

INTERGROWTH-21st

International Fetal and Newborn Growth Standards for the 21st Century

The International Fetal and Newborn Growth Consortium



BASIC NEONATAL CARE MANUAL

September 2009



**Please read this manual carefully and refer to it throughout the study
if any clarification is needed**

This Operations Manual was produced by the INTERGROWTH-21st Neonatal Group, based on the 1st Meeting of the Neonatal Group, Oxford, July 2009. This document reflects the consensus reached by members of the group regarding the definitions of neonatal morbidities and the minimum standards of care to be provided by all centres taking part in the INTERGROWTH-21st study.

INTERGROWTH-21st is a large project involving health institutions from eight geographically diverse countries. It is therefore essential that all participating institutions follow a standardized neonatal care protocol.

Table of Contents

Credits	4
Abbreviations.....	5
Definitions of Neonatal Morbidities	6
<i>Transient Tachypnea of Newborn (TTN).....</i>	<i>7</i>
<i>Respiratory Distress Syndrome (RDS).....</i>	<i>7</i>
<i>Bronchopulmonary Dysplasia (BPD)</i>	<i>8</i>
<i>Meconium Aspiration Syndrome.....</i>	<i>8</i>
<i>Retinopathy of Prematurity (ROP)</i>	<i>8</i>
<i>Periventricular Leukomalacia.....</i>	<i>9</i>
<i>Apnea of Prematurity.....</i>	<i>9</i>
<i>Hypoxic Ischemic Encephalopathy (HIE)</i>	<i>10</i>
<i>Birth Asphyxia</i>	<i>10</i>
<i>Intraventricular Hemorrhage (IVH).....</i>	<i>11</i>
<i>Necrotizing Enterocolitis (NEC)</i>	<i>12</i>
<i>Polycythemia.....</i>	<i>12</i>
<i>Anemia requiring transfusion</i>	<i>13</i>
<i>Acute Bilirubin Encephalopathy</i>	<i>14</i>
<i>Chronic Bilirubin Encephalopathy</i>	<i>14</i>
<i>Hypotension in Neonates</i>	<i>14</i>
<i>Hypoglycemia.....</i>	<i>14</i>
<i>Inborn Error of Metabolism</i>	<i>15</i>
Treatment and Management Recommendations for Neonatal Morbidities	17
<i>Administration of Antenatal Steroids to Women at Risk of Preterm Delivery.....</i>	<i>18</i>
<i>Feeding the Preterm Infant</i>	<i>19</i>
<i>Thermoregulation in Preterm Newborn Babies</i>	<i>21</i>
<i>Administration of Surfactant to Preterm Infants with or at Risk for RDS</i>	<i>25</i>
<i>Use of Nasal CPAP for Respiratory Distress Syndrome (RDS).....</i>	<i>26</i>
<i>Screening for Intraventricular Hemorrhage (IVH) and Periventricular Leukomalacia (PVL).....</i>	<i>27</i>
<i>Periventricular Leukomalacia (PVL)</i>	<i>28</i>
<i>Screening for Retinopathy of Prematurity (ROP)</i>	<i>29</i>
<i>Hypoxic Ischemic Encephalopathy (HIE)</i>	<i>34</i>
<i>Neonatal Hyperbilirubinemia.....</i>	<i>39</i>
<i>Hypotension in Neonates</i>	<i>43</i>
<i>Patent Ductus Arteriosus (PDA) in Preterm Neonates: (<34 weeks gestation).....</i>	<i>45</i>
<i>Sepsis.....</i>	<i>48</i>

Credits

This manual was prepared by members of the INTERGROWTH-21st Neonatal Group and reflects the general consensus reached during the Neonatal Group Meeting, Oxford, 6-7th July 2009, regarding the minimum standards of neonatal care to be provided by all INTERGROWTH-21st centres.

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Abbreviations

LBW	Low birth weight infants, defined as <2500g at birth
VLBW	Very low birth weight infants, defined as <1500g at birth
ELBW	Extremely low birth weight infants, defined as <1000g at birth

Definitions of Neonatal Morbidities to be used for the INTERGROWTH-21st Study

Transient Tachypnea of Newborn (TTN)

TTN is a parenchymal lung disorder characterized by pulmonary edema resulting from delayed resorption and clearance of fetal alveolar fluid.

The onset of TTN is usually at the time of birth and within two hours after delivery with tachypnea being the most prominent clinical feature. Characteristic findings on chest radiograph support the diagnosis and include increased lung volumes, and prominent vascular markings, with fluid in the interlobar fissure. In order to make the diagnosis, other conditions (such as pneumonia, respiratory distress syndrome, pneumothorax, etc) must be ruled out.

Symptoms of TTN usually last for 12 to 24 hours, but may persist as long as 72 hours in severe cases. Infants rarely require supplemental oxygen, but if required they usually respond to oxygen therapy. When oxygen is needed, usually concentrations less than 40 percent are sufficient to achieve adequate oxygenation.

REFERENCE

Guglani, L et al. "Transient Tachypnea of the Newborn." *Pediatr. Rev.* 2008; 29:e59-e65

Respiratory Distress Syndrome (RDS)

An infant is determined to have respiratory distress syndrome if each of the following is true:

- Requires O₂ at 6 hours of life continuing to age 24 hours
 - Demonstrates clinical features within age 24 hours
 - Has need for respiratory support to age 24 hours, AND
 - Has an abnormal chest x-ray within age 24 hours consistent with surfactant deficiency
- OR
- Has received surfactant therapy within the first 24 hours of life

REFERENCE

Fanaroff AA, Stoll BJ, Wright LL, et al; NICHD Neonatal Research Network. Trends in neonatal morbidity and mortality for very low birth weight infants. *Am J Obstet Gynecol* 2007; 196:147.e1-147.e8

Bronchopulmonary Dysplasia (BPD)

BPD defined as 1) Chronic supplemental oxygen needs for >28 days (28 days oxygen need based BPD)

OR

2) Chronic supplemental oxygen needs at either PMA of 36 weeks or discharge from hospital whichever come first (36 weeks Oxygen need based BPD)

REFERENCE

Pascal M. Lavoie, Chandra Pham, Kerry L .Jang. Heritability of Bronchopulmonary Dysplasia, defined according to consensus statement of National Institute of Health.Pediatrics.2008; 122:479-485.

Meconium Aspiration Syndrome

Meconium Aspiration Syndrome (MAS) is defined as respiratory distress in an infant born through meconium stained amniotic fluid (MSAF), whose symptoms cannot be otherwise explained. This disorder may be life threatening complicated by respiratory failure, pulmonary air leaks and persistent pulmonary hypertension.

REFERENCE

Fanaroff AA. Meconium aspiration syndrome: historical aspects. J Perinatol.2008; 28:3-7

Retinopathy of Prematurity (ROP)

ROP a developmental vascular retinopathy occurs only in the incompletely vascularized retina of premature infants, leading to a wide range of outcomes from normal vision to blindness. For a diagnosis of ROP to be documented we need a confirmed diagnosis by an ophthalmologist in the notes according to the staging criteria below;

Staging of ROP:

Stage1: Demarcation line separating the avascular retina anteriorly from the vascularized retina posteriorly, with abnormal branching of small vessels immediately posterior.

Stage 2: Intraretinal ridge; the demarcation line has increased in volume, but proliferative tissue remains intraretinal.

Stage 3: Ridge with extraretinal fibrovascular proliferation.

Stage 4: Partial retinal detachment

Stage 5: Total retinal detachment.

REFERENCES

International Committee for the classification of Retinopathy of Prematurity "The international classification of Retinopathy of Prematurity Revisited" Arch Ophtalmol 2005;123:991-999.

