HEPATITIS C CLINICAL TRAINING

Hepatitis C: Epidemiology, Natural History and Diagnosis

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Training Development and Funding

- This training is designed in collaboration with the NYC Department of Health and Mental Hygiene (DOHMH)

- This training is funded by the NYC City Council

Housekeeping Notes

Have a question for the presenter

- Type the question into the chat box and Meg will read them aloud to the presenter at the end

Claiming CE

- After the training, you will receive an e-mail with instructions, the course number, and the access code
- CE certificate can be printed or stored in your account
- Questions about CEs, contact Joycambe@empireliverfoundation.org

For Additional Information

- Visit https://empireliverfoundation.org/about-us/cme-accreditation/

Disclosures

Consultant- Gilead, Abbvie, Merck, BMS

Speaker's Bureau- Gilead, Abbvie, Merck, BMS

Learning Objectives

By the end of this presentation, participants will be able to:

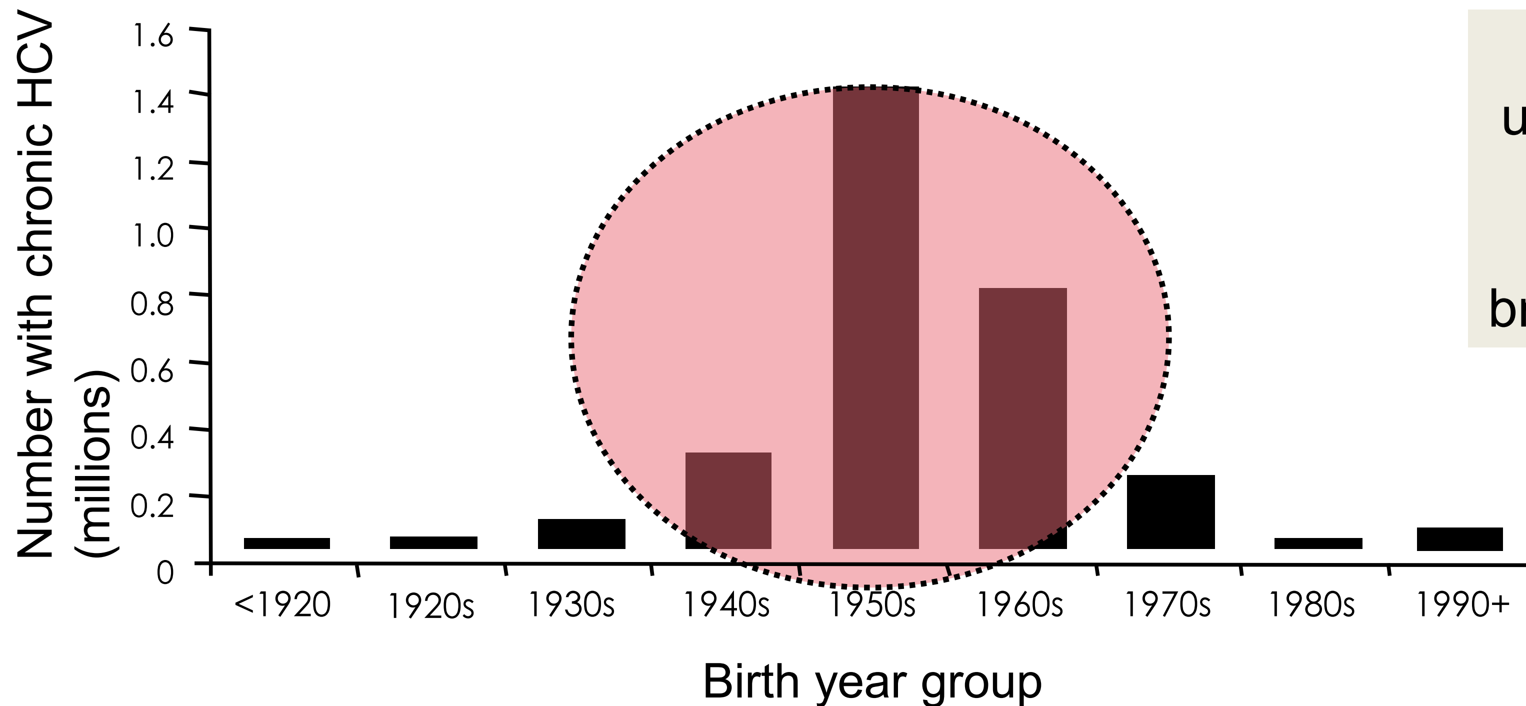
- Recall the epidemiology and natural history of hepatitis C (HCV)
- Identify and interpret diagnostic tests for HCV
- Explain pre-therapy assessment of HCV patients, including assessment of liver fibrosis
- Describe the impact of HCV treatment on patient outcomes

Epidemiology

Hepatitis C

- 200-250 million infections worldwide
- Estimated ~3 million people with HCV in the US
- 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)[3]

1. Centers for Disease Control and Prevention. *MMWR*. 2012;61:1-32; Adapted from Pyenson B, et al. *Consequences of Hepatitis C Virus (HCV): Costs of a baby boomer Epidemic of Liver Disease*. New York, NY: Milliman, Inc; May 18, 2009. http://www.milliman.com/expertise/healthcare/publications/rr/consequences-hepatitis-c-virus-RR05-15-09.php Milliman report was commissioned by Vertex Pharmaceuticals;
3. McGarry LJ et al. *Hepatology*. 2012;55(5):1344-1355.

