Current Global & Regional Epidemiology of HCV Infection in Hemodialysis Units
Strategies for Preventing Transmission

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Université catholique de Louvain
Brussels, Belgium
DISCLOSURES

Research Support: Amgen, Janssen-Cilag, MSD, Otsuka, Roche

Lecturing: Abbvie, Amgen, Menarini, MSD, Vifor-FMCRP

Consulting activities: Astellas, Vifor-FMCRP, MSD

Other : I have cochaired the 2018 update of the HCV in CKD KDIGO Guideline and am cochair of KDIGO
Outline

• Background
• Current magnitude of the problem
• Routes of nosocomial HCV transmission
• Potential preventative strategies
• Attitude when facing a case of acute HCV
• Conclusion
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Transmission of blood-borne viruses (HBV, HCV, HIV)

• Infectivity correlates with viral load:
  after injury with contaminated needle,
  risk of transmission around 30% for HBV (except in vaccinated subjects)
  3% for HCV
  0.3% for HIV

• Massive contamination = 100 microlitres of blood
Current transfusional risk of HCV in high income countries: \( \leq 1 \) case per million blood units
HCV transfusional risk
everything fine globally (1)?

- In 2011, in 39 countries, blood donations not routinely tested for transfusion-transmissible agents, including HCV (WHO)
- Use of rapid tests and poor quality control procedures: thus low sensitivity; in a study involving 17 African countries, sensitivity as low as 80% for HCV (WHO)
- Similar situation in Pakistan reviewed in Thursz and Fontanet
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CDC Urging Dialysis Providers and Facilities to Assess and Improve Infection Control Practices to Stop Hepatitis C Virus Transmission in Patients Undergoing Hemodialysis

CDC has received an increased number of reports of acute HCV infection among patients undergoing hemodialysis. Between 2014 and 2015, CDC has been contacted about 36 cases of acute HCV infection in 19 different hemodialysis clinics in eight states.
Prevalence, incidence, and risk factors for hepatitis C virus infection in hemodialysis patients

Michel Jadoul, Brian A. Bieber, Paul Martin, Takashi Akiba, Chizoba Nwankwo, Jean Marie Arduino, David A. Goodkin and Ronald L. Pisoni

KDIGO
HCV prevalence in prevalent vs. incident (<120 days) patients
Among countries in DOPPS 1+ countries

<table>
<thead>
<tr>
<th>Region/Country</th>
<th>DOPPS Phase</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalent patients</td>
<td></td>
<td>14.3</td>
<td>12.1</td>
<td>9.5</td>
<td>9.4</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(7894)</td>
<td>(6682)</td>
<td>(6245)</td>
<td>(8617)</td>
<td>(10042)</td>
</tr>
<tr>
<td>Incident patients</td>
<td></td>
<td>5.2</td>
<td>5.5</td>
<td>5.2</td>
<td>4.8</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(6186)</td>
<td>(3018)</td>
<td>(898)</td>
<td>(3102)</td>
<td>(4767)</td>
</tr>
</tbody>
</table>

Patient and facility characteristics associated with HCV incidence

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Mean or prevalence by incident HCV</th>
<th>Hazard Ratio (95% CI) of HCV Incidence&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient characteristics (n=946)</td>
<td>(n=37049)</td>
<td></td>
</tr>
<tr>
<td>Age, per 10 years for HR</td>
<td>61.7(14.5) 63.2(14.8)</td>
<td>0.99(0.94-1.04)</td>
</tr>
<tr>
<td>Male</td>
<td>58% 58%</td>
<td>1.00(0.88-1.13)</td>
</tr>
<tr>
<td>Time on dialysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>34% 38%</td>
<td>1.17(0.97-1.41)</td>
</tr>
<tr>
<td>1-2.9 years</td>
<td>21% 23%</td>
<td>1.00(ref)</td>
</tr>
<tr>
<td>3-4.9 years</td>
<td>13% 14%</td>
<td>0.99(0.79-1.24)</td>
</tr>
<tr>
<td>5-9.9 years</td>
<td>17% 15%</td>
<td>1.11(0.90-1.36)</td>
</tr>
<tr>
<td>10+ years</td>
<td>16% 10%</td>
<td>1.36(1.07-1.73)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>39% 43%</td>
<td>1.05(0.91-1.21)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>5% 2%</td>
<td>2.87(2.06-4.00)</td>
</tr>
<tr>
<td>Substance abuse in last 12 months</td>
<td>3% 2%</td>
<td>1.42(0.88-2.31)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>2% 0.4%</td>
<td>2.93(1.79-4.80)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Stratified by country and phase and accounting for facility clustering; adjusted for all variables listed in table; n = 946 events among 37,995 patients; facilities not admitting HCV+ patients were excluded.
## Patient and facility characteristics associated with HCV incidence