M.Subhani, Adriann Coombs, Pamela Weber, Corina Gerontis. Screening guidelines for Retinopathy of Prematurity: The needs for revision in Extremely Low Birth Weight Infants.Pediatrics.2001; 107:656-659

Periventricular Leukomalacia

Damage to the deep white matter (WM) in the centrum semiovale is the main characteristic feature of PVL. The damage may vary from punctuate areas of hemorrhage & necrosis to more extensive injuries including cystic changes, scarring, hypomyelination / demyelination, and even hemorrhagic infarction of the white matter.

REFERENCE

De Vries LS, Eken P, Dubowitz LMS. The spectrum of leukomalacia using cranial ultrasound. Behav Brain Res 1992;49:1-6

Apnea of Prematurity

Clinically significant apnea in infants is defined as breathing pauses that last for > 20 seconds or for > 10 seconds if associated with bradycardia (e.g. < 80 beats per minute) or oxygen desaturation (e.g. O₂ saturation of < 80-85 %).

REFERNECE

Finer N, Higgins R, Kattwinkel J, Martin RJ. Summary Proceedings From the Apnea-of-Prematurity Group. Pediatrics 2006;117:S47-S51.

Hypoxic Ischemic Encephalopathy (HIE)

Hypoxic Ischemic Encephalopathy (HIE) of the newborn is “a clinically defined syndrome of disturbed neurological function in the earliest days of life in the term infant, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, sub normal level of consciousness and often seizures.

REFERENCE

Nelson KB, Leviton A. How much of neonatal encephalopathy is due to birth asphyxia? Am J Dis Child 1991

Birth Asphyxia

Infant satisfying at least one of the following criteria:

- Apgar score of 5 or less at 10 minutes
- Mechanical ventilation or resuscitation at 10 minutes
- Cord pH < 7.1, or an arterial pH < 7.1 or base deficit of 12 or more within 60 minutes of birth
- Evidence of encephalopathy according to Sarnat staging (Sarnat 1976; Finer 1981):
Stage 1 (Mild): hyperalertness, hyper-reflexia, dilated pupils, tachycardia, absence of seizures.

Stage 2 (Moderate): lethargy, hyper-reflexia, miosis, bradycardia, seizures, hypotonia with weak suck and Moro.

Stage 3 (Severe): stupor, flaccidity, small to midposition pupils which react poorly to light, decreased stretch reflexes, hypothermia and absent Moro.

REFERENCE

Sarnat H, Sarnat M. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976 vol. 33 (10) pp. 696-705

Finer N, Tommy P. Controlled evaluation of muscle relaxation in the ventilated neonate. Pediatrics 1981 vol. 67 (5) pp. 641-6

Jacobs SE, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003311.

Postnatal Infection (Sepsis)

Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life.

Late onset sepsis defined as 1 or more positive blood cultures obtained after 3 days of age from infants with clinical features of sepsis

Since culture positive sepsis is relatively rare, a physician documented episode of sepsis would suffice.

REFERENCES

Infectious disease: In Gomella TL, Cunningham MD(eds): a LANGE Clinical manual. Neonatology: Management, procedures, on Call Problems Diseases and Drugs.5th ed. McGraw Hill, 2004.p434-440.

M Gary Karlowickz, E Stephen Buescher Fulminant Late Onset Sepsis in a intensive neonatal care unit, 1987-1997, and the impact of avoiding empiric vancomycin therapy. Pediatrics.2000; 106:1387-1390

Intraventricular Hemorrhage (IVH)

A diagnosis of IVH should be based on a documentation of IVH based on Ultrasonographic findings conducted by a qualified ultrasonographer/ultrasonologist.

Intraventricular hemorrhage is graded by the classification of Papile et al on ultrasonographic examination as follows:

Grade1: Blood in the periventricular germinal matrix regions or germinal matrix hemorrhage.

Grade2: Blood within the lateral ventricular system without ventricular dilatation.

Grade3: Blood acutely distends the lateral ventricles.

Grade4: Blood within ventricular system and parenchyma

REFERENCE

Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr 1978;92(4):529-34.

Necrotizing Enterocolitis (NEC)

A diagnosis and staging of Necrotizing enterocolitis (NEC) should be based on a clinical documentation by treating clinician based on the following criteria:

Stage1: Suspected

- *History of perinatal stress
- *Systemic signs of ill health: temperature instability, lethargy, apnea
- *Gastrointestinal manifestations: poor feeding, increased volume of gastric aspirates, vomiting, mild abdominal distension, faecal occult blood (no fissure)

Stage2: Confirmed

- *Any of the features of stage 1 plus:
 - *persistent occult, or gross gastrointestinal bleeding, marked abdominal distension
 - *abdominal radiograph: intestinal distension, bowel wall oedema, unchanging bowel loops, pneumatosis intestinalis, portal vein gas.

Stage3: Advanced

- *Any of features of stages 1 or 2 plus:
 - *Deterioration in vital signs, evidence of shock or severs sepsis, or marked gastrointestinal hemorrhage
 - *Abdominal radiograph shows any of features of stage 2 plus pneumoperitoneum

REFERENCE

Gastrointestinal disorder: In Roberton's R Text book of Neonatology (3rded). Churchill Livingstone. 1999, p752.

Polycythemia

Polycythemia in term infant is the presence of a venous hematocrit more than 65% or a venous hemoglobin concentration in excess of 22 gm/dl.

REFERENCE

Phibbs RH:Neonatal polycythemia. In Rudolph AB (ed): Pediatrics, 16th ed. Newyork: Appleton Century Crofts, 1997.

Anemia requiring transfusion

There is no consensus on definition of Anemia of Prematurity.

Shown below is the criteria for transfusion taken from US and Canadian collaborative study. Patients are transfused in a volume of 15ml/kg, administered over 2-3 hours.

TABLE 1. Transfusion Criteria

-
- A) Hct 31%–35%
 - Receiving >35% supplemental hood oxygen
 - Intubated on CPAP or mechanical ventilation with mean airway pressure >6–8 cm H₂O
 - B) Hct 21%–30%
 - Receiving <35% supplemental hood oxygen
 - On CPAP or mechanical ventilation with mean airway pressure <6 cm H₂O
 - Significant apnea and bradycardia (>9 episodes in 12 h or 2 episodes in 24 h requiring bag and mask ventilation) while receiving therapeutic doses of methylxantines
 - Heart rate >180 beats/min or respiratory rate >80 breaths/min persisting for 24 h
 - Weight gain <10 g/d observed over 4 d while receiving >100 kcal/kg/d
 - Undergoing surgery
 - C) Hct <21%
 - Asymptomatic with reticulocytes <1%
 - D) Transfuse at any hematocrit value if hypovolemic shock develops
 - E) Do not transfuse
 - To replace blood removed for laboratory tests
 - For low Hct alone
-

CPAP indicates continuous positive airway pressure; Hct, hematocrit.

Table 1 adapted from Donato et al. Pediatrics. 2000;105(5):1066-72.

REFERENCE

Donato H, Vain N, Rendo P, Vivas N, Prudent L, Larguía M, Digregorio J, Vecchiarelli C, Valverde R, García C, Subotovsky P, Solana C, Gorenstein A. Effect of early versus late administration of human

recombinant erythropoietin on transfusion requirements in premature infants: results of a randomized, placebo-controlled, multicenter trial. *Pediatrics*. 2000;105(5):1066-72.

Acute Bilirubin Encephalopathy

A clinical syndrome in the presence of severe hyperbilirubinemia, of lethargy, hypotonia, and poor suck, which may progress to hypertonia (with opisthotonus and retrocollis) with a high-pitched cry and fever and eventually to seizures and coma.

Chronic Bilirubin Encephalopathy

The clinical sequelae of acute encephalopathy with athetoid cerebral palsy with or without seizures, developmental delay, hearing deficit, occlumotor disturbances, dental dysplasia and mental deficiency.

REFERENCE

Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (35 or more week's gestation). Canadian Pediatric Society. *Pediatr Child Health*. 2007; 12:1-12

Hypotension in Neonates

Hypotension is a blood pressure (B.P) >2 standard deviations below normal for age. For infants who are <30 weeks gestation, a mnemonic that is helpful in remembering BP is that the mean BP should be at least the same number as gestational age. For example, a 23 week infant should have a mean BP of 23 mmHg.

