Epstein Barr Virus (EBV) Testing for Infectious Mononucleosis

New EBV screening Protocol

From 6\textsuperscript{th} July 2015 we intend to initially screen requests for EBV infection by measuring EBNA IgG antibodies on the Abbott Architect platform.

This serological marker is detected from 3-4 months after the initial infection and usually persists for the rest of the patient’s life. It is thus a marker of past infection.

• If the EBNA IgG assay is positive, the result will be reported with a comment stating that the patient has had past EBV infection.

• If the EBNA IgG assay is negative, we will then proceed to measure the other markers of EBV infection, VCA IgM and VCA IgG, and report accordingly.

\textit{(EBNA= Epstein Barr Nuclear Antigen, VCA=Viral Capsid Antigen)}

The graph below shows the “natural history” of these three antibodies following EBV infection.

The majority of patients that are tested for EBV turn out to have had past infection. In a recent audit, almost 90\% of all tested patients over the age of 30 showed evidence of past EBV infection. The new algorithm which will be adopted is very effective at selecting only those that have no evidence of previous EBV infection and thus require further testing. It also brings us into line with the majority of other laboratories in New Zealand who also perform initial EBV screening with EBNA IgG.
**EBV Serology Interpretation Chart**

<table>
<thead>
<tr>
<th>VCA IgM</th>
<th>VCA IgG</th>
<th>EBNA IgG</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Past EBV infection</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Primary acute EBV infection</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Recent EBV infection</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>No evidence of past or present EBV infection.</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>-</td>
<td>* EBV infection at some point in the past</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>** Possible EBV reactivation</td>
</tr>
</tbody>
</table>

*A small percentage of people do not produce EBNA IgG antibodies. Therefore for this particular serological picture it is impossible to be sure whether infection has been in the recent or distant past.

** Reactivation is rare in immunocompetent individuals and is generally considered of no clinical relevance. If reactivation of EBV is being queried on immunocompetent individuals please indicate this on the request form so that VCA IgM and IgG can be performed regardless of the EBNA IgG result.*

Reactivation is a more serious problem in severely immunocompromised patients. Such patients may not produce sufficient levels of antibodies to allow accurate diagnosis by serological testing. Please contact the Clinical Microbiologist to discuss the most clinically appropriate testing for these individuals.

**Review of Previous Results**

In addition to the above, when a request for EBV serology is received, we plan to review all previous EBV serology results on the patient. If there is a history of positive VCA IgG or EBNA IgG antibodies from prior testing then a report will go out stating that the current sample has not been tested as the patient has a past history of EBV infection.

The only exception to this would be if EBV reactivation is being considered and is documented on the request form.
Monospot Testing Changes

Monospot testing is an alternative method of laboratory testing for Infectious Mononucleosis. It utilises the ability of heterophile antibodies produced in response to EBV infection to agglutinate horse red blood cells. “Paul Bunnell testing” and “Heterophile antibodies” are other ways of making such a test request.

It has a sensitivity of approximately 80%, except in young children, who have reduced ability to produce heterophile antibodies.

It has little additional value over EBV serological testing using EBNA, VCA IgM & IgG antibodies.

The following changes will be put in place regarding Monospot testing:

1) A request for “Monospot”, “Paul Bunnell testing” or “Heterophile antibodies” will not be performed if EBV serology has also been requested on the same request form.

2) A request for “Monospot”, “Paul Bunnell testing” or “Heterophile antibodies” will not be performed in children under the age of 6, due to poor sensitivity in this cohort. Please request EBV serology for these patients.

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