Hepatitis C Update
Lauri Ann Welch, ARNP-BC, PhD
DISCLOSURES

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SESSION OBJECTIVES

• Discuss HCV epidemiology including transmission, diagnosis and CDC screening guidelines.
• Discuss patient management when diagnosis is made including determining viral load, genotype and the significance of that information.
• Summarize treatment options, both historical and current, including side effects and risks associated with treatment.
• Discuss chronic Hepatitis C including hepatic and extra-hepatic manifestations and factors that can increase or reduce fibrosis progression.
Understanding the Growing Impact of the HCV Epidemic

Lauri A. Welch, FNP-BC, PhD
GI Consultants of Greater Lowell
Epidemiology and Natural History of HCV Infection
Approximately 3.2 Million People in the US Have Chronic HCV Infection

- ~3.2 million people are chronically infected with HCV based on NHANES (1999-2002) population\(^1,2\)
  - ~70% born 1945-1964\(^1\)

- The number chronically infected with HCV in the US may be even higher\(^3\)
  - Accounting for populations not sampled in NHANES
    - Incarcerated
    - Homeless
    - Nursing home residents
    - Hospitalized
    - Those on active military duty

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Distribution of HCV Genotypes in the US

- Genotypes 1a and 1b account for 79%
- Genotype 2 accounts for 15%

Transmission of Hepatitis A, B, and C Virus

<table>
<thead>
<tr>
<th>Route</th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV drug use</td>
<td>![Common]</td>
<td>![Common]</td>
<td>![Common]</td>
</tr>
<tr>
<td>Transfusion</td>
<td>![Common]</td>
<td>![Common]</td>
<td>![Common]</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>![Never]</td>
<td>![Common]</td>
<td>![Common]</td>
</tr>
<tr>
<td>Intra-institutional</td>
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<td>![Never]</td>
<td>![Common]</td>
</tr>
<tr>
<td>Sexual</td>
<td>![Common]</td>
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</tr>
<tr>
<td>Household</td>
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<td>![Common]</td>
</tr>
<tr>
<td>Mother-to-newborn</td>
<td>![Common]</td>
<td>![Never]</td>
<td>![Common]</td>
</tr>
<tr>
<td>Oral-oral contact</td>
<td>![Never]</td>
<td>![Common]</td>
<td>![Common]</td>
</tr>
<tr>
<td>Food-borne</td>
<td>![Never]</td>
<td>![Never]</td>
<td>![Never]</td>
</tr>
<tr>
<td>Fecal (oral)</td>
<td>![Never]</td>
<td>![Never]</td>
<td>![Never]</td>
</tr>
<tr>
<td>Water-borne</td>
<td>![Never]</td>
<td>![Never]</td>
<td>![Never]</td>
</tr>
<tr>
<td>Raw shellfish</td>
<td>![Never]</td>
<td>![Never]</td>
<td>![Never]</td>
</tr>
</tbody>
</table>

IV=intravenous.
Adapted from Dartmouth College. www.epidemic.org/thefacts/hepatitisc/transmission.php.
Natural History of HCV Infection

20%-30% of individuals are symptomatic.

HCC=hepatocellular carcinoma.

HCV-Related Decompensated Cirrhosis and HCC Projected to Rise in the US

- HCV-related decompensated cirrhosis and HCC are rising as manifestations of liver disease in aging population\(^1\)
- 73.4% of HCV-related deaths occurred among persons 45-64 years of age
  - Median age was 57 years; ~20 years less than the average lifespan of persons living in the US\(^2,\)*

*Projection based on a dynamic, multicohort, natural history model of data from the CDC, NHANES, and a review of the medical literature, with conservative estimates of disease progression and complications. Model assumes first-year mortality of 80%-85% for HCC.

*During the period from 1999 to 2007.

HCV Is Leading Cause of Liver Transplants in the US

Primary cause of disease among adults on the liver transplant wait list, 2011

- HCV: 30.1%
- Acute hepatic necrosis: 2.6%
- HBV: 2.8%
- Malignancy: 6.0%
- Alcoholic liver disease: 9.0%
- Cholestatic disease: 23.2%
- All others: 26.4%

Primary cause of disease among adult liver transplant recipients, 2011

- HCV: 23.5%
- Metabolic liver disease: 2.5%
- Acute hepatic necrosis: 4.0%
- Cholestatic disease: 9.1%
- Alcohol liver disease: 17.6%
- Malignancy: 20.9%
- All others: 22.3%

Treatment Goal in HCV Is SVR

- Majority of patients who achieve an SVR do not experience viral recurrence²

cccDNA=covalently closed circular DNA; HBV=hepatitis B virus.

