Hepatitis C

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Disclosures

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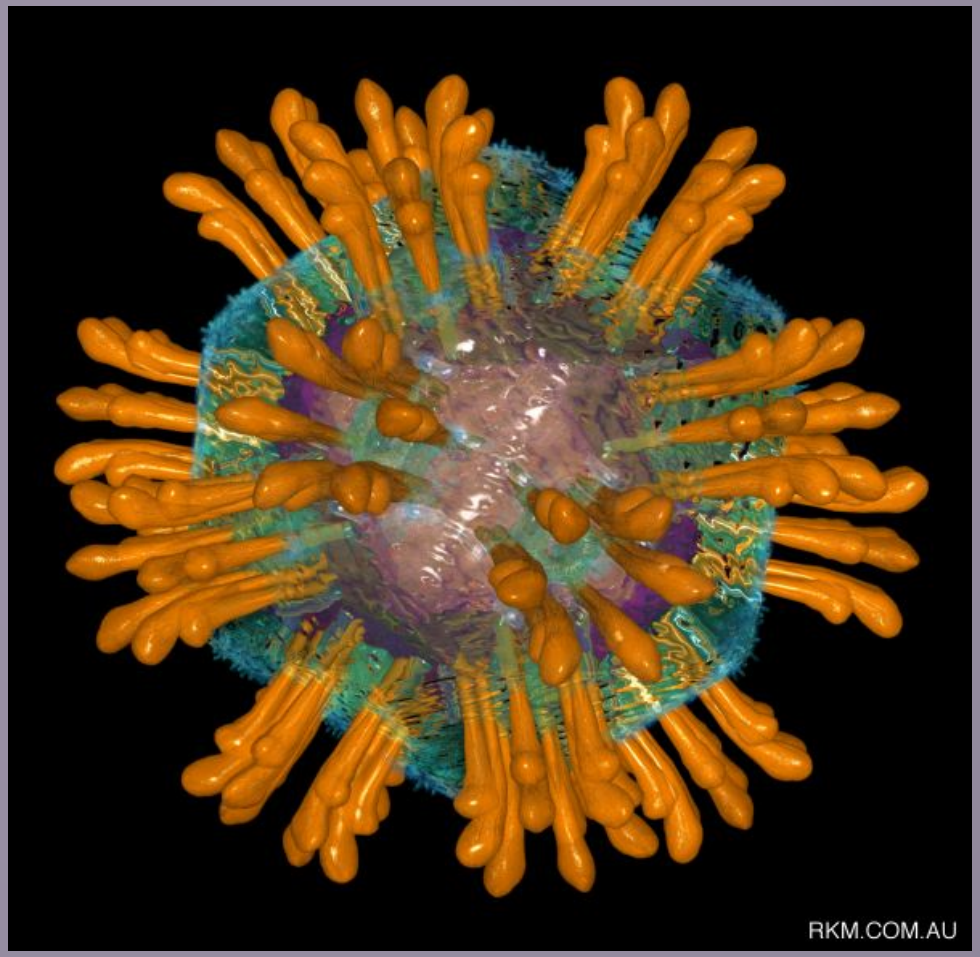


HCV Outline

- Prevalence
- Transmission
- Prevention
- Screening
- Treatment
- Extrahepatic Manifestations
- HCC screening
- Perinatal Transmission
- Adolescents
- Coffee, Herbs and Supplements
- Alcohol
- Cannabis

Learning Objectives

- Describe the prevalence and transmission of HCV
- Describe the extrahepatic manifestations of HCV
- Describe the process of HCC screening
- Describe the risks and benefits of herbs, supplements, coffee and cannabis

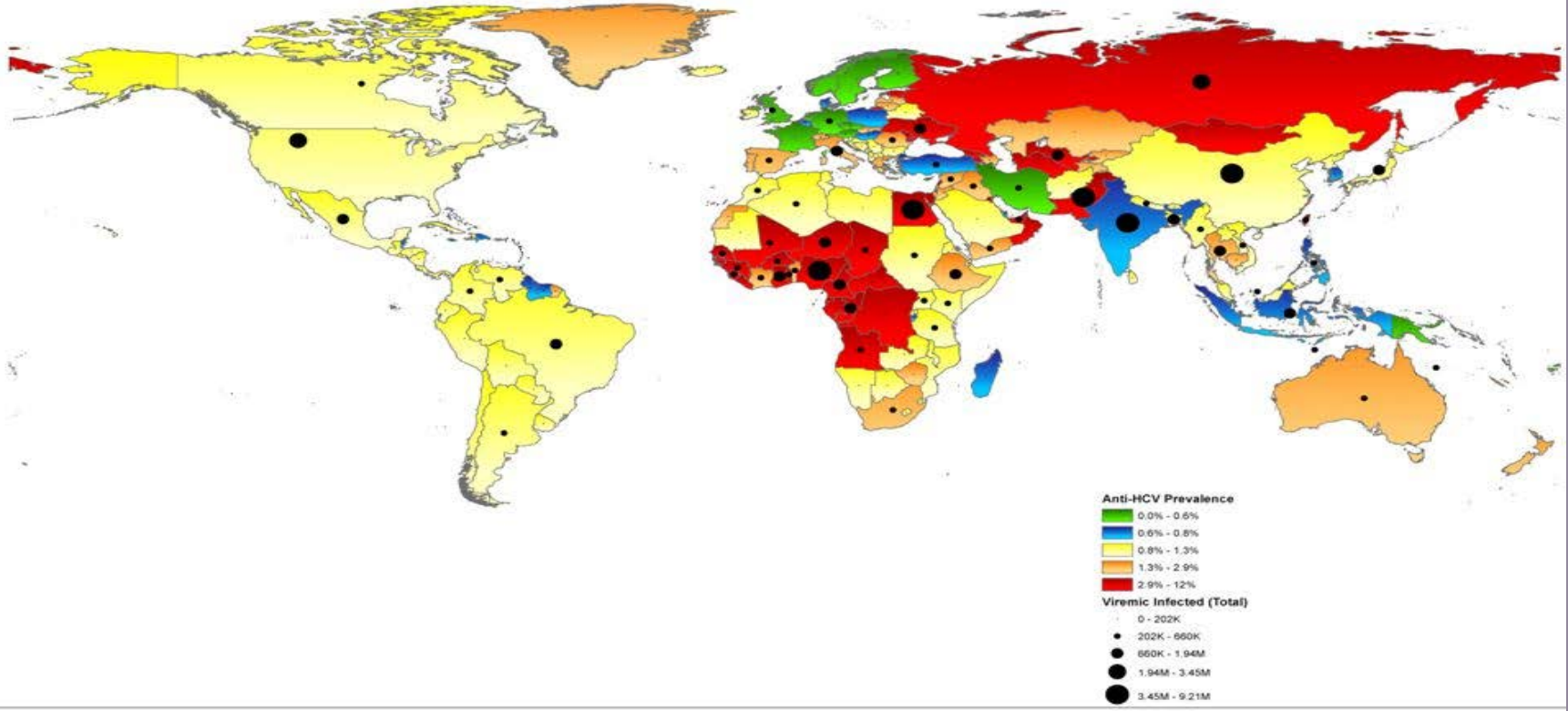
US Prevalence of HCV

- Based on NHANES data, Hepatitis C is the most common blood borne infection.
- NHANES from 2003-2010 estimates a prevalence of 2.7 million persons with chronic Hepatitis C. However this data excludes homeless, military, incarcerated, nursing home and immigrants.
- Because of the populations excluded, others estimate prevalence at 3.5-5.2 million

- Alter MJ. Epidemiology of hepatitis C. Hepatology. 1997;26(3 Suppl 1):62S-65S.
- [PubMed Abstract] -
- Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an
- estimate of true prevalence. Liver Int. 2011;31:1090-101.
- [PubMed Abstract] -

