



Congenital Cytomegalovirus: A Pilot Study

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Special Thanks

Centers for Disease Control and Prevention

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Objectives

- 1) Congenital cytomegalovirus (cCMV) basics
- 2) Minnesota CMV pilot study
- 3) CMV and newborn screening – the case for CMV
- 4) Questions



Cytomegalovirus (CMV) Basics

- It is the MOST common congenital viral infection in the USA
- Common cause of disability
- Infection rate is 0.6-0.7% of live births worldwide
- 15-20% of infected infants have permanent disability
- 6,000 children in the U.S. annually
- Low awareness – clinical impact mostly discussed with organ transplant recipients or HIV-infected individuals



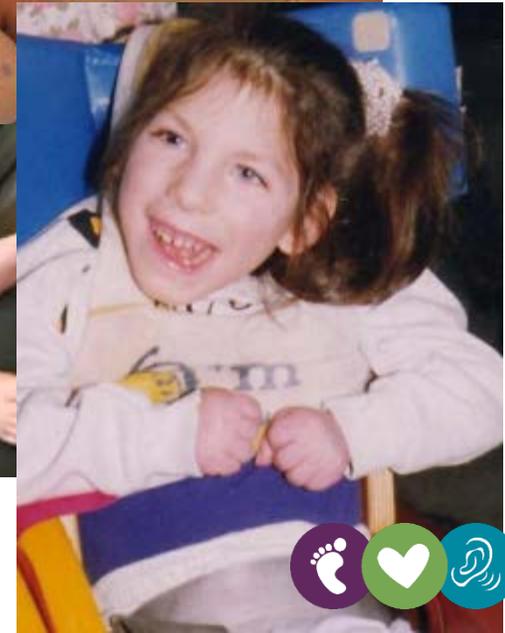
Congenital Cytomegalovirus (cCMV) Infections

- Most common cause of non-hereditary sensorineural hearing loss in children
- Three possible classifications for cCMV
 - Symptomatic – 10-15%
 - Asymptomatic with hearing loss (may or may not be present at birth) – 7-15%
 - Asymptomatic with no clinical concerns – 80%
- Can be treated with antiviral medication if identified early (ganciclovir and/or valganciclovir)
- Congenital vs acquired – distinguishable only within first 21 days of life



