CONGENITAL CMV INFECTION; A NEW ERA OF DIAGNOSIS AND TREATMENT

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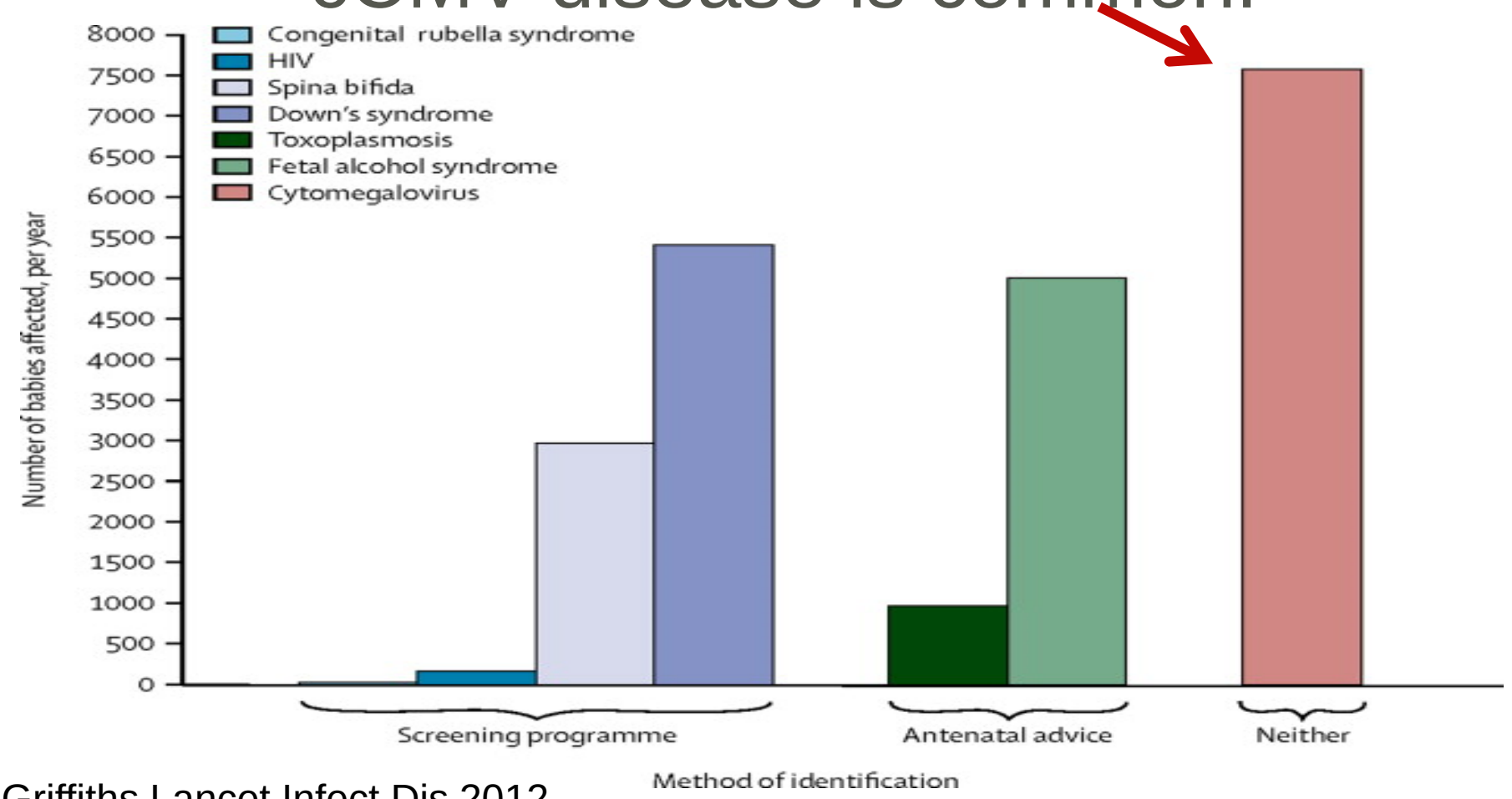
WHAT IS CONGENITAL CMV?

