University Teaching Hospital
Women's and Newborn Hospital &
Lusaka Children's Hospital

Neonatal Intensive Care Unit Protocol

FOREWORD

Neonatal mortality rate (NMR) in Zambia improved marginally following implementation of the Millenium Development Goals (MDG). The Sustainable Development Goals (SDGs) have been introduced with a view to ending preventable neonatal deaths and it prioritizes improving care at birth and care for small and sick newborns, particularly during the first few days after birth.

In order to achieve a reduction in neonatal mortality in high patient flow areas like hospitals, a multi-prong approach is being implemented and this includes investment in specialized equipment, training of specialized manpower and standardising care.

The development of the Zambian Neonatal Protocols and Drug Doses is one of the prongs that has been concluded with a view to standardizing practice in neonatal units in secondary and tertiary level hospitals. The protocols will also provide a basis to achieve best practice and quality standard of care in the neonatal units.

The clinical protocols come in pocket book format for clinicians and an A4 print copy kept on the wards.

Honourable Dr Chitalu Chilufya, MP.
Minister of Health

ACKNOWLEDGMENTS

I wish to thank the team of reviewers headed by Dr Kunda Mutesu-Kapembwa and Dr Yusuf Ahmed who worked diligently and dedicated their efforts towards ensuring that these protocols were reviewed and edited by the listed reviewers in their different capacities.

I also wish to thank the Saving Mothers Giving Life initiative supported by the United States Government and other global partners for finanacially supporting the activities leading to the completion of these protocols.

The Ministry of Health provided the necessary support for concluding works on the protocols.

Dr Jabbin Mulwanda
Permanent Secretary

Adapted from the Cape Town Groote Schuur Neonatal Protocols of 2015.

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IMPORTANT INFORMATION

Please read this carefully before using the booklet.

This booklet is intended as a quick reference guide only. It is beyond the scope of this publication to include all the side effects and handling details . The reader is advised to consult full length formularies whenever prescribing medication for the first time. All doses, normal values and formulae are derived, where possible, from a reputable formulary, textbook or original papers.

North-American recommendations place a greater emphasis on gestational age while British recommendations in the British National Formulary for Children and the BMJ Neonatal Formulary suggest a simpler approach based on the greater contribution of postnatal age and the importance of avoiding under-dosing.

Gestational age scoring is only accurate to ± 2 weeks and despite the trend for greater volumes of distribution and longer elimination times in preterm infants, this is highly variable. The recommendations in this publication follow the simplest regimen to avoid confusion and under-dosing. Some medications are not licensed for use in neonates and the inclusion of drugs in this booklet does not imply approval by the Zambia Medicines Regulatory Authority (ZAMRA). Trade names, if used, are illustrative and do not imply endorsement of a particular drug or product.

Unless otherwise stated, doses and values refer to neonates < 5 weeks old.
Where infusions are described as "in" a certain volume, read "made up to"
Thus, 12 mg/kg"in" 12 ml saline results in a final volume of 12 ml.

NOTICE
The reader is advised to check information in the package insert of each drug and to refer to updated websites: www.uptodate.com and www.neonatalformulary.com. New research and experience may cause rapid changes in recommended treatment.

FORMS
These guidelines are accompanied by supporting forms. These include forms for observation, consent, referral, laboratory, scoring, etc.

Abbreviation	*Term(s)*
µg	Microgram
µmol	Micromol
½ NS	½ normal saline
Aa	Alveolar arterial ratio
ASD	Atrial septal defect
BP	Blood pressure
Bpm	Beats per minutes
BSA	Body surface area
cART	Combination Antiretroviral Therapy
CGA	Corrected gestational age = gestational age at birth + postnatal age in wks
CI	Contraindication
CNS	Central nervous system
Conc	Concentration
CVP	Central venous pressure
D	Day(s)
D10W	10% dextrose water
D5W	5% dextrose water
Dly	Daily
DW	Dextrose water (5 or 10%)
Elem	Elemental
ETT	Endotracheal tube
FeNa	Fractional excretion of sodium
FiO2	Fractional inspired oxygen
GA	Gestational age
GFR	Glomerular filtration rate
GSH	Groote Schuur Hospital
HDN	Haemolytic disease of new born
Hly	Hourly
HR	Heart rate

Abbrevation	*Term(s)*
Hr	Hour
I/T ratio	Immature: total neutrophil ratio
IM	Intramuscular
IV	Intravenous
L	Litre
LAD	Left axis deviation
LAH	Left atrial hypertrophy
LH	Left heart
LVH	Left ventricular hypertrophy
Maint	Maintenance
MAP	Mean arterial pressure
Max	Maximum
MCHC	Mean corpuscular haemoglobin
MCV	Mean corpuscular volume
MDI	Mean dose inhaler
Min	Minutes
Mg	Milligram
Mmol	Millimol
NEB	Nebulizer
Ng	Nanogram
Nmol	Nanomol
NS	Normal saline
PDA	Patent ductus arteriosus
PICC	Peripheral inserted central catheters
PIP	Peak inspiratory pressure
PJP	Pneumocystis jiroverci pneumonia
PO	Per os (by mouth)
Proph	Prophylaxis
Q	Every (qua que)
RAD	Right axis deviation

Abbreviation	*Term(s)*
RAH	Right atrial hypertrophy
Refs	References
RR	Respiratory rate
RSV	Respiratory syncytial virus
Rx	Treatment
SA	South Africa
S-U	Shoulder umbilicus
SC	Subcutaneous
SE	Potential side effects
Soln	Solution
Susp	Suspension
SW	Sterile water for injection
TA	Tricuspid atresia
Tab	Tablet
TAPVD	Total anomalous pulmonary venous drainage
T°	Temperature
UAC	Umbilical arterial catheter
UVC	Umbilical venous catheter
Vit	Vitamin
Wkly	Weekly
ZMW	Zambian Kwacha

ROUTINE CARE

ADMISSION CRITERIA

Babies needing admission to NICU include those with:

- Weight less than 1.8kg
- In respiratory distress
- Temperature greater than 38°C
- Hypoglycaemia unresponsive to feeds
- Macrosomic baby above 4kg
- All Infants of diabetic mums
- Infants with meconium aspiration
- Infants with congenital anomalies
- Asphyxiated babies
- Babies with convulsions
- Babies with Jaundice
- Persistent vomiting
- All infants with a septic risk (PROM >18 hours, maternal UTI etc.)
- Hypothermia (temperature <36°C) unresponsive to warming by radiant warmer/KMC

INFECTION PREVENTION

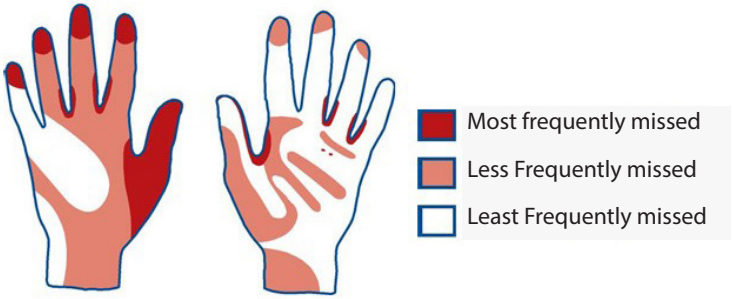
Infection prevention and control is required to prevent transmission of nosocomial or health care associated infections in all neonatal care units.

HAND WASHING

Hand washing is the single most important procedure in infection prevention in any setting.

INFECTION KILLS! Please wash your hands.

The Illustration below shows the areas most commonly missed when we wash our hands



Six Stages of Effective Hand Hygiene

- Take off your outdoor jacket/coat (keep your valuables with you)
- Roll up your sleeves and remove your watch bracelets/rings (except wedding ring)
- Use cold water as this will prevent skin irritation.
- Apply soap and wash your hands, wrists and lower arms
- Rinse your hands thoroughly with clean running water
- Take care not to miss the areas that are easily missed as shown above.
- Dry your hands, wrists and lower arms thoroughly with paper towels provided
- Keep your sleeves rolled up until you leave the unit
- Apply alcohol hand rub before and after touching every baby using the same technique as when washing your hands. Let the spray /rub to dry for a few seconds before handling the baby.
- Wash your hands:
  - ◊ **Every time you enter a ward in which neonates are being nursed,** using the wash basin in the unit
  - ◊ Before and after you touch or handle any infant
  - ◊ Every time you leave the nursery
- Also clean with disinfectant your stethoscope, tape measure, thermometer, phone and ultrasound probe **before and after use.**

Mothers

- **Mothers must wash hands and breasts** before and after breastfeeding or expressing milk
- **Mothers must wash hands** before and after handling baby
- Promote **exclusive breastfeeding**/expressed breast milk to protect baby against infection
- Mothers SHOULD have unrestricted visits

Staff

- **Minimal handling** of babies by staff to avoid unnecessary cross-transfer of infection
- **Consider teaching mothers to feed as this is effective in reducing cross infection**

Public

- **Restricted entry for public** – father, grandparent and family are allowed controlled scheduled visits
- Adults who are infectious are restricted from entering nursery; eg: flu, snotty nose, body rashes, infectious hepatitis
- Retricted entry for people coming from areas of infectious disease outbreak

Intravenous (IV) access Lines

IV access predisposes to infection, use with caution and remove quickly:

- Use Umbilical Venous Catheter (UVC) only where absolutely necessary and peripheral IV drip not possible
- Remove UVC within 7 days or as soon as no longer needed
- IV drips must be removed as early as possible once not needed
- Close monitoring of drip site for signs of infection
- Central Venous Pressure (CVP) lines to be removed within 7-10 days of insertion, monitor closely for signs of infection
- Use aseptic technique when doing invasive procedures and inserting IV line

Incubators

- Sharing incubators predisposes to cross transfer of infection between babies, aim to avoid sharing incubators
- Incubators should be thoroughly cleaned every time a baby is removed and a new baby is to occupy it

Nursery

- Nurseries should be thoroughly cleaned on daily basis with disinfectants.
- Strict scheduled high level disinfection biannual cleaning
- Strict disposal of medical and domestic waste
- Infection prevention posters with short messages to be displayed on the ward
- The unit should have several handwashing points with the six steps handwashing displayed
- The unit should have several alcohol hand rub dispensing points

EXAMINATION OF THE NEWBORN IN POSTNATAL WARD

All newborns must be fully examined within 24 hours of birth and at discharge.

PRE-EXAMINATION **(Use Neonatal Case Record form)**

- Introduce yourself and ask the mother/parents if you may examine their baby.
- Explain the purpose of the examination.
- Check the maternal notes for:
  - ◊ Family history
  - ◊ Booking blood results (HIV, RPR, HBsAg, blood group, blood glucose)
  - ◊ Antitetanus toxoid injections
  - ◊ Antenatal details.
  - ◊ Maternal medical or social problems
  - ◊ Maternal drug history
  - ◊ Antenatal ultrasound results
  - ◊ Details of labour
  - ◊ Risks for infection (PPROM, fever, UTI, GBS, chorioamnionitis, infections of note)

Check neonatal records for:

- Resuscitation details
- Birth weight and gestational age
- Condition of baby since birth (feeding, passed urine and meconium)
- Previous management and follow up plans made

EXAMINATION

Certain observations are made while talking to the mother and while undressing the baby.

Completely undress the baby, ensure that the baby does not become hypothermic.

Examine the following:

- General appearance
- Colour of baby
- Skin lesions
- Heart sounds and murmur
- Palate
- Observe and palpate the abdomen
- Genitalia
- Hips
- Plot anthropometry (weight, length and head circumference)
- Spontaneous activity of infant
- Palpate all pulses
- Patency of the upper airway
- Signs of respiratory distress
- Hernia sites
- Anus (position/patency)
- Spine
- Red reflex in both eyes

Neurological: **Do a Ballard score if premature** *(Form as below and plot on standard growth chart)*

- Head control by pulling to sit
- Moro, grasp and suck reflex
- Truncal control in ventral position
- Palpate anterior fontanelle

NUTRITIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballad Score)

MATURATIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballard Score)

Name _____ Date/Time of birth _____ Sex _____ **SCORE**

Hospital No. _____ Date/Time of exam _____ Birth weight _____ Neuromuscular _____

Race _____ Age when examined _____ Length _____ Physical _____

Apgar score: 1 minute _____ 5 minutes _____ 10 minutes _____ Head circ. _____ Total _____

Examiner _____

Neuromuscular maturity

Neuromuscular maturity sign	Score							Record score here
	–1	0	1	2	3	4	5	
Posture								
Square window (wrist)	 >90°	 90°	 60°	 45°	 30°			
Arm recoil		 180°	 140° to 180°	 110° to 140°	 90° to 110°	 <90°		
Popliteal angle	 180°	 160°	 140°	 120°	 100°	 90°	 <90°	
Scarf sign								
Heel to ear								
							Total neuromuscular maturity score	

Maturity rating

Score	Weeks
–10	20
–5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Source: Gomella TL, Cunningham MD, Eyal FG, Tuttle D: *Neonatology: Management, Procedures, On-Call Problems, Diseases, and Drugs, 6th Edition:* www.accesspediatrics.com

Physical maturity

Physical maturity sign	Score							Record score here
	–1	0	1	2	3	4	5	
Skin	sticky friable transparent	gelatinous red translucent	smooth pink visible veins	superficial peeling &/or rash, few veins	cracking pale areas rare veins	parchment deep cracking no vessels	leathery cracked wrinkled	
Lanugo	none	sparse	abundant	thinning	bald areas	mostly bald		
Plantar surface	heel-toe 40–50 mm: –1 <40 mm: –2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
Breast	imperceptible	barely perceptible	flat areola no bud	stippled areola 1–2 mm bud	raised areola 3–4 mm bud	full areola 5–10 mm bud		
Eye/ear	lids fused loosely: –1 tightly: –2	lids open pinna flat stays folded	sl. curved pinna; soft slow recoil	well curved pinna; soft but ready recoil	formed 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	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large minora small	majora cover clitoris & minora		
							Total physical maturity score	

Gestational age (weeks)

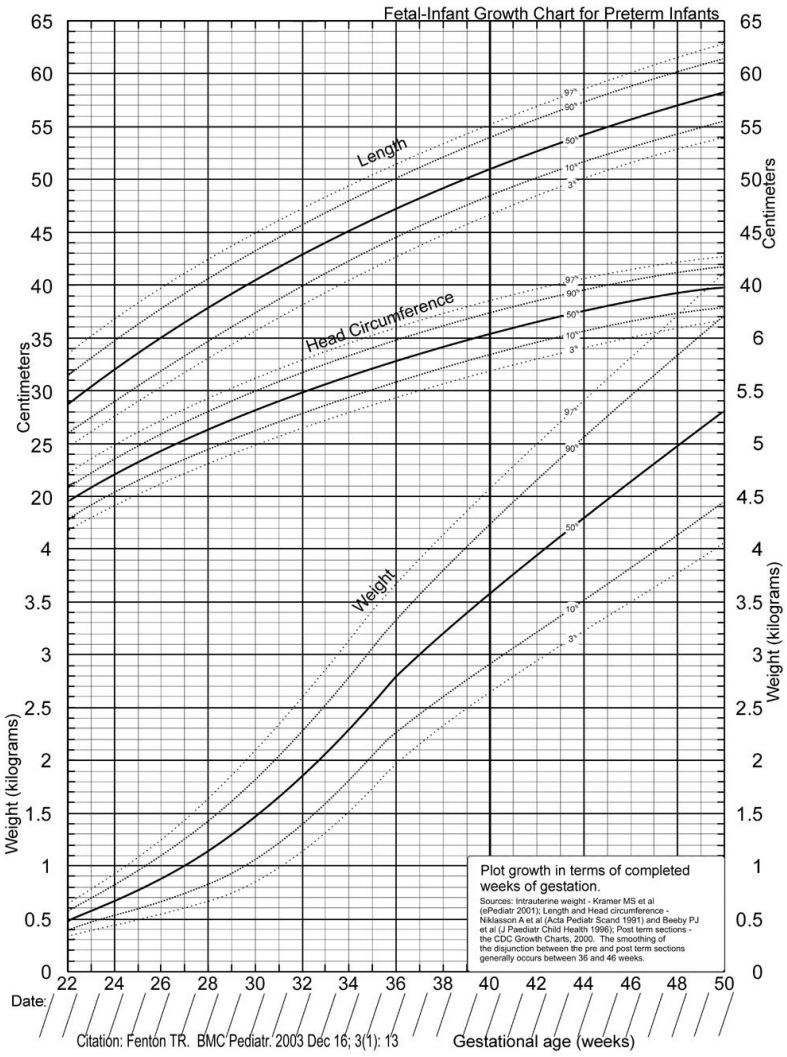
By dates _____

By ultrasound _____

By exam _____

Source: Gomella TL, Cunningham MD, Eyal FG, Tuttle D: *Neonatology: Management, Procedures, On-Call Problems, Diseases, and Drugs, 6th Edition:* www.accesspediatrics.com

FETAL-INFANT GROWTH CHART FOR PRETERM INFANTS



DISCHARGE

- Ensure the baby receives intramuscular vitamin K 1mg
- Give the baby nevirapine syrup if HIV exposed. (see section on HIV Exposed neonates)
- Discharge if there are no clinical problems.
- If a problem is identified, discuss the case with a senior clinician and ensure that a management plan and follow up is instituted.
- Ensure that the breastfeeding technique of the mother is correct and that parents understand how to care for the umbilical stump.
- Tell parents to visit the nearest local clinic when the baby is 3 days old and then at 7 days old. (Ensure that parents understand the follow-up plans; they have all the dates and necessary referral letters)
- Ensure that mother collects a birth record on discharge (mothers whose babies were born alive but died before discharge should receive both the birth record and death certificate on discharge)
- Fill in the Discharge summary form

For neonates discharged within 6 hours:

- Advise parents to seek medical attention if there is a delay in passing urine or meconium beyond 24 hours.
- Give BCG and OPV 0 if available at the hospital. If not, advice the parents to take the baby to the nearest local clinic within 13 days. (also applies for babies born premature)

NEONATAL RESUSCITATION

RECENT MAJOR CHANGES IN RESUSCITATION MANAGEMENT

- Delayed cord clamping of at least 1min for uncompromised infants
  - ◊ confers improved iron status in term infants
  - ◊ Preterm infants require less inotropic support and fewer blood transfusions
  - ◊ Milk the cord 4 times prior to clamping in infants requiring major resuscitation
- Commence resuscitation using room air and use a blender
  - ◊ 100% oxygen confers no advantage over air
  - ◊ Reduced mortality for infant resuscitated in room air
  - ◊ If infant requires chest compressions increase inspired oxygen to 100%

- Use pulse oximeter attached to right hand or wrist to guide use of oxygen to 100%
- Infants < 32 weeks gestation must be placed in a food-grade plastic wrap or bag, without drying, immediately after birth.
- Routine aspiration of meconium is not recommended. (Check management of neonates with Meconium Aspiration Syndrome (MAS)
- If adrenalin is given, the IV route is recommended
- Use capnography in addition to clinical assessment to confirm placement of tracheal tube
- Therapeutic hypothermia offered to newborn infants at term or near term with evolving moderate to severe HIE

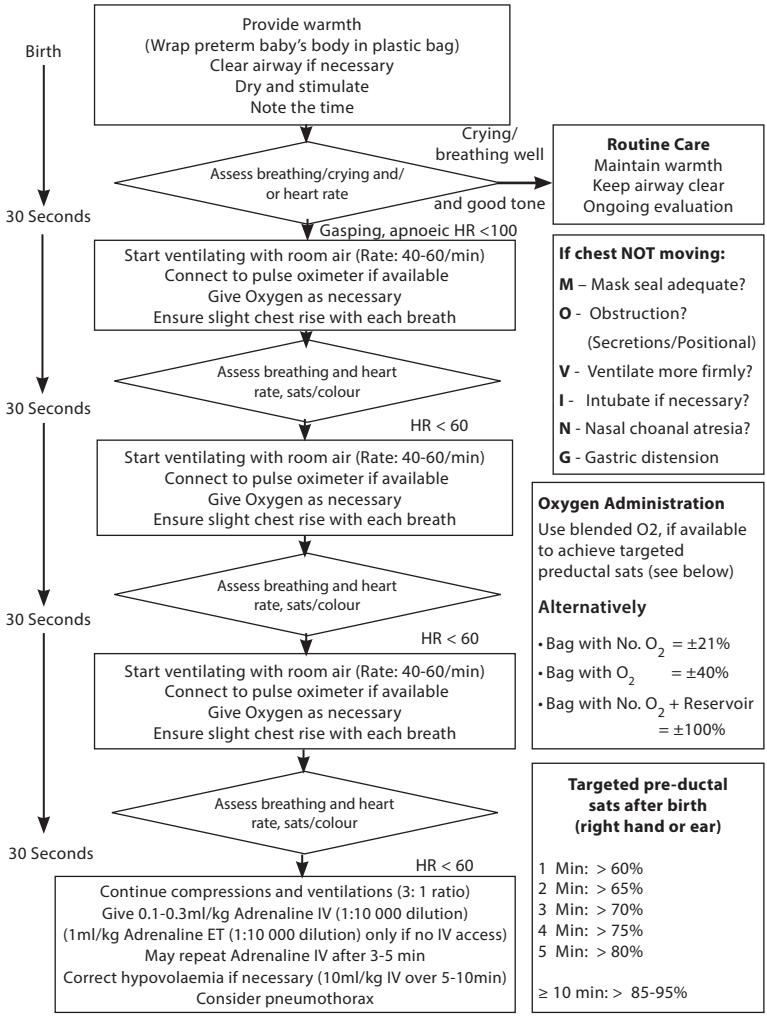
PREPARATION

- Take a detailed history; ask specifically about antepartum and intrapartum risk factors
- Prepare and check equipment

RESUSCITATION

- See resuscitation algorithm
- Start the stopwatch at the time the infant is placed on the resuscitaire
- The most effective step in neonatal resuscitation is ventilating the lungs
- Use oxygen sparingly and blend
- Adapt inflation time to achieve good chest movement
- Use a T-Piece/Neopuff® device if possible
- Avoid overheating in term infants post resuscitation
- Stop resuscitating if no heart beat after 10 minutes
- DO NOT use fluid bolus, naloxone and bicarbonate routinely

NEWBORN RESUSCITATION ALGORITHM



(The algorithm follows the assumption that the previous step was unsuccessful and the newborn is deteriorating)

NEONATAL THERMOREGULATION

Neonates require a stable thermo-neutral environment for optimum metabolism and oxygen demand. Extended periods of cold stress are harmful and detrimental to survival and long-term outcome.

GENERAL INTERVENTIONS

Maintain a set environmental temperature of > 26ºC. Heat exchange can occur by:

- **Conduction:** Prewarm and cover equipment and surfaces
- **Convection:** Avoid draughts and window, maintain 'minimal handling', Use portholes for access and keep radiant heater sides up
- **Radiation:** Avoid incubator walls and direct sunlight, use curtains and covers over the incubator
- **Evaporation:** keep infant skin and bed dry

EARLY THERMAL MANAGEMENT OF THE VLBW INFANT

- All infants should be received into a clean, dry pre-warmed towel
- Infants less than 30 weeks GA or 1200g weight should be placed into a plastic bag up to neck. Cover the head but not the face. DO NOT DRY THESE INFANTS
- Continue to resuscitate with the infant in the plastic bag. Cut holes in bag for limb or umbilical vascular access if needed. Weigh the infant inside plastic bag.
- Keep infant in bag during transfer to neonatal unit. Remove plastic bag once stablilised in the NICU in an incubator
- Document temperature on arrival in NICU and after 1 hour

TRANSFER OF NEONATE

Transfer for procedures or investigations should occur in infant incubators, and remain turned on during the procedure, awaiting their return to the NICU. The neonate's temperature must continue to be monitored during transfers and procedures.

CHOICE OF ENVIRONMENT

Incubator

Any neonate less than 1.5kg should be nursed within an enclosed incubator and should be nested

There are 2 types of incubator temperature control:

1. **Servo-controlled skin probe:** The incubator temperature is servo-controlled to maintain a desired set infant temperature. Avoid placing skin probe on bony prominences and excoriated areas.
2. **Air temperature mode:** The incubator temperature is initially set according to birth weight and postnatal age. Adjust according to measured infant temperature. (See table below). Hypothermic infants may need the incubator temperature raised by 0.5°C every half-to one hour until normothermic.

		Birth weight and temperature range			
		1-1.2kg +/- 0.5°C	1.2-1.5kg +/- 0.5°C	1.5-2.5kg +/- 1.0°C	>2.5kg & 36/40 +/- 1.5°C
Age	0-12 hours	35.0	34	33.3	32.8
	12-24 hours	34.5	33.8	32.8	32.4
	24-96 hours	34.5	33.5	32.3	32.0
	4-14 days	33.5	33.5	32.1	32.0
	2-3 weeks	33.1	33.1	31.7	30.0
	3-4 weeks	32.6	3206	31.4	
	4-5 weeks	32.0	32.0	30.9	
	5-6 weeks	31.4	31.4	30.4	

Radiant warmer bed

Thin, transparent plastic barrier (e.g. cling-wrap) may be used to increase the local humidity and limit air movement, by being fixed to the supporting walls of the radiant warmer in order to create a micro-environment around the baby. These plastic barriers can reduce the insensible water losses by 50-70%.

Open cot

A well neonate who weighs between 1.5 – 1.8kg, may be transferred to a cot depending on ambient room temperature. Ideal ambient temperature is 26-28°C. Neonates should be covered or wrapped in blankets and should wear a hat. Axilla temperature should be checked within 1-2 hours and then be checked 3-4 hourly for the first 24 hours. Space between cots should be 1-3 meters for infection prevention.

Kangaroo care

In Kangaroo care, the baby wears only a small diaper and a hat and is placed in a flexed position between the breasts. The parent should wear a shirt or hospital gown with an opening to the front and a blanket over the wrap for the baby.

HEAT STRESS

The signs and associated problems of heat stress are: Temperature above 37.3ºC and rising, tachycardia, tachypnoea, restlessness, dehydration. The commonest cause of hyperthermia is a dislodged temperature probe.

MANAGEMENT

- Check probe position and environment temperature
- Confirm reading with manual axilla temperature
- Remove external heat sources eg blankets, swaddling and leave the neonate in an extended position to encourage heat loss
- If the cause is not environmental consider infection as a cause of the pyrexia

POSITIONING FOR THE PRETERM OR SICK NEONATE IN NICU

Aims: The preterm or sick infant requires support to facilitate and maintain postures that enhance motor control and physiological functioning and reduce stress.

The developmental goals of positioning are:

- To provide flexion in the limbs and trunk and the facilitation of midline skills.
- To assist the infant in self-regulation and maximize infant stability.
- To preserve energy and promote growth.
- To promote CNS organization

Considerations for positioning

Respiratory needs

- The position should optimise the infant's ability to breathe independently.
- Infants with increased respiratory demands may be more stable in prone.
  - ◊ Prone position provides improved respiration and greater chest wall synchrony and improved gas exchange.
  - ◊ The prone position is thought to help by stabilizing the chest wall and may also reduce extra movement which may compromise the respiratory system.
  - ◊ The prone position may also reduce apnoeas in more mature infants with a history of regular apnoeic episodes.

Posture

- Preterm infants are hypotonic (floppy) less than 28 weeks then start to develop hypertonia (increased resistance) around 30 weeks.
- The use of high boundaries in nesting provides the baby containment and facilitates midline movements (e.g. hands to face).
- This can impact on future gross motor development. When positioning in prone and supine ensure the neck is not in extreme rotation. Movements of preterm infants can be jerky and abrupt initially.

Infant self-regulation

- **Boundaries of nest** need to be high enough to contain the legs and close enough that the baby can brace his feet against it.

Infant stress

- Stress should be minimized by positioning the infant to maximize comfort and enable the infant to self soothe e.g. hands to midline, boundaries close enough for the infant to reach with feet.

Energy conservation and Heat conservation:

- **Prone position can also increase time asleep and decrease energy expenditure compared to supine.**
- The surface area is greatest in supine and therefore greater heat loss.
- Use of nesting with high boundaries can also help reduce heat loss.
- Nesting and ambient heating can be adjusted to achieve both comfort and warmth.

Head shape

- Preterm infants have very soft skulls and time spent too long in one position may result in narrowing of the head or asymmetry of head shape.
- It is important to vary the head position both when prone, side lying or supine.

Skin integrity

The preterm infant requires regular position changes to maintain skin integrity.

Sudden Infant Death Syndrome (SIDS)

- It is widely accepted that sleeping a baby on its back at home reduces the risk of sudden infant death syndrome.
- While the infant is monitored and breathing and self-regulation is more important it is safe to sleep the infant on its side or stomach.
- All infants who are not being monitored should sleep on their back in the nursery unless directed by the clinician.
- Education to parents about the needs of their baby and their progression of positions should be explained.

Attachments and Lines

Care should be taken to ensure attachments and lines are appropriately positioned to ensure function and appropriately visible.

VACCINATION OF THE PRETERM INFANT

- The preterm infants are at higher risk of vaccine-preventable diseases such as Pertusis, H. influenza and Pneumococcal disease. All international guidelines recommend vaccination at chronological and NOT corrected age.
- Studies show that most preterm infants produce antibodies at chronological age even if this is slightly lower than their term counterparts.

  However, the smallest and the sickest infants may not produce sufficient antibodies for some of the less immunogenic strains of vaccines.
- Side effects such as fever and skin reactions are not worse than term infants.
- Pertusis has been implicated in causing apnoea in the preterm infant BUT this is NOT the case for the acellular Pertussis (aP)
- Whole cell (wPertussis) is used in Zambia. It is known to be more effective in neonates

RECOMMENDATIONS FOR PRETERM INFANTS

- BCG- defer until discharge of the infant
- All other vaccinations starting at age 6 weeks to be administered at the chronological age as per EPI schedule
- If infant is acutely unwell, defer vaccinations until recovered
- **NB;** ***clinics are often reluctant to give vaccinations to small infants so parental education and a letter to the clinic explaining the importance and safety of the vaccines is important***

EXPANDED PROGRAM OF IMMUNISATION (ZAMBIAN) SCHEDULE

Birth:	OPV (0)	BCG	
6 weeks:	OPV (1)	RV (1)	DPT/Hib (1)
	HepB (1)	PCV (1)	
10 weeks:	OPV(2)	DPT - HepB (2) Hib (2)	RV (2)
14 weeks:	OPV (3)	DPT - HepB (3) - Hib (3)	PCV(2)
9 months:	Measles (1)	PCV (3)	OPV 4 (If OPV (0) was missed)
18 months:	Measles (2)	DPT	
9 years:	HPV (girl)		

OPV. Oral Polio Vaccine (drops by mouth);
BCG. Bacille Calmette Guerin Vaccine (intradermal R arm);
RV. Rotavirus Vaccine;
HepB. Hepatitis B Vaccine (IM R thigh)
DPT/Hib: (Pentavalent): Diphtheria, Tetanus, Pertussis/ H. Influenza type B (IM L thigh);
PCV. Pneumococcal Conjugated Vaccine (IM R thigh)
HPV. Human Papillomavirus vaccine

HEAD ULTRASOUND SCREENING GUIDELINES

International guidelines vary.

The following indications for head scans in neonates are generally accepted.

- Congenital malformations where CNS involvement is possible.
- Seizure or other suggestive abnormal neurological signs.
- Sepsis
- Repeated apnoea /bradycardia
- Large/sudden decrease in Hb
- Abnormal head growth
- Preterm infants ≤32 weeks gestation/< 1 500 g at birth the following times:
  - ◊ Before day 3 of life: do as soon as possible if intubation, but consider delayed scan if on NCPAP
  - ◊ At age 3-5 weeks
  - ◊ At discharge or 40 weeks cGA, whichever comes first

Most frequent scanning will yield more lesions but cost effectiveness and patient benefit as not been established.

DISCHARGE CHECKLIST

1. **Head circumferance:** All infants must have head Circumferance measurement before discharge
2. **Growth chart complete**
3. **Immunisations.** Baby should be referred to the nearest local clinic to receive BCG, polio vaccine and other subsequent immunisations. Only exception in TB exposed infants on INH prophylaxis BCG deferred for 3 months.
4. **Discharge Summary:** Must be written with problem list and relevant follow up appointments documented.
5. **HIV-exposed infants.** Must have a date for follow up or PCR testing. If different from the 6 weeks follow up dates.
   Also:
   - Feeding choice clearly documented
   - PCR result if tested in the Nursery before discharge (Take note that DNA PCR to be done at birth in New 2016 Guidelines)
   - Separate PMTCT discharge letter to be completed if applicable
   - NVP/AZT given(refer to section on HIV exposed neonates)
6. **Socio-economic support reviewed where indicated**
7. **Kangaroo Mother Care (KMC) established if indicated**
8. **All other appointments documents**

KANGAROO MOTHER CARE (KMC) GUIDELINES

BACKGROUND

- The concepts and benefits of KMC, including breastfeeding, should be explained to the mother as soon as the baby is admitted to the nursery
- Intermittent KMC should be started by all mothers as soon as possible, including those in NICU
- Intermittent KMC sessions of at least 1-hour duration are encouraged
- Weight, oxygen therapy and phototherapy are not contraindications to KMC, provided that the infant is stable

KMC WARD ADMISSION CRITERIA

- The baby should be off oxygen
- Should be on a total fluid intake (TFI) of at least 120ml/kg/day
- Should be at least 1 to 1.5kg but discretion can be used depending on the stability of the baby and reliability of the mother (can be discussed with senior clinician)

MONITORING DURING KMC

Check if the infants':

- Neck position is neutral
- Airway is clear
- Breathing is regular
- Colour is pink
- Temperature is being maintained

DISCHARGE CRITERIA

See predischarge readiness scoring sheet
A total score of 20/20 should be achieved for breastfeeding mothers before discharge
Consider circumstances at home. If difficult social circumstances, be more conservative in discharge weight and don't discharge too early. Also applicable to teenage mothers
If criteria are met, an infant can be discharged if weight is ≥1500g
Some infants may be discharged at lower weight, in discussion with the senior clinician

PREDISCHARGE READINESS SCORING SHEET

KMC Daily Score Sheet **Based on the Intra-hospital KMC training Programme in Bogota, Colombia**				Date	Date	Date
Name: Date of birth…../…./…		Breastfeeding:		Day 1	Day 2	Day 3
Hospital number …..		Formula:		Kg	Kg	Kg
Evaluation	Score					
	0	1	2			
Socio-economic support	No help or support	Occasional help	Good Support System			
Mother's milk production (Must score before discharge. N/A for formula Feeding)	Expresses 0-10 ml breast milk	Expresses 0-20ml breast milk	Expresses 20-30ml breast milk			
Positioning and attaching of the baby on the breast (Not applicable for formula feeding)	Always needs assistance	Occasionally needs assistance	No assistance needed			
Baby's ability to suckle at the breast/cup feeds	Gets tired very quickly	Gets tired infrequently	Takes all feeds well			
Confidence in handling baby, i.e. feeding, bathing, changing	Always needs assistance	Occasionally needs assistance	No assistance needed			
Baby's weight gain per day(must score1 or 2 before discharge)	0-10g	10-20g	20-30g			
Confidence in administering vitamins and iron drops	No confidence	Some confidence	Fully confident			
Knowledge of KMC	No knowledge	Some knowledge	Knowledgeable			
Acceptance and application of KMC	Dose not accept or apply KMC	Partly accepts and applies KMC method	Applies KMC without having to be told			
Confidence in caring for baby at home	Does not feel sure or able	Feels slightly unsure and unable	Feels confident			
TOTAL SCORE per day **Ready for discharge:** **Breastfeeding; If mother and baby score >19** **Formula feeding: if mother and baby score >15**						

DEATH AND BEREAVEMENT GUIDELINES

THE DYING BABY

- A senior clinician, preferably somebody who has been involved with treatment, should counsel parents
- If care is being withdrawn, it is acceptable (within reason) to wait until close family members have has a chance to say goodbye
- Ensure that the baby is not suffering by using appropriate analgesics (opiates). This is a very important aspect, which the parents remember
- Spiritual support should be enabled. This may include baptism/blessing
- Photographs should be encouraged. If the family do not have any photographs, arrange for a photograph to be taken or take one with a camera phone, which can be printed out
- Hand/footprints of the baby can also be done
- Use screens to give privacy to the family
- Some parents prefer to hold their baby for the last few minutes whilst other prefer to leave them on the ventilator
- Be aware that parents of other babies in the unit will also be affected.
- Non viable baby birth policy
- Do not resuscitate policy

AFTER THE BABY HAS DIED

1. Certify the baby's death in the notes. Note time and date
2. Write the death summary
3. If the parents are not present, ask them to come in but try not break the news of the death over the phone
4. Counsel parents in a private space/counseling room

GUIDELINES FOR COUNSELING:

- know the baby's name and gender
- Have a nursing sister present
- Get to the point straight away
- Do not use euphemisms –say your baby has died
- Emphasize the lack of suffering (If this is true)
- Emphasize it is not their fault
- Parents will remember very little – avoid lengthy details
- Allow parents as much time with the baby as they need
- Refer to the social worker/bereavement counsellors if required
- Offer follow-up counseling with the medical team and provide a phone number should they initially decline this.

FORMS

1. Death certificate (also called Notice of Death Form -Medical certificate of cause of death): A doctor needs to complete the form as soon as possible (except in non-viable cases). Indicate in the notes this has been done.
2. Deceased neonate is transferred to mortuary with a death card
3. A cremation form should only be filled in when requested

PROCEDURE FOR REQUESTING A POST MORTEM

1. Discuss with the consultant if necessary before speaking to the next of kin if a post mortem (PM) is considered.
2. Explain the need for the post-mortem to the next of kin.
3. Obtain consent by letting the next of kin fill in the Consent Form (MOH/NEO/001) and signing by signature or thumb print.
   NB: Attach a copy of the consent form to the post mortem request form.
4. After obtaining consent, fill in the Perinatal/Neonatal Post Mortem Request Form (MOH/NEO/004)
5. Advise the next of kin to pay for the post mortem as required. Each institution usually has their own procedures of payments for post-mortem.
6. If the death takes place after hours or during weekends and the paediatrician has deemed a post mortem is necessary, obtain consent for the PM as described above. Handover to staff in the next shift.

   NB: Urgent PM's can be arranged if burial must take place the same/next day due to religious reasons or other extenuating circumstaces.
   Although post mortem provisional results are usually available within seven (7) days, the final results may take up to **six weeks.**
7. Arrange a follow-up visit with the next of kin.

FORENSIC CASES

The following could be considered forensic cases:

- Any death due to deliberate or accidental physical or chemical influence, direct or indirect, or related complications, including accidental errors e.g. incorrect medications or air embolus from intravenous therapy;
- Death related to anaesthaesia or any clinical procedure;
- Where the death is sudden and unexpected, or unexplained; e.g – KMC or home in a baby who was totally well with no symptoms/signs of disease.
- All other deaths deemed unnatural.

Discuss all possible cases with the paediatrician/ neonatal consultant and the (forensic) pathologist on call.

IF the pathologist decides that a medico-legal/ forensic autopsy should be conducted, THEN:

1. Do NOT complete the death certificate.
2. Inform the medical superintendent through established channels of communication.
3. The medical superintendent is responsible for notifying the police who then notify the coroner.
4. The police will need to be notified, a case opened and a case number be assigned
5. The Forensic mortuary must be notified so that they can collect the body
6. Documentation required – a Coroner's Form 2 (available via the Police) with the hospital folder/notes if the infant died in hospital or a detailed referral letter with all
7. Relevant history + copy of RTHC chart if possible.
8. If the forensic pathologist does not think a medico-legal autopsy is needed, then try and get a Clinical post-mortem. Not all SIDS babies will need a medico-legal autopsy but let the pathologist decide.

REQUESTING FOR A PLACENTA EXAMINATION

Fill in the Placenta Examination Request Form (MOH/NEO/003).
The following are indications for requesting a placental examination:

IUGR (birth weight below 2.5 kg or 3rd centile	Maternal pyrexia	2 vessel cord etc.	PROM (more than 36 hours)
Abruption	Fetal hydrops	Abnormal placenta shape	Gestational diabetes
Morbidly adherent placenta	Isoimmunisation – Rh / ABO / Kell / Other	Pre-eclampsia (uncomplicated)	Maternal Gp B Streptococcus
Prematurity (>28 weeks)	Stillbirth – antepartum / intrapartum	Foetal abnormality (specify when sending request to the laboratory.)	Severe fetal distress (requiring admission to NNU)
RPR reactive	Other (must specify)		

QUICK REFERENCE GUIDE TO FORMS

All Deaths

- Certify in the case notes
- Medical certificate of cause of death certificate (except for forensic cases)
- Neonatal Death summary
- Social Worker referral if required
- Cremation Form (MOH/NEO/012)

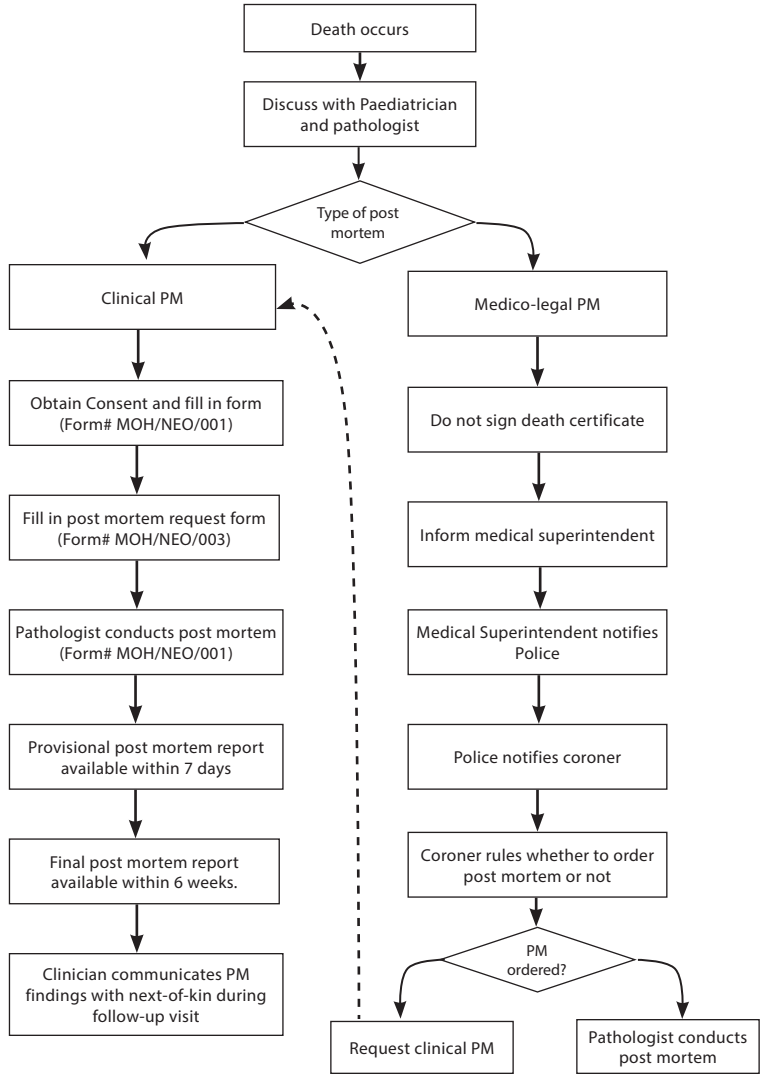
POST MORTEM

- Consent Form for Perinatal/Neonatal Post Mortem (MOH/NEO/009)
- Placenta Examination Request Form (MOH/NEO/010)
- Perinatal/Neonatal Post Mortem Form (MOH/NEO/011)

FORENSIC /MEDICO-LEGAL

- Coroner's Form 2 (Available from Inquests Act CAP 36 of the Laws of Zambia)

ALGORITHM FOR REQUESTING A POST MORTEM



RETINOPATHY OF PREMATURITY SCREENING

ROP screening can be a potentially stressful examination in preterm infants. Efforts should be made to limit the effects of screening. A trained paediatric ophthalmologist should perform the examination. Infants being screened should be monitored for 1-hour post instillation of eye drops for side effects from systemic absorption of cyclopentolate or phenylephrine. Common adverse effects: vasoconstriction, tachycardia, increased blood pressure, apnoea and feed intolerance.

SCREENING CRITERIA:

- All infants with a GA<30 weeks or birth weight<1251gm-this may differ in other neonatal units
- Book infant in ROP diary-to be screened at 4-weeks chronological age
  - ◊ Write the date for screening on the front of the infant record chart
  - ◊ Provide parents with information leaflet
  - ◊ The ophthalmologist must be provided with a list (in order of screening) before the start of the screening session

PROCEDURE

- Ensure that the infant is fit for examination. Ill infants must be rebooked for the week
- The patient must be monitored via pulse oximetry
- Administer cyclopentolate eye drops 1 per eye (max 3 drops), at 15-20 minute intervals starting at least 45 minutes prior to examination until pupils are dilated
- The nasolacrimal duct can be occluded when drops are instilled-this may limit systematic absorption
- Dim the lights to minimize discomfort for the infant after drops have been instilled
- Check for adequate pupillary dilation prior to inserting second/third drops
- Poor or failed pupillary dilation may be an indication of severe ROP
- Benoxinate hydrochloride 0.4% eye drop (local anaesthetic) must be instilled with the last cyclopentolate eye administration
- Swaddle infant during the procedure and place in nest
- Assist ophthalmologist with positioning as required
- Record findings in the infant's notes
- Document follow up date on the infant record chart and in the ROP diary

FLUID AND ELECTROLYTE MANAGEMENT IN PRETERM NEONATES

BACKGROUND

The expected early postnatal weight loss is higher in preterm infants. Preterm infants may lose up to 15% of their body weight.
Hyaline membrane disease may be associated with a delayed postnatal diuresis.
Transdermal water losses are high in very preterm infants.

MANAGEMENT

- All infants < 30 weeks GA/ < 1200 g must be placed into a plastic bag at delivery without drying and the face exposed.
- Monitor the infant's weight daily
- Cover all infants < 30 weeks/ < 1200g and under a radiant heater with clear plastic.

Initiate fluids as below:

	Fluids	D1 (ml/kg/d)	Glucose mg/kg/min
<1000	5% DW	90	3.2
1000g – 1199g	10% Dextrose	80	5.6
1200-1499g	10% Dextrose	70	4.2
> 1500g	10% Dextrose	60	4.2

Note; Neonatolyte (NNL) 10% is the preferred fluid instead of Dextrose 10%

- Maintain glucose 2.6 -7 mmol/l
- If ELBW infant becomes hypoglycaemic, give bolus D10% 3mls/kg then change fluids to 10%NNL/Dextrose
- Increase total fluid intake daily in increments of 10-20 ml/kg/d, dependent on the urinary output, weight and serum sodium (see below)
- After 36-48 hours, change 5% DW to either ¼ strength Darrow's solution in 10% dextrose (or 5% paediatric maintenance solution or 10% Neonatalyte), depending on the blood glucose

NB: *5% dw is suitable for elbw infant because it has low solute load which can easily be handled by the immature kidneys*

MONITOR

Urine output

- > 6 wet nappies indicate good urinary output
- Sicker infants need urine output quantified:
  - ◊ Aim for a minimum urine output of 0.5-1 ml/kg/hr

Sodium

- A useful indicator of hydration status in the first few days of life. A rising sodium indicates dehydration and a falling one indicates over hydration
- Aim to maintain serum [Na] between 135-145mmol/l

Weight

- Excessive changes in weight may reflect rapid changes in fluids status
- Weight loss > 10% of birth weight is of concern

Thermal Energy requirements

Full term infant: 60-80kcal/kg/d in the first week of life and thereafter 80-120kcal/kg/day

Pre-terms: 50-90kcal/kg/day in the first week of life and thereafter 100-150kcal/kg/day

ENTERAL FEEDING

Breast milk feeding must be encouraged for all infants. Donor breast milk is preferable to formula for preterm infants unable to access mother's own breast milk. Fluid and enteral intake prescriptions should be indvidualised for sick infants and infants with risk factors or feed intolerance.

≥ 1 500 G AND ≥ 32 WEEKS

- In the absence of mother's own milk, consider preterm formula
- Start on bolus feeds 2 -3 hourly at 60ml/kg on day 1
- Increase to 75, 100, 125, 150ml/kg/d from D2-D5 as feeds are tolerated

< 1 500 G OR 32 WEEKS

- Start with bolus tube feeds (expressed breast milk (EBM))
- Orogastric tubes are preferable to nasogastric tube
- Start milk on D1 at 12-24 ml/kg/d
- Increase feeds daily by 24 ml/kg/day
- Consider continuous feeds if prolonged significant feeding intolerance – discuss with senior clinician.
- Syringes should be changed every 4 hours for all feeds given via a syringe driver
- Continue until a rate of 10ml/hr or 1 200 g is achieved before challenging 2-hourly bolus feeds
- Stop supplemental IV fluids when an enteral intake of 150 ml/kg/day is achieved (consider individual baby tolerance)
- Increase enteral volume incrementally to 180-200 ml/kg/day
- Add supplements and breast milk fortifier according to guidelines
- The feeding tube must be changed weekly and the administration set three times a week
- Initiate TPN for confirmed prolonged feeding intolerance > 3 days and for confirmed cases of NEC (See TPN Protocol)

HIGH RISK PATIENTS

In the presence of the following risk factors, feeds should be initiated more cautiously in discussion with a senior clinician:

- Neonatal encephalopathy
- Preterm and metabolic acidosis at birth
- Cardiorespiratory instability

CRITERIA FOR NIL PER ORAL (NPO)

- Tense abdominal distension
- Erythema of the abdominal wall
- Decreased bowel sounds
- Gross or occult blood in the stools
- Abdominal tenderness
- Heavy bile stained nasogastric aspirate
- Pneumatosis intestinal on abdominal X-ray
- Vomits after two consecutive feeds with the feeding tube in the correct position

PRETERM SUPPLEMENTS AND PROBIOTICS

1,500G TO 2,500G

Low birth weight infants on feeds at 150ml/kg or more should be given the following for 6 months:

- Multivit 0.6 ml PO daily
- Iron/ferrodrops 0.6 ml (2 to 3mg/kg/day) PO from 28 days or on discharge (whichever occurs first)

< 1500 G

- Add human milk fortifier (e.g FM85) to breast milk 24 hours after 150 ml/kg/day of enteral feeds are achieved
- Initially add 0.5g FM85 per 20ml EBM, followed by 1 g per 20ml EBM from the next day
- Introduce Multivit 0.3 ml PO daily from 48 hours after establishing full feeds
- Ferrodrops 0.2 ml from 28 days of life or discharge (whichever occurs first)
- Continue multivit and Ferrodrops for 6 months. Increase dose once infant > 1.5kg.

Routine sodium and phosphate supplementation is not indicated – appropriately fortified breast milk and preterm formula at 180ml/kg/day will provide adequate daily amounts of most of the nutritional components.

MONITORING AND THE NEED FOR INDIVIDALISED SUPPLEMENTATION

- Phosphate and ALP levels should routinely be monitored 3 weekly in VLBW – see "Metabolic Bone Disease" protocol
- Monitor serum sodium every 3 weeks and supplement if < 130 mmol/l
- Supplement with 0.5 ml 5% NaCl PO 8 hourly, titrate according to severity

PROBIOTICS

2014 Cochrane Review: Enteral supplementation of probiotics prevents severe NEC and all cause mortality in preterm infants. A combination of Lactobacillus and Bifidobacterium species is preferable – Lactobacillus alone can also be used.

INDICATIONS

- ≤ 32 weeks gestational age or ≤ 1 500g birth weight
- Initiate 24 hours after commencing oral feeds
- Indications to stop
  - ◊ NPO > 3 days
  - ◊ Diarrhoea > 3 days
  - ◊ Positive blood culture containing probiotics strains

DOSE

Start with half dose until infant is tolerating 60 ml/kg/day enteral feeds.

Commence with full dose thereafter. Continue until infant reaches weight of 1 500g.

- **Half dose:** 0.1 ml/once daily (2-3 drops)
- Should contain less than < 1.5 x 109 CFU per day
- **Full dose:** 0.2 ml (5 drops)
- Should contain less than 3 x 109 CFU per day
- Administration: Give directly in the mouth. Probiotic drops contain sunflower and MCT oils – substantial losses of CFUs may occur with feeding tube administration.

TOTAL PARENTERAL NUTRITION (TPN)

Total Parenteral Nutrition (TPN) aims to provide nutritional requirements for optimal growth and maturation of the infant. It is a substitute for enteral feeding in circumstances where the establishment of full enteral feeds will be delayed or inadequate. However, the preferred for of nutrition for the neonate remains breast milk.

INDICATIONS FOR TPN

- Prolonged feeding intolerance > 3 days
- Necrotising enterocolitis (NEC)
- Gastrointestinal tract anomalies
- Chylothorax (Failed MCT diet)

COMPLICATIONS

The primary complications of parenteral nutrition are cholestasis and those related to infusion catheter.

Catheter/Venous access options

- **Umbilical venous catheter (UVC)** usage reduces line insertion attempts and does not increase the risk of infection or NEC when compared with PICC lines
- **Peripheral inserted central catheters (PICC lines)** should be used in neonates receiving prolonged TPN > 5 days
- **Peripheral IV cannula:** TPN may be administered via a peripheral line for short term (< 5 days). Phlebitis is a known complication. All venous access sites should be inspected regularly for tissues infiltration or infection.

