Trust Guideline for the Management of Neonatal Jaundice on the Neonatal Intensive Care Unit (NICU)

Document Control:

For Use In:	Norfolk and Norwich University Hospital (NNUH) NICU, Delivery Suite, Midwifery Led Birthing Unit, Postnatal Ward (Blakeney)		
Search Keywords	Jaundice, neonate, newborn, infant, phototherapy, bilirubin		
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Document Owner:	Division 3, Women and Childrens Health		
Approved By:	Clinical Guidelines Assessment Panel		
Ratified By:	Clinical Safety and Effectiveness Sub-board		
Approval Date:	07/08/2024	**Date to be reviewed by:** This document remains current after this date but will be under review	07/08/2027
Implementation Date:	N/A		
Reference Number:	JCG0013v5 - ID No: 1316		

Version History:

Version	Date	Author	Reason/Change
V4.0	05/2020	Sarah Keen Mark Dyke	References to “direct coombs test” replaced with “direct anti-globulin test”. Cross reference added to Transcutaneous Bilirubinometer: Non-Invasive Bilirubin measurements using a Transcutaneous Bilirubinometer Trustdocs Id:12092
V5.0	06/2024	Sarah Keen David Booth	Flow chart altered to include taking blood group and DAT at second bilirubin level. Removal of taking ToRCH screen for prolonged jaundice, as no longer recommended by virology. Change in national guideline. Document transferred to Joint Procedural Document Template.

Previous Titles for this Document:

Previous Title/Amalgamated Titles	Date Revised
None	N/A

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:

- Neonatal Unit Guideline Development Meeting

Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

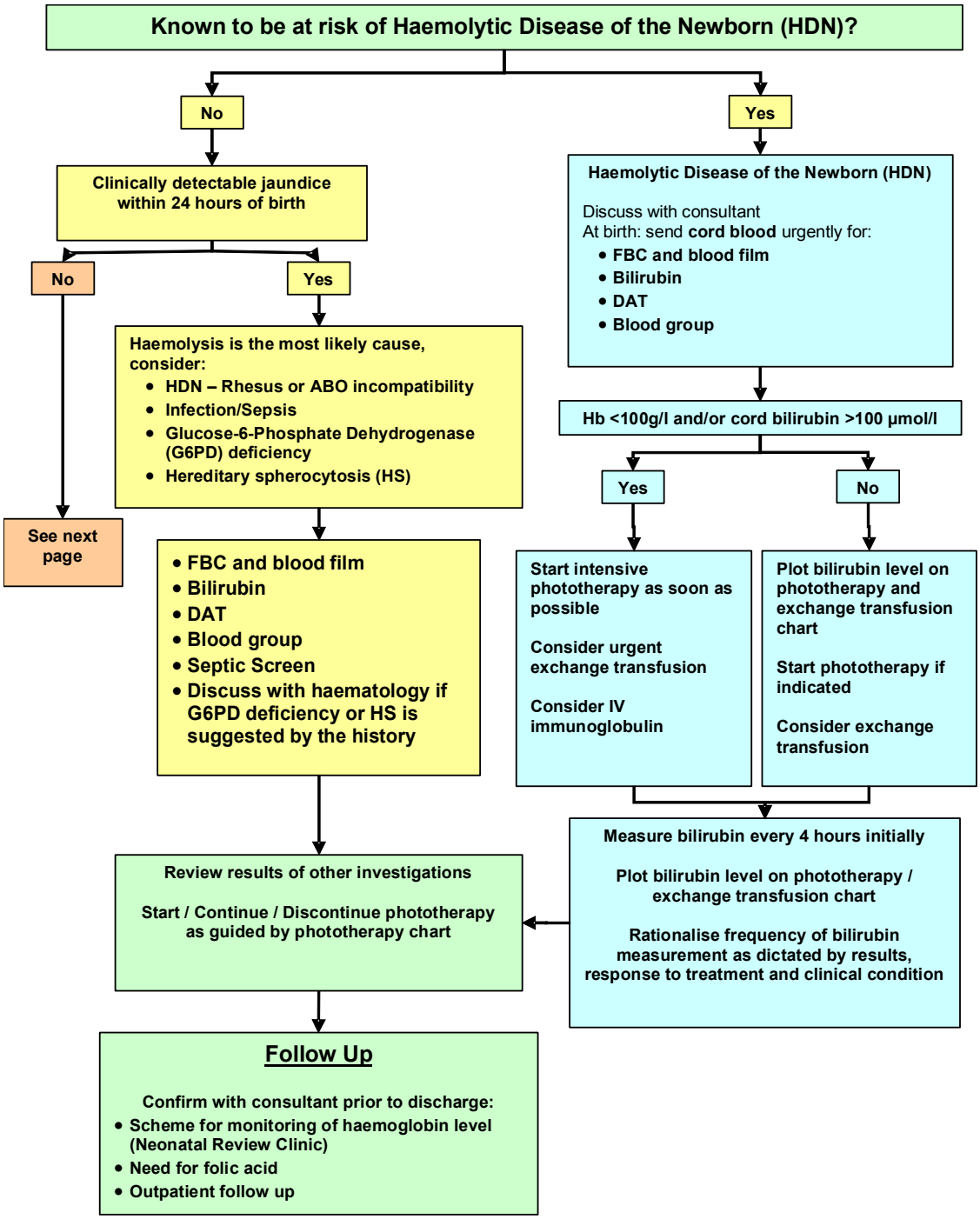
This document is a clinical guideline applicable to individual Trust; please refer to local Trust's procedural documents for further guidance, as noted in Section 4.