- CMV infection that occurs in utero
- Incidence of cCMV is 0.6% of all live births in developed countries
- Most common non-genetic cause of childhood hearing loss
- Leading cause of intellectual disability, second only to Down syndrome
- Most pregnant women have never heard of CMV...

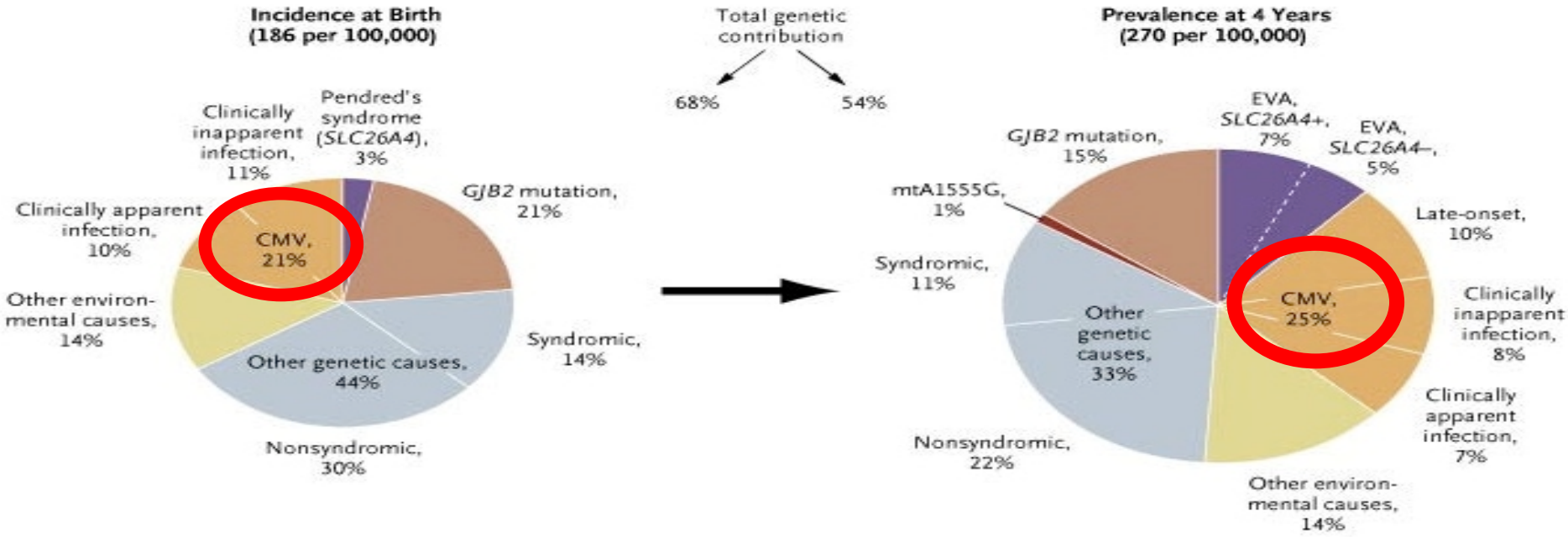
Kenneson Rev Med Virol 200

cCMV disease is common!



Griffiths Lancet Infect Dis 2012

Causes of deafness at birth and 4 yrs



Morton CC, Nance WE. N Engl J Med 2006;354:2151-2164.