PRESCRIBING TPN

- Discuss all cases with senior clinician and dietician.
- Order TPN using the codes for specific formulations (see recommended TPN regimes from manufacturer e.g. Fresenius – Kabi)
- Prescribe total TPN volume, concentration and the rate of infusion on the fluid prescription chart
- The maximum volume of TPN is usually 150 ml/kg/24 hours.
- Order ITNBABY 102 (150ml) or ITNBABY 103 (235 ml) depending on the volume required
- If the infant becomes hyperglycaemic order ITNBABY 105 (7% dextrose; lipid-containing formulation; 150 ml bag)
- Avoid using ITNBABY 100 (5% dextrose; lipid free formulation)

ESTABLISHING FULL TPN

There is no evidence that early versus late introduction of lipid changes neonatal outcomes. There is also no evidence that a gradual increment in the infusion rate of lipid improves fat tolerance. Maximal lipid intake in parenteral nutrition should be limited to a maximum of 3-4 g/kg/day. A maximum volume of 150 ml/kg/24 hours of standardized TPN will prevent excessive lipid intake. Babies can be started on full TPN.

Administration and storage

- TPN must be kept refrigerated at 2-8ºC
- Administer TPN 1 hour after removal from refrigerator
- The TPN bag should be gently agitated and rubbed between the hands prior to administration to redistribute any creaming which may have occurred
- Protect TPN from direct sunlight or phototherapy lights
- A new administration set must be used each time a new bag of TPN is to be infused
- It is recommended that TPN should be administered through a terminal 1.2 micron "in-line" filter
- No additions may be made to the TPN bag
- Adherence to aseptic technique is essential

Duration of infusion:

- TPN should be infused over 24 hours
- Stop TPN when the patient is tolerating 120 ml/kg as enteral feeds
- Remove all central lines ASAP – do no send catheter tips for MCS

Routine TPN monitoring

- Do regular blood glucose levels
- Discuss the need for further blood tests with the senior clinician after 5-7 days of TPN- prolonged TPN administration requires careful clinical and laboratory monitoring.
- In addition to routine observations the following are required for prolonged TPN use:
  - ◊ Weekly: LFTS, ALP, albumin, bilirubin and FBC
  - ◊ UEC, ABG, Ca, Mg, PO4

Hyperglycaemia (while on TPN)

1. If glucose > 10 mmol/l assess infant for a possible underlying cause e.g sepsis, excess intake, corticosteroids or other drugs
2. If glucose persist > 10 mmol/l change to 7% dextrose TPN. If 7% dextrose TPN not available, then decrease the volume of TPN and replace appropriately with an infusion containing 5% dextrose. Plan to return to standard TPN by 48 hours. The goal is short-term treatment of hyperglycaemia.
3. If glucose persists > 10 mmol/l on 7% dextrose TPN or after 48 hours if unable to return to TPN with 10% dextrose then consider insulin infusion. Change back to 10% dextrose TPN- the goal is now improved growth.

IV FLUID CONSTITUENTS

	Na	K	Cl	Ca	Mg	Lactate	HPO4	Dextrose	KJ/L	Osmolarity
	mmol/L(g/L)							g/dl		(mosmol/L)
5% Dextrose Water (DW)	0	0	0	0	0	0	0	55	880	278
5% DW + 0.2% NaCl	34	0	34	0	0	0	0	55	880	346
Neonatalyte (Sabax) in 10% DW	20	15	21	2.5	0.5	20	3.75	110	1760	645
Potassium Free Neonatalyte (Sabax) in 10% DW	33	0	33	5	0	0	0	110	1760	627
Paediatric Maintenance Solution in 5% DW	35	12	47	0	0	0	0	55	880	372
½ Darrows in 5% DW	61	17	51	0	0	27	0	55	880	434
5% DW in 0.45% Saline	77	0	77	0	0	0	0	55	880	406
0.9 % Saline	154	0	154	0	0	0	0	0	0	308
Fresenius Kabi ITNBABY 102 (150 ml) N.0.31g/AA 2.08g/lipid 2.08g/per 100ml + trace elements & vitamins	21.3	16.6	42.4	10.2	1.7	0	10.3	103.9 (10.45) Dextrose	2607.5 (NPE)	928
Fresenius Kabi ITNBABY 103 (235 ml). Similar content to 102 But larger volume	18	12.6	39.4	8.6	1.7	0	7.4	105.2 (10.4%) Dextrose	2640.5 (NPE)	911
Fresenius Kabi ITNBABY 105 (150 ml) Similar content to 102 But less dextrose	21.5	12.6	37.1	6.6	1.7	0	7.5	63 (6.3%) Dextrose	1931.8 (NPE)	677

ACUTE ELECTROLYTE DISTURBANCES

HYPONATREMIA

Serum sodium (Na) < 130
Dangers: hypotonia, apnoea, seizures

Common causes:

- Prematurity – high
- Inadequate Na intake
- Excessive water intake (Fluid Overload)
- Excessive intrapartum maternal fluid intake
- Renal failure due to e.g acute tabular necrosis
- Diuretic therapy
- Diarrhoea, gastric, pleural, csf losses
- 17- hydroxyl-progesterone deficiency
- SIADH – ADH has limited ability to concentrate urine in newborns

Investigation

Do not treat an isolated low Na – repeat the sample
If high Na requirements, consider doing urinary sodium level to estimate replacement needs
FENa is an indicator of normal tubular function, value is limited in preterms due to tubular immaturity

MANAGEMENT

Treatment depends on underlying cause and the severity of the hyponatraemia. It may be difficult to determine whether the main cause of hyponatraemia is excessive water, inadequate body sodium or a combination of both.

Dilutional Hyponatraemia

- Consider if: hyponatraemic and weight gain or absence of weight loss
- Establish the cause: may be secondary to renal dysfunction, cardiac failure, excessive water intake or SIADH
- Restrict fluid intake
- If serum Na <120 mmol/l or symptomatic:
  - ◊ Calculate the Na deficit
  - ◊ Replace deficit with hypertonic saline over 24 hours beware fluid overload

Sodium deficiency

- Consider if: hyponatraemic + weight loss
- Common cause: diuretics, GI or renal losses, osmotic diuresis
- Manage cause, reduce sodium losses and replace sodium deficit. See Sodium Deficit in the FORMULAE AND CALCULATIONS section.

Rapid and complete correction of low serum sodium concentration in adults has been shown to be associated with pontine and extrapontine myelinolysis.

HYPERNATRAEMIA

Serum Sodium (Na) >145 mmol/l

Dangers: Cerebral venous sinus thrombosis, intracellular dehydration and associated intracranial bleeds, acute rehydration can lead to cerebral oedema

Commonest causes

- Excessive water loss
- Very preterm insensible water loss
- Diarrhoea
- Polyuria
- Excess sodium intake – common with sodium bicarbonate infusions and other medications/infusions

MANAGEMENT

Interpret high sodium values in clinical context.

Is the body dehydrated?

Are there ongoing fluid losses?

Is the baby receiving medications or infusions that contain large amounts of sodium?

Hypernatraemia + weight loss = water loss (e.g. Dehydration)

- Increase fluid intake or reduce sodium intake appropriately.

Reduce insensible water loss

Thin, transparent plastic (e.g. Cling –wrap) to increase the local humidity and limit air movement.

- Fix to the walls of the radiant warmer to create a micro-environment around the baby
- Effective in reducing insensible water losses by up to 70%

Chronic hypernatraemia:

- Should be corrected slowly because of the slow dissipation of idiogenic osmols – rapid rehydration will result in brain oedema
- Calculate H2O deficit (in l):
- BW (Kg x 0.7 x [1 – (Na current ÷Na desired)]
- Rehydrate over 48 hours. A correction rate of 0.5mmol/l hours is prudent in patients with hypernatraemia of chronic or unknown duration.

HYPOKALAEMIA

Potassium [K] <3.0mmol/l

Can occur in alkalosis, nasogastric or ileostomy losses, renal tubular disorders. Patients may present with lethargy, ileus or arrhythmia.

Acute cases:

- Monitor ECG and replace intravenously
- Recheck [K] 6 to 12 hourly.

Chronic cases:

- Supplement orally. (See formulary)
- Recheck [K] in 24 to 48 hours.

HYPERKALAEMIA

Potassium [K] ≥7.0mmol/l

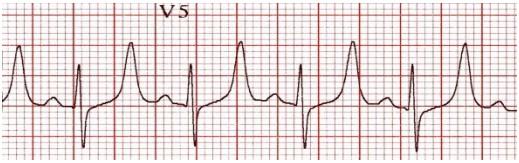
Hyperkalaemia is a potentially life-threatening condition because of effects on cardiac rhythm. It is most commonly seen in infants born extremely prematurely or in infants with impaired renal function. In premature infants, the serum potassium usually reaches a peak at 24 hours of age and declines to normal values by 72 hours of age.

Risk factors for hyperkalaemia in the neonate include:

- Extreme prematurity (<27 weeks gestation)
- Low systemic blood flow
- Acute renal failure (most commonly perinatal asphyxia)
- Chronic renal failure – multiple causes
- Haemolysis/Tissue Injury
- Double volume transfusion/use of "old blood" (Potassium rises after 4 days in stored blood)
- Sepsis
- Haemolysed specimen may falsely elevate potassium. Repeat test if this is suspected. If ECG changes are present or expected result is delayed, institute measures immediately.

ECG changes

- Peaked T waves
- Widened QRS configuration
- Bradycardia, trachycardia
- SVT, VT and VF



MANAGEMENT

Stop all potassium –containing fluid!

If ECG changes or symptomatic:

- 10% calcium gluconate 0.5 ml/Kg IVI over 10 min. NB! Calcium gluconate is incompatible with sodium bicarbonate.
- Insulin infusion: 0.05-0.2U/kg/hr. Give with 2 – 4ml/kg/h 10% DW. Monitor glucose after 30min, then hourly until stable.

- If [K] rise persists:
  - ◊ Salbutamol infusion 4µg/kg in 5mls water over 20minutes (repeat as necessary)
  - ◊ Alternately 0.4mg/kg/dose neb 2 hourly
- Correct acidosis if present with bicarbonate
- In order to reduce the risk of IVH, avoid rapid sodium bicarbonate replacement. Give over one hour in infants born before 34 weeks

Do not use Kexelate® (sodium polystyrene). It has no role in the management of acute hyperkalaemia.

HYPOCALCAEMIA

Ionised [iCa] < 0.9mmol/l
Total corrected serum [Ca] < 1.8mmol/l

Commonly occurs in preterm, or SGA infants, HIE, Infant or diabetic mothers, Di George syndrome. May also occur with hyperphosphataemia, hypoparathyroidism, hypomagnesaemia, renal failure, diuretic therapy.

Symptoms: jitteriness, irritability, high-pitched cry, seizures, stridor, tetany, decreased myocardial function, or ECG abnormalities.

Management
Calcium gluconate 10%. May be repeated if necessary and maintenance calcium dose can be increased in symptomatic.

HYPERCALCAEMIA
Total corrected serum [Ca] > 1.5 mmol/l or [iCa]>1.5mmol/l
Rare in newborns. May cause vomiting, hypotonia and encephalopathy.

Management
- Correct underlying cause, if possible.
- Ensure adequate hydration. Furosemide to increase calcium excretion. Consult with Endocrinology Service.

HYPOMAGNESAEMIA
[Mg] < 0.65mmol/l
Unusual. Associated with persistent hypocalcaemia.

Management
Treatment is MgSO4 IM or SLOW IV over several minutes. Treatment only required if symptomatic.

Hypermagnesaemia
[Mg] > 1.2 mmol/l

Usually occurs secondary to magnesium treatment of the mother with pre-eclampsia. Neonatal symptoms: hypotonia, hyporeflexia, apnoea, haemodynamic instability. The treatment is supportive until magnesium is excreted.

CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

DEFINITIONS

Continuous Positive Airway Pressure (CPAP) is the application of a preset positive pressure throughout the respiratory cycle (i.e. inspiratory and expiratory phases) in a spontenously breathing patient with the aim of opening collapsed lung segments and maintaining patency in already opened air spaces.

Weaning – The process of gradually reducing ventilatory support for the purpose of stopping various forms of mechanical ventilation. Weaning can refer to the reduction in the amount of oxygen (fraction of inspired oxygen-FiO_2), the volume and/or pressure required to maintain adequate ventilation and/or oxygenation.

BENEFITS OF CPAP:

- Reduces the work of breathing
- Maintains functional residual capacity by preventing alveolar collapse during expiration and improving alveolar recruitment
- Maintains a patent upper airway
- Stabilises chest wall

INDICATIONS FOR CPAP:

- Hyaline membrane disease (RDS)
- Apnoea of prematurity
- Post extubation
- Transient tachypnoea of the newborn
- Pneumonia/Sepsis
- Mild meconium aspiration
- Persistent Pulmonary Hypertension of the Newborn (PPHN).

CONTRAINDICATIONS TO USE OF CPAP

- Bronchopulmonary fistula
- Abdominal pathologies (e.g. diaphragmatic hernia, tracheoesophageal fistula etc)
- Craniofacial abnormalities are relative contrainidications

CPAP DEVICES:

Ventilator – variable level of distending pressure
Bubble CPAP – flow has to be altered to ensure proper bubbling
Flow drivers – maintains more uniform pressure

INSTITUTING CPAP:

- CPAP pressures should be optimized to between 4-8cm H_2O
- FiO_2 adjusted to maintain saturations between 90-95%
- Minimal handling – judicious approach to interventions/investigations

FAILED CPAP DEFINED BY ANY OF:

- FiO_2 > 0.6 required to maintain an oxygen saturation of 90-95%
- Persistent pulse oximeter saturation monitor for premature babies <88 and terms <95%
- Respiratory acidosis with a pH <7.2 in the absence of any other metabolic disturbance and fully related to a raised partial pressure of carbon dioxide of more than 6.0kPa
- Recurrent apnoea requiring mask ventilation.

MONITORING WHILE ON CPAP

Weaning:

- First reduce the FiO_2 before reducing the pressure (oxygen is toxic to preterm babies and may cause problems like Retinopathy of Prematurity-ROP, BPD etc)
- Consider changing to nasal prong oxygen if the baby copes at a pressure <5cm H_2O

For bubble CPAP

- First reduce the pressure to 5cm H20 if the saturations are maintained
- Then reduce the oxygen as tolerated
- You can then change to nasal prongs if oxygen saturations are maintained and there are no more apnoeic spells

SIDE EFFECTS OF CPAP

- Gastric distension and vomiting
- Risk of air leak syndrome (e.g. pneumothorax)
- Reduction in cardiac output if increased pressures due to reduced preload by the increased intrathoracic pressures.
- Nasal trauma and necrosis
- Agitation
- Nosocomial infection

HIGH FLOW NASAL CANNULA (HFNC) - VAPOTHERM

DEFINITION

HFNC is the delivery of humidified, heated and blended oxygen/air to flow rates up to 6 (six) times the minute ventilation of the patient via a nasal cannula. Minute Venitilation (MV) is the product of the tidal volume and the respiratory rate.

BENEFITS OF HFNC

- Babies on HFNC appears to be well settled and comfortable
- Less abdominal gaseous distension than other flow devices
- Babies do not require "time off" for nose breaks
- Easy to see more of the baby's face
- Easier access for cranial ultrasound scans.

INDICATIONS FOR HFNC

- Non-invasive ventilation of preterm/extremely preterm infants
- Non-invasive ventilation for infants with parenchymal lung disease (e.g. Hyaline Membrane Disease, pneumonia, Chronic Lung Disease/, Meconium Aspiration Syndrome, pulmonary hypoplasia, bronchiolitis)
- Treatment/prevention of apnoea of prematurity
- Do-not-intubate/ palliative settings
- Cardiogenic pulmonary edema

INSTITUTING HFNC

- Attach appropriately sized nasal cannula
- Cannula should not obstruct or be larger than half the diameter of the nares
- Adjust the flow to the desired rate and place the cannula on the patient
- Operational flow rates range from 1 – 8 l/min
- Start at flow rate of 6-7 l/min
- Flow can be increased in increments of 0.5-1l/min (maximum 8 l/min)
- Minimal handling - judicious approach to interventions/investigations

FAILED HFNC DEFINED BY ANY OF:

- FiO2 > 0.6 required to maintain normal oxygen saturation
- Respiratory acidosis with a pH <7.2
- Recurrent apnoea requiring mask ventilation.

WEANING HFNC

Weaning strategy for preterm babies (flow >4-6 l/min)		
FiO_2 < 0.25	FiO_2 0.25 – 0.30	FiO_2 > 0.30
Reduce by 0.5 l/min 48 hourly	Reduce by 0.5 l/min 48-72 hourly	Weaning < 6 l/min Usually not indicated
Weaning strategy for term babies		
FiO_2 < 0.25	FiO_2 0.25 – 0.30	FiO_2 > 0.30
Reduce by 1 l/min 24-hourly	Reduce by 0.5 l/min 24-hourly	Weaning < 4 l/min Usually not indicated

CONVENTIONAL (INTUBATED) VENTILATION

INDICATIONS

- Inadequate respiratory drive
- Severe circulatory failure
- Failed NCAP: FiO_2 > 0.6 after surfactant or respiratory acidosis with pH < 7.2
- Severe meconium aspiration

GENERAL CONSIDERATIONS

- Surfactant should be given within 2 hours of birth if surfactant deficiency is present
- Circulation, haemoglobin, electrolyte and nutritional status should be optimized
- Sedation after intubation is not usually required if extubation anticipated within 12 hours
- Monitor blood gas after starting ventilation and subsequently depending on abnormality and ventilator changes. A severely abnormal blood gas should be repeated 20 – 40 minutes after changes that are expected to influence it.
- Monitor blood pressure, heart rate and oxygen saturation and record hourly

VENTILATION MANAGEMENT

- Ventilator should be calibrated before use (usually done in advance by technologist)
- Baby's weight and tube details should be entered on the form.
- A Clean flow-sensor should be placed.
- In-line suction should be placed if intubation beyond 12 hours anticipated
- Set humidifier distal temperature sensor at ± 38ºC (the higher of the two options on the humidifier) – unless infant receiving therapeutic hypothermia, then temperature should be ±35º C (the lower of the two options)
- Check tubing – water trap at lowest point and heater wires extended optimally
- If using the AVEA ventilator set bias flow at 8 l/min and trigger sensitivity at 0.5 l/min.

  Only change venitlator settings after discussion with senior clinician.
- Mode: usually synchronized intermittent mandatory ventilation (SIMV) with pressure support. Assist control (A/C) used in discussion with senior clinician.

Initial ventilator settings

- Positive End Expiratory Pressure (PEEP) is usually set at 4-6 cm water. Severe lung disease or abdominal splinting may require higher pressure
- Peak Inspiratory Pressure (PIP) should be just enough to achieve adequate chest movement and expired tidal volumes (VTE) of 4-6 ml/kg BUT not exceeding 30cm H_2O. In a preterm with lung disease initially set PIP at 18cm H_2O. Normal lungs rarely require PIP>12m H_2O

  NB: *On some ventilators e.g. Avea, PIP is set as Inspiratory Pressure above PEEP: hence a PIP of 18 described above would be set on the Avea with a PEEP of 4 and a PIP of 14*
- Rate: initially 60 breaths per administration if lung disease present – decrease after surfactant administration. Use a much lower rate (40) if the lungs are normal
- Inspiratory time (T1): 0.35 – 0.4 seconds. Use the lower T1 for fast rate or A/C mode
- Pressure support: set at 2/3 of PIP initially. (T1 termination to be set by senior clinician/technician ONLY)

Subsequent changes to ventilator settings

Target is: oxygen saturation of 90-95% with progressively decreasing FiO2: $PaCO_2$ 5-7kPa with pH >7.25. PIP and rate are weaned in response to progressive improvement.

NB If pressure support is >2/3 PIP and/or A/C mode is used then weaning the respiratory rate will make no difference as every breath will be supported. Pressure support and/or PIP must be weaned.

- High P/SaO_2 can be achieved by increasing one or more of the following paramters: FiO_2, PIP, T1, PEEP (beware of increased CO_2), pressure support
- Decreased $PaCO_2$ can be achieved by increasing rate and/or PIP.

Consider high frequency oscillatory ventilation (HFOV) if blood gases are abnormal on optimal conventional ventilation (typically if PIP > 22-24 cm H_2O or rate > 65bpm)

Extubation criteria (usually to NCPAP)

Consider extubation if patient has normal respiratory drive: MAP < 8cm H_2O; FiO_2 ± < 0.3; rate < 30bpm.

HIGH FREQUENCY OSCILLATORY VENTILATION (HFOV)

DEFINITION

Is a type of mechanical ventilation that uses a constant distending pressure (MAP) with pressure variations oscillating around the MAP at very high rates (up to 900 cycles per minute).

INDICATION

- Hypercarbia, hypoxia or respiratory acidosis with pH < 7.25 despite optimal conventional ventilation (typically if PIP> 22-24 cm H_2O or rate >65bpm)
- Failure of conventional ventilation in term babies (PPHN and MAS) and preterm babies (Severe RDS, PIE, Pulmonary Hypoplasia) or for reduction of barotrauma when conventional ventilation settings are high.
- Air leaks syndromes (Pneumothorax, Pulmonary Interstitial Emphysema [PIE].

GENERAL CONSIDERATIONS

(In addition to those listed under conventional ventilation)

- Use transcutaneous PCO_2 monitor if available
- In-line suction is required
- Continuous blood pressure monitoring via arterial line is recommended

VENTILATOR MANAGEMENT

- Set humidifier distal temperature sensor at ± 38ºC (the higher of the two options on the MR850 humidifier) – unless infant receiving therapeutic hypothermia, then temperature should be ±35º C (the lower of the two options)
- Set bias flow at 20 l/min for equipment like Sensormedics 3100A and check piston is centered
- Set upper pressure alarm at MAP + 5cm H_2O and lower alarm at MAP – 5 cm H_2O

Initial ventilator settings

Frequency 10Hz

- 1: E Ratio should be 1:2 if using Sensormedics 3100A. Other ventilators e.g. Drager vN500 should be set at 1:1 initially
- Start with mean airway pressure (MAP) at 2cm above that used on conventional ventilation. If air-leak or hyper-inflated previously, then consider lower MAP
- For infants being oscillated without prior ventilation start at 8cm H2O
- Conventional MAP = $\frac{\text{PEEP+ (PIP – PEEP) x Ti}}{\text{(Ti +Te)}}$

Set amplitude (ΔP) to achieve visible oscillation of chest. Usually 30-35 cm H_2O

Subsequent changes

Target is:

- Normal lung inflation of 8-9 posterior ribs on chest x-ray (CXR)
- Normal oxygen saturation with progressively decreasing FiO_2
- $PaCO_2$ 5-7kPa with pH >7.25

MAP

If required FiO2 is higher than on conventional ventilation, then increase MAP at the bedside in 1-2 cm H_2O increment until FiO2 can be weaned. Poor response may indicate over or under inflation. Do not increase MAP 15 cm H_2O without discussion with a senior clinician.

Obtain CXR within 30-60 minutes of starting HFOV.

- Increase MAP to improve SaO2 if CXR show low lung volume and/or until FiO_2 stabilises
- Reduce MAP to improve SaO_2 if CXR shows hyperinflation – titrate to SaO_2. Optimum MAP is the point at which higher or lower MAP results in relatively lower SaO_2. Further CXRs may be required if progressive weaning is not possible within 6-12 hours.

- ΔP and Hz
- Increased ΔP in 5-10 cm H_2O increments in response to a high PCO_2 depending on extent
- Reduced ΔP in 5-10cm H_2O increments in response to a low PCO2 depending on extent
- If ΔP > 45cm H_2O is required due to high $PaCO_2$ consider reducing Hz to 8 -9
- If ΔP < 20cm H_2O is required due to low PCO_2, consider increasing Hz to 11-12

Discuss all frequency (Hz) changes with a senior clinician

WEANING AND EXTUBATION *(REMEMBER TO ADJUST MAP ALARM LIMITS AND CHECK PISTON CENTERING)*

Wean FiO_2 first then wean MAP in steps of 1-2cm H_2O and wean ΔP in steps of 5cm H_2O

When MAP is ≤ 8cm H_2O ΔP is≤ 25 cm H_2O and FiO_2 <0.3 consider extubation to NCPAP if respiratory drive is good

TRANSCUTANEOUS BLOOD GAS MONITORING

- Device measures skin surface PO2 and PCO2 to estimate arterial partial measure of O2 and CO2.
- Transcutaneous measurement of O2 and CO2 is referred to as Ptc O2 and Ptc CO2 respectively.

EQUIPMENT

- Transcutaneous device components:
  - ◊ Dual electrode
  - ◊ Electrode cleaning kit
  - ◊ Electrolyte and membrane kit
  - ◊ Contact solution
  - ◊ Double –sided adhesive rings
  - ◊ Calibration gas cylinder with delivery apparatus
- Digital displays show $P_{tc}O_2$, $P_{tc}CO_2$ and site of sensor

PRECAUTIONS

- Equilibration takes approximately 20 minutes after electrode is placed
- Intermittent correlation with formal blood gas is recommended
- Ptc O_2 may underestimate PaO_2 in presence of hypoxia, BPD, poor perfusion, severe anaemia and acidosis, hypothermia and with concurrent of vasoconstrictive drugs.
- Pressure on the sensor may result in falsely low $P_{tc}O_2$
- Change electrode location 4 hourly to avoid burns

TECHNIQUE

- Ensure all staff are properly trained on the device
- Perform electrode maintenance, if troubleshooting required, remove membrane
- Clean electrode with cleaning kit, rinse with deionised H2O, dry with gauze
- Apply electrolyte solution and place new membrane on electrode
- Perform two-point gas calibration as per manufacturer's instructions
- Use alcohol wipe to clean the skin where sensor to be placed
- Apply double-sided adhesive ring to the sensor
- Apply one drop of contact solution to skin site
- Apply the sensor to the skin over the contact solution
- Secure sensor cable
- Allow time to equilibrate
- Use alcohol wipes to remove adhesive rings when use no longer indicated.

SURFACTANT ADMINISTRATION GUIDELINE

INDICATIONS

(Discuss borderline cases with senior clinician)

- Intubated and ventilated with a diagnosis of surfactant deficiency (HMD or secondary deficiency) with FiO_2 >30%.
- Ncpap (optimized at MAP 4-6cm) or Vapotherm and FiO_2 persistently > 0.35-0.45
- Also consider use (discuss with senior clinician) in the following situations: secondary surfactant disfunction/inactivation or post surfactant slump as seen in Acute Respiratory Distress Syndrome (ARDS), pneumonia, MAS or pulmonary haemorrhage (after stabilization)

SURFACTANT DOSE

Curosurf® (Poractant): 1.5ml = 120mg

- Dose: Recommended does is 1.25 -2.5ml/kg (100 – 200 mg/kg)

  Empiric dosing reduces wastage – refer to table below for empiric dosing

Survanta® (Berctant) - available in Zambia: 4ml = 100mg

- Dose: Recommended does is 4ml/kg (100mg/kg)

  Empiric dosing reduces wastage – refer to table below for empiric dosing

Curosurf®			Survanta®		
Weight (kg)	**Volume**	**Dose (mg/kg)**	**Weight (kg)**	**Volume**	**Dose (mg/kg)**
<1	1.5ml	≥100			
1-1.5	1.5ml	100-80	1-1.5	4ml	100-71
>1.5-2.5	3 ml	160-96	>1.5-2.5	8ml	133-80
>2.5-4	4.5ml	160-90	>2.5-4	12ml	120-75
>4	6ml	≤180	>4	16ml	≤100

TIMING OF FIRST DOSE

- Administer as soon as possible, preferably within 2hours of birth, immediately after intubation and clinical confirmation of correct tube placement (visualisation of vocal cord, bilateral chest wall expansion on bagging the patient, bilateral equal air entry on auscultation and detection of carbon dioxide on capnography or other comfirmatory test of the presence of carbon dioxide)
- Do not wait for X-ray confirmation unless the ETT is staying in and/or the indication is uncertain
- Administration should be followed by immediate ventilation or NCPAP

Repeat dose: review in 12-14 hours and discuss with senior clinician if FiO_2> 0.35 (Consider CXR before repeat doses to rule out other reasons for poor response)
A third dose of surfactant is seldom helpful and should not be given without senior clinician approval.

APNOEA OF PREMATURITY

DEFINITION:
Cessation of respiratory airflow lasting ≥20seconds associated with oxygen desaturation, cyanosis and /or bradycardia.

TYPES OF APNOEA

- **Central:** occurs when inspiratory efforts are absent
- **Obstructive:** where inspiratory effort persists in the presence of airway obstruction
- **Mixed type:** has components of both central and obstructive apnoea.

Apnoea occurs in >50% of neonates <30 weeks and occurrence reduces with advancing gestational age. At 60 days post conceptual age the risk of apnoe in neonates is the same as in the term babies.

Apnoea of prematurity is a diagnosis of exclusion because it is associated with other diagnoses including hypo/ hyperthermia, hypoglycemia, anaemia, hyperbilirubinaemia, sepsis, intraventricular haemorrhage, necrotizing enterocolitis, gastro esophageal reflux etc. Any neonate with apnoea should be evaluated thoroughly!

EVALUATION:

It is important that preterm neonates ≤33 weeks of gestational age are commenced on continuous oxygen saturation monitoring with alarm set at saturations <88% and time lag for alarm to go off at 20 seconds. Prompt response to alarm is required to ascertain cause of desaturation.

If no monitors are available, it is important to observe the neonate for cyanosis, mottling, and lack of breathing/ no chest wall movements.

Work up for apnoea: Glucose, FBC, CRP, blood culture, RBS, serum electrolytes, serum Aminophylline level if possible and cranial ultrasounds scan.

If not tolerating feeds +/- abdominal distension, consider necrotizing enterocolitis

MANAGEMENT

Prevention

- Aminophylline/caffeine is given prophylactically to all preterm neonates <33weeks gestational age or <1500g birth weight.
- **Dose: Aminophyllin: l**oad with 6mg/kg given slowly over 20min then start maintenance at 2.5mg/kg twice daily starting 24hours after loading.
- Aminophylline may be given orally (usually reconstituted into liquid form) to stable preterm neonates at the same dosing. Stop once infant has good suckling and swallowing coordination. (Therapeutic serum level is 9-14mg/l)
- **Dose:** Caffeine as in the drug section

TREATING APNOEA

Establish cause and start treatment for suspected cause.
Commence CPAP with close monitoring and during an apnoea episode stimulate infant, if not arousable provide bag mask ventilation. If episodes are frequent >3 episodes then mechanical ventilation is needed.

NITRIC OXIDE

INTRODUCTION

- Nitric oxide (NO) is a naturally occurring vasodilator, which is present in the vascular endothelium of all blood vessels in the body
- At a cellular level it works by activating guanylyl cyclase leading to an increase in the production of cyclic GMP which in turn relaxes vascular smooth muscle. It is rapidly inactivated in the blood stream with production of methaemoglobin and inorganic nitrates and nitrites.
- When it is given by inhalation (iNO) it dilates the pulmonary blood vessels in ventilated lung, reducing pulmonary vascular resistance, increasing pulmonary blood flow and improving ventilation perfusion mismatch without having any significant effect on the systemic vasculature.

PRESCRIBING NITRIC OXIDE

- iNO is not registered by the Zambia Medicines Regulatory Authority (ZAMRA). iNO must be prescribed on the infusion chart. Start and stop time and dose changes must be charted accurately
- An iNO register should be kept and necessary forms (to be obtained from ZAMRA when iNO is registered) must be completed, including parental consent.

INDICATIONS

- Nitric oxide should be considered in:
- Infants >35 weeks gestation with severe hypoxic failure – PaO_2 cannot be maintained above 6.6kPa or O_2 saturation <90% despite optimal ventilation with FiO2 greater than 0.80 and a normal perfusion.
- PPHN.

Relative contraindications

- Uncontrolled bleeding and profound thrombocytopenia.

Considerations

- Ventilation should be optimized prior to consideration of use of iNO
- Infants should receive optimal cardiovascular management prior to starting iNO
  - ◊ 1st line: dobutamine probably reduces both pulmonary and systemic vascular resistance and is likely to increase cardiac output. Start at 10µg/kg/min (range 2-20µg/kg/min)
  - ◊ 2nd line: adrenalin increase systemic more than pulmonary vascular resistance. start at 0.05µg/kg/min (range 0.05-05µg/kg/min)
  - ◊ Caution: dopamine increases pulmonary and systemic vascular resistance to a similar degree.

Dosage of iNO

Start at 20ppm (higher doses are unlikely to be of benefit and doses >40ppm is associated with methaemoglobinaemia)

- Successful response: O_2 sats rise by 10%; 3kPa rise in post-ductal PaO_2 and pre-ductal PaO_2 >8kPa
- iNO lack of dose response: There is no consistent evidence of a dose response effect with iNO therefore:
  - ◊ Attempts should be made to reduce iNO dose to the minimal effective dose assessed by response to changes in nitric oxide delivery
  - ◊ If no response after one hour, discuss with senior clinician whether ongoing iNO administration is indicated
  - ◊ If no response, wean iNO by 5ppm every 30 minutes

Methaemoglobin monitoring

- iNO can theoretically cause methaemoglobinaemia, although none of the RCTs using doses of 20ppm or less have reported any increase in the incidence of methaemoglobinaemia
- Methaemoglobin levels should be checked at least every 24 hours (MetHb on blood gas analyser) record all MetHb levels on the gas sheet
- If levels rise above 50%, iNO should be reduced or stopped
- If levels are persistently 7% give methylene blue (see dose in formulary section)

Weaning

- There is little evidence to guide the best method for weaning iNO, although some authors have anecdotally noted rebound deterioration on stopping iNO in some babies
- The aim should be to deliver the minimum dose compatible with normal oxygenation and haemodynamics
- As noted above there is little evidence of a dose response relationship with iNO and so if the dose is increased and no effect is observed, then the dose should be reduced as early as possible.

CONGENITAL DIAPHRAGMATIC HERNIA

BACKGROUND

- Congenital diaphragmatic hernia (CDH) is a congenital anomaly that affects 1 in 3000 live births and is associated with a high risk of mortality and morbidity
- The combination of pulmonary hypoplasia and abnormal morphology of the pulmonary vasculature leads to severe respiratory insufficiency in over 90% of cases in the first hours after birth
- Infants with CDH are at increased risk of developing persistent pulmonary hypertension of the new born (PPHN) due to pathological development of the pulmonary vasculature
- Several triggers such as hypoxaemia, acidosis and pulmonary vascular damage caused by mechanical ventilation, sustain PPHN through reactive vasoconstriction and vascular remodeling. Therefore, it would seem best to achieve optimal management of elevated pulmonary arterial pressure and prevent further damage to the lung before undertaking surgical repair of the diaphragmatic defect.

ANTENATAL MANAGEMENT

- Following prenatal diagnosis, lung: head ratio and liver position should be recorded as this aids prognosis
- Delivery should be as close to term as possible, and planned for the daytime (preferably morning and preferably not just before a weekend)
- In the case of preterm labour prior to 34-weeks gestation, antenatal steroids should be given.

AT TIME OF DELIVERY

- More than one doctor should be present at delivery regardless of mode with at least one senior clinician.
- The key principles of successful post delivery management are airway management and the avoidance of high airway pressure while maintaining adequate preductal saturations.
  - ◊ Immediately intubate the infant WITHOUT bag and mask ventilation
  - ◊ Maintain preductal saturations between 80-95%
  - ◊ Use of lowest PIP possible, preferably below 25cm H_2O
  - ◊ Insert naso-or Orogastric tube with intermittent or continuous suction to decompress bowel
  - ◊ Sedation is necessary; Fentanyl is the drug of choice. Do not use neuromuscular blockers
  - ◊ Do not administer prophylactic surfactant.

IN NICU

- Gentle ventilation with the lowest pressures required to maintain preductal saturations between 85%-95%.
- Target $PaCO_2$ should be between 5.5 and 8kPa. pH >7.2, lactate <5mmol/l
- Urine output > 1 ml/kg/hour
- Conventional ventilation:
  - ◊ PIP 20-25cm H_2O
  - ◊ PEEP 5cm HH_2O
  - ◊ Rate 40-60bpm
- HFOV (These are starting points):
  - ◊ MAP 13-17cm H_2O
  - ◊ ΔP 30-50cm H_2O
  - ◊ Hz 10-12
- Wean FiO_2 to saturation targets
- Do CXR initially and repeat, guided by changes in clinical condition and mode of ventilation

Monitoring:

HR, invasive BP, pre-and post-ductal saturations should be monitored routinely
Be guided by BP (appropriate for gestation), capillary refill, urine output, and lactate levels as to whether inotropic agents are required
In case of hypovolaemia, volume expansion with 20ml/kg boluses of 0.9% normal saline may be needed.

PPHN IN CONGENITAL DIAPHRAGMATIC HERNIA

- Echocardiography should be done in the first 24 hours of life
- Inhaled nitric oxide (iNO) is the initial drug of choice in PPHN, however, there is currently no evidence to suggest that iNO improves outcome in CDH. iNO should NOT be used
- Sidenafil may be used in PPHN (in the chronic phase)
- Prostaglandin E1 to re-open the ductus arteriosus can be considered in the case of severe PPHN with suprasystermic pulmonary artery pressures and right to left shunting through foremen ovale.

SURGICAL REPAIR

Surgical repair should only be performed after the patient is physiologically stable. The surgical team should be informed of the patient prior to delivery and updated once the baby has been born.

FLUID MANAGEMENT AND PARENTERAL FEEDING

Fluid requirements are based on gestational age and clinical conditions.

- Term infants should be started on 40ml/kg/day intravenous fluids (including medication infusions)
- Aim for a urine output of 1-2 ml/kg/day/hour
- Start TPN while waiting surgery and in the post-operative period
- enteral feeding may be started postoperatively
- anti-reflux medication may be needed

87% of infants that survive will have long term pulmonary, GIT, or neurological abnormalities. Long term follow-up is required.

MECONIUM ASPIRATION

Acute or chronic hypoxia and/or infection can result in the passage of meconium in utero. In this setting, gasping by the fetus or newly born infant can cause aspiration of amniotic fluid contaminated by meconium.

Meconium aspiration before or during birth can obstruct airways, interfere with gas exchange, and lead to severe respiratory distress

INCIDENCE

- 8 to 25% of births
- Uncommon in preterm infants- most babies are 37 weeks and older
- Common in post-mature and
- Small for gestational age

MANAGEMENT OF INFANTS DELIVERED THROUGH MECONIUM STAINED FLUID

Oropharyngeal and nasopharyngeal suctioning on the perineum and routine tracheal intubation and aspiration of meconium in vigorous infants are not effective in preventing meconium aspiration syndrome (MAS).

Infants should be assessed and intervention reserved for infants who are depressed or have respiratory distress

- **Initial assessment:** at delivery complicated by MSAF, determine whether the infant is vigorous as demonstrated by heart rate >100 beats per minute, spontaneous respiration, and good tone
- **If vigorous:** routine care should be provided regardless of consistency of meconium
- If respiratory distress develops or depressed infant, tracheal intubation under direct laryngoscopy and intratracheal suctioning.

MANAGEMENT OF MAS

Observation:

infants who are depressed at birth and have had meconium suctioned from the trachea are at risk for meconium aspiration pneumonia and should be observed closely for respiratory distress

- CXR – classic findings are diffuse, asymmetric patchy infiltrates, areas of consolidation, often worse on the right, and hyperinflation
- Oxygen saturation monitoring aids assessment of the severity of the condition and avoids hypoxaemia

Care of neonate with MAS

- Minimal handling to prevent agitation (may worsen the condition and predispose to pulmonary vasoconstriction and PPHN)
- Correct hypoglyacaemia
- Pay particular attention to electrolytes particularly calcium and monitor pH (likely metabolic acidosis)
- Restrict fluids to avoid cerebral and pulmonary oedema
- Monitor blood pressure-may require inotropes
- Maintain haemoglobin level above 15mg/dl (improves oxygenation)
- Monitor renal function

Oxygen therapy

- Management of hypoxaemia should be accompanied by increasing FiO2 and monitoring blood gases and pH

Assisted ventilation

- ***CPAP***- considered when saturation is less than 90%, if FiO_2 >0.40
  However, CPAP may sometimes aggravate air trapping and should be instituted with caution if hyperinflation is apparent clinically or radiologically

- ***Mechanical ventilation***
  - ◊ Required if excessive CO_2 retention ($PaCO_2$>60mmHg) or persistent hypoxaemia (PaO_2<50mmHg)
  - ◊ Infants require higher inspiratory pressures (30-35cm H_2O), PEEP (3 to 6 cm H_2O) should be selected based on response. Adequate expiratory time should be permitted to prevent air trapping behind partially obstructed airways
- Useful starting points; inspiratory time of 0.4 to 0.5 seconds at a rate of 20 to 25 breaths per minute. Adjust as required
- HFOV if not coping on conventional ventilation and in those who develop air-leak syndromes

  There are no prospective randomised trials comparing the efficacy of the various ventilator modes in MAS

Medications

- ***Antibiotics:*** difficult to distinguish MAS from bacterial pneumonia. Use broad spectrum antibiotics (e.g. Penicillin and gentamicin)-can be guided by blood cultures
- ***Surfactant:*** Endogenous surfactant can be inhibited by meconium. Should not be routinely used but may be of benefit in those with clinical deterioration and require escalating of support
- ***Sedatives:*** may be warranted if requiring mechanical ventilation(refer to elective intubation chapter)

COMPLICATIONS OF MAS

- **Air leak:** pneumothorax and pneumomediastinum in 15 to 33%. Common with mechanical ventilation, especially in the setting of air trapping
- **PPHN**
- **Pulmonary sequelae:** approximately 5% of survivors require oxygen supplementation at 1 month, may have abnormal pulmonary function including increased FRC, airway reactivity and a higher incidence of pneumonia

PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN (PPHN)

BACKGROUND

PPHN is the failure of the normal physiological decline in pulmonary vascular resistance that occurs after birth, with resulting hypoxia due to shunting of blood flow across fetal channels (e.g. PDA, PFO)

CAUSE OF PPHN

In utero stress, e.g. hypoxia

- Alveolar/interstitial lung disease, e.g MAS, pneumonia, HMD
- Sepsis and acidosis, hypothermia, hypoglycaemia
- Lung hypoplasia
- Congenital diaphragmatic hernia

} Combination of PHT, pulmonary hypoplasia vascular remodeling

- Idiopathic PPHN

DIAGNOSTIC FEATURES

- Severe hypoxaemia – (PaO_2 < 6.4kPa). The severity may not correspond to the extent of lung opacification on CXR, lung fields appear black and organic
- Evidence of right to left shunting, (Postductal sats/PaO2 significantly lower than preductal).
  A difference of >10% between pre-and postductal saturation suggests PDA-dependent lesion or PPHN
- Structurally normal heart with tricuspid regurgitation
- Associated history of possible secondary causes of PPHN

MANAGEMENT

- Transfer baby to intensive care
- Oxygen (oxygen is a potent pulmonary vasodilator) via Nasal prongs or CPAP
- If baby remains hypoxic on high percentage oxygen, consider intubation.
  Aim for a smooth, controlled intubation and ventilation with lowest possible airway pressures. This should be done preferably by an experienced clinician, as pulmonary hypertension may be exacerbated by difficult intubations and high airway pressures.
- Use an appropriately sized ET tube to minimize leak (check ETT size in the appendices)
- Fentanyl is the preferred agent for sedation once baby is intubated. Beware of side effects: Chest wall rigidity, hypotension, urinary retention and hypomotility of the gut.
- The use of muscle relaxant is controversial, NOT TO BE USED WITHOUT DISCUSSION WITH SENIOR CLINICIAN

- Correct hypoglycaemia, acidosis, hypothermia, hypocalcaemia if this exists
- Do a septic work-up and treat empirically with broad spectrum antibiotics for suspected cause and later guided by microbiology sensitivities from the culture.
- Consider surfactant replacement therapy in severe alveolar disease. Discuss with senior clinician
- Ensure that the infant is normotensive; consider inotropic support if this is required. Dobutamine should be your initial drug of choice, start at 10µ/kg/min and titrate according to response. Adrenalin can be added as a second line inotrope. DISCUSS WITH SENIOR CLINICIAN. Inotropic support should be started via central lines and ONLY in cases where central line placement is a challenge or in an emergency should inotropes be given peripherally. The umbilical catheter is another choice but the clinician should be cognisant of its complications.
- Optimise oxygen carrying capacity (Refer to transfusion guidelines section)
- Alkalinisation with sodium bicarbonate is controversial. Discuss with senior clinician before administering

VENTILATION STRATEGY

- Use conventional ventilation initially. If high inspiratory pressures are required, switch to HFOV if available
- Aim for normal PCO2 (between 4-5kPa). Avoid hypocapnoea. More frequent ABG measurement may be required initially when HFOV is started, until baby is stabilized
- Avoid over-expansion of lungs with HFOV (lung fields ≤9 ribs)

DRUGS

inhaled nitric oxide (iNO)

- Refer to nitric oxide protocol

Sildenafil

- Sildenafil is a potent pulmonary vasodilator and may be added to treatment. Used for iNO weaning or when iNO is not available. Dose: 1mg/kg every 6hours to a maximum of 8doses.

ROLE OF ECHOCARDIOGRAPHY

- First –exclude the presence of structural cyanotic heart defects
- Second – estimate pulmonary artery pressures and confirm pulmonary artery pressures
- Third – assess myocardial contractility

PULMONARY HAEMORRHAGE (PH)

Pulmonary haemorrhage is commonly defined as the presence of haemorrhagic fluid in the trachea accompanied by respiratory decompensation requiring increased respiratory support or intubation within 60 minutes of the appearance of fluid

RISK FACTORS

- PDA with a left to right shunt
- Exogenous Surfactant therapy (especially if given prophylactically)
- Sepsis

Other factors include: Prematurity, Intrauterine Growth Restriction, RDS, Asphyxia, Coagulopathy, Polycythaemia, Hypoxemia, DIC, Mechanical ventilation, Hypothermia, male gender, cold injury, multiple births, Oxygen toxicity. Antenatal glucocorticoids are said to be protective

EVALUATION:

History and physical examination

- Elicit risk factors
- Physical exam reveals pink or red frothy fluid in the airway and signs of respiratory decompensation.
- Monitor for apnoea, generalised pallor, cyanosis, bradycardia and a drop in blood pressure
- As increasing amounts of blood are suctioned from the ET, PCO2 starts to rise and so does the need for higher fractions of inspired oxygen.

Radiological evaluation

- CXR may be none specific; shows diffuse fluffy opacities, focal ground-glass opacities or appear as a complete "white out" if the PH is massive

Laboratory studies

- Declining haematocrit
- Metabolic or mixed acidosis
- Evidence of Coagulopathy

TREATMENT

Because the underlying pathogenesis remains unclear, treatment remains supportive

The general approach involves clearing the airways of haemorrhagic fluid and restoring adequate ventilation

- **Provide positive end-expiratory pressure(PEEP):** the use of elevated PEEP of 6 to 8cm of H2O helps decrease the efflux of interstitial fluid into the alveolar space
- **Restore haemodyanamic stability:** Correct haemodynamic instability with volume resuscitation including packed red blood cell replacement, and consider the addition of vasoactive medication, as needed
- **Correct acidosis:** Restore both adequate ventilation and blood pressure to improve acidosis
- **Consider echocardiogram:** An echocardiogram evaluation may assist in the evaluation of ventricular function, the need for vasoactive medications, and the possible contribution of a PDA. Consider pharmacologic or surgical closure of the PDA if haemodynamically significant
- **Identify other predisposing factors:** Additional potential contributing factors such as sepsis and Coagulopathy must be addressed
- **Strategy for ventilation:** It is uncertain whether using high-frequency ventilation to provide high mean airway pressure while limiting tidal volume excursions is more effective than conventional ventilation to minimize further interstitial and alveolar fluid accumulation
- **Role of surfactant:** Improves secondary surfactant deficiency resulting from haemorrhagic airway oedema. However, the potential benefits of surfactant therapy in these cases need further investigation and should be decided on a case by case basis

BRONCHOPULMONARY DYSPLASIA

DEFINITION:
Chronic lung condition that develops in preterm neonates treated with oxygen and positive-pressure ventilation.

	Gestational Age	
	<32 weeks at birth	≥32 weeks at birth
Treatment with oxygen	>21% for at least 28 days	>21% for at least 28 days
Time of assessment	36 weeks CGA or discharge	>28 days or discharge whichever occurs first
	Severity of disease	
Mild	Breathing room air at 36 weeks CGA or discharge	Breathing room air at 56 days of age or discharge whichever occurs first
Moderate	<30% administered oxygen at 36 weeks CGA or discharge	<30% administered oxygen at 56-days postnatal age or discharge whichever occurs first
Severe	>30% oxygen at 36 weeks CGA or discharge	>30% oxygen at 56-days postnatal age discharge whichever occurs first

CGA= Corrected Gestation Age

MANAGEMENT

Ventilation

- Aim to support using "non-invasive" devices
- Aim for lowest possible pressures if mechanically ventilated
- Volume targeted strategies to deliver appropriate tidal volumes

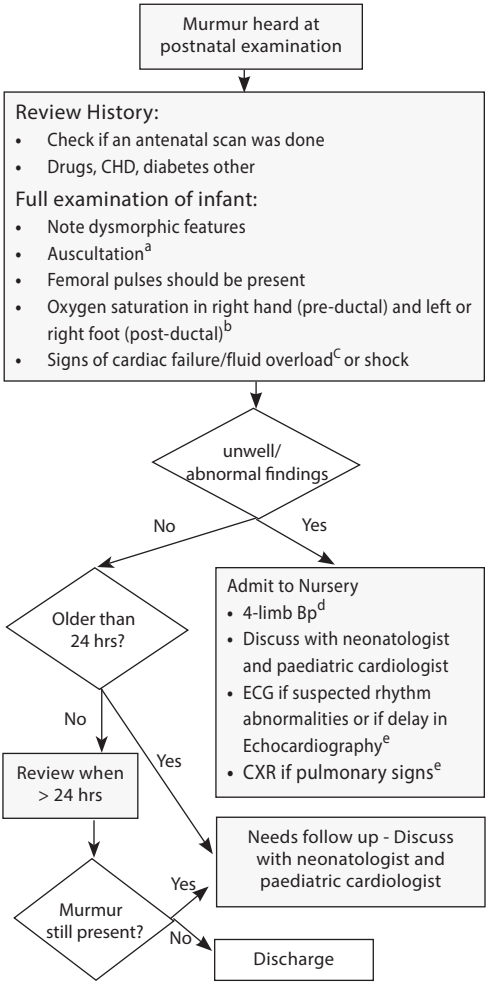
Nutrition

- Ensure calorie intake of a least 120 Kcal/kg/day
- Avoid fluid overload

Corticosteroids

- Consider in an infant who is ventilator-dependent and requiring increasing or persistently high FiO_2.
- Treatment should usually be initiated between 14-21 days of age
- A senior clinician should be involved in the decision
- Contraindications to treatment should be considered
- The parents should be fully informed of the reasoning behind the decision to commence treatment. They should be told that Dexamethasone may increase the chances of their baby surviving, BUT studies suggest that babies who receive Dexamethasone postnatal may have an increase risk of neurological impairment namely cerebral palsy.
- Obtain verbal parental consent and record in notes
- Use the DART regimen for dexamethasone dose (see drug table)
- Hydrocortisone, betamethasone and inhale corticosteroids are not recommended

CARDIAC MURMUR IN A WELL TERM INFANT



a. S1 is heard best at the lowest left sternal border and is usually single.
S2 is heard best along the left upper sterna border – varies with respiration and audibly split in 80% by 48h. An abnormal S2 requires investigation.
A murmur that is persistent, diastolic, loud or harsh in quality is abnormal and requires investigation.

b. Pulse oximetery is abnormal if, when measured after 24h, the oxygen saturation is < 90% in any extremity, oxygen saturation is persistently <95% in both extremities, or a >3% absolute difference in oxygen saturation between upper and lower extremity readings.

c. Signs of failure/fluid overload:
Respiratory distress, hepatomegaly, prominent precordial impulse, poor feeding

d. A BP persistently 20mmHg higher in the arms than in the legs may indicate coarctation or interrupted aortic arch.

e. CXR and ECG do not add sufficient information to change management emergently and are not cost effective if echocardiography is available. However, RVH may indicate Rt obstructive lesion: LVH may indicate Lt obstructive lesions: Rt or Lt axis deviation can indicate ASD or AV canal defect; and ASD can present as incomplete RBBB. dark lung fields on CXR are associated with Rt obstructive lesions

MANAGEMENT OF HYPOTENSION

Hypovolaemia, low systemic vascular resistance, or poor myocardial contractility may cause hypotension.

POOR MYOCARDIAL CONTRACTILITY

The transition to extra-uterine life: In preterm infants, systemic blood flow is typically low during the first 12-24h, associated with relatively high systemic vascular resistance. The transition may be associated with transient hypotension, resolving spontaneously by 36 hours. Most preterm babies, who are hypotensive, are not hypovolaemic and the preterm myocardium is particularly sensitive to afterload. Routine early volume expansion in the absence of hypovolaemia is not beneficial.

Perinatal hypoxia: Hypoxic-ischaemic damage to the ventricles can cause ventricular dysfunction.

Persistent pulmonary hypertension (PPHN): The high pulmonary vascular resistance in babies with PPHN is associated with right ventricular failure and dysfunction. Left ventricular dysfunction may also be present.

HYPOVOLAEMIA

Hypovolaemia (absolute or relative) typically occurs in babies with acute blood loss, sepsis or NEC. Hypovolaemic neonates cannot easily increase the stoke volume by increasing heart rate. There is no evidence that colloid is superior to crystalloid.

MARKERS OF CIRCULATORY FUNCTION

Blood pressure correlates poorly with cardiac output, systemic blood flow and cerebral blood flow.

The use of other signs, including capillary refill time, urine output and serum lactate level improves the diagnostic accuracy of low blood pressure for low systemic blood flow.

