

# Oh, the Places You'll Go! Chronic hepatitis C in 2025

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# Case of XY

- 27 year old Latinx man found to have “abnormal LFTs” during life insurance evaluation.
- No symptoms
- BMI 34 kg/m<sup>2</sup>
- 2-3 beers on the weekends
- Remote history of intranasal cocaine
- No family history of liver disease
- PE: central obesity

**Congratulations!**  
**Today is your day!**  
**You're off to Great Places!**  
**You're off and away!**

**Dr. Seuss**

# Nobel Prize for Medicine goes to Hepatitis C discovery

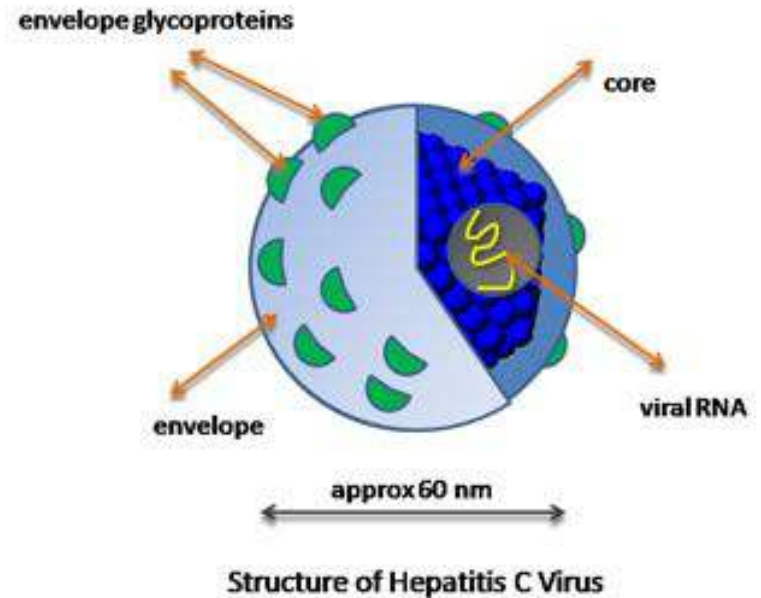


**I met  
him!**

BBC News October 5, 2020

# Hepatitis C: The Basics

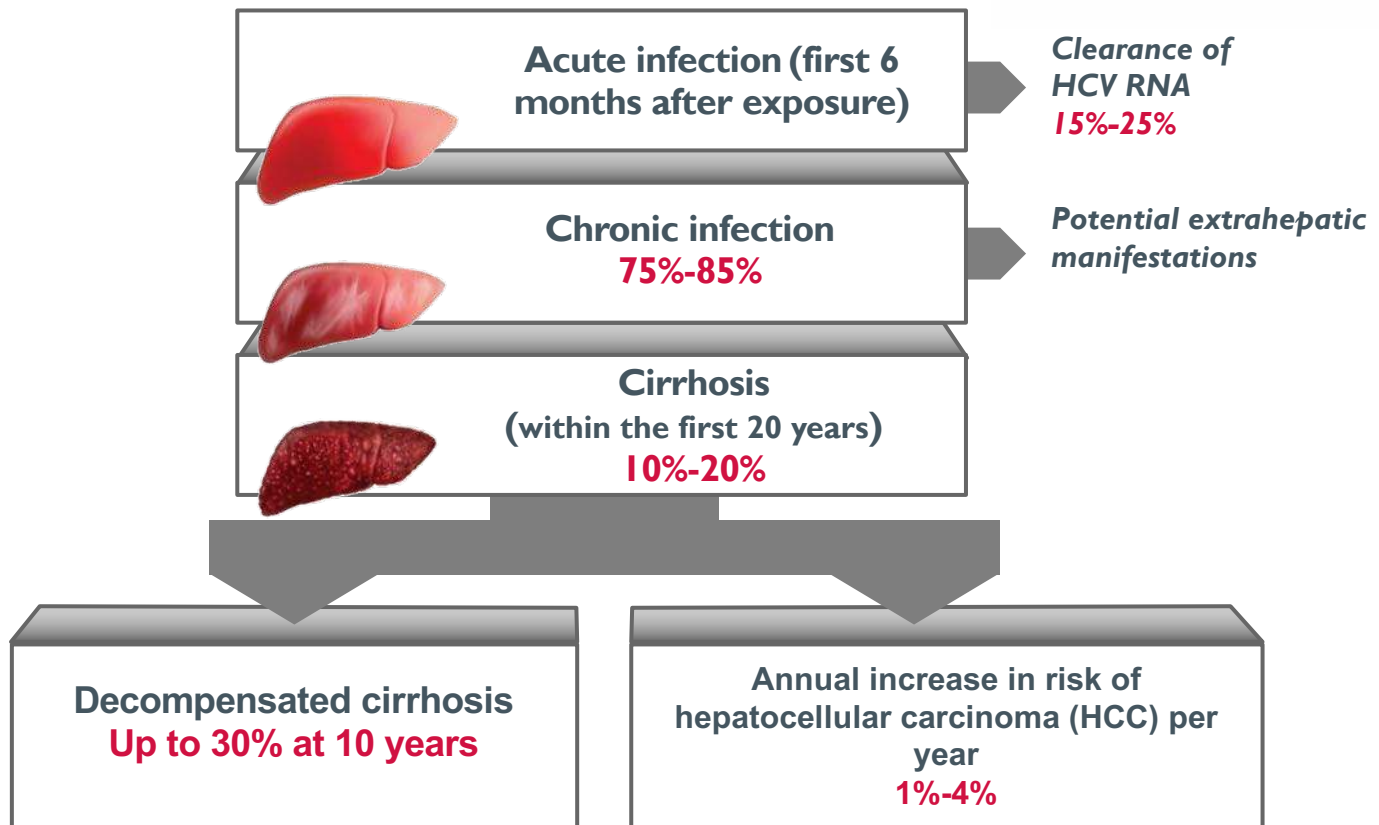
- (+) single stranded linear RNA virus
- Mimics the cellular mRNA (messenger RNA) molecule
- Exploits host cellular apparatus to synthesize proteins during replication



# Hepatitis C: Statistics

- Identified in **1989**
  - Previously known as NANB, post-transfusion hepatitis
- Screening HCV-Ab test first become available in **1992**
- Mode of transmission: blood, sexual, vertical.
- Incubation period: 60~90 days ( range 45~180).
- Genotypes: 1-6
- Vaccine: not available, antibody **NOT** protective