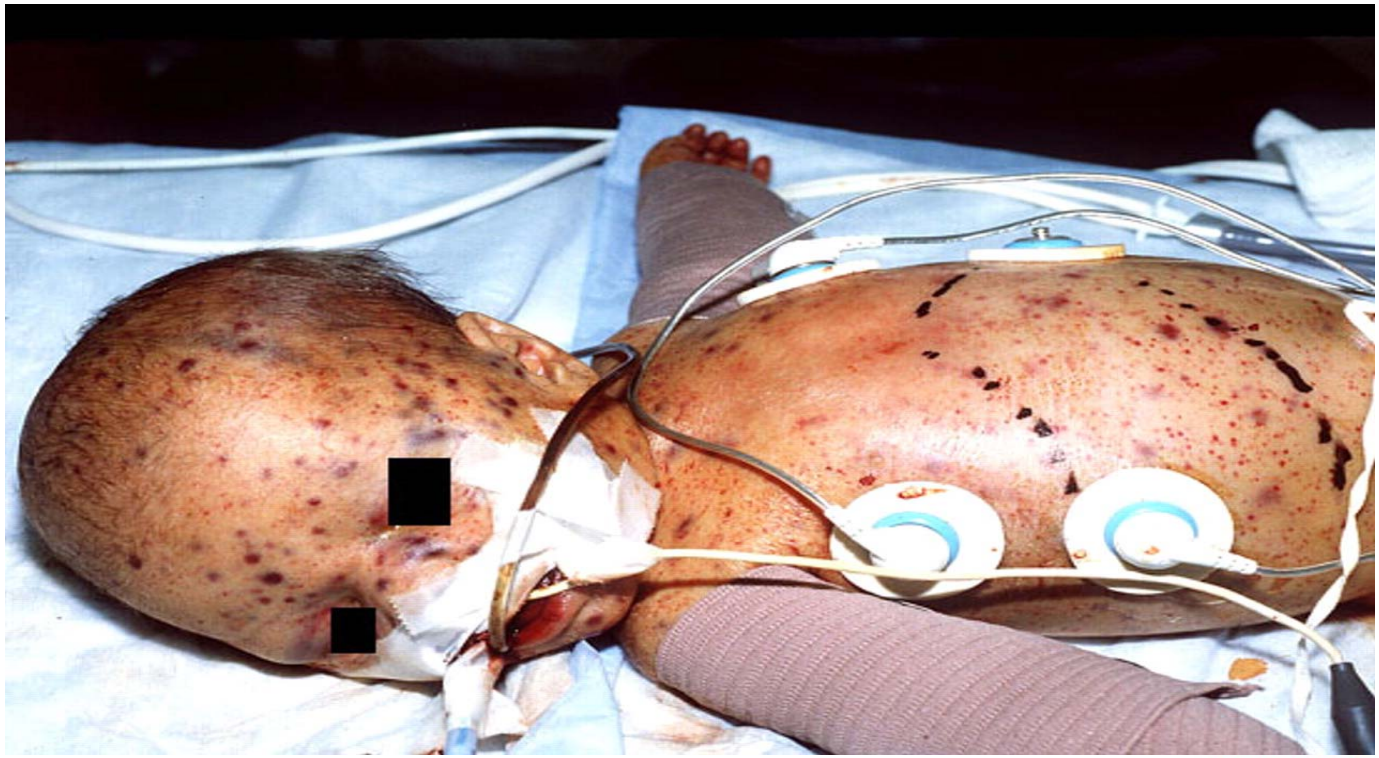
The NEW ENGLAND JOURNAL of MEDICINE

HOW DO NEWBORNS WITH CCMV PRESENT?

- ~10% are symptomatic at birth
  - Most develop neurologic deficits
  - Wide range of severity (can be mild)
  - Diagnosis frequently missed, delayed
- ~90% “asymptomatic” at birth
  - 15% develop permanent hearing loss

Boappana CID 2013; Fowler CID 2013

cCMV rarely looks like this.



Committee on Infectious Diseases et al. Red Book Online 300-305

RED BOOK® ONLINE
The Report of the Committee on Infectious Diseases

Usually it looks like this…

HOW DO YOU DIAGNOSE CMV?

- Requires viral culture or PCR of saliva or urine at <3 weeks of life
  - Very high viral loads in saliva and urine
  - Dried blood spot PCR insensitive (~30%)
  - No role for infant serology
- At ≥3 weeks old, can not determine if infection was congenital or not
- Often suspected too late to definitively diagnose (or treat)

Adler PIDJ 2005; Pass J Peds 2010; Din Pediatrics 2011

Saliva testing for cCMV is easy!