DEFINITIONS

Hypotension can be defined as a blood pressure < 5th centile for age – in the first week of life, this corresponds approximately to the gestational age of the infant. Beyond the first week of life, the lower limit of normal is appropriately equal to the corrected gestational age for preterm infants: in term infants the lower limit increases to 50mmHg by 6 weeks and 60 mmHg by 6 months (oscillometric data). Blood pressure measurements are subject to variability according to the make of equipment and the method used; oscillometric measurements (using a cuff) may be marginally higher than indwelling arterial measurements. See reference table.

TREATMENT THRESHOLDS AND TARGETS

There is no evidence that treating hypotensive preterm infants with vasopressors or inotropes is beneficial. The threshold at which treatment of hypotension is beneficial is not known, guidance is based on limited evidence and consensus opinion.

Preterm infants in the first week of life

Initiate treatment when:

- The mean BP is ≥ 5mmHg below cGA, Or
- Mean BP (mmHg) is <cGA, PLUS one or more of:
  - ◊ Urine output < 0.5ml/h
  - ◊ Delayed capillary refill ≥ 3s
  - ◊ Lactate > 4mmol/l

Once initiated, aim to achieve MBP within 5 mmHg of target (cGA) and resolution of other signs.

Preterm infant with sepsis/NEC

Initiate treatment when the mean BP (mmHg) is <cGA

Term Neonates:

Initiate treatment when the mean BP (mmHg) is < 40 mmHg. For infants with PPHN consider aiming for suprasystemic blood pressure depending on clinical response.

HYPOTENSION TREATMENT CATEGORIES

Acute Blood loss
- Diagnostic indicators: history, low Hb, bleeding
- Management: Normal Saline (NS) and/or emergency blood if available
  - ◊ 10ml/kg initially, consider repeat
  - ◊ Check coagulation status and platelets
  - ◊ Consider dopamine if hypotension persists after fluids resuscitation

Chorioamnionitis/Sepsis/NEC
- Consider hypovolaemia – give 10ml/kg NS and evaluate response
- Dopamine 1st line
- Consider Adrenaline 2nd line (wean dopamine if adrenaline effective)
- Consider hydrocortisone 3rd line

Myocardial Dysfunction
- Avoid volume
- Dobutamine 1st line
- Dopamine 2nd line (max dose 15 mcg/kg/min)
- Consider Adrenaline 3rd line (discontinue dopamine)

Cause Unknown
- Dopamine 1st line
- Consider hypovolaemia – give 10ml/kg NS initially
- Dobutamine 2nd line
- Consider Adrenaline and/or Hydrocortisone 3rd line (wean dopamine if effective response)

Ideally therapy should be modified after assessing circulatory status using functional echocardiography to determine ventricular distension and systemic blood flow.

PATENT DUCTUS ARTERIOSUS

The ductus arteriosus (DA) is functionally closed in the majority of well term and preterm infants by 72 h. Approximately 30% of infants< 30 weeks GA have a persistently patent DA (pPDA) by the age of 3 days.
Current evidence does not support the use of anti-prostaglandins for the routine treatment of, or prophylaxis for, pPDA. There is insufficient evidence to guide treatment. A pragmatic approach involves limiting ductal closure to infants where the pPDA is thought to be the primary cause for persistent ventilator dependency or intractable hypotension and it is haemodynamically significant.

Ibuprofen is as efficacious as indomethacin and is the preferred agent for ductal closure because it causes fewer renal and gastrointestinal effects. The intravenous formulation should be used if available. If access or resource-limitation restricts the use of the intravenous form, then oral formulations with osmolality below 400 mOsm/kg (liase with department pharmacy) may be considered if the risk of off-label use is deemed appropriate by senior attending clinicians.

CLINICAL DIAGNOSIS OF PDA

- Signs of a patent ductus arteriosus include: systolic murmur, full pulses, active precordium, tachycardia, tachypnoea, hypotension, cardiac failure and/or fluid overload, increased pulse pressure or increased vascularity/cardiomegaly on CXR
- In the first week of life clinical signs occur 1-2 days after significant echocardiographic signs.
- The sensitivity and specificity of signs is low in the first day of life, increasing with time until age 7 days
- Preterm infants who present with a murmur after the first week of life as a single sign are more likely to have physiological pulmonary branch stenosis than they are to have PDA. (important to note as this is very common and tends to resolve with time as observed with serial echoes)

ECHOCARDIOGRAPHIC DIAGNOSIS OF HAEMODYNAMICALLY SIGNIFICANT PDA (HDSPDA)

Infants <31 weeks/1500g and >12 hours old:

- Ductal diameter with colour flow: DA> 1.5mm or ≥ 1.4 mm/kg
- Left atrial/aortic ratio>1.5 (using M-mode)
- Unrestrictive pulsatile transductal end diastolic left to right ductal velocity of <2m/s
- Reduced, absent or reversed diastolic flow in the middle cerebral, mesenteric or renal arteries.

Ductal shunting is usually left-to-right or bidirectional – pure right to left shunting is unusual and usually represents additional pathology.

MANAGEMENT OF A SYMPTOMATIC PDA

All infants should be managed with the following basic measures:

- Confirm diagnosis and significance with echocardiography if skills available
- Restrict intravenous fluid to 80% of maintenance (a maximum of 120ml/kg per day)
- Support with NCPAP or humidified high-flow air/oxygen if respiratory distress

- Target oxygen saturation at 90-94% if receiving oxygen
- Transfuse according to standard transfusion guidelines
- Permissive hypercapnoea

If despite the above measures, the signs of cardiac failure/fluid overload persist and a HdsPDA is confirmed echocardiographically:

- Treat fluid overload with hydrochlorothiazide + spironolactone or K+ supplement if hypokalaemia occurs
- Loop diuretics such as furosemide should be avoided (Because neonates already have wasting kidneys and this is worsened by prematurity!)
- Treat hypotension with dopamine as a first line agent

If after the above management, the infant remains dependent on mechanical ventilation, primarily due to the PDA and/or there is intractable hypotension:

- Discuss the use of ibuprofen with a senior clinician
- If, after treatment, the PDA remains the cause of intractable cardiac failure and/or ventilator dependency then repeat ibuprofen or surgical closure should be discussed with a senior neonatal clinician and a paediatric cardiologist.

IBUPROFEN DOSE AND ADMINISTRATION

Intravenous

- Dose: first dose 10mg/kg, 2nd and 3rd dose 5mg/kg
- Give doses 24 hours apart. Stop treatment early if complete ductal closure is proven on echo
- Administer each dose as an infusion over 15 minutes, preferably undiluted
- If dilution is required, then 0.9% saline or 5% dextrose water may be used

Oral

- Manufacturers do not recommend the use of ibuprofen for this indication (PLEASE NOTE)
- If an oral suspension is used, it should have osmolality<400 mOsm/kg (eg Nurofen®) – Nurofen is available in pharmacies in Zambia
- It is given undiluted via the gastric tube, followed by
- 1ml sterile water
- Dose: first dose 10mg/kg, 2nd and 3rd dose 5mg/kg
- Give doses 24 hours apart. Stop treatment when complete ductal closure is proven on echo

CONTRAINDICATIONS TO IBUPROFEN (IMPORTANT TO NOTE!)

- Renal (relative): urea>10mmol/l or creatinine >120µmol/l or oliguria (output <0.6ml/kg/hr in the last 8 hours).
- If not oliguric then treatment is only contraindicated if urea>14mmol/l or Creatinine>140µmol/l
- Haematological: platelet count<60 x 109/l or active abnormal bleeding
- GIT: necrotizing enterocolitis or gastritis
- New untreated sepsis
- Duct-dependent cyanotic heart disease

NEONATAL ARRHYTHMIAS

INTRODUCTION

Sinus dysrrhythmia is most common in infants and is considered a normal variant; the heart rate drops during expiration and increases during inspiration. Arrhythmias are not well tolerated by infants, particularly those with single ventricle physiology and cardiac failure. supportive interventions are as important as treating the abnormal rhythm.

GENERAL MANAGEMENT PRINCIPLES

- Always consult with cardiologist after 12 lead ECG done
- Run continuous rhythm strip during administration of medication or during cardioversion
- Ventilate and sedate infants requiring cardioversion
- Correct electrolyte abnormalities (aim for ionized Ca>1.0, K>4.0 and Mg 1.2-2.0) and maintain normal temperature.

TACHYARRTHYMIAS

Supraventricular tachycardia

- Regular narrow QRS complex tachycardia >230bpm; hidden, normal or retrograde P waves
- May present in utero with hydrops

Management

- Vagal manoeuvre with ice to face (omit if hypotensive); if unsuccessful use adenosine
- Adenosine by rapid injection via good vascular access followed by immediate 2 ml 0.9% saline flush, ensure ECG strip running
- Adenosine dose: dilute 3mg to 10ml 0.9% saline to make 300µg/ml

- Start dose: 200µg/kg/dose
- Increment by 50µg/kg every 2 minutes to max of 300µg/kg until sinus rhythm
- If adenosine unsuccessful; synchronized cardioversion at 1J/kg, repeat at 2J/kg if no response
- Discuss chronic management with cardiologist if SVT persists

Atrial Flutter

- ECG: regular atrial activity, saw-tooth flutter waves, narrow QRS with variable RR interval

  Management
  - Adenosine will disclose flutter Heart block. Discuss with cardiologist
  - Sychronised cardioversion at 1J/kg, repeat at 2J/kg if no response

BRADYARRHYTHMIAS

Heart block

- HR <90bpm awake or <80bpm asleep
- Associations – congenitally corrected TGA, maternal antibodies e.g. Rho/La, drug toxicity
- May present in utero with hydrops
- 1st degree AV block
- Prolonged PR interval, normal QRS
- 2nd degree AV block
  - ◊ P waves dissociated from QRS
  - ◊ Type 1 increased PR interval
  - ◊ Type II normal PR interval
- Complete AV block: P waves unrelated to QRS

MANAGEMENT

- Determine maternal SLE status
- Indications for pacing (discuss with cardiologist)
  - ◊ Haemodynamic instability
  - ◊ Heart rate < 50bpm
  - ◊ Wide QRS escape rhythm on ECG

Non-invasion transcutaneous pacing

Technique of electrically stimulating the heart externally through a set of electrode pads and utilize the external pacing option on compatible defibrillators. It is only a temporary measure until a permanent pacemaker is placed.

1. Place paediatric electrode pads as directed by package insert. Anterior/ Posterior placement of the electrode pads is most commonly used
2. Set defibrillator on external pacing. Start at 100bpm
3. Many transcutaneous pacemakers operate in 2 modes: asynchronous (fixed rate) or synchronous (demand or non-demand mode) **select demand mode pacing (usually default setting)**
4. Set pacing output (mA) to achieve capture – usually between 50-100 (mA)
5. Start at lowest mA and increase slowly. The higher the mA the greater the chance for skin burns
6. Electrodes should be checked every 30 minutes to avoid burns and should not be left on for more than 2 hours
7. Pacing will cause discomfort sedation is recommended

Synchronised cardioversion procedure

1. Ventilate and sedate infants requiring cardioversion
2. Turn the defibrillator on
3. Attach the patient cable and ECG electrodes. Place the electrodes away from defibrillator sites. Some devices allow monitoring and cardioversion via disposable electrode pads placed in the anterior – posterior position
4. Select the lead which provide a tall R wave; if using disposable electrode pads select the "paddles" lead
5. Select the synchronized mode. "Sync markers" should appear above each R wave. If they do not appear, or appear elsewhere on the ECG, adjust the ECG size or gain until they appear on each R wave. If this does not help, select another lead or reposition ECG electrodes
6. Apply defibrillation gel to the paediatric paddles and place in the anterior-posterior position
7. Select the desired energy and charge the defibrillator
8. Reconfirm that the "sync markers" are properly located
9. Push and hold both paddle discharge buttons until the defibrillator discharges
10. After discharge assess patient rhythm and vital signs
11. If a second cardioversion is indicated follow steps as above.

NECROTISING ENTEROCOLITIS (NEC)

BACKGROUND

- NEC is a life –threatening condition that affects the bowel of infants, the majority of whom are preterm. Patients are severity ill, with an acute abdomen
- There is a high rate of morbidity amongst survivors
- NEC should be considered in any preterm infant with abdominal distention
- Aetiology is multifactorial; prematurity is the biggest independent risk factor but infection, hypoxia, feeding regimens and type of feed [hyperosmolar formula], polycythaemia, PDA, indomethacin may play a role
- The use of breast milk is associated with a lower incidence of NEC.

CLINICAL FEATURES

- Can occur in the first few days of life in term patients, but more commonly from the second week onward in preterm infants
- Onset can be insidious but patients with a rapid onset deteriorate quickly
- Lethargy, abdominal distention, absent bowel sounds, bloody stools, vomiting and discoloured abdominal wall are the cardinal signs. Other signs of illness, i.e. tachycardia, respiratory distress and poor perfusion may be present.

Modified Bell's staging

Stage 1. Suspected NEC: clinically ill. AXR normal to mild distension of bowel loops

Stage 2. Definite NEC: mild or moderate systemic illness, absent bowel sounds, abdominal tenderness, metabolic acidosis, low platelets. AXR: pneumatosis intestinalis or portal venous gas.

Stage 3. Advanced NEC severely ill, marked distension, signs of peritonitis, hypotension metabolic and respiratory acidosis, DIC.

AXR: pneumatosis intestinalis, portal venous gas or pneumoperitoneum

MANAGEMENT

1. Resuscitate: Support breathing and intubate if required.
2. Assess circulatory status; apply fluid and inotropic support judiciously
3. Stop enteral feeds immediately. Insert naso-/orogastric tube, leave on free drainage, monitor output
4. Strict input-output monitoring
5. Investigations: Abdominal X-ray. FBC, CRP, blood culture. Consider U&E, ABG and INR/PIT.
6. Start broad –spectrum antibiotics including adequate gram negative cover
7. Serial abdominal examinations
8. **Stage 1:** reassess abdomen in 24-48 hours. Restart small volume feeds cautiously if examination is normal
   Stage 2 and 3: Keep NPO for 5-10 days. Start total parental nutrition preferably via a deep percutaneous venous line by 48 hours NPO.
9. Patients with advanced disease may require repeat FBC, and clotting profile. Blood products (i.e. packed RBC, platelets or FFP) should be transfused if anemic and/or DIC present. Refer to transfusion protocol.
10. Surgery: operative intervention may be indicated if: pneumoperitoneum, fixed bowel loop, abdominal mass palpable or persistent metabolic acidosis. Paediatric surgeons should be consulted after initial stabilization
11. DO NOT GIVE INDOMETHACIN TO AN INFANT with suspected or definite nec
12. Peritoneal drainage can be used in patients who are too unstable for surgery or in whom ventilation is difficulty due to abdominal fluid. Consult with paediatric surgeon present. Restart feeds slowly (20-30ml/kg/day).
13. Continue antibiotics until septic markers are normalized
14. Patients who have had surgery may return to the NICU with a stoma. Feeds may be resumed 5-7-days post surgery once bowel sounds are present and the stoma is functioning.

OUTCOME

- There is a high mortality, especially in more immature infants
- Patients may present with strictures 3 to 6 weeks post NEC, including those who have had surgery
- Other complications include malabsorption, short gut syndrome, structures, and fistula and neurodevelopmental delay. Involve paediatric gastroenterologist in the management of patients to prevent malnutrition and manage these complications

PREVENTIVE MEASURES

- Start small volume feeds to stimulate GIT mucosal development
- Cautious advancement of feeds in small premature infants
- Do not increase feeds if infant has gastric residual of 50% or more
- Freshbreast milk appears protective

DELAYED PASSAGE OF MECONIUM

- Most healthy babies pass meconium within 24 hours of birth.
- Delay beyond 24 hours is unusual and underlying pathology should be considered
- Possible causes are:
  - ◊ Hirschprung's disease
  - ◊ Meconium ileus
  - ◊ Meconium plug
  - ◊ Intestinal dysmotility, especially in growth restricted infants
  - ◊ Imperforate anus
  - ◊ Prematurity

MANAGEMENT

- Review history for any evidence of polyhydramnios. Ensure that no meconium was passed prior to delivery and check the mother's folder for any antenatal ultrasound reports.
- Take a feeding history, asking specifically about bilious vomiting and abdominal distension
- Do a complete examination, paying special attention to the infant's perfusion, presence or absence of abdominal distension and tenderness, and check if the anus is patent
- If the infant is < 48 hours old, well, no vomiting and a normal examination then observe
- If the infant is > 48 hours old discuss with senior clinician
- If the infant at any time has worrying features on history or clinical examination:
  - ◊ Admit to the nursery
  - ◊ Request AXR
  - ◊ Keep NPO until a senior clinician has reviewed the infant
  - ◊ Discuss with the paediatric surgeon in case of an obstruction or if Hirschprung's disease is suspected.

OESOPHAGEAL ATRESIA (OA) AND TRACHEO-OESOPHAGEAL FISTULA (TOF)

BACKGROUND INFORMATION ON OA AND TOF

- Oesophageal atresia may often be suspected prior to the first feeding by a history of polyhydramnios or observation of copious oral secretions that require very frequent suctioning or may be diagnosed antenatally.
- OA and TOF are due to a failure of early embryonic differentiation of the oesophagus and trachea. At least six types are recognized:

1. OA with distal TOF (85.8%).
2. OA without TOF (7.7%). This malformation is almost invariably associated with a "long gap"
3. TOF without OA (4.2%) H-type fistula. This anomaly may be missed in the newborn period because swallowing is possible. It is associated with cough, pneumonia and abdominal distension
4. OA with fistula to both pouches (1.4%). Although rare, this form is found more often than originally thought.
5. OA with proximal TOF (0.8%). Is an uncommon anomaly; the abdomen is airless, and the diagnosis may be missed unless contrast studies are used.
6. Oesophageal stenosis

MANAGEMENT

- Admit to high care or ICU
- Immediate management of infant with OA and TOF includes the prevention of aspiration and treatment of pneumonitis
- A Replogle tube (or NGT if not available) should be positioned into the upper oesophageal pouch to continuously aspire saliva under low-pressure suction (2-5 cm of water). The double-lumen Replogle tube is best for this purpose because the perforations along the side of the tube are located only near the tip of the catheter; this minimizes the possibility of suctioning oxygenated air away from the larynx
- The Replogle tube should be flushed every 15 minutes with 0.5ml of 0.9% NaCl to keep the tube patent
- The infant should be positioned to minimize the reflux of gastric fluid up through the TOF, i.e. head up. The prone position is the most effective in minimizing reflux in the infant. Therefore, wherever possible nurse prone with head elevated.
- Chest X-ray with Replogle tube (or NGT) in situ
- If the tube curls up in blind oesophageal pouch and there is no air in bowel, assume a diagnosis of oesophageal atresia.

- If the tube curls up in blind oesophageal pouch and there is air in the distal bowel, assume a diagnosis of oesophageal atresia with distal TOF
- Keep nil by mouth from birth. Insert IV cannula for IV fluids of 10% glucose
- Avoid bag and mask ventilation and nasal CPAP to prevent over-distension of the stomach. If the baby needs respiratory assistance, intubate the infant
- Inform a senior clinician.
- Insert a PICC line for parenteral nutrition
- Arrange referral to paediatric surgery as soon as possible
- Ensure associated anomalies excluded (VACTERL) before discharge home.

ASSOCIATED ANOMALIES

- Overall incidence 50% to 70%
- The anomalies are most common in cases of OA with TOF and are least common in cases of the H-type fistula
- Cardiovascular anomalies are the most common (35%). Complex cardiac deformities account for most of the deaths associated with OA. The most common single defect is a ventricular septal defect. Other common cardiac anomalies include tetrology, patent ductus arteriosus, atrial septal defect and coarctation of the aorta
- Genitourinary (20%). The defects are varied and include hypospadias, undescended testes, renal agenesis, or hypoplasia, cystic renal disease, hydronephrosis, vesico-ureteral reflux, ureteric duplication, ambiguous genitalia and many more.
- Gastrointestinal (24%). These include anorectal atresia, duodenal atresia, ileal atresia, malrotation, annular pancreas and pyloric stenosis
- Skeletal (13%)
- Associated neurological anomalies (13%)
- VACTERL association (vertebral defects, anal atresia, trachea-oesophageal fistula, oesophageal atresia, renal defects and limb abnormalities)
- Oesophageal atresia is also found in conjunction with the CHARGE association (coloboma, heart defects, choanal atresia, developmental retardation, genital hypoplasia and ear deformities or deafness).

COMPLICATIONS

Early Complications:

- anastomotic leak: the leak at the oesophagotomy occurs in approximately 14-16% of the infants. Most leaks are clinically insignificant and can be managed with adequate drainage and nutrition support
- Oesophageal stricture: it is a common complication of anastomosis of the oesophagus in OA and TOF, but the reported incidence varies widely depending on the criteria used to define a stricture
- Recurrent trachea-oesophageal fistula occurs in 3-14% of the infant after initial operative division of ligation

Late Complications:

- Gastro-oesophageal reflux (GOR): this occurs in 40-70% of infant following repair of OA. It can be a cause of considerable morbidity. The GOR may be related to shortening of the intra-abdominal oesophagus resulting from anastomotic tension, or oesophagaeal motor dysfunction, either acquired as a result of operative manipulation or intrinsic to the congenital anomaly itself.
- Tracheomalacia: 10-20%
- Disordered peristalsis

GASTROSCHISIS AND OMPHALOCELE

BACKGROUND

- gastroschisis is a herniation of abdominal contents through a small right-sided abdominal wall defect, lateral to the umbilical cord. The exposed bowel is never covered by a peritoneal sac. Approximately 10% of infants with gastroschisis have associated abnormalities, usually intestinal atresias.
- Omphalocele is a herniation of bowel, and occasionally other organs including stomach and liver, into the umbilical cord and these are usually covered by a peritoneal sac, which may rupture prior to or during birth. Omphalocele is highly associated (>50%) with other anomalies, especially congenital heart disease, chromosomal abnormalities, pentalogy of Cantrell and Beckwith-Wiedemann syndrome. Therefore, chest X-ray, renal ultrasound, and echocardiogram should be obtained prior to operation.
- Often diagnosed prior to delivery by ultrasound. If not in a major centre, mother must be referred to deliver where appropriate expertise is available.

MANAGEMENT

- Notify paediatric surgeon prior to the delivery of the infant. The surgeon should preferably be present in theatre to place a silo, if gastroschisis is present.
- The neonatal registrar must be present at delivery
- Insert a Replogle tube/or NGT if not available and place on continuous suction to prevent bowel distension
- If the silo is not placed in theatre, fluid losses from the exposed bowel can be massive, so the defect should be wrapped in cling wrap to keep the environment moist. Sterile 0.9% NaCl soaked swabs can be used as an alternative to cover the defect
- Maintain suction while the surgeon places the silo
- Intubate electively if the procedure is difficult or the infant experiences discomfort
- With gastroschisis or large omphalocele, make sure that the blood supply to the bowel is not kinked by the weight of the bowel
- Place baby under radiant warmer to prevent hypothermia from high heat loss from he exposed bowel
- Start IV maintenance fluids and prophylactic antibiotics. IV fluid requirement may be high, especially for gastroschisis.
- Insert a PICC line for TPN

- Monitor and replace NGT aspirates ml for ml with half normal saline + KCl (100ml 0.45% saline 1 ml KCl)
- Each day, the silo is tightened by the surgeons so that the bowel is gradually pushed back into the abdominal cavity
- The final closure is performed in the operating room with removal of the silo and, occasionally, placement of a mesh graft to help close the anterior abdominal wall.
- If there is adequate space within the abdominal cavity, a primary closure of the abdominal wall may be done, often with a gastrostomy tube for decompression. Usually this is possible for omphaloceles, which tend to be small, and is occasionally possible for small gastroschises.
- Risks of the silo include infection and bowel necrosis.

HAEMATEMESIS AND BLOOD IN STOOL OF THE NEWBORN

POSSIBLE CAUSES

- Swallowed maternal/placental blood at delivery
- Swallowed maternal blood from cracked nipple
- Local trauma e.g laryngoscope, NGT
- Over vigorus laryngeal suction
- Fissure-in-ano

Note: It is important to distinguish between maternal (swallowed blood) and fetal blood by using Apts test for fetal hemoglobin.

Other conditions include:

- NEC
- Hemorraghic diasthesis
- Steroid use
- Rare causes e.g. trauma, Meckel diverticulum, malrotation, peptic ulceration, rectal hemangiomas, intussuseption, colitis

HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

DEFINITION

HIE is an acquired syndrome of acute brain injury characterized by Neonatal Encephalopathy (NE) and evidence of intrapartum hypoxia.

- NE is characterized by an abnormal level of consciousness, abnormal tone and abnormal primitive reflexes. Abnormal breathing and seizures may occur
- Intrapartum hypoxia may be suggested by the presence of one or more of the following features:
  An acute intrapartum event, fetal bradycardia or reduced variability, meconium stained liquor, prolonged second stage, need for resuscitation at birth for 5 minutes or longer, a 5-minute Apgar score < 7, acidosis on cord or neonatal blood in the first hour of life (defined as pH < 7 or Base Excess < - 10).

NB: The presence of features that suggest intrapartum hypoxia does not exclude other causes of encephalopathy.

Indications for Admission of Term/Near Neonates Who Required Resuscitation

- Neonates who required cardiac compressions and/or adrenaline at birth
- An abnormal cord or neonatal blood gas in the first hour of life (pH< 7 or Base Excess < -10)
- Neonates who have a 10-minute Apgar score < 8 or grunting respirations regardless of Apgar score.

IMMEDIATE MANAGEMENT ON ADMISSION

- Manage airway, breathing and circulation (refer to newborn resuscitation algorithm)
- Check glucose, perform a general and neurological examination if no multistix available, give glucose at 3mls/kg
- Document congenital anomalies
- Document the Thompson HIE score (chart below)
- If there are signs of encephalopathy:
  - ◊ Keep nil by mouth
  - ◊ Commence IV fluids at 40 ml/kg/day
  - ◊ Apply the aEEG as soon as possible if available

If there are clinical or aEEG signs of moderate-severe HIE, refer to the cooling protocol –discuss all cases with a senior clinician.
Initial investigations of infants with moderate – severe HIE should include:

- Blood gas
- FBC and blood culture
- Sodium, Potassium, Calcium, Magnesium
- If history/signs suggest sepsis, perform a septic screen including a lumbar puncture
- Commence antibiotics – see further in text

HISTORY DOCUMENTATION

The neonatal record from the labour ward will have some of the information, otherwise will need to obtain the following aspects, if necessary from a review of obstetric case notes:

1. **Maternal and Family history**
   Health, consanguinity, congenital abnormalities, perinatal death
2. **Previous Pregnancies**
   Live/still Born or miscarriages or neonatal deaths
3. **Current Pregnancy**
   Gestation, medication, events, booking investigations and scans
4. **Labour and Delivery**
   Augmentation, fetal heart monitoring, medication, sepsis, intrapartum events, length 2nd stage, presentation, method, and indication for delivery
5. **Resuscitation and evidence for intrapartum hypoxia**
   - Blood gas on Cord (umbilical artery or vein) or on infant (preferably arterial) as soon as possible after birth (or acidotic breathing [deep respirations with prolonged expiration])
   - Apgar scores at 1, 5 and 10 minutes
   - Need for intubation and details
   - Time of first gasp and onset of heart rate > 100bpm
   - Time onset of regular (non-gasping) respirations
   - Drugs/fluid administered to infant
6. **Placental information**
   Record appearance and weight – send for histology if there is diagnostic uncertainty.

CLINICAL MANAGEMENT

Temperature and Cooling

- Avoid overheating infants at any stage
- Refer to separate cooling protocol for details of eligibility and method
- All cooled and borderline cases should be discussed with a senior clinician
- It is not necessary to obtain the aEEG result before cooling if infants have obvious moderate-severe encephalopathy on clinical grounds

Ventilation

- Aim for normal $PaCO_2$ and oxygen saturation **(refer to normal values in appendix)**
- If oxygen is needed and respiratory effort is good, nasal cpap or nasal cannulae are often adequate
- Ventilate if apnoea or respiratory acidosis with pH < 7.25 and inform senior clinician
- If pCO_2< 3.3kPa wean ventilation rapidly and recheck within 30mins – consider extubation
- Wean FiO2 and peak inspiratory pressure at the bedside observing saturation and chest wall movement
- If ventilated do blood gases hourly or more often if abnormal – continues until normal

Blood pressure (BP), haemoglobin (Hb) and coagulation management

- Monitor blood pressure and keep it in the normal range (Mean arterial pressure [MAP] = 40-50)
- Give fluid bolus of normal saline at 20mls/kg if suspected hypovolemia
- Metabolic acidosis alone, is not an indication for a fluid bolus
- Transfuse if significant anaemia (PCV < 30%/Hb <10); consider occult bleeding, consider Coombs test
- Check INR/PTT/Fibrinogen in severely anaemic or bleeding infants (e.g. subaponeurotic haemorrhage)
- Treat active bleeding with vitamin K (1-2mg/kg IV) and FFP (15mls/Kg over 30 minutes) – consider cryoprecipitate if poor response or low fibrinogen
- Treat normovolaemic hypotension with inotropes – see separate inotrope guideline (see cardiac care section) usually Dobutamine starting at 5 mcg/kg/min is first line. If not available give Dopamine at 5mcg/kg/min.
- An echocardiogram to assess cardiac function can inform fluid and inotrope management (If ECHO not available, use CRT, urine output and blood pressure where possible as a proxy)
- Central access via UVC or other central line is preferable for sick infants requiring inotropes

Fluid balance, acidosis and metabolic management

Intrinsic renal failure and SIADH commonly occur

- Initially fluid restrict to 40 ml/kg/24 hours
- Initially use potassium-free 10% dextrose solution containing 1/5 – 1/2 normal saline ***(check how many millimoles of each electrolyte).*** Ensure that maximum sodium is adhered to with the fluids available.
- Potassium-containing fluid should only be used if urine output and serum potassium are normal
- Monitor urine output, electrolyte, blood glucose and blood gases
- Remember to palpate for bladder and massage if distented. If not distended and oliguric (<1 ml/kg/hr) or continues to retain fluid after massage, then catheterise
- Catheterise if urine retention or oliguria (<1 ml/kg/hr)
- Hypocalcaemia and hypomagnaesia should be anticipated and treated
- Treat Hyponatraemia< 130 mmol/l with fluid restriction if oliguric – if not oliguric, consider increasing fluids and using 0.9% saline in maintenance fluids
- There is no proven benefit of Sodium Bicarbonate to treat lactic acidosis
- Monitor plasma glucose initially at least 4 hourly
  - ◊ Increase IV glucose concentration if plasma glucose < 2.6 mmol/l
  - ◊ Adjust according to further monitoring
  - ◊ If hypoglycaemia occurs, use 12 or 15% glucose as an infusion solution

Feeding

- Beware of necrotizing enterocolitis
- Preferably feed with breast milk
- Introduce feeds slowly, particularly moderate-severe HIE – usually nil by mouth on admission then commence 3-hourly feeds after 12-24 hours:
- Increment by 12mls/kg/day during the first 3 days and by up to 30m/kg/day thereafter if abdomen exam normal
- Infants with mild encephalopathy who are not cooled can be fed with higher volumes

Sepsis

- Treat with first line antibiotics as per hospital protocol.
- Discontinue antibiotics at 36 hours if sepsis ruled out for follow hospital antibiotic policy.

Seizures

- Refer to seizure management guideline

Communication with Parents

Explain the clinical condition and the potential for other causes

- Explain the management
- Document the parent's version of events
- Prepare them for a potential poor outcome if investigations and signs are suggestive

CLINICAL NEUROLOGICAL ASSESSMENT

Clinical signs vary with time

There are **three stages of encephalopathy**:

- Stage 1(mild): Irritability, increased tone, poor sucking and exaggerated moro reflex
- Stage 2 (moderate): Lethargy, decreased tone and primitive reflexes. Often with seizures
- Stage 3 (severe): Stupor or Coma, flaccid tone and seizures often clinically less apparent

Moderately or severely affected infants typically develop increasingly obvious signs during the first 48-72 hours. Seizures are often clinically silent.

The Thompson HIE score

The Thompson HIE score should be performed on admission, before age 5 hours, and daily until normal or age 7 days (up to 10 days if cooled). The maximum score, based on the clinical signs in the previous 24 hours, is recorded in each category and then totaled for the day. A score of < 5 in the first 5 hours of life is associated with a normal aEEG at 6 and 24 hours.

Score / Grade Sign	1	2	3	Score
Limb Tone	Generally Hypertonic	Generally Hypotonic	Flaccid	
Level of Consciousness	Hyper-alert, staring, or excessive irritability	Lethargic	Comatose or Stuporose	
Visible Fits	Infrequent < 3/day	Frequent > 2/day		
Posture	Fisting and/or cycling	Strong distal flexion	Decerebrate	
Moro	Partial	Absent		
Grasp	Poor	Absent		
Suck	Poor	Absent and/or bites		
Respiration	Hyper-ventilation	Transient apnoea	Apnoea Req IPPV	
Fontanel	Full	Tense		
TOTAL				

If infants are not cooled: A peak score of 10 or less during the first 6 days with a score of 0 by day 7 predicts a normal outcome, a score of 11-15 at any time or a score above 0 on day 7 predicts an abnormal outcome in 65% and a score of above 15 predicts an abnormal outcome in 92%.

Cerebral function monitor, aEEG

- If available, apply aEEG to all infants with signs of HIE as soon as possible.
- Monitor for at least 6 hours if not cooled (preferably 24h). If cooled, continue until rewarm is complete.
- Background pattern should only be used to prognosticate in the "crosshead" mode
- Record in the notes; seizures activity at any time and background pattern at age 6 hours and then every 24 hours
- A severely suppressed background persisting for 6 hours predicts a poor outcome in over 80% and if this persists beyond 48 hours, despite cooling, the prognosis is almost invariably poor
- A normal voltage pattern at 48 hours in cooled infants associated with a good outcome in most infants

Cranial ultrasound

Perform at least on Day 1 and again at Day 7-14. Cranial US shows gross anatomy, established damage at birth and evolving focal or global injury.

MRI

If available, MRI is the most reliable guide to prognosis and diagnosis available. It is best done at 7-14 days for optimal prognostic information.

WHEN TO STOP RESUSCITATION OR OFFER WITHDRAWAL/REDIRECTION OF CARE

- Stop resuscitation after 10 minutes of asystole
- Consider stopping resuscitation if no spontaneous respiration after 20 minutes – first ensure that infant is not hypocarbic and has not been exposed to maternal opiates/benzodiazepines
- Discuss with senior clinician before stopping resuscitation
- Withdrawal of intensive care or ventilation should be discussed with the senior clinician, but should be considered (withdrawal may be mandatory if resources are limited), in the following circumstances:
  - ◊ Infants who initially met resuscitation discontinuation criteria but ventilation was continued and there is persisting isoelectric aEEG and/or coma and persistent apnoea in the absence of sedative drugs
  - ◊ Infants with severely abnormal aEEG (upper and lower margins below 10mcV or burst suppression) persisting beyond 24 hours if not cooled or 48 hours if cooled.

NOTE: high dose midazolam or opiates can affect the clinical and electrical data

◊ Additional factors such as cranial ultrasound and MRI findings and multi-organ failure should also be considered.

Follow-up

Arrange neurodevelopmental follow up at 20 (18-22) weeks (to follow up with local hospital guidelines)

- Document head circumference and neurological exam at birth and at discharge
- Document maximum HIE grade and Thompson score
- Plan and discuss the need for long-term anticonvulsant management (refer to neonatal seizures section). Only discharge on anticonvulsants under exceptional circumstances and in discussion with a senior clinician
- Limited consensus exists concerning the duration of long-term AED therapy and controlling seizures

Normal examination, in particular a normal nutritive suck at age 7 days carry a good prognosis. However, infant who can feed well and visually fix and follow by age 10-14 days can still have significant focal basal ganglia lesions that may lead to an athetoid type of CP with good preservation of intellect and head growth; and Infants with adequate feeding by 2-3 week but often slightly slow visual attention may have significant white matter injury that will lead to relative microcephaly and some slowness in learning without a major motor problem.

If MRI is done after discharge -ensure that a developmental appointment is made soon after to discuss results.

THERAPEUTIC HYPOTHERMIA FOR HIE

CRITERIA FOR THERAPEUTIC HYPOTHERMA

These criteria are based on recommendations in published studies. The resource – limitations and the local data describing the HIE associations in our population have also been considered.
All infants that are considered for cooling should be discussed with senior clinician before cooling.

A. All of the following:

1. ≥ 35-weeks gestation
2. Birth weight > 1800g
3. Able to begin cooling by age 6 hours
4. Absence of: severe congenital anomaly; or uncontrolled bleeding, systemic hypotension, and/or pulmonary hypertension (FiO_2 > 0.8) not responding to treatment

AND

B. Suspected intrapartum hypoxia based on the presence of at least one of the following:

1. First hour blood gas (cord/infant/arterial/capillary/venous): pH ≤ 7 or base deficit ≥ 10mmol/l
2. 5-minutes Apgar < 7 or assisted ventilation at birth continued for ≥ 10 minutes

AND

C. Moderate-severe neonatal encephalopathy base on one of the following:

1. Abnormal amplitude – integrated EEG (aEEG) occurring at any time during the first 6 hours defined by: Moderately abnormal background, suppressed background, discontinuous normal voltage, burst suppression, low voltage, flat trace or seizures.
2. If an aEEG is not available, moderate-severe encephalopathy can be defined by the presence of at least one finding in at least three categories as indicated in the table below or definite seizures.

Category	Moderate Encephalopathy	Severe Encephalopathy
Level of Consciousness	Lethargic	Stupor or coma
Spontaneous activity	Decreased activity	No activity
Muscle tone	Hypotonia	Flaccid
Posture	Distil flexion/complete extension	Decerebrate
Suck or Moro	Weak suck or partial moro	Absent
Autonomic system	Miosis (fixed pinpoint pupils) Bradycardia (<100bpm) Periodic or shallow breathing	Deviated, fixed dilated or non-reactive pupils, variable heart rate, or apnoea

NB: If the aEEG is normal, but cooling has already commenced based on appropriated clinical criteria alone, cooling should be continued for 72 hours. Cooling should not be delayed by aEEG application in severe clinical HIE.

Cooled infants should be entered in a cooling register

DETAILED COOLING METHOD: PART I

Management on admission

- Only commence cooling on instruction from senior clinician
- Check and stabilize vital signs first
- Infant should be kept at a skin temperature of 36.5^{o}C while awaiting decision to cool
- Attach aEEG to all infants as soon as possible – initially only 3 leads need to be applied.

Contrandications to cooling

- Major congenital abnormalities likely to affect neurological outcome or moribund and unlikely to benefit from cooling or uncontrolled bleeding OR
- Severe pulmonary hypertension/system hypotension responding poorly to treatment

SERVO-CONTROLLED GEL-PACK COOLING METHOD

(Should preferably be used with radiant warmers capable of a target infant temperature of 33.5)

- Connect temperature probe from infant to servo crib:
  EITHER: Skin probe between infant and mattress, insulated with reflective cover & tegaderm
  OR: Rectal temperature probe: insert 5cm and stick to buttocks with tegaderm

- Set Target infant temperature on servocrib to **33.5°C** – It must remain at this target until rewarm starts
- Place heat shield over head and shoulders
- Apply 2 to 4 cold soft gel packs from Fridge (NOT FROZEN SOLID) around head
- Do not "nest" infants cooled in this manner
- If infant temperature rises above 34°C:
  - ◊ Check temp. Probe is correctly positioned and covered, adequate sedation, not nested, humidifier set low, gel bags cool and being changed frequently, heat shield covering head and shoulders. If necessary, add more bags around the head, neck and chest.
  - ◊ IF TEMPERATURE REMAINS ABOVE 34°C INFORM DOCTOR
- If infant temperature is below 33°C:
  - ◊ Check probe as above, remove gel bags
  - ◊ IF TEMPERATURE REMAINS BELOW 33°C INFORM DOCTOR
- Always acknowledge servocrib temperature alarms by silencing them
- Re-warm after 72 hour of cooling: Leave heat shield in place and increase servocrib target temperature by 0.2°C every hour until at 36-36.5°C. Then change the probe to a standard surface skin probe with a target temperature of 36.5 °C or, preferably, place the infant in a cot.

SERVO-CONTROLLED COOLING MAT METHOD

- Turn off servocrib
- Insert rectal temperature probe 4-5 and attach to cooling unit
- Refer to separate instructions for operation of cooling unit and rewarming

DETAILED COOLING METHOD: PART 2

Sedation during cooling

- Sedate ALL infants during cooling (unless decreased level of consciousness or adequately sedated with anticonvulsants)
- **Morphine dose:** 0.1mg/kg loading dose PO or IV slowly over 10 minutes; then 0.05 mg/kg 6 hourly IV/PO or IV infusion of 0.008mg/kg/hr (8mcg/kg/hr) until rewarm is commenced. Review need for sedation regularly.

Morphine dilution insructions:

Add 10mg Morphine to 9ml saline to give 1mg/ml solution. Draw up dose from that solution using a 1ml syringe. Add that dose in the 1ml syringe to a further 5ml Saline before infusing bolus, or to a 50ml syringe with saline for continuous infusion.

MONITORING AND RELATED MEDICAL MANAGEMENT

Manage according to HIE protocol. Specific management related to cooling:

- If giving IPPV or NCPAP, then set humidifier to low temperature setting to keep inspired gas to 34 °C
- Heat rate falls by 10bpm per 1 °C fall in temperature. Normal heart rate during cooling: 70-120bpm
- **If heart rate>120bpm exclude the following:**
  - ◊ Inadequate cooling
  - ◊ Seizures
  - ◊ Agitation, pain
  - ◊ Hypotension, blood loss
  - ◊ Excessive inotropes or
  - ◊ Sepsis

aEEG Monitoring and Management

- The interpretation of the aEEG should be clearly documented (and verified by the attending consultants) in the patients notes at the following times: Pre-cooling, 6h, 24h, 48h, 72h; when ever seizures are suspected and whenever there is a change in background pattern
- Use the on screen tool to document medication, clinical abnormalities or events on the aEEG monitor
- Treat seizures according to seizure protocol: Phenobarbital up to 40mg/kg, then midazolam, then Lignocaine, then pyridoxine. NB: Adjust dose of Lignocaine during cooling

MANAGEMENT OF NEONATAL SEIZURES

DEFINITION

An abnormal synchronous electrical discharge of a group of neurons in the central nervous system.
Status epilepticus: continuous seizures lasting 30 minutes or recurrent seizures occupying 50% of the EEG recording for at least 60 minutes.

CLINICAL MANIFESTATIONS

- Clinical manifestation may be:
  - ◊ Absent
  - ◊ Subtle: eye deviation, eyelid fluttering, bucco-lingual movement or pedaling of arms and legs
  - ◊ Focal: tonic or clonic
  - ◊ Generalised: multifocal rhythmic jerking, generalized posturing or myoclonic

IMPORTANT CAUSES

- *Brain damage:* Hypoxia –ischaemia, bleeding, infarction, oedema
- *Brain malformations*
- *Meningitis or encephalitis:* Acute (Bacterial or viral) or Chronic (viral, syphilis)
- *Bilirubin encephalopathy*
- *Biochemical:* Hypoglycaemia, hypomagnesaemia, hypernatraemia,
- hyponatraemia, hyperammonaemia, pyridoxine dependency, other
- *Inborn errors of metabolism*
- *Drug withdrawal:* Maternal opiate or cocaine abuse
- *Iatrogenic:* Air embolism
- *Familial:* Fifth day fits (benign)

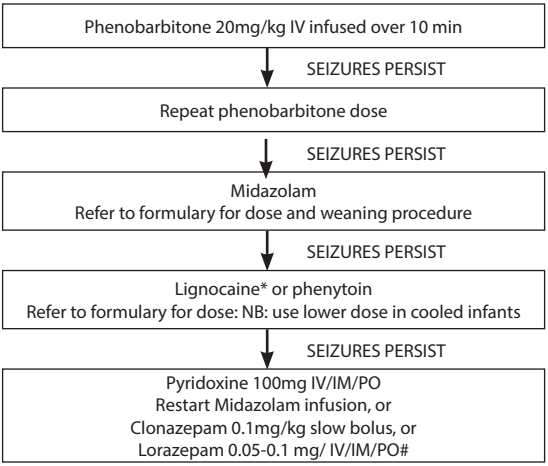
DIAGNOSIS

- History: family, pregnancy, birth, clinical course
- Confirm seizure and monitor response to treatment using aEEG if available
- Measure serum glucose, magnesium, calcium and sodium
- Do a lumbar puncture if sepsis is suspected
- Head ultrasound may be diagnostic if intracranial bleed, structural abnormality or ventriculitis is present
- Consider inborn errors or metabolism if other causes are not obvious
  - ◊ Measure serum lactate, ammonia and amino acid and urine organic acids. Discuss with the consultant need for CSF lactate and glycine levels. Note serum and CSF glycine levels have to be done simultaneously
  - ◊ **Discuss and arrange with the laboratory before taking any samples**

TREATMENT

- Treat electrolyte and glucose abnormalities and sepsis
- Ensure adequate ventilation and perfusion. Commence CFM/Brainz monitor
- Treat seizures (clinical and/or electrical) with anticonvulsants if they are recurrent or last more than 3 minutes.

ANTICONVULSANT TREATMENT ALGORITHM FOR TERM INFANTS



- If IV Phenobarbitone is not available, use midazolam, clonazepam or Lorazepam as first line. In addition, consider treating with oral phenobarbitone as crushed tablets.
- If Lignocaine is not available, use Phenytoin as second line.
- Do not use Lignocaine and Phenytoin in the same patient within 72 hours of each other.
- #Lorazepam: IV use, dilute to 0.1mg/ml. IM use (emergency) dilute to 1mg/ml. Use sugar free suspension for oral use.

ENSURE THE LIGNOCAINE VIAL IS SUITABLE FOR IV USE. Lignocaine infusions must be checked by 2 senior staff before commencement

In preterm infants follow the same algorithm but use phenytoin as second line instead of lignocaine

TREATMENT CONSIDERATIONS

1. When the seizures are controlled, keep the newborn in Phernobarbitone maintenance at 3-5 mg/Kg/day.

   NB: In case of excessive sedation do not discontinue Phernobarbitone (probably the drowsiness is secondary to the underlying condition) and evaluate reduction of Phernobarbitone at lower maintenance dose with close clinical monitoring.

2. In case of acute symptomatic seizures resolved by correction of the underlying etiology and not associated with increased risk of brain injury, AEDs can be discontinued gradually.

3. If the infant is taking medication and seizures recur, increase the dose back to levels at which no seizures occurred and ask for neurological evaluation.

4. Generally, patients who had neonatal seizures that required recommencement of anticonvulsants/continued AEDs; should be discharged on maintenance phenobarbital and followed up montly at least until 3 months of age. The choice to tapper down Phernobarbitone after 1 month should be evaluated case by case considering risk factors for recurrence of seizures.

5. Paediatric neurology evaluation and EEG at 1-3 month for infant at increase risk of epilepsy should be requested where available.

MANAGEMENT OF MENINGOMYELOCELE AND OTHER NEURAL TUBE DEFECTS

BACKGROUND

- Failure of closure of the neural tube during the third week of gestation leads to the constellation of defects observed in patients with meningomyelocele (MMC)
- The open neural tube is continuous with the surface of the skin. For this reason, infants with MMC are at risk for bacterial meningitis due to the spinal defect. Leak of cerebrospinal fluid (CSF) leak is commonly observed
- The major indication for early operative repair (within 48h of delivery) is prevention of infection
- Although it is essential to protect exposed neutral tissue from trauma and drying, the neurological deficit caused by MMC is fixed and rarely improves following repair
- Deterioration, however, can occur

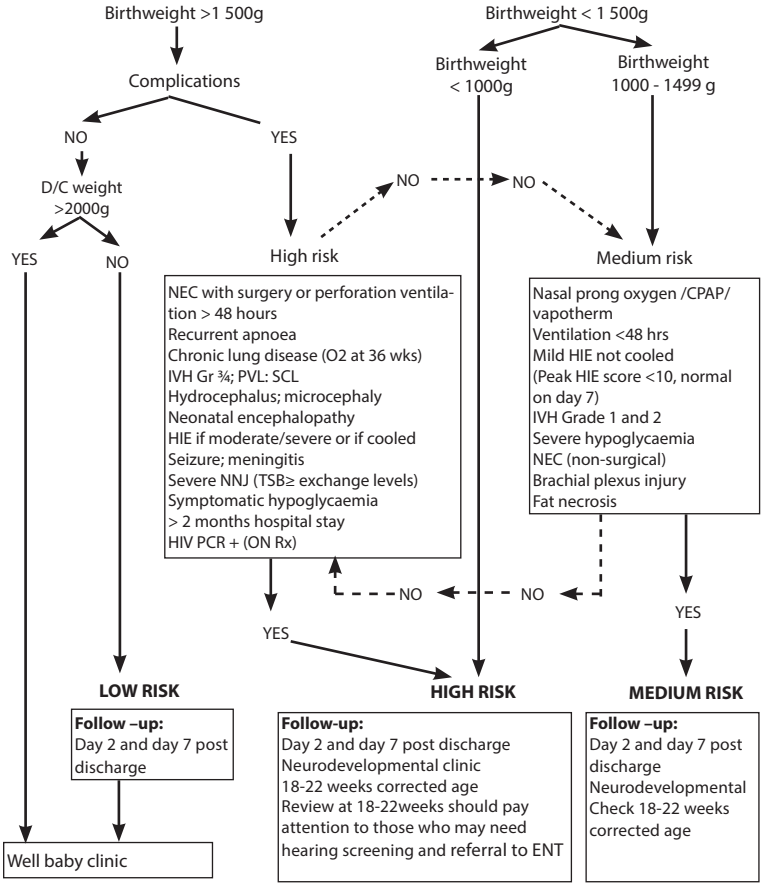
MANAGEMENT

- Notify a senior clinician of the expected delivery
- The senior clinician should be present for delivery, which will almost always be by caesarean section
- Use sterile, non-latex gloves
- After birth, position infant on side or on abdomen. Resuscitate as needed. Although all MMC patients have a Chiari II malformation (hindbrain herniation) visualized on MR imaging; only a minority will be symptomatic at birth. This may consist of stridor and upper airway obstruction
- Carefully examine MMC to estimate the anatomic level of lesion and whether the sac is intact. A small amount of CSF usually "weeps" from the translucent edges of the neural placode. If the sac ruptures, it usually decompresses and drops to the level of the back.
- Place sterile 0.9% saline soaked swabs over the defect and keep the swabs moist.
- Always nurse prone or side-lying position to avoid pressure on the sac or nerves
- Avoid contamination of side and dressing from stool and urine
- Perform a careful full neurological examination and note the presence of any orthopaedic deformities such as clubfeet
- Measure the head circumstance and look carefully for clinical findings of hydrocephalus. Obtain a baseline head ultrasound. The decision to place a ventriculoperitoneal shunt is individualized for each patient. In general, symptomatic hydrocephalus, progressive increase in head size, or leakage of CSF from the repaired defect site are indication for shunt placement. Usually a shunt is placed several days after the initial repair, although infrequently this may need to be done at the same time as the repair.
- Monitor infant closely for signs of meningitis.
- Arrange appropriate referral within 48 hours.

BLADDER MANAGEMENT

- Clean intermittent catheterization is indicated to check postvoid residuals until urologic and renal function assessed.
- If voiding pattern is abnormal, it is important to determine if the aetiology is abnormal bladder emptying, renal function, or both. A serum creatinine level is useful in making this distinction

GUIDELINES FOR HIGH-RISK INFANT FOLLOW-UP AND DEVELOPMENT SCREENING



Calculation of corrected age (date for first neurodevelopment screening visit):
[40-Gestation age at birth (Ballard) +20 = No. of weeks [N]
Date for follow-up =Birth date + [N] (best age for assessment between 18-22) weeks, NOT earlier)

PVL = periventricular leucomalacia: SCL = Subcortical Leucomalacia;
Severe hypoglycaemia is a single reading < 1.6mmo/l or 3 or more reading < 2.6 mmol/l;
Symptomatic hypoglycaemia is any that is associated with clinical signs

NEONATAL PAIN AND STRESS PREVENTION AND MANAGEMENT

INTRODUCTION

Untreated pain and stress has been linked to adverse short and long term outcomes. Acute effects include: elevation of cortisol, catecholamines, and lactate, hypertension, tachycardia, respiratory instability, glucose instability and changes in cerebral blood flow. Chronic pain; affect growth, immune function, recovery, length of hospital stay, effects on long term memory, social and cognitive development and neuroplasticity. Later consequences; decreased pain thresholds in later infancy, altered pain response in childhood, hormonal imbalance with resultant cardiovascular disease and type 2 diabetes in adults.

