NATIONAL GUIDELINES FOR NEWBORN CARE

VOLUME II

- Neonatal jaundice
- Respiratory distress in newborn
- Neonatal infections and antibiotic therapy
- Neonatal seizures
- Post-resuscitation management of a neonate with Hypoxic Ischaemic Encephalopathy (HIE)

Ministry of Health

2020

Family Health Bureau

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World Health Organization

SRI LANKA COLLEGE OF PAEDIATRICIANS

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STATEMENT OF INTENT

The main purpose of these guidelines is to improve the quality of clinical care provided by the health care providers at all levels. These parameters of practice should be considered recommendations only. The ultimate judgment regarding a particular clinical procedure or a treatment plan must be made by the clinician in light of the clinical data gathered from the patient and the diagnosis and treatment options available.

Designed by Ajith Kumara Jayamanne

Preface

Sri Lanka has a vision to have no preventable deaths of mothers, foetuses and newborns, where every pregnancy is planned and wanted, every birth celebrated, and women, babies and children survive, thrive and reach their full potential as per the Maternal and Newborn Health Strategic Plan 2017-2025. For the country to ensure reaching the set vision, goals and objectives evidence based updated guidelines for the use of staff caring for new-borns are essential.

This set of guidelines is updated based on the current updated global evidence in place. As per the previous National Guidelines for Newborn Care 2014, greater emphasis is on improving the quality of neonatal care services in the country with a view of further reducing neonatal morbidity and mortality in Sri Lanka. This is an attempt to improve the quality and uniformity of clinical care with efficiency, cost effectiveness and accountability.

We highly appreciate the contribution made by the Consultant Neonatologists and Consultant Paediatricians from the Sri Lanka College of Paediatricians and Consultant Community Physicians of the Family Health Bureau in updating, adopting and developing these guidelines. Further these guidelines are developed as per national policies, strategies and standards and considering the facilities and resources available in the country. As such this set of guidelines are national guidelines for the conditions described and all health care workers are requested to follow the same.

Dr Asela Gunawardena
Director General of Health Services
Ministry of Health
Sri Lanka

2020

Message from the President of Sri Lanka College of Paediatricians

Sri Lanka has set an example to many developing countries and reached a neonatal mortality rate of 6 per 1000 live births in 2015. However, this accounts for over 70% of infant mortality and regional and district disparities are observed. Reduction of mortality and morbidity remain a challenge despite continuous effort of health care staff, even with a lot of effort put into training of human resources and improving infrastructure. Focusing on the neonate specifically in these areas is a priority which remains unchanged. Simple interventions like preconception folic acid, antenatal corticosteroids for preterm delivery, preventing inadvertent oxygen administration and using a pulse oximeter for neonatal resuscitation, delayed cord clamping, delivery onto abdomen of the mother, using plastic bags for preterm babies, preventing hypothermia, simple inflation and ventilation breaths by the midwife or nurse in unexpected situations, passive head cooling for asphyxia, promotion of exclusive breast feeding on demand could be practiced in low resource settings and has a direct link to reduce neonatal mortality and morbidity. Furthermore, advanced newborn care such as treatment of infections, neonatal ventilation, extra care for premature newborns, surgical interventions, therapeutic cooling and NO therapy are performed with the aim of further reducing neonatal mortality and improving the quality of life of newborns.

A team of Consultant Neonatologists, Consultant Paediatricians and Consultant Community Physicians have been working on revising and updating these newborn care guidelines. These guidelines for newborn care will further go a long way to bring uniformity in standards of neonatal care across the country to further improve quality of care. The health care providers all over the country can utilize these guidelines and care for newborns in a uniform manner using the best standards of care.

I express my sincere gratitude towards all who worked hard to revise this document. I am certain that, these guidelines will have a great impact on improving the quality of care and reducing the mortality and morbidity among newborns in Sri Lanka.

Prof Vasantha Devasiri
President
Sri Lanka College of Paediatricians

Acknowledgements

Revising the existing national newborn care guidelines is a timely need in keeping with the new scientific evidence available globally, thus to improve quality survival of newborns via evidence based practices. Sri Lanka aims at reaching the sustainable developmental goals (SDGs) by the year 2030. Preventing all preventable deaths among newborns cannot be achieved without achieving quality of care. Sri Lanka is already on track to achieve the targeted neonatal mortality rate of 2 per 1000 live births in concordance with the SDG targets.

Quality coverage of newborn care provided at all levels is essential to ensure further reduction of neonatal mortality and morbidity. With 99.9% of births occurring in institutions, care given during birth and immediately after, lead to triple investment including reduction of neonatal deaths.

Publishing the updated National Guidelines for Newborn Care 2020 would not have been possible without the commitment and support from many individuals and organizations. We greatly appreciate the administrative support extended by Dr. Susie Perera, Deputy Director General, Public Health Services II, Ministry of Health.

The Family Health Bureau gratefully acknowledges contributions of all the technical experts of the guideline development committee and the Sri Lanka College of Paediatricians for updating the guidelines despite their busy schedules.

We are thankful to the UNICEF country office Sri Lanka for supporting this activity technically and financially.

Electronic version of these guidelines will be available for ease of reference for all health care workers. The heads of health institutions and technical supervisors are expected to ensure availability of this document in all neonatal units, postnatal units and labour rooms for easy access. We hope the updated national newborn care guidelines will help to improve quality of care for our newborns by adhering to the highest standard of care while maintaining uniformity of health services in Sri Lanka so all newborns may survive, thrive and transform to reach their highest growth potential.

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Content

List of Abbreviations

AC	Assist control
ACD	Acid citrate dextrose
ANC	Absolute neutrophil count
BNF	British National Formulary
CFL	Compact fluorescent lamp
CNS	Central nervous system
CONS	Coagulase negative staphylococcus
CPAP	Continuous positive airway pressure
CPD	Citrate phosphate dextrose
CRP	C-reactive protein
CRT	Capillary refill time
CSF	Cerebro- spinal fluid
CTG	Cardiotocography
CVP	Central venous pressure
CXR	Chest X –Ray
DAT	Direct antibody test
DCT	Direct Coomb's test
DIC	Disseminated intravascular coagulation
ECMO	Extra corporeal membrane oxygenation
EEG	Electroencephalogram
EOS	Early onset sepsis
ESR	Erythrocyte sedimentation rate
FBC	Full blood count
FFP	Fresh frozen plasma
FiO2	Fraction of inspired oxygen
G6PD	Glucose 6 phosphate dehydrogenase
GBS	Group B streptococci
HFOV	High frequency oscillatory ventilation
HIE	Hypoxic ischaemic encephalopathy
IC	Intercostal
IEM	Inborn-errors of metabolism
IL	Interleukin
INR	International normalised ratio
ITR	Immature neutrophils / Total neutrophils ratio
IV	Intra venous

IVIG	Intravenous Immunoglobulin
LED	Light emitting diode
LOS	Late onset sepsis
LP	Lumbar puncture
MAS	Meconium aspiration syndrome
MRSA	Methicillin resistant Staphylococcus aureus
MSAF	Meconium stained amniotic fluid
NG	Nasogastric
NICU	Neonatal intensive care unit
NIPPV	Non – invasive positive pressure ventilation
PCO_2	Partial pressure of carbondioxide
PDA	Patent ductus arteriosus
PFO	Patent foramen ovale
aPEEP	Positive end-expiratory pressure
PPHN	Persistent pulmonary hypertension of the newborn
PT	Prothombin time
RDS	Respiratory distress syndrome
ROM	Rupture of membranes
SIMV	Synchronised Intermittent positive pressure ventilation
SIPPV	Synchronised intermittent positive airway pressure ventilation
SIR	Systemic inflammatory response
SPO2	Percentage of haemoglobin saturated with oxygen
T4	Thyroxine
TCL	Total leukocyte count
TGF-β	transforming growth factor-beta
TNF	Tumour necrosis factor
TORCH	Toxoplasma, rubella, cytomegalovirus, herpes, syphilis
TSB	Total serum bilirubin
TSH	Thyroid stimulating hormone
TTN	Transient tachypnoea of newborn
US	Ultra sound
UTI	Urinary tract infection
VZIG	Varicella zoster immunoglobulin
WBC	White blood cells
WOB	Work of breathing
ZIG	Zoster immunoglobulins

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Disclaimer

These guidelines are based on current best available evidence and consensus opinion of the Consultants involved in the development of guidelines. They are neither intended to replace the process of critical evaluation of every case and nor is it intended to dictate an exclusive course of management or treatment. It must be interpreted with reference to individual patient needs, available resources and limitations unique to the institution and variations in local populations. This guideline on Neonatal Care has been developed based on the best available evidence at the time of preparation. It is the responsibility of the users of the guideline to keep updated with the latest evidence relevant to the management of patients under their care.

Introduction

Clinical guidelines are systematically developed statements which assist clinicians in making decisions about appropriate treatment for specific conditions based on the best scientific evidence at the time of development. Guidelines are not intended to limit the clinical freedom. However, clinicians are expected to follow these recommendations as the basis for their decision making. Availability of resources, the existing situations and the expectations of individual families under their care need to be considered by the clinicians.

These guidelines are developed by the group of consultants in the guidelines development committee. The sources of information that were used as references in preparing the guidelines included the UK NICE (National Institute for Clinical Excellence)guidelines, American Academy of Pediatrics guidelines, SDF Facility Based Care for the Sick Newborn manual, Roberton's Text book of Neonatology, WHO recommendations and relevant research papers from peer reviewed journals. The information from these sources were combined with our local expert opinion and knowledge of available technical facilities in the country when formulating the guidelines. The latest available scientific evidence based recommendations have been made as far as possible. The draft guidelines were presented to the wider forum of paediatricians and neonatologists, in order to obtain feedback after which a consensus was arrived at. The guidelines were then presented to the Technical Advisory Committee on Newborn and Child Health of the Ministry of Health and consensus was arrived at with the participation of a multidisciplinary team including medical administrators, provincial health authorities, representatives of the Sri Lanka College of Paediatricians and other relevant professional colleges and national programme managers and senior nursing officers.

Scope

The guidelines are intended to assist all health care professionals at all levels of institutions where newborn care is being provided, in the clinical management of normal and sick newborns

NEONATAL JAUNDICE

Chapter 7

Neonatal jaundice

7.1 Introduction

Jaundice is yellow discolouration of skin and sclera. Neonatal jaundice is a common problem which often does not require intervention. However, jaundice in the newborn might sometimes signal a serious, potentially treatable illness which may cause neurological damage (bilirubin encephalopathy including subsequent kernicterus), if the bilirubin level is significantly elevated.

7.2 Physiological and pathological jaundice

Jaundice can be seen in 60% of term infants and 80% of preterm infants. It is mostly physiological. However, it can be pathological requiring special treatment and investigations.

7.2.1 Features of physiological jaundice (all of the following)

- Jaundice that first appears between 24-72 hours of age
- Maximum intensity is seen on 4-5th day in term and 7th day in preterm neonates
- Clinically undetectable after 14 days (term); 21 days (pre-term)

NB: Physiological jaundice is a diagnosis of exclusion

7.2.2 Features of pathological jaundice (any of the following)

- Clinical jaundice in first 24 hrs of life
- Total serum bilirubin (TSB) increasing by > 5mg/dl/day (85 µmol/l/day) or 0.5 mg/dl/hr (8.5µmol/l/hr)
- Conjugated or direct bilirubin level greater than 1 mg/dL when the total bilirubin is less than 5 mg/dL or more than 20% of the total bilirubin if the total bilirubin is greater than 5 mg/dL
- Clinical jaundice persisting for > 2 weeks* in full term and >3 weeks in preterm neonates (prolonged jaundice).

(***NB;** Except in the cases of breast-milk jaundice)

7.3 Causes of jaundice

Hyperbilirubinaemia in the first week of life is usually of the unconjugated (indirect) variety. Conjugated hyperbilirubinemia (direct) occurs less commonly, but is always pathological.

Causes of jaundice are usually classified based on the time of onset of jaundice.

7.3.1 Appearing within 24 hours of age

- Haemolytic disease of newborn: Rh, ABO and minor group incompatibility – most common
- Infections: sepsis
- Hereditary haemolytic anaemias; congenital spherocytosis, G6PD deficiency

7.3.2 Appearing after 24 hours of life

- All of the above
- Physiological – most common
- Breastfeeding / starvation jaundice - common
- Polycythaemia
- Concealed haemorrhages: cephalhaematoma, subaponeurotic haemorrhage, subarachnoid bleed, intraventricular haemorrhage.
- Metabolic disorders eg; Galactosaemia, Crigler-Najjar

7.3.3 Prolonged jaundice - duration > 2 weeks

Prolonged unconjugated hyperbilirubinaemia

- New/ persisting sepsis
- Metabolic - hypothyroidism, galactosaemia
- Persisting haemolysis
- Breast milk jaundice

Prolonged conjugated hyperbilirubinaemia

- Neonatal hepatitis – congenital infections, α_1- Antitrypsin deficiency
- Neonatal sepsis – mainly coliform
- Extra hepatic biliary atresia
- Choledochal cyst
- Galactosaemia, tyrosinaemia
- Total parenteral nutrition , inspissated bile syndrome,

7.4 Jaundice within the first two weeks of life

7.4 .1 Approach to a jaundiced baby

The following questions need to be addressed

- What is the gestation?
- What is the birth weight and current weight?
- What is the postnatal age in hours?
- Is the baby clinically ill or well?
- What is the visual estimation of jaundice? (Fig 7.1)

After the initial evaluation, decide whether

- The baby needs further investigations for jaundice?
- The baby needs phototherapy / exchange transfusion?
- The baby has features of encephalopathy?

7.4.2 Assessment of a jaundiced neonate

In the assessment of a neonate with jaundice, the history and examination are directed towards determining aetiology of jaundice, assessing the severity and identifying any complications.

7.4.2.1 Severity of jaundice

When a neonate is clinically jaundiced, the total serum bilirubin (TSB) is usually >5 mg/dl (85 µmol/l). Jaundice in newborn progresses in a cephalocaudal direction and thus the extent of yellowness of the skin is

useful to assess the level of bilirubin. Kramer's criteria are used to clinically estimate severity (Figure 7.1). However, this can be unreliable, especially in dark skinned babies.

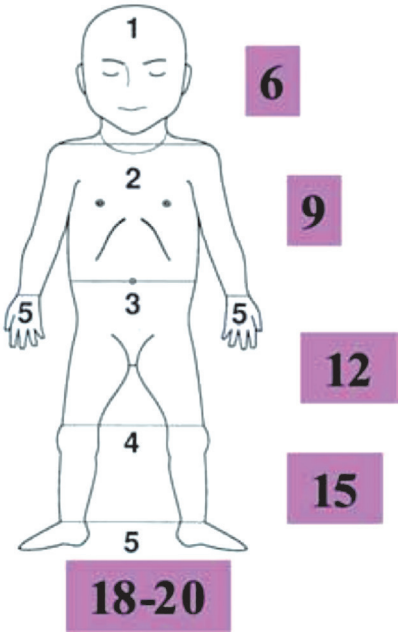

Figure 7.1: Estimation of severity of jaundice(mg/dl) by visual perception, Kramer 1969

Check serum bilirubin level if there is any visual jaundice

Once baby is under phototherapy visual assessment is inaccurate.

A transcutaneous bilirubinometer is a non-invasive method of checking the bilirubin levels in babies >35 weeks gestation. The result is available immediately. However, if the levels are found to be high, a confirmatory test with a serum sample is required.

7.4.2.2 Features of acute bilirubin encephalopathy

The baby needs to be assessed for features of acute bilirubin encephalopathy. These features range from hypotonia, lethargy, poor feeding, irritability to hypertonia of extensor muscles, opisthotonus, respiratory distress, shrill high pitched cry, apnoea, loss of moro reflex, seizures and coma.

7.4.3 Laboratory testing

All visibly jaundiced babies should have a blood sample for total serum bilirubin (TSB) estimation.

Plot these values on gestation specific treatment threshold graphs and decide about intervention. The treatment threshold graphs are available at the end of the chapter.

Management decisions should be based on the total serum bilirubin value and not the unconjugated bilirubin value.

Babies needing phototherapy / exchange transfusion should have a jaundice workup which includes

- Haemoglobin, reticulocyte count, blood picture for evidence of haemolysis
- Blood group: mother and baby - to diagnose Rh or ABO incompatibility
- DCT (Coomb's test) – to diagnose immune mediated hemolysis
- Septic screen if sepsis is suspected
- **Save baby's and mother's blood sample for cross-matching.**

7.4.4 Management

Management of jaundice during the first 2 weeks of life is directed towards, reducing the level of bilirubin to prevent CNS toxicity irrespective of the cause of hyperbilirubinaemia. Specific therapy to alleviate the cause can be used if indicated.

Reduction of serum bilirubin is achieved by increasing the elimination of bilirubin.

1. Optimising breastfeeding and improving hydration decreases the enterohepatic circulation and helps to eliminate bilirubin via stool.
2. Phototherapy converts the bilirubin to a water-soluble form and eliminates it via urine.
3. Exchange transfusion removes the blood with high amount of bilirubin and replaces with blood without bilirubin.

7.4.4.1 Starvation / inadequate breastfeeding jaundice

One of the most common causes of jaundice requiring phototherapy in the Sri Lankan setting is inadequate breastfeeding/starvation jaundice which is due to delayed establishment of breastfeeding.