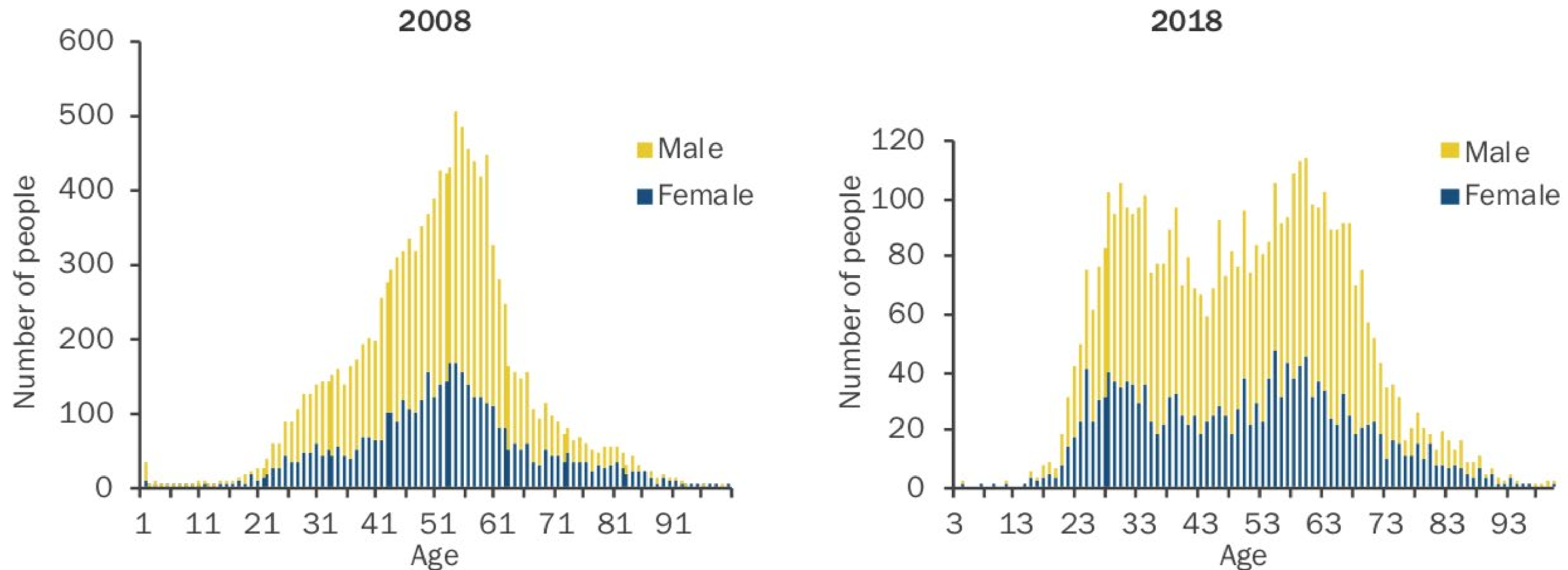
Rising Incidence of HCV in Youth

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 **upstate NY** populations

Zibbel et al. MMWR May 2015
Zibbel et al. Am J Pub Health. 2014

Newly Reported Chronic HCV Age Distribution in New York City, 2012-2018

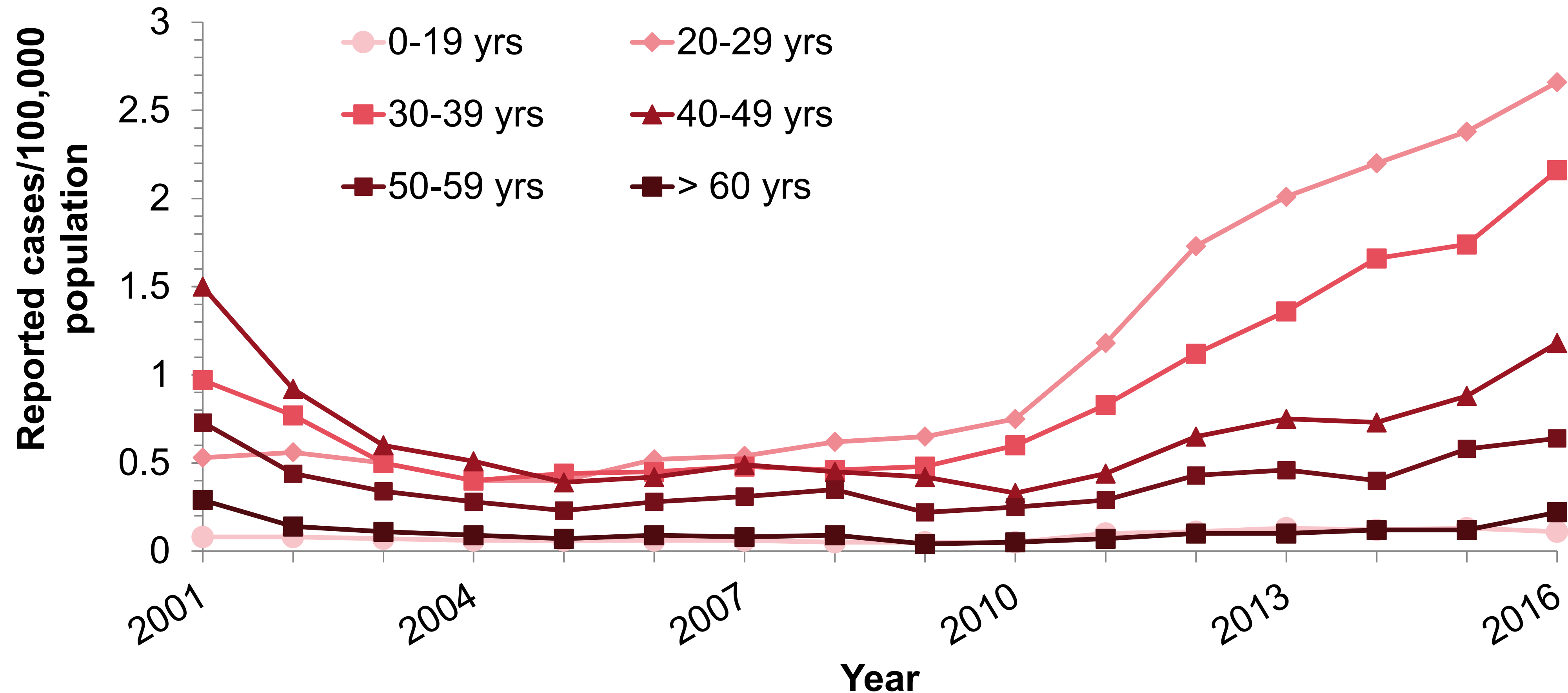


Increase in youth attributed to:

- Transition from oral prescription medication to intranasal then to injection of heroin which is cheaper and easier to acquire
- In NYC, higher percentage of female, residents of Staten Island and whites compared with older HCV-infected persons

www1.nyc.gov. Accessed March 28, 2020

Incidence of Acute HCV, by Age Group – United States, 2001-2016



Source: CDC, National Notifiable Diseases Surveillance System.

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 settings
- Sharing personal care items (i.e. straight razors)
- Being born to a mother who has HCV
- Tattoos, body piercing in unlicensed setting (e.g. jails)
- Sex with an infected person, especially among MSM, and in particular, MSM who are HIV+

Case Study 1

- 65 year old man
- Feels well
- History of injection drug use once as a teenager; currently drinks alcohol, mostly on weekends
- Noted to have ALT 42 on routine PE
- Further testing show HCVRNA 850,000
- Genotype 1a
- Fibroscan F3, S2 disease

Think about what you would do next. We will review at end of presentation.

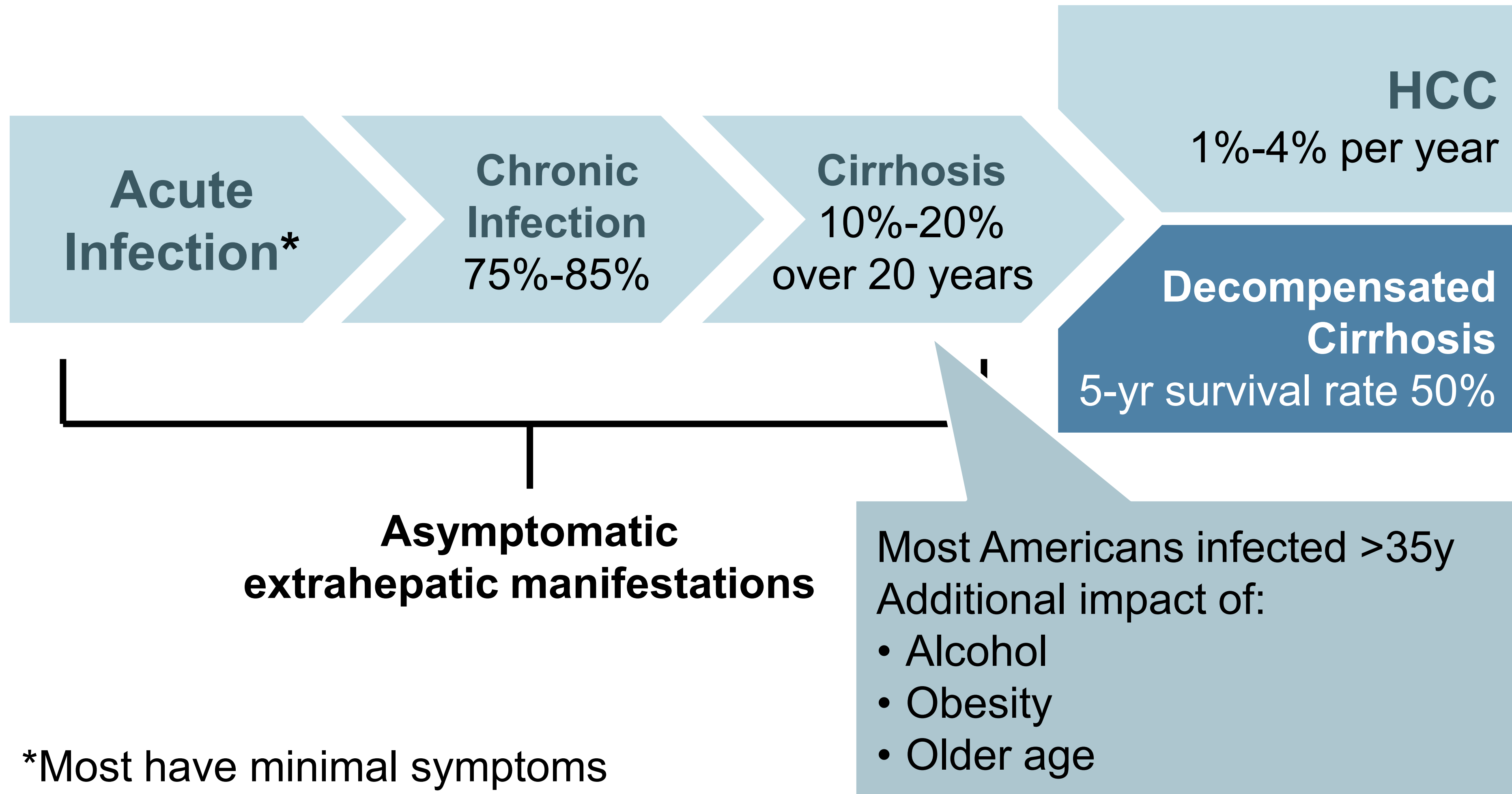
Case Study 2

- 28 year old woman
- Feels well
- Active intravenous drug user
- Noted to have ALT 87 on routine PE
- HCVRNA 550,000
- Genotype 1a
- Fibroscan F1, S0 disease

Think about what you would do next. We will review at end of presentation.