Trust Guideline for the Management of Neonatal Jaundice in the Neonatal Intensive Care Unit (NICU)

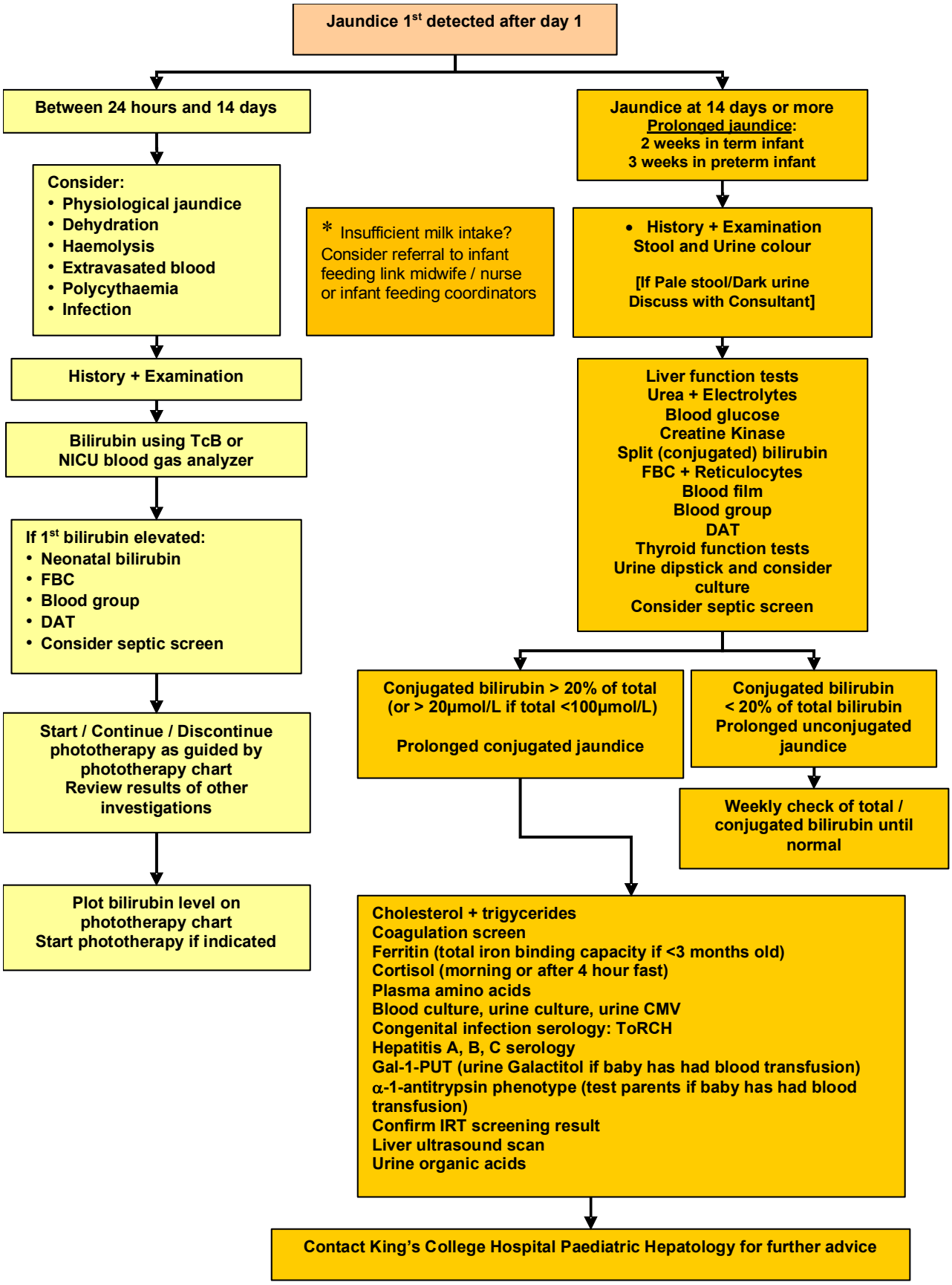
Contents Page

Trust Guideline for the Management of Neonatal Jaundice in the Neonatal Intensive Care Unit (NICU)

Quick reference – Known to be at risk of Haemolytic Disease of the Newborn (HDN)?



Trust Guideline for the Management of Neonatal Jaundice in the Neonatal Intensive Care Unit (NICU)



Phototherapy – Quick reference guide

Introduction

Rationale

More than 50% of all term newborns become jaundiced in the first week of life[2], with total serum bilirubin peaking at between 3-5 days in the majority of these. Preterm infants have a higher incidence of clinically detectable jaundice and the peak tends to be later (5-7 days).

Neonatal jaundice is thought to occur due to the simultaneous occurrence of:

- elevated bilirubin production due to the shortened lifespan of fetal erythrocytes and a relatively high haematocrit at birth and
- reduced hepatic excretory capacity due to low concentrations of ligandin (bilirubin binding protein) and lower activity of glucuronyl transferase (which conjugates bilirubin to glucuronic acid, making it water soluble)

