

# Investigation of Neonatal Conjugated Hyperbilirubinaemia

## *Introduction*

This aid to current investigations of conjugated hyperbilirubinaemia is aimed at General Paediatricians, Neonatologists and Paediatric Gastroenterologists who would typically perform the first line investigations of jaundiced babies before/during discussion with a specialist unit. **It is vital that sick infants and those with pale stools are discussed early with a liver unit** even while awaiting the results of first line investigations. In some cases direct referral to a supra regional liver unit is appropriate to exclude the diagnosis of biliary atresia as quickly as possible. Some Paediatric Gastroenterologists will also perform some of the second line investigations depending on their local radiological and histopathological expertise.

## *Guidelines*

A split bilirubin (total and conjugated) should be checked on any baby who remains jaundiced after 2 weeks of life (3 weeks for preterm infants). If the conjugated fraction is  $\geq 20 \mu\text{mol/L}$  **and**  $> 20\%$  of total bilirubin then investigations for possible liver disease should be instigated. Liver disease in the newborn can present as:

- An ill infant with liver failure (deranged clotting unresponsive to intravenous vitamin K)
- Neonatal hepatitis syndrome
- Biliary obstruction (pale stools).

Early discussion with a supra regional liver unit is necessary for infants presenting with neonatal liver failure or possible biliary obstruction. Do not delay discussion while waiting for the results of all first line investigations.

It is particularly important to diagnose **treatable causes** of liver disease

- sepsis, galactosaemia, tyrosinaemia, endocrine disorders
- surgical causes - biliary atresia, choledochal cyst

It is also important to prevent **serious complications** of cholestasis

- intracranial bleeding from malabsorption of vitamin K
- hypoglycaemia

A table is provided for the results of these investigations. This table can be appended to any transfer/referral letter.

## **Contact Details for Supra regional Liver Units**

The Liver Unit  
**Birmingham Children's Hospital**  
[Liver.Direct@bch.nhs.uk](mailto:Liver.Direct@bch.nhs.uk)  
Phone 0121 333 9999 Bleep 55200  
Fax 0121 3338251

Children's Liver & GI Unit  
**St James's University Hospital, Leeds**  
Phone 0113 2065711  
ask for the paediatric liver SpR  
Fax 0113 2066691

Paediatric Liver Service  
**King's College Hospital, London**  
Phone 020 3299 9000  
Fax 020 3299 3564

Bleep 426 between 9 am and 5 pm  
Bleep 235 between 5 pm and 9 am

## **First Stage Investigations**

These refer to the well child with prolonged conjugated jaundice.

### **Blood sugar &/or BM's pre feed in the first 24 hours of admission**

Full blood count & reticulocyte count

Group and Coomb's

INR, prothrombin time (if prolonged give 300 microg/kg of IV vit K and repeat 12 hours later. If still prolonged contact a Liver unit)

APTT, Fibrinogen

Na, K, Urea, Creatinine, Bicarbonate

Ca, Phosphate

Total & conjugated bilirubin

ALT/AST, Alk Phos, Gamma GT, Albumin

Cholesterol, triglycerides

Infections Blood cultures

Urine culture and CMV

Serology (IgM to Toxoplasma, rubella, CMV, Herpes)

Hepatitis A, B, and C serology

Metabolic Immunoreactive trypsin (up to 8 weeks) or sweat test

Galactose-1-phosphate uridyl transferase

$\alpha_1$  antitrypsin level and phenotype

Plasma and urine aminoacids

Urine organic acids (succinyl acetone)

Ward test urine for protein

Endocrine Thyroid function tests

Cortisol (preferably after 4 hour fast)

– if low – short synacthen test

Ultrasound scan of Abdomen after 4 hour fast, to see if gall bladder present, and if has choledochal cyst

Consultant to see stool colour (save specimen)

## **Second Stage Investigations**

*To be undertaken according to indications from history, examination and laboratory findings and /or after discussion with a specialist consultant.*

Hepatobiliary scintigraphy - pretreat with phenobarbitone 5 mg/kg nocte for at least 3 days, and continue to scan until 24 hours post isotope, if there has been no excretion before then.

Liver biopsy

Syphilis serology

Viral PCR e.g. herpes, CMV

Eye examination for embryotoxon, chorioretinitis, septooptic dysplasia

X ray spine for butterfly vertebrae

Cardiology opinion if murmur heard

Tests for rare disorders (not routine):

Lactate, ammonia, pyruvate

Very long chain fatty acids

Urine and serum for inborn errors of bile salt metabolism

Acyl carnitines

Alpha fetoprotein

Isoelectric focusing of transferrin

White cell enzymes either glycogen or lysosomal storage

CSF for protein and lactate

Tubular reabsorption of phosphate

Ferritin and transferrin saturation

MRI head

Muscle biopsy for mitochondrial cytopathy

Bone marrow for storage disorders

Skin biopsy for fibroblast culture

***Liver Steering Group,  
BSPGHAN, Feb 2007***

## Conjugated Hyperbilirubinaemia – first line investigations

	Test	Date Taken	Result				
<b>Haematology</b>	FBC		Hb	WCC	Plts	Retics	
	Coagulation		INR	PT	APTT	Fib	
	Group and Coomb's		Gp		Coombs		
<b>Biochemistry</b>	U&E		Na	K	Urea	Cr	Bic
	Total/conj bilirubin		Total BR		Conj BR		
	Liver function tests		ALT/AST		Alk phos	γGT	
	Ca/ Phos		Ca		Phos	Alb	
	Cholesterol/triglycerides		Chol		Trig		
	Blood sugar/BM						
<b>Microbiology</b>	Blood culture						
	Urine culture						
<b>Virology</b>	IgM to TORCH		Toxo	Rub	CMV	HSV	
	Hepatitis A,B, C						
	Urine CMV						
<b>Metabolic</b>	IRT/sweat test						
	GAL-1-PUT						
	α <sub>1</sub> -antitrypsin		Level		Phenotype		
	Plasma amino acids						
	Urine amino acids						
	Urine organic acids						
	Ward test urine						
<b>Endocrine</b>	Thyroid function tests		TSH	T <sub>3</sub>	T <sub>4</sub>		
	Cortisol						
	Short synacthen test*						
<b>Radiology</b>	Abdo USS (fasting)						
	CXR/spine X-ray *						
	Radioisotope scan*						
<b>Histology</b>	Liver biopsy*						
<b>Other tests</b>	Ophthalmology review *						
	Stool colour						

\* second line investigations