



# **DED ER GENERAL HOSPITAL**

**NEONATAL INTENSIVE CARE UNIT (NICU)**

**STANDARD TREATMENT GUIDELINES  
(STG) PROTOCOL**

*“Adapted from National STG 2021 4<sup>th</sup> Edition”*

***October 2024***

***Deder, Eastern Ethiopia***

### SMT APPROVAL SHEET

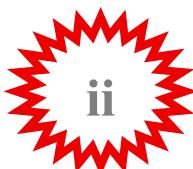
<b>TITLE</b>	<b>Title:</b> NEONATAL INTENSIVE CARE UNIT STANDARD TREATMENT GUIDELINE PROTOCOL <b>Version:</b> 1.0			
	<b>NAME</b>	<b>POSITION</b>	<b>ROLE</b>	<b>SIGN</b>
<b>AUTHORS</b>	Abdi Tofik (BSc, MPH)	Quality Director	Team leader	
	Abdella Aliyi (BSc MW)	Quality Officer	Member	
	Mahammad Aliyi (BSc N)	Reform head	Member	
	<b>Draft Date:</b> July 15, 2016E.C		<b>Approved Date:</b> July 20, 2016E.C	
<b>SMT APPROVAL</b>	<b>Name</b>	<b>Position</b>	<b>Role</b>	<b>Sign</b>
<b>SMT APPROVAL</b>	Nuredin Yigezu (BSc, MPH)	CEO	Chair person	
	Dr. Derese Gosa (GP)	Medical director	Member	
	Dr Isak Abdi (G/Surgeon)	Staff Representative	Member	
	Dr. Dawit Seifu (GP)	IPD Director	Member	
	Abdi Tofik (BSc, MPH)	Quality Director	Member	
	Hamza Jamal (BSc N)	Metron	Member	
	Abrahim Tahir (BSc N)	HR Head	Secretary	
	Obsa Usma'il (BA)	Finance and procurement head	Member	
	Bellisa Usma'il (BSc Pharm)	Pharmacy head	Member	
	Alamudin Usma'il (BSc Lab)	Laboratory head	Member	
	Dine Bakar (BA)	Internal Auditor	Member	
	Redwan Sharafuddin (BSc Pharm)	Planning Head	Member	
<b>REVIEW</b>	<b>Reviewed and updated</b> <b>Review date:</b> July 2018E.C			

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# **SECTION 1:**

# **INTRODUCTION**

## **1.1 Background**

Neonatal mortality remains a significant public health challenge in Ethiopia, with the first 28 days of life being the most vulnerable period. The Neonatal Intensive Care Unit (NICU) at Deder General Hospital serves as a critical referral center for sick newborns in Eastern Ethiopia. Data from the Ethiopian **Fiscal Year (FY) 2016** E.C. identified the top five leading causes of neonatal morbidity and mortality in the NICU as:

- Preterm birth complications
- Birth asphyxia
- Neonatal sepsis
- Hypothermia
- Hypoglycemia

This Standard Treatment Guideline (STG) for the NICU is developed to standardize clinical care, improve outcomes, and reduce preventable neonatal deaths. It is adapted from the *National Neonatal Intensive Care Unit (NICU) Treatment Guideline 2021*, aligned with the Ethiopian Essential Medicines List (EML), and contextualized to the infrastructure, staffing, and patient load at Deder General Hospital.

## **1.2 Purpose of the NICU STG**

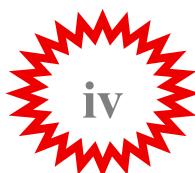
**This NICU-specific Standard Treatment Guideline serves to:**

1. Standardize clinical practice – Ensure consistent, evidence-based management of common neonatal conditions across all shifts and providers.
2. Improve quality of care – Reduce clinical variability, prevent errors, and enhance survival and neurodevelopmental outcomes.
3. Promote rational use of medicines and resources – Align prescribing with the EML and hospital formulary, minimizing waste and overuse.
4. Support antimicrobial stewardship – Guide appropriate antibiotic use to combat antimicrobial resistance (AMR).
5. Facilitate training and mentorship – Serve as a reference for neonatal care for doctors, nurses, pharmacists, and interns.
6. Enable monitoring and evaluation – Provide a framework for auditing clinical performance and outcomes.

## **1.3 Rationale for Hospital-Specific Adaptation**

While the National NICU Guideline provides a robust national framework, local adaptation is essential due to:

- Resource availability: Variability in access to ventilators, CPAP, laboratory services, and medications.
- Patient volume and case mix: High burden of preterm and asphyxiated neonates requiring tailored protocols.
- Staffing capacity: Mix of experienced and newly graduated staff requiring clear, step-by-step guidance.
- Referral system limitations: Delays in referrals necessitate extended in-hospital management.
- Local epidemiology: High rates of sepsis and perinatal asphyxia influencing treatment priorities.



## **1.4 Need for NICU-Specific STG**

The National NICU Guideline is comprehensive but requires contextualization for operational feasibility. This hospital-specific STG ensures that:

- Protocols are practical within Deder General Hospital's resource constraints.
- Treatments are safe and effective using available medicines and equipment.
- Staff have clear, accessible guidance for emergency and routine care.
- Continuity of care is maintained during shift changes and handovers.

## **1.5 Guiding Principles**

The Deder General Hospital NICU STG is built upon six core principles:

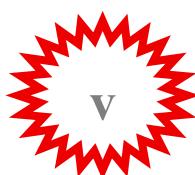
<b>PRINCIPLE</b>	<b>APPLICATION IN NICU</b>
Evidence-Based Practice	Recommendations are based on the National NICU Guideline 2021, WHO guidelines, and latest clinical evidence, adapted to local context.
Equity and Access	All neonates receive standardized, high-quality care regardless of socioeconomic status or referral origin.
Quality and Safety	Emphasis on correct diagnosis, infection prevention, safe medication administration, and reduction of medical errors.
Family-Centered Care	Parents are informed, involved in care decisions, and supported emotionally and educationally.
Cost-Effectiveness	Interventions balance clinical benefit with efficient use of limited resources (e.g., prioritizing CPAP over mechanical ventilation when appropriate).
Sustainability	Protocols are designed for long-term implementation using existing staff, equipment, and supply chains.

## **1.6 Scope of the Document**

### **1.6.1 Target Users**

This STG is intended for use by:

- Neonatologists and pediatricians
- Medical officers and interns
- NICU nurses and nurse practitioners
- Pharmacists and pharmacy technicians
- Laboratory staff involved in neonatal diagnostics



## **1.6.2 Exclusions**

This document does not cover:

- Pediatric conditions beyond the neonatal period (28 days)
- Obstetric and maternal care (managed under MCH protocols)
- Surgical emergencies requiring immediate transfer to pediatric surgery
- Palliative care for non-viable neonates (to be addressed in a separate ethical guideline)

## **1.6.3 Conditions Covered**

This STG includes detailed protocols for the following high-burden neonatal conditions:

1. Neonatal Sepsis
2. Birth Asphyxia and Hypoxic-Ischemic Encephalopathy (HIE)
3. Preterm Birth and Respiratory Distress Syndrome (RDS)
4. Neonatal Hypoglycemia
5. Neonatal Hypothermia
6. Meconium Aspiration Syndrome (MAS)
7. Patent Ductus Arteriosus (PDA)
8. Persistent Pulmonary Hypertension of the Newborn (PPHN)
9. Parenteral Nutrition-Associated Cholestasis

For conditions not listed, refer to the *National NICU Guideline 2021* or specialty references.

## **1.7 Expected Benefits**

### **1.7.1 For Patients (Neonates and Families)**

- Timely, accurate diagnosis and treatment
- Reduced complications and length of stay
- Improved survival and neurodevelopmental outcomes
- Clear communication and family involvement in care

### **1.7.2 For Healthcare Providers**

- Standardized, easy-to-follow protocols
- Reduced clinical uncertainty and decision fatigue
- Enhanced teamwork and handover clarity
- Tool for training and performance evaluation



### **1.7.3 For the Hospital**

- Improved adherence to national standards
- Better data collection for quality improvement
- Strengthened antimicrobial stewardship
- Enhanced reputation as a center of neonatal excellence

### **1.8 Development Process**

#### **1.8.1 Sources of Evidence**

- National Neonatal Intensive Care Unit (NICU) Treatment Guideline 2021
- WHO Guidelines for Perinatal and Neonatal Care
- Ethiopian Essential Medicines List (EML), 6th Edition
- Clinical Reference Manual for Advanced Neonatal Care in Ethiopia
- Local NICU morbidity and mortality data (EFY 2016 E.C.)
- Regional Oromia Health Bureau neonatal care directives

#### **1.8.2 Stakeholder Involvement**

The development involved multidisciplinary input from:

- NICU physicians and nurses
- Pharmacists and laboratory heads
- Hospital management and medical directorate
- Regional neonatal care coordinators
- Ministry of Health representatives

#### **1.8.3 Methodology**

- Review of national and international guidelines
- Adaptation to local drug availability, equipment, and staffing
- Consensus meetings with NICU staff
- Pilot testing of key algorithms
- Finalization and approval by Hospital Clinical Governance Committee

## **1.9 Alignment with National and Regional Strategies**

This STG supports:

- National NICU Guideline 2021: Ensures consistency with MOH standards.
- Essential Medicines List (EML): All medications are EML-compliant.
- Health Sector Transformation Plan II (HSTP-II, 2020/21–2024/25): Contributes to reducing neonatal mortality.
- National AMR Containment Strategy: Promotes rational antibiotic use.
- Oromia Regional Neonatal Care Strategy: Aligns with regional priorities and capacity.

## **1.10 Limitations**

1. Resource Constraints: Limited access to advanced imaging, echocardiography, and inhaled nitric oxide.
2. Infrastructure Gaps: Occasional power outages affecting ventilators and monitors.
3. Human Resource Shortages: High patient-to-nurse ratios during peak times.
4. Supply Chain Issues: Periodic stockouts of key medications (e.g., surfactant, IV dextrose).
5. Scope Limitations: Does not cover rare metabolic or genetic disorders.
6. Evidence Evolution: Requires regular updates to reflect new clinical knowledge.

## **1.11 Sustainability & Updating Plan**

- Review Frequency: Every two years, or earlier if national guidelines change or new evidence emerges.
- Responsible Body: NICU Clinical Guidelines Committee (NICU doctors, nurses, pharmacists, lab, management).
- Feedback Mechanism: Suggestion box and digital form for staff input.
- Capacity Building: Quarterly in-service training on STG updates.
- Orientation Integration: STG training included for all new NICU staff.
- Access: Available in printed manuals at nursing stations and digital format on hospital intranet.

## **1.12 Ethical Considerations**

All NICU providers must adhere to:

1. Informed Consent: Parents/guardians must be informed about diagnosis, treatment options, risks, and prognosis.
2. Confidentiality: Patient information protected per national health data policies.
3. Best Interest of the Neonate: Decisions based on clinical benefit, not parental preference alone.
4. Palliative Care: For non-viable neonates, comfort care and family support must be provided with dignity.
5. Equity: No discrimination based on gender, ethnicity, or socioeconomic status.

## **1.13 How to Use This STG**

### **1.13.1 General Use**

- Use as the primary reference for NICU management.
- Adapt to individual patient needs, comorbidities, and response to therapy.
- For conditions not covered, refer to the *National NICU Guideline 2021*.
- Keep copies at bedside, nursing station, and pharmacy.



### **1.13.2 Format & Navigation**

Each disease chapter includes:

1. Definition
2. Causes & Risk Factors
3. Clinical Features
4. Investigations
5. Management (including pharmacologic and supportive care)
6. Monitoring & Follow-Up
7. Referral Criteria (if higher-level care needed)
8. Prevention & Parent Education

### **1.13.3 Symbols & Notations**

[E]	Medicine in Ethiopian Essential Medicines List
[IV]	Intravenous
[PO]	Oral
[IM]	Intramuscular
[UR]	Use with caution in renal impairment
[P]	Use with caution in preterm neonates

### **1.13.4 Clinical Decision Support**

- Use Downe Score for respiratory distress assessment.
- Apply glucose infusion rate (GIR) calculations for hypoglycemia.
- Use FiO<sub>2</sub> calculation (Finer's formula or STOPROP table) for oxygen therapy.
- Follow ventilator setting algorithms for mechanical ventilation.

### **1.13.5 Documentation Requirements**

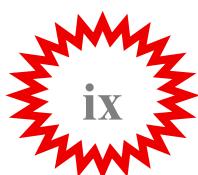
For every neonate:

- Document diagnosis, interventions, and response in NICU chart.
- Record medications, doses, and administration times.
- Note vital signs, BGL, temperature, and feeding tolerance.
- Report adverse drug reactions via national pharmacovigilance system.

## **1.14 Definitions & Acronyms**

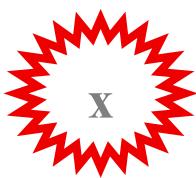
### **1.14.1 Definitions**

- Neonate: Infant aged 0–28 days.
- Preterm: Born before 37 weeks of gestation.
- Low Birth Weight (LBW): <2500 g.
- Very Low Birth Weight (VLBW): <1500 g.
- Ambulatory Care: Not applicable in NICU (all care is inpatient).
- Essential Medicines: As per Ethiopian EML.
- Standard Treatment Guideline (STG): Evidence-based protocol for clinical decision-making.



## **1.14.2 Acronyms**

NICU	Neonatal Intensive Care Unit
BGL	Blood Glucose Level
CPAP	Continuous Positive Airway Pressure
PEEP	Positive End-Expiratory Pressure
PIP	Peak Inspiratory Pressure
FiO <sub>2</sub>	Fraction of Inspired Oxygen
MAS	Meconium Aspiration Syndrome
PDA	Patent Ductus Arteriosus
PPHN	Persistent Pulmonary Hypertension of the Newborn
HIE	Hypoxic-Ischemic Encephalopathy
RDS	Respiratory Distress Syndrome
GIR	Glucose Infusion Rate
EML	Essential Medicines List
MOH	Ministry of Health
WHO	World Health Organization
HSTP-II	Health Sector Transformation Plan II
AMR	Antimicrobial Resistance
STG	Standard Treatment Guideline

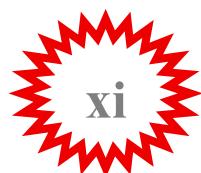


# **SECTION 2:**

## **PURPOSE, RATIONALE, AND**

## **PRINCIPLES OF GOOD PRESCRIBING**

## **& DISPENSING PRACTICE**



## **2.1 Purpose of Good Prescribing and Dispensing in the NICU**

This section establishes a framework for safe, effective, and rational use of medications in the Neonatal Intensive Care Unit. Given the unique vulnerabilities of neonates—especially preterm and low birth weight infants—medication errors can lead to severe morbidity or mortality. The purpose of this section is to:

- Minimize adverse drug events (ADEs) through standardized prescribing practices.
- Ensure accurate dosing based on weight, gestational age, and organ maturity.
- Promote appropriate selection, duration, and monitoring of drug therapy.
- Support interprofessional collaboration between prescribers, pharmacists, and nurses.
- Align with national standards and the Ethiopian Essential Medicines List (EML).

## **2.2 Rationale for NICU-Specific Prescribing Guidelines**

The pharmacokinetics and pharmacodynamics of drugs in neonates differ significantly from older children and adults due to:

- Immature liver enzyme systems (e.g., CYP450) affecting drug metabolism.
- Reduced glomerular filtration rate and tubular function impacting drug excretion.
- Higher body water content and lower fat/protein binding affecting drug distribution.
- Rapid physiological changes in the first days and weeks of life requiring frequent dose adjustments.

Additionally, the NICU environment involves:

- High-risk medications (e.g., inotropes, sedatives, antibiotics, dextrose infusions).
- Complex fluid and electrolyte balance requiring precise calculation.
- Frequent off-label or unlicensed drug use due to limited pediatric formulations.
- High potential for error during transitions of care (e.g., resuscitation, ventilation, feeding changes).

Therefore, standardized prescribing and dispensing protocols are essential to ensure patient safety, therapeutic efficacy, and antimicrobial stewardship.

## **2.3 Principles of Good Prescribing Practice**

### **2.3.1 General Prescribing Principles**

All NICU prescribers must adhere to the following principles:

- Use generic names only to avoid confusion (e.g., *ampicillin*, not “Ampicil” or brand names).
- Prescribe by weight (mg/kg/day or mg/kg/dose) for all medications, recalculated daily as weight changes.
- Specify exact dose, route, frequency, and duration (e.g., “Gentamicin 5 mg/kg IV once daily”).
- Avoid abbreviations that may cause misinterpretation (e.g., write “intravenous” instead of “IV” in narrative notes; “unit” must be spelled out).
- Adjust doses for prematurity, renal/hepatic impairment, and postnatal age (e.g., longer dosing intervals in preterm neonates for aminoglycosides).
- Document indication for each medication (e.g., “Ceftriaxone – for suspected meningitis”).
- Review and revise orders daily during rounds, discontinuing unnecessary medications promptly.

### **2.3.2 Antimicrobial Prescribing Principles**

To combat antimicrobial resistance (AMR) and ensure optimal outcomes:

- Only initiate antibiotics for confirmed or strongly suspected bacterial infection, supported by clinical signs and risk factors (e.g., maternal chorioamnionitis, prolonged rupture of membranes).
- Prefer narrow-spectrum agents when possible (e.g., ampicillin + gentamicin as first-line for early-onset sepsis).
- Base empiric therapy on local susceptibility patterns and hospital NICU infection data.
- Avoid ceftriaxone in hyperbilirubinemic neonates due to risk of bilirubin displacement.
- Limit duration of therapy:
  - If cultures are negative and infant is well, stop antibiotics at 36–48 hours.
  - For culture-proven sepsis, treat for 7–14 days depending on pathogen and site (e.g., 10–14 days for meningitis).
- De-escalate when culture and sensitivity results are available.
- Never use antibiotics for viral illnesses or asymptomatic colonization.

### **2.3.3 Steps in Rational Prescribing (Adapted from WHO Good Prescribing Guide)**

<b>STEP</b>	<b>ACTION</b>
Define the patient's problem	Conduct thorough history (antenatal, delivery, maternal infection), physical exam, and relevant investigations (CBC, CRP, blood culture, CSF analysis if indicated).
Specify the therapeutic objective	E.g., "Eradicate Group B Streptococcus infection," "Maintain blood glucose >45 mg/dL," "Prevent progression of RDS."
Choose the standard treatment	Select first-line drug(s) per this STG and EML (e.g., surfactant for RDS, ampicillin + gentamicin for sepsis).
Write a clear prescription	Include: generic name, strength, dose (mg/kg), route, frequency, duration, and indication. Use pre-printed NICU order sets where available.
Give information, instructions, and warnings	Communicate with nursing staff about monitoring parameters (e.g., pre- and post-dose gentamicin levels, blood glucose checks).
Monitor response and adjust	Assess clinical improvement, lab results, and adverse effects; modify therapy accordingly.

### **2.4 Principles of Good Dispensing Practice**

Pharmacists and pharmacy technicians play a critical role in medication safety in the NICU.

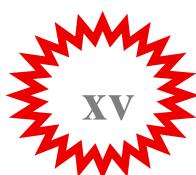
#### **2.4.1 Key Dispensing Principles**

- Prescription Verification:
  - Check completeness: patient name, weight, gestational age, drug, dose, route, frequency, duration, and prescriber signature.
  - Flag illegible or incomplete orders immediately.
  - Confirm dose appropriateness using weight-based calculations.
- Accuracy:
  - Double-check high-alert medications (e.g., potassium, insulin, inotropes, opioids) with a second pharmacist or nurse.
  - Prepare IV medications under aseptic conditions using standardized concentration guidelines (e.g., dopamine 1 mg/mL in D5W).

- **Labeling:**
  - All dispensed medications must be clearly labeled with:
    - Patient's name and medical record number
    - Drug name (generic), strength, total volume
    - Concentration (e.g., mg/mL)
    - Dose (mg/kg) and volume to administer
    - Expiry time (for reconstituted or diluted drugs)
    - Administration instructions (e.g., "Infuse over 30 min")
- Standardization of IV Solutions:
  - Use pre-mixed, centrally prepared bags for common infusions (e.g., dextrose 10%, electrolyte supplements, inotropes) where feasible.
  - Avoid compounding at bedside unless absolutely necessary.
- Storage:
  - Store medications according to stability requirements (e.g., refrigeration for erythromycin, protection from light for nitroglycerin).
  - Separate high-alert medications in designated areas.

#### 2.4.2 Role of the Pharmacist in the NICU

- Participate in daily NICU rounds to review medication regimens.
- Provide dose adjustments based on renal function, acid-base status, and drug levels.
- Educate staff on new medications, interactions, and AMR trends.
- Lead antimicrobial stewardship initiatives (e.g., audit antibiotic use weekly).
- Report and investigate medication errors and near misses.



## 2.5 High-Alert Medications in the NICU

These medications carry a higher risk of causing significant patient harm if used incorrectly. Special safeguards are required:

Medication	Risk	Safeguards
Insulin	Hypoglycemia	Double-check dose; use insulin protocol; frequent BGL monitoring
Potassium Chloride (KCl)	Cardiac arrest if given IV push	Never give undiluted; infuse slowly; monitor ECG and serum K+
Sodium Bicarbonate	Metabolic alkalosis, hypernatremia	Use only for severe acidosis (pH < 7.15); calculate dose carefully
Inotropes (Dopamine, Dobutamine, Epinephrine)	Tissue necrosis, arrhythmias	Use dedicated line; label clearly; monitor BP, HR, perfusion
Opioids (Morphine, Fentanyl)	Respiratory depression	Use lowest effective dose; monitor SpO <sub>2</sub> and apnea; have naloxone ready
Benzodiazepines (Diazepam, Midazolam)	Apnea, hypotension	Use only for seizures or sedation; monitor respiratory status
Aminoglycosides (Gentamicin)	Nephrotoxicity, ototoxicity	Once-daily dosing; monitor trough levels; limit duration
Surfactant	Endotracheal tube occlusion	Administer slowly in aliquots; reposition ETT if needed; suction carefully
Calcium (IV)	Bradycardia, tissue necrosis	Infuse slowly; avoid extravasation; monitor ECG
Hypertonic Dextrose (>12.5%)	Thrombophlebitis, osmotic diuresis	Administer via central line; monitor serum glucose and Na <sup>+</sup>

Note: All high-alert medications require independent double-checks before administration.



## **2.6 Medication Safety Practices**

To reduce errors in prescribing, dispensing, and administration:

- Use standardized order sets and pre-printed charts for common conditions (e.g., sepsis, RDS, hypoglycemia).
- Implement barcode scanning if available for medication administration.
- Conduct daily medication reconciliation during rounds.
- Hold “time-outs” before high-risk procedures (e.g., surfactant administration, exchange transfusion).
- Use weight-based dosing charts posted in the NICU (e.g., mg/kg tables for common drugs).
- Avoid verbal orders unless in emergencies; if used, require read-back and immediate documentation.
- Report all adverse drug reactions (ADRs) using the national pharmacovigilance form.

## **2.7 Documentation Requirements**

Accurate documentation is essential for continuity, safety, and accountability. The following must be recorded:

- Medication administration: Time, dose, route, and initials of administering nurse.
- Vital signs and response: Pre- and post-medication HR, SpO<sub>2</sub>, BGL, temperature.
- Laboratory monitoring: Gentamicin trough levels, serum electrolytes, glucose, bilirubin.
- Adverse events: Any suspected ADR (e.g., rash, apnea, bradycardia).
- Consents: For procedures involving medications (e.g., exchange transfusion, ECMO).
- Discontinuation: Date and reason for stopping any medication.

All entries must be legible, timed, dated, and signed.

## **2.8 Patient and Family Involvement**

Although neonates cannot self-report, families are integral to safe care:

- Inform parents about medications being used, their purpose, and potential side effects.
- Provide written discharge summaries with clear medication instructions (if applicable).
- Encourage questions and clarify misunderstandings.
- Document parental consent for high-risk treatments (e.g., second-line antibiotics, experimental therapies).

## **2.9 Training and Competency**

- All NICU staff must receive orientation on NICU STG, medication safety, and emergency protocols.
- Annual competency assessments required for:
  - Medication calculation skills
  - Ventilator and infusion pump operation
  - Recognition and management of ADRs
  - Resuscitation and emergency drug administration
- Simulation drills (e.g., hypoglycemia response, ETT displacement) conducted quarterly.

## **2.10 Monitoring and Evaluation**

To ensure adherence and effectiveness:

- Monthly audits of:
  - Antibiotic prescribing (appropriateness, duration, de-escalation)
  - Medication error rates
  - ADR reporting compliance
- Feedback reports shared with clinical teams and hospital management.
- Integration with DHIS2 for tracking key indicators (e.g., sepsis mortality, BPD rate, hypoglycemia incidence).
- Quality improvement projects initiated based on audit findings (e.g., reducing vancomycin overuse).

# **Section 3:**

# **Antimicrobial Resistance, Patient Care, and Palliative Care**

### **3.1 Antimicrobial Resistance (AMR) and Antibiotic Stewardship in the NICU**

#### **3.1.1 The AMR Challenge in Neonatal Care**

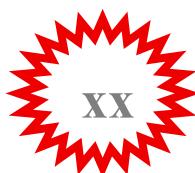
Antimicrobial resistance is a growing threat to neonatal survival, particularly in low-resource settings like Deder General Hospital. Neonates are at high risk due to:

- Frequent use of broad-spectrum antibiotics for suspected sepsis.
- Prolonged hospital stays and invasive devices (e.g., endotracheal tubes, central lines).
- Immature immune systems increasing susceptibility to healthcare-associated infections (HAI).
- Limited microbiology capacity for culture and sensitivity testing.

Local data from NICU surveillance (FY 2016 E.C.) indicate rising resistance patterns, including:

- ESBL-producing *E. coli* and *Klebsiella* – resistant to ampicillin, gentamicin, and third-generation cephalosporins.
- MRSA – though still rare, isolated cases have been reported.
- Carbapenem-resistant organisms (CROs) – not yet confirmed but remain a critical concern.

Without intervention, AMR can lead to treatment failure, prolonged ICU stay, increased mortality, and higher healthcare costs.



### **3.1.2 Principles of Antibiotic Stewardship in the NICU**

To preserve antibiotic efficacy and improve outcomes, the following principles must be implemented:

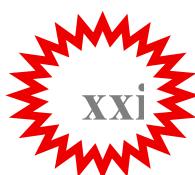
<b>Principle</b>	<b>Practice</b>
Prescribe only when indicated	Avoid antibiotics for non-infectious conditions (e.g., transient tachypnea, hypoglycemia). Use clinical signs and risk factors (e.g., maternal fever, prolonged ROM) to guide initiation.
Use narrow-spectrum agents first-line	Empiric therapy should follow NICU protocol: ampicillin + gentamicin for early-onset sepsis; ceftazidime or amikacin-based regimens only for late-onset or hospital-acquired infections.
De-escalate when possible	If blood cultures are negative and infant improves clinically within 48 hours, discontinue antibiotics. If positive, tailor therapy based on sensitivity.
Limit duration of therapy	- Sepsis (culture-negative): stop at 36–48 hours if well. - Culture-positive sepsis: treat for 7–14 days depending on pathogen and site. - Meningitis: treat for 14–21 days.
Avoid high-risk antibiotics unless essential	Reserve vancomycin, meropenem, and amikacin for confirmed resistant pathogens or life-threatening infections, with approval from senior neonatologist.
Never use ceftriaxone in hyperbilirubinemic neonates	Risk of bilirubin displacement leading to kernicterus.
Monitor treatment response	Track clinical improvement (vital signs, feeding tolerance), CRP trends, and repeat cultures if persistent fever.
Educate staff on AMR risks	Conduct quarterly training on rational antibiotic use, infection prevention, and local resistance patterns.

### **3.1.3 Role of the NICU Antimicrobial Stewardship Program (ASP)**

Deder General Hospital will integrate this STG with a NICU-specific Antimicrobial Stewardship Program to:

- Conduct weekly prescription audits of all antibiotic use in the NICU.
- Provide real-time feedback to prescribers on appropriateness, dose, duration, and de-escalation opportunities.
- Monitor antibiotic consumption using WHO ATC/DDD methodology via DHIS2 reporting.
- Disseminate an annual NICU antibiogram to guide empiric therapy.
- Organize monthly case reviews of culture-positive and multi-drug resistant (MDR) infections.
- Collaborate with microbiology lab to improve blood culture yield and turnaround time.
- Train staff on infection prevention and control (IPC) practices to reduce HAI burden.

Note: All second-line antibiotics (e.g., meropenem, vancomycin) require dual sign-off by a senior neonatologist and pharmacist.



## **3.2 Patient Care in the NICU**

### **3.2.1 Core Elements of High-Quality Neonatal Care**

The NICU provides 24/7 critical care for sick newborns. Key components include:

#### **1. Immediate Stabilization (ABC Approach)**

- Airway: Clear secretions, position head appropriately, use CPAP or intubation as needed.
- Breathing: Initiate oxygen therapy or respiratory support based on Downe score and SpO<sub>2</sub>.
- Circulation: Assess perfusion (CRT, HR, BP), initiate fluid resuscitation if shocked.

#### **2. Comprehensive Diagnostic Workup**

- Perform targeted investigations (e.g., blood culture, CRP, ABG, CXR) guided by clinical presentation.
- Avoid unnecessary or redundant tests to reduce stress and blood loss.

#### **3. Daily Multidisciplinary Review**

- Conduct structured rounds involving neonatologists, nurses, pharmacists, nutritionists, and respiratory therapists.
- Document progress, adjust plans, and identify discharge readiness.

#### **4. Infection Prevention and Control (IPC)**

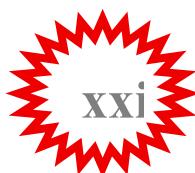
- Strict hand hygiene before and after every patient contact.
- Use sterile technique for invasive procedures (e.g., line insertion, suctioning).
- Change ventilator circuits only when visibly soiled or malfunctioning.
- Implement cohorting during outbreaks (e.g., suspected sepsis clusters).

#### **5. Developmental Care**

- Minimize noise and light exposure; cluster care activities.
- Use kangaroo mother care (KMC) for stable preterm infants.
- Provide non-nutritive sucking (NNS) and sucrose for pain relief during procedures.

#### **6. Early Discharge Planning**

- Begin planning at admission: assess family support, feeding ability, follow-up access.
- Provide clear discharge summaries with medications, warning signs, and clinic appointments.



### **3.2.2 Family-Centered Care**

Parents are essential partners in neonatal care. Practices include:

- Daily updates on baby's condition, treatment plan, and prognosis.
- Informed consent for major interventions (e.g., intubation, surfactant, exchange transfusion).
- Parental involvement in care activities (diapering, bathing, KMC).
- Emotional and psychological support through counseling and peer support groups.
- Education on newborn danger signs, medication administration, and home care.

**Ethical Note:** In cases of poor prognosis (e.g., severe HIE, extreme prematurity), involve parents in shared decision-making with compassion and transparency.

### **3.3 Palliative Care in the NICU**

#### **3.3.1 Definition**

Palliative care in the NICU is the active, holistic care of neonates with life-limiting or non-viable conditions, focusing on relief of pain and distressing symptoms, while supporting families emotionally and spiritually. It applies to:

- Neonates with severe congenital anomalies incompatible with life (e.g., anencephaly, trisomy 13/18).
- Infants with stage III Hypoxic-Ischemic Encephalopathy (HIE) showing no neurological improvement over 72 hours.
- Extremely preterm infants (<26 weeks) where survival is unlikely or with severe complications.
- Terminally ill infants with progressive conditions (e.g., metabolic disorders, advanced cancer).

Palliative care does not mean abandonment of care—it means shifting focus from curative to comfort-oriented treatment.

#### **3.3.2 Goals of Palliative Care**

- Alleviate physical suffering (pain, respiratory distress, agitation).
- Provide emotional, social, and spiritual support to parents and siblings.
- Facilitate honest, compassionate communication about prognosis and options.
- Honor cultural and religious beliefs in end-of-life decisions.
- Support bereavement and mourning after death.



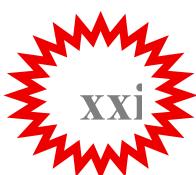
### 3.3.3 Core Principles

Principle	Practice
Holistic Assessment	Evaluate physical symptoms (pain, secretions, dyspnea), family stress, spiritual concerns, and cultural preferences.
Symptom Management	Use evidence-based protocols for pain, respiratory distress, and agitation (see Table below).
Shared Decision-Making	Involve parents in care planning; explain benefits and burdens of continued intensive care.
Ethical Practice	Respect parental autonomy while ensuring decisions are in the best interest of the neonate. Avoid non-beneficial interventions.
Continuity of Care	Ensure seamless transition from intensive to comfort care with consistent nursing and medical oversight.
Bereavement Support	Offer counseling, memory-making (e.g., handprints, photos), and referral to grief services.

### 3.3.4 Symptom Management Protocol

Symptom	Assessment Tool	Management
Pain	NIPS, PIPP-R scores	<ul style="list-style-type: none"> <li>- Non-pharmacologic: NNS, sucrose, swaddling, KMC</li> <li>- Pharmacologic: Paracetamol [E] (10–15 mg/kg PO/PR q6h), Morphine [E] (0.05–0.1 mg/kg IV q4h PRN)</li> </ul>
Respiratory Distress	Clinical observation, SpO <sub>2</sub>	<ul style="list-style-type: none"> <li>- Positioning, gentle suctioning</li> <li>- Low-dose morphine (0.05 mg/kg IV) to reduce air hunger</li> <li>- Oxygen via nasal cannula if desired by family</li> </ul>
Agitation/Seizures	Clinical exam, EEG if available	<ul style="list-style-type: none"> <li>- Midazolam [E] (0.05–0.1 mg/kg IV bolus, then infusion 0.01–0.05 mg/kg/hr)</li> <li>- Phenobarbital [E] (10–20 mg/kg IV loading)</li> </ul>
Excessive Secretions ("Death Rattle")	Auscultation	<ul style="list-style-type: none"> <li>- Positioning (head elevated)</li> <li>- Scopolamine [E] (0.01 mg/kg SC/IV q6h) or Glycopyrrolate [E] (0.01 mg/kg IV q6h)</li> </ul>
Fever/Discomfort	Temp, behavior	<ul style="list-style-type: none"> <li>- Paracetamol [E], tepid sponging, light clothing</li> </ul>

Note: All medications used in palliative care must be clearly documented as part of comfort measures only (CMO).



### **3.3.5 When to Consider Palliative Care**

Initiate palliative care discussions when:

- Neonate has a non-survivable diagnosis (e.g., anencephaly, bilateral renal agenesis).
- After 72 hours of stage III HIE with no improvement in consciousness or brainstem reflexes.
- Parents request limitation of life-sustaining treatment after full counseling.
- There is futility of care despite maximal support (e.g., persistent acidosis, multi-organ failure).

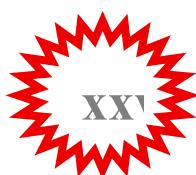
Decision Process:

1. Multidisciplinary team discussion (neonatologist, nurse, social worker, ethics lead).
2. Family meeting with interpreter if needed.
3. Document decision in chart with rationale and parental consent.
4. Transition to CMO orders; discontinue ventilator, inotropes, and lab draws unless for comfort.

### **3.3.6 Integration into NICU Practice at Deder General Hospital**

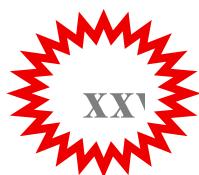
To ensure consistent and compassionate palliative care:

- Develop a NICU Palliative Care Pathway aligned with MOH ethics guidelines.
- Train staff annually on communication skills, symptom management, and ethical decision-making.
- Establish a Palliative Care Committee including neonatology, nursing, pharmacy, chaplaincy, and social work.
- Provide memory boxes (photos, footprints, blanket) to families.
- Conduct debriefings after neonatal deaths to support staff well-being.
- Link with community-based bereavement programs for long-term family support.



# **SECTION 4:**

# **DISEASE SPECIFIC TOPICS**



# CHAPTER 1: CLINICAL MANAGEMENT

## Immediate care of Newborn



### 81. Essential newborn care

Essential newborn care is care given to all newborn infants at birth to optimize their chances of survival.

Standardized procedures in Essential Newborn Care (ENC)

#### Step 1: Dry and stimulate

- Immediately dry the whole body including the head and limbs.
- Keep the newborn warm by placing on the abdomen of the mother
- Stimulate by rubbing the back or slapping or flicking the soles of the feet
- Remove the wet towel
- Let the baby stay in skin-to-skin contact on the abdomen and cover the baby quickly, including the head with a clean dry cloth. Don't let the baby remain wet as this will cool the body and make it hypothermic.

#### Step 2: Evaluate breathing

- Check if the baby is crying while drying him/her.
- If the baby does not cry, see if the baby is breathing properly.

- If the baby is not breathing and/or is gasping: call for help. The assistant can provide basic care for the mother while you provide the more specialized care for the baby who is not breathing. Cut the cord rapidly and start resuscitation.
- If the baby breathes well, continue routine, essential newborn care.
- Do not do suction of the mouth and nose as a routine. Do it only if there is meconium, thick mucus or blood. Do mouth first, then nostrils.

#### Step 3. Cord care

##### Optimal cord care consists of the following:

Clamping/tying the cord: If the baby does not need resuscitation, wait for cord pulsations to cease or approximately 1-3 minutes after birth, whichever comes first, and then place one metal clamp/cord tie two centimetres from the baby's abdomen and the second clamp/tie another two centimetres from the first clamp/tie. Cutting the cord soon after birth can decrease the amount of blood that is transfused to the baby from the placenta, and in preterm babies, is likely to result in subsequent anaemia and increased chances of requiring a blood transfusion



#### **Step 4. Keep the newborn warm (Prevent hypothermia)**

- Keep the baby warm by placing it in skin-to-skin contact on the mother's chest within ten minutes of life.
- Cover the baby's body and head with clean cloth. Keep the room temperature warm at  $28 \pm 2$  °C
- If the room is cool ( $<25$  °C), use a blanket to cover the baby over the mother.

#### **Step 5. Initiate breastfeeding in the first one hour**

- Skin-to-skin contact and early breastfeeding are the best ways to keep an infant warm and prevent hypoglycaemia. Term and low birth weight neonates weighing  $< 2000$ g who do not have complications and are clinically stable should be put in skin-to-skin contact with the mother soon after birth after drying thoroughly to prevent hypothermia.
- Early breastfeeding means breastfeeding within the first hour, with counselling for correct positioning.

#### **Step 6. Administer eye drops/eye ointment**

- Wash your hands with soap and water.
- Clean eyes immediately after birth with a swab soaked in sterile water, using a separate swab for each eye.
- Clean from medial to lateral side.
- Give tetracycline eye ointment/drops within 1 hour of birth usually after initiating breastfeeding.

#### **Step 7. Administer vitamin K Intramuscularly (IM)**

- 1 mg for babies with gestational age of 34 weeks or above.
- 0.5 mg for premature babies less than 34 weeks' gestation.

#### **Step 8. Place the newborn's identification bands on the wrist and ankle**

#### **Step 9. Weigh the newborn when it is stable and warm**

- Place a clean linen or paper on the pan of the weighing scale.
- Adjust the pointer to zero on the scale with the linen/paper on the pan.
- Place the naked baby on the paper/linen. If the linen is large, cover the baby with the cloth.
- Avoid long and unnecessary stay of the baby on the scale especially while naked.
- Record the baby's weight in partographs/ maternal/newborn charts and delivery room
- register
- Inform the mother about the newborn's weight.

#### **Step 10. Record all observations and treatment provided in the registers/appropriate chart/cards**

Note:

- Defer bathing for at least 24 hours.
- Organize transport if necessary.

## Reference

1. Essential Care for Every Delivery, American Academy of Paediatrics.
2. Sara K.Berkelhamer,Douglas D. McMillan, Erik Amick, Nalini Singhal AND Carl L. Bose. Pesiatic October 202-, 146(Supplement2) S112-12

## 82 Neonatal Resuscitation

A person skilled in basic neonatal resuscitation, whose primary responsibility is the newly born baby, should be present at every birth. Delivery of all high-risk infants should be ideally attended by personnel who possess the skills required to perform a complete resuscitation. Anticipation is key to ensure that adequate preparations have been made for a neonate likely to require resuscitation at birth. It is estimated that as many as 10 per cent of neonates require some assistance at birth for normal transition, whereas <1 per cent require extensive resuscitative measures.

A clear understanding of the roles of other team members and coordination among team members is mandatory.

Resuscitation efforts at delivery are designed to help the newborn make the respiratory and circulatory transitions that must be accomplished immediately after birth: the lungs expand, foetal lung fluid is cleared, effective air exchange is established and the right-to-left circulatory shunts terminate.

**The goals in neonatal resuscitation are the following:**

1. Minimizing immediate heat loss by drying and providing warmth, thereby decreasing oxygen consumption by the neonate.
- 2 Establishing normal respiration and lung expansion by clearing the upper airway and using positive pressure ventilation if necessary.
- 3 Increasing arterial PO<sub>2</sub> by providing adequate alveolar ventilation.
- 4 The routine use of added oxygen is not warranted, but this therapy may be necessary in some situations.
- 5 Supporting adequate cardiac output.

### Perinatal conditions associated with high-risk deliveries

Ideally, the obstetrician should notify the paediatrician well in advance of the actual birth. The paediatrician may then review the obstetric history and events leading to the high-risk delivery and prepare for the specific problems that may be anticipated. If time permits, the problems should be discussed with the parent(s). The following antepartum and intrapartum events warrant the presence of a resuscitation team at delivery.

1. Evidence of non-reassuring foetal status
  - a. Foetal distress: late decelerations, recurrent variable decelerations, or bradycardia
  - b. History of an acute perinatal event (e.g., placental abruption, cord prolapse or abnormal foetal testing, or a scalp pH of 7.20 or less)
  - c. History of decreased foetal movement, diminution in growth or abnormalities of Umbilical Vessel Doppler Flow Studies

- 2 Evidence of foetal disease or potentially serious conditions
  - a. Meconium staining of the amniotic fluid and/or other evidence of possible foetal compromise
  - b. Prematurity (<37 weeks), postmaturity (>42 weeks), anticipated low birth weight (<2.0 kg) or high birth weight (>4.5 kg)
  - c. Major congenital anomalies diagnosed prenatally
  - d. Hydrops fetalis
  - e. Multiple gestation
- 3 Labour and delivery conditions
  - a. Significant vaginal bleeding
  - b. Abnormal foetal presentation
  - c. Prolonged or unusual labour
  - d. Concern about a possible shoulder dystocia

Necessary equipment must be present and functioning properly. Each delivery room should be equipped with the following:

1. Radiant warmer with procedure table or bed. The warmer should be turned on and checked before delivery. For a very low birth weight (VLBW) infant, additional warming techniques should be available, which might include prewarming the delivery room to 26°C, plastic wrap for covering the baby, or the use of an exothermic mattress. When used in combination, care should be taken to avoid hyperthermia.
- 2 A blended oxygen source (adjustable between 21 per cent and 100 per cent) with adjustable flow meter and adequate length of tubing. A humidifier and heater may be desirable.

Use room air as the initial concentration of oxygen for term babies and 21 per cent to 30 per cent oxygen for premature babies <32 weeks' gestation.

- 3 Pulse oximeter available for use when oxygen therapy is anticipated. It may take around 60 to 90 seconds to obtain an accurate reading; pulse oximetry may fail if cardiac output is low.
- 4 Flow-inflating bag with adjustable pop-off valve or self-inflating bag with reservoir. The bag must be appropriately sized for neonates (generally about 750 mL) and capable of delivering 100 per cent oxygen.
- 5 Face mask(s) of appropriate size for the anticipated infant
- 6 A bulb syringe for suctioning
- 7 Stethoscope with infant or premature-sized head
- 8 Equipped emergency box or cart
  - a. Laryngoscope with no. 0 and no. 1 blades. For extremely low birth weight infants, a no. 00 blade may be preferred.
  - b. Extra batteries
  - c. Uniform diameter ET tubes (2.5, 3.0, and 3.5 mm internal diameters), or laryngeal mask
  - d. Drugs, including epinephrine (1:1000, and NaCl 0.9% (normal saline). Dextrose 5% and 40%
  - e. Sodium bicarbonate (0.50 mEq/mL) and naloxone are rarely useful and are not part of the usual resuscitation algorithm.
  - f. Umbilical catheterization tray with 3.5 and 5 French catheters
  - g. Syringes (1.0, 3.0, 5.0, 10.0 and 20.0 mL), needles (18 to 25G),

9. End-tidal CO<sub>2</sub> monitor/indicator to confirm ET tube position after intubation.

Initial steps of resuscitation are provided consisting of the following steps:

1. Place the newborn on the warming table.
2. Position head and clear airway as necessary by placing the newborn on the back with head in midline position and with slight neck extension “sniffing position”.
3. Clear the airway as necessary by suctioning the mouth first, and then the nose (M before N) gently and briefly by using a suction bulb or a large-bore suction catheter. Limit suctioning to five seconds at a time and avoid aggressive and deep pharyngeal suctioning. Routine tracheal suction is no longer recommended for non-vigorous babies with meconium-stained fluid.

Dry the infant completely and discard the wet linens, including those on which the infant is lying. Drying should be thorough but gentle; avoid vigorous rubbing or attempts to clean all blood or vernix from the baby. Ensure that the infant remains warm. GA less than 32 and weight less than 1500 may require extra warming techniques such as wrapping the body and extremities in a plastic wrap or bag or the use of an exothermic mattress.

- Stimulation of the infant to breathe
  - Apply tactile stimulation by gently rubbing the back or flicking the soles of the feet two to three times.

- Assess breathing

- If breathing, assess heart rate by auscultation or umbilical pulse or pulse oximetry
- If apnoeic, start positive pressure ventilation (PPV)

If there is no response with the above methods, start bag and mask ventilation within the golden minute.

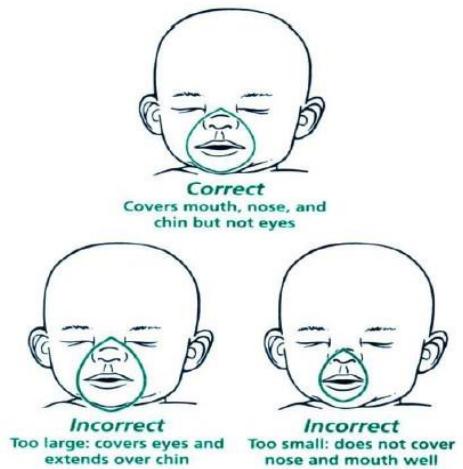
Ventilation of the lungs is the single most effective step in newborn resuscitation.

For in-term infants and preterm ( $\geq 35$  weeks of GA) use room air or 21 per cent FIO<sub>2</sub> for initiating resuscitation.

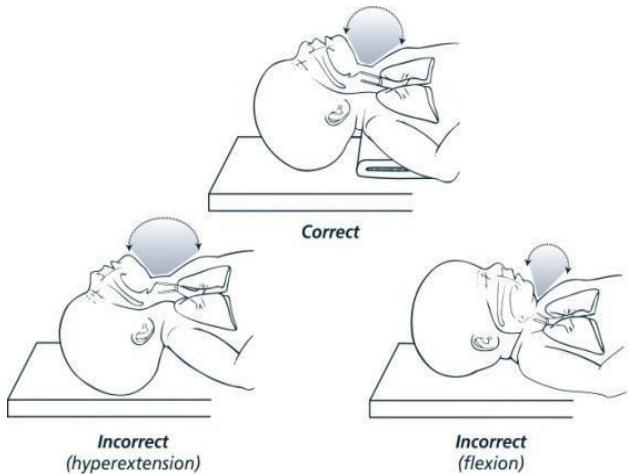
For preterm infants less than 35 weeks GA use 21-30 per cent. If there is no blender, use a self-inflating bag (with O<sub>2</sub> and without reservoir) which provides 40 per cent. The normal pressure required to inflate the lungs is 15 – 40cm H<sub>2</sub>O.

#### Steps:

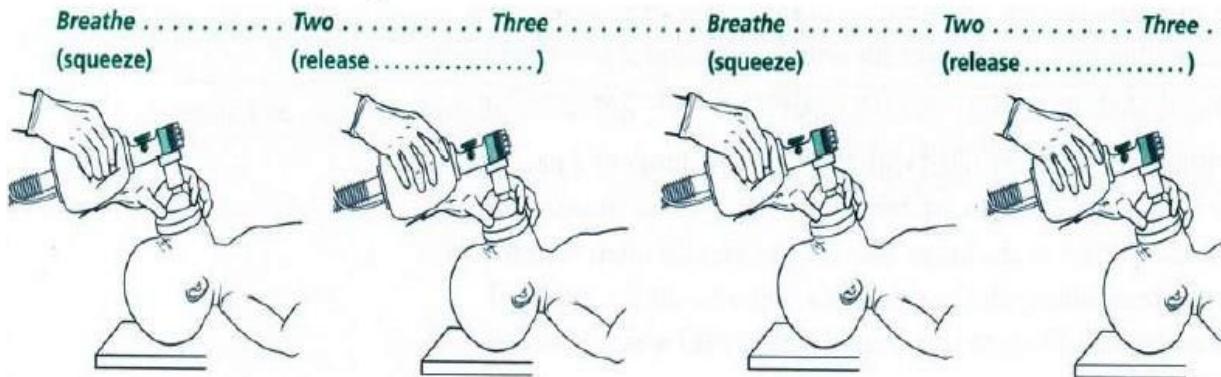
1. Call for help
2. Position the infant correctly with a slight extension at the neck
3. Position the mask correctly and apply a firm seal
4. Provide positive pressure ventilation at a rate of 40 breaths per minute. Check for rising chest, increase in heart rate and colour change.