Images adapted from Soriano V, et al.¹
Sustained Virologic Response (SVR) Achieved After Treatment Is Durable

- **SVR** = HCV RNA negative (by a sensitive assay, <50 IU/mL) at 12 (SVR12) or 24 weeks after cessation of treatment\(^1,2\)

- 99% of patients who achieved an SVR had undetectable levels of HCV RNA in serum samples throughout the follow-up period\(^3,*\)
  - “These data suggest that the recurrence of HCV RNA is extremely rare in patients who achieve an SVR, and it now appears likely that such patients may be considered “cured” from a virologic standpoint”\(^3\)

- For patients with cirrhosis, current guidelines recommend monitoring those who have achieved an SVR at 6-month intervals for the development of HCC\(^1\)

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*After treatment with peginterferon alfa-2a ± ribavirin; mean follow-up, 3.9 years (range, 0.8–7.1 years).

Screening Recommendations for HCV
Current Estimates Show a Significant Gap in HCV Care

Approximately 3.2 million in the US have chronic HCV infection\(^1,2,\ast\)


*Prevalence estimate based on NHANES data from 1999 through 2002.\(^1,2\) NHANES data underestimate the actual prevalence of HCV in the US by not accounting for incarcerated, homeless, hospitalized, nursing home and active military duty populations.\(^6,7\)

1.6 million (50%) diagnosed\(^3,4\)

170,000 – 200,000 (5 – 9%) were successfully treated\(^4,5\)

\(\ast\)NHANES data underestimate the actual prevalence of HCV in the US by not accounting for incarcerated, homeless, hospitalized, nursing home and active military duty populations.\(^6,7\)
Laboratory Diagnosis of Chronic HCV Infection

- RNA testing identifies active disease in HCV-seropositive patients

- HCV antibodies appear by 6–8 weeks following infection\(^1\)
  - Can be detected by EIA\(^2\)

- Serum ALT is not a reliable indicator of liver damage\(^1\)

- FDA-approved rapid point-of-care testing is available\(^3\)
  - OraQuick® HCV Test

ALT=alanine aminotransferase; EIA=enzyme immunoassay; RNA=ribonucleic acid; ULN=upper limit of normal.

Image adapted from MicrobiologyBytes:Virology:HCV\(^1\)
HCV Diagnostic Algorithm Based on Serologic Testing

Anti-HCV Antibody

Positive

HCV RNA

Positive

HCV Genotype
Assess for Fibrosis:
Fibrosure, Fibroscan
Liver Biopsy
Vaccinate for HAV / HBV*

Negative

No Further Testing

Negative

No Active Disease

*If patient lacks pre-existing antibodies to HAV or HBV.
HAV=hepatitis A virus, HBV=hepatitis B virus.
2012 CDC Recommendations for Birth Cohort (1945–1965) Screening

- **Recommendation 1**
  - Adults born from 1945 to 1965 should receive one-time testing for HCV without prior ascertainment of HCV risk
  
  *Grade: strong recommendation*
  *Evidence: moderate-quality*

- **Recommendation 2**
  - All persons identified with HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions as indicated
  
  *Grade: strong recommendation*
  *Evidence: moderate-quality*

2013 Updated USPSTF HCV Screening Recommendations

- **Those at high risk for HCV infection:**
  - Most important risk factor is past or current injection drug use
  - Additional risk factors include:
    - Receiving a blood transfusion before 1992
    - Long-term hemodialysis
    - Being born to an HCV-infected mother
    - Incarceration
    - Intranasal drug use
    - Getting an unregulated tattoo, and other percutaneous exposures

- **Adults born between 1945 and 1965 (“Baby Boomers”)**

*Grade B recommendation for persons at high risk for infection and adults born between 1945 and 1965.*
Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].
Presentation of Patients Infected With HCV

