Hepatitis C Among Pregnant Women

December 13, 2017
About NVHR

• National Viral Hepatitis Roundtable
  – working together to eliminate hepatitis B and C in the U.S.

• ~500 coalition members
  – community-based, advocacy, and grassroots groups
  – healthcare providers
  – health departments
  – other government and industry partners

• www.nvhr.org
Housekeeping: GoToWebinar

• Slides and a recording of the webinar will be sent to everyone who registered and posted on our website.
  • www.nvhr.org

• The Q&A session will follow the last presentation

• Please use the question box to submit your questions and comments
Webinar Overview

Project presentations

- Kimberly Page, Ph.D., MPH, MS
  - Professor and Chief of Epidemiology, Biostatistics & Preventive Medicine, University of New Mexico Health Sciences Center

- Stephen Patrick, MD, MPH, MS
  - Assistant Professor of Pediatrics and Health Policy, Division of Neonatology, Vanderbilt University School of Medicine

- Kathy Sanders, RN, MSN
  - Adult Viral Hepatitis Prevention Program Coordinator, Kentucky Department for Public Health

- Sarah Schillie, MD
  - Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC

Discussion and questions and answer
NVHR Webinar: Hepatitis C Among Pregnant Women

Hepatitis C epidemiology in pregnant women and children
HCV seroprevalence by sex in the U.S.: 1998-2008 (NHANES)
Meta-analysis: Pooled estimates of HCV incidence in female and male PWID (16 studies). F:M ratio was 1.36:1 (95% CI: 1.13, 1.64)

HCV incidence F:M aHR = 1.39 (95% CI 1.12, 1.72)
Women are more likely to spontaneous clear HCV

• Women are significantly more likely than men to show evidence of cleared HCV infection in cross-sectional and retrospective studies.

• Women are significantly more likely than men to spontaneously clear HCV in prospective studies.

• Early viral kinetics differ in women and men and may predict clearance in women, but not men.

• Age appears to modify this: older women are less likely to clear than younger women.
Estimated HCV viral persistence probabilities (in months) among female and male young adult PWID with incident HCV infection.

Proportions of males and female PWID who spontaneously clear HCV by sex and IFNL4*
A tale of two cohorts: the “Irish” and the “German” Anti-D cohorts:

- Rh negative women infected by HCV-contaminated anti-D immunoglobulin during 1970s
- Irish cohort (1977-79): 863 exposed; 682 (79%) infected women followed; 302 (45%) spontaneously cleared;
  - Median age at infection 28 years (range 17-44)
  - BABIES with chronic HCV: 3/380 chronic mothers = 0.79%¹
- German cohort (1978-79): 2867 exposed; 1980 (69%) followed; 883 (48%) spontaneously cleared; (66% of icteric women SC)
  - Median age at infection 24 years (range: 16-34)
  - BABIES with HCV: 3/132 chronic HCV mothers = 2.27%²

¹ Power et al, Lancet 1995; ² Meisel et al., Lancet 1995
Perinatal transmission of HCV

• Transmission from HCV RNA+ mothers\(^1\) (pooled risk)
  • HCV mono-infected: 5.8% (95%CI: 4.2%, 7.8%)
  • HCV/HIV co-infected: 10.8% (95%CI: 7.6%, 15.3%; AOR 2.56 (95%CI: 1.5, 4.5)

• Factors associated with increased risk of transmission
  • Viremia <6 log: 3.9%
  • Viremia ≥ 6 log: 14.3%; OR 4.0 (95% CI 1.3, 12.4)\(^2\)
  • Prolonged membrane rupture (>6 hrs): aOR 9.3 (95%CI 1.5, 180)\(^3\)*

• Not associated with increased risk:
  • Breastfeeding\(^2\#\), Internal fetal monitoring\(^2\^*, Cesarean vs. vaginal delivery\(^2\^\), Mothers age, parity, and HCV genotype\(^1\); IDU mediated by PBMC infection\(^4,5\)

• There is no current recommendation to prevent MTC HCV transmission

HCV in infants

- Passive transfer of antibody (anti-HCV) with gradual loss by 18 months by majority (many by 12 mo.)\(^1\)
- Clearance of viremia among children with transient RNA positivity occurs at the median age of 15 months. \(^2,3\)
- 95% of children diagnosed as uninfected lose maternal antibodies by 12 months of age\(^5\)
- In addition to circulating HCV viremia, the presence of HCV antibodies at \(\geq 18\) months of age has been used as a surrogate measure of infection\(^5\).