Jaundice tends to become visible first on the face and neck, progressing to the trunk and extremities as levels rise (cephalocaudal progression[3]). It tends to resolve in the opposite order. In the vast majority of infants this normal, or "physiological", jaundice causes no harm and clears spontaneously, usually reaching normal levels by about 10 days of age. It may persist for longer in babies who are exclusively breast-fed ("breast-milk jaundice"). Breastmilk jaundice is a rarely a cause for concern and not a reason to stop breastfeeding.

However, in certain situations (e.g. haemolytic disease, prematurity, sepsis) the serum bilirubin may rise to dangerously high levels, causing bilirubin encephalopathy which can, in extreme cases, progress to kernicterus.[4]

Broad recommendations

Neonatal jaundice will be considered as follows:

- Jaundice within 24 hours of birth
- Jaundice occurring between 24 hours and 14 days
- Prolonged jaundice (including prolonged conjugated jaundice)

All parents should be offered a parent information leaflet on neonatal jaundice Jaundice in Newborn Babies Trustdocs Id: 9891

Jaundice within 24 hours of birth

Haemolysis is the most likely cause.

Check**:**

- Serum bilirubin
- Full blood count (FBC)
- Blood film
- Blood group
- Direct Antiglobulin test (DAT)

Review the mother's blood group**:** Consider Haemolytic disease of the newborn, especially Rhesus or ABO incompatibility.

Sepsis is a possible cause of early jaundice and it is reasonable to consider a septic screen in all babies presenting with jaundice within 24 hours of birth.