- Patients often asymptomatic in early stages of infection\(^1\)

**Symptoms may include\(^1\)**
- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Dark urine
- Grey-colored stools
- Jaundice
- Joint pain

**First symptoms may be those of extrahepatic manifestations\(^2\)**
- Arthralgias
- Paresthesias
- Myalgias
- Pruritus
- Sicca syndrome

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Patient Counseling for HCV Precautions and Treatment Expectations
Counseling Recommendations for HCV-Infected Individuals

To Prevent HCV Transmission
- Avoid sharing toothbrushes and dental or shaving equipment
- Prevent blood contact with others
- Stop using illicit drugs; those who continue to inject drugs should take precautions to avoid viral transmission
- Risk of sexual transmission is low, but practice “safe sex”

Additional Recommendations
- Avoid alcohol consumption
  - Excess alcohol may lead to progressive liver disease, increased HCV RNA replication, and reduced response to treatment
- Consider treatment for hepatitis C*
- Vaccinate for hepatitis A and B
- Get tested for HIV
- Encourage family members to get screened

Generally Accepted Indications for HCV Treatment

- Age ≥18 years
- HCV RNA positive and significant fibrosis*
- Compensated liver disease
- Acceptable hematologic and biochemical indices†
- Willingness to be treated and to adhere to treatment requirements
- No contraindications‡

* Bridging fibrosis or cirrhosis.
† Hemoglobin 13 g/dL for men and 12 g/dL for women; neutrophil count 1500/mm³ and serum creatinine <1.5 mg/dL.
‡ Uncontrolled depression, solid organ transplant, autoimmune hepatitis or autoimmune condition known to be exacerbated by pegIFN/RBV, untreated thyroid disease, pregnancy, severe concurrent medical disease (e.g., hypertension, heart failure, coronary heart disease, poorly controlled diabetes, chronic obstructive pulmonary disease), age <2 years

AASLD=American Association for the Study of Liver Diseases.
Summary

- Approximately 3.2 million people in the US have chronic HCV infection\(^1,2,*\)
- If left untreated, HCV infection can lead to advanced liver disease
  - Patients often asymptomatic in early stages of HCV infection\(^3\)
  - There is an increasing burden of liver disease in aging baby boomers due to manifestations of HCV infection acquired 20-30 years ago\(^3\)
- CDC and USPSTF recommend screening all baby boomers in addition to those with other specific risk factors\(^4,5\)
- HCV infection is curable (SVR=virologic cure)\(^6,†\)
  - SVR reduces the risk of mortality and of developing advanced liver disease\(^7,8\)
  - Patients with cirrhosis who achieved an SVR should continue to be monitored at 6- or 12-month intervals for the development of HCC\(^9\)

*Prevalence estimate based on NHANES data from 1999 through 2002.\(^1,2\)
†Outcomes based on 2-drug therapy with PegIFN and RBV.

Extrahepatic Manifestations of HCV
Extrahepatic Manifestations of HCV

- Mixed cryoglobulinemia
- Sjögren (sicca) syndrome
- Lymphoproliferative disorders
- Porphyria cutanea tarda
- Neuropathy
- Membranoproliferative glomerulonephritis
- Cryoglobulinemic vasculitis

**Strongly associated**

- Corneal ulcers (Mooren ulcers)
- Thyroid disease
- Lichen planus
- Pulmonary fibrosis
- Type 2 diabetes
- Systemic vasculitis (polyarteritis nodosa, microscopic polyangiitis)
- Arthralgias, myalgias, inflammatory polyarthritis
- Autoimmune thrombocytopenia

Liver Histology Scoring Systems
# Scoring Systems for Histologic Stage

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Ishak Description</th>
<th>Ishak Score(^1)</th>
<th>META VIR Score(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fibrosis</td>
<td>No fibrosis</td>
<td>0</td>
<td>F0</td>
</tr>
<tr>
<td>Fibrous expansion of some portal areas ± short fibrous septa</td>
<td>1</td>
<td>F1</td>
<td></td>
</tr>
<tr>
<td>Fibrous expansion of most portal areas ± short fibrous septa</td>
<td>2</td>
<td>F2</td>
<td></td>
</tr>
<tr>
<td>Fibrous expansion of most portal areas with occasional portal to portal (P–P) bridging</td>
<td>3</td>
<td>F3</td>
<td></td>
</tr>
<tr>
<td>Fibrous expansion of most portal areas with marked bridging (P–P and portal to central [P–C])</td>
<td>4</td>
<td>F4</td>
<td></td>
</tr>
<tr>
<td>Marked bridging (P–P and/or P–C) with occasional nodules (incomplete cirrhosis)</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>6</td>
<td>F4</td>
<td></td>
</tr>
</tbody>
</table>