Use of oral swabs is much more convenient than urine and equally sensitive

Boppana NEJM 2011

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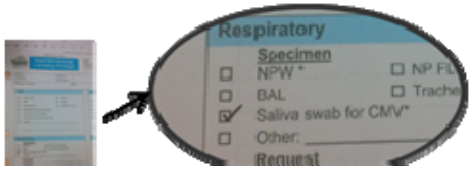
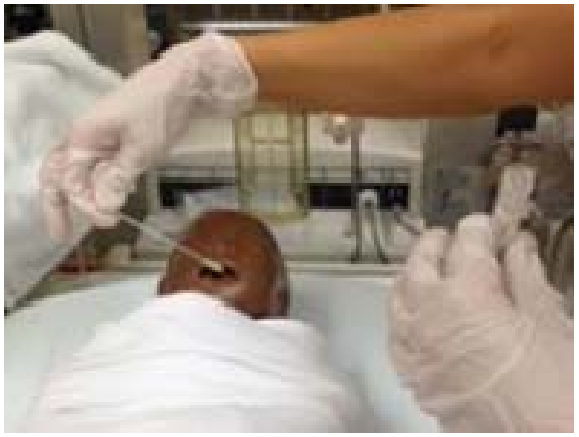
PROCEDURE


eNAT
preservation medium
for nucleic acids


Respiratory
Specimen
NPW *
BAL
Saliva swab for CMV*
Other:
Request



WHY DOES DIAGNOSING CMV MATTER?

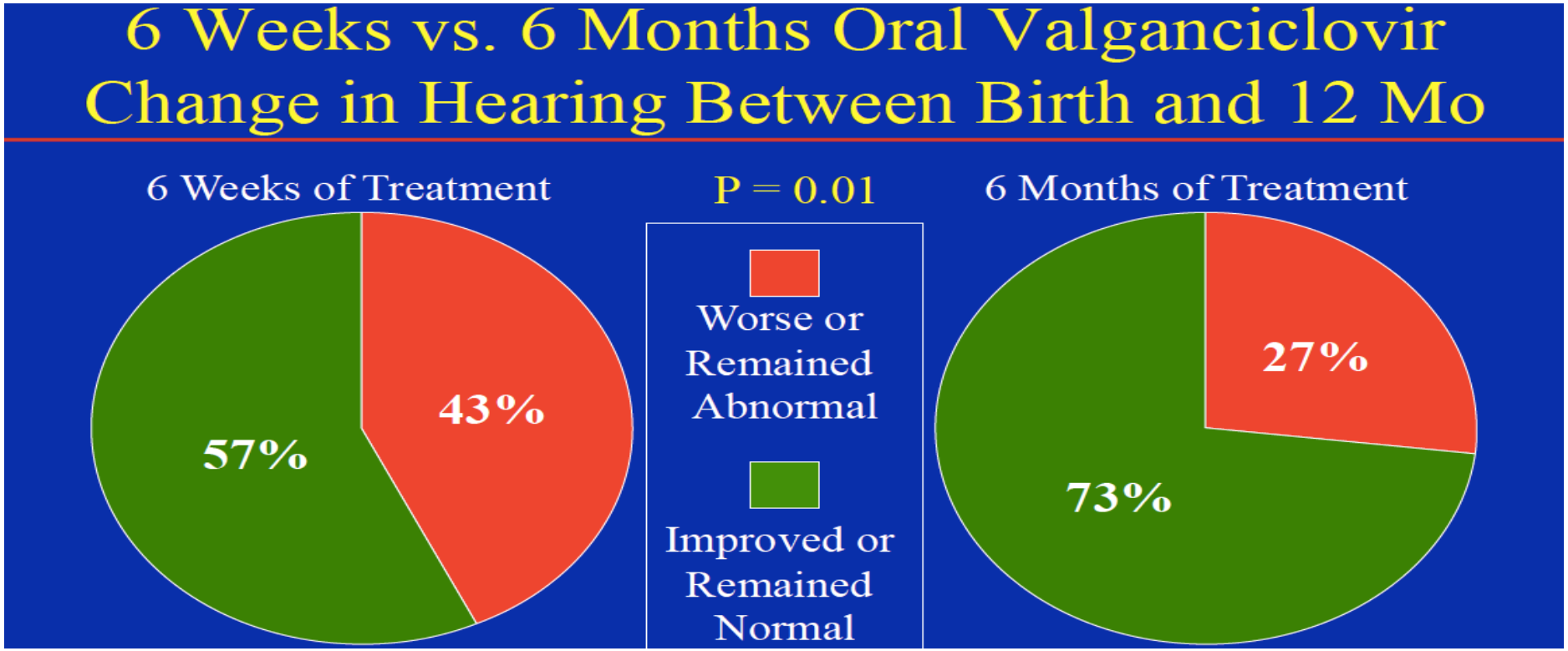
- Treatment of symptomatic neonates with oral antiviral medication is beneficial
  - Improved hearing, cognitive outcomes
  - Safe and well tolerated
- Close follow up for asymptomatic neonates
- Early diagnosis and support for hearing loss

