Brief Review of HIV and Hepatitis C Virus (HCV) Infection  
(with focus on HCV)

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Disclosures

Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.
Medical toll of illicit opioid use

First-initiated substances

Intranasal → IV
Tentative → Compulsive

Acute Illness

- Overdose
- Violence / trauma

Subacute Effects

- Soft tissue infection
- Endocarditis
- Losses / legal issues

Chronic Effects

- Chronic viral hepatitis, liver disease
- HIV infection
- Malnutrition
- Smoking related illnesses
- Premature CHD, cancer
- Homelessness

HIV (and HCV) outbreak among injection drug users in Indiana

Community Outbreak of HIV Infection Linked to Injection Drug Use of Oxymorphone — Indiana, 2015

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On April 24, 2015, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

On January 23, 2015, the Indiana State Department of Health (ISDH) began an ongoing investigation of an outbreak of human immunodeficiency virus (HIV) infection, after Indiana disease intervention specialists reported 11 confirmed HIV cases traced to a rural county in southeastern Indiana. Historically, fewer than five cases of HIV infection have been reported annually in this county. The majority of cases were in residents of the same community and were linked to syringe-sharing among injection drug users. The outbreak was first identified by HIV surveillance.

Injection drug use in this community is a multi-generational activity, with many generations of the same family and multiple community members injecting together. IDU practices include crushing and cooking extended-release oxymorphone, most frequently 40 mg tablets not designed to resist crushing or dissolving. Syringes and drug preparation equipment are frequently shared (e.g., the drug is dissolved in nonsterile water and drawn up into an insulin syringe that is usually shared with others). The reported daily numbers of injections ranged from four to 15, with the reported number of injection partners ranging from one to six per injection event.

Like many other rural counties in the United States, the county has substantial unemployment (8.9%), a high proportion of adults who have not completed high school (21.3%), a substantial proportion of the population living in poverty (19%), and limited access to health care (1). This county consistently ranks among the lowest in the state for health indicators and life expectancy (2).

ISDH worked with the only health care provider in the immediate community, local health officials, law enforcement, community partners, regional health care providers and CDC to launch a comprehensive response to this outbreak. A public health emergency was declared on March 26 by executive order (3). The response has included a public education campaign, establishment of an incident command center and a community outreach center, short-term authorization of syringe exchange, and support for comprehensive medical care including HIV and hepatitis C virus care and treatment as well as substance abuse counseling and treatment. State and local health departments

- 135 cases as of report
- Investigation triggered by HIV surveillance
- Injection of oxymorphone
- Multigenerational use of injection drugs
- 84.4% (114/135) also diagnosed with new HCV infection
HIV and HCV: Quick Comparison

**Epidemiology**

- **HIV**
  - 33 million worldwide
  - 1.2 million in US
  - Up to 25% coinfected w/ HCV
  - Affects 9% of chronic IDUs
  - Mortality decreasing in US (now 12K/yr)
  - Less efficient needle transmission (0.3%)
  - More efficient sexual / perinatal transmission

- **HCV**
  - 150 million worldwide
  - 3.4-4.9 million in US
  - Affects 60-70% of chronic IDUs
  - Mortality increasing in US (now 15K/yr)
  - More efficient needle transmission (3%)
  - Less efficient sexual / perinatal transmission

**Vaccine available?**

- NO

**Whom to screen?**

- 1X testing for all adults age 15-65
  - Risk factor based:
    - High-risk sexual practices or partner
    - IVDU
    - Other STIs
    - Pregnant women

- 1X testing for birth cohort 1945-1965
  - Risk factor based:
    - IVDU
    - Transfusion before July, 1992
    - Chronic hemodialysis
    - Healthcare worker w/ needlestick

**Workup**

- **HIV**
  - HIV Ab / p24 Ag immunoassay
  - HIV viral load
  - CD4 lymphocyte count
  - Antiviral resistance testing
  - Assessment for opportunistic infections

- **HCV**
  - HCV Ab immunoassay
  - HCV viral load
  - HCV Genotype
  - Hepatic staging
  - Assessment for extrahepatic manifestations
HIV and HCV: Quick Comparison