Impact of cCMV

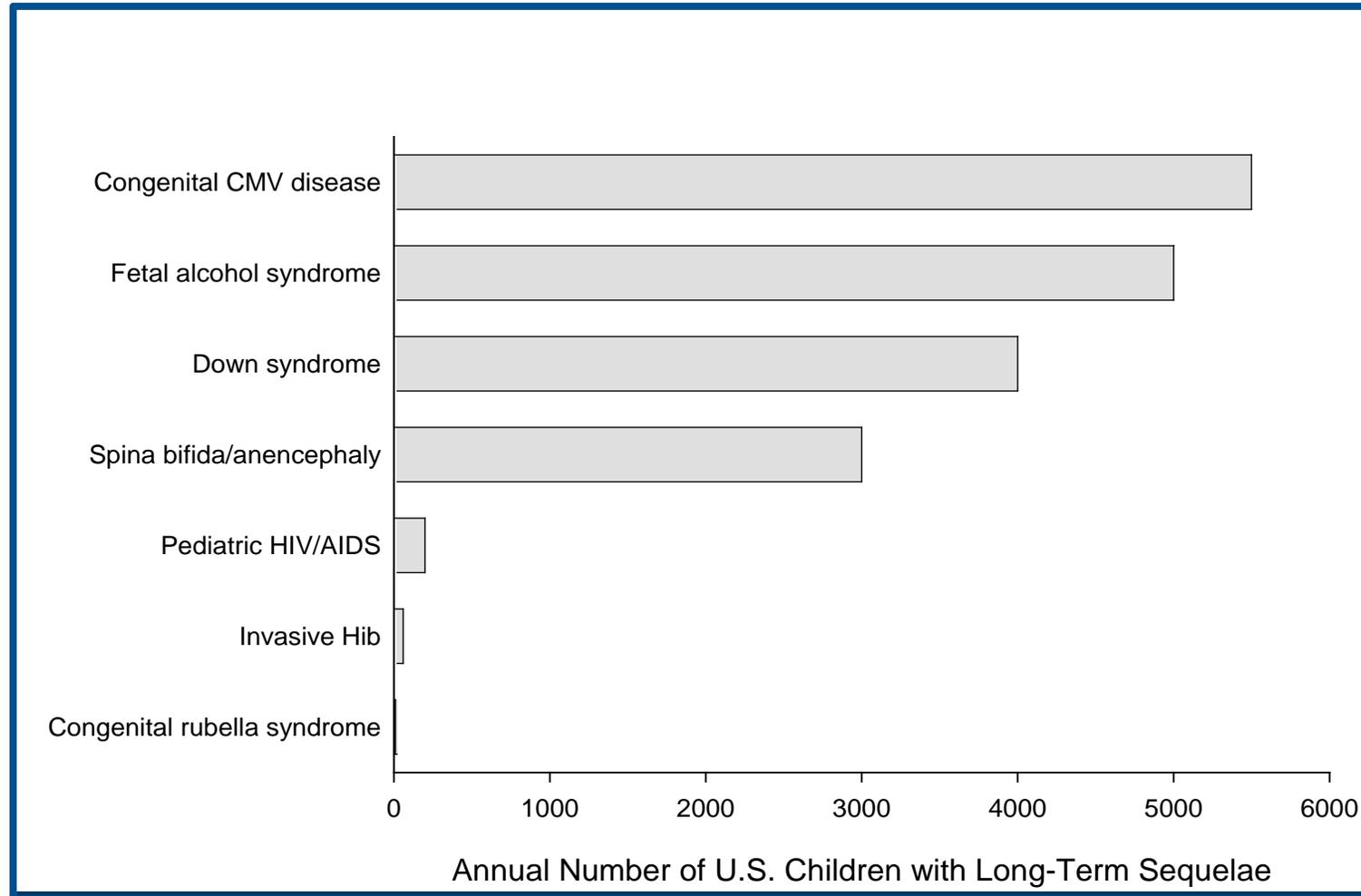
- Prenatal findings can include: echogenic bowel, IUGR, ventriculomegaly, thick placenta
- Newborns can show: prematurity, liver disease, petechiae, thrombocytopenia
- Symptomatic children can present with:
 - Criteria – 2 or more features with CNS involvement
 - Cognitive impairment/mental disability – 55-66%
 - Vision loss – 22-58%
 - Hearing loss – 30-50%
 - Microcephaly
 - Cerebral palsy
 - Seizures
 - Death



* Advocates have dubbed CMV the “birth defects virus”



Childhood Conditions



By the Numbers

Minnesota – birth rate of ~70,000 per year

*assume an infection rate of 1/200

~350 newborns **each year** are born infected



Symptomatic

35 infants



Asymptomatic
with hearing loss

35 infants



Asymptomatic

280 infants



Minnesota Study

- Funded through CDC's Emerging Infection Program (EIP) Cooperative Agreement
- Partnerships with:
 - CDC – Sheila Dollard, PhD,
 - UMN – Mark R. Schleiss, MD
 - Hospitals: Fairview Health (UMMC, Ridges, Southdale) & Allina Health (Abbott Northwestern & United)

