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NICE accredited
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"NICE has renewed accreditation of the process used by **Public Health England (PHE)** to produce **UK Standards for Microbiology Investigations**. The renewed accreditation is valid until **30 June 2021** and applies to guidance produced using the processes described in **UK standards for microbiology investigations (UKSMIs) Development process, S9365', 2016**. The original accreditation term began in **July 2011.**"

Amendment table

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

New or revised documents should be controlled within the laboratory in accordance with the local quality management system.

Amendment number/date	8/18.01.19
Issue number discarded	5
Insert issue number	6
Anticipated next review date*	18.01.22
Section(s) involved	**Amendment**
Whole document.	The whole document has been reformatted to a new more interactive and comprehensive template. All the background, technical, scientific and legal information has been moved to two separate documents: General information and Scientific information that can be accessed from this document via hyperlink.
Footnote.	Updated footnotes to include new references. Defined children age: under 4 years.
Table.	The sentence: “Note: ‘recent infection’ covers infection in the last 2-4 weeks.” Was removed from the reporting table as it is not of any relevance to the context. Table was renamed to “Interpreting and reporting laboratory results”.

*Reviews can be extended up to five years subject to resources available.

1. General information

View general information related to UK SMIs.

2. Scientific information

View scientific information related to UK SMIs.

3. Scope of document

The algorithm considers the interpretation of common Epstein-Barr virus (EBV) serology profiles arising from investigation of acute EBV infection and not those arising from investigation of malaise or persistent lymphadenopathy. Although EBV-specific serology is preferable, properly conducted heterophile antibody tests (eg Paul-Bunnell, Monospot) remain acceptable in appropriate clinical circumstances as described below. EBV IgG avidity testing may be helpful in distinguishing acute and past infections[1, 2].

Refer to Q 7 - Good practice when undertaking serology assays for infectious diseases for information regarding good laboratory practice in serological testing.

This UK SMI should be used in conjunction with other UK SMIs.

4. Safety considerations

The guidance should be supplemented with local COSHH and risk assessments. Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

5. Specimen processing and procedure

5.1 Specimen type

Serum, plasma or refer to manufacturer's guidelines.

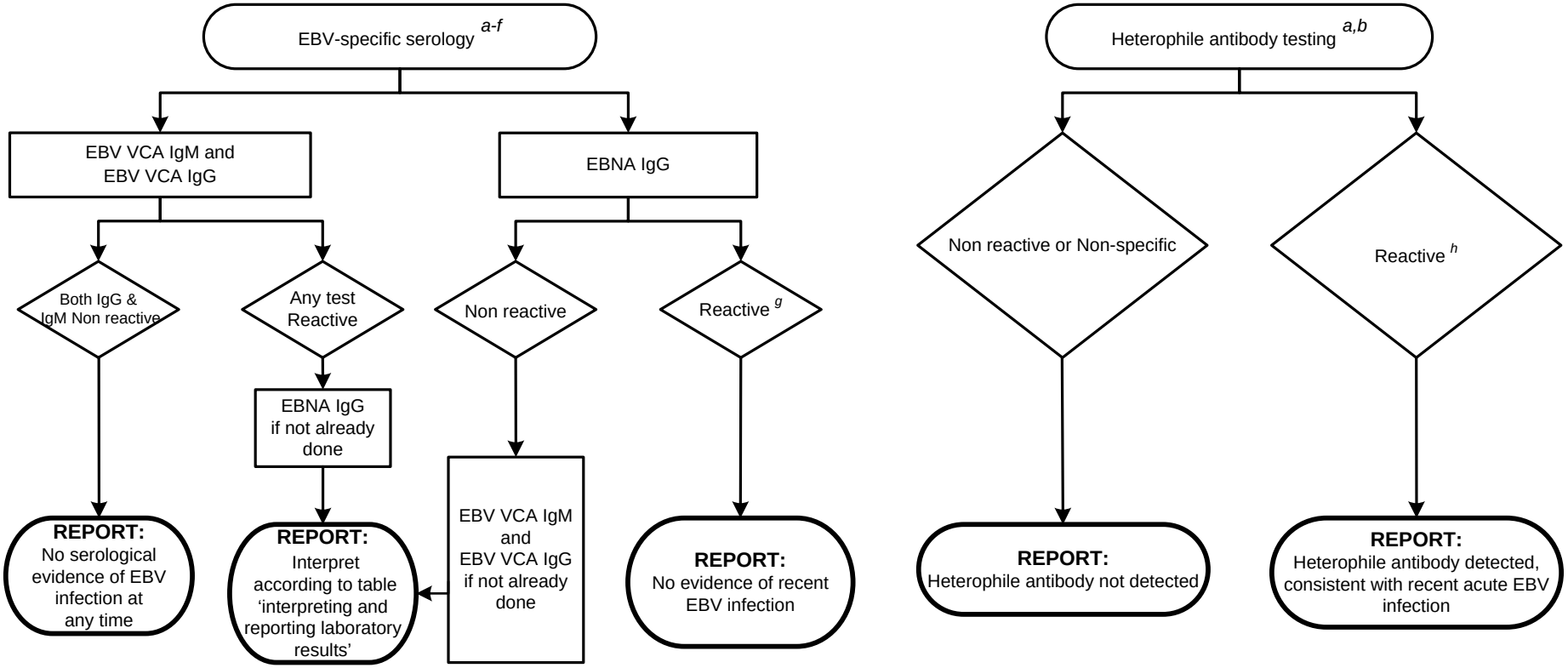
5.2 Specimen transport and storage conditions

