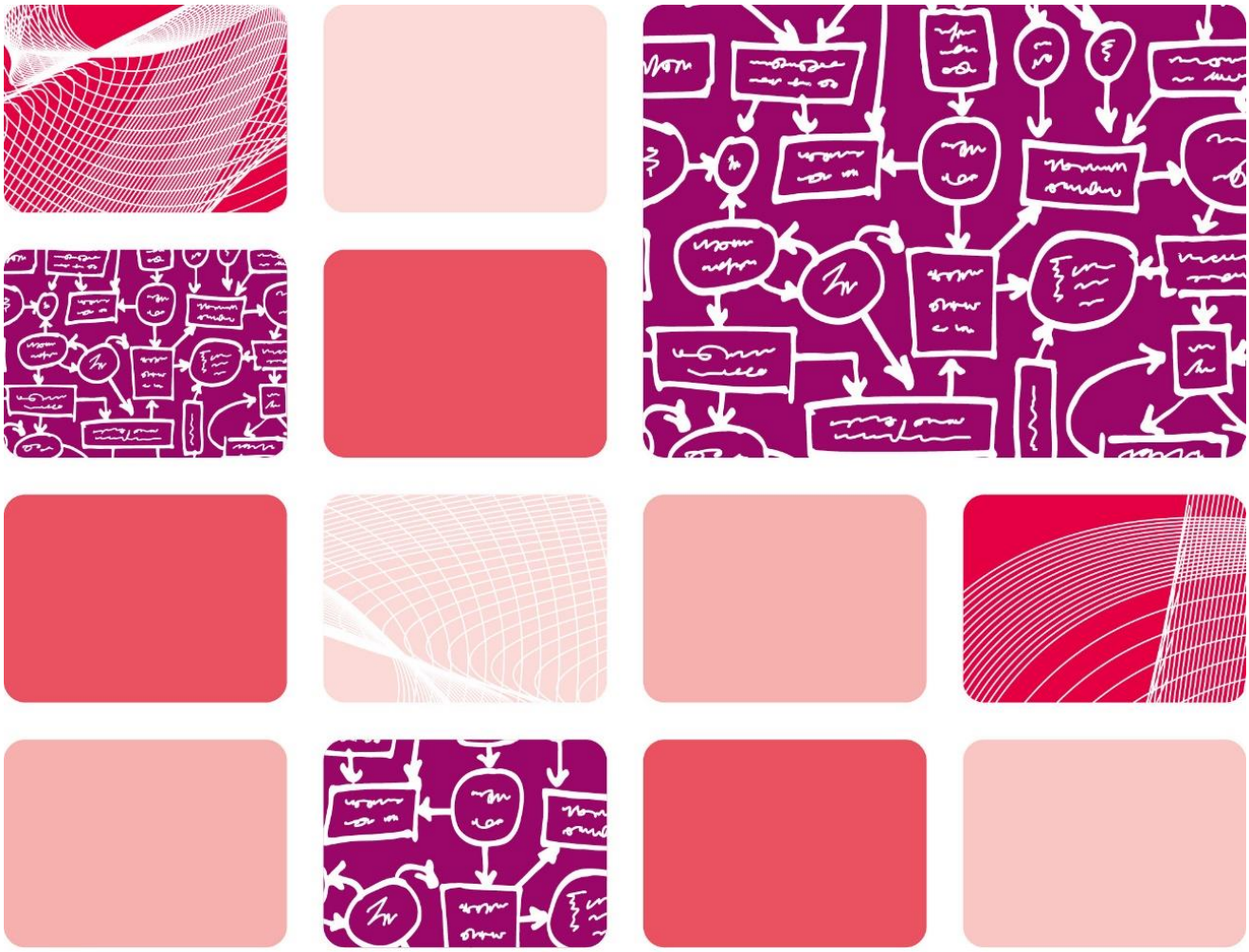
UK Health Security Agency

UK Standards for Microbiology Investigations

Meningoencephalitis



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Acknowledgments

UK Standards for Microbiology Investigations (UK SMIs) are developed under the auspices of UKHSA working in partnership with the partner organisations whose logos are displayed below and listed on the UK SMI website. UK SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee.

The contributions of many individuals in clinical, specialist and reference laboratories who have provided information and comments during the development of this document are acknowledged. We are grateful to the medical editors for editing the medical content.

UK SMIs are produced in association with:

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Contents

Amendment table

Each UK SMI document has an individual record of amendments. The amendments are listed on this page. The amendment history is available from standards@ukhsa.gov.uk.

