Viral Hepatitis Update

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Assistant Professor of Medicine
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Outline

• Hepatitis A
• Hepatitis B
• Hepatitis C
• Hepatitis D
• Hepatitis E
Hepatitis A

- Identified in 1973
- RNA virus (picornavirus)
- Fecal oral transmission
  - (the vowels are in the bowels)
- Lack of adequate sanitation and poor hygienic practices
- Endemic in third world nations
- Can survive outside of the body for months
Risk Factors in U.S.

- International travel (45.8%)
- Contact with a case (14.8%)
- Employee or child in a daycare center (7.6%)
- Exposure during a food or waterborne common-source outbreak (7.2%)
- Illicit drug use (4.3%)
- Men who had sex with men (3.9%)

Hepatitis A

Incidence of Hepatitis A, by year
United States, 1980-2010

Vaccine

http://www.cdc.gov/hepatitis/HAV/HAVfaq.htm
Clinical Presentation

- Age <6 years, 70% of infections are asymptomatic
- Older children and adults, typically symptomatic, with jaundice in >70%
- Incubation period of ~ 30 days
- Fatigue, malaise, nausea, vomiting, anorexia, fever, and right upper quadrant pain
- Acholic stools, dark urine, jaundice, pruritus
- Fulminant hepatitis
Laboratory Evaluation

• ALT/AST 1000’s
• Total Bilirubin up out of proportion to alkaline phosphatase
• + HAV IgM
  – **Can remain elevated even after infection is cleared especially in children\(^1\)
• + HAV IgG late

Hepatitis A

[Graph showing symptoms, IgG and IgM antiHAV, and Fecal HAV over months after exposure.]
Hepatitis A Vaccination

- Children 12-23 months of age
- Travelers except to Australia, New Zealand, Canada, western Europe, and Japan
- Men who have sex with men
- Users of illicit drugs
- Persons with occupational risks (health care professionals, HAV-infected animals)
- Persons with chronic liver disease
Hepatitis A Vaccination

• Single antigen
• Nearly 100% effective in the immune competent and lifelong
• Standard (Havrix, Vaqta)
  – Two doses 6-12 months apart
• Twinrix (HepA/HepB)
  – Month 0, 1, 6
  – Days 0, 7, and 21 to 30 and one year
Hepatitis B

- Australia antigen 1966
- DNA virus (hepadnavirus)

Worldwide
- 400 million chronic carriers
- 9th leading cause of death
- Leading cause of hepatocellular carcinoma (HCC)

United States
- 1.25 million chronic carriers
HBV – Global Prevalence

HBsAg Prevalence

- ≥8% - High
- 2-7% - Intermediate
- <2% - Low
Hepatitis B
Modes of Transmission

- Blood transfusion: 0%
- Other*: 15%
- Unknown: 32%
- Multiple sex partners: 17%
- Injection drug use: 14%
- Hemodialysis: 0%
- Men who have sex with men: 6%
- Sexual contact with hepatitis B patient: 13%
- Household contact of hepatitis B patient: 2%
- Medical employee: 1%

*Other: surgery, dental surgery, acupuncture, tattoo, other percutaneous injury

NNDSS/VHSP. Available at www.cdc.gov/ncidod/diseases/hepatitis/slideset/refugee/refugees.ppt
<table>
<thead>
<tr>
<th></th>
<th>High</th>
<th>Moderate</th>
<th>Low or Not Detectable</th>
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<td></td>
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<td>Breast milk</td>
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</table>
Whom to Screen

- Immigrants and offspring from high prevalence areas
- Household and sexual contacts
- IVDU
- Multiple sexual partners, MSM, inmates, h/o STD
- HCV, HIV
- Pregnant women
- Dialysis
- Immunosuppressive therapy
- Chronic liver disease

Lok AS, McMahon BJ. Hepatology 2009; 50:1-33
Whom to Vaccinate

- Everyone on the prior slide
- All infants, beginning at birth
- All children aged <19 years who have not been vaccinated previously
- Susceptible sex partners of Hepatitis B surface antigen (HBsAg)-positive persons
- Persons seeking evaluation or treatment for a sexually transmitted disease
Whom to Vaccinate

• Health care and public safety workers at risk for exposure to blood or blood-contaminated body fluids
• Residents and staff of facilities for developmentally disabled persons
• Travelers to regions with intermediate or high rates of endemic HBV infection
• Persons with chronic liver disease
Whom to Vaccinate

- Unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (discretion of clinicians for unvaccinated adults with diabetes mellitus who are aged ≥60 years)
- All other persons seeking protection from HBV infection — acknowledgment of a specific risk factor is not a requirement for vaccination
Risk of Chronic HBV

- Neonates: 90%-100%
- Children: 20%-40%
- Adults: <5%

HBV Disease Progression
HBV Disease Progression

>90% of infected children progress to chronic disease

<5% of infected immunocompetent adults progress to chronic disease

HBV Disease Progression

- Acute Infection
- Chronic Infection
- Cirrhosis

>90% of infected children progress to chronic disease

<5% of infected immunocompetent adults progress to chronic disease

30% of chronic HBV-infected individuals

HBV Disease Progression

- Acute Infection
- Chronic Infection
- Cirrhosis
- Liver Cancer (HCC)

>90% of infected children progress to chronic disease

<5% of infected immunocompetent adults progress to chronic disease

30% of chronic HBV-infected individuals

HBV Disease Progression

Acute Infection → Chronic Infection → Cirrhosis → Liver Cancer (HCC)

5%-10% of chronic HBV-infected individuals²

30% of chronic HBV-infected individuals²

>90% of infected children progress to chronic disease

<5% of infected immunocompetent adults progress to chronic disease¹

HBV Disease Progression

Acute Infection → Chronic Infection → Cirrhosis → Liver Cancer (HCC) → Liver Failure ( Decompensation)

5%-10% of chronic HBV-infected individuals²

30% of chronic HBV-infected individuals²

>90% of infected children progress to chronic disease

<5% of infected immunocompetent adults progress to chronic disease¹

23% of patients decompensate within 5 years of developing cirrhosis³

HBV Disease Progression

Acute Infection → Chronic Infection

5%-10% of chronic HBV-infected individuals

>90% of infected children progress to chronic disease

<5% of infected immunocompetent adults progress to chronic disease

Chronic Infection → Cirrhosis

30% of chronic HBV-infected individuals

23% of patients decompensate within 5 years of developing cirrhosis

Cirrhosis → Liver Failure ( Decompensation)

Liver Failure ( Decompensation) → Liver Transplant

Liver Transplant → Liver Cancer (HCC)

Liver Cancer (HCC) → Liver Transplant

Chronic HBV is the 6th leading cause of liver transplantation in the US

References:
HBV Disease Progression

- **Acute Infection**
  - >90% of infected children progress to chronic disease

- **Chronic Infection**
  - <5% of infected immunocompetent adults progress to chronic disease
  - 5%-10% of chronic HBV-infected individuals

- **Cirrhosis**
  - 30% of chronic HBV-infected individuals
  - 23% of patients decompensate within 5 years of developing cirrhosis

- **Liver Failure (Decompensation)**

- **Liver Cancer (HCC)**

- **Liver Transplant**

- **Death**

Chronic HBV is the 6th leading cause of liver transplantation in the US

References:
# Stages of Hepatitis B

<table>
<thead>
<tr>
<th>Test</th>
<th>Naive</th>
<th>Vaccinated</th>
<th>Immune from past exposure</th>
<th>Acute infection</th>
<th>Immune Tolerant</th>
<th>Chronic Active eAg +</th>
<th>Inactive Carrier</th>
<th>Chronic Active eAg -</th>
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<tbody>
<tr>
<td>HBs Ag</td>
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<td>-</td>
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<td>HBs Ab</td>
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<td>+</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HBc Ab</td>
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<td>-</td>
<td>+</td>
<td>+ (IgM)</td>
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<td>+</td>
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<tr>
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<td>-</td>
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<tr>
<td>HBe Ab</td>
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<td>+</td>
<td>-</td>
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<td>-</td>
<td>+</td>
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<tr>
<td>HBV DNA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↑↑</td>
<td>↑↑↑</td>
<td>↑↑</td>
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<td>↑</td>
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<tr>
<td>ALT</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
<td>↑↑</td>
<td>NI</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
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</tbody>
</table>
Chronic HBV – Natural History

