Initiating Hepatitis C Treatment in Your Practice

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University of Virginia Division of Infectious Disease and International Health
Dr. Dillingham has received an investigator-initiated grant from Gilead. She also serves as a consultant to Warm Health Technologies, Inc, an mHealth company.
Hepatitis C Virus

- *Flaviviridae*
- Positive-sense RNA genome with one long ORF flanked by two NTRs which assist with RNA replication
- Replicates in a membranous web in tight association with LDL and VLDL
- Exceptional diversity – much greater than HIV – genotypes (1-7) differ by 33%; subtypes (a-b) by 25%

Natural History of HCV Infection

- 15-45% of those infected with HCV will recover spontaneously.
- 5-20% with chronic infection will develop cirrhosis in 20-25 years.
  - 30% of those with cirrhosis will develop end-stage liver disease.
  - 1-2% per year of those with cirrhosis will develop hepatocellular carcinoma.

Figure 8 Mortality Rates from HBV, HCV, and HIV in United States, 1999-2007.

This graphic shows that when determining age-adjusted mortality rates, hepatitis C-related deaths surpassed HIV-related deaths in 2006. Abbreviations: PY = person years

A Short History of HCV Therapy

- HCV Discovered (Chiron)
- HCV Antibody Testing
- Ribavirin Added
- PEG Interferon + RBV Trials
- Genotype-Specific RGT
- Telaprevir Boceprevir Approval
- Simeprevir Sofosbuvir Approval


SVR:
- 6%
- 12%
- 20%
- 40%
- 54%
- 70%
- 90%

Slide courtesy of Dr. Donald Jensen
Hepatitis C Treatment

Interferon-Based Regimens

50% CURE

Direct Acting Antivirals

95% CURE
Cascade of Care

SVR = Sustained Virologic Response = “Cure”

Yehia 2014, PLoS One
Figure 1. Hepatitis C cascade of care. Steps in the hepatitis C cascade of care were defined to be (1) any positive HCV test, (2) measurement of HCV viral load, (3) active HCV, defined by a positive viral load, (4) linkage to care, defined as a scheduled appointment with an HCV specialty clinic, (5) medication prescribed through the electronic medical record, and (6) SVR, defined as a nondetectable viral load after treatment. The cascade includes all individuals with a positive HCV test within the University of Virginia Health System between 2010 and 2016 who completed cascade steps by December 31, 2017. Abbreviations: HCV, hepatitis C virus; SVR, sustained virologic response.
Figure 1. Hepatitis C cascade of care. Steps in the hepatitis C cascade of care were defined to be (1) any positive HCV test, (2) measurement of HCV viral load, (3) active HCV, defined by a positive viral load, (4) linkage to care, defined as a scheduled appointment with an HCV specialty clinic, (5) medication prescribed through the electronic medical record, and (6) SVR, defined as a nondetectable viral load after treatment. The cascade includes all individuals with a positive HCV test within the University of Virginia Health System between 2010 and 2016 who completed cascade steps by December 31, 2017. Abbreviations: HCV, hepatitis C virus; SVR, sustained virologic response.
Initiating Treatment

• Risk factor assessment
• HPI and Medical History Review
  • Reproductive status
  • History of prior treatment for hepatitis C
  • Current medications
• Laboratory Value Review
  • Hepatitis B
  • Hepatitis A
  • HIV
  • Renal function
• Imaging Review
• Anticipatory Guidance
26yo woman referred for evaluation of positive HCV antibody – Ms. C

• On review, you see that she has a detectable HCV viral load of 1,240,000 copies/ml.

• Her HCV genotype has been completed, and she is infected with Genotype 3 HCV.

• She is visibly anxious.

• Her HCV test was obtained at a local medication-assisted treatment (MAT) clinic where she is prescribed buprenorphine/naloxone.
Your next step should be:

A. Tell her that she needs to be stable at the MAT clinic for six months with negative urine drug screens (UDS) before she can be evaluated.

