INTEGRATED PLAN FOR DETECTION & MANAGEMENT OF NEONATAL JAUNDICE

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DIVISION OF FAMILY HEALTH DEVELOPMENT
MINISTRY OF HEALTH MALAYSIA

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MINISTRY OF HEALTH MALAYSIA
2009 (Revised)

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FOREWORD

Jaundice is one of the most common conditions requiring medical attention in newborns. Jaundice is a treatable condition and should not be allowed to cause morbidity and mortality if addressed in its early stages. In most infants, jaundice reflects a normal transitional phenomenon, however, in some infants the serum bilirubin level may rise excessively, which can be a cause for concern as it can result in death and lifelong neurologic sequelae in infants who survive. For these reasons, the presence of neonatal jaundice frequently results in diagnostic evaluation.

It is essential that a newborn's jaundice be monitored closely by health care professionals as most healthy newborns require only a brief hospital stay. Health education of the population at risk, especially pregnant women, and early referral at primary health care level will reduce the burden of severe neonatal jaundice.

Previous efforts by the Ministry of Health have addressed the issue of jaundice with a special focus on G6PD deficiency. Many factors continue to cause the persistence of severe neonatal jaundice and in addition there are continuing difference between hospital and health in policy and communication. This is a combined document relating to neonatal jaundice that will be used by both hospital and health. Recommendations from this document call for closer vigilance of newborn for early detection of jaundice and effective treatment towards the prevention of kernicterus.

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1. INTRODUCTION

What is neonatal jaundice (Hyperbilirubinaemia)?

About 75% of normal newborns become clinically jaundiced sometime during the first week of life. Jaundice is apparent clinically, when the level of bilirubin in the serum rises above 85µmol/l (5mg/dl).

Physiological jaundice

Physiological jaundice occurs as a result of excessive bilirubin formation and because the neonatal liver cannot clear bilirubin rapidly enough from the blood. In normal term infants, this unconjugated (indirect) hyperbilirubinaemia usually appears between 24-72 hours of age, reaches a maximum on the 4-5th day and becomes undetectable after 14 days.

Pathological jaundice

Jaundice is considered pathological if its appearance, duration, or pattern varies significantly from that of physiological jaundice.
Features of pathological jaundice include:

- Clinical jaundice appearing in the first 24 hours of age
- Increase in the level of total bilirubin by more than 8.5 µmol/l/hour (0.5 mg/dl/ hour) or 85 µmol/l/24hours (5 mg/dl/24 hours).
- Total serum bilirubin more than 340 µmol/l (20 mg/dl) in a full term infant
- Conjugated (Direct) hyperbilirubinaemia more than 34 µmol/l (2.0 mg/dl) or more than15% of total bilirubin)

Prolonged jaundice

Prolonged jaundice refers to jaundice persisting beyond the first two weeks of life in the term infant or three weeks in the preterm infant. Its causes include late onset breast milk jaundice, urinary tract infection, congenital hypothyroidism, biliary atresia and other uncommon conditions.

Causes of neonatal jaundice

- Physiological jaundice
- Haemolysis due to ABO or Rh isoimmunisation, G6PD deficiency, microspherocytosis, drugs
- Cephalhaematoma, Subaponeurotic haemorrhage
- Polycythaemia
- Infection e.g. sepsis, meningitis, urinary tract infection and intra-uterine infection
- Breastfeeding and breastmilk jaundice
- Gastrointestinal tract obstruction: increase in enterohepatic circulation

Risk factors for severe jaundice

- Prematurity (< 36 weeks)
- Low birth weight (< 2.5kg)
- Sepsis
- Infant of diabetic mother
- Onset of jaundice before 24 hours of life
- A sibling with severe neonatal jaundice or exchange transfusion
- Dehydration
- Inadequate breastfeeding
- Mothers with blood group O / Rhesus negative
- G6PD deficiency
- Acidosis
- Asphyxia

Complications of severe jaundice

Although most newborns with jaundice are otherwise healthy, they need to be monitored because bilirubin is potentially toxic to the central nervous system. Sufficiently elevated levels of bilirubin can lead to acute bilirubin encephalopathy and subsequently kernicterus. Kernicterus is associated with a high mortality, and survivors usually suffer sequelae like athetoid cerebral palsy, intellectual disability and high frequency hearing loss. The factors influencing bilirubin toxicity in the brain cells of the neonate are complex and incompletely understood. There is no specific level of total serum bilirubin above which kernicterus can be predicted to happen.

Measures to prevent severe neonatal jaundice

1. Inadequate breast milk flow in the first week may aggravate jaundice. Supportive measures should be present to promote successful breastfeeding. Supplements may be needed temporarily to ensure adequate hydration, especially if there is more than 10% weight loss from birth weight.

2. Interruption of breastfeeding in healthy term newborns is discouraged and frequent breast-feeding (at least 8-10 times every 24 hours) should be continued. Supplementing with water or dextrose water does not lower bilirubin level in healthy, jaundiced and breast-feeding infants.

3. Ideally G6PD status should be known before discharge. If G6PD deficient, it is recommended that the baby is observed for 5 days in the absence of NNJ and longer with moderate jaundice.

4. Infants of mothers with blood group “O” and with a sibling who had severe neonatal jaundice should be observed for at least the first 24 hours of life.

5. If phototherapy is used for infants with haemolytic diseases or is initiated early and discontinued before the infant is 3 to 4 days old, monitor for rebound jaundice and adequacy of breast feeding within the next 24-48 hours.

Follow-up

1. Follow-up should be provided to all babies discharged less than 48 hours after birth, by a health care professional in an ambulatory setting, or at home within 2-3 days of discharge.

2. Babies with serum bilirubin > 340 µmol/l (20 mg/dl) and those who required exchange transfusion should be kept under follow-up in the high-risk clinic for neuro-developmental outcome. Hearing assessment (using BSER, not OAE) should be done at 0-3 months of corrected age.

2. SCREENING AND DETECTION OF NEONATAL JAUNDICE

Neonatal jaundice screening and parental education begins from the antenatal period and extend into the early neonatal period.

Antenatal care

1. Education on neonatal jaudice should be provided for the expectant mother and a pamphlet should be given to her (see Appendix 7.1 for Parent Education Leaflet).

2. All mothers should have blood taken for ABO and Rhesus group.

3. Identify other risk factors for significant jaundice e.g. family history of severe neonatal jaundice, exchange transfusion and haemolytic diseases.

Intrapartum care

1. Take cord blood for G6PD screening.

2. Attempts must be made to obtain G6PD results before the baby is discharged from hospital or as soon as possible in home deliveries.

3. G6PD results must be informed to parents and also be documented in the Home-based Child Health Card and the G6PD register book.

4. If result shows G6PD deficiency, the infant is to remain or be admitted to hospital for observation and monitoring for at least 5 days.

5. When the mother is Rh-negative, a direct Coombs' test, ABO blood type, Rh(D) type, bilirubin level and haemoglobin level (full blood count) on the infant's (cord) blood are required.

Postnatal care

1. Education on neonatal jaundice should be reinforced in the postnatal period.

2. Support the mother to breastfed the infant adequately (at least 8-10 times every 24 hours) to minimize the severity of neonatal jaundice. Supplements may be needed temporarily to ensure adequate hydration. Expressed breast milk should be given. If not available or inadequate use formula milk.

3. Nursing personnel should actively look for signs of jaundice during routine care of the mother and infant.

4. Infants of mothers with blood group “O” should be examined for jaundice before discharge. If jaundiced is noted, serum bilirubin should be done before they leave the ward and managed appropriately. If jaundice is not detected on discharge, the mother should be given written instructions (see Appendix 7.1 for Parent Education Leaflet) to inform the local health staff to review the baby the following day.

Home visit during the postnatal period

1. Home visit should be for all newborns on day 1, 2, 3, 4, 6, 10 and 20. Special attention for jaundice must be taken on day 2, 3 and 4 of life.

2. If the jaundice is detected, daily visits should be conducted to monitor the severity of jaundice.

3. For the infant with jaundice, sunlight exposure is not recommended. Although sunlight provides sufficient irradiance in the 425 to 475 nm band for conventional phototherapy, there is a risk of dehydration and sunburn.

High risk factors for neonatal jaundice

The following newborns are at higher risk of developing severe neonatal jaundice.

1. Prematurity (< 37 week gestation)
2. Low birth weight (< 2.5 kg)
3. Sepsis
4. Infant of diabetic mother
5. Onset of jaundice before 24 hours of life
6. A sibling with severe neonatal jaundice or exchange transfusion
7. Dehydration
8. Inadequate breastfeeding
9. Mother with blood group O or Rh negative
10. G6PD deficiency

Clinical detection of jaundice

Neonatal jaundice first becomes visible on the face and forehead then gradually extend to the trunk and extremities. Jaundice can be detected by blanching the skin with finger pressure. The health care provider should examine the baby under good lighting for presence and severity of jaundice.

The severity of the jaundice is determined clinically by the area of skin involved (see Table 1 and Figure 1). Usually, a total serum bilirubin level is the only testing required.

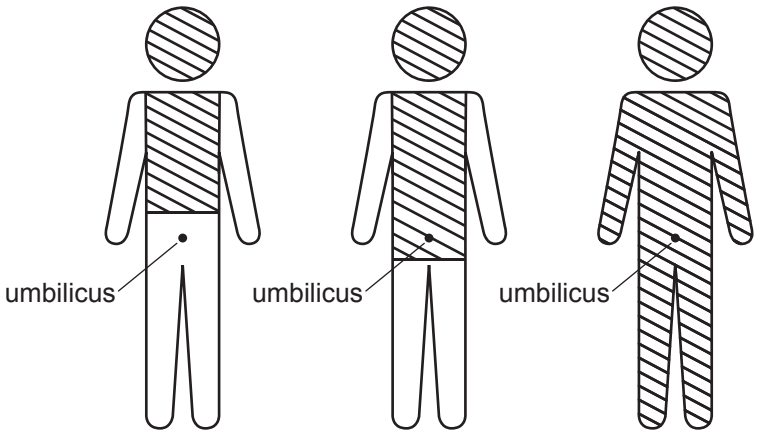
Table 1 : Clinical assessment of neonatal jaundice (Kramer's rule)

Area of the Body	Range of serum bilirubin	
	µmol/l	mg/dl
Head & neck	68-135	4-8
Over upper trunk above umbilicus	85-204	5-12
Lower trunk & thighs (below umbilicus)	136-272	8-16
Arms & lower legs	187-306	11-18
Palms & soles	>306	>18

Note: This may be difficult in dark skinned infants

Visual inspection of the infant, including Kramer's rule, can only be used as a guide to the level of jaundice. There is a wide inter-obsever error in the clinical estimation of the level of jaundice. In equivocal cases a formal serum bilirubin measurement should be done.

