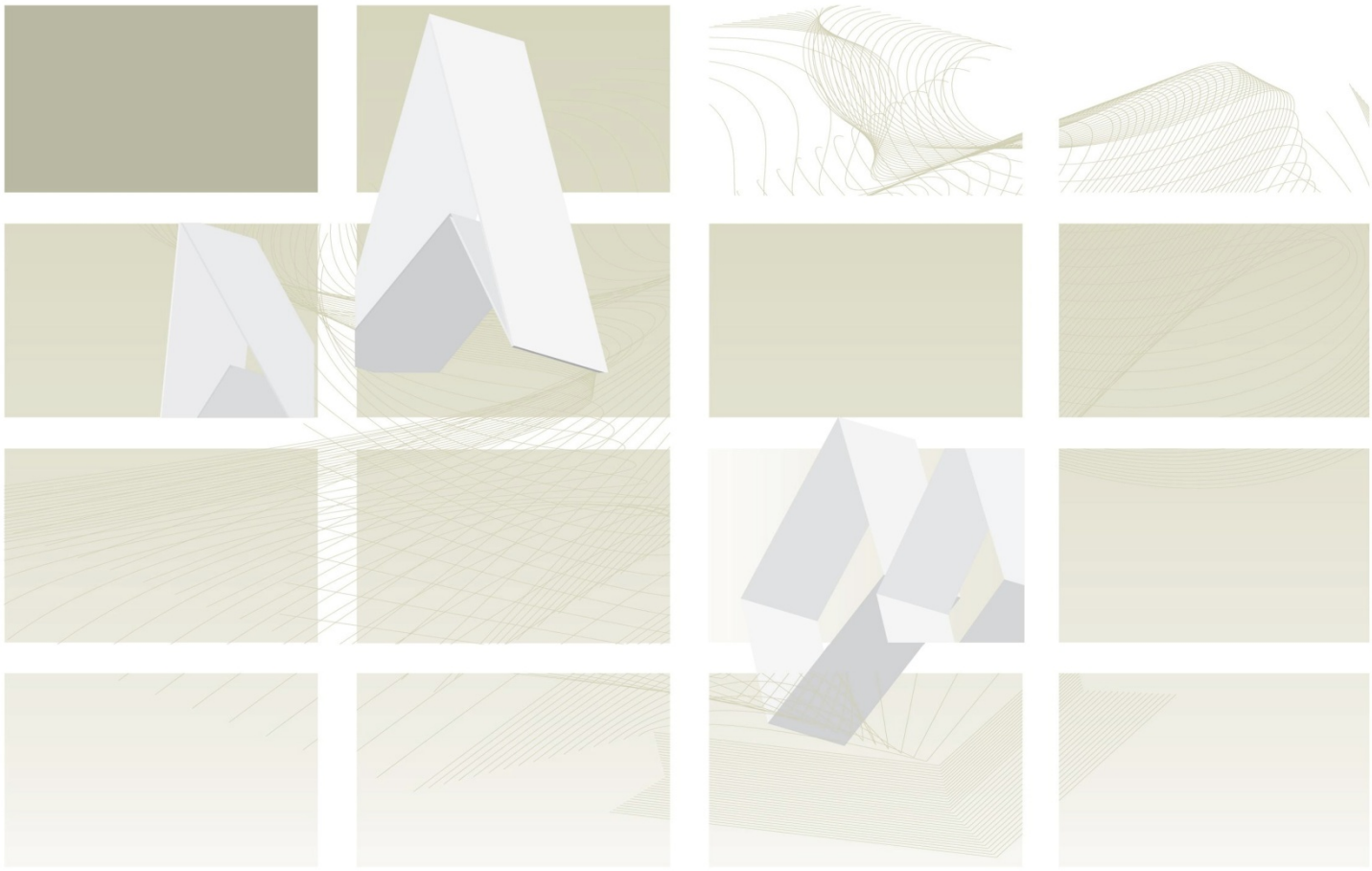
Public Health England

NHS

UK Standards for Microbiology Investigations

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

S5 Meningoencephalitis



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

1st CONSULTATION 08.01.10 – 05.02.10

PROPOSAL FOR CHANGES

Comment Number	1		
Date Received	08/02/2010	**Regional Committee**	SEMSTAG
Section			
Comment			
a. The group felt that this was a realistic presentation of the syndrome All CSF should under go a cell count and culture b. Yeast should be cultured for c. Throat swabs and faeces should be added in as additional sample types d. Prions and Bartonella should be moved to secondary testing e. A statement highlighting the need to consider parasites should be inserted.			
Recommended Action	a. **ACCEPT** The SMI has been amended to include a reference to B 27 which covers this area. b. **ACCEPT** The SMI has been amended to include a reference to B 27 which covers this area. c. **NONE** These sample types are not appropriate for Encephalitis but will be covered in a syndromic algorithm Meningitis. **Please note:** Since these comments were received, this document contains merged algorithms for Meningitis and Encephalitis. d. **ACCEPT** The SMI has been amended to remove the pyrexia section and *Bartonella* from the algorithm. The prions section was also removed. e. **ACCEPT** The SMI has been amended to detect toxoplasma by PCR or serology and a footnote added to cover the rare pathogens.		

