

# ACB SCIENTIFIC COMMITTEE TASK FORCE ON THE STANDARDISATION OF “TEST PROFILES

Draft Proposal for “Liver Function Tests” (LFTs)

Authors: Dr W S A Smellie, Dr J H Barth

Comments to [Julian.Barth@leedsth.nhs.uk](mailto:Julian.Barth@leedsth.nhs.uk)

## Introduction:

“Liver function test” profiles include a varying number of analytes used primarily to detect liver disease, although several of the analytes have additional potential applications. Few measure liver function as such, but provide information about haemolysis, hepatitis and biliary obstruction and hepatic protein synthesis. Current LFT profiles vary between laboratories and historically have contained some or all of the following:

1. Amino aspartate transaminase (AST)
2. Alanine aminotransferase (ALT)
3. Total bilirubin
4. Conjugated/unconjugated bilirubin
5. Alkaline phosphatase (Alk Phos)
6. Gamma glutamyl transferase (gamma GT)
7. 5’ nucleotidase
8. Total serum protein
9. Serum albumin
10. Calculated serum globulins
11. Lactate dehydrogenate (LDH)

Current Keele benchmarking data from 41 participating laboratories suggest that the great majority of laboratories offer total bilirubin, alanine aminotransferase (ALT), and Alkaline Phosphatase. A few offer aspartate aminotransaminase (AST) in place of ALT and a small number offer both. Approximately half of laboratories offer total protein, and slightly over a third offer gamma glutamyl transferase (GGT). None offered conjugated bilirubin or LDH as part of the LFT profile.

## Aim:

The aim of this document is to provide a proposal for a standard “minimum data set” of liver analytes to be included in primary and secondary care LFTs.

## Discussion:

At the outset, it should be noted that in screening exercises, it is estimated that fewer than 1% of subjects with ‘abnormal’ LFTs have liver disease [1].

## Transaminases/Hepatic markers: AST, ALT

ALT offers far greater specificity for hepatic disease than AST which is present in many tissues. Some clinicians make use of AST/ALT ratios in differential diagnosis of disease, although this might be considered as a specialist level investigation not for inclusion in a routine profile and is, in any case, of arguable diagnostic utility. The incremental benefit of AST in addition to ALT appears to be limited. This is consistent with Keele data in which the great majority of laboratories offer ALT alone as a transaminase.

## Indicators of obstructive/cannalicular change: Alk Phos, gamma GT, bilirubin

Alk Phos and GGT are used for assessment of intra and/or extra hepatic obstructive change. GGT is also subject to induction by many drugs and by alcohol. Alk Phos is not liver specific, the second major source being bone. Several consensus guidelines advise the use of GGT only as a secondary investigation to differentiate the potential cause of raised Alk Phos [2][3][4][5][6]. Despite much clinical evidence, many doctors rely incorrectly on GGT possibly because the DVLA continue to use it as a test of alcohol consumption. Minor elevations of GGT are common in primary and secondary care and may well be related to obesity [7] amongst other causes. Moreover, the high number of minor rises of uncertain clinical significance suggest that it may add more confusion than benefit to a routine liver profile, although it remains useful for secondary level investigations, particularly to investigate a raised Alk Phos. It is acknowledged however that Keele data suggest that around one third of laboratories currently offer gamma GT in their LFT profile.

Bilirubin is relevant as a marker of haemolysis as well as intra or extra hepatic obstruction. Isolated rises in total bilirubin not associated with changes in other liver indices, may require further investigation, including differentiating conjugated from unconjugated bilirubin. Bilirubin can be a measure of actual hepatic excretory function. It is measured routinely in LFTs by all participating Keele laboratories.

## Hepatic protein production

Albumin can be an indicator of hepatic synthetic function in the absence of other reasons to explain altered serum protein concentrations, notably falls in serum albumin may reflect one of several processes of impaired synthesis, malnutrition, haemodilution and excessive loss. Serum albumin is also used to adjust the total measured calcium in blood and appears separately in a bone profile. Whilst several of the investigative uses of serum albumin do not directly reflect investigation of liver disease, its role as a potential indicator of hepatic protein synthesis and to identify albumin losing states is useful

Total protein (and the calculated serum globulins) is a non-specific marker which more reflects inflammatory and immune reactions and plasma cell dyscrasias. It should therefore be allocated to a different profile category. However, as dysglobulinaemic states are frequently associated with the same diseases which influence serum albumin, inclusion of total protein in a liver profile could be argued to be appropriate and slightly over half of the participating Keele laboratories currently offer this in LFTs

## Lactate dehydrogenase

LDH is an enzyme found in many cells and offers poor specificity for the liver. Other than specific uses as a tumour marker or ancillary indicator of tissue damage, its routine use in a liver profile appears limited and it is not included in the LFT profile of any of the Keele participants.

## Proposal:

The following tests are proposed as the core liver function test profile:

1. Alanine amino transaminase
2. Alkaline phosphatase
3. Serum albumin
4. Total bilirubin

Inclusion of total protein should be considered on the basis of the response to the consultation exercise but on balance we feel that there does not appear to be a compelling argument to include it.