- HBeAg+ 
- Anti-HBe+ 

**REPLICATIVE PHASE**

**NON-REPLICATIVE PHASE**

→ seroconversion

Time (years) from onset of infection

ALT

HBV DNA

0 10 20 30

0 500

300

200

100

0
Chronic HBV – Natural History

- HBeAg+
- Anti-HBe+

**Replicative Phase**
- Time (years) from onset of infection

**Non-replicative Phase**
- Seroconversion
- Reactivation
HBV – Therapy

• Interferon
• Lamivudine (3TC)- 4 year resistance ~70%
• Emtricitabine (FTC)
• Telbivudine (LdT)
• Adefovir dipivoxil (ADV) – 4 year resistance ~18%
• Entecavir (ETV)
• Tenofovir disoproxil fumarate (TDF)
• Truvada (TDF/FTC)
Hepatitis B Vaccination

• Effective after 3 doses

<table>
<thead>
<tr>
<th>Dose</th>
<th>Infants</th>
<th>Teens and Adults</th>
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<tr>
<td>1</td>
<td>16% - 40%</td>
<td>20% - 30%</td>
</tr>
<tr>
<td>2</td>
<td>80% - 95%</td>
<td>75% - 80%</td>
</tr>
<tr>
<td>3</td>
<td>98% - 100%</td>
<td>90% - 95%</td>
</tr>
</tbody>
</table>

• Less effective with
  – age (>60- 75% protective)
  – male sex, obesity, smoking, and chronic illness
  – cirrhosis

http://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html
Hepatitis B Vaccination

- sAb drops over time
  - No need to boost unless high risk
- High risk population
  - Hemodialysis, HIV, IVDU...
  - Check titer 1-2 months and repeat series if low
- Standard (Recombivax HB, Engerix-B, Twinrix)
  - Three doses month 0, 1, 6
  - Accelerated days 0, 7, and 21 to 30 and one year

http://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html
Post Vaccination Testing

• Infants born to HBsAg-positive mothers
• Health care workers and public safety workers at high risk
• Chronic hemodialysis patients, HIV-infected persons, and other immunocompromised persons (e.g., hematopoietic stem-cell transplant recipients or persons receiving chemotherapy)
• Sex partners of persons with chronic HBV
• Check 1-2 months after last dose
Screening for Hepatocellular Carcinoma

- HBV with or without cirrhosis
  - Cirrhotic (70-80%)
  - Asians Males > age 40, females > age 50
  - Over 40 with h/o ↑ AST/ALT or cirrhotic
  - Africans > age 20
  - Family history of HCC

- Cirrhosis any cause
  - HCV ~50% of cases in U.S.
  - Metabolic syndrome
    - ? independent

References:
El-Serag H. NEJM 2011;365:1118-27
Mittal S. J Clin Gastroenterol 2013;47:S2-S6
Lok AS. Hepatology 2009;50:1-33
Hepatitis C Virus (HCV)

- 9.6 kb, enveloped positive-stranded RNA flavivirus
- Cloned in 1989
- Six major genotypes (1-6)
  - Genotype 1: 72% of infections in the US
  - Genotype 2: 16-19%
  - Genotype 3: 8-10%
  - Genotypes 4-6: 1-2%
HCV - Epidemiology

- 170 million infection worldwide
- >3 million infected in USA
  - 2 Million baby boomers
- 35,000 new infections/year in USA
- 10-20% lifetime risk of death from HCV
- >10,000 deaths/year in USA
- ~50% of injection drug users have HCV viral infection

http://www.cdc.gov/hepatitis/HCV/StatisticsHCV.htm
Hepatitis C

* Actual acute cases estimated to be 13.4 times the number of reported cases in any year

http://www.cdc.gov/hepatitis/HCV/StatisticsHCV.htm
HCV – Clinical Importance

• Prevalence previously expected to quadruple by 2020
• Mortality expected to rise over next 10-20 yrs
• Increased risk of hepatocellular carcinoma
• Most common indication for liver transplantation
• 75% of those infected are unaware of their status

NIH Consensus Statement 2002
HCV – Natural History

• 60-85% of exposures result in chronicity
• Asymptomatic or nonspecific symptoms
• Normal/mild/moderate ALT elevations
• 10-25% develop cirrhosis (>20 years)
• Hepatocellular carcinoma: 1-4% per year once cirrhotic
HCV – Natural History

• Factors affecting progression
  – Age at acquisition
  – Alcohol use
  – Coinfection (HIV, HBV)
  – Obesity
  – Steatosis
HCV – Natural History

• Factors *not* affecting progression
  – Genotype
  – Viral load
  – ALT
  – Mode of transmission
HCV and Alcohol