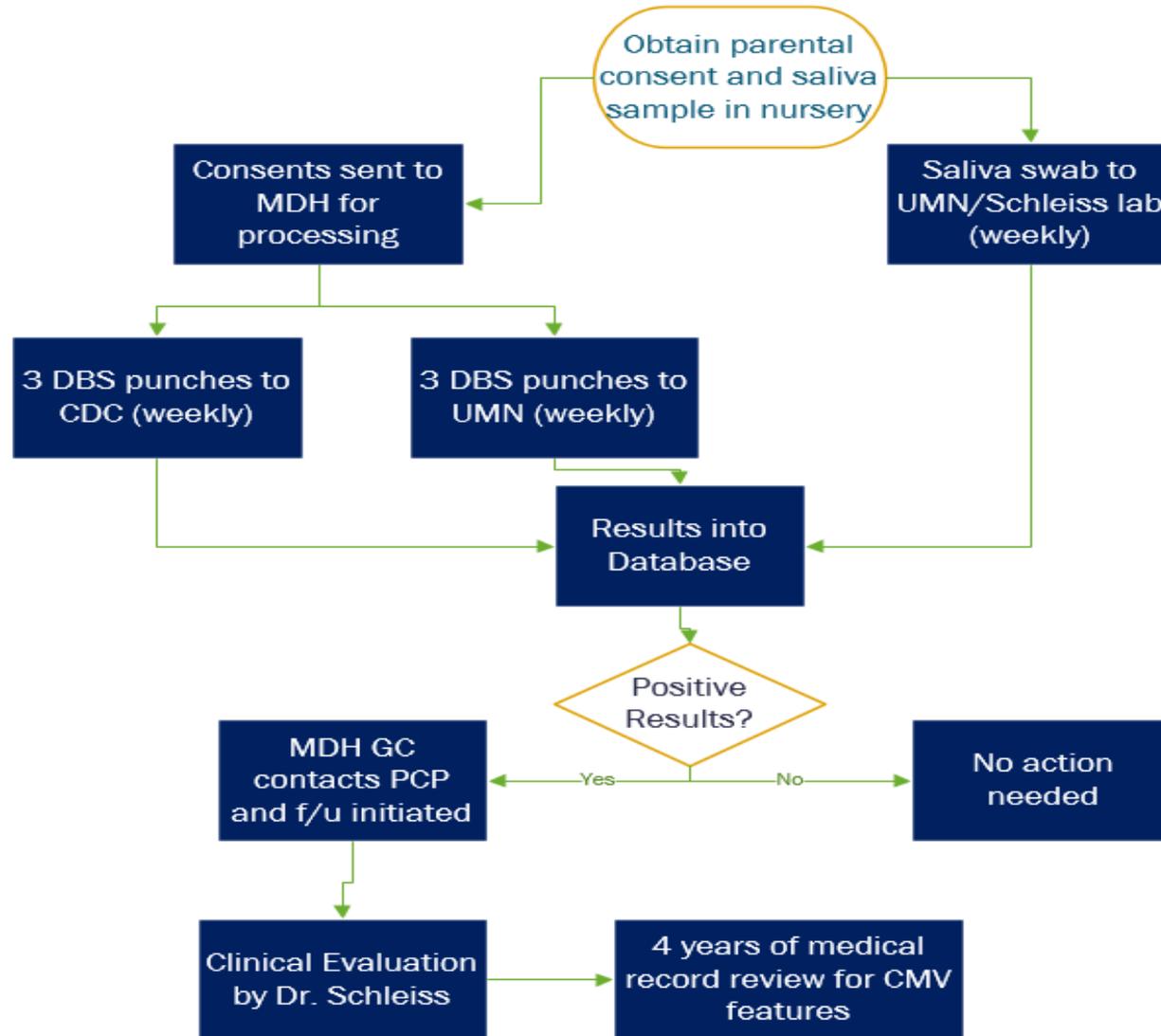


Study Aims

- Clinical sensitivity:
 - Compare two DBS PCR assays performed in independent laboratories (CDC/Dollard and UMN/Schleiss laboratory), using the newborn DBS as a source of CMV DNA
 - Compare DBS PCR results to PCR performed on saliva specimens obtained in the newborn nursery
 - Viral load is known to be higher in urine and saliva
- These results will help clarify which assay is more useful for universal newborn CMV screening
- Target enrollment: 30,000 infants



Study Design



Demographics collected:

GA at delivery
Living children (TPAL)
Birth weight
Head circumference
Race
Ethnicity



Clinical Evaluation

- Infant is evaluated by pediatric infectious disease provider familiar with CMV (to date all infants have seen Dr. Schleiss)
 - Hearing evaluation
 - History and physical exam
 - CNS imaging (selected)
- Positive infants upon clinical evaluation
 - Additional labs obtained for confirmation (Urine)
 - Parents are engaged in a discussion regarding treatment options
 - Hearing assessments at increased frequency – every 3 mo for first 3 years, and every 6 mo until age 4
 - Medical record review annually until age 4



