Medical responses to social diseases: The case of Hepatitis C

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ID Professor’s Evening, June 9, 2016
Disclosures

None to declare
Summary

- A brief history of HCV
- A brief review of HCV epidemiology
- The evolution of HCV treatment
- The marketing of HCV treatment (2013 – present)
- Syndemics, public health and HCV
Confessions

• I believe that HCV can cause bad things in the liver
• I believe the new HCV drugs are very good
• I believe that people should not be denied treatment because they inject drugs
# A Brief History of HCV in Canada

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960/1970’s</td>
<td>Blood tests to diagnose HepB and HepA infections were developed</td>
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<tr>
<td>1972</td>
<td>The Canadian Red Cross implements HepBsAg testing across Canada</td>
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<tr>
<td>1974</td>
<td>A third form of transfusion associated hepatitis is postulated (Non-A Non-B)</td>
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<tr>
<td>1981</td>
<td>NEJM-surrogate marker testing using ALT reduces hepatitis transmission by 40%</td>
</tr>
<tr>
<td>1981</td>
<td>Both US NIH and Canadian Red Cross opt for further study and do not use ALT</td>
</tr>
<tr>
<td>1982</td>
<td>Mark Tyndall starts medical school (largely unnoticed)</td>
</tr>
<tr>
<td>1986</td>
<td>US began screening for ALT and anti-HBc as “surrogate” testing – not in Canada</td>
</tr>
<tr>
<td>1987</td>
<td>Dr. Blajchman / Feinman submit application for a randomized study on ALT</td>
</tr>
<tr>
<td>1988</td>
<td>Chiron Corp discovers Non-A Non-B virus (later HepC)</td>
</tr>
<tr>
<td>1988</td>
<td>Blajchman study approved by NHRDP and Canadian Blood Committee</td>
</tr>
<tr>
<td>1990</td>
<td>Red Cross implements first generation HepC-antibody testing</td>
</tr>
<tr>
<td>1993</td>
<td>Blajchman shows a 70% reduction in HepC transmission in the screened group</td>
</tr>
<tr>
<td>1990-present</td>
<td><strong>Massive numbers of new infections among drug users unrelated to transfusions</strong></td>
</tr>
<tr>
<td>1998</td>
<td>Interferon and Ribavirin approved for treatment but uptake is very low</td>
</tr>
<tr>
<td>2005 - 2012</td>
<td>HepC replicated in test tube - opened the door to Direct Acting Antivirals</td>
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</table>
170 million infected globally
0.3 million infected in Canada
BC Hepatitis Testers Cohort

- De-identified health information for 1.5 million British Columbians tested for HCV, HIV, HBV & TB
- Includes almost all: lab tests/results, medical visits, hospitalizations, prescriptions, cancer outcomes, and mortality
- 25 years of information
- Net costs of services
- Health outcomes by different groups
- Amongst the most comprehensive in the world
March 09, 2015:
- 1,425,589 individuals tested for anti-Hep C
- 76,083 anti-HCV+
  - includes 8,495 seroconverters
  - 4,263 within 24m
Flow of subjects in BC HTC

HCV testers
N = 1,132,855

HCV positive
N = 64,634 (5.8%)

Reported cases
N = 3,092

Total HCV positive
N = 67,726

HCV negative
N = 1,065,129

Died
N = 11,945 (17.6%)

Liver Cancer
1,208 / 65,842
(1.8%)

Alive in 2013
N = 55,781

HCC
915 / 65,842
(1.4%)

Died
N = 74,840 (7.4%)

Liver cancer
1,664 / 980,865
(0.17%)

Alive in 2013
N = 988,381

HCC
1,140 / 98,0865
(0.12%)
Annual age-adjusted liver related mortality rates among HCV infected individuals by sex, BC HTC, 1993-2012

Dark lines smoothened rates; light lines observed data

Associated with large hospitalization costs
3,148 cases of liver cancer (1992-2011)

Liver Cancer
1,136

M/F: 79% / 21%

M/F: 81% / 19%

1,146 (36%)
62 (2%)
62,004 (98%)

804 (25%)
31,279 (97.5%)

Hep C +ve
1990-2012
N=65,842

HBV +ve
1990-2012
N=34,775

Hep C

Alcohol? Obesity?
Estimated lifetime cost of HCV infection ~$65,000

Myers et al. CJGH 2014
Summary:
- Estimated 2.7 million infected not counting homeless and incarcerated.
- Main risk factors were blood transfusion pre-1990 and illicit drug use.
- Highest rates in the less educated and the poor.
- Speculate that falling prevalence due to death.
Incidence of hepatitis C virus infection among injection drug users during an outbreak of HIV infection

David M. Patrick, Mark W. Tyndall, Peter G.A. Cornelisse, Kathy Li, Chris H. Sherlock, Michael L. Rekart, Steffanie A. Strathdee, Sue L. Currie, Martin T. Schechter, Michael V. O’Shaughnessy

CMAJ • OCT. 2, 2001; 165 (7)

Fig. 1: Incidence density rate (and 95% confidence interval) for hepatitis C virus and HIV over 3 years of the Vancouver Injection Drug User Study.