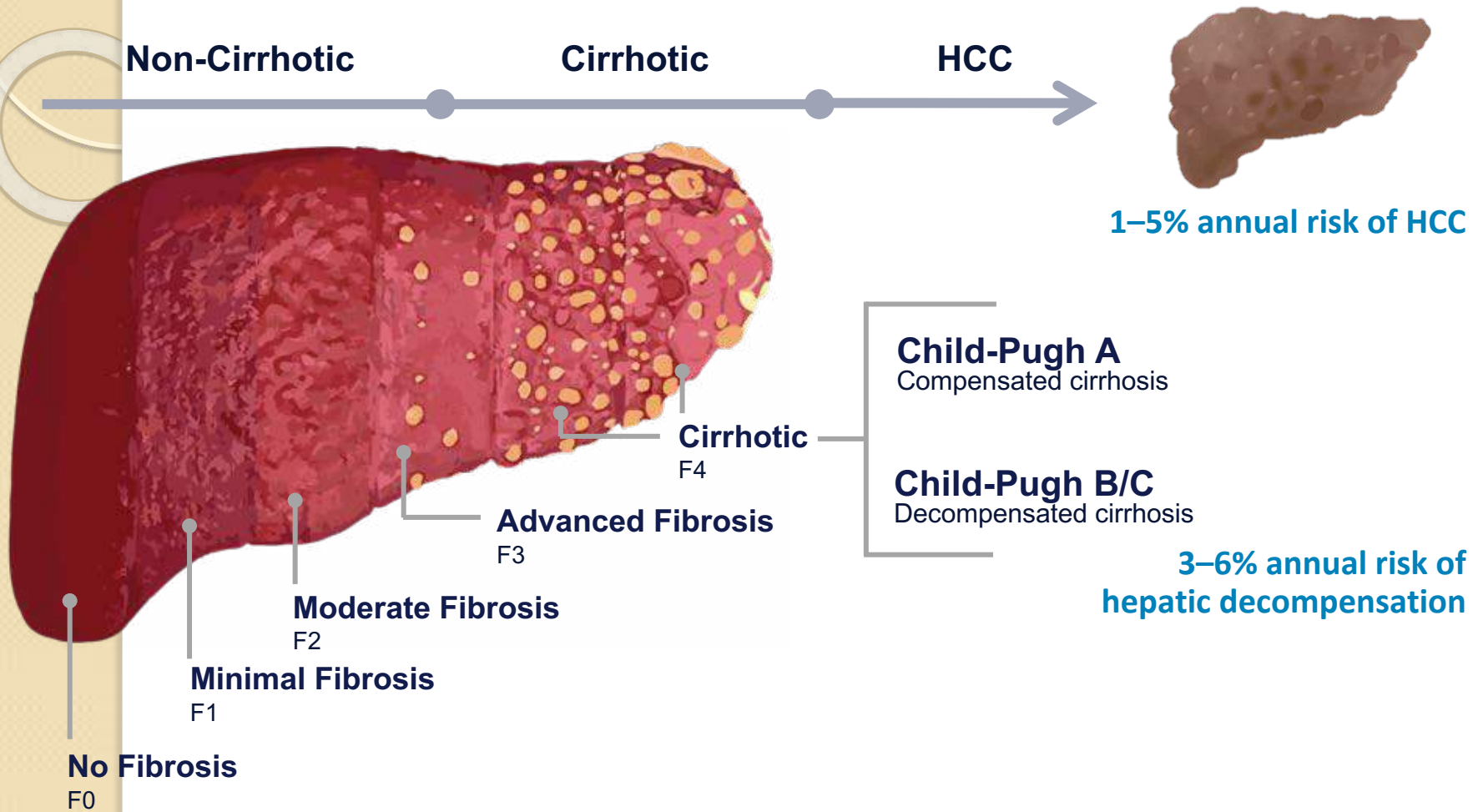
# Natural History of HCV Infection



1-5% will die from the consequences of chronic infection (liver cancer or cirrhosis)

- This equates to 120,000-160,000 deaths out of 3.2 mln currently infected

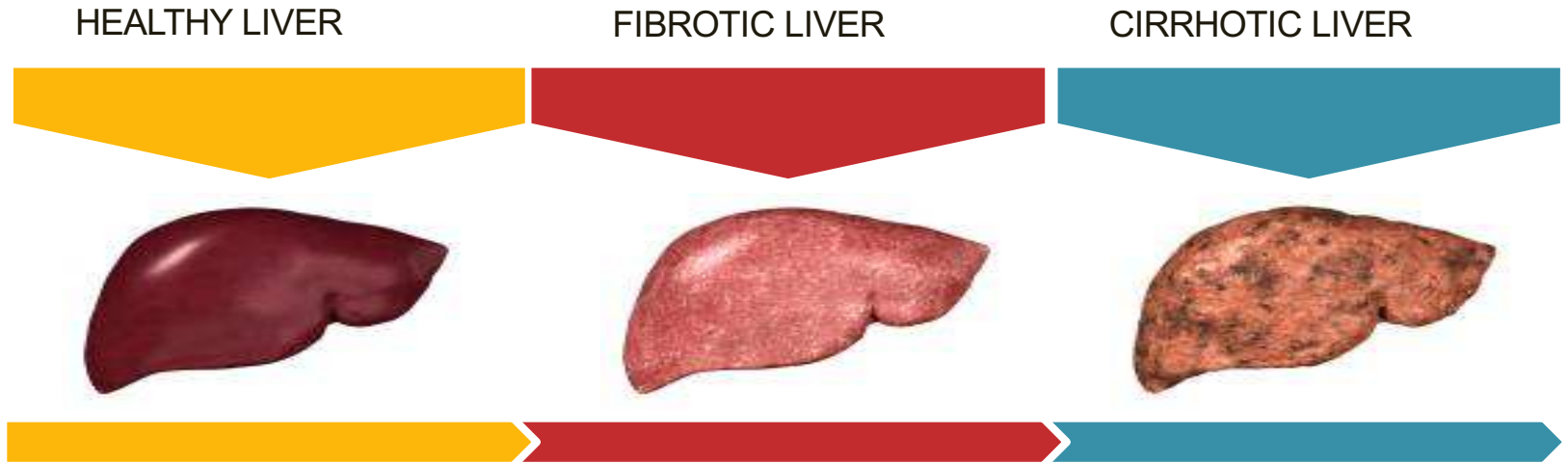
# Liver Fibrosis Progression in Patients With Chronic HCV



Poynard T, et al. Semin Liver Dis 2000;20(1):47-55. 2. CDC. Hepatitis C FAQs for Health Professionals. <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>. Accessed March 2019; 3. AASLD and IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. [www.hcvguidelines.org](http://www.hcvguidelines.org). Accessed March 2019.



# Chronic Hepatitis C Is a Progressive Disease

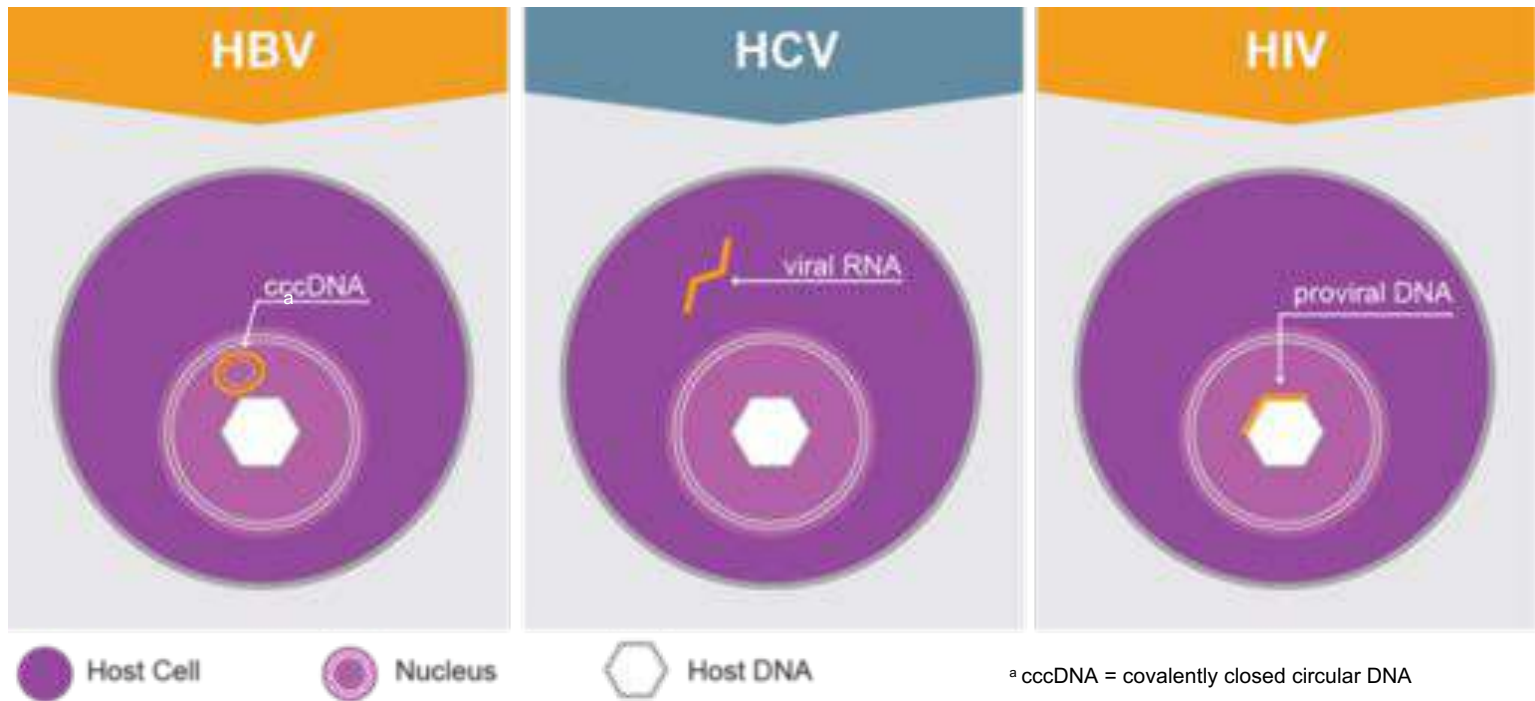


- Few or no symptoms; can progress without signs for decades
- Most pts asymptomatic until serious liver complications arise

1. CDC. MMWR Morb Mortal Wkly Rep. 1998;47(RR-19):1-39.  
2. Heidelbaugh JJ, et al. Am Fam Physician. 2006;74:756-762.

# Why is HCV Curable?

- Unlike some other viruses, HCV RNA is only present in the cytoplasm (not in the nucleus) of the host cell<sup>1</sup>
- Without the stable, genetic-material reservoir of the nucleus created by other viruses, the possibility exists for HCV cure by treatment<sup>1</sup>



1. Soriano V, Perelson AS, Zoulim F. Why are there different dynamics in the selection of drug resistance in HIV and hepatitis B and C viruses? *J Antimicrob Chemother.* 2008;62(1):1-4.