Potential Maternal and Infant Characteristics Associated with Risk of HCV Transmission

* p=0.006;

Figure 1. Reported cases of acute hepatitis C virus infection by year, United States, 2004-2014, NNDSS*
U.S. Temporal Trends in the Rate of HIV, HBV, and HCV During Pregnancy, 1998-2011

- Inpatient hospitalizations for all liveborn singleton deliveries in the US between 1998 and 2011 from Nationwide Inpatient Sample.
- Annual average of 4,473 cases of maternal HCV.
- Maternal HCV rate was 118.6 per 100,000 deliveries, but higher for:
  - drug users (3,931.2),
  - HIV-positive mothers (2,764.9),
  - alcohol abusers (2,222.1),
  - tobacco users (965.7),
  - Women on Medicare/Medicaid (213.8)
- A ~5X increase in HCV/100,000 pregnancy: from 42.0 in 1998 to 210 in 2011.
- 50% to 75% decreased odds of HCV in racial/ethnic minority women compared to Non-Hispanic Whites.

Values expressed in boxes are the annual percent changes (95% CI). <20 years (solid black line); 20–29 years (dashed blue line); 30 years (dotted red line).

Salemi et al., J Med Vir 2016
**HCV detection in women and testing in children 2011-2014**

<table>
<thead>
<tr>
<th></th>
<th>National</th>
<th>Kentucky</th>
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</thead>
<tbody>
<tr>
<td><strong>HCV detection in women of childbearing age</strong></td>
<td>22% increase From 139 to 169/100,000</td>
<td>213% increase from 275 to 862/100,000</td>
</tr>
<tr>
<td><strong>HCV testing in children ages ≤2 years</strong></td>
<td>14% increase From 310 to 353/100,000</td>
<td>151% increase from 403 to 1,011/100,000</td>
</tr>
<tr>
<td><strong>% of infants born to HCV+ women</strong></td>
<td>68% increase From 1/536 (0.19%) to 1/302 (0.32%)</td>
<td>124% increase from 1/142 (0.71%) to 1/63 (1.59%)</td>
</tr>
</tbody>
</table>

*HCV testing (anti-HCV or RNA in population served by Quest Diagnostics; 1.Koneru et al, MMWR 2016*
... and in Wisconsin

- 81% increase in HCV detection in 15–44 year olds (45.7 to 82.6/100,000)
- 43% women
- 93% increase in HCV in pregnancies (2.7 to 5.2 per 1,000) (= to 1/368 to 1/192)
- Among 183 infants born to HCV+ women with evidence HCV, 34% received recommended HCV testing.
### HCV in pregnant women in OAT programs: “cascade” outcomes

<table>
<thead>
<tr>
<th>Author</th>
<th>Setting</th>
<th>N</th>
<th>Anti-HCV screened N (%)</th>
<th>anti-HCV +</th>
<th>HCV RNA test</th>
<th>HCV RNA +</th>
<th>Post-partum referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Page et al, 2017</td>
<td>ABQ, NM: Milagro Clinic 2012-2015</td>
<td>190</td>
<td>178 (97%)</td>
<td>95 (53.4%)</td>
<td>94 (98.9%)</td>
<td>75.6%</td>
<td>na</td>
</tr>
<tr>
<td>Krans et al, 2016</td>
<td>Pittsburgh, PA: Magee Womens Hosp; 2009-2012</td>
<td>791</td>
<td>611 (77.2%)</td>
<td>369 (60.4%)</td>
<td>153 (25%)</td>
<td></td>
<td>77.2% referred; 24.9% attended; 1.6% Tx</td>
</tr>
<tr>
<td>Berkley et al., 2008</td>
<td>ABQ, NM. Milagro Clinic 2000-2006</td>
<td>371</td>
<td>300 (85%)</td>
<td>159 (53%)</td>
<td>26 (16%)</td>
<td>16 (61.5%)</td>
<td>5.5% referred; 1.9% of neonates referred</td>
</tr>
</tbody>
</table>
HCV testing in pregnant women on OAT pharmacotherapy at Milagro Clinic at UNM*

