and skin 7. Decreased movement or tenderness in joints and limbs

Investigations:

1. Swabs or ETT secretions for culture + Swab suspicious lesion 2. Blood cultures 3. Full blood count: neutrophil count <2000 or>15000/mm, platelet count of<100.000, toxic granulation in neutrophils [or if measured, an immature:total (I:T) neutrophil ratio >0.2]	4. Clotting profile (evidence of bleeding diathesis or in severe infection 5. CRP: delay 24 hour between onset of symptoms & rise in serum CRP, for support of diagnosis & follow up 6. Urine microscopy, culture & sensitivity by clean-catch or supra-pubic aspiration	7. Lumbar puncture (LP): IF baby unstable, deranged clotting or thrombocytopenia (consultant advise) CSF for Gram-stain & culture, protein & glucose +/- PCR for bacteria and viruses where indicated 8. Chest X-ray 9. If abdominal distension noted, abdominal X-ray

Treatment:

"Every Hospital Must Have Its Own Protocol"

- Do not use vancomycin routinely
- Do not use oral antibiotics to treat infection in babies
- For babies with indwelling catheters and on parenteral nutrition, unless they are very unwell to treat endotracheal secretion colonisation with CoNS
- When culture results available, always change to narrowest spectrum antibiotic, or stop antibiotics if negative cultures, inflammatory markers not raised and no clinical signs of infection

First Line:

- Flucloxacillin + Gentamicin as initial antibiotics for late onset sepsis in a stable neonate

Second Line:

- Vancomycin + Gentamicin (with caution)
- Vancomicin + Third-generation cephalosporin (e.g. cefotaxime) (in areas where MRSA is prevalent)
- Vancomicin + Piperacillin/Tazobactam

Third Line:

- Meropenem, Ciprofloxacin + Vancomycin

For Meningitis:

First Line:

- Cefotaxime + Amoxicillin + Gentamicin

Second Line:

- Meropenem

Meningitis:

- For all babies with a positive blood culture, other than Coagulase-negative staphylococci (CoNS), discuss the need for an LP.
- Empirical treatment whilst CSF results pending
- CSF visually clear, give first line antibiotics as in late onset sepsis
- CSF cloudy or high clinical suspicion of meningitis, give high dose cefotaxime
- Treat with high dose cefotaxime for 14–21 days, depending on organism

Table of Normal CSF Values

Gestation	White cell count (count/mm3)	Protein (g/L)	Glucose (mg/dl)
Preterm < 28 days	**9**	**1**	**55**
Term < 28 days	**6**	**0.6**	**55**

Values are mean (range)

Note:

Protein levels are higher in first week of life and depend on RBC count. WBC of >21/mm3 with a protein of >1.0 g/L with <1000 RBC is suspicious of meningitis

Subsequent Management:

Fungal Infection:

- Risk factors for prophylactic antifungal treatment to be considered according to consultant opinion
- <1500 g
- Parenteral nutrition
- Indwelling catheter
- No enteral feeds
- Ventilation
- H2 antagonists
- Exposure to broad spectrum antibiotics, especially cephalosporins
- Abdominal surgery

Treatment:

First choice:

- Standard amphotericin starting at 1 mg/kg. Can increase dose as tolerated to 1.5 mg/kg, yet use carefully to avoid its nephrotoxicity & hypokalemia risk
- Liposomal amphotericin 1 mg/kg (if available), increasing to a maximum of 5 mg/kg have less side effects
- Alternatives fluconazole and vefungin

REFERENCES:

1. **The National Institute for Health and Care Excellence (NICE) 2021**
2. **Neonatal guidelines 2019- 2021 (the Bedside Clinical Guidelines Partnership)**
3. **Puopolo et al, 2018 (AAP publications)**
4. **Procianoy & Silveira, 2019**
5. **Odabasi & Bulbul, 2020**
6. **Singh et al, 2021 (StatPearls)**

Nutrition and Enteral Feeding

AIMS:

To Achieve:

⇨ Growth and nutrient accretion similar to intrauterine rates

⇨ Best possible neurodevelopmental outcome

To Prevent:

⇨ Specific nutritional deficiencies

Principles:

- Early enteral feeds promote normal gastrointestinal structure and function, motility and enzymatic activity
- Delayed nutrition can result in growth restriction with long-term complications of parenteral nutrition, dysbiosis of the intestine, poor organ growth and poorer neurological outcomes
- There is robust evidence that feeding maternal colostrum and breast milk is protective for necrotizing enterocolitis (NEC), sepsis and retinopathy when compared to formula milk
- Manage feeding on an individual basis dependent upon gastrointestinal tolerance and availability of breast milk

Nutritional Requirements:

Daily recommended intake of nutrients for stable/growing preterm infants

Nutrient	Term infant	Preterm Infant (Koletzo 2014)	Preterm infant (ESPGHAN 2010)
Energy (kcal/kg)	95–115	110–130	110–135
Protein (g/kg)	2	3.5–4.5	<1 kg: 4.0–4.5 1–1.8 kg: 3.5–4.0
Sodium (mmol/kg)	1.5	3–5	3–5
Potassium (mmol/kg)	3.4	2–5	1.7–3.4
Calcium (mmol/kg)	3.8	3–5	2.5–3.5
Phosphate (mmol/kg)	2.1	2–4.5	2–3
Vitamin A (µg RE/kg)	59	400–1100	400–1000
Vitamin D (units/day)	400	400–1000	800–1000

Feeding Guide:

When to Start Feeding?

- Commence enteral feeds in preterm infants as close to birth as possible (unless clinically contraindicated)

Buccal Colostrum:

Aim:

- To provide the benefits of colostrum to all sick and premature infants who cannot access oral breast feeds
- Place 0.3 mL (0.15 mL per side) colostrum in buccal cavity by syringe/gloved finger at 3-hourly intervals for first 48 hour of life)
- Colostrum is absorbed locally by the buccal mucosa
- Can be administered even to critically-ill, ventilated, fragile infant
- Counsel all mothers anticipating delivery of sick/preterm infant about benefits of colostrum
- Advise mothers to hand express as soon after delivery as possible (ideally within 1 hour)
- Initiate administration of buccal colostrum as soon as colostrum available (ideally within 2 hour of birth)

Patient Group:

- Preterm infants (born <34 weeks' gestation) admitted to NNU or
- Any infant ≥34 weeks' gestation admitted to NNU and not receiving oral feeds

Contraindicated:

- Any contraindication for receiving mother's own milk e.g. maternal HIV infection
- Oral breastfeeding: will receive colostrum orally as first few feeds after birth

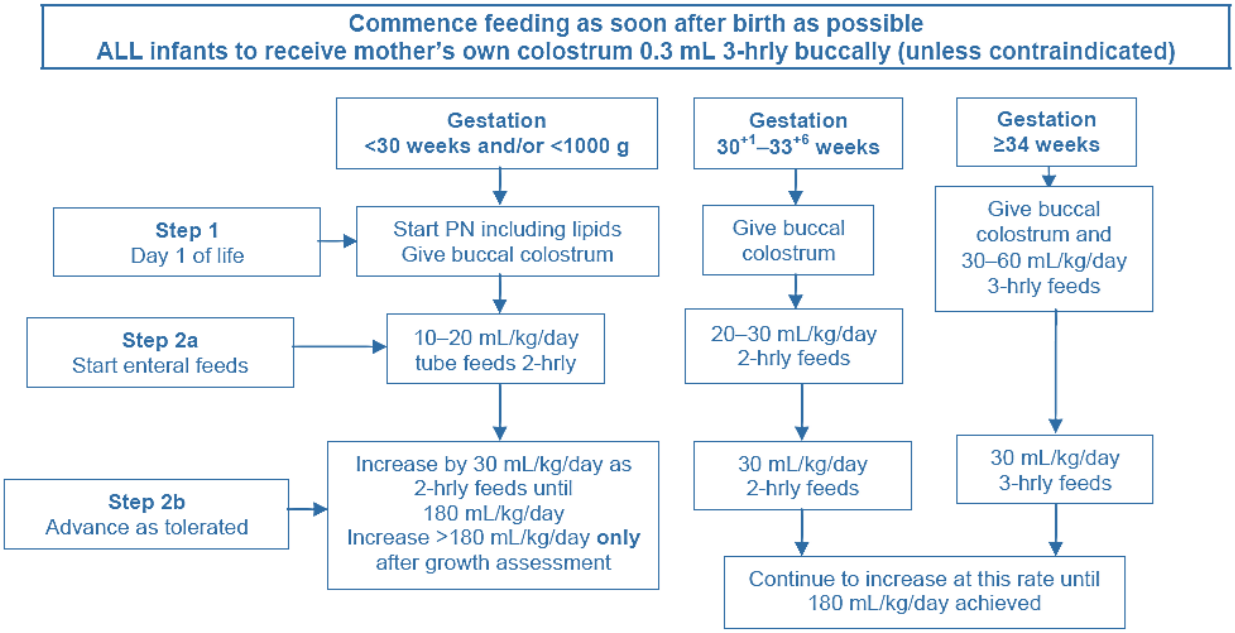
Enteral Feeds:

Route of Administration:

- Infants <34 weeks are not mature enough to co-ordinate sucking, swallowing and breathing to feed effectively and must be tube fed
- Use gastric feeding with either naso- or orogastric tube

Initiating and Advancing Enteral Feeds

- Make every effort to use mother's fresh expressed colostrum and breast milk
- If mother's expressed breast milk (MEBM) not available within 48 hour of birth, use preterm formula



Trophic Feeds:

- Small volumes (10–20 mL/kg/day) of milk given to stimulate the bowel
- Maintain for up to 7 days
- Not intended to contribute to nutrition
- Use in infants where feeds cannot be advanced in order to utilize maternal colostrum and stimulate gut trophic hormones

Which Milk to Use?

MEBM:

- Mother's own breast milk remains the ideal milk for term and preterm infants and should be strongly recommended
- If MEBM still insufficient at 48 hour of life, use alternative feeds as tolerated in line with algorithm above
- Add breast milk fortifier (BMF) when volumes reach ≥150 mL/kg/day and advance to 180 mL/kg/day as tolerated
- Commence gradual introduction of alternative feeds once full volumes achieved (minimum150 mL/kg/day) and infant aged ≥14 days (see Slow change to a different type of milk feed)

BMF:

- All preterm infants born <34 weeks fed exclusively on MEBM require addition of BMF to meet protein requirements for growth
- Add BMF when MEBM volumes reach 150 mL/kg/day
- Increase volume of MEBM + BMF to full feeds of 180 mL/kg/day
- Use full strength
- Prepare as per manufacturer's instructions
- Continue BMF until 37 weeks' CGA
- At 37 weeks' CGA
- If growth velocity adequate stop BMF
- If growth insufficient or catch up required continue BMF as fortified breast milk supplements
- If more than half of feed requirement provided by preterm formula, BMF not required unless there is poor growth and intolerance of volume

Preterm Milk Formula:

- Indicated for infants born <34 weeks' gestation and <2 kg
- Preterm milk formula formulated to meet the nutrient needs of preterm infants <2 kg where insufficient MEBM to meet requirements
- Nutrient enriched post-discharge formula (NEPDF) formulated to meet the ongoing enhanced nutrient needs of infants born <34 weeks, once they reach 37 weeks CGA/≥2 kg/at discharge from NNU
- Not all preterm infants require post-discharge formula for extended periods. Infants with normal growth velocity and no requirement for catch-up growth can be discharged on term formula with appropriate vitamin and mineral supplementation
- NEPDF especially useful for infants who have higher nutritional requirements (e.g. CLD on oxygen) or infants who have ongoing poor growth (e.g. have crossed down >2 centiles on growth chart during neonatal stay)
- Volumes >180 mL/kg are not usually necessary and other reasons for poor growth should be sought before further volume increases introduced (see Inadequate growth)

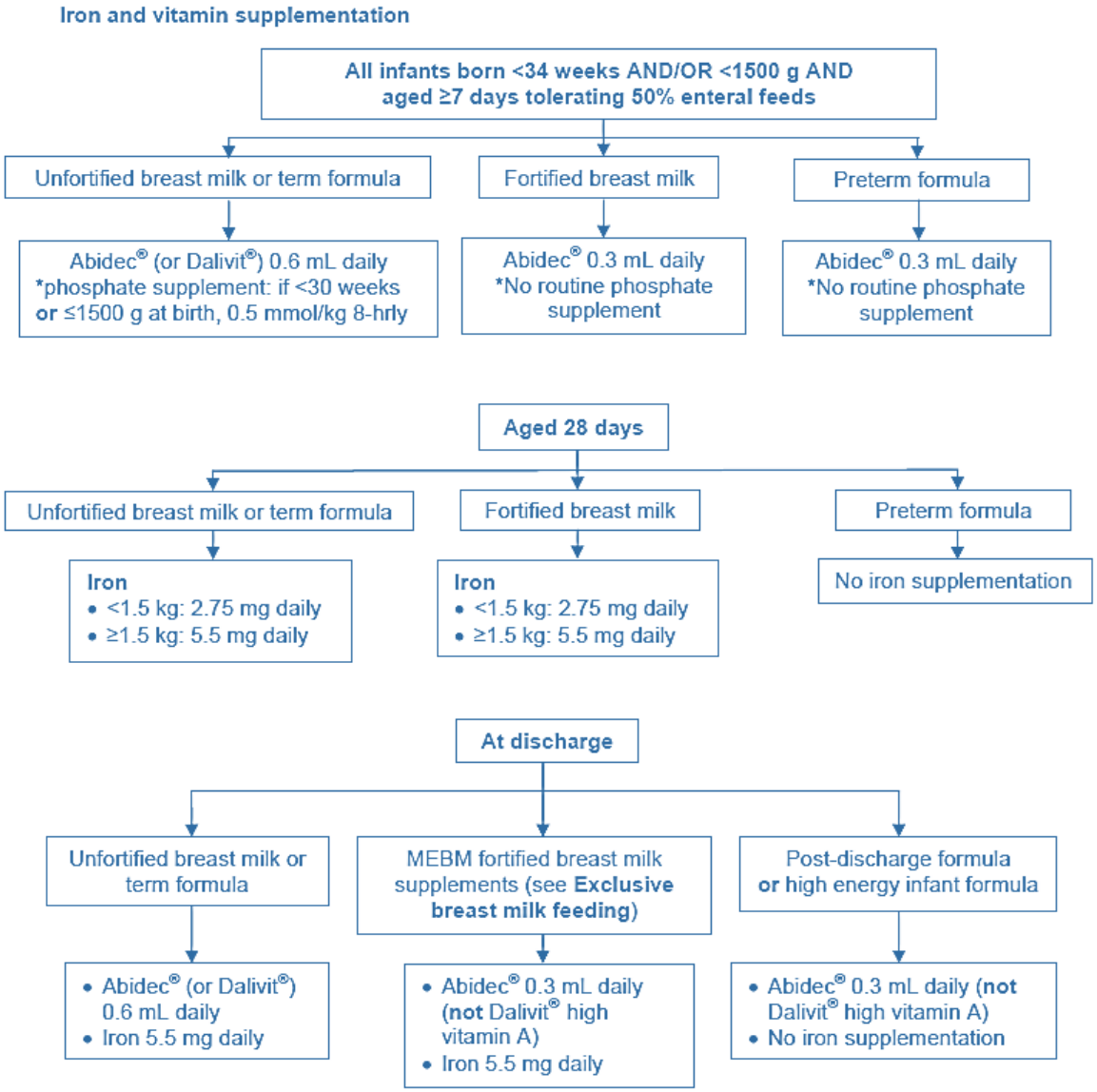
Specialized Preterm Formulas:

- These formulas may be suitable for infants who fail to tolerate/progress on standard preterm formula or have a family history of CMPI or require MCT for proven fat malabsorption
- These formulas do not provide adequate nutrition for preterm infants at standard dilution and will require modification to ensure individual requirements met. Use only where absolutely necessary and always under direction of paediatric/neonatal dietitian

Appropriate Maintenance Feeds for Neonates Based on Gestational Age and/or Weigh

Gestational Age and/or Weight	Maintenance Feed
<30 weeks and/or <1 kg	• D/MEBM + BMF: aim 180 mL/kg/day • Preterm milk formula: aim 165−180 mL/kg/day
Born between or on reaching 30+1–33+6 weeks	• MEBM + BMF: aim 180 mL/kg/day • Preterm milk formula: aim 165−180 mL/kg/day
At 34 weeks and <2 kg	• MEBM + BMF: aim 180 mL/kg/day • Preterm milk formula: aim 165−180 mL/kg/day • Introduce oral feeds (see Progression to oral feeding guideline) • consider fortified breast milk supplements as breastfeeding increases
At 34 weeks and ≥ 2 kg	• MEBM + BMF: aim 180 mL/kg/day • Post-discharge formula: aim 165−180 mL/kg/day • Introduce oral feeds (see Progression to oral feeding) • Allow natural reduction in BMF as breastfeeding increases
Born 34 - 37 weeks **and** <2 kg	• MEBM: aim 160−180 mL/kg/day or modified responsive breastfeeding + half strength BMF • Post-discharge formula modified responsive bottle feeding • Discharge on breast milk or term formula
Born ≥37weeks	• MEBM 180 mL/kg/day via naso-/orogastric tube or modified responsive breastfeeding • Term formula 165−180 mL/kg/day via naso-/orogastric tube or modified responsive bottle feeding
Preterm infants (born<34 weeks) at discharge	• Infants >37 weeks with normal growth velocity and no requirement for catch-up growth • Allow natural reduction in BMF as breastfeeding increases • if insufficient MEBM and growth velocity satisfactory use term formula at discharge • Infants <36+6 weeks CGA and/or poor growth velocity or requiring catch-up growth: • Use fortified breast milk supplements as oral breastfeeding increases • If insufficient MEBM to meet requirements use NEPDF on discharge

