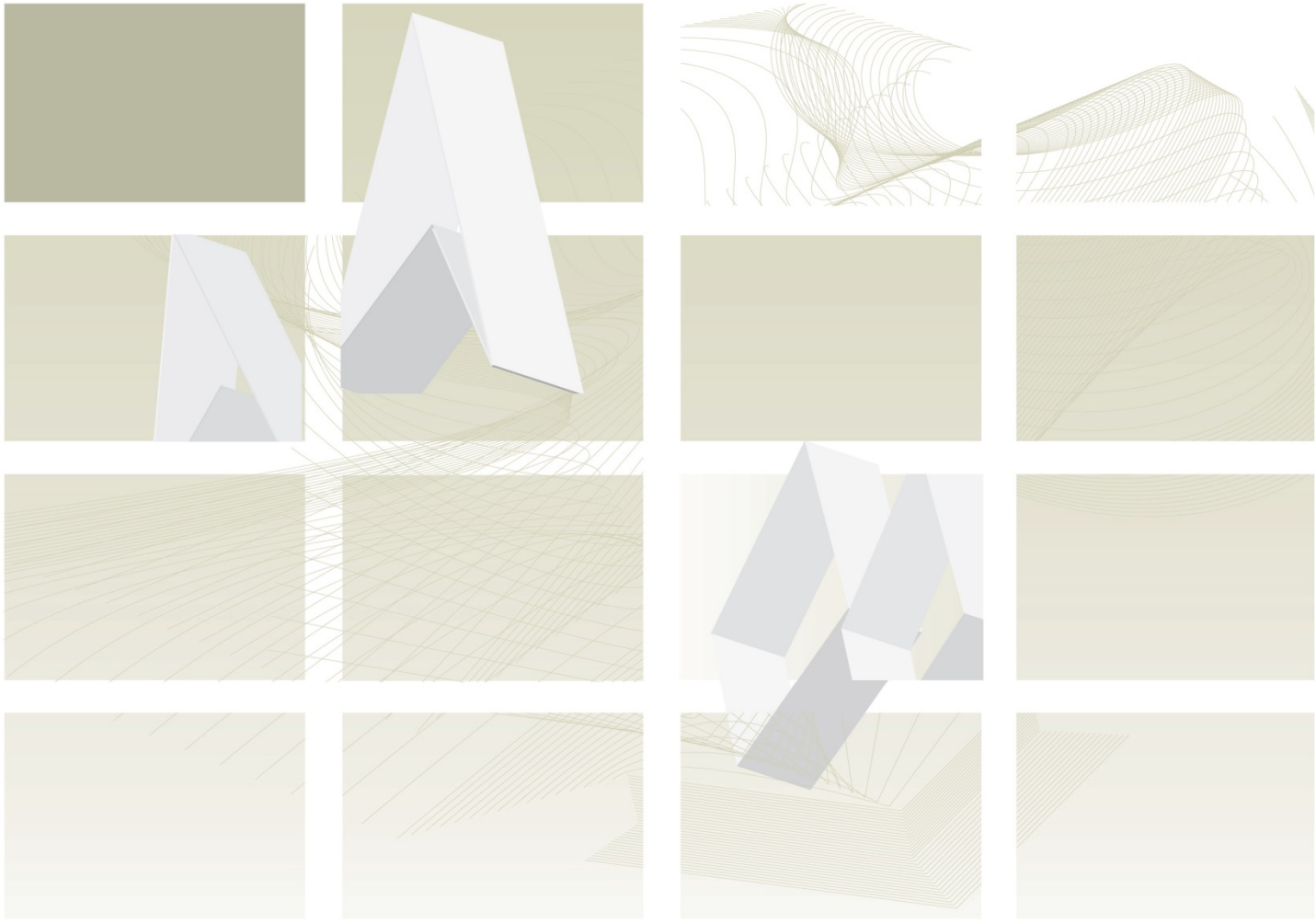
Public Health England

Protecting and improving the nation's health

UK Standards for Microbiology Investigations

Review of Users' Comments received by
Joint Working Group for Syndromic Algorithms

S 1 Acute Infective Hepatitis



NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by Public Health England to produce Standards for Microbiology Investigations. Accreditation is valid for 5 years from July 2011. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.