REFERENCE

Hypotension and shock in Gomella TL, Cunningham MD (eds): a Lange clinical manual, *Neonatology*: 5th ed. McGraw Hill 2004

Hypoglycemia

A normal range for neonatal hypoglycemia has not been properly defined, and there is controversy over safe blood glucose concentration. The World Health Organization designates a blood glucose "operational threshold" <2.6 mmol/L or 46.8 mg/dl as requiring treatment and make no distinction between preterm and term infants.

REFERENCE

Division of Child Health and Development and Maternal and Newborn Health/Safe Motherhood, Hypoglycemia of the Newborn. Review of the literature. World Health Organization.Geneva.1997.1-55

Inborn Error of Metabolism

Inborn errors of metabolism comprise a large class of genetic diseases involving disorders of metabolism. The majority are due to defects of single genes that code for enzymes that facilitate conversion of various substances (substrate) into others (products). In most of the disorders, problems arise due to accumulation of substances which are toxic or interfere with normal function, or to the effects of reduced ability to synthesize essential compounds. Inborn errors of metabolism are now often referred to as congenital metabolic diseases or inherited metabolic diseases, and these terms are considered synonymous.

REFERENCE

Charles Scriver, Beaudet A.L, Valle D, Sly, WS, Vogelstein, B Kinzler. K.W. The online Metabolic and molecular bases of inherited disease. Newyork: McGraw Hill 2001.

Treatment and Management Recommendations for Significant Neonatal Problems

Administration of Antenatal Steroids to Women at Risk of Preterm Delivery

- Single course of corticosteroids for all pregnant women between 24-34 weeks gestation who are at risk of preterm delivery within 7 days
 - Betamethasone 12mg IM x2doses, 24 hours apart, OR
 - Dexamethasone 6mg IM x4doses, 12 hours apart
- Single course of corticosteroids should be administered to all women with PROM < 32 weeks gestation
- Repeat courses (“rescue”) should not be used routinely, but may be considered

REFERENCES

ACOG. “Antenatal Corticosteroid Therapy for Fetal Maturation.” ACOG Committee Opinion No. 402, March 2008.

Sweet et al. “European consensus guidelines on the management of neonatal respiratory distress syndrome.” Journal of Perinatal Medicine. Volume 35, Issue 3, Pages 175–186, June 2007

Garite TJ et al. “Impact of a ‘rescue course’ of antenatal corticosteroids: a multicenter randomized placebo-controlled trial. Am J Obstet Gynecol 2009; 200:248.e1-248.e9

Feeding the Preterm Infant

The goal of this guideline is to promote exclusive breast feeding of the preterm infant at the time of hospital discharge

What to feed in order of preference:

- Mothers own milk from the breast
- Mothers expressed breast milk
- Donor Human Milk if available
- Preterm formula if < 32 weeks gestation

Feed volumes:

Start at around 80ml/kg/day.

Increase fluids by 10-20 ml/kg/day to maximum of around 160 -180ml/kg/day by the end of the first week of life.

Human Milk Supplementation:

Vitamin D 400 IU per day if <1500g

Phosphorus & calcium – some evidence that reduce metabolic bone disease in <1500g

Iron 2mg/kg/d – start by 8 weeks

Multi-component fortifiers – associated with short term increases in weight gain, linear and head growth. There is no evidence of long-term benefits or adverse effects.

Duration of exclusive breast feeding:

6 months in low birth weight infants accompanied with iron supplementation

How to feed:

Orogastric better than nasogastric tube especially if infant has increased work of breathing

No strong evidence for continuous over bolus feeds

Babies should be encouraged to suck at the breast once sucking behaviour is observed

Feed progression:

Most babies > 32 weeks tolerate maintenance enteral feeds on day 1

Babies <32 weeks. Introduce small amounts of trophic feeds (5-10ml/kg/d) on first day of life unless illness severity prevents this.

Babies >32 weeks are likely to tolerate faster increases in volume better than smaller less mature babies.

Table 2. Recommended daily enteral nutrients for pre-term infants >1000g at birth

Nutrient	Birth to 7 days	Period after birth Stabilization to Term
Energy, kJ/kg(kcal/kg)	292-334 (70-80)	438-563 (105-135)
Protein, g/kg	1.0-3.0	3.0-3.6
Fat, g/kg	0.5-3.6	4.5-6.8
Carbohydrate, g/kg	5.0-20.0	7.5-15.5

REFERENCE

Adapted from WHO Technical review: Optimal feeding of low-birth-weight infants, by K. Edmond and R Bahl (2006)

Thermoregulation in Preterm Newborn Babies

At Delivery

The delivery room or operating theatre is always too cold for a VLBW baby. The baby should be thoroughly dried, wrapped, resuscitated and removed to a warmer environment, as soon as possible. Wrapping the baby in a polyethylene film straightaway without prior drying, until after transfer to a warmer or an incubator is an effective way of avoiding hypothermia in the immediate newborn period

Problems Encountered in Premature newborns

- NICU admission temperatures remain sub optimal despite intervention with polyethylene wrap.
- Polyethylene wrap alone is insufficient to maintain an adequate temp if the delivery suite environment is <25°C

Therefore maintaining adequate thermoregulation for the preterm infant in the immediate newborn period is dependent on

1. Adequate environmental temperature in delivery suite >25°C
2. Use of transwarmers for infants < 29 weeks or where a prolonged resuscitation is required
3. Occlusive plastic wrapping at delivery for all infants <32 weeks

There is no evidence that one type of plastic wrap is superior to another

- Utilize sterile plastic bags
- Unwrap and remove paper insert
- Insert baby directly into bag at delivery or immediately on arrival at resuscitaire. NB ensure that the infant's head is not inside the bag.
- Baby should not be dried prior to plastic covering
- Baby can be placed into plastic bag by obstetrician at section as the bag is sterile.
- Cling film wrap may be used if sterile plastic bag is not available
- Access through plastic can easily be made for saturation probes or umbilical access

4. Hats and swaddling

5. Maintaining temperature stability during stabilization in NICU

- Leave in occlusive wrap during initial practical procedures
- Transwarmers should be transferred with the babies
- Limit access during line insertion to port holes – sides should not be lowered.

Incubator Care

A closed incubator provides a baby with high ambient temperature while allowing attendants to work at a lower and comfortable temperature. Air mode is considered more satisfactory for nursing most newborn babies. Temperature settings depend on whether the baby is clothed or naked, on the weight and the postnatal age of the baby. Following values are recommended (Hey, 1975).

Table 3: Average incubator air temperature needed to provide a suitable thermal environment for naked, healthy babies

Birth weight (Kg)	Environmental temperature			
	35° C	34° C	33° C	32° C
1.0-1.5	For 10 days	After 10 days	After 3 weeks	After 5 weeks
1.5-2.0		For 10 days	After 10 days	After 4 weeks
2.0-2.5		For 2 days	After 2 days	After 3 weeks
> 2.5			For 2 days	After 2 days

- In a single-walled incubator, the environmental temperature needs to be increased by 1° C for every 7° C difference between room and incubator temperature
- VLBW infants (< 1 kg) need higher air temperature and a humidified incubator in the first week.

Radiant Warmer:

Table 4: Suggested abdominal skin temperature settings for infants under radiant warmers or Servo-mode incubators (Rutter, 2008)

Weight (Kg)	Abdominal skin temperature (°C)
< 1.0	36.9
1.0-1.5	36.7
1.5-2.0	36.5
2.0-2.5	36.3
> 2.5	36.0

Provision of incubator humidity in premature babies

Evidence and current practice guidelines support the use of humidity in caring for extremely preterm infants (Marshall, 1997; Harpin and Rutter, 1985). However, the infant's needs for humidity reduce substantially after 7-14 days.