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Mean or prevalence by incident HCV</th>
<th>Hazard Ratio (95% CI) of HCV Incidence&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Facility characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation stations</td>
<td>19%</td>
<td>22%</td>
</tr>
<tr>
<td>Facility size, per 20 for HR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>49[38,58]</td>
<td>50[39,63]</td>
</tr>
<tr>
<td>Facility % HCV+&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>15%</td>
<td>20%</td>
</tr>
<tr>
<td>1-5%</td>
<td>16%</td>
<td>23%</td>
</tr>
<tr>
<td>6-10%</td>
<td>23%</td>
<td>25%</td>
</tr>
<tr>
<td>11-20%</td>
<td>24%</td>
<td>21%</td>
</tr>
<tr>
<td>&gt;20%</td>
<td>22%</td>
<td>11%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Stratified by country and phase and accounting for facility clustering; adjusted for all variables listed in table; n = 946 events among 37,995 patients; facilities not admitting HCV+ patients were excluded

<sup>b</sup> Median [interquartile range]

<sup>c</sup> HR (95%)=1.26 (1.14-1.39) per 10% higher facility % HCV
Table 3 | Percentage of facilities within each country or region by number of incident HCV cases during DOPPS follow-up, restricted to facilities with 10+ patients who had at least 2 HCV antibody measurements and whose initial measurement was negative (1996–2015)

<table>
<thead>
<tr>
<th>Facility No. of incident HCV cases</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Facilities, N²</th>
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</thead>
<tbody>
<tr>
<td>Australia–New Zealand</td>
<td>48.6</td>
<td>37.1</td>
<td>8.6</td>
<td>2.9</td>
<td>–</td>
<td>2.9</td>
</tr>
<tr>
<td>Belgium</td>
<td>68.8</td>
<td>16.7</td>
<td>10.4</td>
<td>2.1</td>
<td>–</td>
<td>2.1</td>
</tr>
<tr>
<td>Canada</td>
<td>81.0</td>
<td>16.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2.4</td>
</tr>
<tr>
<td>China b</td>
<td>78.3</td>
<td>21.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>France</td>
<td>57.6</td>
<td>18.6</td>
<td>15.3</td>
<td>3.4</td>
<td>5.1</td>
<td>–</td>
</tr>
<tr>
<td>GCC c</td>
<td>80.0</td>
<td>10.0</td>
<td>10.0</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Germany</td>
<td>64.0</td>
<td>24.0</td>
<td>2.7</td>
<td>4.0</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>Italy</td>
<td>45.3</td>
<td>26.7</td>
<td>13.3</td>
<td>6.7</td>
<td>5.3</td>
<td>2.7</td>
</tr>
<tr>
<td>Japan</td>
<td>42.9</td>
<td>29.5</td>
<td>12.5</td>
<td>8.9</td>
<td>3.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Russia</td>
<td>77.8</td>
<td>11.1</td>
<td>11.1</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Spain</td>
<td>52.1</td>
<td>27.4</td>
<td>9.6</td>
<td>5.5</td>
<td>1.4</td>
<td>4.1</td>
</tr>
<tr>
<td>Sweden</td>
<td>78.7</td>
<td>12.8</td>
<td>4.3</td>
<td>4.3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Turkey</td>
<td>100.0</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>71.9</td>
<td>12.3</td>
<td>8.8</td>
<td>3.5</td>
<td>–</td>
<td>3.5</td>
</tr>
<tr>
<td>United States</td>
<td>62.9</td>
<td>16.5</td>
<td>8.1</td>
<td>4.0</td>
<td>3.7</td>
<td>4.8</td>
</tr>
<tr>
<td>All DOPPS countries</td>
<td>59.1</td>
<td>21.5</td>
<td>9.0</td>
<td>4.8</td>
<td>2.6</td>
<td>2.9</td>
</tr>
</tbody>
</table>
Nosocomial transmission evidence