Natural History of
Hepatitis C

Natural History of HCV



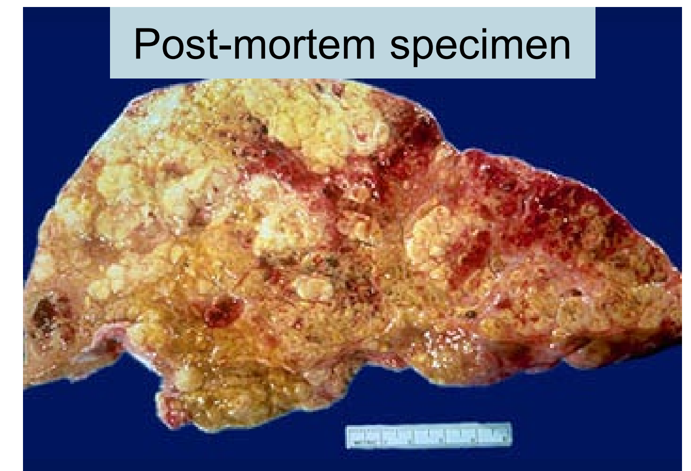
Liver Cancer 101

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 QALY saved

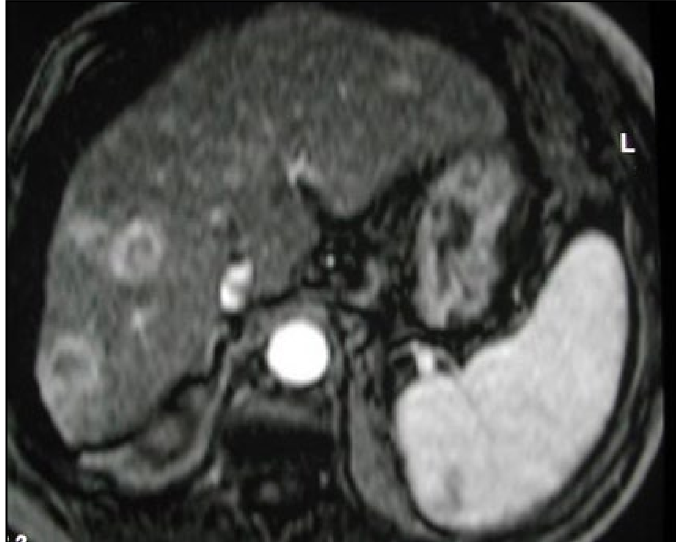
AASLD recommends:
- HCC surveillance should be performed in **cirrhotic patients with ultrasound with AFP**
- Patients should be screened at **6 month intervals**
- Most hepatologists recommend HCC surveillance for HCV patients with stage 3 fibrosis

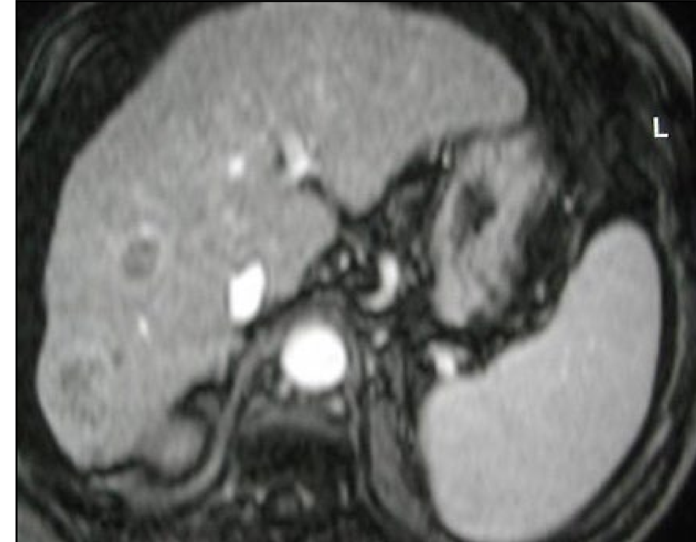
Resection specimen


Post-mortem specimen

Wolf DC. Screening for hepatocellular carcinoma: Is it cost-effective? Liver Transplant 2003;9:682; Marrero JA et al. Diagnosis, staging and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. Hepatology 2018;68:723

