Interpretation of Liver Function Tests (Outside of the Neonatal Period – i.e. beyond 28 days of age)

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Purpose
This guideline is designed to assist with the interpretation of liver function tests carried out in paediatric patients at Sheffield Children’s Hospital

Intended Audience
Clinical staff at SCH who are requesting and are required to be able to interpret liver function test results.
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1. Introduction
This guideline will assist with the interpretation of liver function tests outside of the neonatal period.

For guidance on neonatal and prolonged jaundice please see relevant guidelines:

LFT’s are frequently requested in both the acute and chronic situation. Clinicians need to know how to interpret these tests and to know when LFT results require close/further evaluation. This guideline has been produced to help interpret LFT’s.

It is not possible for this to be a totally comprehensive guideline. Background basic knowledge of hepatology is required. I.e. **It is not meant to replace the requirement for those medical staff that are requesting / interpreting LFT’s to have at least a basic medical knowledge of hepatology.**

**If in doubt then please consult with your seniors / colleagues as outlined at the end of this guideline.**

2. Intended Audience
Clinical staff who are requesting and are required to be able to interpret liver function test results.
3. Guideline Content

A. Standard liver function tests at SCH
B. Basic interpretation of liver function tests
C. How to assess liver function
D. Examples
E. Frequency of monitoring
F. Cautions / available resources

A. A standard set of LFT’s carried out at SCH would be as follows:

NB – If you are assessing the function of the liver it is essential to include clotting studies and glucose (see Section C below).

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (Br)</td>
<td>conjugated and unconjugated</td>
</tr>
<tr>
<td>Alkaline Phosphatase (Alk P)</td>
<td></td>
</tr>
<tr>
<td>Gamma glutamyl transpeptidase (GGT)</td>
<td></td>
</tr>
<tr>
<td>Aspartate aminotransferase (AST)</td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase (ALT)</td>
<td></td>
</tr>
<tr>
<td>Albumin (Alb)</td>
<td></td>
</tr>
</tbody>
</table>

B. Basic interpretation of liver function tests

Aminotransferases (AST and ALT) will be elevated with inflammation/damage (i.e. hepatitis) of the liver cells – both may be marginally elevated or increased into the thousands. AST is less liver specific than ALT (although both may originate from muscle). The degree of rise of AST and ALT alone does not necessarily correlate with the severity of the disease so must be used as part of the whole picture.

AST has a shorter half life than ALT but tends to have a quicker response time – it therefore tends to be elevated quicker and higher than ALT but will fall before ALT will.

**TRANSAMINASES THAT ARE FALLING WHILST BILIRUBIN IS STILL RISING AND/OR ALBUMIN IS FALLING IS AN OMINOUS SIGN – THIS INDICATES THAT THERE HAS BEEN SO MUCH HEPATOCYTE DAMAGE AND NECROSIS THAT THERE ARE NO LIVER CELLS LEFT TO MAKE THESE ENZYMES.**
Conjugated Br – elevated with liver cell dysfunction or with biliary obstruction.

Unconjugated Br – elevated with haemolysis (i.e. non- liver in origin) or genetic defects in Br conjugation pathway. May also be commonly seen in the newborn period secondary to physiological jaundice.

Alk P and GGT reflect bile flow within the liver. They will be elevated in biliary obstruction or biliary inflammation.

Albumin falls when the liver is failing. The liver is no longer able to synthesise the Albumin.

Ammonia can be measured separately which gives an idea of protein catabolism and whether this is proceeding normally.

In order to fully assess the liver from a blood point of view, you also need to know what the glucose level is, along with clotting times and a full blood count.

C. How to assess liver function

SYNTHETIC FUNCTION
When we talk about synthetic function of the liver we are referring to **how well the liver is able to make the things that it is supposed to.**

We tend to assess synthetic function of the liver by looking at the following bloods. It is therefore essential that these tests are also performed when assessing the function of the liver:

- Albumin
- Glucose
- Clotting

In a liver that is failing – either chronically or acutely, albumin levels start to drop below the normal range, glucose is no longer able to be synthesised by the liver with resultant low blood sugars and the liver dependent clotting factors are decreased which result in prolonged clotting times – initially prothrombin times but may progress to also include prolonged APTT and reduced fibrinogen levels.