Progress through Aug 14, 2017

First site began enrolling mid-February 2016

5 sites active with enrollment

Total of 3,395 infants enrolled

Enrollment rate: 55% overall, 72% when discussed

Number of positive infants: 10

Initial clinical evaluation of positive infants:

4 infants – symptomatic with hearing loss

6 infants – asymptomatic without hearing loss (at initial evaluation)

Delayed hearing loss:

1 ‘asymptomatic’ infant developed hearing loss (mild to moderate unilateral) identified on 6 month hearing assessment



Advocacy Efforts



The Case Against Universal Screening

- Lack of awareness of CMV
- So. Many. Babies.
 - This is a HUGE increase in follow-up burden (min. 350 infants per year)
- Asymptomatic infants/children – 80% of those identified
 - Persistent parental anxiety (fragile child syndrome)
 - Unnecessary medical attention



Case Against Cont.

- Treatment options
 - Ganciclovir and Valganciclovir are off-label for cCMV
 - Only treat some of the features – moderately favorable effect on long-term audiologic and neurodevelopmental outcomes in symptomatic children
 - Consensus papers recommend treating symptomatic children – not currently the recommendation for “asymptomatic with hearing loss” children but is occurring clinically
- A vaccine is a better option...
- Lack of validated laboratory method for dried blood spots (DBS)
 - CHIMES study found DBS detection of CMV was low (~ 30% sensitivity) however, their DBS method was proven to be low yield and out-of-date