WHAT DOES FOLLOW UP LOOK LIKE?

- Audiology every 3-6 months
- Early speech and occupational therapy
- Hearing aids/cochlear implants for SNHL
- Trials ongoing for treatment of late onset disease

Kimberlin J Peds 2003; Kimberlin IDSA 2013; Fowler CID 2013

6 Weeks vs. 6 Months Oral Valganciclovir Change in Hearing Between Birth and 12 Mo



A TYPICAL CASE

- Newborn boy fails hearing screen through the BC Early Hearing Program
- ABR at 3 months old shows hearing loss
- No risk factors identified by history
- Physical exam is normal
- Could the hearing loss be due to cCMV?
  - Too late to diagnose (except by blood spot?)
  - Too late to start antiviral treatment based on current studies

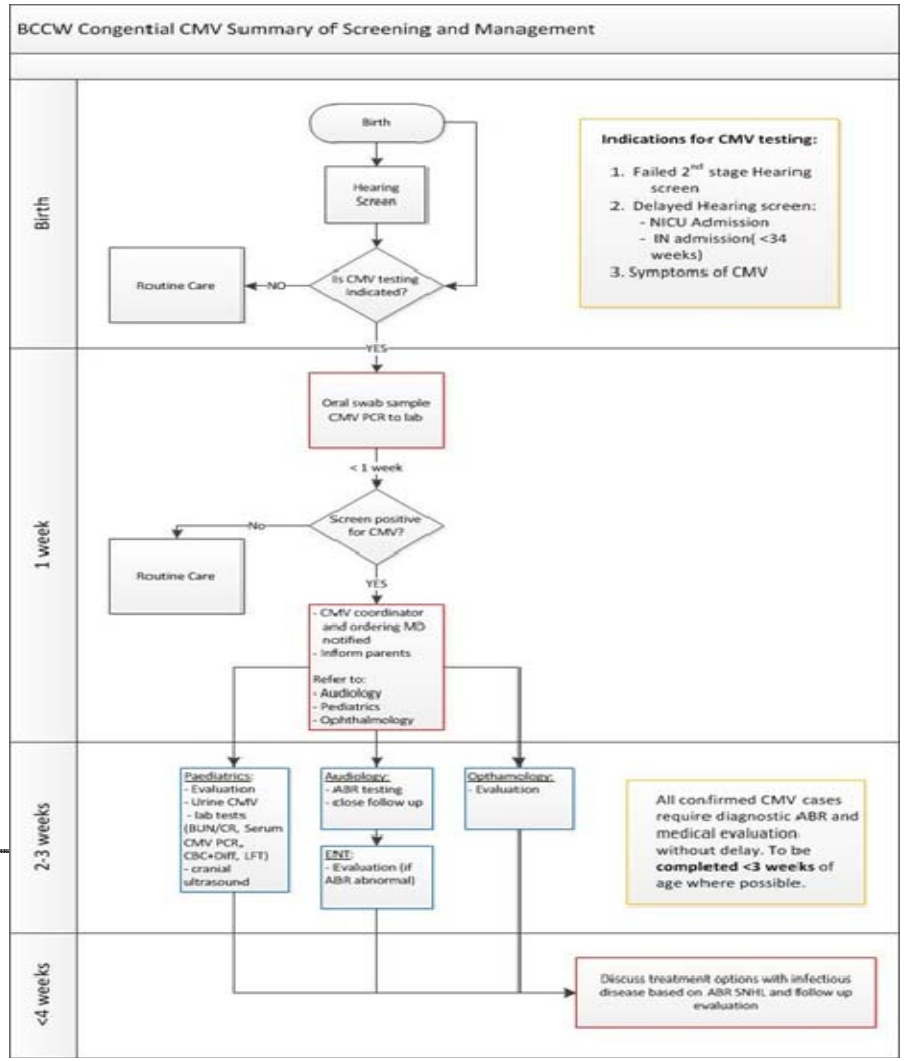
CCMV TESTING-CURRENT STATE

- CMV testing currently only done if there is clinical suspicion (i.e.,"TORCH" infection)
  - Diagnosed in only 10% of symptomatic cases in Canada in a recent national study
  - BC is not any better
- Universal screening requires testing every newborn, not yet standard of care
- Testing of infants with hearing loss
  - Recommended by US Joint Committee on Infant Hearing (2007 Position Statement)
  - Now state law in Utah, Connecticut, others...