B. Inform her that genotype 3 is the worst kind of hepatitis C.

C. Review data about the relationship of HCV viral load and progression of liver disease.

D. Assess her understanding of hepatitis C infection and its treatment.
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B. Inform her that genotype 3 is the worst kind of hepatitis C.

C. Review data about the relationship of HCV viral load and progression of liver disease.

D. Assess her understanding of hepatitis C infection and its treatment.
Initiating Treatment

• Risk factor assessment – “Please tell me what you know about hepatitis C and how you think you got it.”
• HPI and Medical History Review
• Laboratory Value Review
  • Hepatitis B
  • HIV
  • Renal function
• Imaging Review
• Anticipatory Guidance
HCV Transmission and Snorting

Table 1. Detection of hepatitis C virus (HCV) RNA and blood in biological specimens obtained from 38 patients with HCV-positive serum specimens.

<table>
<thead>
<tr>
<th>Assay</th>
<th>No. (%) of persons (n = 38)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood detection with OBTI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal secretions</td>
<td>28 (73.7)</td>
<td>57.8–85.2</td>
</tr>
<tr>
<td>Sniffing straws</td>
<td>3 (7.9)</td>
<td>2.0–21.5</td>
</tr>
<tr>
<td>HCV RNA detection with PCR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal secretions</td>
<td>5 (13.2)</td>
<td>5.3–27.8</td>
</tr>
<tr>
<td>Sniffing straws</td>
<td>2 (5.3)</td>
<td>0.5–18.2</td>
</tr>
</tbody>
</table>

- Systematic review estimated HCV prevalence of those who use drugs intra-nasally to be between 2-35%.

Fig. 1  Hepatitis C risk factor identification among survey participants from Virginia, United States, 2017. HCV hepatitis C virus, MSM men who have sex with men
Initiating Treatment

• Risk factor assessment
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  • Current medications
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  • Hepatitis B
  • HIV
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• Imaging Review
• Anticipatory Guidance
26yo woman referred for evaluation of positive HCV antibody – Ms. C

• Ms. C has a history of opioid use disorder, mainly snorting crushed pills. She started snorting pills 6 years ago.

• She has bipolar disorder and was started on aripiprazole three months ago. This medication has helped to stabilize her mood.

• She has two children (4 and 8 yo) both of whom are cared for by her mother. She is not currently sexually active. She is not on any birth control.

• She has had no prior treatment for hepatitis C, but her mother was treated 15 years ago. The treatment required her mother to stop working, and it did not cure the hepatitis C.
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Barriers to Care: Discrimination Against Substance Users

2017 study of rural Appalachian people who use drugs showed that while 59% contacted a healthcare provider after a positive HCV antibody test, only 8% reported receiving treatment.
Figure 2. Summary 5-year risk (95% confidence interval) of recurrence post-sustained virological response (SVR), by risk group. Presented are the pooled estimates for the 5-year risk of recurrence after achieving an SVR. Also shown are the number of studies that were included to derive each estimate. Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus.
26yo woman referred for evaluation of positive HCV antibody – Ms. C

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Your next step should be:

A. Reassure her that the treatment for hepatitis C infection has improved dramatically since her mother was treated.
B. Assess whether aripiprazole has any interactions with possible treatment options.
C. Ask whether her children have been tested for HCV infection.
D. Recommend that she initiate birth control.
E. All of the above.
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<table>
<thead>
<tr>
<th>HEP Drugs</th>
<th>Co-medications</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Search HEP drugs...</td>
<td>Search co-medications...</td>
<td>Check HEP/ HEP drug interactions</td>
</tr>
</tbody>
</table>

- **A-Z**
- **Indication**
- **Trade**

**Selected HEP Drugs will be displayed here:**
- Adefovir
- Daclatasvir
- Elbasvir/Grazoprevir
- Entecavir
- Glecaprevir/Pibrentasvir
- Lamivudine (HBV)
- Ledipasvir/Sofosbuvir