Page et al, Mat&Child Health J 2016
Other complications and outcomes in HCV+ mothers and infants vs. HCV-:

- **Mothers:**
  - Cholestasis (6.3% vs. 0%)
  - Pre-term delivery (24.5% vs. 14.9%)

- **Neonatal**
  - Birthweight <2500 g (32.9% vs. 17.1%)*
  - Lower gestational age (37.9 vs. 38.4 wks)*
  - Neonatal abstinence syndrome (88.4% vs. 36.4%)

*Berkley et al., Obstet Gyn 2008; *controlling for methadone and tobacco
Conclusions

- HCV is increasing in many groups including women of childbearing age with risk exposures, and there are increasing N/% of infants born to HCV+ mothers.
- Vertical transmission is the leading cause of childhood HCV infection.
- No intervention has been clearly demonstrated to reduce the risk for mother-to-infant HCV transmission. Some may increase.
- Identification of effective management strategies to reduce risk for transmission is an important clinical and public health concern.
- Many gaps in follow up of women and children.
Society for Maternal Fetal Medicine recommendations for obstetric care providers

1) Screen women who are at increased risk for HCV by testing for anti-HCV at first prenatal visit. If anti-HCV negative, repeat later in pregnancy in women with persistent or new risk factors for HCV (eg, new or ongoing use of injected or intranasal illicit drugs) (GRADE 1B).

2) Screen HCV infected pregnant women for other sexually transmitted infections (GRADE 1B).

3) Counsel HCV infected women to abstain from alcohol (Best Practice).

4) HCV direct-acting antiviral treatment should be deferred to post-partum period (not currently approved during pregnancy (GRADE 1C), or only in the setting of a clinical trial.

5) If invasive prenatal diagnostic testing is requested, women be counseled that data on the risk of vertical transmission are reassuring but limited; amniocentesis is recommended over chorionic villus sampling given the lack of data on the latter (GRADE 2C).

6) Recommend against cesarean delivery solely for the indication of HCV (GRADE 1B).

7) Avoid internal fetal monitoring, prolonged rupture of membranes, and episiotomy in managing labor in HCV–positive women (GRADE 1B).

8) Do NOT discourage breast-feeding based on a HCV infection (GRADE 1A).
Recommendations to fill gaps in care and knowledge

• Improve early identification of HCV-infected women of childbearing age, link-treat-cure, and avoid HCV infection during pregnancy, and prevent mother-to-child transmission
• Consider strategies and policies to increase HCV detection among women of childbearing age.
• Improve follow up care and monitoring of both mothers and children.
• All of these require more and better data.
Acknowledgements

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  • Jacqueline Fridge, MD
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  • Larry Lehman, MD
  • Sanjeev Arora, MD
  • Karla Thornton, MD

• Centers for Disease Control
  • John Ward, MD
Hepatitis C Virus in Neonates

Stephen W. Patrick, MD, MPH, MS
NVHR Webinar
December 13, 2017
Neonatal Abstinence Syndrome

- A withdrawal syndrome experienced by drug exposed newborns after birth
- Generally follows opioid exposure, though other drugs have been implicated
  - e.g., benzodiazepines, barbiturates
- 40-80% of heroin and methadone exposed newborns develop NAS
  - ~5% of those exposed to opioid pain relievers
Incidence of Increasing of Neonatal Abstinence Syndrome