Delayed establishment of breastfeeding causes decreased elimination of bilirubin due to increased enterohepatic circulation.

Diagnosis

Weight loss nearing or exceeding 10% of birth weight in an otherwise well child is suggestive of the diagnosis. Baby may have features of dehydration. The blood investigations will be normal except for the elevated bilirubin, unless it co-exists with a haemolytic disease.

Treatment

- The mainstay of treatment is to establish breastfeeding with correct positioning and attachment and thereby decrease the enterohepatic circulation
- Expression of breast milk 2-3 hourly will increase production of breast milk (as poor attachment → reduced emptying of breast → increased feed-back inhibitor → reduced milk production)
- Feeding the baby expressed breast milk via cup after direct breastfeeding may be useful in babies with marked weight loss.
- Intravenous fluids are needed only in the case of severe dehydration – as it does not decrease the enterohepatic circulation
- Phototherapy may be given if above the threshold to increase the elimination of bilirubin.

7.4.4.2 Phototherapy

- Advantages: non-invasive, effective, inexpensive and easy to use

7.4.4.2.1 Optimising phototherapy

Ideal irradiance

- Use of intensive phototherapy with irradiance in blue-green spectrum of at least 20-30μW/cm^2/nm and delivered to as much of the infant's surface area as possible.

- The light waves convert the bilirubin to water soluble nontoxic forms which are then easily excreted.

Optimise the distance and keep the lights parallel and directly above the baby

- Keep babies at the distance recommended by the manufacturer for the phototherapy lights to be maximally effective and safe (avoid hyperthermia).
- In case of fluorescent light phototherapy machines baby should be kept about 18 inches away from the light due to increased heat emission.
- In the case of LED lights baby can be kept 10-15cm from the light due to minimal heat emission

Maximising the area of exposure

- This involves exposure of the naked baby to blue light /CFL/ LED of wave length 450-470nm.
- Use eye shields
- Dress the baby in the smallest possible nappy to prevent soiling with urine and stool.
- Turn baby every 1-2 hours to maximise the area of exposure.

Maximising the time under phototherapy

- Do all nappy changes while baby remains under the light, especially if the bilirubin levels are near or above the exchange level.
- Feed expressed breast milk via cup while baby remains under the light, especially if the bilirubin levels are near or above the exchange level – keep the baby continuously under the phototherapy light until the bilirubin levels are well below the exchange level – after which direct breastfeeding can be resumed.

7.4.4.2.2 Provision of phototherapy

- Generally single phototherapy is initiated
- **Continuous double surface phototherapy**

Indications for *continuous double surface phototherapy*

- Bilirubin level is rising > 0.5mg/dl/hr (8.5µmol/l/hr)
- Bilirubin is at a level within 3mg/dl (50 µmol/l) below the level for which exchange transfusion is indicated
- Bilirubin level fails to respond to single phototherapy (i.e. bilirubin continues to rise, or does not fall, within 6 hours of starting single phototherapy)

Step down to single phototherapy

- When bilirubin level falls to a level of 3mg/dl or 50 µmol/l below the threshold level for exchange transfusion
- Baby will appear bleached when under phototherapy and hence clinical assessment of jaundice is not reliable. Serum bilirubin must be monitored.
- Prophylactic phototherapy does not offer any clinical benefit in the course of hyperbilirubinaemia
- Repeat serum bilirubin measurement 4–6 hours after initiating phototherapy
- Repeat serum bilirubin measurement every 4-6 hours if the serum bilirubin level is rising or not falling while under phototherapy
- Repeat serum bilirubin measurement every 12-24 hours when the serum bilirubin level is stable or falling.
- Stop phototherapy once bilirubin levels are below the phototherapy level by 2 -3 mg/dl (35 - 50µmol/l) as per postnatal age.
- In case of haemolytic jaundice, check bilirubin levels 12 - 18 hours after stopping phototherapy to check for rebound increase.

7.4.4.2.3 Side effects of phototherapy (all are reversible)

- Hypo or hyperthermia: common side effect - therefore monitor temperature regularly.

  Other side effects are not common.

- Increased insensible water loss is rare with LED phototherapy as heat emission is much less

- Loose green stools: ensure hydration is good
- Skin rashes: harmless, no need to discontinue phototherapy
- Bronze baby syndrome: occurs if phototherapy is used in conjugated hyperbilirubinaemia. If so, discontinue phototherapy

Do not use sunlight as treatment for jaundice.

7.4.4.2.4 Biliblanket

In this method of providing phototherapy the baby can be kept on or wrapped in this blanket which emits the phototherapy light. A blue halogen bulb is directed into a fibre optic mat for the purpose.

Advantages

- Problem of the baby becoming irritable when kept alone under the traditional phototherapy light is resolved as baby can be held in the mother's arms.
- Breastfeeding can be continued without interruption while holding baby in this blanket.
- For babies in incubators, the baby can be placed on the biliblanket when double phototherapy is required

Disadvantage - efficacy is slightly less than when using LED

7.4.4.3 Exchange transfusion

- It is an effective and reliable method to reduce serum bilirubin.
- It should be performed if the TSB remains in exchange transfusion range as per treatment threshold graphs **despite effective phototherapy.**
- **Immediate exchange transfusion is indicated if features of bilirubin encephalopathy are evident.**
- If facilities for exchange transfusions are not available at your centre early referral to a higher centre is indicated.
- Delay in treatment may result in permanent brain damage.
- **When referring a baby with jaundice, make sure that either the mother is referred or mother's blood sample is sent.**

- Use a double-volume exchange transfusion (2 x 80 ml/kg)
- Umbilical vessels are the preferred access method for performing an exchange transfusion
- Use acid citrate dextrose (ACD) or citrate phosphate dextrose (CPD) blood less than 5 days old.
- Electrolytes, blood gases and vital signs should be monitored during exchange transfusion

7.4.4.3.1 Type of blood

- **Rh isoimmunisation**

  The best choice would be O negative packed cells suspended in AB positive plasma. O negative whole blood or cross-matched baby's blood group (Rh negative) may also be used.

- **'ABO' isoimmunisation**

  O group (Rh compatible) packed cells suspended in AB plasma or O group whole blood.

- Other situations baby's blood group should be used.
- All blood must be cross-matched against maternal plasma.

7.4.4.3.2 Following exchange transfusion

- Continue double surface phototherapy during and after procedure
- Measure serum bilirubin level within 2 hours and manage according to threshold graphs

7.4.4.4 Role of intravenous immunoglobin (IVIG)

Intravenous immunoglobulin (IVIG) may be used in the dose of 0.5-1g/kg over 4 hours for decreasing the need of exchange transfusion in neonates with proven isoimmune haemolytic jaundice (established hyperbilirubinaemia with positive DCT or blood picture).

Use of fresh frozen plasma, albumin, phenobarbitone and other oral medication for the treatment of jaundice are not warranted.

7.5 Care of babies with prolonged jaundice

7.5.1 Definition

Gestation ≥37 weeks with jaundice lasting more than 14 days

Gestation <37 weeks with jaundice lasting more than 21 days

7.5.2 Clinical features

Look for pale chalky stools and/or dark urine that stains the nappy – seen in conjugated hyperbilirubinaemia

7.5.3 Investigations indicated for prolonged jaundice

- Total bilirubin and conjugated bilirubin
- Full blood count, blood picture, reticulocyte count
- Blood group determination (mother and baby) and DAT (Coombs' test)
- Urine culture
- Routine metabolic screening including screening for congenital hypothyroidism (T4, TSH), galactosaemia (urine reducing substances)

  If all the above investigations are not suggestive of a pathological cause the diagnosis of breast milk jaundice may be considered. Baby should be reviewed until the jaundice disappears.

  Follow expert advice about care of babies with conjugated or direct bilirubin level greater than 1 mg/dL when the total bilirubin is less than 5 mg/dL or more than 20% of the total bilirubin if the total bilirubin is greater than 5 mg/dL because this may indicate serious liver disease.

7.5.4 Conjugated hyperbilirubinaemia

This is rare in the newborn period and is always pathological.

7.5.4.1 Definition

It is defined as conjugated or direct bilirubin level greater than 1 mg/dL when the total bilirubin is less than 5 mg/dL or more than 20% of the total bilirubin if the total bilirubin is greater than 5 mg/dl.

7.5.4.2 Approach

The following questions need to be answered

- Are the stools white or clay coloured?

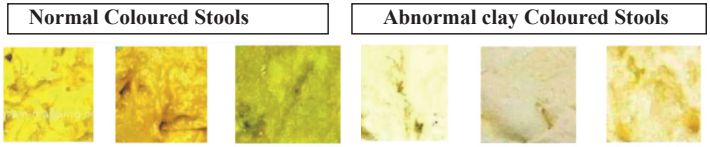

Figure 7.21: Stool colour of the newborne

- Is the urine dark coloured?
- Are liver and spleen enlarged?

7.5.4.3 Investigations to find the aetiology

Baby should be investigated as follows;

- Serum bilirubin with direct fraction
- US scan abdomen
  - Absence of the gall bladder after 4 hours of fasting is suggestive of biliary atresia
  - Altered echogenicity of liver parenchyma is suggestive of congenital hepatitis
  - Presence of choledochal cyst
- Liver function tests – enzymes, alkaline phosphatase, PT /INR
- Urine for reducing substance
- Urine culture
- TORCH screen (toxoplasma, rubella, cytomegalovirus, herpes, syphilis)

Rule out or establish the diagnosis of extra hepatic biliary atresia as early as possible (preferably within 90 days of age) and refer for surgery

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Treatment threshold graph for babies with neonatal jaundice

NHS
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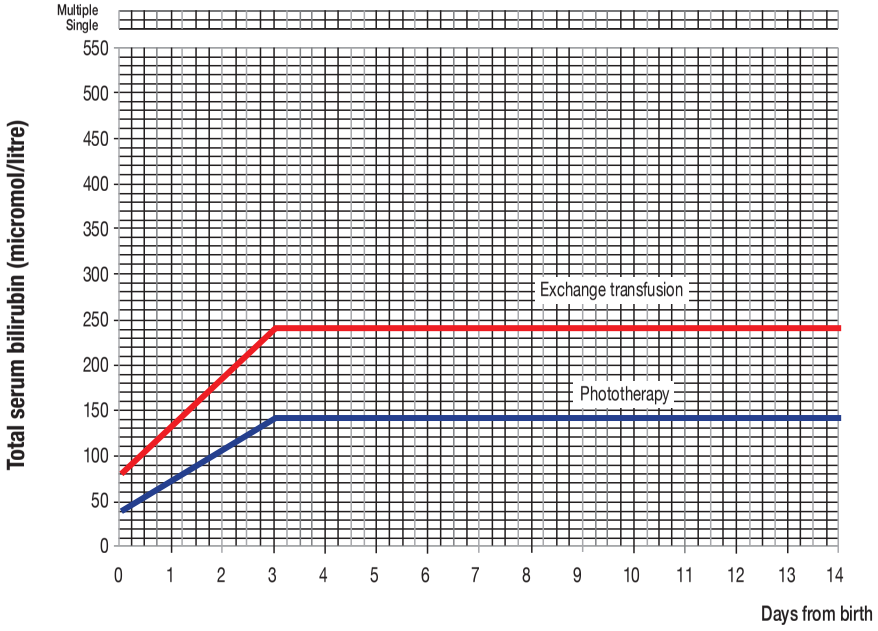
Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **24 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS National Institute for Health and ClinicalExcellence

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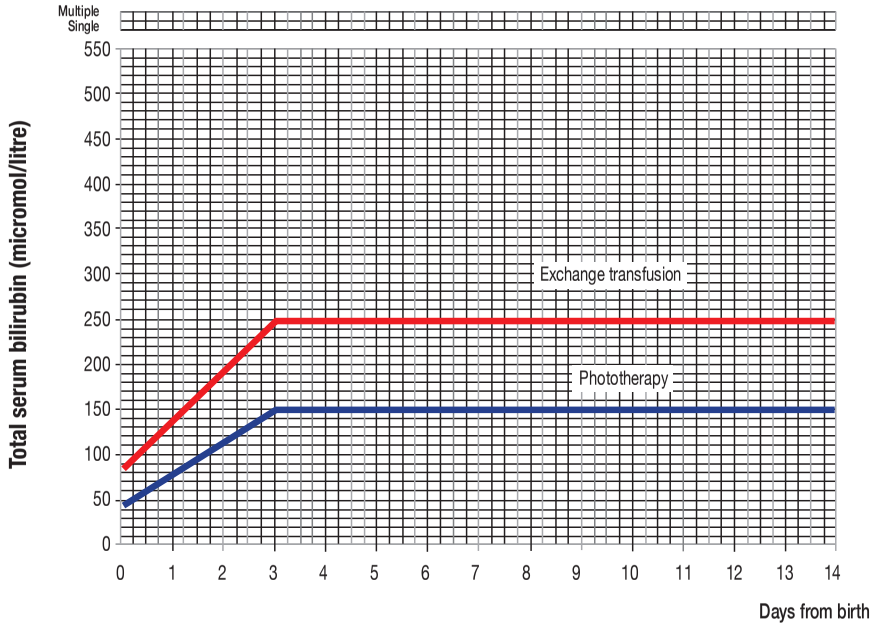
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **25 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS
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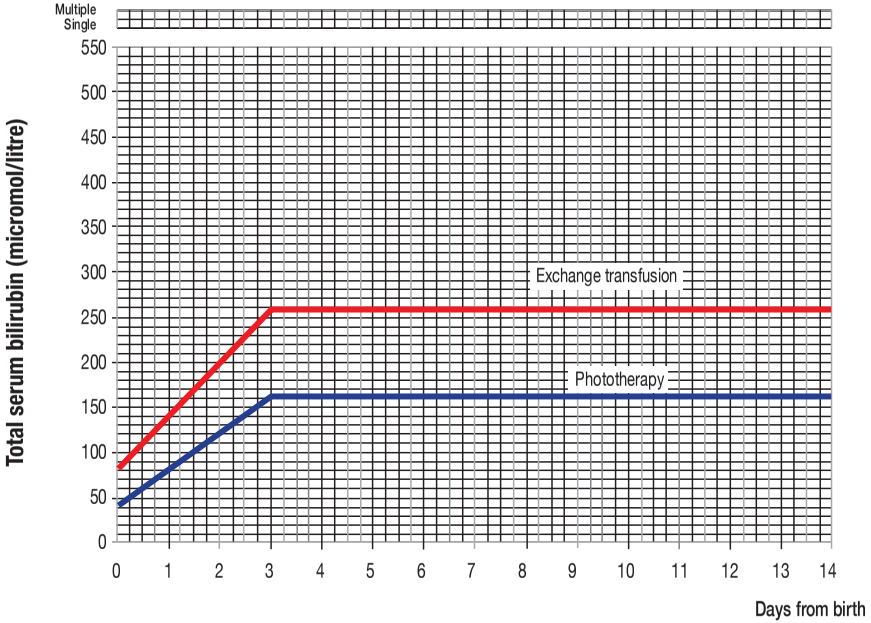
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **26 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS National Institute for Health and ClinicalExcellence

