Management of Conjugated Hyperbilirubinaemia in Newborn Intensive Care Unit

Procedure Responsibilities and Authorisation

Department Responsible for Procedure	Newborn Intensive Care Unit (NICU)
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Document Facilitator Title	Head of Department – NICU
Document Owner Name	Jutta van den Boom
Document Owner Title	Head of Department – NICU
Target Audience	NNPs, CNSs, Registrars, SMOs and Nurses
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Procedure Review History

Version	Updated by	Date Updated	Summary of Changes
04	L Carpenter	Mar 2020	Heading, fat soluble vitamins
05	L Carpenter	Dec 2020	Update Vitamin A dose
5.1	Jutta van den Boom	Nov 2021	Liver sparing criteria
5.2	N Luo	Jan 2023	Addition of stool colour table Length of vitamin treatment
5.3	Jutta van den Boom	August 2023	Insertion of approved form for investigations
V6	Jutta van den Boom	July 2024	Insertion of blood test tubes and volume for Vitamin and Mineral levels Correction of infusion rate for liver sparing Glucose 10%

Management of Conjugated Hyperbilirubinaemia in Newborn Intensive Care Unit

1 Overview

1.1 Purpose

To provide a clear investigative and treatment plan for infants with Conjugated Hyperbilirubinaemia.

1.2 Staff group

Health New Zealand staff working in Waikato hospital NICU e.g. medical staff.

1.3 Patient / client group

Neonates and Infants in NICU.

1.4 Definitions

CNS	Clinical Nurse Specialist
Conjugated Hyperbilirubinaemia	A direct (or conjugated) bilirubin greater than 20 micromol/L or more than 10% of the total bilirubin if the bilirubin is less than 200 micromol/L.
INR / PT	International Normalised Ratio / Prothrombin Time – coagulation measures
IVN	Intravenous nutrition
Medical Staff	This includes Neonatal Nurse Practitioner, Clinical Nurse Specialist, Registrar and SMOs.
NNP	Neonatal Nurse Practitioner
Prolonged jaundice	Jaundice persisting for more than 14 days for term infants and for more than 21 days for preterm infants.
SMO	Senior Medical Officer

2 Clinical Management

2.1 Abnormal Jaundice

- New onset of jaundice after the first week of age.
- Persistence of jaundice beyond 14 days of age in infants with a gestational age of 37 weeks or more, or beyond 21 days in infants with a gestational age of less than 37 weeks.
- Jaundice with pale stools or dark urine.

2.2 Stool Chart

Stool colour is a useful screen for detecting biliary obstruction (primarily, biliary atresia). Stools in biliary obstruction are persistently pale. Urine colour may be dark or orange. Stools that are pale or acholic require investigation. Record colour of the stool in the infant's observation chart.

Refer to Stool Chart in Appendix B
http://www.perinatalservicesbc.ca/Documents/Screening/BiliaryAtresia/StoolColourCard_English.pdf

2.3 Investigations

For investigations refer to
Appendix A: Waikato DHB clinical form - Investigation of Conjugated Hyperbilirubinaemia.

Test	Sample	Tube
Vitamin A and E	1x 0.5ml	red top tube
Vitamin D	1x 0.2ml	red top tube
Vitamin K (light protected)	2x 0.5ml	red top tube
Zinc	1x 0.5ml	pink top
Selenium	1x 1ml	dark green top

2.4 Treatment

All infants undergoing investigation of conjugated hyperbilirubinaemia should commence fat-soluble vitamin supplementation as soon as possible and supplementation should be administered **enterally** until jaundice is resolved, provided there is prior documentation of normal levels on supplementation. As long as the INR/PT is normal, stop Vitamin K supplements once jaundice resolves.

If levels were not normal, document levels at that point, continue supplementation for about 4 weeks after resolution of jaundice, then stop and re-check levels 6 weeks after stopping supplements.