Neonatal Abstinence Syndrome in Rural vs. Urban Communities

Hepatitis C Prevalence Among Pregnant Women

Hepatitis C Prevalence Among Pregnant Women, US 2014

Hepatitis C Prevalence Among Pregnant Women, Tennessee 2014

## Odds of Hepatitis C Infection in Pregnancy

<table>
<thead>
<tr>
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<th>aOR (95% CI)</th>
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<tbody>
<tr>
<td>Age (Year)</td>
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<td>Education (&lt;High School)</td>
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<tr>
<td>Non-Hispanic White</td>
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<td>Non-Hispanic African American Hispanic</td>
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*Model includes: marital status, other sexually transmitted infections (chlamydia, gonorrhea, syphilis, HSV).*
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<tr>
<td>Hepatitis B</td>
<td>16.6 (12.7-21.7)</td>
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Probability Hepatitis C in Pregnancy

**Patient 1:** 27-year-old, smokes cigarettes, late/no prenatal care, lives in rural area and Hepatitis B +

**Patient 2:** 20-year-old, no cigarettes, prenatal care, lives in urban county and Hepatitis B -

* After accounting for marital status, education, race, parity, chlamydia, gonorrhea, syphilis and herpes simplex virus infection
Follow-up of HCV Exposed Inadequate

• Exposed infants must be followed to evaluation for conversion
  • ~6% vertical transmission rate, ~11% with HIV co-infection
  • Maternal antibodies can persist 18 months

• Philadelphia Department of Health
  • 16% of exposed infants tested
  • Estimated 23 HCV Positive Infants Missed

• Wisconsin Department of Health
  • 34% received recommended HCV testing
  • Mother-to-infant (vertical) transmission 4%

Implications

• Hepatitis C is a rising and potentially modifiable risk to maternal and infant health
  • One infant born exposed to Hepatitis C every 40 minutes nationwide in 2014

• Highest rates of Hepatitis C in areas of highest rates of opioid-related complications
  • Abuse deterrent preparations
  • Increase in heroin use
Implications

• Treatment of Hepatitis C
  • Expensive, challenge for Medicaid
  • Not proven/tested in pregnancy or children
  • Time for universal screening of Hepatitis C in pregnancy/preconception?
• Systems of care to follow exposed infants
Acknowledgements

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Carolyn Wester, MD, MPH

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Perinatal Viral Hepatitis in Kentucky

Robert Brawley, MD, MPH, FSHEA
Kathy J. Sanders, RN MSN
Kentucky Department for Public Health
Adult Viral Hepatitis Prevention Program
**State-by-state Trends**

From 2010-2014, Kentucky led the nation in acute HCV rates. In 2015, rates decreased in Kentucky, making the Commonwealth third in the nation.¹
CDC- Top 220 US Counties

CDC - 55 High Risk Counties in Kentucky

County-level Vulnerability to Rapid Dissemination of HIV/HCV Infection Among Persons Who Inject Drugs

Kentucky Viral Hepatitis Surveillance: Successes

- In 2012, Kentucky Viral Hepatitis Prevention Program partnered with selected local health departments (LHDs), including NKIDHD, for HCV laboratory testing pilot project for individuals with identified risk factors.
- Results: Identified a large number of confirmed HCV-positive tests in persons aged 20 - 29 years.
- Raised concerns about the potential for mother-to-child transmission of HCV.
Perinatal Hepatitis C Reporting in Kentucky

- In late December 2013, DPH requested voluntary reporting from healthcare providers across Kentucky for:
  - All HCV-positive pregnant women
  - All infants born to HCV-positive women
  - All HCV-positive children aged 5 years or less
- Reporting was mandated by law in Feb 2015
Cases of Perinatal Hepatitis C Among Mothers and Pregnant Women in Kentucky, 2013-2016

Perinatal Hepatitis C Cases (n=894)
- 0 or Did Not Report
- 1-5
- 6-10
- 11-20
- 21-50
- 21-50
- >50