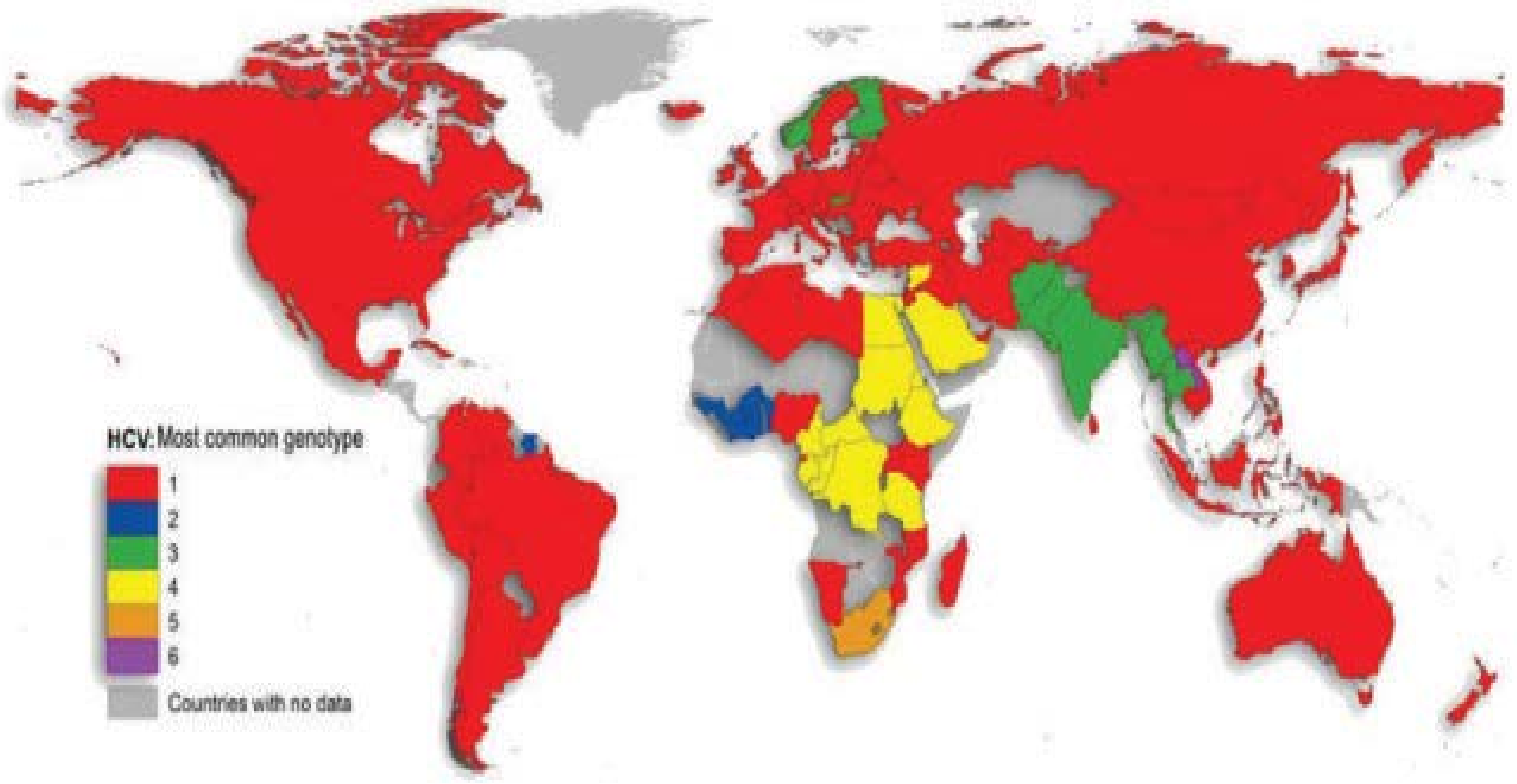
Worldwide Prevalence of HCV

Anti-HCV Prevalence
(Reported + Extrapolated)



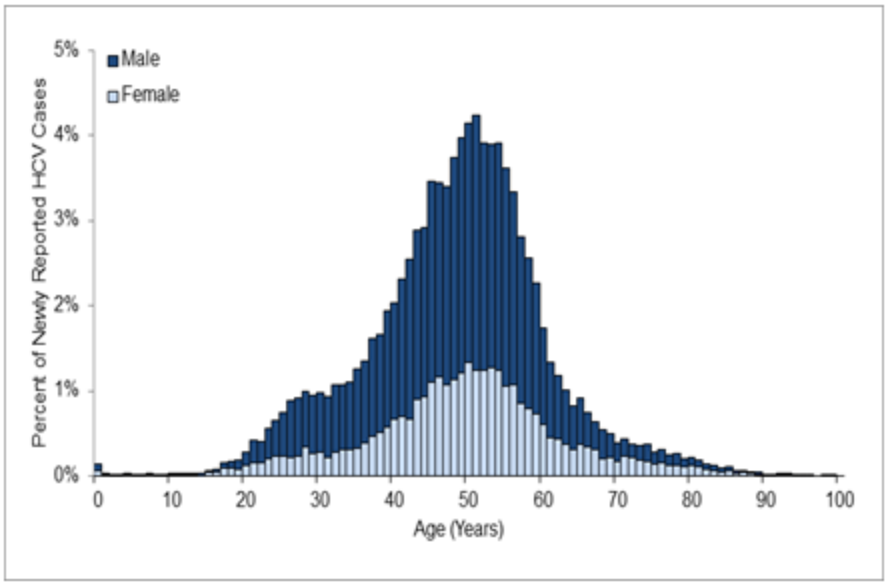
Gower, E., Estes C., Hindman, S., Razavi-Shearer, K., Razavi, H., Global epidemiology and genotype distribution of the hepatitis C virus, *Journal of Hepatology* (2014)

Worldwide distribution of HCV Genotypes

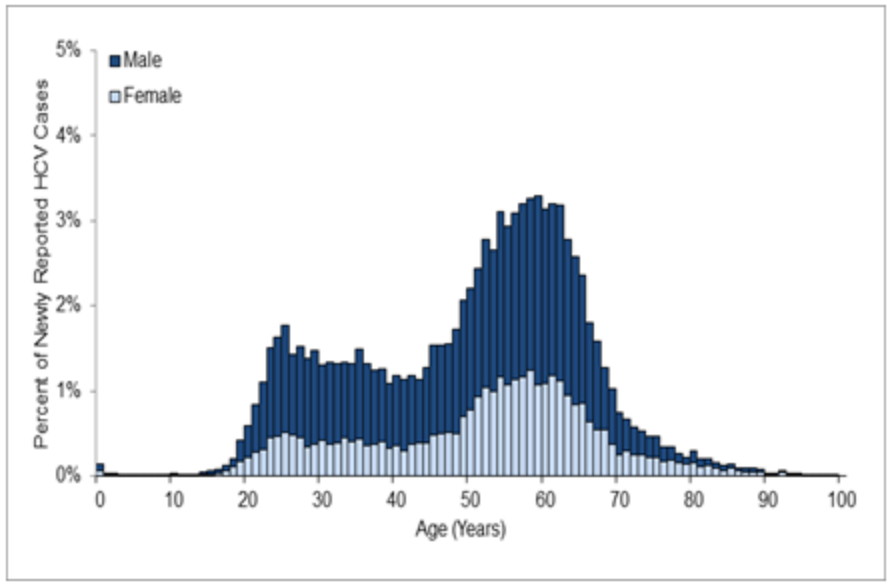


Chronic Hepatitis C – Age Distribution of Newly Reported Cases, California, 2007 and 2015

