NEONATAL GUIDELINES

Chapter 8: Haematology and Jaundice
v2018.2

Specialty: Neonatal Medicine
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Blood transfusion guidelines

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Introduction:

Jaundice is caused by increased haem breakdown (haemolysis), interference with hepatic conjugation (e.g. hepatitis), or impairment of bile excretion (e.g. biliary atresia). Jaundice can, therefore, be either unconjugated or conjugated depending on its cause.

Jaundice can also be categorised according to timing:
Early <24 hours old - Requires immediate investigation and treatment to rule out haemolytic disease
Prolonged >14 days in term babies >21 days in pre-term babies – Requires further investigation to look for an underlying cause

Unconjugated Hyperbilirubinaemia

In normal newborn infants, due to their high intrauterine Hb concentration, there is increased destruction of RBCs. Babies also have immature liver pathways. It is normal or “physiological” for babies to have mild unconjugated hyperbilirubinaemia and up to two thirds will develop jaundice within the first week.

However, unconjugated jaundice is not always harmless.

High levels of unconjugated bilirubin, which is lipid soluble and easily crosses the blood brain barrier, can cause acute bilirubin encephalopathy: lethargy, hypotonia and poor suck followed by irritability and hypertonia in association with fever and high-pitched cry. Left untreated, this may be fatal or lead to high frequency deafness, choreo-athetoid cerebral palsy and severe learning problems. Kernicterus is the name given to the yellow staining of the basal ganglia found at post-mortem in bilirubin toxicity.

The level of bilirubin required to cause encephalopathy varies with gestational age and can also be affected by acidosis and hypoxia which displace bound bilirubin from albumin. Hypoalbuminaemia will also result in more free bilirubin which is able
to cross the blood brain barrier. These factors should be taken into account when assessing jaundice.

Early recognition of jaundice and any associated risk factors and appropriate management with phototherapy and exchange transfusion (if indicated) should mean that kernicterus never happens.

**Conjugated Jaundice**

Conjugated hyperbilirubinaemia occurs in diseases where the flow of conjugated bilirubin into bile or the flow of bile into the intestine is impaired. It suggests an hepatobiliary problem.

It is much less common than unconjugated hyperbilirubinaemia in neonates but it is vital to recognise conjugated hyperbilirubinaemia as it may indicate a serious underlying cause such as biliary atresia which requires surgical intervention within the first 8 weeks of life to be a success.

The conjugated fraction of bilirubin must always be requested in cases of prolonged jaundice and should be considered earlier than this if the clinical picture is suggestive of conjugated jaundice.
Jaundice – Causes and Risk Factors

Identifying babies more likely to develop significant hyperbilirubinaemia

- Gestational age under 38 weeks
- A previous sibling with neonatal jaundice requiring phototherapy
- Known maternal antibodies (e.g., anti-C antibodies) – see Management of the baby with suspected haemolytic disease
- Visible jaundice in the first 24 hours of life.
- Mother’s intention to breastfeed exclusively. Breast feeding in presence of comorbidities like dehydration, marked bruising, haemolytic disease and infection increases risk.
- Significant bruising / cephalhaematoma
- Male sex
- Ethnic minority population

Risk factors for developing kernicterus

- a. Serum bilirubin > 340 micromole/L in term babies.
- b. Rapidly rising bilirubin of > 8.5 micromole/L/hour.
- c. Clinical features of bilirubin encephalopathy.

In the well term infant, problems are rarely seen below 340 micromol/L. In the pre-term infant the blood brain barrier is less developed and bilirubin can be pathological at lower levels. Risk is significantly high above 510 micromol/L.

Always plot the SBR on a NICE treatment graph corresponding with the baby’s gestational age at birth.

Identification of Pathological Jaundice

- Visible in first 24 hours (suggests haemolysis and needs urgent investigation and treatment)
- Jaundice in presence of risk factors.
• Baby is “unwell”
• Total bilirubin >340 mmol/l (term infants) OR Above exchange transfusion line on the NICE jaundice chart
• Rapid rate of rise of bilirubin. The risk is much higher if the increase in serum bilirubin is >8.5 micromol/L/hour and this warrants an exchange transfusion.
• Conjugated hyperbilirubinemia
  o Serum conjugated bilirubin concentration of greater than 25 micromol/L OR
  o more than 20% of the total bilirubin if the total bilirubin is >85 micromol/L.
• Prolonged jaundice
  o > 14 days in term babies
  o > 21 days in preterm babies
• Jaundice which recurs having cleared

**Causes of Unconjugated Hyperbilirubinemia**

a. Physiological Jaundice
b. Acute intravascular haemolysis
   • Haemolytic disease e.g. Rhesus, ABO, Kell
   • Red cell abnormalities e.g. G6PD, hereditary spherocytosis
   • Viral infections e.g. CMV, Herpes, Toxoplasmosis
   • Bacterial infection e.g. sepsis or urinary infection
c. Sequestered blood
   • Excessive bruising, cephalhaematoma
   • Intraventricular haemorrhage
   • Haemangioma
d. Decreased conjugation
   • Sepsis
   • Criglar-Najjar syndrome (deficiency of glucuronyl transferase enzyme)
e. Increased enterohepatic circulation due to decreased gut movement
   • Delayed feeding
   • Constipation or bowel obstruction
f. Breast milk jaundice
Causes of CONJUGATED Hyperbilirubinaemia

a. Neonatal hepatitis
   - Hepatitis A, B or C
   - Other viral hepatitis
   - Congenital viral infections: rubella, CMV, Herpes
   - Galactosaemia

b. Other causes of conjugated hyperbilirubinaemia:
   - Cystic fibrosis
   - Endocrine causes (hypothyroidism, hypopituitarism)
   - Prolonged TPN
   - Biliary atresia
   - Alagille syndrome
   - Choledocal cyst
   - $\alpha_1$ antitrypsin deficiency
   - Inspissated bile syndrome
   - Inborn errors of metabolism
   - Many more
How to Investigate a Jaundiced Baby

This part of the guideline refers to the investigation of a baby who is noted to be jaundiced in the first 2 weeks of life. For the investigation of prolonged jaundice see the separate section on Prolonged Jaundice.

Beware of underestimating jaundice on visual inspection.

- Research has shown that the degree of jaundice estimated by health professionals on inspection does not correlate with serum bilirubin. It is easy to underestimate the level of bilirubin in the blood based on how yellow the baby appears.
- In particular be aware of the risk of underestimating jaundice in Asian or Afro-Caribbean infants.
- Pre-term infants often need treatment when little jaundice is visible.
- Also, beware the baby who has been under phototherapy; the skin may look clear but the blood or tissue bilirubin could still be high.

If a child is visually jaundiced:

For babies <24 hours old:
- Send lab serum bilirubin urgently and plot result on a NICE jaundice treatment chart.
- Start single phototherapy as a precaution whilst awaiting SBR result. This can be stopped if the SBR turns out to be below the phototherapy line.
- If <24 hours old also send FBC, blood film, group and DCT to look for haemolysis/ABO/Rhesus incompatibility and consider a septic screen if risk factors or features of sepsis.

For babies >24 hours old:
- Check bilirubin using a transcutaneous bilirubinometer if available.
- Plot TcBili result on a NICE jaundice treatment chart.
• Send a serum bilirubin to the lab and start single phototherapy in the meantime if:
  o TcB measures Bili > 250
  o TcB is below the treatment line but within 50micromol/L of the line
  o TcB high enough to require phototherapy send an SBR
  o No TcBili available

• If SBR confirms jaundice requiring treatment, send a blood film, blood group and DCT with the next set of bloods to rule out haemolysis.

• Only request a split bilirubin (for conjugated fraction) if there are risk factors for conjugated hyperbilirubinaemia e.g. pale stools, dark urine, prolonged jaundice, features of congenital infection.

NICE Treatment Charts
• These are available on Sharepoint
• Ensure you have selected the right graph for the baby’s gestational age at birth.
  Continue to use this graph. It is not necessary to change graphs when the baby’s corrected gestational age changes.
• Print a copy of the graph, plot the bilirubin against age in hours/days and place it in the baby’s notes.

Additional investigations as suggested by history/examination
• FBC and film and reticulocyte count – to look for evidence of haemolysis
• Group and DCT - to look for evidence of rhesus/ABO incompatibility and haemolysis
• U+E if history or examination suggests dehydration or if SBR very high
• Septic screen
• Split bilirubin for conjugated fraction
• Liver function tests, including coagulation screen
• G6PDH screen
• TFTs
• Cranial USS to rule out intracranial haemorrhage
Management of Unconjugated Hyperbilirubinaemia

Phototherapy is the main treatment for unconjugated jaundice. Phototherapy converts bilirubin to a soluble form allowing its renal excretion. **Indications for phototherapy**

- Phototherapy should be started in any baby whose serum or transcutaneous bilirubin plots above the treatment line on the NICE jaundice treatment chart (available on Sharepoint and via Google) or if the TCB is >250 or within 50 micromol/L of the treatment line. NB Phototherapy started on the basis of a TCB can be stopped again if the SBR is below the treatment line.
- Remember, to ensure you have the correct chart for the baby’s gestation.
- If the infant is sick (e.g. HIE, hypoxia, acidosis, hypoglycaemia, infection) lower thresholds for treatment are necessary.
- If the infant has suspected haemolysis, phototherapy should be started immediately and exchange level is dependent on the rate of rise rather than absolute level - see Management of the Baby with Suspected Haemolytic Disease.

**How to Start Phototherapy**

A. If serum bilirubin is above the treatment line and but more than 50 micromol/L below the threshold for exchange transfusion start **single phototherapy**.

1. Short breaks of up to 30 minutes for breast feeding can be allowed. Use clinical judgement.
2. Repeat serum bilirubin* 4-6 hours after starting phototherapy. Then every 6-12 hours if level stable or falling.
3. Switch to continuous multiple phototherapy if level is not stable or falling. Monitor hydration by daily weighing of babies and checking for wet nappies.
B. If serum bilirubin less than 50 micromol/L below the threshold for exchange transfusion or if haemolytic disease of the newborn is suspected:

- Start continuous multiple phototherapy
- Admit to NICU. Inform consultant if SBR is above the exchange line
- Do not interrupt phototherapy for feeding. Intravenous or NGT enteral feeding can continue. Monitor hydration.
- Repeat serum bilirubin* 4-6 hours after starting phototherapy. Then every 6-12 hours if level stable or falling or every 4 hours if it continues to rise.
- If the SBR continues to rise despite multiple phototherapy calculate rate of rise and consider exchange transfusion if >8.4micromol/hour. Give IV immunoglobulin to bind bilirubin whilst exchange transfusion is being arranged. (See Management of the Infant with Suspected Haemolytic Disease and Exchange Transfusion Protocol).

*Once phototherapy has been started the transcutaneous bilirubinometer is no longer accurate and should not be used. Serum samples must be sent.

