**Viral hepatitis in migrants?**

Jordan J. Feld MD MPH  
Toronto Centre for Liver Disease  
Sandra Rotman Centre for Global Health  
University of Toronto

**Outline**

- **Scope of the problem**  
  - HBV & HCV by the numbers  
  - HBV & HCV – commonalities and differences  
- **Situation in migrants**  
  - To screen or not to screen  
  - When, where and how?  
  - Screening tools  
- **Beyond screening**  
  - Linkage to care & treatment

**Should the “Big 3” be the “Big 4”?**

![Graph showing deaths from various diseases](WHO Global Hepatitis Report, 2017)

**HCV is a MAJOR global public health problem**

![Map showing HCV distribution](WHO)

- 7.1 million people infected  
- No vaccine  
- Leading indication for liver transplant

**HBV: Some sobering facts**

![Map showing HBV distribution](WHO)

- 250 Million people chronically infected  
- 2 billion with evidence of "past" infection  
- 600,000-1 million deaths annually (same as malaria)

**Disclosures**

- Research: Abbvie, Gilead, Janssen, Merck, Wako
- Speaking: None
**Hepatitis is a MAJOR health problem in Canada**

- **Years of Life Lost**
- **Years of Life Equivalents of Reduced Functioning**

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**Dramatic improvement in HCV therapy**

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**WHO takes the lead**

- **Vision:** A world where viral hepatitis transmission is halted and everyone living with viral hepatitis has access to safe, affordable and effective prevention, care and treatment services

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**WHO Elimination Targets**

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**WHO**

- **WHO Global Health Sector Strategy 2016-2021**
- **WHO Elimination Targets**

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**The first cancer vaccine – highly effective!**

- **Global coverage:** 79% in 2012
- **Trend in 3rd dose vaccine coverage in infants global coverage**

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**WHO, NCs 2007, WHO 2017**

- Increasing but plateauing coverage → 79% in 2012 and 82% in 2014
- Only 38% coverage of birth-dose (reduces risk by 8-fold)

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**WHO**

- **WHO Global Health Sector Strategy 2016-2021**
- **WHO Elimination Targets**
**Treatment uptake more important than cure rate**

- Curing the individual is now easy
- Curing the population will take a lot more work...

**SVR in individuals**

**SVR in the population**

![Graph showing SVR rates](image1)

*Improved therapy of no benefit unless treatment rates increase*

**The cascade of care... not just treatment**

*Modeled data for non-VA US population*

*But won’t this all get better with IFN-free therapy?*

**An elimination strategy**

*Reminder in EPR → 32,012 visits → 18,772 (58%) tested → 7,315 Ab+ (4.2%)*

*Left side of the cascade actually more important*

*DAAs only help here*

*Even with effective treatment, major gaps in cascade of care!*

**Why are treatment rates so low?**

**Patients**
- Unaware of infection → feel perfectly well until advanced disease
- May have little interaction with the healthcare system
- Screening and active case finding required

**Doctors**
- Poor awareness – late diagnosis and referral
- Treatment capacity – few hepatologists, GIs, IDs
- PCPs/ Addiction medicine... just starting to enter the field
- Outdated models of care – based on the interferon days
- Treatment access often limited – fibrosis stage, specialists
- Improved access, increased provider base and new models of care required

**What about HBV?**

*Long-term entecavir in eAg+ve HBV*

*Tenofivir vs Tenofiv/entecavirabine in LAM-R HBV*

*Long-term therapy with potent oral nucleotide analogues leads to suppression in almost all patients (even after resistance)*

**Highly effective therapy**

- Current therapy taken long-term
  - Suppresses HBV DNA
  - Normalizes ALT
  - Prevents fibrosis progression
  - Promotes fibrosis regression – even in cirrhosis
  - Prevents and even reverses hepatic decompensation
  - Reduces, but does not eliminate, the risk of HCC

*Highly effective BUT not curative*
HBsAg loss is the real goal of therapy

HBV ≠ HCV: Some key differences
- **Transmission**
  - HBV: At birth, (sexual)
  - HCV: Throughout life – medical, IDU
- **Epidemiology**
  - Some overlap but some key differences
  - HBV: Asia, SS Africa
  - HCV: S. Asia, Egypt, Eastern Europe
- **Natural History**
  - HBV: Dynamic, unpredictable
  - HCV: Slowly progressive
- **Treatment**
  - HBV: Complicated decisions, long-term/indefinite → specialty care
  - HCV: Simple, finite, curative → primary care

