Two “Silent Epidemics” - Chronic Hepatitis B and Hepatitis C: A Primer for Primary Care Practitioners

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Hepatitis B: Objectives
1. Identify
   - when to initiate treatment
   - 3 first line medications
   - common side effects of hepatitis B treatments
   (25 min)
2. Identify
   - recommended monitoring of patients who are pregnant
   - when treatment initiation may be considered in this population.
   (10 min)

Hepatitis C: Objectives
1. Identify the
   - treatment regimen
   - monitoring for patients with hepatitis C genotypes 1, 2, 3.
   (35 min)
2. Identify common side effects of hepatitis C treatments
   (5 min)
3. Identify drug interactions with treatment regimens for hepatitis C genotypes 1, 2, 3.
   (5 min)
4. Q & A (10 min)

Disclosures
Add disclosure details here if there is any development.
1. AbbVie, Viekira Pak
2. Quest Diagnostics

Hepatitis B is a DNA virus and is NOT curable.

Hepatitis B: Natural History
- 800,000-1.4 million C-HBV in US
- 240 million worldwide
- Survives 7 days outside the body
- High prevalence areas >/= 8%, Most of Africa, Asia
- Progression to chronic HBV
  - greatest risk if infected as a child
    - 90% if infant
    - 25-50% if in childhood
- Die prematurely due to cirrhosis or liver cancer
  - If infected at birth or childhood 25%
  - If infected after childhood

http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm#overview
Hepatitis B: Natural History
- no transmission
- breastfeeding, kissing, coughing, sneezing,
- different clinical presentation
- asymptomatic → “Silent Killer”
- hepatic decompensation
- HBV is a reportable condition
- HBV infection rates down 82% since 1991
- routine vaccination
- Hep B is a reportable condition

HBV is a reportable condition

HBV DNA viral count < 2000 IU = low
AST < 19 for females, 30 for males = normal

Hepatitis B: Natural History
- different immunological PHASES, + HBsAntigen
  - IMMUNE-ACTIVE
    - high viral levels, elevated ALT → treat
  - IMMUNE TOLERANT
    - high viral levels, normal ALT, little/no biopsy activity
  - INACTIVE CARRIER
    - low or undetected viral levels, normal ALT
  - LATENT
    - detected viral level, no HBsAg


Hepatitis B: Who/when to Screen
- Foreign-born persons from countries of high HBV endemicity
- Before beginning immunosuppressive therapy (anti-TNF meds, chemo)
- may begin preemptive antiviral therapy
- Hemodialysis patients
- Pregnant women
- ALT/AST elevation of unknown etiology
- Persons with known or suspected exposure to HBV including:
  - infants born to HBV-infected mothers
  - household contacts of HBV-infected persons
  - needle sharing, needlestick
  - sex contacts
  - persons with known occupational or other exposures to infectious blood or body fluids
- HIV-positive persons
- MSM: Men who have sex with men

Hepatitis B: Screening
→ HB surface antigen, HB surface antibody, and HB core antibody
if:
  + HB surface antigen (x 6 mo) = chronic infection
  + HB surface antibody = + immunity
  + HB core antibody AND HB surface antibody
  ● there are gray areas!!
  ● if all are negative:
    - give vaccination series, 3-dose series, 0, 1, 6 months
  ● if + HB surface antigen ....

Hepatitis B: Work up
- treatment / cirrhosis status / infectivity / HCC screening
  - CMP - AST/ALT >19 for Females, >30 for Males
  - CBC - platelets
  - Hep A, Hep C, HIV
  - AFP, AFP-L3, DCP - every 6 months for hepatocellular cancer (HCC) screening
  - Hepatitis B e antigen (HBeAg)
  - Hepatitis B e antibody (HBeAb)
  - hepatitis B virus DNA PCR quantitative
  - Fibrosure (F1-F2-F3-F4)
  - Fibroscan (F1-F2-F3-F4), may replace biopsy
  - Abdominal ultrasound - every 6 months for HCC screen
Hepatitis B: Work up not included

- Hep D
- Liver biopsy
  - useful in certain cases
  - HBV DNA > 2,000 and ALT normal
  - used less and less
  - limitations
    - 25-30% sampling error
    - different interpretations
    - invasive
    - expensive

