NEW YORK STATE
HCV PROVIDER CLASSIFICATION TRAINING
Hepatitis C Pre-Treatment Assessment: The Role of the Primary and HCV Provider

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Objectives

• Review hepatitis C (HCV) basics:
  – Prevalence and incidence.
  – Natural history of HCV infection.

• Discuss responsibilities of the primary provider.
  – Screening for HCV infection.

• Discuss responsibilities of the HCV provider.
A 60 year old woman is referred to you to address:

- Complaints of mild fatigue.
- New findings of HCV Ab and HCV RNA positivity.

**HPI:**

- In excellent health except for mild hypercholesterolemia and mild GERD.
- Complaining of mild fatigue for “a few years”.
- Seen by her primary care provider; underwent HCV testing because of her “Baby Boomer” status.

**ALLERGIES:** none.

**M ED S:**

- Atorvastatin 20 mg qD
- Omeprazole 20 mg qD
Case Study

ROS / PMH:
• Mild fatigue.
• Mild GERD.
• Mild nonspecific pain in legs.

Surgery: none.

Social History:
• Divorced, has two adult children.
• Lives by herself, but is currently “dating”.
• Occupation: dental hygienist.
• Cigarettes: none.
• Drugs: evasive answer, but states “I was a little wild in college”.
• Alcohol: two glasses of wine per night.
Case Study

Physical Exam:
• Normal vital signs.
• Normal lung, heart, abdomen, extremities, neuro exams.

LABS:
• CBC/plt: normal.
• CMP: AST 45 U/L, ALT 50 U/L, otherwise normal.
• HCV studies:
  o HCV Ab positive.
  o HCV RNA positive at 5 million IU/mL

What do you do?
Introduction to HCV

- 200-250 million infections worldwide
- Estimated 5-7 million people with HCV in the USA
- A leading indication for liver transplantation
- A leading predisposing factor to development of hepatocellular carcinoma
Baby Boomers (Born in 1945–1965) Account for 76.5% of HCV in the US

An estimated 33% of undiagnosed baby boomers with HCV currently have advanced fibrosis (F3-F4; bridging fibrosis to cirrhosis)

It’s Not Total HCV in New York (Excluding NYC): Just Baby Boomers

2005

2015

2012

2016

Slide courtesy of NYS DOH Bureau of Viral Hepatitis.
Rising Incidence of HCV in Youth

MMWR May 2015 surveillance data of 2006-2012:

• **364% increase** in acute HCV in persons < 25 y/o from 4 Appalachian states (KY, TN, WV, VA)

• Primarily non-Hispanic White individuals from non-urban communities

• Associated with increased injection of prescription opioid analgesics

• Similar findings were reported in analogous populations in *upstate NY*

Zibbel et al. MMWR May 2015

Reported cases/100,000 population

Source: National Notifiable Diseases Surveillance System (NNDSS)
Transmission of HCV

- Sharing supplies for injection or intranasal drug use
- Transfusion of blood/blood products prior to 1992
- Needle stick injury in health care
- Sharing personal care items (straight razors)
- Being born to a mother who has HCV
- Tattoos, body piercing in unlicensed setting
- Sex with an infected person (blood exposure)
Acute Infection*  
Chronic Infection 75%-85%  
Cirrhosis 10%-20% over 20 years  
Decompensated Cirrhosis 5-yr survival rate 50%  
HCC 1%-4% per year  
Asymptomatic Extrahepatic manifestations  
Most Americans infected >35y  
Additional impact of:  
- Alcohol  
- Obesity  
- Older age  
*Most have minimal symptoms
HCV Treatment: What Should Physicians & Patients Expect?

- Improved symptoms: Likely
- Improved liver chemistries: Yes
- Sustained virological response (i.e. cure): ~ 95-99% likelihood
- Reversal of fibrosis: Maybe
- Stabilize compensated cirrhosis: Hopefully
- Reverse decompensated cirrhosis: Probably not
HCV: Provider Responsibilities

**HCV PROVIDER**
- Take an excellent history
- Perform an excellent physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV
- Assess severity of disease (non-cirrhotic vs. cirrhotic)
- Assess genotype
- Assess patient’s potential for treatment compliance
- Prescribe and monitor treatment

**PRIMARY PROVIDER**
- Screen patients at risk
- If HCV Ab positive, confirm with RNA testing
- Linkage to care
Primary Provider Responsibilities
Screen Patients at Risk

PRIMARY PROVIDER

✓ Screen patients at risk
✓ If HCV Ab positive, confirm with RNA testing
✓ Linkage to care