**Implication**: Once you start…usually very long-term therapy!

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  - Screening tools
  - Beyond screening
    - linkage to care & treatment

**Benefits of screening for viral hepatitis**

**Individual**
- Access to treatment – prevent complications of the disease
- Prevent additional harms to health – alcohol, obesity (even if no treatment)
- Vaccination for HBV – personal & contacts

**Societal**
- Harm reduction – reduce transmission
- Assess burden in the population – plan for the future

**Potential ‘harms’ of screening**

**Individual**
- Diagnosis in asymptomatic individuals
  - Give a well person a ‘disease’
  - Potentially stigmating – may affect employment, immigration
- Potentially ‘harmful’ unless
  - Linkage to care – minimum – information, harm reduction
  - Access to treatment – this is really the key
    - ‘No treatment available’, ‘No doctors available’ or ‘You’re not sick enough for treatment’ or ‘No treatment for you unless you stop using drugs/ETOH’

**Societal**
- Cost of screening
- Cost of treatment → cost effective is not cost saving – huge budget impact…opportunity cost!

**Screening Approaches**

**Risk-based**
- Identify and test only those with risk factors
  - Pros:
    - High yield
    - Cheaper
  - Cons:
    - Contact with HC system
    - Must know & discuss risk factors
    - Test may be stigmatized
    - Miss those without RFs

**Population-based**
- Test a segment of the population eg. baby boomers, newcomers
  - Pros:
    - High coverage rate
    - Easy to implement
  - Cons:
    - Need to choose the population
    - Low yield, expensive
    - May be stigmatizing to population eg. migrants

Not mutually exclusive
Should migrants be screened?

- Probably – in most settings
- But need data to determine optimal approach
  - All migrants or only certain countries?
  - All migrants or only certain types e.g. refugees vs immigrants vs other?
  - Part of population-based screening or separate program?
  - Where, when and how should migrants be screened?

Collecting the data...

- Rarely available for given migrant population in a particular country
- Estimate:
  
  \[ \text{Migrant population (census)} \times \text{prevalence in country of origin} \]

  Caveats: Undocumented migrants missed
  Quality of country-specific prevalence data variable
  HCV antibody vs HCV RNA
  HBsAg vs anti-HBc (exposure)

Migrants: Multiple studies...multiple meta-analyses

Does the type of migrant matter?

Prevalence in migrants vs home country

<table>
<thead>
<tr>
<th>Region</th>
<th>HCV Prevalence</th>
<th>HBV Prevalence</th>
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<tbody>
<tr>
<td>East Asia</td>
<td>8.1%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>9.0%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Western Europe/Central Asia</td>
<td>9.3%</td>
<td>12.3%</td>
</tr>
<tr>
<td>South Asia</td>
<td>6.6%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Americas/Middle East</td>
<td>6.6%</td>
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Less relevant: SS Africa & Eastern Eur/Central Asia (poor vaccine coverage)
Most relevant: S. Asia (better vaccine coverage)

On balance refugees greater burden – more true for HBV than HCV, but variable
Situation worst for undocumented

- Standardized prevalence ratio 2.4 (1.1-5.3) for HBV
- Major issues with access even beyond testing for undocumented

Should migrants be ‘targeted’ for testing?

- Where migrants account for a high % of HCV → screen migrants (France, Germany, Netherlands, UK)
- In countries with high baseline prevalence → screen everyone (e.g. Bulgaria, Poland, Romania)

Same question for HBV?

- Similar conclusions – screen migrants vs whole population but...easier to target
- Migrants account for 25% of HBV in Europe ~50% from 10 countries

Is testing being done when recommended?

- Low awareness of guidelines, concerns about cost & workload by GPs

Where do you get these data?

- HEPscreen – a very useful resource (for Europe)
  Data by country + information for providers, policy-makers and affected population
And in North America?

- High burden of HBV in migrants to US
- Leads to estimates of much higher HBV prevalence

- CDC increasing efforts to improve surveillance
- Efforts underway to collect more robust data

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What happens after a diagnosis is made?

Linkage to care is critical!