Liver Cancer 101

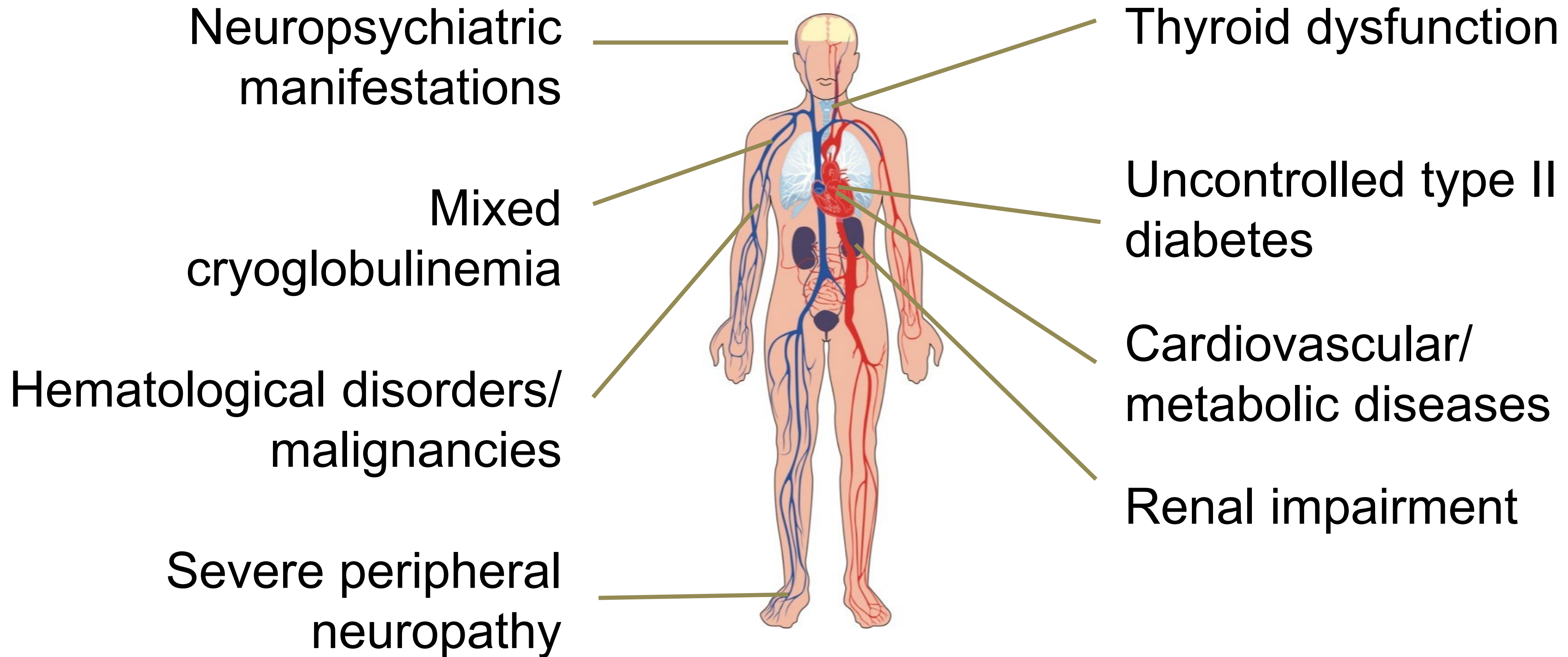




- If there is a suspected nodule on ultrasound → refer for MRI
- Most HCC diagnoses are made radiologically

Bruix J, Sherman M. Management of hepatocellular carcinoma. AASLD Practice Guideline. *Hepatology.* July 2010;
Wolf DC. *Liver Transpl.* 2003;9:682.

Extrahepatic Manifestations of HCV Infection



Cacoub P, *et al. Dig Liver Dis* 2014; **46**(Suppl 5)**:**S165–S173; Negro F, *et al. Gastroenterology* 2015; **149:**1345–1360; Englert Y, *et al. Fertil Steril* 2007; **88:**607–11; Samuel DG & Rees IW. *Frontline Gastroenterol* 2013; **4:**249–254.

Pre-Therapy
Assessment

Acute HCV: Interpretation of Tests

Test	Interpretation
HCV Ab	• Test may be negative during first 6 weeks after exposure • Seroconversion may be delayed or absent in immunosuppressed individuals • Presence of HCV Ab alone does not distinguish between acute and chronic infection
HCV RNA	• Viral fluctuations > 1 $\log_{10}$ IU/ml may indicate acute HCV infection • HCV RNA may be transiently negative during acute HCV infection • Presence of HCV RNA alone does not distinguish between acute and chronic infection
ALT	• Fluctuating ALT peaks suggests acute infection • ALT may be normal during acute HCV infection • ALT may be elevated due to other liver insults, such as ETOH use

www.hcvguidelines.org Accessed August 10, 2018

Diagnosis of Hepatitis C

- Hepatitis C antibody with reflex to HCV-RNA

Primary Care Provider Responsibilities Diagnosing and Confirming HCV

Screen all adults 18-79 years, including pregnant women	In March 2020, USPSTF expanded its recommendation for one-time HCV screening to include all asymptomatic adults ages 18-79 years, including pregnant women: https://jamanetwork.com/journals/jama/fullarticle/2762186
Use HCV antibody with reflex to RNA testing	Since 2017, NYC Health Code requires labs to automatically perform HCV RNA confirmatory test on all positive antibody test for HCV
	Since 2015, NYS Department of Health recommends reflex testing and provides resources for implementation: https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_c/providers/reflex_testing.htm