• DOPPS HCV incidence rates, by facility practice:
  • Do not accept HCV+ patients: 0.6 (0.3,1.3)
  • HCV+ pts treated at a general station: 2.3 (2.1,2.5)

• Clustering of HCV seroconversions in some facilities (mini-outbreaks)
  • 60% of facilities had 0 cases over ~3 years follow-up
  • 3% of facilities had 5+ cases

• Transfusional HCV transmission: currently < 1 case per million transfusions in high income countries

• IV drug users generally much younger than the hemodialysis patients with HCV seroconversion
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Nosocomial transmission of HCV in HD

• Rare event, difficult to study:
  example: if incidence of seroconversion: 5% /year
  \( \leq 5 \text{ events} \) leading to transmission among 100 patients, each 156 sessions a year (3 weekly sessions):
  \( 15600 \text{ sessions} \)

• Best approach: combine
  - epidemiological data (shift, practices, monitors,…) in same unit
  - molecular virology (demonstrated nosocomial HCV transmission)
Incidence and risk factors for hepatitis C seroconversion in hemodialysis: A prospective study

Michel Jadoul, Chantal Cornu, Charles van Ypersele de Strihou, and the UCL Collaborative Group
Molecular virology
common HCV source in pts A-G

Molecular Evidence for Nosocomial Transmission of Hepatitis C Virus in a French Hemodialysis Unit

Jacques Izopet, C. Pasquier, K. Sandres, J. Puel, and L. Rostaing

1Laboratoire de Virologie, CHU Purpan, Toulouse, France
2Service de Néphrologie, CHU Rangueil, Toulouse, France
Nosocomial transmission of HCV in HD

- 20 studies with molecular virology demonstration of nosocomial transmission and some epidemiological data
- 1 to 22 patients newly contaminated from source patient(s)
- N of events?
  - A to B, C and D
  - A to B, B to C, C to D
Nosocomial transmission of HCV in HD

- 2 studies suggested a role for internal circuit of monitor (either hydraulic circuit or pressure transducer) but role of external surfaces not excluded
- 18 studies: transmission by monitor excluded: source patient(s) and newly contaminated patient(s) dialyzed on other monitors (or at same time)
- Several studies with transmission of HCV despite separate monitors for HCV(+) pts
Nosocomial transmission of HCV: which routes?

Vast majority of transmission events occur at same time /other monitors

• External surfaces
• Hands of staff
• Multidose vials or contaminated injectable drugs
Isolation of HCV+ pts or not?

- Isolation by ward would mean 4 wards in units with HBV + pts: B+C+, B-C+, B+C-, B-C-
- Window from infection to seroconversion (EIA) in HD patients: 5 months
- HCV: lower infectivity than HBV
- Risk of infection by multiple HCV genotypes

M Jadoul Semin Dial 1995
3.1: We recommend that hemodialysis facilities adhere to standard infection control procedures including hygienic precautions that effectively prevent transfer of blood and blood-contaminated fluids between patients to prevent transmission of blood-borne pathogens. (IA)

3.1.1: We recommend regular observational audits of infection control procedures in hemodialysis units. (IC)

3.1.2: We recommend not using dedicated dialysis machines for HCV-infected patients. (ID)

3.1.3: We suggest not isolating HCV-infected hemodialysis patients. (2C)

3.1.4: We suggest that the dialyzers of HCV-infected patients can be reused if there is adherence to standard infection control procedures. (2D)
HCV KDIGO Guideline 3: evidence based?