**Treatment rationale**
- HIV: Restore / preserve immune function, Reduce HIV-related end-organ damage, Reduce HIV transmission
- HCV: Prevent HCV-related chronic liver disease, Reduce HCV transmission

**Whom to treat?**
- HIV: Any patient, regardless of CD4 count, More urgent w/ OI or high risk of Xmission, PREP: High risk sexual partner (or drug use?)
- HCV: Advanced liver fibrosis, Those at high risk of Xmission

**How to treat?**
- HIV: Four primary med categories: (NRTIs, NNRTIs, PIs, IIIs)
  - Recommended treatment: 2-NRTI backbone + NNRTI, PI, or II
  - 1-pill regimens available: (e.g., Atripla, Complera, Stribild)
  - PREP: Truvada = 2-NRTI combo (Emtricitabine + Tenofovir)
- HCV: Three types of DAAs: (PIs, polymerase inhibitors, NS5A inhibitors)
  - Recommended treatment: 2 or 3 DAAs combined, based on genotype
  - Combination products available: (e.g., Harvoni, Viekira pak, Zepatier)

**Curative treatment?**
- HIV: NO
- HCV: YES

**Long-term challenges**
- HIV: Treatment adherence, Surveillance for non-AIDS morbidity (CV disease, liver disease, renal disease, cancers, osteoporosis, neurocognitive effects, frailty)
- HCV: Treatment uptake (cascade of care), High cost of drug regimens, Prevention of reinfection, HCC screening (in those with fibrosis)
Hepatitis C: Key Facts

- RNA virus that infects liver cells, causing inflammation and damage.
- Most common and most deadly blood-borne infection in the U.S.
- Transmitted by direct blood to blood contact—primarily needles

Mortality due to Hepatitis viruses and HIV


Source: Centers for Disease Control and Prevention

* Includes cases contracted in the hospital or during childbirth
Hepatitis C: Key Facts

The “Baby Boomer” Hepatitis C cohort

- Highest prevalence 3-4% among “baby boomers” (1945 to 1965 birth cohort) – who should now be screened routinely regardless of risk factors

- New, rising population of infected young adults.

- More than half of patients with Hepatitis C are unaware of their infection


Two Hepatitis C cohorts at MGH Charlestown

Rise of young adults with Hepatitis C in Massachusetts

Source: Onofrey et al. (2011) MMWR 60: 537.
Why treat Hepatitis C?

Natural history of untreated HCV

80% asymptomatic

Exposure

2-12 wk incubation period

Acute infection
Ab + or -, VL +, ALT ↑↑

Viral clearance (15-25%): Ab +, VL -, ALT nl

Promoted by:
- Alcohol use
- Older age, male gender
- HBV or HIV infection
- High BMI, DM, or fatty liver

Chronic infection (75-85%)
Ab +, VL +, ALT ↑

Cirrhosis (30%/30yrs)

Decompensation or Hepatocellular carcinoma (1-4% per year)

More common with:
- Young patients
- Females
- Icteric acute infection

- Exposure
- Acute infection
- Viral clearance (15-25%)
- Chronic infection (75-85%)
- Cirrhosis (30%/30yrs)
- Decompensation or Hepatocellular carcinoma (1-4% per year)
Why treat Hepatitis C?

Chronic infection
Ab +, VL +, ALT ↑

Decompensation or Hepatocellular carcinoma (1-4% per year)

Cirrhosis (30%/30yrs)

New infection

New infection
Workup of Hepatitis C

1) Diagnose and characterize infection:
   - Hepatitis C virus (HCV) Antibody
   - HCV RNA (= viral load)
   - HCV genotype (1-6)

2) Assess for HCV-related liver disease:
   - Physical exam
   - Liver function tests (LFTs), CBC, APRI, AFP
   - HCV FibroSure
   - Liver ultrasound
   - Fibroscan
   - Liver biopsy

HCV FibroSure (Labcorp):