Figure 1 : Diagram showing the degree of neonatal jaundice



(Ref. Kramer, L.I., Am. J. Dis. Childhood, 18: 454, 1969)

Criteria for serum bilirubin testing

1. Any jaundice before 24 hours of life (these infant should be admitted)
2. Any jaundice below the umbilicus after 24 hours of life
3. Any unwell infant with jaundice

See Appendix 7.2 for the technique of capillary blood sampling for bilirubin testing.

3. CRITERIA FOR ADMISSION FOR NEONATAL JAUNDICE

Infants with the following criteria must be admitted:

1. Onset of jaundice within 24 hours.
2. Infant who require phototherapy based on Table 2.
3. Clinical jaundice below umbilicus.
4. Jaundice up to the level of the sole of the feet – likely to need exchange transfusion.
5. Rapid rise of serum bilirubin of more than 8.5µmol/l/hour (> 0.5mg/dl/hour)
6. All G6PD deficient infants with or without jaundice (to keep for at least 5 days)
7. Other haemolytic disorders eg. ABO incompatibility and Rh isoimmunisation.
8. Clinical symptoms / signs suggestive of sepsis.

Table 2 : Guidelines for phototherapy (hospitalisation) in infants > 35 weeks' gestation

Hours of life	Total serum bilirubin levels µmol/l (mg/dl)	
	Healthy term baby	Any risk factor*
< 24	Infants jaundiced at < 24 hours of life are not considered healthy & require admission	
24	170 (10)	135 (8)
48	220 (13)	185 (11)
72	255 (15)	220 (13)
96	290 (17)	240 (14)
> 96	305 (18)	255 (15)

** NB: Risk factors include prematurity (< 37 weeks gestation), low birth weight (< 2.5 kg), sepsis, haemolysis*

Consider admission in the following cases:

The situations listed below require consideration for admission. These infants should be sent to the hospital for review and may be admitted.

1. Jaundice in an infant who has a sibling with past history of severe NNJ / exchange transfusion.
2. Infants with large cephalohaematoma or severe bruising.
3. Jaundice in an infant with logistic problems eg. remoteness / social reasons for follow-up and monitoring.

Infants referred from the health centres for jaundice should be considered for admission as it may have been difficult for health staff to persuade parents to come to hospital. However, in cases where mothers are able to care for their infants and serum bilirubin can be measured, patients with mild jaundice can be allowed to go home and followed up by the local clinic.

Detection and management of NNJ at the postnatal ward in hospitals with and without specialists

Refer to the flow diagrams in the Appendix 7.7 and 7.8 that outline care at these two locations.

4. MANAGEMENT OF INFANTS ADMITTED FOR NEONATAL JAUNDICE

Approach to an infant with jaundice

History

- Age of onset of jaundice
- Previous infants with hemolysis, G6PD deficiency, severe neonatal jaundice or exchange transfusion
- Mother's blood group
- Gestation: the incidence of hyperbilirubinaemia increases with prematurity
- Symptoms of sepsis, apnoea, difficulty in feeding, feed intolerance and temperature instability

Physical examination

- General condition, gestation and weight, signs of sepsis, hydration status
- Signs of kernicterus e.g. lethargy, hypotonia, seizure, opisthotonus, high pitch cry
- Pallor, plethora, cephalhaematoma, subaponeurotic haemorrhage, bruises
- Signs of intrauterine infection e.g. petechiae, hepatosplenomegaly
- Cephalo-caudal progression of severity of jaundice (refer Table 1)

Indications for referral to hospital:

1. Jaundice within 24 hours of life.
2. Jaundice below umbilicus, corresponding to serum bilirubin of 12-15 mg/dl (200-250 µmol/L).
3. Jaundice up to level of the sole of the feet - urgent referral, likely to need exchange transfusion.
4. Family history of significant haemolytic disease or kernicterus
5. Any unwell infant with jaundice
6. Prolonged jaundice more than 14 days (see Prolonged neonatal jaundice - page 18)

Investigations

- Total serum bilirubin
- G6PD status
- Others as indicated:
  - Maternal blood group, infant's blood group, direct Coomb's test
  - Full blood count, reticulocyte count, peripheral blood film
  - Blood culture, urine microscopy and culture (if infection is suspected)

Treatment

Sunlight exposure is not recommended
Although sunlight provides sufficient irradiance in the 425-475 nm band for conventional phototherapy, there is a risk of dehydration and sunburn.

1. Phototherapy

- Conventional phototherapy lights should be maintained with a minimum irradiance of 12 μW/cm^2/nm. Measure intensity of phototherapy light periodically using irradiance meters
- Intensive phototherapy irradiance in the blue-green spectrum (wavelengths of approximately 430 - 490 nm) should be maintained with a minimum irradiance of at least 30 μW/cm2 per nm (measured at the infant's skin directly below the centre of the phototherapy unit)
- Position light source 35-50 cm from top surface of the infant (when conventional fluorescent photolights are used.)
- Expose infant appropriately
- Cover infant's eyes
- Monitor serum bilirubin levels as indicated
- Monitor infant's temperature 4 hourly to avoid chilling or overheating
- Ensure adequate hydration through breastfeeding (at least 8-10 times every 24 hours). Supplements may be needed temporarily to ensure adequate hydration, especially if there is more than 10% weight loss from birth weight.
- Monitor urine output
- Allow parental-infant interaction
- Discontinue phototherapy when bilirubin is 30 μmol/L below phototherapy level.
- For term infants, discontinue phototherapy when total bilirubin is below 240-250 μmol/l (14-15 mg/dl).
- In infants without haemolytic disease, the average bilirubin increase of rebound jaundice after phototherapy is less than 17 μmol/l (1 mg/dl). Discharge from hospital need not be delayed in order to observe the infant for rebound jaundice, and in most cases, no further measurement of bilirubin is necessary.
- Turn off photolights during feeding and blood taking

Indications for intensive phototherapy

- Total bilirubin >300 μmol/l (17.5 mg/dl)
- Early onset jaundice (first 48 hours)
- Rapidly rising jaundice > 8.5 μmol/l/hour (0.5 mg/dl/hour)
- Based on Table 3

Once the baby is on phototherapy, visual observation as a means of monitoring is unreliable. Serum bilirubin levels must guide the management.

Table 3 : Guidelines for phototherapy and exchange transfusion (ET) in hospitalized infants of 35 or more weeks' gestation

Hours of life	Total serum bilirubin levels µmol/l (mg/dl)					
	Infants at lower risk (≥ 38 week & well)		Infants at medium risk (≥ 38 week + risk factors or 35-37 6/7 week & well)		Infants at higher risk (35-37 6/7 week + risk factors)	
	Intensive phototherapy	ET	Intensive phototherapy	ET	Intensive phototherapy	ET
< 24*						
24	200 (12)	325 (19)	170 (10)	290 (17)	135 (8)	255 (15)
48	255 (15)	375 (22)	220 (13)	325 (19)	185 (11)	290 (17)
72	305 (18)	410 (24)	255 (15)	360 (21)	220 (13)	315 (18.5)
96	340 (20)	425 (25)	290 (17)	380 (22.5)	240 (14)	325 (19)
> 96	360 (21)	425 (25)	305 (18)	380 (22.5)	255 (15)	325 (19)

Source: Derived from Figures 2 & 3 - page 11

1. Start conventional phototherapy at TSB 50 µmol/l (3 mg/dl) below the levels for intensive phototherapy.
2. Risk factors - isoimmune hemolytic disease; G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin < 3.0 g/dl.
3. *Infants jaundiced at < 24 hours of life are not considered healthy and require further evaluation.

Note:

1. Failure of phototherapy has been defined as an inability to observe a decline in bilirubin of 17-34 µmol/l (1-2 mg/dl) after 4-6 hours and/ or to keep the bilirubin below the exchange transfusion level.

2. Immediate exchange transfusion is recommended if infants show signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonus, fever, high pitch cry) or if TSB is 85 µmol/l ≥ (5 mg/d) above the intensive phototherapy or exchange transfusion levels.

3. Use total bilirubin level. Do not subtract direct reacting or conjugated bilirubin.

4. ET is recommended if the TSB rises to these levels (Table 3) despite intensive phototherapy.

5. For infants referred for neonatal jaundice - if the TSB level is above the ET level repeat the TSB measurement every 2 to 3 hours and consider ET if the TSB levels remain above the ET level for 6 hours under intensive phototherapy.

6. Infants who are of lower gestation will require phototherapy and ET at lower levels, (please check with your specialist).