Patients at risk are:
• Age cohort 1945-1965
• Risk factors
• Pregnant women
Primary Provider Responsibilities

Confirm HCV Infection

**PRIME CARE PROVIDER**

- Screen patients at risk
- If HCV Ab positive, confirm with RNA testing
- Linkage to care

“Dear Colleague” letter from New York State Department of Health recommends reflex testing and provides resources for implementation.
Primary Provider Responsibilities

Link to HCV Care

PRIMARY CARE PROVIDER

✓ Screen patients at risk

✓ If HCV Ab positive, confirm with RNA testing

✓ Linkage to care
HCV PROVIDER

- Take a history
- Perform a physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV if not immune
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HCV PROVIDER

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✓ Assess patient’s potential for treatment compliance
✓ Prescribe and monitor treatment
HCV Provider Responsibilities

Take a History

Review prescription medications and over-the-counter supplements

- Amiodarone
  - Sofosbuvir $\rightarrow$ bradycardia
- Anti-acid agents
  - Ledipasvir, Velpatasvir $\rightarrow$ absorption
- Statins
- Anti-HIV medications
- Anti-epileptic medications
  - P-gp inducer $\rightarrow$ lower drug levels
- St. John’s wort
  - P-gp inducer $\rightarrow$ lower drug levels
- Rifampin
  - P-gp inducer $\rightarrow$ lower drug levels
- Ethinyl estradiol
- Cyclosporine, tacrolimus

This list is not all-inclusive. Refer to the package insert and online resources:
- www.hep-druginteractions.org
- www.hcvguidelines.org
Extrahepatic Manifestations of HCV Infection

- Neuropsychiatric manifestations
- Thyroid dysfunction
- Mixed cryoglobulinemia
- Type II diabetes
- Hematological disorders/malignancies
- Cardiovascular/metabolic diseases
- Renal impairment
- Peripheral neuropathy

HCV Provider Responsibilities

Take a History

- Take a history
- Perform a physical exam
- **Explain the natural history of disease**
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV if not immune
- Assess severity of disease (non-cirrhotic vs. cirrhotic)
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**Natural History of Hepatitis C**

- **Acute Hepatitis** > 30,500 / year
- **Chronic Hepatitis** 85%
- **Cirrhosis** ~ 20%
- **Liver Failure** 15%
- **HCC** 1-5%

Is a patient with cirrhosis destined to die from liver disease? **NO!**

Survival of patients with HCV cirrhosis 10 years after diagnosis (without liver transplant) is about 70%.
HCV Provider Responsibilities

Counsel to Prevent Transmission

HCV PROVIDER
✓ Take a history
✓ Perform a physical exam
✓ Explain the natural history of disease
✓ **Counsel to prevent transmission**
✓ Obtain basic blood tests
✓ Rule out coexisting liver disease
✓ Vaccinate to prevent HAV and HBV if not immune
✓ Assess severity of disease (non-cirrhotic vs. cirrhotic)
✓ Assess genotype
✓ Assess patient’s potential for treatment compliance
✓ Prescribe and monitor treatment
HCV Provider Responsibilities

Counsel to Prevent Transmission

**Sex**
- Transmission in about 5% of monogamous couples
- Risk factors for sexual transmission
  - Coinfection with HIV
  - Unprotected anal intercourse
  - Coincident ulcerative STDs (e.g. syphilis)
  - Practices that predispose to bleeding

**Household**
- Risk factors:
  - Sharing razors, toothbrushes, nail clippers
  - Contact with blood
- Clean up blood spills with bleach
- Non-risk factors:
  - Sharing utensils, plates, glassware
  - Casual contact: touching, hugging, kissing, sneezing, coughing

**Drugs**
- Risk factors:
  - Sharing drug paraphernalia
  - Both for IVDU and snorting
- Use clean needles

**Maternal**
- 5% transmission rate in from monoinfected mothers to infants
- Breast feeding is safe
HCV Provider Responsibilities

Obtain Basic Blood Tests

**HCV PROVIDER**

- Take a history
- Perform a physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- **Obtain basic blood tests**
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV if not immune
- Assess severity of disease (non-cirrhotic vs. cirrhotic)
- Assess genotype
- Assess patient’s potential for treatment compliance
- Prescribe and monitor treatment
HCV Provider Responsibilities