Usual doses are:

2.4.1 Vitamin A

Preparation: Vitamin A drops (Optimus) (2 drops = 666.7mcg = 0.06mL = 2220.1 IU

Dose: 10 drops daily (= 0.3 mL = 11,100 IU)

Monitoring: Baseline, then three monthly vitamin A levels.

Funding: For Vitamin A funding in community, this form must be completed

https://pharmac.govt.nz/assets/form-alphatocopherylacetate-VitaminE-and-Retinol-vitaminA.pdf

2.4.2 Vitamin D

Preparation: Cholecalciferol oral liquid (Puria®) (188mcg = 1 mL = 7500IU or 400 IU per drop)

Dose: 0.5 mL daily (= 94mcg = 3750 IU)

Monitoring: Baseline, three-monthly levels, adjust the dose as needed.

2.4.3 Vitamin E

Preparation: alpha tocoferil acetate (Micel- E®) (115 mg = 1mL = 156IU)

Dose: 0.5 mL daily (= 57.5 mg = 78 IU)

Monitoring: Baseline level, three monthly levels, adjust the dose as needed.

Funding: For Vitamin E funding in community, this form must be completed https://pharmac.govt.nz/assets/form-alphatocopherylacetate-VitaminE-and-Retinol-vitaminA.pdf

2.4.4 Vitamin K (pytomenadione)

Preparation: Phytomenadione 2mg or 10 mg ampoules (Konakion®)

Dose: 2 mg daily orally or IV

Monitoring: According to INR (dose range 2mg to 10mg daily)

2.4.5 Ursodeoxycholic Acid:

The gastroenterology service at Starship hospital may consider commencing Ursodeoxycholic acid (URSO) at a dose of 20-30 mg/kg/day in 2 divided doses. URSO is a naturally-occurring bile acid that stimulates bile flow.

2.4.6 Liver sparing parenteral nutrition

Indications to commence liver sparing regime include:

- Babies < 34 weeks who have been on PN for > 30 days (this is criterion for intestinal failure)
- Babies > 34 weeks who have been on PN for > 20 days (same)
- Babies > 34 weeks who are very likely to require it >20 days (e.g. major intestinal loss, complex gastroschisis).
- Babies on PN who have a rise in conjugated bilirubin, > 30% of total.

Commence liver sparing regime with total daily fluid volume to be infused over 20h, and the remaining 4h infuse Glucose 10% at a rate of total 10ml/kg/day (over 4h).

2.5 Potential complications

Incorrect dosing of vitamins.

2.6 Tools

Refer Appendix A – Health NZ Waikato clinical form - Investigation of Conjugated Hyperbilirubinaemia
Refer Appendix B – Stool colour chart as a standardised method for colours

3 Evidence base

3.1 Summary of Evidence, Review and Recommendations

Conjugated Hyperbilirubinaemia is a relatively common occurrence in neonates admitted to NICU. Generally it is seen in extremely immature infants who are recovering from illnesses, and who have had prolonged intravenous nutrition.

3.2 Associated Health NZ Waikato documents

- Vitamin K (phytomenadione) for neonates in NICU drug guideline (Ref. 2980)

3.3 Bibliography

- Chin, S & Mouat S. Jaundice – investigation of prolonged. February 2020. https://www.starship.org.nz/guidelines/jaundice-investigation-of-prolonged
- Mckiernan P. Neonatal cholestasis. Seminars in Neonatology. 2002 7 (2): 153 - 165
- Starship Pharmacy and Infectious diseases team. Newborn Services Clinical Practice Committee. Conjugated Hyperbilirubinaemia in the Neonate. March 2020. https://www.starship.org.nz/guidelines/conjugated-hyperbilirubinaemia-in-the-neonate/
- Stool Chart – Retrieved 31/03/20. https://www.childliverdisease.org/wp-content/uploads/2018/01/Yellow-Alert-Stool-Chart-Bookmark.pdf
- Vitamin A – Retrieved from 31/03/20. https://pharmac.govt.nz/assets/form-alphatocopherylacetate-VitaminE-and-Retinol-vitaminA.pdf
- Vitamin E - Retrieved from 31/03/20. https://pharmac.govt.nz/assets/form-alphatocopherylacetate-VitaminE-and-Retinol-vitaminA.pdf
- Perinatal services BC Infant Stool Colour Card http://www.perinatalservicesbc.ca/Documents/Screening/BiliaryAtresia/StoolColourCard_English.pdf