PRINCIPLES OF PREVENTION AND MANAGEMENT OF NEONATAL PAIN AND STRESS

These include:
Neuroanatomic components and neuroendocrine systems of the neonate are sufficiently developed to allow transmission of painful stimuli
Exposure to prolonged or severe pain may increase neonatal morbidity
Infants who have experienced pain during the neonatal period respond differently to subsequent painful events
Severity of pain and effects of analgesia can be assessed in the neonate using validated instruments
Newborn infants usually are not easily comforted when analgesia is needed
A lack of behavioral responses (including crying and movement) does not necessarily indicate the absence of pain

STRATEGIES OF PAIN MANAGEMENT

1. **Non-pharmacological management**
   - ***Environmental and behavioral approaches:***
     ◊ Painful or stressful procedures should be reviewed daily and be limited to those based on medical necessity
   - ***Physiological interventions.*** Consist of taste-mediated analgesia combined with non-pharmacologic strategies (e.g environmental, hand containment or facilitated tucking, pacifier, skin-to-skin holding).
     ◊ **Sucrose analgesia** 0.05ml to 0.5ml solution given orally (on the tongue) 2 minutes before or just prior to the painful procedure. Dose can be repeated if procedure lasts more than 5 minutes
     ◊ **Best combined with other non-pharmacological strategies** such as nonnutritive sucking (e.g. pacifier), eye protection from light, decreased sound/activity around the bed
     ◊ **Breast milk** administration on the tongue before or during painful procedures

2. Pharmacological management

Considerations

- ***Complementary therapies.*** Environmental and behavioral interventions, including sucrose, should be applied to all infants experiencing painful stimuli in conjunction with pharmacological treatments
- ***Prophylaxis versus pain treatment.*** Opioid analgesia given on schedule basis results in a lower total dose and improved pain control compared with "as needed" dosing.
- ***Gestational maturity.*** Pain should be assumed and treatment should be initiated in the immature, acutely ill infant who may be incapable of mounting a stress response to signal his or her discomfort
- ***The routine use of continuous infusions of morphine, fentanyl, or midazolam in chronically ventilated preterm neonates is not recommended due to short term adverse effects and lack of long-term outcome data.***

A. Analgesia for minimally invasive procedures

- ◊ **Sucrose;** dose as above
- ◊ **Topical analgesia**. EMLA, a mixture of Lidocaine and prilocaine, is safe as a topical anaesthetic and can be used in neonates above 37 weeks (avoid in infants on Phenobarbital, sulphurs and acetaminophen)

B. Analgesia for invasive procedures

- ◊ **Opioids** (e.g. morphine or fentanyl)
- ◊ **Sedatives (**e.g. midazolam or Phenobarbital)

Procedures

a. Premedication - required for procedures such as elective intubation, chest tube insertion or removal, peripheral arterial placement and circumcision

b. Intubation – medications as in the procedure section on elective intubation (except in emergency intubation). For the first few days of mechanical ventilation, if analgesia is needed, fentanyl 1 to 3mcg/kg or morphine 0.05 to 0.15mg/kg can be given every 4 hours

c. Circumcision

Pretreatment; both oral (24%) sucrose analgesia, Paracetamol 15mg/kg preoperatively, dorsal penile block or ring block with max Lidocaine dose of 0.5%, 0.5ml/Kg. An infant may benefit from acetaminophen following the procedure

Please note that sedatives and Opioids may cause respiratory depression and their use should be restricted to settings where respiratory depression can be promptly treated by medical staff experienced in airway management.

NEONATAL ABSTINENCE SYNDROME

Babies born to mothers who were dependant on drugs during pregnancy, whether opiates or other substance (e.g selective serotonin reuptake inhibitors, tricyclic antidepressants, methamphetamines or inhalants), may develop signs of drug withdrawals or neonatal abstinence syndrome (NAS).
These signs are listed in the Modified Finnegan Chart (see next page) – each sign is allocated a score that determines subsequent treatment of the infant.
Infant exposed to drugs that cause NAS may initially be asymptomatic, but all should be observed for at least 2 days. Those with opioid or poly-drug use should be admitted and assessed with the Modified Finnegan Chart. The frequency of presentation, time of onset after birth and duration of symptoms varies according to maturity of the infant; and the type and dose of drug. Most infants present within 24-48 hours after birth, but infants of mother on prescription opioids may present at age 60-72 hours. The incidence and severity of NAS is less in preterm infants. All symptomatic infants need to be admitted.

Delivery

- Routine attendance at delivery by neonatal staff is unnecessary
- Narcan (naloxone) is contra-indicated in babies born to mothers suspected of using opiate drugs due to the risk of precipitating a sudden and severe withdrawal in the infant

History

- Record a detailed maternal drug history, including drug detox programmes. Additional information may be available from the midwife or social worker
- All cases must be referred to the social worker before the mother is discharged
- Determine HIV, VDRL, Hepatitis B/C status of the mother

Drug-related maternal infection

- Hep B immunization should be considered in all infants thought to be at postnatal risk based on maternal serology or risk factors
- Hep C positive mother: discuss with senior clinician and paediatrician gastroenterology team

The use of the Modified Finnegan Chart

The scoring interval is the entire period from when the last score was assigned. Scores should reflect symptoms observed over the entire scoring interval, rather than at one set point in the time. Scoring should be performed 30-60 minutes after each feed, before the baby falls asleep (usually 2 to 3 hourly). Don't wake a sleeping infant for an assessment – rather defer until the next feed

NON-PHARMACOLOGICAL MANAGEMENT AND BREASTFEEDING

- Gentle handling, dim light, low noise, avoid waking a sleeping infant
- Swaddling, holding, cuddling, or gentle rocking
- Pacifiers
- Encourage maternal visitation, participation and supervised demand breastfeed
- Consider small, frequent feeds (2-hourly) in persistently unsettled infants
- Maternal therapeutic doses of prescription opioids are usually compatible with breastfeeding
- The medication should not be stopped abruptly and high doses should be avoided. Infants should be monitored for poor feeding, sedation or signs of withdrawal
- Urine toxicology is not routinely required

PHARMACOLOGICAL MANAGEMENT

Use pharmacological treatment if:

- 3 consecutive score are ≥ 8; or
- 2 consecutive score are ≥ 12

For infants of opioid dependent mothers: start morphine – dose and titrate as below. For infants on non-opioid dependent mother start Phenobarbital - dose as below. Treatment titration according to score:

- ≥ 12 – increase dose:
- 9 – 11- no change
- ≤ 8 – decrease dose

Morphine

- Oral morphine (MST Morphine) – dose every 3 hourly
- Start at 0.05 mg/kg/dose - titrate by 10% according to Modified Finnegan score
- Maximum dose 0.15mg/kg/dose
- Add Clonidine if maximum dose morphine reached – if symptoms' remains uncontrolled, add Phenobarbital
- Discontinue once score is ≤ 8 and morphine dose is 0.001mg/kg/24 hr. Then observe for 48 hr.

Clonidine

- Add if morphine dose does not control symptoms (score persistently ≥ 12)
- Start with 0.5 - 1µg/kg, then 0.5 – 1.25µg/kg 6 hourly. Use lowest effective dose
- Discontinue when score is ≤ 8 for 48-hours, clonidine dose is 0.5µg/kg/dose and morphine dose is 0.02 mg/kg/dose

Phenobarbital

Start with 16mg/kg loading dose (oral if no seizures), then 2.5mg/kg/dose 12 hourly
Increase/decrease by 1mg/kg according to Modified Finnegan score
Monitor Phenobarbital levels
Discontinue when score is ≤ 8 for 48 hours and Phenobarbital dose is 1 mg/kg/dose 12 hourly

CONVULSIONS

Convulsions are unusual, but should be treated with IV phenobarbitone (see seizure guideline) and morphine should be commenced if not already done so. Exclude non-NAS causes for convulsions (e.g. hypoglycaemia/infection)

DISCHARGE

In addition to routine unit procedure, ensure

- Referral to social worker when infant is diagnosed, to assess need for supervision/foster care
- Neurodevelopmental follow-up at age 18 – 22 week

Modified Finnegan Neonatal Abstinence Score Sheet																	
System	**Sign and Symptoms**	**Scores**	**AM**							**PM**							**Comments**
Central Nervous Disturbances	Excessive high-pitched (or other) cry <5 mins	2															
	Continuous high-pitched (or other cry >5 mins	3															
	Sleep < 1 hour feeding	3															
	Sleep < 2 hours after feeding	2															
	Sleeps <3 hours after feeding	1															
	Hyperactive Moro reflex	2															
	Markedly hyperactive Moro reflex	3															
	Mild tremors when disturbed	1															
	Moderate-severe tremors when disturbed	2															
	Mild tremors when disturbed	3															
	Moderate-severe tremors when undisturbed	4															
	Increased muscle tone	2															
	Excoriation (chin, knees, elbow, toes, nose)	1															
	Myoclonic jerks (twitcing/jerking of limbs	3															
	Generalised convulsions	5															
Metabolic/Vasomotor/ Respiratory Disturbances	Sweating	1															
	Hyperthermia 37.2 – 38.3ºC	1															
	Hyperthermia 38.4ºC	2															
	Frequent yawning (>3-4 times/scoring interval)	1															
	Motting	1															
	Nasal stuffiness	1															
	Sneezing (>3-4 time/scoring interval)	1															
	Nasal flaring	2															
	Respiratory rate >60/min	1															
	Respiratory rate> 60 with retractions	2															
Gastrointestinal Disturbances	Excessive sucking	2															
	Poor feeding (infrequent/ vomiting uncoordinated suck)	3															
	Regurgitation (≥2 times during/post feeding)	2															
	Projectile vomiting	3															
	Loose stools (curbs/seedy appearance																
	Watery stool (water ring on nappy around stool)																
	Total score																
	Date/Time																
	Initial of Scorer																

HAEMATOLOGY

BLOOD PRODUCTS

REQUESTING BLOOD

1. **The request form must have:**
   - Infant's full name and hospital number
   - Gender
   - Date of birth of infant
   - Ward
   - Name of doctor ordering test, contact number

Always request limited donor exposure (LDEP) infant red blood cell if available.

Larger hospitals should discuss this option with blood transfusion services.
LDEP is currently not available in Zambia. Packed red blood cells can be ordered instead.
Always collect mother's sample and send it along side the baby's sample for grouping until 6 months of age

2. **Specimen sample tube**
   The following information must be on the specimen sample tube label:
   - Infant's full name
   - Hospital number
   - Date of birth of infant
   - Gender

NOTE: At least 1ml of blood needs to be sent. Please use the blood bank labeled tubes. If the baby is on the LDEP programme a repeat blood sample is usually not required.

3. **The Blood samples - The doctor's role**
   - Ensure form is correctly filled in
   - Ensure correct bottle is used and correctly labeled
   - Ensure sample is sent to the laboratory promptly
   - If in doubt on sample requirements, consult the laboratory

OBTAINING BLOOD

Facilities to follow established procedures to obtain blood from blood bank. Ward staff should contact the blood bank and ask if blood products are ready to be delivered. The doctor on duty should make follow up.

ADMINISTRATION OF BLOOD PRODUCTS

Policy checking

- Ensure blood is prescribed on Blood and Blood Product Transfusion Record
- Checking procedure must be carried out by a registered nurse trained to administer intravenous medicines and the doctor both of whom must sign the transfusion prescription sheet.

Record batch number in the infant's file.

- Method of administration
- Ensure that the IV line is working well
- Blood should always be administered through a standard 170-micron filter blood giving set
- Terminal co-infusions into a line containing dextrose is safe and doesn't cause measurable haemolysis

Observation of the Infant

- The infant should be continually monitored during the procedure for heart rate and saturation levels
- Record baseline temperature, HR, respiration and blood pressure pre-transfusion, then hourly until completion of transfusion
- Administer transfusion over 3 hours for routine transfusions.

The cannulation site must be checked at least once an hour or more often if IV access has been difficult

GENERAL POINTS

Screening of donor blood

- All blood in Zambia is currently tested for HIV1-2, syphilis, Hepatitis B and Hepatitis C.
- Screening of donated blood in Zambia currently utilizes chemiluminescent immunoassay (ChLIA or CIA) testing for HIV1 and 2, hepatitis B and C and syphilis. ChLIA testing for HIV P24 antigen or antibodies has the ability to reduce the window period between infection and the test becoming positive to below seven days, remaining a considerable advance in ensuring the safety of the donated blood supply.

Consent

- Always try to get signed consent from the parents before transfusion and document discussions with parents
- In an emergency or where there is no legal guardian the Medical Superintendent give consent
- Each consent is valid for the duration of the acute illness for which the transfusion/s is/are required.

GUIDELINES FOR RED BLOOD CELL (RBC) TRANSFUSION THRESHOLDS FOR PRETERM NEONATES

Assisted ventilation			CPAP/HFNC		Low flow oxygen (<3 l/min)	Room air
<28 days		≥28 days	<28 days	≥28days	FiO_2 ≥0.21	Well in air
Fio2 ≥0.3	FiO_2<0.3	Hb < 10 g/dl	Hb< 10 g/dl	Hb < 8 g/dl	Hb < 7g/dl	Hb < 6 g/dl
Hb <12 g/dl	Hb < 11 g/dl					

RBC transfusion may be considered at higher thresholds than the above for neonates with:

- (Discuss all transfusion with a senior clinician)
- Hypovolaemia (unresponsive to crystalloids)
- Septic shock
- Necrotising enterocolitis
- Undergoing/recovering from major surgery

RBC TRANSFUSIONS

- Dose: 20 ml/kg over 3 hours
- Furosemide should not be routinely given
- Only consider furosemide when additional infusions of platelets or FFP given simultaneously or patient is fluid overloaded (discuss with senior clinician) – dose 1 mg/kg midway through transfusion.

Withhold enteral feeds for the duration of transfusion due to the possible risk of transfusion-associated NEC.

IF PARENTS REFUSE TRANSFUSION (E.G JEHOVAH'S WITNESS) FOLLOW LOCAL UNIT POLICY (Also check far steps in the clinical governance section).

PLATELET TRANSFUSION THRESHOLDS FOR NEONATES

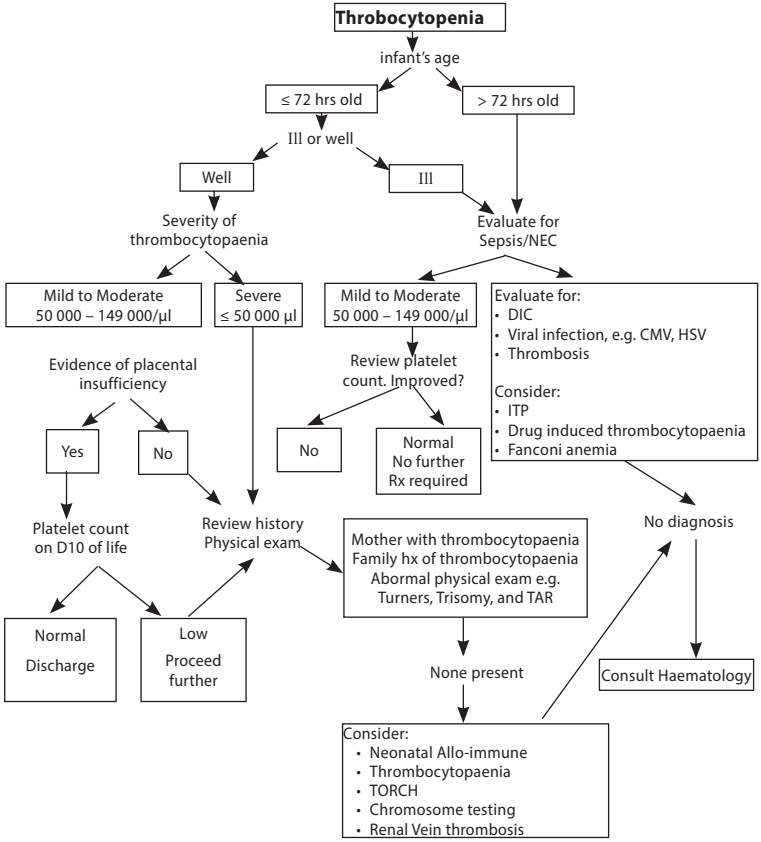
DEFINITION:
Neonatal thrombocytopaenia is defined as a platelet court of <150 x $10^{9/}$l transfusion thresholds

Platelet count (x 10^9/l)	Non-bleeding neonate	Bleeding neonate	*NAITP (proven or suspected)
< 30	Consider transfusion in all patients	Transfuse	Transfuse with **HPA compatible platelets
30-49	Do not transfuse if clinically stable: Consider transfusion if: • <1000g & <1 week of age • Hypotension requiring inotropic support • Previous major bleeding tendency e.g Grade 3-4 IVH • Current minor bleed (e.g Petechiae, punctures, oozing) • Concurent coagulopathy • Respiratory disease requiring • FiO2> 40% or MAP >9cm • Seizures within last 72 hours • Requires exchange transfusion • Pre-surgery (within 24 hours) • Post surgery (within 5 days)	Transfuse	Transfuse with HPA compatible platelets
50-99	Do not transfuse	Transfuse	Transfuse with HPA** compatible platelets if major bleeding present
>99	Do not transfuse	Do not transfuse	Do not transfuse

*NAITP. Neonatal Alloimmune Thrombocytopenia ** HPA: Human Platelet Antigen

ADMINISTRATION
- transfuse 15 ml/kg. Do not waste the unit
- Transfuse over 30 min using the platelet giving set that accompanies the platelets
- Furosemide is not routinely administered

Diagnostic approach to the throbocytopenic neonate



Neonatal autoimmune thrombocytopaenia

- Maternal ITP or SLE causes neonatal autoimmune thrombocytopaenia in 10% of cases. The risk for intracranial haemorrhage is < 1%. Platelets rise spontaneously by Day 7 of life in most cases.
- Check infant platelet count at birth and again at 24 hours.
- In thrombocytopaenic infants check platelets daily for next 4 days

If platelet count <30 x 109/l; treat with 1g/kg/day IVIG for 2 consecutive days

FOLLOW-UP AND REPEAT PLATELETS 2 WEEKS AFTER IVIG WHERE AVAILABLE

FRESHLY FROZEN PLASMA (FFP) TRANSFUSION IN INFANTS

INTRODUCTION

Coagulation times in infants, particular preterm infant are longer than in adults and not necessarily related to the risk of bleeding. Abnormal coagulation test results, in the absence of symptoms or haemorrhagic risk, are not an indication for a FFP transfusion Routine use of FFP to treat coagulopathy in the absence of bleeding has not been shown to reduce morbidity nor mortality.

INIDCATIONS

- Haemorrhagic disease of the newborn secondary to Vit K deficiency where the infant is actively bleeding
- Bleeding (or high risk of bleeding) and coagulopathy
- Treatment of congenital deficiencies of single clotting factors, when the specific concentrate is not available and the infant is bleeding
- Infants with a coagulopathy about to undergo an invasive procedure

Inappropriate indications

FFP is not routinely indicated for:

- Volume expansion
- Hypoproteinemia
- Correction of immune deficiencies
- Correction of congenital or acquired coagulopathies in the absence of bleeding
- Nutritional purposes

Contraindications

- ***Absolute***
  - ◊ Documented intolerance to plasma and its components
  - ◊ Congenital deficiency of immunoglobulin A (IgA) in the presence of anti-IgA antibodies
- ***Relative***
  - ◊ Heart failure and pulmonary oedema

ADMINISTRATION

- Do full cross-match - Group O FFP should never be given to infants who are not Group O due to the potential risk of infusion of significant amounts of anti-A and anti-B antibodies
- FFP should be thawed before use
- Transfuse 15m l /kg over 30 minutes using the giving set supplied by the blood bank
- Furosemide is not routinely indicated.

PLASMA DERIVATIVES

Bioplasma FDP (lyopholised powder for IV infusion) is fresh dried plasma processed from fresh frozen plasma. It is not blood group specific and, where available, may be given to patients of any blood group in an emergency.

A BLEEDING NEONATE

In neonates, there is a decreased activity of several clotting factors, diminished platelet function, and suboptimal defence against clot formation.

DIAGNOSTIC WORKUP OF THE BLEEDING INFANT

A. The history includes:

- Family history of excessive bleeding or clotting
- Maternal medications (e.g. aspirin, phenytoin)
- Pregnancy and birth history
- Maternal history of the birth of an infant with a bleeding disorder
- Any illness, medication, anomalies, or procedures done to the infant

B. The crucial decision in diagnosing and managing the bleeding infant is determing whetehr the infant is sick or well

1. **Sick infant.** Consider DIC, viral or bacterial infection, or liver disease (hypoxic/ ischaemic injury may lead to DIC)
2. **Well infant**. Consider vitamin K deficiency, isolated clotting factor deficiencies, or immune thrombocytopaenia.

   Maternal blood in the infants GIT will cause symtoms in the infant.

   Thorough clinical examination is required to exclude bleeds from anal fissures, umbilical stamp etc
3. **Petechiae, small superficial ecchymosis, or mucosal bleeding** suggests platelet problem
4. **Large bruises** suggest deficiency of clotting factors, DIC, liver disease, or vitamin K defiency
5. **Enlarged spleen** suggests possible congenital infection or erythroblastosis
6. **Jaundice** suggests infection, liver disease, or resorption of large haematoma
7. **Abnormal retinal findings** suggest infection

LABORATORY TESTS

1. The **Apt test** is used to rule out swallowed maternal blood in a child who is well and only GI bleeding is noted. (stool or gastric aspirate/vomitus can be submitted to the lab)
2. **Peripheral blood smear** is used to assess the number, size and granulation of platelets and the presence of fragmented RBCs as seen in DIC. Large platelets reflect either young platelets (implying an immune cause of destructive thrombocytopenia) or congenital macrothrombocytopaenias
3. **FBC;** significant bleeding if platelets under 20,000 to 30,000/mm3 or less , except in alloimmune thrombocytopenia which may cause bleeding in platelet counts up to 50,000 platelets/mm3
4. **Prothrombin time (PT)** is a test of the "extrinsic" clotting system. Factor VII and tissue factor X; Factor Xa activates prothrombin (II) to form thrombin, with factor Va as a cofactor. Thrombin cleaves fibrinogen to fibrin
5. **Partial thromboplastin time (PTT)** is the test of the" intrinsic" clotting system and of the activation of factor X by factors XII, XI, IX, and VIII, as well as the factors of the common coagulation pathway (factors V and II and fibrinogen)
6. **Fibrinogen** can be measured on the same sample as that used for PT and PTT. It may be decreased in liver disease and consumptive states, and the usula functional assay is low in dysfibrinogenemia
7. **D –Dimer** assays measure degradation products of fibrin found in the plasma of patients with DIC and in patients with liver disease who have problems clearing fibrin split products
8. **Specific factor assays and von Willebrand Panels** for patients with positive family history can be measured in cord blood, or by venipuncture after birth. Age specifc norms must be consulted

9. **Bleeding times are to be discouraged in all patients, but especially in neonates.**

Note: Normal ranges for haematological indexes can be found in Appendix 2 & 3

Treatment tips

- In general, treat clinically ill infants or infants weighing <1500g with FFP 10ml/kg if PT or PTT or both are more than 2 times normal for age or
- With platelets (1 unit) if <20,000/mm3 and babies with NAIT (Neonatal alloimmune thrombocytopaenia) can be transfused if <50,000/mm3)

TREATMENT OF BLEEDING SECONDARY TO DIC

1. The underlying cause should be treated (e.g sepsis, NEC, herpes)
2. Confirm that vitamin K1 has been given

3. Platelets and FFP are given as needed to keep the platelet counter over 50,000/ml and to stop the bleeding. (FFP contains anticoagulant proteins which may slow down or stop ongoing consumption)
4. If bleeding persists, one of the following steps should be taken, depending on the availability of blood, platelets ,or FFP):
   - Exchange transfusion with fresh citrated whole blood or reconstituted whole blood (Packed RBCs, platelets, FFP)
   - Continued transfusion with platelets, packed RBCs, and FFP as needed
   - Administration of cryoprecipitate(10ml/kg) for hypofibrinogenemia
5. If consumption coagulopathy is associated with thrombosis of large vessels and not with concurrent bleeding, heparinization without a bolus may be considered (e.g., 10 to 15units/kg/hour as a continuous infusion). Platelets and plasma are continued to be given after the heparin is started. (can only be done in consultation with a haematologist)

Management of specific causes of bleeding is highlighted in the respective chapters

Differential diagnosis of bleeding in a Neonate

Clinical evaluation	Platelets	PT (Prothrombin time)	PTT (partial thromboplastin time)	Likely diagnosis
"Sick"	decreased	increased	increased	DIC
	decreased	normal	normal	Platelet consumption (infection, NEC, renal vein thrombosis
	normal	increased	increased	Liver disease
	normal	normal	normal	Compromised vascular intergrity (associated with hypoxia, prematurity, acidosis, hyperosmolality
"Healthy"	Decreased	normal	normal	Immune thrombocytopaenia, occult infection, thrombosis, bone marrow hypoplasia(rare), or bone marrow infiltrative disease
	normal	increased	increased	Haemorrahgic disease of the newborn (Vitamin K deficiency)
	normal	normal	increased	Hereditary clotting factor deficiencies
	normal	normal	normal	Bleeding due to local factors (trauma, anatomic abnormalities); qualitative platelet abnormalities (rare); factor XIII deficiency (rare)

HAEMORRHAGIC DISEASE OF THE NEWBORN (HDN)

- Occurs in 1 in every 200-400 neonates not given vitamin K prophylaxis
- Vit K is essential in the activation of:
  - ◊ Prothrombin
  - ◊ F II
  - ◊ Coagulation Inhibitors- protein C and S
  - ◊ F VII
  - ◊ F IX
  - ◊ F X
- Acts by carboxilating the glutamic acid residues on the amino-terminal part of these Vit K dependent proteins
- In Vit K def: de-caboxylated proteins are formed- unable to bind Ca and phospholipids- functionally defective
- Two forms:
  - ◊ Vit K1 (Aquomephyton)- source is dietary
  - ◊ Vit K2 (menaquinones)- produced by gut flora
- Vit K crosses the placenta poorly
- 30:1 maternal-infant gradient
- ***Thus all newborns are Vit K deficient***
- After birth, levels depend on diet; breast vs formula

CLASSIFICATION

Early	Classical	Late
Occurs on day one	One to seven days after birth	Two to twelve weeks after birth
Rare Due to medicines which interfere with Vit K metabolism	More common in unwell infants or where there is delayed feeding (prolonged TPN and antibiotics use)	Mainly in exclusively breast fed infants. Associated with: cholestatic liver disease and other malabsorptive states- CF
Examples: anticonvulsants, TB drugs, warfarin	Sites of bleeding: umbilicus, GIT, venopunture sites, surgical sites, brain (uncommon)	Half of all bleeds are serious intracranial bleeds Of these, 30% have "warning bleeds"
Incidence of bleeding; 6-12% (no Vit K)	Incidence: 0.4-0.7 per 100 000 births	Incidence: 5-20 per 100 000 births

INVESTIGATIONS

- In case you suspect HDN carry out FBC, including platelet count, PT and PTT.
- Normal platelet count and prolonged PT and PTT are an indication of HDN

PROPHYLAXIS REGIMEN

- Vitamin K 1mg IMI single dose at birth in every newborn.
- Virtually eliminates Classical HDNB
- Also reduces rate of Late HDNB
- Premature infants: 0,5mg IMI or IVI
- Side effects of Vit K: local effects due to IMI:
  - ◊ Infection
  - ◊ Irritation at injection site
  - ◊ Nerve damage
  - ◊ Muscle damage

Very rare

TREATMENT

- If there's bleeding, 10ml/kg of FFP ***(refer to chapter on FFP transfusion in infants)*** and IV dose of 1mg of vitamin K (correction with vitamin K can take 12 to 48hours)
- If the mother had been treated with warfarin, anticonvulsants or antituberculous treatment, she should be given Vitamin K 24 hours before delivery (10mg of Vitamin K_1 IM)
  - ◊ The newborn should have PT, PTT and platelets counts monitored for bleeding
  - ◊ Vitamin K 1mg should be given at birth and repeated after 24 hours
  - ◊ Repeated (every 8 to 12 hours or a drip of 1ml/kg/hour) infusions of FFP should be given if bleeding occurs
- For delayed HDN, Vitamin K1, 1mg/week should be given orally for the first 3 months

ENDOCRINE

AMBIGUOUS GENITALIA

DEFINITION

- The genitalia of the baby are abnormal and you cannot decide if the baby is male or female.
- Discuss case with senior clinician and/or endocrinologist (see call centre contact numbers)
- Explain to the parents that the genitalia appear abnormal and you are unsure of the gender
- Do not be pushed into pronouncing on the gender if you are not sure
- Reassure the family that baby's sex will be decided definitively as soon as possible
- Refer to the baby as "the baby" and not he or she, and persuade everyone else to do this
- Discourage the parents from choosing a gender-ambiguous name
- The parents should not register the birth until a gender is assigned
- Remember that chromosomal sex may not be the same as the appropriate gender for the child
- Ensure privacy for the baby and family
- Provide parents with literature and refer to support groups if available
- Follow-up and counseling is essential

Apparent Male

- Bilateral non-palpable testes in a full-term infant
- Hypospadias associated with separation of the scrotal sacs
- Undescended testes with hypospadias

Indeterminate

- Ambiguous genitalia

Apparent Female

- Clitoral hypertrophy of any degree
- Foreshortened vulva with single opening
- Inguinal hernia containing a gonad

Evaluation of a patient with ambiguous genitalia

- Examine for signs of dehydration, genital examination (size of phallus, position of urethra, gonads)
- Biochemical studies electrolytes (Na+, K+), glucose,
- Imaging (abdominal ultrasound, genitogram)
- Hormonal studies (LH, FSH, cortisol, 17-hydroxyprogestrone)
- Karyotype
- Note; Involve surgeons, family, social workers and any other relevant disciplines early in the care of the patient

CONGENITAL ADRENAL HYPERPLASIA (CAH)

PRESENTATION

21-hydroxylase deficiency is the commonest cause of ambiguous genitalia, resulting in virilisation of female infants. CAH should be considered the most likely diagnosis in any infant with ambiquous genitalia and in many cases the safest course is to treat before confirming the diagnosis and stop if you are wrong.

In all ill or collapsed infant with possible CAH, give steroids even if all blood and urine testing is impossible – testing with ACTH will establish a diagnosis at a later date. The condition usually presents in the second week of life.
It is important to avert a salt-losing crisis which may result in death or permanent neurological damage.

OTHER PRESENTATIONS OF CAH:

- Salt loss (falling sodium or unusually high sodium requirements)
- Salt-losing crisis (collapse with low blood pressure, low sodium, high/normal potassium)
- Poorly-virilised male infants (not 21-hydroxylase deficiency, but in 3b-hydroxysteroid dehydrogenase deficiency and lipoid adrenal hyperplasia)
- Virilisation in childhood
- Male genitalia may be pigmented in CAH but this is not a reliable sign in practice.

EXAMINATION AND INVESTIGATIONS

- Examine for the presence or absence of hypergimented lesion, document the size of the phallus (normal phallus size is 3.5cm), position of the urethral meatus and presence or absence of testis/gonads
- Monitor hydration status, BP, HR, CRT
- 17-Hydroxyprogesterone levels
- Serum cortisol (which may be normal)
- Careful monitoring of electrolytes and glucose is important (Na+, K+), typically presents with hyponatreamia and hyperkalemia
- Pelvic ultrasound. If the child is a virilised female, the uterus is present. The uterus is fairly large in the neonatal period – about 3 cm long. If you cannot find a uterus at ultrasound, reconsider the diagnosis.

INITIAL MANAGEMENT

- Inform a senior clinician
- Electrolyte and glucose replacement
- A large sodium deficit will require replacement even after steroids are started
- Steroid replacement: give mineralocorticoid and glucocorticoid
- Contact paediatric endocrinologist for management advice

MANAGEMENT OF SALT LOSING CRISIS

- 20 ml/kg of 0.9% NaCl bolus
- IV hydrocortisone 10mg/kg start then 100mg/m2/day as a continuous infusion until stable then provide physiological dose Hydrocortisone po 0.5mg/kg/day in 3 divided doses
- Fludrocortisone 5mcg/kg/day
- NaCl 0.5-1g for every 10kg BW/day

Follow up

- Babies with CAH will require oral sodium supplements (2 – 3 mmo/l/kg/day) until they are weaned
- Do not allow home until electrolytes are stable on steroids and sodium replacement. Arrange regular electrolyte measurement as an outpatient for the first few weeks.
- If surgery is required for ambiguous genitalia, an early referral should be made to surgeons with expertise in this area.
- The need for steroids is life-long. Parents should be clear about the need to increase the dose for illness and to consult medical help if the child vomits the steroids
- Do not discharge home without detailed follow up plan agreed and arranged.

Genetic Advice

CAH is an autosomal recessive disorder. Antenatal treatment with dexamethasone will reduce or abolish virillisation of the female infant. Treatment must start early in pregnancy and thus genetic testing must be arranged in advance

Differential Diagnosis

- 21-hydroxylase deficiency (commonest). Female infants are virillised and male infants normal. May present with salt losing crisis. 17-hydroxyprogesterone is elevated
- 11b-hydroxylase deficiency. Female infants are virillised and male infants normal. 17-hydroxyprogesterone is elevated. Salt –losing crisis does not occur
- 3b-hydroxysteroid dehydrogenase deficiency. Male infants are under virllised and female infants mildly virillised. 17 hydroxyprogesterone is not elevated. There may be very severe salt wasting
- Lipoid adrenal hyperplasia. All steroid hormones are reduced and male infants are under virillised. Presents with a severe salt losing crisis.

Other causes of adrenal insufficiency in neonates:

- Hypopituitarism – usually presents with hypoglycaemia
- Adrenal hypoplasia – almost always boys
- ACTH resistance – hyperpigmented lesions present

MANAGEMENT OF HYPERGLYCEMIA

DEFINITION

The definition of hyperglycaemia remains controversial. Hyperglycaemia that has been associated with adverse outcomes in observational studies is defined as blood glucose >8.3mmo/l. Insulin therapy is usually only started in presence of blood glucose > 10-12 mmol/l and an osmotic diuresis.

An elevated blood glucose concentration >8.3mml/l occurs frequently in VLBW infants, especially during the first days after birth.

Risk Factors

- Increasing prematurity
- Small for gestational age
- Iatrogenic, e.g. increase infusion rates or concentration and inotropes
- Postnatal corticosteroids
- Sepsis
- Stress response, eg. intraventricular haemorrhage

Consequences

Adverse clinical outcomes associated with neonatal hyperglycaemia include death, intraventricular haemorrhage grade 3 and 4, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia and prolonged length of hospital stay. Most severe outcomes were reported when the hyperglycaemia was prolonged.

DIAGNOSIS

The following infants should be screened:

- Infant born <35weeks gestation
- Infants receiving IV fluids and TPN
- Sick infants
- Infants with glycosuria

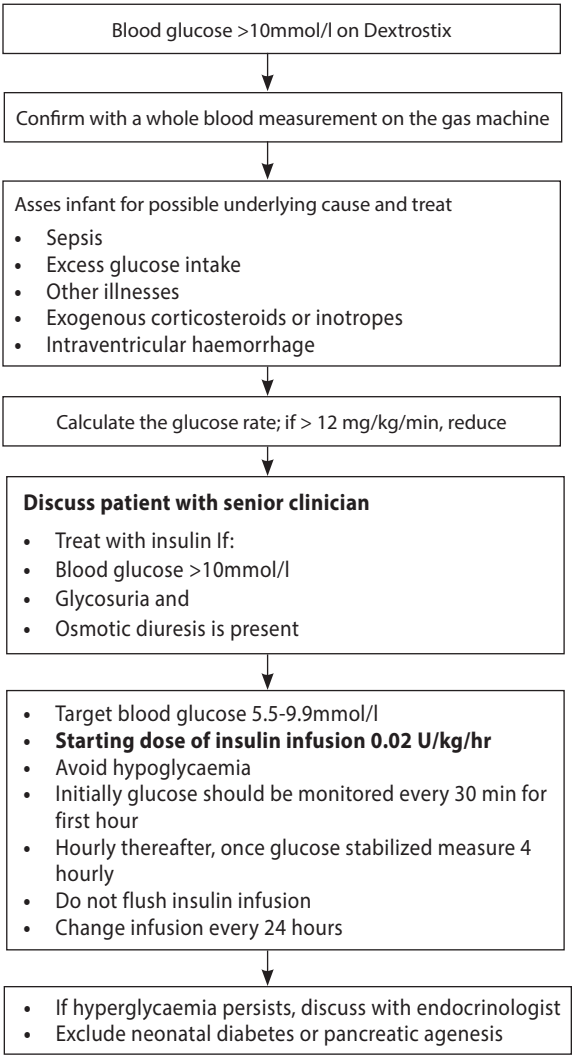
A high reading on the dextrostix must be confirmed with a whole blood measure on the gas machine before starting an insulin infusion if required. Repeated whole blood measurements are not necessary for monitoring treatment.

TREATMENT

Insulin Infusion

See Formulary for Insulin preparation and sliding scale

MANAGEMENT OF HYPERGLYCAEMIA



HYPOGLYCAEMIA

The foetus depends largely on glucose for his/her energy requirements. Glycogen is laid down in the liver with advancing gestation and provides the main source of glucose. Subcutaneous fat stores are also important. In the newborn infant, milk feeds supply most of the required energy

DEFINITION OF NEONATAL HYPOGLYCAEMIA

True whole blood glucose < 2.6 mmol/l
Severe hypoglycaemia: Blood glucose <1.5mmol/l

Normal values

- The fetal serum glucose is usually 2/3 of the maternal value
- Serum glucose is usually 2.5mmol/l to 7.5mmol/l during the first week of life. The normal range of serum glucose is very difficult to define as the levels fall during the first 24 hours after delivery
- The blood glucose levels (measured with reagent strips) are approximately 0.5mmol/l lower than serum levels (measured in the laboratory) due to the high PCV after birth.

Clinical features

- Asymptomatic: hypoglycaemia is detected by screening at risk infants
- Symptomatic: floppiness, jitteriness, apnoea, poor feeding, lethargy, rarely seizures and coma

DIAGNOSIS

Hypoglycaemia should be considered in all at-risk infants:

- Small for gestational age (<10th centile)
- Post-mature infants, especially if wasted
- Infants of diabetic mother
- Prematurity
- Severe rhesus disease
- Polycythaemia
- Septicaemia
- Hypothermia
- Hypoxic ischaemic encephalopathy
- Fluid restriction

Diagnosis is confirmed by blood glucose testing. Normal term infant on the postnatal wards who are feeding do not require screening for hypoglycaemia.

MANAGEMENT

Any baby who has persistent symptoms, is not tolerating enteral feeds, or is unable to maintain normoglycaemia with appropriate enteral feeds alone should be admitted to the Neonatal unit and commenced on an IV infusion of 10% glucose.

- Start IV 10% glucose at 90 ml/kg/day – aim to raise glucose above 2.5mmol/l. This gives 6.25 mg/kg/min of glucose.
- Continue to increase by 30ml/kg/day until glucose above 2.5 mmol/l
- Beware of fluid volumes above 120 ml/kg/day
- If glucose still not maintained, increase the concentration of glucose rather than the volume. If concentration exceeds 12.5% of glucose, insert a long line or umbilical venous catheter. Check the blood glucose after 30 mins after initiation of treatment and then at 2 hours. If recovered can reduce frequency of blood glucose tests
- Glucagon should be given if IV access is delayed. 0.2mg (0.2iU)/kg/dose given intramuscularly
- If baby remains hypoglycaemic despite increasing glucose infusion rate to 12mg/kg/min, draw blood at the time baby is hypoglycaemic for:
- blood glucose, insulin and cortisol
- Babies on IV glucose should still receive breast or enteral feeds whenever possible.

Presence of insulin in the face of hypoglycaemia is indicative of hyperisulinism.

Urine will be found to be negative for Ketones. Discuss with endocrinologist.

- If hyperinsulinism is present, keep glucose > 3.5mmol/l – may need 15-20mg/kg/min of glucose.
- Consider endocrine or metabolic causes and investigate accordingly.
- Clues as to aetiology include micropenis (hypopituitary), virillisation (CAH) and poor feeding/encephalopathy (metabolic disease).
- Hepatomegaly is a feature of several metabolic diseases including glycogen storage disease type 1, fructose1, 6 bisphosphate deficiency and long chain fatty acid oxidation defects.
- Steroid replacement therapy should be considered if there is a clinical suspicion of hypopituitarism or hypoadrenalism.
- Discuss with the senior clinician.
- If normoglycaemia is achieved, attempt to commence weaning the glucose requirement by 1-2 mg/kg/min every 6 hours.

EMERGENCY TREATMENT

Emergency treatment of hypoglycaemia is required if the baby is severely symptomatic or the blood glucose is persistently < 1.5mmol/l

- If the infant has IV access and blood glucose is low despite previous glucose infusion. give a bolus of 3ml/kg of 10% glucose intravenously, followed by an increase in the maintenance glucose infusion. Give glucagon IM if IV access attempts fail.
- In hypoglycaemia unresponsive to maximum glucose infusion rates, glucagon as an IV bolus may be useful – discuss with senior clinician and endocrinologist

CHANGE THE PERCENTAGE DEXTROSE IN A SOLUTION

To change the percentage dextrose in a 10% dextrose solution using 50% dextrose (D50W)

1. Calculate the volume D50W (ml) required = $\frac{\text{(\% change required x final volume)}}{40}$
2. From the 10% dextrose, remove the volume calculated from the final volume
3. Replace the removed volume ml for ml with D50W into the 10% solution.

Example: To make 100ml 15% solution from 10% dextrose solution,
Change required: 15 – 10 = 5%
Final volume = 100ml
Volume D50W = (5 x 100) ÷ 40
= 12.5ml

Therefore, add 12.5 ml D50W to 87.5ml 10% dextrose solution to get final volume of 100ml 15% dextrose –containing solution.

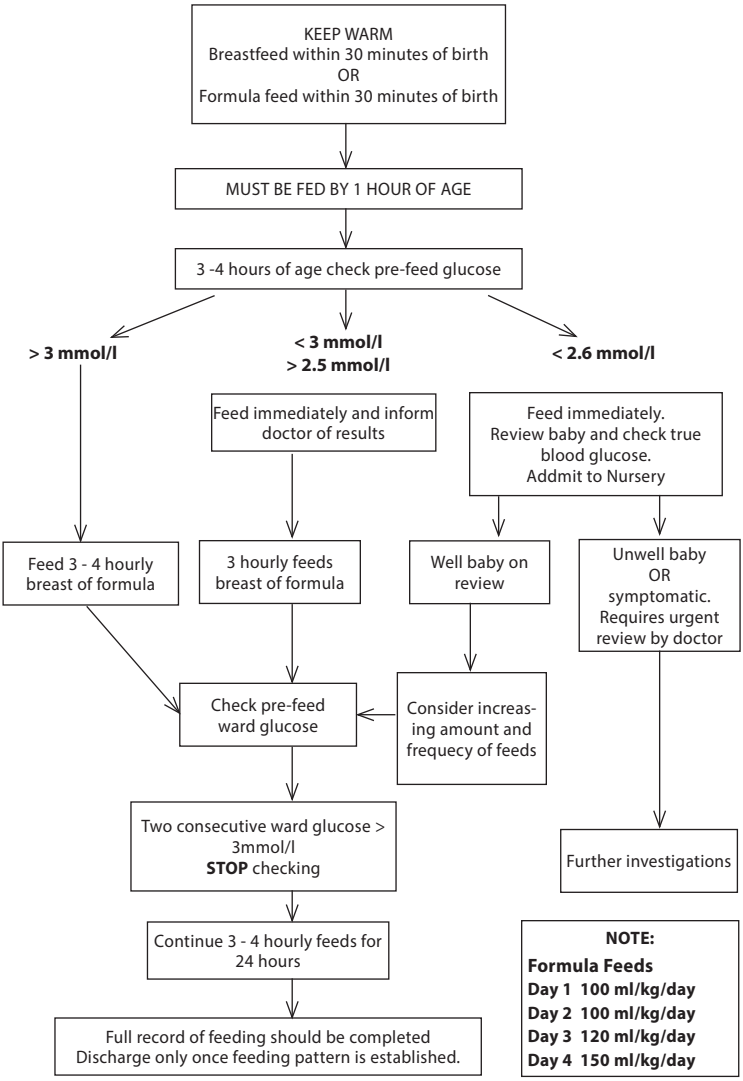
Management of Infants at risk of Hypoglyacaemia on Postnatal Wards (See algorithm)

Gestation Age < 36 weeks Birth weight <10th centile Disproportionate growth (i.e. birth weight ≤ OFC)	Exposed to intra-uterine hypoxia in labour Infant of a diabetic mother

Complications

Symptomatic hypoglycaemia is major risk factor for brain injury and subsequent neuro-developmental handicap.

Babies at risk of hypoglycaemia



INFANTS OF DIABETIC MOTHERS (IDMs)

IDMs require admission to the NICU because they are likely to have the following complications:

General: prematurity and its problems, polcythaemia, Macrosomia (weight higher than the 90th percentile or >4000g), traumatic birth injuries such as clavicular fractures, Erbs palsy or phrenic nerve palsy

CNS: Neurotube defects, anencephaly, holoprosencepahaly

Respiratory: RDS, TTN

Cardiac: Transiposition of the great vessels, VSD, ASD, left obstructive leions such as Hypoplastic left heart,aortic stenosis and COA. Transient hypertrophic subaortic stenosis (Hypertrophic cardiomyopathy) results in heart failure, poor cardiac output and cardiomegaly. Most symptoms resolve by 2 weeks of age and septal hypertrophy resolves by 4 months.(See heart failure management)

GIT: Atresias in any part of the GIT, Jaundice, poor feeding, Small left colon (presents as delayed passage of meconium with generalized abdominal distention (enema usually resolve symptoms) –consider other causes of intestinal obstruction

Renal: renal agenesis, cystic kidneys, renal vein thrombosis (may present with haematuria, flank mass, hypertension or embolic phenomenon)

Metabolic; Hypocalcaemia, hypomagnesemia (refer to treatment in calcium homeostasis below)

Musculoskeletal: caudal regression syndrome, spinal anomalies and syringomyelia

EVALUATION OF IDMS

Resuscitation (refer to neonatal resuscitation guidelines)

In the nursey; **supportive care**

- Provide warmth and respiratory support if required
- Examine thoroughly to exclude congenital anomalies
- Check blood glucose on admission and manage hypoglycaemia as in the previous chapter
- The infant is fed orally or given IV glucose by 1 hour of age
- Check haematocrit on the first day and repeat as required
- Bilirubin should be checked if the infant appears jaundiced
- Calcium levels should be checked and treated if the infant appears jittery or if sick for any reason
- Further laboratory and radiological evaluation will depend on the clinical findings.
- Every effort is made to involve the parents in infant care as early as possible

TOPICS OF CONCERN TO PARENTS

1. **Genetics:** parents of IDMS are concerned about the eventual development of diabetes in their children. There's conflicting data on the incidence of insulin-dependent diabetes in IDMS.
   - **Type 1 diabetes**
     ◊ General population; <1% chance of developing type 1 diabetes
     ◊ If mother has type 1 diabetes, risk of off spring developing the disease is 1-4%
     ◊ If father has type 1 diabetes, risk to offspring is 10%
     ◊ If both parents have the disease, the risk isapproximately 20%
   - **Type 2 diabetes**
     ◊ Average person has a 12 -18% chance of developing diabetes
     ◊ If one parent has the disease, the risk to the offspring is 30%
     ◊ If both parents have it, the risk to the offspring is 50-60%

2. **Perinatal survival**
   With appropriate surveillance and management, a diabetic woman has a 95% chance of having a healthy child

METABOLIC BONE DISEASE

INTRODUCTION

- The foetus accrues approximately 80% of bone mineral content during the third trimester
- Human milk has insufficient Ca and PO4 for normal bone mineral accretion in preterm infants
- Metabolic bone disease (MBD) is a self resolving process
- MBD may be associated with fractures, dolichocephaly and reduced linear growth

RISK FACTORS

- **Decreased mineral intake:**
  ◊ Preterm delivery <32weeks gestation
  ◊ Prolonged total parenteral nutrition
  ◊ Unfortified human milk feeds
  ◊ Bronchopulmonary dysplasia
  ◊ Delayed enteral nutrition
- **Increased Mineral excretion:**
  ◊ Diuretics increases urinary Ca excretion
  ◊ Long-term steroid use

DIAGNOSIS

- Not usually clinically apparent; may appear between the 6th and 12th postnatal week
- ***Biochemical:***
  - Serum: typically, normal Ca, low PO4 and high ALP
    ◊ Urine PO4 excretion is very low or absent. Urine Ca excretion
      - Increases as serum PO4 decreases
  - Vitamin D and parathyroid hormone concentrations are usually normal
- **Radiological:**
  X-rays may reveal osteopaenia, widening of the metaphases, and fractures

MANAGEMENT

Prevention

- Early introduction of enteral human milk feed and supplementation with Breast Milk Fortifier (BMF)
- Screen infants at risk of MBD
  ◊ Infant <32 weeks gestation and/or < 1200g, AND any one of the following:
  ◊ ≥ 4 weeks to reaching full enteral feeds, or
  ◊ Inability to supplement with BMF, OR
  ◊ Infants requiring diuretics, OR
  ◊ Postnatal growth failure
- When to screen:
  ◊ Start at 4 weeks of age and screen every 2-3 weeks thereafter
  ◊ Serum Ca, PO4, ALP
  ◊ X-rays, Urinary Ca and PO4 are rarely indicate

Treatment

- Treat infants with biochemical evidence for MBD PO4< 1.5mmol/l and ALP > 500
- Treat with oral phosphate supplements
- Treat until biochemical evidence of MBD has resolved PO4> 1.8mmol/l and ALP< 400

CALCIUM HOMEOSTASIS IN NEONATES

INTRODUCTION

Ca homeostatic system consists of 3 components:

- Calcium-sensing receptor (CaSR) which senses the ionized calcium concentration
- Parathyroid hormone (PTH) release increases serum Ca
- 1,25-dihydroxyvitamin D, promotes Ca and PO4 absorption from the gastrointestinal tract and reabsorption from the renal tubules

Hypocalcaemia

- Hypocalcaemia is defined by birth weight (BW)
- > 1500g – Serum Ca< 2 mmol/l; ionized Ca< 1.1mmol/l
- <1500g – Serum Ca < 1.75mmol/l or ionized Ca < 1mmol/l
- ***Early hypocalcaemia*** occurs within the first 2-3 days after birth and causes include:
  - ◊ Prematurity
  - ◊ Infants of diabetic mothers
  - ◊ Birth asphyxia
  - ◊ Intrauterine growth restriction
- ***Late hypocalcaemia*** typically occurs at the end of the first week and causes include:
  - ◊ Hypoparathyroidism
  - ◊ DiGeorge syndrome
  - ◊ Maternal hyperparathyroidism
  - ◊ Hypomagnesaemia
  - ◊ Vit D insufficiency
  - ◊ Acute renal failure + hyperphosphataemia

Clinical manifestations

- Most infants are asymptomatic
- Symptomatic features: jitteriness, muscle jerking and seizure

Diagnosis

Routine monitoring is not required

- Screen infants with signs of hypocalcaemia and those with congenital heart disease
- Investigate infants with early hypocalcaemia refractory to treatment, late hypocalcaemia and seizures
- Investigations: 1st line: UEC, Mg and PO4
- Discuss with geneticist and cardiologist if DiGeorge suspected
- 2nd Line: PTH, 25-hydroxyvitamin D and urinary Ca

MANAGEMENT

Only treat symptomatic infants

Direct treatment against the underlying disease

- **Acute:**
  - ◊ 10% Calcium gluconate 1 – 2 ml/kg infused over 10 min (dilute 1:1 with NS). Monitor for bradycardia; stop infusion if HR < 100bpm

  Alternative: Calcium chloride 0.2ml/kg
- **Maintenance:**
  - ◊ 10% calcium gluconate 5 ml/kg/day in IV fluids or divided into 4-6 PO doses with feeds
  - ◊ If PO: dilute by at least 50% with feeds or water (IV solution may be used orally). Can induce gastrointestinal irritability and diarrhea.
- **Hypomagnesaemia**
  - ◊ 50% MgSO4 0.2ml/kg IV/IM 12 hourly x 2 doses. IV infusion over 2 hours

HYPERCALCAEMIA

- Hypercalcaemia is rare is infants
- Defined as serum Ca> 3 mmol/l or ionized Ca> 1.5mmol/l
- Discuss all cases with an endocrinologist
- Untreated hypercalcaemia can have serious renal failure and neurological sequelae

Causes

PTH – independent (elevated Ca; suppressed PTH)

- Subcutaneous fat necrosis (SCFN):

  Presents in the first weeks of life. Cutaneous violaceous rash with indurated painful nodules over the face, trunk, buttock, and arms. Preceding history of birth trauma hypothermia or asphyxia.

PTH-dependent (elevated PTH causing elevated Ca)

- Neonatal severe hyperparathyroidism (NSHPT):
  Caused by a homozygous inactivating mutation of CaSR gene. Present in the first few weeks of life. Severe hypercalcaemia (serum Ca >3.5mmol/l, low serum PO4 and very high PTH levels. Total parathyroidectomy is usually required for neonatal cases.
- Neonatal hyperparathryroidism (NHPT):
- Caused by a de novo heterozygous inactivating mutation of CaSR gene. Hypercalcaemia less marked and symptomatically transient. Early analysis of CaSR gene distinguishes NHPT from NHPT.NHPT also associated with mucolipidosis type II, may be severe and is usually transient.

Management

1. Establish underlying cause and lower Ca to prevent end organ damage
2. Reduce calcium intake and avoid drugs which may cause hypercalcaemia
3. Investigations:
   1st line: PTH, PO4, UEC, ALP, serum and ionized Ca
   2nd line: **(Only if no evidence of SCFN)**
   - Ultrasound of parathyroid and kidneys
   - Skeletal survey
   - SestaMibi scan
   - Store DNA sample

Management (Discuss with endocrinologists)

- Hyperhydration with 0.9% saline
- Furosemide promote natriuresis and hypercalciuria
- Prednisolone useful in SCFN
- Biphosphanates reduce plasma Ca by inhibiting osteoclastic bone resorption
- Cinacalcet used in NSHPT and NHPT as temporizing measure in early symptomatic phase
- Parathyroidectomy for NSHPT

NEONATAL THYROID DISORDERS

BACKGROUND

Thyroid hormones are essential for the normal development of the brain. Maternal thyroid disease influences the thyroid status of the newborn. Both iodine deficiency and excess are associated with transient neonatal hypothyroidism, with potentially negative effects on neurodevelopment. Adverse neurodevelopmental outcomes have been reported in preterm infants with transient hypothyroxinaemia; however, this is confounded by severe illness in this group of patients.

