Top Ten Updates in Viral Hepatitis for the HIV provider

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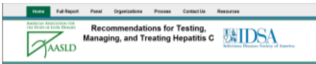
Resources

- **HCV Guidelines** http://www.hcvguidelines.org



- **HBV guidelines**
  AASLD https://www.aasld.org/publications/hepatitis-b-chronic
  EASL https://easl.eu/publication/management-of-hepatitis-b- virus-infection
- **Drug interactions**
  http://www.hep-druginteractions.org www.hep-druginteractions.org
- **HCV Consultation Services "Warmline"**
  www.nccc.ucsf.edu or 844-437-4636
- **Patient education**
  http://www.hcvadvocate.org/

Our case

- 26 year old man, HIV+
- HCV Ab(+) on intake labs – thinks this infection new in past 1-2 years
- Thinks exposed through IDU or MSM, not sure
- Still using methamphetamine IV, but generally uses clean needles

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

Weinbaum AIDS 2005, Rich NEJM 2014

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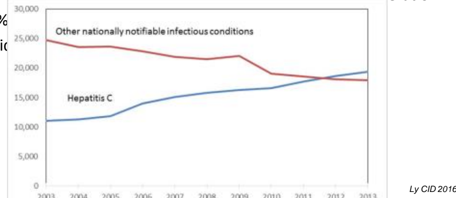
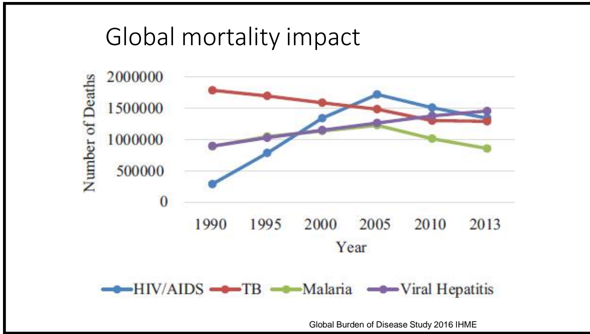


Ly CID 2016



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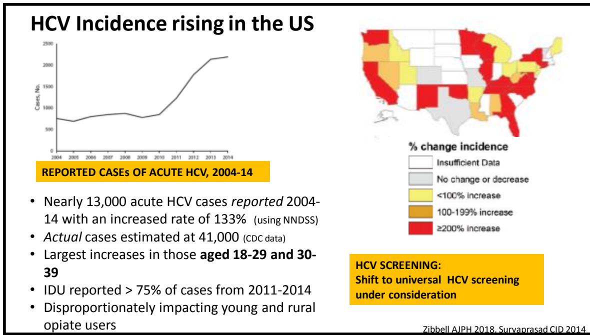

Back to the case: Next steps in HCV Ab+

- 26 year old man, new HCV Ab (+)
- PMH: HIV, GERD
- Meds: bictegravir/TAF/FTC, omeprazole 20 mg QD
- Lives in SRO, intermittently homeless. Has access to clean needles/works through needle exchange
- Labs:
  - **HCV RNA 2.1 million, Genotype 1b**
  - CD4 520, HIV RNA < 40
  - Cr 0.7, AST/ALT 45/41 Alb 4.0 Plts 300
  - Hep A total Ab neg
  - Hep B sAb (-), core ab (+), sAg (-)
  - APRI score is 0.3, suggesting limited fibrosis
    (APRI : AST to PLT ratio- calculator available free on-line)

#2 HAV

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

CDC Centers for Disease Control and Prevention

https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm

Hepatitis A vaccination

Routine vaccination

- **Not at risk but want protection from hepatitis A** (identification of risk factor not required): 2-dose series HepA (Havrix 6–12 months apart or Vaqta 6–18 months apart [minimum interval: 6 months]) or 3-dose series HepA-HepB (Twinrix at 0, 1, 6 months [minimum intervals: 4 weeks between doses 1 and 2, 5 months between doses 2 and 3])

Special situations

- **At risk for hepatitis A virus infection**: 2-dose series HepA as above
  - **Chronic liver disease** → HBV & HCV
  - **Clotting factor disorders**
  - **Men who have sex with men**
  - **Injection or non-injection drug use**
  - **Homelessness**
  - **Work with hepatitis A virus** in research laboratory or nonhuman primates with hepatitis A virus infection
  - **Travel in countries with high or intermediate endemic hepatitis A**
  - **Close personal contact with international adoptee** (e.g., household, regular babysitting) in first 60 days after arrival from country

Expert panel urges hepatitis A shots for homeless in U.S.

https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

Back to the case: HBV serologies

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3 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 Ag(+) to SAb (+)
- Waned Immunity: prior sAb (+) with resolved infection
- Occult HBV: HBV DNA (+), sAg (-)
- False Positive

HBV remains in liver: Risk for reactivation

Adapted from : clinicaloptions.com

Terrault NA, et al. Hepatology. 2018;67:1560-1599.