Figure 2 : Guidelines for intensive phototherapy in hospitalized infants 35 or more weeks' gestation

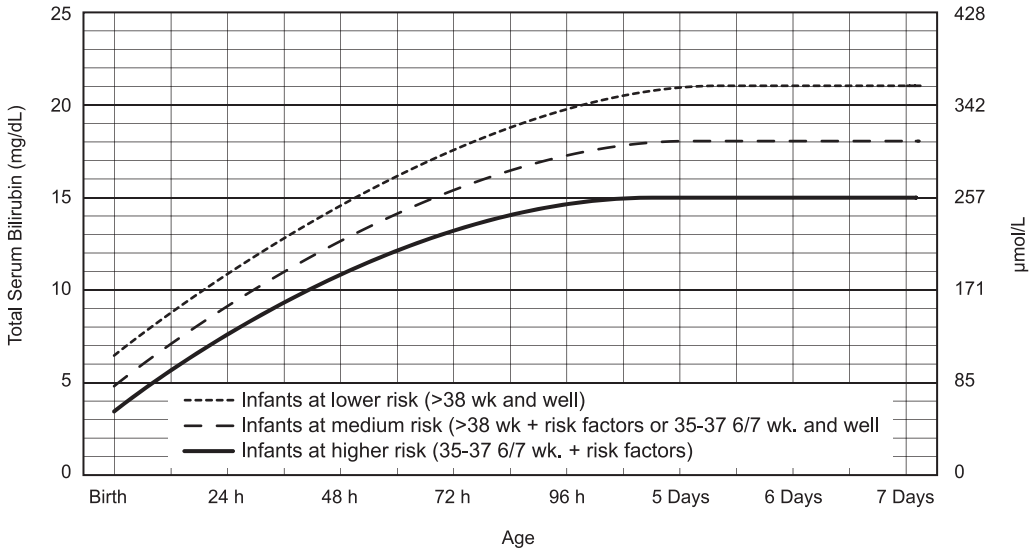
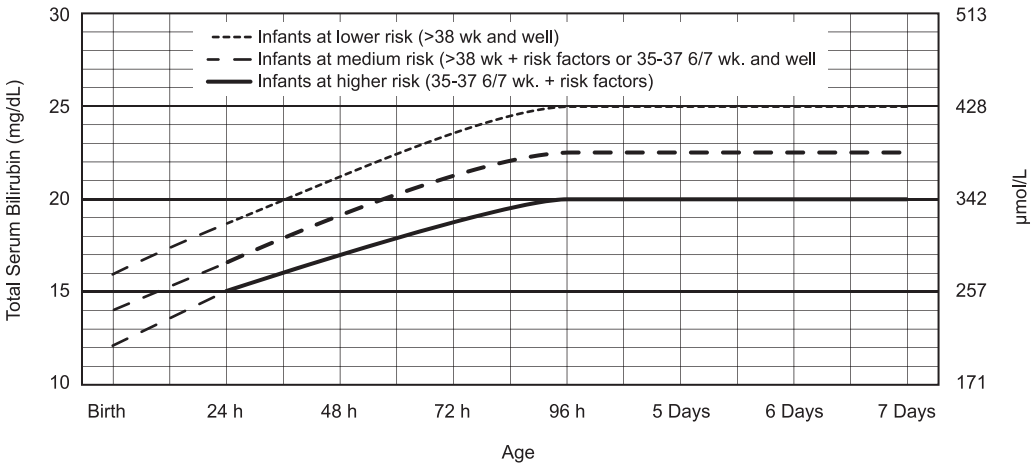


Figure 3 : Guidelines for exchange transfusion in infants 35 or more weeks' gestation



* The dashed lines for the first 24 hours indicate uncertainly due to a wide range of clinical circumstances and a range of responses to phototheraphy.
* Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high piched cry) or if TSB is 25 ml/dl (85 µmol/L) above these lines.

Source : American Academy of Paediatrics. Pediatrics, 2004. 114:297-316

Follow-up

1. Parents should be advised to bring baby to the nearest clinic the next day after discharge for review of jaundice.
2. Babies serum bilirubin > 340 µmol/l (> 20 mg/dl) and those who require exchange transfusion should be kept under follow-up for neuro-developmental outcome. Hearing assessment should be done as early as possible.

2. Exchange Transfusion

Exchange transfusion (ET) is usually indicated for severe hyperbilirubinaemia to lower the serum bilirubin level and reduce the risk of brain damage and kernictirus. Kernicterus has at least 10% mortality and 70% long term morbidity. Neonates with significant neonatal jaundice should be monitored closely and treated appropriately with intensive phototherapy. The mortality within 6 hours of ET ranged from zero death to 3 - 4 per 1000 exchanged term infants. The causes of death include kernicterus itself, necrotising enterocolitis, infection and procedure related events.

Preparation of infant

a. Get a signed informed consent from parent.
b. Resuscitation equipment is available.
c. Stabilise and maintain temperature, pulse and respiration.
d. Set a peripheral line for maintenance intravenous fluid.
e. Proper gentle restraint.
f. Continue feeding the baby and omit only the LAST feed before ET. If less than 4 hours from the last feed, empty gastric content by doing NG aspiration before ET.

Grouping of blood to be used

Rh isoimmunisation	-	ABO compatible, Rh negative blood
Other conditions	-	cross-match with baby and mother's blood
Emergency (rarely)	-	'O' Rh negative blood

Procedure (Exchange Transfusion)

1. Volume to be exchanged is twice blood volume (2x80mls/kg)
2. Use fresh whole blood preferably less than 5 days old
3. Connect baby to cardiac monitor.
4. Take baseline observations (either via monitor or manually) and record down on the neonatal exchange blood transfusion sheet. The following observations are recorded every 15 minutes; apex beat, respiration, oxygen saturation.
5. Doctor performs the ET under aseptic technique with gown and mask.
6. Cannulate the umbilical vein to a depth of NOT > 5-7cm (for push-pull technique ET through UVC).
7. Aliquot for removal and replacement – 5-8 mls/ kg (Not more than 10% of blood volume) Maximum volume per cycle - 20 mls for term infants
8. At the same time the nurse keeps a record of the amount of blood given or withdrawn, and medications given (see below).

Isovolumetric or continuous technique

- Indication – where UVC is not possible e.g. umbilical sepsis, failed cannulation
- Blood is replaced as a continuous infusion into a large peripheral vein while removing small

amount blood from an arterial catheter at regular intervals.

- In smaller infant, e.g. in a 1.5 kg baby, total volume to be exchanged is 240 mls. Delivering 120mls an hour allowing 10 ml of blood to be removed every 5 mins for 2 hours.

Points to note

a) Volume of blood to exchange 160mls/kg body weight (2 x blood volume of 80 ml/kg).
b) Pre-warm blood using a blood warmar, taking care not to overheat the blood.
   i. 1ml of 4.2% NaHCO3 given for every 100mls of blood exchanged
   ii. 1ml of 10% Calcium gluconate for every 160mls of blood exchanged *
   iii. **NEVER give the two solutions (NaHCO3 & Ca gluconate) together.**
   iv. **Dilute and give calcium via peripheral vein as a slow bolus and NOT through UVC.** (Check that the peripheral vein cannula is in situ to prevent extravasation injuries)
   v. **Shake blood bag gently and frequently to prevent settling of red blood cells.**
c) Rate of exchange 4-5 minutes per cycle (1 minute 'out', 1 minute 'in', 1-2 minute 'pause' excluding time to discard blood and draw from blood bag).
d) Total exchange time should be about 90-120 minutes.
e) Exchange should start with removal of blood, so that there is always a deficit to avoid cardiac overload.
f) Remove the UVC after procedure unless a second ET is anticipated and there was difficulty inserting the UVC.
g) Continue intensive phototherapy after the procedure.
h) Repeat ET may be required in 6 hours for infants with high rebound SB
i) Feed after 4-6 hours if patient is well and a repeat ET not required.
j) If child is anaemic (pre-exchange Hb <12 g/dL) give an extra aliquot volume of blood (10 mls/kg) at the end of transfusion at a rate of 5 mls/kg/hr after the ET

Investigations

a. Pre-exchange (1st volume of blood removed)
   i) Serum bilirubin
   ii) FBC
   iii) Blood C&S as indicated (through peripheral venous blood not UVC to reduce contamination)
   iv) HIV, Hepatitis B (baseline)
   v) Others as indicated if patient is unwell

b. Post-exchange - Always discard the blood remaining in the UVC first before sampling
   i) Serum bilirubin
   ii) FBC
   iii) Dextrostix
   iv) Serum electrolytes
   v) Serum calcium
   vi) Others as indicated

c. 4 to 6 hour post-exchange
   i) SB

Follow-up

Long term follow-up to monitor hearing and neurodevelopmental assessment

Complications of exchange tranfusion

1. Catheter related
   - Infection
   - Haemorrhage
   - Necrotising enterocolitis (NEC)
   - Air embolism
   - Portal and splenic vein thrombosis (late sequelae)

2. Haemodynamic problems
   - Overload cardiac failure
   - Hypovolaemic shock
   - Arrhythmia (catheter tip near sinus node in right atrium)
   - Bradycardia with calcium bolus

3. Electrolyte imbalance
   - High potassium
   - Low calsium
   - ↑ or ↓ Blood glucose
   - Acidosis (sometimes late alkalosis due to breakdown of citrate)

Intravenous Immunoglobulins

High dose intravenous immunoglobulin (IVIG) (0.5 to 1 gm/kg single dose) has been shown to reduce the need for exchange transfusions in Rh and ABO hemolytic disease. It can be given after ET or as early as possible if ET is not as yet indicated that is if the TSB is rising despite intensive phototherapy or the TSB level is within 35-50 µmol/l (2-3mg/dl) of the exchange level.

5. SPECIAL AREAS/ ISSUES

Breastfeeding and jaundice

Inadequate breast milk flow in the first week may aggravate jaundice. Supportive measures should be there to promote successful breastfeeding. Supplements may be needed temporarily to ensure adequate hydration. Expressed breast milk should be given. If not available or inadequate use formula milk.

Interruption of breastfeeding in healthy term newborns is discouraged and frequent breast-feeding (at least 8-10 times every 24 hours) should be continued. Supplementing with water or dextrose water does not lower bilirubin level in jaundiced, healthy, breast-feeding infants.

Rhesus & ABO Incompatibility

Maternal prenatal testing should include ABO and Rh(D) typing. Both of these are associated with severe haemolytic neonatal jaundice.

Rh-negative mother should ideally deliver in hospital. When the mother is Rh-negative, a direct Coombs' test, ABO blood type, Rh(D) type, bilirubin level and haemoglobin level (full blood count) on the infant's (cord) blood are required. The infant should be referred to the paediatric team to decide on further management and should not be discharged until there is no risk of severe jaundice.

Infants of mothers with blood group "O" should be examined for jaundice before discharge. If jaundiced, serum bilirubin should be performed on these infants before they are sent home and managed appropriately. If not jaundiced or sent home, the mother should be given written instructions (see Appendix for Parent Education Leaflet) to inform the local health staff to review the baby the next day.

G6PD Deficiency

Magnitude of problem

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common human enzyme deficiency. It is an X-linked recessive condition. It affects 2.5% of newborns locally and is higher in boys (3.1%) and certain ethnic groups (Malays 2.2-3.5%, Chinese 3.1-4.5%, Dayaks 5%, Orang Asli 8- 23%). The contribution of G6PD deficiency to severe NNJ and kernicterus has declined over the years but it remains an important cause of haemolytic neonatal jaundice.

G6PD deficiency screening test

The screening test for G6PD deficiency is the semi-quantitative fluorescent spot test. It has the advantage of being simple and rapid. However, this test has a false positive rate of 13.3 % (sensitivity 97.9% and specificity 86.6%). See Appendix 7.4 and 7.5.