Obtain Basic Blood Tests

- CBC, platelets
- Comprehensive metabolic profile
  - Renal function
  - Liver chemistries
    - Albumin
    - Total bilirubin
    - Alkaline phosphatase
    - Aspartate aminotransferase
    - Alanine aminotransferase
- INR
- Viral studies
  - HIV Ab
  - HAV Ab (total, not IgM!)
  - HBcAb (total, not IgM!)
  - HBsAg
  - HBsAb (quantitative)
- HCV studies
  - HCV RNA (quantitative)
  - HCV genotype
  - NS5A resistance (for G 1a patients who are likely to be treated with elbasvir/grazoprevir)
HCV Provider Responsibilities

Rule Out Coexisting Liver Disease

HCV PROVIDER
✓ Take a history
✓ Perform a physical exam
✓ Explain the natural history of disease
✓ Counsel to prevent transmission
✓ Obtain basic blood tests
✓ Rule out coexisting liver disease
✓ Vaccinate to prevent HAV and HBV if not immune
✓ Assess severity of disease (non-cirrhotic vs. cirrhotic)
✓ Assess genotype
✓ Assess patient’s potential for treatment compliance
✓ Prescribe and monitor treatment
HCV Provider Responsibilities

Rule Out Coexisting Liver Disease

**History**
- Heart disease
- Diabetes, obesity → NAFLD
- Alcohol abuse → alcoholic liver disease
- Family history of autoimmunity
  - Autoimmune hepatitis
  - Primary biliary cholangitis
  - Primary sclerosing cholangitis
- Family history of liver disease
  - Hereditary hemochromatosis
  - Alpha-1 antitrypsin deficiency

**Labs**
- Antinuclear antibody (ANA)
- Antismooth muscle antibody (ASMA)
- Anti mitochondrial Ab (AMA)
- Fe / TIBC / Ferritin
- [Ceruloplasmin]
- [Alpha-1 antitrypsin level & phenotype]
- Alpha fetoprotein

**Scans**
- Ultrasound
HCV PROVIDER

- Take a history
- Perform a physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- **Vaccinate to prevent HAV and HBV if not immune**
- Assess severity of disease (non-cirrhotic vs. cirrhotic)
- Assess genotype
- Assess patient’s potential for treatment compliance
- Prescribe and monitor treatment

HCV Provider Responsibilities

Vaccinate to Prevent HAV and HBV
HCV Provider Responsibilities

Assess Severity of Disease

HCV PROVIDER

- Take a history
- Perform a physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV if not immune
- **Assess severity of disease**
  (non-cirrhotic vs. cirrhotic)
- Assess genotype
- Assess patient’s potential for treatment compliance
- Prescribe and monitor treatment
Progression of Liver Disease

Normal

Chronic hepatitis

Cirrhosis
Liver cancer is curable if caught early.
- Resection cases: cure rate is about 50%.
- Transplant cases: cure rate is about 80%.

Screening patients with cirrhosis is cost effective.
- Costs < $50,000 per quality adjusted life year saved.

AASLD recommends:
- HCC surveillance should be performed in cirrhotic patients with ultrasound.
- Patients should be screened at 6 month intervals.
- Most N.Y. hepatologists recommend HCC surveillance for HCV patients with stage 3 fibrosis.

Liver Cancer 101

• If there is a suspected nodule on ultrasound → refer for MRI.
• Most HCC diagnoses are made radiologically.

HCV Provider Responsibilities

Assess Genotype

**HCV PROVIDER**

- Take a history
- Perform a physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV if not immune
- Assess severity of disease (non-cirrhotic vs. cirrhotic)

**Assess genotype**

- Assess patient’s potential for treatment compliance
- Prescribe and monitor treatment
HCV Provider Responsibilities

Assess Patient’s Potential for Treatment Compliance

- Take a history
- Perform a physical exam
- Explain the natural history of disease
- Counsel to prevent transmission
- Obtain basic blood tests
- Rule out coexisting liver disease
- Vaccinate to prevent HAV and HBV if not immune
- Assess severity of disease (non-cirrhotic vs. cirrhotic)
- Assess genotype
- **Assess patient’s potential for treatment compliance**
- Prescribe and monitor treatment

We cannot afford noncompliance:
- Expense of medications
- Risk of inducing drug-resistance mutations
HCV Provider Responsibilities

Assess Patient’s Potential for Treatment Compliance

HCV PROVIDER

✓ Take a history
✓ Perform a physical exam
✓ Explain the natural history of disease
✓ Counsel to prevent transmission
✓ Obtain basic blood tests
✓ Rule out coexisting liver disease
✓ Vaccinate to prevent HAV and HBV if not immune
✓ Assess severity of disease (non-cirrhotic vs. cirrhotic)
✓ Assess genotype
✓ Assess patient’s potential for treatment compliance
✓ **Prescribe and monitor treatment**
Case Study: Office Visit #1

A 60 year old woman is referred to you to address:

• Complaints of mild fatigue.
• New findings of HCV Ab and HCV RNA positivity.

