Hepatitis C Virus: Maternal and Perinatal HCV
Disclosures for Dr. Cody Chastain

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Objectives

At the end of this lecture, the learner will be able to:

- Identify important trends in hepatitis C virus (HCV) epidemiology among women of child bearing age and children;

- Describe current screening recommendations for HCV in pregnant women and infants born to women with HCV;

- Discuss interventions to reduce mother-to-child transmission of HCV.
Case

- Alice is a 22-year-old woman with a history of opioid use disorder including injection drug use who presents for prenatal care at the beginning of her third trimester.

- Laboratory studies reveal mildly elevated LFTs (AST 50, ALT 60).

  - Is HCV screening indicated?
  - What can reduce maternal and neonatal risk re: HCV?
  - What is the risk of perinatal HCV infection?
  - Should Alice’s infant be screened, and if so how?
  - What treatment options may be available if Alice’s infant is infected?
Outline

- Epidemiology of HCV Among Women and Children
- Screening for Maternal HCV
- Management of Maternal HCV
- Screening for Neonatal HCV
- Management of Pediatric HCV
Maternal → Neonatal → Pediatric
Maternal → Neonatal → Pediatric
Vertical Transmission

- Most common mode of transmission in children
  - Estimated ~ 6%
  - Transmission rate is ~ 11% if mother is co-infected with HIV

- Increased risk of transmission with:
  - Higher viral load
  - Prolonged rupture of membranes
  - Invasive monitoring
  - Instrumentation

European Pediatric Hepatitis C Virus Network

Clin Infect Dis 2005

Vertical Transmission Outcomes

- Acute resolving infection: 20%
- Chronic asymptomatic infection: 30%
- Chronic active infection: 50%
Pregnant Women and HCV in TN

Rate of HCV Among Pregnant Women Per 1000 Live Births in US and TN

Patrick SW et al. MMWR 2017.
Births to Women with Hepatitis C in TN 2005 - 2014

Patrick SW et al. MMWR 2017.
HCV Screening in Vanderbilt ED

- Universal Emergency Department HCV Screening
  - Partnership between Vanderbilt University Medical Center and Gilead FOCUS program 12/2016 – 12/2018
  - Opt-out testing for all adult patients undergoing laboratory assessment during

- Women Between Ages of 18-45
  - 2,622 women screened
  - ~5.9% HCV antibody positive
  - ~2.9% HCV RNA positive

Chastain C et al. IDWeek 2018.
Cost-effectiveness of Universal Hepatitis C Virus Screening of Pregnant Women in the United States

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1Division of Infectious Diseases and Global Public Health, University of California San Diego; 2Perelman School of Medicine, University of Pennsylvania, Philadelphia; 3Department of Internal Medicine, Rush University Medical Center, Illinois, Chicago; and 4Population Health Sciences, University of Bristol, United Kingdom

Results. Universal antenatal screening was cost-effective in all treatment eligibility scenarios (mean ICER <$3000/QALY gained). Screening remained cost-effective at a prevalence of 0.07%, which is the lowest estimated prevalence in the United States (in Hawaii). Screening the ~5.04 million pregnant women in 2018 could result in the detection and treatment of 33 000 women, based on current fibrosis restrictions.

Conclusions. Universal screening for HCV among pregnant women in the United States is cost-effective and should be recommended nationally.
Recommnedation for Universal Hepatitis C Screening in Pregnancy

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
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<tbody>
<tr>
<td>As part of prenatal care, all pregnant women should be tested for HCV infection, ideally at the initial visit. (See Recommendations for Initial HCV Testing and Follow-Up.)</td>
<td>IIb, C</td>
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</table>
“We recommend that obstetric care providers screen women who are at increased risk for hepatitis C infection by testing for anti-hepatitis C virus antibodies at their first prenatal visit.”

“If initial results are negative, hepatitis C screening should be repeated later in pregnancy in women with persistent or new risk factors for hepatitis C infection…”
Risk-Based Hepatitis C Screening in Pregnancy Is Less Reliable Than Universal Screening: A Retrospective Chart Review

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- Retrospective chart review of 1426 pregnancies at University of Maryland

- 1326 were NOT screened for HCV, while 100 WERE screened for HCV

- 50/78 patients with IDENTIFIABLE risk factors for HCV were not screened

- Only 10/100 (0.7% of overall cohort) diagnosed with HCV

Received 29 January 2018; editorial decision 11 February 2018; accepted 15 February 2018. Correspondence: S. Boudova, PhD, 685 West Baltimore Street, Room 480 Baltimore, MD 21201-1509 (sarah.boudova@som.umaryland.edu).