* Two recorded cases did not identify a county of residence.
Perinatal Hepatitis C Rates (per 1000 live births) in Kentucky, 2013-2016

Perinatal HCV Rate (per 1000 live births)
- 0.0 or Did Not Report
- 0.1-5.0
- 5.1-10.0
- 10.1-20.0
- 20.1-50.0
- >50.0

* To avoid double counting, rates were not calculated for counties that reported infants or children only.
<table>
<thead>
<tr>
<th>Mothers or Pregnant Women (n=1890)</th>
</tr>
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<tbody>
<tr>
<td></td>
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<tr>
<td>HCV RNA – Pos</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>HCV Ab - Pos</td>
</tr>
<tr>
<td>HCV Ab – Neg</td>
</tr>
<tr>
<td>No HCV Ab</td>
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<tr>
<td>Total</td>
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Perinatal Hepatitis C Surveillance in Kentucky
Dec 2013 through Dec 2016
<table>
<thead>
<tr>
<th>Year</th>
<th>YES</th>
<th>NO</th>
<th>UNKNOWN</th>
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<tbody>
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<td>2010</td>
<td>260</td>
<td>53,134</td>
<td>196</td>
<td>53,590</td>
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<tr>
<td>2011</td>
<td>380</td>
<td>52,863</td>
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<td>53,380</td>
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<tr>
<td>2012</td>
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<td>52,617</td>
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<td>2014</td>
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<td>2015</td>
<td>995</td>
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<td>2016</td>
<td>1057</td>
<td>51,377</td>
<td>557</td>
<td>52,991</td>
</tr>
</tbody>
</table>
Kentucky Perinatal HCV Data - Vital Statistics Branch

- Data from the Vital Statistics Branch showed that 2,997 of the 166,199 births from 2014 through 2016 had a history of maternal hepatitis C virus (HCV) infection recorded on the birth certificate.
- This maternal infection was recorded for 1.8 percent of the births during this time (i.e., rate of 1,803 per 100,000 births).
- The 2,997 HCV-infected women identified on birth certificates were 1,000 more than the number of HCV-infected pregnant women reported to the DPH Hepatitis Prevention Program by clinics and medical providers.
Underreporting of Perinatal HCV Infections

- Demonstrates known underreporting that can occur with the passive surveillance for perinatal HCV infections
- During 2013 and 2014, reporting of hepatitis C infections in pregnant women and infants to DPH by clinics and medical providers was voluntary.
### Perinatal Hepatitis C Surveillance in Kentucky
**Dec 2013 through Dec 2016**

| Children's HCV Antibody and HCV RNA Results (n=695) |
|---------------------------------|------------------|------------------|------------------|------------------|
|                                | HCV RNA – Pos    | HCV RNA - Neg    | No HCV RNA       | Total            |
| HCV Ab - Pos                   | 26               | 13               | 75               | 112              |
| HCV Ab - Neg                   | -                | 3                | 8                | 11               |
| No HCV Ab                      | 10               | 20               | 542              | 572              |
| Total                          | 34               | 36               | 625              | 695              |
World Hepatitis Day — July 28, 2016

World Hepatitis Day, recognized on July 28, was established by the World Health Organization (WHO) to raise awareness and promote understanding of viral hepatitis, the seventh leading cause of death worldwide (1). Together, hepatitis B and hepatitis C are responsible for most of the 1.4 million annual deaths attributed to viral hepatitis (1). In April 2016, the 69th World Health Assembly adopted a Global Viral Hepatitis Strategy that aims to eliminate hepatitis B and hepatitis C as public health threats by 2030 (1). The strategy includes prevention and treatment targets that, when met, will save millions of lives.