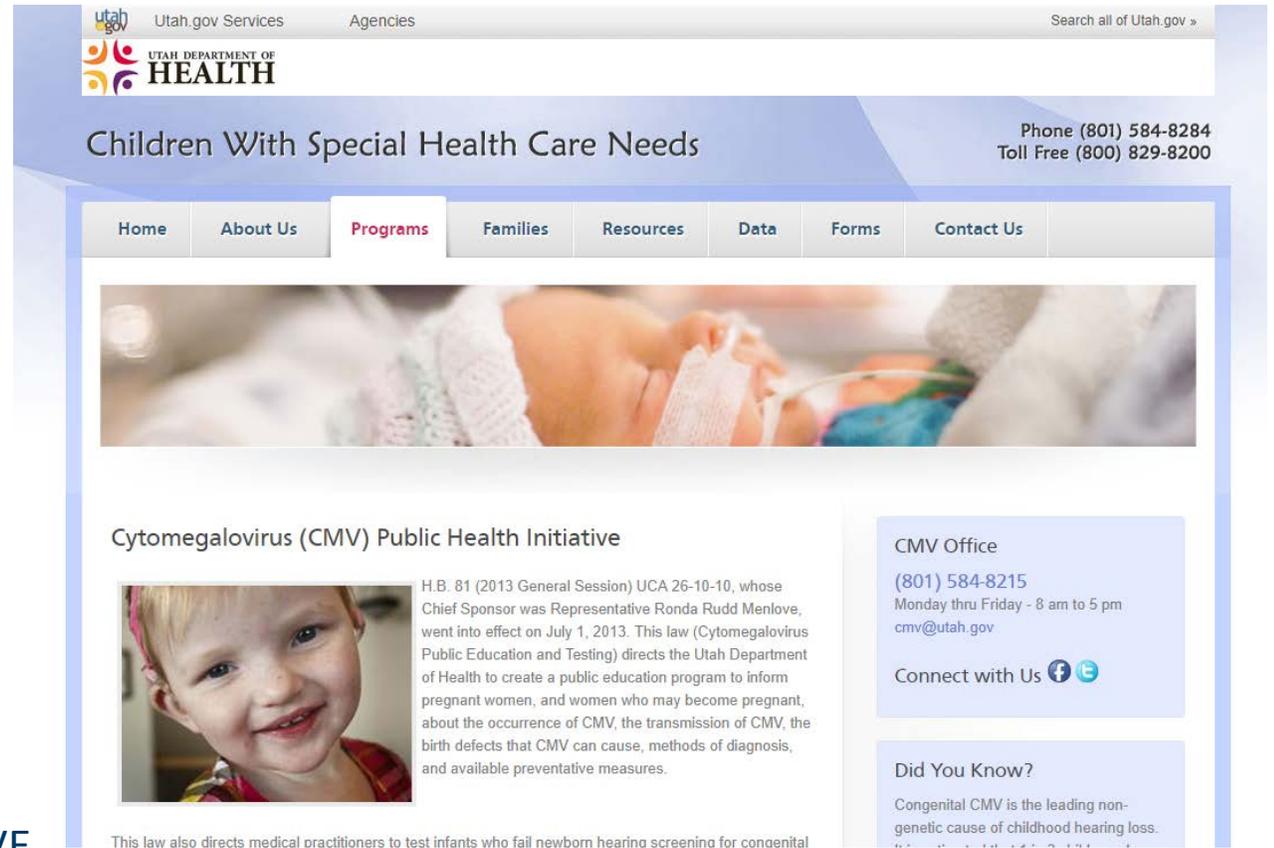
The Case For Universal Screening

- Most CMV-associated disability not evident at birth and therefore not detected
 - Symptomatic infants missed
- Early intervention improves outcomes for these infants
 - Increased monitoring
 - Non-pharmaceutical therapies become an option
- Good evidence for benefit with antiviral tx for symptomatic infants
- CMV screening would avoid diagnostic odyssey for newborns with symptoms



Case For Cont.

- Targeted approaches fall short
 - Utah example: Misses delayed onset hearing loss therefore misses opportunity for treatment
- EHDI programs are unequipped to deal with a laboratory testing platform
- 10 years since CHIMES
 - Technology has changed and improved
- Advocates are organized
 - Universal saliva collection would be EXPENSIVE
 - DBS may be 'good enough'



The screenshot shows the Utah Department of Health website. The header includes the Utah.gov logo, navigation links for Services and Agencies, and a search bar. The main title is "Children With Special Health Care Needs" with contact information: Phone (801) 584-8284 and Toll Free (800) 829-8200. A navigation menu includes Home, About Us, Programs (highlighted), Families, Resources, Data, Forms, and Contact Us. Below the menu is a large image of a newborn baby. The main content area features a section titled "Cytomegalovirus (CMV) Public Health Initiative" with a sub-image of a smiling child and a text block describing H.B. 81 (2013 General Session) UCA 26-10-10. To the right, there is a "CMV Office" contact box with phone number (801) 584-8215, hours, and email cmv@utah.gov, along with social media icons for Facebook and Twitter. A "Did You Know?" box at the bottom right states that congenital CMV is the leading non-genetic cause of childhood hearing loss.

Utah.gov Services Agencies Search all of Utah.gov »

UTAH DEPARTMENT OF HEALTH

Children With Special Health Care Needs Phone (801) 584-8284 Toll Free (800) 829-8200

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Cytomegalovirus (CMV) Public Health Initiative

H.B. 81 (2013 General Session) UCA 26-10-10, whose Chief Sponsor was Representative Ronda Rudd Menlove, went into effect on July 1, 2013. This law (Cytomegalovirus Public Education and Testing) directs the Utah Department of Health to create a public education program to inform pregnant women, and women who may become pregnant, about the occurrence of CMV, the transmission of CMV, the birth defects that CMV can cause, methods of diagnosis, and available preventative measures.

CMV Office
(801) 584-8215
Monday thru Friday - 8 am to 5 pm
cmv@utah.gov

Connect with Us  

Did You Know?
Congenital CMV is the leading non-genetic cause of childhood hearing loss.

This law also directs medical practitioners to test infants who fail newborn hearing screening for congenital

Does it Meet Criteria?

- Medically serious condition with well described case definition
 - Yes
 - However, with 80% unaffected cCMV is unlike any other disorder on the NBS panel
- Accurate, high throughput diagnostic test available
 - No, not currently – working on it
- Effective treatment available
 - Yes - early intervention and promising antiviral treatments for symptomatic newborns

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"If you don't pass, Screen"

* Individual has rolled-off the study

A special **thank you** to all our families for participating in the study!