All infants must have G6PD screening done on cord blood. Ideally the G6PD status should be known before discharge. Any neonate who is discharged without the G6PD status should have

the results obtained within 24 hours and if deficient, the parents should be notified and re-admitted as soon as possible. For home and clinic deliveries the G6PD status should be traced by the health staff.

Management

All infants with G6PD deficiency, including home deliveries, should be observed in hospital for at least 5 days. In the absence of jaundice, the infant can be discharged on day 6. If jaundice is detected, treat accordingly.

Table 4 below outlines the list of drugs and foods/herbs to avoid in children with G6PD deficiency. All parents must be educated and given written guidelines on drugs and foods/herbs that should be avoided.

Table 4 : Agents to be avoided in G6PD deficiency patients

1) Food and herbs to be avoided - Fava Beans (Kacang Parang) - Documented Chinese herbs/medicine Chuen Lin San Chi 13 herbs 12 herbs Other traditional herbs/medications are also not to be taken unless with medical advice **2) Other chemicals to be avoided** - Naphthalene (moth balls) - Mosquito coils and insect repellants which contains pyrethium **3) Drugs to be avoided or contraindicated** - Acetanilide - Doxorubicin - Furazolidene - Methylene Blue - Nalidixic acid - Niridazole - Nitrofurantoin - Phenozopyridine - Promaquine - Sulfamethoxazole - Bactrim	**4) Drugs that can be safely given in therapeutic doses** - Paracetamol - Ascorbic Acid - Aspirin - Chloramphenicol - Chloroquine - Colchicine - Diphendramine - Isoniazid - Phenacetin - Phenylbutazone - Phenytoin - Probenecid - Procainamide - Pyrimethamine - Quinidine - Streptomycin - Sulfisoxazole - Trimethoprim - Tripelennamine - Vitamin K - Mefloquine

Prolonged neonatal jaundice

Definition

Visible jaundice (SB >85 µmol/l) that persists beyond 14 days of life in a term infant or 21 days in a preterm infant.

Causes of prolonged jaundice

It may be unconjugated or conjugated hyperbilirubinaemia (Table 5). Conjugated hyperbilirubinaemia is defined as the direct (conjugated) fraction of bilirubin more than 34 µmol/l (2mg/dl), or more than 15% of the total bilirubin.

Table 5 : Causes of Unconjugated and Conjugated Hyperbilirubinaemia

Unconjugated Hyperbilirubinaemia	Conjugated Hyperbilirubinaemia
Septicaemia Urinary Tract Infection	Biliary Atresia Neonatal hepatitis syndrome Choledochal cyst
Hypothyroidism	Septicaemia or Urinary Tract Infection
Haemolysis – congenital spherocytosis	Congenital Infection (TORCHES)
Breast milk Jaundice	Metabolic Disorders
	Prolonged Total Parenteral Nutrition

Referral

All infants with conjugated hyperbilirubinaemia must be referred to a paediatric department urgently to exclude biliary atresia. Those with unconjugated hyperbilirubinaemia can be investigated first and referred if jaundice does not resolve or a definitive cause found.

Investigations

Table 6 : Investigations for Unconjugated and Conjugated Hyperbilirubinaemia

Unconjugated Hyperbilirubinaemia (Exclude UTI and Hypothyroidism)	Conjugated Hyperbilirubinaemia (Investigate for biliary atresia & neonatal hepatitis syndrome)
Thyroid Function Tests	Admit and observe colour of stool for 3 consecutive days
Trace newborn TSH screening results	Ultrasound of hepatobiliary system
Urine FEME and C&S	Liver Function Tests
FBC, Reticulocyte count & Peripheral Blood Film	TORCHES, VDRL, Urine C&S
Trace G6PD screening results	Metabolic (IEM) screen

Management

Management will depend on the underlying condition. Breast milk jaundice is a diagnosis of exclusion. Infant must be well, gaining weight appropriately, exclusively breastfed and stool is yellow. Management is to continue breastfeeding.

Parental reluctance or refusal for care

Occasionally parents of an infant with **severe NNJ** are reluctant for care or hospital admission. This is often a result of parents having transport problems, waiting for other relatives to arrive, preferring traditional treatment or a true reluctance to come for hospital care.

If parents refuse or are reluctant to bring the infant to hospital, the following actions:

1. Call the medical & health officer (M&HO) responsible for the region.
2. The M&HO has to advise the parents regarding the need to treat NNJ urgently.
3. If this fails, the M&HO is to call the paediatric medical officer (MO) or paediatrician responsible for the region.
4. The paediatric MO or paediatrician is to advise parents of the Child Act and get the baby to a hospital with the aid of the Welfare Department.

6. QUALITY ASSURANCE: SEVERE NEONATAL JAUNDICE AS QA INDICATOR

The QA indicator for severe neonatal jaundice (SNNJ) was designed in 1993 and reviewed in 2001 and 2006. Many districts have remained outliers despite efforts to reduce SNNJ. Among the factors relating to this include machine errors (wrong serum bilirubin levels), failure to detect jaundice at home visits and post natal wards, limited home visits in some regions, failure to identify risk factors for severe NNJ before discharge from hospital and parental refusal for care.

Table 7 : Numbers of babies detected to have jaundice and type of treatment provided

Year	Est. LB	Neonatal Jaundice						
		No. detected	% of LB	Phototherapy	Exchange transfusion	Kernicterus	SNNJ Rate (per 10,000 estimated LB)	Range of SNNJ Rate
2000	518,100	153,291	29.6	44,194	708	152	94.6	8-262
2002	482,945	165,147	34.2	43,832	795	6	91.5	7-285
2004	463,241	181,044	39.1	49,032	1,040	8	91.8	2-179
2006	445,705	201,953	47.3	54,075	744	2	83.0 (2005)	7-230 (2005)

Definition of severe neonatal jaundice

Severe Neonatal Jaundice (SNNJ) is defined as neonate under 14 days of life with serum bilirubin levels > 340 µmol/l (> 20 mg/dl).

Rationale for selection of indicator

1. The rational to monitor and reduce SNNJ is as a proxy for the reduction of bilirubin encephalopathy and kernicterus.
2. It also serves as an indicator for overall neonatal care and morbidity.
3. It is important that kernicterus becomes a notifiable disease and a sentinel event that requires an in-depth investigation.

Formula for incidence rate of severe neonatal jaundice

$$\text{Incidence rate of SNNJ} = \frac{\text{Total number of severe NNJ cases}}{\text{Total number of estimated live births}} \times 10{,}000$$

Standard for severe neonatal jaundice rate

Upper limit

Districts with rates exceeding 150 per 10,000 estimated live births are considered above the accepted level and have a shortfall in quality. These districts need to investigate why there are high rates of SNNJ and whether the care provided has been optimal (Figure 5).

Lower limit

Districts with rates below 50 per 10,000 estimated live births are considered far below the accepted level and have a shortfall in quality. These districts need to investigate why there was such a low detection rate of SNNJ (Figure 6).

Staff responsible for investigation of severe neonatal jaundice

Both hospital and health staff are jointly responsible for the prevention of SNNJ and hence will investigate and institute remedial measures. Regardless of whether the infant was or was not managed in the hospital the following individuals will be responsible for the investigation by the district:

1. Hospitals with specialists - the relevant paediatrician, special care nursery sister, postnatal ward sister, public health matron/ sister of the district (coordinator).
2. Hospitals without specialists - the relevant senior medical officer of the paediatric unit/ family medicine specialist, hospital sister, public health matron/ sister of the district (coordinator).

Data on severe NNJ should be analysed and presented twice yearly at the state perinatal mortality meetings.

Steps in investigation of SNNJ

Figures 4 shows the process of investigation and flow of information and data. An investigation should be conducted if there is a shortfall in quality.

Figure 4 : Flow of data collection for NNJ

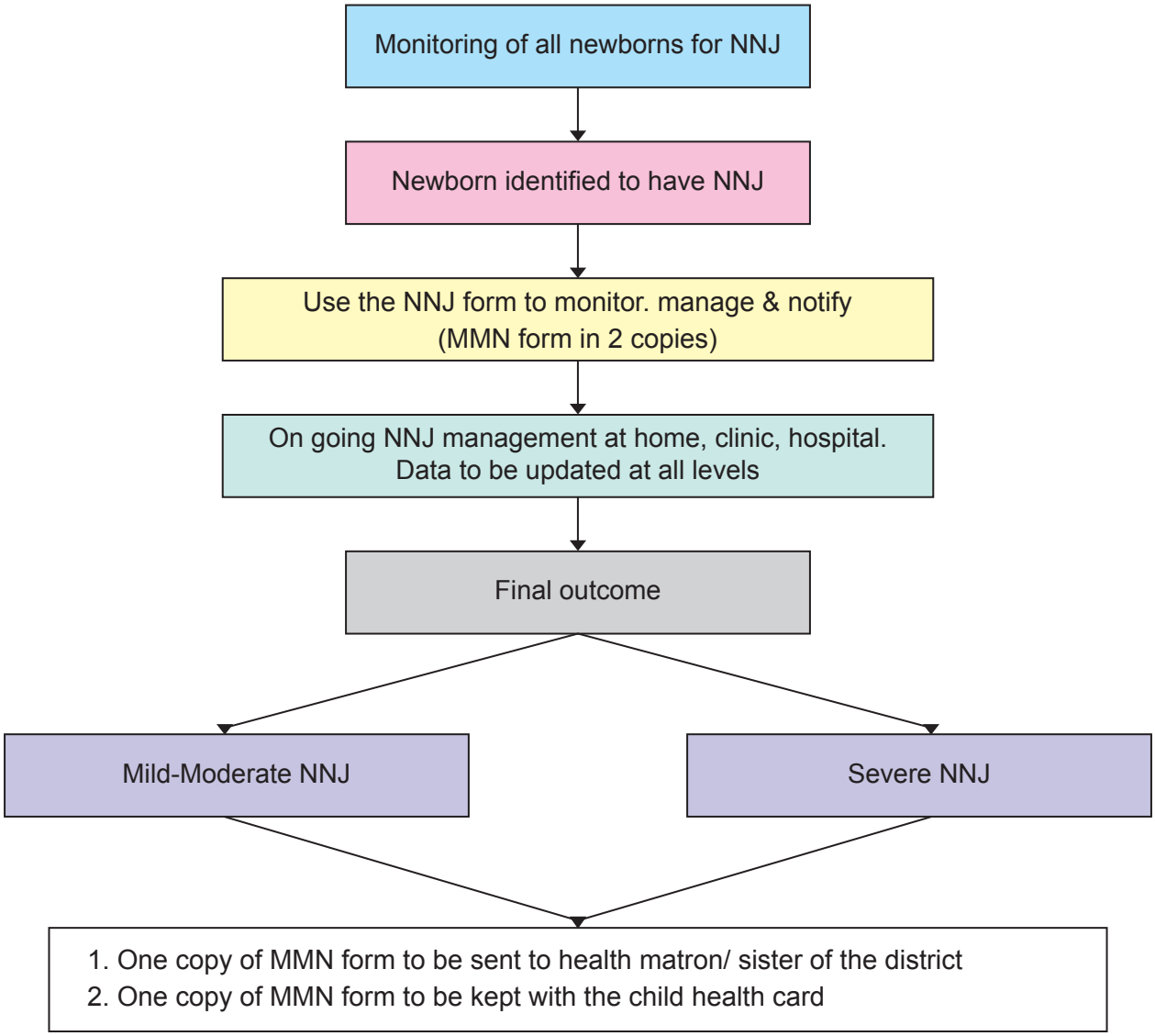


Figure 5 : Investigation for districts that exceed the upper limit of SNNJ rates (>150 per 10,000 estimated live births)