Appendix A – Investigation of Conjugated Hyperbilirubinaemia

Note: this is a sample form only. Forms should be ordered via Atlas using the code W1129HWF.

W1129HWF

Health New Zealand
Te Whatu Ora

Waikato Child and Youth Health

Newborn Intensive Care Unit

Patient Label
Name
NHI DOB dd/mm/yy
Address
or patient details

Conjugated hyperbilirubinaemia investigation

First line investigations

Test	Date taken (dd/mm/yy)	Result
Complete blood count and film		
Total and conjugated bilirubin		
Liver function tests - specify:		
AST		
ALT		
GGT		
ALP		
Blood gas		
Albumin Often low in preterm infants (If assessing synthetic function, consider a coagulation screen)		
INR and/or full coagulation screen		
Blood group and Coombs		
Liver ultrasound scan		
Ferritin		
Thyroid function tests		
a1 Antitrypsin phenotype		
Urine CMV		
Maternal / congenital infection (can be obtained from the obstetric record as necessary)		
Maternal toxoplasma serology		
Maternal Syphilis status		
Maternal Rubella status		
Maternal Hepatitis B status		
Urine sample		
Bacterial culture		
Reducing substances		

SAMPLE

Second line investigations

Test	Date taken (dd/mm/yy)	Result
Urine metabolic screen		
Serum amino acids		
Plasma ammonia		
Plasma lactate and pyruvate		
Herpes simplex PCR (if clinically suspected)		

To be filed in Clinical Record 1 of 2 07/24TM

Health New Zealand Te Whatu Ora | Waikids Waikato Child and Youth Health

Newborn Intensive Care Unit

Patient Label
Name
NHI or patient details DOB dd/mm/yy
Address

Conjugated hyperbilirubinaemia investigation

Other investigations

These should only be ordered after discussion with a specialist from the Paediatric Gastroenterology service and include:

Test	Date taken (dd/mm/yy)	Result
Other acquired and congenital infections:		
Hepatitis A Virus IgM		
Adenovirus serology		
Epstein Barr Virus serology		
Stool Enterovirus (ECHO, coxsackie)		
Parvovirus PCR		
HHV6 PCR		
HCV (very uncommon cause in the initial perinatal period)		
HIV		
Triglycerides and Cholesterol		
Carnitine		
Urine bile acids (bile acid synthetic defects)		
Very long chain fatty acids (peroxisomal disorders)		
White Blood Cell enzymes or Bone Marrow aspirate (storage disorders)		
Karyotype		
Liver biopsy		
Transferrin isoelectric focusing (congenital disorders of glycosylation)		

SAMPLE

Mother (obtain maternal consent)

Test	Date taken (dd/mm/yy)	Result
Antinuclear antibody		
HIV serology		

Note: Wilson's disease has not been described in children <2 years.