Vaudry Peds Child Hlth 2014; Sorichetti J Peds 2015

FUTURE STATE PROCESS

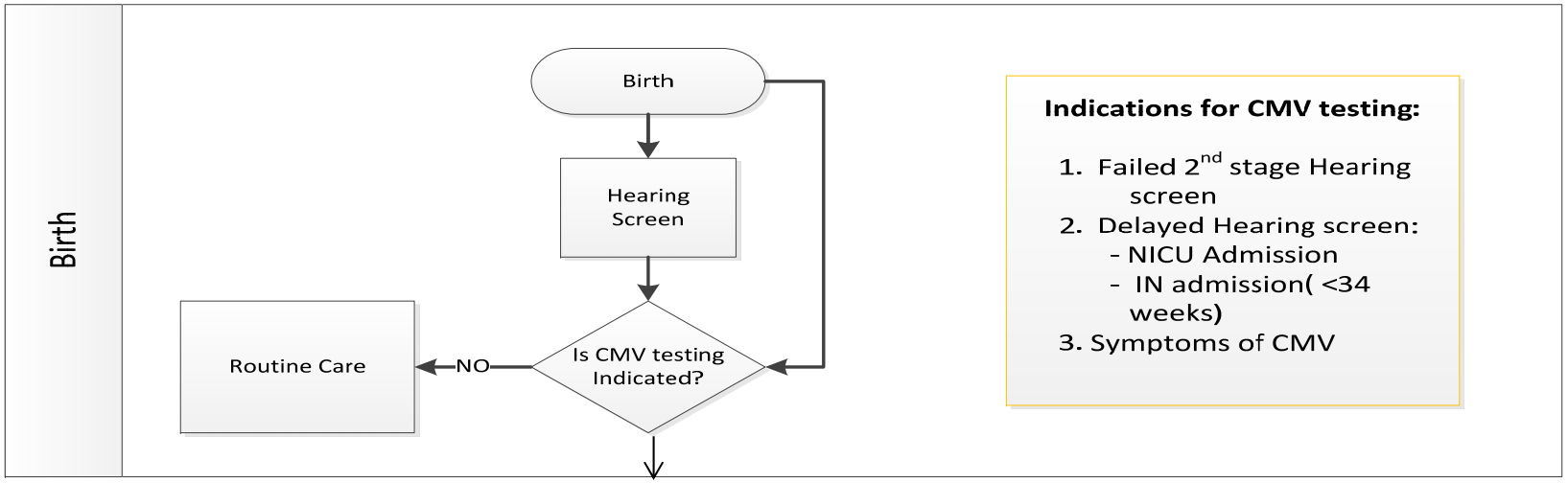
Screening for CCMV at BC Women's



INDICATIONS FOR SCREENING

- Failed newborn hearing screen (unilateral or bilateral).
- Delayed newborn hearing screening for >1 week after birth:
  - All NICU admissions
  - IN admission and <34 weeks gestation at birth
- Symptoms or signs not otherwise explained:
  - Intrauterine growth restriction, small for gestational age, or microcephaly
- Other:
  - Suspicion of primary CMV infection during pregnancy
  - CMV seen on placental pathology