*Figure 3. Appropriate positioning for resuscitation*



*Figure 4. Appropriate mask size selection*



*Figure 5. Method for breathing rate counting*

If no effective ventilation starts, use improved ventilation/take ventilatory corrective steps (MR. SOPA):

**M - Adjust mask in the face**

**R - Reposition the head to open airway.**  
Re-attempt to ventilate. If not effective, then:

**S - Suction mouth then nose**

**O - Open mouth and lift jaw forward.** Re-attempt to ventilate. If not effective, then:

**P - Gradually increase pressure every few breaths until visible chest rise is noted**

**Maximum PIP 30 for PT and 40cm H<sub>2</sub>O for FT.** If still not effective, then:

**A - Artificial Airway (ETT or LMA)**

Evaluate the heart rate after 30–60 seconds of bag and mask ventilation

1. If heart rate is above 100 and infant has spontaneous respiration, discontinue ventilation
2. Heart rate between 60 and 100 – use corrective steps of ventilation
3. Heart rate < 60 beats per minute – ensure ventilation with 100 per cent oxygen and initiate chest compression
4. Pass an orogastric tube if bag and mask ventilation is continued for more than two minutes.
5. If a baby starts to breathe but oxygen saturation (SpO<sub>2</sub>) is not within target range, free-flow oxygen administration may begin at 30 per cent.

6. If the newborn has laboured breathing or SpO<sub>2</sub> cannot be maintained within target range despite 100 per cent free-flow oxygen, consider a trial of continuous positive airway pressure (CPAP).

Intubate if possible.

#### Endotracheal Intubation

Indication:

- Bag and mask are ineffective or prolonged
- Before chest compression
- LBW for administering surfactant
- Tracheal administration of medications is desired
- Congenital diaphragmatic hernia

*Table 2. ET Tube size based on birth weight and gestational age*

Tube size (ID mm)	Birth weight(g)	GA (weeks)
2.5	<1000	<28
3.0	1000-2000	28-34
3.5	2000-3000	35-38
4.0	>3000	>38

(Adopted from NRP 7th edition)

#### Chest compressions:

- Start chest compression if the heart rate is less than 60/min despite good assisted ventilation for 60 seconds.
- Two persons are needed for this step: one to perform chest compression and the other to continue ventilation.

#### Two-thumb encircling hands method:

- Stand at the infant's foot and grip the chest in both hands;
- Two thumbs press at the junction of the middle and lower thirds of the sternum (just below an imaginary line joining the nipples), with the fingers wrapped around and supporting the back. Strictly avoid applying pressure on the xiphoid.

- Continue bag and mask ventilation with 100 per cent oxygen during chest compression.

#### **Rate:**

- The breathing to chest compression ratio should be at 1:3.
- The breathing rate should be 30 breaths/min and compression rate 90 compressions/min.
- Use the “One and two and three and breathe and one and two and three and breathe and...” technique

#### **Compression depth:**

- Compress effectively to one-third of the chest diameter
- Give adequate time for chest compression

#### **Evaluation:**

- After 60 seconds of chest compression, check the heart rate to proceed to the next step.

#### **Medication: Epinephrine**

Epinephrine is indicated when heart rate remains <60 after 30-60 seconds of effective ventilation and another 60 seconds of coordinated compressions and ventilation (at approximately 2 min of life).

**Dose:** 0.1–0.3 ml/kg IV or 0.5–1 ml/kg ET

**Preparation:** use 1:10,000 of epinephrine solution which may be repeated every 3-5 min if required. If the adrenaline concentration is 1:1000, dilute with the adrenaline vial (1ml) with 9ml normal saline to provide 1:10,000 solution.

Endotracheal route is easier, but IV is preferred. Initiate UV cannulation as ET dose is given. Repeat dose of epinephrine as soon as IV is secured, in case first dose is given via ET tube.

#### **Volume expanders:**

Volume expansion should be considered when blood loss is known or suspected (pale skin, poor perfusion and weak pulse) and the infant's heart rate has not responded adequately to other resuscitative measures. Use 10ml/Kg of an isotonic crystalloid solution or blood O negative may be useful for volume expansion in the delivery room.

#### **Post-resuscitation care:**

Infants who require resuscitation are at risk of deterioration after their vital signs have returned to normal. Once adequate ventilation and circulation has been established:

- Stop ventilation.
- Return to mother for skin-to-skin contact as soon as possible.
- Closely monitor breathing difficulties, signs of asphyxia and anticipate need for further care.

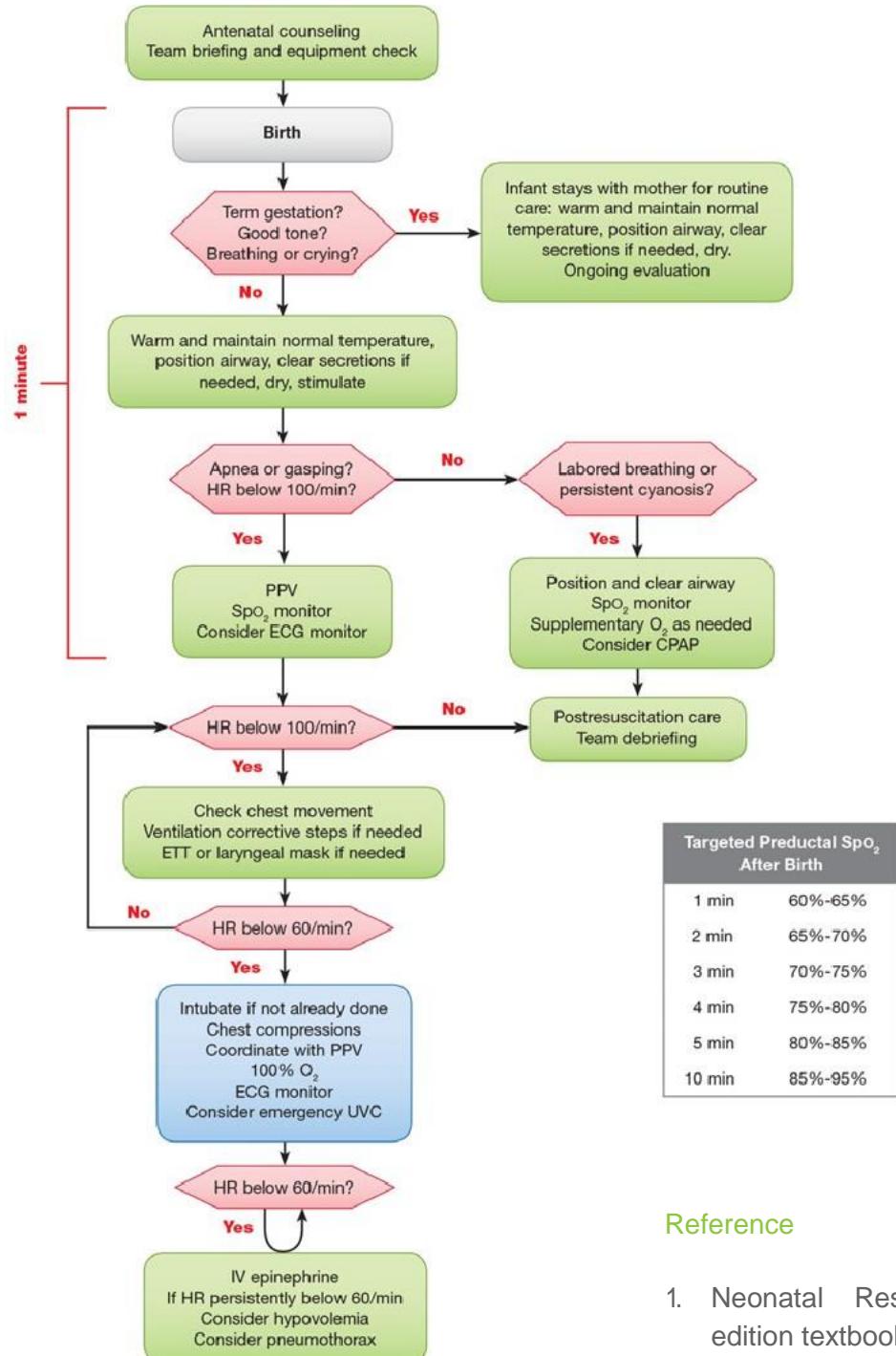
#### **Cessation of resuscitation:**

It is appropriate to consider discontinuing after effective resuscitation efforts if:

- Infant is not breathing and heartbeat is not detectable beyond 10 min, and APGAR at 10 min is zero.
- If there is no spontaneous breathing and heart rate remains below 60/min after 20 min of effective resuscitation, consider transfer to NICU and ventilation or decide case by case.
- Record the event and explain to the mother or parents that the infant has died. Give them the infant to hold if they so wish.



## Neonatal Resuscitation Algorithm-2015 update



### Reference

1. Neonatal Resuscitation Program 7th edition textbook, 2016.
2. Cloherty and Stark's. Manual of Neonatal care. 8th edition.

© 2015 American Heart Association

Figure 6. Neonatal resuscitation algorithm, (AAP)



## Neonatal evaluation

Key elements of newborn evaluation include:

1. History taking (prenatal, birth, family and social)
2. Performing physical examination
3. Evaluating and considering the impact of significant risk factors, history and physical examination findings
4. Determine the need for additional work-up and/or follow-up as indicated
5. Provide education and counselling to parents/legal guardians

### History

When exploring, source the information from the mother, the maternal medical record or through communication with the obstetrician or midwife. These are the main components that need to be included in the history:

1. The mother's medical and obstetric history (age, gravidity, parity, number of live babies, still birth, abortion or prior medical problems)
2. The current pregnancy course (mode of conception, singleton or multiple, gestational age, ANC follow-up, obstetric complications, foetal growth (IUGR, LGA, hydrops))
3. The social and family history (maternal and paternal)
4. Records of antenatal care visits, laboratory studies and medications given

5. Records of the mother's current and prior hospitalizations, interventions and medications given to the mother
6. **Labour record:** rupture of membrane (duration), amniotic fluid (oligohydramnios/polyhydramnios; bloody; purulent; meconium; foul smelling); signs of infection (maternal fever, elevated WBC count, tachycardia, uterine tenderness) foetal tracing (tachycardia, decelerations, etc)
7. **Delivery record:** mode of delivery (indicate if operative delivery), method of anaesthesia, medications used
8. Newborn records (APGAR score, birth weight, what was done/given to the newborn)
9. Reason for referral of the newborn

### Physical examination

Examination of the newborn must be started immediately after birth, with assessment of the newborn's haemodynamic stability and need for respiratory and cardiovascular support.

The first examination will be performed based on the assessment parameters of the APGAR score.

Based on the APGAR score, resuscitation must be decided.



Following resuscitation, further haemodynamic stability will be assessed and one must decide whether to transfer the newborn into a neonatal intensive care unit or not.

The newborn must also be assessed for dysmorphology/malformation/congenital anomaly which may require NICU admission. In the birthing place, it is mandatory to check for choanal atresia by passing thin catheter through both nostrils, check for oesophageal atresia by passing naso/orogastric tubes and check for patency of anus for all newborns. Details of physical examination must be done at admission to NICU.

General examination: look for any sign of acute illness: alertness, movement of the extremities, muscle tone (hypotonia/hypertonia), colour, posture and respiratory distress and address any life-threatening issue before proceeding to the details of the physical exam e.g., if the newborn is lethargic or sleepy, check random blood sugar and address hypoglycaemia.

To perform physical examination, measuring tape, stethoscope, thermometer, pulse oximeter and if possible, ophthalmoscope need to be available.

### Key examination points

#### 1. Take the vital signs and interpret

- Respiratory rate per minute
- Heart rate per minute
- Axillary temperature
- Pulse oximeter with and without oxygen
- Measure blood pressure using appropriate cuff
- Pain assessment score

#### 2. Take anthropometric measurement

- Weight, length and head circumference and interpret based on Fenton growth chart and classify as: Appropriate for gestational age; Small for gestational age, and Large for gestational age (Figure 3.1)
- Appropriate for gestational age if the parameter is between 10th and 90th centile
- Small for gestational age if the parameter is below 10th centile for gestational age
- Large for gestational age if the parameter is above 90th centile for gestational age
  - ▶ Classify based on birth weight
  - ▶ Low birth weight – less than 2500 grams
  - ▶ Very low birth weight – 1500-1000 grams
  - ▶ Extremely low birth weight – less than 1000 grams

#### 3. Gestational age assessment

Gestational age will be assessed using last menstrual age or early trimester ultrasound. If both are not available, do Ballard Score (see Figure 8).

Classify based on gestational age as:

- Extremely preterm – less than 28 weeks
- Very preterm – 29-31 weeks
- Moderate to late preterm – 32-37 weeks
- Term – 37+1 weeks to 42 weeks
- Post term – more than 42 weeks

- 4. Examination of HEENT:** examine the skull (caput succedaneum, subgaleal haemorrhage, cephalohematoma), sutures (craniostosis), fontanel, face, nose, ears, mouth, neck, clavicles, eye discharge, icterus, cataracts
- 5. Mammary glands:** enlargement of breast tissue and discharge (physiologic)
- 6. Respiratory system:** check for signs of respiratory distress, breathing pattern, respiratory rate, air entry to the lungs, presence of abnormal sounds in the lungs, AP diameter and symmetry of the chest, strider
- 7. Cardiovascular:** heart rate, heart murmurs, gallop rhythm, femoral pulses
- 8. Abdomen:** shape (scaphoid, distension), look for any organ enlargement like hepatomegaly, splenomegaly, mass, ascites, kidneys, abdominal wall defect, examination of the umbilical stump (bleeding and discharge), and anal patency.
- 9. External genitalia:** see if there are any abnormalities of the genitalia both in male and female newborns (size of penis, position of testicles, opening of urethral meatus (hypospadias/epispadias), ambiguous genitalia), vaginal bleeding or discharge.
- 10. Musculoskeletal:** limb defects (clubfoot, syndactyly, polydactyly), symmetry and movement of extremities to see fractures and birth injuries, spina bifida, joints (hip should be examined to detect developmental dysplasia of the hip, look for gluteal fold symmetry), enema.
- 11. Skin examination:** rash, jaundice, pallor, plethora, meconium staining, cyanosis, etc. Acral (extremity) cyanosis is a normal finding in newborns.
- 12. Neurological examination:** level of alertness, spontaneous movements, muscle tone, reflexes
  - Rooting reflex, absent or present
  - Grasp reflex (arm and plantar)
  - Sucking reflex, absent, weak or vigorous
  - Tonic neck reflex
  - Moro reflex, check for completeness and symmetry. Moro is a distressing reflex, better to do it at the end of examination.

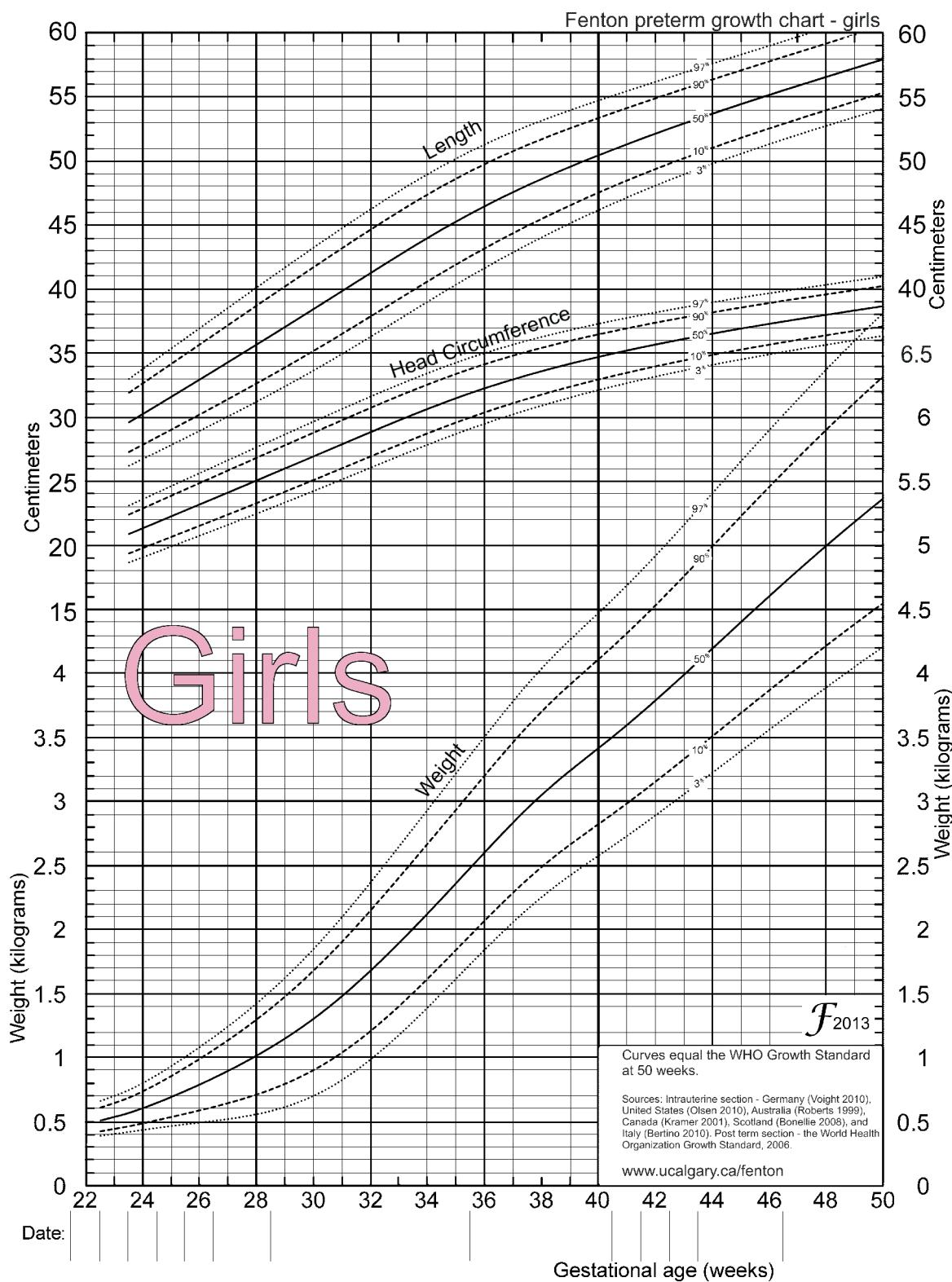


Figure 7. Growth curve for girls

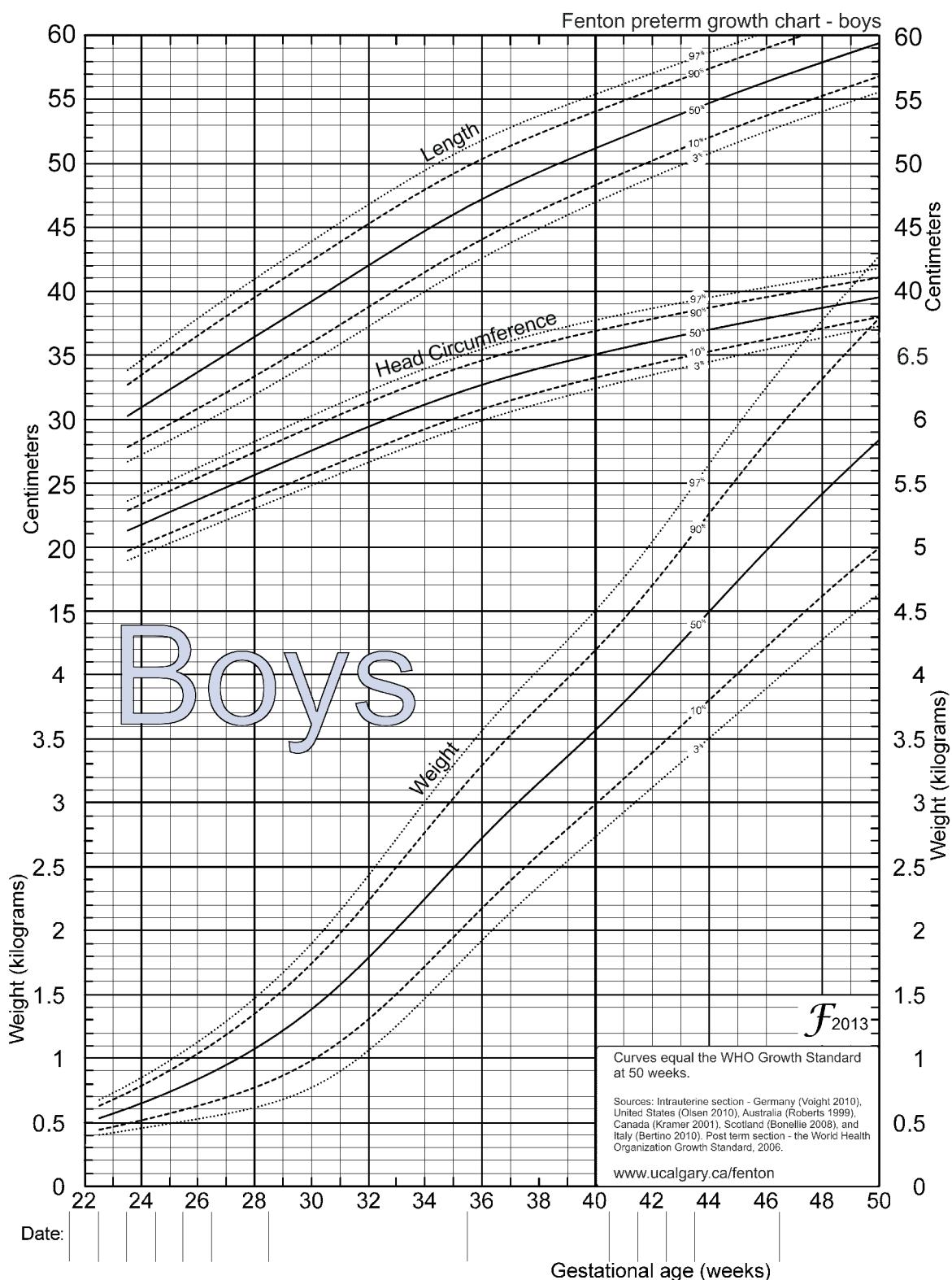


Figure 8. Growth curve for boys

Score	-1	0	1	2	3	4	5
Posture							
Square window (wrist)							
Arm recoil							
Popliteal angle							
Scarf sign							
Heel to ear							

Score	-1	0	1	2	3	4	5																												
Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink; visible veins	Superficial peeling and/or rash; few veins	Cracking, pale areas; rare veins	Parchment, deep cracking; no vessels	Leathery, cracked wrinkled																												
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	Maturity Rating																												
Plantar surface	Heel-toe 40-50 mm: -1 <40 mm: -2	>50 mm, no crease	Faint red marks	Anterior transverse crease only	Creases anterior 2/3	Creases over entire sole	<table border="1"> <thead> <tr> <th>Score</th> <th>Weeks</th> </tr> </thead> <tbody> <tr> <td>-10</td> <td>20</td> </tr> <tr> <td>-5</td> <td>22</td> </tr> <tr> <td>0</td> <td>24</td> </tr> <tr> <td>5</td> <td>26</td> </tr> <tr> <td>10</td> <td>28</td> </tr> <tr> <td>15</td> <td>30</td> </tr> <tr> <td>20</td> <td>32</td> </tr> <tr> <td>25</td> <td>34</td> </tr> <tr> <td>30</td> <td>36</td> </tr> <tr> <td>35</td> <td>38</td> </tr> <tr> <td>40</td> <td>40</td> </tr> <tr> <td>45</td> <td>42</td> </tr> <tr> <td>50</td> <td>44</td> </tr> </tbody> </table>	Score	Weeks	-10	20	-5	22	0	24	5	26	10	28	15	30	20	32	25	34	30	36	35	38	40	40	45	42	50	44
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Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4 mm bud	Full areola, 5-10 mm bud																													
Eye/Ear	Lids fused loosely: -1 tightly: -2	Lids open; pinna flat; stays folded	Slightly curved pinna; soft; slow recoil	Well curved pinna; soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff																													
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae																													
Genitals (female)	Clitoris prominent, labia flat	Clitoris prominent, small labia minora	Clitoris prominent, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora																													

Figure 9. Gestational age assessment: new Ballard score physical and neuromuscular assessment

#### Reference

1. <https://live-ucalgary.ucalgary.ca/resource/preterm-growth-chart/preterm-growth-chart>
2. Maturational Assessment of Gestational Age. Ballard JL et al. New Ballard Score, expanded to include extremely premature infants. J Pediatrics 1991; 119:417



## CHAPTER 2: THERMOREGULATION

### Hypothermia

Neonatal hypothermia after delivery is a worldwide issue and if prolonged can affect the survival of a newborn significantly. In newborn infants, thermal control is more limited than that of an adult due to less insulation and lack of shivering response. Preterm infants are at even higher risk of hypothermia, larger surface area to weight, immature skin and less subcutaneous fat or brown fat.

The temperature range during which the basal metabolic rate of the baby is at a minimum, oxygen utilization is least and the baby thrives well is known as 'Thermo-neutral Range of Temperature' or 'Neutral Thermal Environment'. For each baby, this range of temperature varies depending on gestational age.

*Table 3. Axillary temperature in newborns*

	Temp in Celsius (°C)	Temperature in Fahrenheit (°F)
Euthermia	36.5-37.5	97.7-99.5
Mild hypothermia / cold stress	36-36.4	96.8-97.5
Moderate hypothermia	32-35.9	89.6-96.6
Severe hypothermia	<32	<89.6

(Adopted from WHO Thermal Control of Newborn: A Practical Guide 1999)

The neonatal temperature is monitored per axilla using digital thermometers. Routine core body (rectal) temperature monitoring is not recommended.

#### 1. Prevention of hypothermia in the delivery room

The main strategy to prevent hypothermia in the delivery room for a healthy newborn who doesn't require resuscitation is following essential newborn care.

**Anticipate need for resuscitation before every delivery:** ensure that the radiant warmer is on for at least half an hour and adjust the temperature on manual mode, with 100 per cent heater output.

Warm chain to keep the newborn warm includes the following:

1. Warm delivery room (26–28°C)
2. Always receive the baby in pre-warmed sterile towel
3. Warm resuscitation-radiant warmer

4. Immediate drying – dry the baby under the warmer, remove wet linen and wrap in a pre-warmed towel covering the head. Infants < 32 weeks are covered with a plastic bag prior to drying to prevent evaporative heat loss.
5. Skin-to-skin contact in the first one hour after birth for stable babies
6. Breastfeeding as soon as possible for the stable baby
7. Bathing postponed to after 24 hours of life: do not bathe the baby during hospital stay. Baby may be sponged.
8. Appropriate clothing – all babies, including term normal weight babies, should be covered with warm clothes including cap, socks, mittens and sweater.
9. Mother and baby together – keep the baby with mother in case of normal delivery and stable baby. Initiate KMC in the labour ward for stable LBW babies.
10. Monitor babies at risk of hypothermia.
11. Warm transportation, preferably using transport incubator

### **Management in postnatal wards**

Ensure that the baby is kept warm with a head cap and placed in a warm blanket.

- Practice “Bedding in” whenever possible.
- Kangaroo mother care for stable LBW babies
- Encourage breastfeeding on demand.
- Remove soiled clothes immediately.
- Keep windows closed and fans off.
- Do not bathe the baby.

### **Management in the NICU**

- Ideal NICU room temperature:  $28 \pm 2$  °C. Maintain the baby in Thermal Neutral Environment (TNE) by using heating devices like radiant warmer, incubator or warm cradle.
  - Measure temperature Q 4 h.
- 2. Radiant warmers**
- All unstable neonates, especially unstable preterm (less than 1500 grams) neonates should be managed under radiant warmers.
  - Receive newly born babies admitted for observation under radiant warmer (term and preterm).
  - Keep the warmer on in anticipation of admission in manual mode with 100 per cent heater output for 20 minutes.
  - As soon as the baby is received, change to skin servo control mode.
  - Place the sensor over the abdomen in midline, between umbilicus and xiphisternum. In the prone position place the sensor on the flank. Check position of sensor frequently. Do not apply the temperature probe on bony prominences or on areas of brown fat.
  - Cover the head with pre-warmed hat
  - Set appropriate abdominal skin temperature at 36.5°C. Check axillary temperature of baby Q 4 h. If the axillary temperature is < 36.5 °C, then increase the set temperature to 37.0 °C. Ensure that the skin sensor temperature correlates with the warmer temperature ( $\pm 0.5\%$  accuracy)
  - Monitor the amount of heater output required to maintain normal temperature.

- Need for increasing heater output may be an early sign of sepsis.
- Transfer the infant to an incubator or an open cot as soon as they are stable and their temperature is within the target range.
- For infants less than 32 weeks, cling wrap (plastic roll used to cover vegetables) can be used to cover the entire warmer if the infant is required to stay on the warmer for any extended length of time. Stretch the plastic cling wrap from one wall of the radiant warmer to the opposite wall. This is for ventilated newborns.

### 3. Incubators

Pre-warm an incubator to two degrees above that required by the infant (remember to adjust after the baby has been placed in the incubator).

**Air mode:** Set at Thermo Neutral Environment (Table 4.3)

**Skin mode:** Set at 36.5–37°C

- Preterm stable neonates < 1200 g or less than 32 weeks must be managed in incubators
- All the ports of the incubator must be kept closed.
- For infants < 28 weeks, humidification is required to prevent excessive trans-epidermal water loss.

- If the infant is less than 32 weeks' gestation and requires humidity, a temperature probe must be used to provide a guide to the infant's temperature.
- If the infant's axillary temperature rises above 37.2°C, reduce the air temperature by 0.5°C every hour until the infant's temperature falls within the target range.
- If the infant's temperature falls below 36.5°C, increase the incubator temperature by increments of 0.5°C every hour until the temperature is within the target range.
- Adjust humidity accordingly.
- Recheck within an hour of making any adjustments.
- The temperature probe will provide continuous monitoring during this time.

**Incubator humidity:** it is recommended that infants < 27 weeks' gestation be commenced in an incubator humidity of 80 per cent. However, this should be assessed according to skin integrity, gestational age, corrected gestational age and the set temperature requirement of the incubator.

Weaning of humidity should be alternated with weaning of the incubator temperature until a level is reached that maintains an axillary temperature within the target range.

*Table 4. Suggested values for balance of humidity and incubator temperature*

Incubator temperature(°C)	Humidity (%)
38	80
37	70
36	60
35	50
34	40

Weaning off humidity should be commenced during the first week of life when the infant is able to maintain a per axilla temperature within the target range. Weaning should commence at 5% per cent intervals over the period of a week to around 50 per cent at the end of the first week of life.

During the second week of life, the humidity can be reduced to 40 per cent and thereafter ceased if the incubator is at or less than 32 degrees. Some infants may require humidity until two to three weeks of age. However, this should be discussed with a senior nurse. Incubator humidity is provided by sterile water.

Incubator 'rain out': rain out should not occur. It usually means there is a mismatch between the humidity set and the incubator temperature.

#### **Incubator usage for phototherapy or isolation:**

##### **Phototherapy**

- Reduce the incubator temperature by 0.5°C when phototherapy commences.
- If the infant's temperature > 37.2°C reduce the incubator temperature by 0.5 °C. Infant may need to be transferred into an open cot.

##### **Isolation**

- Can be used in the NICU to isolate a newborn with a contagious infection.

#### **Grading out of incubator:**

thermal challenging should take place on a daily basis once the infant's axillary temperature has remained stable in the target range. Transition

from a thermally regulated environment to an open cot can occur if the following criteria are met:

- Birth weight regained and weight gain following a normal curve on the growth chart (average 15-30 grams per day for a healthy preterm infant).
- Weight greater than 1200 grams.
- Parenteral fluids < 50 per cent of total daily fluid allowance.

#### **4. Cot-nursing in hospital**

- Only stable babies will be cared for under cot.
- If possible, keep the baby and mother on a single bed.
- Adequately clothe the baby (including head and extremities).
- Keep ambient atmospheric temperature warm for baby's weight and postnatal age (28–32°C). Monitor body temperature frequently, at least every three hours, during the initial postnatal days.
- In cold weather, wrap the baby well but in hot weather (or when the baby has a fever) use loose clothes.

##### **Transport of newborn:**

- Always stabilize the baby's temperature before transport.
- Ideally, the baby must be transported in a transport incubator.
- In the absence of a transport incubator, special care needs to be taken to prevent hypothermia.
- The embrace bag can be used for in-hospital transport of stable newborns. The temperature is maintained for a period of four hours.

- Wrap the baby in pre-warmed cotton and swaddle the baby.
- Keep all windows of the vehicle closed.
- For stable babies, Kangaroo care is recommended during transport

Babies at risk of hypothermia:

- All newborn babies at birth.
- Preterm and low birth weight babies.
- Small for gestational age babies.
- Sick neonates.
- Neonates undergoing procedures.
- During transport.

Signs and symptoms of hypothermia

- a. Peripheral vasoconstriction-acrocyanosis, cool extremities, decreased peripheral perfusion
- b. CNS depression-lethargy-bradycardia-apnoea-poor feeding
- c. Increased metabolism-hypoglycaemia-hypoxia-metabolic acidosis
- d. Increase of pulmonary artery pressure distress, tachypnoea
- e. Chronic signs (weight loss, poor weight gain)

### **Management of hypothermic newborn**

#### **Mild Hypothermia**

- Where possible, initiate skin-to-skin contact with the mother to improve thermoregulation and promote maternal bonding and decrease the need to separate the neonate from the mother.

- If the neonatal temperature is still decreasing after 30 minutes of skin-to-skin contact, or if there are any symptoms of neonatal distress, cease skin-to-skin contact. Take the neonate to the ward nursery and place on the radiant warmer, request the medical staff to review the neonate.
- Assess for any risk factors or signs of an underlying pathological condition which may cause neonatal hypothermia.
- When the neonatal temperature returns to the normal range, the neonate may be dressed with warmed clothing, including a bonnet, and wrapped warmly.
- Monitor the neonatal temperature hourly for three hours to ensure that the neonate's temperature remains stable.
- Inform the paediatric resident if the neonatal temperature is unstable despite these measures.

#### ***Moderate hypothermia (32 to 36°C)***

- Skin-to-skin contact should be in a warm room and warm bed.
- Warmer/incubator may be used, if available.
- Continue rewarming till temperature reaches normal range.
- Monitor every 15-30 minutes.
- Temperature increase should be 0.5°C every 30-60 minutes.

#### ***Severe hypothermia***

- Use air heated incubator (air temperature at 35-36°C) or manually operated radiant warmer

- Once the baby's temperature reaches 34°C, the rewarming process should be slowed down by 0.5°C every 30-60 minutes.
- Rapid correction of severe hypothermia could result in peripheral vasodilation and shock
- Check random blood sugar (RBS)
- Bolus of normal saline 10-20ml/kg
- Give oxygen while maintaining normal saturation
- Consider treatment of the underlying cause

**Table 5. Thermo-neutral environment based on weight and age of the baby**

Age	Weight in grams Under 1200	1200-1500 grams	1500-2500grams	Greater than 2500 grams
0-12 hours	34.0-350	33.9-34.3	32.8-33.8	32.0-33.8
12-24 hours	34.0-35.0	33.3-34.3	31.8-33.8	31.0-33.7
24-48hours	34.0-35.0	33.0-34.2	31.5-33.5	30.5-33.3
48-96 hours	34.0-35.0	33.0-34.0	31.2-33.3	30.5-33.0
4-14 days	33.0-34.0	33.0-34.0	31.0-33.0	
2-3 weeks	32.2-34.0	32.2-34.0		
3-4weeks	31.5-33.5	31.5-33.5		

(The range is provided in degree centigrade)

(Source: Fanaroff AA, Klaus MH. The Physical Environment. In: Fanaroff AA, Fanaroff JM, eds. Klaus and Faranoff's Care of the High Risk Neonate. 6th ed. Philadelphia, PA: Elsevier Saunders; 2013:132-150.)

## Hyperthermia

- If the baby's temperature is > 37.5 °C:
  - In the postnatal ward, keep the baby exposed for 15 minutes. Check temperature. If the temperature has normalized, it is most likely environmental, if it persists for more than four hours despite environmental exposure, investigate for infection.
  - Check signs of dehydration and assess fever after hydration.
  - A baby in a spread-eagle posture with plethoric peripheries and warm temperature is more likely to have

hyperthermia due to environmental causes. If the baby is flexed with tummy toe difference, consider endogenous fever and rule out sepsis.

- Paracetamol and tepid sponging are very rarely needed in the newborn period.

## Reference

- Cloherty and Starks's. Manual of Neonatal care 8<sup>th</sup> edition.
- WHO. Managing newborn problems: A guide for doctors, nurses and midwives. 2003.

## Kangaroo mother care

The definition of Kangaroo mother care (KMC) is care of preterm infants carried out skin-to-skin with the mother. Its key features include early, continuous and prolonged skin-to-skin contact between the mother and the baby, and exclusive breastfeeding (ideally) or feeding with breast milk.

Continuous KMC is defined as the practice of skin-to-skin care continuously throughout the day without breaking the contact between mother and baby, while intermittent KMC is the practice of skin-to-skin care alternated with the use of either a radiant warmer or incubator care for the baby.

Continuous KMC is performed for all stable newborns under 2000 grams. This is a strong recommendation from WHO, has shown significant reduction in neonatal mortality and morbidity and has resulted in early discharge from the hospital.

Intermittent KMC, rather than conventional care, is recommended for newborns weighing 2000 g or less at birth, if continuous Kangaroo mother care is not possible. This is strongly recommended.

KMC has benefits both to the newborn and the mother; one of the benefits is prevention of hypothermia for the newborn.

The details of KMC are mentioned In the national guideline, to be used as a reference.

### Reference

1. WHO recommendations on interventions to improve preterm birth outcomes:  
[http://apps.who.int/iris/bitstream/handle/10665/183037/9789241508988\\_eng.pdf?sequence=1](http://apps.who.int/iris/bitstream/handle/10665/183037/9789241508988_eng.pdf?sequence=1)
2. WHO. Managing newborn problems: A guide for doctors, nurses and midwives. 2003.



## CHAPTER 3:

### FLUID AND ELECTROLYTE MANAGEMENT

Transition from foetal to newborn life is associated with major changes in water and electrolyte homeostatic control. Careful fluid and electrolyte management in term and preterm infants is an essential component of neonatal care.

- Total body water for preterm is > 80 per cent of body weight
- Total body water (TBW) = intracellular fluid (ICF) + extracellular fluid (ECF)
- Insensible water loss (IWL) = fluid intake - urine output + weight change

Water is lost through skin and breathing: 40 per cent (Insensible loss) and urine 50-60 per cent (obligatory)

Water and electrolytes are controlled by antidiuretic hormone and kidneys.

#### 1. Renal losses:

Renal function matures with increasing gestational age (GA). Immature sodium and water homeostasis is common in the preterm infant.

#### 2. Extra renal losses:

In VLBW infants, insensible water loss can exceed 150 mL/kg/day owing to increased environmental and body temperatures, skin breakdown, radiant warmers, phototherapy and extreme prematurity.

Respiratory water loss increases with decreasing GA and with increasing respiratory rate; in intubated infants, inadequate humidification of the inspired gas may lead to increased IWL.

Other fluid losses that should be replaced if amount is deemed significant include stool (diarrhoea or ostomy drainage), cerebrospinal fluid (from ventriculostomy or serial lumbar punctures), and nasogastric tube or thoracostomy tube drainage.

**Fluid requirement:** normal healthy term and late preterm newborns usually don't need IV infusions. Fluid usually is started in preterm (G/A <34 weeks or birth weight <1500gm) or critically sick newborns.

**Type and amount of fluid required:** varies with birth weight and postnatal age of the newborn infant.

*Table 6. Estimated maintenance fluid requirements based on weight and postnatal age*

Birth Weight	Fluid Rate (ml/kg/day)			
	Postnatal Age			
	Day 1	Day 2	Day 3-6	≥ Day 7
<750 gm	100-140	120-160	140-200	140-160
750-1,000 gm	100-120	120-140	130-180	140-160
1,000 - 1,500 gm	80-100	100-120	120-160	150
1,500 - <2,500 gm	60-80	80-100	120-160	150
>2,500 gm	60-80	80-100	90-150	

The volume of fluids given should be estimated based on the infant's clinical status.

- Term infants: depending on the tolerance of the previous day's fluid therapy, estimations of IWL and clinical status of the infant, an increase of 10-20 ml/kg/day may be considered.
- VLBW infants (during the 1st week of life): depending on weight and serum sodium levels, fluid therapy should be managed to keep serum sodium at a normal range (135-145 mEq/L).
- ELBW infants (especially <750 gm) may have fluid requirements up to 200 ml/kg/day.
- ↑Daily total fluid intake (+20 ml/kg) for infants under radiant warmers or phototherapy.

Main goal of fluid therapy is:

- Weight loss → 1- 2%/kg/day in the first 7 days
- Urine output → 1- 2ml/kg/hr. (optimal)
- Urine Sp. Gravity → 1.005 – 1.015

#### ■ Euelectrolytemia and Euglycemia

By the end of the first week of life, fluid requirements decrease toward 150 ml/kg/day in VLBW infants as the skin becomes more mature.

**N.B:** Gastric feeding and any medication that needs dilution before administration (e.g., antibiotic, dopamine), the volume should be subtracted from the total IV fluid intake.

#### Choice of fluid:

Term babies and babies with birth weight > 1500g

- DAY 1 - 10% Dextrose to maintain a glucose infusion of 4-6mg/kg/min
- DAY 2 TO 7 - 10% Dextrose and sodium and potassium to be added after 48 hours

Preterm Baby with Birth Weight 1000-1500 Grams

- DAY 1 - 10% Dextrose

- DAY 2 TO 7 - 10% Dextrose and sodium and potassium to be added after 48 hours
- AFTER DAY 7 - Fluids should be given at 150-180 ml/kg/day and sodium supplementation at 3-5 mEq/kg should continue till 32-34 weeks corrected gestational age.

**Table 7. Electrolyte requirement**

Day 1	No routine electrolytes except <b>Ca<sup>2+</sup>:</b> 1 mmol/kg/day Add calcium routinely to less than 1500gm, PNA, infant of Diabetic mother
Day 2 onwards	Add electrolytes <b>Na<sup>+</sup>:</b> 3 mmol/kg/day (very preterm infants may need more) <b>K<sup>+</sup>:</b> 2 mmol/kg/day after 48hours Continue Ca <sup>2+</sup> 1 mmol/kg/day

#### Reference

- Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition.
- NICU neonatal care (FMOH)
- Neonatal Care Pocket Guide for Hospital Physicians, Egypt, 2010

## Hyponatraemia

#### Definition:

- Serum Na<sup>+</sup><135mEq/L
- Normal level 135-145 mEq/L
- Most neonates with Na >125mmol/L are asymptomatic
- If Na <120meq/L lethargy and seizure can occur.
- Acute hyponatraemia is if the hyponatraemia developed within 24 hours
- Chronic hyponatraemia developing >24 hours may have subtle features.

#### Common causes:

- Iatrogenic water overload following birth
- SIADH
- Increasing gastrointestinal losses (vomiting, diarrhoea or nasogastric aspirate)
- Decreasing renal losses (renal tubular disorders, late hyponatraemia of prematurity after relief of obstructive uropathy, salt wasting, congenital adrenal hyperplasia)
- Third space loss (e.g., NEC)
- Diuretic therapy, especially loop diuretics (e.g., furosemide).

#### Clinical manifestations:

- Hypotonia, lethargy and convulsions (with plasma sodium <125mEq/L and partly related to the acuteness of the fall)

- Inappropriate increase of weight with iatrogenic water overload in early postnatal life or decrease of weight with sodium depletion in later postnatal life
- Features of the underlying disease
- SIADH (suspected by decrease in serum Na<sup>+</sup> and urine output)
  - Criteria: decreasing serum Na<sup>+</sup>, increasing urine Na<sup>+</sup> loss
  - urine osmolality > plasma osmolality
  - normal adrenal & renal function

#### **Management:**

- Management is according to the problem
- Management is recommended if Na <130meq/L.
- Management is determined by the presence of seizure/altered consciousness state and fluid status.

Symptomatic hyponatraemia, e.g., seizure/coma or Na <120mEq/L:

- If the serum sodium concentration is less than 120 mEq/L, regardless of whether the hyponatraemia is due to free water overload or total body sodium deficit, then correction of the serum sodium concentration up to 120 mEq/L is recommended with administration of 4 to 6 mL/kg of 3% saline solution (513 mEq of sodium per litre=0.5mEq in 1ml) over 4 to 6 hours, depending on the severity of hyponatraemia and using the above formula.
- With symptomatic hyponatraemia where the serum sodium concentration has reached 120 mEq/L and the risk of acute central nervous system symptoms has been minimized, complete correction of hyponatraemia slowly over the next 48 hours.

#### **Asymptomatic hyponatraemia:**

- In patients with asymptomatic hyponatraemia whose serum sodium concentration is greater than 120 mEq/L, replace Na<sup>+</sup> loss using replacement formula with 5% DW/0.45 to 0.9% saline solution.
- Target of increment should be not more than 10-12meq/L over 24 hours.

#### **SIADH**

- Restrict fluid intake to half to one-third of the daily requirement
- Na<sup>+</sup> replacement using hypertonic 3% NaCl 4-6 ml/kg over 4-6 hours if Serum Na<sup>+</sup> <120 mEq/L or if neurologic signs such as seizures develop.
- Initiate furosemide (1 mg/kg IV Q 6 hrs),
- Once serum Na<sup>+</sup> >120 mEq/L and neurologic signs abort, fluid restriction alone can be utilized.

Total Na<sup>+</sup> replacement = (Desired Na<sup>+</sup> (mEq) - Actual Na<sup>+</sup> (mEq)) × Weight (kg) × 0.7

- Check serum Na<sup>+</sup> after 24 hours of replacement
- Treat the underlying cause.

**N.B.:** Rapid correction of hyponatraemia → pontine myelinolysis.

#### **Reference**

1. Neonatal Guideline 2017-19, NHS Trust, UK.
2. Cloherty and stark's, Manual of Neonatal Care 8<sup>th</sup> edition.
3. Neonatal Care Pocket Guide for Hospital Physicians, Egypt, 2010

# Hypernatremia

**Definition:** Serum Na<sup>+</sup> > 145 mEq/L.

## Common causes:

- Excessive water loss.
- ↓Free water intake (as in lactation failure)
- ↑Trans epidermal water loss (e.g., skin sloughing)
- ↑Renal losses (e.g.,
  - Diuretic phase following acute kidney injury
  - Obstructive uropathy
  - Osmotic diuresis, glycosuria
- ↓GI losses (diarrhoea and vomiting)
- Excess Na<sup>+</sup> intake.
- Sodium-containing solution administration (NaHCO<sub>3</sub> bolus infusion and sodium-containing medications).
- Inappropriate fluid normal saline boluses during resuscitation.
- Inappropriately prepared formula.

## Clinical manifestations:

- Irritability/high pitched cry: unsettled during breastfeeding, poor feeding.
- Usual signs of dehydration (sunken fontanelle, reduced skin turgor) may be absent, weight loss, reduced urinary output, fever.
- Lethargy/altered level of consciousness, tremor, hypertonicity and convulsions.
- Diagnosis may be delayed as signs of hypovolaemia and decreased skin turgor occur late.
- Severe hypernatremia may lead to permanent CNS damage.

It is important to determine the chronicity of hypernatremia when determining the rate of correction.

- Hypernatremia is acute if it has been present for less than 24 hours. Acute hypernatremia is mostly caused by excessive fluid losses; patients may also have manifestations of hypovolaemia. The goal of the treatment is to replace the entire water deficit in 24 hours. Calculate the water deficit with 100ml/kg. Administer half of the calculated deficit in the first 8 hours and the next half in the next 16 hours.
- Hypernatremia is chronic if it has been present for longer than 24 hours. Most patients are asymptomatic due to cerebral adaption, which occurs within one to three days. The goal of this treatment is to lower the serum sodium by a maximum of 10-12 mEq/L in a 24 hour period.

Management: the rate of correction in moderate to severe chronic hypernatremia (plasma sodium ≥ 150 mEq/L for greater than 24 hours) or severe acute hypernatremia (sodium greater than 160 mEq/L) should not exceed a fall of 0.5 mEq/L per hour (i.e., 10 to 12 mEq/L per day).

## Mild hypernatremia (<160mEq/L):

- Manage in postnatal ward or by the mother's side
- Feed baby with EBM/formula milk on measured feeding
- Monitor blood glucose according to the protocol
- Repeat electrolyte and calcium replacement after 24 hours

- Baby improving: continue routine postnatal care
- Start deficit correction with intravenous fluid management if:
  - Oral feeds are not tolerated
  - Baby is unwell
  - Repeat electrolyte replacement shows worsening and hypernatremia is changed to moderate or severe
  - Associated hypocalcaemia

**Moderate(161-175mEq/L) to severe Hypernatremia ( $\geq 175\text{mEq/L}$ ):**

- If sign of shock, resuscitate with boluses to restore circulating blood volume with 20ml/kg 0.9% saline
- Fluid management should then be based on the initial serum sodium.
- Use 5% DW and 0.3-0.45% saline solution IV in volumes equal to the calculated fluid deficit, given over 48-72 hrs.

Water deficit (in L) = [(current Na level in mEq/L  $\div$  145 mEq/L) - 1] X 0.7  $\times$  weight (kg)  
 (or: water deficit per hour = current weight X 4ml/kg X 12mEq/l)

- Reduce serum Na<sup>+</sup> level no faster than 0.5 mEq/L/hr (or no more than 10-12mEq/L reduction over 24 hours)
- The sodium concentration of the fluid to be administered is approximately 10-15mEq/L less than the serum sodium level, 3% sodium solution may be required to achieve this when serum sodium is more than 165 mEq/L
- Rapid fall in serum sodium → cerebral oedema
- Extreme hypernatremia (sodium > 200 mEq/L [ $> 200 \text{ mmol/L}$ ]) should be treated

with peritoneal dialysis, especially if poisoning causes a rapid rise in serum sodium.

- However, maintenance fluid also has to be administered.

**Monitor:**

- Vital signs
- Keep a strict fluid balance chart
- Monitor weight once or twice daily
- Monitor RBS, serum electrolytes and urine volume and specific gravity, adjust fluid administration accordingly.
- Once adequate urine output is noted, add potassium.
- Do not correct hyperglycaemia with insulin, this can reduce plasma osmolality rapidly and precipitate cerebral oedema.