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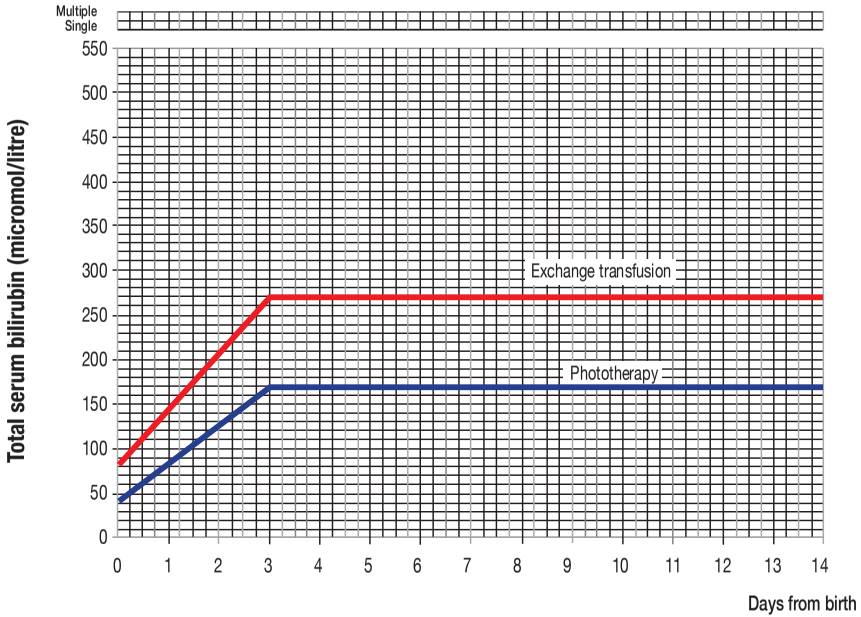
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **27 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS
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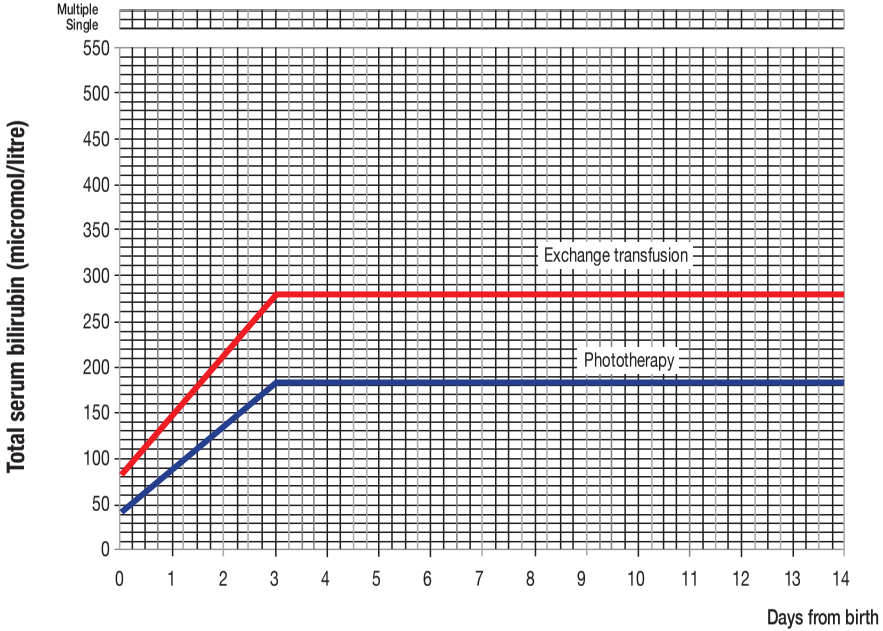
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **28 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS
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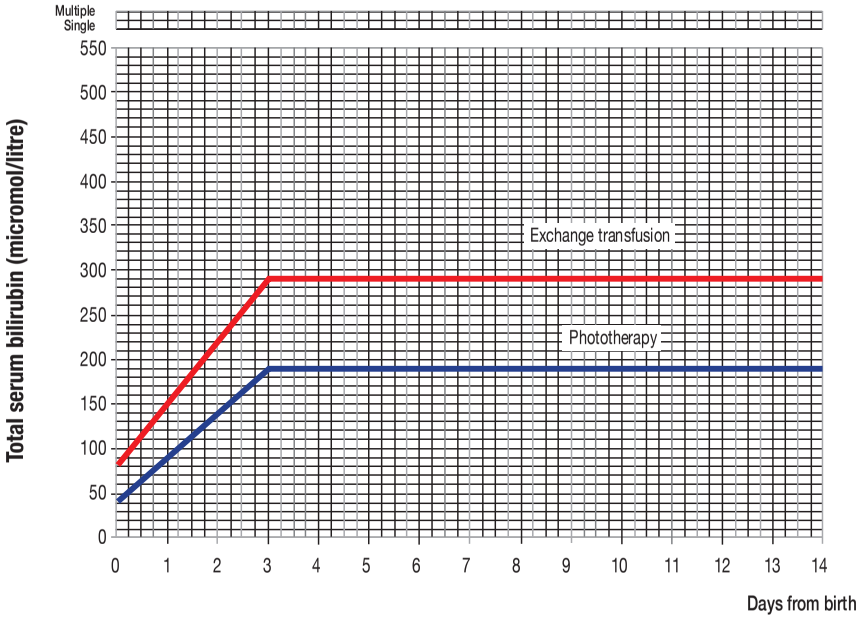
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **29 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

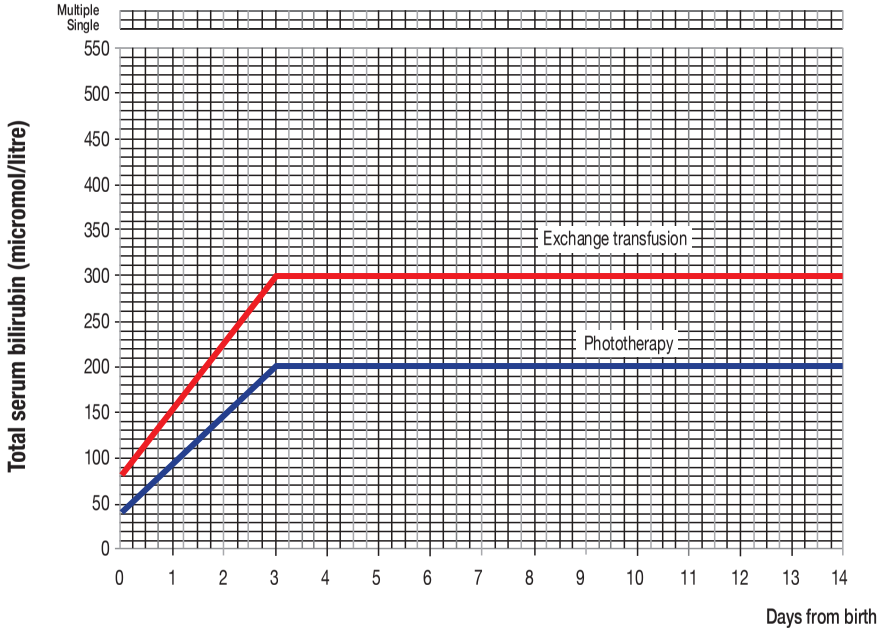
NHS
National Institute for
Health and ClinicalExcellence

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **30 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS National Institute for Health and ClinicalExcellence

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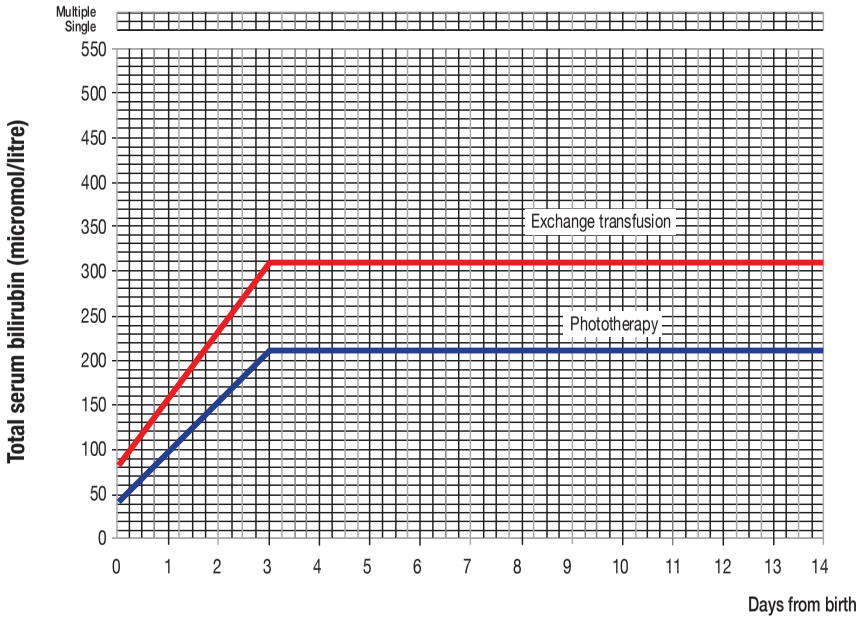
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **31 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

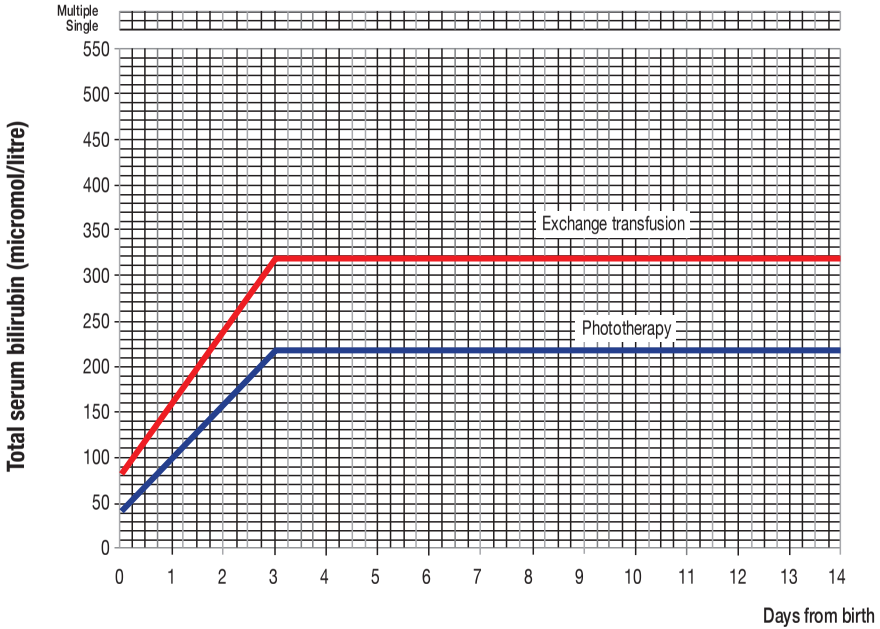
NHS
National Institute for
Health and ClinicalExcellence

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **32 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

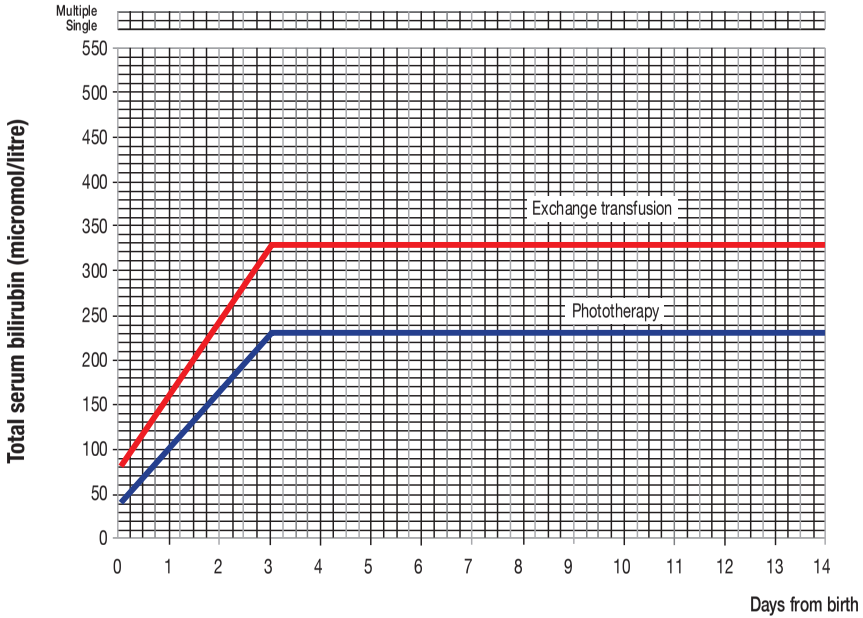
NHS
National Institute for
Health and ClinicalExcellence

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **33 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS
National Institute for
Health and ClinicalExcellence

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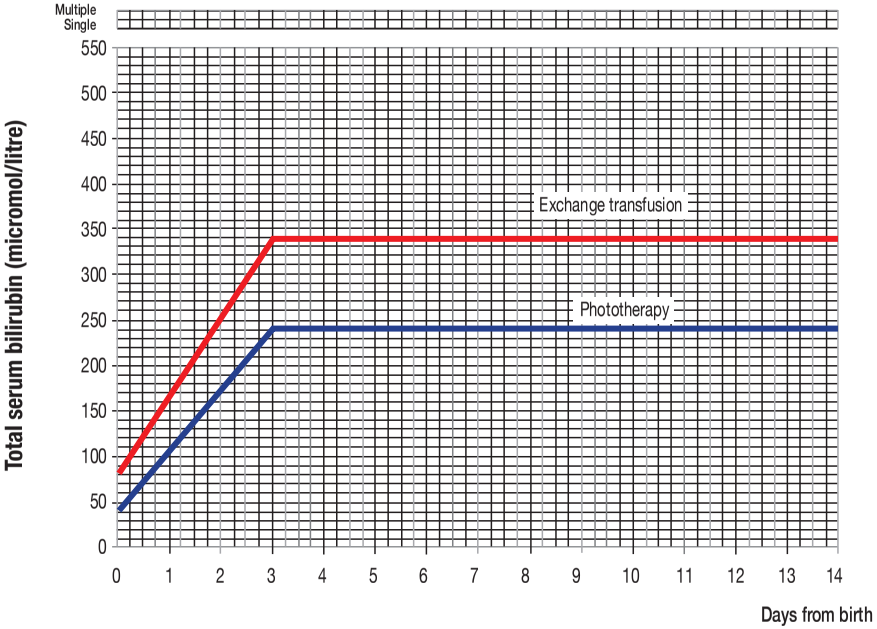
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 34 weeks gestation

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS National Institute for Health and ClinicalExcellence

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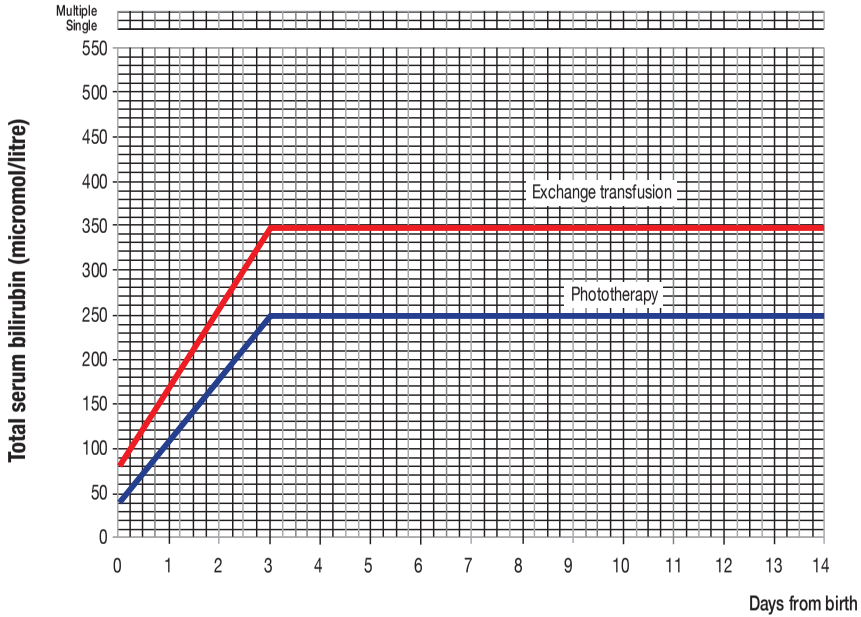
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **35 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

NHS
National Institute for
Health and ClinicalExcellence

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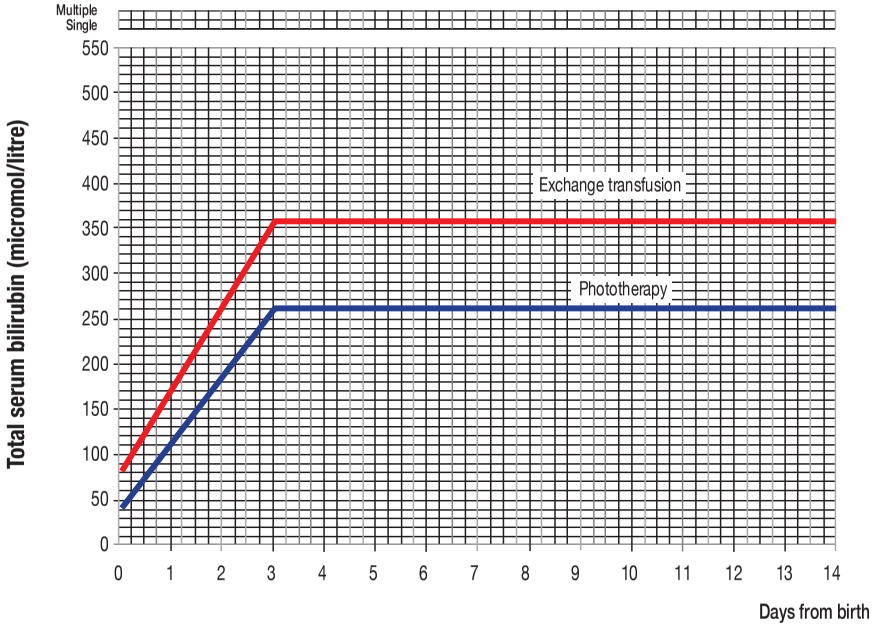
Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 36 weeks gestation

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

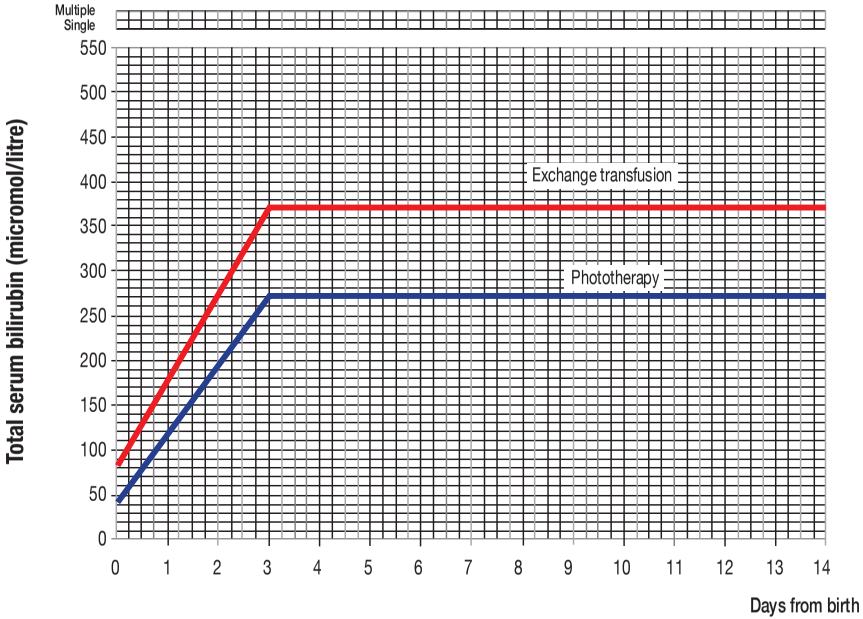
NHS National Institute for Health and ClinicalExcellence