Iron and Vitamin Supplementation



- **Preterm infants fed exclusively on breast milk should receive supplementary phosphorus titrated against normal serum phosphate and ALT levels.**

- **If ≤33+6 weeks' gestation at birth with PO4 <1.8 mmol or >34 weeks' gestation with PO4 <1.4 mmol, send paired urine and blood phosphate to measure tubular reabsorption of phosphate (TRP)**

TRP Calculated As:

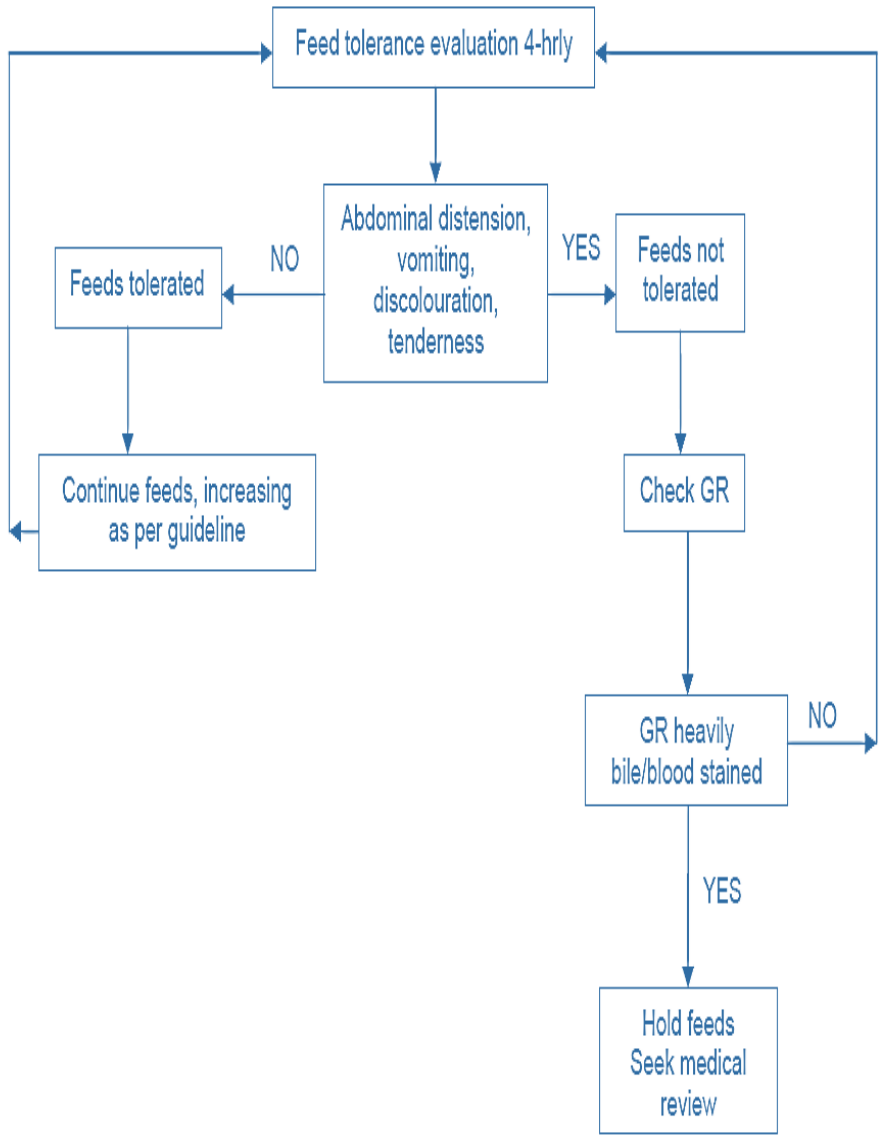
- **1 – (urine phosphate - plasma creatinine/plasma phosphate - urine creatinine) 100% with all units in mmol/L. If >95% start PO4 supplementation - Alkaline phosphate not sensitive or specific to osteopaenia of prematurity**

Evaluation:

Monitoring of feed tolerance, growth and biochemical balance is critical in nutritional management of preterm infants to ensure optimal outcomes

Assessment Feed Tolerance:

- Poor gut motility is common among VLBW/ELBW infants and some will have episodes requiring temporary discontinuation of feeding or delay in advancing feeds
- If failure to progress feeds continues over several days, seek advice early from neonatal/paediatric dietitian assessment of gastric residuals (GR)
- Routine aspiration of GR not recommended in preterm infants
- Advance feeds as tolerated after feed tolerance evaluation 4-hourly (see below)
- Do not use GR volumes in isolation when deciding to limit advancement of feeds



Nutritional Assessment of Enterally-fed Preterm Infants:

Parameter	Frequency of Measurement
Fluid Intake (ml/kg/day) • Enteral intake • Parenteral intake	Daily
Nutritional Caloric Intake (kcal/kg/day)	Daily
Anthropometry	
• Weight (gm) • Length (cm) • Head circumference (cm)	Daily at the same time Weekly Weekly

Biochemical Monitoring:

- Measure plasma urea, electrolytes, calcium, phosphate and albumin weekly in stable preterm infants to monitor nutritional status
- Monitor glucose closely in initial few days

Inadequate Growth:

- Preterm infants with weight gain <16 g/kg/day require further assessment
- Review proportional growth (weight, head, length) on age and gender appropriate growth chart
- Ensure infant prescribed recommended nutritional intake
- Ensure infant receiving prescribed nutritional intake
- Ensure on maximum advised volume of age/weight appropriate feed – see maintenance feed volume/type charts
- Calculate energy and protein intake per kg/day and compare with ESPGHAN recommended requirements for weight/gestational age
- Check adequate total body sodium by ensuring sodium excretion in urine ≥20 mmol/L (only useful in infants not receiving diuretics)
- Add extra supplements as necessary
- In infants receiving MEBM use hind milk (see Breast milk expression guideline)
- If tolerated, increase feed volumes beyond that recommended
- If receiving MEBM + BMF: ≤220 mL/kg/day
- If receiving preterm formula: ≤200 mL/kg/day
- If infant receiving MEBM + BMF does not tolerate increased volumes, or if insufficient MEBM to increase
- Volumes, replace 25−50% MEBM + BMF with gestational age/weight appropriate formula
- <2 kg preterm formula
- ≥2 kg high energy term formula
- Breastfeeding/MEBM: use BMF as a concentrated solution (known as fortified breast milk supplement, give 1 sachet dissolved in 3 mL MEBM via syringe/teat before 4 breastfeeds, equally spread throughout 24 hour period. Reduce BMF by 1 sachet/day every 2 weeks until 6 weeks post-term or 3.5 kg, whichever soonest, then stop fortified breast milk supplements
- Refer to neonatal/paediatric dietitian for assessment and advice

Neonatal Parenteral Nutrition for Preterm Babies, up to 28 Days after Their Due Birth Date

Indications for Starting NPN:

For newborn preterm babies start NPN in:

- Babies born before 31+0 weeks
- Babies born at or after 31+0 weeks if sufficient progress is not made with enteral feeding in the first 72 hours after birth
- Babies who are unlikely to establish sufficient enteral feeding, for example, babies with a congenital gut disorder or critical illness such as sepsis.

For preterm babies who have previously established some enteral feeds start NPN in:

- Babies whose enteral feeds have to be stopped and it is unlikely they will be restarted within 48 hours
- Babies whose enteral feeds have been stopped for >24 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.

When a preterm baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.

Administration of NPN:

Venous Access:

- Use a central venous catheter to give neonatal parenteral nutrition. Only consider using peripheral venous access to give neonatal parenteral nutrition if:
  - It would avoid a delay in starting parenteral nutrition
  - Short-term use of peripheral venous access is anticipated, for example, less than 5 days
  - It would avoid interruptions in giving parenteral nutrition
  - Central venous access is impractical.
- Only consider surgical insertion of a central venous catheter if:
  - Non-surgical insertion is not possible
  - Long-term parenteral nutrition is anticipated, for example, in short bowel syndrome.

Protection from Light:

- Protect the bags, syringes and infusion sets of both aqueous and lipid parenteral nutrition solutions from light

Standardized Bags:

- When starting neonatal parenteral nutrition for preterm babies, use a standardized parenteral nutrition formulation (‘standardized bag’).
- Continue with a standardized bag unless an individualized parenteral nutrition formulation is indicated, for example, if the baby has:
  - Complex disorders associated with a fluid and electrolyte imbalance
  - Renal failure.
- Standardized neonatal parenteral nutrition (‘standardized bags’) should be formulated in concentrated solutions to help ensure that the nutritive element of intravenous fluids is included within the total fluid allowance.

Amounts for Constituents of Neonatal Parenteral Nutrition

If starting NPN in the first 4 days after birth				If starting NPN more than 4 days after birth
	Starting Range on First Day	Increasing From Starting To Maintenance	Maintenance Range	Give
Energy	40-60 kcal/kg/day	Gradually, for example over 4days	75-120 kcal/kg/day	75-120 kcal/kg/day
Glucose	6-9 g/kg/day		9-16 g/kg/day	9-16 g/kg/day
Amino acids	1.5-2 g/kg/day		3-4 g/kg/day	3-4 g/kg/day
Lipids	1-2 g/kg/day	Gradually, for example in increments of 0.5-1 g/kg/day	3 - 4 g/kg/day	3-4 g/kg/day
If starting NPN in the first 48 hours after birth				**If starting NPN more than 48 hours after birth**
	Starting Range on First Day	**Increasing from Starting to Maintenance**	**Maintenance Range**	**Give**
Calcium	0.8-1 mmol/kg/day	After 48 hours	1.5-2 mmol/kg/day	1.5-2 mmol/kg/day
Phosphate	1 mmol/kg/day	After 48 hours	2 mmol/kg/day	2 mmol/kg/day

Ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids

- Use a non-nitrogen energy to nitrogen ratio range of 20 to 30 kcal of non-nitrogen energy per gram of amino acids (this equates to 23 to 34 kcal of total energy per gram of amino acid)
- Provide non-nitrogen energy as 60% to 75% carbohydrates and 25% to 40% lipid.

Monitoring NPN:

Other Constituents of Neonatal Parenteral Nutrition – General Principles	
Iron	• Do not give intravenous parenteral iron supplements to preterm babies <28 days old. • For preterm babies 28 days or older, monitor for iron deficiency and treat if necessary.
Vitamins	• Give daily fat-soluble and water-soluble vitamins (in the intravenous lipid emulsion) fromthe outset or as soon as possible after starting parenteral nutrition.
Electrolytes	• Give sodium and potassium in parenteral nutrition to maintain standard dailyrequirements.
Magnesium	• Give magnesium in parenteral nutrition from the outset or as soon as possible afterstarting parenteral nutrition.
Trace Elements	• Give daily trace elements from the outset or as soon as possible after starting parenteralnutrition.
Lipid Emulsions	• For preterm babies with parenteral nutrition-associated liver disease, consider giving acomposite lipid emulsion rather than a pure soy lipid emulsion.
Phosphate	• Giver higher dosage if indicated by serum phosphate monitoring.

General Principles for Monitoring NPN:

When taking blood samples to monitor neonatal parenteral nutrition:

- Collect the minimum blood volume needed for the tests, and liaise with the local clinical laboratory to retrieve as much information as possible from the sample
- Coordinate the timing of blood tests to minimize the number of blood samples needed.

Minimum Blood Monitoring Requirements

Test	Starting	Maintenance	Increased frequency
Glucose	1-2 hours after first starting NPN	1-2 hours after each change of NPN bag (usually24-48 hours)	• Previous hypoglycaemia or hyperglycaemia • Dosage has been changed • Clinical reasons for concern, for example,sepsis or seizures
Blood pH, potassium, chloride, and calcium	Daily when starting and increasing NPN	Twice weekly afterreaching a maintenance NPN	• If levels have been outside normal range • Dosages have been changed • Clinical reasons for concern, for example,critically ill babies
Serum Triglycerides	Daily while increasing lipids	Weekly after reaching maintenance lipid dosage	• If level is elevated • Clinical reasons for concern, for example, critically ill babies or babies with a lipaemic blood sample
Serum or Plasma Phosphate	Daily while increasing phosphate	Weekly after reaching maintenance phosphate dosage	• If level has been outside normal range • Clinical reasons for concern, for example,metabolic bone disease • Born <32 weeks
Iron Status	Measure ferritin, iron and transferrin saturation if a preterm baby is on parenteral nutritionfor >28 days		
Liver Function	Weekly		• If levels have been outside the normal range • Clinical concerns

Stopping NPN:

Factors to take into account when deciding when to stop parenteral nutrition:

- Tolerance of enteral feeds
- Nutrition being delivered by enteral feeds (volume and composition)
- Relative contribution of parenteral nutrition and enteral nutrition to baby's total nutritional requirement
- Likely benefit of nutritional intake compared with risk of venous catheter sepsis
- Individual baby's circumstances, for example, a baby with complex needs such as short bowel syndrome, increased stoma losses or slow growth, may need long-term parenteral nutrition.

Depending on the above factors, consider stopping parenteral nutrition within 24 hours once the following enteral feed volumes are tolerated

- For preterm babies born before 28 weeks: 140 to 150 ml/kg/day
- For preterm babies born at or after 28 weeks: 120 to 140 ml/kg/day
- ***SOURCE:***
  - **National institute for health and care excellence (NICE)**

Neonatal Parenteral Nutrition for Term Babies, up to 28 Days After Their Birth

Indications for Starting NPN:

For newborn term babies start NPN in:

- Babies who are unlikely to establish sufficient enteral feeding, for example, babies with a congenital gut disorder or critical illness such as sepsis

For term babies who have previously established some enteral feeds start NPN in:

- Babies whose enteral feeds have to be stopped and it is unlikely they will be restarted within 72 hours
- Babies whose enteral feeds have been stopped for >48 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.

When a term baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.

Administration of NPN:

Venous Access:

- Use a central venous catheter to give neonatal parenteral nutrition. Only consider using peripheral venous access to give neonatal parenteral nutrition if:
  - It would avoid a delay in starting parenteral nutrition
  - short-term use of peripheral venous access is anticipated, for example, less than 5 days
  - It would avoid interruptions in giving parenteral nutrition
  - Central venous access is impractical.
- Only consider surgical insertion of a central venous catheter if:
  - Non-surgical insertion is not possible
  - Long-term parenteral nutrition is anticipated, for example, in short bowel syndrome.

Protection from Light:

- Protect the bags, syringes and infusion sets of both aqueous and lipid parenteral nutrition solutions from light.

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- Continue with a standardized bag unless an individualized parenteral nutrition formulation is indicated, for example, if the baby has:
    - Complex disorders associated with a fluid and electrolyte imbalance
    - Renal failure.
- Standardized neonatal parenteral nutrition (‘standardized bags’) should be formulated in concentrated solutions to help ensure that the nutritive element of intravenous fluids is included within the total fluid allowance.

Starting, Increasing and Maintaining NPN

Amounts for Constituents of Neonatal Parenteral Nutrition				
If starting NPN in the first 4 days after birth				If starting NPN more than 4 days after birth
	Starting Range on First Day	Increasing From Starting To Maintenance	Maintenance Range	Give
Energy	40-60 kcal/kg/day	Gradually, for example over 4days	75-120 kcal/kg/day	75-120 kcal/kg/day
Glucose	6-9 g/kg/day		9-16 g/kg/day	9-16 g/kg/day
Amino acids	1-2 g/kg/day		2.5 - 3 g/kg/day	2.5 - 3 g/kg/day
Lipids	1-2 g/kg/day	Gradually, for example in increments of 0.5 -1 g/kg/day	3 - 4 g/kg/day	3 - 4 g/kg/day
If starting NPN in the first 48 hours after birth				If starting NPN more than 48 hours after birth
	Starting Range on First Day	Increasing from Starting to Maintenance	Maintenance Range	Give
Calcium	0.8-1 mmol/kg/day	After 48 hours	1.5-2 mmol/kg/day	1.5-2 mmol/kg/day
Phosphate	1 mmol/kg/day	After 48 hours	2 mmol/kg/day	2 mmol/kg/day

Other constituents of neonatal parenteral nutrition – general principles	
Iron	• Do not give intravenous parenteral iron supplements to term babies <28 days old.
Vitamins	• Give daily fat-soluble and water-soluble vitamins (in the intravenous lipid emulsion) from the outset or as soon as possible after starting parenteral nutrition.
Electrolytes	• Give sodium and potassium in parenteral nutrition to maintain standard daily requirements.
Magnesium	• Give magnesium in parenteral nutrition from the outset or as soon as possible after starting parenteral nutrition.
Trace elements	• Give daily trace elements from the outset or as soon as possible after starting parenteral nutrition.
Lipid Emulsions	• For term babies with parenteral nutrition-associated liver disease, consider giving a composite lipid emulsion rather than a pure soy lipid emulsion.
Phosphate	• Giver higher dosage if indicated by serum phosphate monitoring.
Energy	• For term babies who are critically ill or have just had surgery, consider giving parenteral energy at the lower end of the starting range.

Ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids
• Use a non-nitrogen energy to nitrogen ratio range of 20 to 30 kcal of non-nitrogen energy per gram of amino acids (this equates to 23 to 34 kcal of total energy per gram of amino acid)
• Provide non-nitrogen energy as 60% to 75% carbohydrates and 25% to 40% lipid.

Test	Starting	Maintenance	Increased frequency
Glucose	1-2 hours after first starting NPN	1-2 hours after each change of NPN bag (usually24-48 hours)	• Previous hypoglycaemia or hyperglycaemia • Dosage has been changed • Clinical reasons for concern, for example,sepsis or seizures
Blood pH, potassium, chloride, and calcium	Daily when starting and increasing NPN	Twice weekly after reaching a maintenance NPN	• If levels have been outside normal range • Dosages have been changed • Clinical reasons for concern, for example,critically ill babies
Serum Triglycerides	Daily while increasing lipids	Weekly after reaching maintenance lipid dosage	• If level is elevated • Clinical reasons for concern, for example, critically ill babies or babies with a lipaemic blood sample
Serum or Plasma Phosphate	Daily while increasing phosphate	Weekly after reaching maintenance phosphate dosage	• If level has been outside normal range • Clinical reasons for concern, for example,metabolic bone disease • Born <32 weeks
Liver Function	Weekly		• If levels have been outside the normal range • Clinical concerns

Monitoring NPN:

Stopping NPN:

Factors to take into account when deciding when to stop parenteral nutrition:

- Tolerance of enteral feeds
- Nutrition being delivered by enteral feeds (volume and composition)
- Relative contribution of parenteral nutrition and enteral nutrition to baby's total nutritional requirement
- Likely benefit of nutritional intake compared with risk of venous catheter sepsis
- Individual baby's circumstances, for example, a baby with complex needs such as short bowel syndrome, increased stoma losses or slow growth, may need long-term parenteral nutrition.

Depending on the above factors, consider stopping parenteral nutrition within 24 hours once the enteral feed volume tolerated is 120 to 140 ml/kg/day

Transfusion of RBC in the NICU

Indications:

- Acute blood loss with haemodynamic compromise or 10% blood volume loss.In emergency, use Group O RhD negative blood & transfuse 10 mL/kg over 30 min. Further transfusion based on haemoglobin (Hb)
- Top-up blood transfusion, if Hb below threshold levels quoted in the following situations

<table>
<tr><th>Baby</th><th colspan="3">Hb (g/L)</th></tr>
<tr><td>Post Natal age</td><td colspan="3">Suggested transfusion threshold Hb (g/L)</td></tr>
<tr><td></td><td>Ventilated</td><td>Other non-invasiverespiratory support (CPAP/BiPAPHFNC/O2)</td><td>No Respiratory Support</td></tr>
<tr><td>First 24 hour</td><td>< 120</td><td>< 120</td><td>< 100</td></tr>
<tr><td>Week 1 (day 1-7)</td><td>< 120</td><td colspan="2">< 100</td></tr>
<tr><td>Week 2 (day 8-14)</td><td rowspan="2">< 100</td><td>< 95
< 85 if symptoms of anaemia (e.g. poorweight gain or significant apnoeas) or poor reticulocyte of anaemia (e.g. poorweight gain or significant apnoeas) or poor reticulocyte response (<4% or count <100 X 10^9/L)</td><td></td></tr>
<tr><td>≥Week 3 (Fday 15 onwards)</td><td>< 85</td><td><75 if asymptomatic andgood reticulocyte response (4% or reticulocyte count ≥100 X10^9/L)</td></tr>
</table>

NB: To convert from (g /L) to (mg / dl) divide the number by 100

Pre-Transfusion:

Communication:

- If possible, inform parents that baby will receive blood transfusion.

Cross Match:

- For top-up transfusions in well baby, arrange with blood bank.
- Crossmatch against maternal serum (or neonatal serum if maternal serum not available) for first 4months
- For first transfusion, send samples of baby's and mother's blood

Direct Coombs Testing:

- Laboratory will perform direct Coombs test (DCT) on maternal serum for any atypical antibodies
- If maternal DCT negative, blood issued will be crossmatched once against maternal serum.
- If maternal DCT positive, crossmatching of donor red blood cells against maternal serum is required every time

Premature babies receiving breast milk or with Hb<10 g/dl should receive oral iron supplementation at age 4 weeks

Transfusion:

Volume of Transfusion:

- Give 15 mL/kg of red cell transfusion for non-bleeding neonates irrespective of pre-transfusion Hb
- Give 20 mL/kg of red cell transfusion in case of massive haemorrhage

Rate of Administration:

- Administer blood at 15 mL/kg over 3-4 hour
- Increase rate in presence of active haemorrhage with shock via peripheral venous or umbilical venous line
- Routine use of furosemide is not recommended except with chronic lung disease, with haemodynamically significant PDA, in heart failure with edema or fluid overload

Hazards of Transfusion:

- Infections bacterial/viral
- Hypocalcaemia
- Volume overload
- Citrate toxicity
- Rebound hypoglycaemia (following high glucose levels in additive solutions) thrombocytopenia after exchange transfusion

Use of Furosemide:

- Routine use not recommended
- Consider soon after blood transfusion for babies:
  - With chronic lung disease
  - With haemodynamically significant PDA
  - In heart failure
  - With oedema or fluid overload

Documentation and Good Practice:

- Clearly document indication for transfusion and consent in the note
- Ensure blood transfusion volume and rate is prescribed in appropriate infusion chart
- Observations, including:
  - SpO2
  - Hourly temperature and BP (recorded before, during and after transfusion)
  - Document pre- and post-transfusion Hb levels

SOURCE:

1. **The National Institute for Health and Care Excellence (NICE)**
2. **Neonatal guidelines 2019- 2021 (the Bedside Clinical Guidelines Partnership)**
3. **British Committee for Standards in Haematology recommendations**

NEONATAL HYPOTENSION

Hypovolaemia is an uncommon cause of hypotension in the preterm newborn. Excessive volume expansion can increase mortality.

Definition:

Thresholds for intervention:

⇨ Aim to maintain mean arterial BP (MABP) gestational age in weeks

⇨ Aim for even higher MABP in case of persistent pulmonary hypertension of the newborn

Recognition and Assessment:

Assessment of BP:

- Measure MABP: by direct intra-arterial BP if possible since Dinamap has limited accuracy in hypotensive preterm babies; usually overreads BP in the lower ranges
- Identification of hypotension should not be based solely upon BP thresholds, but must assess other indices of tissue perfusion (e.g. capillary refill time (>3 sec), toe-core temperature difference (>2°C), urine output (<1 mL/kg/hour), rising lactate

Causes of Hypotension:

- Sepsis
- Extreme prematurity
- Tension pneumothorax
- Blood loss
- Large patent ductus arteriosus (PDA)
- Poor myocardial contractility (e.g. VLBW, hypoxia, cardiomyopathy)
- Polyuria secondary to glucosuria
- Third spacing (NEC/perforation/malrotation/obstruction)
- High positive intrathoracic pressure (high MAP on conventional/HFOV)
- Severe acidosis (pH <7)
- Drugs (morphine, muscle relaxants and anti-hypertensives)

Immediate Treatment:

"Aim is to treat cause and improve organ perfusion, not to correct a 'BP reading"

Transilluminate chest to exclude pneumothorax:

Fluid:

- Give if hypovolaemic (not >10 mL/kg) unless there is evidence of fluid/blood loss/sepsis, Otherwise, start inotropes first
- If clinical condition poor, BP very low, or mother has been treated with IV anti-hypertensive agent, give inotrope after fluid bolus
- Use sodium chloride 0.9% 10 mL/kg over 10-15 min except when there is coagulopathy with bruising: give fresh frozen plasma 10 mL/kg over 30 min or acute blood loss: give packed cells 10 mL/kg over 30 min

"Reassess clinically within 10 min of bolus"

Inotropes:

- Start dopamine at 5 microgram/kg/min
- Reassess every 15– 20 min
- If still hypotensive, increase dopamine to 10 microgram/kg/min
- If still hypotensive, add dobutamine at 10 microgram/kg/min
- If still hypotensive, increase dobutamine up to 20 microgram/kg/min
- If still hypotensive, increase dopamine up to 20 microgram/kg/min
- Give hydrocortisone 2.5 mg/kg IV (over 3-4 min) followed by 2.5 mg/kg IV 6-8 hourly for 2 3 days as necessary

"Do not use >20 microgram/kg/min of dopamine"
(alpha effect causes vasoconstriction)

- In babies with poor cardiac function, consider starting dobutamine first (also discuss with cardiologist)
- In term babies requiring inotropes for pulmonary hypertension an infusion of noradrenaline or adrenaline may be required
- Consider milrinone in PPHN after evaluation of cardiac function

Caution:

- Inotropes ideally given via central line
- When peripheral line used during emergency monitor site carefully for extravasation injury

Continuing Hypotension:

- Echocardiogram where possible to assess myocardial dysfunction/congenital heart disease

Refractory Hypotension:

- Seek senior advice before starting adrenaline infusion.
- Discuss alternative agents (e.g. noradrenaline, vasopressin)
- If acidotic with severe hypotension, but not hypovolaemic, give adrenaline 100-1000 nanogram/kg/min & if baby requires >1000 nanogram/kg/min, consider other inotropes but monitor limb perfusion and urine output

Monitoring:

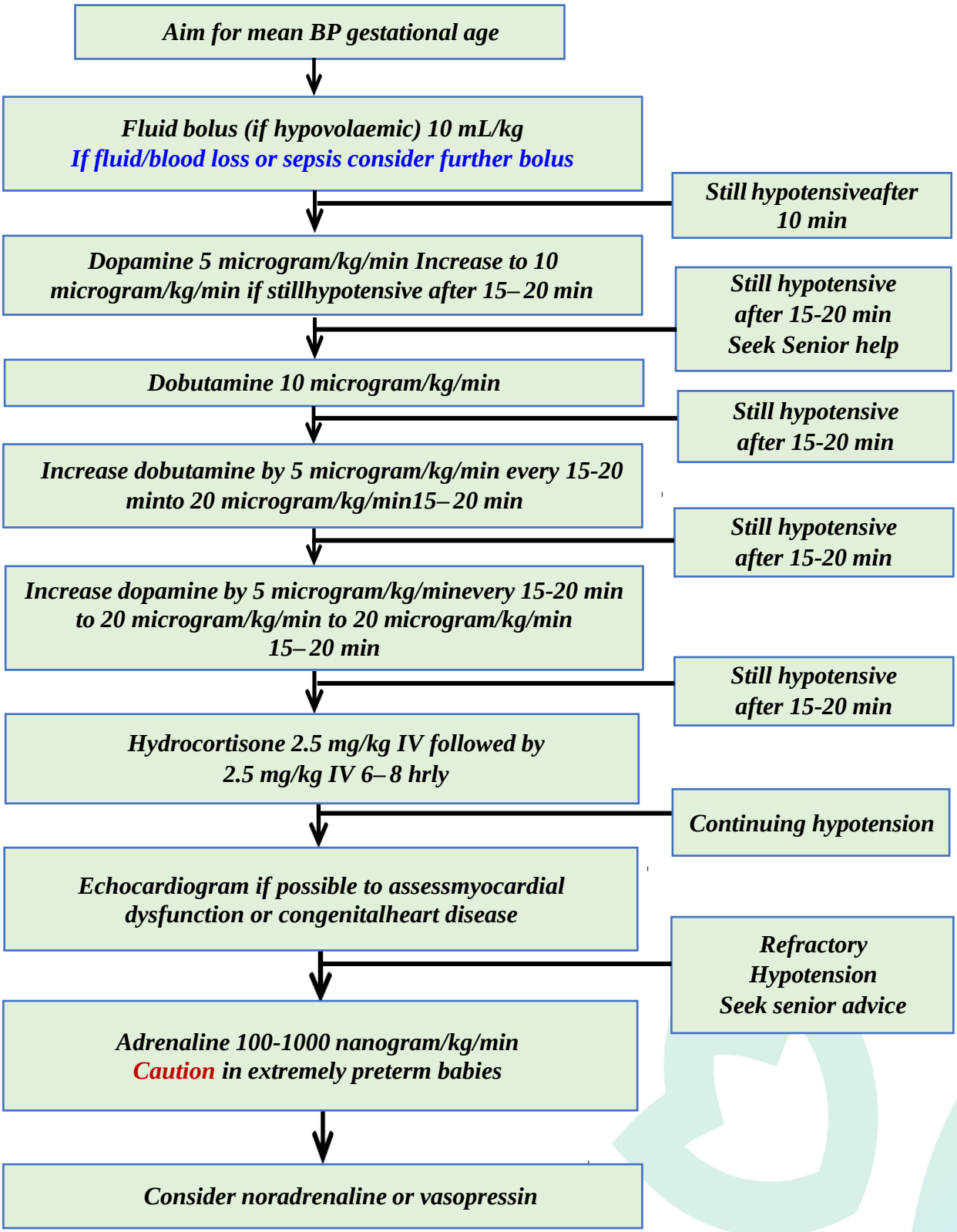
- BP via arterial line
- Check effective delivery of drugs
- Chest X-ray
- Signs of tissue perfusion
- Echocardiogram where possible to assess function and structure

Subsequent Management:

- If already on morphine and muscle relaxant infusion, reduce dosage if possible
- If ventilated, try to reduce mean airway pressure without compromising chest inflation and oxygenation
- If baby acidotic and not responding to treatment, consider sodium bicarbonate
- Weaning inotropes if hypotension improves

Wean inotropes (dopamine or dobutamine) in 5 microgram/kg/min decrements and adrenaline in 100 nanogram/kg/min decrements) as tolerated and directed by senior advice

Flowchart: Management of Hypotension



Neonatal Period by Gestational Age

neonatal period by gestational age

Gestational age (week)	BP %	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)
26-28	50th	55-60	30-38	38-45
	95th	72-75	50-50	57-58
	99th	77-80	54-56	63-63
30-32	50th	65-68	40-40	48-48
	95th	80-83	55-55	63-64
	99th	85-88	60-60	68-69
34-36	50th	70-72	40-50	50-57
	95th	85-87	55-65	65-72
	99th	90-92	60-70	70-71
38-40	50th	77-80	50-50	59-60
	95th	92-95	65-65	74-75
	99th	97-100	70-70	79-80
42-44	50th	85-88	50-50	62-63
	95th	98-105	65-68	76-80
	99th	102-110	70-73	81-85

*Modified from table presented in reference. SBP=Systolic blood pressure, DBP=Diastolic blood pressure, MAP=Mean arterial pressure, BP=Blood pressure

SOURCE:

1. **The National Institute for Health and Care Excellence (NICE)**
2. **Neonatal guidelines 2019- 2021 (the Bedside Clinical Guidelines Partnership)**

MECHANICAL SUPPORT OF RESPIRATION OF THE NEWBORN

Standard CPAP:

Equipment:

- Short binasal prongs and/or nasal mask, Circuit, Humidifier (ESSENTIAL: to have heated humidified gas), CPAP generating device with gas mixing and pressure monitoring
- All require high gas flow (usual starting rate 8 L/min)

Fixing Nasal CPAP Device:

Short binasal prongs (preferred):

A. To avoid loss of pressure, use largest prongs that fit nostrils comfortably
B. Ensure device is straight and not pressed hard against nasal septum or lateral walls of nostrils. Excessive pressure can cause tissue damage

Nasal mask has to fit securely over nose

Consider alternating mask with prongs, particularly if baby developing excoriation or erosion of nasal septum.

Procedure:

Position:

- Prone position is preferable. Avoid excessive flexion, extension or rotation of the head
- After connecting start at 5–6 cm H2O initially and increase by 1 cm H2O increments. Optimum pressure depends on illness type and severity – watch baby and use lowest pressure required to improve work of breathing (Do not exceed 8 cms H2O unless consultant orders)

Reassess frequently:

- If baby not improving CHECK: Air entry, secretions, close mouth, revise flow and pressure delivery, decompress stomach with orogastric tube.
- If still deteriorating, consider INTUBATION

Wean:

- Reduce CPAP pressure one by one after FiO2 is weaned <40%. Disconnect at PEEP 4-5 and FIO2 30%

Conventional Ventilation:

"The aim of MV is to provide "acceptable" blood gases whilst avoiding lung injury"

Ventilator Parameters:

PIP:

- Use lowest possible PIP to achieve visible chest expansion and adequate gas exchange on blood gas analysis
- To minimize lung injury from barotrauma and inadvertent over-distension, avoid excessive PIP.

PEEP:

- Start with a PEEP of 5 cms and increase incrementally up to 8 cm (for babies with RDS) for improving oxygenation (when PEEP >6 cm is necessary consult first)

Inspiratory Time (Ti):

- Usually between 0.3–0.4 sec
- Avoid Ti >0.5 sec except in term babies with parenchymal lung disease (consult first)

Rate:

- Rapid rates (≥60/min) are associated with fewer air leaks and less asynchrony in PRETERM babies compared to slow (20–40/min) rates. Use slower rates in obstructive illness.