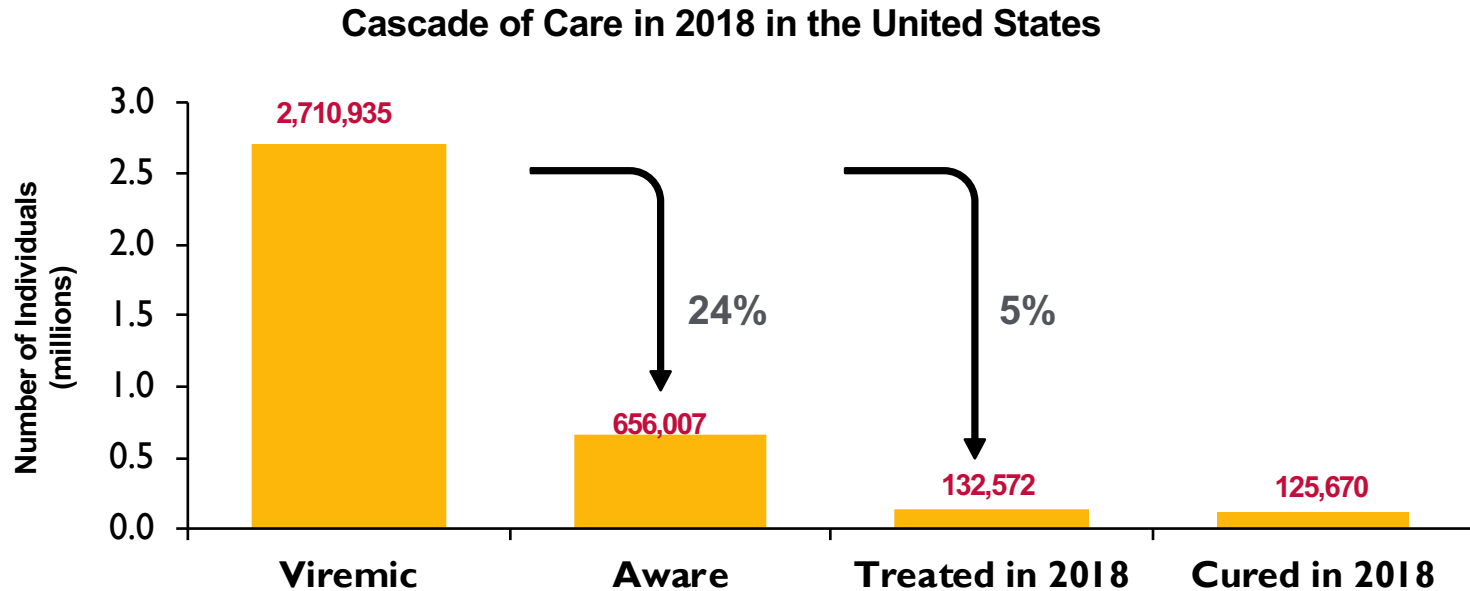
# Defining HCV Cure

- **Goal of treatment is cure**
- Cure = sustained virologic response (SVR12) = undetectable levels of HCV in the blood at 12 weeks after therapy is complete<sup>1,2</sup>
- In some instances, HCV treatment does not result in cure
  - Virus does not reach undetectable levels (non-responder)
  - Virus does not stay undetectable after therapy completion (relapser)



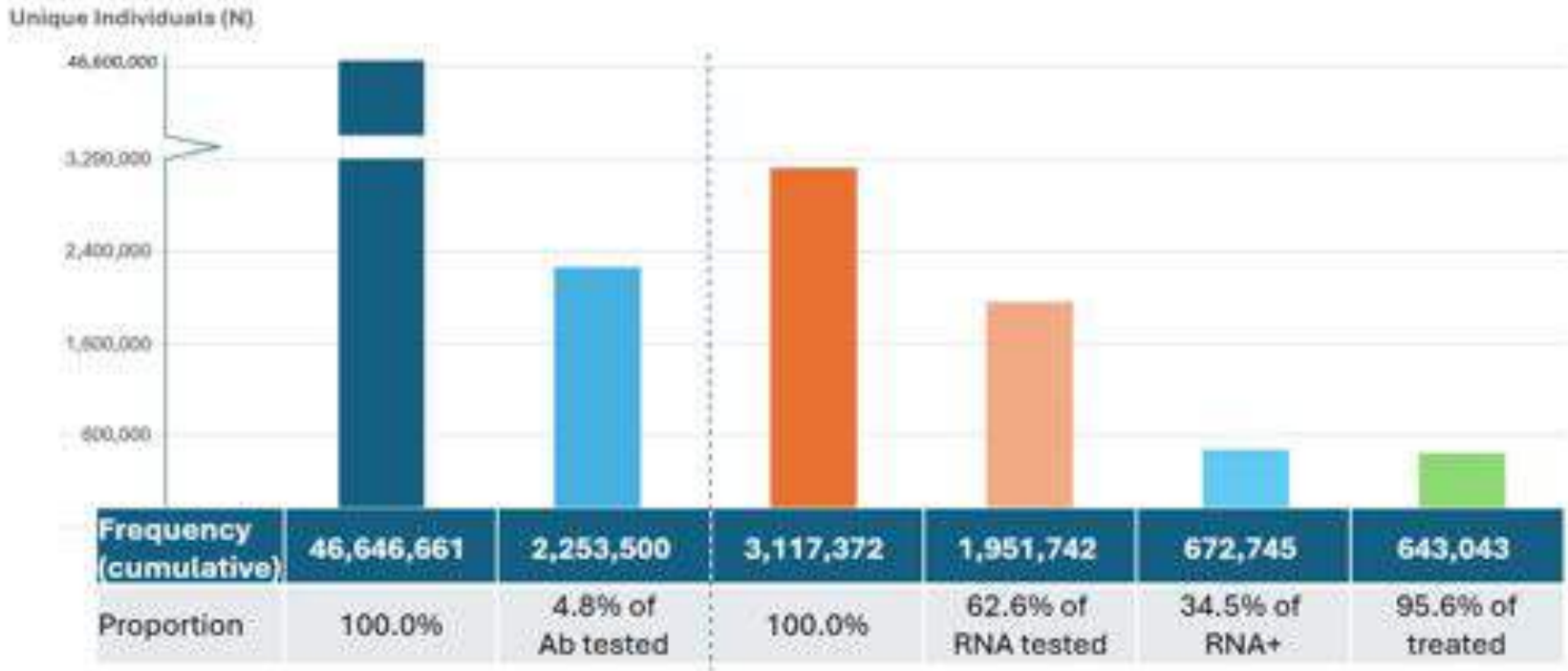
1. US Department of Health and Human Services, Center for Drug Evaluation and Research. Draft Guidance for Industry. Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment. October 2013.
2. AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Accessed December 7, 2015.

# HCV is Underdiagnosed and Undertreated



1. Chhatwal J et al. *APT*. 2019; 2. Zibbell JE, et al. *Am J Public Health*. 2018;108(2):175-181. 2. Data on file 3. Zibbell JE, et al. *Am J Public Health*. 2018;108(2):175-181.