Odds Ratio for Having Cirrhosis

- Teetotaler
- Alcohol Abuser

HCV Negative
- 1
- 15

HCV Positive
- 9
- 147

Lancet 1997;349:825-32
Hepatitis C
Whom to Screen

• High prevalence (90%)
  – Injection drug use
  – Persons with hemophilia
  – Incarceration (26%)
  – HIV (~25%)

• Moderate prevalence (10%)
  – Blood transfusion before 1992
  – Hemodialysis

• Low prevalence (< 5%)
  – Persons born from 1945 through 1965 (3.25%)
    • CDC, AASLD, USPSTF
  – Perinatal
    • 1-5% with high viral load

Tohme RA. Hepatology 2010;52:1497-1505
Mbaeyi C Semin Dial 2013; 26:439–446
HCV – Risk Factors

- Other risk factors
  - STD history
  - Tattooing with shared equipment
  - Multiple sexual partners
  - Men who have Sex with Men
  - Household contacts
  - Monogamous heterosexual couples
    - 1:190,000 sexual encounters

- Unproven risk
  - Acupuncture
  - Body piercing
  - Professional Tattooing
  - Commercial barbering

HCV – Diagnosis

• Whom to test?
  – Risk factors as discussed earlier
  – Elevated liver enzymes

• Antibodies to HCV
  – Sensitivity >99%, specificity 99%

• If HCV antibody positive, check HCV RNA
  – Detectable within 1-2 weeks of infection

NIH Consensus Statement 2002
# HCV – Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>HCV Ab</th>
<th>HCV RNA</th>
<th>ALT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic HCV</td>
<td>+</td>
<td>+</td>
<td>Normal or ↑</td>
</tr>
<tr>
<td>Spontaneous recovery</td>
<td>+</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Sustained Virologic Response (SVR)</td>
<td>+</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>False positive HCV Ab</td>
<td>+</td>
<td>-</td>
<td>Normal</td>
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</table>
HCV
Assessing Disease Severity

• Insensitive and nonspecific methods
  – Physical exam
  – AST:ALT ratio, platelet count
  – Tests of liver function (INR, bilirubin, albumin)
  – Imaging

• Accurate at the extremes of the fibrosis scale
  – Serum fibrosis markers
  – Elastography
HCV
Assessing Disease Severity

• Liver biopsy is gold standard
  – Etiology
  – Disease grade (activity/inflammation)
  – Disease stage (fibrosis)
  – Prognosis
  – Treatment decisions
HCV – Liver Biopsy
Assessing Disease Severity

normal

stage 1

stage 3

stage 4
HCV
What To Do When Seeing a Patient

• Confirm viremia
• Reassurance/counseling
  – Alcohol
  – Weight loss
  – Vaccination against A&B
  – Sharing a razor or toothbrush
• Refer to a specialist
• Screen for hepatocellular carcinoma if found to have advanced fibrosis
HCV – Treatment Goals

• Primary goal: Eradicate HCV

• Secondary goals
  – Slow progression of liver disease
    • 45% lower risk of death
  – Reduce risk of hepatocellular carcinoma
  – Improve health-related quality of life
  – Control extrahepatic manifestations

Treatment

• Pegylated Interferon and Ribavirin
  – GT 1: 30-40% Sustained Virologic Response (SVR)
  – GT 2: 90%
  – GT 3: 80%

• Protease Inhibitors (1st generation) 2011
  – GT 1: 50-80% SVR
  – Telaprevir
  – Boceprevir

• Side effects
New Direct Acting Antivirals

• > 20 new agents in trial
• Minimal side effects
• Multiple drug interactions
• Sofosbuvir NS5B polymerase inhibitor
  – GT1: PegIFN, Riba, Sof x 12-16 weeks
    • SVR: 90%
  – GT2 Riba, Sof x 12 weeks 90-97%
  – GT3 Riba, Sof x 24 weeks 60-80%
    • +/- PegIFN x 12 weeks 87%
• Simeprevir NS3/4A protease inhibitor (1st gen, 2nd wave)
  – GT 1: Peg, Riba, SMV - 70-90% SVR
Sofosbuvir + Simeprevir

12 or 24 weeks of simeprevir + SOF ± RBV

SVR12 (excluding non-virological failures)