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**

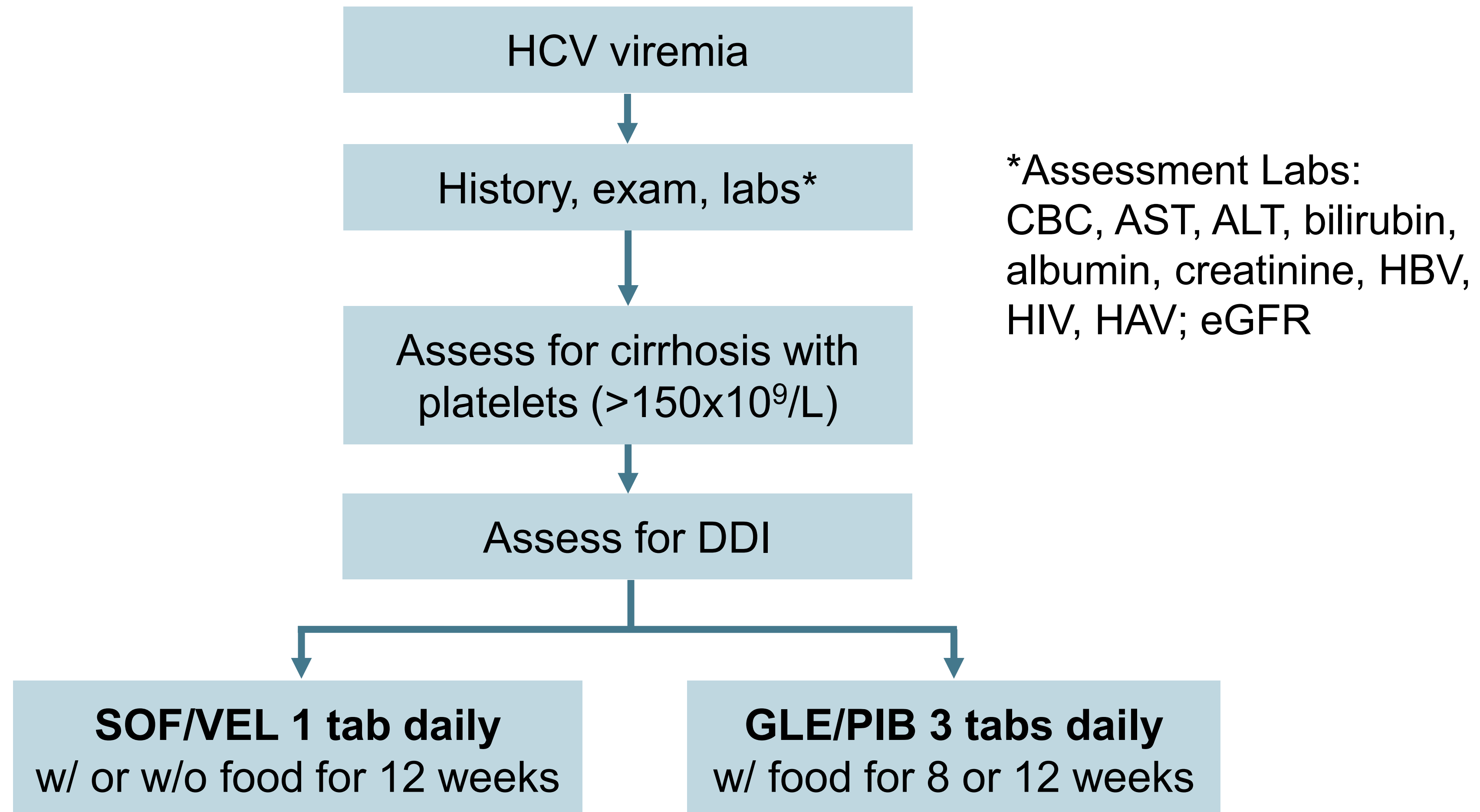
- **Viral studies**
  - HIV Ab
  - HAV Ab (total, not IgM!)
  - HBcAb (total, not IgM!)
  - HBsAg
  - HBsAb (quantitative)

Reactivation of Hepatitis B

- Patients with prior, resolved, or active HBV infection are at <u>risk of reactivation</u> on DAA therapy
- FDA issued black box warning in 2016
  - 29 reactivations reported since 2013
  - 2 died, 1 required liver transplant

http://www.fda.gov/downloads/Drugs/DrugSafety/UCM523499.pdf

How Simple Can Treatment Be For Most Patients?



Dieterich *et al*, Gastroenterology & Hepatology; volume 15, issue 5, supplement 3, May 2019

Counsel to Prevent Transmission

Risk	More Information	Prevention Messages
Sharing drug use equipment	• Transmission rate can exceed 40% • Both injection drug use and snorting	• Use new equipment (needles, cookers, cutters) for drug use
Sex	Transmission in about 5% of monogamous couples. Risk factors: • Coinfection with HIV • Unprotected anal intercourse • Coincident ulcerative STDs (e.g. syphilis) • Practices that predispose to bleeding	• Get partner tested and cured if needed, until then, practice safe sex (use condoms every time)
Household	Risk factors: • Sharing razors, toothbrushes, nail clippers • Contact with blood	• Clean up blood spills with bleach • Avoid sharing personal care items (such as razors, toothbrushes, nail clippers)
Perinatal	5% transmission rate from HCV+ mothers to infants	• Screen and treat (if needed) all women of childbearing age prior to pregnancy

Pre-Therapy Assessment

- Basic labs should include:
  - Genotype at least once in the past
  - Viral load relatively recent
    - Most insurances require within 3 months
  - Assessment of liver function
  - Assessment of renal function (creatinine, GFR)
- Assessment of liver fibrosis
- Drug/alcohol screening only if required by payers

Pre-Therapy Assessment: **Drug-Drug Interactions (DDIs)**

- **Very important** element in pre-therapy assessment
- List of prohibited drugs is relatively short
- Be alert for interactions with common drugs
  - Statins, acid reducing agents, birth control preparations, amiodarone, rifampin
- No herbs!
  - In particular, no St. John’s Wort
- Use online tools to help assess DDI’s
  - ***https://www.hep-druginteractions.org/checker***

Remember: Patients rarely tell you all the pills they are taking!

Importance of Assessing Fibrosis

- Patients with bridging fibrosis or cirrhosis need additional screening
  - Varices
  - Hepatocellular carcinoma
- Allows for selection of proper treatment plan and duration of therapy
- Determines post-treatment follow-up

Methods for Staging Fibrosis

Method	Procedure	Advantages	Disadvantages
Indirect serum markers	APRI, FIB-4	Noninvasive; inexpensive	Limited ability to differentiate intermediate stages of fibrosis
Direct markers	FibroSure, FibroTest, FibroMeter, FIBROSpect II, and HepaScore	Noninvasive; easily accessible	Limited ability to differentiate intermediate stages of fibrosis
VCTE	Shear wave velocity	Noninvasive; assesses large volume of liver parenchyma	May be difficult to interpret in F2 and F3 liver disease; limited availability
MRI elastography	MRI with elastography	Non-invasive, evaluates entire liver	Not FDA approved in US, expensive
Liver biopsy	Pathologic examination	Diagnostic standard; diagnoses concurrent liver disease	Invasive procedure; costly; sampling error