- Humidity should be commenced in all infants born at < 31 weeks gestation.
- Humidity should start at 85% (>85% results in rainout and temperature instability).
- Humidity should be reduced with respect to gestation and temperature stability. The gestation specific parameters are outlined below.
- Humidity should be discontinued in all infants when a level of 40% has been demonstrated to be compatible with thermal stability.

Infants of 28-30 weeks gestation

- If temperature remains stable at 24 hours, start to reduce humidity by 5% daily

Infants of <28 weeks gestation

- Maintain humidity of 85% for first 7 days and then decrease by 5% daily as temperature allows.

Humidity systems

- The water used in the humidity drawer should be sterile water.
- The water in the drawer should never be topped up - a complete exchange of water is necessary if refilling the drawer.
- The drawer should be washed (tap water) and dried thoroughly with hand towels whenever the water is being changed (this should reduce the risk of a bacterial film build up)

Incubator cleaning

- The interior of the incubator should be wiped down daily when in use and kept free of visible particulate matter.
- Incubators should be cleaned in all but the most unstable babies at weekly intervals.
- All signs of physical contamination should be removed.
- Incubators and parts should be dried thoroughly with hand towels after washing. They should not be switched on to run until dry as this will encourage colonization.
- Incubator parts should not be soaked in detergent solutions but should be cleaned as above.

Weaning to Crib:

When the infant's temperature is maintained within a normal range in low incubator temperatures (i.e. $<34^{\circ}\text{C}$) and heater output of less than 50%, then thermal aides can be slowly weaned. Remove them one at a time and assess effectiveness over 6 – 8 hours before making further changes.

What is needed: Overall approval of process, serious concerns (if any), supportive suggestions, agreement that physician order is not required after implementation of the project.

REFERENCES

- Hey E.N. Thermal Neutrality. *British Medical Bulletin*. 1975, 31: 69-74
- Nicholas Rutter. Temperature control and disorders. *Robertson's Textbook of Neonatology. 4th Ed.* Elsevier Churchill Livingstone, 2008, p 274
- Marshall A. Humidifying the environment for the premature infant: maintenance of a thermo-neutral environment. *Journal of Neonatal Nursing* 1997; January: 32-36.
- Harpin V. and Rutter N. Humidity of incubators. *Arch Dis Child*. 1985; 60: 219-224.
- Gelhar D.K., Miserendino C.A., O'Sullivan P.L., Vessey J.A. 1994. *J Obstet Gynecol Neonatal Nurs.* 23: 341-4
- Medoff Cooper B. (1994). Transition of the preterm infant to an open crib (clinical issues). *J Obstet Gynecol Neonatal Nurs.* 23: 329-335.
- Meier P.P (1994). Transition of the preterm infant to an open crib: process of the project group. *J Obstet Gynecol Neonatal Nurs.* 23: 321-6.
8. New K. Flenady V. & Davies M.W. (2006) Transfer of preterm infants from incubator to open cot at lower versus higher body weight. *Cochrane Lib*, 1: (CD004214).

Administration of Surfactant to Preterm Infants with or at Risk for RDS

- Surfactant should be given to infants with RDS as soon as possible after intubation irrespective of antenatal steroid exposure, or gestational age
- Prophylactic (<30min of life) surfactant replacement should be considered for extremely preterm infants at risk of RDS especially if they have not been exposed to antenatal steroids

REFERENCES

William A. Engle and the Committee on Fetus and Newborn. "Surfactant-Replacement Therapy for Respiratory Distress in the Preterm and Term Neonate." *Pediatrics* 2008; 121:419-432

Sweet et al. "European consensus guidelines on the management of neonatal respiratory distress syndrome." *Journal of Perinatal Medicine*. Volume 35, Issue 3, Pages 175–186, June 2007

Use of Nasal CPAP for Respiratory Distress Syndrome (RDS)

- a. When possible, infants < 27 weeks gestation should be intubated and given prophylactic surfactant in the delivery room or as soon as possible after intubation
- b. For babies ≥ 27 weeks, use nCPAP for respiratory distress if:
 1. Low risk for significant RDS and/or mild RDS on x-ray
 2. Infants with a diagnosis of RDS should receive surfactant if they require intubation and supplemental oxygen for respiratory failure
- c. Initial settings: 4-5 (max 7-8) cm H₂O, FiO₂ 0.4-0.5, flow 6-8 lpm
- d. Monitoring:
 1. Clinical: respiratory rate, work of breathing, color/O₂ saturation, perfusion, blood pressure, chest expansion and pneumothorax on CXR, presence of nasal trauma
 2. Blood gas monitoring when available
 3. Centers employing nCPAP should be able to diagnose and manage air leak syndrome
- e. When using nCPAP, if FiO₂ > 0.6, or more than one apneic episode per hour requiring stimulation, or significant work of breathing, the baby should be intubated and mechanical ventilation along with surfactant should be provided.
- f. Extubation to CPAP:
 1. After intubation and administration of surfactant, preterm infants with RDS, regardless of birth weight, can be extubated and stabilized on CPAP if the infant is active, exhibits spontaneous respiratory effort, and is not in respiratory failure (FiO₂ < 50%, PCO₂ < 60 mm Hg on low ventilator settings).
- g. Weaning from CPAP: Wean to CPAP of 5 and discontinue when infant is stable with FiO₂ < 0.30, and recommence CPAP if apnea or FiO₂ increases.

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Welty et al. "Treatment and complications of respiratory distress syndrome in preterm infants." Up To Date, January 2009

Screening for Intraventricular Hemorrhage (IVH) and Periventricular Leukomalacia (PVL)

In 2001, a committee of prominent neonatologists, neurologists, perinatal epidemiologists, and neonatal radiologists was appointed to review the literature and make recommendations concerning the routine neuro-imaging of the at-risk neonate. Their findings were published as a practice parameter that was published in Neurology (2002); 58:1726-38. Dr. Papile participated on this committee, and summarized in their recommendations:

- Only infants < 30 weeks gestation should undergo routine screening for IVH or PVL.
- The initial brain ultrasound exam should not be done until 7-14 days (unless indicated for clinical reasons).
- A repeat cranial sonography should be done at 36-40 weeks (or just prior to discharge) to screen for periventricular leukomalacia (PVL).
- If the initial screening brain ultrasound (at 7-14 days) is normal or shows a grade 1 or grade 2 IVH, no further screening ultrasound exams need to be done prior to the exam at the time of discharge.

REFERENCES

Ment LR, Bada HS, Barnes P, Grant PE, Hirtz D, Papile LA, Pinto-Martin J, Rivkin M, Slovis TL. Practice parameter: neuroimaging of the neonate: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2002 Jun 25;58(12):1726-38.

Periventricular Leukomalacia (PVL)

There seems to be no generally accepted classification for PVL and the best suggested one based on ultrasound guidelines proposed by De Vries, Dubowitz et al is reproduced below:

<u>Classification</u>	<u>Description</u>
1. Flare or echodensity	Periventricular echodense area. Loss of normal pattern of alternating echo-reflectant and echo-poor lines.
2. Fronto parietal cystic PVL	Localised small frontoparietal cysts. Lesions not involving occipital cortex.
3. Parieto-occipital cystic PVL	Multiple cysts in parieto-occipital WM.
4. Subcortical cystic PVL	Multiple subcortical cysts in deep WM (Multicystic Leucoencephalomalacia - MCLE).
5. Porencephalic cysts	Single large cavity adjoining a ventricle and in communication with it.

REFERENCE

De Vries LS, Eken P, Dubowitz LMS. The spectrum of leukomalacia using cranial ultrasound. Behav Brain Res 1992;49:1-6

Screening for Retinopathy of Prematurity (ROP)

Infants with birth weight of <1500 gm or gestational age < 32 weeks and selected infants with a birth weight of 1500-2000gm or gestational age > 32 weeks with an unstable clinical course, including those require cardio respiratory support, are candidates for screening for ROP.

- 1) The following table provides the schedule for detecting ROP potentially damaging to retina with 99% confidence.