Hepatitis B: Treatment Goals

- Suppress the virus... NOT A CURE
- AST/ALT normalization
- Prevent progression of the disease to cirrhosis
- liver failure
- hepatocellular carcinoma (HCC)
  - Pts with HBV have an increased risk of HCC even if
    - NO cirrhosis present
    - on therapy
- Liver regeneration
- Prevent transmission of the disease to newborns

Hepatitis B: Treatment Initiation

Hepatitis B: Treatment Options

At least 5 years, probably for LIFE
- tenofovir disoproxil (Viread)
- entecavir (Baraclude)
- telbivudine (Tyzeka)

Limited time
- PEG-interferon (Pegasys)

... or a combination

Hepatitis B: Treatment Options

tenofovir disoproxil (Viread) 300 mg po once daily
- potent antiviral activity, 76% at 1 year
- suppresses lamivudine, telbivudine or entecavir resistant
- low to no level of resistance
- is used off label in pregnancy
- with or without food

SE: rash, nausea, diarrhea, headache, depression, weakness

entecavir (Baraclude) 0.5 mg or 1 mg po once daily
- potent antiviral activity
- suppresses lamivudine resistant
- may consider use with decompensated cirrhosis
- low level of resistance
- now generic
- copay card

SE: transient elevated ALT, rash, nausea, diarrhea, headache, insomnia

telbivudine (Tyzeka) 600 mg po once daily
- less potent antiviral activity
- suppresses lamivudine resistant
- can develop resistance
- copay card

SE: fatigue, increased CK, nausea, diarrhea, headache, cough, rash

PEG-interferon-alpha 2a (Pegasys), 180 mcg injection weekly x 48 weeks
- potential for loss of HBV DNA (17~30%)
- better for genotype A and B

SE: flu-like symptoms, extreme fatigue, nausea, diarrhea, headache, rash

Hepatitis B: Treatment Summary

- Can take many months to suppress virus
- In most cases treatment is for LIFE
- Occasionally, on therapy will see...
  - Seroconversion of Hepatitis B surface antigen (HBsAg) to Hepatitis B surface antibody (HBsAb)
  - Continue meds for at least 1 year more before considering stopping therapy
  - Check HBV serologies and monitor for HCC every 6 months
Hepatitis B: Transmission in Pregnancy
- most common mode of transmission worldwide
- higher chance for mother to baby transmission if:
  - high viral load, > 10,000,000 IU
  - + HBe antigen
- treat in 3rd trimester if HBV DNA > 10,000,000 IU
- breast feeding if +HBV NOT contraindicated
- breast feeding if on HBV medication IS contraindicated

Hepatitis B: Treatment in Pregnancy
Goals:
- Monitor HBV DNA viral count and ALT
- Suppress maternal viremia
- Prevent mother to baby HBV transmission
  THIS IS OFF LABEL
- tenofovir disoproxil (Viread) 300 mg po once daily
- entecavir (Baraclude) 0.5 mg or 1 mg po once daily
- telbivudine (Tyzeka) 600 mg po once daily
- PEG-interferon-alpha 2 a (Pegasys) 180 mcg injection weekly x 48 weeks

Hepatitis B: Treatment in Pregnancy
- tenofovir disoproxil (Viread) 300 mg po once daily
category B
OFF LABEL USE
- was administered during entire pregnancy

Hepatitis B: Treatment in Pregnancy
telbivudine (Tyzeka) 600 mg po once daily
category B
OFF LABEL USE
Sheng Q, Ding Y, Bai H, et al. Efficacy and safety of telbivudine in preventing mother-to-infant HBV transmission in HBV-infected pregnant women in immune tolerant phase. Program and abstracts of the 65th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD); November 7-11, 2014; Boston, Massachusetts. Abstract 1864
"Telbivudine treatment effectively and safely prevented mother-to-infant transmission of HBV from chronically infected mothers with a high degree of viremia late in pregnancy."