Specimens should be collected in appropriate CE marked leak proof containers and transport in sealed plastic bag.

Specimens should be transported and processed according to manufacturer’s instructions or local validation data[3].

Samples should be retained in accordance with The Royal College of Pathologists guidelines ‘The retention and storage of pathological records and specimens’[4].

6. Investigation: Laboratory diagnosis of acute EBV infection[1,5-11]



Footnotes

a) Some laboratories choose not to routinely test patients above a specific age as the positive predictive value of any test set will be low for diagnosis of acute infection.

b) Although EBV-specific serology is preferable, properly conducted heterophile antibody tests (eg Paul-Bunnell, Monospot) remain acceptable in appropriate clinical circumstances[10]. Heterophile antibody tests are not appropriate for testing children under the age of 4 and immunocompromised individuals due to a high false negative rate[10]. False positives are uncommon but have been described in rheumatoid disease, SLE, leukaemia, lymphoma, infections including malaria, HIV, CMV, rubella, viral hepatitis and tularaemia, and after administration of anti-thymocyte globulin[10].

c) Two different approaches to initial screening for EBV are in common use; either initial anti-EBNA-1 or initial VCA (IgG and IgM) testing are equally valid if appropriate algorithms are followed and due care is given to interpretation of results. Anti-EBNA-1 usually appears after 3-4 weeks from onset of illness and appears in 95% or more of individuals; but may not be present in the immunocompromised individuals or in chronic EBV infections[7]. Some laboratories use antibody to early antigen (diffuse) as an additional test in diagnosis of acute infection[7].

d) EBV DNA PCR must be used to investigate primary or reactivated EBV infection in patients who are immunocompromised and at risk of severe disease as serological tests may be unreliable in the immunocompromised patients[9].

e) EBV DNA PCR on whole blood (EDTA) or plasma may be useful as a confirmatory assay where antibody test results are inconclusive.

f) EBV IgG avidity testing may be helpful in distinguishing acute and past infections[1,2].

g) Interpret with caution as in a small number of cases EBNA IgG may be detectable early - by immunofluorescent antibody testing as early as ten days after the onset of illness in <5%[8].

h) If haematological parameters are consistent with acute EBV infection, regard as confirmed. If haematological parameters are not consistent with acute EBV infection or are not available, regard as unconfirmed and consider doing confirmatory specific EBV serology[11].

7. Interpreting and reporting laboratory results

There are other combinations of results which have not been tabled but which do occur and require individual comments based upon profile and clinical setting, along with a further sample.

	VCA IgM	VCA IgG	EBNA IgG	Interpretative Comment	Notes
1	Not detected	Not detected	Not detected	No serological evidence of EBV infection at any time.	Re-test if recent onset of illness. Consider testing for HIV[12].
2	Not detected	Detected	Detected	Consistent with past EBV infection. Consider testing for HIV if at risk[12].	
3	Detected	Detected	Not detected	Consistent with recent acute EBV infection	Consider possibility of false negative anti-EBNA-1 when reporting.
4	Detected	Not detected	Not detected	Consistent with but not diagnostic of early acute EBV infection. Repeat to confirm in 4-6 weeks.	IgM result may be false, repeat to clarify. EBV DNA PCR may be useful in this situation.
5	Not detected	Detected	Not detected	The EBV serological profile may reflect distant past infection, however recent infection cannot be excluded. Repeat in 4-6 weeks if recent EBV infection is suspected.	Consider EBV PCR and heterophile antibody testing[6,7]
6	Detected	Detected	Detected	Evidence of EBV infection at some time, but this profile is difficult to interpret. Although the IgM reactivity might be false, late primary infection or recent EBV reactivation cannot be excluded.	Some laboratories may be able to establish a cut off for IgM below which most results are false, and can be reported as such, if EBV VCA IgG and anti-EBNA-1 IgG are positive. Unrelated acute infection can result in the non-specific polyclonal activation of memory cells and the release of VCA IgM. Consider testing for CMV IgM, Parvovirus IgM, HAV IgM and HIV[6,7]. EBV PCR and heterophile antibody testing may be helpful. Review in light of clinical details, and the numerical values of the test results and consider repeat to clarify.

References

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