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Figure adapted from Standish RA, et al. *Gut*. 2006;55:569-578.
# Definitions of Virologic Response to Treatment

<table>
<thead>
<tr>
<th>Response Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid virologic response (RVR)</td>
<td>HCV RNA negative at treatment week 4 by a sensitive PCR-based quantitative assay</td>
</tr>
<tr>
<td>Early virologic response (EVR)</td>
<td>≥2 log reduction in HCV RNA level compared with baseline (partial EVR) or HCV RNA negative at treatment week 12 (complete EVR). Predictive of SVR</td>
</tr>
<tr>
<td>End-of-treatment response (ETR)</td>
<td>HCV RNA negative by a sensitive test at the end of treatment</td>
</tr>
<tr>
<td>Sustained virologic response (SVR)</td>
<td>HCV RNA negative at 24 weeks (SVR24) after cessation of treatment. Best predictor of long-term outcomes</td>
</tr>
<tr>
<td>Breakthrough</td>
<td>Reappearance of HCV RNA in serum while on therapy</td>
</tr>
<tr>
<td>Relapse</td>
<td>Reappearance of HCV RNA in serum after therapy is discontinued</td>
</tr>
<tr>
<td>Nonresponder</td>
<td>Failure to clear HCV RNA from serum after 24 weeks of therapy</td>
</tr>
<tr>
<td>Null responder</td>
<td>Failure to achieve a 2 log reduction in HCV RNA after 24 weeks of therapy</td>
</tr>
<tr>
<td>Partial responder</td>
<td>2-log reduction in HCV RNA but still HCV RNA positive at week 24</td>
</tr>
</tbody>
</table>

HCV Treatment
Current standards and AASLD recommendations
Evolution of HCV Treatment

The first advance in treatment for chronic HCV in 10 years
- SVR rates have steadily increased with each advance in treatment
- Protease inhibitors provide another option for previously treated G1 patients

Treatment by Genotype

- **Genotype 1**

  Ledipasvir 90 mg / Sofosbuvir 400 mg
  - once-daily, single-tablet regimen
  - Ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor
  - Sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor
  - Interferon (IFN)-free and Ribavirin (RBV)-free regimen
- The recommended dosage of Ledipasvir/Sofosbuvir for adults is one tablet taken orally once daily with or without food.

**RECOMMENDED REGIMEN AND TREATMENT DURATION IN GT1 CHC PATIENTS**

<table>
<thead>
<tr>
<th>1</th>
<th>Tablet Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-naïve patients with or without cirrhosis</td>
<td>12 weeks$^a$</td>
</tr>
<tr>
<td>Treatment-experienced patients$^b$ without cirrhosis</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment-experienced patients$^b$ with cirrhosis</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

- Relapse rates are affected by baseline host and viral factors and differ between treatment durations for certain subgroups.

*No dose recommendation can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30 mL/min/1.73m$^2$) or with end stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite.*

$a$ 8 weeks can be considered in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL.

$b$ Treatment-experienced patients who have failed treatment with either peginterferon (Peg-IFN) alfa + RBV or an HCV protease inhibitor (PI) + Peg-IFN alfa + RBV.
Ledipasvir/ Sofosbuvir
ONCE-DAILY, SINGLE-TABLET REGIMEN, DELIVERED HIGH SVR12 RATES

<table>
<thead>
<tr>
<th>Subjects Without Cirrhosis</th>
<th>Treatment-naïve</th>
<th>Treatment-experienced&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>96-99% SVR12</td>
<td>95% SVR12 with 12 weeks of treatment</td>
</tr>
<tr>
<td></td>
<td>with 12 weeks of treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>97% SVR12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with 8 weeks of treatment (HCV RNA &lt;6 million IU/mL)</td>
<td></td>
</tr>
<tr>
<td>Subjects with Compensated Cirrhosis</td>
<td>94% SVR12 with 12 weeks of treatment</td>
<td>100% SVR12 with 24 weeks of treatment</td>
</tr>
</tbody>
</table>
In addition to rifampin and St. John’s wort, coadministration is also not recommended with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir. Such coadministration is expected to decrease the concentration of ledipasvir and sofosbuvir, reducing the therapeutic effect.