Hepatitis C: Objectives
1. Identify the -treatment regimen -monitoring for patients with hepatitis C genotypes 1, 2, 3. (35 min)
2. Identify common side effects of hepatitis C treatments (5 min)
3. Identify drug interactions with treatment regimens for hepatitis C genotypes 1, 2, 3. (5 min)
4. Q & A (10 min)

Hepatitis C is an RNA virus and it IS curable.
Hepatitis C: Natural History

- It's curable!!
- 3.2 million in US
- 130-150 million worldwide
- Survives 14 days outside the body
- 4x as prevalent as HIV or HBV
- In 2007 C-HCV surpasses HIV in mortality trends
- The majority (73.4%) of registered deaths related to HCV occurred in adults aged 45 to 64 years, BABY BOOMERS

Hepatitis C: Prevalence

In specific US populations: By population, and NOT S/Sx.
- more males than females
- 75% in the homeless clinic in Austin, whereas in US 52%
- injection drug users
- incarcerated
- 5% vertical transmission rate
- sharing household items such as razors and toothbrushes
- 3-5% chance of contracting HCV if in a mutually monogamous relationship with someone who is HCV +
> 25% chance of contracting HCV if you have multiple partners
- those born between 1945 and 1965
- The #1 risk factor that we are told to focus on now is age. Right now anyone who is 48-66 years of age must be tested

Point of Care Testing for HCV with OraQuick

- FDA approved June 25, 2011
- Hepatitis C antibody test
- Fingerstick
- Results in 20 minutes
- If + f/u w/ laboratory testing
- Accuracy
  - Sensitivity- 99.7%
  - Specificity- 99.9%

This is the only point of care HCV antibody test I know of.

Hepatitis C: ROS

- MANY have no signs or symptoms

May have:
- Fatigue
- Polyarthralgia and polymyalgia
- Fever
- Nausea or anorexia
- RUQ tenderness

PS: The CDC has great posters for your office.

+ Your patient screened positive

Does he/she have chronic hep C?
- We don't know yet.

Is Hepatitis C Curable?
- Yes!!

Remember: Screen, Treat, Cure!!
Hepatitis C: Lab Work up

- CMP, CBC, *fibrosis marker, pt/INR
- ALT: 7-55 u/L → men 30, women 19 !!!
- Fibroscan, Abd U/S,
- HCV antibody
  - 1000s to 1,000,000s to 10,000,000s IU
  - no stratification of meaning
- Fibrosis
- Genotype: 1a, 1b, 2, 3, 4, 5, 6

*fibrosis markers: FibroSure, FibroSpect, ELF, HepaScore, and others

Patterns of ALT Levels in Patients with Chronic Hepatitis C

Hepatitis C: Treatment Goals

- CURE
  - Prevent progression of the disease to cirrhosis
  - liver failure
  - hepatocellular carcinoma (HCC)
  - Potential reversal of fibrosis cirrhosis… yes...cirrhosis!!
  - eradicate HCV by 2036!!!

Hepatitis C: Treatment

- Treatment efficacy & options vary depending on:
  - Genotype- 1a, 1b, 2, 3, or 4
  - Prior treatment status- naïve, relapser, partial/null responder
  - Cirrhotic or not
  - Coinfection: HIV, HBV
  - Obesity
  - Other meds pt is taking

Hepatitis C: Treatment in Pregnancy

- Not recommended
- Ribavirin is category X in pregnancy
- Advise 2 forms of contraceptives while on therapy, and for 6 months post therapy, if EITHER partner is taking ribavirin!!!!!!

Hepatitis C: Treatment History

- 1990’s: Interferon (IFN) - injection, ribavirin (RBV).
  Just two years in and Incivek and Victrelis are:
  - no longer the standard of therapy.
  - not used.

IFN and RBV are still used
Where direct acting antivirals (DAAs) are working.

Hepatitis C: Treatment
Treatment medications and duration are dictated by:
- genotype: 1a, 1b, 2, 3, 4
- prior treatment response: null, partial, relapse
- cirrhosis status: non-cirrhotic, cirrhotic
- insurance
- Express Scripts
- CVS
- other medications the patient is taking
  - http://hep-druginteractions.org/
  - Hep iChart

Hepatitis C: Newer Treatments
2013- simeprevir (Olysio) 150 mg daily, PO
- genotypes 1
  - few side effects - photosensitivity
  - contains sulfonamide moiety
  - low genetic barrier to resistance
  - NOT for monotherapy
  - give with interferon + ribavirin or sofosbuvir