# HCV Screening and RNA Testing Cascade 2014-2021



# HCV is Underdiagnosed and Undertreated

Model Populations

Population	Estimated Size, N	HCV RNA Prevalence, %*
Non-institutionalized	249,177,857	0.89
Unsheltered/Unhoused	212,090	11.10
Incarcerated	2,086,600	9.72
Active-duty military	1,326,200	0.02
Nursing home residents**	1,404,421	0.57
PWID	1,694,500	43.7

HCV RNA Prevalence

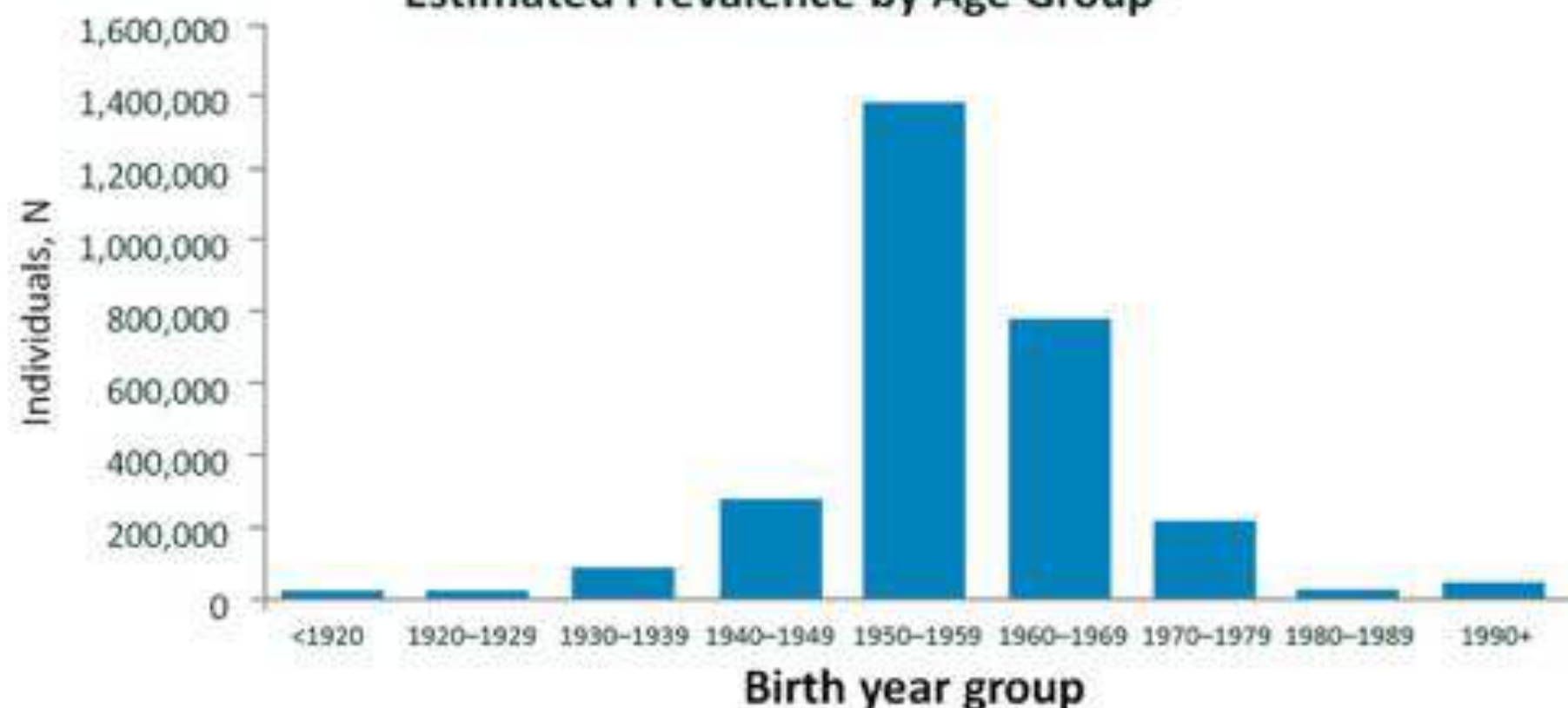


Accounting for PWIDs, estimated US prevalence of HCV is substantially higher than previously reported

## The Majority of HCV Infections are Found in Baby Boomers (Born 1945 – 1965)

Of the 3.4 million chronically infected people in the US,  
~75% are baby boomers<sup>2</sup>

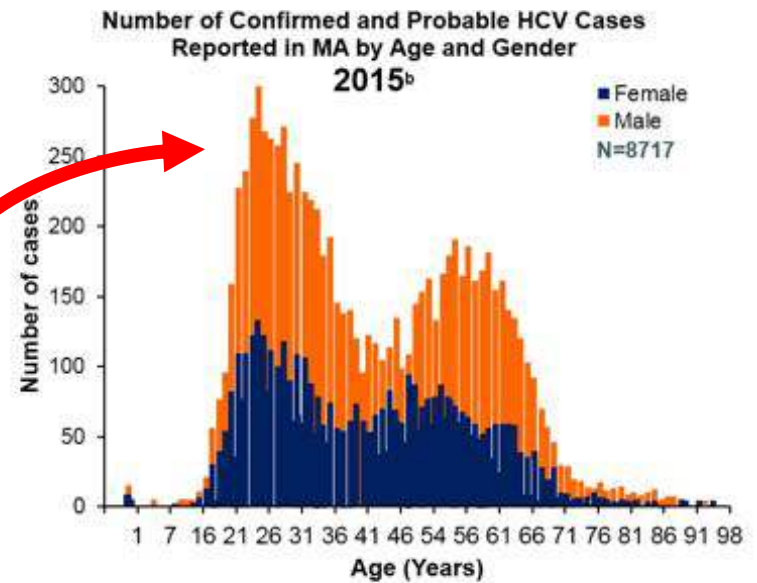
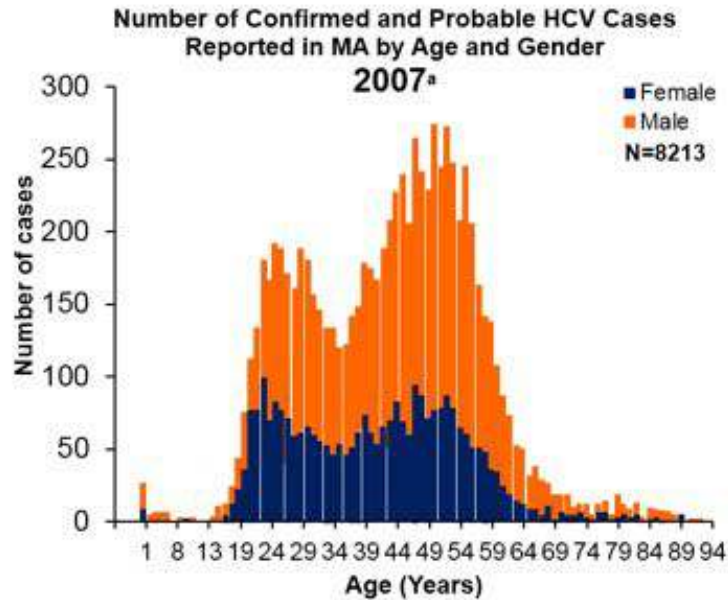
### Estimated Prevalence by Age Group<sup>1</sup>



1. Smith BD, et al. MMWR. 2012;61:1-32.

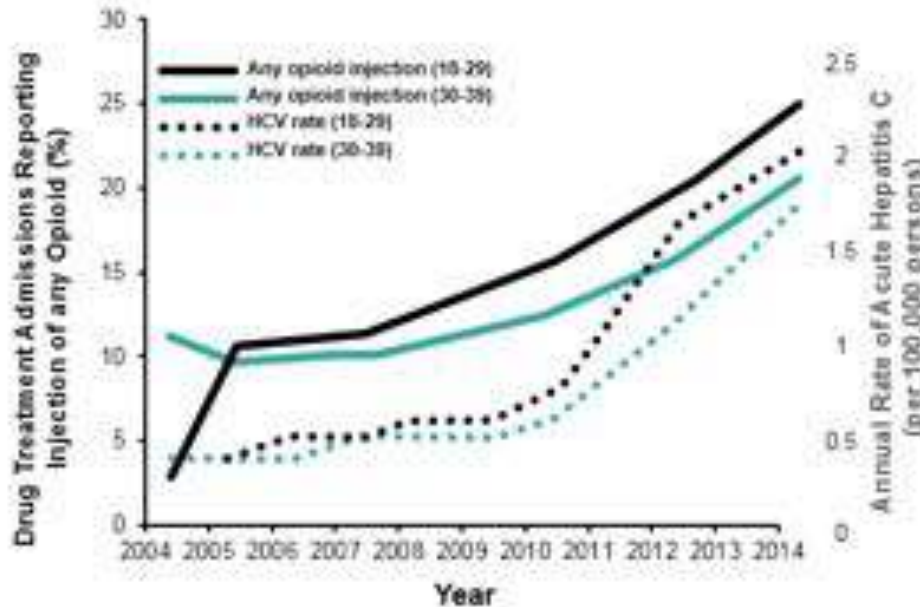
2. Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/hepatitis/populations/1945-1965.htm>