Coadministration is not recommended with simeprevir due to increased concentrations of ledipasvir and simeprevir. Coadministration is also not recommended with rosvastatin or co-formulated elvitegravir/cobicistat/emtricitabine/tenofovir disopropxil fumarate due to increased concentrations of rosvastatin and tenofovir, respectively.
# Concomitant Drug Class: Drug Name

<table>
<thead>
<tr>
<th>Concomitant Drug Class: Drug Name</th>
<th>Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acid Reducing Agents</strong></td>
<td></td>
</tr>
<tr>
<td>Antacids (e.g., aluminum and magnesium hydroxide)</td>
<td>Ledipasvir solubility decreases as pH increases. Drugs that increase gastric pH are expected to decrease concentration of ledipasvir.</td>
</tr>
<tr>
<td>H₂-receptor antagonistsb (e.g., famotidine)</td>
<td>It is recommended to separate antacid and HARVONI administration by 4 hours.</td>
</tr>
<tr>
<td>Proton-pump inhibitorsb (e.g., omeprazole)</td>
<td>H₂-receptor antagonists may be administered simultaneously with or 12 hours apart from HARVONI at a dose that does not exceed doses comparable to famotidine 40 mg twice daily.</td>
</tr>
<tr>
<td><strong>Antiarrhythmics:</strong> digoxin</td>
<td>Proton-pump inhibitor doses comparable to omeprazole 20 mg or lower can be administered simultaneously with HARVONI under fasted conditions.</td>
</tr>
<tr>
<td><strong>HIV Antiretroviralsc</strong></td>
<td>Coadministration of HARVONI with digoxin may increase the concentration of digoxin. Therapeutic concentration monitoring of digoxin is recommended when coadministered with HARVONI.</td>
</tr>
<tr>
<td>Efavirenz/emtricitabine/tenofovir DF (ATRIPLA®)</td>
<td>Monitor for tenofovir-associated adverse reactions in patients receiving HARVONI concomitantly with efavirenz/emtricitabine/tenofovir DF.</td>
</tr>
<tr>
<td>Regimens containing tenofovir DF (VIREAD®) and an HIV protease inhibitor/ritonavir, including</td>
<td>The safety of increased tenofovir concentrations in the setting of HARVONI and an HIV PI/ritonavir has not been established. Consider alternative HCV or antiretroviral therapy to avoid increases in tenofovir exposures. If coadministration is necessary, monitor for tenofovir-associated adverse reactions.</td>
</tr>
<tr>
<td>• atazanavir/ritonavir + emtricitabine/tenofovir DF (TRUVADA®)</td>
<td></td>
</tr>
<tr>
<td>• darunavir/ritonavir + emtricitabine/tenofovir DF</td>
<td></td>
</tr>
<tr>
<td>• lopinavir/ritonavir (Kaletra®) + emtricitabine/tenofovir DF</td>
<td></td>
</tr>
</tbody>
</table>

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aBased on drug interaction studies or predicted interaction; this information is not all inclusive.
bThese interactions have been studied in healthy adults.
cRefer to the appropriate prescribing information for recommendations on renal monitoring with these medications.
No clinically significant drug interactions (observed or expected) when HARVONI is used with the following drugs individually:

**Antiretrovirals**
- abacavir
- atazanavir/ritonavir
- darunavir/ritonavir
- efavirenz
- emtricitabine
- lamivudine
- raltegravir
- rilpivirine
- tenofovir DF