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **37 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



Treatment threshold graph for babies with neonatal jaundice

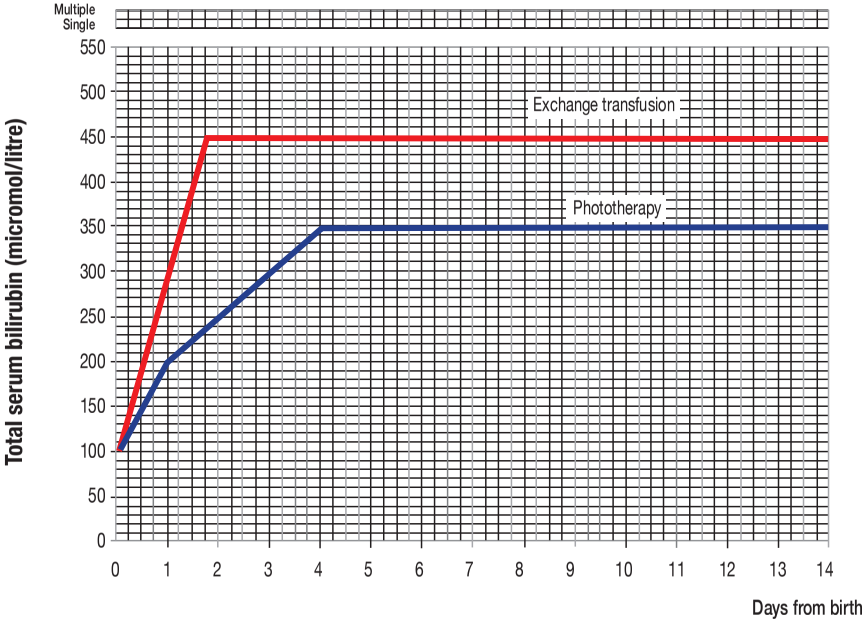
NHS National Institute for Health and ClinicalExcellence

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **38 weeks gestation**

Shade for phototherapy

Baby's blood group _____ Mother's blood group _____



RESPIRATORY DISTRESS IN NEWBORN

Chapter 8

RESPIRATORY DISTRESS IN NEWBORN

8.1 Introduction

Approximately 10% of neonates require respiratory support immediately after delivery whereas 1% of neonates are in need of resuscitation. Respiratory distress is the most frequent cause of neonatal intensive care unit (NICU) admission. Regardless of the cause, if not recognised and managed in advance, respiratory distress can escalate to respiratory failure and cardiopulmonary arrest. Delayed or inappropriate management may result in hypoxic respiratory failure which has high mortality and morbidity.

8.2 Definition

Breathing difficulty or respiratory distress is characterised by any one of the following:

- Respiratory rate > 60 breaths per minute
- Severe chest in-drawing / recessions (subcostal or intercostal)
- Grunting
- Nasal flaring
- Apnoea (not breathing) or gasping.

If the baby is apnoeic or gasping, resuscitate the baby immediately.

8.3 Common causes of respiratory distress

8.3.1 Term baby

- Transient tachypnoea of newborn (TTN)
  - Common in term and late preterm
  - Occur within first 6 hours
  - Presents with tachypnoea and grunting
  - Self-limiting

- Commonly seen after elective caesarian section
- Unable to differentiate from congenital pneumonia

- Meconium aspiration syndrome (MAS)
  - Diagnosed in a baby who develops respiratory distress if born through meconium stained liquor
  - Meconium passes into amniotic fluid due to relaxation of the anal sphincter owing to hypoxia
  - Baby aspirates meconium stained amniotic fluid during gasping
  - Causes obstruction of the airways, chemical pneumonitis, inactivation of surfactant and pulmonary hypertension
  - Pneumomediastinum, pneumothorax are common
  - Presents with all features of respiratory distress
  - Presents immediately or in the transition period
- Congenital pneumonia
  - Commonly acquired at birth, less commonly nosocomial
  - Maternal risk factors for sepsis
  - Presents with all features of respiratory distress
  - Can occur hours or days after birth
- Hypoxic injury (refer Chapter 11)
- Persistent pulmonary hypertension of the newborn (PPHN)
  - Cyanosis with respiratory distress due to right to left shunt
  - Pre and post ductal saturation difference
  - Labile oxygen saturation which worsens with handling
  - Commonly due to MAS, Respiratory distress syndrome (RDS), pneumonia, pulmonary hypoplasia and diaphragmatic hernia, hypoxia
  - Structurally normal heart with right to left shunting via patent ductus arteriosus (PDA) or patent foramen ovale (PFO)

8.3.2 Preterm baby

- Surfactant deficient lung disease
  - Decreased gestational age is inversely related to the risk
  - Prenatal steroids decrease the risk
  - Presents within the first few hours of life
  - Indistinguishable from congenital pneumonia
- Congenital pneumonia (refer Chapter 9)
- Miscellaneous causes: hypothermia, hypoglycaemia (refer Chapters 2 and 6)

8.3.3 Surgical causes (in preterm or term)

- Diaphragmatic hernia
- Tracheo-oesophageal fistula
- Bilateral choanal atresia

8.3.4 Other causes

- Cardiac: congenital heart disease
  - Cyanosis disproportionate to the degree of tachypnoea is suggestive of cardiac disease or persistent pulmonary hypertension. Tender hepatomegaly and cardiomegaly, are features suggestive of congenital heart disease.
- Metabolic: Inborn errors of metabolism
  - Significant tachypnoea without increased work of breathing (WOB) should prompt additional laboratory investigation to identify metabolic acidosis or sepsis

8.4 Approach to respiratory distress

8.4.1 History

A detailed relevant antenatal and perinatal history should be taken based on the common causes:

- Gestation
- Onset of distress / breathing difficulty

- Previous preterm babies with respiratory distress
- Antenatal steroid prophylaxis if preterm delivery
- Rupture of membranes > 18 hours, maternal intrapartum fever, foul smelling liquor
- Prolong labour / assisted delivery
- Meconium stained amniotic fluid (MSAF)
- Perinatal asphyxia
- Maternal diabetes mellitus
- Poor feeding, lethargy, convulsions
- History of excessive frothing

8.4.2 Examination

- Severity of respiratory distress as assessed by score given below
- Neurological status: activity, altered sensorium
- CRT (Capillary refill time)/skin colour
- Axillary temperature
- Hepatomegaly
- Central cyanosis or oxygen saturations on pulse oximetry
- Ill baby with lethargy, poor activity, irritability, poor feeding
- Evidence of malformations / dysmorphism

8.5 Assessment of severity of respiratory distress

The Downe score is preferred to the Silverman-Andersen score to obtain an objective measurement of severity of respiratory distress due to better accuracy, reliability and user friendliness.

Table 8.1: Downe Score

Score	Respiratory rate	Cyanosis	Air entry	Grunt	Retraction
0	<60/min	Nil	Normal	None	Nil
1	60-80/min	In room air	Mild reduction	Audible with stethoscope	Mild
2	>80/min/ apnoea	Present	Marked reduction	Audible with naked ear	Moderate

Table 8.2: Interpretation of Downe score

Degree of respiratory distress	Score
Mild	0-3
Moderate	4-6
Severe / Impending respiratory failure	7-10

8.6 Investigations

The diagnosis is based on the history, clinical examination, x-ray findings and the results of the partial septic screen.

8.6.1 Chest X ray (CXR)

8.6.1.1 When to do the CXR ?

- Babies with respiratory distress should have a chest x-ray with NG tube in situ, 4-6 hours after birth, giving adequate time for absorption of amniotic fluid in the lung.
- Earlier CXR is indicated if the management depends on the radiological diagnosis
  - Diaphragmatic hernia
  - Tracheo-oesophageal fistula
- Confirm endotracheal tube, intercostal tube position

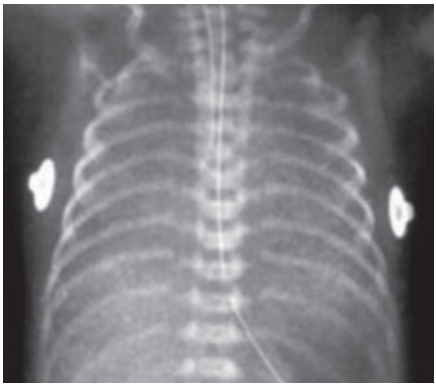


Figure 8.1. Ground glass appearance with air bronchogram and unexpanded lungs

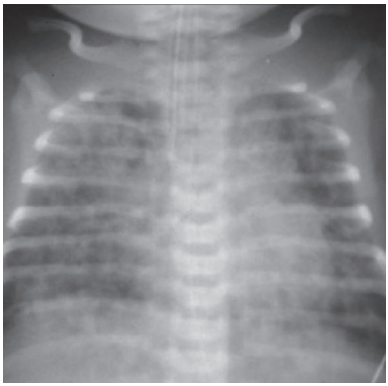


Figure 8.2 Fluffy shadows and hyperexpanded lungs in meconium aspiration syndrome

8.6.1.2 How does the chest x-ray findings help in the diagnosis ?

- Respiratory distress syndrome (RDS) - air bronchogram, decreased lung volume and hazy lungs / whiteout lungs
- Meconium aspiration syndrome (MAS)- bilateral fluffy shadows with hyperinflation.
- Pneumonia – infiltrates
- Pulmonary haemorrhage – multilobar infiltrates
- Other malformations e.g.; diaphragmatic hernia, tracheo-oesophageal fistula

X-ray findings should be interpreted along with the history and clinical examination.

8.6.2 Partial septic screen

8.6.2.1 Components of the partial septic screen

- Full blood count
- C-reactive protein
- Surface swab culture
- Blood culture

8.6.2.2 Indications for partial septic screen in babies with respiratory distress

- Respiratory distress lasting for more than 4 hours from birth
- Unexplained preterm delivery
- Maternal risk factors for sepsis:
  - Intrapartum fever
  - Urinary tract infection
  - Chorioamnionitis
  - Prolonged rupture of membranes (>18hrs)
- Meconium aspiration syndrome
- Poor condition at birth requiring resuscitation

8.6.3 Capillary/venous blood gas (if available)

Should be done in all babies with moderate to severe respiratory distress in order to look for respiratory acidosis (poor ventilation) or metabolic acidosis (lactic acid from anaerobic metabolism resulting from poor oxygenation).

8.7 Management

8.7.1 Supportive management

- Maintain normal body temperature (refer Chapter 2)
- Monitor heart rate, oxygen saturation, respiratory rate and effort, blood sugar, blood pressure
- Target saturation is 90% in preterms and 95% in term babies
- **Start on CPAP if there is increased respiratory effort** (recessions, grunting or nasal flaring)
- Give oxygen, only if baby is unable to achieve the target saturation despite optimal CPAP
- **Consider invasive ventilation if there is a poor response to CPAP or oxygen requirement is > 40% to achieve target saturation**
- **Give oxygen if there is desaturation without respiratory distress**

- Give baby expressed breast milk with tube if not accepting direct breastfeeds
- Maintain adequate perfusion via volume expansion ± inotropes
- Maintain normoglycemia
- Apnoea (see below)

8.7.2 Specific management

8.7.2.1 Mild breathing difficulty (Downe Score 1-3)

- Administer oxygen if saturation is <95%.
- Admit to the neonatal unit if baby cannot be weaned off oxygen within 4 hours or worsening respiratory distress or poor feeding
- Start antibiotics after partial septic screen if the respiratory distress persists for more than 4 hours or if there are risk factors. Once respiratory distress settles and if the partial septic screen is negative (at 48 hours) antibiotics maybe omitted.
- Continue breastfeeding

8.7.2.2 Moderate to severe breathing difficulty (Downe Score 4 - 10)

- Commence respiratory support with continuous positive airway pressure (CPAP) in moderate respiratory distress
- Intubate and ventilate in severe breathing difficulty (score ≥7)
- Administer surfactant if suspecting surfactant deficiency, congenital pneumonia or meconium aspiration syndrome
- Monitor and record the baby's respiratory rate, saturation, presence of chest in-drawing and grunting on expiration and episodes of apnoea
  - every hour until the baby no longer requires oxygen and then every
  - 2 – 4 hourly for an additional 24 hours.
- Insert an oro-gastric tube to empty the stomach of air and secretions (important for all babies with respiratory distress)
- Start antibiotics. (refer Chapter 9)
- Express and feed breast milk via tube if not taking direct breastfeeds

8.7.2.3 Suspected persistent pulmonary hypertension of the newborn (American Heart Association and American Thoracic Society Guidelines 2015)

- Administer even 100% oxygen – aim for saturation > 95%
- Surfactant is useful to treat the underlying parenchymal lung disease
- Intubation and mechanical ventilation - maintain normal lung expansion
- Consider high frequency ventilation (HFOV) if needing high peak inspiratory pressures (PIP > 28cm H_2O) or mean airway pressure (MAP > 15cm H_2O)
- High frequency oscillatory ventilation (HFOV) is useful for babies with parenchymal lung disease with low lung volumes
- Sedate baby with morphine, if not responding use midazolam
- Paralysis with pancuronium should be considered only if not responding to sedatives as it may promote atelectasis and increase the risk of death
- Inhaled nitric oxide is recommended for babies with an oxygenation index (OI) > 25
- Extra Corporeal Membrane Oxygenation (ECMO) is indicated for babies with congenital diaphragmatic hernia with PPHN not responding to medical therapy and for babies with an OI > 40
- Correct acidosis as it increases pulmonary vasoconstriction
- Maintain systemic blood pressure above the pulmonary pressure using inotropes
  - First line - dopamine
  - If there is poor myocardial contractility – dobutamine and milrinone are preferred
- Do not use fluid boluses unless there is intravascular depletion – as it increases right atrial pressure – thereby worsening the right to left shunting

- Use pulmonary vasodilators
    - Selective pulmonary vasodilators (inhaled nitric oxide) are preferred to non-selective vasodilators (sildenafil, intravenous magnesium sulphate)
    - Monitor blood pressure closely when using non selective vasodilators
- Arrange 2D echocardiogram to confirm diagnosis and differentiate from cyanotic heart disease
    - Treat underlying cause

8.7.2.4 Suspected pulmonary haemorrhage

- Resuscitate and restore circulatory volume with colloid boluses on 20ml/kg FFP, blood and platelets
- Intubate and ventilate
- Suction regularly (1-2 hourly) to keep airway patent during active bleeding
- Suction can be weaned off in the absence of active bleeding as unnecessary suctioning can make the haemorrhage worse.
- Ventilate with high pressure to splint alveolar vessels (PIP can be increased to 30 cm H_2O and PEEP to 7-8 cm H_2O)
- Surfactant - single dose improves oxygenation
- Sedate baby
- May need blood transfusion to replace ongoing losses and correct anaemia
- Correct coagulopathy / platelet deficiency
- Diuretics may be needed if there is fluid overload
- Treat underlying cause – take blood cultures and start antibiotics as infection can be a cause.

8.7.2.5 Apnoea

- **Definition**
    - Spontaneous cessation of breathing for more than 20 seconds or any cessation associated with desaturations / cyanosis / pallor and / or bradycardia (heart rate less than 100).

- **Causes**
  - An underlying disease which should be managed appropriately eg; respiratory distress, meconium aspiration, sepsis etc
  - Apnoea of prematurity
  - Obstructive apnoea (floppy or preterm baby)
- **Management**
  - First apnoeic attack
    - Ensure patent airway
    - Provide tactile stimulation
    - Give positive pressure ventilation with bag and mask ventilation until spontaneous breathing occurs
    - Give caffeine citrate / aminophylline for recurrent apnoeic spells if baby is preterm
      - IV aminophylline can be given in a dose of 6mg/kg as a loading dose over 30 minutes followed 12-24 hours later by 3mg/kg/dose 12 hourly. Give aminophylline orally once baby is on oral feeds.
      - Caffeine citrate: available as oral or IV preparation; 20mg/kg as loading dose (1ml = 20mg of caffeine citrate or 10mg of caffeine base). Start maintenance caffeine citrate 10 mg/kg (range 5-15mg/kg) once a day, 24 hours after loading dose.
      - Caffeine or aminophylline should be stopped once the neonate is apnoea free for at least 1 week and may be continued till 34 – 35 wks gestation.
  - Recurrent apnoeic spells
    - Needs investigation
      - CXR
      - partial septic screen to look for infection
    - Start intravenous antibiotics after blood culture
    - Start CPAP / non invasive ventilation
    - If poor response - commence invasive positive pressure ventilation (intubate and ventilate via ambu bag, T-piece resuscitaire or ventilator if available).