# Age Distribution of New HCV Infections in the US Skews Toward Adolescents and Young Adults





# From 2004-2014, HCV and Opioid Injection Drug Use Increased Significantly Among People Aged 18-39 Years



Among people aged 18-29 years<sup>1</sup>:

**622%**  
Admission for opioid injection

**400%**  
Rate of acute HCV

Among people aged 30-39 years<sup>1</sup>:

**83%**  
Admission for opioid injection

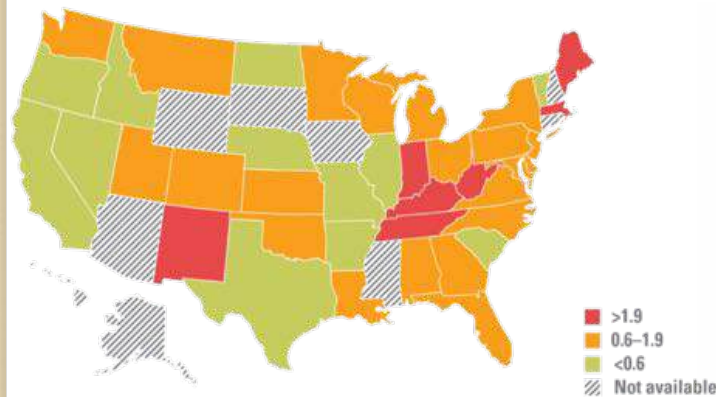
**325%**  
Rate of acute HCV

**The national increase in acute HCV infection is associated with the nation's opioid epidemic.<sup>1</sup>**

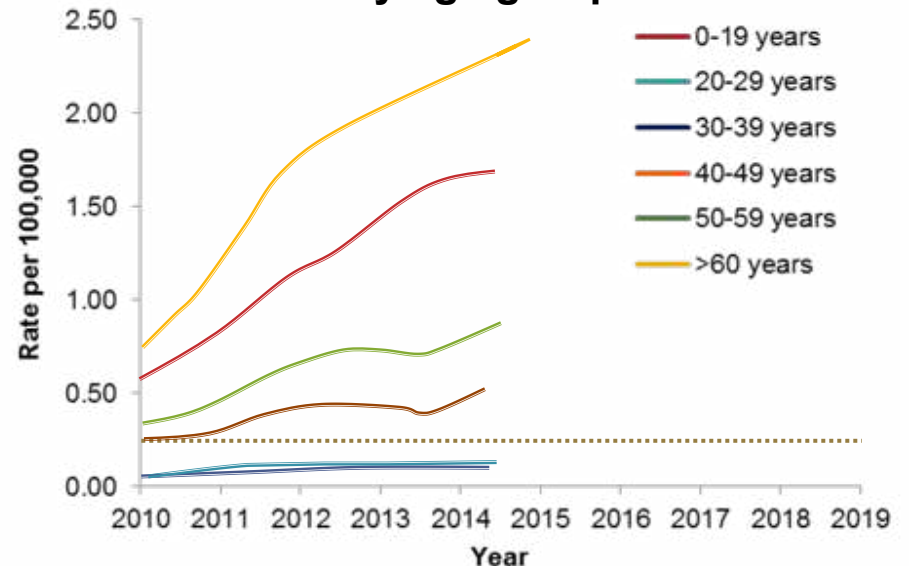
1. Zibbell JE, et al. *Am J Public Health*. 2018;108(2):175-181. 2. CDC. <https://www.cdc.gov/nchstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html>. December 21, 2017. Accessed August 9, 2019.

# HCV Epidemiology: Incidence

- Between 2010 and 2015, new HCV infections rose 294%<sup>1</sup>
  - 7 states  $\geq$  national average in HCV incidence: IA, KY, ME, MA, NM, TE, WV
- Young adults have the highest rates of acute HCV infections, and rates in this group are increasing at a higher rate than other age groups



Incidence rate of reported HCV infections, by age group<sup>2</sup>



1. Campbell CA et al. *MMWR Morb Mortal Wkly Rep*. 2017;66(18):465-469.  
2. Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Progress toward viral hepatitis elimination in the United States, 2017. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, Office of Infectious Diseases, NCHHSTP; 2017. Available at: <https://www.cdc.gov/hepatitis/policy/PDFs/NationalReport.pdf>.

# Hepatitis C: Why to Screen?

- Estimated 3.5 million infected in the US
- Estimated 800,000 additional patients will need treatment
- > 120,000 lives saved
- Effective therapies available now, >90% cure rates
- **Potential for elimination?**

# Hot off the Press: CDC Update

- **Universal hepatitis C screening:** Hepatitis C screening at least once in a lifetime for **all adults** aged 18 years and older
- Hepatitis C screening for **all pregnant women** during each pregnancy

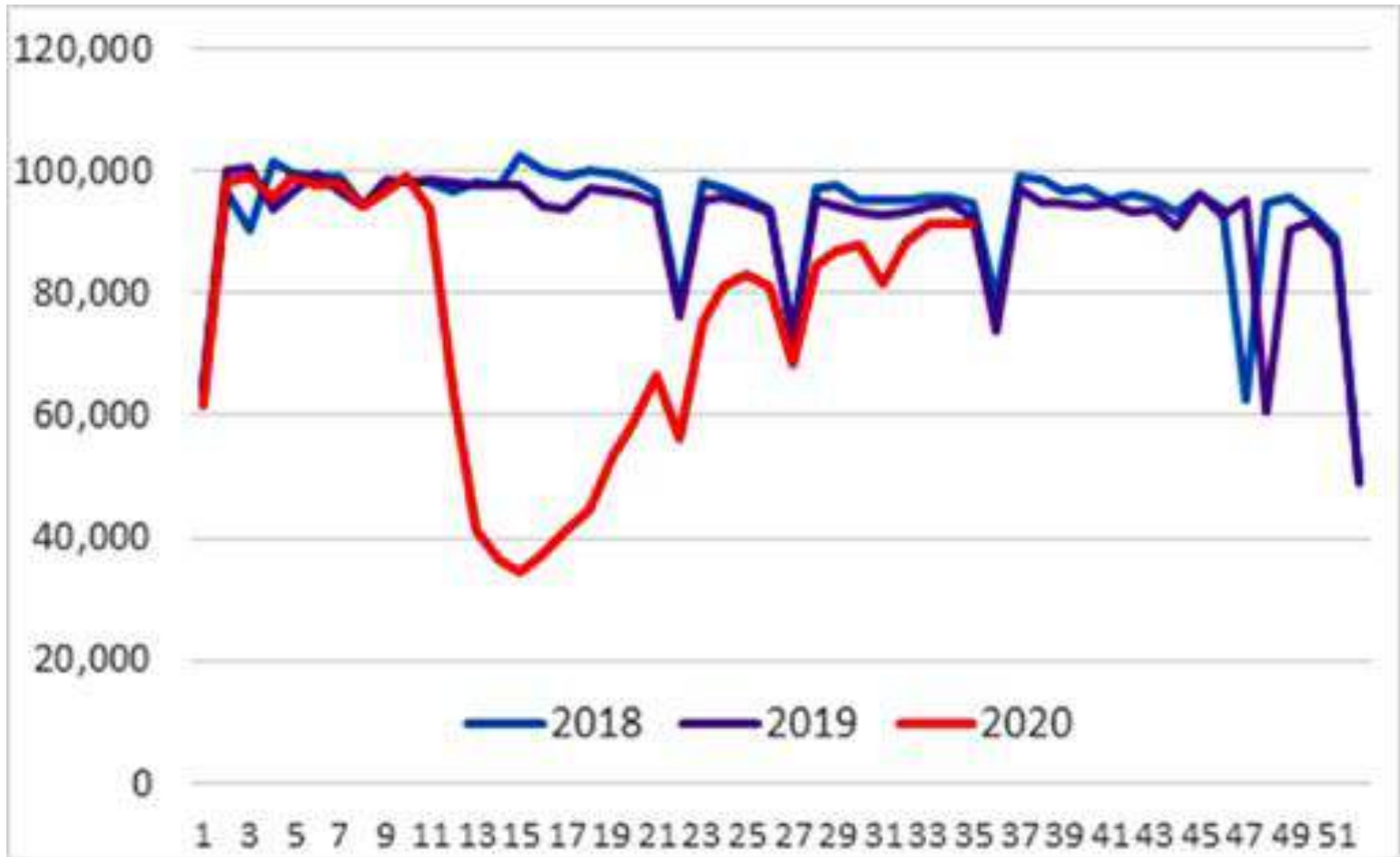


# Hot off the Press: CDC Update

## **One-time hepatitis C testing regardless of age among people with recognized conditions or exposures:**

- People with HIV
- People who ever injected drugs and shared needles, syringes, or other drug preparation equipment
- People with selected medical conditions, including:
  - people who ever received maintenance hemodialysis
  - people with persistently abnormal ALT levels
- Prior recipients of transfusions or organ transplants, including:
  - people who received clotting factor concentrates produced before 1987
  - people who received a transfusion of blood or blood components before July 1992
  - people who received an organ transplant before July 1992
  - people who were notified that they received blood from a donor who later tested positive for HCV infection
- Healthcare, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood
- Children born to mothers with HCV infection
- **Any person who requests hepatitis C testing** should receive it, regardless of disclosure of risk, because many persons may be reluctant to disclose stigmatizing risks