2007*



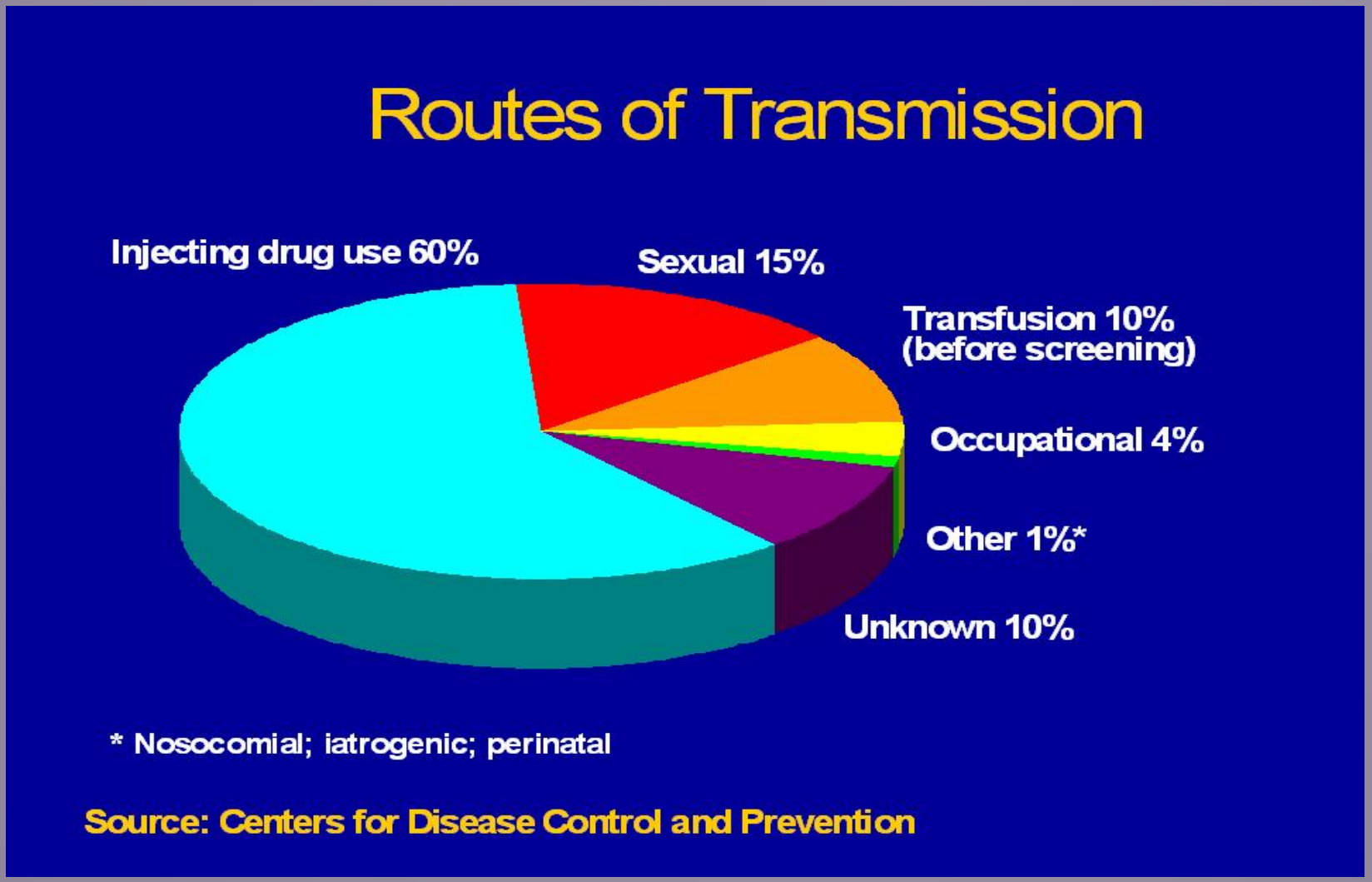
2015†



*N = 41,037; excludes 547 cases with missing age or sex information.
†N = 33,454; excludes 294 cases with missing age or sex information.

"BY THE WAY, I HAVE HEPATITIS C"

Transmission of HCV



Transmission of HCV

- Hepatitis C is transmitted from blood to blood contact
- It is not transmitted from casual household contacts, hugging, kissing, sharing drinks, consuming alcohol

- HCV is primarily transmitted by:
  - Sharing equipment used for injection drug use

- Other risks include:
  - Blood transfusion prior to 1992
  - Clotting factors or organ transplants prior to 1987
  - Hemodialysis (in settings with poor infection control)
  - Tattoos in unregulated settings (especially prisons)
  - Needle stick injury
  - Perinatal transmission 5%; 15-20% if HIV/HCV coinfected
  - Higher risk of sexual transmission among people living with HIV (especially men who have sex with men)

HCV Virus is Durable

- HCV infection from a contaminated syringe is 5-20-fold higher than it is for HIV
- HCV has been detected in all manner of drug using equipment: cookers, cotton, water, filters, even alcohol wipes.

Source: Thibault V, JID 2011

Cleaning as Prevention

- Ideally, a person has a new syringe and all other injecting equipment (cooker, cotton, water, etc.) for each use
- Bleach does kill HCV 99% of the time, so it is better than not cleaning if no other options
- Rubbing alcohol (70% isopropanol) also kills HCV, but you have to rinse and repeat the process 3 times
  - e.g. draw up the alcohol, rinse it and do that at least 2 more times

Source: Binka, OFID 2015

Prevention of HCV Transmission

To Prevent HCV Transmission

- Avoid sharing used toothbrushes, razors, etc.
- Prevent blood contact to non-intact skin/mucous membrane/etc.
- Encourage harm reduction and treatment service access for people who inject drugs, including MAT (i.e. buprenorphine/methadone) for people with opioid use disorders
- "Safe sex" (i.e. condoms + lubricant) recommended generally, but sexual transmission is rare if HIV negative

Other Messages

- Avoid/limit alcohol consumption
- Test for HIV, test & vaccinate for HAV/HBV
- Encourage screening of family members, as applicable
- Potential household exposure, kids born after HCV infection, all "baby boomers"
- Stage of fibrosis important to determine long term prognosis, treatment options, monitoring
- Great treatment options available to cure HCV

Source: Adapted from Ghany, et al. Hepatology. 2009;49:1335-1374

Screening Recommendation

- 1998: CDC recommends risk-based testing
- 2012: CDC expands recommendations to include one-time screening for "Baby Boomers" born between 1945 and 1965
- Some are already screening all persons over the age of 13

Source: CDC and Prevention. MMWR. 2012. RR61:1-32

Risk Based Screening

AASLD/IDSA Risk Based Screening Recommendations

Risk Exposures

- Long Term hemodialysis (ever)
- Getting a tattoo in an unregulated setting
- Healthcare/occupational exposure to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of transfusion or organ transplant
  - Notified that they received blood from HCV+ donor
  - Blood product or organ transplant prior to July 1992
  - Clotting factor concentrate produced before 1987
- Persons who were ever incarcerated

Risk Behaviors

- Injection Drug Use (current or ever)
- Intranasal illicit drug use

Other

- HIV infection
- Unexplained chronic liver disease including elevated ALT
- Solid organ donors (deceased and living)

Source: AASLD/IDSA Recommendations for Testing, Managing and Treating Hepatitis C (www.hcvguidelines.org)

HCV Screening Tests

Hepatitis C Antibody (Ab)

- If positive, tells you that the patient has been exposed to hepatitis C
- Requires follow-up blood draw for confirmatory RNA test
- Antibody is not protective, does not offer any immunity to Hepatitis C

Hepatitis C RNA (by PCR quantitative)

- If positive, tells you whether the patient is currently infected or not
  - ~15-25% of individuals clear HCV infection naturally

Hepatitis C Ab with Reflex to RNA

- Best screening test as it gives you the antibody screening and, if positive, automatically runs the RNA test confirming active infection (without additional blood draw)

Q: What about rapid tests?

- Can be used for quick turn around in 20 minutes for antibody only
- If positive, requires confirmatory blood draw for RNA test

Prescribing Information, Clinical Studies, and Slide Decks
All materials are available for download in their original formats as PDF or PowerPoint.