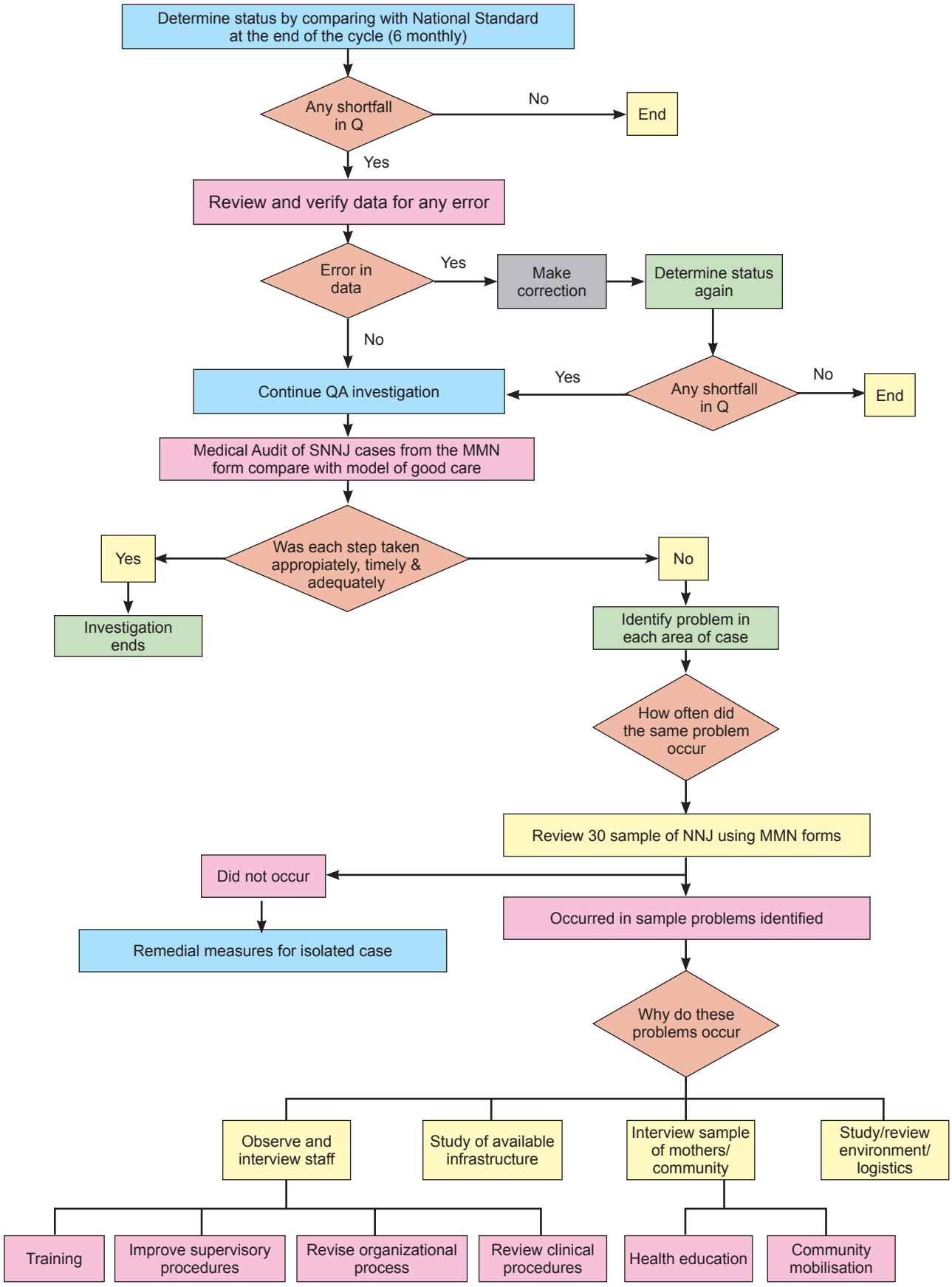
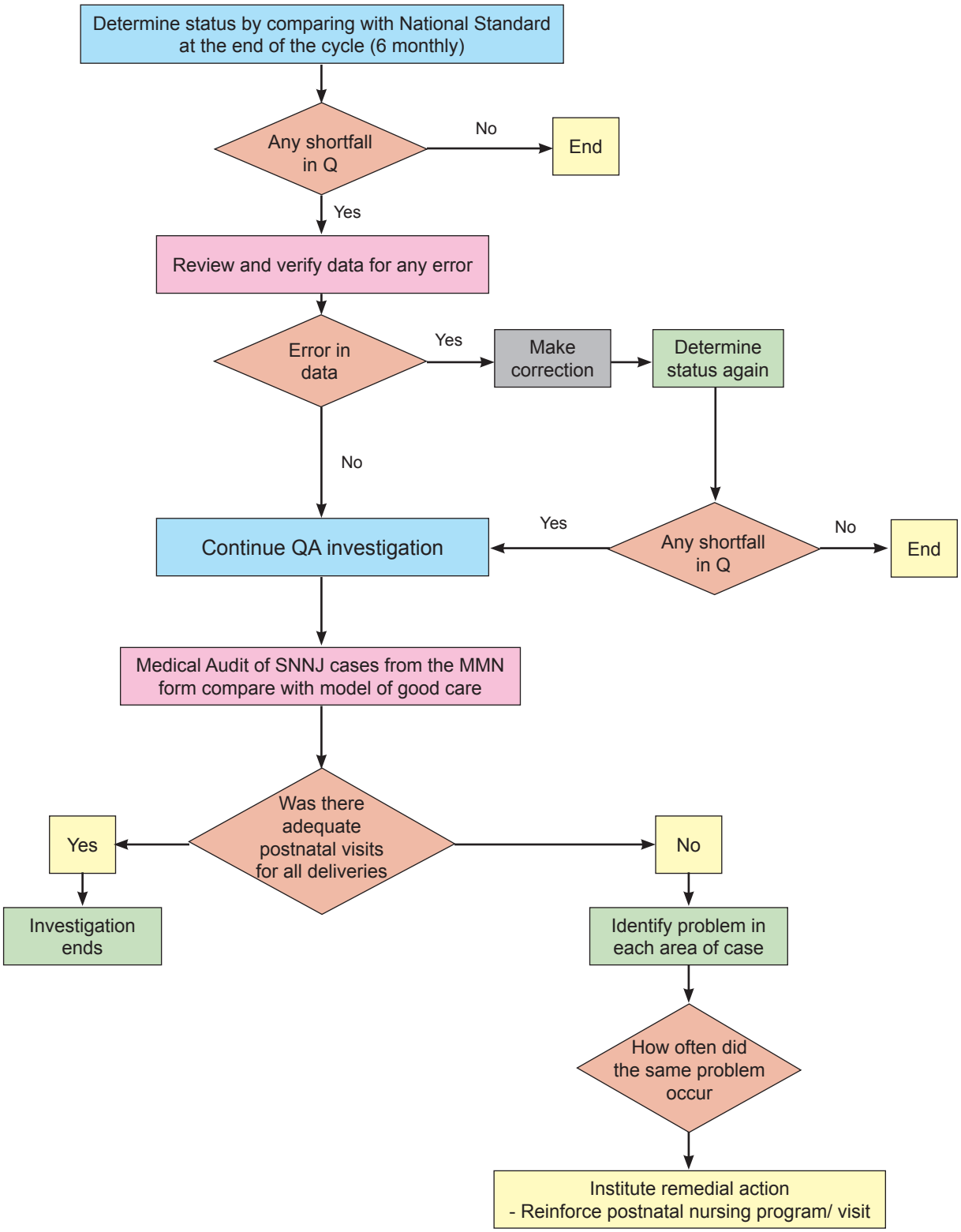


Figure 6 : Investigation for districts that are below the lower limit of SNNJ rates (< 50 per 10,000 estimated live births)



Model of Good Care

Antenatal care

1. Education on neonatal jaundice provided to expecting mother (pamphlet).
2. All mothers should have blood taken for ABO and Rhesus group.
3. Identify other risk factors for significant jaundice e.g. family history of severe neonatal jaundice, exchange transfusion and haemolytic diseases.

Intrapartum care

1. Obtain G6PD screening results.
2. Babies of Rh-negative mother should be managed at hospital.

Postnatal care

1. Support the mother to breastfed the infant adequately with supplementary fluids if required.
2. Prompt notification of postnatal mother to the nearest health centre.
3. Identification of Risk Factors
    - Prematurity (< 36 week gestation)
    - Low birth weight (< 2.5 kg)
    - Sepsis
    - Infant of diabetic mother
    - Onset of jaundice before 24 hours of life
    - A sibling with severe neonatal jaundice or exchange transfusion
    - Dehydration
    - Inadequate breastfeeding
    - Mother with blood group O or Rh negative
    - G6PD deficiency

Detection of neonatal jaundice postnatally

1. Evaluate high risk babies before discharge from postnatal wards.
2. Routine home visits as planned (Day 1, 2, 3, 4, 6, 10 and 20).
3. Daily home visits to monitor severity if jaundice is detected.
4. Refer to clinic or hospital for admission or bilirubin testing and review based on criteria.

