Washington State Department of Health

SCREENING FOR CONGENITAL CYTOMEGALOVIRUS

Washington State Board of Health

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Presenters

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Cytomegalovirus (CMV)

- Part of the herpes family
- Easily contracted through exchange of bodily fluids
  - Saliva, tears, blood, breast milk, etc.
- Symptoms can be mild to severe flu like symptoms
- 50 to 80% of adults have contracted CMV by the age of 40

Congenital CMV (cCMV)

If a pregnant person experiences CMV infection, she can pass it to her baby in utero

Factors that influence risk of transmission/severity of disease

- When in pregnancy it is passed to the baby
- Pregnant person's history of infection
  - Primary infection (more risk)
  - Pre-existing infection that is reactivated (less risk)
  - Individual is infected with a new strain of CMV(less risk)

Congenital CMV (cCMV)

1 in 200 babies are born with cCMV each year

Can have severe and life-threatening impacts on the infant

- Hearing loss
- Cerebral palsy
- Developmental delays
- Liver, lung, and spleen problems
- Vision loss
- Seizures
- Microcephaly
- Hyperbilirubinia

~10% are symptomatic at birth – 50% will develop disabilities

~90% asymptomatic – 10% will develop disabilities

Approaches for cCMV Screening

Targeted screening approach

- Test infants for cCMV when they do not pass their newborn hearing screening

Universal screening approach

- Use the newborn screening dried blood spot to test all infants for cCMV

Targeted cCMV Screening

Urine or saliva is collected from an infant after they do not pass their second newborn hearing screening

Polymerase chain reaction (PCR) test

Helps determine whether cCMV is the cause of a child's hearing loss

Must test for CMV within 21 days of life to determine if CMV infection is congenital

Targeted Screening Reliability

Polymerase chain reaction (PCR) of saliva or urine

- High sensitivity (>97%) and specificity (99%)
- Positive result should be confirmed with second sample (often urine)

Targeted screening lacks sensitivity

- Unable to identify infants with cCMV whose hearing loss develops later or have other impacts
- Approximately 10-15% of children with cCMV will have hearing loss
- Newborn hearing screening identified 57% of all CMV-related hearing loss that occurred in the neonatal period (Fowler et al. 2017)

Six states mandate targeted screening

- UT, IA, VA, NY, CT, IL

Newborn Hearing Screening Considerations

There is no mandate for hearing screening in Washington

Currently 27% of second hearing screenings occur after 21 days of life

- Average age of second screen = 22 days
- Median age of second screen = 15 days

Special considerations need to be made for infants with extended stays in the Neonatal Intensive Care Units (NICU)

Universal NBS for cCMV

Ontario Province

- Quantitative PCR (common method to amplify DNA)
- Multiplex with SCID testing

Universal NBS for cCMV

Ontario Province

5/2018 to 7/2019 – targeted approach

7/2019 onward – universal NBS for cCMV in blood spots

- ~200,000 babies screened
  - Positive rate: 0.14%
    - ~90% of positives were confirmed as cCMV
  - 3% clinically diagnosed (false negative NBS)