Table 5. Timing of First Eye Examination Based on Gestational Age at Birth:

Gestational Age at Birth, wk	Age at Initial Examination, wk	
	Postmenstrual	Chronologic
22 ^a	31	9
23 ^a	31	8
24	31	7
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4
31 ^b	35	4
32 ^b	36	4

Shown is a schedule for detecting pre-threshold ROP with 99% confidence, usually well before any required treatment.

This guideline should be considered tentative rather than evidence-based for infants with a gestational age of 22 to 23 weeks because of the small number of survivors in these gestational-age categories.

- 2) Follow up examination should be recommended by the examining ophthalmologist on the basis of retinal findings classified according to the international classification.
 (See Figure 1)

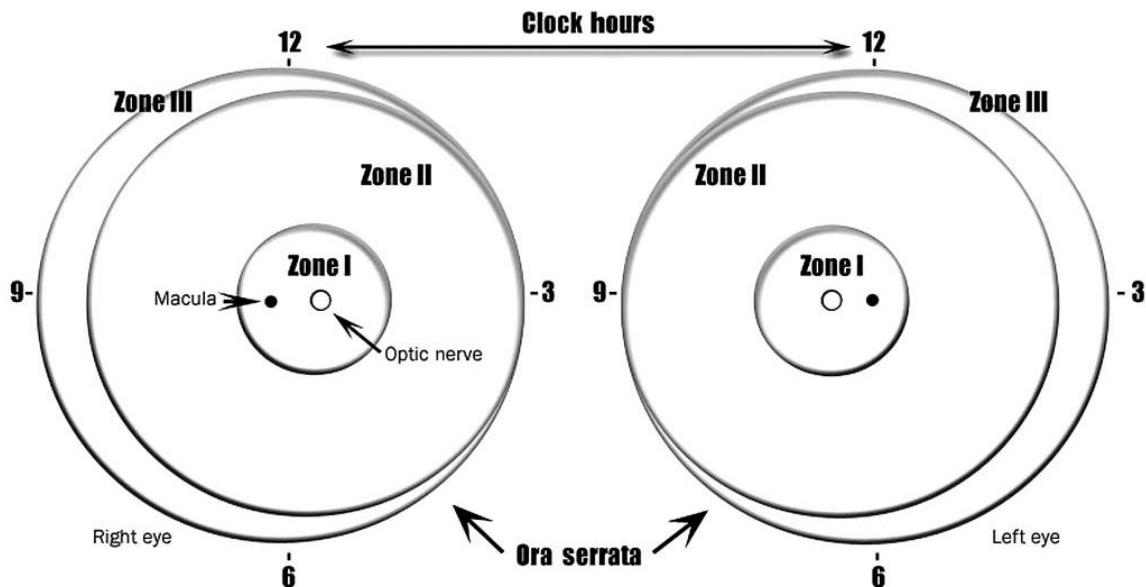


Figure 1 (adapted from American Academy of Pediatrics. Screening examination for Preterm Infants for Retinopathy of Prematurity. *Pediatrics*. 2006; 117:572-576).

Scheme of retina of the right and left eyes showing zone borders and clock hours used to describe the location and extent of retinopathy of prematurity. Diagrammatic representation of the potential total area of the premature retina, with zone I (the most posterior) symmetrically surrounding the optic nerve head (the earliest to develop). A larger retinal area is present temporally (laterally) than nasally (medially) (zone III). Only zones I and II are present nasally. The retinal changes discussed in recommendation 4 are usually recorded on a diagram such as this.

1 Week or less follow up

Stage 1 or 2 ROP: Zone I

Stage 3 ROP: Zone II

1-2 Week follow up

Immature vascularization: Zone I –no ROP

Stage 2 ROP: zone II

Regressing ROP: Zone I

2 Week follow up

Stage 1 ROP: zone II

Regressing ROP: Zone II

2-3 Week follow up

Immature vasularization: Zone II—no ROP

Stage 1 or 2 ROP: Zone III

Regressing ROP: Zone III

One examination is sufficient only if it is unequivocally shows the retina to be fully vascularized in each eye.

REFERENCE

American Academy of Pediatrics. Screening examination for Preterm Infants for Retinopathy of Prematurity. *Pediatrics*. 2006; 117:572-576.

Apnea of Prematurity:

It usually occur in infants who are <34 weeks gestation, weight<1800gm, and have no identifiable cause of the apnea of prematurity

1. General measure: include tactile stimulation, correct anemia, maintain normal body temperature, correct electrolyte imbalance if present.
2. Look for IVH, signs or symptoms of Sepsis, PDA, NEC, and gastro-oesophageal reflux, and treat it accordingly.
3. Specific treatment: Theophylline or caffeine: The choice of drugs depends on availability and neonatologist's preference.

Aminophylline:

Dose for apnea of prematurity: 5-6 mg/kg PO or I/V (infused over 15-30 minutes) as a loading dose, followed by a maintenance dose of 2 mg/ kg q 12 h starting 12 hr after the loading dose.

Adverse effects: hyperglycemia, diuresis, dehydration, feeding intolerance, tachycardia, arrhythmias , hyperreflexia, jitteriness and seizures.

Therapeutic level for apnea: 6-11 mg/ml

Caffeine:

Loading dose: 20mg of caffeine citrate (10 mg of caffeine base) I/V or P/O

Maintenance dose (caffeine base): 2.5-5 mg/kg/day as single dose

Adverse effects: Nausea, vomiting, gastric irritation, agitation, tachycardia and diuresis. Symptoms of over dosage include arrhythmias and tonic clonic seizures

Therapeutic level: 5-25 mcg/ml

- a. Therapy can usually be discontinued by postconceptional age (usually 37 weeks), depending on the weight of the infant (usually 1800-2000g), or if the infant has been apnea free for 7 days. More immature infants will require treatment longer.
- b. If the above mentioned drug trial fails, use **continuous positive air way pressure(CPAP)** via nasal prongs at a rate of 2-4 cm H₂O and continue administration of drug. An alternative to nasal CPAP is to use high flow nasal cannula at 1-2 L /min.
- c) If apnea persists, consider **doxapram** (not commonly used). Doxapram may be efficacious when theophylline and caffeine have failed.

Dosage: 0.5-1.5mg/kg/hr by continuous I/V infusion, decrease the dose when control of apnea is achieved.

d) **Mechanical Ventilation:** Should be continued if apnea and bradycardia cannot be controlled by drug therapy or nasal CPAP. Low pressures are used to prevent apnea.

REFERENCE

Apnea and Bradycardia: In Gomella TL, Cunningham MD (eds): a Lange Clinical Manual, Neonatology: 5th ed. McGraw Hill 2004.210

Hypoxic Ischemic Encephalopathy (HIE)

Table 6. 3 clinical Stages of encephalopathy described are:

Stage 1	1. Duration<24 hrs with hyperalertness 2. Uninhibited Moro and stretch reflexes 3. Sympathetic effects 4. Normal electroencephalogram
Stage2	1. Obtundation 2. Hypotonia 3. Decreased spontaneous movement with or without seizures
Stage3	1. Stupor 2. Flaccidity 3. Seizures 4. Suppressed brain stem and autonomic functions 5. EEG may be isopotential or have infrequent periodic discharges

- 1) Stage 3 or persistence of stage 2 for more than seven days or failure of the EEG to revert to normal is associated with Neurodevelopmental impairment or death.
- 2) Full-term infants who develop long-term neurologic sequelae from intrapartum.
- 3) Asphyxia may not have low Apgar scores but will demonstrate neurological dysfunction within 48 hours⁽²⁾

Postnatal Management:

Management of every asphyxiated baby is individualized. Below is the broad guideline for management of the asphyxiated baby.