Interactions: Remember categories.
- Antibiotics
- Antifungals
- Antivirals
- Steroids
- Anticonvulsants
- Antiarhythmics
- Herbals: St. John’s wort, milk thistle

This is not a complete list.
[Links]

Hepatitis C: Newer Treatments
2013 sofosbuvir (Sovaldi) 400 mg daily, PO
- genotypes 1, 2, 3, 4
  - high genetic barrier to resistance
  - few drug interactions
  - few side effects (HA), fatigue
  - NOT for monotherapy
  - give with interferon + ribavirin or simeprevir

Interactions: Remember categories.
- HIV meds
- Anticonvulsants
- Antimycobacterials
- Herbals: St. John’s wort

This is not a complete list.
[Links]

Hepatitis C: Newer Treatments
2014 sofosbuvir + ledipasvir (Harvoni) 400 mg/90 mg, PO
- genotypes 1 (off-label in genotype 3, 4)
  - high genetic barrier to resistance
  - relatively few drug interactions
  - few side effects (HA), fatigue, nausea
  - one pill once a day

Interactions: Remember categories.
- same as Sovaldi
- PPI/H2B: take equivalent to omeprazole 20 mg at EXACTLY the same time
- Antacids: take 4 hours before or after
  - There are other potential DD interactions that req monitoring.

[Links]
Treatment according to genotype following American Association for the Study of Liver Diseases guidelines.

Starting with genotype 2.

Hepatitis C: Genotype 2 Treatment

Sovaldi + Ribavirin 1000/1200 mg x 12 weeks

Summary of sustained virologic responses (SVR) in research:
- naive, non-cirrhotic SVR 97% (VALENCE)
- naive, cirrhotic SVR 83% (FISSION); 94% (POSITRON), 100% (VALENCE); consider extending to 16 weeks
- prior failure, non-cirrhotic SVR 90-91% (FUSSION, VALENCE)
- prior failure, cirrhotic SVR 78% (FUSSION), consider adding interferon for SVR 93% (LONESTAR 2)

Hepatitis C: Genotype 3 Treatment

1. Sovaldi + Ribavirin 1000/1200 mg x 24 weeks
   - naive, non-cirrhotic SVR 93% (VALENCE)
   - naive, cirrhotic SVR 92% (VALENCE), consider extending to 16 weeks
   - prior failure, non-cirrhotic SVR 85% (VALENCE)
   - prior failure add interferon, x 12 weeks for SVR 82% (VALENCE)

2. Harvoni + Ribavirin 1000/1200 mg x 12 weeks
   - naive, non-cirrhotic SVR 100% (VALENCE)
   - naive, cirrhotic SVR 100% (VALENCE)

Hepatitis C: Genotype 1 Treatment

There are 10 treatment options depending on:
- genotype
- subtype
- prior treatment status
- cirrhosis status

The following is just to give you an idea of where we are in regards to SVR response based on some of the above factors. It is not a complete treatment guide.

Hepatitis C: Genotype 1a Treatment

1. naive, non-cirrhotic
   a. Harvoni x 12 weeks SVR 96% (ION-3) to 98% SVR (ION-1)
   b. Harvoni x 12 weeks SVR 96% (ION-3)
   c. Sovaldi + Olysio x 12 weeks SVR 95% (COSMOS [Pooled Analysis] – F0-3)
   d. Viekira Pak + RBV [with food] x 12 weeks SVR 96% (Sapphire I) to 97% SVR12 [Pearl IV]

2. naive, cirrhotic
   a. Harvoni x 12 weeks SVR 94% (ION-1)
   b. Sovaldi and Olysio x 24 weeks SVR 100% (COSMOS [Pooled Analysis] F4)
   c. Viekira Pak + ribavirin x 24 weeks SVR 95% (Turquoise II)
Hepatitis C: Cost
- very expensive
Many paths to cure
- insurance
- assistance programs
- grants
- donations
- free meds
Ultimately, everyone deserves a chance for a cure.

Hepatitis C: Treatment Summary
- Very high SVR
- Many fewer side effects
- Shorter duration of therapy, in most cases
- Counsel no alcohol
- Still need to watch out for:
  - drug to drug interactions
  - side effects
- We need to advocate for screening and patient treatment.

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Hepatitis C: Cost
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