Comment Number	2		
Date Received	04/02/2010	**Lab Name**	Royal Preston Hospital
Section			
Comment			
a. Footnote a recommends that HHV6 should be tested in age related cases. We wonder if this could be made more specific (which ages?). b. We wonder if secondary testing for immunocompetent patients should include lymes, syphilis, mycoplasma and bartonella (depending on clinical details). c. In immunocompromised patients, we would perform EBV and CMV PCR on CSF. d. For the suspected parainfectious cases, we would recommend campylobacter serology. e. For parainfectious cases, we question the utility of performing PCR in CSF for respiratory and GI viruses. f. We would perform PCR on CSF for CMV and EBV, in HIV positive patients who have subacute encephalitis. g. We question the need for a separate heading for pyrexia. For example, HSV encephalitis can cause fever.			
Recommended Action	a. **ACCEPT** The SMI has been amended to specify that the test should be performed in cases younger than 3 years old. b. **NONE** These documents are minimum guidelines covering common features of encephalitis. **Please note:** Since these comments were received, this document contains merged algorithms for Meningitis and Encephalitis. c. **ACCEPT** The SMI has been amended to detect EBV and CMV by PCR on CSF samples. d. **ACCEPT** The SMI has been amended to remove the parainfectious/post vaccine section. e. **NONE** There is evidence to support the need to test for these viruses however the parainfectious/post vaccine section was removed. f. **ACCEPT** The SMI has been amended to detect CMV and EBV on CSF samples by PCR.		

	g. **ACCEPT** The SMI has been amended to remove the pyrexia section.

Comment Number	3		
Date Received	03/02/2010	**Lab Name**	PHE (formerly HPA), Southampton Lab
Section			
Comment			
Borrelia burgdorferi infection is an uncommon but treatable cause of acute meningoencephalitis and can also cause rare cases of encephalomyelitis (with a subacute or chronic presentation), which is also treatable. It is a shame to miss the opportunity of diagnosing and treating these conditions, as the outcomes of treatment are usually very good. I do not think that tests for Lyme borreliosis should automatically be incorporated into an "encephalitis test menu", but would welcome some comment regarding reviewing the patient's history of potential tick exposure risk (in the UK and abroad) and clinical history and findings for other evidence to suggest Bb infection. Both serum and CSF antibody tests are useful in this situation, with a very high likelihood of positivity. PCR is less useful (< 40% in acute neuroborreliosis, and even lower in late neuroborreliosis. I've attached the new guidelines from the European Federation of Neurological Societies that might be helpful to your group.			
Recommended Action	**ACCEPT** A footnote will be added.		

Comment Number	4		
Date Received	03/02/2010	**Lab Name**	PHE (formerly HPA), Bristol Lab
Section			
Comment			
Pyrexia is a feature of many cases of infective encephalitis. Can’t the bacteria be squeezed in under other headings, or under ‘clinically suspected bacterial infection’ (from CRP, FBC etc).			
Recommended Action	**ACCEPT** The SMI has been amended to remove the pyrexia section.		

Comment Number	5		
Date Received	15/01/2010	**Lab Name**	Royal Infirmary of Edinburgh
Section			
Comment			
Encephlitis and meningoencephalitis have a broad range of potential aetiologies as you will be aware. It is hence difficult to cover all, as history examination and initial radiological and CSF findings including opening pressure, glucose and concurrent serum glucose may give some guidance. Appropriate 'infection' investigations should at least be considered (if not done) for TB (>6mls CSF) syphilis (serology at least) Lyme serology at least if not CSF for PCR Fungal infections espcryptocococcosis (CSF culture, antigen, or serum at least). Endemic mycoses may sometimes be relevant. Toxoplasma CSF PCR These are few quick thoughts, but have not formally reviewed all possibilities.			
Recommended Action	**ACCEPT** The SMI has been amended to ensure the most relevant pathogens are tested for all in scenarios. A footnote for the detection of rare causes of encephalitis will be added. **Please note:** Since these comments were received, this document contains merged algorithms for Meningitis and Encephalitis.		