8.8 Oxygen therapy

- Oxygen is a drug and should only be used if the baby has hypoxia, as it is harmful to eyes, brain and lungs, especially in preterm babies.
- Pulse oximeter should be used to monitor oxygen saturations, which should be maintained in the range of 90 – 94% in preterm babies.
- Saturation below 90% should be treated with oxygen supplementation. However, transient drop in saturations below this level, specially when the baby is moving or crying and improving spontaneously should be ignored.
- At no time should babies under supplemental oxygen have saturations above 95% (exception: In persistent pulmonary hypertension aim for pre-ductal PaO2 of 90-100mmHg).
- Oxygen delivered via nasal prongs without the use of a blender would give 100% oxygen when the flow rate is >0.3L/min for a 1kg baby

Pulse oximetry: Maintain a pre-ductal saturation of 90– 94%

8.8.1 Nasal prongs

- This is a useful method of delivering oxygen.
- Appropriate size prongs, which fit the neonate well, should be used. If a large size of the nasal cannula is used, it may cause blanching of the alae nasi and injure the nose.
- Adjust flow of oxygen (0.5 – 2.0 l/min) to achieve target saturation.

8.8.2 Head box

- Place a head box over the baby's head.
- Ensure that the baby's head stays within the head box, even when the baby moves.
- Adjust the flow of oxygen (3-5 l/min) to achieve the desired oxygen saturation.

8.9 Continuous positive airway pressure

8.9.1 Definition

Maintenance of an increased (positive) airway pressure during the inspiratory and expiratory phases of respiration with the baby breathing spontaneously.

8.9.2 How does CPAP work ?

- Splint open airway – including upper airway; ↓ airway resistance and thereby ↓ work of breathing
- Increases functional residual capacity and ↑ tidal volume
- Decreases ventilation/perfusion mismatch
- Conserves surfactant and ↑ lung compliance
- Lung damage is much less than when positive pressure ventilation via endotracheal tube is used.

8.9.3 How to apply CPAP ?

- Administered via CPAP nasal prongs or special CPAP masks using an appropriate sized CPAP hat to stabilise
- Different types of nasal prongs (commonly used) and nasopharyngeal (rarely used) CPAP are available
- An orogastric tube on open drainage should always be used with CPAP to decompress the stomach
- Use of CPAP requires training of staff
- Fixing of prongs and stabilisation of circuit should be done in a manner to minimise nasal trauma and subsequent head shape abnormalities
- Available CPAP delivery devices include conventional ventilators, infant flow drivers, bubble CPAP
- Baby's vital signs and nasal septal condition should be monitored regularly.

8.9.4 When not to use CPAP

- Diaphragmatic hernia
- Tracheo-oesophageal fistula

- Minimal respiratory efforts or recurrent apnoea (Apnoea of prematurity is avoided by nasal CPAP; however if apnoeic spells are recurrent while on CPAP, non-invasive positive pressure ventilation [short trial] or intubation & ventilation should be done).

8.9.5 High-flow nasal prongs (HFNP)

This is a form of respiratory support that is mainly used in the process of weaning from invasive ventilation. Heated, humidified air / oxygen is given to the infant via flexible nasal prongs. It is less troublesome for baby and easier for nursing care. It produces a continuous positive airway pressure in a manner similar to CPAP. Some experts believe it to be as effective as CPAP. The equipment for providing HFNP respiratory support is generally less expensive.

8.10 Non-invasive (nasal) positive airway pressure - NIPPV

- NIPPV is use of the nasal CPAP prongs to deliver intermittent positive pressure breaths in addition to the continuous positive end expiratory pressure.
- Current evidence indicates that NIPPV after extubation of very premature infants reduces the rate of re-intubation. Its mechanism of action is not very clear but it may improve pulmonary mechanisms, tidal volume and minute ventilation and there is some evidence that NIPPV marginally improves gas exchange.

8.10.1 Failure of CPAP/NIPPV

- Needing >40% FiO2 to maintain target saturation
- Rise in pCO2 >55 mmHg
- Unsettled respiratory distress (recessions/grunting / tachypnoea)
- Respiratory exhaustion
- Apnoeic attacks
- If any one or more of the above occurs proceed to assisted ventilation and transfer if necessary.

8.11 Invasive positive pressure ventilation

- This requires endotracheal intubation – generally done orally (nasal also possible)
- Conventional ventilation includes either pressure control or volume control modes.
- In Sri Lanka currently pressure control ventilator modes are the most commonly available
- The pressure control modes include invasive CPAP, pressure support, controlled intermittent mandatory ventilation, synchronised intermittent positive pressure ventilation (SIMV), assist control (AC) / synchronised intermittent positive airway pressure ventilation (SIPPV).

8.12 High frequency oscillatory ventilation

- Available in Sri Lanka
- Useful when conventional ventilatory methods are failing to achieve adequate oxygenation or ventilation.
- Some authorities believe it causes less lung injury.
- Especially useful in babies with persistent pulmonary hypertension and air leaks such as pulmonary interstitial emphysema in preterm infants and pneumothorax.

Do not use facemasks to deliver oxygen. They are not appropriate for use in neonates.

8.13 Management of improving baby

- When the baby's oxygen saturation is acceptable gradually wean from oxygen. Reduce the oxygen flow rate by ½ litre/min every 30 minutes and observe saturations.
- If the saturations remain in the normal range gradually remove oxygen.
- When the baby begins to show signs of improvement:
  - Allow the baby to begin breastfeeding as the respiratory distress settles. Baby can be put on to the breast while on oxygen by nasal cannula with continuous monitoring.

- If the baby cannot be breastfed, give expressed breast milk using a cup or gastric tube

- When the baby has no difficulty breathing and is feeding well, discharge the baby.

8.13.1 Indications for referral

Remember to refer if,

- Baby with breathing difficulty is worsening while on the maximal respiratory support available at your unit
- Persistent central cyanosis or low oxygen saturations despite oxygen supplementation (for cardiology opinion)
- You suspect / diagnose an associated abnormality – e.g. diaphragmatic hernia – that requires specialist management

Always stabilise before transport

8.14 Discharge advice and follow-up

Babies with respiratory distress should be followed up at 48hrs by the public health midwife. Detailed advice regarding exclusive breast feeding, temperature maintenance and immunisation should be provided.

8.15 Prevention of respiratory distress

- Antenatal steroids to prevent surfactant deficient lung disease
  - To enhance lung maturation.
  - Optimal effect is seen 24 hrs – 7 days after completion of therapy.
  - Betamethasone 12 mg given intramuscularly in two doses or dexamethasone 6 mg given intramuscularly in four doses are the steroids of choice
  - Should be given to all women at risk of iatrogenic or spontaneous preterm birth between 24 weeks gestation to 34+6 weeks of gestation.
  - Should be given to all women for whom an elective caesarean section is planned prior to 38+6 weeks of gestation.

- Intrapartum prophylaxis to prevent Group B streptococcus pneumonia

Summary

- Respiratory distress is common in neonates
- Early identification and timely appropriate management is the key to good outcome
- Use oxygen with caution.
- Antibiotics are not indicated beyond 36-48 hours unless blood culture is positive, septic markers are indicative or clinical features are strongly compatible.

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NEONATAL INFECTIONS AND ANTIBIOTIC THERAPY

Chapter 9

NEONATAL INFECTIONS AND ANTIBIOTIC THERAPY

9.1 Introduction

Neonatal infection is a significant cause of death all over the world. In Sri Lanka 11% of neonatal mortality is due to infection.

If diagnosed early and treated with good supportive care and antibiotics, it is possible to save most babies with neonatal sepsis. Decreasing invasive interventions, promoting breastfeeding and maintaining proper hand hygiene are the best preventive strategies to reduce the occurrence of neonatal sepsis.

Antibiotic use should be rationalised and standardised in order to reduce inappropriate usage and emergence of multi-resistant organisms.

9.2 Definitions and aetiology

Neonatal sepsis is a suspected or proven systemic infection associated with the systemic inflammatory response (SIRS) that occurs in newborns up to 28 days of age.

SIRS is defined as 2 or more of the following criteria:

1) increased or decreased total white blood cells for age or >10% immature neutrophils
2) abnormal temperature (>38.5° or <36°C)
3) increased respiratory rate for age
4) increased heart rate for age

It is an infectious disease of varied aetiology, which determines degrees of inflammatory and metabolic responses. Both proinflammatory cytokines like tumour necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and interleukin-8 (IL-8) and anti-inflammatory cytokines like interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β) are produced rapidly in the setting of neonatal sepsis.

Early onset sepsis (EOS)

Defined as suspected or proven sepsis within 72 hours of birth. Signs of EOS in term infants typically present by the first 6 hours of life. Most cases (80% to 90%) of EOS will present in the first 24 to 48 hrs of life.

The source of the pathogen is the maternal genital tract or the delivery area.

Commonest pathogens are,

- Streptococci (mainly Group B Streptococcus-GBS),
- Escherichia coli, other coliforms and other gram negatives
- *Listeria monocytogenes*

Respiratory distress due to congenital (intrauterine) pneumonia is the predominant manifestation of EOS.

Late onset sepsis (LOS)

Appearance of signs and symptoms suggestive of sepsis 48 – 72 hrs after birth up to 90 days of life. The pathogens are acquired from community or hospital (nosocomial).

Commonest organisms are,

- *Staphylococcus aureus*
- Gram-negative bacilli such as Klebsiella, Escherichia coli, other coliforms
- Coagulase negative staphylococcus (CONS)
- Enterococci
- Pseudomonas, Serratia

LOS commonly presents as septicaemia, pneumonia or meningitis.

9.3 Risk factors for sepsis

Early-onset sepsis is caused by organisms prevalent in the maternal genital tract or in the delivery area.

The risk factors for early-onset sepsis include:

- Invasive Group B Streptococcal infection in a previous baby
- Maternal group B streptococcal colonisation, bacteriuria or infection in the current pregnancy
- Maternal pyrexia >38°C during labour
- Chorioamnionitis, defined by maternal fever, leukocytosis (>15,000 white blood cells [WBCs]/mm3), maternal tachycardia, uterine tenderness, foul odour of amniotic fluid, and fetal tachycardia at delivery

- Mother treated with intravenous antibiotics for invasive bacterial infection (confirmed or suspected) during labour, in the 24-hour periods before and after birth
- Prolonged rupture of membranes >18hrs
- Prelabour rupture of membranes
- Spontaneous preterm delivery (<37 weeks)
- Very low birth weight (<1500g)
- Low APGAR scores
- Prolonged or difficult delivery with instrumentation or ≥3 vaginal examinations after rupture of membranes or presence / removal of cervical suture
- Infection (suspected or confirmed) in another baby in the case of multiple pregnancy
- Maternal urinary tract infection (UTI) during pregnancy
- Unclean delivery and cord separation

Late-onset sepsis is caused by the organisms thriving in the external environment of the home or the hospital. The infection is often transmitted through the hands of the care-providers.

The associated factors of late-onset sepsis include:

- Very low birth weight, prematurity
- Lack of breastfeeding
- Delayed enteral feeding
- Frequent handling/extensive resuscitation with or without invasive procedures
- Disruption of skin integrity with needle pricks and use of intravenous fluids
- Poor hygiene
- Poor maintenance of asepsis in neonatal unit including improper hand-washing techniques
- Superficial infections (eg; skin and umbilical sepsis)
- Previous or prolonged hospitalisation

9.4 Clinical features

Clinical presentation of sepsis in neonates is highly variable. In the early stages, signs may be subtle and, although difficult to define, a mother or nurse may report that a baby is simply 'not right'.

9.4.1 Frequent early signs

- Isolated tachypnoea (respiratory rate sustained above 60 breaths/ min and slight recession)
- Feeding difficulties (not feeding or poor suck)
- Lethargy, poor activity
- Temperature instability – following exclusion of environmental causes and dehydration, axillary temperature below 36°C or above 38.0°C. Hypothermia is much more common in EOS than hyperthermia.

9.4.2 Other signs

- As pneumonia is often the common presenting infection respiratory symptoms are common– apnoea, cyanosis, grunting and dyspnoea (they may even occur in meningitis / sepsis in the absence of pneumonia). For ventilated babies, an increase in ventilation requirements often accompanies generalised sepsis as well as pneumonia.
- Cardiovascular – heart rate ≥160 beats/min; low pulse volume, blood pressure – shock
- Poor cutaneous circulation - mottling and delayed capillary filling (>3 seconds).
- Irritability – may result from pain of a localised infection such as septic arthritis or be an indication of meningitis
- Skin – petechiae, septic spots, paronychia or omphalitis.
- Jaundice - unexplained jaundice; in the absence of other explanation may indicate a UTI.
- Gastrointestinal – vomiting, mild diarrhoea, abdominal distension
- Central nervous system - high-pitched cry, neck retraction, bulging fontanelle and convulsions are late features of neonatal meningitis

- Haemorrhagic diathesis - petechiae and bleeding from puncture sites due to DIC; Thrombocytopaenia without DIC is commoner. Bleeding from the gut or the renal tract are late signs of sepsis.
- Sclerema - diffuse hardening of the subcutaneous tissue resulting in a tight smooth skin that feels bound to the underlying structures; often associated with Gram-negative infection
- Tone – maybe be hypertonic or hypotonic

Examination should include assessment of

- Hydration
- Murmurs or triple rhythm – congenital heart disease and endocarditis
- Abdomen – distension and rigidity, masses, bowel sounds, organomegaly
- Spinal column for defects
- Limbs for signs of osteomyelitis and septic arthritis
- Cannula sites

9.5 Diagnosis

A partial septic screen should be undertaken in all neonates suspected of invasive infection such as pneumonia, sepsis, UTI etc.

Partial septic screen includes:

- Blood culture
- Full blood count
- CRP/micro ESR

Additional investigations should be done depending on the system involvement.

- CXR – if a pneumonia is suspected
- Urine culture – if a urinary tract infection is suspected
- CSF examination – if meningitis is suspected or if the blood culture is positive (25-30% of septic infants have meningitis)

Direct method of diagnosis

- Isolation of microorganisms is diagnostic.
- A blood culture should be sent prior to starting antibiotics in all cases suspected of sepsis.

Collection of samples for blood culture

Inoculation of 1-2 ml of blood (at least 1 ml) is recommended for adequate and appropriate growth in a pediatric blood culture bottle. The ideal ratio of blood to culture medium should be 1:10. The physician should ensure proper aseptic technique during collection of blood to avoid contamination. Before collection of blood, automated system's blood culture bottles should be kept in fridge maintaining a temperature below 25°C and that of conventional broth may be left at room temperature. However, after inoculation of blood in the culture bottle, it should be kept outside at room temperature till it is dispatched to the laboratory for facilitation of growth of microorganisms. Dispatch at the earliest (unless facilities are available to incubate at 37°C).

Indirect methods of diagnosis:

There are a variety of tests which are helpful for screening of neonates with sepsis.

- **White cell count**
  - **Total leukocyte count (TLC) :** A total leucocyte count below 5000/cu mm. TLC upto 30,000 can be normal. A white blood cell machine count can be high due to NRBC
  - **An absolute neutrophil count (ANC)** of < 1500 per cu mm is an indicator of infection. **Neutropaenia is more predictive of neonatal sepsis than neutrophilia.**
  - **Immature neutrophils** (Band cells + myelocytes + metamyelocytes) to total neutrophils ratio (ITR) > 0.20 means that immature neutrophils are over 20 percent of the total neutrophils. This happens because bone marrow pushes even the immature cells into circulation, to fight infection.

- **C-reactive protein (CRP):**
  - A negative CRP does not exclude sepsis. CRP has a lag phase to respond especially in pre-term neonates (upto 48 hours to achieve highest levels in extremely low birth weight infants). Therefore, serial CRPs are more useful.
  - CRP is helpful in excluding infection if two values 24 hours apart with first sample being taken more than 8-24 hours after onset of symptoms are normal
  - The CRP can also be positive in other conditions like prolonged rupture of membranes, maternal fever during labour, fetal distress, perinatal asphyxia, shock, intraventricular haemorrhage, pneumothorax, and meconium aspiration pneumonitis.
- **A negative sepsis screen helps to rule out sepsis; a positive screen may not be confirmatory.**

Positive "sepsis screen" in blood culture negative babies

Two or more positive tests out of the five given below

1. Leukopaenia (TLC <5000/cumm)
2. Neutropaenia (ANC <1500/cumm)
3. Immature neutrophil to total neutrophil (I/T) ratio (> 0.2)
4. Micro ESR (> 15 mm 1st hour)
5. CRP +ve

- **Other investigations that may be used include IL-6 and procalcitonin.**

CSF examination and values of CSF for diagnosing meningitis

- Lumbar puncture (LP) must be performed in all neonates with late-onset sepsis, preferably before starting antibiotics.
- In a neonate with meningitis not showing clinical recovery after initiation of antibiotics, LP should be repeated after 48 hours.
- Ideally, the CSF WBC count & CSF sugar must be performed within 30 minutes of drawing the sample. It must be noted that CSF WBC and glucose rapidly fall with time, giving spurious results.
- The CSF glucose level is sometimes given as a percentage of the serum glucose done at least 30 minutes prior to the lumbar puncture: normal 0.6 (60%).
- Do not consider only one CSF parameter in arriving at a diagnosis.
- For CSF results that are not clear-cut use clinical judgment for diagnosis.
- Neonatal meningitis frequently occurs in the absence of bacteraemia and in the presence of normal CSF parameters. No single CSF value can reliably exclude the presence of meningitis in neonates. The CSF culture is critical to establishing the diagnosis of neonatal meningitis.

