Vertical transmission of hepatitis C: towards universal antenatal screening in the era of new direct acting antivirals (DAAs)? Short review and analysis of the situation in Switzerland

Karoline Aebi-Popp¹*, Andrea Duppenthaler², Andri Rauch¹, Andrea De Gottardi³ and Christian Kahlert⁴

¹ Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Switzerland
² Department of Pediatric Infectious Diseases, University Children's Hospital, Bern, Switzerland
³ Department of Hepatology, University Hospital Bern, Switzerland
⁴ Division of Infectious Diseases, Children's Hospital of Eastern Switzerland, St Gallen, Switzerland

Karoline Aebi-Popp
Consultant Obstetrician/Gynecologist
Department of Infectious Diseases
University Hospital Bern
Switzerland
Outline

- Swiss Hepatitis Strategy
- HCV in pregnant women in Switzerland
- Vertical transmission and missed opportunities
- Antenatal Screening? Future considerations
Viral Hepatitis and HIV-related mortality in Switzerland

HIV, HBV and HCV-related mortality rates (with 95% confidence intervals) from the data of the Swiss Federal Statistical Office.
The Swiss Hepatitis strategy

Network of 80 persons (NGO, medicals, patient initiatives, industry, politicians)

Elimination of viral hepatitis in Switzerland until 2030

Aims:
- reduction of chronic infections of 30% in 2020, of 90% in 2030
- reduction of new infections of 50% in 2020, of 100% in 2030
- no liver cancer and no transplantation due to viral hepatitis in 2030
Hepatitis C: cascade of care Switzerland

36-56% of the total estimated viremic population remain undiagnosed (i.e. 21,000 – 46,100 patients)

1MULLHAUPT et al, PLoS One 2015;10:e0125214
2www.adm.bag.ch; 3IMS Health Pharma GmbH, Rotkreuz

Courtesy Franco Negro
HCV and pregnancy

• No therapeutic agents are available to reduce the risk of mother to child transmission (MTCT) of HVC, which remains 5.8% (95%CI 4.2%-7.8%)

• HCV infection in pregnancy carries risk for preterm birth, low birth weight, cholestasis during pregnancy

• HCV MTCT can be reduced by avoiding fetal scalp electrodes and birth trauma

• If not diagnosed, missed opportunity to refer women for HCV treatment after delivery and close follow up for neonates (HCV infection remains un-diagnosed)
Pregnancy: huge considerations for small numbers

**Should we test during pregnancy?**

**Contra:**
- no measures to avoid perinatal transmission
- upsetting pregnant women

**Pro:**
- follow up for the newborn
- counseling/therapy for the mother after delivery

**Should we test before pregnancy?**

**Contra:**
- When and who?
- Planning pregnancy = eligible for therapy?
- Ethically fair/ correct?

**Pro:**
- HCV therapy before pregnancy, eliminating the risk of MTCT
HBV AND HCV TESTING RECOMMENDATIONS

Past or current use of intravenous or intranasal drugs
Patients infected with HIV

Pregnant women
Birth cohort screening for HCV: population born between 1950 and 1985
Pregnant women and children born to mothers infected with HBV/HCV
Recipient of blood products before 1992 in Switzerland
People who have had tattoos or piercings under unsafe conditions
People who have had tattoos or piercings under unsafe conditions
People who have had tattoos or piercings under unsafe conditions

Patients treated with dialysis
Patients with invasive procedures in health-care facilities with inadequate infection control practices
Patients with elevated transaminases or chronic advanced liver disease

Risk based screening seems inferior to universal screening during pregnancy

Study from Cleveland: **Prevalence in high risk: 0.95% in all women: 3.18%**
Current situation - testing pregnant women for HCV in different Swiss regions 2016 (520 doctors)

% of doctors, who test ALL pregnant women for HCV

### Prevalence of anti-HCV in pregnant women

1.6% of the Swiss population HCV-antibody-positive about 17,939 women are chronically infected with HCV

0.71% of pregnant women HCV seropositive, 75% chronic infection

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Number of women tested (column percent)</th>
<th>No. infected with HCV (percent positive)</th>
<th>Crude odds ratios</th>
<th>Adjusted* odds ratios and 95% CI (p-values from likelihood ratio test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>9,057 (100%)</td>
<td>64 (0.71%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>≤24 years</td>
<td>2,035 (22%)</td>
<td>16 (0.79%)</td>
<td>0.87</td>
<td>0.89 (0.48–1.6)</td>
</tr>
<tr>
<td>25–29 years</td>
<td>3,665 (40%)</td>
<td>33 (0.90%)</td>
<td>1.0</td>
<td>1.0</td>
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<tr>
<td>30–34 years</td>
<td>2,367 (26%)</td>
<td>12 (0.51%)</td>
<td>0.56</td>
<td>0.57 (0.29–1.1)</td>
</tr>
<tr>
<td>35 years and over</td>
<td>990 (11%)</td>
<td>3 (0.30%)</td>
<td>0.33</td>
<td>0.29 (0.09–0.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P = 0.069</td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swiss</td>
<td>5,685 (63%)</td>
<td>43 (0.76%)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Non-Swiss</td>
<td>3,372 (37%)</td>
<td>21 (0.62%)</td>
<td>0.82</td>
<td>0.42 (0.24–0.75)</td>
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<tr>
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<td>P &lt;0.01</td>
</tr>
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</table>
Current situation in Switzerland

- **80 000** deliveries/year, of those **568 (0.7%)** HCV +
- **27** congenital infections expected (if MTCT 6%)
- Notifications Federal Office of Public Health 2005-2014 in children aged 0-14 years
  - Median 11/year

<table>
<thead>
<tr>
<th>Item</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>Median</th>
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<tbody>
<tr>
<td>HCV*</td>
<td>22</td>
<td>18</td>
<td>13</td>
<td>12</td>
<td>17</td>
<td>10</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td><strong>11</strong></td>
</tr>
<tr>
<td>Geburten°</td>
<td>72'903</td>
<td>73'371</td>
<td>74'494</td>
<td>76'691</td>
<td>78'286</td>
<td>80'290</td>
<td>80'808</td>
<td>82'164</td>
<td>82'731</td>
<td>83'753</td>
<td>79'288</td>
</tr>
</tbody>
</table>

* BAG Meldungen total, Alter 0-14J
° Quelle BFS

- BUT: we expect **27** perinatally infected children/year
- Reported are less than **50%** of the expected number
Who cares?

• It is very likely that **more than half of HCV-infected newborns are not diagnosed** as their mothers are not tested during pregnancy.

• Even if 10–20% of perinatally infected children will spontaneously clear HCV infection, a **larger number** of them will have progressive disease that **might not be diagnosed for many years**
Arguments to introduce an universal screening during pregnancy - would you tick the box?

Cost effective?

London: YES !!! (Selvapatt et al J Hepatol. 2015)

Amsterdam: NO !!! (A. T. Urbanus PLOS one 2013)

All depends on cost of DAAs and consideration of „indirect costs“
SUMMARY

• Prior to advent of DAAs HCV was not considered worthy of antenatal screening due to lack of intervention options.

• Screening gives the opportunity to provide appropriate management to reduce perinatal infections as well as monitor the mother and the baby after diagnosis.

• Swiss data shows about 50% undiagnosed children: Consider HCV universal screening in pregnant women.

• Future research: any drugs available to reduce transmission rate during pregnancy, early treatment of children.
Thanks for your attention

mail@aebi-popp.com