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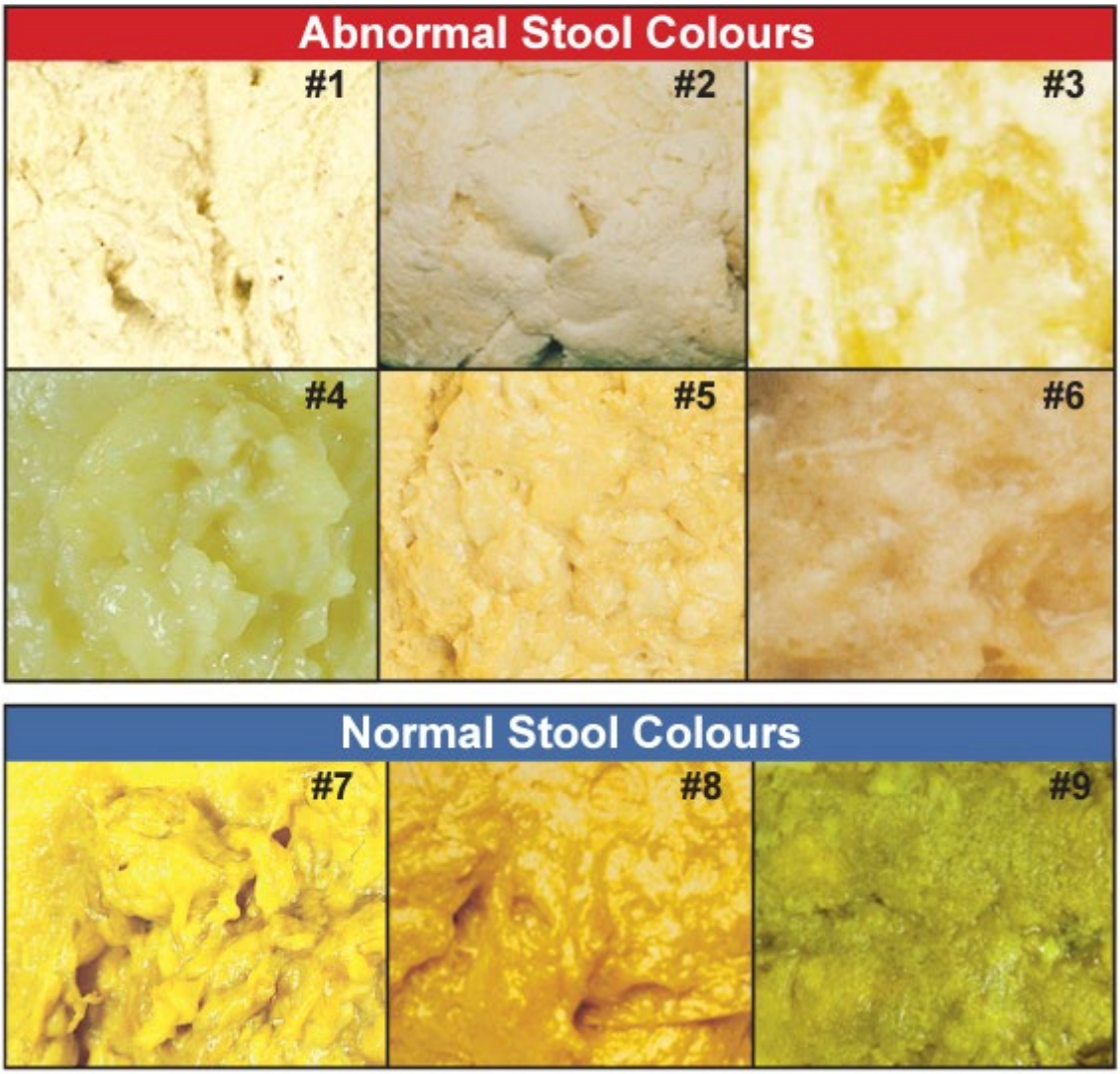
Appendix B – Stool colour chart

If concerned about the colour of the infant's stools, please print this page in colour and record the colour and colour number in the infant's observation chart.

Perinatal Services BC
Provincial Health Services Authority

BC INFANT STOOL COLOUR CARD©
SCREENING PROGRAM FOR BILIARY ATRESIA



http://www.perinatalservicesbc.ca/Documents/Screening/BiliaryAtresia/StoolColourCard_English.pdf