- C-reactive protein (CRP)
- Blood culture
- Consider lumbar puncture (if presents as unwell)
- Consider chest x-ray (with respiratory symptoms)
- Urine dipstick and culture (in babies only with clinical suspicion of urinary tract infection)

Specialist Testing:

1. If the parents' ethnic group (Far East/Middle East/African) is suggestive, consider Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency.
2. Hereditary spherocytosis can also cause an early onset or rapidly progressive hyperbilirubinaemia.

Haemolytic Disease of the Newborn (HDN)

Discuss with consultant.

HDN is usually caused by Rhesus anti-D isoimmunisation of the mother, with trans-placental transfer of IgG antibodies giving rise to fetal haemolysis and a DAT positive haemolytic anaemia.

ABO incompatibility results from isoimmunisation of the fetus with IgG anti-A (most commonly) passing trans-placentally from a group O mother to a group A fetus. This condition is often DAT negative and results in moderate haemolysis, but occasionally it can be as severe as Rhesus isoimmunisation.

When an affected baby is born, cord blood should be taken and sent urgently for **FBC, DAT, blood group** and a **bilirubin.** If cord blood for this purpose has not been obtained, blood from the baby should be sent instead, as soon as possible after birth.

If the Hb is very low (<100g/L) an urgent exchange transfusion should be considered[4]. A very elevated cord bilirubin (>100 micromol/L) is also suggestive of severe haemolysis and increases the likelihood of the need for an exchange transfusion. Intensive (double/triple) phototherapy should be started as soon as possible. Measure bilirubin every 4 hours and extrapolate the line on the phototherapy chart to try to predict when the threshold for exchange transfusion could be reached (refer to NICE Guidance CG98 www.nice.org.uk/guidance/CG98) which contains charts for: Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Ensure adequate fluid intake either by mouth or intravenously depending on clinical status.

In preterm babies

As an approximate guide, bilirubin (in micromol/L) should never be allowed to exceed the gestational age x10, but in haemolytic disease it would be a sensible precaution to deduct 50 micromol/L from these figures.

Intravenous immunoglobulin (IVIg)

Evidence has shown that the administration of IVIg has some therapeutic effect on isoimmune haemolytical disease, in regard to the amount of time phototherapy treatment is required, the need for exchange transfusion and the length of hospitalisation[5]. In the presence of a strongly positive DAT, but where the criteria for exchange transfusion are not immediately met on the cord blood analysis, there are two circumstances where consideration should be given to the use of intravenous immunoglobulin:

- Where the cord results for SBR are very close to threshold for ET and therefore the likelihood of proceeding to ET is considered to be relatively high
- Where the SBR continues to rise at a rate ≥8.5 micromol/L per hour despite adequate phototherapy and fluid administration over a period of 4-6 hours[6].

***IVIg dose**: 500mg/kg intravenous infusion over 4 hours*

Very occasionally, a second dose may be required if, after an initial response (ie a substantial reduction in the rate of rise of SBR), the rate of rise once again exceeds 8.5 micromol/L per hour.

NB: Approval for the use of IVIg must be obtained from the chair of the Drugs, Therapeutics & Medicines Management Committee (DTMM). For request forms click here.

Exchange Transfusion

Exchange transfusion should be strongly considered in an infant with known Rhesus- or ABO-incompatibility who fulfils any of the following criteria:

- Cord Hb <10og/L
- Cord bilirubin >100 micromol/L
- Serum bilirubin rising at rate >10micromol/L per hour in the first 24 hours, despite phototherapy
- Serum bilirubin exceeding threshold for exchange transfusion on the appropriate chart (see chart for appropriate gestation in NICE guidance as above)

For details, see Trust Guideline Performing Exchange Transfusion in Newborn Trustdocs 1304.

Follow up

Babies with significant HDN, whether or not they have received an exchange transfusion, will need to have their level of haemoglobin monitored for several weeks due to the risk of ongoing low-grade haemolysis. Folic acid should be prescribed (500 micrograms/kg once daily)[7]. Discuss with consultant prior to discharge and make a plan for returning to the Neonatal Review Clinic (NRC) with tests required documented clearly.

