## Lack of Awareness and Associated Deaths

<table>
<thead>
<tr>
<th>Virus</th>
<th>Prevalence</th>
<th>% of Population Unaware of Infection Status</th>
<th>Deaths in 2006 Related to Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>800,000 – 1.4 million</td>
<td>About 65%</td>
<td>3,000</td>
</tr>
<tr>
<td>HCV</td>
<td>2.7–3.9 million</td>
<td>About 75%</td>
<td>12,000</td>
</tr>
<tr>
<td>HIV</td>
<td>1.1 million</td>
<td>About 21%</td>
<td>14,016</td>
</tr>
</tbody>
</table>

Sources: CDC; Lin et al. 2007; Hagan et al 2008
Current CDC recommendations for HCV screening

Screen once (no risk assessment)
- **Adults born 1945-1965**
- Signs of liver disease (persistently elevated ALT)

Uncertain
- Long term sexual partner of HCV+
- STIs or multiple sex partners
- Intranasal drug use
- Tattooing/bodypiercing

Screen based on risk for exposure
- HIV-infected
- Past or present injection drug use
- Received clotting factor concentrates prior to 1987 or other blood products made prior to July 1992 or from known HCV+
- Ever on chronic hemodialysis
- Received tissues/organs prior to July 1992
- Infants of HCV-infected mothers
- Occupational exposures (needle stick or mucosal blood exposure)

Of people living with HIV in the US:

1 in 3 are co-infected with HCV
&
1 in 20 are co-infected with HBV
Why the title “golden age”?

1. People get jaundiced on new treatments

2. Refers to an ideal era (albeit mythological) where people were free from suffering

3. They asked me to create a catchy title

4. The new medicines cost a lot of money
Newer strategy for HCV therapy: Direct acting antivirals target life cycle

**PREVIR**
Protease inhibitors
- e.g. telaprevir, boceprevir, ladiprevir, simprevir, dasabuvir, asunaprevir, paritaprevir

**BIVIR**
Polymerase inhibitors
- Nucleos(t)ide analogs: e.g. tenofovir, sofosbuvir
- Non-nucleos: e.g. ledipasvir, daclatasvir

**ASVIR**
NS5A inhibitors: e.g. daclatasvir, ledipasvir, omibitasvir

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Currently used combinations of DAA classes

<table>
<thead>
<tr>
<th>NUC + PI (+/- RBV)</th>
<th>NUC + NS5A (+/- RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUC-SPARING HIV</td>
<td>NUC-SPARING HCV</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Affordability</td>
</tr>
<tr>
<td>Resistance</td>
<td>Provider preference</td>
</tr>
<tr>
<td>Renal Insufficiency</td>
<td>Renal Insufficiency</td>
</tr>
<tr>
<td>Drug-drug interactions</td>
<td>Avoid RBV</td>
</tr>
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<td></td>
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</tr>
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</table>
RBV-free arm with less side effects and dose modifications

<table>
<thead>
<tr>
<th>n (%)</th>
<th>LDV/SOF (N=1080)</th>
<th>LDV/SOF+RBV (N=872)</th>
<th>Total (N=1952)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Event</td>
<td>800 (74%)</td>
<td>745 (85%)</td>
<td>1545 (79%)</td>
</tr>
<tr>
<td>Treatment Related AEs</td>
<td>484 (45%)</td>
<td>617 (71%)</td>
<td>1101 (56%)</td>
</tr>
<tr>
<td>Grade ≥3 AE</td>
<td>46 (4%)</td>
<td>45 (5%)</td>
<td>91 (5%)</td>
</tr>
<tr>
<td>SAE</td>
<td>34 (3%)</td>
<td>17 (2%)</td>
<td>51 (3%)</td>
</tr>
<tr>
<td>Treatment Related SAE</td>
<td>4 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
</tr>
<tr>
<td>AEs Leading to Study Drug Modification/Interruption</td>
<td>6 (1%)</td>
<td>118 (14%)</td>
<td>124 (6%)</td>
</tr>
<tr>
<td>Treatment DC due to AE</td>
<td>6 (1%)</td>
<td>7 (1%)</td>
<td>13 (1%)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Combined safety data from 3 ION studies

Should I start prescribing these meds?
Minimum to Know Pre-Treatment

- HCV genotype/subtype
- Stage of fibrosis
  - Cirrhosis - yes/no
  - If yes, compensated? (e.g., ascites, encephalopathy, etc.)
- Method?
  - Liver biopsy
  - Transient elastography
  - Laboratory biomarkers
  - Imaging
- Prior HCV treatment?
  - Response?
  - DAA used?
- Medications
  - To check for drug interactions
  - Interferon “eligibility” and/or willingness
  - Comorbidities
  - Patient preference
  - Child-bearing potential of patient/partner
  - Ribavirin is a teratogen

YES
HIV/Hepatitis C helpline
1-866-637-2342
Which regimen would you choose for a HIV/HCV-coinfected G1 cirrhotic patient on TDF/FTC + darunavir/r?

1. Peginterferon + RBV + sofosbuvir
2. Sofosbuvir + simeprevir
3. Sofosbuvir/ledipasvir
4. Paritaprevir/r/ombitasvir + dasabuvir + RBV
5. Sofosbuvir + daclatasvir
Which regimen would you choose for a HIV/HCV-coinfected G1 cirrhotic patient on TDF/FTC + darunavir/r?
(After change to compatible ARVS)

1. Peginterferon + RBV + sofosbuvir
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Drug Interactions: Sofosbuvir

- Potent P-gp inducers in the intestine (e.g., rifampin, St. John's wort, phenytoin, phenobarbital) may

↓ SOF

ARV options
Any EXCEPT tipranavir
See package insert for studied interactions
Potential for drug-drug interactions between DAAs and ARVs*

- PTV/OMV/r/DAS
- SOF/LDV
- SOF+DAC
- SOF+RBV

Potential for drug-drug interactions between SOF/LED and ARVs*

Options for patients on TDF + boosted-PI
- Change TDF
- Change PI
- Await another HCV regimen
- If combo required
  - close monitoring recommended
Summary

- Remarkable advances in terms of HCV treatment tolerability & efficacy
  - Continued efforts being made to make shorter, safer, more effective
  - Continued need for therapies without significant drug interactions & that can be used in varied populations (HIV+, ESRD, opiate substitution, etc)
- Successful treatment prevents cirrhosis, end stage liver disease, and hepatocellular cancer
- Challenge now is to scale up efforts to diagnose and treat the millions of people living with HCV

Resources

- HCVguidelines.org
- hepatitisc.uw.edu
- IASUSA.org
- nynjaetc.org

Thank you