Non-invasive Formulae to Assess Fibrosis

AST Level *(IU/L)*

AST (Upper Limit of Normal) *(IU/L)*

APRI = ——— **x 100 =**

Platelet Count *(10^9/L)*

Age *(years)* **x** **AST Level *(U/L)***

FIB-4 = ——— **=**

Platelet Count *(10^9/L)* **x** √ **ALT *(U/L)***

Impact of Treatment on Natural History of Hepatitis C

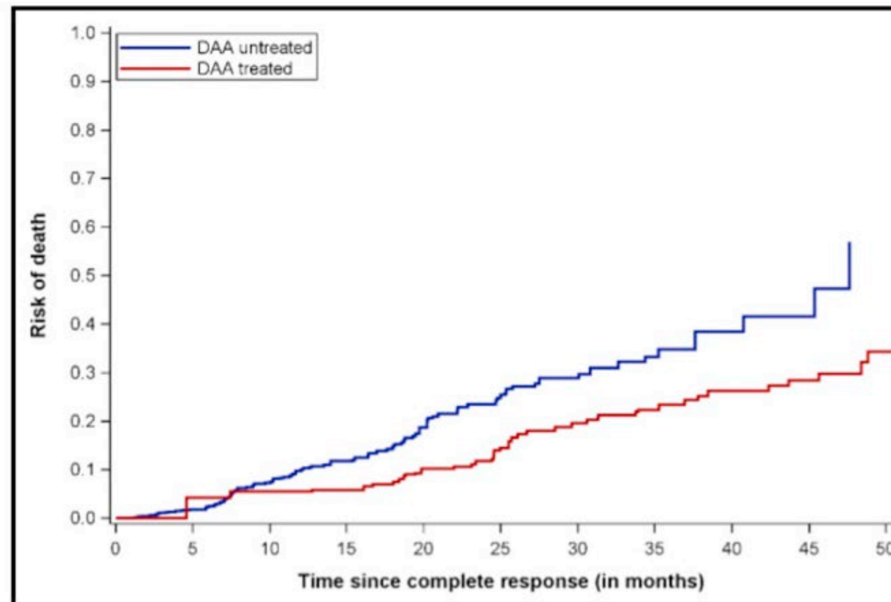
DAA Therapy Associated With Improved Survival in HCC Patients

Methods: Retrospective cohort study of 797 patients with HCV-related HCC from 31 health systems in U.S./Canada

Results:

DAA Treated:
4.6 deaths per 100 person-years follow-up

DAA Untreated:
19.6 deaths per 100 person-years follow-up



Multivariable analysis
- Adjusted for site, age, sex Child Pugh score, AFP, tumor burden and HCC treatment modality

→ **DAA therapy associated with lower mortality: HR: 0.54; 95%CI: 0.33 – 0.90**

Singal AG, al., Gastroenterology. 2019

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- What do you do next?

Case Study 1

- Start anti-viral therapy
- Screen for hepatocellular carcinoma

Case Study 2

- 28 year old woman
- Feels well
- Active intravenous drug user
- Noted to have ALT 87 on routine PE
- HCVRNA 550,000
- Genotype 1a
- Fibroscan F1, S0 disease
- What do you do next?

Case Study 2

- Start anti-viral therapy
- Provide referrals for:
  - harm reduction services (buprenorphine)
  - drug use treatment
  - write prescription for naloxone and syringes

Summary of Key Messages

- Estimated ~3 million people with HCV in the US
- HCV is leading factor in the development of liver cancer which is curable if caught early
- A third of undiagnosed baby boomers with HCV currently have advanced fibrosis; there is a rising incidence of HCV in youth
- All adults 18-79 years, including pregnant women should be screened
- Assess for drug-drug interactions before treatment; list of prohibited drugs is short
- Patients with bridging fibrosis or cirrhosis need additional screening
- HCV treatment is effective and improves liver histology and quality of life

Hepatitis C Treatment Guidelines and Resources

- Treatment Guidelines - HCVguidelines.org
  - Includes a simplified treatment algorithm for use by primary care providers
- Drug-Drug Interactions - https://www.hep-druginteractions.org/