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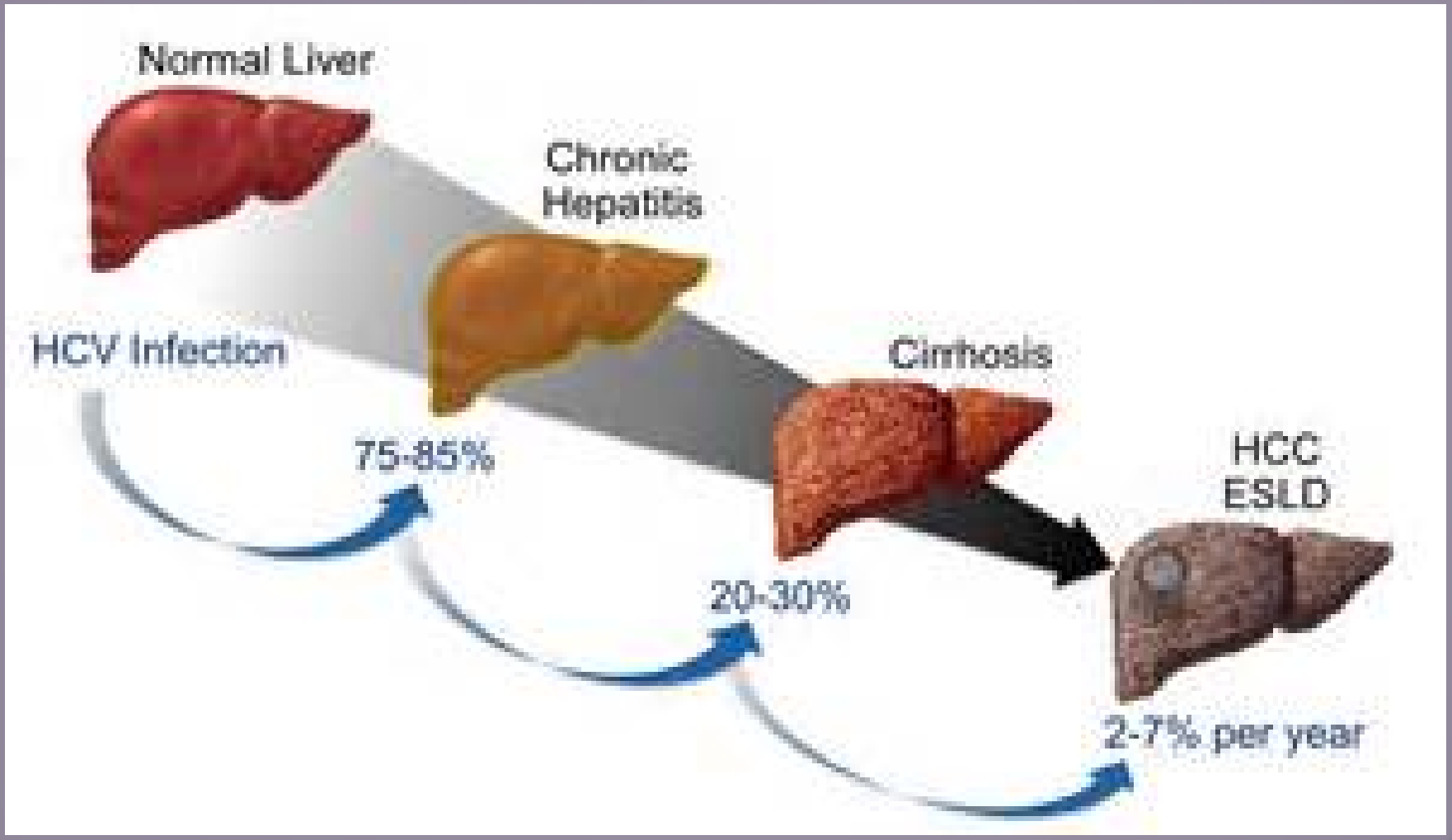
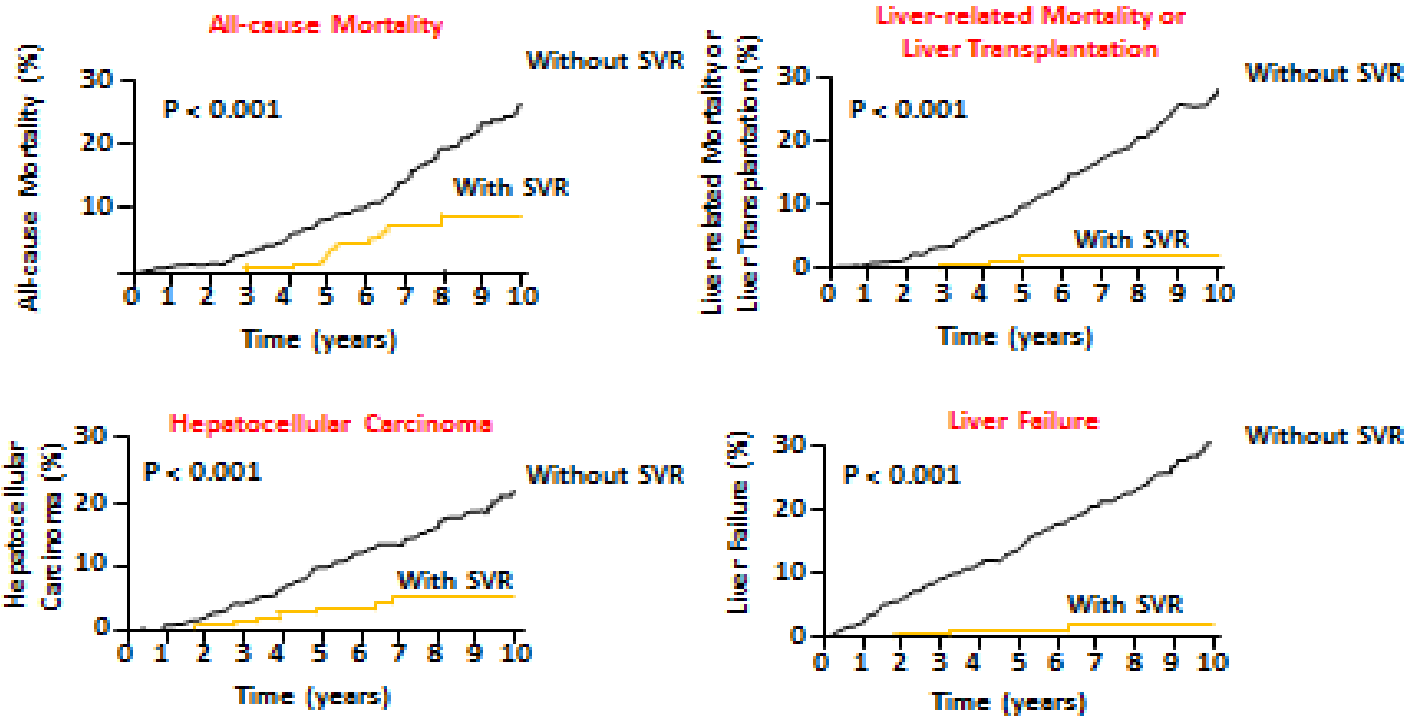
Source: www.hepatitisc.uw.edu; Accessed January 2, 2018

Progression of Liver Disease



Benefits of Treating HCV

SVR and All-Cause Mortality Benefits in Cirrhotics Treated With IFN-Based Therapy



van der Meer AJ et al. JAMA. 2012;308(24):2584-2593.

Summary: Extrahepatic Manifestations of HCV

Table 1. Extrahepatic manifestations of chronic HCV infection.