**Selected Co-medications will be displayed here:**
- Abacavir
- Adefovir
- Abiraterone
- Acalabrutinib
- Acamprosate
- Acrabose
- Aclidinium
- Acebutolol
- Aclofenac

Having trouble viewing the interactions? Click here for the Interaction Checker Lite.

www.hep-druginteractions.org/checker
### HEP Drug Interactions

**HEP Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
</tr>
</tbody>
</table>

**Co-medications**

<table>
<thead>
<tr>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
</tr>
</tbody>
</table>

**Drug Interactions**

- Check HEP/HEP drug interactions

**Switch to table view**

- Potential Interaction
  - Glecaprevir/Pibrentasvir
  - Aripiprazole

- Look for alternatives

---

www.hep-druginteractions.org/checker
Glecaprevir/Pibrentasvir

Aripiprazole

Summary:
Co-administration has not been studied. Aripiprazole is metabolised by CYP3A4 and concentrations may increase due to weak inhibition of CYP3A4 by glecaprevir/pibrentasvir. As aripiprazole has a narrow therapeutic index and unpredictable therapeutic levels, monitor patients closely for signs and symptoms of toxicity.

Description:
(See Summary)

Open in new tab
How many people have access to an internet-connected computer terminal in the examination room?
Testing children for HCV antibody positivity

HCV in Children

Testing

<table>
<thead>
<tr>
<th>Recommendations for HCV Testing of Perinatally Exposed Children and Siblings of HCV-Infected Children</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children born to HCV-infected women should be tested for HCV infection. Testing is recommende...</td>
<td>I, A</td>
</tr>
<tr>
<td>Testing with an HCV-RNA assay can be considered in the first year of life, but the optimal timing ...</td>
<td>IIa, C</td>
</tr>
<tr>
<td>Repetitive testing by HCV RNA is not recommended.</td>
<td>III, A</td>
</tr>
<tr>
<td>Children who are anti-HCV positive after 18 months of age should be tested with an HCV-RNA ass...</td>
<td>I, A</td>
</tr>
<tr>
<td>The siblings of children with vertically-acquired chronic HCV should be tested for HCV infection,...</td>
<td>I, C</td>
</tr>
</tbody>
</table>

www.hcvguidelines.org
Having trouble viewing the interactions? Click here for the Interaction Checker Lite.

---

**HEP Drugs**

- gle
- Glecaprevir/Pibrentasvir
- Glecaprevir/Pibrentasvir

**Co-medications**

- ethin
- Ethinylestradiol
- Ethinylestradiol
- Norethisterone (Norethindrone)

**Drug Interactions**

- Check HEP/HEP drug interactions
- Switch to table view
- Do Not Coadminister
- Look for alternatives

---

www.hep-druginteractions.org/checker
<table>
<thead>
<tr>
<th>HEP Drugs</th>
<th>Co-medications</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>gle</td>
<td>ethin</td>
<td><a href="#">Switch to table view</a></td>
</tr>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>Ethinylestradiol</td>
<td>Do Not Coadminister</td>
</tr>
<tr>
<td>Norethisterone (Norethindrone)</td>
<td>Ethinylestradiol</td>
<td>Look for alternatives <a href="#">Look for alternatives →</a></td>
</tr>
</tbody>
</table>
Other comediations in the same class

Clicking on a symbol will show details of the interaction

The table below shows interactions with other drugs in the same class. The clinical suitability of a drug as an alternative may depend not only on its interaction profile, but also on patient specific information.