# HCV test volume: 2018-2020



# Hepatitis C: How to Diagnose?

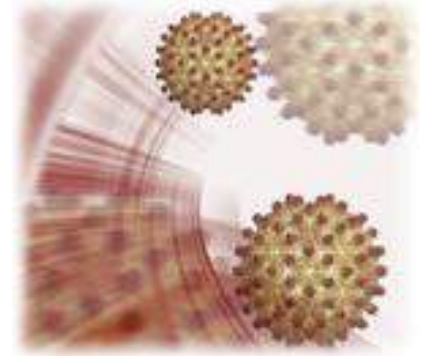
- First step: HCV ab
- If positive: HCV RNA and genotype
- **Vibration Controlled Transient Elastography (VTCE)** : determine degree of fibrosis and urgency to treat
- Biopsy almost never needed

# Hepatitis C antibody test

- It looks for footprints of the virus in your blood 
- If it is positive, patient had been exposed to the virus at some point
- 15-25% of patients clear the virus on their own
- Further testing is necessary to determine active infection



# Hepatitis C RNA



- Viral Load = PCR
- Quantitative, not qualitative
- Presence of virus = chronic Hepatitis C
- Viral load DOES NOT correlate to the severity of inflammation, progression of liver disease or chance of cure.
- Viral load fluctuates over time
  - Monitoring is not needed unless patient is active treatment is planned or in progress

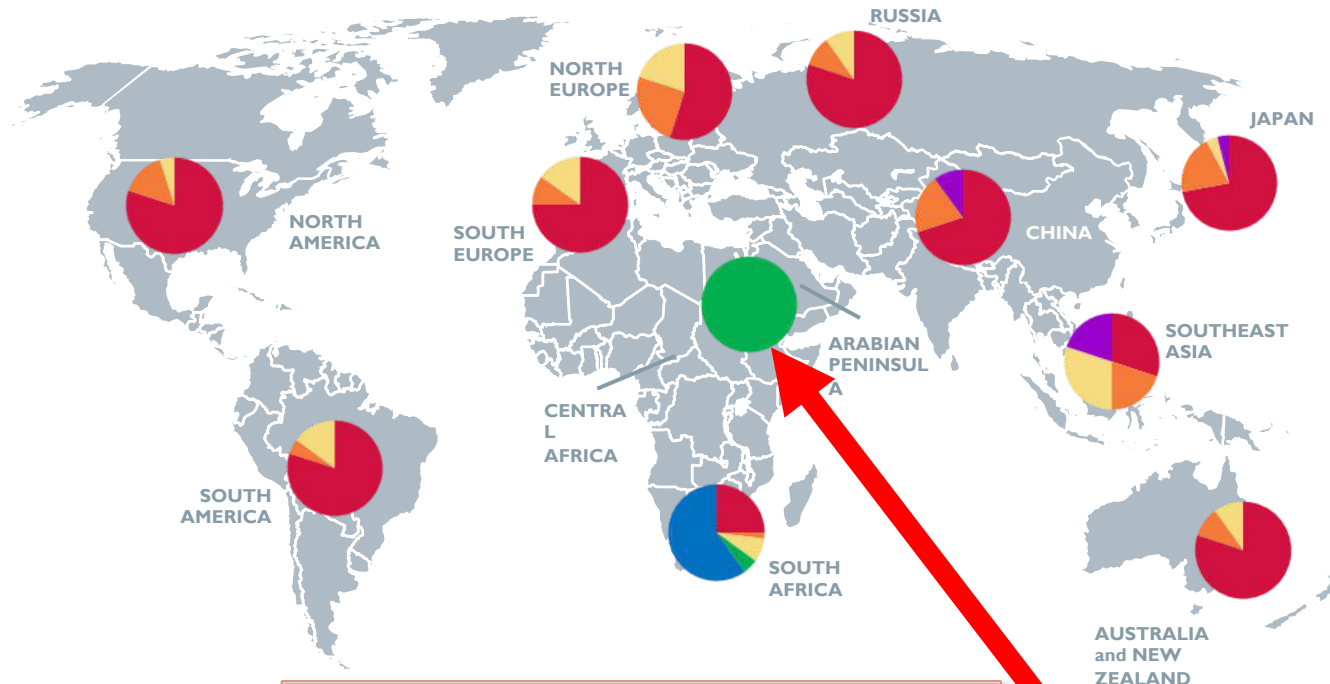
# Hepatitis C Genotype



- Genotypes = different strains of the virus
- 6 known genotypes
- All have similar effects on the liver
- GT 3 is associated with fatty liver and had been previously harder to treat
- Knowing patient's genotype in advance helps to determine appropriate treatment
  - Kind off...



# HCV GENOTYPE (GT) PREVALENCE VARIES GLOBALLY, BUT IS PREDOMINANTLY GT 1, GT 2, AND GT 3 IN THE US<sup>1,2</sup>



**Egypt has the highest prevalence of HCV in the world**

1. World Gastroenterology Organisation. Diagnosis, management and prevention of hepatitis C. 2013.
2. Gerner JJ, et al. *J Clin Microbiol.* 2011;49(8):3040-3043.
3. Manos MM, et al. *J Med Virol.* 2012;84(11):1744-1150.
4. Nainan OV, et al. *Gastroenterology.* 2006;131(2):478-484.

# Schistosomiasis

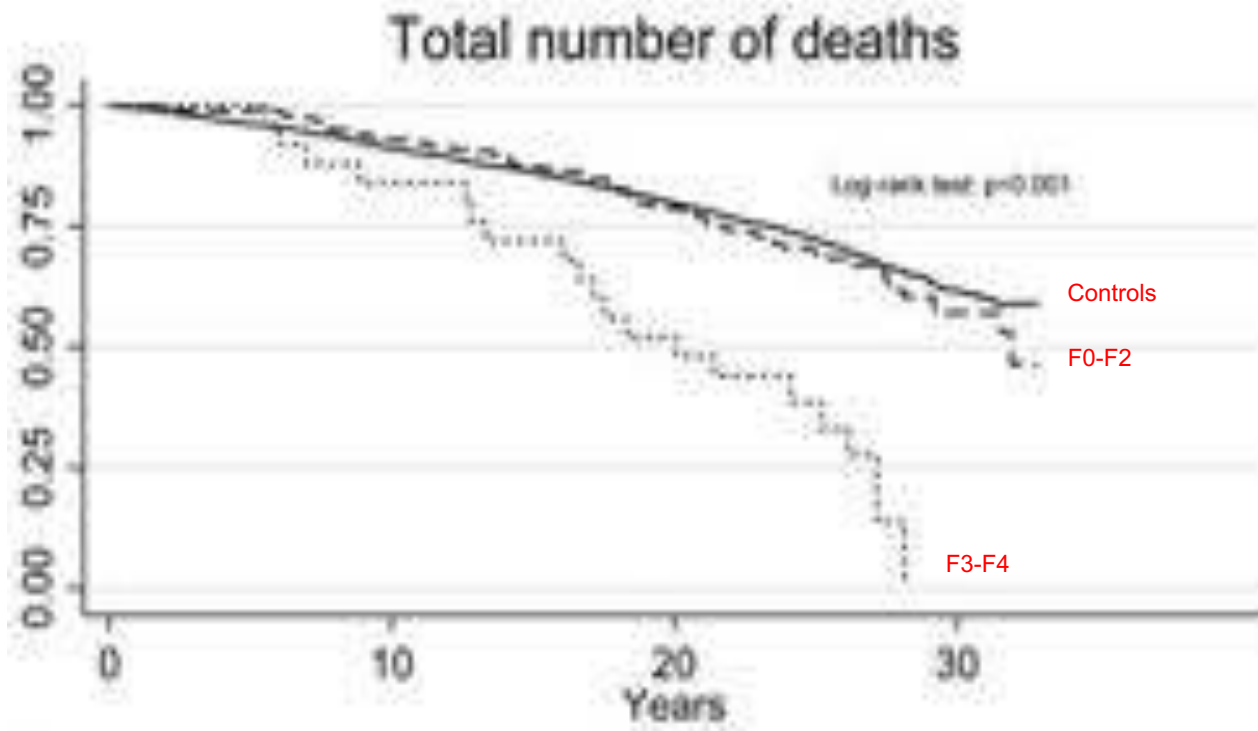
11-year-old boy with abdominal fluid and portal hypertension due to schistosomiasis