Input:
  - Total bilirubin
  - GGT
  - ALT
  - Alpha-2-macroglobulin
  - Haptoglobin
  - Apolipoprotein A-1

Output:
  - Fibrosis score (F0-F4)
  - Necroinflammatory score (A0-A3)
Workup of Hepatitis C

3) Assess for HCV-related conditions:
   - HIV, Hepatitis A serologies
   - Hepatitis B surface antigen and core antibody—a new mandate in 2016
   - Cholesterol, blood sugar, BMI
   - “Extrahepatic” manifestations of HCV
     - Cryoglobulinemia (50%)
     - Low platelets (40%)
     - Autoimmune arthritis (25%)
     - Pruritus, porphyria cutanea tarda (20%)
     - Lymphoma (risk increased by 20%)
     - Diabetes

Source: www.aafp.org
Source: Dartmouth medical photo library
## History of Hepatitis C Treatment

<table>
<thead>
<tr>
<th>Decade</th>
<th>Treatment Description</th>
<th>Weeks</th>
<th>SVR (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>1990s</strong></td>
<td>Interferon-α (IFN) SC + Ribavirin PO</td>
<td>48</td>
<td>10-30%</td>
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<tr>
<td><strong>2011</strong></td>
<td>FDA approval of the first <strong>direct acting antivirals (DAAs)</strong> against Hepatitis C: the protease inhibitors Telaprevir and Boceprevir.</td>
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<td><strong>2011 - 2013</strong></td>
<td>G1: PEG-IFN + Ribavirin + Telaprevir or Boceprevir</td>
<td>24-48</td>
<td>62-80%</td>
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<td>G2/3: PEG-IFN + Ribavirin</td>
<td>24</td>
<td>80%</td>
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<td><strong>Late 2013</strong></td>
<td>FDA approval of two new direct acting antivirals (DAAs):</td>
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<td></td>
<td>- Simeprevir (another oral PI)</td>
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<td></td>
<td>- Sofosbuvir (an oral polymerase inhibitor)</td>
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<td><strong>Allowing the first all-oral, IFN-free treatment!</strong></td>
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</table>

"SVR" = Sustained Virologic Response = Negative HCV viral load 24 weeks after treatment = predictor of a CURE.
Three main types of antivirals as of 2015

**Protease inhibitors**
Suffix: *-previr*

Examples:
- Telaprevir (Incivek)
- Boceprevir (Victrelis)
- Simeprevir (Olysio)

**Polymerase inhibitors**
Suffix: *-buvir*

Examples:
- Sofosbuvir (Sovaldi)
- Dasabuvir (part of Viekira Pak)

**NS5A inhibitors**
Suffix: *-asvir*

Examples:
- Ledipasvir (part of Harvoni)
- Ombitasvir (part of Viekira Pak)