Flow:

- 5–8 L/min is generally sufficient.
- Consider higher flows at faster ventilator rates or shorter inspiratory times (some ventilators auto regulate flow)

Tidal Volume (Vt):

- Target is 4–6 mL/kg

Setting Up Ventilator:

1. Make sure connections are correct, make sure humidifier is set and water is up to the mark
2. Adjust ventilator settings depending on chest movement (chest movement has to be observed but not extensive to avoid over inflation), SpO2, (target and measured Vt).

3. Don't forget to set trigger if synchronization is needed. Trigger is set to almost highest trigger sensitivity (just above the lowest setting (1: bar is mostly unshaded on the dragger machine and set to 0.3 in the preterm <28 weeks on SLE).
4. Sample blood gas within 30 min of commencing ventilator support.

For babies with normal lungs requiring supportive ventilation such as term babies with respiratory depression (asphyxia or drugs), babies with neuromuscular disorders or, in the post-operative period, and preterm babies with recurrent apnoea use low settings with a minimum rate of 40-50/min.

Oxygen is a drug and should be prescribed as with other medications. This should be done by specifying intended target range: for preterm babies: 91–95%, for term babies with PPHN: 96–100%, Target pCO2 > 35 cm H20. If low PCO2 wean ventilation without delay and recheck within 1 hour of low measurement

Modes of Ventilation:

AC, SIPPV, PTV:

- Preferred mode for sick babies.
- Patient triggered: patient decides the rate (make sure the trigger is set to being highly sensitive (very close to the lowest setting), set a backup rate. All other settings are set by the operator (PIP, PEEP, Ti and FiO2)

SIMV:

- Is operator set in all parameters but Trigger sensitivity should be set in order to synchronize set rate with the patient rate.

PSV:

- Patient decides Rate (using trigger) and Ti (set using flow termination criteria which is set to 5-10% of peak flow).
- Operator sets PIP and PEEP. Back up rate is also set.
- Make sure leak is minimal

Targeted Tidal Volume or Volume Guarantee:

- Pre-set the tidal volume required at 5 ml. or use the previous achieved TV noted while on SIMV, make sure there is minimal leak around the ETT. Set pressure limit to 30% higher than the PIP Level that allows adequate chest expansion

If baby is deteriorating , Always Re-Evaluate the Baby Before Raising the Settings:

Blood gas scenario	Recommended action *in order of preference*
Low PaO_2/SpO_2	• Exclude airleak/displaced ETT/overinflation • Increase FiO_2 • Increase PEEP • Increase PIP (but be aware of effect on $PaCO_2$) • Increase T_{insp} [but ensure adequate expiratory time (T_{exp}), especially at fast rates] • Consider further surfactant [see **Surfactant replacement therapy – including less invasive surfactant administration (LISA) technique** guideline] • If above measures unsuccessful, discuss with consultant (may need HFOV/iNO)
High PaO_2	• Decrease FiO_2 (unless already in air) • Decrease PEEP (if >5 cm) • Decrease PIP (especially if $PaCO_2$ is also low)
High $PaCO_2$	• Exclude airleak/displaced or blocked ETT • Increase PIP • Increase rate • Decrease PEEP (only if oxygenation adequate and PEEP >6 cm) after taking senior advice
Low $PaCO_2$	• Decrease PIP • Decrease rate
Low PaO_2/SpO_2 and high $PaCO_2$	• Exclude displaced/blocked ETT • Exclude air leak • Increase PIP • Consider further surfactant • If no response, consider HFOV [see **Ventilation: high frequency oscillatory ventilation (HFOV)** guideline]

- Is baby's chest moving adequately? Is there good bilateral equal air entry? If less on one side: trans illuminate to exclude pneumothorax
- Check Ventilator and tubing, check tidal volume. Are the measured ventilator values markedly different to the set ones? • is there a large (>40%) endotracheal tube (ETT) leak?
- Always exclude airway problems (blocked/displaced ETT) and air leaks in case of deterioration of blood gases.

Babies Fighting Ventilator (Asynchrony):

- Ensure baby is not hypoxic or under-ventilated
- Exclude blocked ETT
- Look for obvious pain e.g. necrotising enterocolitis
- If possible, change to synchronised form of ventilation (SIPPV/PTV/Assist Control/SIMV)
- Ensure adequate sedation

Weaning:

1. Reduce PIP (usually by 1–2 cm) until MAP 7−8 cm reached.
2. Reduce PEEP to 5 cms.
3. Finally reduce rate to 30/min, usually in decrements of 5–10 breaths/min.
4. Extubating to nasal CPAP if baby <31 weeks or to non-invasive PPV (start caffeine before weaning).

Ventilation: High Frequency Oscillatory Ventilation (HFOV):

- Decision to initiate HFOV must be made by a consultant.
- Do not start HFOV unless you have the experience.

Indications for HFOV:

- Rescue following failure of conventional ventilation (e.g. PPHN, MAS).
- To reduce barotrauma when conventional ventilator settings are high.
- Air leak (pneumothorax, PIE).
- Can be used as an initial therapy in babies with RDS to maintain lung open, in experienced hands.

Terminology:

Frequency:

- High frequency ventilation rate (Herz, cycles/sec)

Mean Airway Pressure (cm H2O):

- MAP

Amplitude (Delta P):

- Is the variation around the MAP

Mechanism:

- Oxygenation and CO2 elimination are independent.
- Oxygenation is dependent on MAP (provides constant distending pressure equivalent to CPAP, inflating the lung to constant and optimal lung volume, maximizing area for gas exchange and preventing alveolar collapse in the expiratory phase) and FiO2.
- Ventilation (CO2 removal) dependent on amplitude (The wiggle superimposed around the MAP achieves alveolar ventilation and CO2 removal) and less importantly the frequency.

Management:

Preparation for HFOV:

- If significant leakage around ETT, insert a larger one.
- Optimize blood pressure and perfusion, complete any necessary volume replacement and start inotropes, if necessary, before starting HFOV.
- Invasive blood pressure monitoring if possible.
- Correct metabolic acidosis.
- Ensure adequate sedation.

Setting the Machine:

MAP:

- High volume strategy preferred but consider low volume strategy when air leaks present
- Setting high lung volume strategy (aim to maximize recruitment of alveoli):
  - If changing from conventional ventilation, set MAP 2–4 cm H2O above MAP on conventional ventilation
  - If starting immediately on HFOV, start with MAP 8 cm H2O and increase in 1–2 cm H2O increments until optimal SpO2 achieved
- Setting low volume strategy (aim to minimize lung trauma).
- Set MAP equal to MAP on conventional ventilation.

Frequency:

- Set to 10 Hz.

Amplitude (delta P on SLE ventilator):

- Gradually increase amplitude until chest seen to wiggle well. Wiggle should not be felt below the umbilicus.
- Obtain early blood gas (within 20 min) and adjust settings as appropriate.
- Change frequency only after discussion with consultant.

Adjusting Settings:

Oxygenation:

- Adjusted by changing MAP by 1-2 cms H2O at a time (both over and under-inflation can result in hypoxia. If in doubt, perform chest X-ray)

Ventilation:

- Adjusted by changing amplitude (increase amplitude in high CO2 and vice versa). If wiggle on chest is imperceptible: amplitude is too low!

Monitoring:

- Oxygen saturations
- Amplitude: With chest wiggle (has to be observed)
- Frequent blood gas monitoring (every 30–60 min) in early stages of treatment as PaO2 and PaCO2 can change rapidly (transcutaneous Carbon dioxide monitoring is preferred if available)
- CO2 diffusion coefficient (DCO2): is a reading on the ventilator screen. It is an indicator of CO2 elimination which correlates well with PaCO2 for an individual baby (frequency × (tidal volume)2). Observe its trend (Falling DCO2 : Suggests rising PaCO2)
- Chest X-ray:
  - Within 1 hour to determine baseline lung volume on HFOV (aim for 8 ribs at midclavicular line)
  - If condition changes acutely and/or daily to assess expansion/ETT position, repeat chest X-ray

Troubleshooting On HFOV:

Chest Wall Movement:

- Suction indicated for diminished chest wall movement indicating airway or ETT obstruction (use an in-line suction device to maintain PEEP)
- Increase FiO2 following suctioning procedure
- MAP can be temporarily increased by 2–3 cm H2O until oxygenation improves

Low PaO2

- Suboptimal lung recruitment: increase MAP (consider chest X-ray)
- Over-inflated lung: reduce MAP: does oxygenation improve? Check blood pressure (consider chest X-ray)

ETT Patency:

- Check head position and exclude kinks in tube
- Check for chest movement and breath sounds
- Check there is no water in ETT/T-piece
- Air leak/pneumothorax
- Trans illumination or urgent chest X-ray

High PaCO2

- ETT patency and air leaks (as above)
- Increase amplitude, does chest wall movement increase?
- Increased airway resistance (MAS or BPD) or non-homogenous lung disease, is HFOV appropriate?

Persisting Acidosis/Hypotension

- Over-distension
- Exclude air leaks; consider chest X-ray
- Reduce MAP: does oxygenation improve?

Spontaneous Breathing:

- Usually not a problem but can indicate suboptimal ventilation (e.g. kinking of ETT, build-up of secretions) or metabolic acidosis

Weaning:

- Reduce FiO2 to <0.4 before reducing MAP (unless there is over-inflation: diaphragm below 9th rib: reduce MAP)
- In air leak syndromes (using low volume strategy), reducing MAP takes priority over weaning the FiO2
- Reduce MAP in 1–2 cm decrements to 8–9 cm 1–2 hourly or as tolerated (If oxygenation lost during weaning, increase MAP by 3–4 cm and begin weaning again more gradually).
- Wean the amplitude in small increments (5–15%) depending upon PCO2
- Do not wean frequency
- When MAP <8 cms H2O and amplitude between 20-25 with satisfactory blood gases, switch to CPAP
- In the presence of a lot of chest secretions, switching to low setting conventional ventilation for a short period can be done before extubation

SOURCE:

1. **Neonatal guidelines 2019-2021 (the Bedside Clinical Guidelines Partnership)**

CARE FOR THE ELBW INFANT

1. In utero transport, prenatal steroids to mother and delivery in level 3-4 NICU

2. Special Precautions during Resuscitation (page …)

3. Bundles:

A. Prevention of Hypothermia

- Start from delivery room, warm transport incubator, warm humidified NICU incubator, monitoring temp.

B. Respiratory Support:

- **Blender and pulse oximeter in delivery room**

1. In the spontaneously breathing infant start nasal CPAP at 6-8 cms water with 30% Oxygen. Monitoring pulse oximetry is essential to keep saturation between 90-95%. If oxygen requirement is increasing, give surfactant using the LISA technique
2. If baby not breathing spontaneously, start PPV using a T piece resuscitator (provides regulated PIP and PEEP), low tidal volume (4-5 ml/kg) and rapid rate. This is followed in the NICU by MV with volume guarantee and adequate PEEP. Surfactant therapy should be initiated following intubation as early as possible
3. Caffeine therapy initiated early
4. Avoid hypoxia and hyperoxia. Maintain oxygen saturations at 90-95%

C. Intravenous Access:

1. Under complete aseptic conditions, insert a peripheral catheter soon after birth followed by an umbilical venous catheter within 24 hours
2. By day 7-10 shift to PICC line, if baby still needs long term IV access
3. Minimize punctures

D. Intravenous fluids:

1. Use a humidified incubator
2. If baby is 25-26 weeks give 80-100 ml/kg/day
3. Monitor blood pressure, urine output, daily weight and serum electrolytes (diuresis and natriuresis usually occur by third day, close monitoring for dehydration)
4. Start with Dextrose solution, monitor blood sugar and regulate intake (maintain blood glucose at >45-50 mg/dL). No electrolytes for the first 48 hours unless lab confirmation is available and adequate urine output.

E. Nutrition:

1. Start TPN as early as possible. Initiate protein within day 1 day of life
2. Start trophic feeds with mother own milk early (Day 1-2)
3. Advance feeds regularly as tolerated
4. Provide sufficient calories for growth (target 110-120 kcal/kg/day)

F. Cardiovascular Support:

1. Delay cord clamping in the DR when possible. Maintain blood pressure in normal range (Table)
2. Careful management of fluid boluses for hypotension (limit to 10-20 ml/kg)
3. Dopamine and/or corticosteroids may be used as indicated
4. Avoid fluid overload to promote closure of the ductus (monitor by D2-3)
5. If PDA is hemodynamically significant start medical closure

G. Infection Control:

1. Scrupulous hand washing
2. Minimize punctures and invasive procedures. Close attention to skin care to maintain integrity (emollients)
3. Care of the lines and minimize dwell time by promotion of entral feeds
4. Minimize unnecessary suctioning and promote early weaning from MV

H. Transfusions:

1. Avoid by: Delayed cord clamping, microsampling techniques, essential labs only, strict criteria for transfusion
2. Minimize donor exposure by identifying a specific unit to a patient and splitting it into small aliquots

REFERENCE:

- **Manual of Neonatal Care (2021) - Chapter 13. p 172-185**

TRANSPORT AND RETRIEVAL

Introduction:

The aim of a safe transfer policy is to ensure the highest standard, streamlined care. In the majority of cases transfer will be performed by a dedicated transfer team, but in certain cases the referring team may perform the transfer. In all cases the accept model (Table 1) can be used.

Indications for Transfer:

- Uplift for services not provided at referring unit (including diagnostic and drive-through transfers)
- Repatriation
- Resources/capacity

Table 1: Accept Model

A	**ASSESSMENT**
C	**CONTROL**
C	**COMMUNICATION**
E	**EVALUATION**
P	**PREPARATION AND PACKAGING**
T	**TRANSPORTATION**

Assessment:

- Key questions are:
  - What is the problem?
  - What is being done?
  - What effect is it having?
  - What is needed now?

Control:

- Following initial assessment control the situation:
  - Who is the team leader?
  - What tasks need to be done (clinical care/equipment and resources)?
  - Who will do them (allocated by team leader)?
  - Who will transfer baby (if relevant)?

Clinical Care:

Preparation for transport begins at the referring health care facility with the referring team as soon as decision is made to transfer baby, even if being performed by another team

Airway/Breathing:

- If baby unstable or on CPAP with FiO2 >0.4, intubate and ventilate
- Adjust ETT and lines depending on chest X-ray position; document all positions and adjustments and consider if repeat X-ray required; secure all lines and tubes
- If indicated, give surfactant [see Surfactant replacement therapy including less invasive surfactant administration (LISA) technique guideline]
- If pneumothorax is present, connect chest drains to a flutter valve
- Check appropriate type of ventilator support is available for transfer (e.g. high-flow/BiPAP/SiPAP/volume guarantee/oscillation may not be provided in transport) -if not, discuss other options
- If ventilated perform blood gas and adjust ventilation settings as necessary
- If non-invasive ventilation support, have recent (<6 hour) blood gas result available

Circulation:

- If baby is dependent on drug infusions (e.g. inotropes, prostaglandin), 2 reliable points of venous access must be inserted
- Check whether receiving unit will accept central lines
- If baby is receiving bicarbonate, insulin or inotropes insert double lumen UVC
- Ensure catheters secured with suture and tape
- Check all access is patent and visible
- Optimize blood pressure (see Hypotension guideline)

Drugs:

- Antibiotics [see Infection in first 72 hours of life guideline and Infection (late onset) guideline]
- Decide whether infusions need to be concentrated
- Check vitamin K IM has been given
- Decide whether sedation is needed for transfer

Environment:

- Monitor temperature throughout stabilization – in the extreme preterm baby chemical gel mattress may be required
- Cooling babies [see Cooling in non-cooling centers (referral and preparation of babies eligible for active cooling) guideline]

Fluids:

- Ensure all fluids and infusions are in 50 mL syringes and are labelled
- If requested, change PN to maintenance fluids
- Volume as per Intravenous fluid therapy guideline
- Monitor intake and output

Infection:

- Check if any evidence of infection and inform receiving unit

Parents:

- Update with plan of care
- Discuss how parents will get to receiving unit

Communication:

Referring Center:

- Locate NICU/paediatric intensive care unit (PICU)/specialty bed
- For specialty or other PICU bed,
- Call receiving clinician
- All transfers, provide:
  - Clinical details to transfer team
  - History and clinical details
  - Urgency of transfer
  - Interventions, investigations and results
  - Medications
- Document advice given/received
- Prepare transfer information/discharge summary and arrange for images to be reviewed at receiving hospital

Receiving Center:

- Ensure consultant and nurse coordinator accept referral and agree with advice given

Evaluation:

- Referring clinician, transfer team and receiving team evaluate urgency of transfer and decide who will do it
- Neonatal transfers are classified as:
  - Time critical (e.g. gastroschisis, ventilated tracheoesophageal fistula, intestinal perforation, duct- dependent cardiac lesion not responding to prostaglandin infusion and other unstable conditions)
  - To be performed within 1 hour
  - To be performed within 24 hours
  - To be performed after 24 hours
- In the event of transfer team being unable to respond within an appropriate time period, referring unit may decide to perform transfer themselves in the best interests of the baby

Preparation and Packaging:

- Three components:
  1. Clinical care (see above)
  2. Location and checking of equipment
  3. Allocation of team
- Transport equipment must not be used for any other purpose
- Team undertaking transfer must be trained in use of all equipment and drugs and be competent to perform any necessary procedures en-route
- Ensure air and oxygen cylinders are full before departure
- ETT and lines must be secured before transferring baby to transport incubator
- Baby must be secured in transport incubator

Transport:

Before Leaving Referring Unit:

- Change to transport incubator gases (check cylinders are full)
- Check blood gas 10 min after changing to transport ventilator. Make any necessary changes
- Check lines and tubes are not tangled; check infusions are running
- Record vital signs
- Allow parents to see baby

"Only leave referring unit when team leader is confident that baby is stable for transfer"

- Contact receiving hospital to confirm cot still available.