#4 HBV VACCINATION UPDATES

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

Terrault NA, et al. Hepatology. 2018;67:1560-1599.

New Adjuvanted HBV Vaccine: Heplisav

- 2 doses: 0 and 4 weeks

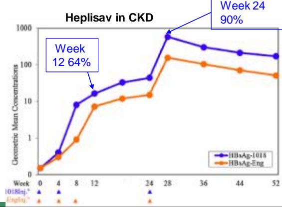
  Compared to standard HBV series: 0/1/6 month or HAV/HBV: 0/1/6 months or 0/7d/30d/1 year
- Improved immunogenicity in older patients and those with DM
- More injection site reactions
- Wholesale price: 230.00 vs. 170-180.00 for standard HBV vaccines

Medical Letter, Issue 1539, 1/18

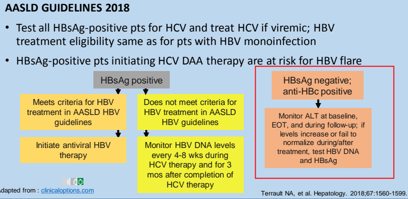
Adapted from : clinicaloptions.com

#5 Heplisav in HIV

- No data for initial vaccination or re-vaccination in non-responder
- Package insert: 2 doses
- CKD study:
  - →Response after 2 vs. 3 doses
- ACTG 5379 study
  - →Heplisav 2 vs. 3 dose in Non-responders
  - → 3 doses in vaccine naive



Update #6: Treating HCV in setting of HBV

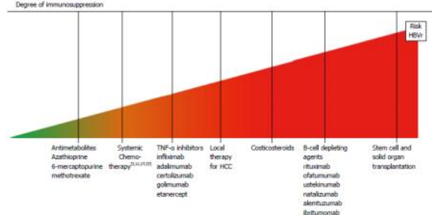


Lancet Meta-analysis of reactivation risk (excluded HIV (+)

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

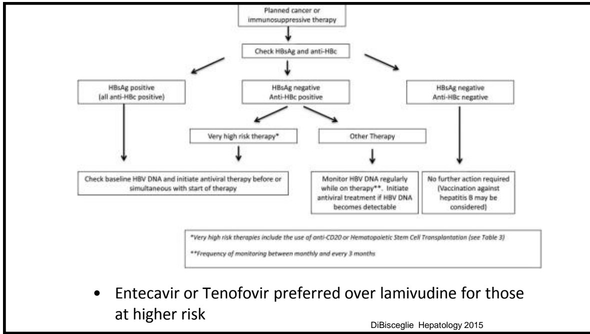
Muckle Lancet Gastro Hep 2018

Risk of HBV reactivation



- Notably: High dose steroids, rituximab, TNF-alpha blockers, chemotherapy

Bessone WJG 2016



- Entecavir or Tenofovir preferred over lamivudine for those at higher risk

DiBisceglie Hepatology 2015

Update #7 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*

Regimen	HCV GT	Duration	Notes
Elbasvir/Grazoprevir (“Zepatier”)	Genotype 1,4	12 weeks	16 weeks if GT1A & NS5a resistance
Glecaprevir/Pibrentasvir (“Mavyret”)	All genotypes	8 weeks	NOW 8 weeks in CIRRHOSIS (except GT3) Expedition-8, AASLD 2018
Sofosbuvir/Ledipasvir (“Harvoni”)	Genotype 1,4	12 weeks	8 weeks if HCV <6 million, non-black, **non-HIV**
Sofosbuvir/Velpatasvir (“Epclusa”)	All genotypes	12 weeks	

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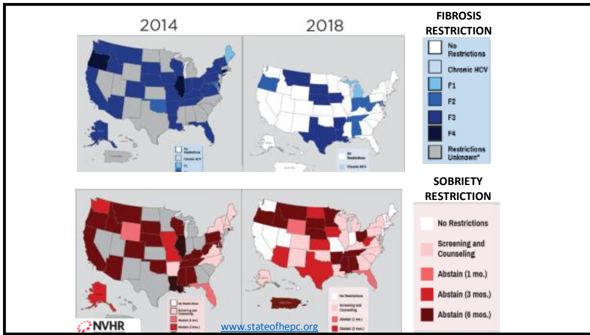
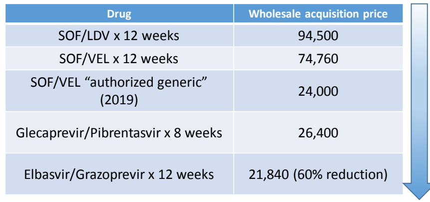