This issue of MMWR features a report revealing the growing risk for perinatal transmission of hepatitis C virus (HCV) in the United States, a risk most pronounced in areas where HCV incidence is increasing among young adults and women of childbearing age. Vaccination-based strategies are highly effective in preventing perinatal hepatitis B virus transmission (2). The report highlights that, in the absence of a vaccine for HCV, there is an immediate need to improve risk screening, scale up HCV testing among persons at risk, including children born to HCV-infected mothers, as recommended by CDC and the United States Preventive Services Task Force, and improve case reporting, particularly among women who are pregnant or planning pregnancy. Additional information and resources are available at http://www.cdc.gov/hepatitis.

References


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Hepatitis C virus (HCV) infection is a leading cause of liver-related morbidity and mortality (1). Transmission of HCV is primarily via parenteral blood exposure, and HCV can be transmitted vertically from mother to child. Vertical transmission occurs in 5.8% (95% confidence interval = 4.2%–7.8%) of infants born to women who are infected only with HCV and in up to twice as many infants born to women who are also infected with human immunodeficiency virus (HIV) (2) or who have high HCV viral loads (3,4); there is currently no recommended intervention to prevent transmission of infection from mother to child (3). Increased reported incidence of HCV infection among persons aged ≤30 years (5,6) with similar

INSIDE
711 Projected Zika Virus Importation and Subsequent Ongoing Transmission after Travel to the 2016 Olympic and Paralympic Games — Country-Specific Assessment, July 2016
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720 Announcement
Results in MMWR indicated that from 2011-2014, HCV detection among women of child bearing age in Kentucky increased 213% from 275 to 862 per 100,000.

1 in 63 births in Kentucky

About 80% have current disease when HCV RNA is reported, i.e., HCV RNA result is reported as “positive”

Multiple risk factors are associated with pregnant women and mothers with HCV

Vertical transmission of HCV is occurring in Kentucky

Not limited to urban centers
Risk Assessments and Testing Recommendations for Hepatitis C Virus Infections - 1

- Adults born during 1945 through 1965 should be tested once (without prior ascertainment of hepatitis C virus (HCV) risk factors)
- HCV-testing is recommended for those who:
  - Have current injecting or intranasal drug use
  - Ever injected drugs, including those who injected/ intranasal once or a few times many years ago
  - Unregulated body piercing and/ or tattoos
  - Sexual contact with a known HCV-positive person
  - History of high risk sexual behavior
  - History of sexually transmitted infection
  - History of incarceration
Screening and Referral Guidance for Hepatitis C Virus (HCV) Infection among High Risk Pregnant Women

Assess pregnant women for high risk factors using the "Kentucky Testing Recommendations for Hepatitis C Virus Infection" and the "Hepatitis C Virus Infection Risk Assessment".

HCV Antibody

No

No further action needed

Provide test results and counseling
Counsel regarding HCV transmission and ways to prevent spread
Assess for and recommend HIV and HBV testing
Assess for and consider HepA & HepB vaccination during pregnancy or postpartum
Recommend repeat HCV antibody testing when admitted for delivery

Yes

Perform HCV Antibody Test

HCV Antibody

No

Assess for ongoing high risk for acquiring HCV infection

Yes

No further testing recommended

HCV RNA

No

Obtain HCV RNA Quantitative Test results in Outreach

Yes

Provide test results regarding meaning of test results
Counsel regarding HCV transmission and ways to prevent spread
Assess for and recommend HIV and HBV testing
Assess for and consider HepA & HepB vaccination during pregnancy or postpartum

HCV RNA

Provide test results and counsel regarding meaning of test results and ways to protect liver
Counsel regarding HCV transmission and ways to prevent spread
Assess for and recommend HIV and HBV testing
Consider HepA & HepB vaccination during pregnancy or postpartum
Report Hepatitis C infection in pregnant woman using the EPID 394 form
Recommend visit to OB/GYN and/or primary care provider
Screening and Referral Guidance for Infants Born to Mothers with Hepatitis C Virus (HCV) Infection

Infant born to mother with a positive HCV Antibody test or positive HCV RNA Test

1. Report to KY DPH using the EPID 394 form and recommend visit to pediatrician or family practice for follow up test at 2 month or 4 month well child visit
2. Provide HBV vaccination
3. No HCV test recommended at time of BIRTH
4. Provide HCV counseling to caregiver on HCV transmission and ways to prevent spread
5. Infant may be breastfed as long as mother's nipples are not cracked or bleeding