Well babies, with a positive Antiglobulin test, but who **do not** show a significant rise in bilirubin (i.e. do not require phototherapy) over the first 48-72 hours, may go home but should have a FBC checked at 2 and 6 weeks to exclude any ongoing haemolysis. Parents should be advised to seek medical advice in the event of signs of significant jaundice or heart failure (e.g. poor feeding, pallor, tachypnoea, sweating). Open access to the Children's Assessment Unit (CAU) is recommended.

Maternal Anti-D Therapy

Administration of anti-D immunoglobulin to the mother during pregnancy can result in DAT being weakly positive in the newborn. Such babies can be treated as normal; parents should be advised to seek midwifery/GP review if significant jaundice develops.

Jaundice occurring between 24 hours and 14 days

This group forms the majority of jaundiced babies seen on NICU. Most will have physiological jaundice requiring no intervention, but in some the bilirubin will have risen to levels which necessitate treatment with phototherapy.

Thorough history and clinical examination are of key importance.

Consider:

- infection
- dehydration or insufficient milk supply
- haemolysis
- breakdown of extravasated blood (e.g. bruising, cephalhaematoma)
- polycythaemia

Special consideration should be given to the difficulty in detecting visible jaundice in babies with darker skin tones, which may lead to delayed diagnosis and treatment.[8]

Following an extensive literature review and update of national guidance in 2023, it is recommended that when examining a baby for jaundice, we should;

- Examine the baby naked, in bright, preferable natural light

- Examine the sclera and gums carefully
- Press lightly on the skin to check for hyperbilirubinemia in 'blanched' skin
- Be aware that jaundice may be less visible in babies with brown or black skin[8,9].

An initial clinical impression of significant jaundice should be corroborated by measuring bilirubin – this is most easily achieved using a transcutaneous bilirubinometer if available (see Transcutaneous Bilirubinometer: Non-Invasive Bilirubin measurements using a Transcutaneous Bilirubinometer (Trust Guideline) Trustdocs Id:12092). There is no strong evidence that TCB measurement is unreliable in babies with darker skin tones, however serum bilirubin measurement remains the gold standard approach.

NICE[9] guidance recommends that this measurement should take place within 6 hours of the initial clinical suspicion of jaundice – in the hospital setting, the measurement should take place as soon as possible and 6 hours should be considered as an upper limit of an acceptable time to obtain a bilirubin measurement.

Necessity for treatment can be determined by plotting the bilirubin level against time on the appropriate phototherapy chart: https://www.nice.org.uk/guidance/qs57

Investigations

- in otherwise well babies who require phototherapy, subsequent laboratory investigation can be limited to **bilirubin**, **FBC, Group and DAT**.
- other investigations, e.g. septic screen (or metabolic tests) should be considered as dictated by the clinical condition of the baby.

Phototherapy

(See quick reference guide)

If the bilirubin level, when plotted on the appropriate phototherapy chart, exceeds the treatment threshold start phototherapy, **using an overhead unit**. Do not use a *biliblanket* as 1st line treatment.

Repeat the bilirubin level after 6 hours of treatment (including group, DAT and FBC if necessary).

Response to treatment should be monitored by measuring the serum bilirubin level every 12 hours during treatment.

Continue phototherapy until the measured bilirubin level is 50µmol/litre below the treatment threshold line.

On cessation of phototherapy, repeat a bilirubin level after 12 hours, to check for rebound hyperbilirubinaemia.

If the bilirubin level remains at least 50µmol/L below the treatment threshold, routine monitoring of bilirubin can be discontinued.

If the bilirubin level has risen to within 50umol/l of the treatment threshold, the level should be repeated after a further 6 -12 hours (depending on the rate of rise).

Special circumstances

Phototherapy with a single overhead unit is the initial treatment of choice unless the serum bilirubin level:

- is rising rapidly (more than 8.5µmol/L/hour) or
- is at a level within 50µmol/L below the threshold for exchange transfusion or
- fails to respond to single phototherapy when assessed at 6 hours of treatment.

If multiple phototherapy units are required, step down to single phototherapy when the level falls to 50µmol/L below the exchange transfusion threshold.