Management

Appropriate management of NNJ in hospital.

Recording & Monitoring

1. Use the “Monitor, Manage & Notify NNJ” form (see page 25).
2. Provide returns to health matron/ district sister.

MMN/NNJ 2010

Bulan/Tahun:____/20 __

MONITORING, MANAGEMENT AND NOTIFICATION OF NNJ /SNNJ

Pejabat Kesihatan Daerah:	POLIKLINIK KOMUNITI:	HOSPITAL:
Nama bayi:	KP Ibu: ☐☐☐☐☐☐☐☐☐☐☐☐	
Tkh Lahir ☐☐-☐☐-☐☐	Alamat Rumah:	
Jarak Rumah Kes dari Hospital terdekat: ☐☐☐ km	**Jarak Rumah Kes dari K.Kes terdekat:** ☐☐☐ km	

Kumpulan etnik:		**Tempat Kelahiran** :		**Gravida Ibu** :	
Melayu :	☐	Rumah:	☐	Primigravida	☐
Cina :	☐	ABC:	☐	2-5	☐
India :	☐	BBA:	☐	≥ 6	☐
Bumi Sarawak	☐	Hospital Kerajaan:	☐	Tidak diketahui	☐
Bumi Sabah	☐	Hospital Swasta:	☐		
Lain-lain :Nyatakan	☐	Lain-lain :Nyatakan	☐		

Faktor Risiko		**Cara Notifikasi Kelahiran**		**Anggota yang Mengesan Jaundis**	
Blood Group O :	☐	Surat Notifikasi :	☐	Bidan	☐
Blood Group Rh-ve :	☐	Lawatan rumah :	☐	Jururawat Masyarakat	☐
Low birth weight (<2.5kg)	☐	Telefon :	☐	Jururawat Terlatih	☐
Prematurity :	☐	Saudara :	☐	Penjaga	☐
H/o SNNJ in siblings :	☐	Kes disambut anggota kesihatan:	☐	Anggota Hospital	☐
Sign / Symptoms of sepsis :	☐	Tiada terima notifikasi	☐	Tidak diketahui	☐
Cephalohematoma/bruises :	☐	Tidak diketahui	☐		
G6PD – Deficient / intermediate :	☐				
Lain-lain (nyatakan):	☐				
		Penjagaan Prenatal ☐ Klinik:..... ☐ Hospital:.....		Penjagaan Postnatal ☐ Klinik:..... ☐ Hospital:.....	

PERGERAKAN KES	HARI POSTNATAL 1	2	3	4	5	6	7	8	9	10	≥ 11
Anak didiscaj											
Notifikasi diterima oleh K. Kesihatan											
Lawatan pertama dan berikutnya											
Jaundis mula dikesan											
Jaundis dikesan di bawah paras umbilicus											
TSB dibuat di: KK(K)/ Hosp(H)/Swasta(S)											
Paras SB (umol/l or mg/dl)											
Rujukan ke hospital											
Paras SB (umol/l or mg/dl)											
Masuk wad *(sekiranya kes tidak masuk wad setelah dirujuk tulis TM pada tarikh rujukan)*											
Paras SB (umol/l or mg/dl)											
Discaj setelah dirawat											
Paras SB (umol/l or mg/dl) discaj											

Jika kes adalah SNNJ nyatakan **Paras SB tertinggi (umol/l or g/dl):** *(mengikut Borang QA FH2)*	**Rawatan**		**'Outcome'**	
	Fototerapi	☐	Hidup	☐
	Fototerapi dan Blood Exchange	☐	Mati	☐
			Kernicterus	☐

Sebab kelewatan rujukan / kemasukan ke wad / menerima rawatan

1. Faktor Pesakit	☐	Nyatakan:
2. Faktor Perkhidmatan Kesihatan	☐	Nyatakan:
3. Faktor Perkhidmatan Hospital	☐	Nyatakan:

RUMUSAN KES (oleh Pegawai Perubatan & Kesihatan / PHN / JK):				**Pelapor:**
Kes Neonatal Jaundis :	☐	**Kes dalam daerah:**	☐	
Kes SNNJ :	☐	**Kes dari luar:**	☐	Tarikh:
Kes SNNJ dikesan dari Format QA FH2:	☐	**Kes tidak dapat dikesan:**	☐	

GARISPANDUAN MENGISI BORANG PENGENDALIAN KES-KES NNJ UNTUK MENGGUNAKAN KES-KES SNNJ

1. Sebaik sahaja NNJ dikesan – borang ini hendaklah digunakan dan diisi.
2. Isikan **dua** (2) salinan.
3. **Salinan Pertama** – dikepilkan di Kad KIK / A (96).
4. **Salinan Kedua** – disimpan hantar kepada Pejabat Kesihatan Daerah.
5. **Ruangan <u>PERGERAKAN KES</u>**:
    i. **Tarikh** anak discaj.
    ii. **Tarikh** notifikasi diterima.
    iii. **Tarikh** lawatan postnatal pertama dan berikutnya.
    iv. **Tarikh** pertama jaundis dikesan.
    v. **Tarikh** jaundis dikesan di bawah paras umbilicus.
    vi. **Tarikh** TSB dijalankan dan **tempat** di mana ujian TSB dijalankan serta paras Serum TSB.
    (K = KK DAN JPL, H = HOSPITAL DAN A&E HOSPITAL, S = KLINIK ATAU HOSPITAL SWASTA)
    vii. **Tarikh** rujukan ke Hospital iaitu (HOSPITAL DAN A&E HOSPITAL) dan paras TSB semasa rujukan.
    viii. **Tarikh** masuk wad dan **paras** TSB semasa masuk wad. *Sekiranya kes tidak masuk wad pada tarikh rujukan sila catatkan **TM** pada ruangan berkenaan*.
    ix. **Tarikh** discaj dan **paras** TSB semasa discaj.
6. Salinan pertama yang telah lengkap perlu diambil semula selepas **PN ke10**, tetapi tentukan kes telah pulih.
7. Kedua-dua salinan perlu dihantar ke Pegawai Perubatan & Kesihatan / Jururawat Kesihatan di KK untuk dibuat rumusan.
8. Jururawat Kesihatan kumpulkan semua borang Salinan Pertama dan hantar bersama reten bulanan setiap bulan ke Pegawai Kesihatan Daerah (Kesihatan Keluarga) / Penyelia Jururawat Kesihatan Daerah / Ketua Jururawat Kesihatan.

Pelapor:

Disemak:

APPENDICES

JAUNDICE IN BABIES

What is jaundice?

Jaundice in newborn babies is seen as a yellowness of the skin and eyes. Up to 75% of all babies develop jaundice.

What causes jaundice?

In the human body, new blood is being made all the time and old blood is being destroyed. One of the breakdown products of blood is 'bilirubin'. Bilirubin is normally processed in the liver and is eliminated from the body in the stool and urine. For the first few days after birth, a baby's liver does not work as efficiently as it does later. So there tends to be a build up of bilirubin in the blood. This causes jaundice in the newborn babies.

Is jaundice harmful?

Severe jaundice or very high levels of bilirubin in the blood can lead to deafness, brain damage and sometimes death.

Are there any long term problems from jaundice?

There are usually no long term problems following jaundice in babies. However, babies with severe jaundice can develop:

- Hearing problems (deafness)
- Learning difficulties
- Intellectual disabilities
- Cerebral palsy

Which babies get severe jaundice?

Babies who may be particularly prone to severe jaundice include:

- Premature infants
- Babies with infection
- Babies with G6PD deficiency
- Babies whose blood group is different from their mother's
  - * Mothers with rhesus negative
  - * Mothers with blood group O

What are the danger signs?

Urgent treatment should be sought if jaundiced babies develop the following signs:

- Jaundice visible within 24 hours after birth
- Jaundice visible below the umbilicus
- Not active, unwell or having fever
- Not feeding well
- Fits or stiffness of the body
- Jaundice persisting beyond 14 days
- Pale coloured stools or tea coloured urine

What should the parents do if their baby develop jaundice?

- Seek early treatment at the nearest health facility
- A blood test will be taken to determine the level of bilirubin in the baby's blood
- Do not put the baby under the sun

How can parents minimise the severity of jaundice in my baby?

- Ensure adequate breastfeeding (at least 8-10 times every 24 hours)
- Avoid taking traditional medication if breastfeeding

Contact Numbers of nearest Health Clinics / Hospitals:

Special Note for parents of babies born to mothers with blood group O:

1. Your baby has a higher risk of developing severe jaundice.
2. Please inform the health staff of the nearest clinic to see your baby the day after discharge to examine for jaundice.

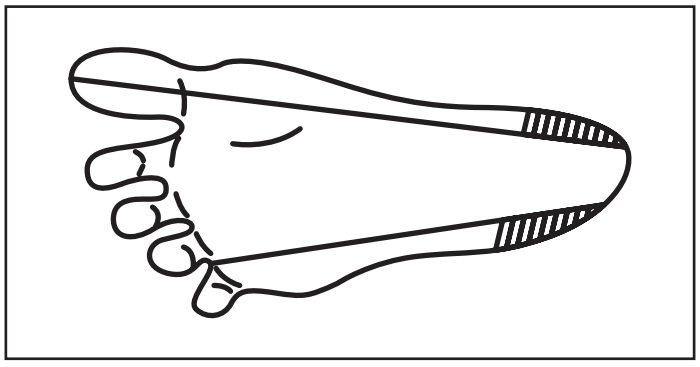
Appendix 7.2

CAPILLARY BLOOD SAMPLING FOR BILIRUBIN TESTING

To obtain the sample:

1. Ensure baby is lying in a safe and secure position
2. Hold the baby's heel
3. Hold the ankle with index and middle finger
4. Use other fingers to steady the baby's leg
5. Partly encircle the baby's heel with the thumb
6. Clean the proposed puncture site with warm water and gauze. Alcohol impregnated wipes should not be used.
7. Allow the area to dry.
8. Gently compress the heel and hold the skin under tension.
9. Puncture the skin in a steady manner.
10. Relax tension and wipe away initial blood flow with cotton wool or gauze.
11. While maintaining grip, hold the heel so that blood is allowed to hang.
12. Gently but firmly compress the baby's heel to form a large droplet of blood.
13. Do not squeeze.
14. Hold the capillary tube (or blood bottle) to the blood droplet and touch.
15. Momentarily release pressure to collect subsequent blood then reapply pressure, allowing the blood to flow.
16. Continue until sufficient blood has been obtained.
17. Once the sample has been obtained, apply pressure to the site with gauze and maintain pressure until bleeding has stopped.