**Immunosuppressants**
- cyclosporine
- tacrolimus

**Opioid**
- methadone

**Oral contraceptives**

**Statin**
- pravastatin

**Calcium channel blocker**
- verapamil
Paritaprevir Boosted with Ritonavir/Ombitasvir/Dasabuvir

- Used With and Without Ribavirin
  - All oral interferon free regimen containing 3 direct acting antiviral agents
    - Paritaprevir-NS3/4A
      - Boosted with Ritonavir
    - Ombitasvir-NS5A
    - Dasabuvir-Non-nucleoside NS5B Polymerase Inhibitor
Paritaprevir Boosted with Ritonavir/Ombitasvir/Dasabuvir

- GT1a without cirrhosis with Ribavirin: 12 weeks
- GT1a with Cirrhosis with Ribavirin: +/- 24 weeks
- GT1b without Cirrhosis without Ribavirin: 12 weeks
- GT1b with Cirrhosis with Ribavirin: 12 Weeks
- 97% Overall SVR
  - 96% in compensated cirrhotic –used with Ribavirin
  - 96% GT1a Non-cirrhotic
  - 100% GT1b Non- Cirrhotic
Side Effects

- Fatigue
- Insomnia
- Nausea
- Headache
- Pruritis
- Skin Reactions
- Cough
- Irritability
- Asthenia
- Anemia
Drug Interactions

- Contraindicated with drugs that are highly dependent on CYP3A for clearance, Strong inducers of CYP3A or CYP2C8 and Strong Inhibitors of CYP2C8
- Ethinyl estradiol – containing preparation are contraindicated – ALT elevations >5X ULN
# Medications contraindicated/ Not recommended

<table>
<thead>
<tr>
<th>Medication</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha Blockers:</strong> Alfuzosin</td>
<td><strong>Anticonvulsants:</strong> Carbamazepine, Phenytoin, Phenobarbital</td>
<td><strong>Antihyperlipidemins:</strong> Gemfibrozil</td>
<td><strong>Antimycobacterial:</strong> Rifampin</td>
</tr>
<tr>
<td><strong>Ergot derivatives:</strong> Ergotamine, Dihydroergotamine, ergonovine, methylergonovine</td>
<td>Ethinyl estradiol containing products</td>
<td>Herbals: St John’s Wort</td>
<td>HIV antiviral: Efavirenz</td>
</tr>
<tr>
<td><strong>HMG-Coa Reductase Inhibitors:</strong> Lovastatin, Simvastatin</td>
<td><strong>Neuroleptics:</strong> Pimozide</td>
<td><strong>PDE5 Inhibitor-Revatio for pulmonary Arterial HTN</strong></td>
<td><strong>Sedatives- Triazolam , Orally administered Midazolam</strong></td>
</tr>
<tr>
<td><strong>Antifungal:</strong> Ketoconazole</td>
<td>Nasal or inhaled Fluticasone</td>
<td><strong>HIV agents:</strong> Darunavir/Ritonavir, Lopinavir/Ritonavir, Rilpivirine</td>
<td><strong>Long acting Beta-Adrenoceptor Agonist- Salmeterol</strong></td>
</tr>
</tbody>
</table>
Monitoring or Dose Adjustments recommended

<table>
<thead>
<tr>
<th>Antiarrythmics- Amiodarone, Bepridil, Disopyramide, Flecaïnide, Lidocaine, Mexiletine, propafenone, Quinidine</th>
<th>Antifungal- Ketoconazole</th>
<th>Calcium Channel Blocker- Amlodipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics- Furosamide</td>
<td>HIV antiviral- Atazanavir/Ritonavir</td>
<td>HMG-CoA reductase inhibitor: Rosuvastatin, Pravastatin</td>
</tr>
<tr>
<td>Immunosuppressants- Cyclosporine, Tacrolimus</td>
<td>Narcotic- Buprenorphine/naloxone</td>
<td>PPI- Omeprazole</td>
</tr>
<tr>
<td>Sedatives- Alprazolam</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Ribavirin

- Contraindicated in Women who are pregnant and men whose partner is pregnant.
- Pregnancy must be avoided during treatment and for 6 months after treatment ends.
- Both men and women on Treatment are advised to use 2 methods of Birth control
- Anemia- monitor CBC, may require Ribavirin dose reduction
Genotype 2
Sofosbuvir and Ribavirin- 12 weeks