Table 9.1: Normal cerebrospinal fluid values

Type of infant	White cell count (count/ mm3)	Protein (g/l)	Glucose (mmol/l)
Preterm <28 days	9 (0-30)	1 (0.5-2.5)	3 (1.5-5.5)
Term <28 days	6 (0-21)	0.6(0.3-2.0)	3 (1.5-5.5)

Courtesy: Roberton Textbook of Neonatology 5th Edition; 2013.

9.6. Management

Supportive care and antibiotics are two equally important components of the management.

9.6.1 Supportive care

- Maintain airway, breathing, circulation. May require ventilation, fluid boluses, inotropes
- Ensure optimum oxygenation (maintain SpO_2 90 - 94%). Aim for higher saturation for babies at high risk of PPHN (e.g. meconium aspiration syndrome)
- Maintenance of temperature
- Maintain normoglycemia
- Vitamin K 1mg IV if there is active bleeding from any site; may need platelets, FFP, cryoprecipitate if in DIC.

9.6.2 Antibiotic therapy

Antibiotic therapy should cover the common causative bacteria when being given empirically. If any of the cultures prove to be positive and a sensitivity pattern is available antibiotics should be revised.

Antibiotics should be commenced as early as possible after obtaining blood +/- CSF, urine cultures.

9.6.2.1 Early onset sepsis

First line

- Benzyl penicillin (or ampicillin) and gentamicin
- Add cefotaxime or replace gentamicin with cefotaxime if meningitis is suspected.
- Consider local antibiotic sensitivities when deciding on change of antibiotics.

Second line

- Remember to choose antibiotic combination to cover Staph. and gram negatives

- Should also consider the prevalent organism in the unit & its antibiotic sensitivity at that particular time period
- Flucloxacillin/cloxacillin with amikacin/ cefotaxime.
- Include cefotaxime with any of the combinations in suspected meningitis

Third line

- Meropenem.+/- vancomycin (consider including vancomycin if staph/MRSA is suspected specially if central lines are used).
- Initial choice of antibiotics is judged by the clinical scenario and is therefore the responsibility of the medical team.
- Subsequently the antibiotic therapy should be adjusted according to blood culture reports and/or clinical response.
- Consider acyclovir if clinical features are suggestive of meningoencephalitis.

Duration of antibiotic therapy

- If blood culture is positive and CSF is normal: treat until blood culture is negative, baby is clinically well and FBC, CRP are normal
- Initially symptomatic baby, screening negative, clinically well in 48 hours: repeat FBC and CRP, if negative: stop antibiotics
- Symptomatic baby, responded to treatment within 48 hours and FBC and/ or CRP positive but blood culture negative:
    - In above situations if the initial CRP was high, it is best to treat until it comes back to normal.
    - Beware of CRP which may be persistently high due to local infection such as cannula site infection or abscess formation.

9.6.2.2 Proven meningitis (positive CSF)

- Empirical therapy for early onset disease- penicillin/ampicillin and cefotaxime
- Empirical therapy for late onset disease- cefotaxime
- Definitive therapy
    - GBS : Benzyl penicillin for 14 days

- Gram negative meningitis: cefotaxime (or according to the culture report) for 21 days
- CSF positive but no organism isolated- Penicillin 14 days and cefotaxime 21 days.

9.6.2.3 Pneumonia

- Duration: Until clinically well, blood tests return to normal and cultures are negative
- Early onset pneumonia
  - Penicillin or ampicillin with gentamicin (alternative option is penicillin and cefotaxime)
- Late onset pneumonia (after 72 hours in ventilated babies)
  - If the baby is already on antibiotics, broaden spectrum to cover coagulase-negative *Staphylococcus aureus (CONS)*, pseudomonas (or antibiotics covering the prevalent/colonised bacteria)
  - Cefotaxime and vancomycin provide a good coverage
- **Un-resolving, non-responsive neonatal pneumonia**
  - Caused by *Ureaplasma urealyticum* or Mycoplasma.
  - Erythromycin/clarithromycin is the antibiotic of choice Also consider possibility of cytomegalovirus

9.6.2.4 Bone and joint infections

- Cefotaxime and flucloxacillin are the first line antibiotics until the culture report is available
- **IV antibiotics** should be continued for 4-6 weeks.
- Vancomycin can be considered as second line therapy

9.6.2.5 Umbilical cord infection

- Umbilical granuloma does not need antibiotic therapy; only requires cauterisation
- When the dried up umbilical cord is separating there can be a wetness / slight discharge without erythema around cord and no malodour; this does not require antibiotic treatment. Baby needs to be bathed regularly and the cord kept dry.

- If there is significant periumbilical erythema or signs of sepsis is/ are present, Start IV flucloxacillin / cloxacillin and gentamicin or flucloxacillin / cloxacillin and cefotaxime
- If the baby is systemically very unwell MRSA cover with vancomycin or cefotaxime is a better option.

9.6.2.6 Skin infection

- Staph. skin sepsis should be differentiated from normal neonatal skin conditions.
- If there are only few small vesicles <10, commence local application of fusidic acid after bathing.
- If large vesicles or > 10, start oral therapy with flucloxacillin/ cloxacillin.
- If systemically unwell, commence IV flucloxacillin/ cloxacillin with gentamicin or cefotaxime.
- Alternatively, for a very sick baby, combination of vancomycin and cefotaxime provide a satisfactory coverage.

9.6.2.7 Varicella infection

- If the mother develops varicella during the 3 weeks prior to delivery, there is a 25% chance for her baby developing the illness.
- Babies born to mothers with perinatal varicella should be isolated from other babies from birth, but baby should be kept with the mother.

Prophylaxis

- Intramuscular varicella zoster immunoglobulin (VZIG) 125 units (/10kg body weight given early as possible after delivery / or exposure but within 72 hours (latest 96 hrs) will prevent / reduce the severity of chickenpox in the neonate.

Indications for prophylaxis with VZIG

- Neonates whose mothers developed chickenpox 5 days before delivery or within 48 hours of delivery
- Neonates born at or before 28 weeks gestation or with a birth weight less than 1000g regardless of the maternal immune status

- Infants born after 28 weeks to a non-immune mother should receive VZIG if there is a significant exposure
- If the siblings get chickenpox and the mother has not had chickenpox

Prophylaxis is not indicated

- Neonates whose mothers develop chickenpox before 5 days of delivery as it ensures adequate transplacental passage of antibodies.
- Neonates who develop chickenpox 3 days after delivery as they are at lower risk of disseminated disease.
- Maternal zoster is not an indication for VZIG.
- The role of prophylactic acyclovir in neonates is unproven.
- An infected mother does not need to be separated from her own her baby. She should be encouraged to breastfeed her baby.
- Both mother and baby should be quarantined together, until all the lesions have crusted.
- If a neonate develops features of varicella, IV acyclovir is the treatment of choice at 20mg/kg 8 hourly.

Use of blood products as adjuvant therapy in the management of neonatal sepsis.

- Routine, prophylactic treatment with FFP and intravenous immunoglobulin (IVIG) in term babies, is/are not recommended when managing neonatal sepsis.
- The routine administration of IVIG to prevent or treat sepsis in very low birth weight infants is not recommended and the available evidence is adequate to state that there is no longer a need for further trials on this subject either.

9.6.2.8 COVID – 19 infection

Babies born to mothers with suspected / confirmed COVID 19
(annexure 1)

- The baby and the mother must be isolated together in a designated area in the hospital.

- Separation of baby and the mother MUST be avoided at all times.
- Kangaroo mother care and breastfeeding are encouraged
- If the mother tests positive for COVID-19, the newborn should be tested every 3rd day till discharge
- All newborns who test negative should be quarantined until 14 days after the mother tests negative
- Mother is advised to take the following measures to minimize the risk for baby contracting the disease from the mother
    - Respiratory hygiene (wear a mask) when handling the neonate / breastfeeding / expressing breast milk
    - Hand hygiene before and after handling the neonate / breastfeeding / expressing breastmilk

Prevent spread

All staff involved in the care of these babies should use

- contact precautions – use personal protective equipment (PPE) – long sleeve full body cover, apron, head cover, shoe cover, face shield / goggles, N 95 mask, boots, double gloves
- hand hygiene
- air droplet precautions – use full PPE during intubation, ventilation, bronchoscopy and minimize suction and nebulization
- disposable equipment where-ever possible

All surfaces contaminated with patient secretions should be disinfected with chlorine for 10 minutes prior to disposal into double layer infection medical waste

Mode of transmission

- Transmission was found to be environmental (70%) and vertical (30%).

Clinical features

- 55% of infected neonates developed symptoms of COVID-19

- Most common symptoms were
  - respiratory (52%) with abnormal lung imaging in 64%
  - fever (44%)
  - gastrointestinal (36%)
  - neurological manifestations (18%)
- Features of sepsis and septic shock may occur in sick neonates

Treatment

- There is no specific treatment
- Treatment should be carried out inside a closed incubator until 14 days if COVID negative since birth or 14 days since becoming COVID negative, in a well ventilated room, preferably with negative suction
- Treat as for sepsis with intravenous antibiotics and treat respiratory distress, circulatory compromise / shock as per national guidelines
- Respiratory care
  - Use lower tidal volumes, higher PEEP, lower PIP < 28
  - prone ventilation
  - in-line suction instead of disconnection
  - closed looped ventilation if available
  - keep the expiratory limb of the ventilatory circuit inside the incubator
- Surfactant, NO, HFOV and ECMO have been found to be useful
- Discard all disposable parts of the ventilator circuits
- Steroids are not recommended
- Visitors other than the mother should not be allowed as per national quarantine guidelines

Discharge criteria

- Temperature of the patient should be normal for more than 3 days
- Symptoms should improve
- Chest X ray / lung ultrasound should show improvement

- Specimens collected from the upper airway secretion (nasopharyngeal and pharyngeal swabs) should show negative 2 consecutive times (with at least 24 hour interval)

9.7 Prevention of neonatal sepsis

It is best to focus on practices that have been shown to reduce nosocomial infections (including hand hygiene, nutrition, skin care and vascular access care) and improving a culture of intensive care that dedicates itself to this goal.

Prevention of infection in hospital

- Adhere to 6 steps of hand washing
- Strict asepsis during procedures and when using central IV lines
- Safe delivery practices
- Early & exclusive breastfeeding
- Early enteral feeds
- Maternal tetanus immunisation
- Early diagnosis and prompt treatment of all maternal infections
- No pre-lacteal feeds
- Cord should be kept clean and dry.
- Avoid overcrowding
- Maintain hygiene
- Minimise invasive interventions such as needle pricks and IV alimentation
- Do not leave currently unnecessary intravenous lines. central venous lines or other lines or catheters such as intercostal tubes, urinary catheters insitu
- Nursery environment should be clean and dry
- Ensure round the clock water supply
- Adequate ventilation
- Maintain environmental temperature at 28 ± 2°C

Hand washing is the simplest and most effective method for controlling spread of infections in the hospital.

9.8 Drug doses

Ampicillin

<7days	30mg/kg 12hrly
7-21days	30mg/kg 8hrly
21-28days	30mg/kg 6hrly

If GBS is suspected

<7days	50mg/kg 12hrly
7-21days	50mg/kg 8hrly
21-28days	50mg/kg 6hrly

In meningitis increase the dose to 100mg/kg/8hrly

Amikacin - Less nephrotoxic than gentamicin

Loading dose	10mg/kg
Then	7.5mg/kg 12hrly

Benzyl penicillin

Neonates under 7 days	50mg/kg 12hrly
Neonates 7-28 days	50mg/kg 8hrly

In meningitis double the dose

In GBS meningitis give IV gentamicin for 5-7 days as well for synergistic action.

Cefotaxime

<7days	25mg/kg 12hrly
7-21days	25mg/kg 8hrly
21-28days	25mg/kg 6-8hrly

Double the dose in severe infections and meningitis

Flucloxacillin / cloxacillin

<7days	25mg/kg 12hrly
7-21days	25mg/kg 8hrly
21-28days	25mg/kg 6hrly

Double the dose in severe infection

Gentamicin

Extended interval dose regimen

<32 weeks	4-5mg/kg 36 hourly
>32 weeks	4-5mg/kg 24 hourly

Use of infusions and the above extended interval dose regime is less nephrotoxic and ototoxic)

Netilmicin

Dose	5mg/kg 24hrly

Meropenem

<7 days	20mg/kg 12hrly
7-28days	20mg/kg 8hrly

Double the dose in severe infection

Vancomycin

<29weeks	15mg/kg 24hrly
29-35 weeks	15mg/kg 12hrly
>35weeks	15mg/kg 8hrly

Summary

- Neonatal sepsis is a major contributor to neonatal mortality
- Signs of neonatal sepsis may be subtle
- Early detection and treatment can save lives
- Neonatal meningitis may not have specific CNS clinical features
- Rational use of antibiotics is essential for prevention of multi-resistant organisms

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NEONATAL SEIZURES

Chapter 10

NEONATAL SEIZURES

10.1 Introduction

A seizure in the neonatal period is an emergency. A seizure is a sudden alteration in neurologic function of a neonate i.e. motor, behavior and/or autonomic function. Seizures can occur due to problems like hypoxic ischaemic encephalopathy (HIE) (commonest cause), birth injuries, meningitis, intracranial bleeding or due to metabolic problems like hypoglycemia, hypocalcemia and hypo or hypernatremia. Inborn errors of metabolism and epileptic syndromes are rare causes of neonatal seizures.

10.2 Common types of Neonatal Seizures

The neonatal seizures are classified based on the involved part of the body or nature of the movements.

Classification according to part of the body involved

- Focal : localised part of the body
- Multifocal : multiple parts of the body
- Generalised : whole body

Classification according to nature of movements

- Subtle
  - **Commonest**
  - Repetitive blinking, eye deviation, or staring
  - Repetitive movements of mouth or tongue (chewing, sucking, lip smacking)
  - Purposeless movements of the limbs, as if cycling, swimming or rowing
  - Systemic – apnoea, tachycardia, blood pressure fluctuations, desaturations
- Clonic
  - repetitive rhythmic jerking, 1-4 times/second
  - usually involving one limb or one side of the body
  - consciousness usually preserved

- Tonic - sustained posturing of the limbs / trunk / deviation of the head
- Myoclonic - rapid isolated jerking of muscles which may be focal or multifocal

10.3 Jitteriness, sleep myoclonus and spasms due to tetanus

These should be differentiated from seizures. The latter is rare in Sri Lanka due to the maternal tetanus immunization programme.

Table 10.1: Comparison of jitteriness, benign neonatal sleep myoclonus, and spasms due to tetanus

Jitteriness	Benign neonatal sleep myoclonus	Spasms due to tetanus
Symmetrical rapid movements of hands and feet	Bilateral or unilateral jerking during sleep	Appears after 48 hours
Provoked by a stimulus	Occurs during active sleep	Involuntary contraction of muscles
Abolished by restraining	Not stimulus sensitive	Fists are persistently and tightly clenched
Not associated with autonomic changes (increased heart rate, blood pressure) or eye movements	Often involve upper>lower trunk	Trismus, opisthotonus
Examination is normal between episodes	Stops if baby is woken up	Triggered by touch, light or sound
EEG is always normal		Baby is conscious throughout; often crying in pain

Excessive jitteriness can be associated with,

- hypoglycaemia (fine jitteriness)
- hypocalcaemia
- hypoxic ischaemic encephalopathy
- intracranial haemorrhage
- drug withdrawal (coarse jitteriness)

10.4 Diagnostic approach

A detailed history should be taken and examination should be done after initial acute management of the seizure to determine underlying cause as neonatal seizures are rarely idiopathic. The identification of cause will help to manage and prognosticate.

The first line tests that need to be done are;

- Blood glucose
- Ionised calcium
- Serum Magnesium
- Serum sodium and
- Blood culture, CRP, full blood count and blood picture
- Ultrasound scan brain – haemorrhage / hypoxia / abnormality

Lumbar puncture (in the absence of any contraindications) for microscopy, protein, glucose and culture should be done if there is no history of hypoxia or drug withdrawal and there is no metabolic derangement or normal findings and the ultrasound scan is normal and cause for seizures cannot be otherwise explained or if there are clinical features or laboratory features (abnormal FBC / CRP) suggestive of sepsis / meningitis.

If the cause is not found from the above, the following investigations will need to be done especially in refractory cases.

- Electroencephalogram (EEG)
- Further Imaging – CT / MRI brain
- CSF studies for metabolic disorders
- Blood / urine investigations for IEM (in-born errors of metabolism)

10.5 Stepwise treatment of a neonate with seizures

- Resuscitate if needed: Place in thermoneutral environment and ensure a patent airway, effective breathing and adequate circulation (TABC).
- Oxygen should be started if required.
- Check capillary blood sugar at the bedside.
- If blood sugar is less than 45 mg/dl (in a baby with convulsions), correct hypoglycemia by a bolus of 2-3ml/kg 10% dextrose followed by a maintenance infusion of 6-8 mg/kg/min.

- Intravenous (IV) access should be secured and blood samples drawn for complete blood count, blood sugar, serum calcium, magnesium and electrolytes, FBC, CRP and blood culture.
- Anti convulsant drugs (ACD); ACD should be given if seizures persists even after correction of hypoglycemia a sample has been sent to check for hypocalcemia.