Hepatitis C Resources in NYC

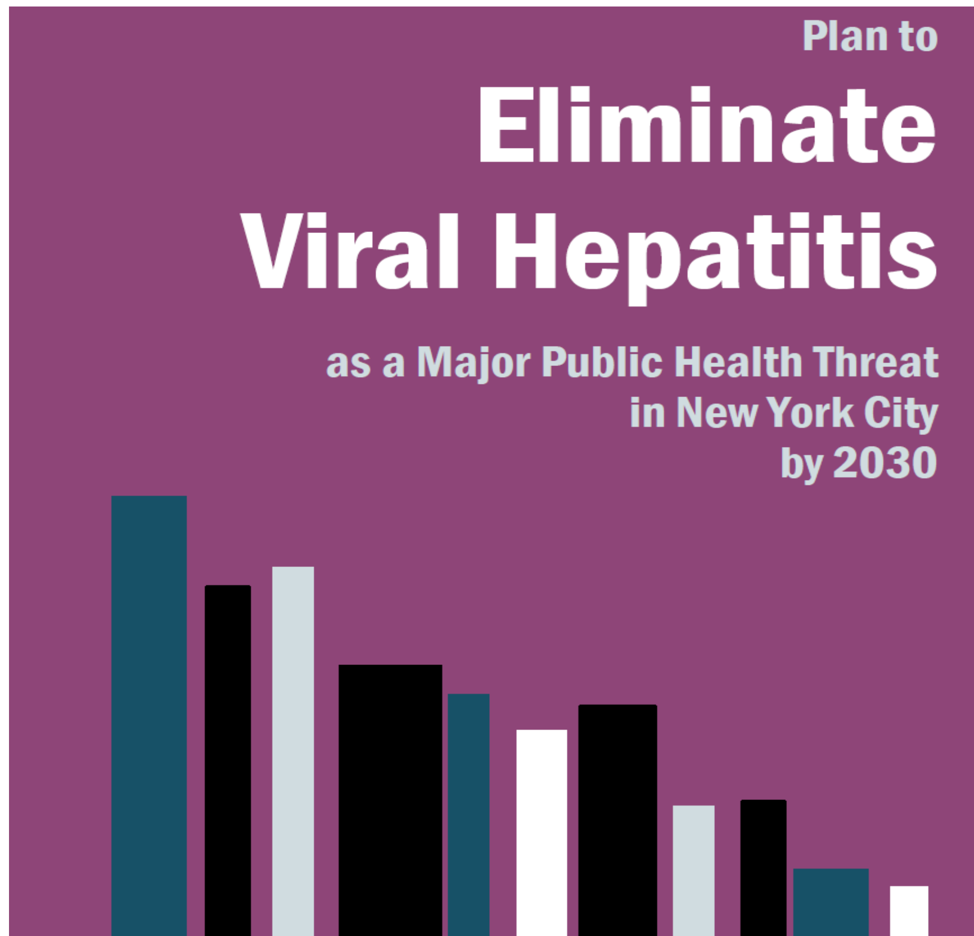
- NYS HCV CEI Clinical Consultation Hotline:
  (866) 637-2342 (leading hepatologist will answer questions)

- www.HepFree.NYC
  - Hep C Task Force
  - Clinical Resources
  - Capacity building tools
  - Advocacy Committee

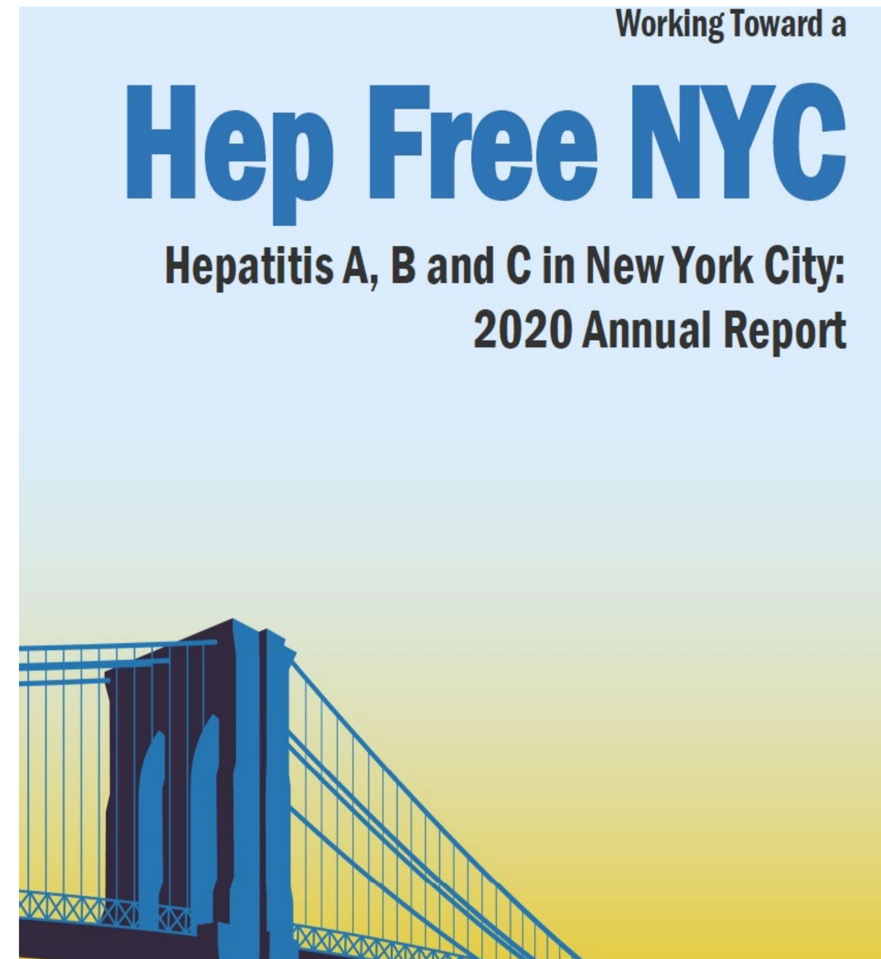
- Hepatitis C patient information page: www.nyc.gov/health/hepc
  - Free or low-cost testing and treatment

Elimination Plan and Annual Report

Find on NYC.gov website here



Find on Hep Free NYC website here



Contact Us

For CMEs or educational opportunities, contact:

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HCV Provider Training Series

Date	Topic
April 21, 2022	Hepatitis C : Epidemiology, Natural History and Diagnosis with Dr. Paul Gaglio
April 28, 2022	Hepatitis C Treatment with Dr. Sonal Kumar
May 5, 2022	Hepatitis C Complications with Dr. Arun Jesudian
May 12, 2022	Hepatitis C Treatment in People Who Inject Drugs (PWID) with Dr. Sara Taki

Upcoming Webinars

Perinatal Hepatitis C with Dr. Kushner May 19 @ 4:30PM EST

PRESENTER

Tatyana Kushner, MD, MSCE
Assistant Professor of Medicine
Division of Liver Diseases
Icahn School of Medicine at Mount Sinai

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1 CME/CNE/CEU offered per webinar. Join both webinars or a single session!