Comment Number	6		
Date Received	15/01/2010	**Lab Name**	Royal Devon and Exeter Hospital
Section			
Comment			
a. The first practical issue in dealing with this syndrome is that patients are not admitted to hospital with the diagnosis “encephalitis” tattooed on their foreheads. Most of the time that we receive CSF with details of “?encephalitis” the diagnosis is something entirely different. Thus the pre-test probability of finding any infective agent is actually very low. I think there is a real problem with an algorithm for this. In principle the number of infective causes of encephalitis is vast and yet in practice the only agents that are detected with any regularity are HSV, VZV and enterovirus with the addition of CMV, EBV and JC virus in immunocompromised. Added to this, most laboratories do not test CSF in house for PCR and even large HPA (now PHE) laboratories			

cannot do tests such as HHV6 in house and therefore it becomes a nightmare trying to get additional tests done when the standard tests are negative. In my view there is a need for a single laboratory that has the critical volume and test repertoire to be able to make this algorithm fly. I honestly think from my own experience it becomes incredibly difficult to get it all to happen in anything approaching a meaningful timeframe.

There is also an issue with an algorithm approach when things are less than clear cut. The implication of the current version is that for non-immunocompromised patients who have negative results for HSV, VZ and enterovirus then a whole raft of other agents have to be done including HHV6, LCM, Adeno, Mumps, Measles and Influenza. Medico-legally this feels fairly uncomfortable to me since a laboratory could end up being criticised for failing to do these when they are stipulated in an SMI. I think there needs to be a much more detailed foot-note to the algorithms which includes some “get out of gaol phrasing” to avoid the need for mindless testing, particularly when often the CSF has normal white cell count and imaging doesn’t confirm the presence of an encephalitis.

b. I recognise that it is very easy to criticise and far harder to come up with something that is better. However I think that rather than going for a classical algorithmic approach, I believe that once one has gone beyond the standard agents it would be more useful to have notes that provided guidance as to what agents should be considered and when. I have held back from doing this myself but would be happy to assist if there were to be helpful.

   The very low yield of PCR testing acellular CSF is well known. It would be very helpful to have a statement about the value or otherwise of investigating for viral causes of encephalitis when a CSF has no white cells and the protein is normal.

   In relation to specific points:

   For immunocompromised patients, surely CMV and EBV testing should be done by PCR on the CSF rather than by serology

c. The far right hand algorithm for pyrexia seems oddly divorced from everything else. Surely all CSF will be cultured for Listeria, so why include that? Toxoplasma should be tested for by PCR and rather than doing this for patients with pyrexia, I would put this down as a test to be considered in the immunocompromised and the HIV positive sub-acute algorithm. Amoebae can be cultured but I would say this should be suspected not on the basis of the presence of a pyrexia but exposure history, together with the clinical response and CSF picture. Bartonella can certainly cause encephalitis but this would normally be diagnosed serologically.

   Mycoplasma pneumoniae does not appear in the algorithms but I believe that this is one of the major causes of encephalitis in children. Similarly Q fever and Chlamydia psittaci can present with encephalitic features. It would seem unwise to omit mention of syphilis since patients can present with acute illness and might be confused with and encephalitis.

Recommended Action	a. **ACCEPT** The SMI has been amended to add a preambule to explain what the algorithm will cover. b. **ACCEPT** The SMI has been amended to add PCR testing for CMV

	and EVB on CSF samples. c. **ACCEPT** The SMI has been amended to remove the pyrexia.

2nd CONSULTATION 16.12.11 – 10.02.12

PROPOSAL FOR CHANGES

Comment Number	1		
Date Received	31/01/2012	**Lab Name**	Royal Infirmary Edinburgh
Section	Flow Diagram		
Comment			
Although the introduction recommends considering tuberculosis none of the testing algorithms included list it as a test. It would be worthwhile citing the British infection Society guidelines on TB meningitis.			
Evidence			
http://www.ncbi.nlm.nih.gov/pubmed/19643501			
Recommended Action	**ACCEPT** UK SMI amended.		