Prolonged jaundice

Definition – clinically detectable jaundice at 2 weeks of age for an infant born at term or at 3 weeks in preterm infants[10]. Most of these babies will be seen in the "Yellow Alert" Clinic, which has its own guideline (Trust Protocol for the Management of Jaundiced Babies referred from Primary Care - CAU1 Version2) - Trustdocs Id: 1528 to view.

This part of the guideline therefore refers to those babies already resident in NICU who go on to develop prolonged jaundice.

The most likely cause remains "physiological" or "breast-milk" jaundice (particularly in exclusively breast-fed infants) but this is a diagnosis of exclusion and more serious causes should be ruled out.

- thorough clinical examination is very important.
- has the baby regained his/her birth weight?
- is he/she growing normally?
- are there concerns about dehydration or infection?
- do not routinely advise additional fluids or feeds based only on the presence of jaundice – only advise if there is evidence of dehydration

Initial investigations should include:

- Liver function tests (LFT) including split (conjugated/unconjugated) bilirubin
- FBC, reticulocytes, blood film,
- Blood group and DAT (if not already done)
- G6PD (if not already done)

- Creatine kinase
- Urea + Electrolytes
- Blood glucose
- Thyroid function tests
- Urine dipstick and culture

Other tests (e.g. septic screen) as dictated by the clinical condition of the baby.

Stool and urine colour

Acholuric (pale, putty-coloured) stools are strongly suggestive of cholestasis in infancy. Babies' urine is normally colourless. Dark urine (which stains the nappy) can be pathological and this again reflects cholestasis.

Try to see the stools yourself.

The Children's Liver Disease Foundation[11] produce a colour chart for standardising stool colour assessment and these charts are available on NICU or via their website (see below for link)

Babies with pale stools and dark urine should be discussed with the consultant regardless of test results.

Conjugated/direct bilirubin levels of >20% total bilirubin (or >20 micromol/L if total bilirubin <100 micromol/L) suggest cholestasis and should prompt further investigation and discussion with the consultant. Jaundiced babies with an elevated conjugated fraction of <20% of the total should ideally have a split bilirubin checked weekly until it normalises.[11]

Most babies with prolonged jaundice have already been discharged from hospital and are in the community. You may, therefore, be telephoned by a midwife or GP concerning a baby with prolonged jaundice. If the baby is well, feeding successfully and gaining weight, a referral to the "Yellow Alert Clinic" should be made for further assessment. Unwell babies should be seen and assessed straight away in the Children's Assessment Unit (CAU).

Prolonged Conjugated Jaundice

Discuss with consultant. In preterm infants this is frequently due to lack of enteral feeding in babies primarily nourished by parenteral nutrition. However, this is a diagnosis of exclusion and should still prompt investigation if the conjugated fraction is >20% total.

Consider the following **additional** investigations in an infant with prolonged conjugated jaundice:

- Blood culture
- Cholesterol and trigycerides

- Coagulation screen
- Ferritin (total iron binding capacity if <3 months old)
- Cortisol (morning or after 4 hour fast)
- Plasma amino acids
- Congenital infection's (PCR), based on specific signs and/or presentation
- Hepatitis A, B, C serology
- Gal-1-PUT (if baby has had blood transfusion, request a Urine Galactitol)
- α-1-antitrypsin phenotype (test parents if baby has had blood transfusion)
- Confirm IRT screening result
- Urine organic acids, urine culture, urine CMV
- Liver ultrasound scan

In general, babies in whom further investigation is being considered should be discussed with the paediatric hepatology registrar at King's College Hospital in London. They will be able to offer up to date advice concerning management and which additional tests are indicated.

Note, the ToRCH screen is no longer recommended in this Trust as a collective test. Please discuss with the duty Virologist as testing is specifically targeted to individual organisms according to the clinical presentation of the infant[12]

Objective

Bilirubin encephalopathy and kernicterus are now rare, but they do still occur[1]. The purpose of this guideline is to identify those babies at risk of encephalopathy, enabling intervention in time to prevent its occurrence.

Elevated bilirubin levels, particularly within the first 24 hours or outside the immediate neonatal period, can also sometimes signify serious underlying disease and it is these babies, also, that we would wish to identify.