**Types of Phototherapy**

- **Overhead lights**
  - These are generally the first choice on NICU and are also available on the postnatal ward.
  - Additional overhead lights can be added to increase the level of phototherapy delivered.
  - Babies can get cold under overhead lights and may need to be in an incubator to maintain their temperature.
- **NeoBLUE Cozy Phototherapy Bed**
  - Available on the postnatal ward and NICU.
  - This is a mattress which delivers phototherapy and allows the baby to be covered with a blanket whilst undergoing treatment.
  - Only delivers single phototherapy but can be used in conjunction with overhead lights to deliver multiple phototherapy.
Caring for a baby receiving phototherapy

- Ensure as much skin exposure as possible. Lay on an open nappy. Remove hat.
- Ensure the eyes are covered with appropriate phototherapy eye protection.
- If using overhead lights, the baby will probably need an incubator or overhead heater to keep warm. The temperature should be measured 4-hourly.
- Phototherapy itself does not increase fluid requirements; however dehydrated babies often have more severe jaundice and an assessment of feeding and hydration should be made. If the SBR is particularly high or is not reducing despite phototherapy send U+Es and consider NG top ups.

When to Stop Phototherapy

- Stop phototherapy once serum bilirubin has fallen to a level at least 50 micromol/litre below the treatment line.
- Check rebound bilirubin 12-18 hours after stopping phototherapy. Babies do not necessarily remain in hospital for this. However, if further phototherapy is required after discharge the baby would need admission to Morriston.

Prior to Discharge

Be aware that the following babies are at risk of ongoing jaundice:

- Near term, i.e. GA 35 – 36/40 at birth
- Cephalhaematoma / bruising
- Exclusively breast fed
- Already received phototherapy on PNW
- Sibling with history of neonatal jaundice requiring phototherapy
- Presence of pathological jaundice, e.g. haemolytic

Ensure that the baby is feeding adequately prior to discharge.

The community midwives will follow babies up at home. In ABMU they carry a transcutaneous bilirubinometer for use on babies who have not already received phototherapy.

For babies who have been under phototherapy, where there is concern about ongoing/worsening jaundice, the midwife will arrange for serum bilirubin to be checked. Kindly liaise with community midwife for any baby who needs continued monitoring in community.
Management of Infants Incidentally Detected to Have Extremely High Bilirubin (Over or Near the Exchange Transfusion Line)

Although the risk of extremely high bilirubin can be antenatally predicted in infants where there is a known risk of haemolytic disease of the newborn, some babies will unexpectedly develop hyperbilirubinemia, which puts them at risk of kernicterus.

If a baby is found to have a bilirubin level that is near or above the exchange transfusion line:

- Inform the parents of the need for immediate treatment and close monitoring.
- Admit to NICU and start multiple phototherapy – Inform consultant if level above exchange transfusion line.
- Take a full history including: age at onset of jaundice, feeding, stools, maternal blood group and antenatal concerns.
- Assess for CNS signs, signs of sepsis, hepatosplenomegaly, pallor.
- Send urgent FBC and blood film, DCT & Group, U+E, Bone profile, LFT, blood gas and PCX glucose.
  - If DCT shows evidence of haemolytic disease of the newborn refer to Management of the Infant with Suspected Haemolytic Disease.
- Undertake a full septic screen and start intravenous antibiotics.
- Ensure adequate hydration, either enteral + parenteral
  - Keep nil by mouth if plan to perform exchange transfusion, or baby unwell.
- Inform blood bank that blood may be required for an exchange transfusion.
- Insert lines in preparation for possible exchange transfusion (UVC/UAC).
- Monitor SBR 2-4 hourly initially until SBR seen to be falling then 6-8 hourly.
- If SBR does not fall or continues to rise, discuss with consultant, give intra venous immunoglobulin (IVIG) and perform exchange transfusion (see Haemolytic Disease of the Newborn and Exchange Transfusion protocols).
Management of the Infant with Suspected Haemolytic Disease or who Develops Jaundice in the First 24 hours

Haemolytic disease of the newborn (HDN) is the pathological break down of red blood cells as a result of maternal antibodies in the baby’s bloodstream. It should be suspected if the mother is known to have blood group antibodies. Most commonly these are Rhesus antibodies but anti-c, C, e, E or Kell antibodies (and others) can also cause HDN. A prediction of the likely degree of HDN can be made by the haematologists.

Treatment with intrauterine transfusion (IUT) is available. Babies who have received this may not require exchange transfusion but will usually continue to have haemolytic anaemia and therefore require follow up (see section on Late Anaemia).

Any baby who has received an IUT must have irradiated blood for any transfusion during the first year of life to avoid GVHD.

In the absence of antenatally detected antibodies, consider HDN in:
- Babies who are jaundiced within the first 24 hours
- Infants of mothers who have had a previously affected infant (Rhesus disease worsens in subsequent pregnancies)
- Babies who are anaemic or hydropic at birth

If you are made aware of a high risk foetus, inform blood bank as soon as possible so that they can cross-match blood against the mother’s serum and have blood available for the infant at short notice.

Blood used for exchange transfusion is of a lower PCV than packs for ordinary transfusions. It needs to be specially prepared and has a shorter shelf life.
In Babies Born to Mothers with Antenatally Detected Antibodies

If the prediction is for moderate or high-risk of haemolytic disease:

- Fresh blood suitable for exchange transfusion should be ordered and delivery of the baby should not take place until this blood is ready in blood bank at Singleton Hospital except in extreme emergency.
- The neonatal team should be made aware of imminent delivery
- Neonatal consultant on-call should be informed prior to the baby’s birth, or as soon as the team becomes aware of the baby’s birth
- Send urgent cord bloods as listed below and chase ASAP
- Admit the baby to SCBU and start prophylactic multiple phototherapy

If the prediction is of mild HDN:

- The neonatal team should be made aware of imminent delivery
- Neonatal consultant on-call should be informed prior to the baby’s birth, or as soon as the team becomes aware of the baby’s birth
- Send urgent cord bloods as listed below and chase asap
- Prophylactic phototherapy should be started on postnatal ward

What to do in the first 24 hours

At delivery:

- Resuscitation as required
- Examine the baby for anaemia, signs of heart failure, oedema and hepatosplenomegaly

Send cord blood urgently for:

- Hb and blood film
- DCT
- Blood group (+ cross-matched if indicated)
- Serum bilirubin
- Clotting screen
NB. Cord bloods are not as accurate as a serum sample from the baby. Use these as an indicator but send a repeat set (preferably venous) from the baby as soon as possible within the first 2 hours of life.

Start prophylactic multiple phototherapy immediately

If a Baby is Found to be Jaundiced within the First 24 Hours of Life

- Always consider HDN as a possible cause so carry out the same investigations as those listed above and commence phototherapy.
- Also send a partial septic screen and start antibiotics as jaundice at <24 hours may be caused by infection and this must not be missed.

Hb at Birth (or within first 24 hours) <120g/L or SBR on or above phototherapy line

- The baby is at high risk of requiring an early exchange transfusion.
- If initially admitted to PNW, transfer to NICU
- Continue multiple phototherapy, and discuss with the on call consultant as a matter of urgency.
- Consider giving IV immunoglobulin whilst preparing the exchange

Hb at Birth (or within the first 24 hours) >120g/L or SBR below phototherapy line

- Continue double phototherapy making sure the baby is as fully exposed as possible (no hats or nappies!).
- Check SBR 4-6 hourly in the first 24 – 48 hours, and calculate the rate of rise. (The baby may still need an exchange transfusion.)
- If rate of rise is >8.4micromol/L/hour or there is a rapid drop in Hb this is an indication for exchange transfusion.
Use of Intravenous immunoglobulin (IVIG)

Acts to bind unconjugated bilirubin preventing it crossing the blood brain barrier.

Recommended for:

- Babies on multiple phototherapy whose bilirubin levels remain above the threshold for exchange transfusion and/or have signs of acute bilirubin encephalopathy while preparing for exchange transfusion.
- Babies with haemolytic disease if serum bilirubin level rises >8.5 micromole/L/hour.

Dosage recommended: 500 mg/kg over 4 hours.

LATE ANAEMIA in babies with haemolytic disease of the newborn

All babies with HDN (even mild cases) can have ongoing haemolysis and are at risk of developing severe anaemia requiring top-up transfusions. Therefore:

- Check haemoglobin prior to discharge
- **Babies with documented haemolysis or Coomb's test >2+ should be commenced on folic acid 500mcg/kg once daily**
- Fill in the referral template on postnatal guidelines and give it to the neonatal secretaries on the same day and request consultant appointment for 6-8 weeks (If the baby has a discharge summary from the unit, this should be attached to the template).
- Organise blood tests in 2 weeks in OPD for FBC, film, reticulocyte count and bilirubin. Add to postnatal ward jobs list for bloods to be chased.
- Further follow up is decided based on these results.
Prolonged jaundice

Defined as jaundice persisting beyond 14 days in term and 21 days in preterm babies

It is vital to establish whether prolonged jaundice is unconjugated or conjugated as this will help direct investigations and further management.

All forms of prolonged jaundice should be investigated thoroughly as it may be an indicator of a serious underlying disease. In particular, conjugated jaundice must be investigated promptly as biliary atresia is a possible cause and its management is time sensitive. Surgery must take place within 8 weeks of birth to be successful.

Causes of Prolonged UNCONJUGATED Jaundice

A. Persistence of unconjugated jaundice from early neonatal period:
   - Haemolytic jaundice (of any aetiology)
   - Infection including UTI
   - Breast milk jaundice – a diagnosis of exclusion only

B. Rare causes of unconjugated jaundice
   - Inborn errors of metabolism (Galactosaemia, tyrosinaemia, lipid-storage disorders, and others)
   - Hypothyroidism
   - Drugs
   - Crigler-Najjar
   - Gilbert’s
   - Intestinal obstruction
   - Cystic fibrosis
Causes of CONJUGATED Jaundice

a. Neonatal hepatitis
   • Hepatitis A, B or C
   • Other viral hepatitis
   • Congenital viral infections: rubella, CMV, Herpes
   • Galactosaemia

b. Other causes of conjugated hyperbilirubinaemia:
   • Cystic fibrosis
   • Endocrine causes (hypothyroidism, hypopitutarism)
   • Prolonged TPN
   • Biliary atresia
   • Alagille syndrome
   • Choledocal cyst
   • α1 antitrypsin deficiency
   • Inspissated bile syndrome
   • Inborn errors of metabolism
   • Many more

Prolonged CONJUGATED Jaundice

This is usually picked up from a serum split bilirubin but there may be a history of pale stools and dark urine.

There are many causes of conjugated jaundice and this must be investigated thoroughly. In particular, biliary atresia must be ruled out early on as this requires surgical intervention within the first 8 weeks of life.

Do base line bloods/urine and discuss with the consultant.
Investigation of prolonged jaundice

- History & examination to elicit cause.
- Look for pale, chalky stool or urine that stains the nappy dark.

