Top 10 Updates in Viral Hepatitis

Annie Luetkemeyer, MD
HIV, ID and Global Medicine, ZSFG, UCSF

Disclosures

I have received research grant support to UCSF related to HCV from the following:

• AbbVie
• Gilead
• Merck
• Proteus
• ACTG (NIH)

Resources

• HCV Guidelines http://www.hcvguidelines.org

• HBV guidelines
  AASLD https://www.aasld.org/publications/hepatitis-b-chronic

• Drug interactions
  http://www.hep-druginteractions.org

• HCV Consultation Services "Warmline"
  www.nccc.ucsf.edu or 844-437-4636

• Patient education
  http://www.hcvadvocate.org/

Case #1

• 26 year old man, seeing you in clinic
• HCV Ab(+) on intake labs – thinks this infection new in past 1-2 years
• Thinks exposed through IDU or sex with men (MSM), not sure
• Still using methamphetamine IV, but generally uses clean needles
• Declines HIV PrEP
ARS: Which is true about the US HCV epidemic?
1) HCV is the 3rd highest cause of infectious disease death in the US.
2) New diagnosis are concentrated in the “Baby Boomer” generation
3) 30% of people living with HCV will spend time in jail/prison
4) Incidence of new HCV cases is on the decline

Update #1: Which is true about the US HCV epidemic?
1) HCV is the 3rd highest cause of infectious disease death in the US.
2) New diagnosis are concentrated in the “Baby Boomer” generation
3) 30% of people living with HCV will spend time in jail/prison & ~20% of incarcerated have HCV
4) Incidence of new HCV cases is on the decline

Update #1: Which is true about the US HCV epidemic?
1) HCV is the leading cause of infectious disease death in the US.

Global mortality impact

Ly CID 2016

Global Burden of Disease Study 2016 IHME
**Update #1:** Which is true about the US HCV epidemic?

1) HCV is the 3rd highest cause of infectious disease death in the US.
2) New diagnosis are concentrated in the “Baby Boomer” generation
3) 30% of people living with HCV will spend time in jail/prison
4) Incidence of new HCV cases is on the decline

**HCV Incidence rising in the US**

- Nearly 13,000 acute HCV cases reported 2004-14 with an increased rate of 133% (using NNDSS)
- Actual cases estimated at 41,000 (CDC data)
- Largest increases in those aged 18-29 and 30-39
- IDU reported > 75% of cases from 2011-2014
- Disproportionately impacting young and rural opiate users

**Update #2**

**HCV SCREENING:** Shift to universal HCV screening under consideration

**Back to the case: Next steps in HCV Ab+**

- 26 year old man, new HCV Ab (+)
- PMH: GERD
- Lives in SRO, intermittently homeless. Has access to clean needles through needle exchange
- Labs:
  - HCV RNA 2.1 million, Genotype 1b
  - HIV RNA (-)
  - Cr 0.7, AST/ALT 45/41 Alb 4.0 PtTs 300
  - APRI score is 0.3, suggesting limited fibrosis
  - Hep A total Ab neg
  - Hep B sAb (-), Core ab (+) sAg (-)

**UPDATE #3**

**Outbreaks of hepatitis A in multiple states among people who use drugs and/or people experiencing homelessness**

[Link to CDC page](https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm)
ARs: Hep B Core Ab (+): What next?

1) Vaccinate him - this is likely false negative
2) Don’t vaccinate - this is resolved infection
3) Repeat all HBV serologies then decide
4) I wish I hadn’t sent these &%$! HBV serologies in the first place.

26 year old man, MSM, IDU, HIV (-), new HCV diagnosis
HepB sAb(-), Core ab (+) sAg(-)

HBV Screening & Isolated Core Ab (+)

**HBV Screening**
- Recommended for all pregnant women, persons needing immunosuppressive therapy, and groups at elevated risk
- Screen for both HBsAg and anti-HBs
- Vaccinate all anti-HBs-negative individuals
- Anti-HBc screening not routinely recommended*

*Except for persons with HIV infection, planning HCV treatment, anticancer, or other immunosuppressive therapy, planning renal dialysis, donated blood/organs.

**Interpretation of Isolated Core Ab (+)**
- Window Period: transitioning from S Ab(+) to sAb (-)
- Waned Immunity: prior sAb (+) with resolved infection
- Occult HBV: HBV DNA (+), sAg (-)
- False Positive

New Adjuvanted HBV Vaccine: Heplets

- 2 doses: 0 and 4 weeks
- Compared to standard HBV series: 0/1/6 month or HAV/HBV 0/1/6 months or Q75d/90d/1 year
- Improved immunogenicity in older patients and those with DM
- Use in prior non-responders & HIV?
- More injection site reactions
- Wholesale price: $230.00 vs. $170-180.00 for standard HBV vaccines

Update #4

**HBV Vaccination Recommendations for Individuals Positive for Anti-HBc Only**
- If person is from low HBV endemicity area and has no risk factors for HBV infection, deliver full HBV vaccine series
- If HBV risk factors present, do not vaccinate unless they have HIV infection or are immunocompromised