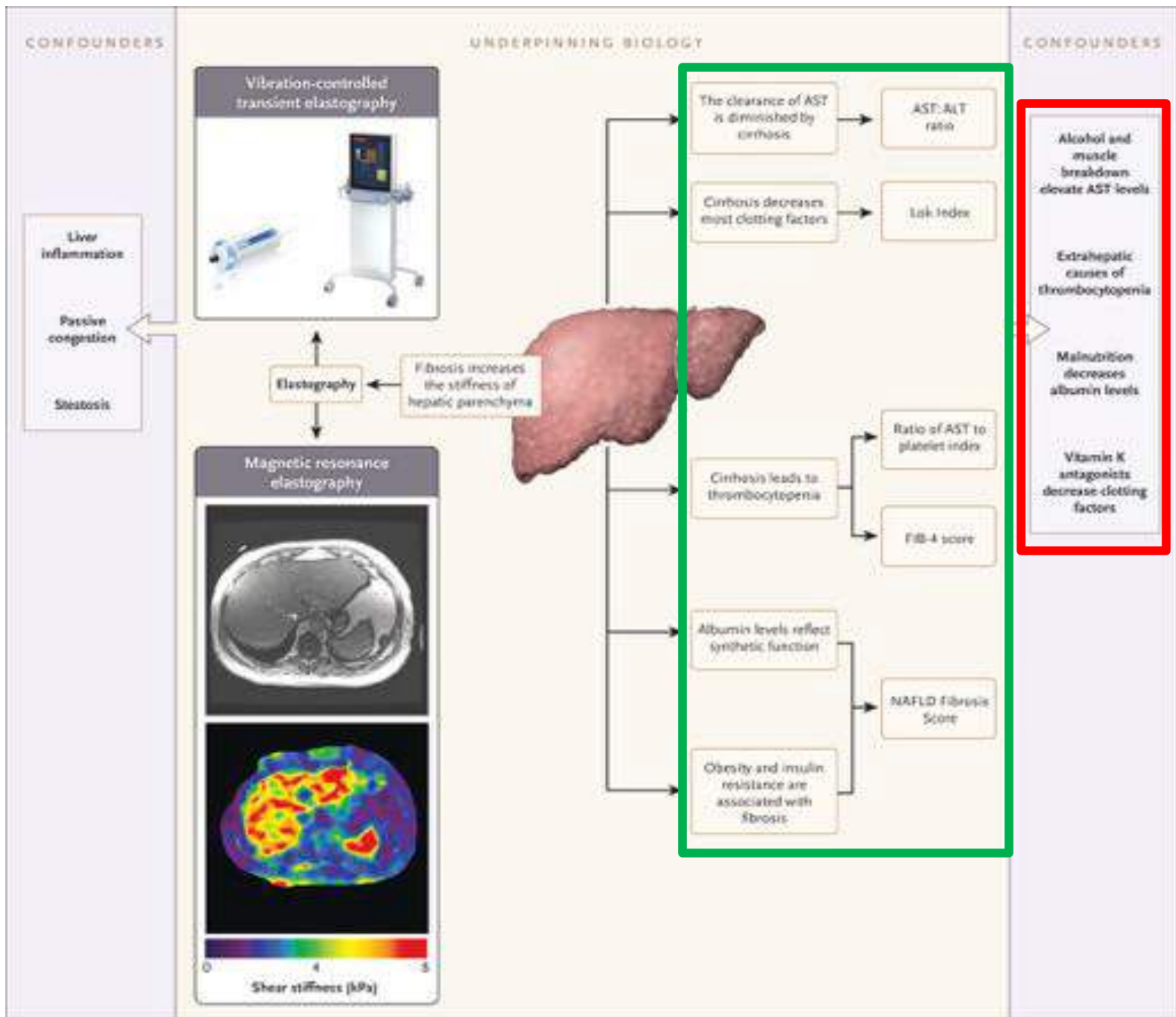
- Caused by parasitic flatworms
- Causes hepatic fibrosis, portal hypertension, kidney failure, infertility, bladder cancer
- Treated with intravenous tartar emetic in the 1950-1980s
- 10-12 IV dose course for everyone infected

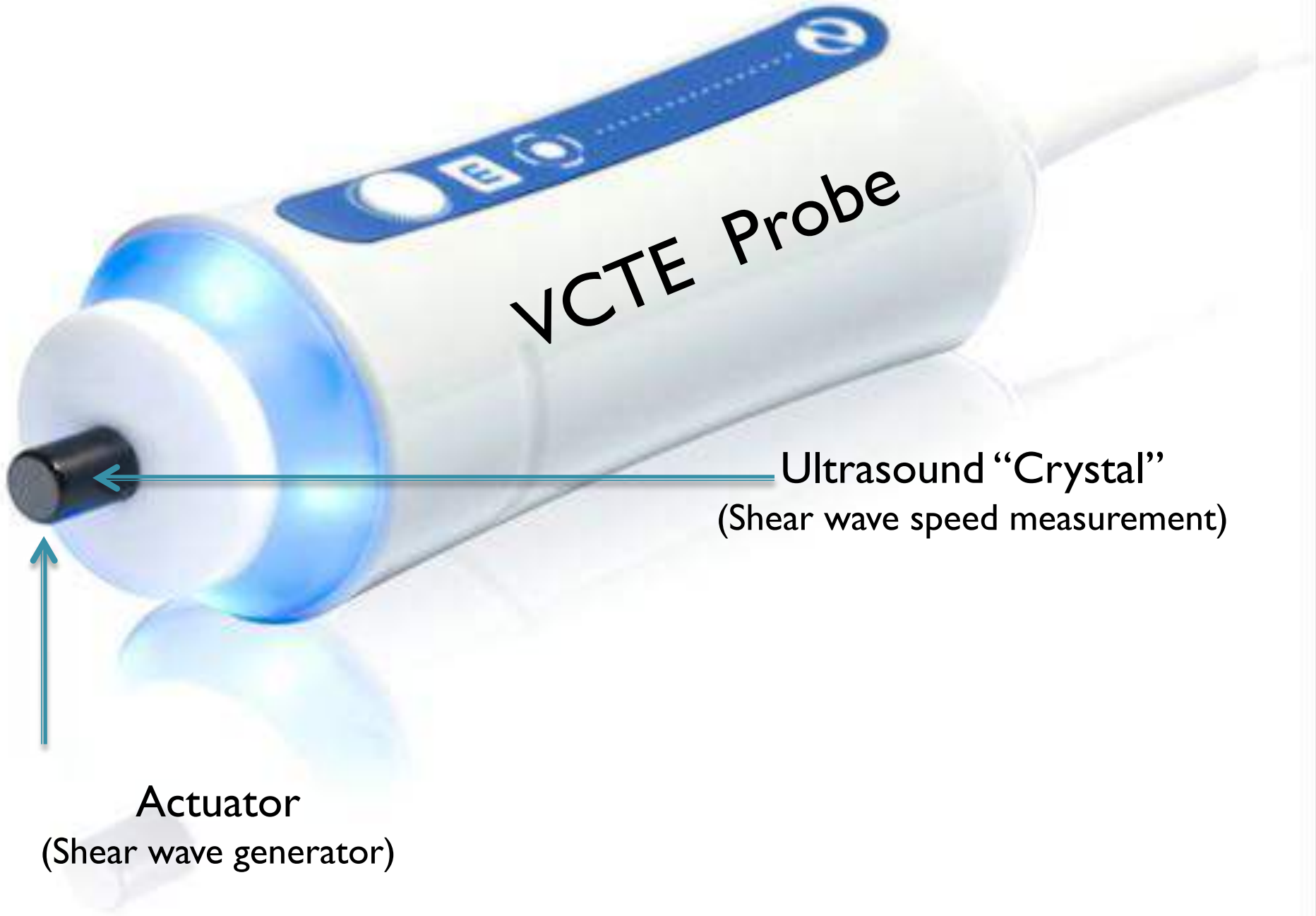
# Who is at the Highest Risk of Complications?