The objective of this clinical guideline is to;

- To clearly set out the pathway for the assessment of babies that are at risk of, or are visibly jaundiced.
- To outline the testing and treatment pathway for babies that are jaundiced.
- To ensure that additional testing is streamlined to those at risk.
- Ensure timely assessment, diagnosis and treatment of babies with jaundice.
- Link information for parents.
- Give easy access to nationally accepted treatment graphs as per birth gestation.

Scope

This document intends to safeguard babies within the delivery suite, midwifery led birthing unit (MLBU), postnatal ward (Blakeney), neonatal intensive care unit (NICU) and babies < 10 days of age brought into the children's assessment unit (CAU) from home with jaundice.

Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
NICU	Neonatal Intensive Care Unit
DAT	Direct Antigen Test
SBR	Serum Bilirubin
FBC	Full Blood Count
NICE	National Institute of Care and Excellence
G6PD	Glucose-6 Phosphate Dehydrogenase
HS	Hereditary Spherocytosis
Hb	Haemoglobin

Responsibilities

- David Booth, Consultant Neonatologist - author
- Sarah Keen, SANNP - author
- Florence Walston, Neonatal Consultant – NICU Lead

Processes to be followed:

- Following identification or suspicion of jaundice, assessment with medical review to be carried out within 6 hours. Depending on timing of suspicion and clinical condition of baby, identification of jaundice may be with transcutaneous monitor or measure of serum bilirubin level.
- If baby has visible early onset of jaundice (<24 hours), the assessing medical staff must consider reason for pathological jaundice, including maternal blood group and/or antibodies and the baby's risk of infection.
- Diagnosis testing to be carried out based on findings above and actioned by the medical team.
- If the baby is jaundiced and requires phototherapy, the neonatal nurse (for babies on the NICU), assessment room nurse (babies on the postnatal ward) or transitional care nurse (babies admitted to transitional care) to commence phototherapy promptly and liaise with medical team on next steps of testing and treatment.
- Blood levels of serum bilirubin to be written and plotted on the NICE phototherapy charts (gestation dependent) only.

Document plan of length of treatment, repeat blood tests and any other diagnostic or treatment plans.

Related Documents

Prolonged jaundice: Trustdocs Id: 1528

TCB Guideline: Trustdocs Id:12092

Gestational jaundice charts: https://www.nice.org.uk/guidance/qs57

PIL: Jaundice-in-Newborn-Baby-2020.pdf (childliverdisease.org)

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11. Children's Liver Disease Foundation, Birmingham – Early Identification of liver disease in infants (2005) Birmingham, UK
12. Coe P. (2017) Microbiology Department User Manual (Norfolk and Norwich University Foundation Trust) Eastern Pathology Alliance*. Document Ref EMC-QUP-011.*

Audit of the process

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
All babies treated for jaundice with phototherapy have neonatal blood group and DAT taken	Local audit of 20 babies per year	Sarah Keen	NICU Governance	Annually

Will be discussed at the Neonatal Governance meeting, presented at the monthly guideline meeting and disseminated via email and safety huddle.

Results will be sent to NNUH clinical governance committee who will ensure that the actions and recommendations are suitable and sufficient. Documentation of phototherapy use is within patient notes and documented on the Neonatal Badger system.

Appendices

There are no appendices for this document.

Trust Guideline for the Management of Neonatal Jaundice in the Neonatal Intensive Care Unit (NICU)

Equality Impact Assessment (EIA)

Type of function or policy	Existing

Division	3	**Department**	NICU
Name of person completing form	Sarah Keen	**Date**	20/06/2024

Equality Area	**Potential Negative Impact**	**Impact Positive Impact**	**Which groups are affected**	**Full Impact Assessment Required YES/NO**
Race	None	None		
Pregnancy & Maternity	None		None	None
Disability	None	None	None	None
Religion and beliefs	None	None	None	None
Sex	None	None	None	None
Gender reassignment	None	None	None	None
Sexual Orientation	None	None	None	None
Age	None	None	None	None
Marriage & Civil Partnership	None	None	None	None
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?		N/A		

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.