Any alterations to this document should be controlled in accordance with the local document control process.

Amendment number/date	1/24.04.25
Issue number discarded	1
Insert issue number	1.1
Section(s) involved	**Amendment**
Whole document.	**This is an administrative point change.** **The content of this UK SMI document has not changed.** **The last scientific and clinical review was conducted on 07.05.2014.** Hyperlinks throughout document updated to Royal College of Pathologists website. Public Health England replaced with UK Health Security Agency throughout the document, including the updated Royal Coat of Arms Partner organisation logos updated. Broken links to devolved administrations replaced. References to NICE accreditation removed. Scope and Purpose replaced with General and Scientific information to align with current UK SMI template.
Section 10: Public health responsibilities of diagnostic laboratories	This section has been added to UK SMI templates to highlight the public health responsibilities that diagnostic laboratories have as part of their duties.

Amendment No/Date.	-/07.05.14
Issue no. discarded.	-
Insert Issue no.	1
Section(s) involved	**Amendment**

1 General information

View general information related to UK SMIs.

2 Scientific information

View scientific information related to UK SMIs.

3 Scope of document

Meningoencephalitis:

The intended scope of this document is to describe which infections, and relevant associated tests, should be considered according to the different clinical presentations of meningoencephalitis. UK SMI B 27 - Investigation of Cerebrospinal Fluid and G 4 - Viral Encephalitis and Meningitis should be referred to for further information.

The syndromes included in this SMI have been selected to reflect the common presenting complaints of patients with meningoencephalitis. Patients who are immunocompromised may have atypical clinical features due to an altered immune response or disseminated infection.

The target organisms for bacterial meningitis include:

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Haemophilus influenzae*
- *Escherichia coli*
- *Listeria monocytogenes*
- Group B Streptococcus

The target organisms for viral meningitis and encephalitis include:

- Herpes Simplex Virus
- Varicella Zoster Virus
- Enteroviruses
- Parechovirus – only in those under three years of age

Meningitis is defined as inflammation of the meninges. This process may be acute or chronic and may result from infective or non-infective stimuli. A wide range ofinfective agents have been shown to cause meningitis, including viruses, bacteria, fungi and parasites.

Encephalitis is part of the spectrum of inflammatory diseases of the central nervous system, characterised by evidence of an inflammatory process involving brain parenchyma.

Encephalitis has over 100 causes, including viral infections (the majority), infection associated with other microorganisms and immune-mediated conditions (including post-infectious inflammatory processes). The time course of disease may be acute (most viral encephalitis), sub-acute, or chronic. Viral encephalitis is usually acute and is often associated with some elements of meningitis (ie meningoencephalitis), although neck stiffness occurs in less than one in three cases[1,2].