Recommendations are listed as ACCEPT/ PARTIAL ACCEPT/DEFER/ NONE or PENDING

Consultation: 27/12/2008 – 21/01/2009

PROPOSAL FOR CHANGES

Comment Number	1		
Date Received	29/12/2008	**Lab Name**	Nottingham University
Section	Various		
Comment			
a. For acute hepatitis in a known IDU - anti-HCV testing is not sufficient, HCV RNA should be a front-line test, as a percentage of patients presenting with acute jaundice due to HCV infection are antibody negative at the time of presentation. b. Asymptomatic hepatitis - for a known exposure to HBV, I thought the standard follow-up protocol was to test for HBsAg at 6 months - the version here says something (not sure what) about testing at 6 weeks. c. Hepatitis in neonates - in the blurb at the top there is something about "neonatal failure" - I suspect this is a misprint - ? meant to be liver failure? d. Hepatitis in neonates - I couldn't see anything about investigating for fulminant HBV infection in a jaundiced neonate - this is well-described, especially in infants of anti-HBe positive mothers - I think Liz Boxall wrote up some cases a while back.			
Recommended Action	a. **ACCEPT** SMI (formerly NSM) amended. b. **ACCEPT** SMI (formerly NSM) amended. c. **ACCEPT** SMI (formerly NSM) amended. d. **ACCEPT** SMI (formerly NSM) amended.		

Comment Number	2		
Date Received	21/01/2009	**Lab Name**	Norfolk & Norwich University Hospital
Section	Acute hepatitis		
Comment			
a. HEV should feature in the farming,occup.group b. Our most common cause of acute hepatitis is EBV –I think it deserves higher prominence than Hep A.			

Recommended Action	a. **ACCEPT** SMI (formerly NSM) amended footnote added to raise awareness of possibility of HEV in some farming. b. **NONE** Due to public health reasons cannot exclude testing for HAV however the algorithm does not exclude testing for EBV which is also patient dependent.

Consultation: 30/06/2009 – 31/07/2009

PROPOSAL FOR CHANGES

Comment Number	1		
Date Received	13/07/2009	**Lab Name**	Nottingham
Section	Various		
Comment			

The lead-into this flow chart contains a number of errors/inaccuracies:

a. Line 3 specifies 3x normal ALT. Why? Surely all patients with abnormal ALT should be investigated for viral hepatitis. I agree that in acute hepatitis, the ALT is likely to be very high, but by stating a lower limit of 3x ULN, you give the false impression that it is OK for someone to walk around with an ALT of, say 2x upper limit of normal, and who don't therefore need investigation.

b. Line 6 "which causes jaundice". Jaundice in acute hepatitis is due to a combination of both hepatocellular damage and intrahepatic biliary obstruction, not simply the latter. I suggest altering to "contributes to jaundice".

c. Line 7 – I agree that acute hepatitis can be asymptomatic, but it can also be fulminant. Why not say that disease presentation can vary from being asymptomatic to being fulminant.

d. Footnote a suggests considering HC PCR in all cases, which is a good idea. It is then a bit difficult to understand why HCV PCR appears in some of the columns but not others. In the absence of additional history, I would always test for hep A, B AND C, but HCV isn't specifically mentioned in this column. HCV can cause fulminant hepatitis – the only strain of HCV that replicates in vitro is the Japanese Fulminant Hepatitis – 1 strain. I agree this is less likely than HAV or HBV, but suggest including HCV PCR as a second line investigation on a par with HEV and Brucella.

e. In a chronic HBV carrier – surely such an individual should always be tested for anti-HCV? HCV PCR is mentioned as an after thought at the bottom, but it should be routine to test a hep B carrier for evidence of HCV infection (past or present) – they share routes of transmission.

f. In the immunocompromised, the supplementary tests include EBV – but there is no stipulation that this should be a viral load test – EBV serology in this setting is not going to help. There is also reference to HHSV6, a virus which, to my knowledge, doesn't exist! If this is meant to be HHV6, then again, I assume the testing should be by DNA not serology, although I confess to not being aware of a