On Arrival at Ambulance:

- Ensure incubator and equipment are securely fastened/stowed
- Plug in gases and electrical connections
- Ensure temperature in ambulance is suitable
- Check all staff are aware of destination
- Discuss mode of progression to hospital (e.g. category of transfer)
- Ensure all staff are wearing seatbelts before vehicle moves

During Road Transit:

- Record vital signs
- If baby requires clinical intervention, stop ambulance in a safe place before staff leave their seats
- Make receiving team aware of any major changes in clinical condition

On Arrival at Receiving Hospital:

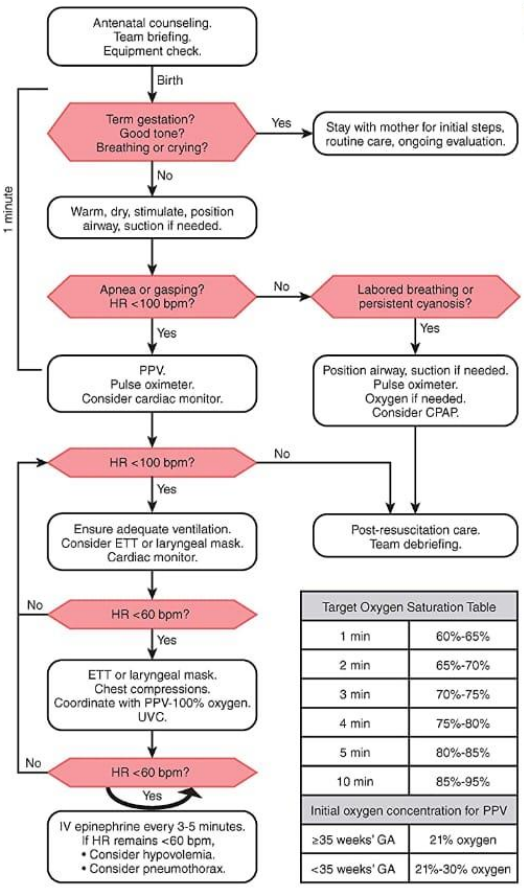
- Follow the ACCEPT structure
- Handover to receiving team then transfer baby to the unit's equipment
- Transfer and receiving teams to agree order in which transfer happens
- After transfer, dispose of any partially used drugs and infusions before returning to ambulance.

N.B: There is an On-Going Plan for a New Protocol for "AVIAN-TRANSPORTATION"

ANNEX

Neonatal Resuscitation Program®, 8th Edition - Reference Chart

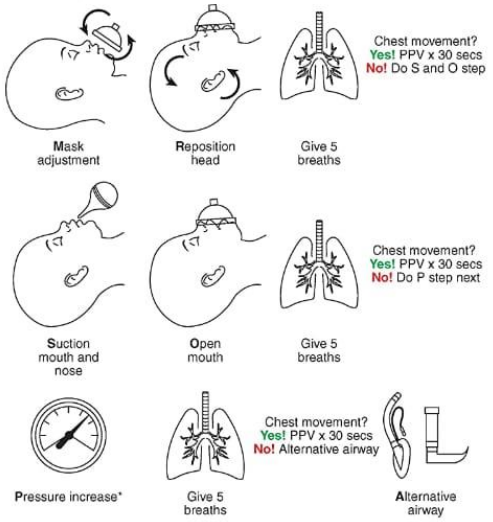
The most important and effective step in neonatal resuscitation is ventilation of the baby's lungs.



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

Ventilation Corrective Steps (MR. SOPA)

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



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

Endotracheal Intubation

Gestational Age (weeks)	Depth of Insertion at Lips (cm)	ET Tube Size (ID, mm)
23-24	5.5	Size 2.5 < 1 kg or < 28 weeks
25-26	6.0	
27-29	6.5	Size 3.0 1-2 kg or 28-34 weeks
30-32	7.0	
33-34	7.5	Size 3.5 > 2 kg or > 34 weeks
35-37	8.0	
38-40	8.5	
41-43	9.0	3.5-4.0

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

Neonatal Code Medications

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

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

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

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NRP339

The recommendations in this publication do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

Hyperglycaemia

- Increase the insulin by increments of 0.05–0.1 units/kg/hour. Target blood glucose while on insulin is 6–8 mmol/L
- Once blood glucose stable, continue to monitor blood glucose 4-hourly
- When a baby is on insulin it is very important to prevent hypoglycaemia – see below

Preventing Hypoglycaemia

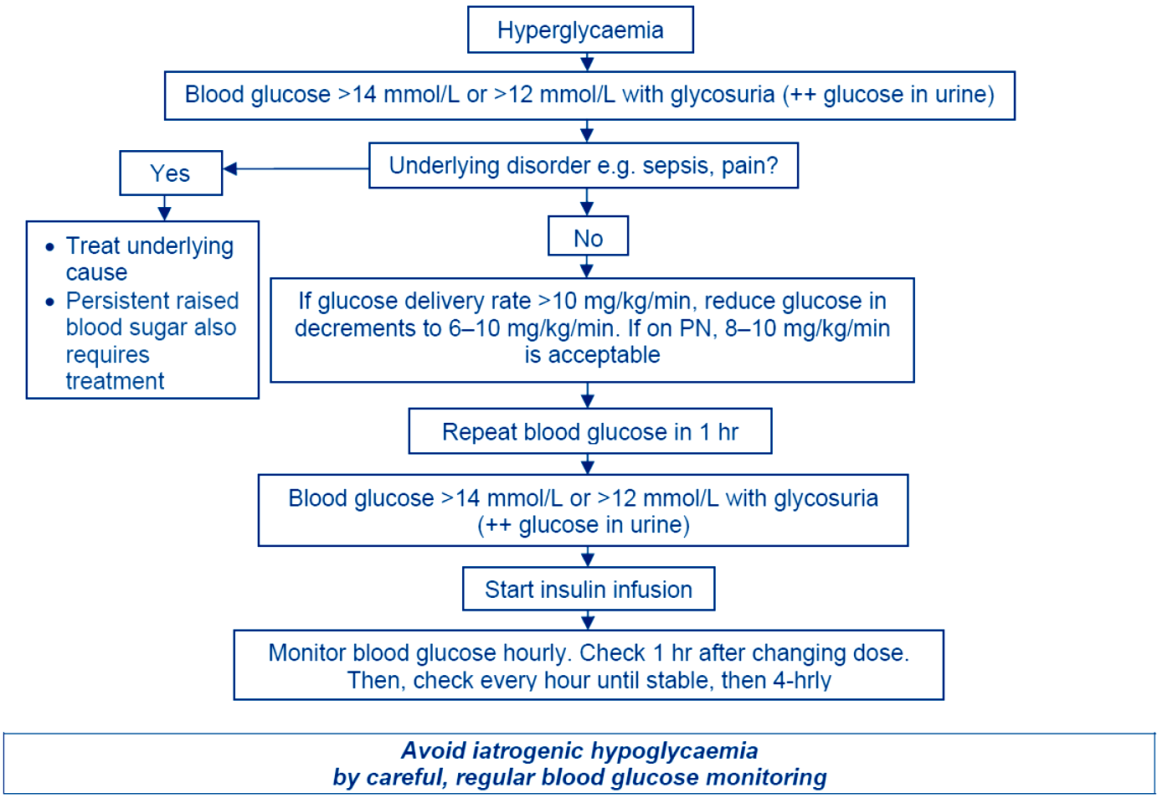
Blood glucose (mmol/L)	Insulin infusion rate
>8	• Increase infusion rate in steps of 0.05–0.1 unit/kg/hr rate of increase will be dependent on rate of fall in blood glucose
6–8	• Maintain at current rate
>4–<6	• Reduce infusion rate in steps of 0.05–0.1 units/kg/hr to maintain blood glucose >4 mmol/L rate of reduction will be dependent on rate of fall in blood glucose
≤4	• Stop infusion

- Recheck blood glucose 1 hour after reducing dose, then 1–2 hourly until stable, then 4-hourly when stable
- If unable to wean off insulin after 1-week, transient neonatal diabetes is possible; consult paediatric endocrinologist
- Early introduction of PN and early trophic enteral feeding will help reduce incidence of hyperglycaemia requiring insulin

Administration of Actrapid Insulin (Soluble Insulin):

- Follow instructions in Neonatal Formulary for making up insulin infusion
- Administer Actrapid insulin infusion via a central line or dedicated peripheral cannula
- Before starting infusion, prime all IV connecting and extension sets and T-connectors with insulin Infusion fluid. Check manufacturer's guide on lumen capacity for priming volumes (insulin can adhere to The plastic of the syringe)

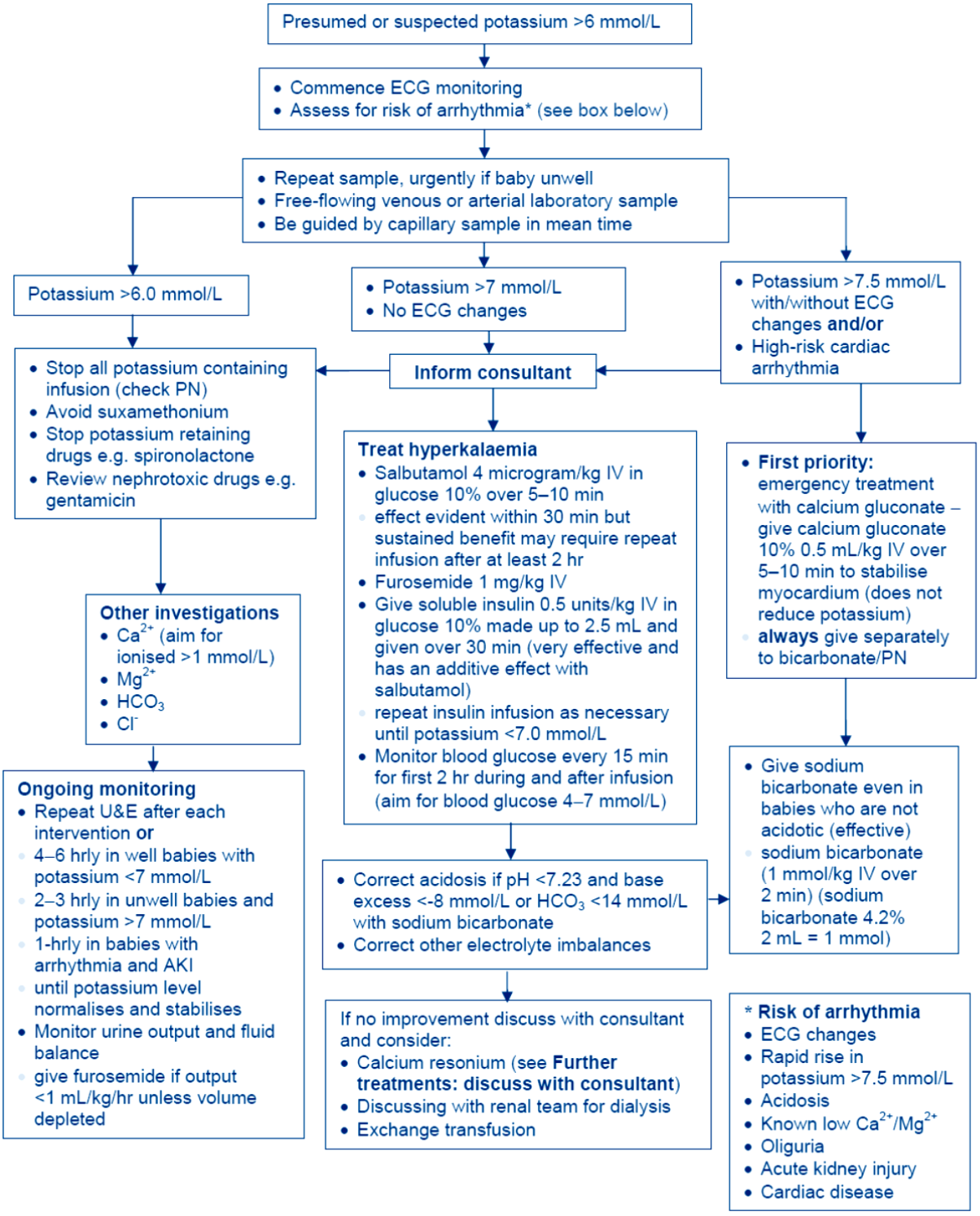
Summary of Neonatal Hyperglycaemia Management



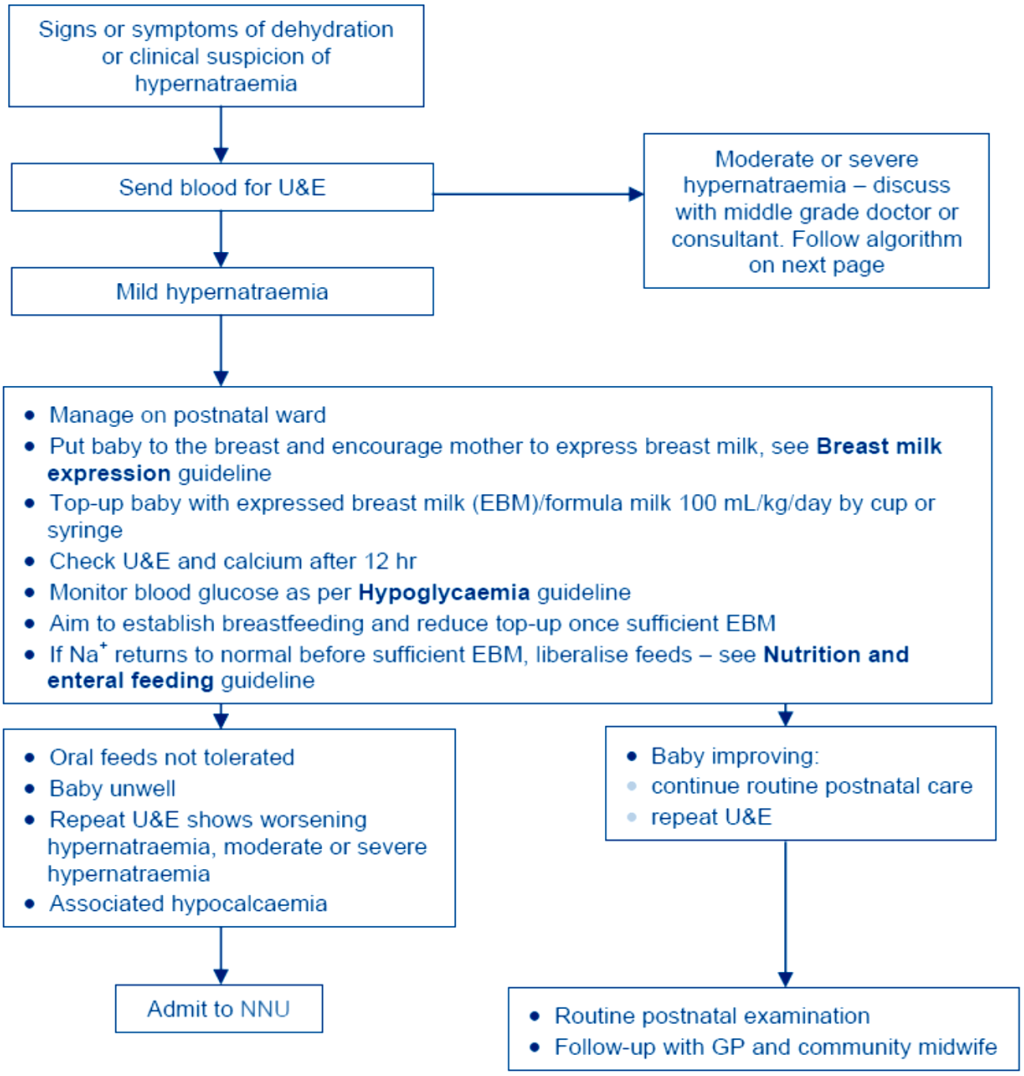
Avoid iatrogenic hypoglycaemia by careful, regular blood glucose monitoring

Hyperkalaemia:

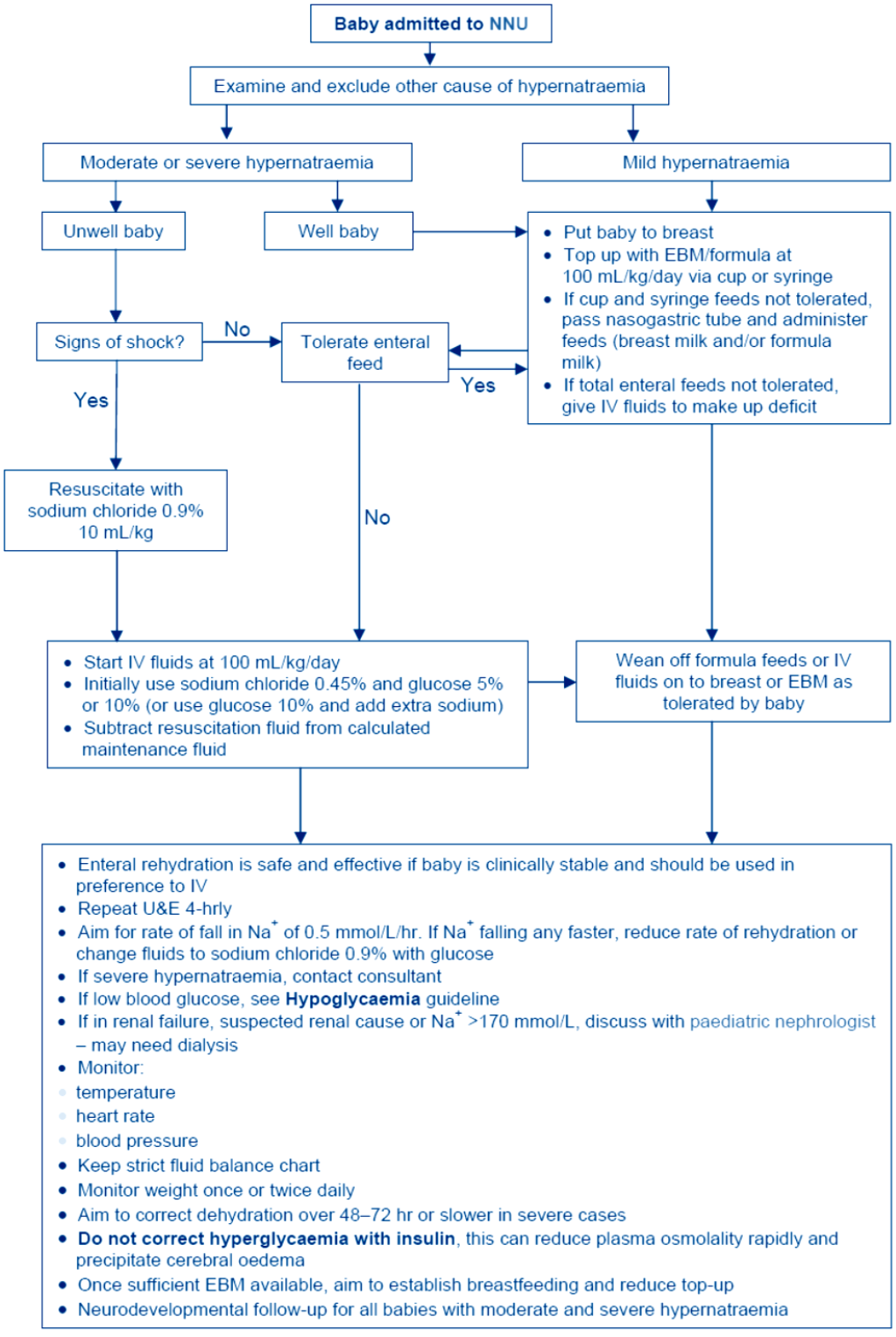
Flowchart: Management of Hyperkalaemia in Neonates



Hypernatraemic Dehydration:

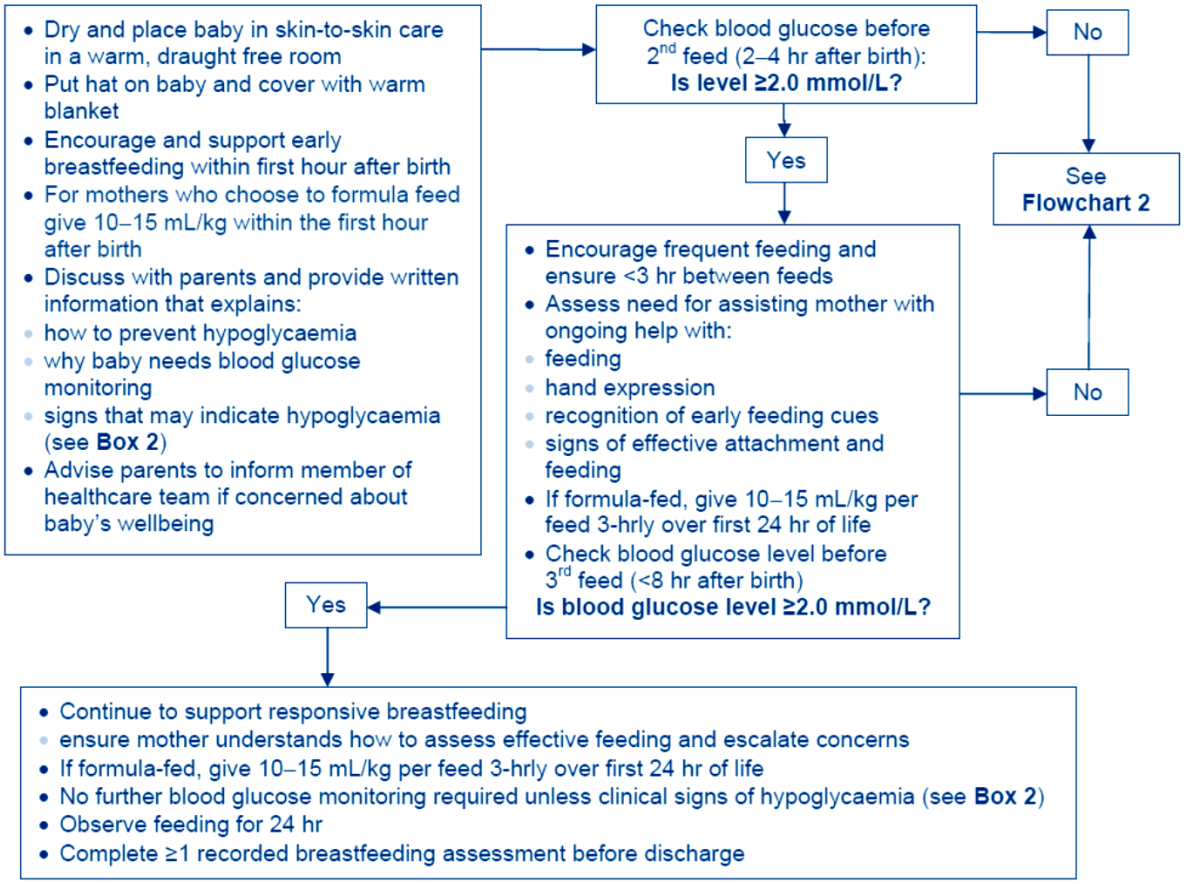


Management


Baby admitted to NNU
Examine and exclude other cause of hypernatraemia
Moderate or severe hypernatraemia
Mild hypernatraemia
Unwell baby
Well baby
Signs of shock?
No
Tolerate enteral feed
Yes
Yes
No
Resuscitate with sodium chloride 0.9% 10 mL/kg
Put baby to breast
Top up with EBM/formula at 100 mL/kg/day via cup or syringe
If cup and syringe feeds not tolerated, pass nasogastric tube and administer feeds (breast milk and/or formula milk)
If total enteral feeds not tolerated, give IV fluids to make up deficit
Start IV fluids at 100 mL/kg/day
Initially use sodium chloride 0.45% and glucose 5% or 10% (or use glucose 10% and add extra sodium)
Subtract resuscitation fluid from calculated maintenance fluid
Wean off formula feeds or IV fluids on to breast or EBM as tolerated by baby
Enteral rehydration is safe and effective if baby is clinically stable and should be used in preference to IV
Repeat U&E 4-hrly
Aim for rate of fall in Na+ of 0.5 mmol/L/hr. If Na+ falling any faster, reduce rate of rehydration or change fluids to sodium chloride 0.9% with glucose
If severe hypernatraemia, contact consultant
If low blood glucose, see Hypoglycaemia guideline
If in renal failure, suspected renal cause or Na+ >170 mmol/L, discuss with paediatric nephrologist – may need dialysis
Monitor:
temperature
heart rate
blood pressure
Keep strict fluid balance chart
Monitor weight once or twice daily
Aim to correct dehydration over 48–72 hr or slower in severe cases
Do not correct hyperglycaemia with insulin, this can reduce plasma osmolality rapidly and precipitate cerebral oedema
Once sufficient EBM available, aim to establish breastfeeding and reduce top-up
Neurodevelopmental follow-up for all babies with moderate and severe hypernatraemia

Hypoglycaemia:

Flowchart 1: Management of babies ≥37 weeks at risk of hypoglycaemia



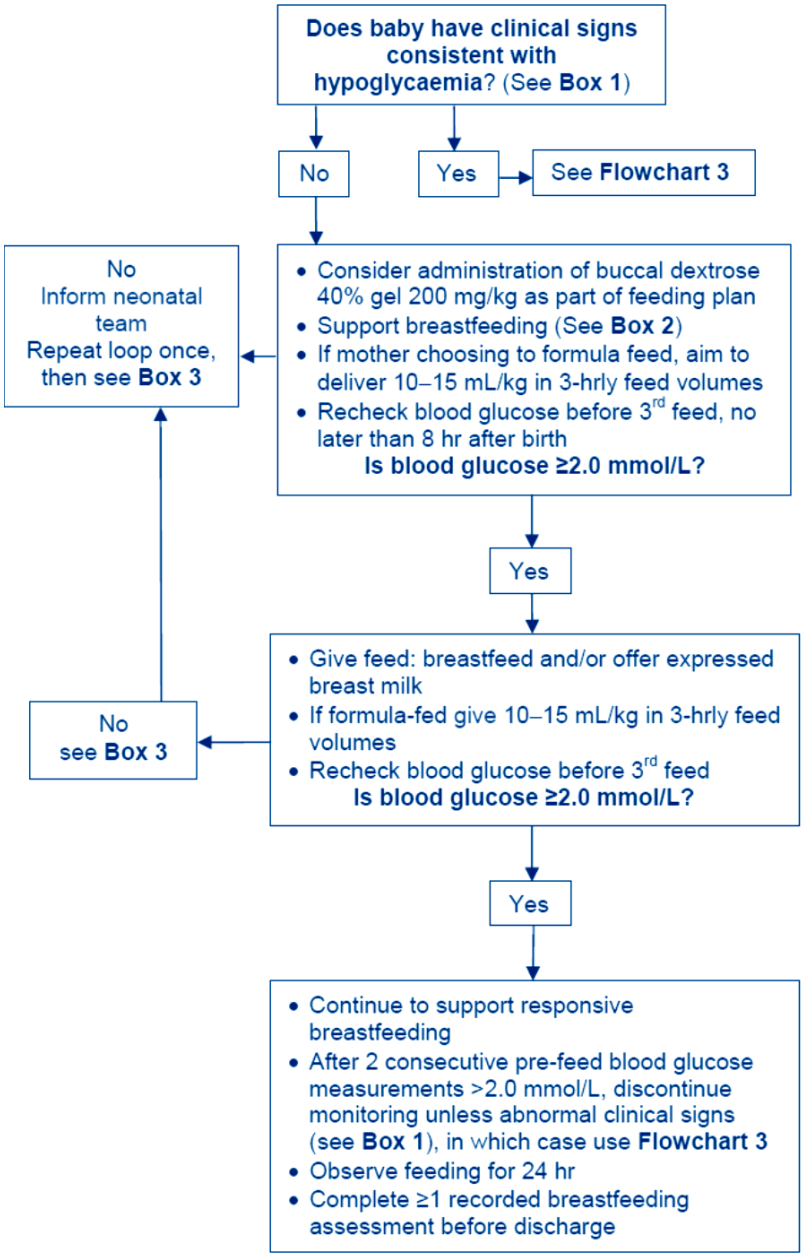
Box 1: Babies requiring routine blood glucose monitoring

- Intrauterine growth restriction (≤2nd centile for gestation, age and sex, refer to BAPM NEWTT thresholds – see **Table 1**) or clinically wasted
- Babies of diabetic mothers
- Maternal beta blocker use

Box 2: Signs that may indicate hypoglycaemia

- Lethargy
- Abnormal feeding behaviour especially after a period of feeding well
- High pitched cry
- Altered level of consciousness
- Hypotonia
- Seizures
- Hypothermia (<36.5°C)
- Cyanosis
- Apnoea

Flowchart 2: Pre-feed blood glucose 1.0-1.9 mmol/L and no abnormal



Box 1: Signs that may indicate hypoglycaemia

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- Abnormal feeding behaviour especially after a period of feeding well
- High pitched cry
- Altered level of consciousness
- Hypotonia
- Seizures
- Hypothermia (<36.5°C)
- Cyanosis
- Apnoea

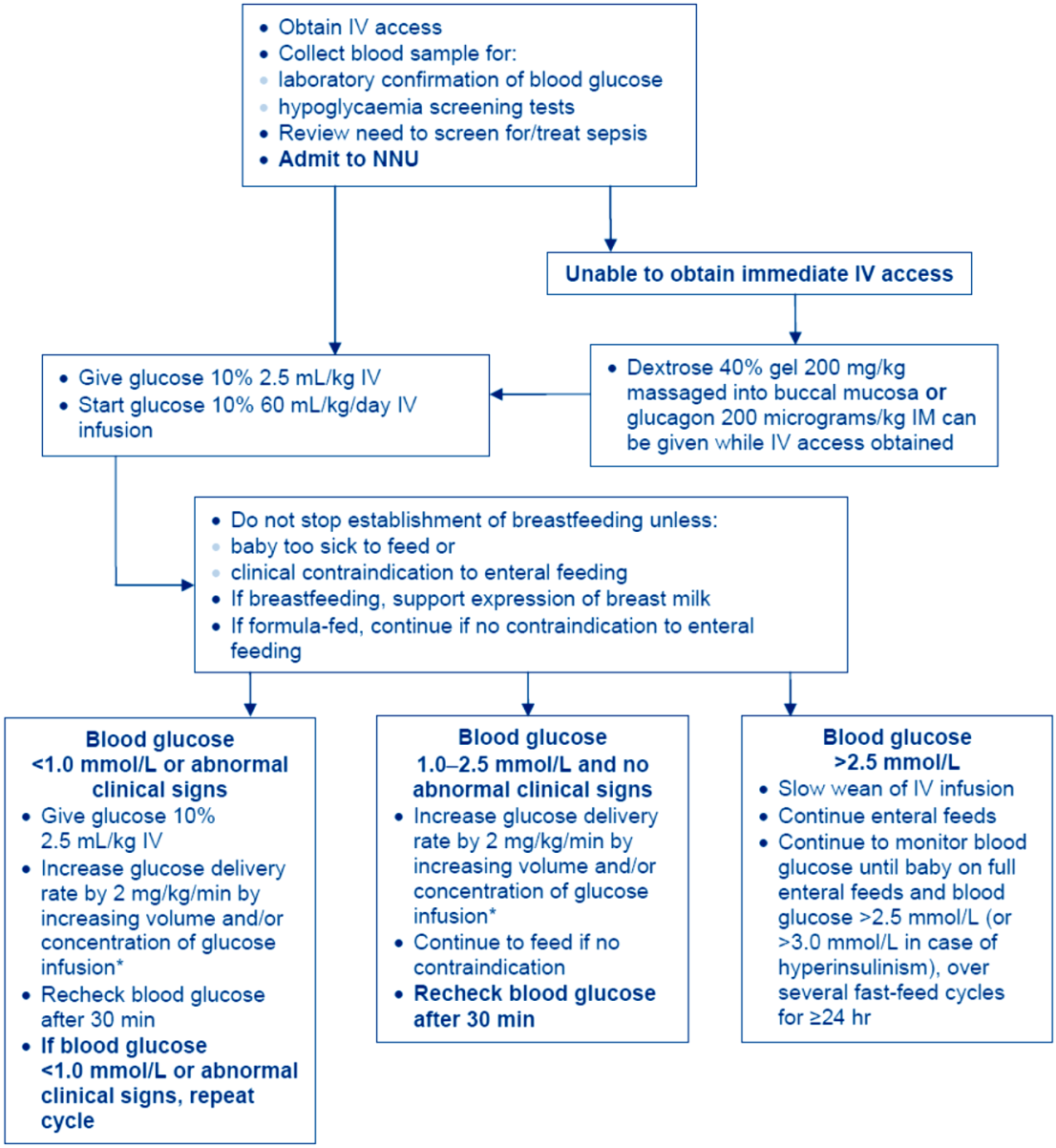
Box 2: Supporting breastfeeding

- Encourage continuous skin-to-skin contact
- Offer breastfeed and if not feeding effectively teach mother to hand express
- Give obtained colostrum to baby by method suitable to parents
- Continue to encourage hand expression ≥8–10 times in 24 hr and support breastfeeding until baby is feeding effectively