CONGENITAL HYPOTHYROIDISM

- Congenital hypothyroidism may result in mental and growth retardation if not treated early in life
- Symptoms and signs include: prolonged neonatal jaundice, constipation, lethargy, poor tone, poor feeding, a large tongue, coarse facies, wide fontanelle, distended abdomen and umbilical hernia.

Definitions

Primary hypothyroidism: High TSH on newborn screen
Secondary hypothyroidism: Low TSH, not detected on newborn screen. Usually associated with other pituitary hormone deficiencies

Cause

- Dysgenesis – agenesis, ectopic, hemithyroid
- Dyshormonogenesis

Screening

- Cord blood is collected for TSH and T4 level
- Normal values for TSH (cord screen) – TSH 1-19 MIU/l or TSH 20-50 MIU/l only if T4 > 100pmol/l
- For infants with an abnormal screen, an urgent blood sample should be collected to test thyroid functions. Do bloods after 48 hours, if abnormal, discuss with a senior clinician/endocrine service
- Start thyroxine at 10µg/kg/dose daily PO
- Repeat thyroid tests at 1 -2 weeks and at 4 weeks
- Treatment is aimed to keep T4 concentration in the upper third of normal and TSH in the normal range
- Consult with endocrine service regarding further evaluation, which may include thyroid scans, ultrasound or antibody tests and bone age X-rays.

TRANSIENT CONGENITAL HYPOTHYROIDISM

Causes

- Iodine deficiency:
  - ◊ Iodine is an essential element for the production of thyroid hormone – deficiency can cause irreversible mental retardation
- Iodine excess
  - ◊ Infants exposed to excess iodine are at risk of iodine overload resulting in transient hypothyroidism. Long term effects are unknown
  - ◊ Use chlorhexidine (instead of iodine –containing solutions) for aseptic procedure

Infants of Mothers with Hashimoto's Thyroiditis

- Infants of mothers with Hashimoto' thyroiditis are at low risk of transient hypothyroidism from thyroid blocking antibodies, and rarely of thyrotoxicosis from coexistent thyroid stimulating antibodies.
- Most infants with transient hypothyroidism will be identified by routine neonatal screening

Infants of Mothers with Graves Disease

- Neonatal thyrotoxicosis is rare but has a significant mortality
- Caused by the transplacental passage of thyroid stimulating immunoglobulins (TSI)
- TSIs may continue to be produced despite ablation of the thyroid gland with surgery or radio-iodine

- Fetal effects: development of a goitre, tachycardia, hydrops associated with heart failure, growth retardation, craniosynostosis, increased fetal motility and accelerated bone maturation
- Neonatal effects: restlessness, tachycardia, tachyarrhythmia, poor feeding and occasionally extreme hunger, severe weight loss and diarrhea. Effects resolve spontaneously within 3 – 12 weeks.

Screening
- Cord blood: TSH, T4 and T3
- Age 2 – 7 days: as above
- Day 10-14: as above, if mother is on antithyroid medication

TREATMENT OF NEONATAL THYROTOXICOSIS
- Discuss with a senior clinician/endocrine service
- Propylthiouracil (PTU): 5-10mg/kg/day in 3 divided doses or carbimazole 0.5 mg/kg/day as a single dose. Both drugs inhibit synthesis of thyroid hormones
- Iodine solutions suppress the synthesis as well as the release of thyroid hormones
  - ◊ Saturated potassium iodide 1 drop daily
  - ◊ Lugol's solution 1-3 drops daily
- Beta –blockers are effective in controlling symptoms due to adrenergic stimulation:
  - ◊ Propranolol 0.25 - .75 mg/kg 8 hourly orally or IV (given over 10 minutes).
- Aim to reduce the HR< 180
- Treat cardiac failure with digoxin and diuretics
- Severely thyrotoxic babies may be treated with prednisone 2 mg/kg/day. Suppresses de-iodination of T4 to T3 and compensates for hypercatabolism of endogenous glucocorticoids induced by T3 and T4.
- Sedatives to manage irritability and restlessness
- Monitor for hyperthermia, aim to achieve a neutral thermal environment
- Assess fluid balance. May have increased fluid requirement
- Breastfeeding: monitor the TFT of infants exposed to antithyroid drugs perinatally
- Mothers on PTU (< 150 mg/day), carbimazole (< 15mg/day) or methimazole can continue breastfeeding.

NEONATAL JAUNDICE

DEFINITION

- Between 50-60% of normal newborns become clinically jaundiced in the first week of life
- Jaundice may be physiological or pathological

Physiological jaundice is due to:

- Increased production of bilirubin (large erythrocyte mass with shortened life span)
- Decreased hepatic excretion of bilirubin (low hepatocyte ligandin level, low glucoronyl transferase activity)
- Increased entero-hepatic circulation of bilirubin (high intestinal B-glucoronidase levels decreased intestinal motility)
- Breast feeding jaundice is thought to be due to feeding problem, which lead to a decreased intake of milk, increased entero-hepatic circulation and sometimes dehydration
- Breast milk jaundice is diagnosed in clinically well breastfed infant who remains jaundiced for several weeks following physiological jaundice. The mechanism is unknown. It is thought that breast milk glucoronidase leads to increased absorption of unconjugated bilirubin via increased entero-hepatic circulation. Diagnosis is by exclusion. Breastfeeding may be continued.

Pathological jaundice may result from an increased unconjugated or conjugated fraction or both

- **Red flags (features of pathological jaundice plus)**
  - ◊ Mother Rh negative
  - ◊ Mother blood group O. If known check total serum bilirubin (TSB) at 6 hours post-delivery
  - ◊ Baby Coombs positive
  - ◊ Anaemia
  - ◊ Evidence of haemolysis
  - ◊ Preterm
  - ◊ Acidosis, hypoglycaemia, hypoxaemia, hypothermia
  - ◊ Features of kernicterus
  - ◊ Bilirubin levels not decreasing despite effective phototherapy, (i.e 17 - 34 µmol/l within 4-6 hours)
  - ◊ Family history of pathological jaundice

Features	Physiological jaundice	Pathological jaundice
Clinical onset of jaundice (after birth)	> 36 hours	≤ 24 hours
Duration of jaundice	Term <10days Preterm <21 days	Term >Day 10-14 Preterm > Day 21
Peak TSB (days after birth)	Term Day 3 Preterm Day 5 – 7	Early or late
Peak TSB	< 275 µmol/l	> 272µmol/l
Rise in TSB (Per 6 hours)		>50 µmol/l
Conjugated serum bilirubin	Only unconjugated fraction increased	>34 µmol/l
Evidence for haemolysis	No	Yes/No
Underlying illness	No	Yes/No
Hepatomegaly	No	Yes/No
Pale stool/dark urine	No	Yes/No

MANAGEMENT

Early onset jaundice (within 24 hours) – caused by haemolytic disease of new born (HDN) (ABO or rhesus)

- Check mother's blood group
- If the mother's blood group is O, ABO likely. Do following investigations:
  - ◊ Infants blood group and Coombs
  - ◊ FBC and peripheral smear
  - ◊ Check TSB 3 hourly
  - ◊ Start phototherapy
  - ◊ In rare cases look for other causes for haemolysis

Jaundice after 24 hours

- Exclude blood incompatibility
- Exclude obvious infection or extravasated blood/bruising
- Check feeding and infant's weight to exclude breastfeeding jaundice
- Exclude polycythaemia
- Often a cause will not be found; in term infants thought to be an exaggeration of physiological hyperbilirubinaemia and in preterm infants due to the immaturity of the conjugation mechanism
- Treatment will depend on the level of the TSB which should be checked daily

Other modes of assessment

Transcutaneous bilirubin (TCB) screening

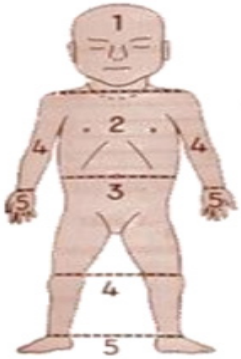
- TCB is a screening tool to select infants who require formal total serum bilirubin (TSB)levels
- TCB screening decreases the number of heel pricks and readmissions for phototherapy
- TCB monitoring should not be relied on in severe hyperbilirubinaemia
- TCB should not be used within 24 hours of phototherapy or an exchange transfusion
- Localised oedema and decreased tissue perfusion affects accuracy of TCB measurements

Technique

- Ensure all staff are properly trained on the TCB device
- Calibrate the TCB device daily in accordance with the manufacturer's specification
- Preferred sites are inter-scapular (for infants < 35 weeks), forehead or sternum
- Measurements should not be made over bruised skin, areas covered by hair or birthmarks
- Measure TCB by gently pressing the tip of the device over the examination site then press the trigger button until the device indicates the measurement is complete
- Take 3 - 5 measurements (device dependent) from the examination site, ensuring consistent placement of the tip and amount of pressure applied
- If the TCB reading is within 20 µmol/L of the phototherapy line do TSB

Kramer's rule

- In a resource limited country like Zambia, laboratory diagnostics may not be available in a timely manner. Clinical examination (e.g Kramers rule) can be used in making the decision to start phototherapy (***It should be known that clinic estimation of jaundice is very unreliable especially in dark skinned infants)***
- Kramer's rule entails visual inspection in natural light. Depth of jaundice progresses from head to toe as the level of bilirubin rises a follows:

Zone	Baby's body area	Approximate bilirubin level	Diagram
1	Head and neck	6 mg/dl (100 µmol/L)	
2	Upper body (chest)	9 mg/dl (150 µmol/L)	
3	Lower body, below the belly button and upper thighs and arms	12 mg/dl (200 µmol/L)	
4	Lower legs and forearms	15 mg/dl (250 µmol/L)	
5	Hands and feet	>15 mg/dl >(250 µmol/L)	

If you can assess the level of jaundice, **any jaundice from the chest and below, you must initiate phototherapy.**

TREATMENT

Phototherapy

High intensity phototherapy (PT) reduces total serum bilirubin (TSB) and decreases exchange transfusions.

- ***Indications***
  - ◊ See phototherapy guideline charts
  - ◊ Indicated for unconjugated hyperbilirubinaemia
  - ◊ In the absence of TCB to help in decision making, DO NOT wait for TSB results before starting phototherapy (Kramer classification can be used if possible)
  - ◊ A low threshold to start phototherapy in high risk infants (e.g. with sepsis, HIE etc)

- ***Contraindications***
  - ◊ Congenital porphyria or a family history of porphyria
  - ◊ Concurrent therapy with metalloporphyrin haem oxygenase inhibitors
  - ◊ Concurrent use of drugs or agents that are photosensitisers

- ***Technique***
  - ◊ Intensive PT is defined as light wavelengths between 430-490nm, delivered spectral irradiance of 30µW/cm2/nm or higher to the greatest exposed body surface
  - ◊ Position the PT unit approximately 40cm from the infant
  - ◊ Measure the irradiance of phototherapy units periodically with the use of a photoradiometer
  - ◊ PT units require adequate ventilation. Do not cover with blankets
- ***Care of the infant receiving PT***
  - ◊ Monitor temp and ensure adequate fluid intake
  - ◊ Cover the eyes with gauze pads and place infant naked under lights (nappy untied)
  - ◊ Remove the eye pads during feeds and observe for conjunctivitis
  - ◊ Turn infant every 2-3 hours
  - ◊ In severe jaundice check the TSB 3 hourly
  - ◊ Visual assessment of jaundice is unreliable once the infant is under phototherapy
- ***Efficacy of PT***
  - ◊ Successful PT should produce a decline in TSB of 17-34 µmol/L within 4-6 hours and TSB should continue to fall
  - ◊ Stop PT if TSB ≥ 50µmol/L below the PT line
- **Complications**
  - ◊ Rashes,
  - ◊ "bronzing"
  - ◊ loose stools
  - ◊ dehydration
  - ◊ hypo/hyperthermia
  - ◊ separation from mother

Intravenous gamma globulin/Polygam®

There is weak evidence that intravenous immunoglobulin (IVIg) reduces the need for exchange transfusion. However, its use might be appropriate in the following situations and should be discussed with a senior clinician:

- Babies with Rh disease unmodified by antenatal treatment
- Babies with potential ABO HDN where a previous sibling has severe HDN requiring exchange transfusion
- Babies with signs of bilirubin encephalopathy
- If there is a delay in obtaining blood for exchange transfusion beyond 4 hours and/or the TSB is continuing to rise > 8.5µmol/hr despite optimal phototherapy and hydration

Dose: 0.5g/kg given over 2 hours

PHOTOTHERAPY

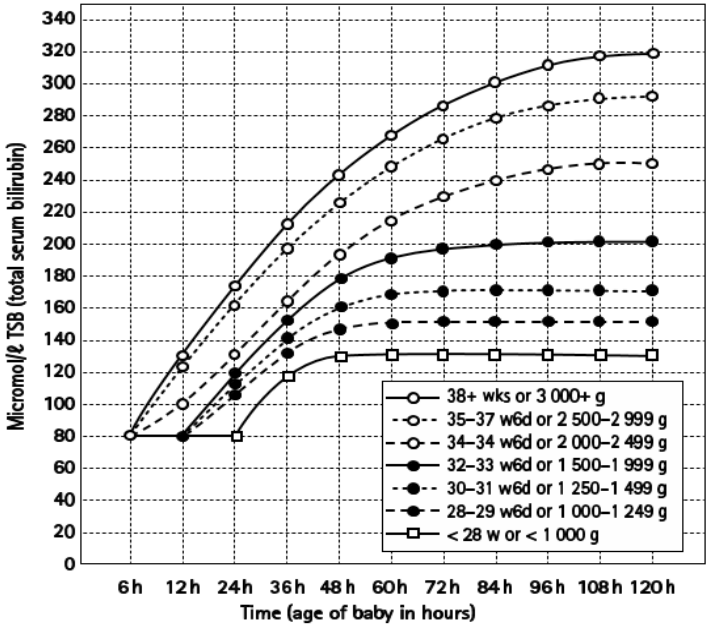
WESTERN CAPE 2006 CONSENSUS GUIDELINES

In the presence of risk factors, use one line lower (the gestation below) until <1000 g
If gestational age is accurate, rather use gestation age (weeks) instead of body weight.

Infants > 12 hours old with TSB level below threshold, repeat TSB levels as follows:
1 - 20 µmol/l below line: repeat TSB in 6 hours or start phototherapy and repeat TSB in 12 - 24 hrs
21 - 50 µmol/l below line: repeat TSB in 12 - 24 hrs
> 50 µmol/l below line: repeat TSB until it is falling and/or until jaundice is clinically resolving

Infants under phototherapy:
Check the TSB 12 - 24 hourly but if TSB > 30 µmol/l above the line, check TSB 4 - 6 hourly.

STOP Phototherapy
If TSB > 50 µmol/l below the line. Recheck TSB in 12 - 24 hours.



Start phototherapy when the TSB is ≥ the line according to gestation or weight.

Exchange transfusion

Introduction

- See exchange transfusion guideline chart
- Method: double volume exchange = 160ml/kg (term) or 180 ml/kg (preterm) whole blood (refer to exchange transfusion procedure below)
  - ◊ Umbilical venous catheter (UVC) method (push/pull): aliquots 5 ml/kg, max 20ml. Each cycle lasts 1-2 minutes
  - ◊ Peripheral method: infuse warm blood into the peripheral IV line at 150ml/kg/hr (12.5ml/kg/5min) and remove 5 ml/kg via an arterial line every 1-2 minutes.
- Often by the time blood is available for the procedure, phototherapy has reduced the TSB to below the exchange value. Do not proceed if exchange is no longer indicated. Return the blood to the blood bank ASAP, store in the refrigerator

Indications

Severe unconjugated hyperbilirubinaemia
Any infant with clinical signs of acute bilirubin encephalopathy
Infants with severe anaemia complicated by cardiac failure who need a blood transfusion; consider an exchange transfusion.

Equipment

- Sterile exchange transfusion (ET) set
- Equipment list according to method (Isovolumetric method is preferred)
- Blood warmer
- Preassembled disposable sets with four-way stopcocks
- Tubes for pre/post exchange blood tests

Isovolumetric method	**Push-pull method**
• Peripheral IV catheter (24g) and giving set • Peripheral arterial catheter and T-connector *OR* • Umbilical arterial catheter • 1 x Three-way stopcock	• Umbilical venous catheter • 2 x Three-way stopcocks
Plus Blood administration set; Male-female leur lock extension set; 20ml syringe; Empty IV bottle for waste receptacle; Heparinised saline (0.5IU heparin/ml)	

PREPARATION FOR PROCEDURE

- Take consent for the ET. Risk of death or severe morbidity; <1% in healthy and 12% in sick infants
- Take cross match from both infant and mother
- Order whole blood for double volume exchange; 160ml/kg(term) or 180ml/kg (preterm)
- Insert lines and clear of air bubbles
- Empty infant stomach and keep NPO for 4 hours prior to procedure, if possible
- Take FBC, UEC, Ca, blood gas, glucose, bilirubin, (TSB) and coagulation pre ET
- Diagnostic blood tests must be done before ET
- Document procedure in infant's hospital record
- Check TSB just before ET. Do not proceed if exchange is not indicated

ISOVOLUMETRIC METHOD

(Total duration: 45-60 minutes)

- Scrub and gown as for major procedure
- Arterial line
- Connect arterial line and T-connector to three-way stopcock
- In case of UAC, attach UAC to stopcock
- Attach male-female leur lock extension set to stopcock and place end in receptacle
- Attach 20 ml syringe to remaining port to stopcock
- Attach venous line to blood administration set
- Allow blood to run through blood warmer
- Start exchange record, document in/out volume and vital signs
- Infuse warm blood into peripheral IV line at 150ml/kg/hr
- Withdraw 5ml/kg blood via the arterial line every 2 minutes and discard in receptacle
- Intermittently flush arterial line with 0.5ml of heparinised saline
- Check peripheral glucose every 30 minutes
- Gently agitate blood bag every 15 minutes to prevent red cell sedimentation

METHOD: PUSH-PULL

(Total duration: 90-120 minutes)

- Attach 2 x three-way stopcocks in series
  - ◊ Proximal stopcock is attached to the UVC and male-female leur lock, place end in receptacle
  - ◊ Distal stopcock is attached to 20ml syringe and blood administration set
- Allow blood to run through blood warmer
- Start exchange record, document in/out volume and vital signs
- Remove and replace blood at rate of 5ml/kg (max 20ml) over 2 minutes for each cycle
- Follow remainder of steps as for isovolumetric method

POST EXCHANGE

- Monitor closely for 6 hours
- Keep NPO for 4 hours after ET
- Monitor glucose 2-4 hourly for 24 hours
- FBC, bilirubin, Ca 4 hours after ET and further as indicated

COMPLICATIONS

- Metabolic: hypocalcaemia, hypo/hyperglycaemia, hyperkalaemia
- Cardiorespiratory: apnoea, bradycardia, hypo/hypertension
- Haemotological: thrombocytopaenia, neutropaenia, DIC
- Catheter related: vasospasm, thrombosis, embolization
- Gastrointestinal: feeding intolerance, NEC
- Infection

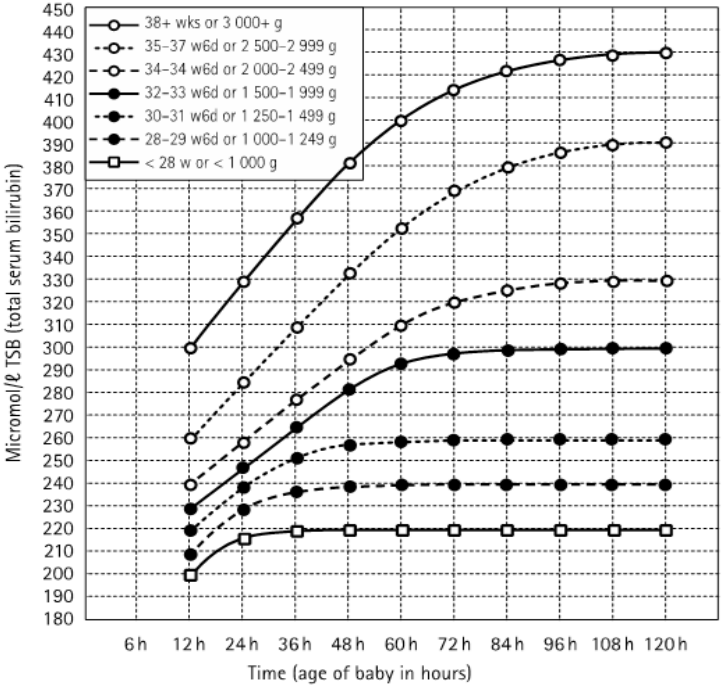
EXCHANGE TRANSFUSION

WESTERN CAPE 2006 CONSENSUS GUIDELINES

In presence of sepsis, haemolysis, acidosis, or asphyxia,
use one line lower (the gestation below) until <1000 g
If gestational age is accurate, rather use gestation age (weeks) instead of body weight.

Note:

1. Infants who present with TSB above threshold should have exchange done if the TSB is not expected to be below the threshold after 6 hours or intensive phototherapy
2. Immediate exchange is recommended if signs of bilirubin encephalopathy and usually also if TSB is > 85 µmol/l above threshold at presentation
3. Exchange if phototherapy contimues to rise



PROLONGED NEONATAL JAUNDICE

- Defined as jaundice lasting >14 days in term infant >21 days in a preterm infant
- Determine whether it is unconjugated or conjugated hyperbilirubinaemia

UNCONJUGATED HYPERBILIRUBINAEMIA

- Determine whether or not the baby is breastfed
- Collect urine for MCS and reducing substances to exclude galactosaemia
- Check liver enzymes
- Exclude hypothyroidism
- Exclude haemolysis, check reticulocytes and Hb
- Hereditary enzyme defects such as Gilbert's and Crigler – Najjar syndromes are rare

CONJUGATED HYPERBILIRUBINAEMIA

- History and examination
- Liver function tests and cholesterol
- Examine stools daily. Acholic (white) stools require urgent referral to exclude biliary atresia
- Exclude infective causes
- Exclude metabolic causes
- Exclude genetic conditions

Cause of conjugated hyperbilirubinaemia

Causes		
Infective	Viral	Hepatitis A, B, CMV, HIV, rubella, herpes simplex
	Bacterial	Syphillis, septicaemia, UTI
	Protozoal	Toxoplasmosis gondii
Biliary	Biliary atresia, choledochal cyst, Alagille's syndrome, bile plugs, cystic fibrosis	
Metabolic/ genetic	Alpha 1-antitrypsin, tyrosinaemia type 1, galactosaemia, wilson's disease, hypothyroidism, hypopituitarism, familial intrahepatic cholestasis, rotor and Dubin-Johnson syndrome	
Drug/toxins	TPN	
Autoimmune	Autoimmune hepatitis Sclerosing cholangitis	

Diagnostic workup for conjugated hyperbilirubinaemia

Investigation	Test	Date Taken	Results
Haemotology	FBC		Hb, WCC, platelets, reticulocytes
	Coagulation		INR, PTT, fibrinogen
	Blood group		
	Coombs		
Biochemistry	U&E		Na, K,urea, Creatinine
	TSB, conjugated bilirubin		TSB, conjugated bilirubin
	Liver functions		AST/ALT, ALP, GGT
	CMP		Ca, Mg, PO4, Albumin
	Cholesterol*		
	Glucose		
Microbiology	Blood culture		
	Urine culture		
Virology	IgM		Rubella, HSV
	Urine CMV		
	Hepatitis A, B, C		
	HIV		
Metabolic	Urine reducing substances		
	GAL-1-PUT*		
	alpha 1-antitrypsin*		
	Plasma amino acids*		
	Urine amino acids*		
	Urine organic acids*		
	Sweat test*		
Endocrine	Thyroid functions		
Radiology	Abdominal U/S		
	CXR/spinal X-ray*		
	Radio-isotope scan*		
Histology	Liver biopsy*		
Other	Stool		
	Ophthalmology*		

**Second line investigations, discuss with senior clinician*

CONGENITAL ANOMALIES

INTRODUCTION

Worldwide, an estimated 276,000 babies die within 4 weeks of birth every year from congenital anomalies. Congenital anomalies can result in long term disability, which may have significant impacts on individual, families, health care systems and societies.

The most common severe congenital anomalies are heart defects, neural tube defects and Down syndrome. Although congenital anomalies may be genetic, infectious, nutritional or environmental in origin, most often it is difficult to identify the exact causes

Some congenital anomalies can be prevented. For example, vaccination, adequate intake of folic acid or iodine through fortification of staple foods or provision of supplements, and adequate antenatal care are keys for prevention. (WHO 2015)

DYSMORPHIC BABY: DIAGNOSTIC WORKUP

History

- Ask for relevant family history, maternal substance use, medications and illnesses
- Check maternal notes for any antenatal scans or screening tests
- History of stillbirths and miscarriages could be a result of unbalanced chromosomal anomalies in parents
- Observe parental features
- Parental age important because the incidence of chromosome aneuploidies is increased in older mothers and fresh autosomal dominant mutations (achondroplasia, neurofibromatosis type 1, etc) are commonly seen with older fathers.
- Ethinicity

Examination

- Examine the baby thoroughly and record all dysmorphic features
- Identify life threatening abnormalities and manage accordingly if possible
- Attempt to assimilate the features to a known syndrome (Downs syndrome, Turners syndrome)
- Record anthropometric measures and plot on centile chart
- Discuss with senior clinician ± genetic consult
- Consider passing a nasogastric tube (NGT) to exclude choanal atresia and oesophageal atresia if clinically indicated

Possible further investigation (depending on other findings)

- Further investigations to be directed by the senior clinician
- May include CXR, AXR, spine XR, echo, eye and hearing examinations

Communication with parents

- Be open and honest with parents. Involve senior clinicians early on in management.

CLEFT LIP AND PALATE

BACKGROUND

- Incidence of 1:700 births
- Clefts can range from an incomplete cleft lip to complete bilateral cleft lip and palate
- A submucous cleft palate is more difficult to detect
- The signs to look for are:
  - ◊ bifid uvula
  - ◊ transparent line down soft palate
  - ◊ presence of notch at junction of hard and soft palate

MANAGEMENT

- Full examination for other anomalies, airway and breathing difficulties
- Babies should ideally be managed with their mothers on postnatal ward
- Early referral to Speech and Language Therapist
  - ◊ Will assess the feeding
  - ◊ Advise for specialist feeding equipment as appropriate
- Encourage breastfeeding and assist with milk expression if not possible
- Referral to the Cleft Lip and Palate service
- The lip and primary palate are usually repaired at around 5 months of age
- The soft palate repair is usually timed around 9 months of age

DOWN'S SYNDROME

BACKGROUND

- Caused by the presence of all or part of an extra chromosome 21
- 1 in 800-1 000 live births
- Increased risk with increasing maternal age: risk < 30 years <1 in 1 000; risk at 35 years 1 in 400; risk at 42 years 1 in 60. However, 75% of babies with Down's syndrome are born to mother <30 years
- Underlying genetics may be:
  - ◊ Trisomy 21 (95%)
  - ◊ Mosaicism (1-2%)
  - ◊ Translocation (2-3%)

ASSESSMENT

- The diagnosis may be antenatal or postnatal
- If the diagnosis is made antenatally, enquire about antenatal cardiac ultrasound and whether Karyotyping had been done
- Perform a full examination, paying particular attention to the cardiovascular and GIT system
- Always discuss the case with a senior clinician
- For postnatal karyotyping, take at least 1 ml of blood and place in lithium heparin tube-send to the cytogenetic lab

CONFIRMED DIAGNOSIS AND FOLLOW-UP

- Check cord thyroid result; if not available do thyroid function test 48 hours after delivery, thereafter at 6 months of age, at 1 year and then annually
- Refer to the cardiology and genetic clinics within 3 months; sooner if heart murmur noted before discharge
- All infants must have a 6-weeks appointment to see the doctor at their nearest facility
- Refer to facilities with additional support for the parents.

INFORMATION THAT MAY BE GIVEN TO PARENTS

The infant will have developmental delay and learning difficulties
High incidence of congenital heart disease (45%)
Potential for feeding problems, hypotonia, visual impairment (squint or cataracts), hearing impairment, duodenal atresia, hypothyroidism (1%), short stature and recurrent URTIs and otitis media.

SINGLE UMBILICAL ARTERY (SUA)

BACKGROUND

- Isolated SUA occurs in up to 2% of all infants
- SUA may be associated with other structural or chromosomal anomalies
- The incidence of other major abnormalities in infants with a SUA is 25%
- There is little yield in investigations without examination findings of other anomalies

MANAGEMENT

- Check if antenatal ultrasound scans detected any other abnormalities
- Examine for dysmorphic features, abdominal masses, or cardiac disease
- If no other abnormalities are found on examination, no investigations are required.

CONGENITAL CYSTIC ADENOMATOID MALFORMATION (CCAM) AND OTHER CONGENITAL LUNG MALFORMATIONS

BACKGROUND

- Congenital lung malformations are often diagnosed on antenatal ultrasound
- CCAM is the commonest congenital lung malformation and is characterized by a lack of normal alveoli and an excessive proliferation and cystic dilation of terminal respiratory bronchioles
- Peak growth occurs at 25 weeks and reaches a plateau at 28 weeks. Many will start reducing in size from 29 weeks
- Single best predictor of fetal death is hydrops
- Generally, outcome is favourable

MANAGEMENT

- A senior clinician must be alerted to the pending delivery of any patient with a congenital lung malformation and must attend the delivery
- All infants must be admitted to the nursery
- Symptomatic infants must be admitted to NICU or high care and reviewed with the senior clinician
- Asymptomatic infants:
- Admit for observations for 12-24 hours
- A CXR is not required
- A Pulmonology OPD follow-up at 4-6 weeks

NB: *Congenital diaphragmatic hernia – see Respiratory Chapter*

NEONATAL INFECTIOUS DISEASES

ANTIBIOTIC POLICY FOR SUSPECTED SEPSIS

Neonatal Unit antibiotics policy is determined by considering the organism known to have caused infection in the unit in the last 6 months. This policy is regularly reviewed and revised as necessary.

A disciplined and consistent approach to antibiotic usage is necessary to provide optimal broad-spectrum cover in suspected sepsis and to limit the emergence of resistant organisms in areas of high usage.

Proposed antibiotics. Decide according to unit cultures and sensitivities

- Early onset sepsis (< 72hrs of age): Penicillin G and gentamicin
- Late onset sepsis (> 72hrs of age): Penicillin/Cloxacillin and gentamicin/ amikacin
- Second line antibiotics: Cefotaxime and cloxacillin
- Third line: Ciprofloxacin/Meropenem
- Meropenem should be used if meningitis or NEC is suspected
- Vancomycin only if the patient has central lines in place and is at risk of Staphylococcus aureus sepsis.

Once started, the duration of treatment should be tailored to clinical circumstances. If cultures come back normal, laboratory indices are normal and the patient no longer shows signs of sepsis, stop antibiotics after 36 – 48 hours. In the absence of proven sepsis, there is no place for "a course" of antibiotics.

RISK FACTORS AND CLINICAL INDICATORS FOR EARLY ONSET INFECTION (<72 HRS OF BIRTH)

Using the following criteria, one can assess the risk of a baby having an early onset infection and therefore the need for antibiotics.

1. ABSOLUTE INDICATION FOR EMPIRIC ANTIBIOTIC TREATMENT

- Maternal invasive bacterial infection requiring antibiotics (eg: septicaemia) – suspected or confirmed (NB: Not prophylaxis)
- Confirmed or suspected infection in twin
- Respiratory distress starting more than 4 hrs after birth
- Mechanical ventilation in a term baby
- Seizures
- Signs of shock

2. START ANTIBIOTICS IF TWO OR MORE ARE PRESENT OF:

Antenatal

- Prelabour ROM
- Preterm birth following spontaneous labour <37 weeks
- ROM ≥18 hours
- Maternal fever ≥ 38ºC or chorioamnionitis
- GBS in previous baby
- Positive GBS screening or infection in this pregnancy

Postnatal

- Altered behavior/tone/responsiveness
- Feeding difficulties (eg. food refusal in a term baby) or intolerance
- Respiratory distress
- Apnoea
- Abnormal heart rate (bradycardia or tachycardia)
- Altered glucose homeostasis (hypo/hyperglycaemia)
- Metabolic acidosis ≥ 10mmol/l
- Temperature abnormality >38º or < 36º not explained by environmental factors

If only one risk factor is present, consider observation for 24 hrs

EARLY ONSET GROUP B STREPTOCOCCAL (GBS) INFECTION

BACKGROUND

Infections in newborns occurring within the first week of life are designated early-onset (EO) disease. Late-onset infections occur in infants aged > 1 week, with most infectious evident during the first 3 months of life. These guidelines are for EO disease only.

MATERNAL PROPHYLAXIS

- Prevention is provided by intrapartum antibiotic prophylaxis (IAP) given to mother at the onset of labour. IAP given at least 4 hours before delivery reduces the risk of neonatal infection by 90% but may be less effective in preterm labour.
- Indication for IAP:
  - ◊ Previous infant with invasive GBS disease
  - ◊ GBS bacteriuria during any trimester of the current pregnancy
  - ◊ Positive GBS vaginal –rectal screening culture in late gestation (35-37 weeks) during current pregnancy
  - ◊ Delivery at <37week gestation when the mother has been in labour
  - ◊ Amniotic membrane rupture ≥ 18 hours
  - ◊ Intrapartum temperature ≥ 38.0^{o}C
- Drug: pen G/ampicillin/cefazolin

NEONATAL PROPHYLAXIS:

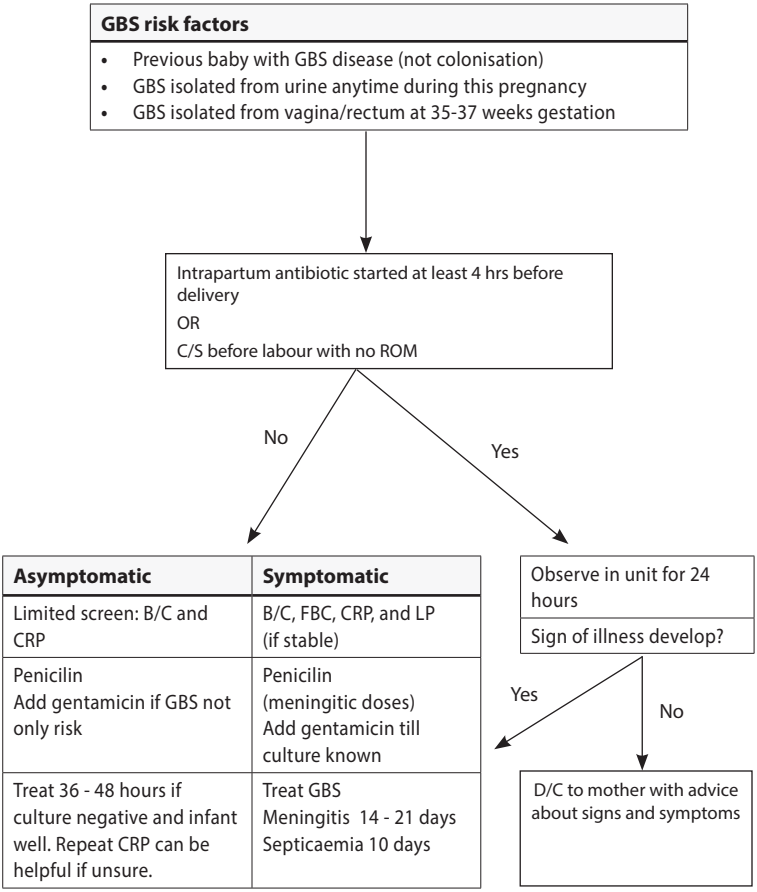
- Indication: if IAP for mother is partially (given <4 hours prior to delivery) or not given
- Drug = pen G (benzyl penicillin) and Gentamicin
- Stop after 36-48 hrs if Blood culture negative and clinically normal

NEONATAL TREATMENT:

- Indications: signs of maternal or neonatal sepsis
- Drug: Pen G (benzyl penicillin IV)
- Meningitis: 100 000 U/kg/dose 8 hourly for 2-3 weeks
- CSF normal: 100 000 U/kg/dose 12 hourly for 10 days

Add gentamicin if GBS not the only risk factor

MANAGEMEN OF BABIES EXPOSED TO GROUP B STREPTOCOCCUS



VARICELLA ZOSTER VIRUS

BACKGROUND

- Varicella is a highly infectious virus. The incubation period is 2 – 3 weeks
- The infectious period is 2 days before the rash until all the vesicles have scabbed
- Early treatment with oral/systemic acyclovir decreases the severity and length of illness
- Herpes zoster (shingles) is caused by re-activation of the patient's varicella virus. Vesicles appear in the dermatome of the affected nerve. Virus is transmissible to susceptible individuals but the risk of transmission is low and the mother's baby will be protected by maternal antibiotics

RISK TO THE FOETUS AND NEONATE

Congenital varicella

- This rare condition affects less than 2% of foetuses whose mothers have chickenpox during the first 20 weeks of pregnancy
- Skin scarring, limb hypoplasia, eye and central nervous system abnormalities can occur

Neonatal varicella

- Mothers who develop chickenpox rash 5 days before delivery till to 2 days after delivery are at high risk of passing on severe chickenpox to their babies who do not have any protective antibodies
- Without treatment 30% of these babies may die
- The infants may get varicella between 0-12 days of life with the highest risk if they manifest the infection between 5-10 days of life
- Prophylactic passive immunization (VZIG) will fail to prevent up to 50% of neonatal cases, however the severity will be reduced
- Neonate exposed to varicella zoster virus from sources other than maternal, i.e. medical staff, other mothers or even other neonates are at risk. High risk neonates (see below) should also receive VZIG if exposed.

INDICATIONS FOR PASSIVE IMMUNIZATION WITH VARICELLA ZOSTER IMMUNOGLOBULIN (IVIG)

1. All infants born to mothers who have developed a chickenpox rash 5 days before delivery until 2 days after delivery. This does not include zoster (shingles)

2. Hospitalised premature infants, less than 28 weeks' gestation or below 1000 g birth weight who are exposed to VZV should receive VZIG, regardless of the maternal history of chickenpox as these infants may not have acquired maternal antibodies. Discuss these infant with a senior clinician.
3. High-risk neonates who are exposed to VZV can be considered for VZIG. There are no international guidelines but very ill babies and preterm babies more than 28 weeks gestation could receive VZIG depending on exposure risk and whether the mother has ever had chickenpox (maternal antibodies should protect these infants). If unsure from maternal history, you could check the mother or baby's blood for antibodies (IgG).

The intramuscular dose of vazigam (>100 IU/ml) is: 0.5 ml for preterm infants and 1 ml for term infants. It should be given as soon as possible, but there is benefit up to 96 hours after exposure.

TREATMENT AND PRECAUTIONARY MEASURES

- Any newborn who develops chickenpox, whether they have had VZIG or not, should receive acyclovir therapy promptly at a dosage of 10 to 15 mg/kg every 8 hour intravenously
- Newborns that have chickenpox must be isolated
- Those who have received VZIG, should as far as possible, be kept isolated from the rest of the nursery (in case they develop chickenpox)
- As the clinical course may be lengthened post VZIG, they should be kept isolated for 30 days (ideally at home)
- Obviously, any adult with chickenpox should not be allowed into the nursery while they are infectious
- When a neonate who received VZIG is discharged home, it should be made clear to the parents that prompt hospital review should be undertaken if the baby becomes unwell or develops a rash.

MEASLES

BACKGROUND

- The incubation period is usually 10-14 days. It is communicable 4 days before to 4 days after rash onset
- Case fatality is as high as 30% (and higher in preterm infants)
- It is a notifiable disease

CONGENITAL MEASLES

- In pregnancy, measles is more likely to cause miscarriage or preterm labour than cause congenital infection or abnormalities

PERINATAL MEASLES

- Exposed pregnant women to receive immunoglobulin within 6 days of exposure
- Mother who develop measles towards the end of their pregnancy can infect the baby via the placenta (10-30%) or by droplet spread after birth
- Babies who develop illness less than 10 days after birth are presumably infected in utero. The measles rash has been described at birth in a few babies
- Continue breastfeeding: IgA measles-specific antibody may help modify the disease
- Measles acquired at 14-30 days of age is transmitted postnatally and is usually milder

DIAGNOSIS

- Recommended work-up: test serum measles IgM or urine for PCR

TREATMENT

- Supportive, antipyretics and fluid as indicated
- Treat superimposed bacterial infection promptly
- Vitamin A 100 000 IU orally x 2/7
- Infants who develop measles must be isolated with their mothers if possible.

PROPHYLAXIS

- Passive immunoglobulin, 0.25ml/kg IM within 72 hours (but effective up to day 6)
- Two formulations available are Beriglobin and Intragam. These are general pooled human immunoglobulins that include anti-measles immunoglobulins.

Prophylaxis should be given to the following:

1. Infant whose mother has measles and the baby does not: Isolate from the mother for 4 days after her rash appeared. Measles may take up to 18 days to develop due to the antibodies given.
2. Infants in the nursery who are exposed to measles through an infected mother/staff member or baby: Only if the mother has never had immunization or measles or baby less than 28 weeks (low antibody transfer).

CONGENITAL INFECTIONS: SYPHILIS, CYTOMEGALOVIRUS, RUBELLA, TOXOPLASMOSIS, HERPES

The following may be present with any of the congenital infections:

Growth restriction	Hepato-splenomegaly	Jaundice (conjugated)
Anaemia	Thrombocytopaenia	Petechiae
Microcephaly	Chorioretinits	Hydrops (non-immune)
Skin rash	Bony changes	Adenopathy

The following point to more specific infections:

Rubella: PDA and cataracts
Toxoplasmosis: Generalised intracerebral calcifications and **Hydrocephalus**
CMV: Periventricular calcifications and microcephaly
Syphilis: Large pale placenta, rash on palms and soles, snuffles, pseudoarthritis, hepatosplenomegaly, growth restriction

Growth restriction alone with no other signs is NOT an indication for investigation for congenital infection.

NB: try to get the PLACENTA sent for histology – this will often assist greatly in making the diagnosis.

CMV

Send urine for CMV PCR or shell vial. If this is positive in an infant less than 3 weeks of age, it confirms congenital CMV. IgM only positive in 50%.

There is evidence that treatment with gancyclovir improves survival in critically ill infants and decreases the incidence of hearing loss. Oral valgancyclovir may also be used. The optimal length of treatment is under study but at least 6 weeks should be given.

Gancyclovir and valgancyclovir are costly and have severe side effects (especially neutropaenia). Each case should be carefully considered. Ophthalmology review and audiology should be done. Neurodevelopmental follow-up is needed.

Syphilis

The most common congenital infection in our setting is syphilis: It is probably worth checking for this first. Even if the mother was RPR/VDRL negative earlier in pregnancy, this does not exclude congenital syphilis – the test only become positive 2 months after infection and with the rapid test we likely to see more false negative tests. Re-check the mother and consider sending a RPR/VDRL on the baby. Specific

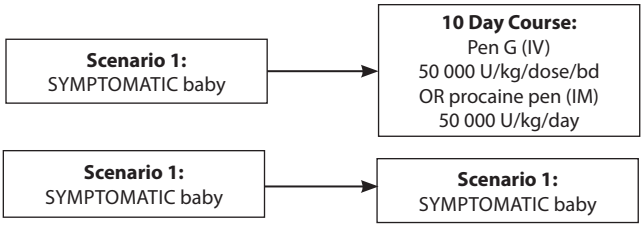
treponemal tests such TPHA are of little use when testing the baby as this will pick up maternal antibodies.

False positive results (usually low titre < 1:16) can occur with EBV, VZV, hepatitis, measles, TB, SLE, lymphoma, mycoplasma or protozoal infections, connective tissue disease and pregnancy itself.

False negative results in rapid tests can be caused when the antibody titre is very high (prozone effect). Laboratory testing can include dilution in suspicious cases.

Treatment:

Only penicillin has been fully tested and should be continued even when other antibiotics are used. If the course is interrupted by more than 24 hours it should be restarted from the beginning.



- There is no need for routine lumbar puncture
- Congenital syphilis is a notifiable disease. Contacts should be treated
- All fully treated infants should have their VDRL/RPR rechecked at 3 months to ensure the titre is decreasing

Rubella

There may be a history of rubella infection in the first trimester. Send urine for rubella PCR. Remember these babies are infectious but there is no specific treatment. Ophthalmology and hearing should be checked. Neurodevelopmental follow-up is essential). Notifiable so fill out form for notifiable disease and send to UTH virology laboratory.

Toxoplasmosis

The placenta is the most useful for diagnosis. Serology can be done but is unreliable. IgA and IgM are the most useful, but liaise with the lab. PCR can also be done.

Treatment is with pyrimethamine and sulphadiazine, possibly with folanic acid (leucovorin). Prednisone is added if there is CNS or eye involvement. Treatment may be for up to a year! Liaise with the infectious disease team if you are considering treatment.

Herpes

This is actually very rarely a true congenital infection and is usually obtained perinatally from the maternal genital tract. Do not rely on a history of herpes lesions from the mother as most of the transmission occurs in maternal primary infection and only 30% of mothers have a known history of herpes ulcers.

Disease usually develops 3-10 days after delivery and is more common in the premature infant.

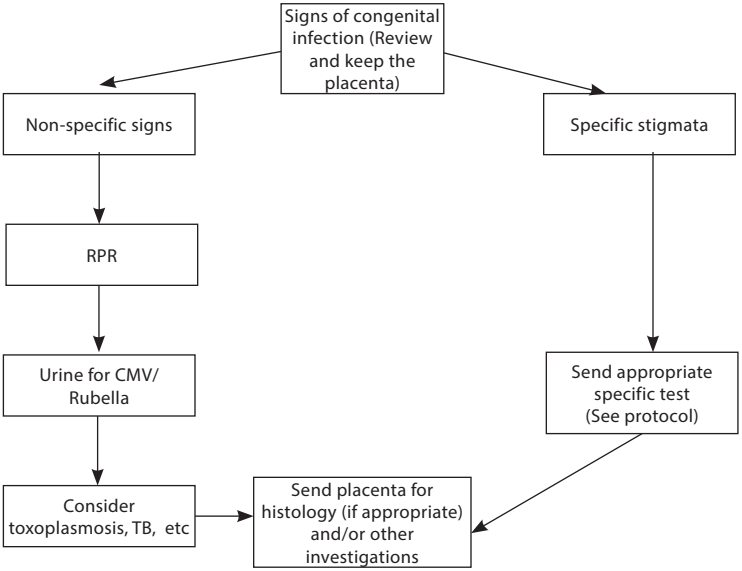
There are 3 methods of presentation:

- SEM- skin/eye/mouth
- Encephalitis
- Disseminated

Only 50% of infants will have any skin lesions and the infant may look as though they have bacterial sepsis. Fever and aseptic meningitis should increase your suspicion of herpes.

Test: IgM very unreliable. Send blood/CSF/vesicle fluid for herpes PCR.
Treatment: high dose acyclovir (20mg/kg 8 hourly) for 2 (SEM only) or 3 weeks.

ALGORITHM FOR INVESTIGATING CAUSE OF SUSPECTED CONGENITAL INFECTION



HEPATITIS B PROPHYLAXIS

BACKGROUND

- Hepatitis B virus can be transmitted to the neonate during birth via blood and secretions
- Mothers who are carriers are hepatitis B surface antigen (HBsAg) positive
- Infected mothers are at high risk of transmitting the virus to their babies if they are hepatitis E antigen (HBeAg) positive OR if the mother has symptomatic acute disease (rare)
- The infants are asymptomatic at birth, with signs only presenting at 2-6 months. This usually consists of mild enzyme elevations. Rarely jaundice, hepatomegaly or liver failure can occur. Hepatitis B investigation should therefore not be part of the routine work-up of unexplained jaundice if the child is less than 6/52 old

CHANCES OF TRANSMISSION

- HBsAg positive and HBeAg negative: 10%
- HBsAg positive and HBeAg positive: 80-90%
- Infants infected at birth have a 90% chance of chronic infection and 15-25% of these will die as adults due to HBV-related liver disease.

PROPHYLAXIS AGAINST HEPATITIS B

- **Active immunization:**
  All babies whose mothers are HBsAg positive should receive Hepatitis B immunization 0.5ml (10mg) IM into the thigh within 24 hours (but preferably within 12 hours)
- **Passive immunization:**

  Give 200 IU into the opposite thigh (this is 2 ml of the hebagam formulation)) to high risk babies (mothers are HBeAg positive OR the HBeAg is not known OR have symptomatic acute disease)

Breastfeeding can continue.

Refer follow-up at 9 months of age for hepatitis B antigen testing. If the infant is discovered to be Hep B infected, they should be referred to a paediatrician.

HEPATITIS A PROPHYLAXIS

Mothers with Hepatitis A have an increased risk of preterm labour and premature rupture of membranes. There have only been 2 cases of intrauterine infection and although vertical transmission can occur in the perinatal period this risk appears to be low. There is no transmission through breast milk.

Newborn infection may be asymptomatic or present at least 2 weeks after exposure with jaundice, loss of appetite, vomiting, fever and hepatomegaly. Treatment is supportive and full recovery usually occurs. Liver failure has never been reported.

Prophylaxis: Some experts advise giving immune serum globulin (0.02 ml/kg intramuscularly [IM]) to the infant if the mother develops symptoms two weeks before to one week after delivery. Beriglobin and intragam are 2 formulations available. The efficacy of this prophylaxis has not been fully established in newborns

TUBERCULOSIS

TB DISEASE

Congenital TB

- True intra-uterine transmission of TB. This is fortunately rare but does occur
- This is by direct haematogenous spread via the umbilical vein or ingestion of infected amniotic fluid
- To make the definition of congenital TB the infant must have proven TB (on microscopy or culture) and one of the following:
  - ◊ Lesions in the first week of life
  - ◊ A primary hepatic complex or caseating hepatic granulomata
  - ◊ Tuberculous infection of the placenta or the maternal genital tract.
- Exclusion of the possibility of postnatal transmission by a thorough investigation of contacts, including hospital staff.
- The infant who acquires TB congenitally may be born with a septic-like picture, hepato-splenomegaly, conjugated jaundice, ascites, pneumonia, fever, papules and petechiae.

Perinatal TB

- TB acquired in utero, intrapartum or during the early newborn period
- Mortality is high, varying from 2-60% depending on delay to presentation and other factors, such as prematurity and co-infection with HIV
- Complications include a high rate of military tuberculosis and meningitis, resulting in seizures, deafness and death

- Impairment of innate pulmonary defences place the infant at high risk of TB, and may result in military or cavitating disease
- Delayed-type hypersensitivity to purified protein derivative may be absent in up to 80% of cases
- Most perinatal cases present after a few weeks with respiratory signs (tachypnoea present in over 80% of the cases)
- Fever, lethargy and hepatomegaly are also common
- Over 50% of the infant have a miliary picture on CXR and 33% of the infants have CSF abnormalities.

INVESTIGATIONS

Microscopy and culture:

- Placenta – histology for TB granulomata
- Gastric washings (x 2)
- Tracheal aspirate (if intubated)
- CSF- Raised protein and lymphocyte predominance

Imaging:

- CXR Miliary pattern/lymph nodes/cavitations
- Ultrasound abdomen: Can demonstrate enlarged lymph nodes indicating abdominal TB

Skin tests:

- Mantoux is the test of choice but is often negative

Other:

- HIV testing if unknown

TREATMENT

Isoniazide (INH) 10mg/kg/day (range 10-15 mg/kg/day)
Rifampicin (RIF) 15 mg/kg/day (10-20mg/kg/day)
Pyrazinamide (PZA) 35 mg/kg/day (30-40 mg/kg/day)

- If milliary/cavitations/extra-pulmonar TBM, spinal:

Duration:	PZA/ INH/RIF	2 months (Intensive phase)
	INH/RIF	10 months (continuation phase)

- If there is CNS involvement:

  INH 15-20 mg/kg/day, RIF 15-20 mg/kg/day, PZA 30-40mg/kg/day, Ethambutol 20mg/kg (15-20mg/kg),
  Duration: 12 months as above.
  Add Prednisone 2-4 mg/kg/day x 4 wks taper over 2 wks.

- In uncomplicated pulmonary TB, treat for 6 months (2 months intensive phase and 4 months continuation phase)
- Discuss with infections disease expert/neurologist.
- Beware liver toxicity – check ALT and watch for jaundice
- If the infant is vomiting - check LFTs and if these are acceptable, split the drugs (give ethionamide separately), note the doses.

NB: Check mother is treated and other family members are screened.

TB EXPOSED INFANT

- An infant is considered TB exposed:
- If he/she is born to a mother with known TB who has received less than 2 months of treatment
- If the mother has been on treatment for longer than 2 months but is noncompliant or still considered exposed. MDR/XDR TB is then a greater possibility
- One should check the sensitivities of the mother in all cases

1 Unwell infant:

- Investigate for TB as above
- Send the placenta for histology if possible
- Start on treatment if clinically indicated

2 Well infant with no physical signs of perinatal TB:

- No investigation
- Start on prophylaxis of INH 10mg/kg daily x 6 months – see dosage chart below
- Baby must be referred to TB clinic for continued prophylaxis and surveillance
- DO NOT give BCG vaccine – this is important as INH may kill the Mycobacterium bovis in the BCG. Also, BCG may confuse the interpretation of tuberculin skin tests if they are subsequently done to try and prove TB disease
- BCG vaccination should only occur at the completion of the TB prophylaxis regimen. Do not give BCG in HIV symptomatic infants

3 If the mother is only diagnosed (or suspected to have TB) around the time of birth:

- If the baby is in the nursery, the mother should only come into the nursery if she is wearing a mask and preferably having started TB treatment
- If the baby is well enough to go to the mother, this may be done as long as the mother has started treatment and the baby is on prophylaxis.