Commence treatment with ACD when:

- Clinically apparent seizure lasts more than three minutes
- More than two brief seizures occur within 20 minutes
- Electroencephalographic seizures are present

  - Inject phenobarbitone 20 mg/kg IV over 20 minutes. Maximum rate 1mg/kg/min. If the baby has no further seizures do not start maintenance

    If seizures persist after 15-20 minutes consider further boluses of phenobarbitone of 10mg/kg every 10 minutes up to a total (including initial bolus) of 40 mg/kg or one additional dose of 20 mg/kg IV

  - Levetiracetam can be used as a second line treatment if seizures are refractory to phenobarbitone.
    - Loading dose not required but may be given if urgent seizure control is required.
    - If loading dose is used, upto 40 mg/kg (initially 20mg/kg) IV followed by maintenance.
    - If no loading dose—10 mg/kg IV twice a day increasing by 10 mg/kg/day to a maximum of 30 mg/kg IV twice daily
    - Dilute to a concentration 5–15 mg/ml and infuse over 15 minutes
    - Maintenance dose may be given orally without regards to feeds; 10 mg/kg/dose orally daily or in two divided doses increasing by 10 mg/kg/day over three days to 30 mg/kg/day
  - If seizures persist - injection phenytoin 20mg/kg IV infused over 20 minutes. Maximum rate 1mg/kg/min. Assess the seizure control after 30 minutes. Give phenytoin slowly with

cardiac monitoring as it is arrhythmogenic. Should only be mixed with saline, as it precipitates in dextrose.

- A midazolam loading dose of 0.15mg/kg over 5 minutes followed by an infusion of 60-400µg/kg/hr can be commenced if further seizures occur.
    - If the seizures are controlled, a maintenance dose of Phenobarbitone (2.5mg/kg 12 hourly, 24 hours after the loading dose) and / or Phenytoin (4-5mg/kg/dose 12 hourly, 12 hours after loading dose). Start maintenance only if seizures continue after the loading doses.
- Other second line agents include lidocaine (lignocaine), topiramate and clonazepam.
- Hypocalcemic convulsions are generally resistant to anticonvulsants.
    a. Trace the calcium level – if low (<7mg/dl) or calcium levels are not available and the fits are still continuing
    b. Give 10% calcium gluconate 2mL/kg IV over 20 minutes.
    c. IV calcium therapy can cause serious cardiac arrhythmia - attach to a cardiac monitor - administer under strict supervision

    IV 10% Calcium gluconate is diluted with 10 fold volume of 0.9% NaCl or 5% dextrose and administered slowly (max. 0.1ml/kg/hr) under cardiac monitoring preferably by an infusion pump. Withhold infusion if HR<100/min). Do not add calcium to maintenance IV fluid; instead give it as a slow bolus preferably using a syringe infusion pump via a central vein eg. umbilical vein.

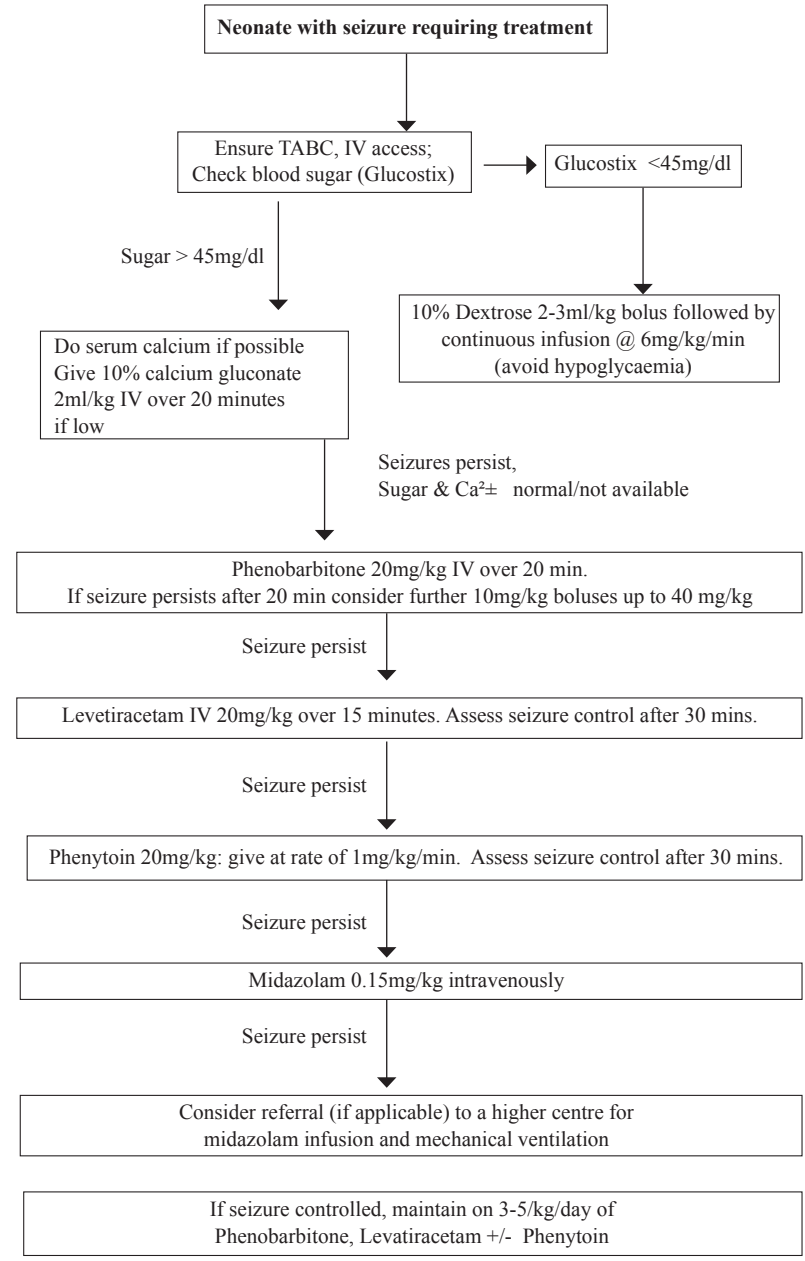
- If seizures are not controlled with phenobarbitone & phenytoin and NICU facilities are not available refer the baby to a centre with NICU facilities
- **Continue supportive treatment and management of underlying cause eg. meningitis**

10.6 When to discontinue ACD

The optimal duration of the ACD should be based on the neurological examination after seizures and associated specialised investigations like the EEG. Putting a baby on long term ACD when not required will produce potential long term adverse effects of the drugs.

Table 10.2: ACD plan according to the status of seizures

Condition	ACD Plan
Neonate with transient metabolic problem as the cause e.g. hypoglycemia, hypocalcaemia, electrolyte imbalance	Treat the cause; Stop the ACD immediately if started initially
Neonatal seizures that needed only one ACD with normal neurological examination and/or normal EEG	Stop ACD once seizures free for >72hours. Tapering not required
Neonatal seizures that are difficult to control (Need of multiple ACD)	If normal neurological examination and/or normal EEG and seizures free for >72hrs, stop the drugs one by one with phenobarbitone being the last to be withdrawn. Will need tapering. Try to stop few drugs prior to discharge. If neurological status is not normal, discharge on phenobarbotone, repeat neurological examination at one month(observe for development and tone) if normal, then taper and stop phenobarbitone over two weeks
If seizures recur during withdrawal of ACD	Reinstate the drug and refer to neurologist
If Neurological examination abnormal at 1 month follow up (abnormal tone, seizure)	Refer the baby to a higher centre for specialized investigations like EEG, neuroimaging and metabolic testing. If normal, then taper and stop Phenobarbitone over 2 weeks.



TABC : Temperature, airway, breathing, circulation

Fig. 10.1: Flow Chart for management of acute neonatal seizures

POST-RESUSCITATION MANAGEMENT OF A NEONATE WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

Chapter 11

POST-RESUSCITATION MANAGEMENT OF A NEONATE WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

11.1 Introduction

Hypoxic Ischaemic Encephalopathy (HIE) is a common neonatal condition that contributes significantly to neonatal morbidity and mortality. It accounts for approximately quarter of neonatal deaths worldwide. Hypoxic Ischaemic Encephalopathy (HIE) is an insult to the fetus or the newborn due to lack of oxygen (hypoxia) and perfusion (ischaemia) to various organs.

11.2 Definition of Hypoxic Ischaemic Encephalopathy (HIE)

HIE is an injury to the brain characterised by the presence of features of encephalopathy, due to poor flow of oxygenated blood to the brain.

- Hypoxia is identified by the presence of acidosis in the cord blood or the infant's blood within first hour of life with pH <7.0 / base excess > -16
- Ischaemia to the brain due to hypoxia
  - Occurs only after subsequent ischaemic damage to other organs, due to redistribution of blood flow as given in table 11.1.
  - Evidence of ischaemic damage to 2 or more organ systems increase the probability of ischaemic damage to the brain

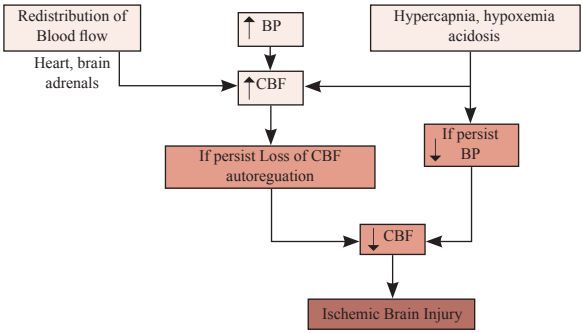


Figure 11.1 –Redistribution of blood flow to the brain in response to hypoxia

CBF – cerebral blood flow; BP – blood pressure
Available from https://img.medscapestatic.com/pi/meds/ckb/57/44457.jpg

Table 11.1 Multi-organ dysfunction seen in HIE

Organ system	Clinical manifestation of ischaemia
Heart (43-78%)	reduced myocardial contractility, severe hypotension, passive cardiac dilatation, tricuspid regurgitation
Lungs (71-86%)	Severe pulmonary hypertension requiring assisted ventilation
Renal (46-72%)	Renal failure presenting as oliguria initially and high output renal failure during recovery
Liver (80-85%)	Elevated liver function test results, AST>>ALT
Haematology 32-54%)	Disturbances include increased nucleated RBCs, neutropenia or neutrophilia, thrombocytopenia, and coagulopathy

11.3 Grading of severity of hypoxic ischemic encephalopathy

The classification of the severity of neonatal encephalopathy is primarily based on the system introduced by Sarnat and Sarnat in 1976[2]. An updated version has been used by the National Institute of Child Health and Human Development Neonatal Research Network[3] to identify newborn infants who may be eligible for neuro-protective treatment (Table 11.2).

Table 11.2 : Features of encephalopathy Based on Sarnat and Sarnat (1976), Shankaran et al. (2005) and Hahn JS (2009)[4]

Features	Severity of encephalopathy		
	Mild	Moderate	Severe
Level of consciousness	Alert or hyperalert	Lethargy	Stupor or coma
Spontaneous activity	May be normal	Decreased activity	No activity
Posture	May be normal	Distal flexion, complete extension	Decerebrate
Tone	Normal / hypertonia	Hypotonia	Flaccidity
Primitive reflexes			
Suck	Weak	Weak	Absent
Moro	Exaggerated	Incomplete	Absent

Features	Severity of encephalopathy		
	Mild	Moderate	Severe
Autonomic function			
Pupils	Dilated	Constricted	Deviated, dilated or non-reactive to light
Heart rate	Tachycardia	Bradycardia	Variable
Respiration	Normal	Periodic breathing	Apnoea
Other features			
Others	Irritability, jitteriness	Brainstem dysfunction	± elevated intracranial pressure
Seizures	Absent	±	Frequent; often refractory to anticonvulsants
EEG background	Normal	Low-voltage, periodic or paroxysmal	Periodic or isoelectric
Outcome	Normal	20-40% abnormal	Death or 100% abnormal

Courtesy: Roberton Textbook of Neonataology 5th Edition, 2013

11.4 Clinical presentation

- HIE may result in adverse effects on all major body systems including the kidney, brain, heart and lungs. The clinical features in asphyxiated babies range from mild to severe impairment.
- The extent of multi-organ dysfunction determines the early outcome of a neonate with HIE.
- The most severely affected babies may manifest with stupor or coma, periodic breathing or irregular respiration, hypotonia and loss of neonatal reflexes like Moro's and sucking.
- About 50% of the babies with moderate to severe HIE may have seizures.
- Severely affected babies may have progressive deterioration of the CNS function in terms of decreasing tone, increasing degree

of coma and prolonged apnoeas over the next 48 hours. These neonates would eventually die or have permanent neurologic sequelae.

11.5 Initial stabilisation and management

The management consists of supportive care to maintain temperature, perfusion, ventilation and normal metabolic state including glucose, calcium and acid-base balance. Early detection by clinical and biochemical monitoring and prompt management of complications must be done to prevent extension of cerebral injury.

- **Temperature:** The temperature should be maintained in the normal range of 36.5 – 37.2°C. **Uncontrolled hypothermia and hyperthermia are detrimental and should be avoided.**
- **Airway & breathing:** Patent airway should be maintained by appropriate positioning and any secretions should be cleared. The breathing should be monitored and supported as required.
- Oxygenation should be kept in the normal range by monitoring oxygen saturation by pulse oximetry if facilities exist. SpO2 should be maintained above 95% in term babies. Hypoxia should be treated with oxygen supplementation and if it does not improve or if the baby has respiratory distress CPAP or mechanical ventilation may be required.
- **Hyperoxia should always be avoided.**
- **IV fluids & enteral feeding:** Fluid administration in the first 24 hours should be at 40ml/kg/day (until urine output is established) provided normoglycaemia and perfusion are maintained. However, after 24 hours, body weight, blood chemistry, urine output and other clinical indicators of adequate hydration should guide fluid administration. Advancement of fluid administration should be guarded. Breast milk feeds should be commenced as early as possible even by nasogastric tube. Start enteral feeds with expressed breast milk (EBM) at 30ml/kg/day and increase as the baby tolerates. In those feeding directly at the breast allow feeding on demand.
- **Blood glucose:** Blood glucose should be monitored for at least first 48 hrs. If the baby is hypoglycemic, treat appropriately (Refer Chapter 6).

- **Calcium: hypocalcaemia is a common metabolic alteration in HIE. A subnormal serum Ca++ level may compromise cardiac contractility and may cause seizures.** Therefore add calcium 1mmol/kg/day to maintenance IV Fluid from day one to maintain calcium level **in the normal range 9-11 mg/dl(2.2-2.7mmol/l).** If a neonate has jitteriness or seizures check serum calcium (and glucose) and manage hypocalcemia if present. (Refer Chapter 10).
- **Vitamin K** 1mg IM must be administered to all those babies who have not received Vitamin K at birth.
- **Blood pressure:** In a neonate with HIE, cerebral blood flow depends on systemic blood pressure. Hence, maintain systemic mean arterial BP at 40 mmHg for term infants. The mean BP for preterm neonates should be maintained equal to gestational age in weeks as mmHg. If the neonate has poor perfusion, inotropes should be commenced early and volume expansion be minimised unless there has been a clear event of volume loss (e.g. abruptio placentae), as the reason for the impaired perfusion is usually poor cardiac contractility. If there is co-existent sepsis volume expansion may be required. In the presence of persistent pulmonary hypertension / meconium aspiration syndrome higher systemic blood pressures may be required.
- **Metabolic acidosis:** This should be confirmed (pH < 7.2 or base deficit > -10) with a cord blood gas or arterial, venous or capillary from the baby within the first hour of birth. If this does not improve with adequate ventilation, and perfusion is inadequate inotropes may be required to achieve adequate perfusion. If there has been an antepartum haemorrhage etc. volume replacement may be required by blood transfusion. Subsequent management of acidosis should be based on further assessment and sodium bicarbonate used very sparingly.
- **Seizures:** For management of seizures (refer Chapter 10).

Steroids, Mannitol, Furosemide & Sodium bicarbonate
HAVE NO ROLE IN MANAGEMENT OF HIE

- Therapeutic hypothermia
    - Therapuetic hypothermia is an established mode of management in newborns with hypoxic ischaemic encephalopathy in developed countries.
    - When using this therapy it is vital to have frequent monitoring of the baby in all clinical parameters including rectal temperature, measured via rectal probe in order to avoid complications of this intervention.
    - There is evidence from the 11 randomised controlled trials included in the 2013 Cochrane systematic review5 (N = 1505 infants) that therapeutic hypothermia is beneficial in term and late preterm newborns with hypoxic ischaemic encephalopathy. Cooling reduces mortality without increasing major disability in survivors. The benefits of cooling on survival and neurodevelopment outweigh the short-term adverse effects. Hypothermia should be instituted in term and late preterm infants with moderate-to-severe hypoxic ischaemic encephalopathy if identified before six hours of age.
- Local guidelines for this would be prepared and circulated once necessary equipment for safe use of this therapeutic modality is available.
- Start early stimulation and multidisciplinary care once stabilised. Early stimulation, physiotherapy, occupational therapy, swallowing assessment and oral stimulation lead to improved outcomes.

11.6 Monitoring

Clinical monitoring

All neonates with moderate to severe HIE must be closely monitored clinically as well as by performing certain bedside tests.