HPI:

• In excellent health except for mild hypercholesterolemia and mild GERD.
• Complaining of mild fatigue for “a few years”.
• Seen by her primary care provider; underwent HCV testing because of her “Baby Boomer” status.

ALLERGIES: none.

MEDS:

• Atorvastatin 20 mg qD
• Omeprazole 20 mg qD
Case Study: Office Visit #1

ROS / PMH:
• Mild fatigue.
• Mild GERD.
• Mild nonspecific pain in legs.

SURGERY: none.

Social History:
• Divorced, has two adult children.
• Lives by herself, but is currently “dating”.
• Occupation: dental hygienist
• Cigarettes: none.
• Drugs: evasive answer, but states “I was a little wild in college”
• Alcohol: two glasses of wine per night
Case Study: Office Visit #1

Physical Exam:
• Normal vital signs.
• Normal lung, heart, abdomen, extremities, neuro exams.

LABS:
• CBC/plt: normal.
• CMP: AST 45 U/L, ALT 50 U/L, otherwise normal.
• HCV studies:
  o HCV Ab positive.
  o HCV RNA positive at 5 million IU/mL

What do you do?
• Order labs.
• Order ultrasound.
• Arrange for follow-up.
• Order medications?
Case Study: Office Visit #2
Assess basic labs

- CBC, platelets
  - Normal WBC, Hgb, Hct
  - Platelets = 150,000

- Comprehensive metabolic profile
  - Renal function
  - Normal kidney function
  - Liver chemistries
    - Albumin: 4.0 g/dL
    - Total bilirubin: 0.6 mg/dL
    - Alkaline phosphatase: 100 U/L
    - Aspartate aminotransferase: 45 U/L
    - Alanine aminotransferase: 50 U/L

- INR: 1.1
Case Study: Office Visit #2
Assess viral studies

• Viral studies
  o HIV Ab negative
  o HAV Ab (total, not IgM!) negative, not immune to HAV
  o HBcAb (total, not IgM!) positive
  o HBsAg negative
  o HBsAb (quantitative) negative

Exposed to HBV in the past. Need to test for HBV DNA.

• HCV studies
  o HCV RNA (quantitative) 5 million IU/mL
  o HCV genotype GT 1a
  o NS5A resistance (for GT 1a patients who are likely to be treated with elbasvir/grazoprevir) ---
Case Study: Office Visit #2
Assess specialized tests

Other Labs

- Antinuclear antibody (ANA)  negative
- Antismooth muscle antibody (ASMA)  negative
- Anti mitochondrial Ab (AMA)  negative
- Fe / TIBC / Ferritin  normal
- Alpha fetoprotein  2.6 ng/mL
Case Study: Office Visit #2
Assess severity of fibrosis

Fibrosis score = 0.74, consistent with F3-F4 fibrosis.

Ultrasound

- Heterogeneous liver architecture.
- No liver mass.
- Spleen size = 12 cm.

Fibroelastography

- Liver stiffness = 15.0 kPa, consistent with F3-4 fibrosis.

**HCV Fibrosure®** (alpha-2-macroglobulin, haptoglobin, apolipoprotein A1, GGTP, T.bili, ALT).

- Fibrosis score = 0.74, consistent with F3-F4 fibrosis.

**Fib4 score**

- Fib4 score < 1.45 c/w F0-F1.
- Fib4 score > 3.25 c/w F3-F4
- Our patient’s score = 2.55: “intermediate risk of advanced fibrosis”
Case Study: Office Visit #2
Order medications

• Review www.hcvguidelines.org
  ▪ Consider…
    ▪ Genotype
    ▪ Disease severity
    ▪ Drug-drug interactions

• Choose a medication
  ▪ What will insurance support?

• Order the medication

• Arrange for monitoring and follow-up
Summary

- Responsibilities of the HCV provider:
  - Perform a history and physical examination.
  - Counsel the patient.
  - Basic and specialized blood tests.
  - Vaccinate against HAV and HBV as needed.
  - Assess severity of liver disease.
  - Assess genotype.
  - Prescribe and monitor treatment.