Affected systems	Reported conditions	Ref. no.
Cardiovascular and circulatory	MC vasculitis Coronary artery disease Carotid aterosclerosis Ischemic heart disease with coronary vasculitis, mitral valvular damage, pericarditis, and congestive heart failure	[7,8]
Endocrine	Insulin resistance T2D Type I diabetes mellitus	
Immune	MC B-cell lymphoproliferative diseases Autoantibodies Monoclonal gammopathies	[8,9]
Integumentary and exocrine	Purpura (main dermatological condition related to MC vasculitis) Raynaud's syndrome, acrocyanosis, livedo reticularis (less frequent) PCT Lichen planus Pruritus, psoriasis, polyarteritis nodosa, necrolytic acral erythema, HCV-related sicca syndrome	[10] [11,12]
Musculoskeletal	Fatigue, arthralgia (main joint condition related to MC vasculitis) HCV polyarthritis /mono-oligoarthritis (less frequent)	
Nervous	Cognitive impairment Fatigue Depression Sensory or sensory-motor polyneuropathy Multiple mononeuropathy	[8,13]
Renal	MC glomerulonephritis (MPG type I) Membranoproliferative glomerulonephritis without MC Membranous nephropathy Glomerulonephritis, focal segmental glomerulosclerosis, IgA nephropathy, fibrillary or immunotactoid glomerulopathy Renal insufficiency	[14] [15]
Respiratory	Subclinical alveolitis Pulmonary intra-alveolar hemorrhages	[8,13]

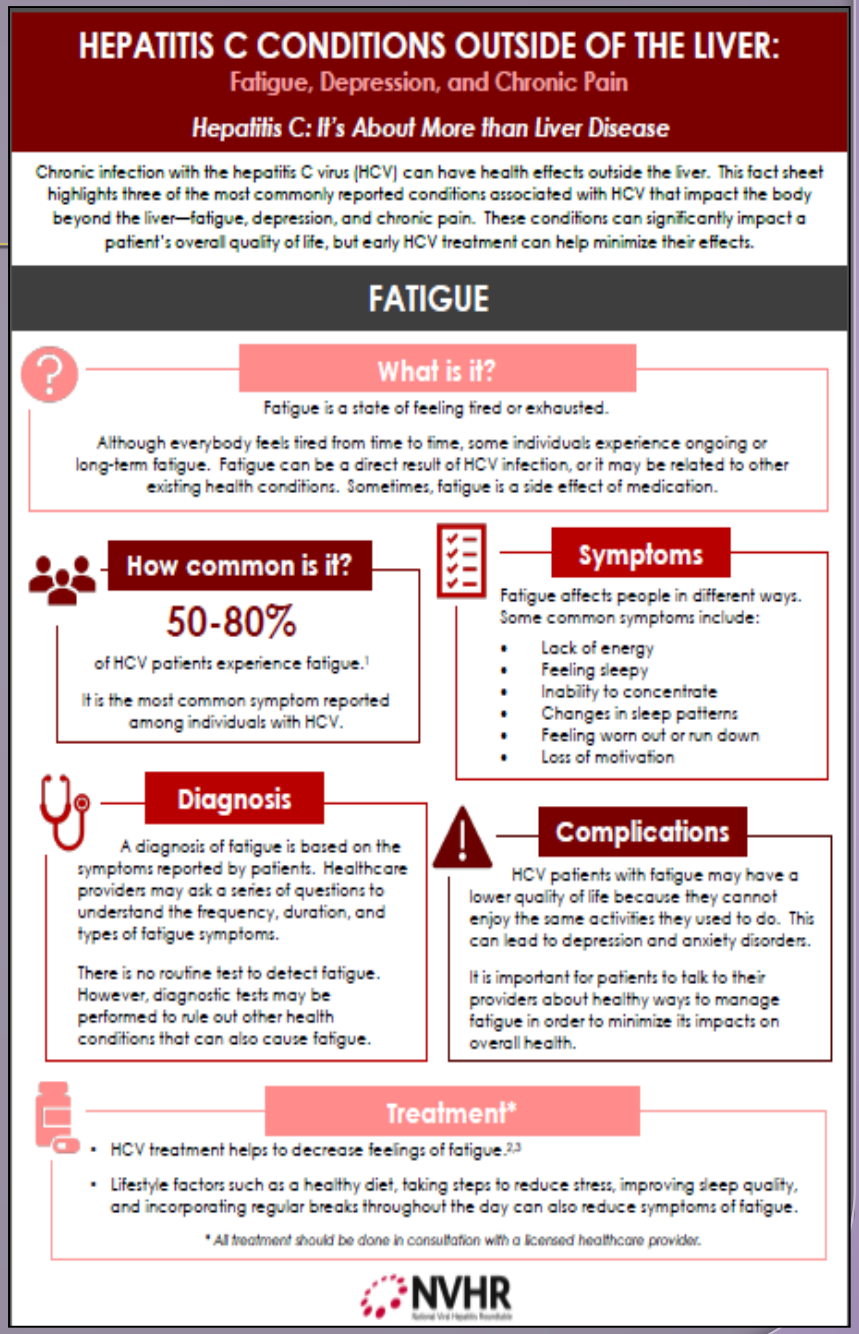
MC: mixed-cryoglobulinemia; MPG: membranoproliferative glomerulonephritis; T2D: type II diabetes mellitus; PCT: porphyria cutanea tarda; HCV: hepatitis C virus.

From Polo ML, Laufer N. Extrahepatic manifestations of HCV: the role of direct acting antivirals. Expert Rev Anti Infect Ther. 2017 Aug; 15(8): 737-746

HCV is a systemic disease!

- Leads to development of immunologic, autoimmune, and viral phenomena throughout the body
- It is estimated that 40% to 74% of patients with chronic HCV will develop at least one extrahepatic manifestation throughout the course of their illness, leading to ↑ treatment cost and overall economic burden

http://nvhr.org/sites/default/files/.users/u34/EHM%20Fact%20Sheet%203.pdf



HEPATITIS C CONDITIONS OUTSIDE OF THE LIVER:

Fatigue, Depression, and Chronic Pain

Hepatitis C: It's About More than Liver Disease

Chronic infection with the hepatitis C virus (HCV) can have health effects outside the liver. This fact sheet highlights three of the most commonly reported conditions associated with HCV that impact the body beyond the liver—fatigue, depression, and chronic pain. These conditions can significantly impact a patient's overall quality of life, but early HCV treatment can help minimize their effects.

FATIGUE

What is it?

Fatigue is a state of feeling tired or exhausted.

Although everybody feels tired from time to time, some individuals experience ongoing or long-term fatigue. Fatigue can be a direct result of HCV infection, or it may be related to other existing health conditions. Sometimes, fatigue is a side effect of medication.

How common is it?

50-80%

of HCV patients experience fatigue.[1]

It is the most common symptom reported among individuals with HCV.

Symptoms

Fatigue affects people in different ways. Some common symptoms include:

- Lack of energy
- Feeling sleepy
- Inability to concentrate
- Changes in sleep patterns
- Feeling worn out or run down
- Loss of motivation

Diagnosis

A diagnosis of fatigue is based on the symptoms reported by patients. Healthcare providers may ask a series of questions to understand the frequency, duration, and types of fatigue symptoms.

There is no routine test to detect fatigue. However, diagnostic tests may be performed to rule out other health conditions that can also cause fatigue.

Complications

HCV patients with fatigue may have a lower quality of life because they cannot enjoy the same activities they used to do. This can lead to depression and anxiety disorders.

It is important for patients to talk to their providers about healthy ways to manage fatigue in order to minimize its impacts on overall health.

Treatment*

- HCV treatment helps to decrease feelings of fatigue.[2,3]
- Lifestyle factors such as a healthy diet, taking steps to reduce stress, improving sleep quality, and incorporating regular breaks throughout the day can also reduce symptoms of fatigue.