- The neurological status should be monitored by using the modified Sarnat score given in Table 11.2, every 8 hrs which has been found to be useful to detect improvement or further deterioration
- The respiratory status must be monitored by meticulous record of the respiratory score (Downe's score) every 2-3 hours (hourly if ventilated).

- The cardiovascular status assessment should include heart rate, colour, CRT, peripheral pulses, pulse oximetry and blood pressure.
- Gut ischaemia should be suspected and enteral feeds should be withheld if there is tense abdominal distension, tenderness or blood stained gastric aspirate.
- The hourly urine output should be calculated based on the urine output over a 6-hour period. It should normally be > 1ml/kg/hr after the first 24 hrs of life. If it remains < 1mL/kg/hr fluid status should be reassessed. Check serum electrolytes, blood urea and serum creatinine every 24 hours.
- Blood sugar should be monitored 6-8 hourly in first 24 hrs and then as required.
- Liver enzymes, serum creatinine & electrolytes coagulopathy screen (and troponin I if possible) should be done after 12-24 hours to see the extent of ischeamia due to hypoxic insult.

11.7 Poor prognostic factors

The presence of one or more of the following features may point towards poor neurodevelopmental outcome in the long term. These are:

1. Need for positive pressure ventilation for 5 days or longer
2. Onset of seizures within 12 hours
3. Severe HIE (See Table 11.2)
4. Inability to establish direct oral feeds by 1 week

11.8 Investigations for prognostication

EEG, amplitude integrated EEG and magnetic resonance imaging with spectroscopy (to identify metabolic status of the brain) is extremely useful in prognostication. Lactate-N-lactate/N-acetyl aspartate (Lac/NAA) peak/area ratio has a better prognostic accuracy than conventional and diffusion-weighted MRI for neurodevelopmental outcome after HIE. The pattern of injury on the MRI is also useful for prognostication and should be done if available.

Ultrasound scan of brain has a 50% sensitivity in identifying HIE and may prove useful in the local setting where MRI is not readily accessible. Imaging is a valuable asset in prognostication which is very useful when counselling parents, where white matter involvement indicates a better outcome compared to involvement of the thalami and the basal ganglia which indicate a poor outcome.

11.9 Post discharge & follow-up advice

- All neonates discharged with diagnosis of HIE must attend the follow up clinic for monitoring of growth and development, vision, hearing screening, assessment for possible cerebral palsy and need for early intervention, seizure control and family psychological status.

Summary

- Hypoxic ischemic encephalopathy is a significant cause of morbidity and mortality in neonates.
- A consensus definition accepted worldwide is not yet available.
- Post asphyxia management aims to minimise further insult to the brain and other organ systems
- Multi-system problems are seen in the acute stage which may require intensive care management. and neurodevelopmental impact is the most significant long term manifestation.
- Therapeutic hypothermia minimises post asphyxial brain insult with improvements in neurodevelopmental outcome and reduction in mortality.

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ANNEXURES

Annexure 01

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சுகாதார மற்றும் சுதேச வைத்திய சேவைகள் அமைச்சு
Ministry of Health and Indigenous Medical Services

Provincial Directors of Health Services
Regional Directors of Health Services
All heads of institutions,

Interim guidelines on management of newborns suspected or confirmed to have COVID-19
(Date: 24th April 2020)

This interim guideline for management of a neonate suspected/ confirmed of COVID-19, is prepared based on the all published literature on COVID-19 in neonates and those born to pregnant mothers with COVID-19, the WHO Guideline and the Chinese Expert Consensus on Perinatal Medicine and considering the prevailing situation, to provide optimal care for newborns during the current COVID-19 pandemic. This will be effective until further notice.

1. Background

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, SARS-CoV-2, that was first recognized in Wuhan, China, in December 2019. It is a beta corona virus, which is closely linked to the SARS virus. Coronavirus is an RNA virus in the family Coronaviridae, order Nidovirales, which is found in humans, mammals, and birds and can cause infections of the respiratory tract, gastrointestinal system, and nervous system.

2. Case definitions

Case definitions are taken as per definitions given by the Epidemiology Unit, Sri Lanka.

2.1 Suspected COVID-19

a) A newborn with acute respiratory illness AND having been in close-contact with a confirmed or suspected COVID-19 case during the last 14 days prior to onset of symptoms OR currently in quarantine (mother or caregivers with contact history of COVID 19)

OR

b) A newborn with acute respiratory illness with a history of fever (at any point of time during this illness) with a history of travel to or residence in a location designated as an area of high transmission of COVID-19 disease as defined by the Epidemiology Unit, MoH during the 14 days prior to onset of symptoms

OR

c) A newborn with acute pneumonia or respiratory distress regardless of contact history as decided by the treating Neonatologist/ Paediatrician

OR

d) A newborn, irrespective of the presence of symptoms, born to a mother suspected/ confirmed with COVID 19 according to the case definitions issued by the Epidemiology Unit, MoH

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2.2 Confirmed COVID-19

A neonate with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms

3. Point of care for COVID-19 suspected/ confirmed neonates

3.1 **All newborns should receive the usual standards of care in keeping with the clinical status, in a designated area. Management of these newborns should NOT be delayed under any circumstances pending COVID-19 test result.**

3.2 All newborns fitting to the 'suspected' case definition **should be admitted and transferred along with the mother** to the designated hospital for confirmatory testing and management. This should be done **only after stabilization** and in prior consultation with the designated hospital, adhering to necessary infection prevention and control (IPC) measures. All confirmed neonates should be transferred to the COVID-19 management centre.

3.3 All hospitals where deliveries occur should have an identified isolation room/ ward/ area to care for the neonate along with the mother until the baby is transferred.

3.4 There should be a separate isolation room/ ward for suspected neonates in the designated hospitals.

3.5 Negative pressure rooms with a minimum of 12 air changes or 160/L/s/patient facilities with natural ventilation should be used where available.

3.6 The isolation room should have facilities to provide respiratory support and intensive care to the neonate until the baby is transferred.

3.7 There should be a proper procedure to enter and exit from the isolation ward and for hand hygiene. The deployment of protective equipment should be strictly followed.

3.8 The presence of unnecessary individuals inside the room should be avoided.

3.9 All neonates confirmed of COVID-19 should be transferred to the COVID-19 treatment centre.

3.10 **All babies born to mothers suspected/ confirmed of COVID-19 should be isolated with their mothers**

In the event that the mother suspected of COVID-19 delivers the baby prior to transfer

a) Baby can be isolated with the mother, if the baby is well and does not require intensive care

b) Baby should be provided intensive care in a separate isolated room and stabilized prior to transfer, if the baby is sick.

3.11 **Attending the delivery of a mother suspected/ confirmed to have COVID-19**

a) All hospitals where deliveries occur should have a separate/ isolated delivery room and operation theatre.

b) The designated neonatal team in the isolation room comprising of the Medical Officer and Nursing Officer attending the delivery need to use standard, droplet, contact and airborne precautions including full PPE and N95.

c) Delayed cord clamping, skin to skin care and initiating breastfeeding within the first hour is recommended as there is no evidence of the virus in breast milk, neonatal disease is very mild and benefits outweigh the risks (Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected, Interim Guidance, World Health Organization, 13 March 2020).

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d) Mother and baby should be kept together facilitating uninterrupted breastfeeding.

3.12 **Breastfeeding the neonate of a mother suspected/ confirmed to have COVID-19**

a) All mothers should be provided with information and counseling on safe infant feeding and appropriate infection protection measures to prevent COVID-19 virus transmission as follows;

According to current evidence,

I. No vertical transmission is documented.
II. COVID 19 virus is not transmitted via breastmilk
III. Virus transmission can occur via droplets and contact with surfaces
IV. Benefits of breastfeeding including;
   - Protection against morbidity and death in the post-neonatal period and throughout infancy and childhood.
   - The strong protective effect against infectious diseases through direct transfer of antibodies and other anti-infective factors as well as long lasting transfer of immunological competence and memory.

V. Relatively a few cases of COVID 19 have been reported among newborns, who had only mild illness.

b) Basic psychosocial support and practical feeding support should be provided to all mothers with suspected or confirmed COVID-19.

c) Mother should be supported to practice the following:

I. Respiratory hygiene (wear a mask) when handling the neonate/ breastfeeding / expressing breast milk
II. Hand hygiene before and after handling the neonate/ breastfeeding/ expressing breastmilk
III. Clean surfaces, where mother has been in contact with

d) If the mother is too sick to provide direct breastfeeding, mothers should be encouraged and supported to express milk and safely provide breastmilk to the neonate applying appropriate IPC

e) The European Institute for Breastfeeding and Lactation recommends sterilization of all used vessels in addition to adequate hand hygiene

3.13 Separate doctors and nurses should be allocated to care for these babies including resuscitation at birth, stabilization, neonatal examination, supporting breastfeeding, monitoring and transfer of this baby to the designated hospital

3.14 Full PPE including airborne precautions with a N95 mask if available, needs to be taken when attending any airway procedure such as resuscitation, intubation, applying CPAP, airway suction etc.

3.15 No visitors will be allowed due to risk of transmission to other patients and health care staff.

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4. Investigations of symptomatic neonates born to mothers confirmed with COVID 19 or neonates presenting with respiratory symptoms suspected of COVID 19

4.1 Microbiological investigations

a) Blood cultures to exclude bacterial infection

I. Collect blood cultures for bacteria that cause pneumonia and sepsis, before antimicrobial therapy.

II. DO NOT delay antimicrobial therapy to collect blood cultures.

b) Specimens from respiratory tract

- Baby should be tested for COVID 19 PCR immediately after birth.

I. Upper respiratory tract (URT; nasopharyngeal and oropharyngeal)

- All suspected neonates for diagnosis
- To demonstrate viral clearance

II. Lower respiratory tract (LRT; endotracheal aspirate, or bronchoalveolar lavage in ventilated patient)

- When readily available – intubated patient – only LRT specimen can be used for diagnosis
- When URT specimen is negative for diagnosis in a symptomatic neonate
- In severe illness / pneumonia (single URT negative sample does not exclude the diagnosis)
- To demonstrate viral clearance

III. Sputum induction should be avoided due to increased risk of aerosol transmission

IV. Do not sample from nostrils or tonsils.

V. Use viral swabs and viral transport media.

VI. Dual infections have been demonstrated – therefore test for other viral and bacterial pathogens as well.

VII. Co-infections with Arbovirus infections like Dengue can occur - Positive diagnostic test for dengue does not exclude COVID-19

4.2 Other investigations

a) Full blood count - Normal or decreased leukocytes / Decreased lymphocytes / Mild thrombocytopenia

b) Other findings include elevated of Creatinine kinase, Alkaline phosphatase, Alanine aminotransferase, Aspartate aminotransferase, Lactate dehydrogenase

c) Imaging - Chest X Ray – features suggestive of pneumonia, Abdominal X ray – intestinal ileus.

5. Asymptomatic newborns born to COVID positive mothers or with contact history will need only COVID testing via upper respiratory tract and not the other investigations

The baby should be observed for any symptoms. Any significant concern with the baby should raise the suspicion of COVID 19 and the baby should be **re-tested with PCR test.** It does not need to be typical symptoms of COVID 19 as in adult patients.

6. Management of a baby with confirmed COVID-19 (for the designated hospitals)

The present evidence indicates that all affected neonates have been shown to have mild illness. None have been reported to have severe illness.

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6.1 Management of mild illness

a) Clinical features suggestive of a mild illness (Uncomplicated URT infection)

Nasal congestion, fever, cough without difficulty in breathing/ tachypnea, vomiting/ diarrhoea

b) Treatment of a mild illness

I. No specific treatment is needed
II. Isolate with mother
III. Use Paracetamol for fever

6.2 Management of severe illness

a) **Clinical features of severe illness**

I. Oxygen saturation via pulse oximetry < 95%
II. Features of respiratory distress; respiratory rate > 60/min, recessions grunting, nasal flaring
III. Cyanosis, inability to breastfeed, lethargy, convulsions
IV. Features of sepsis
    - Abnormality in temperature > 38C fever / < 36C **OR** Low white blood count **AND**
    - Tachycardia > 180/min **OR** Tachypnoea > 60/min
V. Features of septic shock
    - Hypotension (MAP < gestational age) **AND** 2 -3 of the following;
        - Lethargy / irritability
        - Tachycardia (> 180/min) and bradycardia (<100min)
        - Prolonged capillary refill (CRFT> 2s)/ poor pulse volume
        - Respiratory rate > 60/min
        - Mottling / petechial or purpuric skin rash
        - Increased lactate
        - Oliguria (<1ml/kg/hr)
        - Hypo / hyperthermia

b) **Treatment of severe illness**

I. Treat inside a closed incubator. Do not use open incubators.

II. Treat as for sepsis and treat with empirical antibiotics after blood culture within 1 hour of identification according to national treatment guidelines.
    - Inappropriate use of antibiotics, especially broad-spectrum antibiotics, should be avoided.

III. NO features of respiratory distress, in otherwise well baby with saturation < 95%
    - Start oxygen via nasal prongs 2L/min and titrate until saturation is ≥95%
    - A head cover is recommended by the Chinese Expert consensus Group

IV. Features of respiratory distress in otherwise well baby
    - Provide respiratory support with high flow oxygen therapy/ noninvasive ventilation using continuous positive airway pressure (CPAP) or noninvasive mandatory ventilation (NIMV)
    - Intubate and ventilate if no improvement/ incomplete resolution of respiratory distress after 1 hour

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V. **If mechanical ventilation is needed use;**
   - Low tidal volumes, lower peak inspiratory pressures < 28 cmH_2O with higher PEEP, lower target pH values on blood gas 7.15 – 7.30, prone ventilation for 12-16 hours a day,
   - Avoid disconnecting baby from the ventilator for suctioning – due to atelectasis
   - Use in-line suctioning and clamp ET tube when disconnecting (transfer to the transport ventilator)
   - Discard all disposable parts like ventilator circuits, infusion tubings etc and clean non disposable items using instructions given above

VI. Conservative fluid management strategy without tissue hypo perfusion

VII. Treat septic shock as per national guidelines

VIII. The following have been found to be useful with severe respiratory distress
   - Surfactant therapy
   - Inhaled nitric oxide (iNO)
   - High-frequency oscillatory ventilation (HFOV)
   - Continuous renal replacement therapy (CRRT)
   - Extracorporeal membrane lung (ECMO) therapy are required.

- **There is no evidence supporting the effectiveness of steroids, gamma globulin, interferon, or hormone therapy.**

7. Newborn care and screening

7.1 In addition to what is mentioned above, routine neonatal care should be provided.

7.2 Neonatal examination should be done within 24 hours, once the baby is stabilized.

7.3 BCG should be given before discharge.

7.4 Newborn screening for congenital hypothyroidism, critical congenital heart disease and congenital deafness should be done before discharge.

8. Discharge and follow up

8.1 Discharge criteria for **COVID positive newborn**

I. When the newborn is clinically well.

II. Fever free for more than 72 hours.

III. Two (2) negative PCR (nasopharyngeal and pharyngeal swabs) more than 24 hours apart.

IV. Chest X ray/ lung ultrasound should show improvement in previously severe infection

V. If the newborn is initially asymptomatic, but PCR positive, repeat PCR on day 10 and day 14 and discharge when two (2) negative PCR (nasopharyngeal and pharyngeal swabs) more than 24 hours apart become negative.

8.2 Discharge criteria for **COVID negative newborn of a COVID positive mother**

When the mother is ready for discharge, PCR (nasopharyngeal and pharyngeal swabs) testing of the newborn for COVID 19 should be conducted along with the second PCR test of the mother. If the PCR becomes negative, the baby can be discharged with the mother.

8.3 On discharge the patient should follow strict home isolation for minimum of 21 days (3 weeks).

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8.4 When planning the discharge of the newborn and mother, contact the Medical Officer of Maternal and Child Health in the district that the mother resides in and plan the mother and newborn to be transferred to their home for self isolation.

8.5 If the newborn becomes symptomatic, immediate PCR should be carried out and managed as COVID suspected newborn.

8.6 All neonates born to COVID positive mothers and COVID positive newborns should be reviewed at MOH clinic at one month following discharge from the hospital and referred to the nearest Paediatrician if necessary.

9. **In high risk areas**, consider all airway procedures including resuscitation, intubation, suction, non-invasive ventilation as high risk procedures and wear a tight surgical mask with head shield, gown with long sleeves and gloves.

10. **Preserve PPE or N95** for neonates born to COVID suspected mothers or for neonates presenting with clinical features suggestive of COVID-19.

For more details on use of PPE, refer "Guidance on the rational use of personal protective equipment (PPE) in hospitals in the context of COVID-19 disease" issued on 15th March 2020 (Annexure 01) and "Rational use of PPE and Infection Prevention and Control of COVID-19, Health care settings in Sri Lanka" issued on 2nd of April 2020. (http://www.epid.gov.lk/web/images/pdf/Circulars/Corona_virus/sri_lanka_ppe_covid-19_english.pdf) by Epidemiology Unit, Ministry of Health.

Refer "Environmental Cleaning Guidelines to be used during the COVID-19 outbreak – 15/03/2020" issued by the Epidemiology Unit, Ministry of Health (Annexure 02) for details on environmental cleaning.

The COVID-19 is a highly evolving illness. This guideline will be updated with the availability of new evidence.

You are advised to consider this as a top priority and give urgent attention to implement the above recommendations. This information must be urgently communicated to all relevant health staff in your respective institutions.

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