COSMOS

<table>
<thead>
<tr>
<th>Cohort 1 (Null/F0–2)</th>
<th>Cohort 2 (TN/Null/F3–4)</th>
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<tbody>
<tr>
<td>GT 1b</td>
<td>GT 1a no Q80K</td>
</tr>
<tr>
<td>17/17</td>
<td>18/18</td>
</tr>
<tr>
<td>30/30</td>
<td>38/40</td>
</tr>
<tr>
<td>24/27</td>
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Lawitz et al. EASL 2014
Sofosbuvir + Ledipasvir

- Ledipasvir 90mg QD + Sofosbuvir 400mg QD +/- Riba for 12 or 24 weeks

<table>
<thead>
<tr>
<th>Rate of BL NS5A RAVs (%)</th>
<th>All 16%</th>
<th>Baseline NS5A resistance 14%</th>
<th>Overall SVR 12%</th>
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<tr>
<td>ION 1 (TN / 12-24 wks)</td>
<td>98/849</td>
<td>96/135</td>
<td>100/865</td>
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<tr>
<td>ION 2 (TE / 12-24 wks)</td>
<td>97/427</td>
<td>89/55</td>
<td>97/440</td>
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<tr>
<td>ION 3 (TN F0-3 / 8-12 wks)</td>
<td>94/609</td>
<td>90/104</td>
<td>94/647</td>
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</table>

- The majority of pts. with virologic failure had NS5A resistant variants
- Analysis of NS5A RAVs with high level of resistance?
- Approx. 50% of patients with virolog. treatment failure had baseline NS5A RAVs

Mangia et al., NEJM 2014; Afdahl et al., NEJM 2014; Kowdley et al., NEJM 2014
Ombitasvir + Paritaprevir + Dasabuvir +/- Ribavirin

- Ombitasvir 25mg QD + ABT-450r 150mg QD + Dasabuvir 250mg BID +/- Riba for 12 or 24 weeks

<table>
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<th>Virologic failure (n)</th>
<th>1a</th>
<th>1b</th>
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<tr>
<td>Sapphire 1 (TN / non-cirrhotic)</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Sapphire 2 (TE / non-cirrhotic)</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Turquoise 2 (cirrhotic)</td>
<td>16</td>
<td>1</td>
</tr>
</tbody>
</table>

- The majority of pts. with virologic failure had NS3 / NS5A / NS5B resistant variants
- Correlation of virologic failure with pre-existent resistant variants not disclosed

Feld et al., NEJM 2014; Zeuzem et al., NEJM 2014; Poordad et al., NEJM 2014
Daclatasvir + Sofosbuvir

12 or 24 weeks of SOF (± SOF lead-in) + daclatasvir ± RBV

SVR12 (%)

Treatment-naïve
GT 1

<table>
<thead>
<tr>
<th></th>
<th>12 W</th>
<th>24 W</th>
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<tr>
<td>80/82</td>
<td>44/44</td>
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BOC/TVR failures
GT 1

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<th>24 W</th>
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<tr>
<td>40/41</td>
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</table>

Treatment-naïve
GT 2 or 3

Re-treatment and 12-week treatment duration not studied

<table>
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<tr>
<th></th>
<th>12 W</th>
<th>24 W</th>
</tr>
</thead>
<tbody>
<tr>
<td>91</td>
<td>41/44</td>
<td></td>
</tr>
</tbody>
</table>

BOC: boceprevir; TVR: telaprevir

Recommended Regimens for GT1

- LDV/SOF (daily) ± RBV for 12-24 wks
- OMV/PTV/RTV (two tabs daily) + DSV (BID) ± RBV for 12-24 wks
  - Not recommended for pts with prior PI failure
- SMV (daily) + SOF (daily) ± RBV for 12-24 wks
  - Not recommended for pts with prior SOF or PI failure
- DCV (daily) + SOF (daily) +/- RBV for 12-24 wks
- Regimens no longer recommended for GT1
- SOF + RBV, PegIFN, boceprevir, telaprevir

AASLD/IDSA HCV Guidelines (www.hcvguidelines.org)
Recommended Regimens for GT2

- SOF + RBV x 12 weeks (naïve), 16 or 24 weeks (experienced)
- DCV + Sof x 12 weeks (naïve) , 24 weeks +/- RBV (experienced)