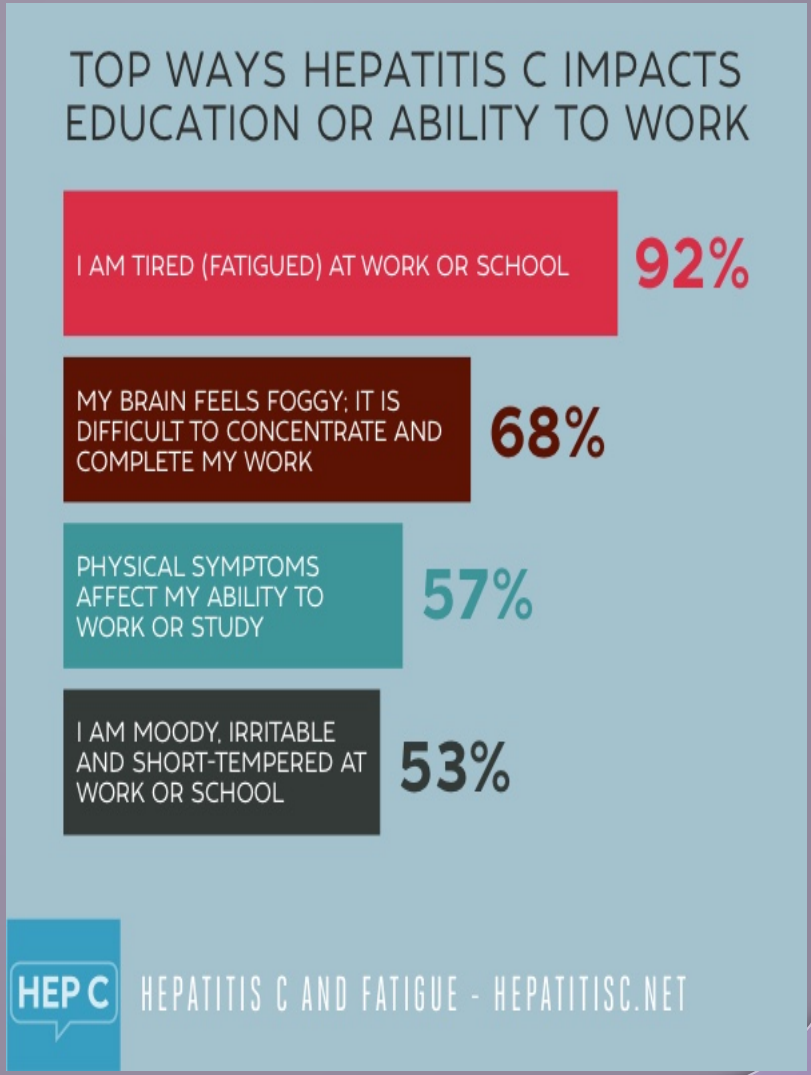
** All treatment should be done in consultation with a licensed healthcare provider.*

NVHR


I'M AFRAID MY BRAIN HAS LEFT FOR THE DAY

HCV and the Brain

- Can lead to cognitive impairment ("brain fog")
  - Memory impairment, fluctuating disorientation, mental fatigue
- Increases risk of cerebrovascular events, including stroke



Insulin Resistance and HCV

- HCV interferes at several steps in the signaling pathway via an increased proteasomal degradation of insulin receptors and other protein synthesis pathways (2,3)
- There is evidence for both hepatic and peripheral insulin resistance, and this is in spite of the fact that HCV only directly infects the liver. (4,5)
- Insulin resistance occurring in patients with HCV recognizes dual pathogenesis, both direct and/or indirect action of the virus and host factors. (4,5)
- Insulin resistance is an independent risk factor for accelerated fibrogenesis and for the development of hepatocellular carcinoma (1).

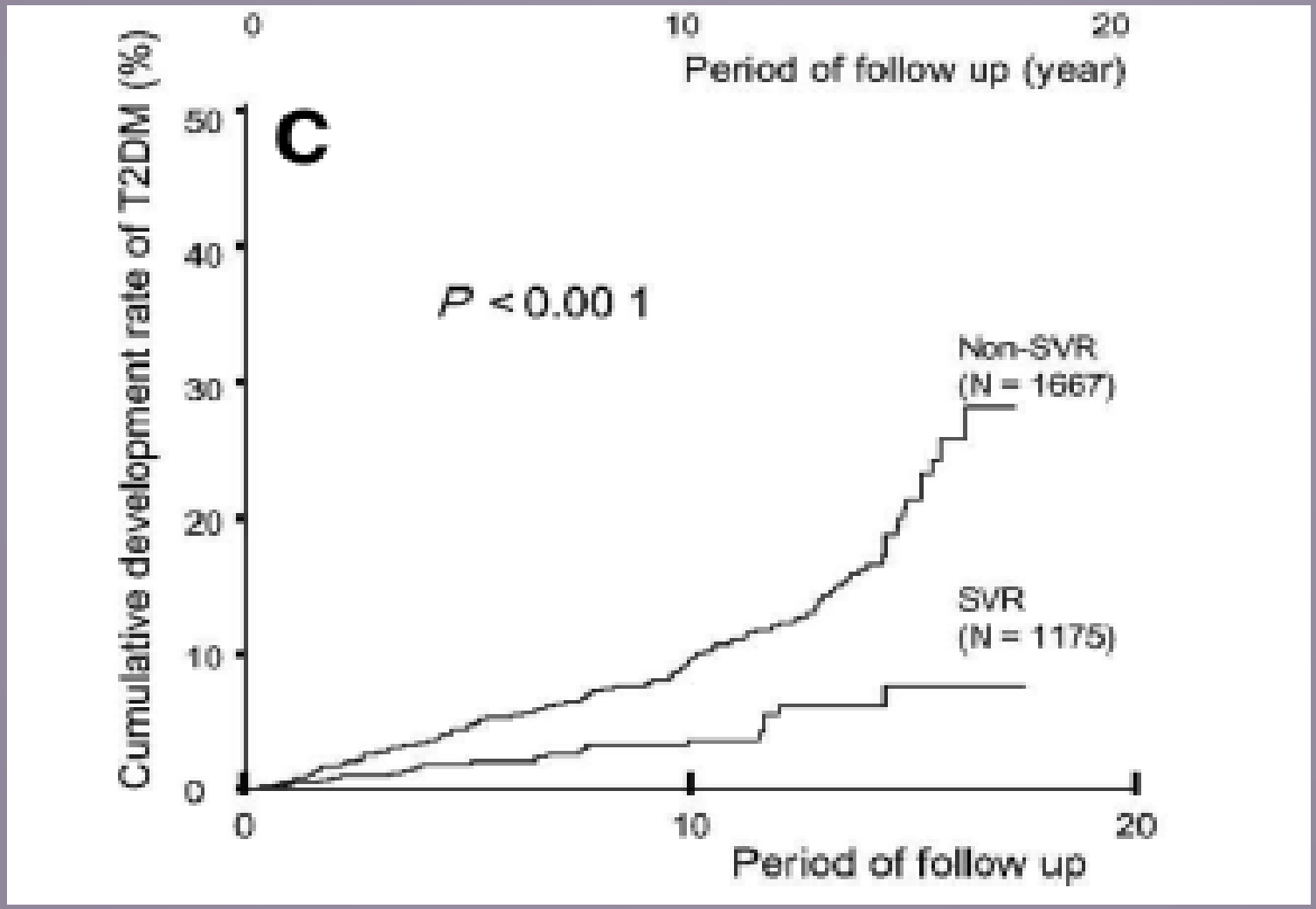
- 1. Bugianesi, E, Salamone, F, Negro, F. The interaction of metabolic factors with HCV infection: does it matter? J Hepatol 2012, 56(suppl 1):S56-S65.
- 2. Aytug, S, Reich, D, Sapiro, LE, Bernstein, D, Begum, N. Impaired IRS-1/PI3-kinase signaling in patients with HCV: a mechanism for increased prevalence of type 2 diabetes. Hepatology 2003, 38:1384-1392.
- 3. Kaddai, V, Negro, F. Current understanding of insulin resistance in hepatitis C. Expert Rev Gastroenterol Hepatol 2011, 5:503-516.
- 4. Vanni, E, Abate, ML, Gentilcore, E, Hickman, I, Gambino, R, Cassader, M, et al. Sites and mechanisms of insulin resistance in nonobese, nondiabetic patients with chronic hepatitis C. Hepatology 2009, 50:697-706.
- 5. Milner, KL, van der Poorten, D, Trenell, M, Jenkins, AB, Xu, A, Smythe, G, et al. Chronic hepatitis C is associated with peripheral rather than hepatic insulin resistance. Gastroenterology 2010, 138:932-941, e931-933.