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Treatment During Pregnancy

- As ribavirin teratogenic, prior HCV treatment regimens not used during pregnancy
- Pregnant women excluded from direct-acting antiviral (DAA) trials
- Single study performed to date
Phase 1 Study of LDV/SOF In Pregnant Women with HCV

- Open-label, phase 1 study
- HIV-negative pregnant women with HCV GT 1 enrolled between 23-24 weeks of gestational age
- 28 women screened, 8 enrolled, and 7 completed follow-up
- SVR12 100% and healthy delivery at term with ongoing infant follow-up
Direct-acting antivirals should only be used in a clinical trial or postpartum.

Counsel women re: invasive prenatal diagnostic testing

Recommend against caesarean delivery solely for indication of HCV

Avoid internal fetal monitoring, prolonged rupture of membranes, and episiotomy

Do not discourage breast feeding
Maternal → Neonatal → Pediatric
Neonatal HCV

- Limited epidemiology data

- In TN Medicaid Study 2005-2014
  - 4072 infants exposed to HCV
  - 23% tested
  - Infants whose mothers were white, smoked, and/or HIV positive more likely to be tested

## Infant HCV Testing “Guidelines”

<table>
<thead>
<tr>
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<th>HCV-Ab</th>
<th>Initial HCV RNA Testing</th>
<th>Repeat HCV RNA Testing</th>
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<tbody>
<tr>
<td><strong>AAP</strong></td>
<td>After 18 months</td>
<td>At 1-2 months</td>
<td>No recommendation</td>
</tr>
<tr>
<td><strong>NASPGHAN</strong></td>
<td>After 18 months</td>
<td>At least 2 months</td>
<td>If HCV RNA positive in early infancy, should be repeated after 12 months</td>
</tr>
<tr>
<td><strong>IDSA/AASLD</strong></td>
<td>At or after 18 months, should be performed even if earlier HCV RNA testing done</td>
<td>Optimal timing of HCV RNA is still unknown, but 2-6 months after birth is reasonable</td>
<td>No value in repeated testing prior to 18 months</td>
</tr>
<tr>
<td><strong>CDC</strong></td>
<td>18 months</td>
<td>At 1-2 months</td>
<td>HCV RNA testing should be repeated at a subsequent visit, independent of initial HCV RNA test result</td>
</tr>
</tbody>
</table>
VANDERBILT CHILDREN’S HOSPITAL ALGORITHM
Testing algorithm for child with confirmed exposure

Patient less than 18 months?

YES

Obtain 2 HCV RNA quant tests 6 months apart, starting after 2 months old

Negative x2

STOP

Positive

REFER

NO

Obtain HCV IgG antibody

Positive

HCV RNA Quant (REFER)

Negative

STOP

Patient less than 18 months?

Positive

REFER

Negative

STOP

Obtain HCV IgG antibody

Patient less than 18 months?

Positive

REFER

Negative

STOP

Obtain HCV IgG antibody

Patient less than 18 months?

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Obtain HCV IgG antibody

Patient less than 18 months?

Positive

REFER

Negative

STOP

Obtain HCV IgG antibody
Testing algorithm for child with **suspected** exposure

- **Examples:** Mother HCV Ab + / RNA unavailable; adopted child with risk factors

```
Able to confirm maternal status

Review maternal HCV RNA quant and HCV IgG results during pregnancy

- IgG negative, RNA negative: No infection STOP
- IgG positive, RNA negative: Prior infection STOP*
- IgG positive, RNA positive: Active infection TEST PER FIRST ALGORITHM

Unable to confirm maternal status

Infant HCV IgG

- Positive: REFER
- Negative: STOP**

** Consider the possibility that mother had acute HCV earlier in the pregnancy but cleared the infection prior to RNA testing. If any intrauterine exposure suspected, then refer (or go down the first algorithm).

** Consider the possibility of acute HCV infection within 2-4 weeks of delivery, prior to seroconversion. If any peripartum exposure suspected, then refer (or go down the first algorithm).
Other Approaches?

- HCV RNA testing once after 2 months only
- HCV RNA testing once after 12 months only
- HCV Ab once after 18 months only
Maternal → Neonatal → Pediatric
Management of HCV-Infected Children

- Serial monitoring until eligible for treatment

- Current DAA Recommendations
  - 3 to <12 years old
    - LDV/SOF x 12 weeks for GT 1, 4, 5, and 6
  - 12 years old and older
    - GLE/PIB for 8-12 weeks for GT 1-6
    - LDV/SOF for 12 weeks for GT 1, 4, 5, and 6
QUESTIONS?