Base line investigations:

- Split SBR (total and direct SBR- the direct SBR is the conjugated fraction)
- Conjugated hyperbilirubinemia defined as serum conjugated bilirubin: *(Definition from North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition)*
  - greater than 25 micromol/L (definition by NICE guidance CG98)
  - more than 17 micromol/L if total bilirubin is < 85 micromol/L.
  - more than 20% of the total bilirubin if the total bilirubin is > 85 micromol/L.
- FBC. Group and DCT. Blood film.
- LFT & coagulation screen
- TFTs
- Urine culture, Septic screen if clinically indicated
- Urine for reducing substances

Further investigations in case of conjugated jaundice

- Hepatitis A, B and C
- Gal-1-put
- α1 antitrypsin phenotype. *(NB, since α1 antitrypsin is an acute phase reactant, it may be raised in any intercurrent illness and may be normal even if there is a deficiency. Hence the need for the typing.)*
- TORCH screen
- Serum amino acids and organic acids, and urine organic acids
- Urgent Liver USS (to exclude choledochal cyst, and look for signs of biliary atresia).
  - Baby should be NBM for at least 4 hours prior to the USS.
  - If no gall bladder is visualised in the fasted USS refer to a specialised unit for further investigations
• HIDA scan if no gall bladder seen on liver USS (radio-isotope scan of the liver to detect biliary atresia)
• X-ray spine (hemivertebra in Alagille syndrome)
• Eye examination (posterior embryotoxin)

Breast milk jaundice

• This is a diagnosis of exclusion. Excessive investigations may cause anxiety to parents, and lead mother to stop breast feeding. Jaundice is not a reason to stop breast-feeding but fluids may need to be increased.
• If the baby is well and is normal to examine, and has normally pigmented stools, check the baseline investigations (see above).
• If these are normal, no further investigations are needed unless the clinical picture changes or the jaundice clinically becomes darker, in which case, a further split SBR should be checked.
• If the jaundice does not resolve in a week, then the split SBR should again be repeated, but if it remains unconjugated and the baby is well, no further tests are needed.

Further Reading:
1. NICE clinical guideline 98. Neonatal Jaundice. Issue date: May 2010
Appendix 1: Jaundice management algorithm for postnatal ward

Management of babies noted to be visibly jaundiced on the postnatal ward

**Baby appears jaundiced**

- **<24 hours old**
  - Send SBR, FBC, Group, DCT and septic screen
  - Start single phototherapy and IV antibiotics

- **>24 hours old**
  - Measure TcBili if criteria met (or serum SBR) and plot on NICE jaundice chart

  - **TcBili >250 or within 50 micromol/L of treatment line**
    - Send SBR and start phototherapy
  - **TcBili >50 micromol/L below treatment line**
    - Review and repeat TcBili 6-8 hours

- **SBR above or within 50 micromol/L below the exchange transfusion line or suspected haemolytic disease**
  - Start continuous multiple phototherapy. Admit to NICU. Start IV fluids and antibiotics. Inform consultant.

- **SBR above treatment line but below exchange line by >50 micromol/L**
  - Continue single phototherapy or if haemolytic disease suspected* start multiple phototherapy

  - **SBR stable/falling**
    - Repeat SBR in 4 hours
    - Stop phototherapy when SBR below treatment line by >50 micromol. Check rebound in 12 hours.

  - **SBR rising**
    - Admit to NICU. Continuous multiple phototherapy. IV fluids and antibiotics. Investigate

- **SBR rising**
  - Calculate rate of rise. If >8.4 micromol/L/hr or SBR above exchange line, prepare for exchange transfusion. Give IVIG.

- **SBR stable/falling**
  - Repeat SBR 6-12 hourly. Stop phototherapy when SBR >50 micromol/L below treatment line. Check rebound in 12 hours.

---

*Inform the neonatal consultant of any baby with an SBR above the exchange transfusion line or a rate of rise of SBR >8.4 micromol/L

*Babies with suspected haemolytic disease due to antenatally detected maternal antibodies should receive prophylactic phototherapy at birth

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Appendix 2: Flow chart: Infants with visible jaundice in community within ABMU health board (To be used in term babies < 14 days and preterm babies < 21 days only)

Criteria for eligibility for bilirubin estimation using bilirubinometer.
- Gestational age >35 weeks
- Babies more than 24 hours of age.
- Babies who have not received phototherapy.
- Babies in whom the TsB reading is less than 250 micromol/L.

Any baby with visible jaundice in the community
Support mother with feeding and CHECK BILIRUBIN.

If baby fits criteria as per Transcutaneous Bilirubinometer protocol

Use Transcutaneous Bilirubinometer
Check level against NICE charts. Plot and put copy of chart in patients notes

Levels are below treatment zone, but within 50 micromol/L from the cut off for phototherapy treatment on the NICE chart or in the high risk group.

Review baby in 6-12 hours and recheck Bilirubin with TsB and support with feeding.
If there is a persistent rise in two bilirubin readings even if it remains below the treatment zone, discuss with Paediatric Registrar / Consultant in appropriate referral centre.

Levels are above treatment zone or if value is >250 micromol/L

Laboratory estimation of bilirubin (blood sample) and phototherapy

Does NOT fit criteria as per Transcutaneous Bilirubinometer protocol
Laboratory estimation of bilirubin required

> 24 hours
Refer to Paediatrician at appropriate neonatal unit.

< 24 hours
Refer to Paediatrician at appropriate neonatal unit.
URGENTLY

Babies at High Risk for Jaundice
- Gestational age <38 wks.
- A previous sibling with neonatal jaundice requiring phototherapy.
- Mother’s intention to breastfeed exclusively.
- Visible jaundice in the first 24 hour.

Refer to Paediatrician at nearest appropriate hospital for treatment ASAP.
1. Morriston Hospital, Paediatric assessment unit. (PAU)
2. Princess of Wales Hospital, PAU
3. Singleton NICU (Only if baby likely to need exchange transfusion)

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Appendix 3: Guideline for the use of JM-105 (Dräger) Transcutaneous bilirubinometer at Singleton Hospital

Transcutaneous bilirubinometry is used for non invasive estimation of serum bilirubin in neonates. The gold standard for estimation of serum bilirubin is laboratory estimation of total serum bilirubin (TSB). The JM-105 provides measurement of transcutaneous bilirubin (TcB), identifying neonates who require a serum bilirubin measurement. This guideline is designed for using JM-105 (Dräger) transcutaneous bilirubinometer in the neonatal unit and postnatal ward in Singleton Hospital.

Who can use the bilirubinometer?
Currently in 2015 use is restricted to doctors and ANNPs in the neonatal team who have been trained in the use of the device. This could be later extended to nursing and midwifery staff with appropriate training.

Which babies are eligible to have their bilirubin levels assessed using transcutaneous bilirubinometer?
The JM-105 is appropriate for use on neonates who are:
1. ≥24 weeks gestational age at birth
2. less than 14 days of age. Above this age conjugated hyperbilirubinaemia should be ruled out by a blood test.
3. not undergoing phototherapy or have not undergone phototherapy or exchange transfusion.

A blood sample to estimate lab serum bilirubin should be sent for any baby who
1. is <24 hours of age with suspected jaundice.
2. has a TcB reading >250micromol/L.
3. has a TcB reading high enough to require phototherapy as per NICE treatment charts or has a TCB reading within 50micromols/L from phototherapy threshold. Phototherapy can be started following the high bilirubinometer reading, pending lab results.
Method of use

The bilirubinometer should be adequately charged. When not in use, it should be docked in the docking station. The doctor/ANNP using it should ‘sign out’ in the log book when taking it out of the docking station and ‘sign in’ when returning it. Ideally daily pre-use checkout should be performed if the device is being used for the first time for the day. The result of the daily check should be documented in the record book available near the bilirubinometer. A monthly check will be carried out by the medical physics team.

Daily operational checkout procedure

1. Remove the JM-105 from the docking station.
2. Press the power switch on. This may come on automatically if it's been recently used.
3. Select CHECKER and touch OK to save selection.
4. Open the checker lid on the charging unit.
5. When the green READY light illuminates, place the tip of the JM-105 perpendicular on the reading checker circle. Press down until you hear a click.
6. The ‘L’ (long), ‘S’ (short), and Delta values must be within the reference values posted under the checker lid. If not, clean the tip and repeat. If values are still out of range, the device is out of calliberation and should not be used. During 9 AM to 5 PM you can contact the medical physics team at Singleton Hospital to get a replacement pre-charged bilirubinometer.

Do not use a JM 105 bilirubinometer which has failed the calibration check.

7. Once every month the medical physics team will undertake a routine check on the JM 105 bilirubinometers. A routine calibration will be undertaken and the machine will be evaluated for any obvious faults. Any pending data from machine will be uploaded to limited access folder in ABMU shared drive by the medical physics team. The bilirubinometers will undergo a more detailed review & calibration every year by the Draegar team. The medical physics team will organize this. (Gary – bleep 5732 OR phone – 35750 or 35178)
Disinfecting the Bilirubinometer

The JM-105 bilirubinometer must be cleaned properly before and after each use. Prior to use in NICU, wipe the machine clean using a medical instrument detergent (e.g., Tuffie wipes) and then wipe clean using a gauze piece. Use 70% alcohol solution (Sani-Cloth 70) to clean the measuring tip of the JM 105 bilirubinometer and make sure the meter is dry of disinfection solution before use. Do not disassemble the device for cleaning. Wipe exterior surfaces only. Do not autoclave. Do not use any steam cleaning device.

The JM 105 can also be disinfected if soiled with blood or body fluids with Actichlor by Ecolab which is available in Singleton NICU. However, if disinfection is required, wipe the device down again with a moist gauze piece and wipe dry to remove any residual disinfectant.

Skin preparation:
Wash your hands. Use alcohol gel. Use non-sterile gloves.

In babies admitted to the neonatal unit, prepare a small area of skin over the sternum using appropriate skin disinfection agent. Skin cleansing swab with 70% isopropyl alcohol can be used to gently wipe area clean. Allow alcohol to dry before measurement. Use an area of unbroken skin only for measurement.

In term babies being tested outside the NICU in the postnatal ward, the JM 105 should be disinfected as above before and after use. Skin preparation in term babies in postnatal ward and can be used with discretion by the operator. Use over unbroken skin only.

