Discontinuation of Herpes Simplex virus (HSV) IgM Testing

Presenter:
Elitza S. Theel, Ph.D., D(ABMM)
Director, Infectious Diseases Serology Laboratory
Co-Director, Vector-Borne Diseases Service Line

Department of Laboratory Medicine and Pathology
at Mayo Clinic, Rochester, Minnesota
Disclosures

• None

Herpes Simplex Virus Types 1 and 2: The facts and stats

• HSV-1 and HSV-2 are common, lifelong infections

• 2015-2016 NHANES seroprevalence data:
  • HSV-1: 47.8%
  • HSV-2: 11.9%

• Primary infection/secondary reactivation typically manifest with painful blisters or sores at the site of infection

• Transmission occurs through direct contact with a lesion, mucosal surface or genital/oral secretions
  • HSV-1: typically orolabial
  • HSV-2: mostly genital
Diagnostic Assays for Detection of HSV-1/HSV-2

- Molecular assays for detection of HSV DNA (i.e., real-time PCR)
  - Swab of orolabial, anogenital or other mucocutaneous ulcers/lesions
  - Cerebrospinal fluid
  - Blood (e.g. neonatal HSV, etc.)
- Serology for detection of IgM and/or IgG-class antibodies to HSV
  - IgM becomes detectable ~10-21 days post-infection, with IgG developing around the same time
  - IgM persists for months following resolution and may or may not develop during recurrent infection, whereas IgG persist indefinitely
  - IgG assays, based on the HSV glycoprotein G (gG), are type-specific
  - IgM serologic assays do not distinguish between HSV-1 vs. HSV-2
    - IgM serology is NOT type-specific

HSV-1/-2 Serology Utilization Recommendations

- When/What to Use:
  - HSV type-specific IgG testing may be useful in the following scenarios:
    - Recurrent genital or atypical symptoms with negative HSV RT-PCR or culture
    - Clinical diagnosis of genital herpes without laboratory confirmation
    - Patients whose partner has genital herpes
    - Persons presenting for an STD evaluation, especially those with:
      - Multiple sex partners
      - Persons with HIV infection
      - MSM at increased risk for HIV acquisition
- When/What NOT to Use:
  - Screening of general population
  - Do not use HSV IgM tests
Recommended HSV-1/-2 Serology Utilization Rules

MMWR. Sexually Transmitted Diseases Treatment Guidelines, 2015

When/What NOT to Use:
- Screening of general population
- **Do not use HSV IgM tests**


A Guide to Utilization of the Microbiology Laboratory for Diagnosis
of Infectious Diseases: 2018 Update by the IDSA and the ASM

HSV serology is useful primarily for immunostatus and exposure status testing. IgM serology is no longer recommended.

HSV IgM Utilization at Mayo Clinic Laboratories (MCL)

- 3,390 to 6,500 HSV IgM orders/month (!!)
- Retrospective review of all HSV tests (RT-PCR and serology) ordered between May-July 2018 through MCL
- 22,683 total HSV tests
- 20% of all HSV-related testing includes HSV IgM serology
- HSV IgM serology associated with low (2.3%) positivity rate
- Among patients tested by both HSV RT-PCR and HSV IgM, ~50% were RT-PCR positive/HSV IgM negative

- **HSV IgM testing is overutilized** with questionable value added to patient care

Table 1. Positivity Rates for HSV1/2 RT-PCR and Serologic Testing (IgM and IgG) from May to July, 2018 at Mayo Clinic Laboratories

<table>
<thead>
<tr>
<th>HSV Test Ordered</th>
<th>Number of Tests Performed</th>
<th>Positivity Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT-PCR alone</td>
<td>0,990</td>
<td>HSV1: 15.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HSV2: 14.2%</td>
</tr>
<tr>
<td>IgM alone</td>
<td>4,584</td>
<td>2.3%</td>
</tr>
<tr>
<td>IgM and IgG</td>
<td>8,100</td>
<td>IgM only: 2.3%</td>
</tr>
<tr>
<td>Serologic Panel</td>
<td></td>
<td>HSV1 IgG only: 4.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HSV2 IgG only: 21.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HSV1 IgG and HSV2 IgG: 13.4%</td>
</tr>
<tr>
<td>IgM and RT-PCR</td>
<td>171</td>
<td>RT-PCR only: 49.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IgM only: 2.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RT-PCR and IgM: 4.7%</td>
</tr>
</tbody>
</table>

Serum and swab samples collected within 7 days of each other.
Discontinuation of HSV IgM Testing at MCL

• As of late October, 2019, HSV IgM testing will no longer be performed at MCL
• The following test codes will be discontinued:
  • HSV IgM (MHSV/87998)
  • HSV Types 1 and 2, IgM/IgG (HSV/84422)
    • Alternative: HSV Types 1 and 2 Ab, IgG (HSVG/84429)
  • ToRCH Profile IgM (TCHM/39858)
    • Alternatives:
      • Toxoplasma Ab, IgM (TXM/39856)
      • Cytomegalovirus Ab, IgM (CMVM/34971)

References


6. Jung, S. and Theel, E.S. *Overutilization of IgM Serologic Assays for Herpes Simplex Virus.* Accepted: *Journal of Applied Laboratory Medicine*
Thank you!