Dropping Prices



Drug	Wholesale acquisition price
SOF/LDV x 12 weeks	94,500
SOF/VEL x 12 weeks	74,760
SOF/VEL "authorized generic" (2019)	24,000
Glecaprevir/Pibrentasvir x 8 weeks	26,400
Elbasvir/Grazoprevir x 12 weeks	21,840 (60% reduction)

TAKE HOMES:

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

Great options for previously harder treat populations

Renal Failure including ESRD	• Glecaprevir/Pibrentasvir • Elbasvir/Grazoprevir

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Cirrhosis including decompensated disease	• Sofosbuvir/Velpatasvir (SOF/VEL) • Sofosbuvir/Ledipasvir (SOF/LDV) *(If decompensated, add RBV and treat in collaboration with liver transplant team if feasible)*

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Active substance use and/or alcohol use disorder	Data support excellent outcomes, additional support may be necessary

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Active substance use and/or alcohol use disorder	Data support excellent outcomes, additional support may be necessary
People living with HIV & HCV coinfection	Equivalent outcomes to HIV-uninfected & compatible with ART

 # 8 1 minute HCV/HIV drug interactions overview

- EBR/GZR: not compatible with PIs or Elvitegravir/Cobi
- GLE/PIB: not compatible with PIs but can give with ELV/COBI
- SOF/VEL & LED/SOF: compatible with most ART but NOT with PPIs
- LED/SOF: only agent compatible with Efavirenz

Excellent drug interaction resources
https://www.hep-druginteractions.org/

	EBR/ GZR	GLP/ PIB	LED/ SOF	SOF/ VEL	SOF/ VEL/ VOX
HIV Drugs					
Entry/Integrase Inhibitors					
Bictegravir/FTC/TAF	◆	▲	◆	◆	◆
Dolutegravir	◆	◆	◆	◆	◆
Elvitegravir/cobi /FTC/TAF	●	◆	◆	◆	◆
Elvitegravir/cobi/FTC/TDF	●	◆	■	■	■
Maraviroc	◆	◆	◆	◆	◆
Raltegravir	◆	◆	◆	◆	◆
NNRTIs					
Efavirenz	●	●	■	●	●
Etravirine	●	●	◆	●	●
Nevirapine	●	●	◆	●	●
Rilpivirine	◆	◆	◆	◆	◆
NRTIs					
Abacavir	◆	◆	◆	◆	◆
Didanosine	◆	◆	◆	◆	◆
Emtricitabine (FTC)	◆	◆	◆	◆	◆
FTC + Tenofovir alafenamide	◆	◆	◆	◆	◆
Lamivudine	◆	◆	◆	◆	◆
Stavudine	◆	◆	◆	◆	◆
Tenofovir-DF (TDF)	◆	◆	■	■	■
Zidovudine	◆	◆	◆	◆	◆
Protease Inhibitors					
Atazanavir	●	●	◆	◆	●
Cobicistat (with ATV or DRV)	●	■	■	◆	■
Darunavir	●	●	◆	◆	■

Update #9: 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 evaluating 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!
  - Need more data but opens the door to more research on prenatal treatmetn

Chaillon CID 2019, Chappell CROI 2019, Abstract #87

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

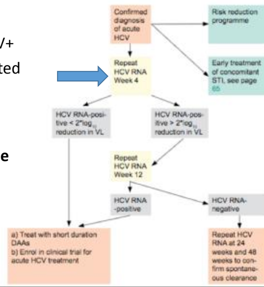
ARS #2: When would you treat this patient with acute HCV infection?

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

- **PROBE-C:** 12% spontaneous clearance in acute HCV in HIV+
- >2 log drop at week 4 predicted 96% of those who cleared
- Consider monitoring for spontaneous clearance at **one month**

(*rather than 3-6 months*)



Boeseke CROI 2019 #576
Adapted from EACS Guidelines version 9.0
www.eacsguidelines.org

Acute HCV

- Consider treatment without waiting for clearance:
  - -HCV transmission prevention
  - - Reduce risk of clinical complications (ex: already cirrhotic)
  - - Concern for LTFU in 3-6 months
- Generally same regimen as for chronic
  - SWIFT-C 8 weeks SOF/LDV – 100% SVR
- No indication for HCV PEP

Naggie #196 AASLD 2017

After the HCV Cure

- HCV Ab may remain positive for life- screen with RNA
- Counsel about Reinfection: IDU & MSM routes
- If cirrhotic, continue to screen for hepatocellular carcinoma with q 6-12 month imaging EVEN IF markers of cirrhosis regress

  …thus need to establish fibrosis staging *before* treatment

Thank you!

Question-and-Answer

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IAS–USA