D. In portal hypertension with resultant splenomegaly and hypersplenism, the platelet count will drop followed by the white cell count and ultimately also the haemoglobin with a picture of pancytopaenia. **Examples**

When interpreting LFT’s, look at the results along with a clinical assessment of the patient. Below are some examples of different scenarios:

| Raised AST and ALT, normal/ raised Br (conj), normal albumin, glucose and clotting | Indicates a hepatitis of some origin. May be acute or long standing. If acute, need to be aware that this may progress to liver failure and will require |

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close monitoring that includes LFT’s, clotting and glucose.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conj Bilirubin rising with falling AST/ALT</td>
<td>Signs that the hepatitis is severe and may be progressing to liver failure.</td>
</tr>
<tr>
<td>Raised AST, ALT, normal/raised Br with any of the following – dropping albumin, hypoglycaemia or prolonged clotting</td>
<td>Indicates that the hepatitis has progressed with synthetic function now affected. This liver is showing signs of failing. If clotting is prolonged, then by definition this has progressed to liver failure.</td>
</tr>
<tr>
<td>Raised Br (conjugated), raised GGT and Alk Phos. Minimally raised/normal AST/ALT</td>
<td>Cholestatic picture – often seen with biliary obstruction.</td>
</tr>
<tr>
<td>Normal LFT’s except albumin, with prolonged clotting, +/- hypoglycaemia</td>
<td>May be a sign of chronic liver disease/chronic liver failure. Often seen in end stage fibrosis/cirrhosis. No active “hepatitis” but synthetic function failing. Likely to be associated with portal hypertension with changes seen on abdominal ultrasound and FBC.</td>
</tr>
<tr>
<td>Raised Br (unconjugated) with normal LFT’s</td>
<td>May be a sign of haemolysis if no suggestion of liver disease. Some genetic conditions such as Gilbert’s syndrome or Crigler Najar syndrome can lead to isolated elevation of unconjugated Br.</td>
</tr>
<tr>
<td>Elevated AST/ALT along with elevated CPK (creatinine phosphokinase)</td>
<td>If CPK is also elevated, this suggests that the transaminitis is secondary to muscle involvement and not liver although in situations such as severe hypoxia there may be both liver and muscle involvement.</td>
</tr>
</tbody>
</table>

E. Frequency of monitoring

Frequency of monitoring will depend on the clinical situation. This may vary between several times per day (in the case of a child in acute liver failure) to only requiring bloods once per year in a child with a known chronic liver disease that is stable.

In a child with a previously unknown liver condition who presents with an acute hepatitis/acute liver failure, the frequency of monitoring will be guided by

1. The clinical status of the child – If the child is unwell then at least daily.
2. The degree and rate of rise of hepatitis (i.e. very high and rapidly rising levels of transaminases require more frequent monitoring – at least daily)
3. Synthetic function; with any drop in synthetic function necessitating close and frequent monitoring – at least daily and sometimes up to three times per day.

4. Decreasing transaminases whilst rising Br requires close monitoring – at least daily and sometimes more frequently

F. **Cautions / available resources**

If a child is in/thought to be in acute liver failure then please follow the management of acute liver failure as per the “Acute Liver Failure” guideline available on the intranet. This guideline contains sections on investigation, management and guidance for onward referral in acute liver failure.


As stated in the introduction, this guideline is not meant to be used in isolation. In order to interpret LFT’s correctly, the requesting clinician must ensure they have sufficient hepatology knowledge to be able to interpret the results.

Please discuss results with your seniors, gastroenterology team, Dr Sally Connolly (Consultant Hepatology at SCH) or Leeds liver team if in any doubt.