Systemic management: The corner stone of management following hypoxia ischemia is supportive care and the careful maintenance of systemic homeostasis⁽³⁾

Figure 2. Summary of initial management of asphyxiated neonates

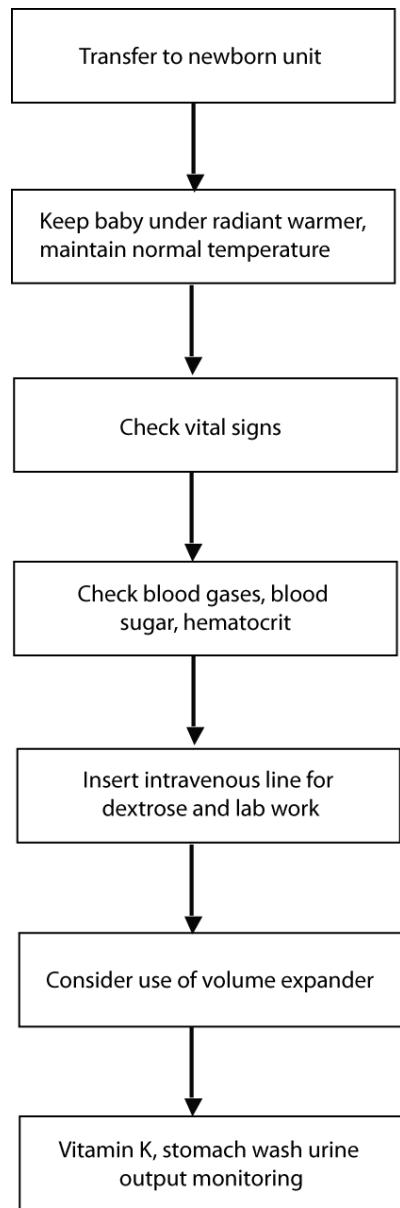


Figure Adapted from: Aggarwal R, Deorari AK, Paul VK. Post-resuscitation management of asphyxiated neonates. Indian J Pediatr. 2001 Dec;68(12):1149-53.

Transfer the baby to NICU/ special care unit:

A baby who fails to initiate and sustain respiration at birth is at risk of hypoxic brain injury and needs regular monitoring. Infants with moderate hypoxia (APGARS 4-6 at one minute of age) may be transferred to the mother. However, these infants should also be monitored frequently in the first 48-72 hours for features suggestive of HIE. Infants with severe asphyxia (Apgar score 0-3 at 1 minute or need

for prolonged bag and mask ventilation >5 minute) should be transferred to NICU for observation and treatment.

Thermoregulation:

Place the baby under radiant warmer after drying the baby. Maintain normal body temperature of the baby.

Monitoring of vital signs:

Immediate clinical assessment should be made by recording respiration, heart rate, blood pressure, capillary refill time, temperature and oxygen saturation. Urine output monitoring should be done.

Start intravenous fluids:

Give two third of the maintenance fluid due to the possibility of syndrome of inappropriate secretion of anti-diuretic hormone (SIADH).

Check blood sugar, hematocrit and blood gas (if needed).

Consider infusion of Volume Expanders:

Volume expanders: Use normal saline, Ringer lactate or if needed blood product to maintain intravascular volume.

If capillary refill is >3 seconds or if there is metabolic acidosis, volume expansion with normal saline (or Ringer lactate) 10mg/kg should be instituted, may repeat if necessary

Subsequent management ⁽⁴⁾

Fluid and electrolytes:

Judicious fluid management is needed and fluid overload should be avoided.

Give 10% Dextrose/water at 40-60ml/kg/day on 1st day of life and increase fluid and electrolytes according to day of life, serum level and neurologic condition of baby.

Maintain normal calcium level: Calcium should be provided in a maintenance dose of 4 ml/kg/day (10% calcium gluconate) for 1-2 days. This can be given in 1:1 dilution under cardiac monitoring.

Treat metabolic acidosis:

If metabolic acidosis is severe or persistent then sodium bicarbonate may be used but caution is advised as rapid infusion increases serum osmolality and alkaliification may decrease cerebral blood flow.

Avoid hypoglycemia and hyperglycemia:

Maintain adequate perfusion:

Global ischemia may affect the myocardium and cardiovascular support may be needed to improve perfusion. The markers for normal perfusion are normal blood pressure, capillary refill time of <3 seconds, normal urine output and absence of metabolic acidosis. The blood pressure should be maintained to the upper normal range. This can be achieved with the judicious use of volume expanders and vasopressor agents.

Vasopressors: Dopamine Is the drug of first choice in the treatment of neonatal hypotension.

Dosage: 4-20 mcg/kg/min

Route: Intravenously

Adverse effects: may cause ectopic heart beats, tachycardia, hypotension, hypertension and excessive diuresis

Dobutamine: If dopamine fails to improve BP, dobutamine is recommended as second line drug. In neonates it is usually given together with dopamine infusion.

Dosage: 2-10mcg/kg/min by continuous infusion. Maximum: 20mcg/kg/min

Route: Intravenously

Adverse effects: dose related. Ectopic heart beats, increased heart rate, and blood pressure elevations

Renal failure management:

Manage renal failure if urine output is <0.5ml/kg/hr after 48 hours of life.

Respiratory support may be necessary for babies with Hypoxic Ischemic Encephalopathy.

Prevent cerebral edema and avoid fluid overload:

Restrict maintenance fluids (by up to 70%) if cerebral oedema is suspected on the basis of neurologic signs. Observe for hypertension and SIADH (hyponatremia, volume overload and decreased urine output). Manage SIADH with restriction of maintenance fluids.

Treat seizures:

Metabolic disturbances should be excluded before initiating anticonvulsant therapy.

Phenobarbitone: Is the initial drug of choice. Initially a 20mg/kg loading dose of phenobarbitone is used (watch breathing if not ventilated). If no effect a further 10-20 mg/kg loading may be given, followed by a maintenance dose of 3-5 mg/kg PO or IV every 12 hours, started 12-24 hours after the loading dose.

Phenytoin is usually added when seizures are not controlled by phenobarbitone. The loading dose is 15-20mg/kg I/V followed by maintenance dose of 4-8 mg/kg/day.

Clonazepam may be useful as a second line 100-200 microgram/kg loading followed by an 100 microgram/kg/day.

Gastrointestinal Care:

Keep NPO. Pass Orogastric tube and attach it with bag on gravity to decompress gut. Look for signs of NEC. If the patient is clinically stable, start feeding gradually according to feeding guideline.

Hematologic Care:

If there is thrombocytopenia and coagulopathy (prolonged PT, APTT) correct it accordingly by platelet and plasma administration.

Nutrition:

Asphyxiated infants are at risk of developing necrotizing enterocolitis. They are at risk also of aspiration if there is pharyngeal incoordination. There may be intolerance to feed because of reduced small intestinal motility, therefore enteral feeding should be commenced cautiously.

Brain or Total Body Cooling:

There are increasing data to support cooling therapy in the treatment of neonatal hypoxic ischaemic encephalopathy. Such treatment will be guided by local or national protocols.

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6. Jacobs SE, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. **Cochrane Database Syst Rev.** 2007 Oct 17;(4):CD003311.

Neonatal Hyperbilirubinemia

Guideline for Neonatal Hyperbilirubinemia

Hyperbilirubinemia is very common and usually benign in the term newborn infant and the late preterm infant at 35 to 36 completed weeks' gestation. Critical hyperbilirubinemia is uncommon but has the potential for causing long-term neurological impairment.

Clinical assessment: Clinicians should ensure that all infants are routinely monitored for the development of jaundice. Clinically jaundice is assessed by blanching the skin with digital pressure revealing the underlying color of the skin and subcutaneous tissue. The assessment of jaundice should be performed in a well lit room, or preferably in day light. Jaundice is seen first in the face and progress caudally to the trunk and extremities¹.

Laboratory measurements: measurement of total serum bilirubin (TSB) and/or total cutaneous bilirubin (TcB) should be performed in every newborn who develops jaundice in the first 24 hours and repeating of TSB will depend on the first bilirubin value, the age of infant and the evolution of jaundice².