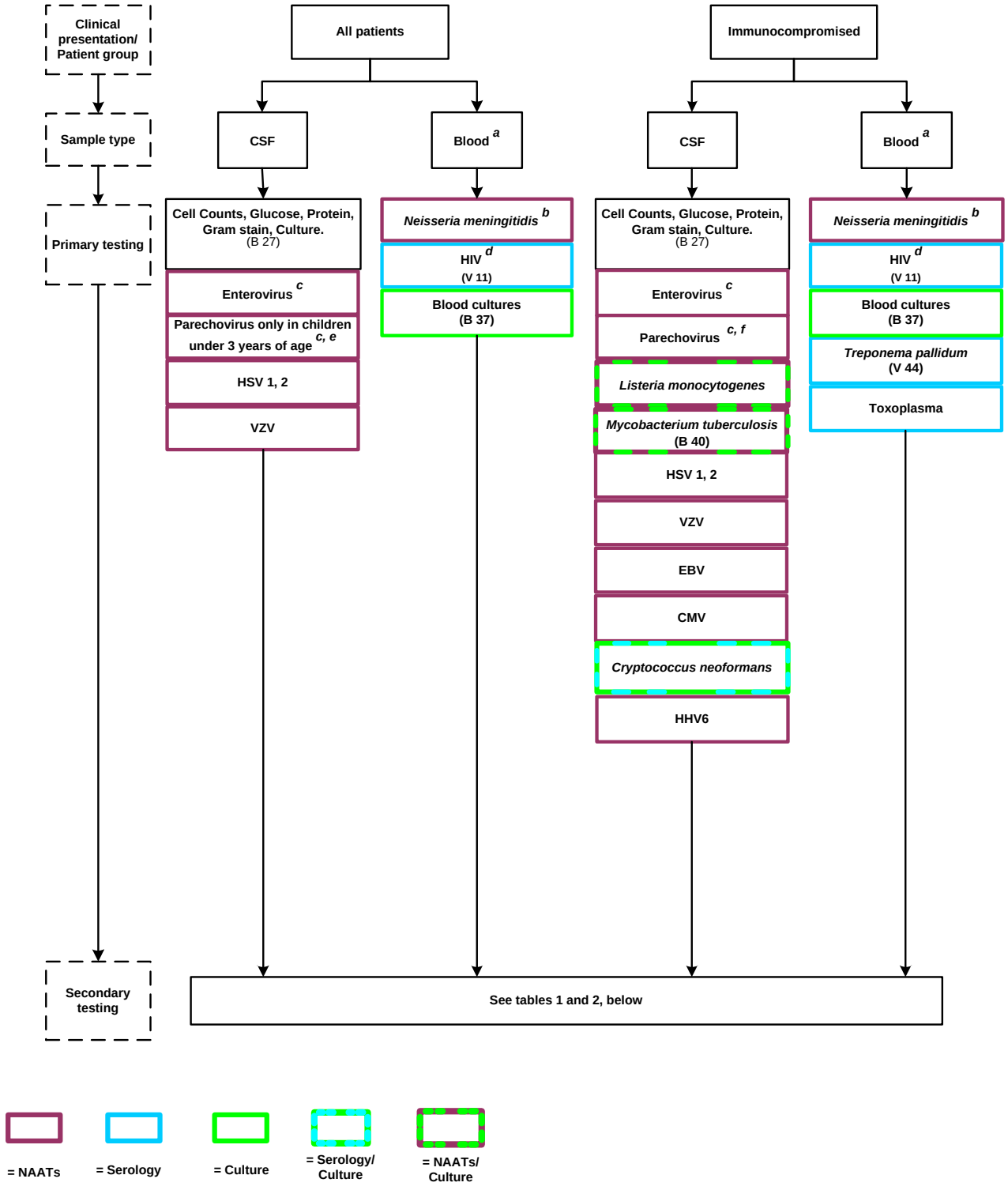
Most studies report that the aetiology of encephalitis is unclear in at least 40% of cases. AUK wide study on the Aetiology of Encephalitis found an infectious cause in 42% of cases most commonly herpes simplex virus (19%), varicella zoster virus (5%) and *Mycobacterium tuberculosis* (5%)[2]. A further 21% of cases had acute immune-mediated encephalitis, and 37% were of unknown aetiology[2]. Arboviruses and rabies, are common causes of meningoencephalitis in some parts of the world.

A useful case definition for encephalitis is encephalopathy (altered level of consciousness, cognition, behaviour or personality persisting for more than 24 hours) and two or more of the following[2]:

- Fever or history of fever (≥38°C)
- Seizures and/or focal neurological findings
- CSF pleocytosis (>4 WBC/µL)
- EEG findings compatible with encephalitis
- Abnormal results of neuroimaging (with evidence of brain parenchyma involvement)[2]

Most have fever, headache and changes to behaviour or level of consciousness. Prognosis may depend on early initiation of appropriate treatment and thus the importance of making an aetiological diagnosis cannot be overemphasized. A systematic approach should be followed for initial investigation, although clinical features, season and travel history are vital for formulating the differential diagnosis.

4 Meningoencephalitis[1-8]



To view associated SMI documents please access from:
https://www.rcpath.org/profession/publications/standards-for-microbiology-investigations.html

Footnotes

a) A blood sample taken at the same time as the CSF can be helpful when interpreting the NAAT test results of CSF contaminated with blood.

b) This should be done for suspected meningitis[9,10].

c) Throat swabs and faeces are additional, appropriate, sample types for diagnosis of enteroviruses. Detection of virus in these samples is suggestive, but not diagnostic, of the cause of illness.

d) HIV testing is recommended for all adults with meningoencephalitis. Consult guidelines for advice on testing children. In all cases a risk assessment and consideration of other features should be made[11].

e) Prevalence suggests testing under the age of 3 in the immunocompetent. Testing outside of this age is not recommended. This test is not freely available in all laboratories and this may cause delay in the results[12,13].

f) Immunocompromised patients can present with a wider range of pathogens, in this context HPeV should be considered in all age groups.