**Complications:**

- Venous and arterial thrombosis, subdural and cerebral haemorrhage, cerebral oedema (especially during rehydration), seizures (especially following rehydration) and cerebral infarction
- Apnoea and bradycardia
- Hearing impairment – may be transient
- Renal failure, hypertension
- Long term developmental delay, cognitive impairment

**Reference**

1. Neonatal Guideline 2017-19, NHS Trust, UK
2. Cloherty and Stark's, Manual of Neonatal Care 8<sup>th</sup> edition
3. Neonatal Care Pocket Guide for Hospital physician, Egypt, 2010

## Hypokalaemia

### Definition:

- Serum K+ < 3.5 mmol/L
- Normal level 3.5-5.5 mEq/L

### Severity of hypokalaemia:

- Mild hypokalaemia 3.0 to 3.4 mEq/L
- Moderate hypokalaemia 2.5 to 2.9 mEq/L
- Severe hypokalaemia < 2.5 mEq/L
- Symptoms rarely occur if potassium level > 2.5 mmol/L

### Common causes:

- Inadequate intake
- Metabolic alkalosis
- Renal causes
- Diarrhoea, ileostomy drainage
- Medications (including diuretic therapy, sodium bicarbonate infusions, insulin, salbutamol)

### Symptoms and signs:

- Muscle weakness and paralysis

### ECG changes:

- Increased amplitude and width of P wave
- Prolongation of PR interval
- T wave flattening and inversion
- ST depression
- Prominent U waves (best seen in precordial leads)
- Apparent long QT interval due to fusion of T and U waves

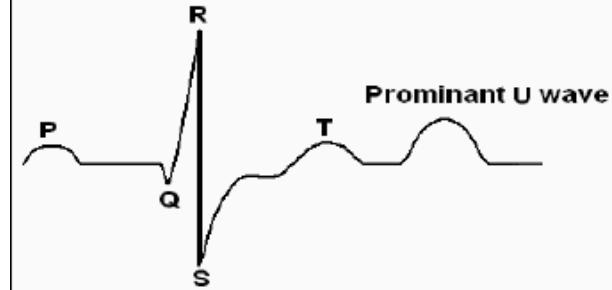


Figure 10. ECG changes in hypokalaemia

### Management:

Treatment will depend on the underlying cause and the severity of the hypokalaemia.

- Mild (serum level 3–3.5 mmol/L)
  - No intervention needed
- Moderate hypokalaemia (serum level 2.5 to <3 mmol/L)
  - Treat by Oral potassium supplementation
  - Oral therapy: 0.5-1 mEq/kg/day divided and given with feedings
- Severe hypokalaemia (serum level <2.5 mmol/L)
  - Treat by slow potassium replacement IV
- (1 mEq/kg KCl → ↑ serum K+ by 1 mEq/L), with dose adjustment based on serum K+ level.
- For emergency treatment of symptomatic hypokalaemia (arrhythmias), KCl (0.5-1 mEq/kg IV) may be given over 30-60 minutes, and then reassess (maximum infusion rate is 1 mEq/kg/hr).
- Maximum concentration of K+ is 40 mEq/L for peripheral venous infusion and 80 mEq/L for central venous infusion.

- Dose dependent on potassium correction=  $(\text{Desired K} - \text{actual K}) \times \text{weight} \times 0.7$
- **CAUTION:** Consider delayed treatment or monitor carefully if urine output is low or renal function is abnormal.

#### Patient monitoring:

- Continuous ECG monitoring
- Monitor potassium levels according to clinical need
- For babies on IV fluids with mild hypokalaemia (potassium 3-3.5 mmol/L), check daily
- Check more frequently in significant hypokalaemia (serum level <3 mmol/L) and symptomatic hypokalaemia
- Once plasma/serum potassium level is normal, continue potassium supplementation for a further week if baby is orally fed, to allow replenishment of total body (intracellular) potassium stores.

- Mild (5.5–6.5 mmol/l),
- Moderate (6.5–7.5 mmol/l)
- Severe (>7.5 mmol/l)

#### Common causes:

- Non oliguric hyperkalaemia in the first 72 hours of life of the very preterm infant.
- ↑Potassium administration
- ↓Potassium clearance (e.g., renal failure & CAH)
- ↑Potassium release (e.g., IVH, cephalhematoma, intravascular haemolysis, bowel infarction and hypothermia)
- Oliguric renal failure (e.g., due to hypoxic event)
- Hyperkalaemia is believed to be exacerbated by:
  - metabolic acidosis, due to exchange of intracellular  $K^+$  with extracellular  $H^+$
  - renal impairment and hypovolaemia

#### Reference

4. Neonatal Guideline 2017-19, NHS Trust, UK
5. Manual of Neonatal Care 8th edition.
6. Neonatal Care Pocket Guide for Hospital Physiciansl, Egypt, 2010

## Hyperkalaemia

#### Definition:

- Serum potassium level >6 mEq/L in a non-haemolyzed specimen
- Symptomatic hyperkalaemia may begin at a serum K level >6 mEq/L.
- hyperkalaemia can be classified according to serum potassium into: -

#### Clinical manifestations:

- It may be asymptomatic or may result in arrhythmias and cardiovascular instability.
- ECG changes:
  - Peaked T-waves
  - flattened P waves,
  - Prolonged PR interval
  - Broadened QRS complexes
  - Disappearing of the P-wave
  - bradycardia, tachycardia, SVT,
  - Ventricular tachycardia, ventricular fibrillation and impaired AV conduction.



**Figure 11. ECG changes in hyperkalaemia**

- Electrocardiography (ECG) monitoring is mandatory in patients with serum potassium >6.5 mmol/l. If ECG is not available, put the baby on monitor with chest leads.

**Treatment:** in patients with moderate to severe hyperkalaemia (>6.5 mmol/l), especially those with renal impairment, therapeutic strategies include:

1. Discontinue all exogenous sources of potassium.
2. Stabilize the conducting system by 10 % Calcium gluconate (1-2 ml/kg) IV over one hour
3. Intracellular shifting of K+
  - Human regular insulin (a bolus of 0.05 unit/kg), with D10W (2 ml/kg), followed by a continuous infusion of insulin 10 units/100 ml, at a rate of 1 ml/kg/ hr (0.1unit/kg/hr), with 2-4 ml/kg/hr D10W. Monitor for hypoglycaemia.
4. Salbutamol: 4 micrograms/kg over 10 min nebulized
5. Inhaled Salbutamol seems to be generally well tolerated.
6. Enhanced Kexcretion
  - a. Furosemide 1 mg/kg/dose (if there is adequate renal function).

7. NaHCO<sub>3</sub> 1-2 mEq/kg (slowly, at least over 30 minutes). Avoid rapid infusion (may lead to IVH, especially in infants <34 weeks' gestation and younger than three days).
8. Exchange transfusion or peritoneal dialysis
  - a. Peritoneal dialysis or double volume exchange
  - b. Use fresh whole blood (<24 hours).

#### Patient monitoring:

- Continuous ECG monitoring
- Recheck serum K+ every four to six hours
- Monitor blood glucose every 30 min for first two hours during and after infusion
- Monitor urine output and maintain good fluid balance
  - If urine output <1 mL/kg/hr and unless baby volume depleted, give furosemide 1 mg/kg IV until volume corrected
- Treat any underlying cause (e.g., renal failure)

#### Reference

1. Neonatal Guideline 2017-19, NHS Trust, UK
2. Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition
3. Neonatal Care Pocket Guide for Hospital Physician., Egypt, 2010

## Hypocalcaemia

#### Definition:

- Total serum calcium <7 mg/dl (<1.75mmol/L) or ionized calcium <4 mg/ dl (<1 mmol/L)

### **Common causes:**

- Early onset hypocalcaemia occurs within the first three days of life, and is associated with IDM's, asphyxia and prematurity.
- Late onset hypocalcaemia develops after the first week of life and usually has a specific cause (e.g., high phosphate intake, malabsorption).

### **Clinical manifestations:**

- Often asymptomatic but may show jitteriness, twitches, apnoea, seizures and abnormalities in cardiac function.

### **Management:**

- Prevented by infusion of 20-45 mg/kg/day (up to 70-80 mg/kg/day for preterm infant) elemental calcium in IV fluids.
- If asymptomatic and total serum Ca<sup>+2</sup> >6.5 mg/dl or an ionized Ca<sup>+2</sup> >0.8-0.9 mmol/L → observe closely.
- If biochemical abnormality persists (total serum Ca<sup>+2</sup> <6.5 mg/dl or ionized Ca<sup>+2</sup> <0.8-0.9 mmol/L) → give additional elemental calcium IV (10-20 mg/Kg for 4-6 hrs).

- If active seizures → give calcium therapy (10-20 mg/Kg elemental calcium by IV infusion over 10-15 min).
- Care should be taken in administering the IV calcium
  - Monitor HR while giving Calcium, discontinue infusion if <100/min.
  - Infants who are on digoxin should receive calcium only by constant infusion.

Check the IV site before & during administration.

### **Reference**

1. Cloherty and Stark's. Manual of neonatal care, 8<sup>th</sup> edition
2. Neonatal Care Guideline for Hospital Physicians. Egypt, 2010

## CHAPTER 4:



# Hypoglycaemia and hyperglycaemia

### Hypoglycaemia

Hypoglycaemia is one of the most common metabolic problems seen in neonatal intensive care units (NICU). Confirming a diagnosis of clinically significant hypoglycaemia requires interpretation of blood glucose values within the clinical context. The definition of hypoglycaemia as well as its clinical significance and management remain controversial. Blood glucose levels in the first hours of life are typically lower than normal values of older children or adults.

The thresholds for treating hypoglycaemia depend on the presence of symptoms, the age of the infant in hours and the persistence of hypoglycaemia.

According to the Paediatric Endocrine Society, by 48 to 72 hours of life glucose control should be similar to that of older children and adults, and plasma glucose levels should be >60 mg/dL. Bedside whole blood glucose measurements are 15 per cent lower than plasma levels.

#### Screening:

- Serial blood glucose levels should be routinely measured in infants who have risk factors for hypoglycaemia and in infants who have symptoms that could be due to hypoglycaemia.

#### Common causes of hypoglycaemia in neonates:

↓Glucose stores and ↓ production

- IUGR or SGA
- Preterm or post-term neonates
- ↓Caloric intake
- Delayed feeding

↑Glucose utilization (hyperinsulinism)

- IDM or LGA infants
- Erythroblastosis fetalis
- Abrupt cessation of high glucose intake
- Beckwith-Wiedemann syndrome
- Islet cell hyperplasia
- Insulin producing tumours
- After exchange transfusion
- Maternal drugs (intrapartum glucose infusion)

↑Glucose utilization and/or ↓ Production

- Perinatal stress (hypothermia, sepsis, asphyxia, respiratory distress, shock)
- Polycythaemia
- Maternal drugs ( $\beta$ - blockers, steroids)
- Endocrine deficiency (adrenal haemorrhage, CAH, hypothyroidism)
- Inborn errors of metabolism (galactosemia, glycogen storage disease, tyrosinemia)
- Congenital heart diseases

### Clinical manifestations:

- Signs are non-specific and can be similar to signs of many other problems.
- Asymptomatic hypoglycaemia is a common transient problem in most neonates.
- A smaller proportion of infants with hypoglycaemia can be symptomatic. Symptomatic hypoglycaemia is an emergency and requires intravenous treatment.
- Symptoms include: jitteriness, tremors, irritability, seizures, coma, apnoea, cyanosis, lethargy and poor feeding, weak or high-pitched cry, hypothermia and respiratory distress. Episodes of sweating, sudden pallor, hypothermia and cardiac arrest have also been reported.

**N.B:** Clinical signs of hypoglycaemia should be alleviated with concomitant correction of plasma glucose levels.

If clinical signs attributable to hypoglycaemia persist despite intravenous glucose, then other causes of persistent/resistant hypoglycaemia should be explored.

### Prevention:

- At birth, dry the baby, avoid hypothermia and encourage skin-to-skin care.
- Encourage early enteral feeding (within one hour of age) and frequently thereafter (at least eight feeds/day).
- Perform serial blood glucose monitoring in infants at risk of hypoglycaemia, starting from the first 1-2 hours of life and do not allow them to wait for >3 hours between feedings.

- Monitor blood glucose values until full feedings and three normal pre-feeding readings  $>45$  mg/dl are taken.
- Initiate tube-feeding with EBM or formula in infants who are not able to suck adequately. Feed hourly to start off, and increase the interval between feeds if blood glucose remains  $>45$  mg/dl and the infant tolerates feedings.
- Initiate IV D10W if the infant is unable to tolerate nipple or tube feedings, with blood glucose monitoring.

### Management:

- Serum glucose levels should always be evaluated and treated in high-risk infants in which hypoglycaemia is anticipated or when the neonate is symptomatic
- Management includes anticipation of neonates at risk, correction and investigation and treatment of the cause.
- Asymptomatic hypoglycaemia: 25mg/dl to 45mg/dl
- Enteral feeding
- Start enteral feeding at 60-80mL/kg/day if there are no contra-indications.
- If persistent, consider admission to NICU and administration of IV fluid

### Monitoring:

- Repeat BGL after 30 minutes of treatment; if normal, then check at three hours.
- Asymptomatic infants with BGL  $< 25$  mg/dl or symptomatic hypoglycaemia
- Admit to NICU immediately for IV supplementation.
- Give bolus of 200mg/kg that is 2mL/kg of 10% dextrose

- Continue IV glucose supplementation with maintenance fluid 10% dextrose at 6-8mg/kg/min recheck glucose after 15-30 minutes
- If hypoglycaemia continues then aim to increase GIR by 2mg/kg/min
- Increasing GIR
- Increase dextrose concentration or increase total fluids by 20mL/kg/day
- If the concentration of dextrose is > 12.5%, don't use the peripheral line, use central access.
- When increasing the total fluid to increase GIR, always consider the daily fluid requirement, better not to go beyond 20m/kg increment
- Monitoring
  - Recheck BGL at 15-30 minute intervals until BGL is  $\geq$  45mg/dl.
  - Once BGL is  $\geq$  45mg/dl then check 3 hourly.
  - If two consecutive three hourly BGL is normal, then can extend to six hourly BGLs

#### **Recurrent / Persistent hypoglycaemia:**

This condition should be considered when an infant fails to maintain normal BGL despite a GIR of 12 mg/kg/min or when stabilization is not achieved by seven days of therapy. High

levels of glucose infusion may be needed in the infant to achieve euglycemia.

Besides increasing GIR for resistant hypoglycaemia, certain drugs may be tried. Before administration of drugs, take serum insulin and cortisol during low sugar level to investigate the cause.

Drugs that are used include the following:

- Hydrocortisone 10mg/kg/day IV in two divided doses for 24 to 48 hours
- Glucagon 100 mg/kg subcutaneous or intramuscular (max 300 mg) – maximum of three doses.
- Diazoxide can be given orally 10-25 mg/kg/day in three divided doses.
- Octreotide (synthetic somatostatin in dose of 2-10  $\mu$ g/kg/day subcutaneously, two to three times a day.
- Surgery if tumour is the underlying cause.

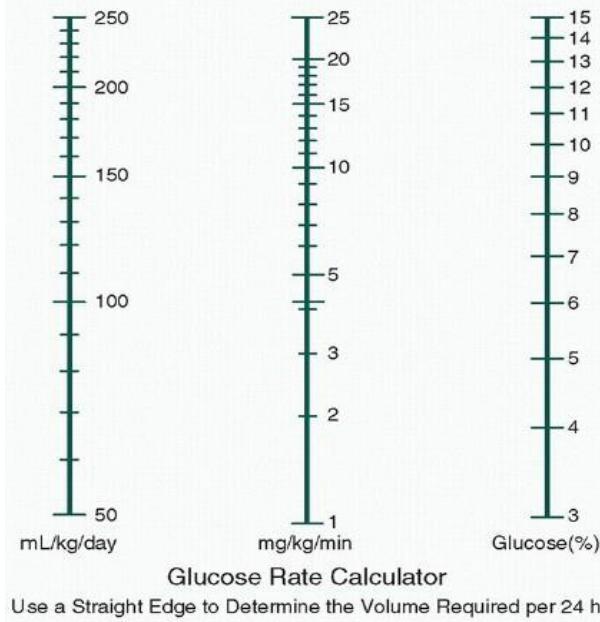
If blood glucose is maintained at more than 45 mg/dl for more than six to eight hours, reduce GIR by 2 mg/kg/min every four to six hours. If glucose is less than 45mg/dl during tapering, resume the previous GIR.

**Decreasing GIR:** can be done by reducing concentration of dextrose, reducing rate and introducing of feeding.

#### **Glucose infusion rate calculation**

$$\text{GIR (mg/kg/min)} = \frac{(\text{Fluid rate (ml/hr)} \times \text{Glucose concentration})}{(6 \times \text{Weight (kg)})}$$

$$\text{GIR (mg/kg/min)} = \frac{(\text{Total Fluid (ml/kg/day)} \times \text{Glucose concentration})}{(6 \times \text{Weight (kg)})}$$



**Figure 12. Glucose infusion rate calculator**

Formula to Calculate Special Dextrose Solutions (Pearson's Square):

How to mix two solutions, differing in concentration, to provide a third solution.

The final concentration must lie somewhere between the strengths of its components, that is, the mixture must be stronger than its weakest component and weaker than its strongest.

To prepare the fluid, use the following formula. We need to prepare  $x\%$  DW from  $a\%$  DW and  $b\%$  DW:

**General formula is**

$$V_b = \frac{(a - x) T_v}{(a - b) + (x - b)} \quad V_a = \frac{(x - b) T_v}{(a - b) + (x - b)}$$

Where

$$\begin{aligned} x &= \text{conc. of DW wanted} & V_b &= \text{volume of b} \\ a &= \text{highest conc. of DW} & V_a &= \text{volume of a} \\ b &= \text{lowest conc. of DW} & T_v &= \text{total volume} \\ & & & \text{needed} = (V_b + V_a) \end{aligned}$$

**Example 1: How to prepare total volume ( $T_v$ ) of 10% DW from 40% DW & 5% DW.**

Given

$$\begin{aligned} x &= 10\% & V_b &= \text{Volume of 5\%} \\ a &= 40 & V_a &= \text{Volume of 40\%} \\ b &= 5\% & T_v &= \text{total volume} \\ & & & \text{needed} = (V_b + V_a) \end{aligned}$$

Using the general formula

$$\begin{aligned} V_b &= \frac{(40 - 10) T_v}{(40 - 10) + (10 - 5)} & V_a &= \frac{(10 - 5) T_v}{(40 - 10) + (10 - 5)} \\ V_b &= (30) T_v / 35 & V_a &= (5) T_v / 35 \end{aligned}$$

Total daily fluid volume required by a baby girl weighing 3000gm (3kg) is -

$3 \times 100 = 300$  ml/day and type of fluid to be given is 10% DW:

**Therefore**

$$\begin{aligned} T_v &= 300 \text{ml}, V_b = 30 \times 300 / 35, V_a = 5 \times 300 / 35 \\ &= 257.1 \text{ml} & &= 42.85 \text{ml} \end{aligned}$$

$$\begin{aligned} \text{Thus, total volume} &= V \text{ of } b (257.1) + V \text{ of } a (42.85) \text{ ml.} \\ &= 299.95 \text{ml} (\sim 300 \text{ ml}) 10\% \text{ DW} \end{aligned}$$

## Hyperglycaemia

**Definition:**

- There is no established definition of hyperglycaemia.
- Whole blood glucose  $>125$  mg/dl or plasma glucose  $>145$  mg/dl

## Clinical Features

- Osmotic diuresis leading to dehydration
- Poor weight gain

## Risk factors

- Immaturity of pancreatic function (e.g., extremely premature infants and small-for-gestational-age)
- Insulin resistance
- Glucose overload (e.g., exogenous parenteral glucose, administrator error)
- Stress (e.g., infection, pain)
- Side effects of a medication (e.g., glucocorticoid, aminophylline treatment)
- Neonatal diabetes mellitus

## Management:

1. Reduce dextrose intake
    - Prevention of hyperglycaemia by carefully adjusting GIR and frequently monitoring blood glucose should be the primary goal.
    - If the neonate has signs of dehydration or is in shock, treat accordingly
    - Decrease glucose infusion by 2 mg/kg/min to 4 mg/kg/min as required
    - Glucose concentration less than 5% dextrose should be avoided
    - If the newborn was not on infusion, put on 5% glucose at a rate of 4 mg/kg/min (approximately 60ml/kg/day)
  2. Insulin
    - Exogenous insulin therapy has been used when glucose values exceed 250 mg/dL, despite efforts to lower the amount of glucose delivered.
- i. Bolus insulin infusion
    - Dose: 0.05 to 0.1 units/kg every four to six hours as needed (PRN)
    - Infuse over 15 minutes via syringe pump
    - Monitor glucose every 30 minutes to one hour
    - If glucose remains >200 mg/dL after three doses, consider continuous infusion of insulin.
  - ii. Continuous insulin infusion
    - Rate of infusion is 0.05 to 0.2 units/kg/hour (usual starting dose is 0.05 units/kg/hour).
    - Check glucose levels every 30 minutes until stable enough to adjust the infusion rate.
    - If glucose remains >180 mg/dL, titrate in increments of 0.01 unit/kg/hour.
    - If hypoglycaemia occurs, discontinue insulin infusion and administer IV bolus of D10W at 2 mL/kg 10% dextrose × 1 dose
    - Monitor potassium level.
    - Monitor for rebound hyperglycaemia.
    - Treat suspected risk factors
    - N.B Don't stop maintenance fluid infusion to reduce high glucose level; that is dangerous.

## Reference

1. Neonatal Clinical Practice Guideline, Hospital for sick kids & Sunnybrook Hospital. 2015 Cloherty and Stark's. Manual of Neonatal Care 8th edition
2. Neonatal Care Guideline for Hospital Physicians. Egypt, 2010



# CHAPTER 5: Nutrition

## Enteral nutrition

Energy intake of 105-135 kcal/kg/day is recommended for the growth of most preterm infants. High intake (130-150kcal/kg/day) is recommended in case of infants with severe and prolonged BPD and IUGR. Lesser intakes (85 to 100 kcal/kg/day) may sustain intrauterine growth rates where parenteral nutrition (PN) is used.

Early enteral nutrition soon after birth, preferably day one or two, is recommended for all to facilitate gut maturity.

Start with gut priming/trophic feeding and advance. Tube feeds are recommended for preterm newborns less than 34 weeks or under 1500 grams. Orogastic tubes are preferred to nasogastric tubes. Infants < 34 weeks and < 1500 grams must be started on IV fluids with gut priming.

Contraindications for breastfeeding/gut priming:

1. Suspected or confirmed NEC, severe haemodynamic instability, ileus and severe asphyxia.
2. Major GIT malformation: Prior to start of feeding, confirm oesophageal and anal patency and review antenatal ultrasound for major GIT malformation such as duodenal atresia and jejunal atresia.
3. Suspected inborn errors of metabolism involving protein/carbohydrate metabolism.

**Feeding initiation and progress:** initiation of feeding, volume and the rate of advance of feedings are related to birth weight, gestational age and the infant's tolerance to feeds. General guidelines include:

- Start IV fluids when infants are < 34 weeks or < 1500 grams, with minimal enteral nutrition.
- Infants ≥34 weeks and ≥1500gm and who are doing well can be started on full feeds (80ml/kg)
- Infants ≥34 weeks and ≥1500gm and critically sick will be started on IV fluid
- Feedings shouldn't be advanced if there are any signs that the infant is not tolerating feeds.
- A small volume feeding, even if not advanced, is much better than nothing at all. Even very small volumes stimulate maturation of gut motility and production of enteric peptides.

The goals for “full feedings” are:

- **Volume:** up to 180 ml/kg/d
- **Calories:** 110-130 kCal/kg/d (some SGA infants will require a higher intake for consistent weight gain).

**Table 8. Volume of feeding for preterm neonate advancement of feed volume**

Gestational age	Weight(grams)	Initial feeds	Progression of feeds /advance as tolerated
<28 weeks	<1000	10 -20ml/kg/day	10-20 ml/kg/day
28 – 32weeks	1000– 1500	20-30 ml/Kg /day	Increase by 20-30 ml/kg/day
32- 34 weeks	1500 – 1800	30ml/kg/day by NG/CUP	Increase by 30 ml/kg/day
> 34 weeks	>1800	30-60ml/kg/day	Increase by 35 ml/kg/day – to attain full feeds

Feeding intolerance: definition of feed intolerance is presence of any one of the following:

- Abdominal distension of more than 2 cm from the previous measurement
- Vomiting ≥2 episodes in the past six hours
- Gastric aspirate blood stained, blood in the stool
- >2 episodes of voluminous gastric aspirates in a six hour period

Routine pre-feed aspirations are not recommended. It is recommended to aspirate only if there is

- Abdominal distension/increase in abdominal girth by more than 2 cm
- Abdominal wall erythema
- Baby is NPO

Indications for stopping/withholding feeds:

- Haemodynamic instability
- Suspected NEC
- If aspirate volume is more than 50 per cent of six hours' feed
- Bilious vomiting or bloody/bilious gastric aspirate, bloody stool

Bilious aspirates may be present in preterm infants. If associated with abdominal distension or any of the above signs, feeds may need to be withheld.

Any aspirate not fulfilling the criteria of feed intolerance should be kept back and the recommended feed given. If the feed is skipped, the IV fluids should be increased by the corresponding amount.

In preterm infants of GA less than 34 weeks and weight less than 1500grams and antenatal Doppler results of one of the following, feeding should not be started in the first 24 hours.

- Estimated foetal weight < 3rd centile
- Umbilical artery doppler perfusion index I > 95<sup>th</sup> centile
- Middle cerebral artery doppler perfusion index < 5<sup>th</sup> centile
- Absent or reverse diastolic flow

Discuss with the consultant before initiation of feeding/use of different protocol.

Fortification and supplementation for preterm infants: preterm milk has higher protein, sodium, magnesium and chloride than mature

milk; the difference stays only up to 21 postnatal days. The nutrient content of unfortified breast milk is insufficient to meet the requirements of preterm infants. Approximately 30 per cent to 50 per cent of very low birth weight (VLBW) infants who are fed unfortified human milk or term infant formulas have decreased bone mineral content compared with a foetus of comparable weight or gestational age. As a consequence, preterm and VLBW infants fed unfortified milk have abnormalities in calcium-phosphorus balance and increase in serum alkaline phosphatase activity compared with infants fed fortified preterm milk.

### Human milk fortifier

In infants < 32 weeks, multicomponent fortifier leads to short term increase in weight gain, linear growth, head growth and mineralization. It should be considered once the infant has reached 100 ml/kg/day.

In infants of more than 32 weeks, HMF is to be used in babies who have attained feed volumes of 180 ml/kg of EBM and don't have weight gain. Preterm formulas are the option when human milk fortifiers are not available.

### Supplements

**Iron:** Stores of iron in preterm infants is low. Start iron at two weeks of life. Babies < 1000g must be given 3-4 mg/Kg/day of iron and babies >1000 g must be given 2-3 mg/Kg/day of iron. Continue until one year of age.

**Vitamin A:** Daily supplementation of 750 – 1500 IU/ Kg/day is recommended.

**Vitamin D:** Daily supplementation of 400 IU/day

#### Calcium and phosphorus:

- Give maintenance oral calcium 150 -200 mg/kg/day, once 50 per cent of feeds is reached and continue till the baby weighs 4-4.5 kg.
- The phosphorus requirement is 60-90 mg/kg/day. Use a calcium preparation with a Ca:P ratio of 2:1. Use a preparation with both calcium and phosphorus.
- Investigate for osteopenia of prematurity by serum calcium, phosphorus and alkaline phosphatase at two weeks.

### Growth monitoring

It is believed that in the preterm infant who is receiving adequate nutrition, the postnatal growth should mimic intrauterine growth.

**Table 9. Desired gains in anthropometric parameters**

	Preterm	Term
Weight	>15-20 g/Kg/day	20-30 g/day
Length	1 cm/week	2cm/month
Head circumference	1 cm/week	0.5 cm/week

Weight should be measured daily till the birth weight is crossed and the infant is found to consistently gain weight for three consecutive days, then measure biweekly till discharge. Length and OFC should be measured once weekly. Growth should be plotted on Fenton's intrauterine growth curves. See Fenton chart on newborn evaluation.

#### Reference:

1. Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition
2. Feeding of Low birth weight infants. All India Institute of Medical Sciences protocol for neonatology. 2019

## Total Parenteral Nutrition (TPN)

The goal of parenteral nutrition is to provide adequate calories and amino acids in order to prevent negative energy and nitrogen balance. Suboptimal nutrient intake during the neonatal period has been associated with both short and long term morbidities.

The preterm infant loses 1 per cent of endogenous protein each day after birth, if not adequately replenished.

Parenteral nutrition should be started on day 1.

#### Indications:

1. Prematurity <30 weeks' gestation and/or <1200 grams.
2. Prematurity <32 weeks' gestation and/or <1500 grams and unable to achieve reasonable enteral feeds (about 50 per cent) by day three.
3. Infants >32 weeks and/or >1500 grams who are unlikely to achieve at least 50 per cent enteral feeds by day five.

4. Necrotizing enterocolitis
5. Surgically correctable gastrointestinal tract anomalies (oesophageal atresia, gastroschisis, atresia of intestine, volvulus and short bowel syndrome).

#### Components of parenteral nutrition:

contains all the nutritional requirements of the body: calories, minerals, vitamins and electrolytes.

The ideal distribution of calories should be 50-55 per cent carbohydrates, 10-15 per cent proteins and 30-35 per cent fats.-

#### Carbohydrate

- Different concentration of dextrose is the source of carbohydrate in the TPN.
- The calorie value of dextrose is 3.4 kcal/g
- Dextrose infusions should be initially 4-6 mg/kg/min in term and as high as 4-8 mg/kg/min in preterm infants to avoid hypoglycaemia.

Glucose infusion rate can be increased 1-2 mg/kg/min every day or if there is hypoglycaemia with a goal of 11-12mg/kg/min.

#### Proteins

- Crystalline amino acids provide the nitrogen source of PN.
- The caloric value of amino acids is 4 kcal/g.
- Amino acids should be initiated on the first day of life to avoid negative protein balance; one should start with at least 2 to 3 g/kg/d and then increase by 1 g/kg/d to a maximum of 3.5 g/kg/d and up to 4 g/kg/d in ELBW infant. Start with 2 g/kg/d in ELBW infants.

## Lipids

- 20 per cent lipid concentration is preferred over 10 per cent because of the lower phospholipid: triglyceride ratio, thus leading to higher lipid clearance time.
- In preterm neonates, lipids can be started on day one of life at a dose of 1 g/kg/d and increased by 1 g/kg/d to a maximum of 3.5 g/kg/d; apply a slower advancement in neonates with GA of less than 27 weeks and IUGR babies.
- Lipid syringes and tubing should be covered by wrapping in aluminium foil if exposed to phototherapy.
- Carnitine is administered in neonates receiving PN for more than 2-4 weeks (10-20 mg/kg/d) to increase oxidation of fat. The rate of infusion should not be >0.15g/kg/hr.

**Electrolytes:** suggested amounts to be included in TPN are:

- Sodium: 2-5mEq/kg/day
- Potassium: 2-4mEq/kg/day
- Magnesium: 0.3-1mEq/kg/day
- Calcium: 1-3mEq/kg/day
- Phosphorus: 0.5-2mEq/kg/day
- The ratio of calcium to phosphorus to avoid precipitation is 1.1: 1 to 2:1 mEq/Mm

**Vitamins:** start from day one by adding to the IVF-intravenous fluid mixture.

## Administration of TPN:

- Can be done through either peripheral or central line.
- Peripheral line glucose concentration must not be more than 12.5 per cent, in central line maximum of 35 per cent glucose and 6 per cent amino acids.
- Hypertonic solution >900 mOsm/L or anticipated TPN for >1 week needs central venous line
- In case of central line, the position of the tip of the catheter needs to be in a large vessel, preferably the superior or inferior vena cava outside the heart with position confirmed by x-ray.
- Central line should contain 0.5-1.0 unit of heparin/ml continuous infusion.
- The venous access used for PN should not be interrupted for giving antibiotics or other medications.
- Infusion sets to be changed every day.
- Reuse of nutrient solutions is best avoided. However, the bottles can be shared between patients administered TPN on the same day.
- A strict sterile aseptic technique is essential for the preparation and administration of TPN.

*Table 10. Monitoring while on TPN*

Laboratory test	Frequency
<b>Weight</b>	<b>Daily</b>
<b>Blood</b>	
<b>Electrolytes:</b> sodium, potassium, chloride, bicarbonate	Daily until stable, then serially as indicated
<b>Glucose</b>	Daily TID until stable, then serially as indicated
BUN, creatinine, calcium, phosphorus, magnesium, alkaline phosphatase, liver function studies (bilirubin, alanine and aspartate aminotransferases)	After the first week and then serially on an alternate week, schedule as indicated
<b>Triglycerides</b>	At maximum lipid infusion and weekly thereafter

When to stop TPN:

- Volume of 100 ml/kg by enteral route, lipids can be stopped. Amino acids can be continued till full feeds.
- TPN-associated complications: cholestasis, metabolic bone disease, line infection and sepsis, infiltration and sloughing of the skin, and air embolus.

Reference

1. Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition
2. Parenteral nutrition. All India Institute of Medical Sciences protocol for neonatology. 2019



## CHAPTER 6:

# Oxygen monitoring in neonates

## Oxygen saturation monitoring of neonate

Neonates Who Require Saturation Monitoring  
The following infants require continuous

oxygen saturation monitoring using pulse oximeter ( $\text{SpO}_2$ ));

- Neonates requiring resuscitation.
- Neonates with signs of respiratory distress, such as grunting, retraction, tachypnoea or nasal flaring.
- Neonates with a history of meconium-stained liquor.
- Neonates following a 'dusky episode'.
- Neonates who appear pale or cyanosed.
- Neonates with an identified cardiac murmur.
- Preterm infants less than 32 weeks.
- Neonates on CPAP, MV or other respiratory support.

### Procedure:

- Saturation monitors provide measurement of haemoglobin-oxygen saturation with a high level of accuracy (+/- 3%).
- Turn on the  $\text{SpO}_2$  monitor; it can take 60 seconds for the correct reading to be displayed.
- During resuscitation and on infants with suspected cardiac murmurs, the probe should be attached to the right wrist (preductal), with the light part of the sensor placed on the inside of the wrist. Later, the foot may be used unless it is cold or blue.
- Acceptable preductal saturations are variable and dependent on age. Oxygen should not routinely be given during this time.

*Table 11. Target oxygen saturation after delivery (NRP 7th edition)*

Age after delivery	Target saturation
1min	60- 65%
2min	65-70%
3min	70-75%
4min	75-80%
5min	80-85%

<b>10min</b>	<b>85-95%</b>	necessary.
After this initial period of adaptation, if oxygen saturation levels are constantly below 92 per cent, give oxygen and request medical assessment.		<ul style="list-style-type: none"> <li>■ If postnatal infants whose oxygen saturation levels are normal i.e., &gt;95 per cent and who continue to grunt, check blood glucose level (normal level &gt;45mg/dl), check temperature (normal level &gt;36.5) and feed and warm the infant as</li> </ul>
		<ul style="list-style-type: none"> <li>■ If baby is still grunting after the above actions, start oxygen and inform/refer to NICU</li> <li>■ If there is suspected congenital cardiac lesions, saturation monitoring may be required both pre and postductally; right arm = preductal, left arm or either leg = postductal</li> </ul>

*Table 12. Normal oxygen saturation ranges and alarm set*

<b>Infants</b>	<b>Saturation range</b>	<b>Alarm set</b>
Preterm < 37 weeks	90 – 95%	89 – 96%
Term Infant > 37 weeks	90 – 95%	89 – 96%

Pulse oximetry is liable to inaccuracy in the following instances:

- Movement artefact
- Cool/poorly perfused peripheries
- Ambient light (causing interference with the probe's spectrophotometer)
- Infants with high total carboxyhaemoglobin levels (CarboxyHb has a similar absorbance to oxyhaemoglobin and may falsely elevate pulse oximeter readings)

Responding to the Oxygen Saturation Alarm: when the oxygen saturation monitor sets off an alarm, the following steps should be followed:

1. Silence alarm and evaluate the patient and monitor.
2. What is the infant's HR, RR and colour?
3. Is suctioning or repositioning required?
4. Is the waveform accurate?
5. Stay at the bedside until  $\text{FiO}_2$  &  $\text{SpO}_2$  have stabilized.

**Table 13. set oxygen saturation alarm**

Managing oxygen desaturation during handling or procedures	High SpO2 alarm	Moderately Low SpO2 alarm (SpO2 > 70%)	Significantly Low SpO2 alarm (SpO2 < 70%)
1. Increase oxygen by 5% to 10% before handling or procedures	After 2 minutes, if the SpO2 does not return to the SpO2 target range, every 2 minutes, continue to decrease oxygen in decrements of 2% until SpO2 has stabilized within target range	After 2 minutes, if the SpO2 is not increasing, every 2 minutes, continue to increase oxygen in decrements of 2% until SpO2 has stabilized within target SpO2 range	1. If saturation is not increasing, increase oxygen by 25% to 50% to bring the SpO2 up to > 80%.
2 Post-procedure, once SpO2 has stabilized within target range, wean oxygen as fast as necessary but only in decrements of 2% until FiO2 is back to baseline			2 Once SpO2 has stabilized, if possible, wean oxygen as fast as necessary but only in decrements of 2% until FiO2 is back to baseline

## Reference

- Neonatal Clinical Guideline 2018, NHS Trust, UK

## 14.1. Blood Gas Analysis

Arterial blood gas (ABG) measurements. Arterial PO<sub>2</sub> (PaO<sub>2</sub>) and PCO<sub>2</sub> (PaCO<sub>2</sub>) are direct indicators of efficiency of pulmonary gas exchange in infants with acute lung disease. PaO<sub>2</sub> measured under steady state conditions from an indwelling catheter is the “gold standard” for oxygen monitoring.

The sample should be analysed immediately within 15 minutes of collection.

Venous blood can be used for venous blood gas analysis. If alveolar ventilation and circulatory function are normal, venous PCO<sub>2</sub> usually

exceeds arterial values by 5 to 6 mm Hg. The difference is unpredictable in hypoventilation and in circulatory collapse. Venous samples can be used to assess ventilation and acid base status but not oxygenation.

**Capillary blood gases:** PCO<sub>2</sub> and pH values obtained from properly collected capillary blood samples can closely reflect arterial values.

### Sample collection:

- Arterial samples could be collected from umbilical arterial catheter or from radial artery.
- Dry heparinized syringe should be used for sample collection; too much heparin may decrease PH.

- Air in the sample will elevate PaO<sub>2</sub>.
- Total parenteral nutrition/lipids may lower PH.
- Blood sample of 0.2-0.5 ml could be enough for most ABG machines.

#### **Indications for ABG analysis:**

- Severe respiratory or metabolic disorders
- Clinical features of hypoxia or hypercarbia
- Shock
- Sepsis
- Decreased cardiac output
- Renal failure

- Ideally any baby on oxygen therapy/ respiratory support
- Inborn errors of metabolism

#### **Arterial blood gases should be drawn:**

- Within 30 minutes of initiating mechanical ventilation or making a parameter change.
- Every 2-4 hours during acute phase of illness.
- Every 4-6 hours on stable infants requiring minimal ventilator manipulations.
- Every 1-7 days in infants with chronic lung disease.
- Whenever clinical condition indicates.

*Table 14. Acceptable newborn ranges of blood gas*

	Arterial	Capillary	Venous
pH	7.30-7.45	7.25-7.35	7.25-7.35
PCO <sub>2</sub> (mmHg)	35-45	40-50	40-50
PO <sub>2</sub> (mmHg)	50-70	35-50	35-45
HCO <sub>3</sub> (mEq/L)	20-24	18-24	18-24
SaO <sub>2</sub> (%)	92-96	70-75	70-75
Base excess or deficit	(-4) -(+4)		

#### **Interpretation of blood gases:**

- Evaluate pH, PCO<sub>2</sub> and HCO<sub>3</sub>-
- Determine primary abnormality by matching pH with PCO<sub>2</sub> or HCO<sub>3</sub>-

#### **Acidosis:**

- Acidosis is a downward shift in pH <7.35. It is either metabolic acidosis or respiratory acidosis.

- Metabolic acidosis: decreased HCO<sub>3</sub>-
- Respiratory Acidosis: increased PCO<sub>2</sub>

#### **Alkalosis:**

- Alkalosis is an upward shift in pH >7.45. It is either metabolic alkalosis or respiratory alkalosis.
- Metabolic acidosis: increased HCO<sub>3</sub>-
- Respiratory Acidosis: decreased PCO<sub>2</sub>

### Anion gap:

- Serum (Na<sup>+</sup>) – (Serum [Cl<sup>-</sup>] + Serum [HCO<sub>3</sub><sup>-</sup>]) (normal: 8-16 mEq/L)

### Causes of metabolic acidosis in newborns:

#### Increased anion gap (>15 mEq/L)

- Acute renal failure
- Inborn errors of metabolism
- Lactic acidosis
- Late metabolic acidosis
- Toxins (e.g., benzylalcohol)

#### Normal anion gap (<15 mEq/L)

- Renal bicarbonate loss
- Renal tubular acidosis
- Acetazolamide
- Renal dysplasia
- Gastrointestinal bicarbonate loss
- diarrhoea
- Cholestyramine
- Small-bowel drainage
- Hyperalimentation acidosis

#### Treatment:

- Whenever possible, treat the underlying cause.
- IV Na bicarbonate or Na acetate is most commonly used to treat arterial pH <7.25. Estimate bicarbonate deficit from the

following formula:

- Deficit = 0.4 × body weight × (desired bicarbonate -actual bicarbonate)

### Causes of metabolic alkalosis in newborns:

- Iatrogenic – bicarbonate therapy
- Use of diuretics
- Following blood transfusion – citrate in blood gets converted to bicarbonate
- Persistent vomiting – congenital adrenal hyperplasia
- Prolonged gastric aspiration
- Urea cycle disorder

**Treatment:** treat underlying cause

### Respiratory acidosis:

- Due to decreased minute ventilation
- Tube block
- Tube dislodgement
- Increased dead space – long endotracheal tube, adapters and small-bore tube
- Opening of ductus (PDA)
- Pulmonary interstitial oedema
- Pulmonary air leak
- Collapse, consolidation

*Table 15. Blood gas status and the possible change(s) in ventilator settings*

Blood gas scenarios	Ventilator settings which will achieve it (using pressure-type ventilator)
Low PaO <sub>2</sub> /SpO <sub>2</sub>	<ul style="list-style-type: none"> <li>■ Exclude air leak/displaced ETT/over inflation</li> <li>■ Increase FiO<sub>2</sub></li> <li>■ Increase PEEP</li> <li>■ Increase PIP (but be aware of effect on PaCO<sub>2</sub>)</li> <li>■ Increase Tinsp [but ensure adequate expiratory time (Texp), especially at fast rates]</li> <li>■ If above measures are unsuccessful, may need HFOV/iNO if available</li> </ul>
High PaO <sub>2</sub>	<ul style="list-style-type: none"> <li>■ Decrease FiO<sub>2</sub> (unless already in air)</li> <li>■ Decrease PEEP (if &gt;5 cm)</li> <li>■ Decrease PIP (especially if PaCO<sub>2</sub> is also low)</li> </ul>
High PaCO <sub>2</sub>	<ul style="list-style-type: none"> <li>■ Exclude air leak/displaced or blocked ETT</li> <li>■ Increase PIP</li> <li>■ Increase rate</li> <li>■ Decrease PEEP (only if oxygenation adequate and PEEP &gt;6 cm)</li> </ul>
Low PaCO <sub>2</sub>	<ul style="list-style-type: none"> <li>■ Decrease PIP</li> <li>■ Decrease rate</li> </ul>
Low PaO <sub>2</sub> /SpO <sub>2</sub> and high PaCO <sub>2</sub>	<ul style="list-style-type: none"> <li>■ Exclude displaced/blocked ETT</li> <li>■ Exclude airleak</li> <li>■ Increase PIP</li> <li>■ If above measures unsuccessful (may need HFOV if available)</li> </ul>

### Practical ABG analysis

You should come up with your own approach, but the following sequence generally works:

1. Look at the K+, Hb and glucose. You now won't miss a life-threatening potassium/glucose levels or profound anaemia.
2. Look at the PaO<sub>2</sub> and arterial oxygen saturations to determine how hypoxic the patient is. Note what the inspired oxygen concentration is! (i.e., PaO<sub>2</sub> of 12kPa, or 95 % arterial oxygen saturations or breathing 80 % oxygen is NOT good! As a rule of thumb, the expected PaO<sub>2</sub>
  - in the absence of oxygenation defects
  - should be about 10 kPa less than the

inspired oxygen partial pressure i.e., 40 % FiO<sub>2</sub> should result in PaO<sub>2</sub> of 30 kPa)

3. Look at the pH: acidosis (<7.35) or alkalosis (>7.45)?
4. Is the PaCO<sub>2</sub> abnormal? If so, has it changed in a direction which accounts for the altered pH?
5. Is the HCO<sub>3</sub><sup>-</sup> abnormal? If yes, is the change in the same direction as the pH?

### Reference

1. Blood gas analysis. All India Institute of Medical Sciences protocol for neonatology. 2008

- 2 Neonatal Guideline, 2017-19NHS Trust, UK,

## 142 Capnography (End-Tidal CO<sub>2</sub> monitoring)

Refers to the non-invasive measurement of the partial pressure of carbon dioxide in exhaled breaths, expressed as the CO<sub>2</sub> concentration over time.

The relationship of CO<sub>2</sub> concentration to time can be represented graphically as a waveform or capnogram, and can be used to determine the maximum CO<sub>2</sub> concentration at the end of each tidal breath, or end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>).

### Mechanism:

- 1 Analyses exhaled carbon dioxide in the airway.
- 2 The level of carbon dioxide in the airway is dependent upon the patency of the airway, ventilation and perfusion within the lung and metabolism.

### Indications:

- 1 Measures lung function ventilation and/or perfusion of alveolar units and predicts severity and recovery of lung disease.
- 2 Evaluates effectiveness of mechanical ventilation and spontaneous breathing.
- 3 Facilitates weaning from mechanical ventilation and assesses the ability to tolerate changes
- 4 Used to verify endotracheal intubation.

### Factors affecting accuracy:

- If lungs are poorly ventilated or if perfused carbon dioxide in the airway is low
- Presence of lung disease results in a wide gradient between arterial PCO<sub>2</sub> and

expired PCO<sub>2</sub>; it may be more than 20 mmHg (in normal lungs the gradient is less than 5mmHg).

## 143 Transcutaneous CO<sub>2</sub> monitoring (PtcCO<sub>2</sub>)

Transcutaneous CO<sub>2</sub> monitoring (PtcCO<sub>2</sub>): Estimates the PaCO<sub>2</sub> through electrochemical measurements of CO<sub>2</sub> gas diffusing through body tissue and skin.

A sensor is warmed to approximately 42° to 43°C to induce a local hyperaemia, resulting in vasodilation of the dermal capillary bed below the sensor and increasing arterial blood flow. This vasodilation also facilitates diffusion of CO<sub>2</sub>. PtcCO<sub>2</sub> is often slightly higher than the corresponding measured PaCO<sub>2</sub> value.

Some clinical situations may lead to an increased discrepancy between the PtcCO<sub>2</sub> and PaCO<sub>2</sub>. These include: improper probe placement or application, factors associated with increased distance from probe to capillaries (such as body wall oedema, thickness of the patient's skin or subcutaneous tissue), poor perfusion of the site of probe placement, or hyperoxemia (PaO<sub>2</sub> >100 torr).

Transcutaneous carbon dioxide tension exceeds that of arterial blood by a mean of 4 mm Hg in the normal range, but this gradient may more than double in the presence of hypercapnia.

### Reference

- 1 Blood gas analysis. All India Institute of Medical Sciences protocol for neonatology. 2008.
- 2 Neonatal Guideline, 2017-19, NHS Thrust, UK

# Respiratory support in neonates

## Oxygen administration

### Indication

Respiratory distress with Downe score of 1-3.  
Unable to maintain SPO<sub>2</sub> more than 90 per cent in room air.

### Sources of oxygen

Oxygen sources are oxygen cylinder, oxygen concentrator and oxygen pipeline from source. The concentration of oxygen to be administered to the patient i.e., fraction of inspired oxygen (FIO<sub>2</sub>) has to be based on the oxygen saturation of the patient with a goal of keeping SPO<sub>2</sub> between 90-95 per cent in most sick newborns.

Use of blended oxygen is preferable to using 100 per cent oxygen especially for preterm newborns and when high flow oxygen is delivered.

Blenders function as gas/compressed air and oxygen mixers and provide oxygen concentration of 21-100 per cent.

The concentration of oxygen varies from source to source; cylinders and pipelines of oxygen deliver 100 per cent and concentrators deliver up to 90-96 per cent but it is important to understand for each type of concentrator how much concentration it performs, there are concentrators with the ability to concentrate up to 70 per cent.

### Methods of oxygen administration

*Table 16. Methods of oxygen administration*

Method	Flow and Concentration	Oxygen Administration
Bi-Nasal Prongs	<ul style="list-style-type: none"><li>Low = 0.5 -1 L per minute</li></ul>	<ul style="list-style-type: none"><li>Low flow of oxygen required</li><li>Constant concentration of oxygen if applied correctly</li></ul>
Nasal Catheter	<ul style="list-style-type: none"><li>Low = 0.5 L per minute</li><li>Moderate = 0.5 to 1 L per minute</li><li>High = more than 1 L per minute</li></ul>	<ul style="list-style-type: none"><li>Low flow of oxygen required</li><li>Constant concentration of oxygen if applied correctly</li></ul>
Head box	<ul style="list-style-type: none"><li>Low = 3 L per minute</li><li>Moderate = 3 to 5 L per minute</li><li>High = more than 5 L per minute</li></ul>	<ul style="list-style-type: none"><li>Warms the oxygen</li><li>Can give a high Concentration</li></ul>

Method	Flow and Concentration	Oxygen Administration
Face mask	<ul style="list-style-type: none"> <li>• Low = 1 L per minute</li> <li>• Moderate = 1 to 2 L per minute</li> <li>• High = more than 2 L per minute</li> </ul>	<ul style="list-style-type: none"> <li>• Oxygen can be administered quickly</li> <li>• Convenient for administering oxygen for short periods of time</li> </ul>
Incubator	<ul style="list-style-type: none"> <li>• If using a head box inside the incubator, see above</li> <li>• If connecting oxygen directly to the incubator, follow the manufacturer's instructions</li> </ul>	<ul style="list-style-type: none"> <li>• Warms the oxygen</li> </ul>

Humidification of oxygen should be done using sterile water when giving oxygen to newborns in order to prevent formation of nasal blockage by mucus.