Figure 7 : Diagram to show location where heel prick should be done



Appendix 7.3

CORD BLOOD SAMPLING & COLLECTION OF SPECIMENS FOR SCREENING G6PD DEFICIENCY

Collection

The specimen is dried blood spots on filter paper. A specific type of filter paper is used and it see section on filter paper type and it is easy to transport to the laboratory from remote areas.

Method

1. Blood can also be obtained directly from the cut end of the maternal portion of cord.
2. Sampling is carried out after the cord has been cut between the clamps or ties normally applied at delivery.
3. Blood must not be drawn from the portion of cord still attached to the baby because of the serious risk of bleeding.

After cleaning

1. Release the clamp or tie on the maternal part of the cord.
2. Using a gloved hand, gently squeeze blood along the cord to the end.
3. Drop the blood into a sterile gully pot.
4. A minimum of 1 ml of blood should be collected.
5. Use a syringe or dropper to transfer the blood onto filter paper.
6. Drop blood from the syringe or dropper directly onto the circle of filter paper, without touching the syringe or dropper to the paper.

Note:

Dropping the blood directly onto the filter paper from the end of the cord, results in poor control of the amount of blood going onto the paper (usually too much spilling over the edge of the circle). This alternative can be used if there is no other option.

Appendix 7.4

GUIDELINES ON THE METHOD FOR G6PD SCREENING (BLOOD COLLECTION AND SCREENING FORM)

Blood for screening purposes should be obtained from the umbilical cord at birth. For infants not screened at birth, blood should be obtained by a heel prick as soon as possible.

1. Collection of blood for G6PD screening at birth

Before delivery

- Fill up the test request form with the name of mother, address, sex, ethnic group, telephone number, e-mail address, etc. (see below)
- Label G6PD screen filter paper strip with the registration number for cases delivered in hospital or use the Identification Card number (I/C) for cases delivered at Alternative Birthing Centers or home.

At delivery

- Completely wet one end of the filter paper strip with cord blood (minimum soak diameter 1 cm).
- Staple the other end of the filter paper strip to corresponding place on the G6PD screen form.
- Complete other relevant information required on the form.
- Put the form in the envelope and address it to the laboratory to which the form is to be sent for testing. For cases delivered in Alternative Birthing Centers or at home forms should be sent to nearby health centers with U/V box.
- Send the form by hand or post as soon as possible.

For infants who's cord blood screening has not been done

- Blood is to be obtained by heel prick (refer Appendix 7.2).
- Completely wet G6PD filter paper strip with heel blood at one end.
- Label the strip, staple it to the form, label the form, label the form and fill in the necessary particulars and send it to the laboratory as soon as possible.

2. Screening for G6PD enzyme deficiency in the laboratory

- All G6PD specimens must be treated as URGENT and processed on the day of arrival, even if there is only a single specimen to be tested.
- Record all details in the book for G6PD screening.
- Follow procedure for G6PD screening provided in the laboratory.
- Fill in the results on the G6PD form and send them back immediately.
- For guidelines on procedure for detection of G6PD enzyme deficiency by laboratory personnel refer Appendix 7.5.

3. Notifications and Documentation of results - Hospital & Health

- See Appendix 7.6

G6PD SCREENING FORM

UJIAN PENGESANAN KEKURANGAN G6PD

Nama Ibu : .....
No. Pendaftaran : .....
Alamat Tetap Ibu (Penjaga) : .....
Hospital/ Klinik : .....

Perihal Bayi
Jantina : Lelaki Perempuan
Bangsa :
Tarikh Lahir :

Contoh Darah dihantar pada :

Contoh Darah diambil pada :

Contoh Darah diterima pada :

Letakkan kertas strip yang bercelup darah disini :

*Keputusan : Tandakan (√) dalam ruangan yang berkenaan
Biasa ( ) Tidak Tentu (Intermediate) ( )
Ujian Tidak Dijalankan ( ) Kekurangan (Deficient) ( )

Nama makmal : _____
Nama & tandatangan : _____
Tarikh : _____

PERHATIAN:
Bagi Kes-Kes " tidak tentu" atau "kekurangan"
i. Kalau bayi kuning (jaundice walaupun sedikit sahala), bawalah segera untuk rawatan
ii. Jauhi dari segala jenis ubat melainkan yang diberi oleh doctor
iii. Ujian ini hendaklah dibuat sekali lagi dalam tempoh 3 bulan

Appendix 7.5

GUIDELINES FOR LABOATORY PERSONNEL (U/V FLUORESCENCE SCREENING METHOD FOR G6PD DEFICIENCY)

Principle

This fairly simple and foolproof screening for G6PD deficiency is based on that of Beutler (1966). G6PD catalyses nicotinamide adenine dinucleotide phosphate (NADP) to it's reduced form NADPH in erythrocytes. NADPH protects cells from oxidative damage. The conversion of NADP is the basic diagnostic testing for the deficiency. The screening method was modified by White (1972) to be used on samples collected on blotting paper or filter paper. The absence of fluorescence in U/V light would mean deficiency of the enzyme.

Reagents

All reagents can be obtained from SIGMA

1. Oxidised glutathione (GSSG) 8 mmol/l
   M.W = 612.7 (49.016 mg/10 ml buffer).
2. Nicotinamide Adenine Dinucleotide Phosphate (NADP)
   7.5 mmol/l
   M.W = 765.44
   Prepare fresh solution
   (5 7.4 05 mg/10ml buffer)
   The solution, if stored deep frozen, remains stable for a week

3. G-6-P (Gluocose-6-Phosphate) 10 mmol/l
   M.W =358.2 (35.82 mg/10ml buffer)

4. Tris-HCl Buffer, 0.75mol/l, pH = 7.8
   Tris (hydroxymethyl) aminomethane = 90.825 g/l (45.412 gm/500 ml).
   250 ml Tris + 33ml N HCl=0.75 M Tris – HCl Buffer
   (Accuracy of buffer solution should be adjusted to the first decimal place). It is essential to use a PH electrode which is suitable for Tris.

Method

1. 0.1 ml working reagent is placed in a 10 x 75 min labeled test tube.
2. Disc of 6 min punched from sample strip (using TOHO eyelet punch in similar) is placed into tube.
3. Ideally the tube should be incubated at 37˚C X 15 min. However the incubation can be done at room temperature for the same length of time.
4. Using a capillary tube, spot the test mixture on a Whatman No.1 filter paper* and allow it to dry thoroughly, preferably using a hair drier.
5. Examine under U/V lamp for fluorescence.
   Fluorescence + + + = No G6PD deficiency
   Fluorescence Nil = G6PD deficiency

Work procedure

a) Large numbers of tests may be done at the same sitting.
b) *Use “Chromatography Paper” Whatman No.1 (7.5 cm x 100m. Basic weight 87 gm/m, thickness 0.16 mm. Medium Flow Rate.
c) The mixture of the working reagent should be prepared at district hospital and issued at weekly intervals to the peripheral clinics. This reagent should be transported in a ice-flask. In the peripheral clinics, the reagent should be stored in the freezer compartment.
d) Filter paper should be made available to the peripheral clinics.

Control

A known normal blood sample must be run as a control. Check the reagent daily before each batch of tests to make sure it is working properly.

Interpretation of results

Specimens from normal persons shows strong fluorescence. Red cells with less than 20% normal activity will show no fluorescence.
G6PD normal – normal follow up
G6PD Deficient – admit for observation for at least 5 days
G6PD Intermediate - Consider quantitative analysis at 3 months or older of age. If this diagnostic facility is not available, to treat patient as deficient.

Precautions

1. This method will miss some female heterozygotes but is reliable for detecting deficiencies among males.
2. Check the expiration dates of commercial kits.

Appendix 7.6

NOTIFICATION OF G6PD DEFICIENCY SCREENING RESULTS

Hospital

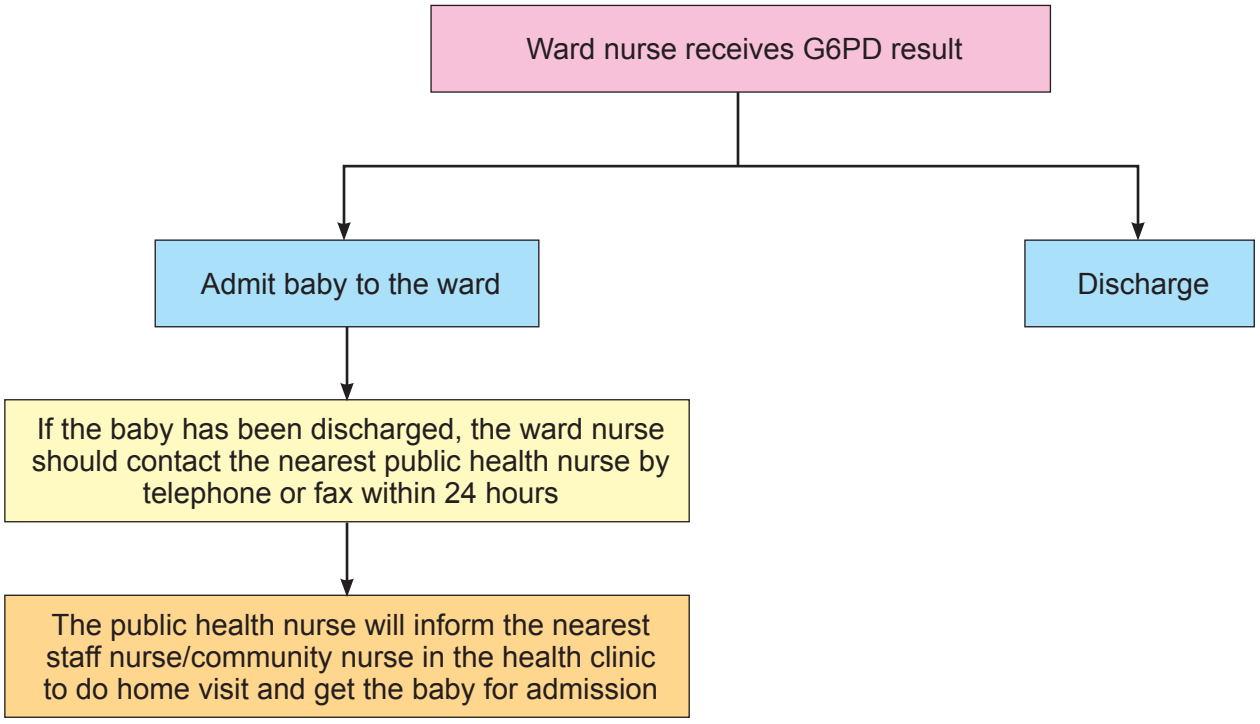
The result should be made available before the baby is discharged. In a busy unit with many deliveries a day, some babies may discharged prior to receiving the laboratory results. There must be a recall system to call back the baby urgently to be admitted to Peadiatric Unit if the result is abnormal.