Table 1: Secondary testing to be considered for all patients (dependent on epidemiological factors and clinical findings)

Bacteria	**Test**
Bartonella henselae	Serology
Brucellosis	Serology, NAAT
Chlamydophila species	Serology, NAAT
Coxiella burnetii (Q fever)	Serology
Cryptococcus neoformans	Antigen detection, culture, microscopy
Leptospirosis	Serology, NAAT
Listeria monocytogenes	Blood culture, NAAT
Borrelia species	Serology
Mycobacterium tuberculosis	Microscopy, Culture, NAAT
Mycoplasma species	Serology, NAAT
Neisseria meningitidis	NAAT
Streptococcus pneumoniae	NAAT
Treponema pallidum	Serology, NAAT
Whipple's disease	NAAT
Unknown bacterial pathogen	16S PCR
Viruses	**Test**
Adenovirus	NAAT
CMV	NAAT
EBV	NAAT
Human Parvovirus B19	Serology, NAAT
Flaviviruses	Serology, NAAT
HHV6*	NAAT
HHV7*	NAAT
Influenza	NAAT
Lymphocytic choriomeningitis	Serology
Measles	Serology, NAAT
Mumps	Serology, NAAT
Rotavirus*	NAAT

Other	Test
Amoebae	Microscopy
Aspergillus species	Microscopy, galactomannan, NAAT
Antibody-associated encephalitis	Immunology

*Should be considered in children under three years of age.

Table 2: Additional testing to consider for returning travellers

Advice should be sought from a regional or national specialist in infectious disease for other possible causes of meningoencephalitis.

For more information regarding possible causes of encephalitis from foreign travel see the British Infection Association Guidelines.

See the European Federation of Neurological Societies.

Pathogen	Test(s)
Japanese encephalitis virus (Flavivirus)	Serology, NAAT
West Nile virus (Flavivirus)	Serology, NAAT
Tick-borne encephalitis virus (Flavivirus)	Serology, NAAT
Murray Valley encephalitis virus (Flavivirus)	Serology, NAAT
St Louis encephalitis virus (Flavivirus)	Serology, NAAT
Eastern, Western and Venezuelan equine encephalitis virus (Alphavirus)	Serology, NAAT
Chikungunya virus (Alphavirus)	Serology, NAAT
La Crosse virus (Bunyavirus)	Serology, NAAT
Colarado tick fever virus (Coltivirus)	Serology, NAAT
Nipah virus (paramyxovirus)	Serology, NAAT
Hendra virus (paramyxovirus)	Serology, NAAT
Rabies, Lyssavirus (Rhabdoviruses)	Serology, NAAT
Eosinophilic meningitis – angiostrongyliasis, gnathostomiasis, other parasites	Microscopy, Serology
Trypanosoma species	Microscopy, Antigen detection
Dimorphic fungi including *Coccidioides* species and*Histoplasma* species	Serology, Culture, Antigen detection
Rickettsia species	Serology, NAAT
Ehrlichia and Anaplasma	Serology

5 Notification to UKHSA [14,15] or Equivalent in the Devolved Administrations[16-19]

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify UK Health Security Agency (UKHSA) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days.

For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local UKHSA Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to UKHSA. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to UKHSA and many UKHSA Health protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

Note: The Health Protection Legislation Guidance (2010) includes reporting of Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCAIs) and Creutzfeldt–Jakob disease (CJD) under ‘Notification Duties of Registered Medical Practitioners’: it is not noted under ‘Notification Duties of Diagnostic Laboratories’.

https://www.gov.uk/guidance/specialist-and-reference-microbiology-laboratory-tests-and-services

Other arrangements exist in Scotland[16,20], Wales[18] and Northern Ireland[19].

6 Public health responsibilities of diagnostic laboratories

Diagnostic laboratories have public health responsibility as part of their duties. Amongst these are additional local testing, or referral to further characterise the organism as required, primarily for public health purposes e.g. routine cryptosporidium detection; serotyping or microbial subtyping; and a duty to refer appropriate specimens and isolates of public health importance to a reference laboratory.

Diagnostic laboratory outputs inform public health intervention, and surveillance data is required to develop policy and guidance forming an essential component of healthcare. It is recognised that additional testing and referral of samples may entail some costs that has to be borne by the laboratory but in certain jurisdictions these costs are covered centrally.

Diagnostic laboratories should be mindful of the impact of laboratory investigations on public health and consider requests from the reference laboratories for specimen referral or enhanced information.

References

An explanation of the reference assessment used is available in the scientific information section on the UK SMI website.

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