When indicated, infants should be treated with phototherapy or exchange transfusion: recommendation for treatment is given in fig 3 and 4.

Acute bilirubin encephalopathy: Immediate exchange transfusion is recommended in any infant who is jaundiced and manifests the signs of moderate to advanced encephalopathy (hypotonia, arching, retrocollis, opisthotonus, fever, high pitched cry) even if the TSB is falling.

Fig 3. Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation¹

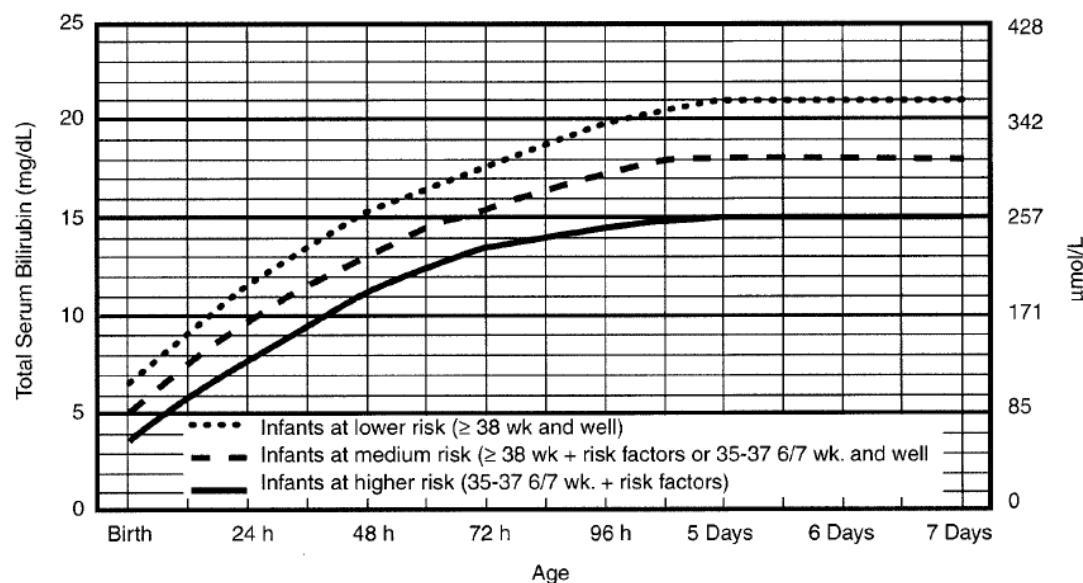
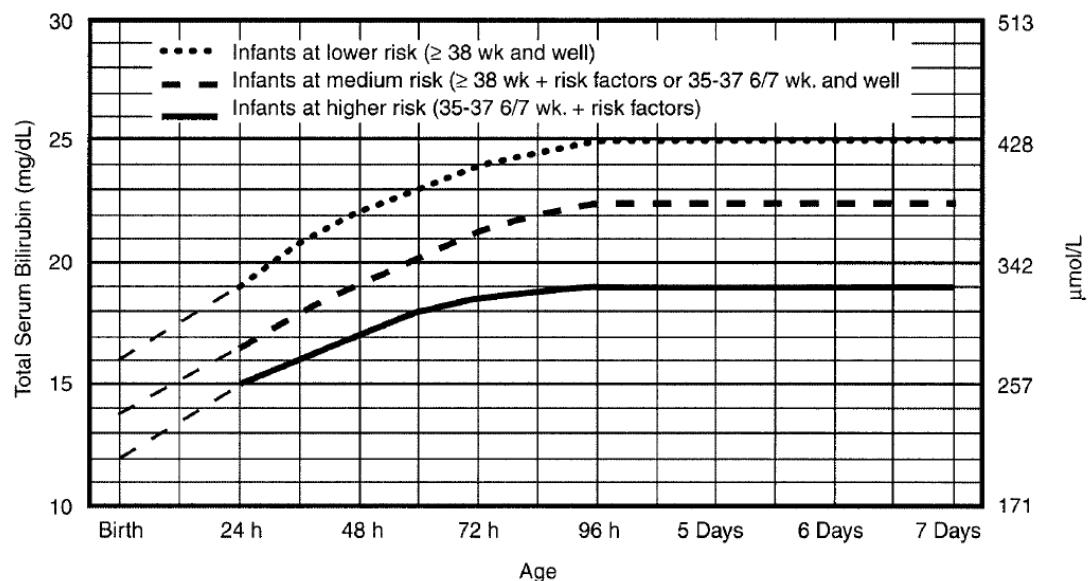


Fig 4. Guidelines for exchange transfusion in infants 35 or more weeks' gestation¹



Hyperbilirubinemia in preterm and low birth weight babies:

Basic pathophysiology of jaundice is the same in term and preterm babies but lower gestation babies are at higher risk of developing hyperbilirubinemia and require close surveillance and monitoring. TSB for intervention also vary in term, near term, and preterm neonates <35 weeks period of gestation.

Clinicians should ensure that all premature infants are routinely monitored for the development of jaundice. TSB should be measured at 24 hour of age with follow up estimation every 12-24 hours until the level stabilizes. TSB should be repeated within 12- 24 hours of stopping phototherapy or sooner if clinical jaundice reappears.

The American Academy of Pediatrics recommends guideline for neonates >35 weeks of gestation, the management of preterm infants are still a grey zone, and most centers have individual treatment guidelines. The following tables provide guidelines for intervention in LBW and/or preterm babies³.

Guidelines for the use of phototherapy and exchange transfusion in low birth weight infants based on birth weight³

Table 7. Total bilirubin level (mg/dl ($\mu\text{mol/L}$))*

Birth weight (g)	Phototherapy†	Exchange transfusion‡
≤ 1500	5-8 (85-140)	13-16 (220-275)
1500-1999	8-12 (140-200)	16-18 (275-300)
2000-2499	11-14 (190-240)	18-20 (300-340)

*Consider initiating treatment at these levels. Range allows discretion based on clinical conditions or other circumstances. Note that bilirubin levels refer to total serum bilirubin concentrations. Direct reacting or conjugated bilirubin levels should not be subtracted from the total.

 Used at these levels and in therapeutic doses, phototherapy should, with few exceptions, eliminate the need for exchange transfusions.

 Levels for exchange transfusion assume that bilirubin continues to rise or remains at these levels despite intensive phototherapy.

Guidelines for use of phototherapy and exchange transfusion in preterm infants based on gestational age³

Table 8. Total bilirubin level (mg/dl (μmol/l))			
Gestational age (weeks)	Phototherapy	Exchange transfusion	
		Sick*	Well
36	14.6 (250)	17.5 (300)	20.5 (350)
32	8.8 (150)	14.6 (250)	17.5 (300)
28	5.8 (100)	11.7 (200)	14.6 (250)
24	4.7 (80)	8.8 (150)	11.7 (200)

Guidelines for initiating phototherapy and exchange transfusion in ELBW infants³

Table 9. Birth weight (g)	Aggressive management		Conservative management	
	Phototherapy begins	Exchange transfusion	Phototherapy begins	Exchange transfusion
501–750	ASAP after enrollment	$\geq 13.0 \text{ mg/dl}$	$\geq 8.0 \text{ mg/dl}$	$\geq 13.0 \text{ mg/dl}$
751–1000	ASAP after enrollment	$\geq 15.0 \text{ mg/dl}$	$\geq 10.0 \text{ mg/dl}$	$\geq 15.0 \text{ mg/dl}$

Bilirubine conversion values:

>8.0 mg/dl >136.8 μ mol/L

>10.0 mg/dl > 171 μ mol/L

>13.0 mg/dl > 222.3 μ mol/L

>15.0 mg/dl > 256.5 μ mol/L

REFERENCES

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2. American Academy of Pediatrics. Clinical practice guideline. Management of hyperbilirubinemia in the newborn infants 35 or more weeks of gestation. *Pediatrics*.2004;114:297-316.
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Hypotension in Neonates

Table 10. Blood pressure ranges¹

Birth weight (g)	Mean pressure	Systolic (mm Hg)	Diastolic (mm Hg)
501–750	38–49	50–62	26–36
751–1000	35.5–47.5	48–59	23–36
1001–1250	37.5–48	49–61	26–35
1251–1500	34.5–44.5	46–56	23–33
1501–1750	34.5–45.5	46–58	23–33
1751–2000	36–48	48–61	24–35

Assessment for the cause of hypotension: Assess the baby to find out the cause of hypotension. The basic decision is whether the infant requires volume replacement or administration of inotropic agents.

