

NATIONAL STANDARD METHOD

EPSTEIN-BARR VIRUS SEROLOGY

VSOP 26

Issued by Standards Unit, Evaluations and Standards Laboratory
Centre for Infections



UK Clinical Virology Network



Association of Medical Microbiologists
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STATUS OF NATIONAL STANDARD METHODS

National Standard Methods, which include standard operating procedures (SOPs), algorithms and guidance notes, promote high quality practices and help to assure the comparability of diagnostic information obtained in different laboratories. This in turn facilitates standardisation of surveillance underpinned by research, development and audit and promotes public health and patient confidence in their healthcare services. The methods are well referenced and represent a good minimum standard for clinical and public health microbiology. However, in using National Standard Methods, laboratories should take account of local requirements and may need to undertake additional investigations. The methods also provide a reference point for method development.

National Standard Methods are developed, reviewed and updated through an open and wide consultation process where the views of all participants are considered and the resulting documents reflect the majority agreement of contributors.

Representatives of several professional organisations, including those whose logos appear on the front cover, are members of the working groups which develop National Standard Methods. Inclusion of an organisation's logo on the front cover implies support for the objectives and process of preparing standard methods. The representatives participate in the development of the National Standard Methods but their views are not necessarily those of the entire organisation of which they are a member. The current list of participating organisations can be obtained by emailing standards@hpa.org.uk.

The performance of standard methods depends on the quality of reagents, equipment, commercial and in-house test procedures. Laboratories should ensure that these have been validated and shown to be fit for purpose. Internal and external quality assurance procedures should also be in place.

Whereas every care has been taken in the preparation of this publication, the Health Protection Agency or any supporting organisation cannot be responsible for the accuracy of any statement or representation made or the consequences arising from the use of or alteration to any information contained in it. These procedures are intended solely as a general resource for practising professionals in the field, operating in the UK, and specialist advice should be obtained where necessary. If you make any changes to this publication, it must be made clear where changes have been made to the original document. The Health Protection Agency (HPA) should at all times be acknowledged.

The HPA is an independent organisation dedicated to protecting people's health. It brings together the expertise formerly in a number of official organisations. More information about the HPA can be found at www.hpa.org.uk.

The HPA aims to be a fully Caldicott compliant organisation. It seeks to take every possible precaution to prevent unauthorised disclosure of patient details and to ensure that patient-related records are kept under secure conditions¹.

More details can be found on the website at www.evaluations-standards.org.uk. Contributions to the development of the documents can be made by contacting standards@hpa.org.uk.

Please note the references are now formatted using Reference Manager software. If you alter or delete text without Reference Manager installed on your computer, the references will not be updated automatically.

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AMENDMENT PROCEDURE

Controlled document reference	VSOP 26
Controlled document title	Epstein-Barr virus serology

Each National Standard Method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from standards@hpa.org.uk.

On issue of revised or new pages each controlled document should be updated by the copyholder in the laboratory.

Amendment Number/ Date	Issue no. Discarded	Insert Issue no.	Page	Section(s) involved	Amendment
3/ 05.03.08	2.1	3	All	All	This document was formerly known as VSOP 6.2 - Hepatitis, jaundice and abnormal LFTs. This document has been separated for better understanding, renamed and labelled VSOP 26 – Epstein-Barr virus serology
			Front page	Front page	Northern Ireland logo added
			All	All	Hyperlinks to relevant NSMs inserted
			5	Algorithm	Revised and improved
			6	Table for serological profiles	Added