Box 3: If >2 blood glucose measurements 1.0–1.9 mmol/L, inform neonatal team

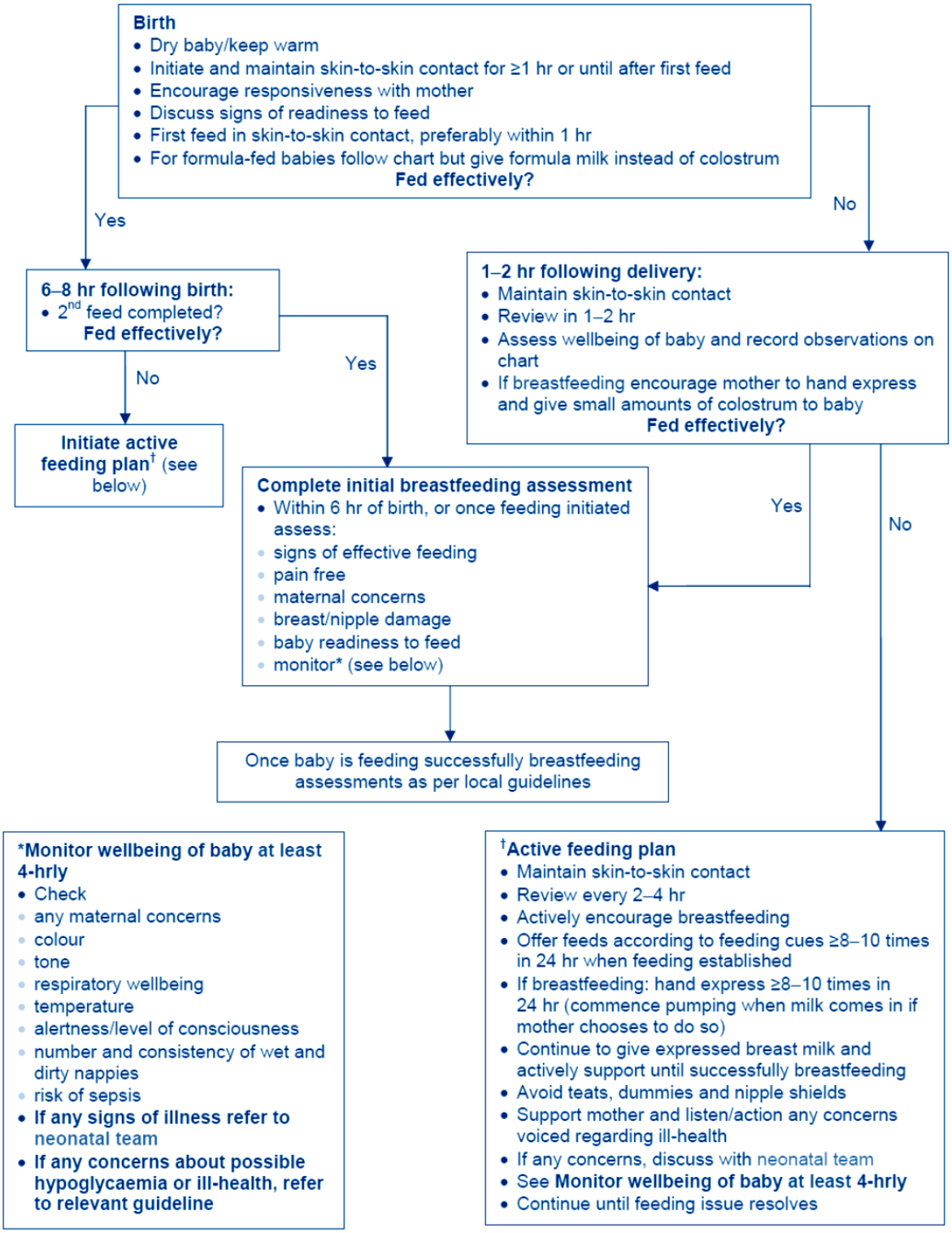
- Investigate for causes of hypoglycaemia, consider sepsis
- Consider increased feed frequency, NGT insertion or glucose 10% IV infusion

Flowchart 3: Blood glucose <1.0 mmol/L and/or clinical signs consistent with hypoglycaemia



*** If glucose infusion rate >8 mg/kg/min, test for hyperinsulinism**

Flowchart 4: Management of reluctant feeding in healthy breastfed infants ≥37 weeks



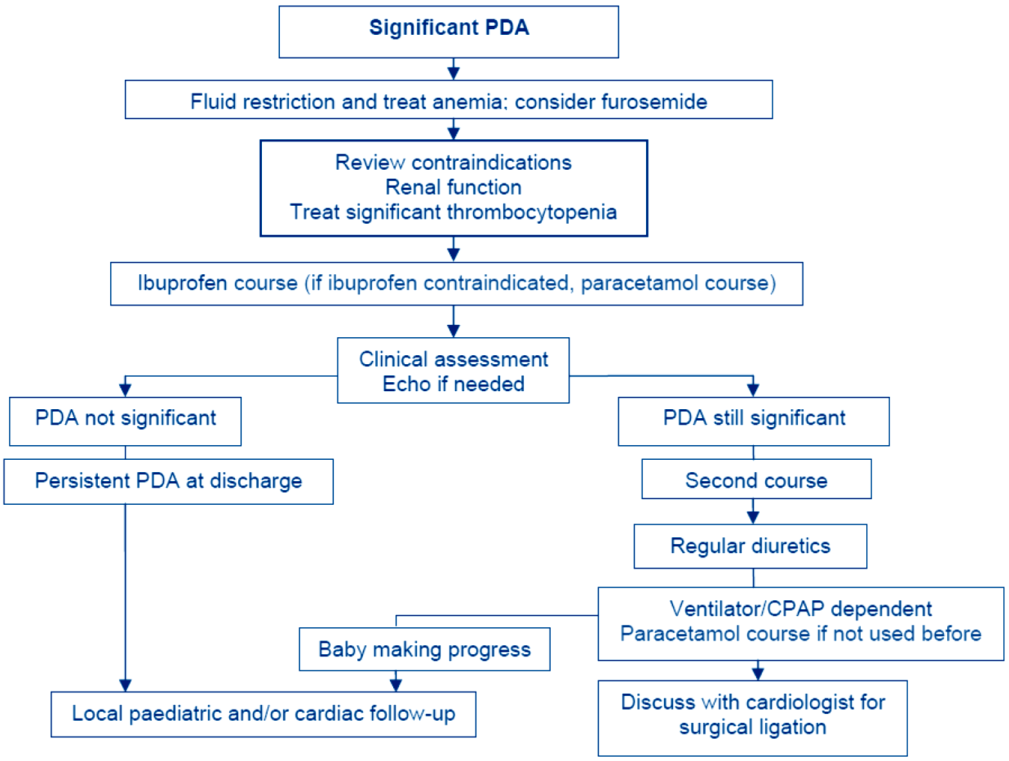
Patent Ductus Arteriosus:

- Prostaglandin inhibitor not indicated (≥34 weeks with cardiac failure not controlled by diuretics)
- Prostaglandin inhibitor ineffective (usually after giving second course). Paracetamol used as third course If not used before, while considering surgical ligation
- Discuss further cardiac assessment and surgical ligation of PDA with cardiologist at regional cardiac Center and transport team − follow local care pathway (e.g. West Midlands PDA Ligation Referral Pathway)
- After surgical ligation, keep baby nil-by-mouth for 24 hour before gradually building up feeds (because of risk of NEC)

Discharge Policy for Persistent PDA:

- If PDA persistent clinically or echocardiographically at discharge or at 6 weeks follow-up, arrange further follow-ups in cardiac clinic (locally or at cardiac center depending on local practice)
- If PDA reviewed locally still persistent at aged 1 yr or if clinically significant during follow-up (cardiac failure or failure to thrive), refer to paediatric cardiologist at regional cardiac center to consider closure (first option is usually catheter closure)

Medical Treatment of Persistent PDA <34 weeks' gestation



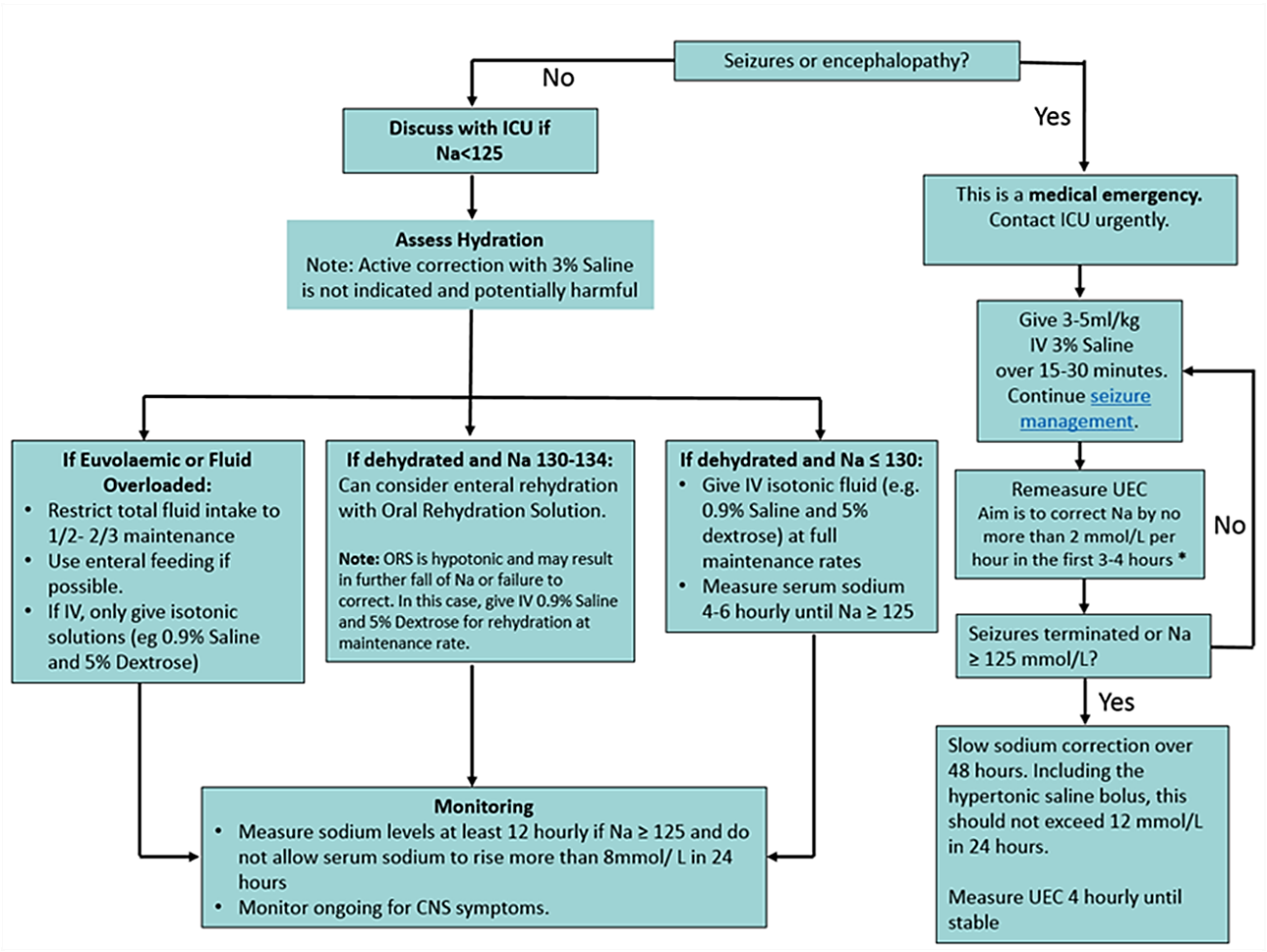
Hypocalcaemia:

Asymptomatic Infants	Symptomatic Hypocalcaemia
•Most infants with early onset hypocalcaemia recover with nutritional support; so early feeding provides adequate calcium •Infants requiring IV fluid: add calcium gluconate 10% 0.46 mmol/kg/day (= 2 mL/kg/day) to IV fluid and give as continuous infusion •Infant tolerating oral feeds: give 0.25 mmol/kg oral 6-hourly	•If seizures, prolonged QT interval, apnoea, unstable or poor feeding give IV calcium gluconate 10% 0.11 mmol/kg (= 0.5 mL/kg) over 5−10 min followed by maintenance •Dilute with sodium chloride 0.9% or glucose 5% 4 mL to each 1 mL calcium gluconate 10% to give a concentration of 45 micromol/mL. Can be given undiluted via central line in an emergency •Doses up to 0.46 mmol/kg (= 2 mL/kg calcium gluconate 10%) have been used •Maximum rate of administration 22 micromol/kg/hour

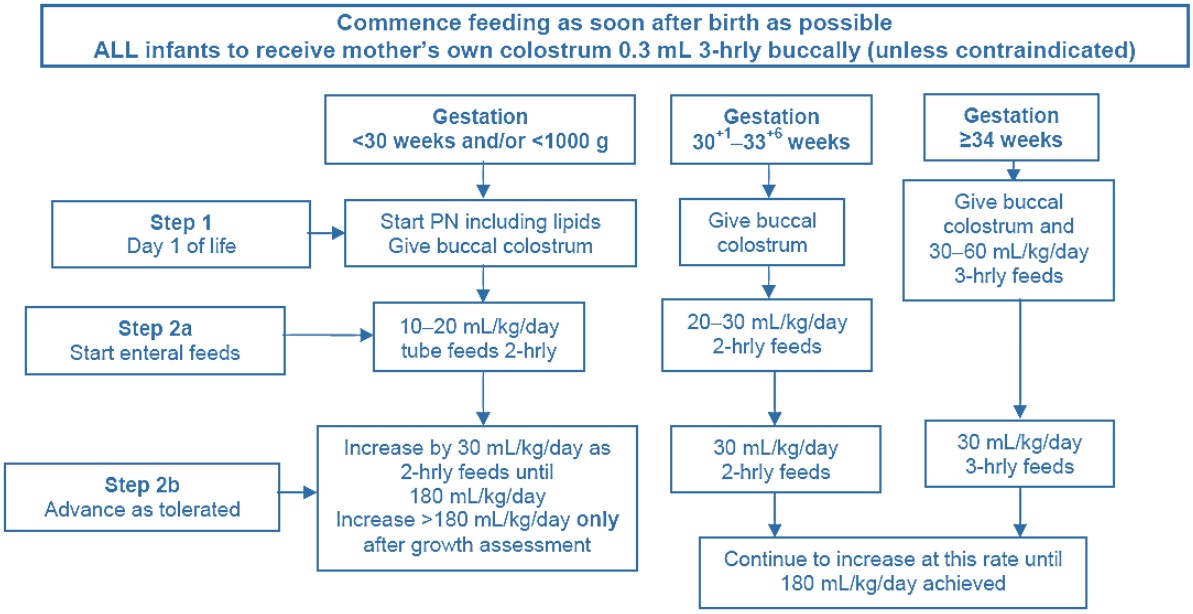
SOURCE:

- **2019–21 Bedside Clinical Guidelines Partnership (University Hospital of North Midlands NHS Trust) - Page:155**

Hyponatraemia:



Initiation and Advancing Enteral Feeding:



- If mother's expressed breast milk (MEBM) not available within 48 hr of birth, use donor expressed breast milk (DEBM) if criteria met, or preterm formula
- If unable to advance enteral feeds over several days refer to neonatal/paediatric dietitian

Neonatal Resuscitation Program (Quick Equipment Checklist):

Neonatal Resuscitation Program® Quick Equipment Checklist

This checklist includes only the most essential supplies and equipment needed at the radiant warmer for most neonatal resuscitations. Tailor this list to meet your unit-specific needs. Ensure that an equipment check has been done prior to every birth.

	• Preheated warmer
	• Warm towels or blankets
	• Temperature sensor and sensor cover for prolonged resuscitation
	• Hat
	• Plastic bag or plastic wrap (<32 weeks' gestation)
	• Thermal mattress (<32 weeks' gestation)
	• Bulb syringe
	• 10F or 12F suction catheter attached to wall suction, set at 80 to 100 mm Hg
	• Meconium aspirator
	• Stethoscope
	• Flowmeter set to 10 L/min
	• Oxygen blender set to 21% *(21%-30% if <35 weeks' gestation)*
	• Positive-pressure ventilation (PPV) device
	• Term- and preterm-sized masks
	• 8F feeding tube and 20-mL syringe
	• Equipment to give free-flow oxygen
	• Pulse oximeter with sensor and cover
	• Target oxygen saturation table
	• Laryngoscope with size-0 and size-1 straight blades (size 00, optional)
	• Stylet (optional)
	• Endotracheal tubes (sizes 2.5, 3.0, 3.5)
	• Carbon dioxide (CO_2) detector
	• Measuring tape and/or endotracheal tube insertion depth table
	• Waterproof tape or tube-securing device
	• Scissors
	• Laryngeal mask (size 1) and 5-mL syringe
	Access to
	• 1:10,000 (0.1 mg/mL) epinephrine
	• Normal saline
	• Supplies for placing emergency umbilical venous catheter and administering medications
	• Electronic cardiac (ECG) monitor leads and ECG monitor

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Phototherapy and Exchange Transfusion Guidelines for Preterm Infants < 35 Weeks Gestational Age:

Use total bilirubin (add conjugated and unconjugated bilirubin). If conjugated bilirubin is > 50% of total serum bilirubin, consult staff physician to determine levels for therapy.