- No Randomized Controlled Trial for prevention
- « old » high quality evidence supporting hygienic precautions (WHO, CDC,....)
<table>
<thead>
<tr>
<th>Region/Country</th>
<th>HCV+ patients not accepted</th>
<th>Treated at an isolation station</th>
<th>Treated at a general station</th>
<th>No policy</th>
<th>N Facilities</th>
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</thead>
<tbody>
<tr>
<td>Australia-New Zealand</td>
<td>25.0</td>
<td>75.0</td>
<td></td>
<td></td>
<td>16</td>
</tr>
<tr>
<td>Belgium</td>
<td>15.8</td>
<td>84.2</td>
<td></td>
<td></td>
<td>19</td>
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<tr>
<td>Canada</td>
<td>15.0</td>
<td>75.0</td>
<td>10.0</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>China</td>
<td>19.5</td>
<td>75.6</td>
<td>4.9</td>
<td></td>
<td>41</td>
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<td>France</td>
<td>16.7</td>
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<td>16.7</td>
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<td>GCC-6</td>
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<td></td>
<td></td>
<td>16</td>
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<td>30.0</td>
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<td></td>
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<td>22.2</td>
<td>66.7</td>
<td>11.1</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>5.0</td>
<td>80.0</td>
<td>15.0</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>United States</td>
<td>4.4</td>
<td>33.1</td>
<td>37.5</td>
<td>6.0</td>
<td>83</td>
</tr>
</tbody>
</table>

All DOPPS countries  | 4.4                        | 33.1                            | 37.5                          | 3.1       | 388          |

a. As reported by medical directors at each DOPPS facility; Supplemented by nurse study coordinator response where missing medical director response
b. Gulf cooperation council countries — includes Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates
CHAPTER 3
PREVENTING HCV TRANSMISSION IN HEMODIALYSIS UNITS

3.2: We recommend hemodialysis centers examine and track all HCV test results to identify new cases of HCV infections in their patients. (1B)

3.2.1: We recommend aggressive measures be taken to improve hand hygiene (and proper glove use), injection safety, and environmental cleaning and disinfection when a new case of HCV is identified that is likely to be dialysis-related. (1A)

3.3: Strategies to prevent HCV transmission within hemodialysis units should prioritize adherence to standard infection control practices and should not primarily rely upon the treatment of HCV-infected patients. (Not Graded)
Most common errors

• Preparing IV drugs in a contaminated area
• Sharing multidose vials (heparin, saline)
• Emergency situations (less time to change or at least withdraw gloves)
• Inadequate transport of contaminated waste, disseminating blood in the environment
Key points for the prevention of nosocomial HCV in HD

- Hand Hygiene (hydroalcoholic solution or water and soap) before contact with patient and after gloves withdrawal
- Wear gloves, to be changed between patients/stations
- Prepare (injectable) drugs in clean area
- Do not return unused material from contaminated to clean area
- Clean/disinfect surfaces of HD environment (including external surface of monitor) before next session
- Dedicate small items (tourniquet, tape, ...) to a single patient (if not, disinfect between patients)
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CHAPTER 1
DETECTION AND EVALUATION OF HCV IN CKD

HCV screening of patients with CKD

1.1.1: We recommend screening all patients for hepatitis C virus (HCV) infection at the time of initial evaluation of chronic kidney disease (CKD). (1C)

1.1.2: We recommend screening all patients for HCV infection upon initiation of in-center hemodialysis or upon transferring to another dialysis facility or modality. (1A)
1.1.2.1: We recommend using immunoassay followed by NAT or NAT alone. (1A)

This should be part of the infection control strategy of any HD unit
Suspecting/Diagnosing acute hep C

• Even mild increase of transaminase level (ALT) above baseline is abnormal in HD
  ALT level rising from 8-12 IU to 45 IU (NI <40 IU) : acute hep C? test by NAT for HCV-RNA

• Window between infectivity (PCR= NAT+) and EIA +: around 5 months
Attitude in case of suspected nosocomial HCV transmission

- Check epidemiology in HD unit (map with already HCV+ patients, etc…)
- Recent (last year) transfusion? If yes, look back at donor(s)
- Other risk factors (IVDU?)
- Look after ongoing additional transmission
  Test for HCV-RNA all potentially exposed patients, twice within 2-12 weeks (KDIGO 2008 and 2018)
- Identify errors, explain, check
Can HCV transmission be fully prevented?

Success will depend on

• Educational material adapted to local characteristics, level of education of staff: simplicity!
• Repeating educational courses
• Checking the impact on day to day practices
• Support of local leaders (nephrologists, head nurses…)
Conclusion

- HCV transmission is still substantial within HD units
- Preventative strategies
  - 1st priority: safety of blood transfusions (OK in high-income countries)
  - nosocomial transmission could/should be reduced by low-cost educational interventions

unless done, reinfections will occur in HD units despite cures by highly active DAA regimens