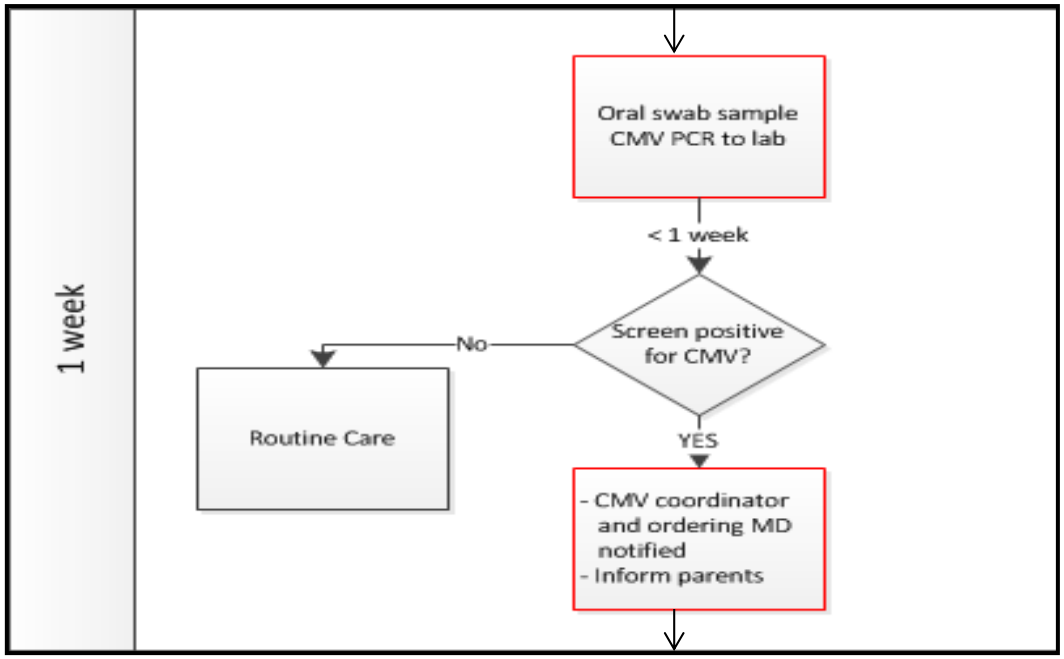
HEARING SCREENING AND IDENTIFICATION



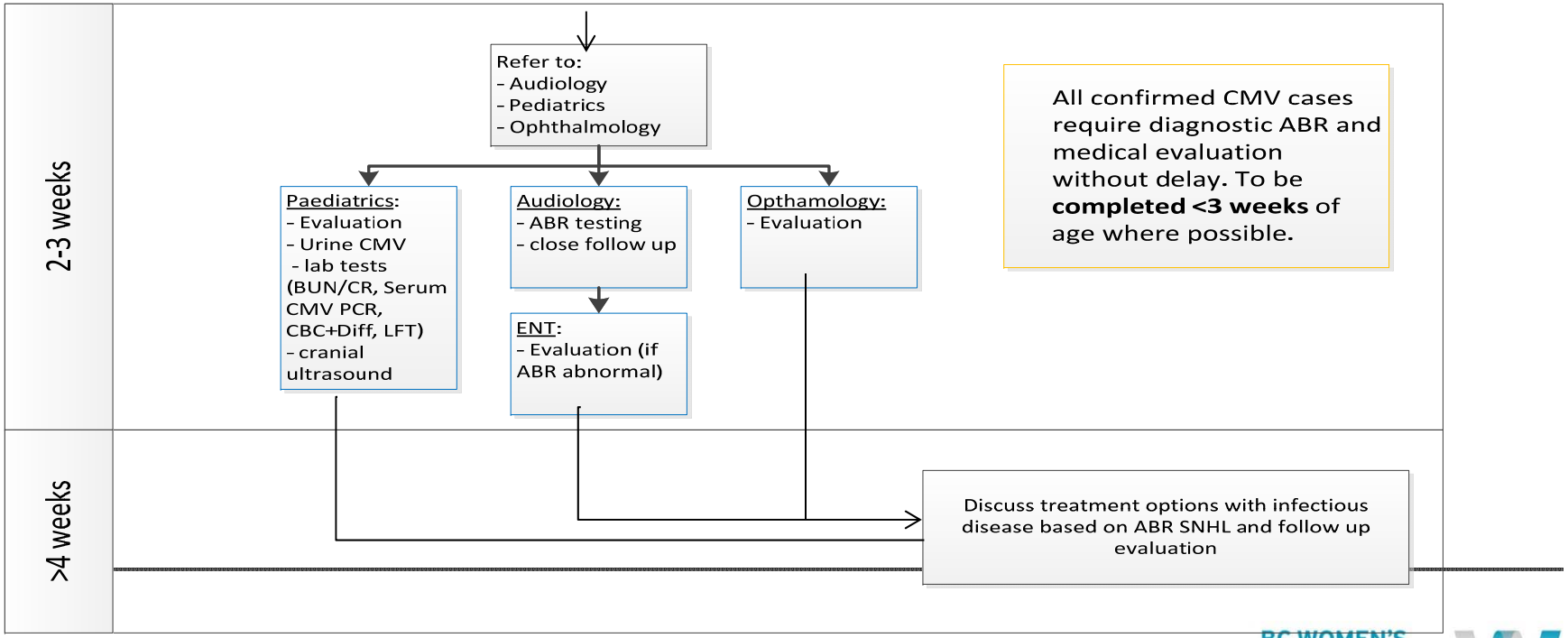
Indications for CMV testing:

1. Failed 2nd stage Hearing screen
2. Delayed Hearing screen:
   - NICU Admission
   - IN admission(<34 weeks)
3. Symptoms of CMV

SAMPLE COLLECTION AND REPORTING



FOLLOW-UP AND TREATMENT



EDUCATION AND COMMUNICATION

- Education Days
- Admission Order Set (NICU)
- Eduquick
- Policy
- Patient Pamphlet
- Hearing Screeners
- Care Providers

EVALUATION

- Process Evaluation
  - At 3, 6 and 12 months
- Feedback from staff re: logistical issues
- Assess number of swabs received by lab from:
  - NICU
  - IN
  - Postpartum
- Failed hearing screens
- Positive CMV results.

TAKE HOME MESSAGES

- CMV is a common cause of hearing loss
- Need to diagnose affected newborns early to give appropriate treatment and care
  - Effective, safe oral treatment available
- Testing is simple, accurate and inexpensive
  - Saliva CMV PCR at <3 wks of life
- Targeted testing to go live at BCWH
  - Plan to expand province-wide
- Universal screening may be warranted

Adler PIDJ 2005; Pass J Peds 2010;
Cannon Rev Med Virol 2014

THANK YOU!

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QUESTIONS OR COMMENTS?