*JM 105 devices being used in the postnatal ward should not be used to test babies in the NICU. Please use devices designated for NICU only for checking babies in NICU.*
Transcutaneous Bilirubin measurement procedure using JM 105 bilirubinometer

1. Clean the bilirubinometer as described above.
2. Press the power switch on. This may come on automatically if it’s been recently used.
3. Select MENU, select MEASURE, and press OK.
4. Enter User ID and Baby ID.
   a. By Barcode scanner from the meter by pressing SCAN on screen or
   b. By key entry by pressing KEY on screen.
5. Select measurement site. The neonate’s mid-sternum is preferred. The skin must be clean, dry and unbroken.
6. Place the bilirubinometer probe tip flat against on the baby’s skin, not at an angle, and press lightly until you hear a click. Lift the device from the skin between measurements and pause until the green READY light illuminates again. Repeat the testing procedure for 3 times.
7. Take the reading from the screen in micromol/L after the third testing.
8. Record the actual reading on the patient’s notes and plot it and record against the charts for assessing neonatal jaundice in the neonatal protocol. Take appropriate action based on the chart. If baby requires phototherapy, commence phototherapy and send a blood sample to lab for serum bilirubin estimation. (Be aware that transcutaneous bilirubinometer reading could have an error of ±50 micromol/L from the actual lab value.)
**Uploading data from JM105 bilirubinometer to limited access data file on ABMU server** *(Medical physics team or authorised personnel only)*

1. Connect the docking station to the designated PC with USB cable provided.
2. Press power switch and turn on JM 105 bilirubinometer.
3. In the bilirubinometer menu scroll down to select
   - Config → press ok → Memory → press ok → Change ‘Mem only’ to ‘Link on’ → press ok.
4. Place the bilirubinometer in the docking station.
5. Touch OK on the screen of the bilirubinometer to confirm transfer of data.
6. Right click on the SW JM-S1W software logo on the computer. 2 choices preferences and exit will open. Click on ‘preferences’ to open the software box. Tick box to allow changes. Click Ok.
7. JM 105 screen will confirm data has been sent. Press ok to go back to menu screen.
8. Confirm data has uploaded to the JM 105 folder in Z drive (ststorage2, Women & Children’s folder).
9. Select Config → press ok → Memory → press ok → Change ‘Link on’ to ‘Mem only’ → press ok.
10. Replace JM 105 in docking station.

References:
1. NICE clinical guideline 98, Neonatal Jaundice. Issue date: May 2010
3. Dräger Jaundice Meter Model JM-105 Instructions for Use.
5. Dräger UK addendum to jaundice meter cleaning and disinfection guide.
Appendix 4: Guideline for use of Dräger Transcutaneous Bilirubinometer JM- 103 based on NICE guideline for POW Hospital postnatal ward and ABMU community midwives

Transcutaneous bilirubinometer is a device used for non invasive estimation of serum bilirubin in neonates. The gold standard for estimation of serum bilirubin is a laboratory estimation of bilirubin. This protocol is designed for using the transcutaneous bilirubinometer in a community setting by appropriately trained medical personnel (midwives, doctors, ANNP) within ABMU health board as part of the pilot project called ‘Jaundice Community Project’.

Who can use the bilirubinometer?
Newborn Examiners, Midwives, Doctors, ANNP in ABMU health board who have been trained in the use of the device.

Which babies are eligible to have their bilirubin levels assessed using transcutaneous bilirubinometer?

1. Term and near-term babies more than 35 weeks gestation with visible jaundice.
2. Babies more than 24 hours of age.
3. Babies who have not received phototherapy.
4. Babies in whom the transcutaneous bilirubinometer reading is less than 250 micromol/L.

The bilirubinometer can be used in babies with any skin tone (Caucasian, African, Asian etc)

A blood sample to estimate lab serum bilirubin should be sent for any baby who

1. Is less than 24 hours of age with suspected jaundice.
2. Has a transcutaneous bilirubinometer reading more than 250 micromol/L.
3. Has a transcutaneous bilirubinometer reading high enough to require phototherapy.
(Phototherapy can be started following the high bilirubinometer reading pending lab results)

**Which babies should not have bilirubin estimated using transcutaneous bilirubinometer?**

1. Babies < 35 weeks gestation.
2. Babies < 24 hours old.
3. Babies who have received or is receiving phototherapy.
4. Babies with transcutaneous bilirubinometer reading > 250 micromol/L.

**Method of use:**
The bilirubinometer should be adequately charged. When not in use it should be docked in the docking station which is connected to a power source. The doctor/ANNP/midwife using it should ‘sign out’ in the log book when taking it out of the docking station and ‘sign in’ when returning it.

The calibration check must be done daily and highlighted on “Weekly update” form. If it fails the calibration check, clean tip using alcohol wipe and recheck calibration. If readings are outside the calibration limits the machine could be faulty and should not be used for estimation of bilirubin. (In addition to daily calibration the device will need annual calibration which is arranged by Draegar medical in association with ABMU medical physics team)

1. Switch device on. Wait for green light indicating device is ready.
2. Ensure that device is set to be in units ‘micromole/L’ and is set to measure average of 3 values. (This is the default setting).
3. Clean the tip using an alcohol wipe.
4. Keep tip perpendicular to sternum of baby and press gently until a red light flashes at the tip. Direct contact with skin is needed. Repeat process 3 times. If the red light does not flash wait a few seconds and try again.
5. Take the reading from the screen in micromole/L after the 3rd flash.
6. Record the actual reading on the patient’s notes and plot it and record against the charts for assessing neonatal jaundice in the neonatal protocol. Take appropriate action based on

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the chart. If baby requires phototherapy refer the baby for treatment to an appropriate hospital (Morriston PAU, POW or Singleton NICU) as per referral pathway. Only babies that need exchange transfusion should be sent to Singleton NICU.

* Be aware that transcutaneous bilirubinometer reading could have an error of +/- 50 micromol/L from the actual lab value. This need not be deducted from any results you read off the machine while plotting on the charts.

A baby whose value fall within +/- 50 mmol/l, must be reassessed and TsB rechecked within 24 hours to ensure that the levels do not rise. Parents to be advised on feeding.

References:

Appendix 5:

Referral form for baby with jaundice from Community midwife team to Hospital in ABMU Health Board

<table>
<thead>
<tr>
<th>Baby's Details</th>
<th>Mother's Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>Name:</td>
</tr>
<tr>
<td>DoB:</td>
<td>DoB:</td>
</tr>
<tr>
<td>ToB:</td>
<td>Hospital number:</td>
</tr>
<tr>
<td>Hospital number:</td>
<td>Address:</td>
</tr>
<tr>
<td>Hospital born:</td>
<td>Phone number:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Birth weight:</th>
<th>Is baby eligible for TSB testing: Yes / No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current weight:</td>
<td>Bilirubin level by TSB:</td>
</tr>
<tr>
<td>Day of life:</td>
<td>Date test done:</td>
</tr>
<tr>
<td></td>
<td>Time of test:</td>
</tr>
</tbody>
</table>

Level in NICE bilirubin chart: Below photozone

*(Circle as appropriate)*

Below photozone

In photozone

In Exchange zone

Reason for referral:

Name of doctor baby has been discussed with:_____________________

Designation of doctor baby has been discussed with:_________________

Name of midwife making referral:_____________________________

Phone number of midwife making referral:_________________________

*(Kindly inform the midwife the outcome of the baby)*

Hospital referred to: Morriston PAU  Princess of Wales PAU  Singleton NICU  GP

*(Circle as appropriate)*

Other:_________________

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Guidelines for RBC transfusions in neonates

Dr. Gareth Davies, Dr. Nitin Goel

- The most common form of transfusion used in the neonatal unit is a small volume packed red cells transfusion (top up), usually 10-20ml/kg. This is to correct lower levels of Haemoglobin (Hb) which are often the result of reduced production (Anaemia of prematurity) and repeated blood sampling. A higher Hb allows for the same level of tissue oxygenation with a lower cardiac output.

- Blood transfusion for neonates is obtained from pedipaks, i.e., a donor pack of O RhD negative for 280mls subdivided into 4-8 packs of 30-50ml. This is done to reduce the donor exposure. Donor blood is CMV negative, leuco-depleted and centrifuged and then resuspended in SAGM (saline adenine glucose mannitol) to give a final haematocrit of 0.5-0.7.

- The lifespan of each donor pack is 30-35 days, however they are usually split on day 6, and therefore pedipaks have a shelf life of around 28 days when they are split at the Welsh Blood Transfusion Service. Thus by the time they arrive in Singleton, that may be shorter still. Within those 28 days, there is no evidence of difference in ‘quality’ of blood at different storage ages.

- **Volume and Rate:** Larger volume (15-20ml/kg) RBC transfusions lead to larger rises in Hb and fewer overall transfusions than small volume transfusions (≤10ml/kg). Volumes over 20ml/kg are not recommended due to the increased risk of transfusion-associated circulatory overload. BCSH recommends using 15 ml/kg for non-bleeding neonates in most cases, in context of data supporting restrictive transfusion thresholds. A rate of 5ml/kg/hr is usually recommended for the non bleeding infant; i.e. 15ml/kg over 3-4 hours. Transfusion of each pack should not exceed 4 hours due to risk of bacterial proliferation when PRBC’s are not refrigerated.

- Micro-aggregate filters should be used for all transfusions. Blood warmers should be used for massive transfusions, rapid blood replacement and exchange transfusion.

- Adhering closely to strict transfusion guidelines reduces transfusion number and donor exposure. The most appropriate RBC transfusion strategy for sick neonates is a large volume
restrictive approach directed by strict guidelines using dedicated products from a single donation.

**Following is a table of suggested RBC transfusion triggers (Hb g/L):**

<table>
<thead>
<tr>
<th>Postnatal age</th>
<th>Suggested transfusion threshold Hb (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ventilated</td>
</tr>
<tr>
<td>First 24 hours</td>
<td>&lt;120</td>
</tr>
<tr>
<td>Day 1-7 age</td>
<td>&lt;120</td>
</tr>
<tr>
<td>Day 8-14 age</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Day 15 onwards</td>
<td>&lt;100</td>
</tr>
</tbody>
</table>

Table 1. From the British Committee for Standards in Hematology (BCSH), 2016 – suggested transfusion thresholds for preterm neonates. *depending on the clinical situation*

The above table does not include suggested thresholds for moderate to late preterm (≥32 weeks gestational age at birth) or term neonates, as there is little evidence regarding the appropriate thresholds for these groups. Clinicians may consider similar thresholds to those used for preterm babies off oxygen.

- RBC transfusions may be considered at higher Hb concentrations than recommended above. Examples include:
  - Acute hypovolaemia due to blood or other fluid loss where Hb concentration is an unreliable indicator of anaemia
  - Septic shock
  - Nectrotising entercolitis
  - Major surgery
  - Signs of congestive heart failure
  - Poor growth, lethargy, increasing frequency of desaturations and bradycardias.

- The Hb thresholds for triggering RBC transfusion are only guidelines and some neonates will have no clinical compromise at these Hb concentrations and therefore will not automatically require a RBC transfusion. In babies that are spontaneously breathing and older than 28 days, always evaluate reticulocyte count before deciding on a transfusion. There is no justification for top-up transfusion simply because the baby is about to be discharged.
• When a baby receives a transfusion, clearly document in the notes the clinical indication for the transfusion.

• Infants <4 months old do not need to be cross matched provided there is no evidence of haemolytic disease (i.e., DCT negative, no maternal antibody). The transfusion service will need an initial maternal sample to group and antibody screen and an infant sample to group and DCT. After this no samples are required, until the infant is 4 months old. If maternal blood is unavailable, the antibody screen can be done on the baby.