Management of DM/ Metabolic Syndrome

- **DM, HTN, hyperlipidemia**
  - Obesity associated with accelerated fibrosis progression
  - Aggressively manage metabolic syndrome risk factors
  - Check lipid panel and HbA1c annually
- **Weight loss of 7-10% of total body weight improves both steatosis and inflammation**
  - Restrict caloric intake:
    - 1200 – 1500 kcal/day for women
    - 1500 to 1800 kcal/day for men
  - Encourage aerobic exercise to decrease intrahepatic TG and increase hepatic insulin sensitivity
  - Increase baseline steps per day to goal of 10-12,000 per day
  - Exercise 2.5 hours aerobic plus resistance training per week for NAFLD
- **Pharmacotherapy (if indicated)**
  - Statins are OK in liver disease, monitor for increase in ALT
  - Treat diabetes appropriately
  - Vitamin E increases risk of cardiovascular events in persons with DM and NAFLD
- **Treat and cure HCV**

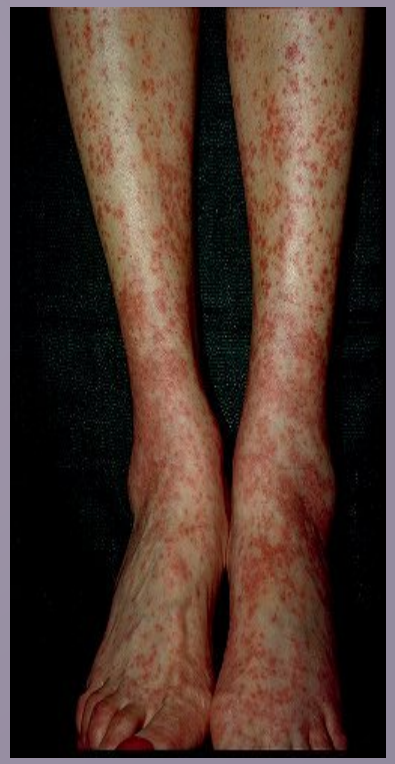
- *Marchesini, et al. Hepatoloogy, 2015.*

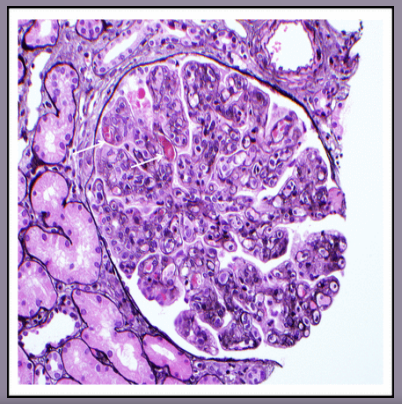
Lower risk of Diabetes After SVR



HCV-Associated Rheumatologic Disorders

- Wide range of complications: includes frank auto-immune and rheumatic diseases (i.e. arthralgia, myalgia, arthritis, sicca syndrome, vasculitis)
  - Mixed cryoglobulinemia vasculitis (CryoVas): systemic vasculitis → clinical manifestations ranging from purpura, arthralgia and fatigue to more serious lesions with neurologic and renal involvement





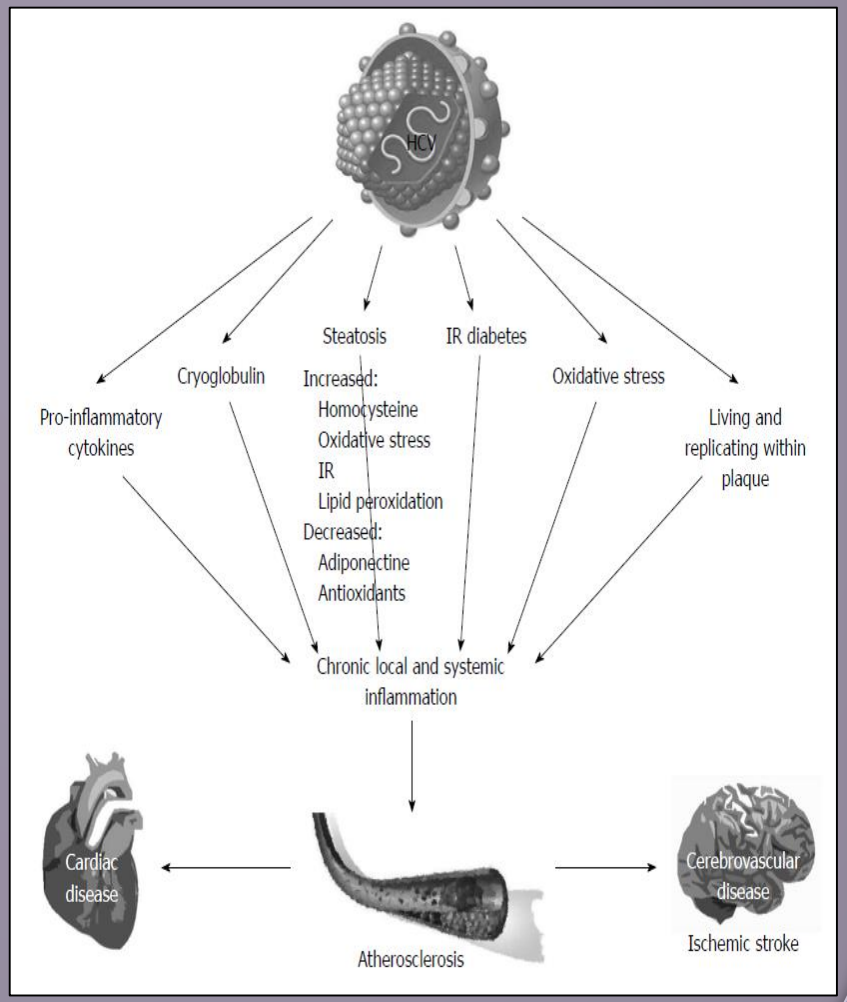
Circulating mixed cryoglobulins detected in 40–60% of patients with chronic HCV; overt CryoVas observed in only 5–10%.

Cardiopulmonary Manifestations

- ~17-37% of people living with chronic HCV have HCV-related heart disease
- Most common manifestations: cardiomyopathies, myocarditis, cardiovascular disease (stroke, atherosclerosis, coronary artery disease), peripheral artery disease

- Primary (*direct*) pulmonary outcomes include: COPD, idiopathic pulmonary fibrosis, asthma, interstitial lung diseases

Can also *indirectly* affect lungs and pulmonary vasculature via mixed cryoglobulinemia, hepatopulmonary syndrome, portopulmonary hypertension



Adinolfi LE, Zampino R, Restivo L, et al. Chronic hepatitis C virus infection and atherosclerosis: clinical impact and mechanisms. World J Gastroenterol. 2014 Apr 7; 20(13): 3410-3417.