History: A careful history should be obtained to rule out birth asphyxia, blood loss (antenpartum or postpartum), drug infusion, birth trauma (adrenal hemorrhage or liver injury), and cardiac problem.

Physical examination: a careful physical examination will often reveal which organ system is involved

Chest X-ray: A small heart is seen in volume depletion; a large heart is seen in cardiac disease.

Management:

Empirical volume expansion with crystalloid (normal saline) (10ml/kg intravenously over 30 minutes) should be started if unsure of the cause of hypotension

If there is a response, continue volume expansion (Volume administration is less effective in the immediate postnatal period, and its extensive use is associated with significant untoward effects, especially in preterm infants)

Provide respiratory support: as needed

Correct metabolic acidosis: If there is no response,

An inotropic agent should be started:

Dopamine: See Section on HIE (page 36)

Dobutamine: See Section on HIE (page 36)

Refractory hypotension:

During the course of their disease, some of the sickest newborns become unresponsive to volume and pressor administration; this is called as refractory hypotension.

Definition: Refractory hypotension is defined as mean arterial pressure < than the gestational age despite a total inotrope dose of 20 microgram/kg/minute ⁽²⁾. In these cases, stress dose of hydrocortisone 1mg/kg 8 hourly for 5 days rapidly up regulates cardiovascular adrenergic receptor and decreases the requirement for pressor support in the critically ill newborn with volume and pressor resistance hypotension⁽³⁾

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3. Baker CF, Barks JD, Engmann C, Vazquez DM, Neal CR. Hydrocortisone Administration for the Treatment of Refractory Hypotension in the Critically ill Newborns. J Perinatol.2008; 28:412-419.

Patent Ductus Arteriosus (PDA) in Preterm Neonates: (<34 weeks gestation)

Preterm infants have a high incidence of persistent PDA, about 40-60%. A clinically symptomatic PDA has been associated with significant morbidity in this high risk population.

Clinically significant PDA: PDA diagnosed on the basis of continuous or systolic murmur heard best in the left subclavicular area associated with hyperactive precordium and a wide pulse pressure or bounding pulses.

Heart failure is assessed on the basis of one or more of the following clinical findings: tachycardia, gallop rhythm, hepatomegaly, cardiomegaly, deteriorating respiratory status, and radiologic evidence of increased pulmonary vascularity or pleural fluid.

Echocardiography: PDA is echocardiographically significant when ductal size > 1.5 mm or the left atrial to aortic root ratio >1.4.

Management of PDA in newborn <34 weeks gestation:

1) The following should be tried initially:

- a) Fluid restriction:** Fluid should be restricted to 2/3 rd of maintenance fluid.
- b) Furosemide:** 1 mg/kg intravenously twice a day
- c) Digoxin** (if there are signs and symptoms of cardiac failure)

If no improvement:

Then consider:

2) Non steroidal anti inflammatory drugs: Indomethacin or Ibuprofen

Randomized controlled trials have demonstrated similar efficacy in ductus closure with these two agents in infants born at up to 34 weeks of gestation ⁽¹⁾

1) Indomethacin:

Dose: 0.2mg/Kg/day, enterally or parenterally, 3 doses. Second and third doses are given 12 and 36 hour after the first dose. The second and third doses are 0.1mg/kg/dose if the infant is <7 days old and the infant is <1250 g birth weight. If the infant is either > 7 days old or >1250 g, then the second and third dose are also 0.2mg/kg ⁽²⁾

Monitor: urine output, serum creatinine, and platelet count.

Measure serum creatinine and platelets before each dose, hold the drug if serum creatinine is >2 mg/dl, platelet count is <60,000 or urine output is <1.0ml/kg/day, or if there is evidence of NEC or bleeding disorders.⁽³⁾

Feeding should be given cautiously and monitor for aspirates, abdominal distension, and other signs and symptoms of necrotizing enterocolitis.

After a course of indomethacin, assess the baby clinically, and if possible by echocardiography. If there is still a significant PDA consider a second course of indomethacin. In 20-30% of cases, the ductus will reopen after the first course of indomethacin. A significant proportion of these cases will benefit from a second course of indomethacin.

Side effects: Renal dysfunction, gastrointestinal hemorrhage, necrotizing enterocolitis, intraventricular hemorrhage, platelet dysfunction.

2) Ibuprofen: Oral Ibuprofen (as shown in various studies) is as effective as indomethacin in ductal closure⁽⁴⁾

Dose: 10mg/kg followed by 2 additional doses of 5mg/kg on consecutive days

Clinical improvement after medical treatment: Murmur abolished or decreased in intensity, if on ventilator parameters decreased. Signs and symptoms of heart failure improved.

Surgical Ligation: Failure of ductus to close after one or two courses of drug therapy along with persistence of heart failure and ventilator dependence.

Algorithm for management of PDA in Preterm Neonates

Step 1

Fluid Restriction

Furosemide

Digoxin (If signs and symptoms of cardiac failure Present)

Step 2

NSAIDs: Indomethacin: 0.2mg/kg followed by 0.1mg/kg if <1250gm or >7days old, the dose is same if weight>1250gm or >7 days old given at, 8 and 36 hours

Or

Ibuprofen: 10mg/kg at 0hour then at 5mg/kg at 24hr and 48hr

Step 3

Consider surgical ligation if medical treatment fails along with persistence heart failure or ventilator dependency

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Sepsis

Criteria for suspecting sepsis:

The signs and symptoms of neonatal sepsis often are nonspecific. Most, but not all, infants with sepsis have respiratory signs, including cyanosis or apnoea. Other signs such as feeding difficulties or lethargy are nonspecific and may be subtle or insidious. Thus, a high index of suspicion is required to identify and evaluate at-risk infants.

Presenting features of early onset systemic infection in preterm infants

- Respiratory distress
 - Unstable temperature
 - Floppiness
 - Irritability
 - Poor feeding
 - Early onset jaundice
 - Apnoea
 - Poor perfusion
 - Tachycardia
 - Seizures
-

REFERENCE

William McGuire, Linda Clerihew, Peter W Fowlie. Infection in the preterm infant. BMJ 2004;329:1277-1280

Investigations:

- Blood culture
- Take into consideration urine culture and cerebral spinal fluid culture also

Specific Management:

After blood culture, first line antibiotic therapy should be started without delay. Local guidelines for antibiotics should exist, taking into account the prevalence and sensitivities of organisms within each unit. Consider changing antibiotics if there is no clinical improvement or according to culture-sensitivity report.

Prevention

- Spacing
- Avoid overcrowding
- Good handwashing before and after touching the baby
- Application of alcohol gel

Supportive management:

- Provide thermoneutral environment
- Provide supplemental O₂ if required, Ventilatory support may be required in some cases.
- Monitor vital signs, peripheral perfusion and urine output.
- Monitor renal function to avoid aminoglycoside toxicity.
- Fluid resuscitation. If there is poor peripheral perfusion (capillary refill>3 sec, give normal saline 10ml/kg IV bolus. Continue IV fluids. IV bolus can be repeated if necessary.
- Treat convulsions if present.
- Give blood products as indicated.
- Monitor and correct electrolyte imbalance if present.
- Blood sugar monitoring

REFERENCE

Edwards MS: Postnatal Bacterial Infections. In Fanaroff AA, Martin J: Neonatal Perinatal Medicine: Diseases of the Fetus and Infant, 8th ed. Mosby. 2006. P791-804.