<table>
<thead>
<tr>
<th>Contraceptives and Hormone Replacement</th>
<th>Glicaprevir/Pibrentasvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desogestrel</td>
<td>Do Not Coadminister</td>
</tr>
<tr>
<td>Dienogest</td>
<td>Potential Interaction</td>
</tr>
<tr>
<td>Drospirenone</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Estradiol</td>
<td>Potential Weak Interaction</td>
</tr>
<tr>
<td>Ethinylestradiol</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Etonogestrel (implant)</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Etonogestrel (vaginal ring)</td>
<td>Potential Interaction</td>
</tr>
<tr>
<td>Levonorgestrel (COC)</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Levonorgestrel (Emergency Contraception)</td>
<td>Potential Interaction</td>
</tr>
<tr>
<td>Levonorgestrel (HRT)</td>
<td>Potential Weak Interaction</td>
</tr>
<tr>
<td>Levonorgestrel (implant)</td>
<td>Potential Interaction</td>
</tr>
<tr>
<td>Levonorgestrel (IUD)</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Levonorgestrel (POP)</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Medroxyprogesterone (depot injection)</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Medroxyprogesterone (oral)</td>
<td>No Interaction Expected</td>
</tr>
<tr>
<td>Norethisterone (Norethindrone)</td>
<td>No Interaction Expected</td>
</tr>
</tbody>
</table>

www.hep-druginteractions.org/checker
Pilot study finds HCV treatment safe in pregnancy

March 8, 2019

SEATTLE — A small pilot study of hepatitis C treatment in pregnant women found that the treatment was effective in achieving hepatitis C cure and identified no safety concerns associated with treatment, according to findings presented at CROI.

Although guidelines from the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases recommend that all women be tested for HCV at the initiation of prenatal care, treatment during pregnancy is not recommended. However, the rate of HCV infection among pregnant women is rising in the United States, increasing the risk for perinatal transmission, according to Catherine A. Chappell, MD, MSc, assistant professor of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh, and colleagues.

“Over the last decade there has been about a twofold increase in hepatitis C among pregnant women delivering at my hospital,” Chappell said in a news conference. “That’s particularly important because of the babies that are delivered from those women, about

SEE ALSO

PCP-driven care safe, effective for HCV

10 recent HCV reports: SVR outcomes, continued DAA treatment

Some other key history questions

• Nausea/vomiting/heartburn?
• Headaches?
• Fatigue?
• Joint pain in the hands?
• Rashes? Spiders?
• Abdominal bloating?
• Confusion?
• Family history of liver disease?
• ALCOHOL?
Initiating Treatment

• Risk factor assessment
• HPI and Medical History Review
  • Reproductive status
  • History of prior treatment for hepatitis C
  • Current medications
• Laboratory Value Review
  • Hepatitis B
  • Hepatitis A
  • HIV
  • Renal function
• Imaging Review
• Anticipatory Guidance
Hepatitis B - Oh My!!

- Status of *exposure* and *immunity* must be assessed prior to initiating treatment.
  - Risk of reactivation of the disease while on HCV treatment.
  - Communicable
  - Preventable
1981 - Hepatitis B vaccine becomes available.  
2006 – Hep B vax routine for all children.
ANTIGENS

SURFACE ANTIGEN
HBsAg
+VE = INFECTION
VACCINE = HBsAg

E ANTIGEN
HBeAg
RELEASED DURING REPLICATION
+VE = ACUTE PHASE
↑LEVEL = ↑INFECTION VIBRACY

CORE ANTIGEN
HBeAg
NOT IN THE BLOOD
MIDDLE OF VIRUS (CORE)