Adapted from: clinicaloptions.com


Medical Letter, Issue 1539, 1/18
**Update #5: Treating HCV in setting of HBV**

- Test all HBsAg-positive pts for HCV and treat HCV if viremic; HBV treatment eligibility same as for pts with HBV mono-infection
- HBsAg-positive pts initiating HCV DAA therapy are at risk for HBV flare

**Lancet Meta-analysis of reactivation risk**
- HBsAg (+): 24% with DNA↑, 9% with hepatitis.
- Resolved infection (sAg (-), core Ab (+)): 1.5% with DNA↑, NO risk of hepatitis (associated with HBV)

**Update #6 California HCV Prescribing landscape**

**As of 7/18:** Medi-cal now adheres to AASLD/IDSA guidelines: Treat all regardless of extent of fibrosis if not dying of non-HCV cause

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>12 weeks</td>
<td>16 weeks if GT1A &amp; NS5a resistance</td>
</tr>
<tr>
<td>Giletrix/Pibrentasvir</td>
<td>8 weeks</td>
<td>NOW 8 weeks in CIRRHOSIS (except GT3)</td>
</tr>
<tr>
<td>Sofosbuvir/Ledipasvir</td>
<td>12 weeks</td>
<td>8 weeks if HCV &lt;6 million, non-black, non-HIV</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>12 weeks</td>
<td></td>
</tr>
</tbody>
</table>

**Treatment saves lives, regardless of cirrhosis**

- Mortality rate
- 3x No cirrhosis
- 7x With cirrhosis

---

*Adapted from: clinicaloptions.com, Muckle Lancet Gastro Hep 2018*
### Update #7 Great options for previously harder treat populations

| People living with HIV & HCV coinfection | Equivalent outcomes to HIV-uninfected & compatible with ART |
| Renal Failure including ESRD | Glecaprevir/Pibrentasvir (G/P) |
| Cirrhosis including decompensated disease | Sofosbuvir/Velpatasvir (SOF/VEL) |
| Cirrhosis including decompensated disease | Sofosbuvir/Ledipasvir (SOF/LDV) (If decompensated, add RBV and treat in collaboration with liver transplant team if feasible) |
| Active substance use and/or alcohol use disorder | Data support excellent outcomes, additional support may be necessary |
Update #8: HCV in pregnancy

- Rising HCV rates in women of childbearing age & doubled in pregnant women from 2009->2014
- AASLD/IDSA guidelines recommend testing in all pregnant women (ACOG does not)
- More cost effective than risk based screening
- Phase 1 data supporting SOF/LDV in late 2nd trimester
  - 100% SVR12 (n=8)
  - No adverse fetal events
  - Caveat: SOF/LDV limited to GT 1,4
  - 170 HCV viremic women identified in 2 yrs!

Chaillon CID 2019, Chappell CROI 2019, Abstract #87

Update #9 Dropping Prices

<table>
<thead>
<tr>
<th>Drug</th>
<th>Wholesale acquisition price</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF/LDV x 12 weeks</td>
<td>94,500</td>
</tr>
<tr>
<td>SOF/VEL x 12 weeks</td>
<td>74,760</td>
</tr>
<tr>
<td>SOF/VEL &quot;authorized generic&quot; (2019)</td>
<td>24,000</td>
</tr>
<tr>
<td>Glicaprevir/Pibrentasvir x 8 weeks</td>
<td>26,400</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir x 12 weeks</td>
<td>21,840 (60% reduction)</td>
</tr>
</tbody>
</table>

TAKE HOMES:
- Ongoing formulary changes with price decreases
- Price should NOT be the major barrier to HCV care

Back to your patient

- You treat him with 8 weeks of G/P due to formulary preference and he is cured
- Given ongoing risk for HCV acquisition through MSM sexual contact, you continue to screen him with HCV RNA every 6-12 months
- Unfortunately, 1 year after his cure from HCV, his RNA is now detectable at 2.4 million IU/ML, Genotype 2, consistent with new infection

ARS: When would you treat this patient with acute HCV infection?

1) Now
2) If his HCV RNA remains detectable in 3-6 months
3) If his HCV RNA has not declined 2 fold in 4 weeks
4) I would not retreat him until his risk for being reinfected is decreased.
5) Insurance where I practice will not permit treatment of HCV reinfection
Update #10 Acute HCV Considerations

- Consider monitoring for spontaneous clearance at **one month** (rather than 3-6 months)

Adapted from EACS Guidelines version 9.0 www.eacsguidelines.org

Acute HCV Considerations (2)

- Consider **immediate** HCV treatment:
  - HCV transmission prevention
  - Reduce risk of clinical complications (ex: already cirrhotic)
  - Concern for LTFU in 3-6 months
- IF follow-up HCV RNA undetectable, repeat at least 12 weeks later to confirm clearance
- Your patient opts for immediate treatment given ongoing risk for sexual transmission to others

After the cure: HCC screening

- If F3/F4 (on scale of F0-F4) at time of treatment, continue to screen for hepatocellular carcinoma with q 6 months imaging, **even if fibrosis regresses**

- This “one size fits all approach” will **overscreen** some with F3/F4s and **underscreen** some at risk w/o fibrosis
- Consider using HCC risk estimator: www.hccrisk.com

Thank you!