4 Premature babies

- In the very premature baby who has feeding difficulties, prophylaxis can be deferred until the baby is on full feeds as long as the mother is thought to be a low infection risk (been on treatment for longer than 2 weeks and wearing a mask)
- It is essential to remember to start the prophylaxis later as this can be easily forgotten – make a note in the folder)

5 MDR/XDR confirmed or suspected

- Speak with infectious disease team
- Standard INH dosing

Body weight (Kg)	Daily isoniazid (INH) 100 mg tablet
2-2.4	¼
2.5-4.9	½
5-7.4	¾
7.5-9.9	1
10-19.9	2
20-24.9	2 ½
>25	3

MANAGEMENT OF HIV EXPOSED INFANTS

Maternal combined ART (cART) coupled with infant ARV prophylaxis significantly reduces the risk of MTCT.

2016 Recommendations

Infant ARV prophylaxis in high-risk infants=AZT +NVP for 12 weeks
HIV virologic testing concurrent with Expanded Program for Immunisation (EPI visits)

High-Risk HIV-exposed infants		
Case scenario	**Management of the mother at delivery and in Postnatal care**	**Infant ARV prophylaxis and Nucleic acid testing**
1. Born to women with established HIV infection not on ART; or: 2. Born to women with established HIV infection and having received less than 12 weeks ART at the time of delivery; or: 3. Born to women established HIV infection with viral load>1000 copies/mL within the four weeks before delivery, if viral load measurement available.*	Start or continue cART	All exposed infants to be put on AZT/ NVP for 12 weeks
Known for positive who refuses ART	Continue counselling for need to start therapy. Suggest to start ART with the possibility of stopping after delivery (Option B) while counselling continues toward their mother accepting lifelong cART (Option B+)	Prophylactic ART (AZT/NVP) until confirmed final outcome HIV negative after complete cessation of breastfeeding

*All HIV positive pregnant women on cART should have a viral load done 1 to 4 weeks before delivery

Low-Risk HIV-Exposed Infants		
Case scenario	**Management of the mother at delivery and in Postnatal care**	**Infant ARV prophylaxis and Nucleic acid testing**
Known for HIV-positive women on ART for more than 12 weeks	Continue ART	All exposed infants to be put on (AZT/NVP) for 6 weeks
HIV-negative women with known positive partner	Pre-Exposure Prophylaxis and provide HTS every 3 months	NAT on the mother, and if the positive NAT on the baby

*All HIV positive pregnant women on cART should have a viral load done 1 to 4 weeks before delivery

HEI ARV prophylaxis in complicated cases

Case scenario	**Management of the mother at delivery and in postnatal are (PNC)**	**Infant ARV prophylaxis and Nucleic acid testing (NAT)**
Woman with an HIV positive test in ANC who starts cART in ANC and has been ART for >12 weeks. She has a home delivery. Infants does not receive AZT/NVP at birth, but presents >72 hours after birth	Continue cART	Do NAT: if positive, start cART. If negative, start AZT/NVP for 6 weeks and repeat NAT at 6 weeks of age. *If NAT results are delayed, start AZT/NVP immediately
Woman with unknown antenatal HIV status who has a home delivery and has an HIV positive test in postnatal clinic>72 hours after delivery Born to woman with established HIV infection who received less than 12 weeks of ART at the time of delivery; OR Born to woman with established HIV infection with viral load >1000 copies/mL in four weeks before delivery, if viral load measurement available	Start (or switch to) cART	AZT/NVP for 24 week NAT testing
Woman with an HIV negative test in ANC and has an HIV positive test in L&D or during breastfeeding period*		

For scenarios not found in tables above, consult the Advanced Treatment Centres or call the toll-free line **7040,** which is the University Teaching Hospital HIV Expert Hotline.

Simplified infant prophylaxis dosing

Infant age	Dosing of NVP	Dosing of AZT
Birth to <6 weeks		
Birth weight 2000g-2499g*	10mg once daily (1ml of syrup once daily)	10mg twice daily (1ml of syrup twice daily)
Birth weight ≥2500g	15mg once daily (1.5ml of syrup once daily)	15mg twice daily (1.5ml of syrup twice daily)
>6 weeks to 12 weeks		
	20mg once daily (2ml of syrup once daily or half a 50mg tablet once daily)	Use treatment dose 60mg twice daily or a 60mg tablet twice daily

*For infants weighing <2000g and older than 35 weeks of gestational age, the doses are: NVP 2mg/kg per dose once daily and AZT 4mg/kg per dose twice daily. Premature infants younger than 35 weeks of gestation age should be dosed using expert guidance

RENAL ABNORMALITIES

HYPOSPADIAS

- Hypospadias is a common condition that affects 1 in 300 newborn males.
- An increased incidence is documented with low birth weight and growth restricted babies
- Some evidence suggests that placental dysfunction early in gestation increases the risk for hypospadias.
- There is a familial incidence, with 7-10% of first degree relatives affected. The genetics is not well understood

The three key features of hypospadias are:
(Not all three are necessarily present in each case)

- Abnormal ventrally positioned urethral meatus
- Ventral curvature of the penile shaft (chordae)
- Hooded dorsal foreskin

MANAGEMENT

1. No immediate management is required provided:
   - The meatus is not stenosed
   - The infant is passing urine
   - Both testes are palpable

   Scrotal examination is of extreme importance particularly in cases of severe hypospadias.

   NB: Patient with impalpable testes requires emergency assessment by a senior clinician to exclude a possible disorder of sexual development.

2. Parents should be advised not to circumcise the infant as the prepuce is sometimes used in reconstructive surgery
3. Current professional opinion recommend repair between 6 and 12 months of age. Ensure that the infant has a Urology OPD (±3 months) appointment at a major referral centre before discharge.

POSTNATAL MANAGEMENT OF ANTENATALLY DETECTED HYDRONEPHROSIS

DEFINITION

1. This is hydronephrosis that has been detected by an antenatal anomalies scan.
2. Discuss each case with a senior clinician
3. Infant can remain with mother in postnatal ward if well and passing urine
4. Ensure that the infant has passed urine prior to discharge
5. Only transfer to nursery if concerns:
    - Infant not passing urine
    - Posterior urethral valves (PUV) suspected
    - Antenatal history of oligo-/anhydramnios
    - Suspicion of infection
6. In case of PUV [suggested by bilateral hydronephrosis and thickened bladder wall on ultrasound, palpable distended bladder or history of poor urine stream]- pass a urinary catheter to decompress upper renal tract
7. Routine U&E is not required if the patient is well and passing urine
8. Routine prophylactic antibiotics for UTI prevention are not required
9. Prior to discharge discuss follow up plan with senior clinician and arrange referral:
    - Unilateral lesions should be followed up with an ultrasound within the first week.
        ◊ If AP diameter < 20mm can repeat at 6 weeks for a ultrasound and MAG3/DMSA. May need referral for nuclear scan.
        ◊ If AP diameter >20mm, discuss with urologist/nephrologist.
    - Unilateral pelvi-ureteric junction obstruction >15 mm on antenatal scan will require follow up in one week for a postnatal ultrasound
    - All bilateral lesions will be followed up within one week for an ultrasound and MCUG to rule out VUR/PUV
10. Arrange referral [discuss with urologist/nephrologist] and ensure that patient has a copy of the referral letter-(**call the nephrologist/urologist directly if possible**).
11. At discharge discuss danger signs, i.e. irritability, lethargy, poor feeding or vomiting, with parents as detailed in the referral letter.

POSTERIOR URETHRAL VALVES

- Congenital malformation of posterior urethra
- Obstruction to urinary bladder outflow results in hypertrophy of the bladder muscle and may result in reflux into the kidneys with risk of renal dysplasia
- Several modes of presentation including antenatal diagnosis, severe oliguria, pulmonary hypoplasia, poor urine stream, urinary ascites, patent urachus, renal failure, urinary sepsis
- Discuss suspected cases with senior clinician [neonatologist, nephrologist, urologist]
- Catheterize the bladder as soon as possible after stabilizing the patient-some neonates may be difficult to catheterize thus if failed on two attempts discuss with senior clinician and preferably urologist to avoid unnecessary trauma to the urethra.
- UEC, FBC, urine M/C/S, Sepsis screen
- Check for other malformations e.g. VACTER
- Treat urinary infection for 7-10 days depending on condition-choice of antibiotic?
- Remember that these infants are at risk of post-obstruction diuresis and electrolyte imbalances. THEREFORE, monitor neonate's urine output hourly, weigh 6 hourly if possible and daily UEC until patient is stable. Aim to keep electrolytes within normal range. Use ½ normal saline to replace excess fluid loss through polyuria [greater 5ml/kg/hr]
- Patient may have severe renal failure (see renal failure protocol page) and may require renal replacement therapy thus early involvement of nephrology service is important.
- Arrange for postnatal scan within the first week as soon as possible.
- MCUG-will demonstrate valves, reflux, trabeculated bladder
- MAG3/DMSA to determine individual kidney function.
- Consult urology service ASAP to arrange for definitive repair [valve ablation] or if this is not possible then placement of a vescicostomy.
- BEFORE DISCHARGE ensure patient has a referral letter detailing relevant history and ensure has appointment to see urologist and nephrologist for follow-up.

URINARY TRACT INFECTION

- Occurs more commonly in boys than girls in infancy
- May be an important signal of possible structural renal anomalies
- Usually non-specific symptoms like fever, lethargy, poor feeding. Often detected as part of sepsis screen, neonates with known renal anomalies, or passing cloudy malodorous urine
- Obtain urine specimen for urine m/c/s by in /out catheter using size six foleys catheter or feeding tube. If unable to use suprapubic aspiration [discuss with senior clinician]
- Any growth greater than 103 /ml in appropriately collected supra-pubic specimen indicates UTI or 105/ml organisms for in/out catheter specimen or any gram negative bacilli.
- Any child with UTI proven by culture should have a KUB ultrasound done
- For neonates; always parenteral route for treatment. Treat for at least 7 days
- Generally antibiotic prophylaxis not advisable but can be given on discussion with urologist/nephrologist in special cases

ACUTE KIDNEY INJURY

Acute renal failure is a sudden potentially reversible inability of the kidney to maintain normal body chemistry and fluid balance. See the table below for the neonatal AKI KDIGO classification- table 1.
Important to recognize AKI because studies have shown increased mortality even in neonates with only mild renal dysfunction

NEONATAL AKI KDIGO CLASSIFICATION

Stage	Scr	Urine Output
0	No change in Scr or rise < 0.3 mg/dl	0.5 ml/kg/h
1	Scr rise> 0.3 mg/dl within 48h or Scr rise > 1.5-1.9 x reference Scr within 7 days	< 0.5ml/kg/h for 6-12 h
2	Scr rise > 2.0-2.9 x reference Scr	<0.5 ml/kg/h for > 12hr
3	Scr rise> 3x reference Scr or Scr > 2.5mg/dl or receipt of dialysis	< 0.3 ml/kg/h for 24 h or anuria for >12 h

CAUSES

Pre-renal	Intrinsic	Post-renal
• Asphyxia • RDS • Fetal/neonatal hemorrhage • Renal hypoperfusion e.g hypovolaemia, peripheral vasodilation, circulatory failure • Surgical fluid loss • Septic shock • Drugs e.g indomethathacin	• Drugs e.g. Indomethacin, • ATN • HUS • DIC • Renal malformations e.g polycystic kidneys, bilateral renal aplasia • Renal vein artery thrombosis	• Posterior urethral valves • Neurogenic bladder e.g. spina bifida, HIE • Extrinsic kidney compression e.g. sacro-coccegeal tumours

MANAGEMENT OF RENAL FAILURE IN NEONATES

- Stabilize cardio-pulmonary status
- Evaluate neonate for prerenal, intrinsic and postnatal causes
- Detailed clinical history include antenatal(ultrasound), maternal (nephrotoxic drugs), birth history, postnatal events e.g. hypotesive episode, nephrotoxic drugs

- Investigations are guided by likely cause. Serum UEC, calcium, magnesium, phosphate, KUB, ultrasound, platelets, hemoglobin, sepsis screen,urine m/c/s
- Strict in-put/output. Note that upto 60% of neonates with AKI secondary to HIE or drug toxicity may have a normal urine output.
- If prerenal failure is suspected, judicious use of NS boluses at 20ml/kg over 30-60 minutes if patient thought to have hypovolemia after excluding pulmonary odema, optimize systemic blood pressure with vasopressors if necessary
- If post –renal failure ensure patient has bladder catheter inserted, consult urology for upper tract obstructions for possible nephrostomy/ureterostomy
- Remove any suspected nephrotoxic drugs
- Renally adjusted drug doses

On-going care

- Fluids; if fluid depleted correct the deficit. If fluid overloaded restrict fluid intake to 400ml/m2 plus fluid output in preceeding 24hrs (urine output,nasogastric losses, surgical drains e.t.c)
- Hourly urine out-put monitoring-catheterise
- Monitor fluid intake
- Discuss use of furosemide [1mg/kg/hr] infusion in fluid over loaded, anuric babies with senior clinician (risk of ototoxicity and electrolyte imbalance)
- Weigh daily
- Initially 6 hourly UEC, Ca, Mg

Indications for dialysis

- Hyperkalaemia
- Severe fluid overload
- Electrolyte imbalance, acidosis not corrected by conservative management
- Anticipation of prolonged oliguria, so that space can be made for dietary intake
- Urea >30 mmol/L

Note: Ideally peritoneal dialysis, CRRT(Continuous Renal Replacement Therapy) possible but technically more complex than peritoneal dialysis

Recovery phase

- Watch out for diuresis after recovery of renal function. Continue to monitor urine output and weigh 6 hourly.
- May require fluid replacement if polyuric.

OBSTETRIC BRACHIAL PLEXUS INJURIES (OBPI)

GENERAL FEATURES

- Brachial plexus injuries occur in 0.5%-2% of all deliveries
- Brachial plexus injuries include weakness or total paralysis of muscles innervated by the brachial plexus C5-C8 and T1.
- Factors associated with OBPI:
  - ◊ Large birth weight > 3.5 kg
  - ◊ Multiparous mother
  - ◊ Shoulder dystocia
  - ◊ Assisted delivery, forceps or vacuum
  - ◊ Prolonged 2nd stage
- Note if there was shoulder dystocia
- Erb's palsy refer to involvement of C5 and C6 ± C7
- Klumpke's palsy refers to involvement of C6-T1
- Horner's syndrome may be present if T1 is injured
- Most children recover from OBPI, and return of muscle strength at 3 months is a good predictor of full recovery
- Infants with extensive lesions and those who have little elbow flexion at 3 months will need assessment for surgery

CLINICAL FEATURES

Erb's palsy:

- Results in paralysis of the arm and shoulder. The hand muscles remain intact
- The involved extremity is adducted, prone and internally rotated
- There is decreased shoulder abduction, shoulder external rotation elbow flexion, supination, wrist and finger extension producing the "waiters tip" posture
- There is an asymmetrical Moro reflex

Klumpke's palsy:

- Occurs when the nerve roots C6-T1 are injured
- The upper arm and shoulder movements are normal
- The wrist and hand are paralysed

Horner's syndrome:

Presents with a drooping eyelid and a contracted pupil

MANAGEMENT

Conduct a full neurological examination, meticulously documenting all findings
Exclude fractures and check that peripheral pulses are present and record this in the infant's notes
X-rays of chest and entire length of affected arm (CXR needs to include both clavicles and all ribs)
All patients must be referred to the physiotherapist. IF the physiotherapist cannot see the patient before discharge, ensure that an appointment is booked as an outpatient.
All patients should be followed up at 6 weeks post discharge at an orthopaedic clinic, (preferably a specialized hand clinic)
Encourage the parents to continue the exercises as shown by the physiotherapist.

TALIPES EQUINOVARUS

BACKGROUND

- Congenital Talipes Eqninovarus (clubfoot) is a developmental deformity
- Incidence of 1.2 per 1000 live births
- Twice as common in boys and is bilateral in 50% of cases
- Idiopathic but may be associated with other conditions in 20% of cases:
  - ◊ Spina bifida
  - ◊ cerebral palsy
  - ◊ arthrogryposis

DIAGNOSIS

- The foot point downwards at the ankle (equinus)
- The heel is turned in (varus)
- The midfoot is deviated towards the midline (adductus)
- The first metatarsal points downwards (plantar flexion).
- The deformity is not passively correctable by the examiner
- The diagnosis is clinical and radiography

MANAGEMENT

- Infant should be referred to orthopaedic service
- The current preferred treatment for clubfoot is the Ponseti method
- This is a method of manipulation and casting without major surgical releases.

DEVELOPMENTAL DYSPLASIA OF THE HIPS

BACKGROUND

- Incidence of 1-2:1000, more common in females
- Risk factors include:
  - ◊ Breech position
  - ◊ Family history
  - ◊ Infant with neuromuscular problems
- Detection is not always easy. Screening reduces the incidence of "late" presentations by about 50%

CLINICAL DIAGNOSIS

Barlow manoeuvre

- Adduct the hip (bringing the thigh towards the midline) while applying light pressure on the knee, directing the force posteriorly
- If the hip is dislocatable the test is positive

Ortolani maneuver

- Flex the hips and knees to 90 degrees placing anterior pressure on the greater trochanters, gently and smoothly abducting the infant's legs.
- A positive sign is a distinctive 'clunk" which can be heard and felt

MANAGEMENT

- Infants with confirmed dislocation of the hip to be referred to Orthopaedic Surgeon

Imaging

- Ultrasonography after 3 weeks is the preferred screening imaging method for high-risk infants. (Resources permitting)
- Ultrasound performed earlier can lead to a high rate of false positives
- Ultrasound is not necessary for infants with a positive Ortolani or Barlow test (findings will not change the need for orthopaedic consultation)
- Plain radiographs become the preferred imaging modality after 4 months.

MANAGEMENT OF AN INFANT WITH A FRACTURE

SUSPECTED FRACTURE:

1. Admit infant to the observation unit
2. Inform the senior clinician
3. Document a full history including delivery in the baby's note
4. Examine the baby fully to exclude any other injury, check pulses, colour of limb, etc and document fully in the notes
5. Consider the need for analgesia. Oral paracetamol is often all that is required
6. Inform the parents of your findings and explain the need for X-ray investigation
7. Nursing observations:
    - (Regular observations including vascular and pain assessment to be included in the Nursing Care Plan)
    - Observe for colour, perfusion, swelling and movement
    - Document these findings in the notes
    - Hourly for the first 4 hours then 4-hourly for 24 hours.
    - Encourage parents to be awrare and report any changes they observe

8. If X-ray confirms a fracture tell the parents and inform the senior clinician
9. In the absence of trauma, consider other causes of fracture, e.g ELBW, ostegenesis imperfecta or osteopaenia due to decreased intrauterine movement.
10. Liaise with paediatric orthopaedic specialist if available. Most fractures can be managed conservatively in the nursery.
11. An outpatient appointment at the orthopaedic clinic must be booked at the time of discharge.

ACCIDENTAL STAFF INJURY/EXPOSURE TO BLOOD AND BLOOD STAINED BODY FLUIDS

DEFINITIONS:

Accidental exposure includes:

- Needle-stick injuries
- Injury with other sharp objects
- Splashes of blood or body fluids onto mucous membrane of eyes, mouth or nose
- Exposure of non-intact skin to blood or body fluids

Source patient: a patient whose blood or potentially infectious material has come into contact with a staff member by splashing onto the mucous membranes or onto broken skin or by accidental injury

Immediate care area: the area where emergency management of the injured staff member is carried out.

PROCEDURE

Immediately after exposure to **HIV exposed blood:**

1. Clean the site: wash skin wounds with soap and running water. DO NOT SQUEEZE.
2. If the exposed area is an eye or mucous membrane, flush with copious amounts of clean water. DO NOT USE BLEACH or other caustic agents/disinfectants to clean the site.
3. Contact your in-charge or supervisor
4. Consult the clinical officer or the medical officer, who does the following:
    - Determine the need for post exposure prophylaxis (PEP) based on the risk of transmission and risks and benefits of taking or (not taking) cART.
    - Counsel regarding PEP's risks and benefits. Start PEP (table below) preferably within 2 hours of the exposure. If 72 hours have passed since exposure, do not provide PEP because of lack of effectiveness.
5. For high risk exposure arrange immediate HIV testing and counselling. If HIV Testing and Counselling will likely last ≥ hour, give first dose PEP before HIV Testing and Counselling.
6. Do not give PEP to already exposed employees who refuse HIV testing or HIV positive at initial test. Instead, refer to cART clinic for assessment of cART eligibility. **Observe confidentiality.**
7. Send baseline creatinine (FBC if starting AZT)
8. Complete the appropriate government PEP register.

FOLLOW UP

1. HIV testing on the day of the exposure
2. If negative retest at 6weeks, 3 months and 6 months after exposure.
3. Retest for HIV whenever acute illness includes fever, rash, myalgia, fatigue, malaise and lymphadenopathy
4. See clinical officer within 72hours after starting PEP and monitor for side effects for at least 2 weeks.

Post exposure prophylaxis recommendations by risk category

Risk category	Combined antiretroviral therapy (cART)	Duration
No risk: intact skin	Not recommended	
Medium risk: invasive injury, no blood visible on needle	TDF + XTC + ATV-r* AZT + 3TC +LPV-r (children <10 years)	28 days
High risk; large volume of blood/fluid, known HIV-infected patient, large bore needle, deep extensive injury		
Penetrative sexual abuse		

*For intolerance to ATV-r, use LPV-r.
PIs are preferred ARVs for PEP because of concerns for transmitted resistance to NNRTIs; For patients with CrCl <50ml/min, replace TDF with AZT; TDF should not be used in children <10 years.

Exposure to Hepatitis B exposed blood

- After washing the affected area as outlined above (HIV section), blood of the affected staff should be drawn for the purposes of checking for Hepatitis B surface antigen status.
- If Hepatitis B surface antigen test is positive, check for the Hepatitis B core antibodies in order to determine if the infection is active.
- If IgM core antibody is negative, repeat test within 6 months
- If IgG core antibody positive, check titers and start treatment as per prevailing national standard of care (consult infectious disease specialist/Internist)

INADVERTENT EXPOSURE TO ANOTHER MOTHER'S BREAST MILK: POST EXPOSURE PROPHYLAXIS (PEP) AND MANAGEMENT

To prevent this occurrence, all babies should be identified carefully with clear name tags before they are fed.

1. Immediately aspirate the milk via a gastric tube.
2. Immediately report incident to senior clinician and sister in charge.
3. Inform parents as soon as possible after discussion with senior clinician. Counsel parents about small, but possible risk of HIV and Hepatitis B.
4. After informed consent, test both mothers for HIV and Hepatitis. Send 2 x EDTA (purple top) tubes to laboratory requesting hepatitis B surface antigen and HIV ELISA and only if HIV ELISA test is negative to do HIV DNA PCR test.

   NB: *test even if mother reports she is HIV negative and even if she has had a recent negative HIV rapid or ELISA test. If mother is known to be HIV positive, she does not need re-testing.*

5. If a mother is not available for testing or refuses testing, obtain consent for testing the infant from superintendent on call, but do not delay initiation of PEP. Send 2 x EDTA (purple top) microtainers to laboratory requesting HIV ELISA and only if HIV ELISA test is positive to do HIV DNA PCR test.
6. Assure parents that confidentiality will be maintained
7. Do not introduce parents to one another
8. If recipient infant was HIV exposed before the milk exposure, do HIV DNA PCR test on the infant (1 x EDTA (purple top) microtainers). A positive PCR confirms infections prior to inadvertent milk exposure, but a negative test does not exclude prior infection in these infants.
9. Do baseline FBC/differential and ALT on recipient infant.
10. Commence post exposure drug prophylaxis (AZT/NVP) as soon as possible, preferably within 1 hour of exposure.
11. Do not wait for HIV test results to initiate post exposure prophylaxis
12. Document test dates and results clearly in recipient baby's notes and the incident report
13. Determine and document the reason for incorrect milk administration
14. Doctors and nurses who reported or who were involved in the management of the incident must write incident reports. Completed incident reports should be given to the senior clinician and sister in charge of the area. Ensure that folder numbers and contact details of both infants are recorded on this form.

DURATION OF HIV PEP AND FOLLOW-UP

- Complete a 28-day prophylactic course unless:
- The donor mother is PCR negative on current testing, THEN STOP HIV PEP

- The recipient infant's HIV DNA PCR test is positive, in which case the infant's treatment should be reviewed by a Paediatric HIV clinician
- At 2 and 4 weeks post commencement, do FBC/differential and ALT
- Do follow-up PCR at 6 weeks, and if negative, repeat at 14 weeks
- At discharge, a copy of the discharge summary with the follow-up plans and contact details must be given to the senior clinician, so that parents can be kept informed.

SPECIAL CIRCUMSTANCES

In the following situations, discussion with a Paediatric HIV clinician is recommended but must not delay initiation of PEP:

- If the recipient is already receiving nevirapine because of intra-uterine exposure
- If the breast milk was pasteurized before exposure (transmission risk is likely to be minimal)
- If the exposed infant is preterm or <2 weeks of age (inadequate dosing and safety data on Kaletra® and lamivudine)

HEPATITIS B EXPOSURE

If either mother is hepatitis B surface antigen positive, give hepatitis B immunoglobulin (HBIG 200 IU intramuscularly) and the first dose of HBV vaccine within 24-48 hours of exposure. Administer HBIG and vaccine at different sites. Since protection from HBIG decreases dramatically after 48 hours and hepatitis serology results for the mothers may not be available within 24-48 hours of exposure, HBIG and vaccine may be administered prior to result being available. Follow-up as indicated according to hepatitis B exposure guidelines.

CRITICAL INCIDENT REPORTING

The doctor and/or nurse involved in the incident should immediately report the matter to the sister in charge of the neonatal unit, and to the senior clinician of the specific area. If after hours, the on call senior clinician should be notified.

The nursing service manager as well as relevant medical superintendent must be informed on the same day. If the incident occurs after-hours, the matron and/or senior clinician on call should inform the medical superintendent on call at their discretion

The incident must be well documented in the involved patient's clinical notes, stating time of event and any interventions applied as a direct result of the stated incident. Incident report forms must be completed by all involved in the incident, i.e. doctors and nurses, and sister in charge on the same day/shift. Ensure that patient's name and folder number are correctly recorded on the forms.

The required documentation must be completed by the sister in charge of the

neonatal unit. All incident report forms and documentation must be duplicated and copies sent to relevant nursing service managers, the medical superintendent on the same day or the next day if after hours. One copy must be filed in the incidents folder (incident folder will be kept in the department offices).

GENERAL WARD MANAGEMENT

MORTALITY AND CLINICAL AUDITS FOR IMPROVED PATIENT MANAGEMENT

- Use of evidence based management of patients should be the ultimate goal
- Weekly Extraordinary Committee (EXCO) meetings consisting of representation from all sections of the unit to improve communication and smooth running of the unit
- To help copying of stress by mothers; explaining condition, prognosis, assurance, professional counseling and referring to relevant people that can help. Family centered approach should be encouraged. Social workers should be utilised in helping assess the social situation of the mothers as required
- Stressed staff; team work, consulting each other and ombudsmen (senior staff taking a fatherly role), hospital policy

CONSULTATION RULES

- The JRMO/SHO (first on call) should call the registrar (second on call) who should then call the senior registrar for input
- The senior registrar should then call the consultant
- Hotlines/phone numbers for specialists to posted on the ward notice board for ease of consultation (for consideration)
- The Second-on-call will be the direct Liaison person for queries from labour ward. They will be the person responsible to assist with resuscitations, and take over the lead in resuscitation from the First on Call, in the event this is required.

HAND OVER RULES

Morning handover meetings should be done every day. The team post call should hand over patients to the day team including handing over results, social issues and further management.

MEDICO-LEGAL ISSUES

Medico-legal issues in the ward include:

- Parents wanting to take their baby against medical advice
- Parents refusing lifesaving procedures like blood transfusion
- Refusing certain drugs/treatments deemed to be lifesaving and safe by the attending paediatrician
- Decision to withdraw care, not to escalate care or DNR (Do not resuscitate)

Procedure to follow

1. Report the matter to the medical superintendent/ Head Clinical care
2. The medical superintendent then writes to the magistrate for a restraining order on the parents/caregivers wishing to take the baby
3. The consultant is allowed to sign on behalf of the parents
4. The Medical Superintendent can also sign on behalf of the parents
5. In situations regarding withdrawal of care or not to escalate or DNR, the senior clinicians should meet to agree on level of care to be offered. This can be based on resources available and the expected outcome. The consultant should then discuss with the family regarding the options but giving the family autonomy over the matter.

DOCUMENTATION ON THE NEONATAL UNIT

BACKGROUND

Good clinical records are a prerequisite to delivering high-quality, evidence–based healthcare, particularly where a number of different clinicians are contributing simultaneously to patient care. Unless everyone involved in clinical management has access to the information they require, duplication of work, delays and mistakes are inevitable.

Why keep good clinical notes?

- Administrative and managerial decision making within hospitals
- Meeting current legal requirements
- Assisting in clinical audit
- Supporting improvements in clinical effectiveness through research
- Providing the necessary factual base for clinical negligence claims

What makes good clinical notes?

- History – relevant to the condition (get detailed notes from the mother's folder)
- Examination of the patient – all systems and identification of the baby with the tag
- All-important findings, both positive and negative
- Differential diagnosis
- Investigations – details of any investigations arranged
- Referral – details of any referral made
- Information given to the parents concerning risks and benefits of treatments
- Consent – details of consent given to proposed treatments or procedures
- Treatment – details of the main doses of drugs
- Follow-up – arrangements for follow-up tests and future appointments
- Progress – any further consultations, how the baby has progressed

Good clinical notes should have the following attributes:

- Legible and understandable when handwritten
- Legibly signed with the date, time, name and designation
- Objective and factual
- Free from subjective comments about patients or parents

- Contemporaneous – at the time of the incident
- Correction to notes should be dated with name of the person amending it
- To correct an entry run a single line through it so it can still be read
- Abbreviation should be unambiguous and universally recognized

SPECIFIC DOCUMENTATION

- Ensure that you have a well-kept box folder for the patients notes whilst in admission
- On admission, fill in detailed contacts including phone numbers of the parents in the contact records form provided
- On discharge, make a discharge summary on the provided form
- If the patient has died, make a death summary as this helps in the mortality audit
- Complete all the paper work first thing in the morning after the patient dies to avoid parents/relatives waiting the whole morning for the medical certificate of death.

REFERRAL

- Call the hospital you are referring to before you refer the patient to enable them prepare for the patient
- Preferably, contact the doctor on call with the details of the condition
- Complete the referral form with relevant details when referring a patient
- Staff accompanying the baby being referred should have skills in neonatal resuscitation

INSERTION AND WITHDRAWAL OF CENTRAL VENOUS CATHETER (ICC LINES)

INDICATIONS

To provide prolonged access for parenteral nutrition, high strength glucose infusions or inotropes.

EQUIPMENT

- Sterile PICC line pack
- Sterile gown, sterile gloves
- Chlorhexidine in 70% alcohol, and 0.9% NaCl
- Sterile central venous catheter (e.g Premcath®)
- Strapping/Tegaderm (op-site 6 cm x 7cm)
- 2 x 2 ml syringe
- 24 gauge needles/yellow cannula x 2
- 2-port intravenous connector

METHOD OF INSERTION

1. Identify a large vein for the site of insertion
2. Determine the length of the catheter to be inserted by measuring from the site of insertion to the xiphoid for the leg and the sternal angle for the arm.
3. Place the baby in a comfortable position.
4. The procedure is an aseptic one. First wash hands and dry with a sterile towel and put on a sterile gown and gloves.
5. Prime the catheter lumen with 0.9% NaCl and leave the syringe on for flushing. Cover the catheter with a piece of sterile gauze.
6. Clean the identified leg or arm with Chlorhexidine alcohol and let it dry. The whole limb should be cleared, from groin to toes, or armpit to fingertips as well as the whole circumference. To prevent chemical burns of the skin, clean away the antiseptic solution within 0.9% NaCl.
7. Place the sterile towels around the site of insertion and leave the leg or arm accessible for the procedure by placing it through a hole in a sterile towel
8. Change your gloves
9. Identify the vein and insert the cannula into the vein until there is a good flow of blood
10. Use the non-toothed forceps to hold and thread the catheter slowly (1-2 mm at

a time) until the desired length is obtained. Sometimes threading the catheter into the vein can be difficult. Be patient and keep pushing the catheter slowly at 1-2mm at a time until you reach the 5cm mark. Once the 5cm mark is reached, the catheter is making it way into the vein

11. Flush the catheter slowly with 0.9% NaCl to ensure patency
12. Use the gauze swab to put pressure on the catheter at the site of entry and remove the cannula
13. Press until bleeding stops. This may take up to 10-15 minutes
14. Use the Steristrip to tape the catheter to the skin in the same way that you use Stristrip to secure an IV cannula
15. Place a small piece of gauze underneath the hub and use Steristrip to tape the remaining catheter to the skin (if the catheter on the skin's surface is long make loops and use Steristrips to tape on the skin). The insertion site should remain clearly visible and free from loops of catheter so if the catheter has to be withdrawn it can be done without removing all the Steri-strips, etc.
16. It is essential to wait until bleeding has stopped before applying the gauze or further dressing; failure to do this, increases the risk of line infection.
17. Use the Tegaderm to cover the site and the blue hub. Ensure that the entire catheter is enclosed
18. Flush the catheter again to ensure the patency of the line and leave the syringe attached so the PICC line can be kept patent by connecting the syringe to a syringe pump
19. X-ray the baby to determine the position of the tip of the catheter
20. If the catheter has a guide wire in situ, leave the guide wire in situ for the X-ray.
21. Contrast is required for catheters without the guide wire. Use 0.5ml of radiopaque contrast medium
22. Once the tip is in position (superior or inferior vena cava) the line can be used for infusions
23. Document the whole procedure in the baby' notes, record the limb used for insertion, length line inserted to and show that the position has been checked on X-ray, along with the date, time and name of the person undertaking the procedure.

NB: *Migration of the line into the heart may be associated with pericardial effusion, leading to tamponade. Exclude a pericardial tamponade in any infant with a central line who suddenly deteriorates.*

WITHDRAWING THE CATHETER

1. If the catheter has been inserted into the heart it must be withdrawn under aseptic condition
2. Calculate the length to be withdrawn using the position you see on the X-ray

3. Use a new sterile PICC line pack, clean gown, gloves, Steri-strips and Tegaderm
4. Clean the Tegaderm and prepare the limb as before
5. Remove the Tegaderm over the insertion site and only using sterile forceps and scissors and take care not to damage the line
6. Loosen the Steri-strips and pull the catheter back the required distance
7. Re-secure with Steri-strips after you have ensured that the bleeding has stopped, taking care to ensure that the catheter does not become kinked
8. Cover the site with a new piece of Tegaderm
9. Document this procedure fully in the baby's notes.

INSERTION OF UMBILICAL CATHETERS

Umbilical Arterial Catheter UAC	Umbilical Venous Catheter UVC
• For frequent measurement of arterial blood gases • For continuous arterial blood pressure monitoring • For exchange transfusion	• For inotropes and high glucose concentrations • For TPN • For exchange transfusion

INDICATIONS

EQUIPMENT

- Sterile umbilical pack
- Sterile gown, sterile gloves
- Umbilical Venous catheter: size 3.5, 5 or 8Fr
- Umbilical Arterial catheter: size 3.5Fr
- 3-way tap
- Umbilical tape
- Scalpel blade
- Tegaderm/strapping
- Chlorhexidine solution
- 5 ml syringe 10 ml of Saline

1. Determine the length of the catheter to be inserted: See Umbilical Catheter lengths in appendix
2. The baby should be normothermic and stable. If not, consult with a senior clinician before the procedure
3. Inspect the baby's legs and buttock for discolouration
4. Place the baby in the supine position

METHOD OF UAC INSERTION

1. The procedure is an aseptic one. First wash hands and dry with a sterile towel and put on a sterile gown and gloves
2. Attach the 3-way tap to the catheter. Prime the catheter with NaCl using the 5ml syringe
3. Clean the umbilical cord area with 0.05% Chlohexidine solution.
4. Place the sterile towels around the umbilicus, leaving the feet and head exposed. Observe the baby closely during the procedure for vasospasm in the leg or signs of distress
5. Tie an umbilical tape around the base of the umbilical cord, tight enough to minimize blood loss but loosely enough for the catheter to be passed easily through the vessel. Cleanly cut the umbilical cord with scalpel, leaving a stump of 1-2cm
6. Identify the arteries – there are two arteries and one vein; the arteries have relatively thick walls and a small lumen when compared with the vein. They are usually located at 4-7 o'clock
7. Using the curved artery forceps, grasp the end of the umbilicus to hold it upright and steady
8. Using fine forceps and a blunt-ended dilator, greatly open the artery
9. Once the artery is sufficiently dilated, greatly insert the catheter and advance the catheter slowly
10. Gently insert the UAC into the artery to the required length. Blood should flow back freely
11. Obstruction may be encountered at:
    1-2 cm: This is where the vessels turn downwards. Try turning the umbilical stump toward the baby's head.
    4-5cm: This is probably due to spasm and kinking of the artery at the origin of the iliac vessels. Use gentle sustained pressure to overcome this
12. Secure the catheter
13. Insert the baby's legs for any new discoloration. If the leg or toes are blue or white, remove the catheter
14. X-ray the chest and abdomen to confirm the UAC position. If the UAC is in the artery the catheter will dip down first towards the pelvic bone then turn upwards as it enters the iliac artery, finally lying to the left of the spine. A high UAC should lie at the level of the diaphragm (T4-T8 vertebrae on CXR) and a low UAC between L3 and L5. Never leave a UAC at the level of L1, i.e. opposite the origin of the renal arteries.
15. Attach the UAC to an infusion and invasive BP monitoring system
16. Document the whole procedure in the baby's notes, record the limb used for insertion, the length to which the line was inserted and show that the position has been checked on X-ray, along with the date, time and name of the person undertaking the procedure.

METHOD OF UVC INSERTION

1. The procedure is an aseptic one. First wash hands and dry with a sterile towel and put on a sterile gown and gloves
2. Attach the 3-way tap to the catheter. Prime the catheter with 0.9% NaCl using the 5 ml syringe
3. Clean the umbilical cord area with 0.05% chlorhexidine solution. Place the sterile towels around the umbilicus, leaving the feet and head exposed. Observe the baby closely during the procedure for vasospasm in the leg or signs of distress
4. Tie an umbilical ape around the base of the umbilical cord, tight enough to minimize blood loss but loosely enough for the catheter to pass easily through the vessel. Cleanly cut the umbilical cord with the scalpel, leaving a stump of 1-2cm
5. Identify the vein – there are two arteries and one vein. The arteries have relatively thick wall and a small lumen when compared with the vein. The vein is usually located at 12 o'clock
6. Using the curved artery forceps, grasp the end of the umbilicus to hold it upright and steady
7. Using fine forceps, gently open the vein
8. Gently insert the catheter and advance the catheter slowly
9. Gently insert the UVC into the vein to the required length. Blood should flow back freely. If feeling resistance or "bouncing" the catheter is probably coiled in the liver
10. Secure the catheter
11. Inspect the baby's legs for any new discolouration. If the leg or toes are blue or while, remove the catheter.
12. X-ray the chest and abdomen to confirm the UVC position
13. Document the whole procedure in the baby's notes, record the limb used for insertion, the length to which the line was inserted and show that the position has been checked on X-ray, along with the date, time and name of the person undertaking the procedure.

REPOSITIONING THE CATHETER

Never push a catheter in if it is too short; discuss the need to replace it with a senior clinician.

If the catheter is inserted too far it can be safely pulled back providing the following method is used. This procedure is not sterile.

1. Decide the length to be withdrawn and identify this using the markings on the catheter
2. Gradually withdraw until the desired length is reached.

REMOVAL OF UAC OR UVC

INDICATIONS

Urgent removal:

- Persistent discolouration of toes, foot, limb or buttock
- Remember if the baby is shocked and hypovolaemic at birth an umbilical arterial catheter may significantly reduce the flow of blood in an artery. Hypovolaemia should be treated appropriately.

Planned removal:

- UAC and UVC should be removed as soon as the baby no longer requires extensive treatment or monitoring. The incidence of infection in these catheters rises substantially the longer the catheter remains in place.

EQUIPMENT

- 1 dressing pack
- Chlorhexidine solution

PROCEDURE

This procedure should only be carried out by a doctor, an experienced neonatal nurse or be carried out under their guidance or supervision

1. The trolley is prepared as for aseptic technique
2. Place the dressing pack on the top shelf and the remaining items on the bottom shelf
3. Wash hands and dry with ordinary hand towel
4. Open the dressing pack and make sure not to contaminate the contents of the pack
5. Turn the baby supine and get a nurse/doctor to hold the baby's leg still
6. Wash hands again and dry with sterile towel
7. Put on sterile gloves
8. Clean the area around the umbilical catheter with Chlorhexidine solution
9. Drape the area around the umbilical catheter with a sterile towel
10. The UAC and UVC is withdrawn about 1cm every 15-20 seconds
11. Have the sterile gauze available to put pressure on the umbilical stump until it stops bleeding. If the umbilicus continues to bleed seek advice from a senior clinician
12. If bleeding is excessive you will need to stop this quickly. Place your finger

and thumb either side of the umbilicus about 1-1.5cm apart. Squeeze the abdominal wall together between your finger and thumb. This applies direct pressures to the umbilical vessel as they pass through the abdomen to the aorta. This is a very effective way to stop bleeding especially if there is no stump.

13. Ensure the area is dry and clean. Do not apply a dressing
14. After the procedure, leave the baby in a supine position with the umbilicus exposed so that observations can be made in case the umbilical stump oozes blood
15. If no oozing has occurred after one hour the baby can be placed prone.

ELECTIVE INTUBATION OF NEONATES

EQUIPMENT

- Monitor heart rate and oxygen saturation
- Neopuff circuit/bag with suitable sized mask
- Oxygen supply
- Two working laryngoscopes of suitable size
- Suction equipment with suction catheter attached (5Fr, 6Fr or 8Fr)
- Suitable selection of ET tubes
- Introducer (use optional but must be available)
- Resuscitation equipment

DRUGS USED WHERE INFANT WILL REMAIN INTUBATED

- **Atropine IV bolus: 0.01 mg/kg**
  Dilution: add 1 ml of 0.5mg/ml to 4 ml sterile water to give 0.1 mg/ml
  (The dose is 0.1ml/kg of the diluted solution)

  ◊ **Fentanyl IV bolus: 2 µg/kg**
  Dilute for accurate dosing: add 1 ml of 50µg/ml to 9ml 0.9% NaCl =5µg/ml
  (The dose is 0.4 ml/kg of the diluted solution)

- **Suxamethonium IV bolus: 1 mg/kg/dose**
  Provides 5-10 minutes of muscle paralysis
  Dilution: add 0.2ml of 50mg/ml to 4.8 ml 0.9% NaCl to give 2mg/ml
  (Dose is 1 mg/kg = 0.5ml/kg)

DRUGS USED WHERE INFANT WILL IMMEDIATELY BE EXTUBATED TO CPAP (I.E. FOR INSURE SURFACTANT ADMINISTRATION)

- Fentanyl as induction
- Atropine as above
- **Reversal of opiate:** naloxone 0.02 mg/kg (0.05 ml/kg IV before extubation, followed by 0.02 mg/kg/(0.05ml/kg) IM at 15 minutes post extubation, sooner if hypoventilation)

NB: ensure that all equipment and drugs are available and have been checked before commencing intubation sequence!

PATIENT CHECKLIST

- Check for previous reaction or family history of reaction to anaesthetic agents
- Check whether any previous intubation was difficult
- Ensure there is no evidence of micrognathia
- Ensure there is no evidence of stridor
- Ensure there is no upper airway abnormality e.g. cleft
- Ensure potassium level is within normal range before suxamethonium is used
- Ensure liver function is not grossly deranged
- Check patient has been starved for 6 hours.

If any of the above conditions are not met, discuss with senior clinician before intubating.

ETT TUBE SIZE

Tube size (mm) (Internal diameter)	Weight	Gestation age (weeks)
2.5	Below 1000	Below 28
3.0	1000 – 2000	28-34
35	2000 – 3000	34-38
35-4.0	Above 3000	Above 38

ETT DEPTH

Orally intubation: depth = Wt + 6cm
Nasal intubation: depth = Wt + 7cm

Intubation procedure

1. Use a size 2mm ETT for in/out procedure
2. Insert nasogastric tube and aspirate content of stomach
3. Give oxygen by facemask for a few minutes to achieve oxygen saturations of 99%
4. Give atropine followed by fentanyl – note that many babies will become apnoeic after morphine and will therefore require T-piece and mask ventilation
5. Give dose of suxamethonium once fentanyl has produced desired sedative effect
6. Ensure adequate T-piece and mask ventilation
7. Intubate once suxamethonium has caused paralysis. This occurs within a minute
8. Secure tube
9. Confirm correct endotracheal position of the ET tube.

INSERTION AND REMOVAL OF INTERCOSTAL CHEST DRAIN (ICD)

INDICATIONS

Drainage of pneumothoraces or pleural effusions.

EQUIPMENT

- Sterile chest drain pack and sterile gown
- Sterile gloves
- Chlorhexidine solution
- Lignocaine 1% 3mg/kg, 5ml syringe and 25G (Orange) and 23G (blue) needles
- Intercostal drain: <2.5 kg = 8F, 2.5-3.0kg = 10F, 3 – 3.5kg = 12F and > 3.5kg = 14F
- Tegaderm/strapping and Steri-strips
- Scalpel blade
- Underwater collection bottle
- Underwater suction (if needed)

PROCEDURE

1. Ensure adequate sedation and analgesia
2. Use aseptic technique
3. Remove trocar from the intercostal drain
4. Position baby with the arm fully abducted and chest elevated by 45º to horizontal (on the side of insertion) for pneumothoraces, or supine for pleural effusions
5. Clean skin with chlorhexidine

6. Infiltrate insertion site (4th intercostal space mild-axillary line) with 1% lignocaine (3mg/kg) and wait 2 minutes
7. Make a small (0.5-1cm) skin incision parallel to and at the upper border of the rib below (far from the breast bud)
8. Bluntly dissect through the muscle layers to and through the pleura
9. Introduce the drain into the pleural space using the artery forceps and advance 2-3 cm
10. For pneumothoraces, aim anteriorly and apically; for effusions, aim posteriorly and basally
11. Connect the drain to the underwater collection bottle and watch for bubbling/ swinging with respiration
12. Use the Tegaderm/strapping to close the skin incision around the drain
13. Only use a suture if the skin incision is too large to adequately close with Tegaderm/strapping
14. Apply Tegaderm/strapping over the drain site to create an air tight seal
15. Request a CXR to check the position of the drain and assess for improvement of the pneumothorax/effusion

COMPLICATIONS

- Haemorrhage
- Lung parenchymal injury
- Pericardial injury
- Thoracic duct injury
- Phrenic nerve injury
- Scarring

Removal of Intercostal Drain

Remove ICD when bubbling and swinging has stopped for at least 12-24 hrs.

1. If unsure whether ICD should be removed, clamp the drain and observe over the next 6 hours for re-accumulation clinically or request CXR
2. Remove the dressing
3. Withdraw the draw and rapidly pinch the wound closed with the finger (wearing sterile gloves)
4. Use Steri-strips and Tegaderm/strapping to close the incision and create an airtight seal
5. Observe for signs of re-accumulation and request a CXR only if re-accumulation is suspected.

LUMBAR PUNCTURE

INDICATIONS

- Patients with sepsis and suspected CNS infection

CONTRAINDICATIONS

- Platelet count is less than 50 x 10-9/l
- Local infection over lower lumbar spine
- Be especially cautions in infants who have cardiorespiratory compromise

METHOD

6. Employ a strict aseptic technique
7. An assistant is required to hold infant, be careful not to flex the neck
8. With baby in a lateral decubitus position, disinfect the lumbosacral area with chlorhexidine solution only and create a sterile field
9. Site of entry is between the 4th and 5th lumbar spinous processes, at the level of the iliac crests
10. DO NOT attempt above the L3, as the neonatal spinal cord extends till L3
11. A 25G spinal needle or a butterfly may be used to collect CSF
12. Collect 0.5ml to 1ml CSF in 2 sterile tube for chemical pathology and microbiology labs, and 1 sodium fluoride-containing tube for glucose determination
13. Remember to do a blood glucose test at the time of CSF collection.

INSERTION OF A NASOGASTRIC TUBE (NGT)

EQUIPMENT REQUIRED

- An appropriately sized nasogastric tube
  - ◊ 5Fr
  - ◊ 6Fr if on ventilation or NCPAP
  - ◊ 8Fr for free drainage for all surgical babies
- A stethoscope
- 5ml syringe
- Blue litmus paper

PROCEDURE

1. Wash and dry hands after assembling all supplies and put on clean gloves
2. Measure length of tubing to be inserted by extending the tube from sternal notch to the xiphoid process, double this length and add 2cm
3. Insert tube into selected nostril and advance it to the posterior pharyngeal wall, using gentle pressure. Direct the tube along the floor of the nostril and towards the ear on that side (have the baby suck on a pacifier if appropriate). Continue to insert the tube until the mark is at the nostril.
4. Test the position of the tube:
   - by using the blue litmus paper or
   - by introducing 1 ml of air into tube and simultaneously listening over gastric region with a stethoscope. A distant popping and swooshing should be heard
5. Clean baby's check and then apply a small piece of Granuflex® to protect the skin
6. Secure the tube with a piece of Tegaderm/strapping. Once it is established that the tube is in the stomach, the tube is ready to be used for feeding.
7. The tube will need to be changed at least 3 times a week
8. Document the date of insertion on the nursing charts
9. If there is difficulty passing the NGT it could be because the baby has a congenital abnormality of the nose, oesophagus, etc. such as choanal atresia or trachea-oesophageal fistula.

When removing the tube, wait at least 2 hours following the feed, if not, aspirate prior to removal of the tube
Pinch the feeding tube with your thumb and forefinger when removing the tube. This prevents the milk from flowing into the baby's lungs.
always test tube placement prior to feeds

BLADDER CATHETERISATION

INDICATIONS

- Obtain urine for culture
- Quantify urine output in an infant
- Relieve urinary retention

CONTRAINDICATIONS

- Blood at the meatus
- In coagulopathic infants risks and benefits must be considered

TECHNIQUE

Equipment

All equipment must be sterile

- Sterile gloves
- Disposable surgical pack
- Sterile 0.9% NaCl
- Surgical lubricant
- Urinary catheter
  - ◊ 3.5, 5, 6.5 and 8Fr silicone urine catheters are available
  - ◊ 5 Fr infant feeding tubes and 3.5 or 5 Fr umbilical catheters may be used
- Sterile container for specimen collection or collection bag for indwelling catheter
- Adhesive surgical dressing

Precautions

- Use aseptic technique
- Ensure adequate lighting
- 3.5Fr catheter is recommended in infants<1000g and 5 Fr for larger infants
- If catheter does not pass easily, do not use force
- To avoid knotting or curling only insert the catheter as far as necessary to obtain urine
- Remove the catheter as soon as possible to avoid infection
- If the catheter cannot be removed easily, do not use force; consult urologist

Male infants

- Prepare equipment and squeeze small amount of lubricant onto the sterile field
- Position infant supine in the frog-leg position
- Wash hands and wear gloves

- Stabilise the penile shaft with the non-dominant hand
- Retract the foreskin (foreskin cannot be fully retracted) just enough to expose the meatus
- Apply the free pressure at the base of the penis to prevent reflex urination
- Use the free hand for the remainder of the procedure
- Clean the glans with the sterile NaCl. Begin at the meatus and work outward down the penile shaft
- Drape towels over lower abdomen and legs
- Place the wide end of the catheter into the specimen container
- Lubricate the tip of the catheter
- Insert the catheter through the meatus until urine is seen in the catheter
- If the meatus is not visualized insert the catheter through the preputial ring in an inferior direction
- If resistance is found at the external sphincter, hold the catheter in place, applying minimal pressure; spasm will relax after a brief period, allowing easy passage thereafter
- Do not move the catheter in and out, increases the risk of urethral trauma
- Standard insertion depth 6cm in term infants
- Do not insert extra tubing length to stabilize, increase risk of trauma and knotting
- Collect specimen for culture if indicated
- For indwelling catheter, connect catheter to collecting bag and secure to the inner thigh.

Female infants

- Follow first 3 steps of technique for male infant
- Retract the labia minora, use sterile gauze with non-dominant hand
- Avoid separating the labia too widely to prevent the fourchette from tearing
- Use the free hand for the remainder of the procedure
- Clean the area between the labia minora, swab in an anterior to posterior direction
- Drape towels over lower abdomen and legs
- Place the wide end of the catheter into the specimen container
- Lubricate the tip of the catheter
- Visualise the meatus; the most prominent structure is the vaginal introitus. The urethral meatus lies immediately anterior between the clitoris and introitus
- Insert the catheter through the meatus until urine is seen in the catheter
- Standard insertion depth 5cm for term infants

COMPLICATIONS

- Infection
- Trauma
- Catheter malposition
- Knotting

BLOOD CULTURES

- The management of neonates with possible infection is influenced by the result of a blood culture
- In general, a negative blood culture is taken to mean the absence of bacteraemia and antibiotics may then be stopped
- The reliability of blood culture results (both false negatives and false positives) is therefore of critical importance. Volume of blood sample is an important factor for the sensitivity while correct blood collection technique is important for the specificity of the test. Only perform a blood culture if the intention is to start antibiotics.