huge literature on HHV6 induced hepatitis in the immunosuppressed. g. In the glandular fever column, I would suggest adding in HBsAg testing. I have seen patients who present with generalised lymphadenopathy, a skin rash, and polyarthralgia, who've then turned yellow a few days later, who had acute HBV, and this is well described in the text books. h. Asymptomatic Hepatitis The columns relating to hepatitis B and C include data relating to timing eg HBsAg – HBV – at 6 weeks, HCV: HCVrt PCR at 12 weeks, HCV: IgG 12 weeks after exposure, HCV: IgG 24 weeks after exposure. These don't make any sense to me in the context of an algorithm for investigation of a patient presenting with abnormal LFTs without symptomatic hepatitis. They obviously relate to the timing of appropriate tests after a known exposure incident such as a needlestick. But why conflate investigation of asymptomatic hepatitis (which is, after all, the title of this page), with post-exposure testing? An individual with an exposure does not have asymptomatic hepatitis!!!! I would suggest this will lead to confusion (at least I am confused), and I also suggest simply separating an algorithm for testing of asymptomatic hepatitis from a separate algorithm for testing for infection post exposure.	
Recommended Action	a. **ACCEPT** SMI (formerly NSM) amended. b. **ACCEPT** SMI (formerly NSM) amended. c. **ACCEPT** SMI (formerly NSM) amended. d. **ACCEPT** SMI (formerly NSM) amended. e. **ACCEPT** SMI (formerly NSM) amended. f. **ACCEPT** SMI (formerly NSM) amended. g. **ACCEPT** SMI (formerly NSM) amended. h. **ACCEPT** SMI (formerly NSM) amended to make this section clearer.

Comment Number	2		
Date Received	23/07/2009	**Lab Name**	Royal Devon & Exeter Foundation Trust

Section	Various
Comment	

a. IDU with acute Hepatitis

Hepatitis C is clearly an unusual cause of acute Hepatitis but there may be flares of chronic infection. Is it necessary in all patients to undertake PCR testing as well as HCV antibody testing?

b. No additional history

We and other laboratories in the South West had noted the rarity of cases of acute Hepatitis A infection and were having problems with tests for acute Hepatitis A infection in elderly patients who not infrequently, produce reactive HAV IgM tests which are almost certainly, non-specific, although this is difficult to prove. We overcome this by being much more selective about the criteria for testing for Hepatitis A IgM.

c. Fulminant Hepatitis

I am not sure how this is defined but certainly, a recent case we had locally had no overt risk factors for leptospirosis but in fact, this was the ultimate diagnosis. Although rare, I am absolutely certain that this is a more likely diagnosis than acute brucellosis in the absence of foreign travel.

d. Immuno-compromised

I was very surprised to see that adenovirus was to be diagnosed by serology. This is most likely to occur in allograft patients and my understanding is that serology is almost useless in that situation and that diagnosis should be made on the basis of PCR on blood and any specimens such as liver biopsy that may be obtainable.

e. I was under the impression that HHV6 serology was no longer available and surely this again should be a PCR test.

f. In relation to aspergillosis, again, my understanding is that even in the National Reference Laboratory, PCR is not a routinely established test and therefore, it seems unrealistic to put it into a algorithm of this sort.

g. As far as Candida is concerned, I think it needs to be more specific about what sample isolation should be attempted from. Presumably, in general, this would be blood cultures.

h. Occupational/Farming Water exposure

Brucella is no longer endemic in the UK and I think the value of Brucella serology is highly debatable, even as a supplementary test. In cases of acute Brucellosis, the diagnosis should be possible using blood cultures anyway.

Suspected bacterial sepsis including biliary sepsis

I was truly amazed to see Brucella as a routine initial test in this setting. What possible justification is there for this?

i. Hepatitis in neonates

Serum

My experience of *Treponema pallidum* IgM has been less than encouraging. Does the data support use of this test as a means of determining whether

infection has been transmitted to the neonate? j. Faeces and Throat swabs I note that enterovirus cell culture is listed but my understanding is that certainly for the vast majority of the country, cell culture has been replaced by PCR. Is it therefore sensible to include this? k. CSF Has *Treponema pallidum* been validated for CSF? Certainly the Reference Lab doesn't include this as a routine test, according to their information on the HPA website. l. Foot notes E I don't understand the phrase 'however farming is not considered to be of risk' Does this mean farming in general? m. Footnotes F I don't understand the term 'positive cholestatic jaundice'	
Recommended Action	a. **NONE** The two tests give different information. b. **NONE** Testing for HAV is necessary with this clinical picture. c. **ACCEPT** Removed from this column. d. **ACCEPT** SMI (formerly NSM) amended to reflect PCR. e. **ACCEPT** SMI (formerly NSM) amended to reflect PCR. f. **NONE** There are cases where this pathogen needs to be considered as a second line test. g. **NONE** It is a second line test and will be replaced with PCR at the next review. h. **ACCEPT** SMI (formerly NSM) amended to remove Brucella. i. **ACCEPT** It does have a role to play in this kind of diagnosis. j. **ACCEPT** SMI (formerly NSM) amended to reflect PCR.

	k. **NONE** In certain patient groups it can give useful information. l. **NONE** It does mean farming in general. m. **ACCEPT** SMI (formerly NSM) amended.