AASLD/IDSA HCV Guidelines (www.hcvguidelines.org)
Recommended Regimens for GT3

• Treatment naive:
  – SOF/RBV + PegIFN x 12 weeks
  – SOF/RBV x 24 weeks (interferon intolerant)
  – DCV + SOF +/- RBV x 12-24 weeks (SVR 60-90%)

• Prior treatment failure to PegIFN/RBV without SOF
  – SOF/RBV + PegIFN x 12 weeks
  – SOF/RBV x 24 weeks (interferon intolerant)
  – DCV + SOF +/- RBV x 12-24 weeks

• Prior treatment failure to SOF/RBV
  – DCV + SOF + RBV x 24 weeks
  – SOF/RBV + PegIFN x 12 weeks if tolerant to interferon

AASLD/IDSA HCV Guidelines (www.hcvguidelines.org)
Recommended Regimens for GT 4

Data are limited but AASLD/IDSA guidance make the following recommendations:

• SOF/LDV x 12 weeks
• OMV/PTV/RTV (without DSV) + RBV x 12 wks
• SOF + RBV x 24 wks
• Recommended in Rx-experienced and alternative for Rx-naive pts: SOF + RBV + PegIFN x 12 wks
• Alternative for Rx-experienced pts: SOF + SMV ± RBV x 12 wks

AASLD/IDSA HCV Guidelines (www.hcvguidelines.org)
<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
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</thead>
<tbody>
<tr>
<td>NS3/4A protease inhibitor</td>
<td>Sovaprevir (ACH-1625)</td>
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<tr>
<td>NS3 protease inhibitor</td>
<td>Asunaprevir</td>
</tr>
<tr>
<td>NS3/4A protease inhibitor</td>
<td>Grazoprevir (MK-5172)</td>
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<td>NS5A inhibitor</td>
<td>GS-5816</td>
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<td>Elbasvir (MK-8742)</td>
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<td>Samatasvir (IDX 719)</td>
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<tr>
<td>NS5A inhibitor</td>
<td>ACH-3012</td>
</tr>
<tr>
<td>NS5A inhibitor</td>
<td>PPI-668</td>
</tr>
<tr>
<td>NS5B nonnucleoside polymerase inhibitor</td>
<td>Beclabuvir (BMS-791325)</td>
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<tr>
<td>NS5B non-nucleoside polymerase inhibitor</td>
<td>ACH-3422</td>
</tr>
<tr>
<td>NS5B non-nucleoside polymerase inhibitor</td>
<td>Mericitabine (R7128)</td>
</tr>
</tbody>
</table>

Combination regimen to be released in late 2015
Investigational Drugs

• Targeting mRNA
  ‣ Miravirsen - inhibits miR-122 liver specific micro RNA; 5 weekly subcutaneous injections.
  ‣ RG-101 - single subcutaneous injection

Hepatitis D Virus (HDV)

• Delta agent, a defective virus
• Endemic in Mediterranean basin
• Uncommon in Western countries except IVDU and hemophiliacs
• Requires presence of HBV for virus assembly
Hepatitis D Virus (HDV)

• Acute coinfection
  – Indistinguishable from acute HBV
• Superinfection
  – Severe acute hepatitis in unrecognized HBV carrier
  – Exacerbation of chronic HBV
• Interferon-alfa is the only FDA-approved treatment
Hepatitis E Virus (HEV)

- Single stranded RNA virus
- Suspected 1983 seen on EM, sequenced 1990
- Enteric transmission, Swine reservoir
- Self-limited infection
- Highest incidence in Asia, Africa, Middle East, Central America
- 2.3 Billion infected worldwide
- NHANES- sero-prevalence 21% in U.S.
Hepatitis E Virus (HEV)

• More severe disease than HAV
  – HAV is more readily transmitted and is more widely distributed worldwide

• Rare fulminant hepatitis
  – Occurs more frequently during pregnancy

• Chronic infection in immunosuppressed patients
Hepatitis E Virus (HEV)

- High perinatal morbidity/mortality with vertical transmission
- Treatment is supportive for acute infection
- Chronic infection
  - Reduce immunosuppression
  - Ribavirin +/- PegIFN
- No commercially-available vaccine
- Put back in the differential
Summary

- Screen for hepatitis A, B and C in at risk populations - Key is identification
- Vaccinate for HAV and HBV
- Screen for HCC in chronic HBV and advanced liver disease of any cause
- HCV therapy is rapidly changing with high cure rates
- Hepatitis E is not just a problem of the third world
Questions?