To Test or Not To Test: The Conundrum of Congenital Cytomegalovirus (cCMV) Screening in the Newborn Nursery

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Objective
To review the evidence related to cCMV hearing-targeted screening and to highlight the utility of screening in the newborn nursery.

Outline
• Congenital CMV background
• Pertinent Review of Recent Literature on Hearing Targeted Screening (HTS)
• Cost-effectiveness of hearing targeted screening vs universal screening
• Questions
Background

cCMV is most common non-genetic cause of congenital SNHL.

Average prevalence of 0.64-0.70%.

90% of infants will be asymptomatic, of which 10-15% will develop SNHL.


Vertical transmission of cCMV results in 90% of infants being asymptomatic, of which 10-15% will develop SNHL.

Manifestations of cCMV

- Microcephaly
- Ventriculomegaly
- Intracerebral calcifications
- Periventricular echogenicity
- Cortical/cerebellar malformations
- Chorioretinitis
- Sensorineural hearing loss
- Hepatomegaly
- Elevated LFTs
- Splenomegaly
- Thrombocytopenia
- IUGR


cCMV Hearing Loss

- Sensorineural
- Progressive and fluctuating
- Delayed onset
- Valganciclovir shown to improve hearing & developmental outcomes.
Congenital CMV PCR Tests

<table>
<thead>
<tr>
<th></th>
<th>Urine</th>
<th>Saliva</th>
<th>Dried Blood Spot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>100%</td>
<td>97%</td>
<td>34.4%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.1%</td>
<td>99%</td>
<td>99.9%</td>
</tr>
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</table>

*Positive saliva CMV tests must be confirmed with urine CMV PCR test within the first 3 weeks.

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Case

You are the director of a newborn nursery. One of your coworkers has heard of a few local institutions that have recently implemented hearing targeted screening and suggests that CMV targeted screening be implemented at your institution.

What would be your response?

A. Yes, let’s do it!
B. No, I would prefer universal screening
C. No, I don’t think we should screen at all
D. I don’t know/prefer not to respond at this time
Public Health Screening Criteria by Wilson & Jungner

1. Measures of magnitude of health problem
2. Availability of effective therapies
3. Expected benefits and harms from early detection & treatment
4. Perceived validity and cost of screening tests


Efficacy of Hearing Targeted Screening (CHIMES study)

~100,332 infants b/w 2007-2012 across 7 US medical centers received a newborn hearing screen (NHS) AND were screened for cCMV.

*43% of CMV positive infants with SNHL would have been missed with hearing targeted screening alone.

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### Take Away Points

- Newborns with cCMV have a significantly higher newborn hearing screen (NHS) referral rate than CMV negative infants.
- HTS misses cCMV+ infants who pass initial NHS but are at risk for late onset hearing loss.

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### Results from a Hearing-Targeted Cytomegalovirus Screening State Program

Screening protocol
1. Infants who fail both their inpatient AND return outpatient screening
2. Infants who fail first hearing screening if it occurs after age 14 days.

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Take Away Points

- Compliance suboptimal with outpatient testing.
  -- Associated with maternal education & location of infant’s birth.

- Expect 20-30 (out of 103,000 infants) with cCMV related hearing loss utilizing HTS.
  -- 6 identified with cCMV related hearing loss

Yale-New Haven Health System cCMV Targeted Screening Program

Screening protocol:
Infants who fail newborn hearing screen (inpatient) -> saliva CMV PCR -> if saliva positive, urine CMV PCR sent for confirmation
Results

Take Away Points

• Excellent compliance with inpatient testing.

• Anticipated 4-9 (out of ~10,000 infants) with cCMV related hearing loss utilizing HTS.
  – 1 infant identified with cCMV related hearing loss.

Is newborn screening for cCMV infection cost-effective?

• Estimated cost-effectiveness of universal and targeted cCMV screening

• Assumptions:
  – Prevalence of 0.5% of cCMV at birth
  – Referral rate of 1.5%; 10% with confirmed hearing loss
  – 12% reduction in costs due to earlier ID of hearing loss
Cost of Universal vs Targeted Screening

Cost to identify 1 case of cCMV hearing loss

<table>
<thead>
<tr>
<th>Cost</th>
<th>Universal Screening</th>
<th>Targeted Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>$166</td>
<td>$1,000</td>
<td>$27,460</td>
</tr>
<tr>
<td>$566</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cost to identify 1 case of cCMV

<table>
<thead>
<tr>
<th>Cost</th>
<th>Universal Screening</th>
<th>Targeted Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>$3,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$5,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$10,000</td>
<td></td>
<td></td>
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<tr>
<td>$15,000</td>
<td></td>
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<tr>
<td>$20,000</td>
<td></td>
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<tr>
<td>$25,000</td>
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<tr>
<td>$30,000</td>
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*Assumes $10/test


Net Cost/Savings Per Newborn Excluding Loss of Productivity Costs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Universal Screening</td>
<td>-$6.83</td>
</tr>
<tr>
<td>Targeted Screening</td>
<td>+$4.95</td>
</tr>
</tbody>
</table>

*Assumes screening test cost $10/newborn


Net Cost/Savings Per Newborn Including Loss of Productivity Costs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Universal Screening</td>
<td>+$37.97</td>
</tr>
<tr>
<td>Targeted Screening</td>
<td>+$27.31</td>
</tr>
</tbody>
</table>
Take away points

• Universal and targeted screening cost-effective when there is an effective anti-viral treatment and when loss of productivity costs included.

• Under assumption of no treatment, targeted screening is associated with a net cost ($2.01 vs $1.80) and involves testing fewer newborns.

<table>
<thead>
<tr>
<th>Wilson &amp; Jungner Screening Criteria</th>
<th>Yes</th>
<th>No</th>
<th>Nonconclusive or inconclusive</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The condition should be an important public health concern</td>
<td>✗</td>
<td>✔</td>
<td></td>
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<tr>
<td>2. There should be an accepted treatment for patients with recognized disease</td>
<td>✗</td>
<td>✔</td>
<td></td>
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<tr>
<td>3. Facilities for diagnosis and treatment should be available</td>
<td>✗</td>
<td>✔</td>
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<td>4. There should be a recognizable latent or early symptomatic stage</td>
<td>✗</td>
<td>✔</td>
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<tr>
<td>5. There should be a suitable test or examination</td>
<td>✗</td>
<td>✔</td>
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<td>6. The test should be acceptable to the population</td>
<td>✗</td>
<td>✔</td>
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<tr>
<td>7. The natural history of the condition, including development from latent to declared disease should be adequately understood</td>
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<td>✔</td>
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<tr>
<td>8. There should be an agreed policy on who to treat as patients</td>
<td>✗</td>
<td>✔</td>
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<tr>
<td>9. Total cost of finding a case should be economically balanced in relationship to medical expenditure as a whole</td>
<td>✗</td>
<td>✔</td>
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<tr>
<td>10. Case finding should be a continuous process, not a &quot;once and for all&quot; project</td>
<td>✗</td>
<td>✔</td>
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</tbody>
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Discussion

• More studies needed on psychosocial impact of screening; provider perspectives.

• Outcome of ValEAR trial

• Focus on cCMV education for families and providers.
References


Questions?