HCV RNA Quantitative Negative

- No further action needed

HCV RNA Quantitative Positive

- Ongoing evaluation and follow up by pediatrician or family practice as high risk infant
- Update and resend the EPID 394 form to report a HCV Antibody positive test

1. Recommend physician assessment and evaluation for HCV RNA Quantitative test at 2 month or 4 month well-child visit, or the HCV antibody test at 18 months of age
2. Counsel caregiver on transmission and ways to prevent spread
3. Provide test results and counseling
4. Update and resend the EPID 394 form to report a HCV RNA Quantitative positive test
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  effective in 2015
Development of Guidance for Perinatal HCV Testing and Prevention

Sarah Schillie, MD, MPH, MBA

NVHR Webinar
December 13, 2017

The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention
Changing Epidemiology of HCV Infection

- 2.9 fold increase in reported cases of acute HCV from 2010-2015
  - Predominantly from injection drug use (64% of reports with information)

- Increase among males and females
  - Rates similar among males and females (0.9 and 0.7 cases per 100,000 population, respectively)

CDC 2010-2015 Surveillance Data
Reported Number of Acute Hepatitis C Cases — United States, 2000–2015

33,900 cases when adjusting for under-reporting/under-ascertainment

CDC 2015 Surveillance Data
Incidence of Acute Hepatitis C by Age Group — United States, 2000–2015

CDC 2015 Surveillance Data
2015 State Acute Hepatitis C Incidence Compared to Healthy People 2020 National Goal*

CDC National Notifiable Diseases Surveillance System (NNDSS)
*National goal: 0.25 cases/100,000 population
Births to HCV-Infected Women of Child-Bearing Age

- The number of reproductive-aged women with acute and past/present HCV-infection doubled from 15,550 in 2006 to 31,039 in 2014*
  
  - Applying a laboratory-derived infection rate to annual live births from 2011-2014, an estimated 29,000 HCV-infected women gave birth to 1,700 HCV-infected infants each year.

*National Notifiable Diseases Surveillance System (NNDSS)
Ly et al, 2017
Perinatal HCV Transmission

- Estimated to occur in 5.8% of infants born to HCV-infected, HIV-negative mothers

- Transmission increases with:
  - Maternal HIV co-infection (occurs in 10.8% of infants)
  - High maternal viral load (>6 log: 14.3%; <6 log: 3.9%)
  - Prolonged rupture of membranes >6 hrs (odds ratio=9.3)

HCV Treatment

- HCV can be cured in >90% of persons with direct acting antiviral agents (DAAs) administered daily for 8-12 weeks
- Treatment guidance from IDSA/AASLD
- Safe/effective for 12-17 year-olds
  - Treatments for children aged 6-11 years with HCV: coming soon

HCV Treatment, cont.

- **Safety and efficacy during pregnancy not yet established**
  - Challenges regarding Medicaid treatment restrictions (e.g., in drug treatment programs); a priority for some Medicaid programs (e.g., California)

- **Treatment before pregnancy optimal to prevent infant infection as well as maternal disease progression**
  - Treatment after pregnancy cures the mother and prevents infection in the next pregnancy
Existing HCV Testing Recommendations (U.S. Preventive Services Task Force, CDC)

- **Risk-based recommendations** (apply also to pregnant women)
  - Injection drug use
  - Blood transfusion before 1992
  - Long-term hemodialysis
  - Being born to an HCV-infected mother
  - Incarceration
  - Intranasal drug use
  - Receipt of an unregulated tattoo
  - Other percutaneous exposures (such as in health care personnel or from having surgery before the implementation of universal precautions)

- **Persons born during 1945-1965 (Prevalence-based recommendation)**
  - anti-HCV prevalence: 3.25%
  - Likely past child-bearing age