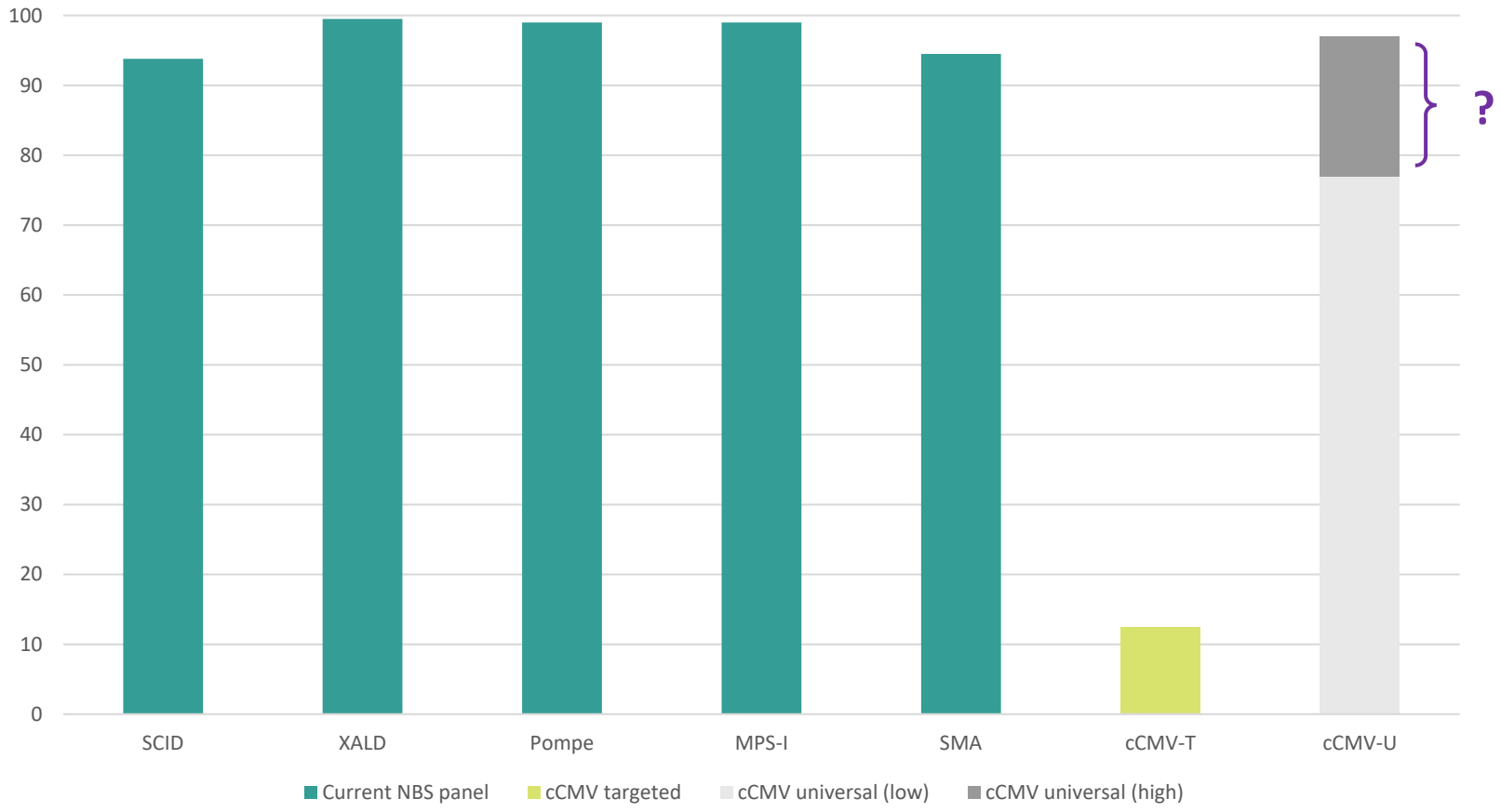
Universal NBS for cCMV

Ontario Province

- ~16% of babies with cCMV were symptomatic at diagnosis
  - Only 4% were clinically recognized
    - Remaining had non-specific or sub-clinical symptoms

- Prevalence: ~1:800 births
  - Why is prevalence lower than expected (1:167)?
    - Is the test not sensitive enough? – collaborating with MN
    - Is the prevalence of cCMV in Ontario lower than other populations?
      - Did COVID-19 lock-down in Ontario dramatically reduce the prevalence?

Comparison of NBS Test Sensitivities



Treatment Improves Outcomes

Audiologic monitoring

- Hearing evaluations every 3-6 months for the first three years of life and then annually until the child turns 18

Early intervention to reduce impact of hearing loss or other disabilities (e.g., physical therapy, occupational therapy, speech and language therapy)

Antiviral treatment

- Ganciclovir or Valganciclovir
  - Newborns with moderate to severe symptoms
  - 6-month course of treatment
  - Shown to modestly improve long-term hearing and developmental outcomes

Access to Diagnostic and Treatment Services

University of Washington, Seattle Children's Hospital, and independent national labs (like Quest and LabCorp) can do the PCR test for CMV

Pediatric audiology clinics statewide

Early intervention programs are available throughout Washington

- Administered through the Department of Children, Youth and Families (DCYF) Early Support for Infants and Toddlers (ESIT) Program
- Both cCMV and hearing loss are diagnoses that establish eligibility for services

Access to Treatment Services

All infants with cCMV should be referred to a pediatric infectious disease specialist, audiology, otolaryngology, and ophthalmology

Pediatric infectious disease physicians are located at:

- Seattle Children's Hospital, Seattle
- Mary Bridge Hospital, Tacoma
- Swedish Hospital, Seattle
- Providence Infectious Disease Clinic, Spokane

Unresolved Questions

- How effective are treatments at reducing mortality and morbidity?
- Screening test performance
  - Targeted approach – low sensitivity (10-15%)
  - Universal approach – limited data on blood spot test
    - one small study (MN)
    - one new program during pandemic (ON)
  - Saliva testing has highest sensitivity

Unresolved Questions

- How is diagnostic testing coordinated?
  - No “official” diagnostic test for cCMV
- What success have educational campaigns had in reducing cCMV?
- Is there capacity among audiologists to absorb the increased case load?
- Uncertainty of benefits for babies identified with cCMV
  - A small percentage will derive large benefits
  - Remainder will derive marginal or no benefits

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