PHOTOTHERAPY INITIATION LEVELS
Total serum bilirubin (TSB) (micromol/litre)

- For infants > 1000 grams use INTENSIVE phototherapy (irradiance ~30µW/cm2/nm)
- For infants ≤ 1000 grams use STANDARD phototherapy (irradiance ~10µW/cm2/nm) unless TSB is rapidly rising or TSB continues to rise while receiving phototherapy (less irradiance used to reduce risk of oxidative tissue injury by phototherapy in extremely immature infants)

Gestational Age (weeks)	Age in Hours	<24 hours	24-48 hours	49-72 hours	> 72 hours
	<28 0/7 and at risk*	70	80	80	90
	<28 0/7	80	90	90	100
	28 0/7 to 29 6/7 and at risk*	80	90	90	100
	28 0/7 to 29 6/7	90	100	120	140
	30 0/7 to 31 6/7 and at risk*	90	100	120	140
	30 0/7 to 31 6/7	100	120	140	170
	32 0/7 to 33 6/7 and at risk*	100	120	140	170
	32 0/7 to 33 6/7	100	130	170	200
	34 0/7 to 34 6/7 and at risk*	110	140	170	200
	34 0/7 to 34 6/7	110	160	210	230

NB: To Convert from (Mmol/L) to (mg / dl) divide the number by 17

EXCHANGE TRANSFUSION LEVELS

Total serum bilirubin (TSB) (micromol/litre)

- Exchange transfusion is recommended for infants whose TSB levels continue to rise to exchange levels despite receiving intensive phototherapy to the maximal surface area
- Exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, high-pitched cry); even if below exchange levels (but note that these signs can be subtle in very low birth weight infants and may be difficult to detect)

Gestational Age (weeks)	Age in Hours	<24 hours	24-48 hours	49-72 hours	> 72 hours
	<28 0/7 and at risk*	190	190	210	220
	<28 0/7	190	200	210	240
	28 0/7 to 29 6/7 and at risk*	200	200	210	220
	28 0/7 to 29 6/7	200	210	220	240
	30 0/7 to 31 6/7 and at risk*	220	220	230	260
	30 0/7 to 31 6/7	220	230	260	270
	32 0/7 to 33 6/7 and at risk*	240	240	260	300
	32 0/7 to 33 6/7	240	250	290	300
	34 0/7 to 34 6/7 and at risk*	250	260	290	310
	34 0/7 to 34 6/7	260	270	310	320

NB: To Convert from (Mmol/L) to (mg / dl) divide the number by 17

***INFANTS AT GREATER RISK for BILIRUBIN TOXICITY**

Risk factors for bilirubin toxicity include:

- serum albumin level < 25 g/L
- rapidly rising TSB levels, greater than 8.5 micromol/litre/hour suggesting haemolytic disease
- clinically unstable infants*

*Clinically unstable infants:

if one or more of the following in the preceding 24 hours:

- blood pH < 7.15
- blood culture positive sepsis
- apnea and bradycardia requiring cardio-respiratory resuscitation (bagging and/or intubation)
- hypotension requiring pressor treatment
- mechanical ventilation at time of blood sampling

Providing and Discontinuing Phototherapy:

- The purpose of phototherapy is to prevent the need for exchange transfusion. With phototherapy, the serum bilirubin should decrease by approximately 20-35 micromol/litre in 4-6 hours.
- Use gestational age for the first 7 days of age and then postmenstrual age for determining phototherapy initiation levels. For example, if the infant is born with a gestational age of 29 2/7 weeks, use the 28 0/7 to 29 6/7 weeks category until the infant is 7 days of age; then after 7 days of age, use the TSB level for 30 0/7 weeks.
- Discontinuing phototherapy: discontinue phototherapy when the TSB is 20-35 micromol/litre below the initiation level. Check TSB 6-12 hours after discontinuing phototherapy to assess for rebound.

Rationale for Levels (see reverse for references):

- Treatment thresholds are based on published expert opinion that utilized best available, but limited data.
- Phototherapy levels in the first 24 hours of age were adapted from National Institute for Health and Clinical Excellence (NICE) United Kingdom (U.K.) guidelines.
- Phototherapy levels between 24 and 72 hours of age were adapted from a combination of NICE guidelines and Maisels et al (2012) guidelines.
- Exchange levels before 72 hours of age were adapted from Maisels et al (2012) guidelines.
- Phototherapy and exchange levels beyond 72 hours of age, (EXCEPT for GA 34 weeks): levels were adapted from Maisels et al (2012) guidelines as these treatment thresholds are lower than NICE guidelines.
- Phototherapy and exchange levels beyond 72 hours, for gestational age (GA) 34 weeks: levels were adapted to align with AAP/CPS levels for GA ≥35 weeks.

REFERENCES:

Phototherapy table adapted from:

1. Maisels MJ, Watchko JF, Bhutani VK, Stevenson DK. An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation. Journal of Perinatology (2012) 32, 660–664.
2. National Institute for Health and Clinical Excellence. Neonatal Jaundice. National Institute for Health and Clinical Excellence, 2010, www.nice.org.uk/CG98
3. Morris BH, Oh W, Tyson JE, Stevenson D, Phelps DL, O'Shea TM et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight. New Engl J Med 2008; 359: 1885–896.
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Exchange transfusion table adapted from:

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3. American Academy of Pediatrics. Subcommittee on hyperbilirubinemia. Clinical practice guideline: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004; 114: 297–316.

PPHN:

Nitric Oxide (inhaled)	In newborns >34 weeks' gestation, the maximum recommended dose of nitric oxide is 20 ppm and this dose should not be exceeded. Starting as soon as possible, and in the first 4 to 24 hours of therapy, the dosage must be reduced gradually to 5 ppm or less, titrating it to the needs of the individual patient. Treatment can be continued until the oxygen desaturation is resolved and the patient is ready for gradual withdrawal. The required duration varies but should be as brief as possible, and is typically less than 4 days
Epoprostenol (intravenous)	Initially 2 nanograms/kg/minute adjusted according to response; usual maximum dose 20 nanograms/kg/minute (rarely up to 40 nanograms/kg/minute) by continuous intravenous infusion.d
Magnesium Sulfate (intravenous)	Initially 200 mg/kg (0.8 mmol/kg Mg2+) magnesium sulfate heptahydrate over 20–30 minutes; if response occurs, then 20–75 mg/kg/hour (0.08–0.3 mmol/kg/hour Mg2+) by continuous intravenous infusion for up to 5 days.d
Milrinone (intravenous)	0.25 to 0.75 micrograms/kg/min by continuous intravenous infusion for up to 35 hours.g
Sildenafil (oral)	Initially 250–500 micrograms/kg every 4–8 hours, adjusted according to response; max. 30 mg daily; start with lower dose and frequency especially if used with other vasodilators.d
Sildenafil (intravenous)	A trial (NCT01720524) is ongoing using intravenous sildenafil at a loading dose of 0.1 mg/kg over 30 minutes followed by a maintenance dose of 0.03 mg/kg/hour for a minimum of 48 hours and maximum of 14 days

SOURCE:

- **Pulmonary hypertension in neonates:**
  - **Sildenafil Evidence summary Published: 29 March 2016**
  - **www.nice.org.uk/guidance/esuom51**

Management of Persistent Pulmonary Hypertension of the Newborn:

Background: To recommend evidence based or best practice for management of persistent pulmonary hypertension (PPHN) in the newborn term and preterm infant. PPHN is failure of the circulatory transition from intra- to extra-uterine life, resulting in high pulmonary pressures leading to extra-pulmonary right to left shunting (across PDA/PFO) causing hypoxaemia.

Consider PPHN diagnosis:
- Often term or near term infant
- Onset at birth or few hours after
- Profound hypoxia – low arterial PaO_2 on blood gas may be associated with low, normal or high $PaCO_2$
- **Always consider congenital cardiac disease presenting with a right to left shunt**

Investigations:
- **Echo** – gold standard; exclude congenital cardiac disease (TAPVD difficult); diagnose PPHN with raised pulmonary pressures and tricuspid regurgitation
- **Oxygen saturations** – Pre (right hand) and post-ductal (feet) differential of 10-15%; measure simultaneously
- **CXR** to exclude other pathology and guide respiratory management – lung expansion, RDS requiring surfactant etc. may be normal
- **Bloods** – FBC, coag, U&E, LFT, lactate, Ca^{2+}, Mg^{2+}
- **Cranial ultrasound** – if ECMO referral

General measures
- Minimal handling, reduce noise (minimuffs) and light (goggles)
- Normothermia
- Central access – UAC and double lumen UVC
- Antibiotics
- Sedation and muscle relaxation if intubated

Specific measures to consider if iNO not available or effective – on advice of tertiary/ECMO centre
- Milrinone
- Adenosine
- Alprostadil
- Epoprostenol
- Tolazoline
- Magnesium sulphate

Outcomes
- Mortality 10-20% - highest with hypoplastic pulmonary vasculature
- Often neurodevelopmental, cognitive and hearing problems (approx. 25%)

Oxygen Index = $\frac{\text{MAP (cmH20) x FiO2 x 100}}{\text{Post-ductal } PaO_2 \text{ (mmHg)}}$
(1KPa = 7.5mmHg)

OI > 15 consider iNO OI > 25 refer to ECMO

Take: the nitric tray and spare nitric cylinder
Additional saturation monitor

Use a multi-system, simultaneous approach to A,B, C

A - Intubate

B – Optimise oxygenation
- Give oxygen to achieve arterial PaO_2 >10 or saturations >95% (pre-ductal)
- Increase mean airway pressure as required
- Give surfactant if indicated (RDS, MAS)
- Optimise haemoglobin (transfuse if <140)
- Give sedation and muscle relaxation

Maintain normal PCO_2 4.5-5.5 KPa
Maintain normal pH 7.35 – 7.45
- Use sodium bicarbonate or THAM as needed

C – Optimise systemic blood pressure
- Term baby aim mean BP >50mmHg (may need to be higher, saturation gap should start to close)
- Give volume 10-20ml/kg 0.9% sodium chloride
- Give 'useful' volume eg. Packed cells, FFP if appropriate
- Optimise Ca^{2+}
- Start **dopamine** 5 microgram/kg/min, assess after 10 mins, increase to max 10 microgram/kg/min
- Start second agent early (dopamine @10 microgram/kg/min)
- **Dobutamine** 5-20 microgram/kg/min
- **Adrenaline** 0.05 microgram/kg/min to 1 microgram/kg/min

If poor response discuss with tertiary and/or ECMO centre
- **Hydrocortisone 2.5mg/kg/ iv QDS**
- **Noradrenaline** start at 0.1microgram/kg/min

OR
- **Vasopressin (Argipressin)** start at 0.009-0.03 units/kg/hr (seek ECMO centre advice for starting dose and use of higher doses)

Start iNO at 20ppm
- Consider use in preterm infants >26 weeks on an individual basis where there is evidence of PPHN

Reassess every 20 minutes
Consider referral to ECMO if OI>25

ECMO – refer via Embrace (through CenTre)
Exclusions:
- Known non-reversible underlying condition
- <34 weeks gestation
- <2kg
- Significant intracranial injury (need cranial ultrasound)

SOURCE:

- **Sheffield Children's (NHS) Foundation Trust**
- **Nair J, Lakshminrusimha S. Update on PPHN: Mechanism and Treatment Semin Perinat. 2014 March; 38 (2) 78-91**
- **North Trent Neonatal Network Clinical Guideline Persistent Pulmonary Hpyertension of the Newborn**
- **Guy's Paediatric Formulary Monograph Argipressin (8-Arginine vasopressin) July 2015**

Practical Approach Persistent Pulmonary Hypertension of the Newborn:

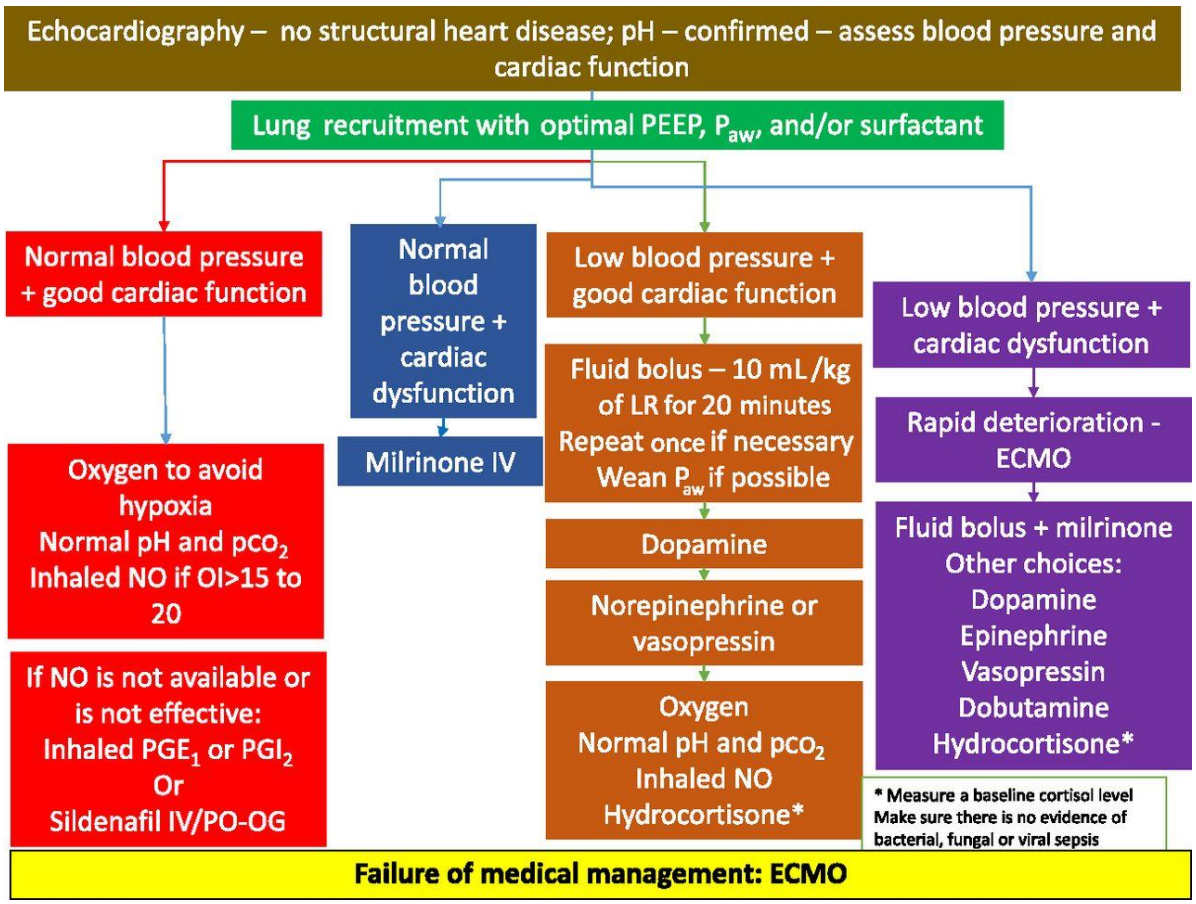

Figure Legend:

- Algorithm showing practical approach to persistent pulmonary hypertension of the newborn (PPHN) based on oxygenation, systemic blood pressure, and cardiac function. See text for details.
- ECMO=extracorporeal membrane oxygenation; IV=intravenous; LR=lactated ringers solution; NO=nitric oxide; OI=oxygenation index; Paw=mean airway pressure; PEEP=positive end-expiratory pressure; PGE1=prostaglandin E1; PGI2=prostaglandin I2; PO-OG=per oral or orogastric.

SOURCE:

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Prophylaxis of Respiratory Syncytial Virus (RSV)

RSV accounts for approximately 50% of all cases of pneumonia and up to 90% of the reported cases of bronchiolitis in infancy.

RSV infection frequently progresses to the lower respiratory tract, where it can cause wheezing, cough, and dyspnea in infants, these symptoms usually appear 1 to 3 days after the onset of rhinorrhea.

High Risk population

- Higher-Risk Populations Include Preterm Infants and Children <2 Years Old With BPD or HSCHD.
- Hospitalization rates are higher in high-risk groups, including premature infants and those with underlying cardiac or pulmonary diseases.

Prophylaxis: Palivizumab

Passive prophylaxis with palivizumab decreases the frequency of hospitalization for RSV in high-risk infants. It is cost-effective only for infants at high risk of hospitalization.

1-Children born at 35 weeks of gestation or less and less than 6 months of age at the onset of the RSV season.

2- Children less than 2 years of age and requiring treatment for bronchopulmonary dysplasia within the last 6 months.

3- Children less than 2 years of age and with hemodynamically significant congenital heart disease.

NB:

- Palivizumab should be administered up to a maximum of 5 monthly doses (15 mg/kg per dose administered intramuscularly once every 30 days) during the RSV season to infants who qualify for prophylaxis in the first year of life.
- A child with a history of a severe allergic reaction following a dose of Palivizumab should not receive additional doses.
- Palivizumab is not approved or recommended for the treatment of RSV disease
- Palivizumab does not interfere with routine childhood immunizations.

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