Fraction of oxygen inspired (FIO<sub>2</sub>) by the patient could be calculated using the Finer's formula:

Or a "STOPROP" table can be used reference attached.

$$FIO_2 = \frac{(0.79 * \text{Oxygen flow ml/min}) + (0.21 * VE)}{VE}$$

Where VE=Minute volume

If the patient's condition is deteriorating or the respiratory distress score worsens, the next step of management is use of continuous positive airway pressure.

### References

1. WHO: Oxygen therapy for children: a manual for health workers. 2016
2. Benaron DA & Benitz WE "Maximizing the Stability of Oxygen Delivered Via Nasal Cannula" Arch. Pediatr. Adolesc Med 148: 294-300, March 1994

3. Finer NN, Bates R, Tomat P. Lowflow oxygen delivery via nasal cannula to neonates. Pediatric pulmonology. 1996;21(1):48-51

## 15.1. Continuous positive airway pressure (CPAP)

In premature infants with respiratory distress, CPAP expands collapsed alveoli, splints the airway, reduces the strain of breathing and improves the pattern and regularity of respiration.

The key determinants of VILI (ventilator induced lung injury): atelecto-trauma (repeated opening and collapse of the alveoli), biotrauma (intubation of the airway) and volutrauma (overstretching of the alveoli) are minimal or absent with CPAP.

### Indications:

- To put the neonate on CPAP, the presence of good respiratory effort is the prime requirement.
- Recently delivered preterm infant with minimal respiratory distress requires low supplemental oxygen (to prevent atelectasis).

- Respiratory distress and requirement of FiO<sub>2</sub> above 0.30.
- Recurrent apnoea not responding to medical management.
- Post-extubation from mechanical ventilation
- Term neonates with respiratory distress and saturations less than 88 per cent on hood oxygen.
- Initial stabilization in the delivery room for spontaneously breathing, extremely preterm infants (25 to 28 weeks' gestation).
- Initial management of premature infants with moderate respiratory distress

**NB:** Preterm infants with RDS who require FiO<sub>2</sub> above 0.4 on CPAP should be intubated, ventilated and given surfactant replacement therapy.

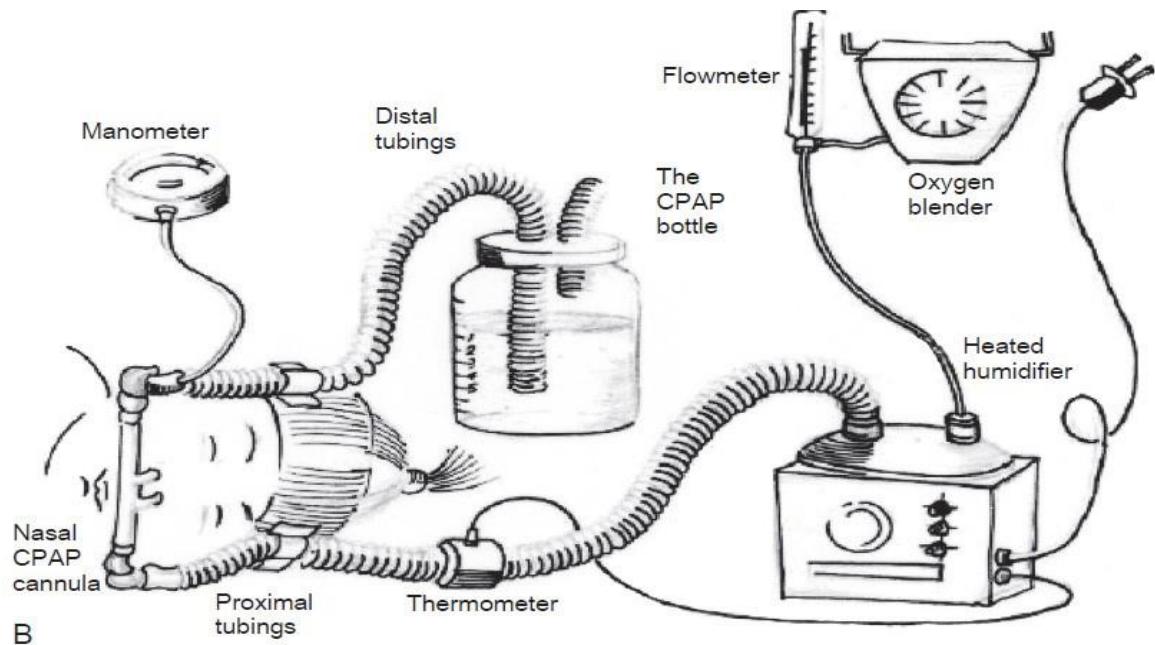
- Contraindications
- Poor respiratory efforts
- Congenital diaphragmatic hernia, tracheoesophageal fistula, choanal atresia and cleft palate.
- If severe cardio-vascular instability, better to put on a ventilator.
- ABG = pH is less than 7.25 and PaCO<sub>2</sub> >60 mm of Hg.

#### **Methods and machines to deliver CPAP:**

- CPAP can be delivered using the variable flow or continuous flow method.
- Variable flow uses the mechanical ventilator as a gas source and is not commonly used.
- Continuous flow uses a standalone CPAP device and is a method where a blended gas flow is administered to the baby after the gas is heated and humidified via binasal prongs and the expiratory limb is submerged under a water seal or water bubble.
- The bubble CPAP method is used with different modifications in Ethiopia; there is also a locally made CPAP which has been used for almost a decade and its detail is available in the national guideline.
- Currently there is a concentrator device with an incorporated CPAP system called Diamedica CPAP which is available in most of the level 3 hospitals, the details of which are described below.

#### **CPAP delivery interfaces**

- Can be delivered using binasal prongs and nasal masks; different devices may have different methods of CPAP delivery.
- Starting and weaning a patient on CPAP
- The details are available on Diamedica CPAP; follow that for other CPAP devices.



*Figure 13. Bubble CPAP used in the current era*

#### **Diamedica Baby CPAP**

Diamedica CPAP delivers gas by the concentrator mechanism; there is no need to attach it to oxygen and compressed air. It needs an electric source for operation. In centres where there is high power interruption, it is better to put a reserve cylinder in case of power interruption to use the local CPAP.

#### **The Diamedica CPAP contains:**

Two flowmeters that can go up to 10 l/min oxygen and 10 l/min medical air,

A self-contained unit that generates 95 per cent oxygen and its own medical air,

A voltage protector that is fitted to all CPAP machines, protecting the machine from unstable power surges,

A humidifier that ensures warmth and moisture for the air and oxygen delivered to the patient,



*Figure 14. Diamedica CPAP*

A clear oxygen/air mixing chart that allows for easy setting of flow rates, and

Inexpensive to run – no need for costly oxygen and air cylinders.

### Flow oxygen/air mixing chart:

- Flowmeters allow for a variable gas mixture containing oxygen from 21% - 95% concentration
- Recommended total flow of 10 litres a minute to start  
Example: if you give 5 litres of oxygen and 5 litres of air FIO<sub>2</sub>= 57.5%
- Adjust flows to achieve desired FIO<sub>2</sub> levels

### The CPAP system:

- The concentrator has also been modified so that warm waste air from the concentrator's compressor is directed towards the humidifier bottle.
- This increases the temperature of the inspired gases, raising the dew point of the water and thus providing enhanced humidification to the device.

- Pressure is maintained throughout the respiratory cycle by directing the gas flow to a container of water at the distal end of the circuit via a tube with an open end at an adjustable depth beneath the surface.

### Air filter:

- This is available at the back of the machine with a sponge cover for the part trapping air.
- Remove dust from the air filter daily.
- Keep the machine 30 cm away from walls or curtains.
- In between patients, wash it with water and soap and let it dry adequately.

### Power on:

- Once power is turned on, the yellow light will stay illuminated until the concentrator reaches and exceeds 85 per cent, then the light will turn off. This takes approximately 10 minutes.

Oxygen/air mixing chart										
		Air Flowmeter (l/min)								
		0	1	2	3	4	5	6	7	8
1		95.0	57.5	45.0	38.8	35.0	32.5	30.7	29.4	28.3
2		95.0	70.0	57.5	50.0	45.0	41.4	38.8	36.7	35.0
3		95.0	76.3	65.0	57.5	52.1	48.1	45.0	42.5	40.5
4		95.0	80.0	70.0	62.9	57.5	53.3	50.0	47.3	45.0
5		95.0	82.5	73.6	66.9	61.7	57.5	54.1	51.3	48.8
6		95.0	84.3	76.3	70.0	65.0	60.9	57.5	54.6	52.1
7		95.0	85.6	78.3	72.5	67.7	63.8	60.4	57.5	55.0
8		95.0	86.7	80.0	74.5	70.0	66.2	62.9	60.0	57.5

Assuming an oxygen concentrator output of 95% oxygen

Figure 15. Oxygen/air mixing chart available on the machine

## CPAP application

Position the patient: neutral supine position to maintain an open airway.

Elevate the shoulders using a towel or blanket. Ensure clear airway- suction the nares with a catheter or bulb syringe if needed.

**Apply interface/nasal prong:** Hudson prongs are supplied with the machine, if available RAM cannulas can also be used.

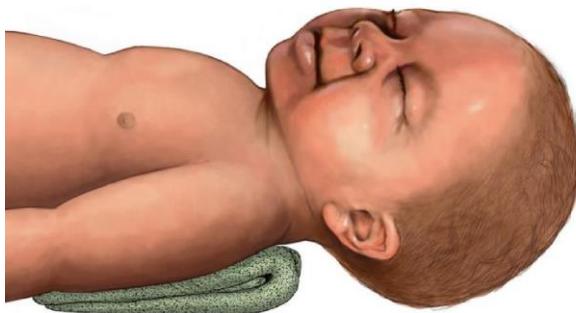


Figure 16. Positioning of newborn for CPAP application

## Applying Hudson Prongs

In order to create CPAP, Hudson prongs require full occlusion of the nares.

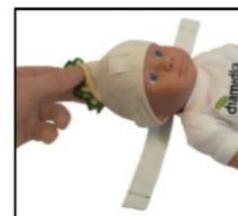
The machine is supplied with prongs of eight different sizes .

0 = the smallest, 7 = the largest

Each prong has its size stamped on it.

Select the appropriate size for your patient.

There are also bonnets of 4 sizes supplied with the prong; select the appropriate size that will help to fix the tubing.



a) Place the bonnet on patients head, centering the "securement line indicator"

b) With the bonnet centered at nape of neck, place remaining bonnet on infant

c) Close the top of bonnet by twisting bonnet until tightly secure to head crown.

d) Secure with ribbon provided

e) Cut self-adhesive Velcro in half and secure to the bonnet

f) Attach chin strap to the infant and secure to Velcro

g) Place the nasal prong into the infants nostril

g) Place the nasal prong into the infants nostril

Figure 17. Steps of attaching the Hudson prong and bonnet

May need to lubricate prongs with water or saline solution.

Place the prongs curved side down and direct into nasal cavities.

Be careful when selecting the appropriately sized prong.

Large prongs to the side of nares cause nasal irritation.

Small prongs to the side of nares cause air leak and loss of pressure and decrease the CPAP effect.

### Initiating CPAP

In the NICU, CPAP should be initiated based on the presence of respiratory distress.

Respiratory distress is assessed using clinical parameters of respiratory rate, intercostal and subcostal retraction, grunting, cyanosis, nasal flaring and air entry.

Downe score can be used for clinical assessment of respiratory distress (see Table 17 below).

### When to start

If the preterm newborn has respiratory distress with a Downe score more than or equal to four (Table 17), CPAP must be started: early initiation is recommended in preterm infants with signs of RDS.

In preterm newborns who were initiated on CPAP at the delivery room, CPAP must be continued in the NICU till the baby has a Downe score of less than four.

In late preterm and term newborns, oxygen concentration greater than 30 per cent or 0.5 L/min is required to maintain SpO<sub>2</sub> of more than 90 per cent.

### How to start CPAP

Initial flow 10 L/min = FIO<sub>2</sub> of 57.5 %

- 5 L/min air
- 5 L/min oxygen

Increase or decrease FIO<sub>2</sub> based on patient saturation

### Initial CPAP depth

- If RAM cannula is available, start at 6 cm H<sub>2</sub>O and increase to 10 cm H<sub>2</sub>O
- Hudson prongs start at 5 cm of H<sub>2</sub>O and increase to 10 cm H<sub>2</sub>O

Put orogastric tube, attach open syringe at the end and leave it open to remove air from stomach

### Monitoring on CPAP

Continuously monitor SPO<sub>2</sub> and heart rate, if possible also monitor RR

Every 2-4 hours, monitor and document:

- Vital signs (temp, RR, HR)
- Downes' score
- Securing and position of nasal prongs
- Condition of nares, nasal septum and skin
  - check for pressure points

### Signs of improvement

- Oxygen saturations increasing – oxygen requirement decreasing
- Signs of respiratory distress improving
- Downes' score decreasing
- Baby appears more comfortable

## Weaning from CPAP

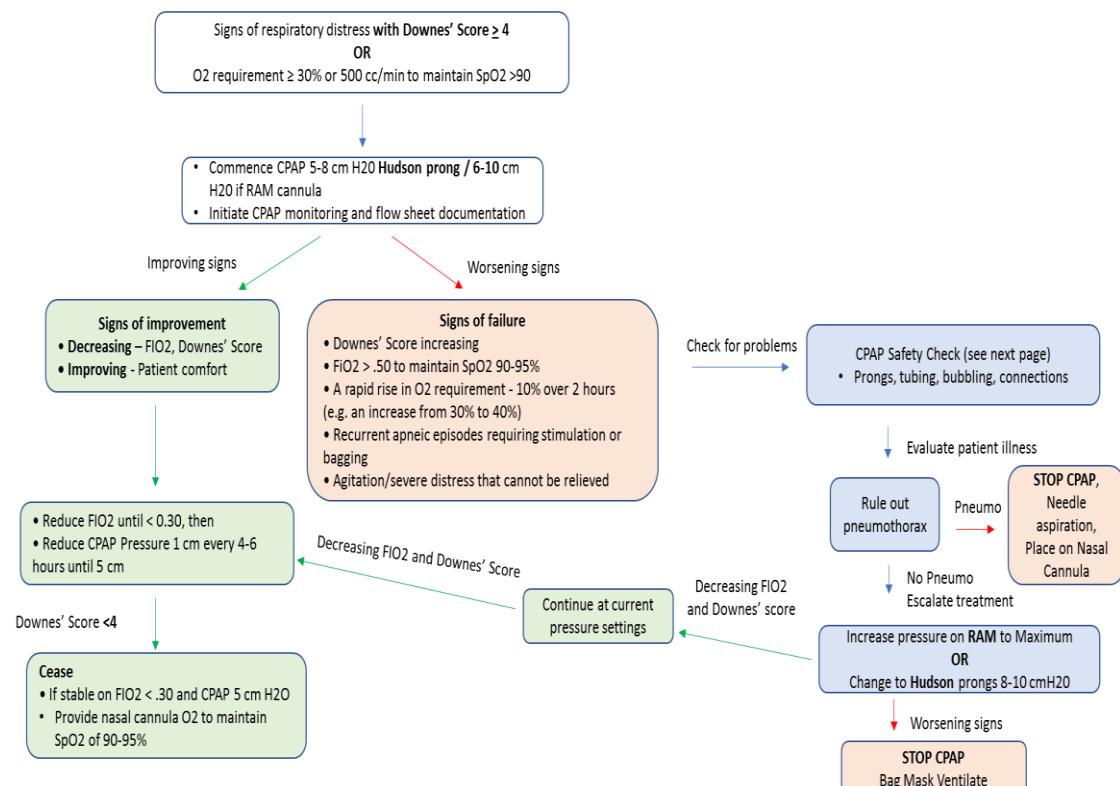
1. Reduce FIO<sub>2</sub> to minimum level (FIO<sub>2</sub> <30%)
2. Reduce pressures by 1 cm slowly until 5 cm

3. When baby is maintaining SpO<sub>2</sub> 90-95 per cent at minimum FIO<sub>2</sub> and CPAP 5 cm for several hours, change to nasal cannula oxygen.
4. After CPAP discontinuation, monitor continuously for respiratory deterioration.

**Table 17. Downes' score for assessment of respiratory distress**

Downes' score	0	1	2
Respiratory rate	<60Breaths per min	60-80	>80
Retractions	None	Mild	Severe
Cyanosis	None	Cyanosis relieved by oxygen	Cyanosis not relieved by oxygen
Grunting	None	Audible with stethoscope	Audible with ear
Air entry	Good bilaterally	Mildly decreased	Markedly decreased

## Guideline for initiation of CPAP



**Figure 18. CPAP initiation and monitoring algorism for preterm and term newborns with respiratory distress**

(Fig. modified from FMOH, UNICEF and VON training material)

## **Monitoring of infants on CPAP**

Monitor and record every 2-4 hours:

- Vital signs
- SpO<sub>2</sub> (preferably right hand)
- Downes' Score
- FIO<sub>2</sub>
- CPAP pressure, Gas flow
- Humidifier and circuit
- Water level in humidifier
- CPAP interface positioned correctly, septal integrity, securing that devices are not causing indentation, pitting or periorbital oedema.

## **Performing CPAP safety check**

- Assess nares for blockage, need for suction and injury to nares – put saline nasal drops every 3-4 hours.
- Verify nasal prong size.
- Check for water in CPAP tubings, empty if water is present.
- Check that corrugated CPAP tubings are connected and fixed in place
- Verify that water level in CPAP chamber is filled to the zero, remove water if needed.
- Verify that CPAP level is correctly dialled.
- Check for water bubbling in the CPAP chamber.
- Check the water level of the bubbling chamber daily, to check water level dial to 0 cm H<sub>2</sub>O.
- CPAP as there is a tendency of water to evaporate.

## **If no bubbling**

1. Check CPAP prongs for occlusion.
2. Check for leaks in tubing or disconnection or occluded tubing.

3. Large air leak from the mouth
4. Chinstrap or pacifier may help
5. Increase CPAP level
6. Increase flow

## **Reference**

1. Cloherty and Stark's. Manual of Neonatal Care. 8th edition
2. Shashidhar a, suman rao pn, joe jose. Downes score vs. Silverman Anderson Score for assessment of respiratory distress in preterm newborns. Pediatric oncall Journal July - September 2016. Volume 13 Issue 3.
3. Diamedica Baby CPAP Instruction for use manual. 2018
4. Diamedica training for Bubble CPAP Operation.2018

## **152 Humidified High Flow Nasal Cannula (HHFNC)**

- Usually refers to the delivery of blended, heated and humidified oxygen at flows >1 L/minute via small binasal prongs.
- Is currently replacing the use of NCPAP and other means of oxygen administration.
- Is used when oxygen is given at more than 2 litres/minute.
- Allows delivery of distending pressure to the infant's airway with a simpler patient interface.

## **Physiologic benefits include:**

1. Flushing the upper airway dead space of CO<sub>2</sub> and allowing for better alveolar gas exchange.
2. Providing a flow adequate to support inspiration, thereby reducing inspiratory WOB.

3. Improving lung and airway mechanics by eliminating the effects of drying/cooling.
4. Reducing or eliminating the metabolic cost of gas conditioning.
5. Providing end distending pressure.

Reported advantages to HHFNC include ease of use, a simpler patient interface and a lower incidence of nasal breakdown compared to conventional CPAP.

Randomized clinical trials have demonstrated its efficacy to be similar to NCPCAP in post extubation management of infants less than 32 weeks' gestation.

Potential disadvantages include more variable distending pressure delivery (both low and high) and a tendency for a longer duration of respiratory support compared to CPAP.

### 153. Intubation in neonate

Elective intubation: neonates in intensive care often require intubation and mechanical ventilation for a period of time. Elective intubation refers to the practice of inserting an endotracheal tube (ETT) for the purpose of providing mechanical ventilation in a non-emergency setting, i.e., the neonate is not requiring resuscitation.

Equipment for intubation: prepare all equipment before the procedure is started.

- Neonatal laryngoscope – check to ensure that the light source is working and is adequate for illumination.
  - Miller blade size 0 for full term and 00 for preterm infant,
- Endotracheal tube (ETT) internal diameter size appropriate for the neonate, and another a size smaller.

*Table 18. Recommended ETT size*

Tube size (internal diameter mm)	Weight in grams	Gestational age (weeks)
2.5	<1000	<28 weeks
3.0	1000-2000	28-36 weeks
3.5	2000-3500	>38 weeks
4.0	>3500	>38 weeks

*Table 19. Recommended ETT length*

Weight (kg)	ETT Length (cm)
<1	6.5-7
1-2	7-8
2-3	8-9
3-4	9-10



Oral length = weight (kg) + 6cm or measure from the mouth to the tragus + 1

- Suction
- Plaster for baby to secure tube, ETT fixing device, forceps and scissors.
- End tidal CO<sub>2</sub> detector if available.
- Oxygen blender if available.
- Oxygen with pressure limiting device and T-piece or 500 mL bag and appropriate size mask.
- Set pressure limits (PIP): 30 cm H<sub>2</sub>O for term babies and 20 - 25 cm H<sub>2</sub>O in preterm babies.

#### Preparation:

- Ensure intravenous cannula is in place and working.
- Ensure all drugs are drawn up, checked, labelled and ready to give.
- Check that there are no contraindications to drugs.
- Ensure monitoring equipment is attached and working reliably.
- If the nasogastric tube (NGT) is in place, aspirate stomach (particularly important if the baby has been given enteral feeds).

#### Premedication:

Intubation has been identified as a painful procedure and is associated with physiologic side-effects including bradycardia, desaturation, increased blood pressure and increased intracranial pressure which may be associated with intraventricular haemorrhage. Choice of drugs depends on local practice. In emergency situations, it may be appropriate to intubate without premedication.

#### Preoxygenation:

- Give 100% oxygen for 2 minutes, before drug administration, through facemask
- Continue to give 100% oxygen until laryngoscopy and between attempts if more than one attempt is necessary.

#### Sedatives: Morphine or Fentanyl

Opioid analgesics, which provide sedation throughout the procedure, prevent systemic hypertension and reduce endocrine and endorphin responses to painful procedures.

Morphine has a longer onset of action than Fentanyl: peak analgesic effect is obtained after 15 minutes for morphine in comparison to in less than 3 minutes for Fentanyl.

If morphine is utilized as a premedication prior to intubation, staff must wait for the onset of action to optimize prior to administering other premedications and proceeding with elective intubation.

Fentanyl: IV 1-4 microgram /kg/dose: duration of action for 2-4 hrs.

- Infusion 1-5 microgram/kg/hr
  - Add 50 microgram/kg in 50ml of D5%W and give 1 microgram/kg/hr = 1ml/kg/hr.

#### Atropine:

Increases the heart rate, blocks the vagal response that placement of a laryngoscope and ETT may induce and minimizes oral secretions improving visibility of the vocal cords.

Onset of action: expected within two minutes.  
Half-life: > 4 hours.

Flush with saline following Atropine dose to ensure dose enters circulation.  
Atropine 20 mcg/kg/IV stat.

Muscle relaxants: prevent the increase in intracranial pressure reported during endotracheal intubation and reduce duration of and number of intubation attempts and hence reduce hypoxia. Muscle relaxants used for intubation are either Suxamethonium or Pancuronium.

Administer muscle relaxants only if you are confident that the team can intubate the baby quickly. Do not use a muscle relaxant unless adequate analgesia has been given.

#### Suxamethonium:

- Onset of action: 30-60 seconds
- Duration of action: 4-6 minutes
- Contraindicated in the presence of hyperkalaemia and family history of malignant hyperthermia.

#### Order of administration:

- Morphine; wait 15 minutes; atropine; wait two minutes; Suxamethonium; intubate
- Atropine; wait two minutes; fentanyl; wait two minutes; Suxamethonium; intubate

#### Procedure:

- Lift laryngoscope. Do not tilt.
- Avoid trauma to gums.
- Cricoid pressure: by person intubating or an assistant.

- Suction secretions only if they are blocking the view as this can stimulate the vagal nerve and cause a bradycardia and vocal cord spasm.
- Insert ET tube (ETT).
- Advance ETT to desired length at the lips.
- General recommendation is to advance ETT no further than the end of the black mark at the end of the tube (2.5 cm beyond cords), but this length is far too long for extremely preterm babies.
- Remove stylet if used and check to ensure it is intact before proceeding.
- Auscultate chest to check for bilateral equal air entry.
- If air entry is unequal and louder on the right side, withdraw ET by 0.5 cm and listen again.
- Stabilize tube using ETT fixation method in accordance with unit practice.
- Request chest X-ray: adjust ETT length so that the tip is at level of T1–2 vertebrae and document on nursing chart and in baby's hospital notes.
- Repeat until air entry equal bilaterally.

#### Reference

1. Neonatal Clinical Guideline 2018, NHS Trust, UK

#### 154. Endotracheal tube Suction

ETT suctioning is necessary to clear secretions and to maintain airway patency, and to optimize oxygenation and ventilation in an intubated patient. The goal of ETT suctioning should be to maximize the amount of secretions removed with minimal adverse effects.

### **Indications:**

- Increase in oxygen requirement
- Increase in CO<sub>2</sub>
- Apnoea and/or bradycardia
- Decreased air entry/increased work of breathing
- Audible crepitus
- Visible secretions
- Irritable, agitated baby
- Radiological changes: consolidation, collapse
- Decreased minute volumes

### **Preparation:**

- Wash hands and put on surgical gloves.
- Auscultate chest before suctioning.
- Ensure full monitoring of heart rate and SpO<sub>2</sub> is in place.

- Ensure baby is adequately oxygenated; consider increasing FiO<sub>2</sub> by up to 10 % before procedure, e.g., if the baby is receiving FiO<sub>2</sub> of 0.3 (or 30 % oxygen), increase oxygen delivery to up to FiO<sub>2</sub> 0.4 (or 40 % oxygen).
- Ensure the baby is positioned appropriately for secretion clearance and stress reduction.

### **Equipment:**

- Sterile disposable gloves
- Sodium chloride 0.9 %, not routinely
- 1 mL syringe
- Check function, suction tubing connected, pressure prior to suction.
- Use a maximum pressure of 100 mmHg (~13kPa).
- Suction catheter (the smaller the better):

*Table 20. Frequency of suctioning*

<b>ETT Size (mm)</b>	<b>Suction Catheter Size</b>
2.5	5-6 Fr
3.0 - 3.5	6-7 Fr
4.0 - 4.5	8 Fr

- Suctioning is not a routine practice; the need to suction should be assessed on an individual basis. Ventilated babies with respiratory distress syndrome have minimal secretions. In the first 72 hours, the need for suctioning should be minimal.
- Wait at least 4-8 hours after surfactant administration.

This is a two-person procedure at all times. The first person performs suction, the second assists and supports the baby during the procedure.

Follow the steps below to suction baby:

1. Auscultate lung fields
2. Measure length required (just beyond tip of ET tube)

3. Ensure that the PIP is set at no more than 4 cmH<sub>2</sub>O above the given working inspiratory pressure (PIP).
4. Silence ventilator alarms, remove flow sensor and reconnect circuit to ETT.
5. Insert catheter through one-way valve to pre-measured length and provide suction on removal. To avoid hypoxia, suctioning should not exceed six seconds.
  - This method of suctioning provides a hybrid between open and closed suction.
6. If the baby desaturates or it is anticipated that the baby will be unstable, escalate respiratory support as follows:
  - Increase the PEEP by 1-2 cmH<sub>2</sub>O, up to a maximum PEEP of 8 cmH<sub>2</sub>O
  - Increase FiO<sub>2</sub>
  - Give a manual inflation, which will give an inflation at your set PIP
  - Turn back the PEEP and FiO<sub>2</sub> to prescribed settings as soon as the baby has recovered from the suction
7. Gently suction oropharynx using a separate larger catheter.
8. Saline (NaCl 0.9%) instillation is only used if secretions are deemed to be thick and tenacious on individual assessment. Do not use sodium chloride 0.9% instillation routinely. Sodium chloride 0.9% ≤ 0.5 mL may be instilled before suctioning if secretions are thick and tenacious and cannot be extracted by suctioning alone.

#### **Complications of ET suctioning:**

- Hypoxia
- Bradycardias/arrhythmias
- Increased cerebral blood flow and intracranial pressure

- Mucosal trauma and injury
- Destruction of mucociliary transport
- Pneumothorax/perforation
- Infection
- Atelectasis
- Decrease in lung compliance

#### **Management of complications/troubleshooting (DOPE):**

- Displacement of the ETT (into right main bronchus or out of trachea) or disconnected tubing: inspect all connections from the ETT back to the ventilator. Observations of neonate for alteration in vital signs (heart rate and SpO<sub>2</sub> deterioration), observe for equal, bilateral chest movement and auscultate for equal, bilateral air entry.
- Obstruction with mucus plug or with kinked ETT or respiratory tubing: auscultate chest for air entry, inspect tubing and suction ETT.
- Pneumothorax: observe neonate for equal chest movement on right and left, auscultate for equal, bilateral air entry, inform medical staff immediately and prepare neonate for transillumination of the chest/chest x-ray and potential thoracentesis and/or insertion of a chest drain
- Equipment failure: ensure there is an inspected and functioning T piece resuscitator or ambu bag ready with appropriately sized neonatal facemask.

Educate the parents on the procedure, including the reason for intubation, requirement for respiratory support, safety aspects they need to be mindful of when interacting with their baby and how they can still interact with and assist with their baby's care.

## Aftercare

Documentation:

- Record colour, type, number of secretions, baby's tolerance of the procedure and ventilator setting required during suctioning on observation chart.

Monitoring:

- Ensure that monitoring of heart rate and SpO<sub>2</sub> continues after procedure
  - Auscultate baby's chest after procedure and document any changes observed
  - If FiO<sub>2</sub> was adjusted before procedure, return to original settings, or ensure that baby's target FiO<sub>2</sub> is maintained.

## Reference

1. Neonatal clinical guideline 2018, NHS Trust, UK

## 155. Mechanical ventilation in neonate

The principal benefits of neonatal mechanical ventilation during respiratory failure are as follows:

- Improve gas exchange, primarily by lung recruitment to improve ventilation/perfusion (V/Q) matching
- Decrease the strain of breathing
- Provide adequate minute ventilation (i.e., carbon dioxide removal) in infants with respiratory depression or apnoea

Indications for ventilation: assisted ventilation should be initiated when respiratory failure occurs.

Respiratory failure is verified by one of the following:

- Respiratory acidosis, documented by an arterial pH <7.2 and partial pressure of

arterial carbon dioxide (PaCO<sub>2</sub>) > 60 to 65 mmHg.

- Severe hypoxia documented by an arterial PaO<sub>2</sub> < 50 mmHg despite oxygen supplementation, or when the fractional inspired concentration (FiO<sub>2</sub>) exceeds 60% on nasal continuous positive airway pressure (nCPAP).
- Prolonged and frequent apnoea not resolved with NCPAP.
- Shock requiring more than two inotropes.

Ventilation is commonly used for the following conditions:

- Respiratory distress syndrome (RDS).
- Apnoea due to prematurity or perinatal depression.
- Initiation of exogenous surfactant therapy in infants with RDS.
- Stabilization of the sick unstable infant, e.g. necrotising enterocolitis, shock
- Downs score of 8-10 despite CPAP.
- Postoperative recovery.
- Persistent pulmonary hypertension.
- Meconium aspiration syndrome.
- Congenital pulmonary and cardiac anomalies, such as congenital diaphragmatic hernia.

Types of conventional mechanical ventilators: The time-cycled, pressure-limited (TCPL) ventilator is the most commonly used ventilator in neonates.

The following settings are used in the TCPL ventilator, which determine the type of breath delivered to the patient:

- Regulation of inspiratory gas flow either by pressure or volume control (ventilatory modalities):

- When pressure is controlled (i.e., pressure-limited), the tidal volume delivered will fluctuate depending on the lung compliance of the patient.
- When volume is controlled (i.e., volume-targeted), the pressure needed to deliver a targeted tidal volume will vary depending on lung compliance of the patient.
- Initiation of the breath (ventilatory modes)
  - breaths can be either mandatory or triggered by the spontaneous breath of the patient. The same mandatory or synchronized options for ventilatory modes are available for both pressure and volume-regulated ventilation.
- Time of inspiration and expiration.
- Positive end-expiratory pressure (PEEP) is the distending positive pressure during expiration.

#### **Choice of ventilation mode:**

- Most units would prefer to use AC in small ELBW babies to maximize support for every breath in such babies.
- SIMV is a very popular ventilation mode more suitable for bigger babies and often used in stable phase and weaning.
- PSV is an excellent mode in babies with good respiratory drive, relatively mild lung disease and during weaning. It does not always work so well in babies with stiff lungs such as in those with bad chronic lung disease.
- Recent Cochrane review has suggested that use of volume guarantee ventilation reduces the combined outcome of death or chronic lung disease. Volume guarantee should be considered when lung compliance is changing rapidly or there is

increased risk of atelectasis due to stiff lungs and increased airway resistance. It can be used in conjunction with other modalities of synchronised ventilation.

#### **Parameters of MV**

##### **Peak inspiratory pressure (PIP):**

- Adjust PIP initially to achieve adequate tidal volume (V<sub>t</sub>), as reflected by chest excursion and adequate breath sounds.
- PIP up to 25 cm H<sub>2</sub>O in preterm and up to 30 cm H<sub>2</sub>O in full term may be required in infants with decreased lung compliance.
- Decrease PIP gradually with improvement of lung disease down to 10 to 12 cm H<sub>2</sub>O.
- Too low PIP → ↓V<sub>t</sub> → hypoxia
- Too high PIP → ↑V<sub>t</sub> → barotraumas, BPD and ↓venous return

##### **Positive end expiratory pressure (PEEP):**

- PEEP can be adjusted as low as 3 cm H<sub>2</sub>O to as high as 8 cm H<sub>2</sub>O (moderate PEEP = 4 to 6 cm H<sub>2</sub>O).
- High PEEP (>8 cm H<sub>2</sub>O) → ↓V<sub>t</sub>, ↓venous return, air leaks & CO<sub>2</sub> retention
- Ventilated newborns should have a minimum physiologic PEEP of 2 to 3 cm H<sub>2</sub>O.
- Inadvertent PEEP: the chosen PEEP may be increased if the expiration time is too short or airway resistance is increased → gas trapping & increased risk of air leak.

##### **Fraction of inspired oxygen (FiO<sub>2</sub>)**

- The simplest means of improving oxygenation
- FiO<sub>2</sub> is adjusted to maintain an adequate oxygenation; it can be as low as 21 per cent and as high as 100 per cent.

### **Rate (RR) or frequency/minute**

- Adjust RR according to the GA & the underlying disease.
- RR 40-60 breaths/min is usually sufficient in most cases; it can be decreased to 20 breaths/min during weaning.
- Increasing RR, while keeping the Ti the same → air trapping.

### **Inspiratory time (Ti)**

- Ti is a measure of how rapidly gas can get in and out of the lungs.
- Adjust between 0.35 to 0.6 second depending on the pulmonary condition.
  - Small preterm infants with RDS have very short time constants and should be ventilated with Ti of 0.35 second or less.
  - Larger infants or those with increased airway resistance (e.g., chronic lung disease or meconium aspiration) have longer time constants and require longer Ti up to 0.5 second.
  - $Ti = G.A \text{ in wks} / 100$

### **Inspiratory time (Ti)/expiratory time (Te) ratio (I: E Ratio)**

- Primarily affects MAP and oxygenation
- Physiological ratio: 1:1 or 1:1.5
- Prolonged expiratory rates (1:2 or 1:3) can be used in MAS and during weaning.

Total breath Time or one cycle = 60 seconds/  
Breath Rate

Example: Rate = 30, Total time =  $60/30 = 2$  seconds.

One cycle is 2 seconds. Hence if  $Ti = 0.4$ ,  $TE = 1.6$  seconds.

Flow Rate [volume of gas passed/time unit (litre/minute)]

- Flow rates of 4 to 8 litres/minute are sufficient in most cases.
  - Low flow rate → effective PIP will not be reached
  - High flow rates → increased risk of alveolar rupture

### **Mean airway pressure (MAP)**

- MAP will be augmented by PIP, PEEP, Ti & flow rate.
- Adjust MAP between 10 to 12 cm H<sub>2</sub>O; higher levels are associated with an increased risk of air leaks.

### **Tidal volume**

- Set TV 4 to 6 ml/kg.

### **Minute ventilation**

- $MV = RR \times TV$

### **Initiation of mechanical ventilation:**

Setting up ventilator: switch on humidifier and follow manufacturer's recommended settings for optimum temperature and humidity.

1. Check that you are not starting with a pneumothorax.
2. Sedate the patient with a drug that does not cause histamine release (e.g., Propofol or Fentanyl instead of Morphine). Short-acting agents are best: the patient is often extubated in a matter of 2-24 hours. If appropriate treatment isn't working, Ketamine can be used (with a benzodiazepine); this dissociative anaesthetic is also a bronchodilator.
3. Paralyse the patient.
4. Start with a high FiO<sub>2</sub>: 100% O<sub>2</sub> initially, then adjusted according to ABG analysis.
5. Start with low PEEP.
6. Start with a low RR and low TV, allowing plenty of time for the patient to breathe

out. Look at the graphics on the ventilator and make sure that expiratory flow stops before inspiration starts.

7. Accept high PaCO<sub>2</sub>s and acidemia.
8. Keep the lungs moist. In some cases, 2ml saline should be squirted down the ETT and not immediately suctioned back. This is to try and loosen secretions. However, routine saline is not recommended.
9. BE PATIENT. With appropriate therapy, it will all get better.

#### Setting 1:

- During admission of a preterm baby requiring ventilatory support
  - Rate 60/min
  - PIP 16–18 cm H<sub>2</sub>O
  - PEEP 5 cm H<sub>2</sub>O
  - Tinsp 0.3–0.4 sec
  - FiO<sub>2</sub> 0.4–0.6
  - Flow 6–8 L/min (not applicable to SLE)
- Adjust ventilatory settings depending on chest movement, SpO<sub>2</sub>, and measured Vt.
- Sample blood gas within 30 minutes of commencing ventilatory support.

#### Setting 2:

- For babies with normal lungs requiring supportive ventilation such as: term babies with respiratory depression (asphyxia or drugs), babies with neuromuscular disorders or babies in the post-operative period, and preterm babies with recurrent apnoea, set ventilator at the following settings:
  - Rate 40/min
  - PIP 14 to 16 cm H<sub>2</sub>O
  - PEEP 4 cm H<sub>2</sub>O

- Tinsp 0.35–0.4 sec
- FiO<sub>2</sub> 0.21–0.3

#### Adjusting ventilatory settings:

##### Adjusting FiO<sub>2</sub>

- Oxygen is a drug and should be prescribed as with other medications. This should be done by specifying the intended target range of SpO<sub>2</sub> on the baby's drug chart.
- Suggested target SpO<sub>2</sub> ranges:
  - Preterm babies: 90 to 95 per cent.
  - Term babies with PPHN: 96 to 100 per cent.

##### Paralysis and sedation:

- Not routinely indicated.
- If the infant is fighting the ventilator, sedation using morphine, midazolam, phenobarbital and fentanyl, or paralysis with pancuronium can be used (Volume expanders may be required, because paralysis results in 3rd spacing of fluid).

##### Suctioning:

- Suctioning should be done to prevent the atelectasis, especially in premature infants.
- Continuously monitor SaO<sub>2</sub> by pulse oximetry.
- During suction, the catheter should not be inserted beyond the lower end of the ETT.
- During accompanying ambu-bagging (manual ventilation), FiO<sub>2</sub> may be increased by 10 per cent over the infant's current requirement.
- No routine saline for suction.

Babies fighting ventilator: if the baby is asynchronous with the ventilator (fighting):

- Ensure the 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, which is usually an intravenous infusion of morphine (10-20 microgram/kg/hr). Muscle relaxation is seldom necessary and is used only if morphine infusion already commenced.

#### **Monitoring the infant on MV:**

- Continuous electronic monitoring of heart rate, ECG, respiratory rate, SpO<sub>2</sub> and temperature.
- Daily monitoring of intake, output and weight.
- Maintain SaO<sub>2</sub> between 90 to 95 per cent.
- Hourly measurement of colour, and measured ventilator parameters: if there is a sudden drop in Vt, check air entry.
- Obtain an initial blood gas within 30 minutes of starting mechanical ventilation.
- Obtain a blood gas within 30 minutes of any change in ventilator settings.
- Obtain a blood gas q6 hours if available unless a sudden change in the infant's condition occurs.

#### **Complications of MV:**

- **ETT complications:** accidental displacement (into main stem bronchus, hypopharynx, or oesophagus), accidental extubation, or obstruction.

- Airway injury: subglottic stenosis, oedema of the cords (hoarseness and stridor), palatal groove (with prolonged orotracheal intubation), and necrotizing tracheobronchitis.
- Pneumonia, infections, BPD/oxygen toxicity.
- Air leak syndromes (related to MAP (>14 cm H<sub>2</sub>O).
- Miscellaneous (IVH, ↓cardiac output, feeding intolerance).

#### **Weaning from MV**

##### **When to wean?**

- If the infant is clinically stable, as evidenced by decreased work of breathing, maintaining normal saturation, increased chest expansion and aeration by chest auscultation, and radiographic evidence of improved lung volume
- If the infant has an efficient spontaneous respiratory drive
- If the infant is able to maintain satisfactory blood gases; if available:
  - PaO<sub>2</sub> >50 mm Hg
  - Optimal PaCO<sub>2</sub> varies according to disease state. For very immature infants or infants with air leaks, a PaCO<sub>2</sub> of 50 to 60 mm Hg may be tolerated as "permissible hypercarbia", provided that pH is >7.25.

#### **Steps:**

- ↓PIP as tolerated and as noted by adequate chest rise.
  - Reduce PIP (usually by 1–2 cm) until MAP of 7-8 cm is reached.

- If Assist/Control (A/C) mode is used, switch to SIMV when FiO<sub>2</sub> <0.4 and PIP <12 cm H<sub>2</sub>O.
- Reduce rate to 20/min, usually in decrements of 5–10 breaths/min.

#### **Extubation:**

- Provide FiO<sub>2</sub> as needed.
- Begin with postural drainage and suctioning.
- Connect the ETT to the ambu bag and give a prolonged sigh of 15 to 20 cm H<sub>2</sub>O to the infant while the ETT is extracted.
- Follow the infant by pulse oximeter.
- Do blood gas two hours after extubation.
- If the infant is stable, resume feeding four hours after extubation.
- Steroids are not routine before extubation (if there is prolonged intubation or previous failed attempts of extubation, give dexamethasone 0.25 mg/kg/dose q12 hours beginning 48 hours before extubation).

- If stridor (laryngeal oedema) develops after extubation, racemic epinephrine aerosols and steroids may be helpful.
- Tracheostomy must be considered if the baby cannot be extubated for at least four times over several weeks.
- For infants weighing <1,750 gm, when PIP <12 cm H<sub>2</sub>O, FiO<sub>2</sub> <0.3 and RR is 20 breaths/min, wean directly to nasal CPAP or HFNC and NIPPV.
- Larger infants can be weaned to nasal prongs or to a head box.

#### **Reference**

1. Wales Neonatal Network Ventilation Guideline, 2013
2. Handbook of Mechanical Ventilator, UK, 2015
3. Neonatal Care Protocol for Hospital Physicians, Egypt, 2010
4. Neonatal Guideline2017-19, NHS Thrust, UK,



# CHAPTER 7: RESPIRATORY SYSTEM DISORDERS

## Apnoea in neonate

Apnoea is defined as cessation of breathing for longer than 20 seconds or of any duration associated with cyanosis/bradycardia <100/min/poor tone.

The incidence of apnoea increases with decreasing gestational age. Essentially, all infants with <28 weeks' gestational age have apnoea. As many as 25 per cent of all premature infants who weigh <1,800 g (~34 weeks' gestational age) have at least one apnoeic episode.

Apnoea of prematurity generally occurs one or two days after birth. If it does not occur during the first seven days, it is unlikely to occur later.

### Causes of apnoea:

1. Idiopathic: apnoea of prematurity.
2. Temperature: Hypothermia / Hyperthermia.
3. Central nervous system: Intracranial haemorrhage, seizures; drugs: depressant, maternal narcotics and magnesium sulphate.
4. Respiratory: hypoxia, RDS, pneumonia, obstructive airway lesions, laryngeal reflex, pneumothorax, nasal occlusion and tracheal occlusion caused by neck flexion.
5. CVS: heart failure, hypotension, hypertension, hypovolaemia, PDA.
6. GIT: GERD, NEC
7. Infection: pneumonia, sepsis, meningitis.

8. Metabolic: acidosis, hypoglycaemia, hypocalcaemia, hyponatraemia, hypernatremia, inborn errors of metabolism
9. Haematological: anaemia, polycythaemia.

### Monitoring:

- All babies of less than 34 weeks' of gestational age should be monitored continuously for at least the first week of life or until there is an absence of apnoeic episodes for at least seven days. Babies >34 weeks' gestational age should be monitored if they are sick.
- Pulse oximeter is an effective way of monitoring apnoea. Though it does not detect chest wall movement, it detects the most important clinical consequences of apnoea, i.e., hypoxia and bradycardia.
- When a monitor alarm sounds, one should remember to respond to the infant, not to the monitor, checking for bradycardia, cyanosis, and airway obstruction.

### Management of apnoea:

#### Immediate measures:

- Most apnoeic spells in preterm infants respond to tactile stimulation.
- If the infant fails to respond with stimulation, then the infant should be ventilated with a bag and mask, starting with a fractional concentration of inspired oxygen ( $\text{FiO}_2$ ) equal to the  $\text{FiO}_2$  used before the spell to avoid marked elevations in arterial oxygen tension.

- After the first apnoeic spell, the infant should be evaluated for a possible underlying cause if a cause is identified. One should be particularly alert to the possibility of precipitating cause in infants who are >34 weeks' gestational age.
- Evaluation should include a history and physical examination; it may include arterial blood gas measurement, complete blood count, measurement of blood glucose, calcium, and electrolyte levels and sepsis work-up.

#### **General measures:**

- If an underlying factor has been identified, correct it/treat it.
- The optimal range of oxygen saturation for preterm infants is not certain. However, supplemental oxygen should be provided if needed to maintain oxygen saturation ( $\text{SpO}_2$ ) values in the targeted range at 90 to 95 per cent.
- Care should be taken to avoid reflexes that may trigger apnoea. Suctioning of the pharynx should be done carefully and tolerance of oral feedings when appropriate should be closely monitored.
- Positions of extreme flexion or extension of the neck should be avoided to reduce the likelihood of airway obstruction. Prone positioning stabilizes the chest wall and may reduce apnoea.
- Correct anaemia: packed cell transfusion if PCV <30 per cent and there are recurrent apnoeas.

#### **Methyl xanthine:**

Caffeine is the preferred methyl xanthine. It reduces apnoeic spells and the need for mechanical ventilation. Survival without neurodevelopmental disability is improved and reduces the rate of BPD/CLD.

#### **Indications for caffeine**

1. Preterm infants < 34 weeks if there is recurrent apnoea (> 2 apnoeas/hour or > 3 apnoeas in 2 consecutive hours).
2. Prophylactically started for <1250 gram or less than 32 weeks.
3. Prior to extubation in preterm infants <1250g.

**Dose:** loading dose of 20mg/kg caffeine citrate (10mg/kg of caffeine base) orally or intravenously, followed by maintenance doses of 5-8 mg/kg of caffeine citrate (2.5 to 5 mg/kg of caffeine base IV or Oral) in once daily dosing beginning 24hrs after loading dose.

If apnoea continues, give an additional loading dose of 10 mg/kg caffeine citrate and increase maintenance dose by 20 per cent. Therapeutic serum levels of caffeine are 5 to 20 mcg/ml.

#### **Caffeine is discontinued:**

- 48 hours after extubation.
- Apnoea free for seven days.
- If started Prophylactically for <1250 gram or less than 32 weeks, it is generally discontinued at 34-36 weeks of corrected age.
- Effect of caffeine likely remains for approximately one week after discontinuation. If caffeine is stopped, the baby should be monitored for apnoea for 5 to 7 days.

Caffeine is currently not available in Ethiopia but this is one of the drugs that has shown a significant impact on the survival of preterm infants. It is better to urge for its availability.

Aminophylline can also be used with a loading dose of 5 mg/kg, followed by 2 mg/kg /dose TID IV or Oral. However, the therapeutic index of aminophylline is narrower, leading to higher side effects. It is administered in more frequent dosing, unlike caffeine which is required once daily. It takes up to two days for aminophylline to be totally eliminated from the neonate.

**Ventilation:** if the apnoeas are very frequent, mandating immediate respiratory support despite methylxanthines:

- Nasal CPAP: at 4 to 6 mm of Hg.
- NIPPV (Non-invasive positive pressure ventilation)
- PIP – 12-15 cm H<sub>2</sub>O, PEEP - 5, Rate - 20-30/min, FiO<sub>2</sub> - 0.21 for normal lungs.
- Invasive ventilation with minimal settings if all other interventions are unsuccessful
- PIP – 12-13 cm H<sub>2</sub>O, PEEP - 5, Rate - 20-30/min, FiO<sub>2</sub> - 0.21.

#### Reference

1. Apnea. All India Institute of Medical Sciences protocol for neonatology. 2019
2. Neonatal Guideline2017-19, NHS Thrust, UK,
3. Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition
4. Michigan Manual of Neonatal ICU 3<sup>rd</sup> edition

## Respiratory distress syndrome (RDS)

Formerly known as hyaline membrane disease (HMD), respiratory distress syndrome describes a disease typical of preterm infants that is caused by insufficient pulmonary surfactant in alveoli.

Preterm infants are particularly prone to RDS because alveolar type II cells do not develop until early in the third trimester, and their number and capacity to produce surfactant increase throughout the third trimester. The development of RDS is inversely related with gestational age. The role of surfactant is to reduce the surface tension at the alveolar level. Absent or insufficient surfactant due to developmental immaturity of alveolar type II cells, spontaneous or inherited mutations of surfactant-related genes, or inactivation of surfactant due to inflammation, chemical modification, or lung injury, result in high surface tension and atelectasis.