Mera MMWR 2016

Diagnosis needs simplification

Step 1
See the doctor

Loss to F/U

Step 2
To the lab for HCV Ab

Loss to F/U

Step 3
See the doctor for result

Loss to F/U

Step 4
To the lab for HCV RNA

Loss to F/U

Step 5
See the doctor for result

Loss to F/U

Step 6
Start DAA therapy (may be additional steps:
heroin assessment, approvals etc)

Loss to F/U

Lots of places to ‘get lost’... particularly if HCV not a priority

Reflex HCV RNA testing

Total tested: Quest 415,000, LabCorp 205,000

Improving diagnostics

- Some improvements but variable quality (few WHO pre-qualified)
- Very variable cost – sometimes more than therapy!
  - Ideally – finger prick, treatment, finger prick...it can be that easy!

LabCorp – continues requirement for second specimen
Barriers to treatment: Restrictions

- Restrictions based on alcohol and/or drug use
- Restrictions based on fibrosis
- Restrictions based on coverage – major issue for migrants
- Restrictions based on provider type
- No evidence for any of this!

Access should be the only barrier... it does not get much easier

SOF + Velpatasvir (NS5A) x 12 wks in G1, 2, 4, 5, 6 – Naïve/Experienced +/- cirrhosis

1-3 pills, once a day for 8 to 12 weeks → >95% cure all populations

Total 1a 1b 2 4 5 6

SVR12 (%) 618 624 206 210 117 118 104 104 116 116 34 35 41 41

Feld NEJM 2015, Foster NEJM 2015

The elephant in the room... cost!

- Even at high costs, still cost-effective – especially with cirrhosis & PWID (prevention benefit)
- But high quality generics available (< $50 per course) – excellent experience with Buyers Clubs – >90% 90%

No reason for HCV to be treated in specialty care!

Improving linkage to care – get help!

Linkage can work well

Strengths:
- Testing well accepted
- Good fit – 100% Ab+, RNA tested
- Multidisciplinary care – culture & language

But treatment suboptimal:
- 2/3 (5%) cirrhosis – DAAs & SVR
- 6 others ‘high risk of progression’ – treated IFN
- 12 others no treatment!

Sagnelli Ann Hepatol 2018

Arora NEJM 2011

Kattakuzhy Annals Int Med 2017

Andrew Hill, World Hepatitis Summit, Sao Paulo 2017

Andrew Hill, World Hepatitis Summit, Sao Paulo 2017

Kattakuzhy Annals Int Med 2017
Make sure you're ready…

Have your ducks in order...before you start

- Key elements for successful screening & linkage for migrants
- Involve patients in design and delivery of care
  - Screening – peer screeners
  - Peer navigators
- Communication
  - Language - interpreter facilities
  - Culture sensitivity – address & discuss stigma
  - Confidentiality
- Avoid loss to follow-up
  - Ensure screening leads to diagnosis – e.g. HCV Ab followed by HCV RNA
- Strategies for linkage and treatment (ideally same place) before screening
  - Assistance for access to therapy – navigating the bureaucracy

Seedat Lancet © 2018

Even more complicated for HBV...

Immunotolerance
Imune Clearance
E Negative
Chronic HBV (precore mutant)

HBV DNA
ALT
Treatment
Immunosuppression (Chemo/HIV/BMT)

Dynamic disease...not everyone needs therapy...therapy may be long-term/indefinite

Treatment challenges

**HCV**
- Access
- Simple diagnosis
- Everyone needs treatment
- Treatment is near 100% effective
- Minimal or no monitoring required
- Drugs are well tolerated & generic

**HBV**
- Complicated serology
- Determining if and when to start therapy
- And if and when to stop therapy
- Long-term monitoring
- Long-term coverage
- Liver cancer surveillance
- Treatment?

So, how are we doing?

HCV Elimination Targets

- On Track
- Working Toward
- Not On Track

CDA 2017: Polaris Observatory (http://centerfortoa.com/polaris/)

Summary

- Viral hepatitis is a major global public health problem
- Migrants shoulder a disproportionate burden of disease
  - Lack of access to prevention (vaccination)
  - Unsafe or no healthcare (HBV, HCV)
- Screening strategies need to be country-specific depending on the local epidemiology and the migrant population (type & origin)
- Screening is just the beginning...linkage to care is critical
- For HCV – treatment can and should be delivered in primary care
- For HBV – a bit more complicated but can be done in primary care
- Need to address the entire cascade with a focus on migrants if we have a hope of reaching WHO 2030 elimination targets