SAMPLE VOLUME

1 ml blood volume is required for culture inoculation
A good sample volume minimizes false negatives but must be balanced against:

- Pain to the baby from repeated attempts
- Transient bacteraemia from inserting a needle through non-sterile skin
- Anaemia from blood loss
- The need for other blood tests

TECHNIQUE

- Wash hands thoroughly
- Wear sterile gloves
- Prepare dressing pack and clean skin with Chlorhexidine solution and leave to dry

The following techniques are approved (in order of preference)

1. Closed technique using a butterfly and syringe – technically the most difficult in small babies, and does not allow the same vein to be used for inserting a cannula
2. Open cannula "syringe" technique - let the blood fill the hub without spilling onto the skin. Use a sterile needle/cannula and syringe and aspirate the blood repeatedly. The cannula may then be left in place for antibiotics etc.

GENERAL

- Inoculate the culture bottle as soon as you have completed drawing the blood sample. Only remove the sealed culture bottle-cap at the last moment prior to inoculation
- Record that a blood culture has been taken in the bacteriology sheet and the notes and give the indication for the blood culture.

REMOVAL OF NON-FUNCTIONAL EXTRA DIGITS

INDICATIONS

- Prevention of accidental avulsion or torsion around narrow base
- Cosmetic correction at parental request

CONTRAINDICATIONS

- Unwell infant
- Bleeding diathesis
- Base of extra digit >2mm wide
- Bone crossing the isthmus between extra digit & hand

EQUIPMENT

- All sterile
- Chlorhexidine cleaning solution
- Gauze/swabs
- Surgical blade and handle
- Straight mosquito haemostat
- Surgical silk suture, 3.0 or 4.0
- Adhesive bandage
- Local anaesthetic cream

PRECAUTIONS

- Perform procedure on healthy infants only
- Consider surgical review if
  - ◊ base is >2mm
  - ◊ extra digit is on the radial side of hand or is a duplicated thumb
  - ◊ there appears to be a joint at the base or bony structures within the digit

TECHNIQUE

- Discuss the procedure and get signed consent from parents
- Apply local anaesthetic cream to the extra digit including the base. Wait the indicated time before proceeding further
- Clean the digit and surrounding skin with Chlorhexidine and allow to dry
- Clamp haemostat as close as possible to the base of extra digit, to allow for closer amputation without residual bump and faster auto-amputation
- Tie suture tightly around the base of extra digit between the haemostat and hand
- Keep haemostat in place until extra digit turns white (at least 5 minutes)
- Using the edge of the haemostat farthest from the hand as a cutting guide, excise the digit

- Remove the haemostat and observe for haemostasis, leaving the ligature in place. If there is any bleeding, reapply the haemostat and reposition the ligature
- With ligature in place, cover with adhesive bandage until residual stump auto-amputates

COMPLICATIONS

- Haemorrhage
- Infection
- Incomplete ligation leading to traumatic neuroma

DRUG DOSES

Trade names, if used, are illustrative and do not imply endorsement of a particular drug or product.

Acyclovir	
20 mg/kg/dose 8 hly IV over I hour Extended dosage interval to 12 hly if <34 weeks PMA, or in renal /hepatic failure. Treat for: • 21 days if disseminated or CNS disease • 14 days if localized simplex • 7-10 days if chickenpox **Oral suppressive therapy following neonatal HSV disease:** 300 mg/m^2/dose 8 hly PO: begin after completion of IV course above.	*Dilute solution to 5 mg/ml before infusing. (250mg vial + 10ml SW/NS. Then add 2ml of this solution of 8 ml NS. Use diluted solution within 12 hours). Do not refrigerate.* Follow blood count, and renal and hepatic function

Acetylcysteine (N-acetylcysteine)	
Loading dose: 150 mg/kg **PO or IV over 30min** **Thereafter: 70 mg/kg 4 hly PO** **or as IV infusion over 4 hr** Treat for 3 days. Parvolex® is 2g/10ml = 200 mg/ml = 20% solution	Part of anti-oxidant cocktail for neonatal liver failure due to neonatal haemochromatosis. The rest of the cocktail for 2-4 weeks is: • Selenium 3 mg/kg IV over 24 hr • Vit E 25 IU/kg daily • Prostaglandin E1 IV infusion 0.4-06µg/kg/hr • Desferrioxamine 30 mg/kg/24 IV infusion over 8 hr until ferritin <500 µg/l

Adenosine	
200µg/kg/dose fast IV Chase with 2 ml NS stat. Increase dose by 50µg/kg increments every two minutes until sinus rhythm returns **Usual maximum dose = 300 µg/kg** May be repeated several times. (Half – life < 30s).	*Dilute 3 mg to 10ml with NS to make 300µg/ml solution for boluses* *Do not refrigerate.* **SE:** apnoea

Adrenaline (bolus for resuscitation)	
Use **1: 10 000** solution: **IV: 0.1 -0.3 ml/kg/dose** **ETT: 1 ml /kg** (Only if IV access is unavailable) Chase with 1 ml NS	*1ml 1: 1000 + 9ml NS = 10 ml 1:10 000* *(1:10 000 solution = 0.1 mg/ml)* May repeat highest dose x 3

Adrenaline infusion	
Usual dose: 0.05 – 1 µg/kg/min Use central line. 0.6mg/kg in 20 ml DW @ 0.2 ml/hr = 0.1 µg/kg/min	1 ml 1:1000 adrenalin = 1mg adrenalin Protect from light during storage. **SE**: arrhythmias, high BP, hypokalaemia
Adrenaline for nebulization	
0.5 ml 1:1000 (1mg/ml) Made up to 5ml with NS	Nebulise 2 hly prn (monitor heart rate) (FOR STRIDOR)
Albumin 20%	
5ml /kg IV over 3-4 hours (± 1mg/kg furosemide) Primary used to treat hypoproteinaemia associated with protein losing states	Hypoalbuminaemia can cause hypovolaemia with secondary salt and water accumulation. **Indications for the use of albumin are contentious**
Amikacin	
15 mg/kg/dose IV/IM Give as a slow bolus or dilute to sufficient volume (5-10ml) and infuse over 30 min. Dose interval 1st week of life < 32 week CGA: 36 hly ≥ 32 week CGA: 24 hly After 1st week: 24 hly for all gestations Increase dose interval by 12 hours if renal failure or treatment with additional nephrotoxic. Measure trough every 3rd dose in these infants and also in infants who are < 30 weeks PMA and <10 days old. In other infants measure the trough at the 5th dose.	Trough (mg/l): 0.1-2 is ideal, < 8 acceptable (1µg/ml = 1mg/l = 1.71µmol/l) Trough level and suggested dose interval alterations. ≤ 5 Reduce interval to a minimum 24 hly dosing 5.1-8 No change 8.1-10.5 Increase interval by 12 hours (48 hly maximum) ≥10.6 Change to less nephrotoxic agent. Re-check levels in 24 hours.

Aminophylline (IV)	
Loading: 8 mg/kg/ IV over 30 min **Maintenance: 2.5-3.5 mg/kg/dose** 12 hly (dilute to 5mg/ml with NS for IV use. Stable for 4 days when refrigerated) 8mg/kg/IV single dose	**Therapeutic ranges** Apnoea of prematurity: 9-14 mg/l Bronchospasm: 10-20 mg/l (1mg/l = 5.55 µmol/l) For oral dosing see: theophylline
Amiodarone	
IV: Loading: 5 mg/kg Infuse Over 30 min **Maintenance: 7-15µg/kg/min** IV dose preferably via central line **PO: Loading: 15mg/kg** **Maintenance: 5mg/kg/dose 12-24 hly** (Start maintenance 24 hr after loading. Hyperosmolar: only give with feeds)	Dil*ute IV solution to 5mg/ml with D5W (not NS), before infusing.* *Make fresh solution daily.* *Oral solution: Crush 200 mg tab in 20 ml 1% methylcellulose. Add 20 ml simple syrup for a 5mg/ml formulation.* *Stable for 6 weeks at room temperature.* *Protect from light in storage.*
Amlodipine	
0.05-0.3 mg/kg/ PO 24 hly	*Dissolve 5 mg tab* *May cause reflex tachycardia*
Amoxicillin	
Preterm and term: **25-50mg/kg/dose PO** in well infants tolerating full feeds	1st week of life 12 hly >1-3 weeks old 8 hly >3 weeks 6 hly
Amphotericin B	
1st week of treatment: 1 mg/kg 24 hly **Thereafter: 1 mg/kg 48 hly** Infuse IV over 4 hours. (No test dose required for neonates, but watch for anaphylaxis during 1st dose). Withhold dose for 3-5 days if serum creatinine doubles or other signs of toxicity. Usual total Rx duration = 2 weeks after the culture is negative or 4 weeks total. Liposomal amphotericin B: 5mg/kg/day over 1 hour	Infusion is painful – consider analgesia Protect from light during storage. **SE:** anaphylaxis, hypokalaemia, hyponatraemia, convulsions, leucopaenia, anaemia, renal damage. Rapid infusion can cause hyperkalaemia *Each dose should be individually diluted and dispensed by pharmacy.*

Ampicillin

50 mg/kg/dose slow IV push on IM

Meningitis and group B streptococcal sepsis: 100 mg/kg

1st week of life	<2 kg	12 hly
	> 2kg	8 hly
> 1 week	< 2kg	8 hly
	> 2kg	6 hly

Increase dose interval in severe renal failure.

SE: very high doses can cause CNS excitation or seizure activity.

Max. IV concentration = 100 mg/ml (use IV solution within 1 hr of mixing)

Arginine (L-arginine)

250-400 mg/kg (1-2mmol/kg) bolus over **90-120min** Thereafter maintenance **250 mg/kg/d (1.2mmol/kg/d)**	**25-35 mg/kg/6 hly IV/PO in OTC deficiency** IV route is preferable in acute hyperammonaemia. Arginine administration aims at maximizing ammonia excretion through the urea cycle

Atropine

0.01-0.03 mg/kg/dose IV (over 1 min) or IM or ETT (Flush with 1 ml NS) **Oral: 0.02-0.09 mg/kg/dose 4-6 hly**	For sinus bradycardia/Intubation **NOT used in resus of newborn at delivery**. SE of overdose: apnoea, seizures. Ten times higher doses may be needed for digoxin toxicity.

AZT (Zidovudine)

PO:	**≥ 36 wks GA:**	**≥2kg:**	**1.2 ml (12mg) (NOT per kg) 12 hly**
		<2kg:	**4mg/kg/dose 12 hly**
	30-35 wks	**2mg/kg/dose**	**12hly for 2 wks, thereafter 4mg/kg**
	< 30 wks:	**2mg/kg**	**12hly for 4 wks**

IV administration: Infuse over 1 hour

≥35 wks:	**1.5mg/kg/dose**	**6 hly**
<35 wks:	**1.5 mg/kg/dose**	**12 hly**

SE: anaemia, neutropaenia

<table>
<tr><th colspan="2">Azithromycin</th></tr>
<tr><td>PO: 10-20 mg/kg/dose 24 hly
IV: 10mg/kg/dose 24 hly</td><td>Chlamydia: 20 mg/kg/dose IV or PO 24 hly for 3 days</td></tr>
<tr><th colspan="2">Biotin</th></tr>
<tr><td>5-10 mg/day IV or PO
Some patients may require up to 100mg/day</td><td>Indications: holocarboxylase synthetase or biotinidase deficiency. Part of initial empiric regimen for suspected inborn error of metabolism with acidosis and or ketonuria.</td></tr>
<tr><th colspan="2">Bupivicaine 0.5% (5mg/ml)</th></tr>
<tr><td>Infiltrative local anaesthesia or epidural block
Up to 2 mg/kg
(2mg = 0.4ml of 0.5% solution)</td><td>Maximum effect after 30 min.
Last 2-8 hour
Toxicity: apnoea, arrhythmia, seizures.</td></tr>
<tr><th colspan="2">Caffeine base (1 mg caffeine base is contained in caffeine citrate</th></tr>
<tr><td>Doses given are for Caffeine base which is the raw format used in extemporaneous preparations
Loading: 10mg/kg PO
Maintenance: (12-24 hr later):
2.5-5 mg/kg/dose 24 hly</td><td rowspan="2">Most references refer to caffeine citrate. GSH Pharmacy uses Anhydrous Caffeine (Base) + Water for injection + Sodium Benzoate
Caffeine base on its own is not used intravenously
Indications: GA<35 weeks, central apnoea, weaning respiratory support
Therapeutic trough = 10-35µg/ml
Toxicity if > 50mg/l (1mg/l = 5.14 µmol/l)
Some infants may benefit from a repeat loading dose or maintenance dose.</td></tr>
<tr><td>Caffeine Citrate (PO/IV)
Loading: 20 mg/kg/PO
Maintenance (12-24 hr later):
5-10 mg/kg/dose 24 hly</td></tr>
</table>

Calcium Gluconate - e.g. Frescenius 10%®

Symptomatic hypocalcaemia: 1-2ml/kg IV over 10 min (dilute 1:1 with NS)
Monitor for bradycardia: stop infusion if HR<100bpm

Maintenance: 5ml/kg/d in IV fluids or divided into 4-6 doses PO with feeds
If PO: dilute by at least 50% by feeds or water (IV solution may be used orally).

Hyperkalaemia: 0.5 ml/kg IV over 10 min
Incompatible with sodium bicarbonate and phosphate

Note: 1 ml 10% Ca gluconate = ± 100mg Ca gluconate = 9.3mg elemental Ca = 0.23 mmol Ca

Calcium lactate gluconate tablets *(e.g. Sandoz® Calcium Forte)*	
For long-term calcium supplementation. **0.5-2 mmol/kg/day** Each tablet contains 500mg elemental Ca Dissolve tab in 50ml SW = 0.25mmol/ml Then give 2-8ml/kg/day divided into feed	Isolated long-term calcium supplementation is unusual. Phosphate supplementation is usually required and calcium supplementation might not be indicated.

Captopril	
0.01-0.5 mg/kg/dose 8-12 hly PO Increase dose carefully as necessary On advice of cardiologist or nephrologist Maximum 2 mg/kg per day	**SE**: cerebral/renal hypoperfusion Dissolve tablets in water to give 1 mg/ml Solution – stable 24 hours. Or ask pharmacy for specially prepared solution. NOTE: Older children are treated with much higher doses.

Carbamazepine	
Loading Dose: **5-20 mg/kg PO** **Maintenance Dose:** **5-8 mg/kg/dose 8-12 hly PO**	Must be approved by neurologists. Induces cytochrome P450 – dose may need to be increased after 2 weeks. **SE:** Leucopaenia, dystonia, can exacerbate myoclonic seizures, avoid if cardiac/hepatic/ renal disease

Carnitine (L-carnitine)	
25 mg/kg/dose 6 hly PO	Urgent IV treatment of hyperammonaemia: 4mg/kg/hr IV continuous infusion.
Cefepime	
≤ 2 weeks old: 30mg/kg/dose 12 hly **> 2 weeks old: 50 mg/kg/dose 12 hly** **Severe infections or meningitis:** 8 hly	IV infusion over 30 min in IM. *Reconstituted solution stable for 24 hours at room temperature or 7 days refrigerated.*
Cefotaxime	
50 mg/kg/dose slowly IV/IM 1st week of life 12hly > 1-3 weeks old 8hly > 3 weeks 6hly This dose treats meningitis.	Renal failure: increase dose interval unless already 12hly *Reconstituted solutions stable for 24 hours at room temperature or 7 days refrigerated.*

Ceftazidime	
25 mg/kg/dose slowly IV/IM **Meningitis: 50 mg/kg/dose** 1st week of life 24hly > 1-3 weeks old 12hly >3 weeks 8 hly	Renal failure: increase dose interval unless already 12 hly. *Reconstituted solution stable for 24 hours at room temperature or 3 days refrigerated.*

Ceftriaxone	
Sepsis: 50mg/kg/dose 24hly **Gonococcal ophthalmia:** **50 mg/kg/dose x 1** dose if not complicated. (Max dose 125mg) Otherwise daily x 5-7 days. **Meningitis (if Cefotaxime unavailable):** **Loading dose: 100 mg/kg/dose 24 hly** **Maintenance 80 mg/kg/dose 24 hly**	Slowly IV/IM (For IM administration, use 2ml 1% lignocaine to reconstitute 250mg, thus make solution of 125ml/ml) Reconstituted IV solution is stable x 3 days at room T° or 10 days refrigerated. NB: Incompatible with calcium-containing IV infusions.
Cefuroxime	
Slowly IV/IM: 25-50mg/kg/dose 1st week of life 12 hly 1-3 weeks old 8hly >3 weeks 6 hly	**PO: 15 mg/kg 12hly** Renal failure: increase dose interval unless already 12 hly.
Chloroquine base	
Malaria prophylaxis: 5 mg/kg weekly **Treatment: 10 mg/kg IV/PO thereafter 5 mg/kg daily x 3 days starting 6 hours after the loading dose**	Resistance: consider mefloquine. Consult: *http://www.whoint/ith/en/* After chloroquine, eradicate liver organisms with primaquine 0.3 mg/kg PO daily x 2 weeks If G6PD deficiency: 0.5mg/kg weekly x 8 weeks. Toxicity: hypotension, arrhythmias, seizures, sedation.
Chlorpromazine	
1 mg/kg 4-8 hly PO	Neonatal abstinence and sedation of chronically ventilated agitated infants.

Cimetidine	
Treat: 5 mg/kg/dose PO or IV over 15 min 6-12 hly **Prophylaxis: ½ above dose** Ranitidine is a preferable agent.	*Dilution before IV use:* *Add 100 mg (1ml) of IV solution to 9ml NS to make 10mg/ml (stable 48hr).* **SE:** Inhibit cytochrome P450 causing potential drug interactions: relaxation of ductus arteriosus
Ciprofloxacin	
<34 wks CGA **7.5 – 15 mg/kg 12 hly** **≥34 wks CGA** **12.5-25 mg/kg 12 hly** **Transfuse over 30 min if given IV**	**SE**: longer ½ life of theophylline and caffeine. Rash, leucopaenia and elevated LFT can occur in high dosages.
Clavulanic acid/amoxicillin *(e.g. Augmentin®)*	
25 mg/kg/dose PO 8 hly	Based on amoxicillin content.
Clindamycin	
5 mg/kg/dose PO or slow IV 1st 2 weeks 8hly > 2 weeks 6hly	Only for deep tissue infections Do not use for meningitis **SE**: pseudomembranous colitis

Clonazepam	
50-100µg/kg IV slow bolus Then same dose IV 24 hly. Do not use infusion.	Aim for levels: 30-100µg/l (1 µg/l = 3.16 nmol/l) Levels > 125µg/l may cause seizures
Clonidine	
0.5-1.25µg/kg PO 4-6 hly Dissolve 25 µg tab in 5ml sterile water = 5µg/ml. Refrigerate and use within 24 hrs.	Used to potentiate sedation and analgesia. Limited long term safety data in neonates.
Cloxacillin	
25-50 mg/kg/dose IV 100 mg/kg/dose for osteitis or intracranial infection.	1st week of life 12hly >1-4 weeks 8hly >4 weeks 6hly

Colistin	
IV/IM: 40 000 U/kg/dose 12 hly if used in the 1st week of life 8hly if patient older than 1 week. Renal failure: decrease dose by 25-50%	Used for resistant *Acinetobocter.* *(*Requires MCC authorization, maternal consent and progress reports.) 30 000 U = 1 mg Colistin base.

Cotrimoxazole	
PO: 4 mg/kg trimethoprim (0.5ml/kg/dose) **IV: 4mg/kg trimethoprim (0.25ml/kg/dose)** 1st week of life 24hly >1 week 12hly **Treatment for PJP (Rx for 21 days):** <4 weeks: as above (start with IV) >4 weeks: give 6hly **Prophylaxis: PJP/asplenia/SCID:** 2.5ml/dose (or 0.5 ml/kg/dose) PO daily.	Suspension contains 40 mg trimethoprim (tmp) and 200 mg sulphamethoxazole (smx) per 5ml IV formulation: tmp 80 mg/smx 400mg/5ml **NB:** Avoid if hyperbilirubinaemia.
Cyclopentolate	
e.g. Cyclomydril® = cyclopentolate 0.2% + phenylephrine 1% 1 drop at least 10 min before retinoscopy.	Apply pressure to lacrimal sac during and for 2 min after to minimize systemic absorption. Observe closely for 30 minutes post instillation

Dexamethasone (IV/PO)	
Chronic lung disease: **DART trial regimen** **(Total dose 712µg/kg over 10 days)** • **60µg/kg 12 hly for 3 days** • **then 40µg/kg 12hly for 3 days** • **then 20µg/kg 12hly for 2 days** • **then 8 µg/kg 12 hour for 2** days *Only to be used after risk & benefits discussed with parents.*	**Laryngeal oedema:** 0.2 mg/kg 4 hr before extubation then 8 hly x 2 doses has been used in infants older than 4 weeks **SE:** hyperglycaemia, hypertension, GI perf/bleeding, sodium and water retention, hypokalaemia, hypocalcaemia, increased sepsis risk. **At much higher doses and longer course:** increased incidence of cerebral palsy, osteopaenia, growth inhibition, pituitary suppression

Diazepam	
0.3mg/kg IV or 0.5mg/kg PR (single dose)	Not an ideal anticonvulsant in neonates. **SE:** apnoea
Diazoxide (PO/IV)	
2-6 mg/kg/dose 8 hly Use if hyperinsulinism. May add hydrochlorthiazide to enhance efficacy and prevent fluid retention. Wean dosage only if blood glucose remains above 3.5mmol/l	25 mg capsule can be suspended in 2.5 ml water to make 10mg/ml solution. Protect from light. Stable for 48 hr. **SE:** severe hypotension
Digoxin (0.05mg/ml)	
PO/IV: 0.005 mg (0.1ml/kg/dose **<37/40 PCA: 24 hly** **≥37/40 PCA: 12 hly** IV slowly over 10min or PO **Therapeutic level:** 1-2ng/ml (µg/l) = 1.25-2.5 nmol/l **Toxicity:** arrhythmias (AV block), feed intol, diarrhea, lethargy Treat AV block with atropine and correct hypokalaemia. (Use *Digibind*® if severe)	**Loading dose:** Only give loading dose for acute CCF or arrhythmias in discussion with cardiologist. The following loading doses are given over 24 hr as 3 divided doses <29/40: 0.015 mg/kg IV or 0.02 mg/kg PO 30-36/40: 0.02mg/kg IV or 0.025 mg/kg PO > 37/40: 0.03 mg/kg IV or 0.04mg/kg PO

Digoxin immuneFab *(Digibind®)*	
Dose **no. of vials=** $\frac{\text{serum digoxin (ng/ml) x wt (kg)}}{100}$	Infuse over 30 min through a 0.22 micron filter. CI if renal failure.
Dobutamine infusion	
2-20 µg/kg/min Avoid doses>15µg/kg/min **Central line infusion (preferable):** 12mg/kg in 20ml D5W @1ml/hr = 10µg/kg/min	**For peripheral infusions:** 6mg/kg in 50 ml D5W@1ml/hr = 2µg/kg/min OR 9mg/kg in 50 ml D5W@1 ml/hr = 3µg/kg/min **Make fresh solution daily.**

Dopamine infusion	
2-20 µg/kg/min Avoid doses>15µg/kg/min **Central line infusion (preferable):** 12mg/kg in 20ml D5W @1ml/hr = 10µg/kg/min	**For peripheral infusions:** 6mg/kg in 50 ml D5W@1ml/hr = 2µg/kg/min OR 9mg/kg in 50 ml D5W@1 ml/hr = 3µg/kg/min **Make fresh solution daily.**

Enoxaparin *(e.g. Clexane®* - low molecular weight heparin)	
Initial treatment of thrombosis: **Preterm: 1.7 mg/kg/dose SC 12 hly** **Term: 2mg/kg/dose SC 12 hly** Individualise according to serum anti-Xa levels. Adjust in 0.5 mg increments. Target: anti-fXa level 0.5-1U/ml Measure Xa concentrations 4 hrs post dose.	**Low –risk prophylaxis**: 0.75 mg/kg/dose SC 12 hly Target: anti-fXa level 0.1-0.4U/ml Re-adjustments needed twice a month, more often with renal/hepatic dysfunction.
Erythromycin (PO) (Erythromycin Estolate)	
Chlamydia/Pertussis: **12.5mg/kg/dose PO 6 hly x 14 d.** **Other infections: 10 mg/kg/dose 8 hly**	CI with cisapride. **SE**: lower plasma clearance of midazolam and theophylline **Neonatal gut dysmotility:** **6-12.5 mg/kg/dose 6 hly**
Erythromycin lactobionate (IV)	
5-10 mg/kg/dose 6 hly Infuse IV over 1 hr.	**SE:** anaphylaxis, diarrhoea cholestasis, IV irritation.

Esmolol	
SVT: 100 µg/kg/min infusion Increase by 50-100 µg/kg/min per 5 min until control achieved. **Post-op hypertension: 50 µg/kg/min** Increase by 25-50 µg/kg/min per 5 min until target is achieved	Requires cardiologist approval. **Infusion:** 120 mg/kg/in 20ml D5W @ 1ml/hr = 100µg/kg/min **SE:** hypotension, phlebitis.

Fentanyl	
Sedation: 2-5 µg/kg/dose IV 2-4 hly or 1-5µg/kg/hr infusion **Anaesthesia:** **10µg/kg loading dose, then 5µg/kg/hr** **Infusion via syringe driver:** *200 µg/kg in 20ml D5W@ 0.2 ml/hr =2µg/kg/hr*	**If no syringe driver available:** 250µg/kg in 100 ml D5W @ 2 ml/hr = 5µg/kg/hr **SE:** stiff chest or laryngospasm: reversible with naloxone. Beware still chest syndrome with boluses and high doses.
Ferrous lactate	
Routine supplement: **0.2ml PO daily (5mg)** (mixed milk feed) Start from age 4 weeks as soon as full feeds are tolerated. **At discharge, increase dose to 0.6ml PO daily** Indications: Birth weight <1.8 kg. Anaemia at birth. Hb < 12 g/dl	This is an empiric dosing regimen for all weights and gestations: fortified breast milk and preterm formula usually contains 1-2 mg/150 ml thus this practical approach ensures that the highest dose of 6mg/kg/day goes to the smallest infants. This level of supplementation decreases the need for blood transfusions later.
Ferrous sulfate	
Routine supplementation: 0.8ml (5mg) After 4 weeks age as soon as full feeds are tolerated. Increase to 2.5ml at discharge.	Use if Ferrous lactate is unavailable. Ferrous sulfate mixture (BPC) contains 6 mg elemental iron per 1 ml.

Flucloxacillin (PO)	
25 mg/kg/dose 6 hly	
Fluconazole	
Systemic infections: **< 2 wks old** 12 mg/kg loading dose, then 6 mg/kg/day thereafter **>2 wks old** 24 mg/kg loading dose, then 12 mg/day thereafter IV infuse over 30 min or PO. **Thrush:** Give a 6 mg/kg loading dose and then 3 mg/kg once a day by mouth.	**Renal failure:** Increase dose interval to 48 hly after the 1st two doses. IV solution undiluted has been used PO if oral solution not available. **SE:** increases ½ life of midazolam. Monitor renal and liver function.

Flumazenil	
(Benzodiazepine reversal) **IV: 5-10µg/kg over 15 s** Repeat every 45s, until response. (max dose = 50µg/kg) Then 10µg/kg/hr infusion. **Intranasal: 20µg/kg/each nostril** **Rectal: 15-30µg/kg/dose** May repeat after 15 minutes	**Infusion:** 0.2mg/kg in 20 ml D5W @ 1 ml/hr = 10µg/kg/hr **SE:** hypotension, re-sedation Use may unmask seizures suppressed by benzodiazepine

Folic acid	
Supplementation is contentious (preterm anaemia or haemolysis) **0.5 mg weekly OR** **Give ¼ tab PO weekly**	Crush 5mg tablet if no solution (1/4 tab = 1.25mg) Megaloblastic anaemia: 1 mg/day

Fucidic acid (IV=sodium fucidate)	
PO: 15 mg/kg/dose 8 hly (susp.) **IV: 10mg/kg/dose 12 hly** Infuse 1V dose over 6 hr.	Monitor transaminases and reduce dose if raised AST/ALT.

Furosemide	
1-2 mg/kg/dose IV/PO **Preterm: 24 hly** **Full term: 12 hly** NB: ½ life may be up to 67 hr in very preterm neonates.	May increase daily oral dose to 6mg/kg, if smaller doses do not produce diuresis. Beware electrolyte imbalances, hypercalciuria, and ototoxicity.

Ganciclovir	
6 mg/kg 12 hly IV over 1 hr Until oral treatment can start with valganciclovir 16mg/kg 12 hly PO. Continue treatment for 3 months.	Monitor hydration and neutropaenia. If < 500 cells/mm^3 then reduce dose by half.

Gentamicin	
≤ 2 kg BW 5mg/kg/dose IV/IM <1kg <2 weeks old 48hly >2 weeks old 24-48 hly 1-2kg <1 week old 48 hly >1 week old 24-48 hly **> 2kg BW 4mg/kg/dose IV/IM** <1 week old 24 hly > 1week old 12-24hly Increase dose interval by 12 hrs if renal failure or treatment with additional nephrotoxic drugs. Measure trough every 3rd dose in these infants and in infants who are< 30 week PMA or <10 d old. In other infants measure the trough at the 5th dose.	Give as a slow bolus or dilute to sufficient volume (5-10 ml) and infuse over 30min. Trough (mg/l): 0.1-2mg/l (1µg/ml = 1mg/l) Suggested dose interval alternations after 3rd dose levels. <0.8mg/l: If using intervals > 24 hr then check peak level 0.8-2 mg/l: No change 2.1-3.2 mg/l: Increase interval by 12 hr to a max of 48 hr ≥3.3 mg/l: Change to less nephro-/ototoxic drug

Glucagon	
Bolus: 0.2 mg (0.2 U)/kg/dose IV/IM/SC (max dose 1 mg) Infusion: start at 0.1µg/kg/min Titrate to max 0.9 µg/kg/min	**Infusion:** 1.2 mg/kg in 20ml D5W@ 0.1ml/h = 0.1µg/kg/min SE: vomiting, tachycardia, Prepare fresh solution daily

Glyceryl trinitrate OR nitroglycerin	
Low output cardiac failure: **0.6-3 µg/kg/min IV** **Infusion:** 2.4mg/kg in 20ml DW or NS @ 0.3 ml/hr =0.6µg/kg/min	Extravasated dopamine/a-line complications: 1cm/kg 2% glyceryl trinitrate ointment

Glycopyrrolate	
0.01-0.05 mg/kg/dose PO 8-12 hly	To decrease secretions, or as premed or as reversal of neuromuscular blockade. Anticolinergic.

Heparin	
Arterial lines: Add 1 000 U heparin to 1litre 0.45% saline then infuse at 0.5-1 ml/hr Full anticoagulation: (indications are not well established). Load with 50U/kg IV over 10 min then infuse at 25 U/kg/hr. **Infusion:** 1 250 U/kg in 50 ml saline @ 1 ml/hr = 25 U/kg/hr	Measure APTT after 4 hours. Adjust infusion rate to obtain an APTT of 1.8-2 times normal. CI to full anticoagulation: Intra-cranial/gastric haemorrhage, thrombocytopaenia < 50 x 10^9/l and IM injections are contra-indicated. Antidote: see protamine sulfate.
Hepatitis B immunoglobulin	
200 IU (2ml) IM Within 24 hr of birth Indicated for babies of high risk HBsAg+ mothers (HBeAg + or anti-HBe neg, or HBe status unknown)	Give at the same time as Hep B vac (opposite thigh) See hepatitis B protocol

Hepatitis B vaccine
10µg in 0.5 ml IM within 24 hr of birth to all infants of mothers who develop Hep B during pregnancy or are HBsAg+. Infants born to high risk mothers also need HBIg within 24 hr of birth (see above). Thereafter continue with national schedule. This offers 95% protection. Breastfeeding is safe. See hepatitis B protocol and Vaccination protocol
Hyaduronidase
For acute severe extravasation tissue injury: clean the site. Infiltrate with 0.3 ml/kg preservative free lignocaine. Make 3 small pricks into the skin surrounding the lesion, then inject 500-1000 U hyaluronidase into the subcutaneous area of the damaged tissue and irrigate with 25-100 ml 0.9% saline. Cover with paraffin gauze dressing.

Hydralazine	
IV: 0.15-0.6mg/kg 4 hly **PO: 0.25 -1.0 mg/kg 6-8 hly** **Max: 7.5mg/kg/day**	Drug interaction with diazoxide: severe hypotension Tachycardia and fluid retention are common SE. (Consider addition propranolol)

Hydrochlorothiazide	
1-3 mg/kg/dose PO 6-12 hly (Ask pharmacy to make 2.5 mg/ml solution)	Monitor electrolytes and glucose. May add spironolactone or KCl supplements **Do not confuse with Chlorothiazide**
Hydrocotisone (IV/PO)	
Hypotension: **2mg/kg IV single dose** Thereafter, 1 mg/kg IV 8 hly **Stress/hypoglycaemia:** **0.5-1 mg/kg/dose 6 hly** (or 7-13 mg/m^2/dose 8hly)	**Endocrinologist supervision:** **Congenital adrenal hyperplasia:** 5-7 mg/m ^{2}/dose B hly plus fludrocortisones 200 µg PO daily as starting dose **Physiological replacement:** 0.2 mg/kg/dose 8 hly (3mg/m ^{2}/dose 8 hly). Might increase 10-fold during illness. **Addisonian crisis**: 10mg IV stat, then 100mg/m ^{2}/day continuous IV infusion until stable, then physiological doses
Ibuprofen	
PDA closure: **1st dose 10mg/kg** **2nd and 3rd doses 5mg/kg** 24hly dosing PO/IV.	Same relative contraindications as indomethacin See PDA protocol
Imipenem	
20 mg/kg/dose IV 1st week of life 12hly 1-4 wks 8hly 2-4 wks 6hly Infuse over 30 min.	Not recommended for CNS infections. May cause seizures if meningitis or preexisting CNS pathology present. (Lower threshold for neurotoxic encephalopathy). **Renal failure:** decrease frequency.

Immunoglobulin (intravenous) (e.g. *Polygam*®)	
Iso immune haemolysis: **0.5g/kg IV over 2 hr** (Indicated if bilirubin levels continue to rise towards exchange transfusion threshold despite phototherapy).Dose may be repeated. Always discuss with senior clinician Results from recent studies show less effectiveness than originally shown.	**Neonatal allo/autoimmune** Thrombocytopaenia If platelet court < 30 x 109/l; treat with 1g/kg/day IVIG for 2 consecutive days. **See protocol on neonatal jaundice** Monitor HR and RR while administering.

Indomethacin

PDA closure:

Age	Dose (mg/kg)		
	1st	2nd	3rd
6-24hr	0.1	0.1	0.1
<48hr	0.2	0.1	0.1
2-7dats	0.2	0.2	0.2
>7 days	0.2	0.25	0.25

3 doses 24 hly IV over 30min

IVH/PDA prevention:
For GA< 28 wks, 0.1 mg/kg IV 24hly x 3.
1st dose at age 6-12 hr.

Relative CI:

Urea> 14mmol/l
Creat > 140µmol/l
Plt <60 x 10^9/l
Urine output <0.6 ml/kg/hr
Abnormal bleeding, NEC.

Note: There is no evidence that IVH is a contraindication. There is good evidence that 0.1mg/kg doses do not result in extension of IVH

See PDA protocol

Insulin infusion

Usual dose: 0.02-0.5 U/kg/hr

Note: it may be necessary to increase dose to 1U/kg/hr but use with extreme caution.

Infusion:
1st add 1 ml (100 U) actrapid to 10ml NS
Then of this solution add 1 ml/kg (=10 U/kg) to 0.9% saline, to make a final volume of 50ml
THEN 0.1 ml/hr =0.02 U/kg/hr

Monitor blood glucose ½ - 1 hly until stable and monitor potassium.

NB. Because insulin adheres to plastic, the lines must be flushed with at least 20 ml of the final solution and then allowed to stand or at least 20 min to saturate binding sites in plastic tubing.

Start dose at:
Blood sugar>25mmol/l 1ml/hr
Blood sugar 20-25: 0.5ml/hr
Blood sugar 18-19: 0.4ml/hr
Blood sugar 15-17: 0.3ml/hr
Blood sugar 12-16: 0.2ml/hr
Blood sugar 8-11: 0.1ml/hr
Blood sugar <8: STOP

If no response to starting dose then increase rate by 0.3ml/hr sequentially until glucose starts to fall.

If doses above 2 ml/hr are persistently required then increase infusion concentration to 50U/kg in 50ml
So 0.1 ml/hr = 0.1U/kg/hr

Hyperkalaemia (last resort Rx):
0.05-0.5 U/kg/hr
May need up to 0.6 U/kg/hr + IV glucose (may need 15% at 120 ml/kg).

Isoniazid (INH)

INH 10 mg/kg/dose 24 hly PO x 6 months
See TB exposure guidelines

INH toxicity:
Treat seizures with pyridoxine 1 mg IV/PO for every mg of excess INH.

Isoprenaline (isoproteranol)	
0.02-02µg/km/min Use lowest possible dose.	**Infusion:** 0.3mg/kg in50 ml NS @0.2 ml/hr = 0.02µg/kg/min

Ketamine	
Anaesthesia: **(premed 10µg/kg Atropine**) **IV: 0.5-2 mg/kg/dose over 1 min** (onset in 30 s, lasts 10min) May repeat once OR infuse at 5-10µg/kg/min. **IM: 4mg/kg (lasts 15min)** **PO: 10 mg/kg/dose** (onset 15-30 min, duration variable)	**Infusion:** 12 mg/kg in 20 ml DW @0.5ml/hr = 5µg/kg/min Not well studied in neonates. Discuss with senior clinician. **SE:** laryngospasm (can avoid by premed with atropine).
Labetalol *(Trandote®)*	
Use in consultation with nephrologists to determine target range. **Start at 0.5mg/kg/hr and double dose every 3 hr until in systolic range.** Maximum dose is 3 mg/kg/hr (3ml/hr)	**Infusion:** *50mg/kg in 50 ml DW or NS* *@0.5 ml/hr = 0.5 mg/kg/hr* *Solution is stable. Does not need to be prepared fresh daily.* **SE:** bradycardia, hypotension, hypoglycaemia (use glucagon). Use with caution if cardiac failure.
Lamivudine (3TC)	
1st 28 d of life: 2 mg/kg/dose 12hly **> 28 d old: 4mg/kg/dose PO 12hly**	Refer to institutional guidelines for indications and duration of Rx.

Lamotrigine	
0.3 mg/kg daily x 2 weeks, then bd x 2 weeks. Titrate to maximal daily dose 4mg/kg.	Very limited data in neonates. Only use in discussion with neurologist. Concomitant use of liver enzyme inducing drugs increase the elimination of lamotragine. **SE**: rash, avoid in renal/liver failure.

Lignocaine (Lidocaine)

1% IV solution = 10 mg/ml
2% IV solution = 20 mg/ml

CHECK if the vial states that it is preservative-free and adrenaline-free and is appropriate for IV use

Infiltrative local anaesthesia:

Use undiluted lignocaine – 3mg/kg provides 1 to 2 hours anaesthesia.

SE/toxicity: arrhythmia (mostly bradycardia and severe hypotension. If these side effects occur, stop infusion immediately and treat symptomatically.

DO NOT USE LIGNOCAINE IF PHENYTOIN HAS BEEN USED.

Safe dosage not yet established for preterm infants.

Seizures in term infants: (third line agent)
Infusion Preparation:
100 mg/kg made up to 50ml in DW or NS @ 1ml/hr = 2mg/hr

A. loading Dose: 2 mg/kg over 10 min

1ml of prepared infusion = 2 mg/kg. Dilute with 10ml NS – infuse at 60ml/hr over 10min

B. Continuous infusion: *it is critical to write clear instructions on the times that the infusion rate must change*

Normothermic	**Weight (Kg)**	**1st 4 hours**	**Next 12 hours**	**Next 12 hours**
	2-2.5	6mg/kg/h	3 mg/kg/h	1.5 mg/kg/h
	>2.5	7 mg/kg/h	3.5mg/kg/h	1.75 mg/kg/h
Hypothermic	Weight (Kg)	1st 3.5 hours	Next 12 hours	Next 12 hours
	2-2.5	6mg/kg/h	3 mg/kg/h	1.5 mg/kg/h
	>2.5	7 mg/kg/h	3.5mg/kg/h	1.75 mg/kg/h

Linezolid

10mg/kg/dose IV over 30 min
<1kg: PNA < 14 days 12hly
1-2kg: PNA < 7 days 12 hly
All other neonates 8 hly

For Methicillin – resistant Staphylococcus and vancomycin –resistant Enterococcus.

SE: morrow suppression if >10 d.

Lopinavir/ritonavir suspension (80/20mg/ml) (Kaletra)	
Dose according to lopinavir component: **300 mg/m² rounded up to nearest 0.1ml PO 12 hly**	Consult with infectious Diseases Unit. ECG, U&E, LFT, osmolality testing and monitoring recommended in neonates.

Lorazepam	
0.05-0.1 mg/kg slow IV/IM/PO **Do not exceed 0.1 mg/kg 24 hly due to long half-life** (18-73 hours in neonates)	**IV use:** *dilute to 0.1 mg/ml* **IM use (emergency):** dilute to 1mg/ml. Use sugar-free suspension for oral use.

Magnesium sulfate (50% solution = 1g/2ml = 2mmol/ml)	
Hypomagnesaemia or hypcalcaemia: **0.1ml/kg IM/IV 12 hly x 2-3 doses** PPHN: 250 mg/kg in 5ml NS IV over 10 min Then infusion of 20-75mg/kg/hr. **Infusion** *1g/kg in 20 ml NS or DW @ 0.4 ml/hr =20mg/kg/hr*	**USE IN PPHN CONTROVERSIAL** Discuss with senior clinician. Only use after commencing inotropes and volume loading. Monitor HR. Stop infusion if bradycardia. Suggested therapeutic serum levels = 3.5-5.5 mmol/l. (Monitor 24hly)

Mefloquine	
Prevention: 5 mg/kg weekly Start 2 weeks before entering endemic area, continue until 4 weeks after leaving **Treatment: 15mg/kg PO then 10mg/kg 12 hrs later.**	Indicated for chloroquine resistant malaria. **SE**: nausea, vomiting, diarrhea, headache, abdominal pain, lethargy

Meropenem			
20 mg/kg IV (slow bolus)			Infuse over 30 min Use 12 hly dose interval if renal failure. Omit dose if anuria. Reconstituted vials may be kept at 4°C x 24 hr.
< 1kg	< 14 days	12hly	
	> 14 days	8 hly	
> 1kg	1st week of life	12 hly	
	>1 week	8 hly	
Meningitis, NEC or pseudomonas Infections: 40 mg/kg IV 8 hly			

Methadone	
(For neonatal abstinence) **Start: 0.1 mg/kg/dose 6 hly (IV/PO)** Increase by 0.05 mg/kg/dose until control of withdrawal. **Rx for seizures (caused by withdrawal):** 0.25mg/kg – monitor for apnoea.	After 24 hours of satisfactory control, the total daily dose is divided 12 hly and given at midday and midnight. The dose should then be reduced by 10-20% each day until 0.05 mg/dose is achieved. Observe for 48 hr following discontinuation of therapy.

Methylene blue	
IV: 1 mg/kg over 1 hr Can repeat dose after 1-3 hr. **Oral: up to 2mg/kg/dose 24 hly** (Vit C 500 mg 24 hly is also effective).	*1% solution contains 1 mg/ml.* *Dilute to 0.1 mg/ml with D5W before infusing.*

Metoclopramide	
Infant: 0.03 -0.1 mg/kg/dose IV/PO 8 hly Increases gastric emptying but does not improve GOR **Mother: 10-15 mg PO 8 hly** Increases breast milk production	Taper over 5-10days **SE:** (overdose): high HR, agitation, diarrhoea, methaemoglobinaemia, dystonic posturing.

Metronidazole

Loading: 15 mg/kg IV/PO slowly, thereafter:

< 1kg :	≤14 days:	7.5mg/kg/dose	48 hly
	15 to 28 days:	15 mg/kg/dose	24 hly
1 to 2 kg:	≤7 days:	7.5mg/kg/dose	24 to 48 hly
	8 to 28 days:	15 mg/kg/dose	24 hly
> 2kg:	≤7 days:	15mg/kg/dose	24 hly
	8 to 28 days	15mg/kg/dose	12 hly

Miconazole	
Oral thrush and additional treatment for candida dermatitis: 1 ml Daktarin® oral gel **in mouth 6 hly after feeds.** Continue treatment until 2 days after thrush clears.	**Candida dermatitis:** Tropical cream 12 hly x 10 days

Midazolam	
Sedation IV Bolus: **mg/kg.** *Dilute in 5ml NS, infuse over 5min.* **IV infusion: 0.02-0.05 mg/kg/hr** *Use lowest effective dose* **Buccal: 0.2 mg/kg/dose (IV solution)** **Oral: 0.25 mg/kg/dose (oral susp)** **Prepare Infusion:** *5mg/kg in 50 ml D5W @ 1 ml /hr* *=0.1mg/kg/hr*	**Anticonvulsant** **Buccal: 0.5mg/kg (IV solution) OR** **IV Bolus: 0.05 mg/kg dilute in 5ml NS and give over 10 min.** **Then start IV infusion: 0.15mg/kg/hr.** **If seizures persist, increase dose very 10min by 0.05mg/kg/hr.** **Maximum infusion rate: 0.5mg/kg/hr** Wean when seizures free for 6 hours by 0.05mg/kg/hr hly until 0.15 mg/kg/hr. Then wean by 0.05mg/kg/hr every 6 hours. Doses higher than 0.25mg/kg/hr may affect aEEG. Half-life: T½ = 6-22 hrs. Tolerance may occur.

Morphine	
Sedation/analgesia on IPPV: **Load 0.1-0.15mg/kg IV over 1 hour** Then 10-20µg/kg IV infusion (Up to 40µg/kg/hr may be required if tolerance develops). **Severe pain on IPPV/Pre-procedure:** Additional 20 µg/kg bolus 4 hly prn. **Short-term pain relief (no (IPPV):** **0.08 -0.1 mg/kg IV/IM/PO 4-6 hly bolus**	**Infusion:** *0.4mg/kg in 20ml D5W* *(or 1mg/kg in 50ml D5W @ 0.5 ml/hr* *=10µg/kg/hr* OR If no syringe pump: 1 mg/kg in 100 ml D5W @ 1ml/hr =10µg/kg/hr **SE:** apnoea, hypotension
Morphine for NEONATAL ABSTINENCE: Oral (MST Morphine) – dose 3 hly Start at 0.05mg/kg/dose –increase/decrease by 10% according to Modified Finnegan score. Maximum dose 0.15 mg/kg/dose. Discontinue once score is ≤ 8 and morphine dose is 0.01 mg/kg/24 hr. Then observe for 48 hr	**Oral solution** (for use oral formulation from pharmacy): **To make 1 mg/ml concentration, add 1 ml of 10mg/ml IV solution to 9 ml preservative-free NS. Protect from light.** **Refrigerate.** **Stable for 7 d.**

Mupirocin

Topical application to skin (or nares of MRSA carriers) 8 hly x 10 d

Naloxone

mg/kg IV/IM (standard preparation = 0.4 mg/ml)

Note: Not recommended as part of initial resuscitative efforts in the delivery room or neonates with respiratory depression; support ventilation to improve oxygenation and heart rate IV route preferable. Onset of action within 2 min.

ETT route not recommended.

Duration of action after IV route is short, so follow with IM dose. IM onset of action within 15 min duration of action up to 24 hr.

Reversal of respiratory depression following therapeutic opioid administration: 0.02 mg/kg (0.05ml) IV followed by 0.02 mg/kg (0.05ml) IM.

IV doses may be repeated as needed to maintain opiate reversal.
Naloxone is CI in maternal narcotic addiction.

Neostigmine

Diagnostic dose for myasthenia gravis:
IM 0.1 mg/kg (30 min pre feed) or 1 mg/kg PO (2 hr pre feed)

IM Rx gives response duration of 2-4 hr after 20-30 min latent period.

SE: salivation, respiratory arrest – reverse with Atropine 0.015 mg/kg IV.

Short-term Rx: titrate dose
IM/SC: 0.1- 0.3 mg/kg 4 - 8 hly or PO: 1 - 2 mg/kg 3 hly

Long –term Rx: 1-2 mg/kg PO 3 hly: Pyridostigmine 1 mg/kg PO 4 hly
Reversal of Pancuronium: 0.04 - 0.08 mg/kg IV plus Atropine 0.02 mg/kg.

Nevirapine

SIMPLIFIED INFANT PROPHYLAXIS DOSING

Infant age	Dosing of NVP	Dosing of AZT
Birth to 6 weeks		
Birth weight 2000-2499g*	10mg once daily (1ml of syrup once daily)	10mg twice daily (1ml of syrup twice daily)
Birth weight ≥2500g	15mg once daily (1.5ml of syrup once daily)	15mg twice daily (1.5ml of syrup twice daily)
> 6 weeks to 12 weeks		
	20mg once daily (2ml of syrup once daily or half a 50mg tablet once daily)	No dose established for prophylaxis; use treatment dose 60mg twice daily i.e. 6ml of syrup twice daily or a 60mg tablet twice daily

*For infants weighing <2000 g and older than 35 weeks of gestational age, the suggested doses are: NVP 2 mg/kg per dose once daily and AZT 4 mg/kg per dose twice daily.

Premature infants younger than 35 weeks of gestational age should be dosed using expert guidance

Nitric oxide

Starting dose: 20 ppm. Assess response after 30min: Successful = 3kPa rise in post ductal PaO_2 and post ductal PaO_2 > 8kPa **Wean iNO if:** Unsuccessful = non-responders or Successful and FiO_2 < 0.6	See PPHN section and nitric oxide for indications and management strategy. CI: thrombocytopaenia < 50 x 10^9; coagulopathy: INR > 2, PTT > 72 s.

Nitroprusside	
Start at 0.25 to 0.5 µg/kg/min, increase till desired effect. Usual maintenance: 0.2-0.5 µg/kg/min Titrate to effect. Doses above ≥1.8 µg/kg/min associated with cyanide toxicity Maximum dose: 8µg/kg/min (for < 10min) *Prepare IV solution: 50 mg in 250 ml D5W =0.2 mg/ml (protect from light).* *(Add 500 mg of sodium thiosulphate to above solution to prepare a 1:10 ratio to prevent cyanide accumulation from the start. Mixture stable for 7 days).* **Infusion***: 1.2 mg/kg in 20ml D5W @ 0.5 ml/r =0.5 µg/kg/min*	Monitor: HR, BP, RBC cyanide (should be < 200 ng/ml), acidosis, serum thiocyanate (should be < 50µg/ml), renal and hepatic function **SE:** severe hypotension, tachycardia and cyanide toxicity Signs of cyanide toxicity: Arrhythmia, acidosis/met Hb above 4% Antidote for cyanide toxicity: 0.3ml/kg of 3% sodium nitrate, then 0.8 ml/kg of 50% IV sodium thiosulphate.
Nystatin	
Prophylaxis: 1 ml (100 000 U) PO 8 hly **Rx:** 1 ml PO 6 hly (2 ml in term babies) -continue until asymptomatic for 3 days	**Topical (cream):** 6 hly until asymptomatic for 3 days.
Octreotide	
Hyperinsulinaemic hypoglycaemia: 1µg/kg/dose SC 6 hly- titrate upwards to max dose to 10µg/kg/dose OR 0.01-1.7 µg/kg/hr as IV/SC infusion	**Chylothorax:** **IV/SC infusion at 1µg/kg/hr** – titrate up to max 10µg/kg/hr. (Median response dose 3 µg/kg/hr) **Infusion:** 0.1mg/kg in 50ml D5W @ 0.5ml/hr =1µg/kg/hr.
Omeprazole	
0.5-1.5 mg/kg/dose PO daily *To prepare 2 mg/ml oral liquid: dissolve contents of 2 x 20mg capsules in 20ml 8.4% sodium bicarbonate. Mix well.*	*Stable x 30 d refrigerated. Protect from light. Dilute each dose of the above solution with equal volume of water immediately before administration.*

Palivizumab

15 mg/kg IM (anterolateral thigh) monthly for 3-5 months, from start of RSV season 48 to 72 hours prior to discharge; or during an outbreak in hospital.
SE: mild URTI, anaphylaxis rare.

Pancreatin

Titrate lipase 2000 to 5000 units per milk feed (formula or breast milk)	Dose according to amount of fat in stool. Liaise with Gastro-enterology

Pancuronium

IV Bolus:0.1 mg/kg/dose 1-4 hly (Half dose may be adequate after the 1st dose). OR IV infusion: 0.02 -0.04 mg/kg/hour	**Antidote:** neostigmine 50µg/kg and atropine 20µg/kg.