#### Prevention:

Antenatal corticosteroid is the only preventive strategy to decrease occurrence of RDS.

- Indicated for 24-34 weeks' gestational age.
- Betamethasone or dexamethasone.
- **Dose:** 2 doses of betamethasone is administered 12 mg IM at an interval of 24 hours or doses of dexamethasone, 6 mg each at an interval of 12 hours. Effect starts 24 hours (possibly as early as 4 hours) after the first dose and continues for seven days.
- A repeat course of steroids is to be considered if they were taken more than seven days ago, gestation is <32 weeks and delivery is likely.

#### Antenatal screening:

- Lecithin/ Sphingomyelin ratio(L/S)

RDS risk is low when the L/S ratio is >2, but notable exceptions to this include maternal diabetes, erythroblastosis fetalis, and intrapartum asphyxia.

- Lamellar body count

Lamellar bodies are the organelles in alveolar type II cells that receive, concentrate, and store surfactant constituents for regulated secretion.

Lamellar body count >50,000 per microliter of amniotic fluid has been correlated with lung maturity.

#### Clinical presentation:

- RDS usually presents immediately after birth or hours after birth, with grunting, tachypenia, subcostal and sternal retractions, nasal flaring, bilateral poor air entry on auscultation and cyanosis in room air.

#### Diagnosis:

- Shake test is a reliable means of diagnosing RDS in preterm infants less than 34 weeks, especially in resource limited settings. Perform the shake test on the gastric fluid within one hour of age by passing a nasogastric tube into the stomach. From all babies, 0.5 ml of gastric fluid is obtained then mixed with an equal volume of normal saline for 15 sec; Add 1 ml of 95 to 100 per cent ethanol and agitate the mixture for 15 sec. Let it stand for 15 min, then examine for bubbles.

*Table 21. Shake test*

Observation	■ Interpretation	■ Risk of RDS
Immature	■ No bubbles	■ High (60%)
1+	■ Very small bubbles in meniscus extending one-third or less of circumference (magnifying glass may be used)	■ Intermediate (20%)
2+	■ Single rim of bubbles extending one third to all the way around the test tube	■ Moderate
3+	■ A rim of bubbles all the way around the test tube with double row in some areas	■ Low (<1%)
4+	■ A double row or more of bubbles all the way around the test tube indicates lung maturity.	■ Nil

- Chest X-ray - Low volume in poorly inflated lungs is typical finding.
  - Fine homogeneous reticulogranular pattern (grade 1)
  - Widespread air bronchograms become visible (grade 2)
  - Cardio pulmonary differentiation difficult due to alveolar shadowing (grade 3)

- Complete white-out of the lung fields (grade 4)
- Chest x-ray may be repeated after CPAP initiation; the goal is to expand the lungs up to 8 to 9 rib.
- Arterial blood gas analysis shows hypoxemia and hypercarbia.
- Sepsis screen - Sepsis and RDS may co-exist; thus, all infants with respiratory distress should be investigated appropriately and treatment with antibiotics should be considered.

#### **Management principles:**

- Basic supportive care (thermoregulatory, circulatory, fluid, electrolyte, and respiratory) is essential while functional residual capacity (FRC) is established and maintained.
- For preterm infants with respiratory distress, CPAP should be initiated as early as possible(refer to CPAPprotocol).
- Respiratory support with mechanical ventilators should be considered for infants not improving with CPAP.
- Administer surfactant based on indication.
- Address fluid and electrolyte based on the gestational age and postnatal age and put umbilical vein catheter if required. Avoid excessive intravenous (IV) fluid administration as pulmonary oedema exacerbates RDS.
- Antibiotics should be considered unless the risk of pneumonia and sepsis is negligible.
- Enteral feeding should be started per nutrition protocol, but feeding can be delayed in very sick newborns not maintaining adequate saturation.

#### **Surfactant administration:**

It is proven to reduce early mortality, air leak and chronic lung disease or death at 28 days. The incidence of BPD, IVH, NEC, health care-associated infections, ROP, and PDA, has not changed with surfactant replacement.

Surfactant replacement is effective for larger and more mature preterm infants with established RDS.

#### **Surfactant preparation:**

Three types of exogenous surfactant are available:

1. Surfactant derived from animal sources e.g., Survanta – bovine, Infasurf - calf and Curosurf - porcine lung extract.
- 2 Synthetic surfactant without protein components, e.g., Exosurf.
- 3 Synthetic surfactant with protein components, e.g., Lucinactant.

Dosing needs to be decided based on the available surfactant to achieve phospholipids of at least 100 mg/kg.

#### **Prophylaxis or preventive versus treatment or rescue surfactant:**

- A prophylactic or preventive is defined as intubation and surfactant administration to infants at high risk of developing RDS and is administered in the delivery room within 10 to 30 minutes. Results in increased rate of intubation and mechanical ventilation. In infants who would have managed successfully with CPAP, it is not recommended.
- Rescue or treatment surfactant is given only to preterm infants with established RDS.

Early Rescue is administered within a few hours (two hours) of birth selectively preferred. Late rescue is administered after well-established RDS >two hours.

Early initiation of CPAP with subsequent selective surfactant administration in extremely preterm infants results in lower rates of BPD/death when compared with treatment with prophylactic surfactant therapy.

#### Indications:

- Rescue therapy is considered for all preterm infants with respiratory distress and  $\text{FiO}_2 > 0.4$ .
- Preterm infants born at <30 weeks' gestational age who need mechanical ventilation because of severe RDS should be given surfactant after initial stabilization.
- Rescue surfactant may be considered for infants with hypoxic respiratory failure attributable to secondary surfactant deficiency (e.g., pulmonary haemorrhage, meconium aspiration syndrome, or sepsis/pneumonia).
- Repeat dose: if the baby is still on a ventilator and MAP is > 8 and  $\text{FiO}_2$  is > 0.4, a repeat dose of surfactant may be administered. The duration for the second dose depends on the type of surfactant used.

#### Methods of surfactant administration:

- Given via endotracheal intubation
- Ventilated babies the tube remains for mechanical ventilation
- For CPAP receiving babies, ETT will be removed after surfactant (INSURE= Intubation Surfactant Extubation).
- Check for comparable air entry after intubation before surfactant administration.

- Routine chest x-ray is not recommended to see the placement of ETT.
- The ETT should be secured after intubation to avoid mispositioning of the tube during dosing.
- To minimize reflux up the ETT, administration via a sterile feeding tube inserted into the ETT with the tip at or above the end of the ETT is preferable.
- Providing the dose in 2 to 4 aliquots and allowing for recovery on mechanical ventilation between aliquots can help to minimize obstruction of the ETT or large airways by the viscous surfactant preparation.
- In non-mechanically ventilated infants, the assistant will ventilate using bag mask ventilation in between aliquots.
- Positional manoeuvres are not necessary and should be avoided because they could result in ETT malposition or extubation.
- Aerosolization devices for surfactant administration are currently in clinical trials.

#### MV indication:

- If  $\text{FIO}_2$  requirement is more than 0.4 to 0.6 to achieve target  $\text{PaO}_2$  or  $\text{SpO}_2$
- When  $\text{PCO}_2$  is more than 60 to 65 mm Hg with PH less than 7.20
- Recurrent apnoea despite NCPAP
- Poor respiratory effort
- Severe respiratory distress - Downe score of more than 6
- Cardiovascular collapse – shock, HR <60 beats per minute calls for Cardiopulmonary resuscitation (CPR)
- Congenital malformations - congenital diaphragmatic hernia, choanal atresia
- Airway obstructions - Severe micrognathia, oropharyngeal mass

Modes and parameters of mechanical ventilation:

- Volume controlled
  - Volume target (VT) 4-6mL/kg
  - Rate 30 to 60 bpm
  - I-time 0.30 to 0.35 second
  - PEEP 5 to 8 cm H<sub>2</sub>O
  - PS to achieve ~% set VT
- Pressure controlled ventilation
  - Low PIP - 10 to 20 cm H<sub>2</sub>O
  - Moderate PEEP – 5 to 6 cm H<sub>2</sub>O
  - Relatively rapid rate (40 to 60/min)
  - If retractions persist, increase PEEP to a maximum of 7 cm H<sub>2</sub>O.
- After surfactant is given, the pressures should be reduced over the next one hour. Volume guarantee is a good mode post surfactant to avoid volutrauma.

Arterial blood gas goals in ventilated RDS newborns:

- pH 7.25 to 7.35
- PaO<sub>2</sub> 50 to 70 mm Hg
- PaCO<sub>2</sub> 45 to 55 mm Hg

### Reference

1. Apnea. All India Institute of Medical Sciences protocol for neonatology. 2019
2. Neonatal Guideline 2017-19, NHS Thrust, UK,
3. Cloherty and Stark's. Manual of Neonatal Care 8th edition
4. Michigan Manual of Neonatal ICU 3rd edition

## Meconium Aspiration Syndrome

Meconium-stained liquor occurs in 10 to 15 per cent of births and among these between 3 to 4 per cent of infants born with MSAF develop MAS. Among this 30 to 50 per cent require either BIPAP or mechanical ventilation.

Incidence of MAS increases from 0.24% to 1.42% between 38 and 42 weeks. But it is rare before 34 weeks.

In the delivery room:

- Note the following points in case of meconium-stained amniotic fluid
  - The character and colour of meconium.
  - Approximate estimation of gestational age (preterm vs term).
  - Presentation (vertex vs breech).
  - Evidence of foetal distress.
- Keep the appropriate resuscitation equipment ready.
- Resuscitation is the same as any normal delivery. The current NRP guidelines 2015 recommends that endotracheal suction in a non-vigorous baby is NOT routinely required. However, suction of mouth and nose is indicated.
- Collect cord arterial blood gas to help diagnose presence of in utero hypoxia.
- If the baby develops respiratory distress in the labour room, start the baby on DR-CPAP with PEEP settings of 5cm of H<sub>2</sub>O and shift to NICU.

### In the NICU:

The infant with MAS may be cyanosed, tachypnoeic, grunting with nasal flaring, retractions, with a hyper inflated chest (barrel shaped chest) and coarse breath sounds on auscultation. They may have marked swings in oxygen saturation due to intra and extra-pulmonary shunting. Poor perfusion may result from impaired cardiac function.

Assess distress score using the Downe score: mild is 1 to 3, moderate 4 to 6, severe >6

- Cord ABG
- ABG on admission (if cord ABG is not collected or clinically indicated)
- X-ray chest if moderate to severe respiratory distress or mild RD persisting for more than two hours.
  - Patchy atelectasis
  - Heterogeneous fluffy or nodular opacities
  - Dirty lung fields
  - Hyperinflation and air leak
- Asphyxia monitoring and work-up
- Sepsis work-up
- Other investigation as indicated

Care for neonate with meconium aspiration syndrome:

- Treat with antibiotics until sepsis is excluded.
- Optimal temperature/glucose regulation, calcium level.
- Minimal handling: typically, infants with MAS are very sensitive to handling. Frequency of routine cares and handling should be discussed among staff for clustering of cares.

- Circulatory support with normal saline or packed red blood cells should be provided to patients with marginal oxygenation.
- Oxygen therapy: providing adequate oxygenation therapy forms the mainstay of PPHN therapy. Some authors recommend maintaining higher saturation targets for O<sub>2</sub> saturation (94 to 98 per cent) and preductal PaO<sub>2</sub> (60 to 100 mm Hg).
- Administer IV fluids as required if there is ventilated or severe asphyxia. For infants with mild RD, give gavage feeds.

### Ventilation:

#### CPAP

1. If FiO<sub>2</sub> requirements exceed 0.40, a trial of CPAP may be considered. CPAP is often helpful, and the appropriate pressures must be individualized for each infant.
2. Do not use CPAP > 6 cm H<sub>2</sub>O. Do not give CPAP if there is air leak, hyperinflated lungs, or high PaCO<sub>2</sub>.

#### MV:

Indications are Downe score  $\geq 6$  and ABG: paO<sub>2</sub><50 on 0.8 FiO<sub>2</sub> or paCO<sub>2</sub>>60 or pH<7.25  
Start with patient triggered ventilation:

- Pressure controlled
  - PIP - 18 to 20 cm H<sub>2</sub>O
  - PEEP – 4 to 6 cm H<sub>2</sub>O
  - Ti = 0.3 to 0.5 sec. Adequate Te – 0.5 to 0.7 sec.
  - limit rate to  $\leq 30$
  - PS  $\sim \frac{2}{3}$  set PIP
- Volume targeted ventilation
  - VT 5 to 6 mL/kg
  - Limit rate to  $\leq 30$
  - PEEP 4 to 6 cm H<sub>2</sub>O
  - Pressure Support to achieve  $\sim \frac{1}{2}$  set VT

The findings on the CXR can guide the ventilatory settings. If it shows low volume, higher PEEP can be used. If it shows hyperinflation, avoid auto PEEP. Give adequate time for expiration.

**Surfactant** – Meconium is a strong surfactant in activator. Consider surfactant if the baby is requiring high ventilator parameters, i.e.,  $\text{FiO}_2 > 0.6$  or  $\text{PIP} > 20 \text{ cm H}_2\text{O}$ , especially if the CXR shows low volume lungs with atelectasis.

- Sedation and analgesia.
- Target  $\text{SaO}_2$  is 92 to 98 per cent.
- Target ABG (without PPHN):
  - pH 7.3 to 7.4
  - $\text{PaO}_2$  60 to 80 mm Hg
  - $\text{PaCO}_2$  35 to 45 mm Hg

### Complications

- Persistent pulmonary hypertension.
- Air leak.
- Abnormal pulmonary function.

### Reference

1. Avery's disease of the newborn. 10<sup>th</sup> edition
2. Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition
3. Michigan Manual of Neonatal ICU 3<sup>rd</sup> edition

## 161. Pneumothorax

Spontaneous pneumothorax occurs in 0.07 per cent of otherwise healthy-appearing neonates. One in 10 of these infants is symptomatic.

Risk factors for air leak are associated with primary lung disease or ventilation of the newborn.

### Pulmonary pathology:

- Meconium aspiration, pneumonia, congenital malformations
- RDS, TTNB, pulmonary hypoplasia

### Ventilator related risks:

- Higher PIP, especially in the 24 hours preceding pneumothorax
- Long Ti (>0.5 seconds)
- Frequent suctioning in the eight hours before pneumothorax

The incidence of pneumothorax has decreased

significantly since the advent of exogenous surfactant.

### Pathophysiology:

- Pneumothorax results from the over distension and rupture of an alveolus when the air is travelling up the vascular sheath into the mediastinum and into the pleural cavity. Uneven ventilation and air trapping both contribute to air leak.
- Air in the mediastinum seldom produces enough tension to cause circulatory embarrassment but when it does, compression of mediastinal structures can impede venous return and cause circulatory collapse.
- High pressures within the pleural space collapse the lung and result in hypoxia and hypercapnia.

Clinical presentation: the condition may present as a sudden deterioration in the infant's clinical state, in the resuscitation room or as marked respiratory distress.

There is usually:

- Decreased air entry on the affected side.
- Cyanosis/fall in the oxygen saturations.
- Tracheal deviation to the contralateral side of the pneumothorax.

#### Investigations:

Transillumination of the chest with an intense beam of light is a useful method of making the diagnosis in an emergency.



Figure 19. Transillumination test

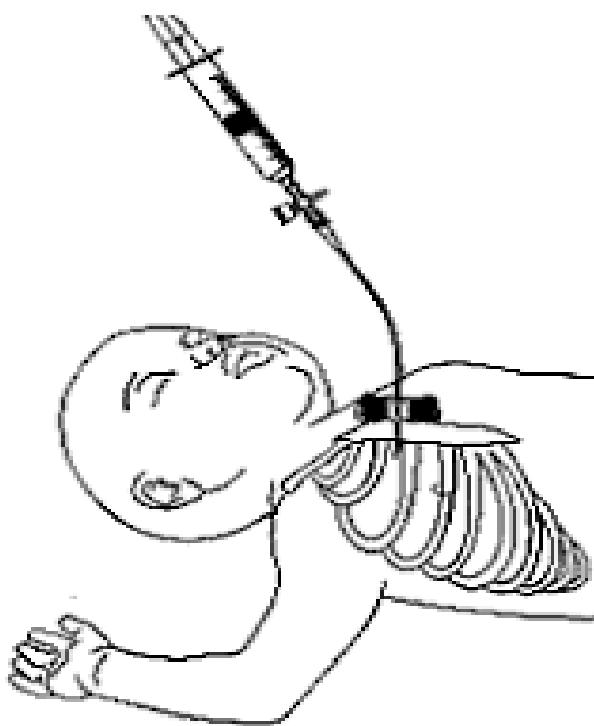
Confirmation by X-ray should be done only if the infant is stable.

If the infant is unstable, immediate draining of air is imperative.

Chest ultrasound – absent sliding sign.

#### Management:

- Small pneumothoraxes may require no specific treatment apart from observation including progress X-rays and blood gases.
- Waiting for a CXR when the infant is deteriorating can be fatal; therefore, aspiration should happen immediately after transillumination, if transillumination is positive.
- This can be done either with needle aspiration or insertion of an intercostal catheter.
- Needle aspiration.  
Needle drainage should be used only for diagnostic and prompt symptom relief purposes. Needle drainage should be implemented at: 23G or 25G butterfly needle; syringe; three-way stop valve
- Neonate should be supine.
- In the identified side, in second ICS in the midclavicular line, the butterfly is inserted at the upper border of the third rib.
- Maintaining closed system with three-way valve and syringe.
- Air is aspirated till there is no further release of air. Urgent preparation should be made to insert an intercostal device (ICD).



*Figure 20. Needle aspiration of pneumothorax using butterfly needle, three-way valve and syringe*

#### **ICD insertion guideline**

Equipment:

- Chest tube catheters of French size 10 or 12 or
- Pigtail catheter of French size 8 or 10 are preferred if available.

Ensure adequate asepsis during procedure.

Use local anaesthesia, lidocaine.

Sedation – injection of fentanyl 2microgram/kg or Morphine

Titrate oxygen as needed.

At the fourth/fifth ICS, ICD is inserted with a small mosquito, after identifying the length to be inserted (2 inches), with the end

clamped. This is connected to a sealed bottle underwater.

The ICD is secured with purse string sutures around the catheter. The ends of the suture are braided over the tube. The column movement should be documented at the end of the procedure.

Take a chest x-ray after the procedure.

ICD is clamped when there is no column movement or air-bubbling and there is adequate chest expansion.

If the baby continues to be stable, the ICD is removed, usually after the baby is off all positive pressure ventilation.

Pneumomediastinum, pneumopericardium and pneumoperitoneum may all also occur. Pneumopericardium and pneumomediastinum occasionally present as emergencies under tension, requiring urgent intervention. The outcome of pneumopericardium when it causes circulatory collapse is invariably fatal unless the air is drained immediately.

#### **Reference**

1. Neonatal Guideline, NHS, UK, 2017-19
2. Cloherty and Stark's. Manual of Neonatal Care 8th edition
3. Michigan Manual of NICU 3<sup>rd</sup> edition

## **162 Bronchopulmonary dysplasia (BPD)**

This is a major form of chronic lung disease in newborns. The aetiology appears to be ventilator support with high pressure and FiO<sub>2</sub> for prolonged periods of time.

Other contributory factors are infection, patent ductus arteriosus, and immaturity of the air way.

### **Definition:**

For infants born at <32 weeks' gestational age who received supplemental oxygen for their first 28 days, BPD at 36 weeks' postmenstrual age (PMA) is defined as:

- Mild when there is no supplemental O<sub>2</sub> requirement
- Moderate when supplemental O<sub>2</sub> requirement <30 per cent
- Severe when supplemental O<sub>2</sub> requirement ≥30 per cent and/or on CPAP or ventilator

For infants born at ≥32 weeks, BPD is defined as the supplemental O<sub>2</sub> requirement for the first 28 days with severity level based on the O<sub>2</sub> requirement at 56 days.

Physiologic definition of BPD - The need for supplemental oxygen is based on oxygen saturation (SpO<sub>2</sub>) during a room air challenge performed at 36 weeks' PMA (or 56 days for infants >32 weeks' PMA) or before hospital discharge. Persistent SpO<sub>2</sub> <90 per cent is the cut-off below which supplemental O<sub>2</sub> should be considered.

### **Investigations:**

- Blood gas analysis
- Chest X-ray
  - Homogenous opacification of lung fields after first week of life (Type 1) or coarse streaky opacities with cystic translucencies in lung fields (Type 2)
- Echocardiography to rule out pulmonary hypertension or structural pathology
- Electrocardiography (ECG) to rule out pulmonary hypertension

### **Management:**

Involvement of a neonatologist in the management is mandatory.

Use lowest possible ventilator pressures to deliver appropriate tidal volumes to minimize barotrauma and volutrauma.

Volume-targeted/volume guarantee ventilation, if available, may help prevent development of BPD.

### **Optimise nutrition:**

- Ensure adequate calorie intake (at least 120 Kcal/kg/day) because of increased work of breathing.
- Avoid fluid overload.

### **Corticosteroids:**

- If the infant is ventilator-dependent and requires increasing or persistently high oxygen intake, consider using corticosteroids.

Diuretics: chlorothiazide or spironolactone can be used.

Bronchodilators: via metered dose, inhalation can be used to relieve bronchospasm and trachea-bronchomalacia.

MV: ventilator management is challenging. Volume-targeted ventilation is preferred.

### **Reference**

1. Cloherty and Stark's. Manual of Neonatal Care 8th edition
2. Michigan Manual of NICU 3rd edition

# CHAPTER 8:

## Cardiovascular problems

### Stabilization of the neonate with acute cardiac disease

A high index of suspicion for neonates who present with “cyanosis” or signs of circulatory failure from the first minutes to the first few weeks of life is required.

**Presentation:** the presentation of CHD in the neonatal period is variable and the yield from clinical assessment is low.

CHD should be suspected in neonates who present with cyanosis, systemic hypoperfusion (shock) and pulmonary over circulation (congestive heart failure).

Of greatest concern is the early identification of cardiac lesions where either pulmonary (duct-dependent pulmonary circulation) or systemic blood flow (duct-dependent systemic circulation) is compromised.

Timely administration of a prostaglandin infusion (PgE1) to sustain ductal patency may be lifesaving in these cases.

In addition, early detection may also improve neurodevelopmental outcomes as preoperative hypoxaemia and systolic hypotension are predictive of white matter injury.

*Table 24. Ductal dependent congenital heart disease*

Duct dependent pulmonary circulation		Duct dependent systemic circulation
Tricuspid atresia	Transposition of great arteries	Congenital mitral stenosis
Ebstein anomaly		Hypoplastic left heart syndrome
Critical pulmonary stenosis		Interrupted aortic arch
Tetralogy of Fallot		Coarctation of the aorta
Double outlet right ventricle		

### Investigations:

- Pre- and post-ductal oxygen saturations ( $\text{SpO}_2$ ) should be monitored in all cases to help with diagnosis and monitor response to therapeutic interventions (e.g., iNO, PGE<sub>1</sub>).
- An arterial blood gas (ABG) and plasma lactate hypoxaemia, metabolic acidosis and elevated lactate are markers of duct-

dependent lesions and can be used to monitor the efficacy of therapeutic interventions.

- Chest X-ray – yield is low abnormal cardiac size.
- Electrocardiogram (ECG) - dysrhythmia, conduction defect or cardiac chamber enlargement.
- Echocardiography

The hyperoxia test should be performed on all neonates with suspected duct-dependent CHD.

The test is performed by placing the neonate in 100 per cent oxygen for at least 10 minutes and performing an ABG, preferably from the right radial artery.

A failed hyperoxia test is defined by a  $\text{PaO}_2 < 150 \text{ mmHg}$  in 100 per cent O<sub>2</sub>.

$\text{PaO}_2 > 100\text{mmHg}$ : Parenchymal lung disease/PPHN most likely

$\text{PaO}_2 < 50 - 100\text{mmHg}$ : CHD or PPHN

$\text{PaO}_2 < 50 \text{ mmHg}$ : Duct-dependent pulmonary circulation most likely

Differentiating a Duct-dependent Pulmonary Circulation (DDPC) from Persistent Pulmonary Hypertension of the newborn (PPHN):

- Clinical signs usually overlap.
- Hyperopia test is not always reliable.
- PPHN - history of respiratory failure, pulmonary parenchymal disease or birth asphyxia and more likely to require mechanical ventilation and cardiotropic support.
- A duct-dependent pulmonary circulation should be considered in neonates with early hypoxaemia and any clinical cardiovascular sign.
- On many occasions both conditions co-exist, and the diagnosis becomes less clear.
- Irrespective of the underlying diagnosis, a simple approach to acute stabilization, including commencing prostaglandin infusion, will ensure safe transfer of neonates with both conditions.

Differentiating a Duct-dependent Systemic Circulation (DDSC) from other forms of Neonatal Shock

- DDSC and sepsis are the most common causes of circulatory collapse in the neonatal period; however, distinguishing these conditions may be difficult.
- Inborn errors of metabolism, cardiomyopathy and arrhythmias may also present as circulatory collapse.
- The timing of presentation of DDSC is variable; however, most cases present in the first seven to 14 days of life.
- Oxygen saturations may be normal, high (reflects excessive pulmonary blood flow with decreased systemic utilization) or low in cases of obstructed systemic blood flow.

### Management:

#### Stabilization

If possible, transfer to a cardiac centre where the definitive surgery can be done.

#### Prostaglandin E1 Infusion

The decision to administer PGE1 should be based on the presenting clinical scenario; as the risks associated with treatment are low, a low threshold for administration should be adopted. PGE 1 is recommended in the following scenario:.

1. Antenatal diagnosis of a duct-dependent cardiac lesion or a cardiac lesion presenting with profound cyanosis or circulatory compromise
2. Low dose PgE1 (0.01  $\mu\text{g}/\text{kg}/\text{min}$ ) is normally recommended in this situation; however, if the clinical situation deteriorates, the dose should be increased to a maximum of 0.1  $\mu\text{g}/\text{kg}/\text{min}$ .

3. Early neonatal cyanosis or hypoxaemia in the presence of clinical signs of CHD (e.g., murmur, abnormal pulses) or abnormalities on radiological or ECG evaluation
4. Inability to clinically distinguish a duct-dependent pulmonary circulation from

PPHN. PGE<sub>1</sub> should not be withheld as there may be beneficial pulmonary vasodilator effects.

5. Critically ill neonates with signs of cardiogenic shock or circulatory collapse. Even if there are risk factors for sepsis or metabolic disease, PGE<sub>1</sub> should not be withheld as failure of administration may lead to the patient's demise. Prostaglandin could result in apnoea as a complication.

#### Ventilation:

Routine intubation of all neonates when PGE1 treatment is administered should not be mandatory. Although there is an increased risk of apnoea, the risk is low at doses <0.05 µg/kg/min.

#### Intubation indications:

- Respiratory failure,
- Clinical signs of cardiogenic shock and/or need for cardiotropic support,
- Profound metabolic or lactic acidosis,
- Prematurity (< 28 weeks gestation) and
- Associated airway disorder

Ventilation goal is PaCO<sub>2</sub> of 40 to 50 mmHg and an arterial pH of 7.25 to 7.35 to avoid excessive pulmonary blood flow in patients with single ventricle type physiology.

#### Oxygen administration:

Oxygen administration in the setting of suspected CHD can be both "beneficial" and "harmful".

Both PPHN and duct-dependent CHD have been associated with abnormal neurodevelopmental outcomes and hypoxaemia is thought to be a major contributory factor.

- PPHN - oxygen is a pulmonary vasodilator and an essential part of the treatment.
- Duct-dependent systemic circulation - oxygen therapy may decrease pulmonary vascular resistance (PVR) and could decrease right to left shunt, and result in inadequate systemic perfusion.
- This makes decisions related to desired oxygen saturation extremely challenging when the diagnosis is unconfirmed.
- The implementation of an oxygen weaning strategy may be a useful "diagnostic test" to help differentiate these PPHN and CHD.
- In general, most neonates with a duct-dependent pulmonary lesion will tolerate weaning O<sub>2</sub> slowly and will remain stable with oxygen saturations between 75 to 85 per cent in room air, unless there is a coexisting pulmonary hypertension.
- Neonates who required 100 per cent oxygen were more likely to have a diagnosis with restricted pulmonary blood flow and had a greater need for mechanical ventilation and cardiotropic support.
- Neonates with PPHN and an extremely reactive pulmonary vascular bed will not tolerate any wean and will develop very low oxygen saturations that will normally respond to reinstitution of O<sub>2</sub>.

- Oxygen should not be withheld from neonates with a clear diagnosis of PPHN, CHD in association with PPHN or where  $\text{SpO}_2$  is <75 per cent.

#### **Cardiotropic support:**

The goal of treatment is to ensure blood pressure is sustained within a range where adequate systemic perfusion is maintained.

Monitoring heart rate, urinary output, arterial pH and lactate are essential components of the stabilization and ongoing care of neonates with CHD.

Treatment includes:

- Crystalloid is useful in neonates with abnormal right ventricular performance; hence, it may play an important role in PPHN or duct-dependent pulmonary circulations (e.g., pulmonary atresia, severe TOF).
- Inodilator agents (dobutamine, milrinone) and pressors (dopamine, epinephrine, vasopressin)

Milrinone has been shown to reduce both mortality and low cardiac output syndrome in post-operative cardiac patients and in many centres; it is the first line cardiotropic agent.

High-dose dopamine and epinephrine are rarely recommended due to their adverse effects on both myocardial and vascular resistance.

Other interventions:

- Inhalational Nitric Oxide is a selective pulmonary vasodilator.
- Profound or sustained hypoxaemia ( $\text{PaO}_2$  <40 mmHg) may result in pulmonary vasoconstriction and elevated PVR.

- Therefore, it is not surprising that PPHN may coexist in neonates with compromised pulmonary blood flow.
- The administration of iNO to neonates with profound hypoxaemia in a setting of PPHN and TGA has been shown to be life-saving.

#### **References**

1. Cloherty and Stark's. Manual of Neonatal Care 8<sup>th</sup> edition
2. The Hospital for Sick Children, Programme Manual, 2013

#### **Pulse oximeter screening of critical congenital heart disease (CHD)**

**Critical CHD** – critical CHD refers to lesions requiring surgery or catheter-based intervention in the first year of life. This category includes ductal-dependent and cyanotic lesions, as well as less severe forms of CHD that are not dependent on the patent ductus arteriosus (PDA). Critical CHD accounts for approximately 25 per cent of all CHD.

Incorporation of pulse oximeter to the assessment of a newborn infant can enhance detection of critical congenital heart disease (CCHD).

Appropriate equipment, trained health workers to perform the pulse oximeter and appropriate management of positive cases is mandatory.

The screening is targeted toward healthy newborn infants in the newborn nursery or postnatal room.

Screening should be performed with motion-tolerant pulse oximeters.

Screening should not be undertaken until 24 hours of life or as late as possible if early discharge is planned.

Oxygen saturations should be obtained from the right hand and one foot.

Screening that has a pulse oximeter reading of ≥95 per cent in either extremity, with a ≤3 per cent absolute difference between the upper and lower extremity, would be considered a pass and the screening would end.

If the pulse oximeter reading is between 90 to 94 per cent or the difference between upper and lower extremity is more than 3 per cent, a repeat test must be done after one hour. If the finding is the same, repeat one more time. If it persists on the second test, this will be considered as a fail and immediate evaluation is mandatory.

Infants with saturations <90 per cent should receive immediate evaluation.

In the event of a positive screening result (failed pulse oximeter screening), CCHD needs to be excluded with a diagnostic echocardiogram. Infectious and pulmonary causes of hypoxaemia should also be excluded.

## 181. Arrhythmias

Neonatal arrhythmias are relatively common, especially supraventricular tachycardias. These arrhythmias may or may not be associated with underlying structural heart problems.

Post-operative arrhythmias usually occur in those that have had open cardiac surgery.

If an arrhythmia is suspected, rapidly assess the infant for signs of respiratory or cardiac decompensation. Emergency management of shock should precede definitive diagnosis. Immediately run a rhythm strip from the bedside monitor and perform a blood gas to determine acid base, electrolyte, blood glucose and haemoglobin status.

If the newborn is stable, perform a 12-lead ECG. It is also important to perform a 12-lead ECG after the rhythm returns to normal. All arrhythmias should be discussed with the duty NICU consultant.

### Narrow Complex Tachyarrhythmia

#### Sinus Tachycardia:

Most common cause of tachycardia

- Heart rate between 180 to 220 beats per minute
- Causes are anaemia, stress, fever, high levels of circulating catecholamines, hypovolaemia, and xanthine (e.g., aminophylline) toxicity.

Treatment - Correct the underlying cause.

#### Supraventricular Tachycardia:

They are the most common symptomatic arrhythmias in all children, including neonates.

SVTs usually have:

- i. Rate >200 beats per minute, frequently “fixed” with no beat-to-beat variation in rate,
- ii. Rapid onset and termination (in re-entrant rhythms)
- iii. Normal ventricular complexes on the surface ECG

#### Causes:

- An atrial ectopic site which has a faster intrinsic rate than the sinus node
- Re-entry in which there are two routes for conduction: the normal atrioventricular node-His-Purkinje system and the accessory pathway (e.g., Wolff-Parkinson-White syndrome).
- 10 to 15 per cent of cases could have structural heart disease. Screening should be performed for all neonates.

#### Treatment:

Type of initial therapy depends on the presence or absence of SHOCK (Clinical findings and metabolic acidosis).

#### If there are no signs of shock:

- Vagal (e.g., Ice to face)
- Adenosine
- Synchronous cardioversion
- Amiodarone/Digoxin (after discussion with cardiologist)

#### Atrial flutter

- Uncommon (unless associated with right atrial problems)
- Variable AV block
- Saw tooth/irregular baseline
- Adenosine may be used as a diagnostic tool by a cardiologist to determine if the narrow complex tachycardia is an SVT or flutter; with flutter, adenosine will temporarily slow the ventricular rate.

#### Treatment:

- Synchronised low dose(0.5J/kg) cardioversion

- Preventative treatment is not usually required; amiodarone can be used.
- Avoid atropine like drugs. Avoid agitation and keep prone.

#### Wide-Complex Tachycardia

##### Ventricular Tachycardia (VT)

- Rare in neonates
- Usually associated with severe medical illnesses including hypoxaemia, shock, electrolyte disturbances, digoxin toxicity and catecholamine toxicity
- It may rarely be due to an abnormality of the electrical conducting system of the heart, such as prolonged QTc syndrome and intramyocardial tumours.
- Haemodynamic compromise common
- ECG usually diagnostic - AV dissociation
- No response to adenosine.

#### Treatment:

- Urgent treatment depends on two simple clinical features: are pulses present?. If yes, is shock present?
- If pulses are present and no shock is present, consider Amiodarone 5mg/kg as first line.
- Immediate synchronous cardioversion if pulseless/shock - commence at 4J/kg (ensure adequate analgesia/sedation)
- Lignocaine 1mg/kg may have a role in prophylaxis of recurrent VT/VF.

#### Ventricular Fibrillation (VF):

Uncommon and usually terminal event, more likely in:

- Severe hypertrophy or myocardial disease
- Severe electrolyte disturbance
- Prolonged QT interval

- Wolf-Parkinson-White Syndrome
- May also result from degeneration of haemodynamically unstable SVT or VT

#### Treatment

- Cardioversion (unsynchronised) – starting dose of 1-2J/Kg

### Bradyarrhythmias

#### Sinus (Baseline) Bradycardia

P wave before every QRS. Commonly, the heart rate is between 80 and 100 beats per minute.

Causes could be hypoxia, acidosis, and elevated intracranial pressure.

Treatment: underlying cause

#### Heart block

- First-degree atrioventricular block
- Occurs when the PR interval is >0.16 seconds.
- Causes could be a nonspecific conduction disturbance, medications (e.g., digoxin), myocarditis, hypothyroidism, or association with certain types of congenital heart disease (e.g., complete atrioventricular canal or ventricular inversion).
- No specific treatment is generally indicated.

#### Second-degree atrioventricular block

- Mobitz I (Wenckebach phenomenon).
- Mobitz II (intermittent failure to conduct P waves, with a constant PR interval).
- Second degree atrioventricular block may occur with SVT, digitalis toxicity or a nonspecific conduction disturbance.

- Nonspecific treatment is usually necessary in addition to diagnosis and treatment of the underlying cause.

#### Complete heart block

- It refers to the complete absence of conduction of any atrial activity to the ventricles.
- It typically has a slow and constant ventricular rate that is independent of the atrial rate.
- Frequently detected in utero as foetal bradycardia.
- Most common causes include anatomic defects (ventricular inversion and complete atrioventricular canal) and foetal exposure to maternal antibodies related to systemic rheumatologic disease, such as lupus erythematosus.
- In cases of in utero complete heart block (CHB) caused by maternal antibodies related to lupus erythematosus, the prognosis may be poor.
- If there is a high risk of developing CHB (previous foetus with CHB, miscarriage, abnormal foetal echocardiography), treatment in pregnancy with dexamethasone, azathioprine, IV gamma globulin, or plasmapheresis should be considered.

#### Irregular rhythms:

##### Premature atrial contractions (PAC)

- These are common in neonates, usually benign and do not require specific therapy.
- Most PACs result in a normal QRS morphology, distinguishing them from premature ventricular contractions (PVCs).

## Premature ventricular contraction (PVC)

- Are “wide QRS complex” beats that occur when a ventricular focus stimulates a spontaneous beat before the normally conducted sinus beat. Isolated PVCs are not uncommon in the normal neonate and generally do not require treatment.
- PVCs may be caused by digoxin toxicity, hypoxaemia, electrolyte disturbances, catecholamine or xanthine toxicity. PVCs occurring in groups of two or more (i.e., couplets, triplets, etc) are pathologic and “high grade”) may be a marker for myocarditis or myocardial dysfunction and further evaluation should be strongly considered.

## Reference

1. Neonatal Guideline 2017-19, NHS Trust, UK
2. The Hospital for Sick children, Programme Manual. 2013

## Patent ductus arteriosus in preterm neonates

### Definition:

Persistent patency of the ductus arteriosus (PDA) is a failure of functional ductal closure by 48 hours or anatomical closure by three weeks. Failure of the ductus arteriosus to close within 48-96 hours of postnatal age results in a left-to-right shunt across the ductus and overloading of the pulmonary circulation.

The incidence of PDA is inversely related to gestational age and birth weight.

### Factors associated with delayed closure:

- Prematurity (significant PDA affects approximately 30 per cent of very-low birth weight babies)
- Lack of antenatal corticosteroid prophylaxis.
- Respiratory distress syndrome.
- Hypoxaemia.
- Liberal fluid therapy/Volume overload.

### Adverse effects of PDA:

- Haemodynamic consequences of left-to-right shunt in preterm babies can prolong ventilatory support and are associated with mortality and morbidity (chronic lung disease, pulmonary haemorrhage, intraventricular haemorrhage, necrotising enterocolitis and retinopathy of prematurity).
- Congestive cardiac failure which manifests clinically with wide pulse pressure and bounding pulses.
- Increased pulmonary blood flow (leading to increased work of breathing and respiratory deterioration).
- Reduced systemic blood flow (leading to acidosis and hypotension).

### Clinical manifestations:

- Onset in preterm infants is usually two to seven days after birth; however, it can be absent even in the presence of a significant duct in the first seven days of life.
- Apnoeic spells/bradycardia may be the initial signs.
- A significant left-to-right shunt is suggested by:

- bounding pulses and wide pulse pressure (i.e., >25 mmHg)
- hyperdynamic precordium (excessive movement of precordium)
- low-pitched systolic or continuous murmur over left upper sternal edge (absence of a murmur does not exclude significant PDA).
- Signs of cardiac failure (tachypnoea, tachycardia, hepatomegaly, pulmonary oedema, generalized oedema etc.)
- Poor perfusion (hypotension, poor capillary refill, mottled skin and persistent acidosis)
- Increased ventilator setting requirement
  - Typically, a preterm infant with RDS shows some improvement during the first few days after birth. This is followed by an inability to wean the infant from the ventilator or a need to increase ventilator settings or O<sub>2</sub> requirements.
- Poor weight gain

#### **Indicators of ductus opening on a ventilated baby**

The following signs should raise clinical suspicions of a symptomatic PDA:

- Metabolic acidosis not attributable to hypoperfusion and sepsis,
- Deteriorating respiratory status on days three to four after a period of relative stability,
- Increasing ventilatory requirements on days three to four,
- Unexplained CO<sub>2</sub> retention,
- Fluctuating FiO<sub>2</sub> requirements and
- Recurrent apnoea in a ventilated baby

#### **Investigation:**

- SpO<sub>2</sub> monitoring
- Chest X-ray: cardiomegaly? pulmonary plethora?
- Echocardiography
  - to detect duct-dependent cardiac lesions and other cardiac pathologies that are difficult to exclude clinically
  - if considering treatment with prostaglandin inhibitor

Echocardiographic assessment of significant PDA includes:

- Size of PDA (>1.5 mm)
- Volume loading of left atrium (LA/aorta ratio >1.5)
- Volume loading of left ventricle
- Velocity and flow pattern of ductal flow

#### **Immediate treatment: general measures:**

- Optimise oxygenation by appropriate ventilatory management.
- Use of a higher PEEP (i.e., ≥5 cm H<sub>2</sub>O) can help minimise effects of pulmonary oedema and risk of pulmonary haemorrhage.
- Treat anaemia – maintain Hb ≥10 g/dL with blood transfusion (consider concurrent dose of furosemide IV).
- Before starting medication, restrict fluid intake to 60–80 per cent.
- If there is fluid overload or pulmonary oedema, give one dose of furosemide IV.
- In intractable CHF, use frusemide in a dose of 1 mg/kg/dose 12 hourly.
- Digoxin has no role in management of PDA.

### **Specific measures:**

- Aim to convert haemodynamically significant PDA into insignificant PDA as complete duct closure may take weeks or months.

Pharmacological treatment with prostaglandin inhibitor to initiate closure:

- Ibuprofen is the drug of choice for this purpose.
  - Ibuprofen dose is 10 mg/kg stat followed by 5 mg/kg/dose x 2 doses at 24-hour intervals given orally.
  - It has an equal efficacy as compared to indomethacin with fewer side effects.
- Paracetamol may also be considered as an oral course in infants who have previously not responded to indomethacin or ibuprofen for the closure of a PDA with possibly fewer adverse effects. A five-day course of 15mg/Kg 6 hourly is recommended.
- Indomethacin (prostaglandin antagonist) can also be used. The closure rate with indomethacin is 80 per cent.
- Pharmacological treatment is best used aged  $\leq$  two weeks but can be effective  $\leq$  six weeks.

### **Indications:**

- Babies born  $<34$  weeks' gestational age with significant PDA – on clinical and/or echocardiographic assessment.
- Includes ventilatory/CPAP dependent babies or PDA with haemodynamic effects (i.e., cardiac failure or poor perfusion).
- Monitor babies with non-significant PDA carefully and treat if it becomes significant.

### **Contraindications to ibuprofen:**

- Duct-dependent cardiac lesion.
- Significant renal impairment: urine output  $<1$  mL/kg/hr or creatinine  $>120$  micromol/L
- Significant thrombocytopenia, i.e., platelet count  $<50$  to  $109$ /L (course started or next dose given only after platelet transfusion).
- Suspected or definite necrotising enterocolitis (NEC).
- Active phase of significant bleeding (gastrointestinal or severe intracranial) – treat coagulopathy before starting course.
- Calculate carefully and prescribe individually on single dose part of prescription chart so that contraindications are checked before each dose.
- Ibuprofen has a similar efficacy to indomethacin but fewer renal side effects (can be used in babies with mild or previous renal dysfunction).

Subsequent management: monitoring pharmacological treatment

### **Check before each dose:**

- Creatinine in the normal range.
- Urine output (maintained  $>1$  mL/kg/hr).
- Platelet count (kept  $\geq 50 \times 10^3$ /dL with platelet infusions if needed).
- Concomitant nephrotoxic drug, e.g., gentamicin/vancomycin (monitor levels carefully or use alternative non-nephrotoxic drug).
- Feed tolerance (feeds cautiously initiated or continued during treatment – briefly stopped during actual infusion).
- Clinical signs of PDA and baby's progress.
- Echocardiography (if clinically indicated), repeated after two to three days of completion.

Fluid gradually liberalised after treatment based on:

- Daily weight (weight gain suggests fluid retention)
- Serum sodium (dilutional hyponatraemia common)

Persistence or recurrence of asymptomatic PDA

- Persistence of murmur does not necessarily indicate return of PDA.
- Echocardiogram sometimes demonstrates physiological branch pulmonary stenosis.
- If a baby with asymptomatic murmur is making progress, plan echocardiography before discharge to decide follow-up.

Persistent significant PDA and surgical referral:

- If PDA significant after 48 hours of completion of first course of prostaglandin inhibitor, use second course of ibuprofen.
- If PDA still significant but the baby is making progress (i.e., can be extubated or come off CPAP):
  - Commence regular diuretics (furosemide + spironolactone) to help control haemodynamic effects.

Surgical ligation is indicated (if available):

- If PDA is still significant and baby is ventilatory or CPAP dependent.
- Prostaglandin inhibitor contraindicated.
- Prostaglandin inhibitor ineffective (usually after giving second course).
- Heart failure not controlled by diuretics

#### Reference

1. Neonatal Guideline 2017-19, NHS Trust, UK

2. PDA . All India Institute of Medical Sciences protocol for neonatology. 2014Cloherty and Stark's. Manual of Neonatal Care 8th edition

## 182 Persistent pulmonary hypertension of the newborn (PPHN)

#### Definition:

PPHN is defined as the failure of the normal postnatal fall in pulmonary vascular resistance, which leads to the persistence of right to left shunts across the foetal channels (ductus arteriosus and foramen ovale) and resultant hypoxia. PPHN is an uncommon condition and mainly affects term or post-term babies; however, it may be present in the preterm infant.

PPHN can be primary (idiopathic) or secondary.

Primary PPHN is the form of PPHN which most closely fits the classical definition, typically presenting soon after birth with hypoxaemia in a baby with clinically and radiologically normal lungs. This condition is probably due to a primary dysfunction in the pulmonary endothelial vasodilating mechanisms.

Secondary PPHN is PPHN which is secondary to a disease in the parenchyma of the lungs. In these babies, the pulmonary vasoconstriction is probably secondary to hypoxia, acidosis and high ventilatory pressures.

#### May be associated with:

- Severe lung disease (e.g., meconium aspiration (MAS), surfactant deficiency)
- Perinatal asphyxia

- Infection (e.g., Group B streptococcal (GBS) pneumonia)
- Structural abnormalities: pulmonary hypoplasia, congenital diaphragmatic hernia, A-V malformations, congenital cystic adenomatoid malformation (CCAM)
- Maternal drugs: aspirin, non-steroidal anti-inflammatory drugs, SSRIs

#### Clinical features:

- Usually present in the first 12 hours of life.
  - SpO<sub>2</sub> <95 per cent or hypoxia in FiO<sub>2</sub> 1.0.
  - Mimics cyanotic heart disease.
  - CVS: tricuspid regurgitant murmur, right ventricular heave, loud second heart sound and systemic hypotension.
  - Idiopathic PPHN: respiratory signs mild or absent.
  - Secondary PPHN: features of underlying disease.

#### Investigations:

- Blood gas shows hypoxaemia (PaO<sub>2</sub> <6 kPa) with oxygenation index <20 (underlying disease will produce a mixed picture).
- SpO<sub>2</sub> >5 per cent difference in pre and postductal saturations (pre > post)
- Hyperoxia test (100 per cent oxygen for 10 min)
- SpO<sub>2</sub> may improve to ≥95 per cent in early stage.
- Chest X-ray: variable findings depending on underlying diagnosis (normal or minimal changes in idiopathic PPHN)
- Electrocardiograph is often normal.
  - Can sometimes show tall P waves in lead 2/V1/V2 or features of RVH (i.e., tall R waves V1/V2, right axis deviation or upright T waves in V1/V2)

- Echocardiogram (although not mandatory for initial diagnosis and management) is useful:
  - to exclude cyanotic heart disease
  - to assess pulmonary pressure
  - to evaluate ventricular function
  - ≤1 of the following confirm PPHN in the presence of normal cardiac structures:
    - significant tricuspid regurgitation
    - dilated right side of heart
    - right-to-left shunting across PFO and/or PDA
    - pulmonary regurgitation

#### Management

The aim of the management is to:

- Lower pulmonary vascular resistance.
- Maintain systemic blood pressure.
- Reverse right-to-left shunting.
- Improve arteriolar oxygen saturation and oxygen delivery to the tissues.
- Minimise barotraumas
- Treat any underlying condition

#### General measures:

- Minimal handling, nurse in quiet environment.
- Secure arterial and central venous access.
- Maintain normal temperature, biochemistry and fluid balance.
- Keep Hb ≥12 g/dL.
- Give antibiotics (sepsis, particularly GBS, is difficult to exclude).
- Surfactant may be beneficial in MAS or GBS sepsis.
- If perfusion is poor, fluid bolus [sodium chloride 0.9% 10 mL/kg] or if coagulopathy, fresh frozen plasma.

- Correct metabolic acidosis to maintain pH 7.35–7.45 using full correction with sodium bicarbonate over one hour. If repeating the correction is necessary, slow bicarbonate infusion of calculated dose can be given over six to 12 hours.

#### **Oxygen and ventilation:**

- Start in 100 per cent oxygen and reduce as tolerated.
- Maintain saturations in the normal range 95 to 100 per cent, aiming to maintain  $\text{PaO}_2$  between 60 to 100 mmHg in term infants.
- Maintain normal  $\text{pCO}_2$  in the range 35 to 40 mmHg;  $\text{pCO}_2$  lower than this may cause cerebral vasoconstriction.
- Use conventional ventilation to start with (targeted tidal volume 5- 6 mL/kg).
- Monitor oxygenation index (OI).
- $\text{OI} = \frac{\text{mean airway pressure (cm H}_2\text{O)} \times \text{FiO}_2 \times 100}{\text{postductal PaO}_2 (\text{kPa}) \times 7.5}$

#### **Sedation and muscle relaxation:**

- Use sedation and muscle relaxation in babies with high ventilatory and oxygen requirements and/or ventilator asynchrony.