HEPATITIS B

ANTIBODIES

SURFACE ANTIBODY
HBsAb
RESPONSE TO HBsAg
+VE = VACCINATED OR INFECTION

E ANTIBODY
HBeAb
RESPONSE TO HBeAg
+VE = BEEN THROUGH ACTIVE PHASE – IMMUNE RESPONSE

CORE ANTIBODY
HbcAb
RESPONSE TO HbcAg
+VE & +VE HBsAg

ACUTE INFECTION CHRONIC
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBSAg anti-HBc</td>
<td>negative</td>
<td>Susceptible (vaccinate)</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBSAg anti-HBc</td>
<td>negative</td>
<td>Resolved HBV infection</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBSAg anti-HBc</td>
<td>negative</td>
<td>Vaccinated</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBSAg anti-HBc</td>
<td>positive</td>
<td>Active HBV infection (usually chronic)</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>*If anti-HBc IgM present, may represent acute infection.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBSAg</td>
<td>negative</td>
<td>Various possibilities:</td>
</tr>
<tr>
<td>HBCAb</td>
<td>positive</td>
<td>distant resolved infection (most common)</td>
</tr>
<tr>
<td>HBsAb</td>
<td>negative</td>
<td>recovering from acute infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>false positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>occult hepatitis B</td>
</tr>
</tbody>
</table>
For HBsAg-positive patients who are not already on HBV suppressive therapy, the following are recommended:

- For patients whose HBV DNA level meets AASLD criteria for treatment, antiviral therapy for HBV should be initiated.

- For patients whose baseline HBV DNA level does not meet criteria for treatment, one of two approaches may be taken:
  
  - Initiate prophylactic antiviral therapy for those with low or undetectable HBV DNA levels. If this course is elected, pending further data, prophylaxis should be continued until 12 weeks after completion of DAA therapy.

- Monitor HBV DNA levels during and immediately after DAA therapy for HCV. Antiviral treatment for HBV should be given in the event of a rise in HBV DNA >10-fold above baseline or to >1000 IU/mL in those with a previously undetectable or unquantifiable HBV DNA level.

https://www.hcvguidelines.org/evaluate/monitoring
San Diego’s hepatitis A update: death total holds at 20, case count continues to climb

Two year outbreak with significant, unexpected mortality.

West Virginia Roiled by Side Effect of Opioid Crisis—a Major Hepatitis A Outbreak

This disease can be transmitted by unwittingly consuming traces of contaminated feces

By Dina Alpert Moran on August 27, 2018

Notes from the Field: Hepatitis A Outbreak Associated with Drug Use and Homelessness — West Virginia, 2018

Weekly / April 12, 2019 / 68[14]:330–331

Erica Wilson, MD; Megan G. Hofmeister, MD; Shannon McBee, MPH; Janet Briscoe, MBA; Erica Thomasson, PhD; R. Henry Olaisen, PhD; Ryan Augustine, MPH; Ellana Duncan, MSc; Sapna Banrah Morris, MD; Loreta Haddy, PhD (View author affiliations)
About 25% of PLWH in the U.S. also Have HCV Infection\(^\text{17,21}\)
Large cohort study demonstrated faster fibrosis in co-infected independent of other risk factors.
Options for those with renal impairment – even with end-stage renal disease!

Recommended regimens listed by evidence level and alphabetically for:

**Patients With CKD Stage\(^a\) 4 or 5 (eGFR <30 mL/min or End-Stage Renal Disease)**

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>GENOTYPE</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</td>
<td>1a, 1b, 4</td>
<td>12 weeks</td>
<td>I, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)(^b)</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>8 to 16 weeks(^c)</td>
<td>I, B(^c)</td>
</tr>
</tbody>
</table>

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\(^a\) Chronic kidney disease (CKD) stages: 1 = normal (eGFR >90 mL/min); 2 = mild CKD (eGFR 60-89 mL/min); 3 = moderate CKD (eGFR 30-59 mL/min); 4 = severe CKD (eGFR 15-29 mL/min); 5 = end-stage CKD (eGFR <15 mL/min)

\(^b\) This is a 3-tablet coformulation. Please refer to the prescribing information.

\(^c\) Patients in this group should be treated as would patients without CKD. Duration of glecaprevir/pibrentasvir should be based on presence of cirrhosis and prior treatment experience (please refer to appropriate section). As such, strength of rating may be lower for certain subgroups.

https://www.hcvguidelines.org/unique-populations/renal-impairment
Initiating Treatment

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  • History of prior treatment for hepatitis C
  • Current medications
• Laboratory Value Review
  • Hepatitis B
  • HIV
  • Renal function
• Imaging Review
• Anticipatory Guidance
Figure 3. Liver stiffness measurements are performed on the right lobe of the liver in intercostal position using FibroScan®.