Table 3: Cox proportional hazards model of independent predictors of HCV seroconversion among IDUs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate hazard ratio (and 95% CI)</th>
<th>Adjusted hazard ratio (and 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>1.69 (1.02–2.80)</td>
<td>2.29 (1.35–3.89)</td>
</tr>
<tr>
<td>Use of cocaine or speedballs (or both)</td>
<td>3.60 (1.88–6.90)</td>
<td>2.42 (1.22–4.79)</td>
</tr>
<tr>
<td>Frequent injection*</td>
<td>3.54 (2.03–6.20)</td>
<td>2.02 (1.09–3.77)</td>
</tr>
<tr>
<td>Frequent attendance at needle exchange program†</td>
<td>3.69 (2.12–6.43)</td>
<td>2.56 (1.37–4.79)</td>
</tr>
</tbody>
</table>
Drivers of HIV incidence among drug users

- Cocaine injection (Strathdee, AIDS 1997; Tyndall, AIDS 2002)
- Difficulty Accessing syringes (Wood, CMAJ 2002)
- Requiring help injecting (Wood, CMAJ 2001)
- Female gender (Spittal, CMAJ 2002)
- Aboriginal Ethnicity (Craib, CMAJ 2002)
Mortality in a large community-based cohort of inner-city residents in Vancouver, Canada

Figure 2: Mortality in the inner-city cohort, by year of follow-up. Drug-, liver- and HIV-related deaths are defined in Methods. Error bars = 95% confidence intervals.
### Table 4: Mortality and excess mortality related to drug use, viral hepatitis and liver disease, and HIV infection among the 2913 participants*

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>No. of deaths</th>
<th>Rate per 10 000 person-years (95% CI)</th>
<th>SMR† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>374</td>
<td>223 (201–247)</td>
<td>7.1 (6.4–7.9)</td>
</tr>
<tr>
<td>Men</td>
<td>263</td>
<td>220 (195–248)</td>
<td>5.8 (5.1–6.6)</td>
</tr>
<tr>
<td>Women</td>
<td>111</td>
<td>230 (191–277)</td>
<td>15.4 (12.8–18.5)</td>
</tr>
<tr>
<td>Drug-related‡</td>
<td>53</td>
<td>32 (24–41)</td>
<td>12.0 (9.1–15.7)</td>
</tr>
<tr>
<td>Men</td>
<td>36</td>
<td>30 (22–42)</td>
<td>9.3 (6.7–12.9)</td>
</tr>
<tr>
<td>Women</td>
<td>17</td>
<td>35 (22–57)</td>
<td>30.3 (18.8–48.7)</td>
</tr>
<tr>
<td>Liver-related§</td>
<td>22</td>
<td>13 (9–20)</td>
<td>5.9 (3.9–8.9)</td>
</tr>
<tr>
<td>Men</td>
<td>15</td>
<td>13 (8–21)</td>
<td>4.5 (2.7–7.4)</td>
</tr>
<tr>
<td>Women</td>
<td>7</td>
<td>15 (7–30)</td>
<td>17.9 (8.5–37.6)</td>
</tr>
<tr>
<td>HIV-related¶</td>
<td>78</td>
<td>46 (37–58)</td>
<td>24.9 (20.0–31.1)</td>
</tr>
<tr>
<td>Men</td>
<td>54</td>
<td>45 (35–59)</td>
<td>18.7 (14.4–24.5)</td>
</tr>
<tr>
<td>Women</td>
<td>24</td>
<td>50 (33–74)</td>
<td>96.8 (64.9–144.5)</td>
</tr>
</tbody>
</table>

Note: CI = confidence interval; ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th revision; SMR = standardized mortality ratio.

*Causes of death for participants in the “unknown status” group (i.e., those whose HCV status and HIV status were both unknown, and those whose status was unknown for either HCV or HIV and who had a negative HIV or HCV result, respectively) are shown in Appendix 3 (available at www.cmajopen.ca/content/1/2/E68/suppl/DC1).