#### **Inotropes:**

- Myocardial function is frequently poor, despite reasonable blood pressures.
- Aim to keep the mean arterial pressures above 50mm Hg in term infants or higher if RV pressure is calculated to be greater than this.
- Use volume (initially normal saline) and inotropic support: dopamine and/or dobutamine, both starting at 5-10 mcg/kg/min. If the systemic pressure increases and pulmonary pressure stays the same, R-L shunt will diminish.

- Adrenaline infusions may be indicated if there is severe myocardial dysfunction.

#### **Pulmonary vasodilatation:**

##### **Sildenafil**

- Sildenafil is a phosphodiesterase 5 inhibitor which results in vasodilation by selectively reducing pulmonary vascular resistance.
- 0.5 to 2mg/kg/dose 6 hourly.

##### **Milrinone**

- Milrinone causes pulmonary vasodilation by inhibiting phosphodiesterase 3.

##### **Inhaled Nitric oxide (NO)**

- If OI >20 or needs 100 per cent oxygen, or significant PPHN on echo, use inhaled nitric oxide (NO) (if available) as a selective pulmonary vasodilator.

Magnesium sulphate may be used in refractory cases. The use of MgSO<sub>4</sub> is controversial but may be indicated in selected instances.

#### **Outcomes:**

- Persistent pulmonary hypertension of the newborn has a 10-20 per cent mortality. Survivors have significant morbidities including cognitive delays, hearing loss and risk of rehospitalization.

#### **Reference**

1. Parenteral nutrition. All India Institute of Medical Sciences protocol for neonatology. 2019 Cloherty and Stark's. Manual of Neonatal Care 8th edition
2. Neonatal Guideline 2017-19, NHS Trust, UK

# CHAPTER 9: CARE OF THE SMALL BABY



## Introduction:

Advances in neonatal care have dramatically improved the survival of premature infants. However, morbidity outcomes have not seen the same extent of progress and are a significant concern, particularly among the most fragile infants.

While recognizing that each infant is unique and requires individualized care, prematurity related disease processes have similar trajectories that permit the implementation of standardized guidelines. Although the population of focus is the VLBW & ELBW infants, the principles on which this protocol is based are also applicable to larger preterm infants.

**Intrauterine growth restricted (IUGR) Infant:** infants with a rate of foetal growth that is less than normal for the population.

**Thermoregulation:** neonatal thermoregulation is defined as the environmental temperature in which an infant is not required to increase or decrease heat production above natural resting levels and has minimal oxygen consumption.

Small, immature infants require an alternate heat source to maintain normothermia.

## Measures to maintain normothermia

### Decrease evaporative heat losses:

- Dry infants immediately after birth using warm towels/blankets.
- Minimize rubbing due to risk of abrasive skin injury.

- Admit preterm infants to pre-warmed and pre-humidified isolettes.
- Provide humidity as outlined in the transepidermal water loss (TEWL) section.
- Polyethylene plastic wrap before drying is recommended for preterm infants less than 32 weeks to reduce water losses, oxygen consumption, heat convection and heat demands.

### Decrease radiant heat losses

- Use a pre-warmed, humidified and double-walled isolette.
- Place an insulating cover over the isolette.

### Decrease convective heat loss:

- Maintain constant air temperatures (use isolette temperature range chart).
- Limit air currents.
- Minimize removal of infant from isolette (i.e., for weighing), especially during the first week of life.

### Decrease conduction heat loss:

- Place infant on pre-warmed blankets and mattresses.
- Pre-warm surfaces such as scales, x-ray plates etc.

### Humidity and transepidermal water loss:

- Premature infants have increased transepidermal water losses that are inversely related to gestational age, increasing their risk of developing dehydration and temperature instability.
- Increasing ambient humidity levels reduces TEWL and improves fluid balance.

- TEWL in infants born at 24-25 weeks in 50 per cent humidity is about 60g/m<sup>2</sup>/h (about 140ml/kg/day). It falls by day three to ~36g/m<sup>2</sup>/h (100cc/kg/day) and by day 28 to ~24g/m<sup>2</sup>/h (~66cc/kg/day)
- TEWL is 15 times higher in infants born at 25 weeks' gestational age compared to full term infants.
- Transepidermal water losses increase by ~50 per cent under a radiant warmer.
- Polyethylene plastic wrap improves temperature stability (once warm) and reduces TEWL.
- Increasing humidity above 50 per cent further reduces TEWL. A 1000g infant's TEWL can be reduced to 40ml/kg/day in 90 per cent ambient humidity.
- Conversely, TEWL increases by 100 per cent when isolette humidity is reduced from 60 per cent to 20 per cent (dry incubators) in infants <26 weeks.
- Epidermal maturation after seven days of age is facilitated in moderate humidification levels. Higher levels of humidity inhibit skin maturation. Premature infants maintained in high humidity environments during the first month of life may experience a delay in skin maturation and barrier function.
- Reducing the relative humidity to 50 per cent at seven days of age has been shown to reduce TEWL at 28 weeks when compared to infants cared for in 75 per cent humidity with no effect on fluid or electrolyte balance.
- Infants <1800 grams are to be admitted to a pre-warmed, pre-humidified isolette

**Table 25. Recommended isolette humidity levels**

<1000 g	Day 0-7	Isolette humidity level ~75-80%
	Day 8	Gradually reduce isolette humidity level to 50% over 12-24 hours by reducing humidity level by ~5% every four hours. To ensure tolerance to changing humidity levels, measure temperature q3h. No supplemental humidity required after the first month of life.
1000-1250 g	Day 0-7	Isolette humidity level ~ 70%
	Day 8	Gradually reduce isolette humidity level to 50% over 12-24 hours by reducing humidity level by ~5% every four hours. To ensure tolerance to changing humidity levels, measure temperature q3h. No supplemental humidity required after the first month of life.
1250-1500 g	Day 0-7	Isolette humidity level ~60-70%
	Day 8	Gradually reduce isolette humidity level to 50% over 12-24 hours by reducing humidity level by ~5% every four hours. To ensure tolerance to changing humidity levels, measure temperature q3h. No supplemental humidity required after the first month of life.
1500-1800 g	Day 0-7	Isolette humidity level ~40-50%
>1800g	Day 8	No humidity required after the first week of life. No supplemental humidity required.

## Skin care

### Minimize epidermal stripping:

- Minimize adhesive use as much as possible.
- Use hydrogel-based cardiorespiratory leads. Remove only when not functioning.
- Use a semi-permeable barrier between skin and the adhesive (e.g., Tegaderm) to secure umbilical catheters, temperature probes and nasogastric tubes.
- Avoid adhesive removal. But if adhesive removal is necessary use cotton balls soaked with warm sterile water to facilitate removal.
- Avoid bonding agents (e.g., tincture of benzoin). Rates and effects of percutaneous absorption are unknown.
- To reduce skin pressure and the development of pressure sores, use gel mattresses.
- Ensure infant is not lying on foreign objects that may result in pressure injuries (i.e., needle caps, IV luer locks).
- Transcutaneous monitor probes should use the lowest effective temperature.

### Bathing:

- Bathing may result in hypothermia, increased oxygen consumption & respiratory distress. The first bath is to be delayed until vital signs are stable and there is clinical stability present for several hours. Bathing should be gentle with minimal infant stress incurred.
- Universal precautions (e.g., gloves) must always be employed but is of particular importance before and during the first bath to prevent exposure to pathogens in body fluids.

- Gloves should continue to be used if vernix or other body fluids remain on the infant after the first bath.
- Premature Infants <1500gram
  - Use sterile and warm water for removal of maternal bodily fluids.
  - Clean skin surfaces with warm sterile water for the first week of life.
  - When soap is needed due to soiling, a neutral pH synthetic soap should be used to minimize interruption of the acid mantle (i.e., Dove).
- Infants <1500 grams should have non-immersion bathing only.
- Immersion bathing, except the head and neck, is only commenced when infants are clinically stable, at least 3 weeks of age, >1500 grams and they are able to maintain their temperature.
- Rubbing or scrubbing can easily injure and must be avoided.
- Completely rinse skin with warm water after cleansing agents or antiseptics are used.

### Emollient use:

- Emollients can provide a mechanical barrier to water loss and promote skin integrity and function. Use of topical emollients is not a routine recommendation. Emollients like petroleum and vegetable oil can be considered on a case by case scenario.

### Maintaining fluid and electrolyte balance:

- Fluid and electrolyte management in the immature infant can be very challenging and requires an understanding of the physiologic processes (body composition, renal function, neuroendocrine control and IWL) that regulate fluid and electrolyte homeostasis.

- Failure to manage the physiologic processes appropriately can easily lead to fluid and electrolyte imbalances that may potentially affect short- and long-term outcomes. For example:
  - Hindering postnatal diuresis: delaying or impeding the expected normal postnatal contraction of extracellular fluid space significantly increases the risk for the development of a patent ductus arteriosus and chronic lung disease.
  - Dehydration: the development of dehydration (usually hypernatremia dehydration) increases the risk of IVH. Immature infants are susceptible to dehydration and hypertonicity due to high insensible water losses and limited urine concentrating ability.
- Adjustments in total fluid intake (TFI) must be based on the assessment of urine output, sodium balance, weight changes and fluid balance.
- Fluid intake must be based on the assessment of fluid deficits, maintenance requirements and ongoing fluid losses. Fluid intake is also dependent on the clinical condition and physiologic requirements.
- If significant fluid deficits develop, which is often manifested by excessive weight loss and hypernatremia, fluid deficits will need to be replaced and a more rapid increase in TFI administered (sometimes as high as 180 to 200cc/kg/day). Once homeostasis is established, a reduction in the TFI may be necessary to avoid fluid overload.
- Calculating the TFI Example: 100cc/kg/day in 0.8kg infant
- $100\text{cc} \times 0.8\text{ kg} / 24\text{hours} = 3.3\text{cc/hour}$

#### **Monitoring fluid balance:**

- Use isolettes with bed scales. Weigh q12h for the first five days and then daily. Only weigh q12h if bed scales in isolettes; otherwise, removal from isolette for weighing must be based on clinical stability and no more frequent than q24h.
- Appropriate rate of weight loss is 2% per cent to 5% per cent per day up to 10 per cent to 20 per cent.
- Assess fluid balance q8-12h for two to three days, and then as clinically indicated but at a minimum of every 24 hours.
- Assessment includes evaluation of weight gain/loss, urine output, fluid balance (negative or positive) and electrolyte levels.
- Use birth weight for fluid calculations until the infant's weight returns to birth weight and after the normal postnatal weight loss has occurred. Typically, birth weight is used for the first one to two weeks of life.

#### **Electrolyte balance (Na, K, Chloride):**

- Sodium is an indicator of both water and sodium balance.
- Early sodium supplementation may increase the risk of fluid overload by delaying the physiological loss of body water and normal postnatal adaptation process due to persistent expansion of the extracellular space.
- Hyponatraemia is generally an indicator of water excess in the first few days of life.
- Hypernatremia is generally an indicator of water deficit in the first week of life.
- Early electrolyte evaluation is essential to establish baseline electrolyte status; it can be used as one measure in the early identification and prompt treatment of hyponatraemic dehydration due to increased insensible water losses.

- Mild hyponatraemia (i.e., >126mmol/L) in the first 12 hours is indicative of dilutional hyponatraemia (unless there is an identifiable cause for Na loss) and not sodium depletion. Fluid intake should not be increased. Supplemental sodium is generally not required and patience should be exercised while waiting for the diuretic phase to begin.
- Sodium requirements generally increase after the first week of life due to increased fractional excretion of Na because of renal insensitivity in the immature kidney to aldosterone and a smaller number of renal sodium selective channels.
- Sodium is an important element in growth and development.
- Potassium levels often rise in the first 24-72 hours and this may lead to the development of non-oliguric hyperkalaemia; even in the absence of oliguria and potassium intake. This is due to a relative hypoaldosteronism, immaturity of renal distal tubules and a shift of potassium from the intracellular to extracellular space.
- Hyperkalaemia may be exacerbated by IVH, pulmonary haemorrhage, bruising and renal failure.
- It is important to remember that pH affects potassium levels:
  - acidosis increases K levels (H<sup>+</sup> shifts intracellular and K<sup>+</sup> extracellular)
  - alkalosis decreases K<sup>+</sup> levels (H<sup>+</sup> shifts extracellular and K<sup>+</sup> intracellular)

## Sodium and potassium intake recommendations

### Pre-diuretic phase (Usually day 1 to 2 of life):

- No sodium or potassium intake is required during this phase. Use only 10 per cent D/W or sodium and potassium free parenteral nutrition (PN).
- TFI BW <1000g: 100cc/kg/day
- BW 1000-1500g: 80cc/kg/day

### Diuretic phase (variable; usually between day one to five of life):

- Add sodium once the diuretic phase has begun and after ~ a five to six per cent weight loss below birth weight (usually between day two to three of life).
- Generally, the sodium level should be <140mmol/L before supplementing the sodium.
- Add potassium once urine output is well established and serum potassium levels begin to decline and are less than 5.0mmol/L in a non-haemolyzed sample.
- Typically, TFI is increased by 20cc/kg/day until 150-160cc/kg/day is reached.

### Post-diuretic phase (Variable; usually between day two to five of life):

- Sodium requirements often increase after the diuretic phase has been completed (usually after the first week) due to high renal sodium losses.
- Maintenance requirements are 150-160cc/kg/day, which generally represents the level at which fluid and nutritional homeostasis and growth can be maintained.

## **Sodium, potassium and chloride monitoring recommendations:**

### **Measure serum electrolytes (Na, K, chloride).**

- <1000-gram infants: every 12 hours x 3 days, then daily until day five of life. Thereafter, as clinically indicated and as per PN monitoring guidelines
  - 1000-1250 grams: every 12 hours x 3 days, then as clinically indicated and as per PN monitoring guidelines
  - >1250-1500 grams: every 24 hours x 3 days, then as clinically indicated and as per PN monitoring guidelines
- All preterm infants should have once weekly electrolyte levels.

### **Calcium:**

- Preterm infants have inadequate calcium stores because the majority of foetal calcium is accrued in the last trimester of pregnancy. Calcium supply is abruptly terminated at delivery and there is a physiologic fall in calcium levels postnatally due to a relative hypoparathyroidism (PTH) with a nadir reached at 24 to 48 hours.
- Supplemental calcium is started early in life in immature infants as calcium reserves are rapidly depleted.
- Premature infants, infants of diabetic mothers and asphyxiated newborns are at risk of clinically significant hypocalcaemia due to diminished response to PTH and increased calcitonin release (holds calcium in bones).
- Hypocalcaemia should be treated because of the major physiologic importance of calcium in all cellular systems.
- Ionized calcium is the physiologic active fraction of calcium.

- Hypocalcaemia: ionized Ca <0.9mmol/L. Total Calcium: Term <2.0 mmol/L; preterm <1.75 mmol/L

## **Calcium intake recommendations:**

### **Day 1**

<1000g infants: Start calcium 0.5 to 1.0mmol/kg/day.

### **Day 2**

<1000g infants: Gradually increase calcium intake up to 1 to 2mmol/kg/day.

>1000 g infants: Start calcium 0.5 to 1.0 mmol/kg/day.

## **Calcium monitoring recommendations:**

- <1000 grams: ionized calcium level at 12 and 24 hours of age, then q24h x 2 days and then between day 5 to 7 of life. Ongoing measurements are as clinically indicated.
- 1000-1500 grams: ionized calcium levels q24h x 3 days, then between day 5 to 7 of life. Ongoing measurements are as clinically indicated.
- After the second week of life, all preterm infants <1500 grams should have weekly phosphate, calcium and alkaline phosphatase levels to monitor osteopenia.

## **Glucose balance:**

- Immature infants are at risk of hypoglycaemia due to poor glycogen reserves and immature postnatal adaptive mechanisms. Endocrine and enzymatic control of glucose-ketogenesis and lipogenesis as an alternate fuel source is limited in very premature infants.
- Immature infants are at risk of hyperglycaemia due to incomplete suppression of hepatic glucose production

in the presence of hyperglycaemia, resistance to insulin (higher levels of insulin are required to achieve euglycemia) and impaired proinsulin processing to insulin.

- Hyperglycaemia increases the risk of osmotic diuresis, water loss and the development of dehydration.

#### **Glucose intake recommendations:**

- Start Glucose Infusion Rate (GIR) 4 to 6mg/kg/minute.
- Increase to 10 to 12mg/kg/min as tolerated.
- Adjust intake according to glucose control and nutritional requirements.
- Hyperglycaemia: minimum GIR is approximately 3mg/kg/min. Insulin therapy may be required if there is persistent hyperglycaemia at a lowGIR.
- Hypoglycaemia: Increase GIR to 10 to 12mg/kg/min in a step wise manner and then consider glucagon for persistent hypoglycaemia.
- For persistent hypoglycaemia, obtain critical labs when blood glucose is <45mg/dL.
- Critical labs: are blood gas, electrolytes, glucose, insulin, beta-hydroxybutyric, cortisol, growth hormone, free fatty acids, lactate/pyruvate and urine ketones.

#### **Glucose monitoring recommendations:**

- Measure glucose on admission, then q12h x 3 days unless clinical circumstances or abnormal values mandate more frequent testing.
- Dayfourtofive: dailyglucosemeasurement.
- Measure glucose or glucometer with all routine labs.
- For glucose levels >110mg/dL, dip urine to assess for glucosuria.

- Refer to NICU Glucose Monitoring Guidelines for recommended management of hypoglycaemia.

#### **Haematology—CBC monitoring recommendations:**

- Complete CBC on day one and day three; thereafter, measurements are as clinically indicated but at a minimum once weekly for the first three weeks and then every two weeks until discharge.
- Routine coagulation evaluation is not required; measurements are based on clinical indication.

#### **Nutrition and growth – enteral and parenteral nutrition:**

- Very low birth weight (VLBW) and extremely low birth weight (ELBW) infants have unique nutritional requirements in order to maintain tissue integrity, metabolism and growth.
- Growth in the early weeks of life has been associated with improved neurodevelopmental scores. On the other hand, poor early nutrition may predispose these infants to health issues later in life.
- The provision of nutrition for preterm infants may consist of either parenteral nutrition (PN), enteral nutrition (EN) or a combination of both. PN is provided to compensate for the inability of the preterm infant to meet their metabolic needs in the first few weeks of life with EN alone.
- Efforts should be made to provide IV amino acids as soon as possible after birth to prevent a state of catabolism.
- A minimum of 1.5 g/kg/d is necessary to provide neutral/positive nitrogen balance and as much as 3 g/kg/d as soon as possible after delivery will further enhance protein deposition leading to earlier growth.

- As much as 4 g/kg/d of IV protein may be necessary to maintain stores and facilitate optimal growth, especially in very preterm infants.

#### **Acid base balance:**

- Generally, treatment of metabolic acidosis with sodium bicarbonate should only be instituted in cases of moderate to severe metabolic acidosis when there are concerns of cardiac dysfunction developing (i.e. pH <7.15).
- Sodium bicarbonate is hyperosmolar and may lead to IVH. If required, it should be administered slowly.
- Common causes of metabolic acidosis in the preterm infant include, but is not limited to, patent ductus arteriosus, intraventricular haemorrhage, sepsis, hypovolaemia and renal bicarbonate loss (renal immaturity).
- Metabolic acidosis should focus on treating the underlying cause of the acidosis. For example, if hypovolaemia results in decreased perfusion, treat with volume replacement.
- Normal serum HCO<sub>3</sub> is 16 to 20mmol/L in preterm infants (full term 19 to 21mmol/L) due to low renal tubular bicarbonate threshold, functional immaturity of renal collecting duct, decreased bicarbonate reabsorption in proximal tubule and limited renal acid excretion.

- Acid and NH<sub>4</sub> excretion in preterm infants increase with maturation but rates remain lower for up to four months.

#### **Blood gas monitoring recommendations:**

- Frequency of blood gas measurements is to be based on clinical stability.
  - <1000 grams: at a minimum, blood gas should be measured q12h x 3 days, then daily until day five of life. Even in the presence of respiratory stability, metabolic acidosis can quickly develop due to renal immaturity and increased renal bicarbonate losses.
  - 1000-1500 grams: stable preterm infants require blood gas measurement at a minimum q24h for the first four days of life. Even in the presence of respiratory stability, metabolic acidosis can quickly develop due to renal immaturity and increased renal bicarbonate losses.
- After the first week of life, blood gas measurements should be completed one to two times weekly. More frequent measurements are often clinically indicated.

#### **Reference**

1. Small Baby Protocol, Neonatal Intensive Care Unit, The Hospital for Sick Children, 2011

# CHAPTER 10: Neurologic disorders



## Perinatal asphyxia

**WHO definition:** Failure to initiate and sustain breathing at birth.

AAP and ACOG Criteria for diagnosis of perinatal asphyxia:

- An arterial cord pH <7.0 and base deficit more than 12.
- Apgar score of less than seven at five minutes.
- Evidence of altered neurological status (altered level of consciousness, seizures, hypotonia and obtundation).
- Evidence of multiple organ involvement (such as that of kidneys, lungs, liver, heart and intestine).

In term infants with asphyxia, renal, CNS, cardiac and lung dysfunction occur in 50 per cent, 28 per cent, 25 per cent and 25 per cent cases, respectively. The extent of organ system dysfunction determines the early outcome of an asphyxiated neonate.

Hypoxic ischemic encephalopathy (HIE) refers to the CNS dysfunction associated with PA.

### Evolution of HIE:

- HIE evolves gradually beginning from the time of insult to hours and days later. The initial hypoxic-ischemic event results in infarction of the brain tissue (primary energy failure). The subsequent injury – secondary injury – is mediated by reperfusion and free radicals in an area surrounding the necrotic area (penumbra).
- The penumbra undergoes programmed neuronal death (apoptosis) even after the hypoxic insult is over.
- The time gap between these two phases could be six to 24 hours and provides a window to institute specific therapeutic intervention.
- Classification of HIE in term neonates was proposed by Sarnat and Sarnat.

*Table 26. Sarnat and Sarnat stages of HIE*

Signs	Stage 1	Stage 2	Stage 3
Level of consciousness	Hyper alert	Lethargic	Stuporous, coma
Muscle tone	Normal	Hypotonic	Flaccid
Posture	Normal	Flexion	Decerebrate
Tendon reflexes/clonus	Hyperactive	Hyperactive	Absent
Myoclonus	Present	Present	Absent
Moro reflex	Strong	Weak	Absent
Pupils	Mydriasis	Miosis	Unequal, poor light reflex
Seizures	None	Common	Decerebration

<b>Signs</b>	<b>Stage 1</b>	<b>Stage 2</b>	<b>Stage 3</b>
Electroencephalographic findings	Normal	Low voltage changing to seizure activity	Burst suppression to isolectric
Duration	<24 hour if progresses; otherwise, may remain normal	24 hour-14 days	Days to weeks
Outcome	Good	Variable	Death, severe deficits

### **Management of a neonate with perinatal asphyxia:**

#### I. Initial management

1. In the delivery room, follow the resuscitation guideline.
2. Transfer the baby to NICU. A baby who fails to initiate and sustain respiration at birth is at risk of hypoxic brain injury and needs regular monitoring. All these babies should have a cord gas analysis performed.
3. Place the baby under the radiant warmer after drying the baby. Maintain normal temperature of the baby. Maintain normal temperature 36.5–37.5°C. Avoid both hyperthermia and hypothermia.
4. Maintain normal oxygenation and ventilation.
  - Maintain saturation between 90 per cent and 95 per cent and, avoid hypoxia and hyperoxia.
  - Assisted ventilation is required if there is apnoea, spontaneous respiration is inadequate or there is continuing hypoxia or hypercarbia.
  - Measure arterial blood gas to see if any respiratory or perfusion

abnormalities are present (maintain PaO<sub>2</sub> between 60 and 90 mmHg and PaCO at 35 to 45 mm Hg). Avoid both hypocarbia (reduces cerebral perfusion) and hypercarbia (increases cerebral perfusion and intracranial pressure and predisposes to intracranial bleed).

5. Ensure normal perfusion, i.e., capillary refill time of less than three seconds, absence of tachycardia and metabolic acidosis, normal blood pressure, and adequate urine output.
  - If tissue perfusion is inadequate, infuse normal saline or Ringer's lactate at 10 mL/kg over 5 to 10 min.
  - Administer dobutamine (preferred) or dopamine to maintain adequate cardiac output, as required.
  - Do not restrict fluids routinely because it may predispose to hypoperfusion; restrict fluids only if there is hyponatraemia (sodium <120 mEq/L) secondary to syndrome of inappropriate secretion of ADH(SIADH) or if there is renal failure.

- ▶ Echocardiography in neonates requiring inotropic support to evaluate decreased contractility due to asphyxia related cardiogenic shock.
6. Check blood glucose and maintain blood glucose levels between 75 mg/dL and 100 mg/dL.
  7. Check haematocrit; correct anaemia and maintain haematocrit between 45 per cent and 55 per cent.
  8. Check blood gases to detect metabolic acidosis; maintain pH above 7.30 in case of severe asphyxia.
  9. Provide calcium in a maintenance dose of 2 mL/kg/day of 10 per cent calcium gluconate for one to two days as a continuous infusion or as 1:1 diluted boluses, slowly under cardiac monitoring; maintain serum calcium concentration in the normal range.
  10. Use of antibiotics should be based on assessment of risks for sepsis; for stage two and three HIE do blood culture at admission and sepsis screen at 6-12 hours. Antibiotics should be initiated at admission based on sepsis protocol. LP should be performed if sepsis screen is positive or blood culture positive or seizure after 24 hours of life.
  11. Fluids and feeding
    - ▶ For severe asphyxia/stage three HIE or haemodynamic instability, initiate intravenous fluid on day one of life and decide initiation of feeding with subsequent monitoring with the attending physician.
  - ▶ Start oral feeding once the neonate is haemodynamically stable, off vasopressor support and has normal abdominal examination findings (no distension and normal bowel sounds).
  - ▶ For haemodynamically stable moderate HIE: feeding can be started on day one of life.
  - ▶ Check for signs of feeding intolerance and NEC.
12. Treat seizure per seizure protocol-re
  13. Neurologic monitoring:
    - ▶ Monitor the neurological condition of the infant using Sarnat and Sarnat staging.
    - ▶ If available, connect to Electro Encephalogram (EEG) monitor continuously.
    - ▶ Amplitude-integrated electroencephalography (aEEG) is a simple, reliable, non-invasive technique which can be applied at the bedside in NICU for monitoring EEG continuously.
    - ▶ MRI is the best imaging modality for determining prognosis in term neonates. Diffusion weighted MRI can detect abnormalities within 24 to 48 hours after birth (optimal time is 2 to 3 days), whereas conventional MRI can show abnormalities in the first 3 to 4 days (though optimal time is later during the first week of life).
    - ▶ Cranial USG is not good for detecting changes of HIE in term neonates. However, hypoechoic areas can be seen in very severe cases (having large areas of infarction).

- ▶ CT has a role in initial evaluation if MRI is not readily accessible. In acute stage of HIE, CT in term neonates shows a generalized low attenuation of brain parenchyma.
- ▶ Baseline renal function test, serum electrolyte, complete blood count, coagulation profile, liver function test, CRP, blood culture.

**Follow the tests every 12-24 hours based on clinical judgment.**

1. Resuscitation decision in the NICU, based on the daily Sarnat staging, preferably avoid CPR for stag III HIE. Discussion should be made with the parents about the outcome of the baby on a daily basis.
2. Decision to stop mechanical ventilation if the baby is on ventilator should be done based on neurologic examination and stage III HIE with no improvement on stage for the first three days; need to involve parents and stop the care.

## II. Specific therapy

### Therapeutic Hypothermia (TH)

Institution of moderate therapeutic hypothermia (33°C to 34°C), initiated within four to six hours and continued for 72 hours of age in ICU, has been shown to reduce mortality and neuro-morbidity by 18 months of age in infants of at least 35 weeks' gestational age with moderate to severe encephalopathy.

The Cochrane review (8 RCTs; 638 term neonates with moderate/severe encephalopathy and evidence of intrapartum

asphyxia) showed that TH reduced the combined outcome of mortality or major neurodevelopmental disability by 24 per cent in infants at 18 months of age.

TH can be instituted by selectively cooling the head or the whole body. It is a safe modality in settings where intensive care facilities to manage sickest neonates are available.

TH has now become the standard of care in developed countries. However, this is not the case in low to middle income countries (LMIC) where the patient profile is different (higher risk of IUGR, infection and nutritional deficiencies). There is a paucity of intensive care and many births occur at home.

Indeed, a few studies have shown increased mortality following TH in these settings. But recent studies from India showed that with proper monitoring and optimal supportive care, TH is feasible using indigenous cooling methods like gel-packs.

### Mechanism of action:

TH has been shown to be protective at critical cellular and vascular sites of cerebral injury. It acts by the following mechanisms to reduce the extent of brain injury:

- Decreased cerebral metabolism and blood flow: Decrease in energy requirement and cerebral oedema.
- Decreased brain lactic acid, glutamate, and nitric oxide concentrations: Less excitotoxic and oxidative injury.
- Inhibits protease activation, mitochondrial failure, free radical damage, lipid peroxidation: Less apoptosis and necrosis.

**Indication:**

- Postmenstrual age (PMA)  $\geq$ 36 weeks, BW  $\geq$ 2,000 g and one of the following;
- Evidence of foetal distress or neonatal distress as evidenced by one of the following: pH  $\leq$ 7.0 or base deficit  $\geq$ 16 mmol/L in cord gas or postnatal blood gas obtained within first hour of life
- 10 minute Apgar score of  $\leq$ 5
- Assisted ventilation initiated at birth and continued for at least 10 minutes,
- Evidence of moderate to severe neonatal encephalopathy by exam and/or aEEG.

## Cooling devices:

## 1. Whole body cooling devices

- High technology devices: Examples
  - Tecotherm TM, Blanketrol TM, MedithermTM
- Low technology devices: Example – Miracradle TM

These devices usually have a circulating water/coolant system. The water/coolant flows over and around the heating/cooling element located in the circulating reservoir. The heated or cooled water/coolant then flows out of the reservoir to the circulating pump and through connecting hoses over a water temperature sensor to the blanket. The water circulates through the blanket(s) and returns to the unit.

## 2 Selective head cooling device: Examples - Olympic cool cap system TM

These devices use the phase change material (PCM) technology to induce therapeutic hypothermia. PCMs are special thermal energy storage materials that store and release heat at a particular temperature. The thermal energy transfer occurs when the material changes a phase from solid to liquid or liquid to solid.

**Initiating therapeutic cooling:**

- Counsel the parents about indications, benefits and risks of therapy, and take informed consent.
- Prepare the cooling system for operation.
- Set the cooling blanket temperature to 33.50C.
- Monitor and document the infant's pre-cooling vital signs.
- Place and secure central and arterial lines before starting hypothermia.
- Gently insert the rectal probe 2 cm into the infant's rectum, and secure to the infant's leg with tape.
- Place the infant on the warmer in the supine position with the entire head and body resting on the cooling blanket.
- The infant must lie directly on the cooling blanket, wearing a diaper only.

*Table 27. Monitoring while cooling*

Parameter	Day 1	Day 2	Day 3
Vital signs including invasive blood pressure monitoring	Q 1 hour	Q 1 hour	Q 1 hour
Neurologic monitoring	Q12 hours	Q 12 hours	Q 12 hours
Urine output	Q 6 hours	Q 6 hours	Q 6 hours
Skin integrity	Q 6 hours	Q 6 hours	Q 6 hours
Serum electrolytes	Once	Once	Once
Renal function	Once	Once	Once
Blood sugar	Q6hours	Q6hours	Q6hours
PT INR	Once	If required	If required
Hb TC DC plt	Once		Once
SGOT/SGPT	Once		If required
Blood gas	Q 6 hours or as indicated by condition of baby	Q 12 hours or as indicated by condition of baby	Q 12 hours or as indicated by condition of baby
aECG	Continuously	Continuously	Continuously
Neurosonogram	If indicated	If indicated	If indicated

#### Rewarming:

1. Increase the infant's core temperature by 0.50C every hour until 36.50C has been reached.
2. When the infant's core temperature is 36.50C, remove the patient from the cooling blanket/device.
3. Re-activate the radiant warmer, monitor and document the infant's temperature with the skin probe.
4. Problems while rewarming: seizures and hypotension.

#### Supportive care while on cooling:

- Sedative or analgesia – morphine or fentanyl can be used.
- Feeding/nutrition – start minimal enteral nutrition if haemodynamically stable.
- Platelet transfusion – if platelet count is less than 100,000/ mm<sup>3</sup>
- Fresh freshen plasma – if bleeding.

#### Follow up:

Follow up for neonates with stage II and III; early identification and intervention is important for neurologic problems.

Among the neonates who survive severe HIE, the sequelae include mental retardation, epilepsy and cerebral palsy. CP can be in the form of hemiplegia, paraplegia, or quadriplegia. Such infants need careful evaluation and support. They may need to be referred to specialized clinics capable of providing coordinated comprehensive follow-up care.

Hearing and visual evaluation has to be included in the follow up.

Prognosis and long-term outcome  
Predictors of mortality and neurological morbidity after perinatal hypoxic ischemic insult:

1. Extended very low APGAR scores (at 20 minutes or more)
2. Time to establish spontaneous respiration (for 30 or more minutes)
3. Neonatal neurological examination (severe HIE)
4. Brain imaging (USG, MRI)
5. Other investigations (EEG, aEEG)

**Stage III HIE** - death up to 80 per cent, while 20 per cent of survivors have neurological sequelae. Up to 80 per cent of neonates who survive severe HIE develop serious complications, 10 to 20 per cent develop moderately serious disabilities and up to 10 per cent are normal.

**Stage II HIE** - death is up to five per cent. Among the neonates who survive moderately severe HIE, 30 to 50 per cent may suffer from serious long-term complications and 10 to 20 per cent with minor neurological morbidities.

**Stage I HIE** - are free from death or any neurological sequelae.

### Reference

1. Post resuscitation management of Asphyxiated neonate. All India Institute of Medical Sciences protocol for neonatology. 2019
2. Cloherty and Stark's. Manual of Neonatal Care 8th edition
3. Neonatal Guideline 2017-19, NHS Trust, UK

## Intraventricular haemorrhage (IVH)

### Introduction:

Intraventricular haemorrhage (IVH) is the most common type of intracranial haemorrhage in the neonate. It occurs primarily in preterm infants  $\leq 32$  weeks' gestational age but is occasionally seen in near term and term infants. The incidence ranges from 15 percent to 20 per cent in newborns born at  $< 32$  weeks' GA, decreases with advancing gestational age and is uncommon in the term newborn. It is influenced by certain perinatal risk factors.

### Pathogenesis:

Most IVH is secondary to hypoxic ischaemic reperfusion injury of the germinal matrix. The factors that make the preterm infant particularly prone to this type of injury are outlined below.

#### 1. Intra-vascular factors:

- Impaired cerebral autoregulation.
- Fluctuating cerebral blood flow (related to fluctuating arterial blood pressure).
- $\uparrow$  cerebral blood flow (e.g., due to hypercarbia, excess volume expansion).
- $\uparrow$  cerebral venous pressure (e.g., with pneumothorax, asphyxial heart failure).
- Hypotension and reperfusion.
- Rapid boluses of intravenous volume are frequently administered to preterm neonates and have been associated with IVH.

- Disturbances of coagulation common to the preterm infant may be associated with an increase in minor grades of IVH.

2. Vascular factors:

- Germinal matrix, a highly vascular structure with poor capillary support, is present in <35 weeks old infants and is a critical factor in pathogenesis of IVH.
- Germinal matrix capillaries are very vulnerable to hypoxic-ischemic injury.
- Arterial development: acute transition from large vessels to a capillary network without gradual arborization.
- Venous drainage: “hairpin loop” configuration in germinal matrix is conducive to outflow obstruction and is important in pathogenesis of periventricular haemorrhagic infarction.

3. Extra-vascular factors:

Preterm infants have –

- Increased fibrinolytic activity
- Poor vascular support in cerebral tissue
- ↑ risk of hypoxia, hypercarbia and acidosis due to immature respiratory system

**Grading of IVH:**

The extent of the haemorrhage, associated ventricular distension and parenchymal involvement is the basis of the classification system of Papile. This classification system is routinely used to describe IVH in infants.

**Grade I haemorrhage:** bleeding is isolated to the subependymal area.

**Grade II haemorrhage:** there is bleeding within the ventricle without evidence of ventricular dilation.

**Grade III haemorrhage:** IVH with ventricular dilation.

**Grade IV haemorrhage:** there is intraventricular and parenchymal haemorrhage.

**Grade IV IVH,** also known as periventricular haemorrhagic infarction, often develops after a large IVH because of venous congestion.

**Ventriculomegaly** is defined as mild (0.5 to 1 cm dilation), moderate (1.0 to 1.5 cm dilation) or severe (>1.5 cm dilation).

**Timing of IVH:**

Nearly all intraventricular haemorrhages occur within 72 hours of birth and the vast majority occurs within the first 48 hours of life. Many occur on the first day and about 30 per cent occur within the first six hours of life. These very early onset haemorrhages probably have their origins in antenatal/intrapartum events.

**Clinical presentation:**

- **Catastrophic:** acute IVH with bulging fontanel, split sutures, change in level of consciousness, pupillary and cranial nerve abnormalities, decerebrate posturing, and often with rapid decrease in blood pressure and/or haematocrit.
- **Saltatory:** gradual deterioration in neurological status may be subtle abnormalities in level of consciousness, movement, tone, respiration and eye position/movement.
- **Asymptomatic:** 25 to 50 per cent of IVH. Discovered on Ultrasound. Fall in haematocrit or failure of haematocrit to rise with transfusion should cause concern.

### **Diagnosis of IVH:**

- Diagnosis is by clinical assessment and ultrasound evaluation.
- Ultrasound screening
- Formal diagnosis is made by cranial ultrasound.

All infants <32 weeks' gestational age should have at least two examinations performed by an ultrasonographer.

### **First ultrasound:**

The first formal ultrasound should routinely be performed between days five and seven of life. This is the optimal time for a single ultrasound examination as all cases of IVH and >90 per cent of associated parenchymal haemorrhages will be evident. However, as many haemorrhages occur on the first day of life and the vast majority by 48 hours earlier, ultrasound examination may be performed on the basis of clinical concerns. If any IVH is seen in U/S, subsequent examinations depend on the clinical course.

### **Second ultrasound:**

The second cranial ultrasound should routinely be performed around day 28 of life. By this stage, parenchymal abnormalities and/or ventriculomegaly will be evident, providing important prognostic information and guidelines for further management. Repeating U/S at this time is important for detection of cystic PVL.

### **Complications:**

IVH may be asymptomatic and without long term consequences. However, potential complications are:

- Death
- Neuro-developmental handicap
- Post haemorrhagic hydrocephalus

### **Prevention of IVH**

#### **Antenatal Interventions:**

- Prevention of prematurity.
- Maternal transfer to a tertiary neonatal centre:
  - Attempts should be made to transfer all women at risk of preterm delivery to an appropriate perinatal centre.
- Corticosteroids:
  - The administration of antenatal corticosteroids to the mother 48 hours prior to delivery significantly reduces the incidence of IVH and should be considered for all women at risk of preterm delivery.
- Management of preterm premature rupture of membranes (PPROM):
  - The use of antimicrobial therapy in the expectant management of preterm premature rupture of the membranes is associated with a reduction in chorioamnionitis, neonatal sepsis and IVH.

#### **Postnatal:**

- Skilled resuscitation to avoid hypoxia and hypercarbia
- Correction of coagulation abnormalities
- Slow infusion of colloids and hyperosmolar solutions
- Avoid hypotension and avoid fluctuations in arterial BP

## **Management:**

- Supportive care:
  - Maintain normal BP and circulating volume.
  - Maintain normal acid base balance & electrolytes.
  - Transfuse with packed RBC's in large IVH.
  - Correct thrombocytopenia and coagulation disorders using fresh frozen.
  - Treat seizures if present.
- For progressive ventricular dilatation (PWD) (post-haemorrhagic hydrocephalus), the essential point is early recognition.
- Management of PWD: serial cranial ultrasonography, serial lumbar punctures, surgical diversion of CSF flow and, rarely, drugs to ↓CSF production (acetazolamide and furosemide).
- Head circumference does not increase until after there has been considerable ventricular dilatation. Therefore, do serial head U/S examinations in infants with IVH ≥grade II. Some cases of ventricular dilatation will respond to serial lumbar punctures and/or acetazolamide (carbonic anhydrase inhibitor) or other diuretics (to decrease CSF production).
- Persistent and progressive ventricular dilatation requires a ventriculoperitoneal shunt by a neurosurgeon.

## **Reference**

1. Neonatal Care Pocket Guide for Hospital Physicians, 2010
2. Intraventricular Haemorrhage (IVH) Intensive Care Nursery House Staff Manual, the Regents of the University of California, 2004

## **Neonatal Seizures**

Seizures are paroxysmal alterations of neurologic function, including behavioural, motor and/or autonomic changes. Seizures occur more frequently in the neonatal period than at any other time of life.

### **Aetiology**

- Hypoxic ischemic encephalopathy:
  - The most common cause of neonatal seizures, accounting for 50 per cent to 75 per cent of cases
  - Seizures usually occur within 24 hours after the insult.
- Perinatal stroke is the second most common cause of seizures in the newborn period, accounting for up to 20 per cent of neonatal seizures.
  - Arterial infarction (neonatal arterial stroke): infants usually appear normal before and after seizures.
  - Venous infarction (secondary to systemic infection, polycythaemia or dehydration and in association with IVH in preterm infants): infants usually have a depressed mental status between seizures.

### **Intracranial haemorrhage (ICH)**

- ICH is responsible for 10 per cent to 15 per cent of neonatal seizures.
- Central nervous system (CNS) infection
  - CNS infections account for about five per cent of neonatal seizures.
  - Congenital TORCHS infections, meningitis or septicaemia
- Acute metabolic disorders
  - Account for approximately five per cent of neonatal seizures.

- Include hypoglycaemia, hypocalcaemia, hypomagnesemia and hypo/hypernatremia
- Less common causes
- Inborn errors of metabolism
  - Pyridoxine (vitamin B6) dependency
  - Folinic acid responsive seizures
- Brain anomalies
- Epileptic syndromes
  - Benign familial neonatal seizures: autosomal dominant, occur in the first 48-72 hrs of life and disappear by age two to six months.
  - Benign idiopathic neonatal seizures (fifth-day fits): occur on day five of life (four to six days) in normal-appearing neonates; multifocal seizures for <24 hrs.
- Maternal drug withdrawal
- Kernicterus

### Clinical manifestations:

#### Subtle seizures

- The most common subtype (~50 per cent) of all seizures (more common in full-term infants).
- Not associated with EEG seizures and have poor response to conventional anticonvulsants.
- Despite the “subtle” expression of this seizure category, these infants may have suffered significant brain injury.

#### Tonic seizures

- Stiffening of parts of the body (either focal or generalized)
  - Focal tonic seizure is often associated with EEG seizures.

#### Clonic seizures

- Stereotypic and repetitive biphasic movements (a fast contraction phase and a slower relaxation phase); the rhythm is usually slow, 1 to 3 movements/second.
- They may be unifocal, multifocal or generalized.

#### Myoclonic seizures

- Brief jerks of extremities or bodies that tend to involve distal muscle groups, lacking the slow return phase of the clonic movement complex.

#### Laboratory investigations:

##### Primary tests

- Blood glucose
- Serum electrolytes
- Serum calcium and magnesium
- CBC with differential
- Arterial blood gas
- CSF analysis and culture
- Blood culture

##### Other tests:

- Search for specific suspected causes (TORCH titers, ammonia level, amino acids in urine, etc).
- EEG (normal in one third of cases) or video EEG monitoring.
- Cranial ultrasound, Brain CT scan or MRI.
- Amplitude-integrated electroencephalography (aEEG) may help to determine which infants are at highest risk of developmental sequelae of neonatal brain injury. The aEEG background voltage ranges, signal patterns and

rates of normalization, as assessed at various points in the first hours and days of life, can provide valuable prognostic information, with positive predictive value of 85 per cent and negative predictive value of 91 to 96 per cent for infants who will have adverse neurodevelopmental outcome. Unfortunately, even with recent improvements in technology, aEEG still has difficulty detecting seizures, particularly those that are brief or originate far from the electrodes. Sensitivity of aEEG for seizure detection, when used by a typical reader, is <50 per cent. For this reason, conventional EEG montage with concurrent video of the patient is preferred for seizure monitoring.

#### **Benign movements simulating seizures:**

##### **Jitteriness**

- Differs from clonic seizures in these aspects:
  - Flexion and extension phases are equal in amplitude.
  - Infant is alert, with no abnormal gaze or eye movements.
  - Diminished by passive flexion or repositioning of the limb, and provoked by tactile stimulation (may be spontaneous).
  - No EEG abnormalities are present.
- Jitteriness is often seen in infants with hypoglycaemia, drug withdrawal, hypocalcaemia, hypothermia and in SGA infants.
- These spontaneously resolve within a few weeks.
- Benign neonatal sleep myoclonus
- Occurs in healthy preterm and term infants during active sleep and is rapidly abolished by arousal.

- May be precipitated by gentle rhythmic rocking or tactile stimuli, and gentle restraint may increase them.
- Resolve spontaneously within a few months.
- Sleep apnoea
- Not associated with abnormal movements, but is usually associated with bradycardia.

#### **Management of neonatal seizures:**

##### **Initial management:**

- Achieve a patent airway, adequate breathing and circulation.
- Correct the underlying cause
- Hypoglycaemia: D10W IV (2 ml/kg) over one min, followed by a continuous infusion.
- Hypocalcaemia: calcium gluconate 2ml/kg IV slow infusion, with observation of HR repeat q6 hrs over the first 24 hrs.
- Sepsis: antibiotics after obtaining appropriate culture

##### **Anticonvulsants:**

- **Phenobarbitone:** preferred initial drug.
  - An initial IV loading dose of 20 mg/kg may be followed by increments of 10 mg/kg IV to a total of 40 mg/kg, with higher doses associated with improved efficacy. Maintenance dose should be started at 5 mg/kg/day divided twice daily.
  - If there is no IV, use oral dose as above and reload after four to six hours as the absorption of oral doses takes long hours.
  - Careful monitoring of cardiac and respiratory function is required for vulnerable infants. Advantages of Phenobarbitone include reduction of cerebral metabolic rate and free radical scavenger.

- **Phenytoin:** it is the second agent selected when Phenobarbitone fails. Loading dose is 20 mg/kg; maintenance dose is 4 to 6 mg/kg daily.
  - benzodiazepines (Diazepam): is used in status epilepticus, when immediate cessation of seizure activity is required. It should be administered after dilution of 0.2 ml of diazepam with 0.8 ml of normal saline. Initial dose is 0.1 to 0.3 mg/kg slowly IV until seizures stop.
  - Disadvantage: It contains sodium benzoate which interferes with binding of bilirubin to albumin --- jaundice. It has short anticonvulsant effect but prolonged respiratory suppressant effect.
  - Lorazepam: the current recommended dose is 0.05 mg/kg/dose over two to five minutes.
- Refractory seizures: give pyridoxine 50 to 100 mg IV with EEG monitoring “therapeutic trial”; seizures will stop within minutes if pyridoxine dependency is the cause. In such cases, maintain an oral pyridoxine (10 to 100 mg/day).
- Give a trial of folinic acid for 24 to 48 hrs in infants failing to respond to anticonvulsants and pyridoxine (starting dose is 2.5 mg twice/day, but it can be increased to 8 mg/kg/day).

#### **Follow up anticonvulsant medications:**

If the neonate takes more than one anticonvulsant medication, phenobarbitone will be the last one to be tapered and discontinued.

Discontinuation of drugs before discharge from the NICU is generally recommended, because then clinical assessments of arousal, tone, and behaviour will not be hampered by a medication effect.

However, newborns with congenital or destructive brain lesions on neuroimaging or those with persistently abnormal findings on neurologic examination at the time of discharge may require a slower taper off medication over several weeks or months.

Indications for discontinuations of antiepileptic drugs:

- Normal findings on examinations
- Absence of recurrent seizure
- Non-epileptic EEG

#### **Complications:**

- Cerebral palsy
- Hydrocephalus
- Epilepsy
- Learning disability, mental retardation

#### **Prognosis:**

- Long-term sequelae in infants with neonatal seizures, including cerebral palsy and intellectual disabilities, still occur at a high rate of up to 30 per cent to 35 per cent with post neonatal seizures occurring up to 20 per cent. The most important factor affecting outcomes for infants with neonatal seizures is the underlying aetiology. For instance, normal development can be expected in infants with benign idiopathic neonatal seizures and in 90 per cent of those with primary subarachnoid haemorrhage, whereas only 50 per cent of those with HIE, and even fewer with a brain malformation, will have normal outcome.

#### **References**

1. Fanaroff and Martin's Neonatal- Perinatal Medicine 9th edition

## CHAPTER 11: INFECTIOUS DISEASE IN NEONATES

### Sepsis in the newborn

#### Introduction:

Neonatal sepsis is a clinical syndrome of bacteraemia characterized by systemic signs and symptoms of infection in the first month of life. Neonatal sepsis encompasses systemic infections of the newborn including septicaemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infection.

Sepsis is the most common cause of neonatal mortality and is probably responsible for 30 to 50 per cent of the total neonatal deaths each year in developing countries. Sepsis related mortality is largely preventable with rational antimicrobial therapy with aggressive supportive care. The manifestation of illness is earlier than the time limit of one week (24 hour=85 per cent, 24 to 48 hour=5 per cent, 2 to 6 days=10 per cent)

#### Classification:

Early onset neonatal sepsis (EONS): EONS usually presents within the first 72 hours of life. In severe cases, the neonate may be symptomatic in utero (foetal tachycardia, poor beat to beat variability) or within a few hours after birth.