• 93% overall SVR
  – Treatment Experience- SVR 90%
  – Treatment Naïve- SVR 97%

Genotype 3
Sofosbuvir and Ribavirin- 24 weeks

• 84% overall SVR
  – Treatment Experienced-SVR 77%
  – Treatment Naïve-SVR 93%
Genotype 4:

- **Sofosbuvir, Pegylated Interferon and Ribavirin – 12 weeks**
  - 96% SVR in Treatment naïve
  - No Data for treatment experienced Estimated ~70 % SVR
## Sofosbuvir containing Regimen side effects:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Placebo 12 weeks</th>
<th>SOFOSBUVIR + RBV&lt;sup&gt;a&lt;/sup&gt; 12 weeks</th>
<th>SOFOSBUVIR + RBV&lt;sup&gt;a&lt;/sup&gt; 24 weeks</th>
<th>Peg-IFN alfa + RBV&lt;sup&gt;b&lt;/sup&gt; 24 weeks</th>
<th>SOFOSBUVIR + Peg-IFN alfa + RBV&lt;sup&gt;a&lt;/sup&gt; 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>24%</td>
<td>38%</td>
<td>30%</td>
<td>55%</td>
<td>59%</td>
</tr>
<tr>
<td>Headache</td>
<td>20%</td>
<td>24%</td>
<td>30%</td>
<td>44%</td>
<td>36%</td>
</tr>
<tr>
<td>Nausea</td>
<td>18%</td>
<td>22%</td>
<td>13%</td>
<td>29%</td>
<td>34%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4%</td>
<td>15%</td>
<td>16%</td>
<td>29%</td>
<td>25%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>8%</td>
<td>11%</td>
<td>27%</td>
<td>17%</td>
<td>17%</td>
</tr>
<tr>
<td>Anemia</td>
<td>0%</td>
<td>10%</td>
<td>6%</td>
<td>12%</td>
<td>21%</td>
</tr>
<tr>
<td>Asthenia</td>
<td>3%</td>
<td>6%</td>
<td>21%</td>
<td>3%</td>
<td>5%</td>
</tr>
</tbody>
</table>
## Genotype 4

<table>
<thead>
<tr>
<th>Concomitant Drug Class: Drug Name</th>
<th>Should not be used with SOFOSBUVIR</th>
<th>Coadministration with SOFOSBUVIR not recommended</th>
<th>No clinically significant interaction with SOFOSBUVIR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antimycobacterials:</strong> rifampin</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Herbal supplements:</strong> St. John’s wort</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antiretroviral:</strong> tipranavir/ritonavir</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td><strong>Anticonvulsants:</strong> carbamazepine, phenytoin, phenobarbital, oxcarbazepine</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Antimycobacterials:</strong> rifabutin, rifapentine</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Antiretroviral:</strong> darunavir/ritonavir, emtricitabine, efavirenz, raltegravir, rilpivirine, tenofovir disoproxil fumarate</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Immunosuppressants:</strong> cyclosporine, tacrolimus</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td><strong>Opioids:</strong> methadone</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>
Genotype 5 & 6:

- **Genotype 5**
  - **Pegylated Interferon and Ribavirin - 48 weeks**
    - ~ 60-70% SVR

- **Genotype 6**
  - **Pegylated Interferon and Ribavirin – 48 weeks**
    - ~ 70-80% SVR
Warnings Pegylated Interferon

- May cause or aggravate neuropsychiatric, autoimmune, ischemic and infectious disorders
- Require close supervision and follow-up, including monitoring WBC and platelets
Warnings Ribavirin

- May Cause birth defects and/or fetal defects- extreme care must be taken to prevent pregnancy during for r6 months following treatment
- Causes Hemolytic anemia- requires careful monitoring
- Anemia may cause worsening of cardiac disease
Side Effects

- Fatigue
- Headache
- Nausea
- Insomnia
- Pruritus
- Anemia
- Neutropenia
- Asthenia
- Worsening Psychiatric illness/ Suicidal Ideation
Summary

- Hepatitis C ~3.2 million people infected in US, ~170 Million Worldwide
- ~ 50% Diagnosed
- ~5-9% treated effectively
- Leading cause of liver transplants in US
- CDC recommends Screening at risk individuals as well as those born between 1945-1965
- Many New more effective interferon free treatments are available
THANK YOU!

Questions?