<table>
<thead>
<tr>
<th>Genotype 1 Options</th>
<th>Duration</th>
<th>SVR for tx naïve pts</th>
<th>SVR for tx experienced or cirrhotic pts</th>
<th>Cost</th>
<th>Side Effects</th>
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</thead>
<tbody>
<tr>
<td>Harvoni (Sofosbuvir / Ledipasvir)</td>
<td>• 8 wks (no cirrhosis, low VL)</td>
<td>98-99%</td>
<td>97% (24 wks)</td>
<td>$94,500 (12 wks)</td>
<td>Fatigue (18%) Headache (17%) Nausea (9%) Diarrhea (7%) Insomnia (6%)</td>
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<td></td>
<td>• 12 wks (high VL)</td>
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<td></td>
<td>• 24 wks (cirrhosis)</td>
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<tr>
<td>Viekira Pak (Peritaprevir / Ombitasvir / Dasabuvir) + Ribavirin</td>
<td>• 12 wks (no cirrhosis)</td>
<td>97%</td>
<td>95% (24 wks)</td>
<td>$83,319 (12 wks)</td>
<td>Fatigue (34%) Nausea (22%) Pruritus (18%) Insomnia (14%) Asthenia (14%)</td>
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<td></td>
<td>• 24 wks (cirrhosis)</td>
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<td>Zepatier (Elbasvir / Grazoprevir)</td>
<td>• 12 wks (no cirrhosis)</td>
<td>92-99%</td>
<td>97% (16 wks)</td>
<td>$54,600 (12 wks)</td>
<td>Fatigue (11%) Headache (10%) Abdominal pain (2%) Diarrhea (2%) Irritability (1%) Depression (1%)</td>
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<td>• 12-16 wks (cirrhosis)</td>
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<td>Genotype 1 Options</td>
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<tr>
<td>Simeprevir/Sofosbuvir</td>
<td>• 12 wks (no cirrhosis)</td>
<td>97%</td>
<td>99% (24 wks)</td>
<td>$150,000 (12 wks)</td>
<td>Headache (17%)</td>
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<td></td>
<td>• 24 wks (cirrhosis)</td>
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<td>Fatigue (16%)</td>
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<td>Nausea (14%)</td>
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<td>Rash (12%)</td>
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<td>Diarrhea (6%)</td>
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<td>Dizziness (3%)</td>
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<td>Epclusa (Velpatasvir/Sofosbuvir)</td>
<td>• 12 wks (no cirrhosis or cirrhosis)</td>
<td>98-99%</td>
<td>99%</td>
<td>$74,760 (12 wks)</td>
<td>Headache (22%)</td>
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<td>Fatigue (15%)</td>
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<td>Nausea (9%)</td>
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<td>Asthenia (5%)</td>
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<td>Insomnia (5%)</td>
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<td>Irritability (5%)</td>
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<tr>
<td>Daclatasvir/Sofosbuvir</td>
<td>• 12 wks (no cirrhosis)</td>
<td>96%</td>
<td>76-100% (24 wks)</td>
<td>$63,000 (12 wks)</td>
<td>Fatigue (14%)</td>
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<td>• 24 wks, +/- Ribavirin</td>
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<td>Headache (14%)</td>
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<td>(cirrhosis)</td>
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<td>Nausea (8%)</td>
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<td>Diarrhea (5%)</td>
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<td><strong>Genotype 2 Options</strong></td>
<td><strong>Duration</strong></td>
<td><strong>SVR for tx naïve pts</strong></td>
<td><strong>SVR for tx experienced or cirrhotic pts</strong></td>
<td><strong>Cost</strong></td>
<td><strong>Side Effects</strong></td>
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<tr>
<td>Epclusa (Velpatasvir / Sofosbuvir)</td>
<td>• 12 wks (w/ or w/out cirrhosis)</td>
<td>98-99%</td>
<td>99%</td>
<td>$74,760 (12 wks)</td>
<td>Headache (22%) Fatigue (15%) Nausea (9%) Asthenia (5%) Insomnia (5%) Irritability (5%)</td>
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<tr>
<td>Daclatasvir/Sofosbuvir</td>
<td>• 12 wks (no cirrhosis)</td>
<td>&gt;95%</td>
<td>&gt;95% (24 wks)</td>
<td>$63,000</td>
<td>Fatigue (14%) Headache (14%) Nausea (8%) Diarrhea (5%)</td>
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<td>Genotype 3 Options</td>
<td>Duration</td>
<td>SVR for tx naïve pts</td>
<td>SVR for tx experienced or cirrhotic pts</td>
<td>Cost</td>
<td>Side Effects</td>
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<tr>
<td>Epclusa (Velpatasvir / Sofosbuvir)</td>
<td>• 12 wks (w/ or w/out cirrhosis)</td>
<td>98%</td>
<td>93%</td>
<td>$74,760 (12 wks)</td>
<td>Headache (22%) Fatigue (15%) Nausea (9%) Asthenia (5%) Insomnia (5%) Irritability (5%)</td>
</tr>
</tbody>
</table>
| Daclatasvir/ Sofosbuvir | • 12 wks (no cirrhosis)  
• 24 wks, +/- Ribavirin (cirrhosis) | 97% | 85-90% (24 wks) | $63,000 (12 wks) | Fatigue (14%) Headache (14%) Nausea (8%) Diarrhea (5%) |
THANK YOU!!

Questions?