Table 1. Comparison of various techniques to assess liver stiffness

<table>
<thead>
<tr>
<th>Method</th>
<th>Product name</th>
<th>Vibration mode/source</th>
<th>Frequency</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static elastography</td>
<td>Quasi-static compression</td>
<td>None</td>
<td>Not applicable</td>
<td>Widely available in ultrasound scanners</td>
<td>Qualitative only</td>
</tr>
<tr>
<td>Magnetic resonance elastography</td>
<td>Shear wave</td>
<td>Continuous mechanical actuator</td>
<td>50–60 Hz</td>
<td>2D/3D stiffness mapping, frequency controlled vibration, other organs</td>
<td>Expensive, metal implants (pace makers, bone implants)</td>
</tr>
<tr>
<td>Acoustic radiation force impulse</td>
<td>Shear wave</td>
<td>Transient radiation force</td>
<td></td>
<td>Ascites, other organs</td>
<td>Accuracy, limited clinical data</td>
</tr>
<tr>
<td>Vibration-controlled transient elastography</td>
<td>Shear wave</td>
<td>Transient mechanical actuator</td>
<td>50 Hz</td>
<td>Largely validated, frequency controlled vibration</td>
<td>Sensitive to body habitus (obesity, ascites, bowel interpolate)</td>
</tr>
</tbody>
</table>

FIBROSCAN SCORE

**F0/F1**
NO. OR MILD FIBROSIS
Indicates no or minimal liver fibrosis and no evidence of progressive liver disease

**F2**
MODERATE FIBROSIS
Indicates significant liver fibrosis and evidence of progressive liver disease

**F3**
SEVERE FIBROSIS
Indicates severe liver fibrosis and high risk progression to cirrhosis

**F4**
CIRRHOSIS
Indicates extensive liver fibrosis consistent with cirrhosis
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  • Hepatitis B
  • HIV
  • Renal function
• Imaging Review
• Anticipatory Guidance
Initiating Treatment

• Anticipatory Guidance
  • Household contact
  • Sex
  • Reduce or preferably eliminate alcohol – especially in the case of advanced fibrosis
  • No more than 2 grams per day of acetaminophen
  • Exercise
  • Blood sugar control
  • Fruits and vegetables
  • Avoid vitamin A and iron supplementation
  • Flu (for everyone) and pneumococcal vaccines (esp for those with advanced fibrosis)
  • Coffee 😊
### Table 2. Association of Baseline Coffee Intake with Liver Disease Progression in 766 Participants of the HALT-C Trial

<table>
<thead>
<tr>
<th></th>
<th>RR per Cup/Day</th>
<th>Nondrinkers</th>
<th>&gt;0 to &lt;1 Caps/Day</th>
<th>≥1 to &lt;3 Caps/Day</th>
<th>≥3 Caps/Day</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort, person-years (%)</td>
<td>404 (16.8)</td>
<td>678 (28.2)</td>
<td>1039 (43.2)</td>
<td>286 (11.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, no. (%)</td>
<td>45 (19.6)</td>
<td>82 (35.7)</td>
<td>85 (37.0)</td>
<td>18 (7.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude RR (95% CI)</td>
<td>0.88 (0.79–0.98)</td>
<td>1.00 (ref)</td>
<td>1.09 (0.76–1.57)</td>
<td>0.73 (0.51–1.05)</td>
<td>0.56 (0.33–0.97)</td>
<td>0.0013</td>
</tr>
<tr>
<td>Multivariate adjusted RR*</td>
<td>0.85 (0.76–0.96)</td>
<td>1.00 (ref)</td>
<td>1.11 (0.76–1.61)</td>
<td>0.70 (0.48–1.02)</td>
<td>0.47 (0.27–0.85)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Multivariate RR additionally adjusted for general health score†</td>
<td>0.85 (0.76–0.96)</td>
<td>1.00 (ref)</td>
<td>1.12 (0.77–1.63)</td>
<td>0.70 (0.48–1.02)</td>
<td>0.47 (0.27–0.84)</td>
<td>0.0003</td>
</tr>
<tr>
<td>RR additionally adjusted for markers of liver function‡</td>
<td>0.91 (0.81–1.02)</td>
<td>1.00 (ref)</td>
<td>1.15 (0.78–1.70)</td>
<td>0.87 (0.58–1.29)</td>
<td>0.66 (0.36–1.19)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