**Aetiology:** the most common organisms in developing countries include Klebsiella, Staphylococcus Aureus, and Escherichia coli

Early onset Neonatal sepsis is associated with certain high risk obstetric factors:

- Birth asphyxia
- Unclean vaginal examination
- Prolonged labour (>24 hours) and prolonged rupture of membranes (>18 hours)
- Preterm and low birth weight Neonates
- Chorioamnionitis, Maternal fever (temp >38°C) during labour or within 24 hours after delivery, uterine tenderness or foul-smelling amniotic fluid
- Maternal urinary tract infection or bacteriuria in current pregnancy
- Meconium-stained amniotic fluid
- Home delivery

Late onset neonatal sepsis (LONS): LONS usually presents after 72 hours of age. The source of infection is either nosocomial or community-acquired and neonates, usually present with septicaemia, pneumonia or meningitis. Factors that may increase risk of community-acquired late onset sepsis include poor hygiene, poor cord care, bottle-feeding and prelacteal feeds. Breast-feeding, on the other hand, prevents infection in neonates. Various factors that predispose to an increased risk of nosocomial sepsis include NICU admissions, low birth weight, prematurity, invasive procedures, parenteral fluid therapy and invasive ventilation.

Most are caused by gram negative bacteria like klebsiella, enterobacter, E-coli, pseudomonas and salmonella.

### **Clinical features:**

- Non-specific features of sepsis: the earliest signs of sepsis are often subtle, nonspecific and need a high index of suspicion. Early manifestations could be changed in behaviour or feeding patterns. But gradually/sometimes suddenly, signs and symptoms develop. It may be complicated to multiple organ failure, shock, cerebral oedema, bone marrow failure and DIC.

Babies with sepsis may present with one or more of the following symptoms and signs:

- Hypothermia or fever (former is more common in low birth weight babies), lethargy, poor cry, refusal to suck, poor perfusion, prolonged capillary refill time, hypotonia, absent neonatal reflexes, Bradycardia; tachycardia, Respiratory distress, apnoea and gasping respiration, hypoglycaemia, hyperglycaemia, metabolic acidosis

Specific features related to various systems:

- Central nervous system (CNS): Bulging anterior fontanelle, blank look, high-pitched cry, excess irritability, not arousable, comatose, seizures, neck retraction. Presence of these features should raise a clinical suspicion of meningitis.
- Cardiac: Hypotension, poor perfusion, shock

- Gastrointestinal: Feed intolerance, vomiting, diarrhoea, abdominal distension, paralytic ileus, necrotizing enterocolitis (NEC)
- Hepatic: Hepatomegaly, direct hyperbilirubinemia (especially with UTI)
- Renal: Acute renal failure
- Haematological: Bleeding, petechiae, purpura
- Skin changes: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge

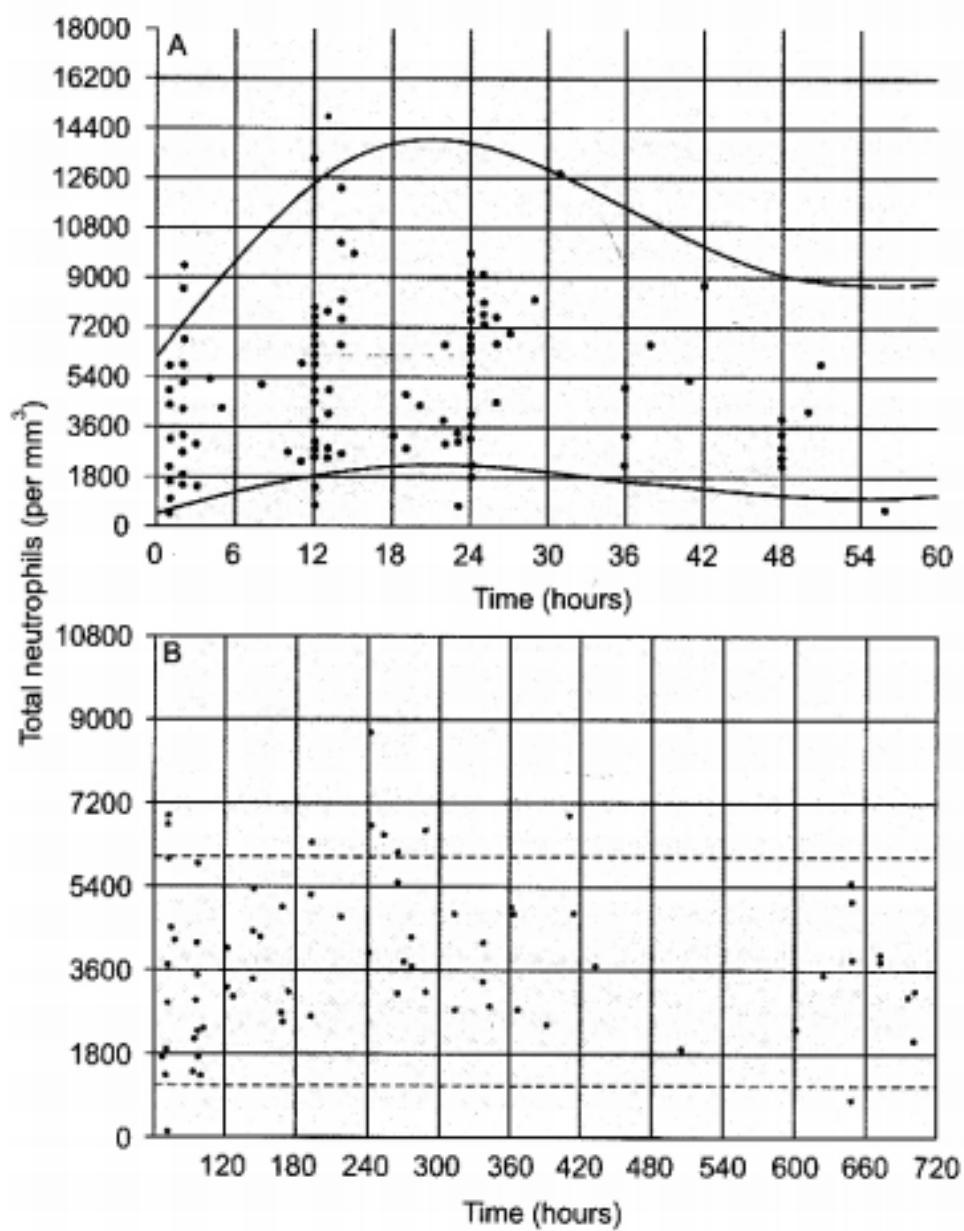
### **Investigations**

It is important that the supportive and antimicrobial therapy of a neonate with sepsis is instituted quickly.

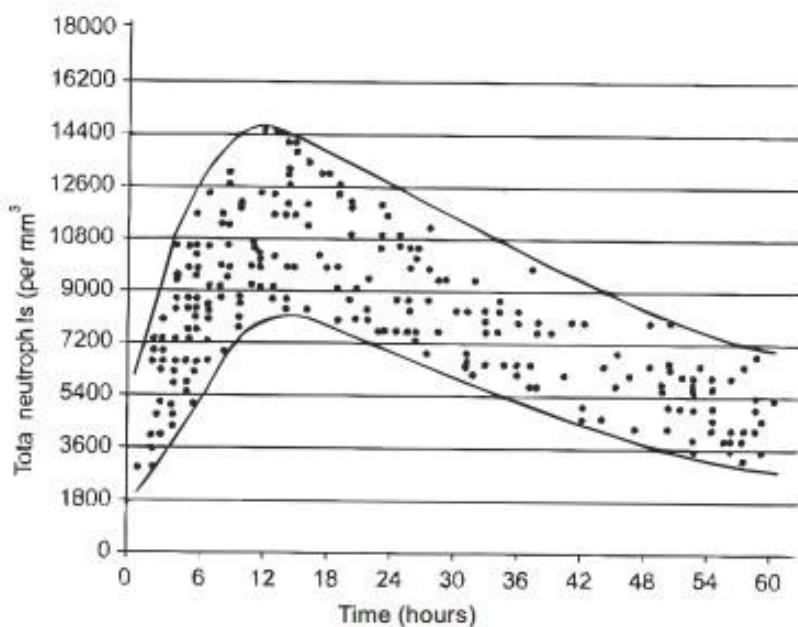
Septic screen: all newborns suspected to have neonatal sepsis should have a septic screen to corroborate the diagnosis of sepsis. However, if there is a strong clinical suspicion of sepsis, the decision to start antibiotics need not be conditional to a sepsis screen.

### **Septic workup:**

- Consider blood culture and antimicrobial sensitivity whenever possible and modify the treatment accordingly.
- CBC (Complete Blood Count) with differential. Should be concerned for sepsis if:
  - Total WBC is abnormal (<5,000 or >20,000)
  - Absolute neutrophil count as per Manroe chart or Mouzinho's chart



*Figure 22. Mouzinho's chart for absolute neutrophil count in very low birth weight neonates*



**Figure 23. Manroe's chart for absolute neutrophil count for term neonates**

- **CRP:** There should be concern for sepsis if positive.
- N.B Do CBC and CRP after 6 to 8 hours of life in suspected early onset sepsis.
- Consider urinalysis and gram stain if there are symptoms of urinary tract infection or more general concerns for sepsis in infant >1 week old.
- Consider lumbar puncture if concerned for meningitis:
  - Lethargy, irritability, convulsions, bulging fontanel if age <72 hours old
  - For all newborns after 72 hours of life
- Consider chest x-ray if there is respiratory distress or oxygen desaturation.

#### **CSF analysis suggestive of meningitis:**

- Identification of organism on gram stain or culture.
- WBC count ranges 0 to 30 cells/mm<sup>3</sup>. PMN (%) more than 60 per cent.

- Low glucose (less than two third of serum value) and.
- Protein greater than 150 mg/dl.

**Management:** for suspected serious infection in a symptomatic infant, carry out a full septic infection screen.

**Supportive:** attention should be given to basic supportive care for a sick child.

- Thermo-neutral environment in order to avoid hypothermia/ hyperthermia.
- Oxygen administration and monitoring oxygen saturation.
- Monitored for hypoglycaemia/ hyperglycaemia.
- Colloids and inotropes should be used for maintaining normal tissue perfusion and blood pressure.

- Enteral feeds should be avoided till the baby is haemodynamically stable.
- Packed cells and fresh frozen plasma for the management of anaemia and bleeding diathesis.

#### **Antimicrobial therapy:**

- The choice of antibiotics depends on the prevailing flora responsible for sepsis in the given unit and their antimicrobial sensitivity.
- Decision to start antibiotics is based upon clinical features and/or a positive septic screen. However, duration of antibiotic therapy is dependent upon the presence of a positive blood culture and meningitis.

#### **Choice of antibiotics:**

Empirical antibiotic therapy should be unit specific and determined by the prevalent spectrum of etiological agents and their antibiotic sensitivity pattern. Antibiotics, once started, should be modified according to the culture sensitivity reports. Guidelines for empirical antibiotic therapy have been provided in the table below.

The empirical choice of antibiotics is dependent upon the probable source of origin of infection. For infections that are likely to be community-acquired and where resistant strains are unlikely; a combination of ampicillin or penicillin with gentamicin may be a good choice for first line therapy.

For infections that are acquired during hospital stay, resistant pathogens are likely and a combination of ampicillin or cloxacillin with gentamicin may be instituted.

In nurseries where this combination is ineffective due to the presence of multiple resistant strains of klebsiella and other gram-negative bacilli, a combination of a third-generation cephalosporin (cefotaxime or ceftriaxone) with gentamycin may be appropriate.

**Treatment of neonatal sepsis with meningitis:**  
**Antibiotics:** the same as for sepsis but with higher dose and prolonged duration (Gentamycin for two weeks, the rest for three weeks). Cefotaxime or Ceftriaxone should be added for treatment of meningitis where resistant strains are likely.

**Table 28. Empirical choice of antibiotics for treatment of neonatal sepsis**

Clinical situation	Septicaemia & Pneumonia	Meningitis
Early onset sepsis	Ampicillin and Gentamicin	Ampicillin and Cefotaxime/ gentamycin
LONS - Hospital-acquired	Vancomycin and ceftazidime	Vancomycin and ceftazidime
LONS- community onset	Ampicillin and Gentamycin	Ampicillin and Cefotaxime/ gentamycin

### **Reserve antibiotics:**

Ciprofloxacin is another antibiotic with excellent activity against gram-negative organisms, although it does not have very good CSF penetration. Hence, ciprofloxacin may be used for the treatment of resistant gram-negative bacteraemia after excluding meningitis.

Meropenem is effective against most bacterial pathogens except methicillin resistant staphylococcus aureus (MRSA) and enterococcus. It should be reserved for situations where sensitivity of the isolate justifies its use.

Methicillin resistant staphylococcus aureus (MRSA) should be treated with a combination of either ciprofloxacin or vancomycin with gentamycin.

For sepsis due to enterococcus, a combination of ampicillin and gentamicin is a good choice for initial therapy. Vancomycin should be used for the treatment of enterococcus resistant to the first line of therapy.

### **Adjunctive therapy:**

Exchange transfusion (ET): the role of a single double volume exchange transfusion in septic neonates with sclerema has been evaluated and demonstrated to show a 50 per cent reduction in sepsis related mortality in the treated group.

If response to therapy is absent, consider non-bacterial infections such as herpes simplex (add acyclovir) and systemic candidiasis (add amphotericin).

*Table 29. Antibiotic dosing chart for newborns*

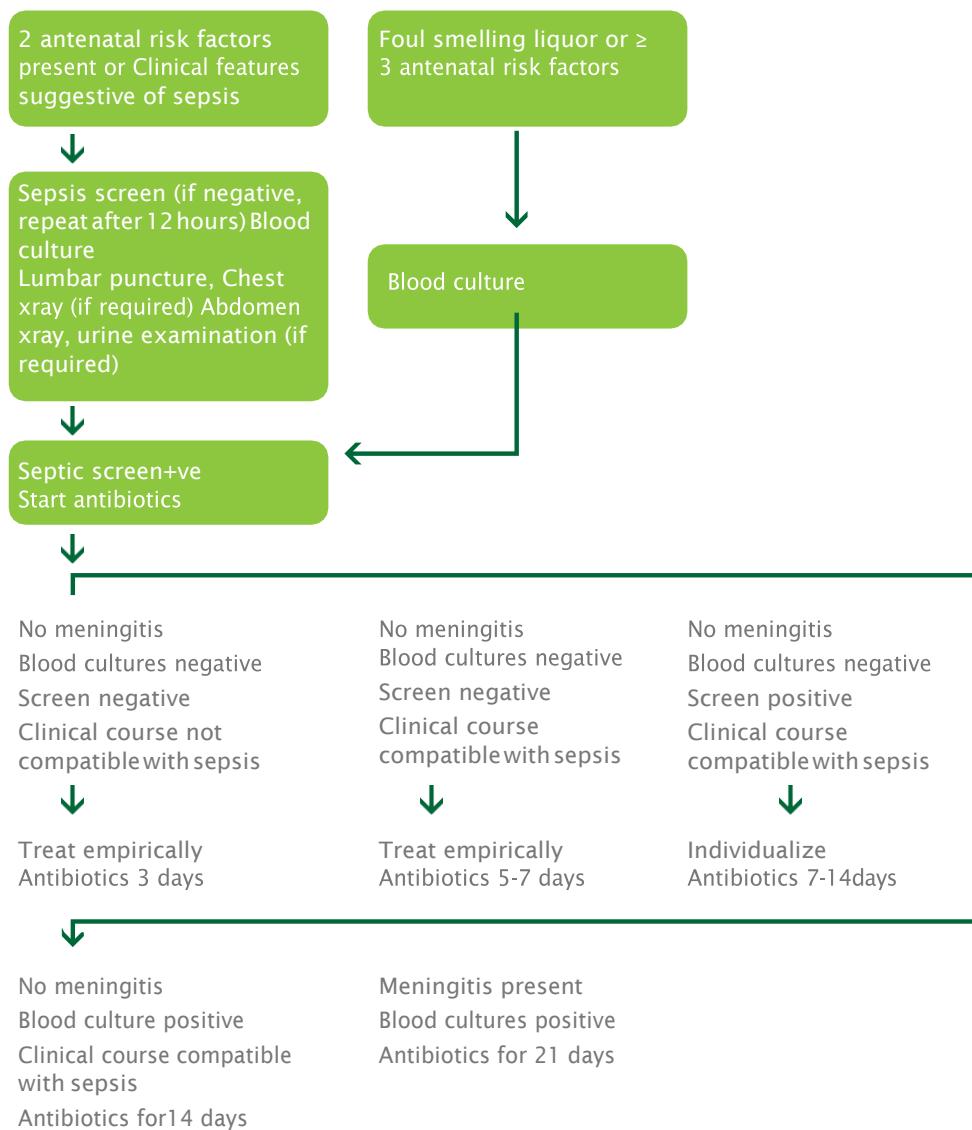
Antibiotic Dosing Chart for Newborns				
Medication	Dose/Frequency			Comments
	< 14 days		> 14 days	
	<u>&lt; 35 weeks</u> PMA* (if PMA not known use current weight <u>&lt; 2.0 kg</u> )	> 35 weeks PMA* (if PMA not known use current weight > 2.0 kg)		
Ampicillin or Cloxacillin	150 mg/kg/dose IV every 12 hours If meningitis ruled out: 50 mg/kg/dose IV every 12 hours		50 mg/kg/dose IV every 6 hours Meningitis: 100 mg/kg/dose IV every 6 hours	-
Gentamycin	3 mg/kg IV once a day and once in 48 hrs in very preterm babies.	4 mg/kg IV once a day		Use newborn dose through the first month.
Cefotaxime	50 mg/kg IV every 12 hours	50 mg/kg IV every 8 hours	50 mg/kg every 6 hours	Preferred over Ceftriaxone due to improved safety profile
Ceftriaxone	50 mg/kg IV every 12 hours for sepsis/meningitis: 50 mg/kg x1 IM for pus draining from eye For IM injection, dilute to 350 mg/mL. Maximum dose: $\frac{1}{2}$ mL = 175 mg			Contraindicated in setting of jaundice or within 48 hours of IV calcium administration
Metronidazole	7.5 mg/kg IV every 24 hours	7.5 mg/kg IV every 12 hours	7.5 mg/kg IV every 8 hours	Anaerobic coverage including treatment of necrotizing enterocolitis
Acyclovir	20 mg/kg IV every 12 hrs	20 mg/kg IV every 8 hours		Treatment of herpes simplex infection: 14 days if localized, 21 days if disseminated
	20 mg/kg PO every 6 hours if IV acyclovir not available			

Duration of antibiotic therapy is dependent upon the presence of a positive blood culture and meningitis.

Duration of antibiotic therapy in neonatal sepsis:

Diagnosis	Duration
Meningitis	21 days
Blood culture positive (no meningitis)	14 days
Culture negative but definite clinical sepsis	10–14 days
Culture negative, clinically probable sepsis, screen positive	7–10 days
Culture negative, clinically probable sepsis, screen negative	5–7 days

## Protocol for sepsis



*Figure 24: Neonatal sepsis treatment algorism*

NB. If no response is seen within 48–72 hours of starting treatment, a repeat blood culture should be obtained to determine the appropriate choice and duration of antibiotic therapy. A lumbar puncture should be repeated in gram negative meningitis to assess for response to therapy.

### **Neonate of Hepatitis B exposed mother**

Hepatitis B is a DNA virus with an estimated 240 million chronically infected individuals worldwide.

The prevalence in antenatal population is not well characterized; there is a suggestion that antenatal prevalence is about 1 per cent.

Risk of vertical transmission:

For a newborn born to a HBsAg positive mother, there is a risk of vertical transmission as high as 90 per cent, if no prophylaxis is given.

The risk of vertical transmission is associated with the following:

- Hepatitis B DNA viral load
- Hepatitis B e antigen status: 90 per cent in HBeAg positive vs 30 per cent in HBeAg negative

#### **Other considerations:**

Mode of delivery: No trials support a difference between vaginal or c-section births in hepatitis B vertical transmission rates.

Breast-feeding: There is no evidence that breast-feeding increases the risk of HepB transmission.

#### **Prevention:**

For known HepBsAg positive mother:

There is evidence to suggest that hepatitis B immunoglobulin alone, hepatitis B vaccine alone and hepatitis B vaccine plus hepatitis B immunoglobulin given at birth prevents hepatitis B occurrence in the newborn.

Management of the baby of an HBsAg-positive woman:

- Screen all women in early pregnancy for hepatitis B carriage
- If available, all HBsAg-positive pregnant women should also be tested for HBeAg and should have HBV DNA measured.

Give the baby hepatitis B protection as follows:

Age	Action to be taken
Birth	Hepatitis B immunoglobulin 100–110 IU and Hepatitis B vaccine 5 µg
6 weeks	DTaP-OPV-HepB/Hib
10 weeks	DTaP-IPV-HepB/Hib
14 weeks	DTaP-IPV-HepB/Hib
9 months	Take a blood test to check for hepatitis B infection (HBsAg) and for vaccine

- Induced immunity (anti-HBs).
- If HBsAg is positive at age nine months, the baby has become infected despite prophylaxis: refer to an appropriate specialist.
- If HBsAg is negative and anti-HBs level is >10 IU/L at age nine months, immunity is proven.

- If HBsAg is negative and anti-HBs level is  $\leq 10$  IU/L at age nine months, give one to three further doses of hepatitis B vaccine at least four weeks apart. Recheck serology four weeks after each dose to determine if further doses are necessary (i.e., if anti-HBs is still  $\leq 10$  IU/L). If there is no seroconversion after the third dose of hepatitis B vaccine, discuss with a specialist.

For unknown HepBsAg status mother:

- The newborn should receive hepatitis B vaccine at birth. Mother should be tested for hepatitis B serology and if HBsAg positive, the infant should also receive hepatitis B immunoglobulin within 48 hours.
- Follow the routine vaccination schedule from six weeks.
- If the mother was determined to be HBsAg positive, then the infant should have HepB serology tests at nine months of age.

For HBsAg negative mother:

- Follow the routine vaccination schedule from six weeks.

#### Efficacy

- If the recommended immunisations are completed, the baby's risk of becoming infected is reduced by about 95 per cent.

## Congenital syphilis

Syphilis is a sexually transmitted disease, caused by the bacteria *Treponema Pallidum*, that can result in serious congenital conditions if contracted during prenatal development. Mother-to-child transmission of syphilis is preventable and curable.

Clinical signs:

- Neonate could be asymptomatic
- Often low birth weight
- Palms and soles: red rash, grey patches, blisters or skin peeling
- 'Snuffles': rhinitis with nasal obstruction which is highly infectious
- Abdominal distension due to big liver and spleen
- Jaundice
- Anaemia
- Some VLBW babies with syphilis have signs of severe sepsis with lethargy, respiratory distress, skin petechiae or other bleeding

Diagnosis:

- Venereal disease research laboratory (VDRL) test
- CSF analysis for VDRL, cell count and protein
- CBC
- Long bone radiography

Treatment:

- Asymptomatic neonates born to VDRL positive women should receive
  - Crystalline penicillin G, 100,000–150,000 U/kg/day, administered as 50,000 U/kg/dose IV every 12 hours during the first seven days of life and every eight hours thereafter for a total of 10 days or
  - Benzathine benzyl penicillin 50,000 units/kg in a single intramuscular dose
- Symptomatic infants require treatment with:
  - Procaine benzyl penicillin 50,000 units/kg as a single dose daily for 10 days or



- Crystalline penicillin G, 50,000 units/kg every 12 hours IM or IV for the first seven days of life and then every eight hours for a further three days.
- Treat the mother and partner for syphilis and check for other sexually transmitted infections.

## **Herpes Simplex infection**

Only 30 per cent of mothers whose infants have neonatal herpes have a history of symptomatic genital herpes. Any infant with vesicular lesion(s) must have investigations performed and have acyclovir treatment commenced regardless of maternal history. Both HSV-1 and HSV-2 can cause neonatal infection. Around 85 per cent of transmission occurs perinatally, 10 per cent in the postnatal period and a small amount antenatally.

Intrapartum/postnatal infection can become manifest up to four to six weeks of age: disseminated infection usually occurs in the first two weeks and can mimic bacterial sepsis; localised CNS or SEM (skin, eye, mucous membrane) disease usually becomes manifest during the second and third week.

The risk of HSV infection in an infant born vaginally to a mother with a first episode or primary genital infection is 33-50 per cent (hence caesarean section usually performed) and such infant warrant acyclovir treatment once investigations have been performed. The risk from recurrent genital HSV infection is 3-5 per cent at most and empiric therapy is not recommended. Cultures can be taken at 24-48 hours if the infant is asymptomatic and acyclovir only initiated if HSV is identified. CNS

infection may occur as an isolated condition or as part of a disseminated multi-organ disease. In either situation, brain involvement may become extensive and result in adverse outcomes. Therefore, in infants presenting with seizures and no other apparent cause, herpes simplex encephalitis should be considered and there should be a low threshold for acyclovir treatment. Duration of treatment is 10 to 21 days based on the clinical condition of the neonate.

## **Reference**

1. Cloherty and Stark's Manual of neonatal care 8<sup>th</sup> edition
2. Neonatal Guideline, UK, NHS, Trust, 2017-2019
3. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. J Pediatr 1979;95: 89- 98.
4. Mouzinho A, Rosenfeld CR. Revised reference ranges for circulating neutrophils in very-low - birth - weight neonates. Pediatrics 1994; 94:76-82

## **Fungal infections**

Fungal infection is common in neonatal ICU, especially as a cause of late onset neonatal sepsis. The incidence and severity are inversely related to gestational age. Some centres provide prophylaxis antifungal especially for those infants under 1000 grams.

### **Aetiologies**

The most common cause is candida infection; the leading among the candida species is C. Albicans.

**Risk factors for fungal infection in neonates:**

- Extreme prematurity
- Prolonged use of antibiotics > 5 days or use of two or more antibiotics.
- Complicated gastrointestinal disease
- Lack of enteral feedings
- Intralipid use > 7 days
- Use of central venous catheter
- Endo-tracheal intubation and mechanical ventilation
- Hyperglycaemia
- Use of steroids/H<sub>2</sub> blockers

**Clinical features:**

- Term infants can have non-invasive localized infection while preterm babies will have a more aggressive systemic infection.
- Common features include frequent apnoea, lethargy, GI symptoms (distension of abdomen, bloody stools, gastric aspirates), respiratory distress, increased oxygen requirement, thrombocytopenia, hyperglycaemia, metabolic acidosis, hypotension and elevated leukocyte count.
- There could be various organ involvements in a fungal infection;
- Renal – UTI/renal abscess
- CNC – meningitis, ventriculitis, abscess
- Gastro-intestinal – peritonitis, intestinal perforation
- Respiratory – pneumonia
- Eye – endophthalmitis, chorioretinitis
- Heart – endocarditis and thrombi
- Bones and joint – septic arthritis and osteomyelitis
- Serial monitoring with abdominal X-rays and abdominal girth monitoring is recommended.
- Consultation with a paediatric surgeon for further management.

**Diagnosis:**

- Blood culture – is the gold standard, 90 per cent of the fungus grows in 72 hours, slow growing species can take 10 days.
- Urine culture – collected under sterile technique, gram stain of the urine can be done for looking at fungal elements/hyphae.
- Obtain culture from CSF, peritoneal fluid organ specific screening like ultrasound for brain and kidney and eyescreening.

**Treatment:**

Remove central lines

**Antifungals:**

- Amphotericin B deoxycholate 1mg/kg is first line for systemic infection and meningitis
- Or Fluconazole 12 mg/kg intravenous or oral daily, is an alternative in neonates who have not been on fluconazole prophylaxis.
- The recommended duration is two weeks (three weeks for meningitis), after documented clearance of candida species from the bloodstream

**Prophylaxis:** initiated mainly for VLBW infants with a high rate (> 10%) and moderate (5-10%) of invasive candidiasis in the NICU.

**Reference**

1. Cloherty and Stark's Manual of neonatal care 8th edition
2. Fungal sepsis. All India Institute of Medical Sciences protocol for neonatology. 2019

Surgical management: absolute indication for surgery

- Pneumoperitoneum (indicating bowel perforation)

- Presence of necrotic bowel (severe and persistent metabolic acidosis, thrombocytopenia and presence of fixed loop on x-ray).

#### **Surgical options include:**

- Laparotomy
- Primary peritoneal drainage (PPD): Consider PPD if unstable to undergo laparotomy.

#### **Prognosis**

- Overall mortality rate is 20-40% but could reach to 100% in case of severe disease.

#### **References**

1. Cloherty and Stark's. Manual of Neonatal Care. 8<sup>th</sup> edition
2. Necrotizing Enterocolitis. All India Institute of Medical Sciences protocol for neonatology. 2019

# CHAPTER 12: NEONATAL JAUNDICE (NEONATAL HYPERBILIRUBINEMIA)

## Indirect hyperbilirubinemia

Jaundice is common in the first week of life, occurring in 60 per cent of term and 80 per cent of preterm newborns and it is the most common cause of readmission after discharge. Can be classified as pathologic and physiologic jaundice.

### Pathologic jaundice:

- Visible jaundice in the first 24 hours of life.
- Yellow palms and soles anytime.
- Serum bilirubin concentration or transcutaneous bilirubin increasing by more than 0.2 mg/dL/hour or more than 5 mg/dL in 24 hours.
- If total serum concentration is more than 95th centile as per age specific bilirubin nomogram.
- Associated signs of illness such as vomiting, lethargy, poor feeding, excessive weight loss, apnoea, tachypnoea or temperature instability.
- Clinical jaundice persisting beyond two weeks in term and three weeks in preterm neonates.

### Causes and risk factors for jaundice:

- Increased bilirubin production
  - RBC disorders
  - Isoimmunization (e.g., Rh ABO and minor blood group incompatibility),
  - Erythrocyte biochemical abnormalities - glucose 6 phosphate deficiencies
  - Abnormal erythrocyte morphology such as hereditary spherocytosis
  - Sepsis

- Sequestered blood due to bruising or cephalohematoma, subgaleal haemorrhage
- Polycythaemia
- Decreased bilirubin clearance
  - Crigler-Najjar syndrome due to either absent uridine diphosphoglucuronosyltransferase (UGT) activity (type I) or reduced UGT activity (type II) results in severe hyperbilirubinemia.
  - Gilbert syndrome results from a mutation in the promoter region of the UGT1A1 gene, reducing production of UGT, and is the most common inherited disorder of bilirubin glucuronidation.
  - Infants of diabetic mother.
  - Congenital hypothyroidism
  - Galactosemia
- Increased enterohepatic circulation
  - Breastfeeding – inadequate breastfeeding
  - Breast milk Jaundice
  - Obstructive cause – idiopathic hypertrophic pyloric stenosis

### Approach to a newborn with jaundice:

- History
  - Record the hours of onset of jaundice and birth weight.
  - Family history – jaundice, anaemia, splenectomy, liver disease.
  - Jaundice in previous sibling (blood group incompatibility).
  - Maternal history – diabetes, intrauterine infection, utero-placental insufficiency.

- Labour and delivery history – oxytocin administration, delayed cord clamping, perinatal asphyxia.
  - Feeding history – initiation, type and frequency of feeding.
  - History of delayed meconium passage, high coloured urine and pale stools.
  - Symptoms of bilirubin induced encephalopathy.
  - Presence of risk factors
- Physical examination
- Age in hours, weight, gestational age – SGA/AGA/LGA.
- Visual assessment of jaundice from face to soles.
  - Pallor, plethora, petechiae
    - Bruise, cephalhematoma, subgaleal bleed.
    - Hepatosplenomegaly
    - Signs of sepsis
    - Adequacy of breastfeeding
    - CNS examination: poor Moro's reflex, poor feeding, lethargy, tone abnormality, altered cry (signs of acute bilirubin encephalopathy).

*Table 31. Acute bilirubin encephalopathy/bilirubin induced neurologic dysfunction*

Clinical signs	BIND score	ABE
<b>Mental status</b>		
Normal	0	None
Sleepy but arousable; decreased feeding	1	Subtle
Lethargy, poor suck and/or irritable/jittery with strong suck	2	Moderate
Semi-coma, apnoea, unable to feed, seizures, coma	3	Advanced
<b>Muscle tone</b>		
Normal	0	None
Persistent mild to moderate hypotonia	1	Subtle
Mild to moderate hypertonia alternating with hypotonia, beginning arching of neck and trunk on stimulation	2	Moderate
Persistent retropcollis and opisthotonus—bicycling or twitching of hands and feet	3	Advanced
<b>Cry pattern</b>		
Normal	0	None
High pitched when aroused	1	Subtle
Shrill, difficult to console	2	Moderate
Inconsolable crying or cry weak or absent	3	Advanced
	Total BIND score	0-3 mild BIND 4-6 Moderate 7-9 Severe

Laboratory/investigation:

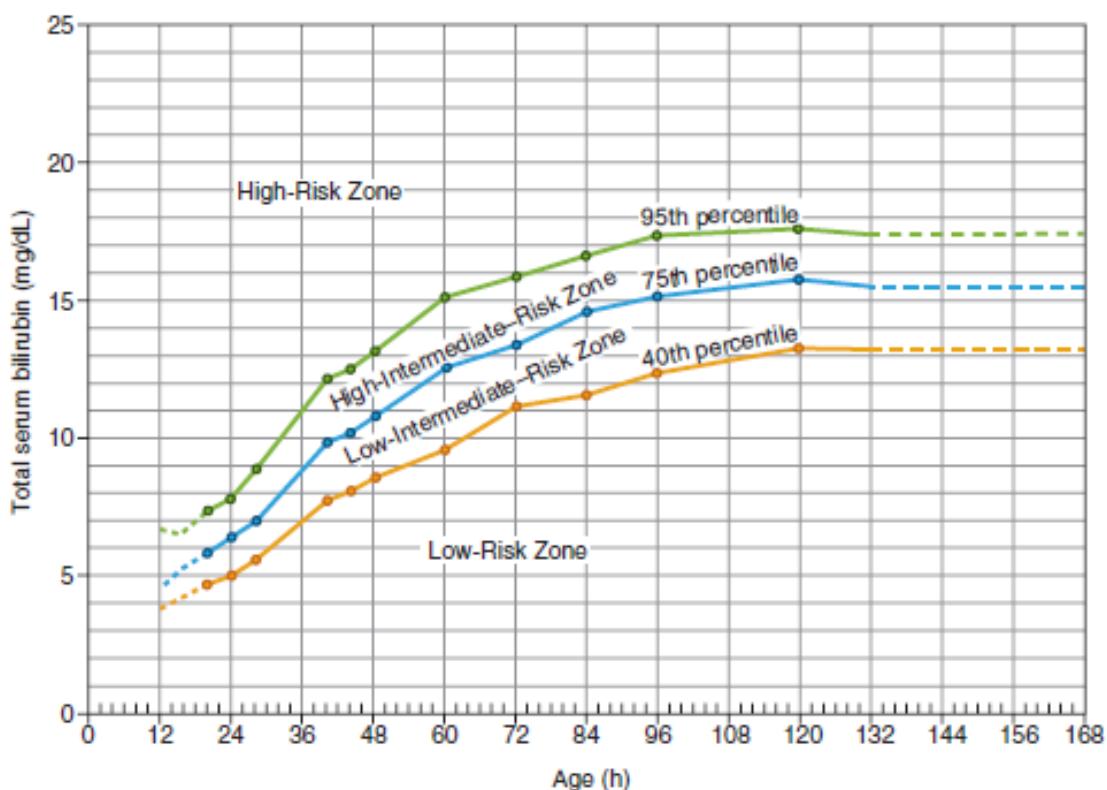
- Mother's and baby's blood group and Rh typing.
- Direct Coombs test (DCT) for the baby.
- Serum bilirubin (Total and direct) (TSB)
- Hb, HCT, reticulocyte count and peripheral smear for RBC morphology.
- Other investigations to be done as per clinical indication.

All babies born to Rh-ve or O+ve blood group should have their cord blood group done and collected as soon as possible. Determine blood group, bilirubin and haemoglobin/haematocrit from cord blood.

All newborns must be evaluated clinically for the presence of jaundice in the first three to five days; if jaundice is present, transcutaneous bilirubin (TcB), if available, will be screened for. If the TcB value is more than 12-14 mg/ dl, confirm level by TSB. If TcB is not available, TSB has to be determined.

Interpretation of TCB and TSB is based on Bhutani's hour specific bilirubin nomogram for term and near-term healthy neonates.

Interpretation is based on the age of the newborn and the presence of risk factors. This interpretation is very important in deciding discharge, follow up and also time to do repeat serum bilirubin.



**Figure 25. Predischarge hour-specific serum bilirubin for subsequent hyperbilirubinemia.**

(Source: Bhutani VK, Johnson L, Sivieri EM. Predictive ability of predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinaemia in healthy term and near-term newborns. Pediatrics 1999; 103:6-14.)

**Table 32. Recommendations for management and follow-up according to risk factors**

Predischarge bilirubin measurements, gestation and risk factors for subsequent hyperbilirubinemia			
Designated risk zone	GA 35-37+6/7 + other risk factors	GA 35-37+6/7 +no other hyperbilirubinemia risk factors Or GA $\geq$ 38 and other risk factors	GA $\geq$ 38 and no other risk factors
High	Evaluate the need for phototherapy and TSB in 4-8 hours	Evaluate the need for phototherapy and TSB in 4-24 hours	Evaluate the need for phototherapy and TSB in 4-24 hours
High intermediate	Evaluate the need for phototherapy and TSB in 4-24 hours	Evaluate the need for phototherapy and TSB in 24 hours	Follow up in 2 days, TSB on follow up
Low Intermediate	If discharging less than 72 hours, follow up in 2 days TSB on follow up	If discharging less than 72 hours, follow up in 2 days	If discharging less than 72 hours, follow up in 2-3 days
Low	If discharging less than 72 hours, follow up in 2 days	If discharging less than 72 hours, follow up in 2-3 days	If discharging less than 72 hours, follow up based on presence of other factors, not jaundice

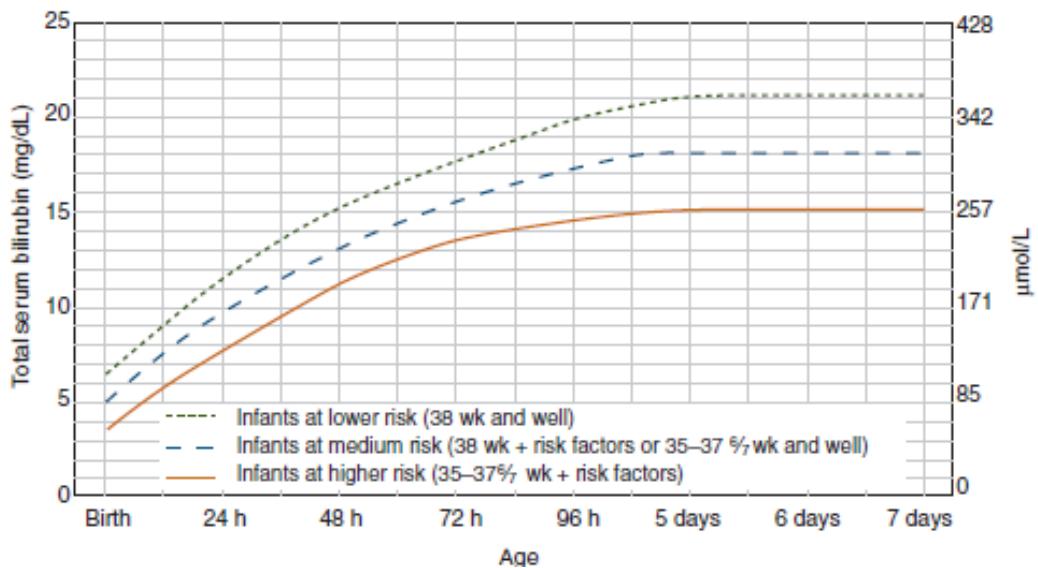
Source: Maisels MJ, Bhutani VK, Bogen D, et al. Hyperbilirubinaemia in the newborn infant  $\geq$ 35 weeks' gestation: an update with clarifications. *Pediatrics* 2009; 124:1193-1198.

### Management:

AAP provides two age-specific nomograms – one each for phototherapy and exchange transfusion. The nomograms have lines for three different risk categories of neonates (Fig. A & C).

- Lower curve – For lower risk babies (38 weeks or more AND no risk factors).

- Middle curve – For medium risk babies (38 weeks or more WITH risk factors, or 35 to 37 weeks AND WITHOUT any risk factors).
- Upper curve – For higher risk (35 to 37 weeks and WITH risk factors). Risk factors include presence of iso-immune haemolytic anaemia, G6PD deficiency, asphyxia, temperature instability, hypothermia, sepsis, significant lethargy, acidosis and hypoalbuminaemia.



**Figure 26. Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation**

Source: Management of hyperbilirubinaemia in the newborn infant 35 or more weeks of gestation. *Pediatrics* 2004;114: 297-316

Preterm infants less than 35 weeks' GA have different cut off values

**Table 33. Guideline for phototherapy and exchange transfusion in preterm newborns based on GA**

<b>Phototherapy</b>		<b>Exchange transfusion</b>
Gestational age (week)	Initiate phototherapy total serum bilirubin (mg $\text{dl}^{-1}$ )	Total serum bilirubin (mg $\text{dl}^{-1}$ )
<28 0/7	5–6	11–14
28 0/7–29 6/7	6–8	12–14
30 0/7–31 6/7	8–10	13–16
32 0/7–33 6/7	10–12	15–18
34 0/7–34 6/7	12–14	17–19

(Source: Maisels MJ, Watchko JF, Bhutani VK, et al. An approach to the management of hyperbilirubinaemia in the preterm infant less than 35 weeks of gestation. *J Perinatol*. 2012; 32:660–664, with permission (footnotes modified).

**Table 34. Guideline for phototherapy exchange transfusion in preterm newborns based on birth weight**

BIRTHWEIGHT	Total Serum Bilirubin Level (mg/dL)				
	Healthy		Sick		
	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion	
<1000 g	5–7	11 - 13	4–6	10 - 12	
1001–1500 g	7–10	12 - 15	6–8	11 - 13	
1501–2000 g	10–12	15 - 18	8–10	13 - 15	
2001–2500 g	12–15	18 - 20	10–12	15 - 18	

### 1. Phototherapy

Initiating and follow-up

Check all lights are on

To increase the efficacy:

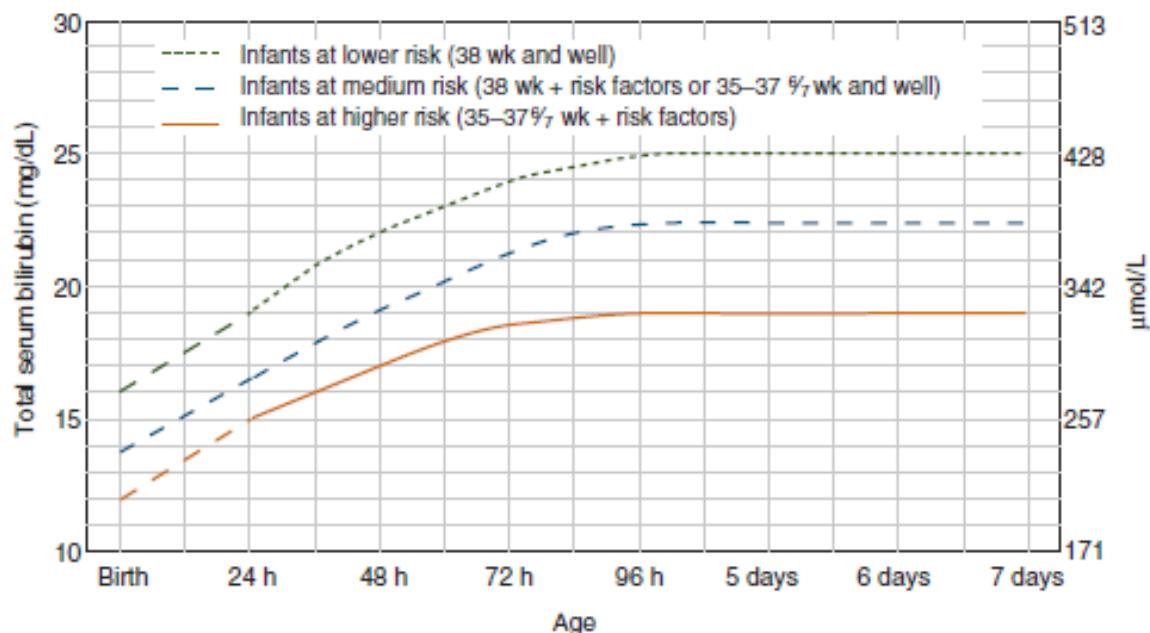
1. Shorten the distance to as close as possible and maintain eutherma
2. Change position two hourly,
3. Use double unit phototherapy.,
4. Use the phototherapy unit with the highest flux,
5. Cover the phototherapy unit with a white sheet to increase reflection,
6. Use special blue lights - Philips TL 52 /20 W.
  - Monitor temperature every two hourly
  - Monitor weight daily.
  - Record intake and output chart.
  - Give frequent breastfeeding. Ensure that the baby is passing stools daily.
  - Shield eyes from light source with appropriately sized eyepads.
  - Give continuous phototherapy (except during feeding).
  - Monitor side effects (dehydration, hypo/hyperthermia, increased stool frequency).

- Measure irradiance, with use of flux meter, monthly (intensive phototherapy -> 30  $\mu\text{w}/\text{cm}^2/\text{nm}$ ) and preferably use a chronometer to measure time of use of phototherapy lights.
- If a flux meter is not available, change tubes of phototherapy after 2000 hours of use.
- Watch for danger signs – vomiting, lethargy, poor feeding, fever, high pitched cry, dark urine, light stools.
- Stop phototherapy when bilirubin is <13 mg/dl in term or two consecutive values are lower than age specific cut offs and < 1-2 mg/dl or less than the starting value in preterm infants.
- Assess clinically for rebound after discontinuing phototherapy and do TSB and direct if required, especially in haemolytic jaundice.

### 2. Exchange transfusion

#### Indications:

- Severe hyperbilirubinemia based on nomogram



*Figure 28. Guidelines for exchange transfusion in infants of 35 or more weeks*

- If the TSB is above exchange level, exchange transfusion is indicated if the baby has received intensive phototherapy.
- If the value is above exchange cut off and the baby has not received phototherapy previously, start intensive phototherapy. Arrange everything, including blood for exchange, but repeat bilirubin in two hours and do an exchange if there is no significant reduction in bilirubin (at least 2 mg/dl). By six hours, TSB should be below exchange cut off level.
- Immediate exchange transfusion is indicated if the baby shows features of BIND (hypertonia, arching, retrocollis, opisthotonus, fever, high pitched cry) or TSB is > 5 mg/dl than exchange level.
- Use total bilirubin. Do not subtract direct fraction unless > 50%.
- Measure serum albumin.

*Table 35. Indication for exchange transfusion based on serum bilirubin to albumin ratio*

Risk category	B/A ratio at which exchange transfusion should be considered
38 0/7 and well	8
35-37 6/7 and well or 380/7 and risk	7.2
35 -37 6/7 and risk	6.8

*Table 36. Guideline for phototherapy exchange transfusion in preterm newborns based on GA*

<b>Phototherapy</b>		<b>Exchange transfusion</b>
Gestational age (week)	Initiate phototherapy total serum bilirubin (mg dl <sup>-1</sup> )	Total serum bilirubin (mg dl <sup>-1</sup> )
<28 0/7	5–6	11–14
28 0/7–29 6/7	6–8	12–14
30 0/7–31 6/7	8–10	13–16
32 0/7–33 6/7	10–12	15–18
34 0/7–34 6/7	12–14	17–19

(Source: Maisels MJ, Watchko JF, Bhutani VK, et al. An approach to the management of hyperbilirubinaemia in the preterm infant less than 35 weeks of gestation. *J Perinatol.* 2012; 32:660–664, with permission (footnotes modified).

*Table 37. Guideline for phototherapy exchange transfusion in preterm newborns based on birth weight*

BIRTHWEIGHT	Total Serum Bilirubin Level (mg/dL)			
	Healthy		Sick	
	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion
<1000 g	5–7	11 - 13	4–6	10 - 12
1001–1500 g	7–10	12 - 15	6–8	11 - 13
1501–2000 g	10–12	15 - 18	8–10	13 - 15
2001–2500 g	12–15	18 - 20	10–12	15 - 18

#### Other indications for exchange:

- Hyperbilirubinemia with BIND.
- An exchange transfusion soon after birth is indicated in haemolytic jaundice if:
  - Cord bilirubin is  $\geq 4.5$  mg/dl
  - Cord Hb is  $\leq 11$  mg/dl, PCV < 30
  - The bilirubin is rising by  $> 1$  mg/dl/hour despite phototherapy
  - The haemoglobin level is between 11 and 13 mg/dl and bilirubin level is rising by  $> 0.5$  mg/dl /hour despite phototherapy.

#### Choice of blood:

- Fresh whole blood (preferably < 72 hrs, up to five days is acceptable).
- Rh isoimmunisation – ABO compatible Rh –ve blood is always used. However, in emergency situations O –ve blood can be used without cross matching. For the first exchange, blood cross matched against mother's serum should be used. For subsequent exchanges, irrespective of baby's ABO blood group, O –ve blood cross matched against baby's serum should be used.

- In ABO incompatibility – O Rh negative blood group or Rh compatible blood group with mother and baby.
- In other situations – fresh ABO and Rh compatible blood should be used.
- Blood should be cross matched with baby and mother. The blood should be warmed to 37°C with a blood warmer if available.
- If the haematocrit is < 35%, partial exchange transfusion with 80 ml/kg PRBC (haematocrit 70%) should be first performed and the exchange completed with another 80 ml/kg of whole blood.
- If possible, irradiated and leukoreduced blood is preferred.

#### **Volume:**

Usually involves double the volume of the infant's blood (160 ml/kg) and is known as double volume exchange transfusion (DVET). This replaces 87 per cent of the infant's blood volume with new blood. In preterm infants, the blood volume should be calculated from the nomogram.

Post double exchange transfusion, bilirubin reduces to half of original value but again increases to 70-80 per cent of previous level afterwards.

#### **Preparation:**

- Obtain informed consent.
- Equipment for umbilical catheterization. It is preferable to have vital signs, saturation or apnoea monitor attached to the baby.
- Use blood warmer if available.
- Check potassium if blood is > 7 days old and particularly if metabolic abnormalities are noted following ET.
- Ensure the stomach is empty. Aspirate

stomach and keep orogastric tube on free drainage. Do not feed during the procedure.