If the result is normal, the mothers should be notified (Fig. 8). The ward nurse in-charge should inform the public health nurse at the clinic nearest the parents home. The public health nurse should endorse the G6PD results in the Home Based Child Health Card.

Health Centre

If the result is abnormal, the nurse or the relevant health staff should be informed immediately, by the Medical Laboratory Technologist, by phone or fax. The baby should be referred to the hospital for admission.

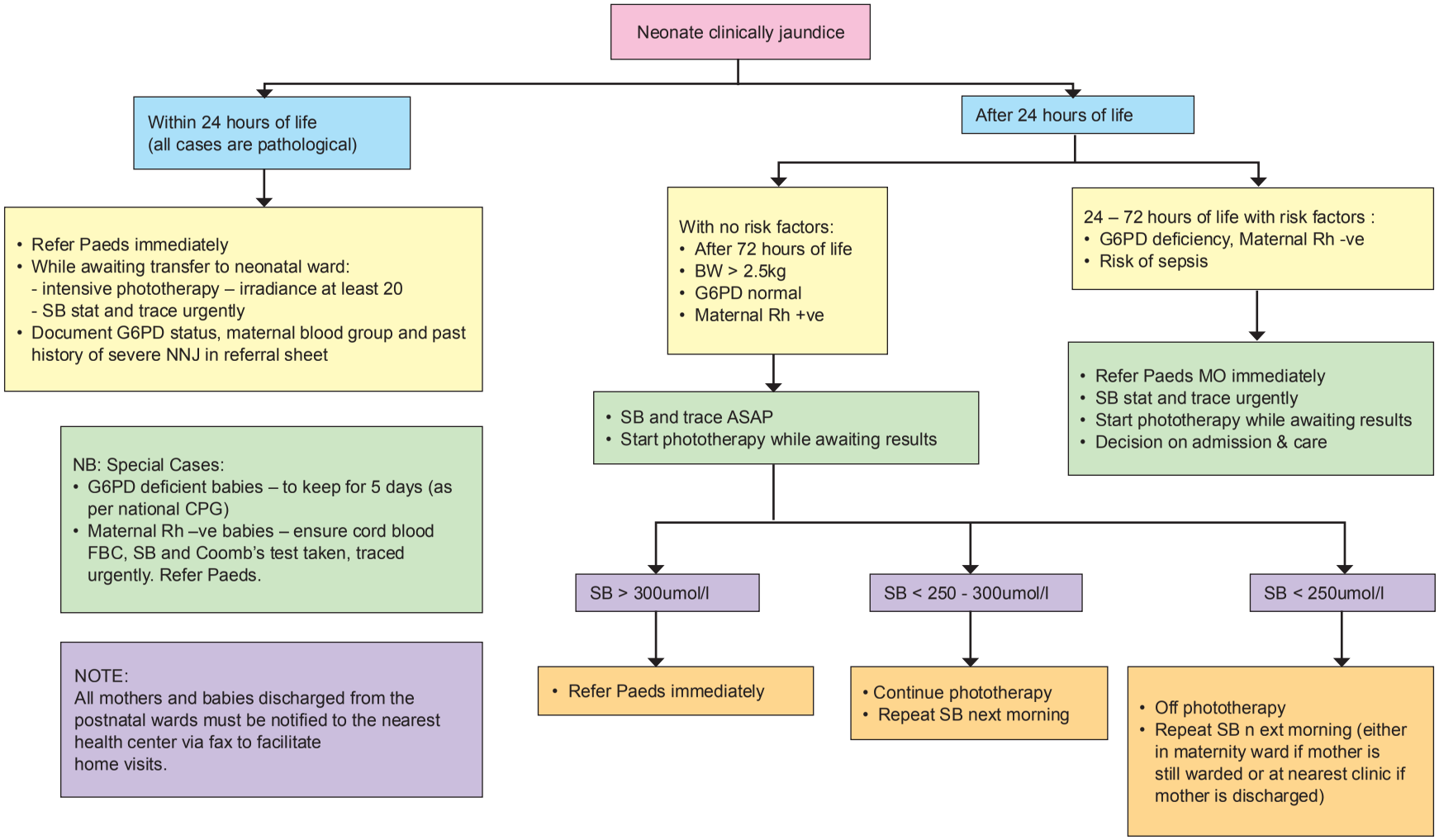
Figure 8 : Flow chart on notification of G6PD deficiency screening results



Appendix 7.7

STANDARD OPERATING PROCEDURE FOR DETECTION OF NEONATAL JAUNDICE IN HOSPITALS WITH SPECIALISTS

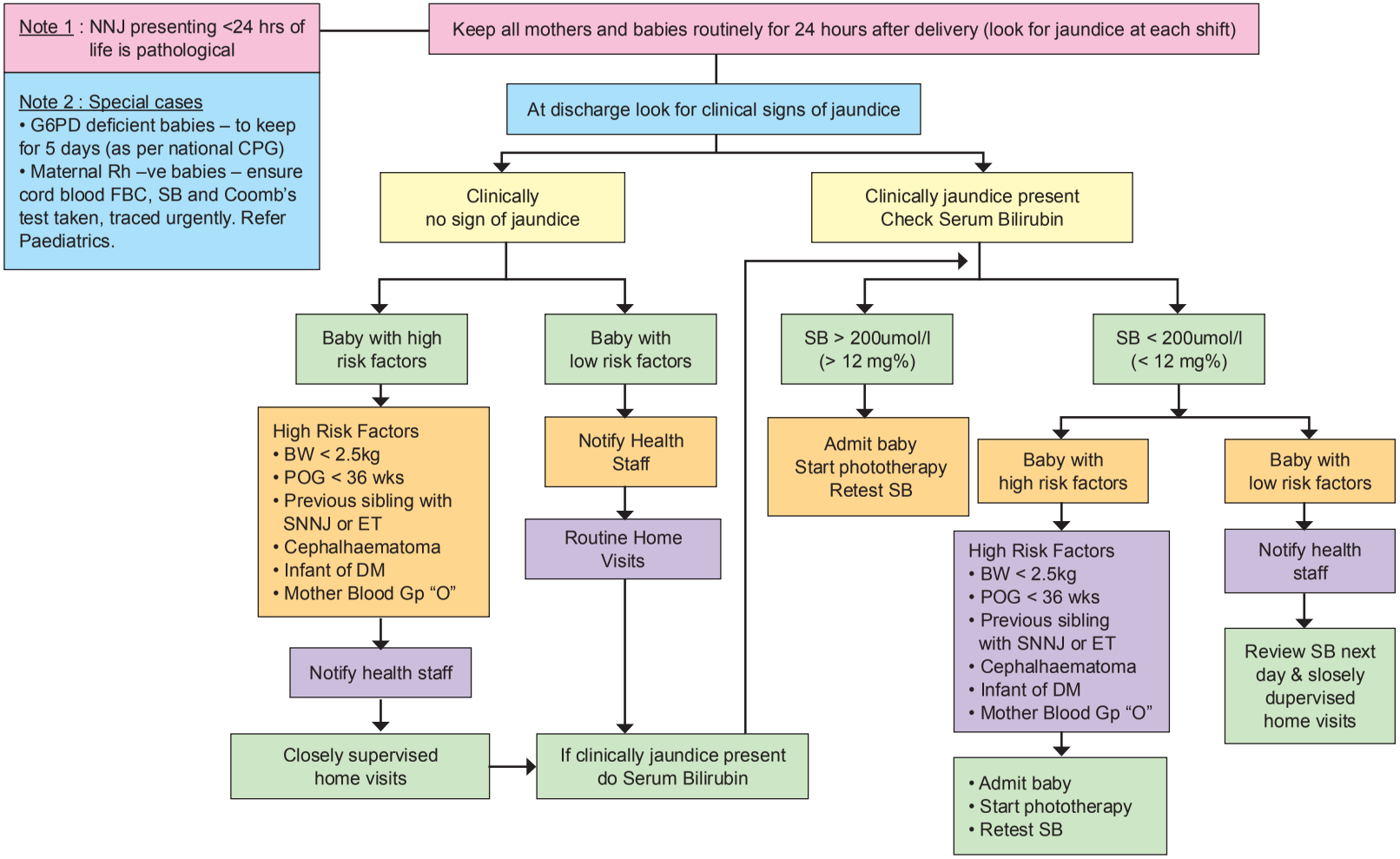
This SOP enables immediate and effective actions through cooperation between the paediatric and obstetric teams for early detection of NNJ and to avoid exchange transfusion.



Appendix 7.8

STANDARD OPERATING PROCEDURE FOR DETECTION OF NEONATAL JAUNDICE IN HOSPITALS WITHOUT SPECIALISTS

Rationale : Many attempts to reduce the incidence of Severe NNJ in the past have not brought about significant change This SOP is to enable early detection of NNJ resulting in immediate and effective action via cooperation between paediatric and obstetric teams with the public health staff.



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ABBREVIATIONS

BW	Birth weight
C&S	Culture & sensitivity
CPG	Clinical Practice Guidelines
DM	Diabetes mellitus
ET	Exchange transfusion
G6PD	Glucose-6-Phosphate dehydrogenase
IVIG	Intravenous Immunoglobulins
LB	Live birth
MOH	Ministry of Health
MO	Medical officer
NIA	National Indicator Approach
NNJ	Neonatal jaundice
Q	Quality
POG	Period of gestation
SB	Serum bilirubin
SNNJ	Severe neonatal jaundice
SOP	Standard Operating Procedure
TORCHES	Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex, Syphilis
TSB	Total serum bilirubin
VDRL	Venereal Disease Research Laboratory test

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