Paracetamol

Oral: Loading dose: 24mg/kg **Maintenance: 12 mg/kg/dose** **Rectal: Loading dose: 30 mg/kg** **Maintenance: 20 mg/kg/dose**	Gestation — Dosage interval Term infants: — 6hly Preterm: ≥ 32 weeks — 8 hly < 32 weeks — 12hly

Paracetamol IV

Loading dose 20 mg/kg infused over 15 min for all gestations. Maintenance infused over 15 min according to CGA.	CGA (weeks) — Dose — Interval ≥37 — 15mg/kg — 6hly 31-36 — 12.5mg/kg — 6hly <30 — 10mg/kg — 6hly

Penicillin (benzyl penicillin) 50 000U = 30mg	
50 000 – 100 000 U/kg/dose slow IV Preterm: 1st week of life 12 hly >1 to 3 weeks old 8hly Term: 8hly The high dose is adequate for group B strep (GBS) bacteraemia and most GBS meningitis. However, if GBS meningitis is confirmed or strongly suspected use the even higher doses below. **Confirmed GBS meningitis:** week old: 100 000 U/kg/dose 8hly > 1 week: 125 000 U/kg/dose 6 hly Also give gentamicin until CSF is sterile or for the 1st week of treatment.	A lower dose of 50 000 U/kg can be used for certain infections, including congenital syphilis and osteitis. Duration of treatment: Pneumonia: 5-7 days Septicaemia: 10-14 days Meningitis: 2-3 weeks Osteitis: 4 weeks Syphilis: 10 days **Congenital syphilis:** see protocol **Osteitis:** 4 weeks – consider oral penicillin V 25 mg/kg 6 hly to complete the course. **Severe renal failure:** ½ dose, and 12 hly. **SE:** bone marrow suppression and hepatitis are rare.
Penicillin – benzathine	
50 000 U/kg/dose IM x 1 dose	For asymptomatic infants born to mothers with syphilis who are untreated, partially treated or treated in the last month of pregnancy: see protocol
Penicillin –procaine (IMI ONLY)	
50 000 U/kg/dose IM 24 hly x 10d **NOT IV (IV use causes anaphylaxis)**	For symptomatic congenital syphilis (notifiable): see protocol

Phenobarbitone	
Loading dose: 20mg/kg IV over 10min If seizures persist, repeat this dose. **Maintenance: 4 mg/kg/day PO/IV/PR** Increase to 5 mg/kg/day if needed for > 2 weeks Phenobarbitone coma using very high dose phenobarbitone (VHDPB) may be effective when all other anticonvulsants fail. Further 10-20 mg/kg dose are given until seizure control or 100mg/kg is accumulated, or levels of 100µg/ml or 450µmol/l are attained. Long term effects of these doses are unknown. (Only use in discussion with senior clinician).	If IV preparation is not available: Use crushed dissolved tablets (in water). Give single dose 40 mg/kg and also give stat dose of midazolam 0.15 mg/kg IV or 0.3 mg/kg buccal. Or load with Phenytoin. Therapeutic level = 20-40 µg/ml (90-180 µmol/l) **SE**: sedation, respiratory depression. **Hyperbilirubinaemia/cholestasis:** 5 mg/kg IM/PO daily.
Phenytoin	
Loading dose: 20 mg/kg IV over 30 min **Maintenance:** (rarely used) 1st week life: 4-8 mg/kg 24 hly >1 week 2-8 mg/kg/dose 8hly	Do not give IM. *Do not mix with dextrose.* *Flush with saline before and after.* Use cardiac monitor. **Therapeutic level**: 6-18µg/ml (30-70µmol/l)
Phosphate	
Treat PO4 < 1.5 mmol/l **0.50 mmol/kg PO 8-12 hly** Titrate to phosphate levels (aim for 1.8-2.5mmol/l)	*1ml Joules solution (NaHPO4)* = 1 mmol 1mmol = 30mg elemental Phosphate.

Piperacillin OR Piperacillin –Tazobactam

100 mg/kg/dose IV over 30 min or IM

Birth weight	Age	Dose Interval
< 1kg	≤ 2 week	12hly
	> 2 week	8 hly
≥ 1 kg:	≤ 1 week	12 hly
	> 1 week	8 hly

Monitoring levels in critically ill patients:

- Peak: 150µg/ml
- Trough: 15-50µg/ml

Potassium chloride ORAL

Treatment for hypokalaemia:
1-3 mmol/kg/day

Divide daily dose into all feeds

Potassium Chloride IV

Increase conc in IV fluids to max of 4 mmol/100ml (for hypokalaemia) by adding 15% KCl (2 mmol/ml)

Do not infuse faster than 0.2 mmol/kg/hr

NNL/ Dextrose 10% = 3 mmol/100 ml K
15% KCl = 2 mmol/ml

Add 1 ml 15% to 200ml NNL/Dextrose 10% bag = 4mmol/100ml

Propofol

2.5mg/kg IV over 10 s should induce anaesthesia within 30 s.
Add a further 1-2 mg/kg if anaesthesia inadequate. Anaesthesia lasts about 10min.

Propranolol

Hypertension/arrhythmia:
PO: 0.25 mg/kg/dose 6 hly, increase to max 3.5mg/kg/ dose 6 hly.

IV: 0.01 mg/kg over 10 min increase to cumulative max of 0.15mg 6 hly.

Neonatal thyrotoxicosis:
PO: 0.25-0.75 mg/kg 8 hly
(+Lugol's iodine: 1 drop 8 hly and propylthiouracil 5 mg/kg 12 hly + sedation)

Proliferating infantile haemangioma
Initial 0.5-1 mg/kg/day 2-3 divided doses

Titrate gradually to maintenance dose: 3 mg/kg/day in 2-3 divided doses.

Prostaglandin E2 (PO)	
Give ¼ tab *crushed in 2ml water* **per nasogastric tube 1-2 hly (or 50µg/kg/dose 1-2 hly)**	1 tablet = 500µg May give ½ tab hly if > 2.5kg.
Prostaglandin E1 (IV) (alprostadil)	
Initial dose: (titrate) **0.05-0.1 µg/kg/min** **Maintenance:** **0.01 - 0.1µg/kg/min**	**Infusion:** 0.12mg/kg in 20 ml DW @ 0.5ml/hr =0.05µg/kg/min **SE:** apnoea, bradycardia, hypotension, seizures, diarrhoea.
Protamine sulfate	
Time since last Heparin dose: / **Protamine dose per 100 U heparin received** **<30 min:** **1mg IV** **30-60min:** **0.5-0.75 mg IV** **60-120 min:** **0.375-0.5 mg IV** **> 120 min:** **0.25-0.375 mg IV**	Give as slow IV push over 5 min or IM. **SE**: bleeding thrombocytopaenia, hypotension, bradycardia, dyspnoea.

Pyridoxine	
Diagnosis of pyridoxine dependent seizures: **50-100 mg per day IV/IM (not/kg)**	**Maintenance:** 50-100mg PO 24 hly.
Pyrazinamide (PZA)	
30 mg/kg/dose 24 hly	(See TB exposure guidelines**)**
Pyrimethamine	
Congenital Toxoplasmosis **Oral load: 2 mg/kg daily for 2 days** Then 1 mg/kg daily for 6 months. 6-12 months: Mon/Wed/Fri only **Empirically add throughout duration:** Sulphadiazine 50 mg/kg PO 12 hly Leucovorin 15 mg PO twice weekly	**CNS disease:** add prednisolone 2 mg/kg/day **Ocular disease**: consider clindamycin SE: thrombocytopaenia, leucopaenia and megaloblastic anaemia.

Quinine	
Malaria: treatment **IV: Loading dose of 20 mg/kg over 4 hours** Followed by 10mg/kg 12 hly infused over 2-4 hours. **PO: 10 mg/kg/dose 8 hly x 7 days**	**Infusion:** *50 mg/kg in 50 ml D5W: 1 ml/hr = 1 mg/kg/hr* Give ¼ tab Fansidar® once on final day of treatment.

Ranitidine	
PO: 2 mg/kg/dose 8 hly **IV: (**slowly to avoid arrhythmia) **Term: 1-1.5 mg/kg/dose 8 hly** **Preterm: 0.5mg/kg/dose 12 hly** **Renal failure: 12 hly dose interval**	*Crush 150mg tab in 60 ml sterile water=2.5mg/ml.* *Stable for 28 days refrigerated.* *Alternatively, use diluted IV solution PO.* IV dilution: 10mg in 10ml NS = 1 mg/ml solution Stable for 7 days refrigerated.

Remifentanil	
Pain relief/intubation: **1-2 µg/kg bolus IV slowly over 30 s** **Continuous infusion:** *1.2 mg/kg in 20 ml D5W @ 0.5 ml/hr =0.5µg/kg/min* Start with 0.5µg/kg/min Range: 0.1 - 1µg/kg/min.	Pain relief occurs within 1 minute of administration and lasts for 5-10. **SE:** apnoea, muscle rigidity if high doses given. Antidote for stiff chest = naloxone 0.1 mg/kg IV or suxamethonium

Rifampicin	
Tuberculosis: **PO: 10-20 mg/kg/dose daily** **(**see TB treatment guidelines) **IV: 5-10 mg/kg/dose 24 hly –over 3 min**	**Meningococcal contact:** 5 mg/kg/dose PO 12 hly for 2 days. **HIB contact:** 10mg/kg/dose 24 hly x 4 days **Pruritus from cholestasis:** Give 5-10 mg/kg 12 hly

Salbutamol	
NEB: 1-2.5 mg in 4 ml saline 6-8 hly (may repeat dose) **PO: 0.1 mg/kg/dose 6-8hly** **To treat hyperkalaemia:** 4µg/kg IV over 5-10 min Decreases K^+ by1.5 mmol/l for 2 hr. **Alternatively:** 0.4 mg/kg/dose neb 2 hly.	IV solution preparation: Add 0.5 mg salbutamol to 50 ml NS. Draw up 0.4ml/kg (4µg/kg) of this solution and make up to 10ml with NS. Infuse this 10 ml over 10min.

Sildenafil	
Dose range: 0.5-2 mg/kg/dose hly Strategy: start at 0.5 mg/kg/6 hly. Maximum dose: 2 mg/kg/dose 4 hly Double dose if no response in 30 min. Success = O2 sats rise by 10% or PaO2 increases by 3kPa. Wean dose by 25% when FiO2 < 0.6. Continue to wean 12 to 24 hly. **CI:** same as iNO **SE:** hypotension (decrease dose and only use with inotropic agents).	**PPHN:** Same indications as for Nitric Oxide (iNO). Consider use where iNO is not easily available or where response to iNO is poor. See PPHN protocol Oral solution: make 5mg/ml, 1:1 mixture of 1% methylcellulose and simple syrup. Protect from light. Stable 3 months refrigerated. Hyperosmolar: *dilute with 4 parts water before administration.* Limited but accumulating neonatal data.

Sodium benzoate and sodium phenylbutyrate	
Acute hyperammonaemia: **IV Loading dose: 250 mg/kg of each drug, given over 90 minutes**, followed by a continuing maintenance infusion of each drug at 10mg/kg per hour. Co-infusion is safe. **Long-term management:** **PO: 250 mg/kg/day sodium benzoate in 3-4 divided doses.** **Sodium phenylbutyrate 600 mg/kg/day in 3-4 divided doses.** If ammonia > 200µmol/l start with treatment and refer for dialysis if it continues to increase.	SE: nausea and vomiting. Overdose can cause metabolic acidosis and fatal encephalopathy. Sodium overload (500 mg of sodium benzoate = 3.5 mmol sodium; 500 mg of sodium phenylbutyrate =2.7 mmol of sodium) Consider haemodialysis if ammonia levels are very high.

Sodium bicarbonate	
For metabolic acidosis **Symptomatic hyperkalaemia:** **Refer to protocol on fluids and electrolytes**	Requires good IV access. Watch for extravasation.

Sodium chloride	
Correct if: serum Na < 120 mmol/l Correct over 15-24 hours Supplementation (Selected infants) Preterm < 30 weeks 2 mmol/100 ml formula 3-4 mmol/100 ml breast milk	Calculating Na deficit: (140-Na value) x (kg) x 0.6 = mmol Na 0.9% NaCl contains: 1 l = 154 mmol Na 10 ml = 1.5 mmol Na
Sodium polystyrene sulphonate (kexalate®)	
500-1000 mg/kg PR Repeatable 12 hly (Premix in pharmacy with methyl cellulose or 25% sorbitol or mix in ward with 6 ml/kg water.	Do not use PO in neonate. Do not use in acute hyperkalaemia Ensure evacuation by rectal or colonic irrigation with 5ml NS after 12 hr. SE: hypocalcaemia, hypernatraemia.
Sodium valproate	
20 mg/kg load PO, then 10 mg/kg/dose 12 hly Very limited data in neonates.	Monitor LFTs and ammonia level. Suspend/decrease treatment if ammonia level > 250 µmol/l. Trough: 40-100 mg/l
Spironolactone	
1-2 mg/kg/dose daily PO **(**If liver disease with ascites, increase dose up to 3.5 mg/kg 12 hly) Usually combined with hydrochlorthiazide or furosemide	Simple syrup suspension: *Crush 8 x 25 mg tabs into 50 ml simple syrup = 4 mg/ml.* **Stable 1 month refrigerated.** Hyperosmolar: *Dilute with 4 parts water before administration.*

Steroid potencies (equivalent activity in mg)			
Steroid	Glucocort	Mineralocort	Biological T ½ (hours)
Dexamethasone	0.75	0	36-54
Betamethasone	0.75	0	36-54
Methylprednisone	4	0.5	12-36
Prednisone	5	0.8	12-36
Hydrocortisone	20	1	8-12
Cortisone	25	0.8	8-12
Fludrocortisone	0	20	18-36

Streptokinase	
Arterial thrombi: **3000 U/kg IV slowly, then 1000 U/kg/hr infusion:** 0.4 ml (20 000 U)/ kg in 20 ml D5W@ 1 ml/hr =1 000 U/kg/hr **Monitoring:** Aim for fibrinogen of 1-1.4g/l Stop if < 1 g/l	**Blocked catheters:** *10 000 U diluted in 2 ml NS.* Fill catheter dead space. Aspirate after 1 hr. Flush with heparinised saline. Antidote: tranexamic acid 10 mg/kg over 10min, repeat if necessary after 8-12 hours.
Sucralfate	
10-20 mg/kg PO 6 hly Avoid prolonged usage.	NB: Beware bezoar formation. *Ulsanic*® suspension: 200 mg/ml
Sucrose	
0.5-2ml of 25% sucrose on tongue, 2 minutes before painful procedure.	

Surfactant (*See surfactant guidelines)*	
Beractant (e.g. Survanta®) **100 mg/kg (4 ml/kg) as a bolus via ETT** Warm to room temp in the hand before administration.	Manufacturers recommend up to four doses, 6 hr apart, in the 1st 48 hr of life.
Bovine lipid extract surfactant (e.g. *Liposurf)* **135 mg/kg (5ml/kg) as an intratracheal bolus via ETT** Warm to room temp in the hand before administration	Repeat same dose as needed up to a maximum of four doses within the first five days of life
Poractant alfa (*Curosurf*®) **100 mg/kg (1.25 ml/kg) as a single bolus, intra-tracheal.** Warm to room temp in the hand before administration.	Repeatable at 12 hly intervals to a total of three doses if necessary. Some references suggest an initial dose of 200mg/kg, then 100 mg/kg thereafter.

Suxamethonium	
Intubation: 1-2 mg/kg will provide 5-10 of muscle relaxation. See intubation guidelines	Use the lower dose if extubation is expected imminently and always give after opiate because fasciculation is painful.

Teicoplanin	
Load: 16 mg/kg **Maintenance: 8 mg/kg IV/IM** 24 hly x 7d **Endocarditis prophylaxis:** 6 mg/kg teicoplainin + 2 mg/kg gentamicin IV/IM 30-60 min before procedure.	**Severe renal failure:** Double dosage interval. Trough level: 10-15 mg/l.

Theophylline (PO)	
Load: 6 mg/kg **Maintenance: 1 mg/kg/dose 6 hly OR** **2.5 mg/kg/dose 12 hly**	Therapeutic range for apnoea of prematurity 9-14 ml/l

Thiopental sodium	
Anaesthesia: 5mg/kg IV gives 5-10 min deep sleep within 45 s (double dose gives double anaesthesia but causes hypotension) **Infusion for seizures:** 5-10mg/kg IV load then 2.5 mg/kg/hr	Check infusate for haziness. Beware tissue accumulation. Extravasation can cause tissue necrosis.

Thyroxine (levothyroxine)	
10-15µg/kg/dose daily PO Monitor fT4 and TSH after 2 and 4 weeks.	Discuss with endocrinologists.

Tobramycin	
5 mg/kg IV/IM if < 4 weeks old **6 mg/kg IV/IM if > 4 weeks old** (max 8 mg/kg at a year). A slow 30 min infusion is not necessary when this drug is given IV. Dilute to concentrate of 5mg/ml with NS for IV use. Dose interval: 1st week of life: <32 week CGA: 36 hly ≥32 week CGA: 24 hly After 1st week: 24 hly for all gestations Increase dose interval by 12 hly if renal failure or treatment with additional nephrotoxic drugs	Measure trough every 3rd dose in these infants and in infants who are < 30 week PMA or < 10 old. Trough (mg/l): 0.5-2mg/l Peak 1 hr post dose: 8-12mg/l (1µg/ml = 1mg/l = 2.14µmol/l). Suggested dose interval alterations after 3rd dose trough. <0.8 mg/l: If using intervals > 24 hr then check peak level. 0.8-2mg/l: No change. 2.1-3.2 mg/l: increase interval by 12 hr to a max of 48 hr. ≥3.3 mg/l: Change to less nephrotoxic or ototoxic drug if possible.

Urokinase	
Blocked catheter: 5 000 U in 2 ml NS Leave in catheter x 2 hr, then aspirate. Flush with NS thereafter.	Antidote: tranexamic acid 10 mg/kg over 10 min.
Ursodeoxycholic acid	
15-30 mg/kg/day PO 24 hly or in 2 divided doses (1/4 or 100 mg tab = 25mg).	Reduces the bilirubin level and decreases pruritus where cholestasis is due to biliary atresia, cystic fibrosis, Allagille syndrome or prolonged parenteral nutrition.
Valgancyclovir	
16 mg/kg 12 hly PO	Monitor hydration and neutropaenia
Valoron	
0.5-1 mg/kg PO 6 hly 8-12 hly if preterm or liver failure. Limited neonatal data.	Dilute 0.1ml (10mg) up to 1m with D5W, to make 10mg/ml. Then dose is 0.1ml/kg of the diluted mixture.

Vancomycin	
15mg/kg/dose for all gestations infused over 1 hour. ***(****Dilute small doses to 5ml and infuse at 5ml/hr).* PMA (weeks) Interval (hours) ≤29 24 30-36 12 37-44 8 >44 6 *Reconstituted vial (10ml SW in 500 mg vial= 50mg/ml) Stable 4 d refrigerated.* *Further dilution to 5mg/ml made by adding10ml of above solution to 90ml NS minibag.*	Levels: Peak (30 min after end infusion) =30-40µg/ml Trough =5-15µg/ml (1µg/ml = 1mg/l = 0,67 µmol/l) Trough of 15-20µg/ml is acceptable, and possibly desirable when treating meningitis. Routine measurement of levels is contentious but trough measurement is only required if efficacy is questioned. **SE:** nephrotoxicity and ototoxicity-risk with aminoglycosides, rash, hypotension, neutropaenia, phlebitis.

Varicella zoster immune globulin (VZIG)	
1ml IM for all gestational ages, within 3 days of exposure (Some benefit up to 5 d after exposure).	(Vazigam® IM contains At least 200 U (320 mg)/2 ml). See protocol in Varicella zoster section for indications

Vecuronium	
Load: 0.1 mg/kg IV slowly **Maintenance:** 0.05 mg/kg/dose 1-2 hly as needed	(Reverse with atropine/neostigmine)
Vigabatrin	
25 mg/kg PO 12 hly May increase to 75 mg/kg PO 12 hly after 3 d.	**Renal failure**: increase dose interval to 24 hr

Vidaylin® drop/Multivitamin	
≥**1.2 kg: 0.3 ml PO bd** This exceeds the minimum requirements for vitamins A, B, C and D. But vitamin E and iron are absent. < 1.2kg: 0.3ml PO daily (on fortified EBM or preterm formula) Indications: give to all preterm and term infants as soon as full enteral feeding has been established ad continue until mixed feeding is well established. Iron supplements need to be given separately or alternatively use vidaylin/ Multivitamin with iron.	0.6ml = Vit A 5000 U Vit D 400U Vit B1 1.5mg Vit B2 1.2mg Vit B6 0.5mg Nicotinamide 10mg Vit C 50mg Discharge on 0.6ml PO daily.

Viday® plus iron	
≥1.2 kg: 0.5 ml PO bd. This exceeds the minimum requirements for vitamins A, B, C, D and E and iron. <1.2 kg: 0.5ml PO daily (on fortified EBM or preterm formula)	1ml = Vit A 1500 U Vit D 400U Vit B1 0.5mg Vit B2 0.6mg Vit B6 0.5mg Nicotinamide 8mg Vit C 34mg Vit E 5U Iron 10mg Discharge infants on 1ml PO daily
Vitamin D	
Vitamin D2 (Ergocalciferol) **Recommendations for routine minimum requirement vary:** **150-400U/kg/day** This is usually provided in routine vidaylin/ multivitamin or equivalent supplementation. *Additional vitamin d supplements are required if malabsorption or chronic renal failure:* **Malabsorbtion:** 1000 U/day PO or 30 000 U IM monthly. **Renal disease:** Use a-Calcidol.	(**Calciferol®** oily solution: 5 000 IU/ml) 1ml = 28 drops drops = 360 IU OR ml = 500IU a- Calcidol (1 alpha –hydroxyvitamin D3) 0.05-0.1 µg/kg daily Larger doses in Vit D resistant rickets.

Vitamin E (1U= 1mg)

Deficiency: 25 UPO 24 hly
Malabsorption:
50 U PO 24 hly (or 10U IM twice/month)

Abetalipoproteinaemia: 75 U PO 24 hly

High doses of vitamin E inhibit iron absorption if given simultaneously.

Vitamin K

Prophylaxis at birth: 1 mg IM
(Preterm < 1000 g: 0.3 mg IM)

Raised INR: Give 1-2 mg/kg IV

Cholestasis: 1 mg PO 24 hly

FORMULAE AND CALCULATIONS

Aa ratio mmHg	$\frac{PaO_2 \text{ (mmHg)}}{(713 \times FiO_2) - (PaCO_2 \text{ (mmHg)} \times 1.25)}$ **NB: FiO_2 is as a decimal**
Aa ratio kPa	$\frac{PaO_2 \text{ (kPa)} \times 7.5}{(713 \times FiO_2) - (PaCO_2 \text{ (kPa)} \times 9.4)}$ **NB: FiO_2 is as a decimal**
Anion gap	= Na – (bicarb + Cl) Normal is 5-15 in neonates
Base deficit Correction	**Total** bicarbonate deficit (mmol)= BE x Wt (kg) x 0.4 *(use BE x wt x 0.3 in babies older than 1 month)* Usually give **HALF** of this, using 4% Sodabic (IV over 30 min), then check blood gas after 30-60min **(NB**: 4% Sodabic = 0.5 mmol/ml and 8% Sodabic = 1mmol/ml)
Blood volume	**Term:** 80 ml/kg **Preterm:** 90ml/kg
DEXTROSE INFUSION RATE: mg/kg/min	**(10% DW = 10 g/100 ml) mg/kg/min= (ml/kg/24 hr) x (%DW) x 0.007** *e.g if baby on 100ml/kg/24 hr of 10%DW; mg/kg/min = 100 x 10 x 0.007 = 7mg/kg/min*

ENDOTRACHEAL TUBE SIZES (Protex®)	**Wt**	**ID (mm)**	**OD(mm)**
Some brands e.g Vygon®have an	<1kg	2.5	3.7
Outer diameter (OD) which is 1mm	1-2kg	3	4.4
Wider than the same sized	2-3kg	3-3.5	4.4 - 4.8
Portex® tube	>3kg	3.5-4	4.8 – 5.5

ENDOTRACHEAL TUBE LENGTH to mid trachea:

Parameter	**Orotracheal length**	**Nosatracheal length**
Weight (kg=cm)	Wt + 6cm	Wt + 7 cm
Sternal notch to tip xiphisternum	Length + 1 cm	Length + 2 cm
Base of nasal septum to tip ear tragus	Lengh + 1 cm	Length + 2 cm

Exchange transfusion	Double volume exchange = 160 ml/kg (term) or 180 ml/kg (preterm) **UVC method (push/pull**) Aliquots 5ml/kg, max 20ml. Each cycle over 2 min. **Peripheral method (*preferable*)** Infuse warmed blood into peripheral IV at 150ml/kg/hr (5ml/kg/2min) and remove arterial aliquots of 5ml/kg as equivalent volume is infused every 2 mins.

FeNa (%)	$= 100\% \times \frac{U_{Na}\ (mmol/l) \times P_{cr}\ (mmol/l)}{P_{Na}\ (mmol/l) \times U_{cr}\ (mmol/l)}$ **(NB: 1st convert P_{cr} from µmol/l to mmol/l by dividing by 1 000)**
GFR ml/ min/1.73m²	**Preterm =** $\frac{33 \times \text{length (cm)}}{\text{Serum creatinine (µmol/l)}}$ **Term =** $\frac{45 \times \text{length (cm)}}{\text{Serum creatinine (µmol/l)}}$ **(Normal: Preterm:** 14±3 **Term: < 1 wk:** 21±4 **1-2 wk:** 50±10**)**
GFR ml/kg/min (the preferred estimation in neonates)	**All gestations:** < 1 wk = 72/serum creatinine (µmol/l) > 1 wk = 66/serum creatinine (µmol/l) **Normal range (post conceptional age in weeks)** **27-29:** 0.2-1.2 **30-32:** 0.3-1.3 **33-35:** 0.5-1.5 **36-38:** 0.6-1.6 **39-41:**0.7-1.7
Mean airway pressure	$= \frac{(PIP \times Ti) + (PEEP \times Te)}{(Ti + Te)}$ **or** $\frac{(PIP\text{-}PEEP) \times Ti + PEEP}{(Ti + Te)}$
Osmolality serum	=2Na + glucose + Urea (mmol/l) *(Normal = 275-295mOsm/kg)*
Oxygenation index	$OI = \frac{MAP \times FiO_2(\%)}{\text{Post ductal } PaO_2\ (mmHg)}$ *> 25=50% mortality > 40=80% mortality.*
Partial exchange	**Volume of exchange** = (blood vol) x $\frac{\text{Observed Hct – Desired Hct}}{\text{Observed Hct}}$ (*Desired Hct usually = 55)*
Renal failure indices in the *oliguric* neonate	**Indices** / **Prerenal** / **Intrinsic renal failure** U_{Na}(mmol/l) / 10-50(term-preterm) / 30-90 U/P creat / 29.2 ±1.6 / 9.7±3.6 U/P urea / >10 / <10 U/P osmolality / >2 / <1 FeNa / <1.5% (<5% preterm) / 2-6%
Sodium deficit	mmol Na needed = (135-[Plasma Na] 0.6 x Wt(kg) ml saline needed = Wt x 4 x (135-[Na]% saline)
Sodium excretion	*Esitmated (mmol/kg/day)* =90 urine Na/urine creatinine (mmol/l)
Sodium correction	In hyperglycaemia, true serum sodium is = Na + 0.3 x (glucose -5.5)

Tubular reabsorption of phosphate (TRP)

TRP = 1 - {urine PO4 (mmol/l) x plasma creatinine (mmol/l)} x 100%
{urine creatinine (mmol/l) x plasma PO4 (mmol/l}

(1st convert plasma creatinine from µmol/l to mmol/l by dividing by 1000)

Normal = > 80%

Urine volume

Estimated urine vol (ml/kg/day) = 90/urine creatinine (mmol/l)

Umbilical catheter lengths

UVC (aiming for tip between diaphragm and LA, T8-T10.)
=2/3 *suprasternal notch-umblicus (SNU) length*

UAC low (L3/L4) *= 2/3 SNU length minus 0.5cm*

UAC high (T8-T10) is preferable *= Total SNU length + 1.5cm*

SNU length (cm)	UVC T8-T10)	UAC low (L3/L4)	UAC (HIGH)
9	6	5.5	10.5
10	6.5	6	11.5
11	7	6.5	12.5
12	8.0	7.5	13.5
13	8.5	8	14.5
14	9.5	9	15.5
15	10	9.5	16.5
16	11	10.5	17.5
17	11.5	11	18.5
18	12	11.5	19.5

Ventilation index

$$VI = \frac{PaCO_2 \text{ (mmHg)} \times RR \times PIP}{1000}$$

Body surface area (m^2)

$$BSA = \frac{(\text{weight in kg} \times 4) + 7}{\text{Weight in kg} + 90} \quad \textbf{or} \quad BSA = (0.05 \times kg) + 0.05$$

NUTRITIONAL REQUIREMENTS OF LOW BIRTH WEIGHT INFANTS

NUTRIENTS	Enteral recommend-ations per 100 kCal	Per 150ml EBM	7.5g FM 85	150 ml EBM + 7.5g FM85	Nan 150ml	Pelargon 150ml	Alfare 150 ml
Fat (g)	4.1-6.5	5.3	0.3	5.6	5.12	5.09	5.37
Protein equivalent (g)	2.5-3.8	2.4	1.5	3.9	2.25	2.24	3.69
Whey (g)		1.68	1.5	3.18	1.35	1.12	3.69
Casein (g)		0.72	0	0.72	0.9	1.12	0
Carbohydrate (g)	5.4-15.5	10.95	5.03	15.98	11.46	11.36	11.63
Energy (kcal) (kJ)	100	100.5	27	127.5	100.5	100.5	108
	420	422	111	531	422	422	448.5
Calcium (mg)	67-200	37.95	112.5	150.45	63	63	90
Phosphorous (mg)	40-127	22.05	67.5	89.55	31.5	31.5	52.5
Ca: PO_4 ratio	1.6:1-2.1:1	1.7:1	1.7:1	1.7:1	2:01	2:01	1.7:1
Magnesium (mg)	5.3-3.6	5	3.6	8.6	6.75	8.1	13.35
Sodium (mg)	46-105	43.95	30	73.95	24	24	58.5
Potassium (mg)	52-106	73.95	63	136.95	99	99	112.5
Chloride (mg)	71-226	88.95	25.5	114.45	69	63	112.5
Iron (mg)	1.33-3.64	0.135	1.95	2.085	1.2	1.2	1.35
Copper (Mg)	80-136	57	60	117	60	60	60

Nutritional requirements of low birth weight infants *(continued)*

NUTRIENT	Prenan 150ml	Monogen (Fat=90% MCT) 150 ml	Neocate 150 ml	Similac special care advance 20 150ml	0.3ml Vidaylin	0.5ml vidaylin + iron
Fat (g)	5.85	3.15	5.25	5.4		
Protein equivalent (g)	3.45	3	2.925	2.71		
Whey (g)	2.4			2.71		
Casein (g)	1.05			0		
Carbohydrate (g)	13.65	18	12.15	10.3		
Energy (kcal) (kJ)	120	113.3	106.5	100		
	501	469.5	447	420		
Calcium (mg)	120	67.5	73.5	180		
Phosphorous (mg)	78	52.5	52.5	100		
Ca: PO_4 ratio	1.5:1	1.3:1	1.4:1	1.8:1		
Magnesium (mg)	13.2	9.15	7.65	12		
Sodium (mg)	43.5	52.5	27	43		
Potassium (mg)	129	94.5	94.5	129		
Chloride (mg)	69	56.3	65.25	81		
Iron (mg)	1.8	1.11	1.58	0.4		5
Copper (Mg)	105	90	90	250		

Nutritional requirements of low birth weight infants *(continued)*

NUTRIENT	Enteral recom-mend-ations per 100 kCal	Per 150ml EBM	7.5g FM 85	150 ml EBM + 7.5g FM85	Nan 150ml	Pelargon 150ml	Alfare 150 ml
Vit A (IU)	467-1364	72	750	822	357	35	379.5
VitD (IU)	100-364	12	150	162	61.5	61.5	64.5
Vit E (IU)	4-10.9	0.6	4.5	5.1	1.22	1.2	1.29
Vit K (MG)	5.63-9.1	3	6	9	8.1	8.1	8.7
Vit C (mg)	12-21.8	6.75	15	21.75	10.05	10.05	10.8
Thiamin (B1) mg)	0.21-0.22	0.014	0.075	0.089	0.075	0.075	0.075
Riboflavin (B2) (mg)	0.17-0.33	0.041	0.15	0.191	0.15	0.15	0.165
Niacin (B3) (mg NE)	2.4-4.4	0.3	1.2	1.5	1.05	1.05	1.05
Folic acid (µg)	17-45	4.95	60	64.95	9	9	9
Vit B6 (mg)	0.1-0.19	0. 009	0.075	0.084	0.08	0.08	0.08
Energy distribution							
Protein as % of total energy	9.0-12.0	9.5		12	9	9	13.5
Fat as % of total energy	40-50	47.2		39	46	46	44
Carbohydrate % of total energy	40-50	43.3		49	45	45	42.5
Renal solute load (mOsm/l)	133-173	106		171	96	96	156
Potential renal solute (mOsm/l)	200-233	138		234	128	128	209
Osmolality (mOsm/kg)	<400			390	290		195

Nutritional requirements of low birth weight infants *(continued)*

NUTRIENT	Prenan 150 ml	Monogen 150ml	Neocate 150ml	Similac Special care Advance 20 150 ml	0.3ml Vidaylin	0.5ml Vidaylin + iron
Vit A (IU)	367.5	283.5	395	1250	2500	750
VitD (IU)	120	69.3	76.5	150	200	200
Vit E (IU)	2.4	1.05	1.11	4.0	0	2.5
Vit K (MG)	14.4	5.55	4.8	12		
Vit C (mg)	19.35	9.3	9	37	25	17
Thiamin (B1) mg)	0.075	0.09	0.09	0.25	0.75	0.25
Riboflavin (B2) mg)	0.15	0.135	0.135	0.62	0.6	0.3
Niacin (B3) (mg NE)	1.2	1.02	2.25	5	5	4
Folic acid (µg)	70.5	12.3	8.55	37		
Vit B6 (mg)	0.15	0.105	0.12	0.25	0.25	0.25
Energy distribution						
Protein as % of total energy	11.5			11		
Fat as % of total energy	43.5			49		
Carbohydrate % of total energy	45			40		
Renal solute load (mOsm/l)	140	160				
Potential renal solute (mOsm/l)	196			175		
Osmolality (mOsm/kg)	390	280		211		

NORMAL RANGES

Appendix 1. BIOCHEMISTRY	
Alanine aminotransferase (IU/l)	Up to 40
Albumin (g/l)	**GA(wks) 0-7d 7-14 d 14-21 d 21-28 d** 27 21-33 29-33 22-35 35 22-36 >36 28-43 30-43 27-44 32-44
Alkaline phosphatase (IU/l)	**>36 wks 36 wks 34-35wks 32-33wks 30-31wks** 28-300 88-326 113-320 110-398 112-450 **28-29 wks 26-27wks** 119-465 35-604 *(values range widely with method)*
Alpha-1-antitrypsin (g/l)	< 1.6 suggests deficiency in infants with prolonged jaundice
Alpha-fetoprotein (U/ml) (according to PMA)	30 wks 38 910-2 034 000 32wks 15 960-988 900 34 wks 6 548-480 000 36 wks 2 686-233 800 38 wks 1 102-113 700 40 wks 452-55 270 42 wks 185-26 870 44 wks 76-13 070
Ammonia (µmol/l)	Up to 100 in healthy term infants (up to 200 if sick/preterm)
Aspartate aminotransferase (IU/l)	Up to 100 (*ranges vary with method*
Calcium total (mmol/l)	**0-7 days >7days** Term: 1.83-2.85 2.1-2.98 Preterm: 2.14-2.65
Chloride (mmol/l)	**Preterm (1 500-2 750g, 7 days old):** 101-116 **Term:** 97-108
Calcium ionized (mmol/l)	**1 d 3 d 5 d** **Term:** 1.05-1.37 1.1-1.44 1.2-1.48 **Preterm: (25-36wks):** 0.81-1.41 0.72-1.44 1.04-1.52
Cholesterol (total) (mmol/l)	**Term: Day 0:** 1.0-2.4 **Day 7:** 2.0-4.3
Cortisol(mmol/l)	**Term 0-14 days:** 0-800 >**15 days** 55-700 **<28 weeks GA 0-14 days** 73-562
Creatine Kinase (IU/l)	**Cord blood 5-8 hr 24-33hr 71-100hr 1month** 70-380 214-1175 158-1230 87-725 50-305

C-reactive protein	< 1mg/dl *(< 10mg/l)*
Creatinine (µmol/l)	**Gest age (weeks)** / **Birth** / **Peak (hr)** / **48 hr** / **7 d** / **14 d** 27-29 / 77±12 / 179± 21(39h) / 116±40 / 84±32 / 72±32 30-32 / 65±4 / 139±19 (33h) / 104±38 / 83±41 / 69±32 33-35 / 73±6 / 120±20(15h) / 93±39 / 68±44 / 55±36 > 36 / 65±5 / / 75±38 / 50±36 / 38±20
Ferritin (ng/ml) (25th -97th percentile)	**Preterm: 3 d:** 80-500 **28 d:** 93-383 **42 d**: 60-460 **Term:** 140-674 (lower at birth)
Fibrinogen (g/l)	**1d** / **5 d** / **30 d** **Term:** 2.83±0.58 / 3.12±0.75 / 2.7±0.54 **Preterm:** 1.5-3.73 / 1.6-4.2 / 1.5-4.1
FSH (follicle stimulating hormone) (IU/l)	**1 wk-2 month:** **male:** < 20 **female:** < 45 **2-4 months:** **male:** < 18 **female: <** 80
Gammaglutamyl transferase (IU/l)	Term: < 2 wks: < 250 2-4 wks: <150
Glucose (fasting) (mmol/l) serum	**12-24hr** / **1-3 d** / **4-7 d** / **>7 d** 2.4-5.4 / 2.9-5.6 / 3.2-6.1 / 3.9-7.0 (*whole blood = 10-15% lower)*
Growth hormone (ng/ml=µg/l)	**Term:** < 2 wks: 15-40 > 2 wks: < 20 **Preterm: <** 2 months: 15-40 > 2 months: < 20
17-hydroxyprogestrone (nmol/l)	**Term 2 -10 days:** 0.7-12.4 (2-3 x higher if sick/preterm)
IgA (g/l) Undetectable at birth in 99%)	**Preterm: 7 d:** 0-0.01 **14 d:** 0-0.08 **28 d:** 0-0.12 **Term: <2 wks:** 0-0.08 **2-4 wks**: 0.02-0.15
IgE (g/l)	Term: Up to 35
IgG (g/l)	Preterm: **7d**: 1.86-7.28 **14 d:** 1.19-6.37 **28 d**: 0.9-4.5 Term: <**2 wks**: 5-17 **2-4 wks:** 3.9-13
IgM (g/l)	Preterm: **7d**: 0.02-0.39 **14 d:** 0.04-0.41 **28 d**: 0.06-0.33 Term: <**2 wks**: 0.05-0.2 **2-4 wks:** 0.08-0.4
Immunoreactive trypsin (µg/l)	Up to 120 (plasma) Up to 70 (blood spot)
Insulin: glucose ratio (MU/l: mmol/l)	**Term:** 0.5-10 **Preterm:** 0.2 - 8
Iron (µmol/l)	**Term:** 10-33 (may be higher at birth) **Preterm: (3 d):** 1.6-22 (10th -95th centile)

Ketone bodies (mmol/l)	**Preterm (3 d):** 0.01-0.51 Term (3d): 0.01-2.06
Lactate (fasting) (mmol/l)	Term: **1 hr**: 0.9-2.7 2**4hr**: 0.8-1.2 **7 d**: 0.5-1.4
Lactate dehydrogenase (U/l)	357-953
LH (luteinizing hormone) (IU/l)	1 wk-2 month: male: 10-40 female: 6-40 2-4 month: male: 5-20 female: 5-30
Magnesium (mmol/l)	**Preterm (0-28 d):** 0.62-1.24 **Term (0-28 d):** 0.72-1.05
Non-esterified fatty acids (mmol/l)	**Preterm (3 d):** 0.01-1.04 **Term (3 d):** 0.04-1.34
Osmolality (mOsm/kg)	Term: 275-295
Phosphate	Term: **1-3 d:** 1.9-2.9 **4-6 d:** 1.7-2.7 **7-12 d:** 1.5-2.9
Potassium (mmol/l) (serum 10% higher than whole blood)	**Preterm (serum) 7 d:** 4.6-6.6 **21 d:** 4.6-7.0 **Term (serum)** **<1 wk:** 3.5-6 **1-4wk:** 3.7-6.6
Protein (g/l) (total)	Term: 54-70 (*preterm babies have lower values)*
Renin (plasma renin activity) ng/ml/hr	**< 5 d** **5 d – 1 month** **3 month-1 yr** 1-40 1-175 1-15
Sodium (mmol/l)	**Preterm:** **7 d:** 133-146 **Term:** **<1 wk:** 133-146 **1-4 wks:** 134-144
Testosterone (nmol/l)	**Cord:** **male:** 0.9-2.1 **female:** 0.7-1.7 **0-48hr:** **male:** 3.5-17.3 **female:** 0.17-2.8 **48 hr-1 wk:** **male:** < 3.5 **female:** <0.9
Thyroxine (free) (pmol/l)	**Preterm 4-10 d:** 10-30 **Term:** **4-10 d:** 13.7-28
TSH MIU /l (=nmol/l)	Preterm > 7 days 0.8-12 Term> 3 days 0.5-6
TSH (CORD SCREEN) (accepted normal values)	1-19 MIU/l or TSH 20-50MIU/l only if T4 > 100pmol/l
Triglyceride (fasting)	Term < 30 days: 0.24-2.08 mmol/l (20-140 mg%)
Urea (mmol/l)	**48 hr** **1 wk** **0-30days** **Preterm:** 5(4-9) 0.5-4.2 **Term:** 0.7-5.7
Urate (µmol/l)	< **2 d:** 200-500 **2-3 d**: 190-395 **3-7 d:** 150-290

URINE BIOCHEMISTRY	
Calcium (mmol/1.73 m^2/24 h) (< 1 wk)	Preterm: < 1.5 Term 1st week: < 0.6
Calcium: creatinine ratio mmol/mmol	Term 1-4 weeks: < 2.4
Nephrotic range protein: creatinine ratio	> 200mg/mmol
Potassium excretion (mmol/kg/24 h)	< 5
Sodium: potassium ratio	< 1
Sodium excretion (mmol/kg/24 h)	**Preterm: < 28 wk** < 7 d: < 22 **Preterm: 29-32 wk** < 7 d: < 12 **Term:** < 1
Tubular phosphate reabsorption	> 80% (higher in preterm babies)

CSF Values – (Meningitis may be present despite normal CSF values)				
	WBC/ mm^3	**%polys**	**Protein-g/l (mean)**	**csf/blood glucose**
Term < 7 d	0-30	0-66%	0.3-2.5 (0.6)	At least 50% of serum. Usually 70-80%. Low CSF levels may persist for weeks after IVH.
Term > 7 d	0-10		0.2-0.8 (0.5)	
Preterm < 7 d	0-30	0-28%	0.5-2.9 (1)	
Preterm > 7 d	2-70	0-60%	0.5-2.6 (0.9)	
Contamination with < 10 000 RBC/mm^3 may not influence the white cell count. *Calculating RBC: WBC ratios are unreliable – rather repeat CSF in 24 hr if in doubt.*				

Appendix 2. HAEMATOLOGICAL VALUES – TERM INFANTS

	Cord	12 hr	24 hr	3 d	7 d	4 wk
Hb (g/dl)	14-20		19.3±2.2	18.8±2	17.9±2.5	12.7±1.6
Hct (%)	43-63		61±7.4	62±9.3	56±9.4	36±4.8
Rb (x 10^{12}/l)	4.2-5.8		5.14±0.7	5.11±0.7	4.86±0.6	3.6±0.4
Reticulocytes (% RBC)	3-7		3.2±1.4	2.8±1.7	0.5±0.4	0.9±0.8
Nucleated RBC /mm³ (/100 WBC)	200-600 (2.9-8.7)		200-500 (2.9-7.3)	0-5 (<0.1)	0	0
MCV (fl)	100-120		119±9.4	116±5.3	118±11.2	101±8.1
MCHC (g/dl)	32-40		31.6±1.9	31.1±2.8	32±1.6	34.9±1.6
Platelets (x 10^9/l)	150-350		150-350	150-350	150-350	150-350
WBC (x 10^9/l) or /mm³)	9-30	13-38	9.4-34		5-21	5-19.5
Total neutrophil	1.8-6.2	7.5-14.4	7.2-12.6	1.8-7	1.8-5.4	1.8-5.4
Immature neutrophils	0-1.1	0-1.4	0-1.3	0-0.6	0-0.5	0-0.5
I/T ratio	0-0.16	0-0.16	0-0.16	0-0.14	0-0.12	0-0.12
	I/T ratio > 0.2 suggests sepsis, but upper limit of normal rises to 0.27 at 4 hours					
Lymphocyte	3.5-8.5	3-8	3-6	2 -5	3.5-7	5.5-9
Monocyte	0.5-1.6	0.9-2	0.8 - 2	0.3-1	0.5-1.7	0.7-1.7
Eosinophil	0.2-2.2	0.1-2	0.1 - 2.2	0.2-1	0.2-1	0.3-0.8
APTT (s)			42.9 ± 5.8			40.4 ± 7.4
PT (s)			13 ± .43			11.8 ± 1.2
Fibrinogen(g/l)			2.8 ± 0.6			2.7 ± 0.5

LEUCOCYTE INDICES IN HEALTHY TERM INFANTS AT 4 HOURS OLD		
	Mean	Range (10^{th}-90^{th})
WBC (x 10^9/l or/mm³)	24.1	16.2 – 31.5
Total neutrophils	15.6	9.5-21.5
Immature neutrophils	2.5	0.7 – 4.3
I/T ratio	0.16	0.05 – 0.27

Appendix 3. HAEMATOLOGICAL VALUES – PRETERM INFANTS < 1,500g (5^{th} -95^{th} centile) (not on EPO or antibiotics)					
	Day 1 (28-35 wks)	**Day 3**	**Day 12-14**	**Day 24-26**	**Day 40-42**
Hb (g/dl)	16.5-21.7	11.6-19.3	10.8-18.4	8.9-16.5	7.9-14.9
Hct (%)	52-69	36-59	32-55	27-50	24-47
RBC (x 10^{12}/l)	3.87-5.76	3.3-4.9	3-5.2	2.6-4.8	2.5-4.6
Reticulocytes (% RBC)	2.3-10	0.7-24.1	0.3-7.3	0.3-6.4	0.4-8.3
MCV (fl)	112-144.5				
Platelets (x 10^9/l)	112-380	75-400	110-543	128-600	133-619
WBC (x 10^9/l)	5-19	4-33.8	7.5-22.1	6.4-15.8	6.1-14.1
or /mm^3)		Antenatal steroids probably resulted in high upper limit on day 3			
Total neutrophil	2-9	1-23.1	1.8-12.4	0.8-6.1	0.9-5.8
	Neutropaenia in infants < 1, 500g is defined as < 1.1 x 10^9/l				
Immature neutrophil	0-1.1	0-1.4	0-1.3	0-0.6	0.5
I/T ratio	2-9	1-23.1	1.8-12.4	0.8-6.1	0.9-5.8
	In a study of 24 healthy infants < 33 weeks gestation during the first 5 days of life, only 5 had an I/T ratio > 0.2.				
Lymphocyte	2-5	1.5-4.5	4-8	4-8	
Monocyte	0.4-1.5	0.3-1.3	0.8-1.8	0.7-1.5	
Eosinophil	0.1-1.1	0.1-0.9	0.3-1.7	0.3-2.8	
APTT (s)	27.5-79.4			26.9-62.5	
PT (s)	10.6-16.2			10-13.6	
Fibrinogen(g/l)	1.5-3.73			1.5-4.14	

Appendix 4. ECG
1small square = 1 mm = 0.04 sec @ 25mm/sec (standard)
10mm amplitude = 1 mV

2^{nd} -98^{th} centile)	0-2 days	3-7 days	1-3 weeks	1-2 months
Term rate	91-159	91-166	107-182	121-179
ORS axis*	59-190	64-190	65-161	31-113
PR interval, (sec) (II)	0.08-0.16	0.07-0.14	0.07-0.14	0.07-0.13
ORS duration (sec)V5	0.03-0.07	0.03-0.07	0.04-0.08	0.03-0.08
VI, R. amplitude (mm)	5.3-26.9	2.8-24.2	3.2-20.8	3.3-18.1
VI, S amplitude	0-22.7	0-16.8	0-10.8	0-12.4
V6, R amplitude	0-12.2	0.3-12.1	2.6-16.4	5.2-21.4
V6, S amplitude	0-9.6	0.9.8	0-9.8	0-6.4
PRETERM rate	109-182	134-200	134-200	128-203
Sleeping rate			140±5	144±6
ORS axis*	75-194	75-165	17-171	17-140
PR interval, (sec) (II)	0.09-0.11	0.09-0.11	0.09-0.11	0.09-0.11
ORS duration (sec)V5	0.04	0.04	0.04	0.04
VI, R. amplitude (mm)	2-12.6	2.6-14.9	3.8-16.8	6.2-21.6
VI, S amplitude	0.06-17.6	1-16	0.15	1.2-14.0
V6, R amplitude	3.5-21.3	5-20.8	4-20.5	8.3-21
V6, S amplitude	2.5-26.5	2.6-26	3-25	3.1-26.3
QT_c interval	=**QT/√RR**	**Normal = < 0.4 (Term)**		**< 0.44 (Preterm**)
T waves	**Age**	**Upright**	**±**	**Inverted**
	0-2 d	V6	V1, aVF	aVR
	2-5 d	I, II, V5, V6	V1, aVF	aVR
	> 5 d-teens	I, II, V5, V6, aVF	V1, aVR	aVR

ECG NOTES

1. RAD: secundum ASD, TGA, RVH, hypoplastic LH, Ebstein's, Fallot's
2. LAD: primum ASD, AV canal defect, LVH
3. Superior axis: ext rt axis = AVSD, ext it axis & cyanotic = tricuspid atresia
4. RAH: primum ASD, Fallot's, Ebstein's TA, hypoplastic LH, obst TAPVD
5. LAH: primum ASD, PDA
6. RBBB: last peak in V1 ABOVE isoelectric line (rSR) ("M")
7. LBBB: last peak in V1 BELOW isoelectric line (RSr) ("W")

ECG INTERPRETATION

- P wave: determine rate, rhythm, axis (normal sinus rhythm P waves upright in II, III and AVF)
- **P-ORS relationship:** 1.1 association, PR interval < 0.12 sec
- **ORS complex:** determine rate, rhythm, broad or narrow.

RVH	OR in V1 and V4R. Upright T in V1 from 5 d to adolescence. R in V1 > 20 mm at any age or > 98th centile for age. S in V6 > 10mm in term infants or > 98th centile for age.
LVH	Inverted T in V5, V6 from 2 d (may be biphasic or "asymmetric") R in V1 or S in V6 > 98th centile for age. Deep Q in V6 (> 2mm < 48hr, > 3mm > 48hr) or absent Q in V6
Septal hypertension	Deep Q in V5 & V6 (> 2mm <48 hr, >3mm > 48hr) + tall R in V1
Bivent hypertension	Voltage criteria for both LVH and RVH
RAH	P ≥ 2.5 mm – best seen in II, V1
LAH	P longer than 0.09 s ± bifid

Appendix 5. BLOOD PRESSURE NORMAL VALUES (mmHg) (liimits = 95% CI)							
PMA =GA + Postnatal age	Systolic		Diastolic		Mean blood pressure		Pulse pressure (mean)
	High limit	Low limit	High limit	Low limit	High limit	Low limit	
24	66	33	47	15	55	22	20
25	68	35	48	16	56	23	20
26	70	38	49	17	57	24	20
27	72	40	50	18	58	25	20
28	73	42	51	19	60	27	22
29	75	44	52	20	61	28	23
30	78	45	53	21	62	29	25
31	79	48	54	22	63	30	25
32	80	49	55	23	64	31	26
33	82	50	56	24	66	33	26
34	85	52	57	25	67	34	27
35	87	55	58	26	68	35	27
36	88	56	59	27	70	37	29
37	90	58	60	28	71	38	30
38	92	59	61	29	72	39	30
39	94	61	62	30	73	40	30
40	95	62	63	31	74	41	32
41	96	65	64	32	76	43	33
42	98	68	65	33	77	44	34
43	99	69	66	34	78	45	34
44	100	70	67	35	80	47	36
45	101	71	68	36	81	48	36
46	102	72	69	37	84	51	40

Appendix 6. NORMAL BLOOD GAS VALUES						
Age	Term	Preterm	Term	Preterm	Term	Preterm
	PaO_2		$PaCO_2$		pH	
	kPa	kPa	kPa	kPa		
1-6 hr	8-10.6	8-9.3	4.7-6	4.7-6	7.31-7.34	7.32-7.38
6-24 hr	9.3-10	8-9.3	4.4-4.8	3.6-5.3	7.37-7.43	7.36-7.45
2-7 d	9.3-11.3	10-0.6	4.4-4.8	4.3-4.5	7.36-7.38	7.32-7.4
14 d			4.8-5.2	5.1	7.37	7.32
21 d			5.3	5.1	7.38	7.31
28 d			5.2	4.9	7.39	7.31

Multiply by 7.5 to convert kPa to mmHg

Appendix 7. SATURATION TARGETS FOR INFANTS RECEIVING OXYGEN			
Infants	**PaO_2 (kPa)/(mmHg)**	**Saturation range**	**Alarm limits**
Preterm < 36 weeks (< 2 400g)	6.5-9.0 (50-70mmHg)	88-92%	86-94%
CLD **AND** 36 weeks PMA	8.0-10.0 (60-75mmHg)	90-95%	88-96%

My personal notes

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