• If there is evidence of haemolytic disease the blood for transfusion must be cross matched against the mother (or infant, if maternal blood is unavailable). The group of the blood issued must be compatible with the mother and the infant and antigen negative for the causative antigen.

• **Practical considerations on RBC transfusions to infants** (0-4 months old)

  o **Small volume transfusion** (most common)
    ▪ Metabolic concerns governing choice of blood do not apply
    ▪ Freshness of blood is irrelevant

  o **Large transfusion** (usually pathological blood loss)
    ▪ Metabolic concerns DO apply
    ▪ Freshness of blood is irrelevant
    ▪ Coagulopathy is a possibility, consider other blood products,

  o **Massive transfusion** (typically exchange transfusion)
    ▪ Discuss with blood bank – pre-arrange
    ▪ Metabolic concerns DO apply
    ▪ Freshness of blood is relevant

**Pre-transfusion Testing:**

- Maternal sample
  1. ABO/ RhD group
  2. Antibody Screen

- Infant sample
  1. ABO/ RhD group
  2. Direct antiglobulin test (DAT)
  3. Antibody screen (if maternal sample unavailable - neonatal sample should be screened for atypical antibodies)

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A. **Atypical antibodies present:**

The presence of atypical antibodies in the maternal or neonatal sample or a positive DAT on the neonatal red cells, may reflect the presence of haemolytic disease of the newborn (HDN). In such cases, special serological procedures will be necessary to determine the infant’s blood group and allow selection of appropriate blood for transfusion.

**In this situation: the choice is:**

1. Use O Rh (D) negative blood, and cross match using the indirect antiglobulin test against the baby’s plasma to ensure compatibility.
2. If maternal sample is unavailable, blood should be cross-matched using the indirect antiglobulin test against the baby’s plasma to ensure compatibility.

B. **No atypical antibodies in maternal/or infant’s serum and the DAT test on infant’s blood is negative:**

- Further top-up transfusions can be given repeatedly during first 4 months of life without further serological testing.
- In repeated massive transfusions, repeat antibody screening of recipient is required (as rarely Abs may develop in these situations).

**Hazards of neonatal transfusions**

The safest blood transfusion is the one not administered. Early recognition and prompt treatment of acute reactions will minimise any adverse consequences. Hence close monitoring during the transfusion is a must. There are non-infectious and infection-related hazards. The Blood Transfusion Lab should be notified of any suspected reactions, as they will normally request the remaining blood to be returned for analysis.

**Non-infectious Complications:**

1. Hypocalcaemia (ionized calcium < 0.8 mmols/L):
   - This is rare. It results from the use of CPD (citrate phosphate dextrose) additives which prevent blood clotting.
   - Can occur with exchange transfusion.
• Warming the blood minimises its effect.

2. Citrate Toxicity:-
   • Induces alkalosis
   • Especially noted in premature neonates
   • If confirmed give calcium gluconate.

3. Hyperkalaemia may result from rapid transfusion (tends not to occur if transfused at usual rate of 5ml/Kg/hour).

4. Thrombocytopenia:-
   • Dilutional in most cases
   • Rule out DIC

5. Hypervolaemia may occur in compromised babies.

6. Hypoglycaemia may occur especially with large volume transfusion, e.g. exchange transfusion, or when there is reduced intake of substrate during the transfusion.

7. Non-immune haemolysis of RBC may result from a variety of causes: overheating, using fluids other than 0.9% NaCl or hypo-osmotic fluids, mechanical damage from rapid transfusion through small gauge (<24G) needle.

8. GVHD (Graft versus Host Disease) Mediated by T-cells. An exceptionally rare problem of intra-uterine and neonatal transfusion. It results from proliferation of donor derived T lymphocytes. There is no effective treatment for this fatal condition. Irradiated blood (which destroys any nucleated cells) is thus used to avoid GVHD in at risk groups:-
   a) Congenital cellular immune deficiency, e.g. 22q11 Di George.
   b) Intra-uterine transfusion and any subsequent transfusion or exchange transfusion in neonates who received IUT.
   c) Donations from first degree relative e.g. maternal blood

   Irradiated blood should be used within 4 days for top-up transfusions and 24 hours for exchange transfusions

9. Haemolytic transfusion reactions in necrotizing enterocolitis. This is a rare, serious complication due to destruction of T-activated autologous red cells by the natural anti-T in transfused plasma. The Blood Transfusion Laboratory should be notified to enable
the diagnosis of T activation to be investigated in any case of NEC.

**Infectious Complications:**

1. CMV – no longer a risk, as all blood used in the UK for transfusing babies below 1yr old is CMV negative.
2. HIV – estimated risk per adult unit transfused: 1 in 1,779,000.
3. HCV – estimated risk per adult unit transfused: 1 in 1,613,000.
4. HBV – estimated risk per adult unit transfused: 1 in 171,000.
5. Bacterial infection: less common than from platelet products as the latter are not-refrigerated, therefore bacteria may multiply more readily.
6. No tests are available to look for prion diseases such as vCJD, so theoretical risk always remains.

**Babies who have received intra-uterine transfusions**

Babies who have received intra-uterine transfusions should have haemoglobin electrophoresis done at birth in order to see the percentage of adult haemoglobin (i.e. transfused blood) in the circulation. Any exchange transfusions or subsequent transfusions for the first year of life should be given as **IRRADIATED BLOOD**. The notes should be marked on the front that irradiated blood is to be given and the mother should be told that only irradiated blood is to be given to reduce the risk of inadvertently giving non-irradiated blood. When a baby receives intra-uterine blood transfusions the marrow becomes suppressed, there is then a theoretical risk that lymphocytes from subsequent blood transfusions may engraft causing graft versus host disease, which is a very serious problem. Radiation causes death of the nucleated cells in the pack – that is any white blood cells that may have escaped removal on leucodepletion.

**References**


3. Blood transfusion service, ABMU HB.

4. Refer to the Blood Transfusion website for Product specification: www.wbs.wales.nhs.uk


Managing Infants Whose Parents do not Wish to Consent to Blood Product Transfusion

Occasionally infants are born to parents whose beliefs preclude them from consenting to blood product transfusion eg members of the Jehovah’s Witness religious group. This can lead to difficulties in decision-making, but when managed carefully and considerately, these situations rarely need to be referred to court.

If there is time, we should engage with parents before birth and clarify their beliefs and feelings. There may be opportunities to explain the possible need for blood products and explain our duty as healthcare professionals including our wish to respect the views of parents as far as we possibly can. There may be some blood products that are acceptable to parents. For members of the Jehovah’s Witness organisation, there is a Jehovah’s Witness Hospital Liaison Committee that parents may wish to contact during discussions. For further details, see link: https://www.jw.org/en/medical-library/hospital-liaison-committee-hlc-contacts/united-kingdom/

<table>
<thead>
<tr>
<th>Emergency Transfusions :</th>
</tr>
</thead>
</table>
| If the need for blood products constitutes an emergency, we have a duty of care to the baby at all times, and if it is in the baby’s best interests, we should administer the blood transfusion without the parents’ consent.

UK law is clear on this:

The Children Act 1989

1 Welfare of the child.

(a) When a court determines any question with respect to—

   (a) the upbringing of a child; or

   (b) the administration of a child’s property or the application of any income arising from it, the child’s welfare shall be the court’s paramount consideration.

When the welfare of the child is in question, the court will have the child’s best interest as its primary focus. There is a presumption in favour of prolonging life.

There is also a wealth of case law concerning the administration of blood transfusions to children of non-consenting Jehovah’s Witness parents where courts have permitted the transfusions to be given. On each occasions1(1) Children Act 1989 above has been applied.

Even in acute situations, we should always try to engage the parents in discussion and
inform them of our intentions if there is time to do so – this is so that they have the opportunity to ask questions, understand the necessity of transfusion and seek any support or help that they would like.

**Non-Emergency Blood Product Transfusion**

In the case of a baby who requires a non-urgent transfusion and if there is time, we should discuss with the parents the reasons for the transfusion and why we feel the transfusion is necessary. A senior neonatologist should always be involved in these cases. It is very helpful if we consider the following measures to reduce the need for blood products:

- Delayed cord clamping. Provided it is safe to do so this has been shown to reduce transfusion requirements.
- Minimum blood sample volume. Use microsamples for blood gas estimation when safe to do so rather than full samples, and the range of blood tests requested should be only those necessary.
- Minimum blood test frequency. Perform each blood test only as frequently as necessary. This will vary according to the results and the baby’s status but for each blood test ask yourself if it is important to know the result at that time.
- Conservative haemoglobin thresholds for transfusion. There may be scope for reducing standard thresholds provided there are no signs of compromise.
- Use of Erythropoietin (EPO). There is some evidence that this is associated with reduced requirement for transfusion in preterm infants.
- Early use of Iron supplementation. Enteral Iron supplementation is usually started at day 28, but consideration can be given to starting earlier, especially if the infant is on EPO, which tends to increase iron requirements.

When a decision about transfusion is needed, it is usually possible to discuss with parents and reach an agreement that, though they will not consent to transfusion, they understand that we as healthcare professionals have a duty of care to the baby. It is also appropriate for us as healthcare professionals, if there is time, to inform parents of any intention to use blood products and allow them time to discuss with others if they so wish. They can then ask any questions they wish and be supported at the time of transfusion by their families and advisors. All discussions should be carefully recorded in the notes.
**When there is No Agreement**

If parents object to the use of blood products and do not agree that the neonatal team makes decisions in the baby’s best interests, then a “best interests” meeting can be held in which the relevant health professionals sit with parents and anyone they would like to support them and discuss the decision to administer a transfusion. Detailed notes should be taken and recorded in the notes. If possible, two consultant neonatologists should attend (or one consultant and another member of the neonatal medical team). It may be possible to have an agreement during this meeting, but if not, an application to court may be necessary.

**Application for a Court Order**

If every effort is made to reach an agreement and this has not been successful, an application for a court order may be necessary in order to allow the medical team to administer a blood product. This should be a rare event as it is almost always avoidable.

A senior member of the health board will need to be notified (usually the Medical Director) and the departmental (or duty) manager. The application is made by notifying the Health Board’s Legal Services Team (Patient Experience, Risk & Legal Services, Headquarters, Baglan) via the ABM Claims e-mail address: ABMclaims@wales.nhs.uk. A witness statement will be required from the consultant neonatologist to explain the baby’s history and condition, the reason for the transfusion and the evidence for and against the transfusion, including any supporting guidelines or literature.

If, in the judgement of the clinical team, the transfusion cannot wait until the court makes a decision, and the transfusion is considered an emergency to avoid death or harm to the infant, the transfusion should be given when considered to be in the patients best interest and this should be documented in the baby’s health records.