*USPSTF; MMWR 2012*
Considerations for HCV Testing during Pregnancy

- **Universal**
  - Will identify most HCV-infected pregnant women
  - Operationally simplest
  - Align with other infectious disease testing recommendations during pregnancy

- **Risk-based**
  - Requires acknowledgement of risk factor
  - Women may deny risk factors fearing loss of custody of infant

- **Prevalence-based**
  - Requires data on prevalence
  - May be desirable in low-prevalence regions
Pros and Cons of Universal HCV Testing during Pregnancy

- **Pros**
  - Pregnancy a time for interaction with healthcare system
  - Opportunity to link infant-maternal health
  - Will identify most HCV-infected pregnant women
  - Operationally simplest
  - Aligns with other infectious disease testing recommendations during pregnancy

- **Cons**
  - Not a ‘pregnancy-specific’ disease
  - No treatment during pregnancy
  - Relatively low transmission risk
  - Will require extra counseling (e.g., C-section, breastfeeding, significance of HCV-antibody-positive/RNA-negative results)
Considerations for HCV Testing of Exposed Infants

- **HCV RNA testing: age 2-6 months**
  - Up to 20% of infants with virus identified will clear spontaneously by age 5 to 7 years
  - RNA-positive infants need further testing, linkage to care, and virologic monitoring
  - Expensive test

Polywka et al, 2006; Mac et al, 2012; European Paediatric Hepatitis C Virus Network, 2005
Considerations for HCV Testing of Exposed Infants, cont.

- **HCV antibody: age 18 months**
  - Passively acquired maternal antibody may be detected up to 18 months
  - Children with negative HCV antibody at age 18 months are not HCV-infected and need no further testing (~95% of children born to HCV-infected mothers)
  - Concerns about loss-to-follow-up

- **Optimal timing for infant testing remains unknown**

Polywka et al, 2006; Mac et al, 2012; European Paediatric Hepatitis C Virus Network, 2005
CSTE Case Definition: Public Health Reporting and National Notification of Perinatal Hepatitis C Virus Infection

- **Clinical criteria**
  - Diagnosis of HCV in an infant between 2-36 months of age, or diagnosis of HCV in a pregnant woman

- **Laboratory criteria**
  - Report all infants under 36 months of age with evidence of HCV infection as evidenced by the following tests: HCV RNA or a positive test indicating presence of hepatitis C viral antigen(s) (HCV antigen), or other evidence of HCV viremia (e.g., genotype testing). Also report all infants between 18-36 months of age with positive HCV antibody results and no or unknown HCV RNA, antigen or genotype results
  - Report all pregnant women with evidence of HCV infection as evidenced by the following laboratory tests: positive HCV RNA OR positive test indicating presence of HCV antigen, OR other evidence of HCV viremia (e.g., genotype testing)
Criteria for epidemiological linkage:

- When possible, in order to verify infection source for an infant that has been reported as having evidence of HCV infection status, the HCV status of the mother should be determined, using the acute and/or chronic HCV infection case definition as a guideline for which cases would be considered confirmed.
Engage Federal Advisory Committee: CDC/HRSA Advisory Committee for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (CHAC)
- CHAC supports universal HCV testing during pregnancy

Consider enhanced risk-based testing
- Prenatal care setting a venue for which HCV testing recommended
- Other potential venues: Syringe Service Programs, drug treatment clinics, Emergency Departments
- Re-define risk-populations (include infants with Neonatal Abstinence Syndrome)
- Specify testing algorithm (need for repeat testing)
Summary

- Increasing HCV incidence in women of child-bearing potential
- Highly effective DAA treatment not approved for use during pregnancy
- Universal HCV testing during pregnancy identifies infants who need testing/follow-up
  - Cons: no treatment during pregnancy, not ‘pregnancy-specific’ disease
- Optimal infant testing algorithm (including timing of tests) unknown
- Enhanced risk-based testing
  - Including prenatal care setting as venue for HCV testing
Thank You
Questions?

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