3rd CONSULTATION 07.06.13 – 30.08.13

PROPOSAL FOR CHANGES

Comment Number	1		
Date Received	19/06/2013	**Lab Name**	Cardiff Virology
Section	All patients - CSF		
Comment			
a. Do the majority of UK labs currently perform testing for parechovirus? b. To my knowledge there are no commercial assays available, so this would require in-house testing. Would it be appropriate for this investigation to be under secondary testing (especially if <3 yrs old), as prevalence appears to vary depending on season and year? c. 'b' refers to 'Throat swabs and faeces together with serology may be appropriate sample types for this pathogen'. Are you suggesting to not have CSF? d. What serology are you referring to? Enterovirus can remain in the stool of children for weeks.			
Evidence			

Wolthers et al. CID 2008, 47: 358-363	
Financial Barriers	
Cost	
Recommended Action	a. **NONE** We are aware that the majority of UK laboratories don't have this test at this time. b. **PARTIAL ACCEPT** A footnote has been added for clarification. c. **NONE** The footnote states that the other sample types are additional not instead of. d. **ACCEPT** Serology has been removed from the list.

Comment Number	2		
Date Received	08/08/2013	**Lab Name**	Aberdeen
Section	Pages 9, 10, 11		
Comment			
a. Page 9: for non-immunocompromised, is parechovirus being recommendedregardless of age? b. Page 10: at (b) suggest replace "may be" with "are additional" c. Page 11: at HHV7, suggest add *, as at HHV6			
Evidence			
Page 9: parechoviruses are mainly found in those under 3 years of age Page 10: think suggestion is better wording! Page 11: HHV7, like HHV6, is usually acquired in the first 3-4 years of life.			
Recommended Action	a. **ACCEPT** A footnote has been added to this effect b. **ACCEPT** The document has been amended c. **ACCEPT** An * has been added to the document.		

Comment Number	3		
Date Received	27/08/2013	**Lab Name**	Newcastle
Section			

Comment

Flowchart P10

a. HHV6. Previous SOPs have included HHV6 as routine under age 3. HHV6 is a relatively common cause of encephalitis in young children. We believe this should be done routinely in this age group, not just considered. A caveat re CIHHV6 would be needed.

b. Parechovirus. Recent evidence / literature highlights that parechovirus infections are principally a problem in the very young. We would propose limiting parechovirus testing to those < 3years for purposes of the algorithm

c. Adenovirus should be included in the tests recommended in the immunocompromised.

P11

d. Footnote b) We do not believe that enterovirus serology testing provides benefit over or in addition to PCR. I am not aware that a serological assay exists for parechoviruses. It needs to be made clear that testing for entero/parech on faeces and throat swab can provide evidence of recent infection, but not evidence that CNS presentation is due to the virus.

e. Footnote c) re HIV testing. HIV should be recommended in both encephalitis and meningitis and footnote is therefore not required.

P12/14

f. This long list is of limited value and gives little information on when testing should be considered. Referral to G 4 - investigation of Viral Encephalitis and Meningitis which provides more detailed information might be more useful.

Recommended Action	a. **PARTIAL ACCEPT** A note has been added to emphasise that this should be considered in children under 3 but the test remains in secondary testing. b. **ACCEPT** A footnote has been added. c. **NONE** It is included for all patients in secondary testing. d. **ACCEPT** This footnote has been made clearer. e. **PARTIAL ACCEPT** The footnote has been broadened to include more scenarios and more patient groups. f. **NONE**

	A cross reference to relevant UK SMIs is already contained in the document.

Comment Number	4		
Date Received	30/08/2013	**Lab Name**	British Society of Antimicrobial Chemotherapy
Section			
Comment			
It is felt that the document should include more mention of *S. aureus* in this context. *S. aureus* septicaemia can present with these features (also as 'cerebritis' on scans) and may be a cerebral presentation of endocarditis.			
Recommended Action	**NONE** This is covered by the inclusion of blood culture bottles.		

OUTSIDE OF CONSULTATION PERIODS

Comment Number	1		
Date Received	28/12/2012	**Lab Name**	University of Nottingham
Section			
Comment			
Thank you for sending me this to comment on. I thought it was straightforward, and of interest, indeed, to such an extent that I thought I ought to look up the National guideline for the management of suspected viral encephalitis in adults. Only problem was that the reference isn't given in full. I looked it up in Pubmed, and it says Epub ahead of print 18th November. I then went to the Journal of Infection and looked for articles in press and couldn't find it. Perhaps it would be sensible to delay issuing this guidance until such time as the reference is actually available.			
Recommended Action	**ACCEPT**		

RESPONDENTS INDICATING THEY WERE HAPPY WITH THE CONTENTS OF THE DOCUMENT

Overall number of comments: 3			
Date Received	01/07/2013	**Lab Name**	NHS Ayrshire & Arran
Date Received	22/07/2013	**Lab Name**	Aberdeen Royal Infirmary
Date Received	21/08/2013	**Lab Name**	Dundee