At all times documentation of discussion is extremely important and seeking the opinion of a second senior member of the neonatal team is good practice.
References


Neonatal Guidelines
Chapter 8 – Haematology and Jaundice v2018.2   Valid until 31st January 2021

Neonatal thrombocytopenia

Definition:
A platelet count of < 150 X 10^9/litre. But some large population studies have shown that average counts at birth are 120, and 105 in preterm babies <32/40. Prevalence:

- 1% of term babies – who have platelet count checked!
- 40 – 50% of babies on Neonatal Units develop thrombocytopenia at some stage during their admission
- Up to 80% of sick or very preterm babies develop thrombocytopenia

Causes:
The most useful clinical classification of the causes of neonatal thrombocytopenia divides them according to time of onset. Some babies are born with a low platelet count, i.e. have a foetal onset, some become evident in the first 72 hours of life, and the rest have an onset later than 72 hours.

- Fetal Onset Thrombocytopenia – detected at birth
  - NAIT (neonatal alloimmune thrombocytopenia – see later)
  - Congenital infection, especially CMV
  - Maternal autoimmune antibodies, e.g. SLE, even in the absence of clinical disease in mother
  - Maternal ITP
  - Aneuploidy (Turner syndrome, trisomies 13, 18 & 21)
  - Severe Rh incompatibility disease
  - Other, rare congenital causes, e.g. Wiskott-Aldridge syndrome, other familial conditions, including Fanconi & TAR which have associated upper limb anomalies.

- Early Onset Thrombocytopenia – within 72 hours of birth
  - 75% are due to placental insufficiency (see later)
  - 10 – 15% are due to perinatal infection, especially bacterial, most importantly GBS. Here the platelet count is usually 20 – 50 X 10^9/litre
2% are due to HIE. Here the platelet count may be as low as 5 – 50 X 10^9/litre

- NAIT (see later)
- Disseminated Intravascular Coagulation
- Maternal autoimmune antibodies, e.g. SLE, even in the absence of clinical disease in mother
- Maternal ITP

- Late Onset Thrombocytopenia – after the first 72 hours of life
  - Late onset bacterial sepsis or NEC account for 90% of late onset thrombocytopenia. A drop in the platelet count may be the first sign of sepsis. Thrombocytopenia may be severe and prolonged – up to several weeks; due to both increased consumption and reduced production
  - Post natal viral infections, e.g. CMV, HIV, HSV.
  - Post natal fungal & parasitic infections, Candida, Toxoplasma gondii.
  - Disseminated Intravascular Coagulation – not related to sepsis.

SPECIFIC CONDITIONS:
**Neonatal Alloimmune thrombocytopenia (NAIT)**

Introduction:
The incidence is about 1 in 1500 births. The condition occurs in a mother who is negative for a particular platelet antigen, and whose infant is positive for that antigen, where the mother becomes sensitised (a similar situation to Rhesus incompatibility) and produces antibodies which cross the placenta and react against the fetal platelets.

Incompatibility of HPA-1a (human platelet antigen1a) accounts for the majority of cases, followed by incompatibility of HPA-5b, and HPA-3a. Two percent of women are HPA-1a negative and therefore potentially at risk of developing NAIT in their pregnancies, however, NAIT most likely develops in women with certain HLA-DR antigens.
Subsequent pregnancies of a mother who had an infant with NAIT are at high risk, and severity increases with each pregnancy. However, unlike Rhesus disease, NAIT may occur in the first pregnancy, and may be severe enough to have resulted in ICH.

**Presentation:**

- Usually a well baby
- Muco-cutaneous bleeding is common
- The risk of intracranial haemorrhage (ICH) may be as high as 10-20% of HPA-1a incompatibility. Some occur in utero. Hence, all infants should have an USS of head as soon as possible after birth.

**Diagnosis:**

The diagnosis is suggested when an infant develops petechiae and purpura and has thrombocytopenia within hours of birth. Platelet counts may fall below 10 in the first day of life. The maternal platelet count is normal, helping to distinguish this condition from neonatal thrombocytopenia secondary to maternal ITP.

**Investigations:**

Other causes of neonatal thrombocytopenia should be excluded e.g. infection, maternal ITP.

Determine the infant’s platelet count 6 hourly in first 24 hours and then daily for several days.

Screen the mother’s and infant’s serum for anti platelet antibody – often difficult to detect. Unlike Rh alloimmunization, maternal anti-platelet antibody titers are NOT predictive of the degree of fetal thrombocytopenia.

**Immunophenotype the maternal and paternal platelets for HPA-1a & HPA-5b:**

- Samples from parents = 20ml in EDTA, 10ml clotted
- Samples from infant = 2 X 0.5ml in EDTA
- Store at room temperature – not in fridge
- Send samples, preferably by courier, to Welsh Blood Service (WBS) at Llantrisant
Pre-natal Management:
Counselling following the diagnosis of the first baby is necessary, as the severity of the pre and post natal haemorrhages tends to worsen in later pregnancies. The pregnancy should be monitored regularly with ultra-sound examination from mid-term, especially looking for evidence of fetal ICH.
Administration of IVIG to the pregnant mother may increase the platelet count.
More invasive measures as intra-uterine platelet transfusions.
Elective C.S should be considered for babies at risk.

Post-natal Management:
Examination and cranial ultrasound scan.
Mainstay of treatment is transfusion with HPA-1a and HPA-5b negative platelets (see details below):
- In a well infant with no ICH or bleeding elsewhere, transfuse when platelet count falls below $30 \times 10^9$/litre
- If any bleeding occurs, transfuse when count is $30 - 49 \times 10^9$/litre
- If major bleed or ICH, transfuse when platelet count is below $99 \times 10^9$/litre

If no suitable platelets are available, IVIG (1g/Kg/d) for two consecutive days is also effective in raising the platelet count, but rise in platelet count may be delayed for 24 hours.

If NAIT is prolonged lasting more than 2 weeks and platelet count is falling and approaching critical values despite more than two units of HPA-1a/5b negative platelet transfusion, then intra-venous immunoglobulin (1g/kg/day) should be considered. This may need to be repeated every 1-3 days until the platelet count is more than 50-100 x $10^9$/L. In most cases however, one dose is often adequate.

Platelet transfusion in NAIT:
- Transfuse with HPA-1a & HPA-5b negative platelets.
  - Obtained from WBS, with authorisation from consultant haematologist at WBS
  - Contact numbers for WBS: 01443622000 (24-hour service)
  - Remember that if these are not available in WBS, they would need to be transported from other Blood Transfusion Services in the UK, thus taking longer to arrive
• As a last resort, or while awaiting arrival of HPA-1a & HPA-5b negative platelets, transfuse with random-donor platelets in infants with serious haemorrhage
• Maternal platelets - washed and irradiated (after carrying usual donor screen) were used in the past, but can no longer be recommended.

**Infants of mothers with ITP**

In contrast to NAIT, there is a milder thrombocytopenia at birth, and the distinguishing factor is that both mother and infant have low platelet counts.

Infants do need to be monitored, as the platelet count may drop in the first few days. A count < 50 is only seen in 3% at birth, therefore the risk of serious bleeding is very low.

Note that many pregnant women develop mild thrombocytopenia towards end of pregnancy, probably dilutional effect of increased plasma volume; this is not ITP.

**Management of thrombocytopenia secondary to maternal ITP:**

Degree of maternal thrombocytopenia is a poor indicator of the infant’s platelet count.

Cord blood may be sent for platelet count, and then repeat FBC checked on baby every day, depending on counts. The risk of bleeding is lower than NAIT but treatment should be considered if platelet count is less than 30 in a well baby. If at risk of bleeding, treatment with IVIG for the first 2 days may be useful.

Dose: IV immunoglobulin 1g/Kg per day.

**Thrombocytopenia due to placental insufficiency**

Prevalence:

This represents 75% of early onset neonatal thrombocytopenia.

Pathophysiology:

In pregnancies complicated by maternal hypertension, PET, diabetes or IUGR, where there is underlying placental insufficiency, the fetus is exposed to chronic hypoxia. This results in raised erythropoetin levels which drive red cell production in the presence of already adequate Hb levels. This phenomenon has been termed
‘lineage steal’, i.e. the pluripotent haemopoietic stem cells are driven to produce more red blood cell precursors, at the cost of less platelet and granulocyte precursors. Hence, in newborns affected by placental insufficiency, there is often a triad of thrombocytopenia, polycythemia and neutropenia.

Platelet counts < 150 are seen at birth, falling to a nadir of 50 – 100 X 10^9/litre between day 3 to 5, and then spontaneously normalising by day 10 -14.

Management:
As the platelet count rarely falls below 50, there is no need for transfusion. Other causes of thrombocytopenia should be looked for if the count falls too much or if the condition persists beyond 2 weeks.
**Indications for platelet transfusion**

Transfused platelets last for a questionable period of time, and there is no evidence that they prevent haemorrhage before it occurs. Levels at which platelets should be transfused have always been controversial, but there is some evidence that the trauma and the stress of birth can very rarely precipitate intracranial or internal bleeding when platelets are <30.

The following are agreed guidelines published by the British Committee on Standards in Haematology. If in doubt, please discuss with consultant.

<table>
<thead>
<tr>
<th>Platelet Count</th>
<th>Who to transfuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 30 X 10^9/litre</td>
<td>Consider in all neonates</td>
</tr>
<tr>
<td>30 – 49 X 10^9/litre</td>
<td>Do not transfuse if clinically stable</td>
</tr>
<tr>
<td></td>
<td>Consider transfusion in:</td>
</tr>
<tr>
<td></td>
<td>• Bt wt less than 1000g &amp; less than 1 week old</td>
</tr>
<tr>
<td></td>
<td>• Clinically unstable</td>
</tr>
<tr>
<td></td>
<td>• Unstable blood pressure</td>
</tr>
<tr>
<td></td>
<td>• Current bleeding, oozing from puncture sites</td>
</tr>
<tr>
<td></td>
<td>• Previous major bleed, e.g. IVH</td>
</tr>
<tr>
<td></td>
<td>• Co-existing coagulopathy</td>
</tr>
<tr>
<td></td>
<td>• Pre-surgery / pre exchange transfusion</td>
</tr>
<tr>
<td>50 - 99 X 10^9/litre</td>
<td>Bleeding neonate</td>
</tr>
<tr>
<td>More 99 X 10^9/litre</td>
<td>Do not transfuse</td>
</tr>
</tbody>
</table>
Further reading:
**Approach to neonatal coagulopathy**
*(Section Author: Shabeena Hayat and Jean Matthes)*

The signs and symptoms of bleeding in an infant require assessment to determine the cause and optimal treatment. In the neonate the cause is usually secondary to an underlying disease process, rarely is it due to bleeding disorder e.g. Haemophilia.

It is also important to recognise that bleeding at a single site is more likely to have an anatomic or structural component and that major bleeding from any primary cause may induce a secondary DIC, which may mask the original pathology.