CI, confidence interval; no., number; RR, relative risk.

*Adjusted for age, body mass index, education, ethnicity, sex, baseline Ishak fibrosis score, total energy intake, lifetime alcohol intake, pack-years of cigarette use, and tea intake.

†Adjusted for age, body mass index, education, ethnicity, sex, baseline Ishak fibrosis score, total energy intake, lifetime alcohol intake, pack-years of cigarette use, tea intake, and SF-36 general health score.

‡Adjusted for age, body mass index, education, ethnicity, sex, baseline Ishak fibrosis score, total energy intake, lifetime alcohol intake, pack-years of cigarette use, tea intake, SF-36 general health score, albumin, AST/ALT ratio, bilirubin, esophageal varices, hepatic steatosis grade, and platelets.
Fig. 1. Proposed mechanism for the antifibrotic effect of caffeine in CLD. Caffeine is a known antagonist of the $A_{2a}$ adenosinergic receptor expressed on activated HSCs and other liver myofibroblasts. Stimulation of $A_{2a}$AR has several downstream profibrogenic effects, including rearrangement of stress fibers, chemotaxis in response to PDGF and other stimuli, and secretion of fibrillar collagen, all of which may be inhibited by caffeine.
26yo woman referred for evaluation of positive HCV antibody – Ms. C

• Ms. C’s records show the following:
  • HBV Surface antibody negative
  • HBV Core antibody negative
  • HBV surface antigen negative
  • Hepatitis A IGG total antibody positive
  • HIV negative
  • Pregnancy test negative
  • Normal renal function
  • ALT 3x normal
26yo woman referred for evaluation of positive HCV antibody – Ms. C

• The best next recommendations should include:
  A. HBV vaccination; HAV vaccination; appointment to have etonogestrel implant for birth control; counseling for prevention of reinfection.
  B. HBV vaccination; appointment for birth control pill containing ethinyl estradiol; discontinuation of aripiprazole; counseling for prevention of reinfection.
  C. HBV vaccination; discussion of monitoring of side effects of aripiprazole; appointment for etonogestrel implant for birth control; counseling for prevention of reinfection.
  D. Counseling about prevention of reinfection; abstinence counseling; discontinuation of aripiprazole.
26yo woman referred for evaluation of positive HCV antibody – Ms. C

• The best next recommendations should include:
  A. HBV vaccination; HAV vaccination; appointment to have etonogestrel implant for birth control; counseling for prevention of reinfection; recommendation for testing her children.
  B. HBV vaccination; appointment for birth control pill containing ethinyl estradiol; discontinuation of aripiprazole; counseling for prevention of reinfection; recommendation for testing her children.
  C. HBV vaccination; discussion of monitoring of side effects of aripiprazole; appointment for etonogestrel implant for birth control; counseling for prevention of reinfection; recommendation for testing her children.
  D. Counseling about prevention of reinfection; abstinence counseling; discontinuation of aripiprazole; recommendation for testing her children.
26yo woman referred for evaluation of positive HCV antibody – Ms. C

• Stay tuned for:
  • Medication choice and access!
  • Follow up post treatment

• QUESTIONS?