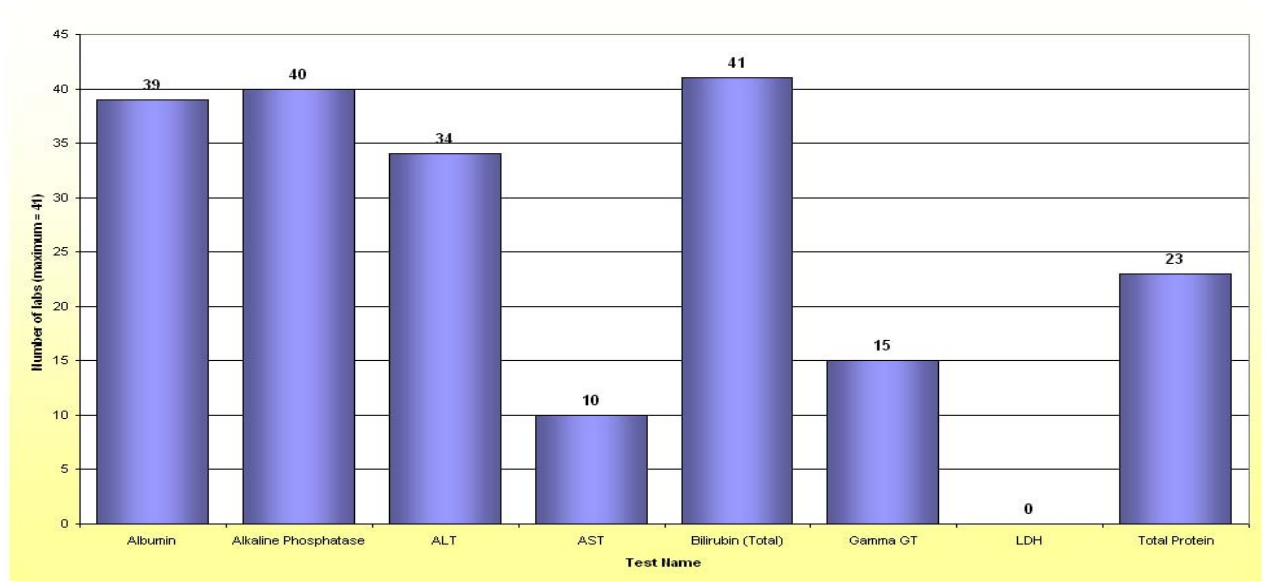
## Conclusion:

The LFT profile may evolve and the outcome of this proposal may only be first stage in this process. Additional tests such as gamma GT, AST, conjugated/unconjugated bilirubin and/or LDH should be available for second line testing dependent on specified situations but would not appear to add significantly to the routine investigation profile. The merits of tests such as serum total protein may be limited in the context of liver disease. Its removal may be unpopular with users who normally receive it but a balance must be made between the removal of a test and the additional work created by tests performed/added subsequently. These factors should not impede efforts to move to the most clinically appropriate profile even if this is an incremental process.

## References:

1. Johnson PJ. Role of the standard "liver function tests" in current clinical practise. *Ann Clin Biochem* 1989;26:463-471.
2. Guidelines and Protocols Advisory Committee. Evaluation and interpretation of abnormal liver chemistry in adults. BC Health Services  
[www.health.gov.bc.ca/msp/protoguides](http://www.health.gov.bc.ca/msp/protoguides)
3. Minuk GY. Canadian Association of Gastroenterology Practice Guidelines: Evaluation of abnormal liver enzyme tests. *The Canadian Journal of Gastroenterology*  
[http://www.pulsus.com/Gastro/12\\_06/mini\\_ed.htm](http://www.pulsus.com/Gastro/12_06/mini_ed.htm) Accessed 5th October 2005.
4. Titcomb CP. Liver function tests: what is the risk? *J Insur Med* 2003;35:26-35.
5. Pratt DS, Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients. *N Engl J Med* 2000;342:1266-1271.
6. Giannini EG, Testa R, Savarino V. Liver enzyme alteration: a guide for clinicians. *CMAJ* Feb 1, 2005;172(3):367-379
7. <http://www.mylaboratoryquality.com/ggtwf2.pdf> accessed 8th March 2007

Number of labs performing each test as part of a Liver Function Test profile



Albumin	Alkaline Phosphatase	ALT	AST	Bilirubin (Total)	Gamma GT	LDH	Total Protein	Number of labs	Percentage of labs
	X	X		X				2	4.88%
X		X		X				1	2.44%
X	X		X	X				1	2.44%
X	X		X	X			X	4	9.76%
X	X		X	X	X		X	2	4.88%
X	X	X		X				8	19.51%
X	X	X		X			X	8	19.51%
X	X	X		X	X			4	9.76%
X	X	X		X	X		X	8	19.51%
X	X	X	X	X				1	2.44%
X	X	X	X	X			X	1	2.44%
X	X	X	X	X	X			1	2.44%

Figure 1. LFT tests performed in Keele benchmarking cohort (41 laboratories) 2006