Causes of bleeding include:

<table>
<thead>
<tr>
<th>A ‘well’ neonate</th>
<th>A ‘sick’ neonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune thrombocytopenia</td>
<td>Disseminated intravascular coagulopathy</td>
</tr>
<tr>
<td>(Alloimmune or autoimmune e.g. maternal ITP)</td>
<td>(secondary to sepsis, asphyxia, severe RDS or NEC)</td>
</tr>
<tr>
<td>Vitamin K deficiency, PIVKA</td>
<td>Consumption thrombocytopenia without depletion of coagulation factors</td>
</tr>
<tr>
<td>Inherited coagulation factor deficiencies (haemophilia)</td>
<td>Liver failure</td>
</tr>
<tr>
<td>Bleeding from anatomic lesions (haemangioma, A-V malformation)</td>
<td></td>
</tr>
</tbody>
</table>

If bleeding is evident in a neonate consider coagulation screens, alongside an FBC and Group and save if bleeding is significant.

**Sampling for coagulation screens**

Coagulation screens are performed by taking 1.3mls of blood and sent in the blue topped citrate coagulation bottles. This is the minimum amount required for neonatal and paediatric sampling on this unit. Samples are to be processed urgently by informing the lab prior to sending the sample.

The initial request for a coagulation screen should include PT, APTT, fibrinogen and TCT (see below).

**Please Note:** Several technical factors can produce prolonged PT and APTT:
- A long difficult blood draw with numerous small fibrin clots
- Heparin in the sample will prolong the APTT with minimal effect on PT.
- The presence of haematocrit >65% will increase the ratio of citrate to plasma and prolong both PT and APTT.

Thrombin Clotting Time (TCT)
As of July 1st 2011 a thrombin clotting time (TCT) is to be requested on all coagulation screens in neonatal patients, whether heparin may have contaminated the sample or not.

As even the smallest amount of heparin can produce erroneous results the TCT will allow more accurate interpretation of results and requires no extra blood. The laboratory technician will know that a Hepenzyme correction will need to be carried out if the TCT is prolonged. If the TCT is normal they will proceed to carry out further correction tests for factor deficiencies.

The laboratory will carry out this test on all samples. However, the request must also be made on the appropriate form.

As always, adequate and legible information of the clinical problem and of the sample source must be provided. Whether the sample is venous or taken from a heparinised central or peripheral arterial line this information must also be written in free text on the request form.

What do they measure?
Figure 1 shows the coagulation pathway

![Coagulation pathway diagram]

TF = Tissue Factor
APTT measures the intrinsic pathway (all clotting factors except VII and XIII).
PT measures the extrinsic pathway (does not measure factors VIII, IX, XI, XII and XIII).
In true cases of prolonged PT and APTT a fibrinogen and ‘fibrin split products’ (also known as D Dimers) will need to be analysed. If DIC is suspected then please add ‘fibrin split products’ to the request. An elevated fibrin split products and decreased fibrinogen suggests DIC, the most common and potentially life threatening cause of impaired homeostasis in neonates. When DIC is present the underlying cause must be identified as is always a secondary event.

**PIVKA - Proteins Induced by Vitamin K Antagonism or Absence**
The PIVKA test should be considered as a modified PT that detects deficiencies in Vitamin K dependant factors II, VII, and X. Because the clotting times are longer than the PT, the test may be more sensitive than the PT for abnormalities in these factors (please refer to SharePoint for more information on PIVKA).
This is a specialised test, and the sample is sent away for analysis, so please discuss with the haematologists in advance.

Table 1 - shows the normal parameters for a coagulation screen in neonates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age</th>
<th>Full Term Ref Range</th>
<th>30-36 weeks Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin Time (Premature) secs</td>
<td>D1 - D91</td>
<td>8.5 - 14.1</td>
<td>8.5 - 17.0</td>
</tr>
<tr>
<td>APTT secs</td>
<td>D1 - D4</td>
<td>29.0 - 51.5</td>
<td>27.5 - 79.4</td>
</tr>
<tr>
<td></td>
<td>D5 - D21</td>
<td>28.0 - 55.0</td>
<td>26.9 - 74.1</td>
</tr>
<tr>
<td></td>
<td>D22 - D89</td>
<td>28.0 - 50.0</td>
<td>26.9 - 62.5</td>
</tr>
<tr>
<td>Fibrinogen g/L</td>
<td>0Y – Adult</td>
<td>1.7 - 4.0</td>
<td>1.7 - 4.0</td>
</tr>
<tr>
<td>Thrombin clotting time secs</td>
<td>0Y – Adult</td>
<td>12.5 -17.4</td>
<td>12.5 -17.4</td>
</tr>
</tbody>
</table>

Diagram 1 in the next page shows how to interpret a coagulation result in clinical context:
Bleeding infant

Screening tests
- Activated ThromboPlastin Testing Time (APTT)
- Thrombin clotting time (TCT)
- Prothrombin time (PT)
- Fibrinogen
- Platelet count

All test normal

- APTT prolonged
  - TCT prolonged
    - Hereditary deficiency of FXIII α2.PA and PAI, vWF
    - Specific factor assays
      - Heparin contamination, heparin therapy
        - Rarely dysfibrinogenaemia
      - Fbg antigen
      - Reptilase time
  - TCT normal
    - PT prolonged
      - Vitamin k deficiency
        - Oral anticoagulants
          - PT, apt, TCT fib abnormal
          - DIC
            - Liver failure
            - Rarely a dysfibrinogenaemia
            - Assay FV, FVII, FVIII, Fbg antigen, Reptilase time
            - Well infant
            - Ill infant
              - Maternal ITP, hereditary NAIT
              - DIC, asphyxia, Sepsis
## Appendix 6 – Other investigations in coagulopathy – normal ranges

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age</th>
<th>Full Term Ref Range</th>
<th>30 - 36 weeks Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha 2 Antiplasmin IU/DL</td>
<td>D1 - D4</td>
<td>55 - 115</td>
<td>40 - 116</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>70 - 130</td>
<td>49 - 113</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>76 - 124</td>
<td>55 - 123</td>
</tr>
<tr>
<td>APTT secs</td>
<td>D1 - D4</td>
<td>29.0 - 51.5</td>
<td>27.5 - 79.4</td>
</tr>
<tr>
<td></td>
<td>D5 - D21</td>
<td>28.0 - 55.0</td>
<td>26.9 - 74.1</td>
</tr>
<tr>
<td></td>
<td>D22 - D89</td>
<td>28.0 - 50.0</td>
<td>26.9 - 62.5</td>
</tr>
<tr>
<td>Anti Thrombin (Functional) IU/DL</td>
<td>D1 - D4</td>
<td>39 - 87</td>
<td>14 - 62</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>41 - 93</td>
<td>30 - 82</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>48 - 108</td>
<td>37 - 81</td>
</tr>
<tr>
<td>Factor 2 IU/DL</td>
<td>D1 - D4</td>
<td>26 - 70</td>
<td>20 - 77</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>33 - 93</td>
<td>29 - 85</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>34 - 102</td>
<td>36 - 95</td>
</tr>
<tr>
<td>Factor 5 IU/DL</td>
<td>D1 - D4</td>
<td>34 - 108</td>
<td>41 - 144</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>45 - 145</td>
<td>46 - 154</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>50 - 134</td>
<td>50 - 134</td>
</tr>
<tr>
<td>Factor 7 IU/DL</td>
<td>D1 - D4</td>
<td>28 - 104</td>
<td>21 - 113</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>35 - 143</td>
<td>30 - 138</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>42 - 138</td>
<td>21 - 145</td>
</tr>
<tr>
<td>Factor 8 IU/DL</td>
<td>D1 - D4</td>
<td>50 - 178</td>
<td>50 - 213</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>50 - 154</td>
<td>53 - 205</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>50 - 157</td>
<td>50 - 199</td>
</tr>
<tr>
<td>Factor 8 (Chromogenic) IU/DL</td>
<td>D1 - D4</td>
<td>50 - 178</td>
<td>50 - 213</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>50 - 154</td>
<td>53 - 205</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>50 - 157</td>
<td>50 - 199</td>
</tr>
<tr>
<td>Factor 9 IU/DL</td>
<td>D1 - D4</td>
<td>15 - 91</td>
<td>19 - 65</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>15 - 91</td>
<td>14 - 74</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>21 - 81</td>
<td>13 - 80</td>
</tr>
<tr>
<td>Factor 10 IU/DL</td>
<td>D1 - D4</td>
<td>12 - 68</td>
<td>11 - 71</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>19 - 79</td>
<td>19 - 83</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>31 - 87</td>
<td>20 - 92</td>
</tr>
<tr>
<td>Factor 11 IU/DL</td>
<td>D1 - D4</td>
<td>10 - 66</td>
<td>8 - 52</td>
</tr>
</tbody>
</table>
### Appendix 6 – Other investigations in coagulopathy – normal ranges

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age</th>
<th>Full Term Ref Range</th>
<th>30 - 36 weeks Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 12 IU/DL</td>
<td>D1- D4</td>
<td>13 - 93</td>
<td>10 - 66</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>13 - 83</td>
<td>9 - 69</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>17 - 81</td>
<td>11 - 75</td>
</tr>
<tr>
<td>Fibrinogen g/L</td>
<td>0Y - Adult</td>
<td>1.7 - 4.0</td>
<td>1.7 - 4.0</td>
</tr>
<tr>
<td>Plasminogen (Functional) IU/DL</td>
<td>D1 - D4</td>
<td>39 - 83</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet ADP (Content) nm/10^9 Plts</td>
<td>D1 - Adult</td>
<td>17 - 47</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet ATP (Content) nm/10^9 Plts</td>
<td>D1 - Adult</td>
<td>35 - 55</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet Total (Content) nm/10^9 Plts</td>
<td>D1 - Adult</td>
<td>52 - 102</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet ATP / ADP (Content) Ratio</td>
<td>D1 - Adult</td>
<td>1.2 - 2.5</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet ADP (Release) nm/10^9 Plts</td>
<td>D1 - Adult</td>
<td>15 - 27.5</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet ATP (Release) nm/10^9 Plts</td>
<td>D1 - Adult</td>
<td>7 - 15.0</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet Total (Release) nm/10^9 Plts</td>
<td>D1 - Adult</td>
<td>22 - 42.5</td>
<td>Not known</td>
</tr>
<tr>
<td>Platelet ATP / ADP (Release) Ratio</td>
<td>D1 – Adult</td>
<td>0.43 - 0.79</td>
<td>Not known</td>
</tr>
<tr>
<td>Protein C (Functional) IU/DL</td>
<td>D1 - D4</td>
<td>17-53</td>
<td>12 - 44</td>
</tr>
<tr>
<td></td>
<td>D5 - D29</td>
<td>20 - 64</td>
<td>11 - 51</td>
</tr>
<tr>
<td></td>
<td>D30 - D89</td>
<td>21 - 65</td>
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<tr>
<td>Protein S (Free) IU/DL</td>
<td>D1 - D6</td>
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<td>W1 - W8</td>
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<td>60 - 98</td>
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<td>W17 - W24</td>
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<td>D57 - D112</td>
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<td>15 - 30</td>
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<td>W1 - W8</td>
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<td>W9 - W16</td>
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<td>W17 - W24</td>
<td>64 - 105</td>
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<td>Prothrombin Time (Premature) secs</td>
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<td>8.5 - 17.0</td>
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<td>D2 - D5</td>
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### Appendix 6 – Other investigations in coagulopathy – normal ranges

<table>
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<th>30 - 36 weeks Ref Range</th>
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<td>D29 - D90</td>
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<td>vWF : RiCof IU/DL</td>
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<td>50 - 287</td>
<td>78 - 210</td>
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<td>D6 - D28</td>
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<tr>
<td></td>
<td>D29 - D90</td>
<td>50 - 206</td>
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### References

- H. William Taeusch, Roberta A. Ballard, Christine A. Gleason, Mary Ellen Avery Avery's diseases of the newborn. Elsevier Health Sciences, 2005
- Nick Dorward – Haemotology & Coagulation Lab, Moriston Hospital, 2014.
Polycythaemia (PCT)

Polycythaemia can be defined as a central venous haematocrit (Hct) >65% for both term and preterm infants.