†Reference group was the population of Vancouver.

‡Deaths from mental and behavioural disorders due to psychoactive substance use (ICD-10 codes F11–16, F19), accidental poisoning by drugs (X40–44), suicide by drugs (X60–64), assault by drugs and medicaments (X85), poisoning by drugs or medicaments undetermined if accidental or intentional (Y10–14), and adverse effects of drugs and medicaments (Y40–574, Y577–79, Y598, Y880).

§Deaths from viral hepatitis (B15–19), liver cancer (C22), alcoholic liver disease (K70) and nonalcoholic liver disease (K71–77).

¶ICD-10 codes B20–24.
Continued low uptake of treatment for hepatitis C virus infection in a large community-based cohort of inner city residents

Maryam Alavi¹, Jesse D. Raffa², Gregory D. Deans³, Calvin Lai⁴, Mel Krajden⁵, Gregory J. Dore¹, Mark W. Tyndall⁶ and Jason Grebely¹

Liver Int. 2013 Oct 27.

Fig. 2. Cumulative proportion of HCV treatment in a large, community-based cohort in the inner city of Vancouver (n = 1257), bars represent 95% confidence intervals.
Drug labs that promote HCV transmission
First Direct Acting Antiviral approved in 2013

- Approved for use with INF/ribavirin
- Price US$84,000 for 12 week treatment or about $1000 per pill
- Price in Canada is about $60,000
- Not including about $30,000 for INF/ribavirin
Profits

Gilead racked up $5 billion in Sovaldi sales in the first half of 2014. According to a JAMA viewpoint article, it may have cost Gilead $11 billion to "develop" Sovaldi - this is based on the price Gilead paid to acquire Pharmasset, which discovered and initially tested Sovaldi. If all of the approximately 3.6 million Hep C patients with chronic liver disease in the United States were treated with Sovaldi at current prices, Gilead would net more than $300 billion dollars, or better than a 27-to-1 return on its investment, "suggesting that pricing is inappropriately high."
Market Watch

Even in the highly mercurial pharmaceutical industry, Gilead Sciences' growth in 2014 was nothing short of astonishing, with revenues more than doubling in a single year from $11bn to $24.5bn, while profits quadrupled to $12bn. The cause was the company's spectacularly successful hepatitis C drug Solvadi, launched at the end of 2013, followed by combination treatment Harvoni in late 2014. Together those two products contributed first year sales of more than $12bn, rocketing Gilead into the global Top 10 pharmaceutical companies. That kind of growth will be hard to maintain. The key challenge facing Gilead is to maintain steady development in the face of numerous rival drugs now entering the market, all priced well below Solvadi's staggering $85k cost for a three-month course.
Syndemics

A central tenet of syndemic theory is that diseases do not exist in a social vacuum nor solely within the bodies of those they inflict, and thus their transmission and impact is never merely a biological process. Ultimately, social factors, like poverty, racism, sexism, ostracism, and structural violence may be of far greater importance in the extent of disease spread and the toll taken in human well-being than the nature of pathogens or the bodily systems they infect. As a result of such factors and the resulting interactions among pathogens or other health conditions, the total burden of disease is far greater among those subjected to structural disadvantage compared to populations that are not so encumbered resulting in significant disparities in both social suffering and years of life lost.
Why HCV is so prevalent among drug users?

Medical/Epidemiologic analysis

• Very easily transmitted through exposure to small amounts of blood – needles and drug paraphernalia

• Acute infection is generally asymptomatic and people may be unaware that they are infected

• Disease progression is extremely slow but variable
  – Studies from medical clinics show cirrhosis in 22% by 20 years while studies following transfusion related HCV show cirrhosis in just 4% after 20 years

• The people that are potentially infectious are in the community for decades
Why HCV is so prevalent among drug users? Syndemic analysis

- Structural factors promote transmission by forcing people into practices that they know are unsafe
- The combination of trauma, mental illness, substance abuse drive HCV infection
- The combination of poverty, stigma and criminalization perpetuate the epidemic
Way forward

- Treat those who need treatment for medical indications - even if HCV treatment could be quickly scaled up there will still be more people getting infected than getting treated
- Scale-up harm reduction to prevent new infections and re-infections – education, needles, social support, housing, access to detox, access to drug treatment, better methadone/suboxone programs, supervised injection sites
- Continue to address upstream social determinants of addiction and poverty
- Challenge the drug pricing
- Develop a Provincial strategy that has clear goals and recognizes the syndemics of the epidemic