Patients with more severe fibrosis have markedly worse outcomes



Prognostic hierarchy from Loomba, et al. *Gastroenterology*. 2015;  
Ekstedt et al. *Gastroenterology* 2015.



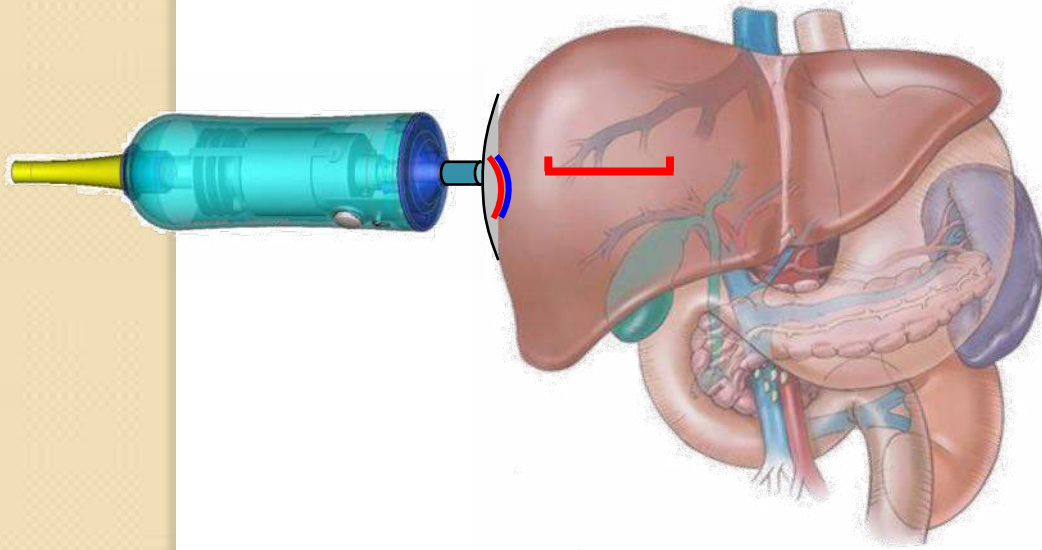


# VCTE Probe

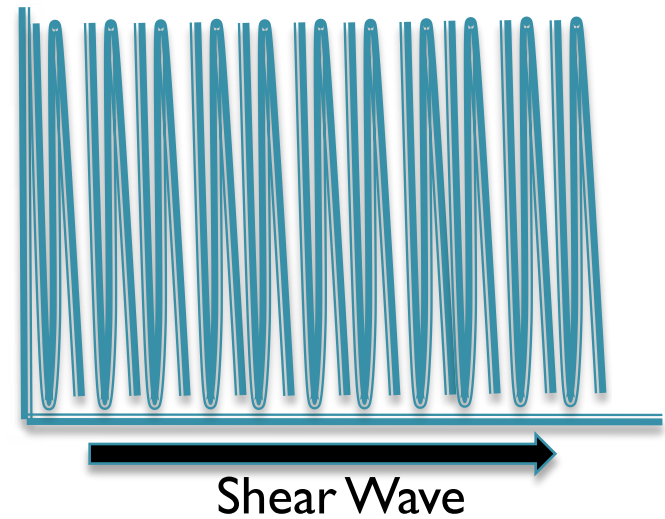
Ultrasound "Crystal"  
(Shear wave speed measurement)

Actuator  
(Shear wave generator)

# Shear Wave Induction

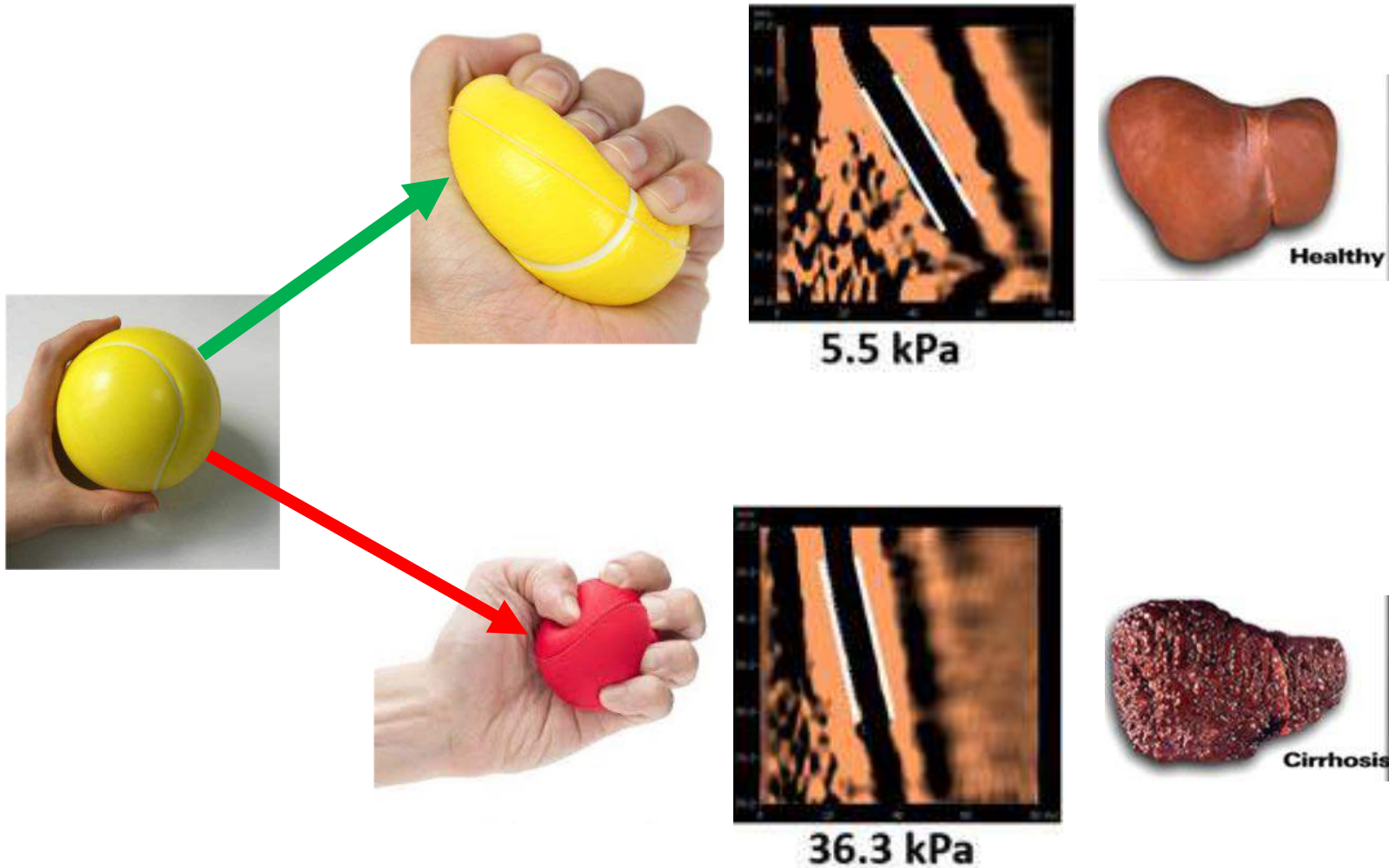


Probe mechanically induces  
shear wave ...





# VCTE: Surrogate Marker of Fibrosis



## Peer Review Cutoff Value Reference

Disease	F0-F1	F2	Significant Fibrosis F3	Cirrhosis F4
HBV	$\leq 6.0$	$> 6.0$	$\geq 9.0$	$\geq 12.0$
HCV	$\leq 7.0$	$> 7.0$	$\geq 9.5$	$\geq 12.0$
HCV-HIV	$\leq 7.0$	$\leq 10.0$	$\geq 11.0$	$\geq 14.0$
Cholestatic	$\leq 7.0$	$\geq 7.5$	$\geq 10.0$	$\geq 17.0$
NAFLD/NASH	$\leq 7.0$	$\geq 7.5$	$\geq 10.0$	$\geq 14.0$

# Hepatitis C: How to Treat?

“You have brains in your head.  
You have feet in your shoes.  
You can steer yourself  
any direction you choose.  
You're on your own. And you know what  
you know.  
And YOU are the one who'll decide where  
to go...”

Dr. Seuss

# Acknowledgements

- Dr. Naoky Tsai
- Dr. Theodor Seuss Giesel