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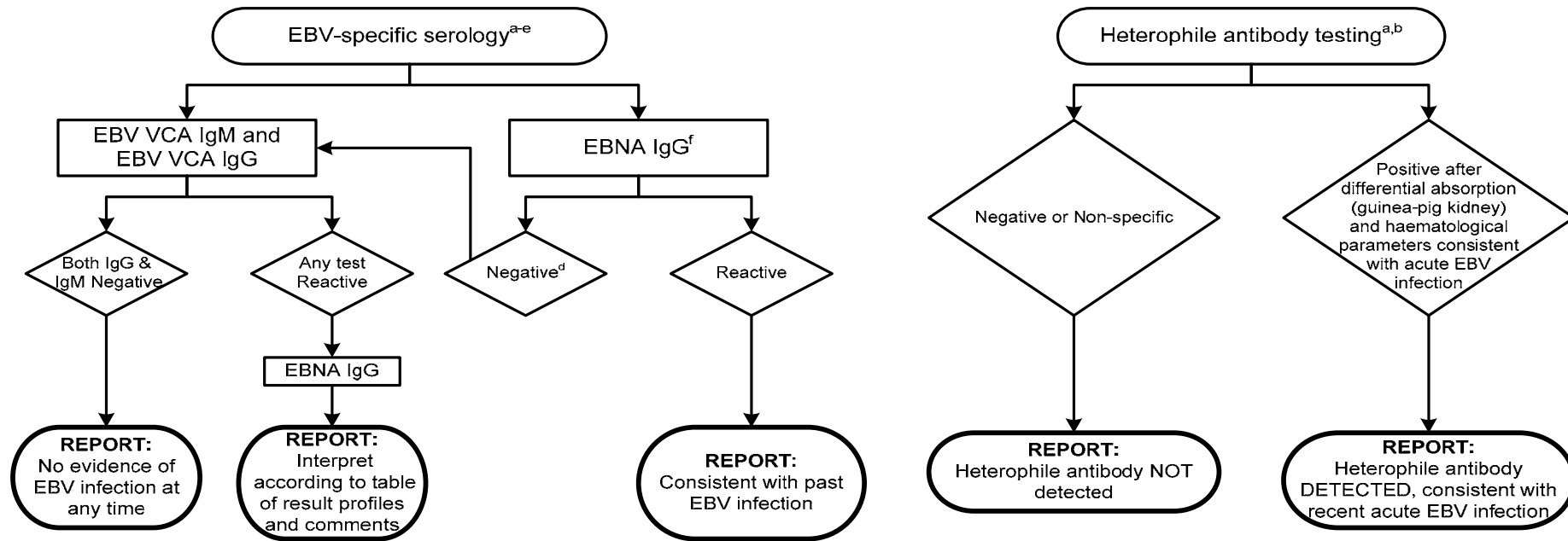
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COMMON EPSTEIN-BARR VIRUS (EBV) SEROLOGY PROFILES - FOR LABORATORY DIAGNOSIS OF ACUTE EBV INFECTION^{2,3}

(See [VSOP 6 - Hepatitis, jaundice and abnormal LFTs](#))



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- ^a Some laboratories choose not to test patients above a specific age as predictive IgG will be low.
- ^b Although EBV-specific serology is preferable properly conducted heterophile antibody tests (eg Paul-Bunnell, Monospot) remain acceptable in appropriate clinical circumstances. Heterophile antibody tests are not appropriate for testing children and immunocompromised individuals (high false negative rate). False positives are uncommon but have been described in situations including rheumatoid disease, Hodgkins disease, tularaemia, and administration of anti-thymocyte globulin.
- ^c Two different approaches to initial screening for EBV are in common use; either initial anti-EBNA 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 can sometimes appear early.
- ^d EBV DNA PCR must be undertaken when assessing patients who are immunocompromised for primary or reactivated EBV infection, as serological tests may be unreliable in the immunocompromised.
- ^e EBV DNA PCR on whole blood (EDTA) or plasma may be useful as a confirmatory assay where antibody test results are inconclusive. EBV DNA PCR is also useful in assessing reactivation of EBV.
- ^f Interpret with caution as EBNA IgG may appear early.

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COMMON EBV SEROLOGICAL PROFILES AND SUGGESTIONS FOR REPORT COMMENTS

VCA IgM	VCA IgG	EBNA IgG	Interpretative Comment
Neg	Neg	Neg	No serological evidence of EBV infection at any time. Re-test if recent onset of illness.
Neg	Pos	Pos	Evidence of past EBV infection (>8 weeks ago).
Pos	Pos	Neg	Consistent with recent acute EBV infection. (consider possibility of false negative anti-EBNA when reporting.)
Pos	Neg	Neg	Consistent with but not diagnostic of early acute EBV infection. As IgM result may be false repeat to clarify in 2-6 weeks. (BV DNA PCR may be useful in this situation).
Neg	Pos	Neg	Consistent with fairly recent or past EBV infection. As no anti-EBNA IgG antibody is detectable, please repeat in 4-6 weeks to clarify.
Pos	Pos	Pos	EBV infection at some time, but these results are difficult to interpret. Although the IgM may be a false positive result, late primary infection or recent EBV reactivation cannot be excluded. Repeat to clarify. 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 IgG are positive. Consider testing for 'cross-reactive' or polyclonal IgM especially CMV IgM and Parvovirus B19 IgM. Testing for EBV,CMV and parvovirus DNA may be required.

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This National Standard Method was initiated and developed by the National Standards Working Group for Clinical Virology (http://www.hpa-standardmethods.org.uk/wg_virology.asp). The contributions of many individuals in clinical virology laboratories and specialist organisations who have provided information and comment during the development of this document, and final editing by the Medical Editor are acknowledged.

The National Standard Methods are issued by Standards Unit, Evaluations and Standards Laboratory, Centre for Infections, Health Protection Agency, London.

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2. Chapter 14. In: Lennette E.H. SN, editor. Diagnostic procedures for viral and rickettsial diseases. 5th ed. Washington: APHA; 1979.
3. Prevalence of primary versus reactivated Epstein-Barr virus infection in patients with VCA IgG-, VCA IgM- and EBNA-1 antibodies and suspected infectious mononucleosis. 2007. p. 292-7

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