- Check and match the bag number on the bag and the form.
- Equipment: cap, mask, sterile gown, surgical gloves, extension tubing Set, blood and infusion warmer.
- Exchange transfusion record chart, cardiorespiratory monitor, consent form for parents, antiseptic solution for line insertion.
- Personnel: doctor and assistant needed as feasible.

#### **Method:**

- Push-pull technique – umbilical exchange through UVC: the tip should be in the IVC to get a good backflow of a few cm. Do not perform exchange transfusion through a UVC if the tip is in the portal circulation. This may cause NEC by reducing bowel blood flow.
- Peripheral exchange – withdraw from artery and infuse through vein. Aliquots < 3-5% (5-10ml/kg) of blood volume; the sicker and smaller the baby, the smaller the aliquot.
  - 5 ml for infants under 1500 gm.
  - 10 ml for infants 1500 to 2500 gm.
  - 15 ml for infants 2500 to 3500 gm.
  - Each aliquot should take 3-5 minutes.
- Keep moving the bag intermittently to prevent RBCs from settling
- Keep the syringe vertical with its nozzle facing down to prevent air embolism. Never leave the umbilical catheter end open.
- Use the three-way/four-way stopcock

- Flush the withdrawal catheter with heparinized saline every 10-15 min to prevent clotting.
- During the procedure, the operator(s) must call out the volume in and out with each infusion and withdrawal (e.g., ten in ten out). A second person must keep a written timed running record of each infusion and withdrawal and of cumulative volumes to be sure that the volumes infused and withdrawn are equal.
- FiO<sub>2</sub> may have to be increased in a ventilated newborn.
- Take 45-60 minutes for a double volume exchange transfusion in a vigorous baby and longer in a sick one. The rate is 1-2 ml/kg/min.
- Routine calcium injections, during exchange transfusion is not recommended. But if there is unexplained tachycardia or arrhythmia, give slow IV calcium.
- Continue phototherapy immediately after the procedure.
- No routine antibiotics after DVET unless umbilicus looks unhealthy or there is breach of asepsis
- Procedure of exchange transfusion 1 - 1.5 hrs.
- After 4-6 hours – send a repeat serum bilirubin.

Monitoring during transfusion: every 10 minutes during the procedure, check and document HR (vital monitor), respiratory rate, temperature, colour and SaO<sub>2</sub> probe.

Monitor vitals and abdominal girth half hourly for two hours. If constant, start feeds. Check blood sugar at the end of the procedure, at 30 min, at one hour and two hours.

#### **Complications related to procedure and blood:**

- Hypocalcaemia and hypomagnesemia.
- Hypoglycaemia.
- Acid base imbalance.
- Hyperkalaemia.
- Infection.
- Bleeding.
- Thrombocytopenia
- Thrombosis, embolization.
- Perforation of vessel, vasospasm.
- Volume overload.
- Cardiac arrhythmias and arrest.
- Haemolysis (haemoglobinuria, hyperkalaemia)
- Hypo/hyperthermia.

#### 1. Intravenous immunoglobulin

Binds to FC receptors and reduces haemolysis

The AAP recommends the administration of IVIG in immune mediated haemolytic disease if the TSB is rising despite intensive phototherapy and the TSB level is within 2–3 mg/dL of the exchange level.

#### 2 Hydration

Adequate hydration should be given to babies with severe hyperbilirubinemia and signs of dehydration.

### **23.1. Cholestasis, or conjugated hyperbilirubinemia**

Conjugated hyperbilirubinemia is defined by a direct or conjugated bilirubin level > 1 mL/dL or >15% of the TB level.

It may be associated with hepatomegaly, splenomegaly, pale stools and dark urine.

Common age of onset is at two weeks of life.

#### **Causes:**

1. Obstructive bile duct disorders: biliary atresia, choledochal duct cysts.
2. Infectious causes include sepsis and urinary tract infections, as well as infections caused by numerous viral, bacterial and other organisms.
3. Metabolic disorders.
4. Immunologic disorders: gestational alloimmune liver disease.
5. Endocrine disorders: hypothyroidism and panhypopituitarism.
6. Toxic disorders: prolonged courses of total parenteral nutrition (PN), including lipid.
7. Isoimmunise haemolysis. May occur in a small proportion of infants with excessive haemolysis such as ABO/Rh incompatibility and may persist for two weeks.

#### **Diagnosis:**

1. History and findings on physical examination may support a specific diagnosis. Acholic stools suggest obstruction.
2. Laboratory studies to evaluate liver function should include total and direct or conjugated bilirubin, serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase and coagulation studies. Specific laboratory studies should be performed based on findings from the history and physical examination.

3. These include tests for infections and metabolic, genetic or endocrine disorders.

Abdominal ultrasonography may suggest biliary atresia by failing to visualize the gallbladder or the presence of the triangular cord sign. Choledochal duct cyst, gallstones or vascular malformations may be identified.

Hepatobiliary scintigraphy with technetium-labelled iminodiacetic acid analogues may distinguish biliary atresia from other causes of cholestasis such as neonatal hepatitis.

#### **Percutaneous liver biopsy**

#### **Management of PN-associated cholestasis:**

- Most cholestasis in the NICU is due to inability to tolerate enteral feeding and prolonged exposure to PN.
- Enteral feedings, even at minimal volumes of 10 mL/kg/day, are initiated as soon as possible. If enteral feedings can be established, infants with persistent cholestasis and abnormal liver function tests (LFTs) are supplemented with fat-soluble vitamin supplements (ADEK).
- If cholestasis persists as enteral feedings are increased, consider use of ursodiol.
- In infants unable to take enteral feedings and who continue on PN, LFTs are checked weekly; discontinue lipid administration.

#### **Reference**

1. Cloherty and Stark's. Manual of Neonatal care 8<sup>th</sup> edition
2. Avery's Disease of the Newborn 10<sup>th</sup> edition

# CHAPTER 13: HEMATOLOGIC DISORDERS



## Neonatal anaemia

Anaemia is defined as haematocrit (Hct) or haemoglobin (Hgb) concentration > 2 SD

below the mean for age. Anaemia is defined as Hct < 45% in a term infant. The table below gives some normal haematological values for preterm and term newborn infants.

*Table 39. Average haematological values for term and preterm infants.*

Gestation(weeks)	Hct (%)	Hgb (g/dL)	Retic (%)
37-40	53	16.8	3-7
32	47	15.0	3-10
28	45	14.5	5-10
26-30	41	13.4	-

### Causes of anaemia in the neonate:

Anaemia in the newborn infant results from one of three processes: (1) loss of RBCs, or haemorrhagic anaemia, the most common cause; (2) increased destruction of RBCs, or haemolytic anaemia; or (3) underproduction of RBCs, or hypoplastic anaemia. The major physiologic impact of anaemia is ↓ oxygen delivery to tissue, resulting in both compensatory responses (see "symptoms") and acute or chronic consequences including poor growth, decreased activity and limited cardiovascular reserve.

#### A. Blood loss

1. Obstetric causes of blood loss include the following malformations of placenta and cord:
  - Abruptio placentae
  - Placenta previa
  - Incision of placenta at caesarean section.
  - Rupture of anomalous vessels (e.g.,

vasa previa, velamentous insertion of cord or rupture of communicating vessels in a multilobed placenta).

- Haematoma of cord caused by varices or aneurysm.
- Rupture of cord (more common in short cords and in dysmature cords).

#### 2 Occult blood loss

- Fetomaternal bleeding may be chronic or acute. Many conditions may predispose to this type of bleeding.
- Fetoplacental bleeding
- Twin-to-twin transfusion

#### 3 Bleeding in the neonatal period may be due to the following causes:

- Intracranial bleeding: massive cephalohematoma, subgaleal haemorrhage or haemorrhagic caput succedaneum.
- Intra-abdominal bleeding: retroperitoneal bleeding, ruptured liver or spleen, adrenal or renal haemorrhage.



- Gastrointestinal bleeding: such as peptic ulcer, NEC.
- Bleeding from umbilicus.
- Latrogenic causes: excessive blood loss may result from blood sampling

## B. Haemolysis

1. Immune haemolysis: Rh incompatibility, ABO incompatibility, minor blood group incompatibility (e.g., c, E, Kell, Duffy) and maternal autoimmune disease (e.g., lupus)
2. Hereditary RBC disorders
  - RBC membrane defects such as spherocytosis, elliptocytosis or stomatocytosis
  - RBC enzyme defects such as glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate-kinase deficiency
  - Haemoglobinopathies
3. Acquired haemolysis
  - Infection, disseminated intravascular coagulation
  - Microangiopathic haemolytic anaemia, haemangioma, renal artery stenosis

## C. Diminished RBC production

- Diamond-Blackfan syndrome
- Congenital leukaemia
- Infections, especially rubella and parvovirus
- Drug-induced suppression of RBC production
- Physiologic anaemia or anaemia of prematurity

### Clinical findings:

Clinical manifestation varies with the severity of anaemia and other associated conditions. There may be no signs with mild anaemia. With more severe anaemia, findings include:

- Pallor
- Tachycardia
- Tachypnoea
- Apnoea
- ↑ O<sub>2</sub> requirements
- Lethargy
- Poor feeding
- Hepatosplenomegaly (haemolytic disease)
- Jaundice
- Wide pulse pressure
- Hypotension
- Metabolic acidosis with severe anaemia
- ↓ tolerance of labour with foetal anaemia

Diagnostic approach to anaemia in the newborn:

- The family history should include questions about anaemia, jaundice and splenectomy.
- The obstetric history should be evaluated.
- The physical examination may reveal an associated abnormality and provide clues to the origin of the anaemia.
  - Acute blood loss leads to shock, with cyanosis, poor perfusion and acidosis.
  - Chronic blood loss produces pallor, but the infant may exhibit only mild symptoms of respiratory distress or irritability.
  - Chronic haemolysis is associated with pallor, jaundice and hepatosplenomegaly.

- Complete blood cell count, reticulocyte count, blood smear, Coombs test and bilirubin level
- Apt test on gastrointestinal blood of uncertain origin
- Kleihauer-Betke test for fetomaternal haemorrhage
- Ultrasound of abdomen and head
- TORCH infection Studies
- Bone marrow (rarely used, except in cases

of bone marrow failure from hypoplasia or tumour).

#### **Treatment:**

##### **A. Blood Transfusion.**

Severe anaemia (normovolaemic or hypervolaemic) causing cardiac failure, as in hydrops fetalis, is best treated with a partial exchange transfusion using packed RBCs.

$$\text{Volume of packed RBC} = \frac{\text{Blood volume (mL/kg)} \times (\text{Desired HCT} - \text{Patient's HCT})}{(\text{PRBC HCT} - \text{Patient's HCT})}$$

Blood volume of a neonate varies from 80 to 90 ml/kg depending on the gestational age.

#### **Indications for transfusion:**

*Table 40: Guidelines for PRBC transfusion thresholds in preterm neonates (<32 weeks)*

Baby Postnatal age	Haemoglobin(g/dL)		
	Suggested transfusion threshold (g/dL)		
	Ventilated	respiratory support (NIPPV/CPAP)	No respiratory support
First 24 hr	<12	<12	<10
Week 1 (day 2–7)	<12	<10	<10
Week 2 (day 8–14)	<10	<9.5	7.5-8.5
≥Week 3 (day 15 onwards)	<10	8.5	7.5 if asymptomatic

Adapted from British Committee for Standards in Haematology recommendations 2016

*Table 41: Guidelines for PRBC transfusion thresholds in term neonates*

Condition	Hb (g/dL)
Severe pulmonary disease	<12
Moderate pulmonary disease	<10
Severe cardiac disease	<12
Major surgery	<10
Symptomatic anaemia	<7

#### **Haemoglobin targets:**

- Infants with low cardiac output state (e.g., cardiac lesion/shock) and/or diminished oxygen carrying capacity (e.g., cyanotic cardiac lesion or severe pulmonary disease with significant hypoxemia): aim to maintain haemoglobin > 12 g/dL.
- Preterm Infants
  - < / = 2 weeks of age: aim to maintain haemoglobin > 10 g/dL
  - Preterm infants > 2 weeks in oxygen or with poor weight gain, lethargy, frequent apnoea or an increase in apnoea and bradycardia events: use a threshold for transfusion of 9-10 g/dL
  - Stable preterm infants > 2 weeks: aim to maintain haemoglobin > 8-9 g/dL

#### **Amount of packed Red Cell Transfusions**

Give 15 ml/kg of packed red blood cell transfusions. The transfusion should be administered at 5 mL/kg/h. If it is whole blood 20 ml/kg is used.

#### **Volume and rate of transfusion**

- The rate of infusion is 5 mL/kg/hr in the absence of cardiac failure. Rate should not be more than 2 mL/kg/hour in the presence of cardiac failure.

- If more volume is to be transfused, it should be done in smaller aliquots.

#### **Expected response:**

Each transfusion of 9 mL/kg of body weight should increase haemoglobin level by 3 g/ dL. Meticulous monitoring of input, output and vital signs are mandatory during blood transfusion.

#### **A. Prophylaxis**

##### **1. Term infants**

According to the 2010 AAP recommendation, breastfed infants should be started on iron supplementation at the age of four months. Non-breastfed infants should be sent home from the hospital on iron-fortified formula (2 mg/kg/day).

##### **2 Premature infants.**

- Iron supplementation in the preterm infant introduced. Use supplement iron in premature infants at two to four weeks at a dose of 2 to 4 mg of elemental iron/kg/ day once full enteral feeding is achieved.
- Mother's milk or formulas similar to mother's milk, in that they are low in linoleic acid, are used to maintain a low content of polyunsaturated fatty acids in the RBCs.

- Vitamin E (5 to 25 IU of water-soluble form) is given daily until the baby is 38 to 40 weeks' postconceptional age (this is usually stopped at discharge from the hospital).
- These infants should be followed up carefully, and additional iron supplementation may be required.

## Thrombocytopenia

Thrombocytopenia is defined as a platelet count of less than 15000/cubic mm. Thrombocytopenia has been observed in 1–5% of newborns at birth.

*Table 42. Suggested thresholds for neonatal platelet transfusion*

Platelet Count	Condition
<25,000 /cubic mm	Neonates with no bleeding (including neonates with neonatal alloimmune thrombocytopenia if no bleeding and no family history of ICH)
<50,000 / cubic mm	<ul style="list-style-type: none"> <li>• Neonates with bleeding</li> <li>• Evidence of coagulopathy</li> <li>• Before surgery</li> <li>• NAIT if previously affected sibling with ICH</li> </ul>
<1,00,000 / cubic mm	<ul style="list-style-type: none"> <li>Major bleeding e.g., significant IVH</li> <li>Major surgery</li> </ul>

Female Rh-negative infants should receive platelets from Rh-negative donors to prevent Rh sensitization from the contaminating red blood cells.

It is also preferable to have ABO compatible platelets as far as possible (at least until one year of age).

The usual recommended dose of platelets is 1 unit of platelets per 10 kg body weight (unit volume = 45 mL), which amounts to 5 mL/kg. The predicted rise in platelet count from a 5 mL/kg dose would be 20 to 60,000/cubic mm. Doses of up to 10 to 20 mL/kg may be used in cases of severe thrombocytopenia.

The recommended rate of infusion is 10–20 mL/kg/hr.

## Fresh frozen plasma

The valid indications for transfusing FFP in a newborn include:

- Disseminated intravascular coagulation (DIC)
- Vitamin K deficiency associated bleeding
- Neonates with clinically significant bleeding or prior to invasive procedures with a risk of significant bleeding and with abnormal coagulation profile (PT or aPTT significantly above the normal gestational and postnatal age-related reference ranges).

FFP should not be used for simple volume replacement/expansion, enhancement of wound healing or routinely for prevention of IVH.

FFP should not be routinely used to correct abnormalities of the coagulation screen alone with no evidence of bleeding. Other rare indications include patients with

afibrinogenemia, von Willebrand factor deficiency, congenital antithrombin III deficiency, protein C deficiency and protein S deficiency when specific factor replacement is not available. Typically, the transfusion volume is 15–20 mL/kg at a rate of 10–20 mL/kg/hr. Preferably, ABO compatible plasma should be selected as far as possible. Group O plasma must only be given to O recipients.

**Table 43. Neonatal dosing of blood components**

Component	Dose	Expected increment
Packed Red Blood Cells	10-15 mL/kg	haemoglobin increases 2-3g/dL
Fresh Frozen Plasma	10-15 mL/kg	15-20% rise in factor levels (assuming 100% recovery)
Platelets	5-10 mL/kg	50,000/ $\mu$ L rise in platelet count (assuming 100% recovery)

Holding of feeds during red blood cell transfusions:

A temporal relationship between red blood cell transfusion and the development of necrotizing feeds will be held before and after red cell transfusions for all infants in the NICU. Start RBC transfusion at a minimum of one hour after feed and restart enteral feeds at the next scheduled feed but at a minimum one hour after completion of RBC transfusion. No additional IV is necessary unless there are concerns of glucose stability (e.g., intrauterine growth restricted or infant of diabetic mother). Babies with necrotising enterocolitis (NEC) Give direct transfusion rather than exchange transfusion.

#### **Special considerations:**

##### **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.
- Document pre- and post-transfusion Hb levels.
- Ensure blood transfusion volume and rate is prescribed in appropriate infusion chart.

- Observations, including:
  - continuous ECG
  - SpO<sub>2</sub>
  - hourly temperature and BP (recorded before, during and after transfusion)
- Appropriate labelling of bag to ensure compliance
- Unless clinically urgent, avoid transfusion out-of-hours
- To reduce the need for blood transfusion, minimize blood sampling in babies (micro-techniques, non-invasive monitoring) and avoid unnecessary testing.
- Volume overload
- Citrate toxicity
- Rebound hypoglycaemia (following high glucose levels in additive solutions)
- Thrombocytopenia after exchange transfusion

### Hazards of transfusion

#### Most important are:

- infections – bacterial or viral
- hypocalcaemia

### Reference

1. Blood component transfusion. All India Institute of Medical Sciences protocol for neonatology. 2019
2. Neonatal Guideline UK, NHS, TRUST 2017-2019
3. Intensive Care Nursery House Staff Manual, The Regents of the University of California, 2004

# CHAPTER 14: Birth injuries



Injury may occur antenatally, intrapartum or during resuscitation.

Risk factors:

Primiparity, cephalopelvic disproportion, dystocia, prolonged or unusually rapid labour, oligohydramnios, abnormal presentation of the foetus, VLBW or extreme prematurity, macrosomia, foetal anomalies and forceps use or vacuum extraction.

## Head injuries

Caput succedaneum

Oedema over the presenting part of the scalp during a vertex delivery.

Clinical manifestations:

- A soft swelling, usually a few millimetres thick and that may be associated with overlying petechiae, purpura or ecchymoses; its size is maximum just after birth.
- It has poorly defined margins and may extend across the midline of the skull and across suture lines.

## Management:

- Usually resolves spontaneously within several days, and treatment is often not required.
- It only needs observation and reassurance.

## Cephalhematoma

Subperiosteal collection of blood overlying a cranial bone.

## Clinical manifestations:

- The bleeding is sharply limited by periosteal attachments to the suture lines (i.e., no extension across suture lines).
- Usually occurs over one or both parietal bones, less often involves occipital bones and very rarely, frontal bones. The overlying scalp is not discoloured.
- It may not be apparent for a few hours after birth.
- It may feel fluctuant and a few days later, it is often bordered by a slightly elevated ridge of organizing tissue (false sensation of a central bony depression).
- It may be associated with skull fractures – usually linear.
- It usually resolves within six to 12 weeks, occasionally with a residual calcification.

## Management:

- Not needed for treatment in uncomplicated cases.
- Incision or aspiration is contraindicated (risk of infection).
- Blood transfusion is required with marked blood loss.
- Significant hyperbilirubinemia requires phototherapy or exchange transfusion depending on bilirubin level.
- Associated linear fractures do not require specific therapy, but require follow-up radiographs at four to six weeks. Depressed fractures require immediate neurosurgical consultation.

## Subgaleal haemorrhage (SGH)

Collection of blood in the soft tissue space between the galea aponeurotica and the periosteum of the skull.

Predisposing factors: difficult instrumental delivery (the most common), coagulopathies, prematurity, macrosomia, foetal dystocia and precipitous labour.

It may result from an associated skull fracture.

### Clinical manifestations:

- Early manifestations are pallor, hypotonia and diffuse swelling of the scalp.
- A fluctuating mass straddling cranial sutures, fontanelles or both is highly

suggestive of the diagnosis. It can spread across the entire calvarium.

- Haematoma may grow slowly or increase rapidly → hypovolaemic shock.
- Ecchymotic discolouration of the scalp, pitting oedema and progressive posterior spread toward the neck and lateral spread around the ears (displacing ears anteriorly); periorbital swelling and ecchymosis are common.

**N.B.:** - SGH should be considered in infants who show signs of hypoperfusion and falling Hct after attempted or successful vacuum delivery, even in the absence of a detectable fluctuant mass.

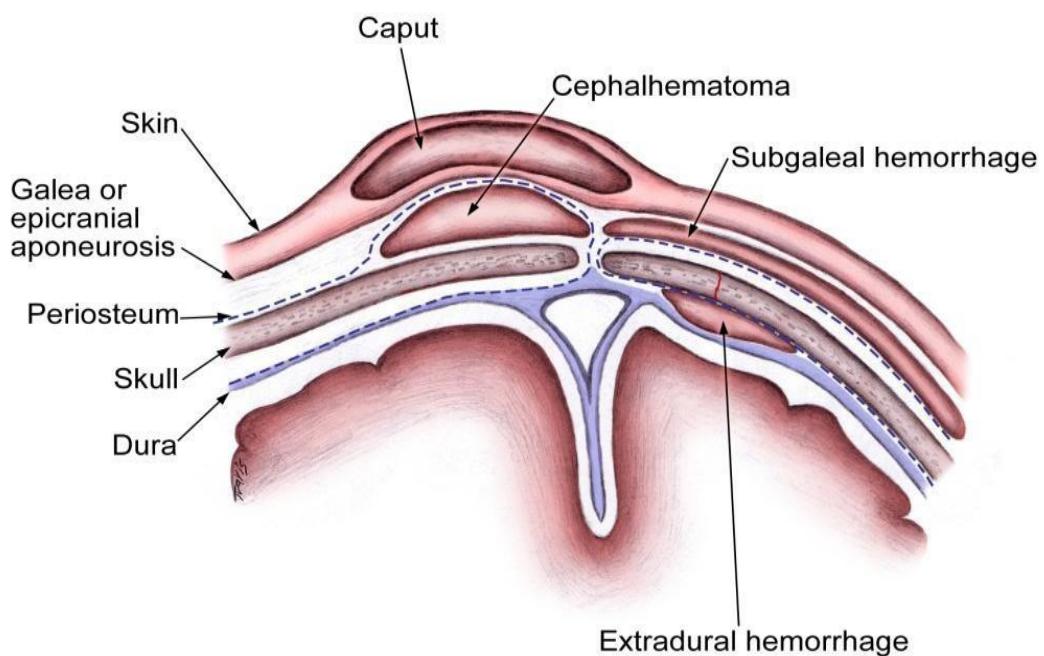


Figure 30. Extracranial site of injuries

### **Management:**

- Newborns with this lesion should be admitted and observed for signs of hypovolaemia and progression.
- Assess and treat shock.
- Prompt restoration of blood volume with FFP or blood.
- Phototherapy provision if hyperbilirubinemia develops.
- Investigation for coagulopathies, in case there is no evidence of trauma or instrumental delivery.
- In the presence of continued deterioration, surgical drainage may be considered.
- Daily HC measurement and HCT follow-up.
- Minimize manipulation because it is painful.

## **Injuries to the neck and Shoulders**

### **Fractured clavicle**

Most clavicular fractures are of the greenstick type, but occasionally the fracture is complete.

Aetiology: difficult delivery of the shoulders in vertex presentations and extended arms in breech deliveries.

### **Clinical manifestations:**

- Decreased movement of the ipsilateral arm
- Pain on passive movement
- Tenderness, crepitus over the clavicle
- Absent Moro reflex on the involved side
- About one-third of the cases present with a palpable mass (callus) at seven to 14 days of life.

- An x-ray confirms the diagnosis.

### **Management:**

- Immobilize the affected arm and shoulder for seven to 10 days.

## **Brachial palsy**

**Aetiology:** excessive traction of the head, neck and arm during birth (e.g., shoulder dystocia and breech presentation)

### **A. Erb's paralysis (the most common form)**

- Results from injury of C5, C6 and occasionally C7 roots.
- Affected infant is frequently large and asphyxiated.
- The affected arm is held in adduction, internal rotation, with extension at the elbow and pronation of the forearm and flexion of the wrist. Moro, biceps and radial reflexes are absent on the affected side. Grasp reflex is intact.
- Signs of respiratory distress indicate an accompanying ipsilateral phrenic nerve root injury.

### **Management:**

- Partial immobilization of the affected extremity for 1–2 weeks in a position opposite to that held by the infant.
- Gentle massage and passive exercises after 1–2 weeks.
- If no improvement, refer to a neurosurgeon.

### **B. Klumpke's paralysis**

- Results from injury of C7, C8 and T1 roots.
- The hand is paralyzed and voluntary movements of the wrist cannot be made. Grasp reflex is absent and deep tendon reflexes are intact.
- Dependent oedema and cyanosis of the hand and trophic changes in the fingernails. After some time, there may be flattening and atrophy of the intrinsic hand muscles.
- Usually ipsilateral Horner's syndrome (ptosis, miosis and enophthalmos) is also present.

#### C. Total brachial plexus injury

- The entire arm is paralyzed; completely motionless, flaccid and powerless, hanging limply to the side.
- All reflexes are absent and the sensory deficit may extend almost to the shoulder.

#### Phrenic nerve paralysis (C3-4-5)

- Results in diaphragmatic paralysis and rarely occurs as an isolated injury; mostly unilateral and associated with ipsilateral upper brachial plexus palsy.
- Difficult breech delivery is the most common cause.

#### Clinical manifestations:

- Recurrent episodes of cyanosis, with irregular and laboured respirations.
- Breathing is almost completely thoracic (i.e., no bulging of the abdomen with inspiration on the affected side).

- ↓ Breath sounds over the affected side.
- Tachypnoea, weak cry and apnoeic spells (in severe cases).
- Chest x-ray reveals elevation of the corresponding copula of the diaphragm.
- Ultrasonography or fluoroscopy of the chest reveals elevated hemidiaphragm with paradoxical movement of the affected side with breathing.

#### Management:

- Most infants require only non-specific medical treatment.
- Positioning of the infant on the involved side.
- Oxygen administration for cyanosis or hypoxaemia.
- IV fluids may be necessary for the first few days. If the infant begins to show improvement, progressive oral or gavage feedings may be started.
- Antibiotics are indicated if pneumonia occurs.
- Infants with more severe respiratory distress (those with bilateral phrenic nerve palsy) may require MV.
- If no improvement after one month, plication of diaphragm should be considered.

#### Intra-abdominal injuries

#### Clinical manifestations

- History of a difficult delivery.

### **Liver (subcapsular) haematoma**

- Generally asymptomatic at birth.
- Signs of blood loss (as pallor, poor feeding, tachypnoea, tachycardia) and jaundice developing during the first 1–3 days after birth; rupture → circulatory collapse.

### **Splenic injury**

- A mass is sometimes palpable in the left upper quadrant.
- Abdominal radiograph shows displacement of stomach bubble medially.

### **Adrenal haemorrhage**

- Adrenal insufficiency (poor feeding, vomiting, diarrhoea, dehydration, irritability, hypoglycaemia and shock).

### **Investigations:**

- Abdominal ultrasound
- Adrenal function tests

### **Management:**

Prompt transfusion with packed RBCs, and recognition and correction of any coagulation disorder.

- Laparotomy with evacuation of the haematoma and repair of any laceration.
- Adrenal insufficiency may require steroid therapy.

**N.B:** Intra-abdominal trauma should be suspected in any newborn with shock and abdominal distension or pallor, anaemia and irritability without evidence of external blood loss.

### **References**

1. Cloherty and Stark's, Manual of neonatal care

# CHAPTER 15: PAIN ASSESSMENT AND MANAGEMENT



## Introduction

Neonates communicate their pain and stress through a number of autonomic, motor and behavioural cues. The caregivers in NICU must recognize these cues and modify the environment to reduce stress and pain, and facilitate self-regulatory mechanisms to promote organization of the neonate.

## Key recommendations:

- Routine assessments to detect pain using a validated assessment tool.
- Reduce number of painful procedures.
- Prevent/reduce acute pain from invasive procedures using non-pharmacological and pharmacological methods.
- Anticipate and treat post-operative pain.

## Types of pain:

- Acute pain – skin-breaking procedures or tissue injury caused by diagnostic or therapeutic interventions.
- Established pain – occurs after surgery, involves localized inflammatory conditions and birth-related trauma.
- Prolonged/chronic pain – results from severe diseases, e.g., necrotising enterocolitis (NEC) and meningitis.
- Pathological pain state – persisting beyond normal tissue healing time.

## Symptoms and signs

### Physiological changes:

- Increase in: heart rate, blood pressure, respiratory rate, oxygen consumption,

mean airway pressure, muscle tone, intracranial pressure and skin blood flow.

- Decrease in: oxygen saturation and transcutaneous oxygen levels, apnoea, shallow breathing and fixed heart rate.

### Behavioural changes:

- Change in facial expression: grimace, brow bulge, eye squeeze, deepening nasolabial furrow, nasal flaring, tongue curving, crying, whimpering, 'silent' cry (intubated babies), decreased sleep and heightened responses.

### Anatomical changes:

- Dilated pupils, sweating, flushing, pallor.

### Body movements:

- Fisting, tremulousness, thrashing limbs, limb withdrawal, writhing, arching back, head banging, finger splaying, cycling.
- Sudden pain and distress may indicate acute deterioration, e.g., bowel perforation.

### Pain assessment tools:

- Assessment of pain, an integral part of any pain prevention program, is challenging in neonates.
- Use validated pain assessment tool; Premature Infant Pain Profile (PIPP).
- Note gestational age.
- Observe the baby's behaviour for 15–30 seconds, then gently touch baby's limb to determine muscle tone/tension (can be done during routine handling).
- When score is above tool's recommended thresholds, initiate comfort measures or analgesia.

*Table 45. Premature infant pain profile (PIPP) pain assessment tool*

Process	Indicators	Date	
		Time	
Chart	Gestational age	36 weeks or more days	0
		32–35 weeks + 6 days	1
		28–31 weeks + 6 days	2
		less than 28 weeks	3
Observe infant for 15 seconds	Behavioural state	Active, awake, eyes open, facial movements	0
		Quiet, awake, eyes open, no facial movements	1
		Active, awake, eyes closed, facial movements	2
		Quiet, asleep, eyes closed, no facial movements	3
		0 bpm increase	0
		5–15 bpm increase	1
		15–24 bpm increase	2
		≥ 24 bpm increase	3
Observe baseline HR and O <sub>2</sub> sats for 30 secs	O <sub>2</sub> sats	92–100%	0
		89–91%	1
		85–88%	2
		84% or less	3
		none	0
		minimum	1
		moderate	2
		maximum	3
Observe infant's facial actions for 30 seconds	Eye squeeze	none	0
		minimum	1
		moderate	2
		maximum	3
	Nasio-labial furrow	none	0
		minimum	1
		moderate	2
		maximum	3

Process	Indicators	Time	Date
Total score			
Procedure			
	Score 0– 6	No action	
	Score 7– 12	comfort measures e.g., positioning, NNS, sucrose	
Intervention	Score > 12	Pharmacological intervention	
Effectiveness Y/N			
Signature initials			

Adapted from KEMH Perth WA

#### **Frequency of assessment:**

All babies should have pain assessment within one hour of admission; score generated will dictate frequency of assessment.

- Intensive care: hourly with observations.
- High dependency: four hourly or if signs of distress/discomfort.
- Special care: as condition dictates or subsequently if signs of distress/discomfort are present.
- Post-operatively: hourly for the first eight hours, then four hourly until 48 hours post-op (more frequently if there are signs of distress/discomfort).

#### **Pain management:**

Non-pharmacological measures are environmental and behavioural interventions that do not use pharmacological agents. They are thought to alleviate pain by activating gate control mechanisms, secretion of endogenous endorphins and diversion of attention. The following measures in combination are followed to minimize pain:

- Avoid bright light, loud noise.
- Limit the number of painful procedures and handling.
- Swaddling, facilitated tucking, distraction measures like talking, music, etc.
- Tactile stimulation like stroking, massaging.
- Gently repositioning baby.
- Comfort/containment holding.
- Reducing light, noise and activity around baby.
- Soothing voice.
- Nappy change.
- Kangaroo care.
- Mother's expressed breast milk – no additives.
- Sucrose/glucose solution induced analgesia.
- Breastfeeding/breast milk supplementation.
- Non-nutritive sucking using pacifiers (dummy or gloved finger).

**Sucrose analgesia:**

- Sucrose administration is particularly useful for short procedures like venepuncture, heel prick, etc. Oral administration of concentrated sucrose solution (24% to 50%) acts through the release of endogenous opioids like beta-endorphin. Analgesic effect lasts for five to eight minutes.

- Use in conjunction with environmental and behavioural measures to relieve pain (e.g., positioning, swaddling, containment holding, Kangaroo care). Alternative to sucrose is dextrose, which is less commonly used.

**Table 44. Dose of sucrose/dextrose for analgesia**

<b>Concentration</b>	<b>For babies who are NPO</b>	<b>Preterm (&lt;32 weeks)</b>	<b>Late PT/Term</b>
24% Sucrose / 25% Dextrose  The sucrose solution is given orally by a syringe 2–3 min before procedure and may be repeated one to two minutes after the procedure. Intragastric administration has no analgesic effect. Don't give for neonate less than 28 weeks of gestation.	0.1–0.2 mL	0.1–0.5 mL	0.2–1 mL

**Breastfeeding and breastmilk supplementation:**  
Almost as effective as sucrose analgesia in reducing pain in newborns undergoing single painful procedures.

Reassess after 30 minutes:

- If pain score is in upper range, institute comfort measures and administer prescribed analgesia/seek medical review.
- If score continues to rise, consider increasing the dose of analgesia and reassess after 30 minutes.
- If clinical concerns – medical review.
- If score constantly below baseline and analgesia is maintained, reduce dosage.

- Record effectiveness of pain management in a plan.

**Pharmacological measures**

The pharmacological measures can be broadly divided into

- Local anaesthetic agents
- Systemic agents: opioids, acetaminophen

Non-steroidal anti-inflammatory agents (NSAID) are generally not used in newborns as analgesics.

## Local anaesthetics

Local anaesthesia is particularly useful for management of acute procedure related pain, with the exception of heel lances. It can be either topically applied on intact skin or injected subcutaneously.

The common topical preparations marketed are:

1. Eutectic mixture of local anaesthetics (EMLA): is a mixture of two local anaesthetics namely lidocaine and prilocaine that is available as 5% cream.
2. Tetracaine (4%)

The dose of EMLA is 1–2g with a contact period of 30 minutes to 1 hour. Apply the cream over a 2–3 cm area with a 1–2 mm thickness and cover with transparent (tegaderm) dressing. For maximal analgesic effect, the topical anaesthetics should be

combined with other non-pharmacological measures like sucrose analgesia or breast milk supplementation.

## Opioids

Opioid drugs are the mainstay in the management of severe pain related to mechanical ventilation.

Indications for continuous infusion of opioids in ventilated neonates are:

- Post-operative patients especially in the first 48–72 hours.
- Illnesses like meconium aspiration syndrome or congenital diaphragmatic hernia with PPHN.
- Asynchrony or fighting with a ventilator. Rule out causes like ventilator malfunction, tube block or inappropriate settings before the infant is sedated for this indication.

**Table 46. Analgesic measures for specific procedures**

Procedure	Intubated	Non-intubated
Arterial puncture/ cannulation lumbar puncture	<ul style="list-style-type: none"><li>■ Inj Morphine 0.1-0.2 mg/kg IV</li><li>■ EMLA cream locally</li><li>■ Sucrose analgesia</li></ul>	<ul style="list-style-type: none"><li>■ EMLA cream locally</li><li>■ Sucrose analgesia</li><li>■ General measures</li></ul>
Chest tube placement	<ul style="list-style-type: none"><li>■ Inj Morphine 0.1-0.2 mg/kg IV</li><li>■ Local infiltration with Lidocaine 2%</li><li>■ Sucrose analgesia</li></ul>	<ul style="list-style-type: none"><li>■ Inj Morphine 0.1 mg/kg IV</li><li>■ Local infiltration with Lidocaine 2%</li><li>■ Sucrose analgesia</li></ul>
Chest drain removal	<ul style="list-style-type: none"><li>■ Inj Morphine 0.1– 0.2 mg/kg</li><li>■ Sucrose analgesia</li><li>■ General measures</li></ul>	<ul style="list-style-type: none"><li>■ EMLA cream locally</li><li>■ Sucrose analgesia</li><li>■ General measures</li></ul>
CT/MRI - for sedation	<ul style="list-style-type: none"><li>■ Inj Morphine 0.1– 0.2 mg/kg IV</li><li>■ Inj Midazolam 0.1– 0.3 mg/kg IV</li></ul>	<ul style="list-style-type: none"><li>■ Oral Chloral hydrate 50 –100 mg/kg</li><li>■ IV Midazolam 0.1–0.2 mg/kg IV single dose</li></ul>

Avoid use of midazolam, especially in preterm neonates. Do not use paralytic agents routinely in ventilated neonates.

In non-ventilated babies, while using opioids – watch for apnoea/respiratory depression; IV Naloxone should be kept ready and used in case of respiratory depression or apnoea

(0.1 mg/kg or 0.25 ml/kg IV); Inj fentanyl may be substituted for Inj morphine; dose 1–4 mcg/kg slow IV over three to five minutes.

Even ventilated patients on opioid infusion during procedures needs additional analgesic measures.

*Table 47. Analgesia measures for routine bedside procedures*

Procedure	Analgesia measure recommended			
	General measures	Sucrose analgesia	Breast milk	Facilitated tucking
Venepuncture sampling	+	+	±	+
Heel prick	+	+	+	+
Subcutaneous/IM injection				
	+	+	+	+
Adhesive tape removal	+	+	+	+
IV cannulation	+	+	±	+

#### Reference

1. Pain Assessment and Management. All India Institute of Medical Sciences protocol for neonatology. 2019

2. Neonatal Care Pocket Guideline for Hospital Physicians. Egypt. 2010



## Annexes

### 351. Normal hematologic values

First Two Weeks of Life in the Term Infant.

Value	Cord Blood	Day 1	Day 3	Day 7	Day 14
Hb (gm/100ml)	16.8	18.4	17.8	17.0	16.8
Haematocrit (%)	53.0	58.0	55.0	54.0	52.0
Red cells (cu.mm. x 10 <sup>6</sup> )	5.25	5.8	5.6	5.2	5.1
MCV (m 3)	107	108	99.0	98.0	96.0
MCH (yy)	34	35	33	32.5	31.5
MCHC (%)	31.7	32.5	33	33	33
Reticulocytes (%)	3-7	3-7	1-3	0-1	0-1
RBC (cu.mm.)	500	200	0-5	0	0
Platelets (1000's/cu.mm.)	290	192	213	248	252

### 352 The White Blood Cell and the Differential Count

First Two Weeks of Life

Age	Leukocytes	Neutrophil							
		Total	Seg	Band	Eosinophils	Basophiles	Lymphocytes	Monocytes	
<b>Birth</b>									
Mean	18,100	11,000	9,400	1,600	400	100	5,500	1,050	
Range	9.0-30.0	6.0-26			20-850	0-640	2.0-11.0	0.4-3.1	
Mean %	-	61	52	9	2.2	0.6	31	5.8	
<b>7 Days</b>									
Mean	12,200	5,500	4,700	830	500	50	5,000	1,100	
Range	5.0-21.0	1.5-10.0			70-1100	0-250	2.0-17.0	0.3-2.7	
Mean %	-	45	39	6	4.1	0.4	41	9.1	
<b>14 Days</b>									
Mean	11,400	4,500	3,900	630	350	50	5,500	1,000	
Range	5.0-20.0	1.0-0.5			70-1000	0-230	2.0-17.0	0.2-2.4	
Mean %	-	40	34	5.5	3.1	0.4	48	8.8	

### 353. Hematologic values in low birth weight neonates

Determination	1-3 Days	4-7 Days	2 Weeks	4 Weeks	6 Weeks	8 Weeks
<b>Birth weight less than 1200g</b>						
Haemoglobin	15.6	16.4	15.5	11.3	8.5	7.8
Reticulocytes as % of RBC	8.4	3.9	1.9	4.1	5.4	6.1
Platelets	148,000 ± 61,000	163,000 ± 69,000	162,000	158,000	210,000	212,000
Leukocytes	14,800 ± 10,200	12,200 ± 7,000	15,800	13,200	10,800	9,900
Segmented Neutrophils	46	32	41	28	23	23
Band Neutrophils	10.7	9.7	8.0	5.9	5.8	4.4
Juvenile Neutrophils	2.0	3.9	5.3	3.6	2.6	2.0
Lymphocytes	32	43	39	55	61	65
Monocytes	5	7	5	4	6	3
Eosinophils	0.4	6.2	1.0	3.7	2.0	3.8
Nucleated RBC as % of total RBC	16.7	1.1	0.1	1.0	2.7	2.0
<b>Birth weight 1200-1500g</b>						
Haemoglobin	20.0	18.0	17.1	12.0	9.1	8.3
Reticulocytes as % of RBC	2.7	1.2	0.9	1.0	2.2	2.7
Platelets	151,000 ± 35,000	134,000 ± 49,000	153,000	189,000	212,000	244,000
Leukocytes	10,800 ± 4,000	8,900 ± 2,900	14,300	11,000	10,500	9,100
Segmented Neutrophils	47	31	33	26	20	25
Band Neutrophils	11.9	10.5	5.9	3.0	1.4	2.1
Juvenile Neutrophils	5.1	2.4	2.7	1.8	1.7	1.6
Lymphocytes	34	48	52	59	69	64
Monocytes	3	6	3	4	5	5
Eosinophils	1.3	2.2	2.5	5.1	2.6	2.3
Nucleated RBC as % of total RBC	19.8	0.8	0	0.4	1.4	1.0
Haemoglobin	20.0	18.0	17.1	12.0	9.1	8.3
Reticulocytes as % of RBC	2.7	1.2	0.9	1.0	2.2	2.7

### 354. Downe-Vidyasagar Score for grading respiratory distress in a term baby

SCORE	Respiratory Rate	Nasal flaring	Cyanosis	Grunt	Auscultation Oliver
0	<60	Nil	Absent	Absent	Good air entry
1	60 – 80	Mild	Present on room air	Audible on Stethoscope	Breathing delayed or decreased
2	>80 or apnoea	Moderate to Severe	Present on FiO <sub>2</sub> 40%	Audible without the stethoscope	Breathing barely audible

Grades of severity according to the total score: 1 – 3 - mild; 4 –6 - moderate, >6 - severe

### 355. Parkin method of clinical assessment of Ga

External sign	0	1	2	3	4
Skin colour	Dark red	Uniform red	Pink pale variable over the body	Pale only pink over the ear palms and sole	
Skin texture	Very fine gelatinous	Fine and smooth	Smooth medium thickness skin rash peeling	Mild thickness skin with peeling hand and feet	Thick like parchment
Breast	No breast tissue	Breast tissue in one or both sides <0.5 cm of the diameter	Breast tissue in one or both sides 0.5-1cm of the diameter	Breast tissue in one or both sides >1 cm of the diameter	
Ear	Smooth early folded doesn't turn back	Smooth easily folded returns back slowly	Cartilage over the top smooth returns fast	Firm ear returns very fast	

Point	1	2	3	4	5	6	7	8	9	10	11	12
GA	30.6	31.7	32.8	33.9	35.1	36.2	37.3	38.4	39.4	40.6	41.7	42.8



### 356. Blood pressure measurement table

Weight in Kg	Gestational Age				
	28	30	32	34	36
1	35-45	36-46	37-47	38-48	39-49
1-2	37-47	38-48	39-49	40-50	41-51
1-4	39-49	40-50	41-51	42-52	43-53
1-6	41-50	41-51	42-52	43-53	44-54
1-8	42-52	43-53	44-54	45-55	46-56
2	43-53	44-54	46-56	47-57	48-58
2-2	45-55	46-56	47-57	48-58	49-59
2-4	47-57	48-58	49-59	50-60	51-61
2-6	48-58	49-59	50-60	51-65	52-62
2-8	50-60	51-61	52-62	53-63	54-64
	8-18hs	19-32hs	33-54hs	55-96hs	97-124hs
	+2	+4	+6	+8	+10

### 357. Apgar score assessment

Apgar score	If at 1st minute <6 assess at 5th minute			1st minute	5th minute	10th minute	20th minute
	0	1	2				
Heart rate	Absent	<100/min	>100/min				
Respiratory effort	Absent	Slow, irregular	Good, crying				
Muscle tone	flaccid	some flexion of extremities	active motion				
Reflex irritability	no response	Grimace (slight response)	vigorous cry, cough, sneezing etc.				
Colour	Blue, pale	Pink body, extremities pink blue	Completely blue				

Score: Total

- 0-3: Severely depressed (URGENT RESUSCITATION)
- 4-6: Moderately depressed
- -10: Good condition

### 358. Composition of breast milk and daily requirement

Status at delivery	Composition	Post-delivery days				
		3	7	14	21	28
Pre term	Calorie	0.51kcal/ml	0.67	0.72	0.65	0.70
	Protein	0.032gm/ml	0.024	0.021	0.018	0.018
Term	Calorie	0.48	0.60	0.64	0.68	0.69
	Protein	0.022	0.18	0.015	0.015	0.014

#### PROTEIN requirement /24 hrs

- In the first week →1-3 gm/dl/24hrs
- After 7 days →up to 6 gm/dl/24hrs preterm  
every 2 hrs- Time of feeding

#### CALORIE requirement/24 hrs

- In the first week →120kcal/24hrs
- After 7 days →up to 160kcal/24hrs

#### Time of feeding

- Preterm every 2 hrs
- Term every 3 hrs

Example of daily requirement for 28 days old and 4.2Kg

- CALORIE =TBM X 0.7 X 8 x 4.2kg
- $60ml \times 0.7 \times 8 \times 4.2 = 80\text{kcal/day}$ ; which is low. So we have to increase it by 10 to 20ml/day/kg according to their GA and post-natal age
- PROTEIN =TBM X 0.018 X 8 x 4.2kgm.
- $60ml \times 0.018 \times 8 \times 4.2 = 2\text{gms /dl/day}$ . This is also low and we have to increase the amount.

## FREQUENCY OF MONITORING

### 1. Department level Monitoring:

- ❖ **Monthly audits** will be performed on randomly selected cases to evaluate adherence to key performance indicators.
  - ✓ For areas with recurring non-compliance, specific action plans with timelines and responsible personnel will be developed.
  - ✓ The implementation of these plans will be monitored during subsequent audits to ensure progress.

### 2. Quality Unit Monitoring:

- ❖ The hospital's quality unit should perform **quarterly monitoring** of protocol adherence across all departments, utilizing standardized monitoring tools.
  - ✓ Findings from these reviews will be summarized in quarterly reports that highlight trends, successes, and areas requiring improvement.
  - ✓ Any deviations identified during monitoring will be addressed through corrective action plans with timelines and responsible personnel developed collaboratively by the Quality Unit and Department teams.

## STG UTILIZATION MONITORING TOOL FOR NICU

### **Objective:**

To monitor adherence to the Standard Treatment Guidelines (STG) within the neonatal intensive care unit, ensuring appropriate use and timely review of clinical protocols.

Monitoring tool for the **Standard Treatment Guideline (STG) Utilization** related to the clinical practice protocol for selected neonatal cases:

Monitoring Area	Indicator	Compliance Check (Y/N)	Findings	Comments/Action Required
Diagnosis	Diagnostic criteria followed as per STG			
	Correct diagnostic tools and assessments used			
Thermoregulation	Temperature monitored within recommended frequency			
	Thermoregulation interventions used			
Fluid & Electrolyte Management	Fluid requirements calculated as per guideline			
	Electrolyte levels monitored within protocol			
Hypoglycemia Management	Screening for at-risk neonates (RBS)			
	Treatment per guideline dosage and frequency			
Nutrition	Feeding volume and frequency assessed			
	Breastfeeding and supplements given per protocol			
Oxygen Monitoring	Oxygen saturation monitored within guidelines			
	Oxygen therapy provided as recommended			
Respiratory Disorders	Interventions for respiratory distress syndrome (RDS) per STG			

	Interventions for Meconium Aspiration Syndrome (MAS) per STG			
<b>Pain Assessment</b>	Pain assessed/documentated per scoring system			
	Pain relief provided as per recommendations			
<b>Care of the Small Baby</b>	Low birth weight/preterm care per STG			
	Feeding, temperature, and growth monitoring			
<b>Neurological Disorders</b>	Interventions for Perinatal asphyxia (PNA) per STG			
	Interventions for Neonatal Seizures per STG			
<b>Neonatal Sepsis</b>	Sepsis screening and risk assessment per protocol(			
	Antibiotic treatment as per STG			
<b>Hematologic Disorders</b>	Blood Transfusion done for severe anemia per STG			
<b>Jaundice Management</b>	Monitoring and management of bilirubin levels			
<b>Birth Injuries</b>	Screening for birth injuries (Caput succedaneum, Cephalhematoma and Subgaleal haemorrhage (SGH))			
	Interventions based on guideline recommendations			
<b>Parent involvement/engagement</b>	Education provided and Parent engaged in decision making process as per protocol			
<b>Documentation and Record-Keeping</b>	Complete documentation of treatments			
<b>Follow-Up and Outcome Tracking</b>	Consistent follow-up on outcomes			
<b>Infection Prevention Practices</b>	Compliance with infection protocols			



# **DED ER GENERAL HOSPITAL**

**NEONATAL INTENSIVE CARE UNIT (NICU)**

**STANDARD TREATMENT GUIDELINES  
(STG) PROTOCOL**

*“Adapted from National STG 2021 4<sup>th</sup> Edition”*