Causes / risk factors for PCT include IUGR, maternal diabetes, maternal hypertension, maternal smoking, delayed cord clamping, cord stripping, twin-twin transfusion, maternal-fetal transfusion, Beckwith-Wiedeman syndrome, hypo- and hyperthyroidism, perinatal asphyxia and trisomies.

When dealing with an infant with PCT always consider whether the cause needs investigation +/- treatment

Symptoms:

Not present at birth, but usually become evident within first 24 to 48 hours.
They include lethargy, hypotonia, vomiting, irritability, poor response to light, tremulousness.

Complications:

Neurological:
- Seizures
- Stroke
- Developmental delay
- Reduced IQ.

Cardiopulmonary:
- Respiratory distress,
- Pleural effusions,
- Pulmonary hypertension.

Metabolic:
- Hypoglycaemia,
- Hypocalcaemia,
Others:
- Necrotizing enterocolitis,
- Renal vein thrombosis,
- Proteinuria, renal tubular damage,
- Hyperbilirubinemia,
- Thrombocytopenia

Treatment:
Always discuss with consultant before treating

Capillary Hct >65%

Confirm with venous Hct, exclude dehydration
(Check weight loss)
Treat dehydration if present

Symptomatic
PET (see below)
Maintain hydration, watch for symptoms

Asymptomatic
Hct 65 - 75%

Hct >75% and not decreasing
Consider PET
Technique for Partial Exchange Transfusion (PET)

Fluid: Normal saline
Volume: 20 ml per kg

Infuse saline by peripheral cannula at rate of 40 ml/kg/hour and withdraw 20 ml/kg of blood from the umbilical venous cannula at the same rate. Aim to complete exchange over 30 minutes. Do not allow the infant to get cold, and check blood glucose after the procedure. Stop feeds for 2-4 hours.
Guidelines for the management of neonatal thrombosis
(Adapted from UHW guidelines – section author – Sujoy Banerjee)

Neonatal thrombosis is rare and occurs in 2.4/1000 admissions to the neonatal unit. The evidence base for the management of neonatal thrombosis is minimal and is largely based on case series and extrapolated data from adult literature.

Predisposing factors: Include indwelling intravascular catheters, congenital heart disease, polycythaemia, poor deformability of neonatal red cells, shock, sepsis and dehydration.

Congenital prothrombotic disorders account for 5-20% of all thrombotic episodes and they should be considered in any neonate with a clinically significant thrombosis, spontaneous thrombotic events, unanticipated or extensive venous thrombosis, ischaemic skin lesions, purpura fulminans or family history of purpura fulminans.

VENOUS THROMBOSIS

Venous thrombosis constitute about 65-75% of all neonatal thromboses. Over 80% are central line related. Hence umbilical venous catheters should be appropriately placed (in the IVC- not in the portal veins) and used for as short a period as possible.

Clinical presentation will depend on thrombus location, but in general occurs with loss of catheter patency, swollen, painful and discoloured limb. Superior vena caval obstruction presents with swelling of the face and neck and chylothoraces. Pulmonary thromboembolism presents with respiratory compromise. Renal vein thrombosis presents as a palpable flank mass, haematuria, proteinuria, renal impairment and thrombocytopenia. Oedematous, cold, discoloured lower limbs may indicate extension of the thrombus into the IVC. Portal vein thrombosis is usually clinically silent. An USS of the portal system may be considered if there is unexplained thrombocytopenia in a sick neonate.

Management:

1. Remove the indwelling catheter.
2. Doppler ultrasound and discuss with radiology regarding contrast venogram.
3. Thrombophilia screen for non catheter related extensive thrombosis.
4. Monitor limb swelling, temperature and discolouration.
5. Monitor renal function and blood pressure if renal vein thrombosed, arrange nephrology referral.
6. Anticoagulation: Consider for any extensive deep vein thrombosis, renal vein thrombosis with IVC extension or renal failure. Start low molecular weight heparin (LMWH), enoxaparin at a dose of 1.7mg/kg BD subcutaneously (monitor anti-factor Xa levels), treatment is recommended for 3-6 months. LMWH is preferred in neonates due to reduced risk for bleeding, no need for venous access and reduced monitoring requirements. Use unfractionated heparin (UFH) if LMWH is unavailable, or in cases where there may be a need to stop the anticoagulation or reverse the effects quickly (e.g. patient requiring surgery or bleeding) and in renal failure (LMWH is excreted by kidneys). Please see the LMWH and heparin guidelines.
7. Parents should be fully informed of potential risks and benefits of anticoagulation, trained to administer enoxaparin prior to discharge and given an anticoagulation card (yellow card). Maintain a record of dose and factor Xa level in clinical notes and the parent held record.
8. Check thrombus size at regular intervals (every 2-3 months) during therapy as it guides duration of therapy.
9. Thrombolitics are rarely indicated in venous thromboembolism

ARTERIAL THROMBOSIS

Arterial thromboses account for 25-35% of all neonatal thromboses and are almost exclusively secondary to indwelling arterial catheters. UA catheters should always be appropriately placed at T6-T10 or between L3-L5. Careful monitoring of colour, temperature, capillary refill time and pulses are important for early detection.

Management

1. Remove any indwelling catheter.
2. Anticoagulation: 70% of thrombi will resolve with anticoagulation alone. Use LMWH or UFH, please see the guidelines for LMWH and UFH.
3. Thrombolysis should be considered if thrombus is limb life or organ threatening. Start alteplase (t-PA) at 0.3-0.5mg/kg/hour for 6 hrs. Give FFP
10-20ml/kg at least 30 minutes prior to starting thrombolytic therapy. Monitor fibrinogen and aim to keep above 1g/l (please see the t-PA guideline).

Contraindications for thrombolysis:

- Active bleeding.
- General surgery within the previous 10 days or neurosurgery in the previous 3 weeks.
- Infants <32 weeks (relative contraindication)

Stuck long lines: Reported between 1 and 12% in older children and adults, no neonatal data available. Venospasm is the main cause for difficulty in removal although other causes include infection, fibrin formation and endothelial thrombosis. It usually occurs in medium sized veins especially basilic and cephalic veins.

Management:

1. Firm but gentle traction and tape down securely, release and try again after 20-30 minutes, repeat 4 hourly.
2. If unsuccessful try warm compresses to entire limb and gentle massage and milking of the skin overlying the vein (Kim et al).
3. Infusion of warm 0.9% Sodium Chloride (available in the warming cabinet on labour ward or Ward 20) in a line distal to long line, it should not be warm to touch.
4. Consider radiological examination to delineate knots.
5. Surgical cut-down may be needed if unsuccessful.
6. Consider using Urokinase 5000 U/kg/hour IV or t-PA 0.1 mg/kg/hr for 12-24 hours (E Chalmers personal communication).

Congenital Prothrombotic disorders:
The International Society of Thrombosis and Haemostasis (ISTH) recommends the following screening tests to be done if concerned about the possibility of congenital thrombophilia. These should be done at 6 months of age or at presentation if presenting with purpura fulminans. These tests require 5 neonatal clotting bottles and 3 Li heparin neonatal bottles. Consider testing the parents at the same time.
1. Antithrombin, Protein C and Protein S.

2. Factor V Leiden (activated protein C resistance) mutation, prothrombin G 20210A, MTHFR T677T and/or fasting homocysteine level.

3. Lipoprotein(a), Lupus anticoagulant, anticardiolipin antibodies.

4. Sickle cell screen or hemoglobin electrophoresis.


Any abnormal results should be repeated in 3-12 months, after discontinuation of anticoagulation therapy. Consider performing further sophisticated blood tests if the initial screening results are negative and there is a strong family history of thrombosis, recurrent or life threatening thrombosis. Please see ISTH reference.

References


(Adapted from UHW guidelines 2010)
Appendix 7: Blood for neonatal exchange transfusion:

PRODUCT*: Plasma reduced RC (Hct 0.55 - 0.60) ideal

AGE of blood: Within 5 days of collection

BLOOD GROUP: ABO group of neonate, or an alternative provided that it is compatible with maternal ABO antibodies. Otherwise use designated group O Rh compatible units.

ANTIBODY SCREEN: Exclude high anti-A,B titres (group O donation) and other significant irregular blood group antibodies.

ANTI-CMV STATUS: Negative in all blood for babies below 1 year of age
If plasma reduced RC is not available:-
Whole blood: About 120 mls of plasma should be removed prior to use to provide an acceptable haematocrit

RC CONCENTRATE: Hct 0.55 - 0.75 are less satisfactory:-
require simultaneous administration of plasma expander e.g. saline or 4.5% albumin (do not use FFP as plasma expander to reduce risk of exposure to multiple donations).

SAG-M BLOOD: Unsuitable at present due to potential metabolic, haemostatic and oncotic pressure problems
**Appendix 8: Choice of ABO Group for Blood Products for Administration to Children**

<table>
<thead>
<tr>
<th>Patient’s ABO Group</th>
<th>Red Cells</th>
<th>Platelets</th>
<th>FFP*</th>
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<tbody>
<tr>
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<td>O</td>
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<tr>
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</tr>
<tr>
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</table>

* Group O fresh frozen plasma (FFP) should only be given to patients of group O. Although group AB FFP can be given to people of any ABO blood group, supplies are usually limited.

Group O components which test negatively for ‘high titre anti-A and anti-B’ are provided by WBS.

Platelet concentrates of group B or of group AB are not normally available at the WBS.
Appendix 9: Selection of non-UK sourced MB treated/removed Fresh Frozen Plasma for neonates and children born on or after 1 January 1996
(Extracted from BCSH Guidelines on FFP, 2004)

FFP Selection by ABO Group

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<thead>
<tr>
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