HCV and the Cardiovascular System

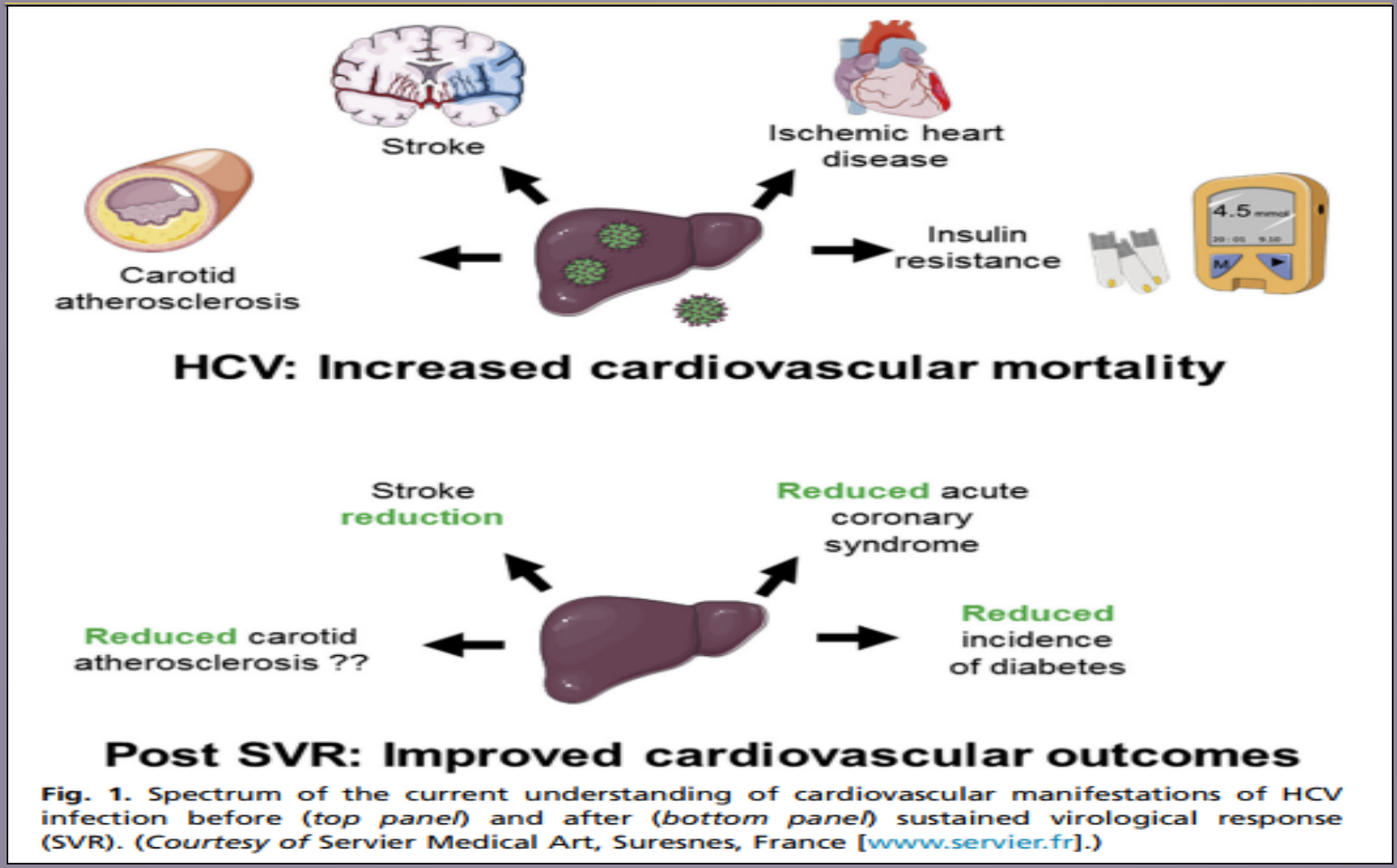


Fig. 1. Spectrum of the current understanding of cardiovascular manifestations of HCV infection before (*top panel*) and after (*bottom panel*) sustained virological response (SVR). (*Courtesy of* Servier Medical Art, Suresnes, France [www.servier.fr].)

HCV and the Kidney

- Renal involvement can be one of HCV's most severe extrahepatic manifestations
- Broad spectrum of histopathologic lesions
- Clinical presentation ranges: completely asymptomatic (mild urinary abnormalities) → end-stage renal failure

Need eGFR > 30 mL/min/1.73 mm^2 for some HCV treatment medication

Table 1
Histopathological features of hepatitis C virus–related renal involvement

Renal Disease Pattern	Histologic Features	Frequency
Diffuse or focal MPGN	Mesangial cells proliferation plus deposits of immune complexes, including HCV particles, complement fragments, immunoglobulins with/without cryoprecipitation capability; frequently, double contour appearance of the capillary wall	Typically found
Mesangial proliferative GN	Diffuse mild mesangial matrix expansion and mesangial cells proliferation	Occasionally found
Tubulointerstitial nephritis[a]	Interstitial fibrosis and infiltrating leukocytes, usually focal, with negative immunofluorescence	Rare
Membranous GN	Subepithelial deposits of immune complexes and C3	Rare
IgA nephropathy	Mesangial IgA deposits	Rare
Thrombotic microangiopathy[b]	Arterioles showed intimal thickening, swollen endothelium, narrowed glomerular capillary lumen, and thrombi that may extend into afferent arterioles	Rare
Focal segmental glomerulosclerosis	Sclerosed glomeruli and tubular atrophy, negative immunofluorescence, deletion of podocytes of epithelial cells (electronic microscopy)	Anecdotal
Immunotactoid glomerulopathy fibrillary GN	Extracellular deposits of microfibrils within the mesangium and glomerular capillary walls; Ig (mainly IgG4) and C3 immunofluorescence	Anecdotal

Abbreviation: GN, glomerulonephritis.
[a] Interstitial fibrosis and infiltrating leukocytes are associated with greater than 60% MPGN, whereas an isolated interstitial nephritis is rare.
[b] Endoluminal thrombi are frequently associated with other pathologic patterns (>50% of MPGN); besides, a peculiar form in the context of a hemolytic uremic syndrome was rarely described in renal transplanted patients.

Acetaminophen vs Ibuprofen

Acetaminophen

- NSAID w/minor effects on Cox-1 and Cox-2, produces analgesia by ↓ pain thresholds through inhibition of nitric oxide pathway
- Harmless at low doses, hepatotoxic >7.5g
- Therapeutic doses can → transient ↑LFT
- Injury due to direct toxic effect of high usually >15 gram dose.
- Hepatic injury starts in 24 to 72 hours with marked ↑ ALT and AST >2000 U/L, followed at 48 to 96 hours by: jaundice, confusion, hepatic failure and in some death. Possible renal insufficiency. LFT ↓ promptly, recovery is rapid if the injury is not too severe.

Acetaminophen is preferred over NSAID in liver disease, up to 2g a day.

Ibuprofen

- Potent inhibitor Cox-1 and Cox-2
- Can → asymptomatic flares of chronic HCV
- ↑ ALT occur full doses of 2,400 to 3,200 mg daily up to 16%
- Overdose >5-10 grams starts in 3 to 6 hours with agitation and stupor followed by coma, respiratory depression and lactic acidosis which can be fatal.
- Inhibits renal prostaglandins which → renal vasoconstriction and ↓ response to diuretics
- Can precipitate ARF
- ↑ Risk of GI bleed
- **Avoid in all patients with cirrhosis**
- Livertox.nlm.nih.gov

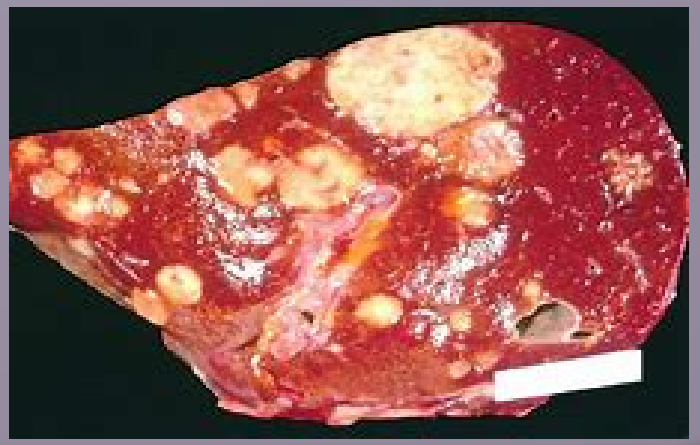
Hepatocellular Carcinoma (HCC) Screening

- Screen anyone with stage 3-4 fibrosis
- Ultrasound with or without alpha-fetoprotein (AFP) every 6 months.
- The added value of AFP to ultrasound in surveillance has been questioned. AFP no longer included in 2011 IDSA/AASLD guidelines.
- Consider cross sectional imaging (MRI or CT if liver is dense and poorly penetrated by ultrasound)

- ***Bruix J & Sherman M - AASLD guidelines; Hepatology 2011:53:1020-1022***

HCC Surveillance in Persons with Advanced Fibrosis

- IDSA/AASLD Guidelines
  - In pts with chronic HCV, insufficient evidence to suggest surveillance before developing cirrhosis
- HALT-C cohort: HCV positive patients with at least advanced fibrosis, median f/u nearly 7 years
  - Of 427 pts w/cirrhosis: 11.2% developed HCC (Metavir F4/4, Ishak 6/6)
  - Of 621 pts w/advanced fibrosis w/out cirrhosis, 6.4% developed HCC (Ishak 3-5/6)



- *Tayob N, CGH 2015, epub ahead of print*
- *Bruix J & Sherman M - AASLD guidelines;*
- *Hepatology 2005;42:1208-1236*

Alpha-Fetoprotein (AFP)

- AFP as a screening test:
  - 40% *with* HCC have normal AFP
  - Up to 25% *without* HCC have abnormal AFP
- The higher the AFP, the more likely the diagnosis of HCC
- DCP (PIVKA-II) and AFP-L3 not better than AFP and don't clearly add additional information
- ***Trevisani F, J Hepatol 2001;34:570; Marrero JA et al. Gastroenterology 2009;137:110-118***

Perinatal HCV transmission

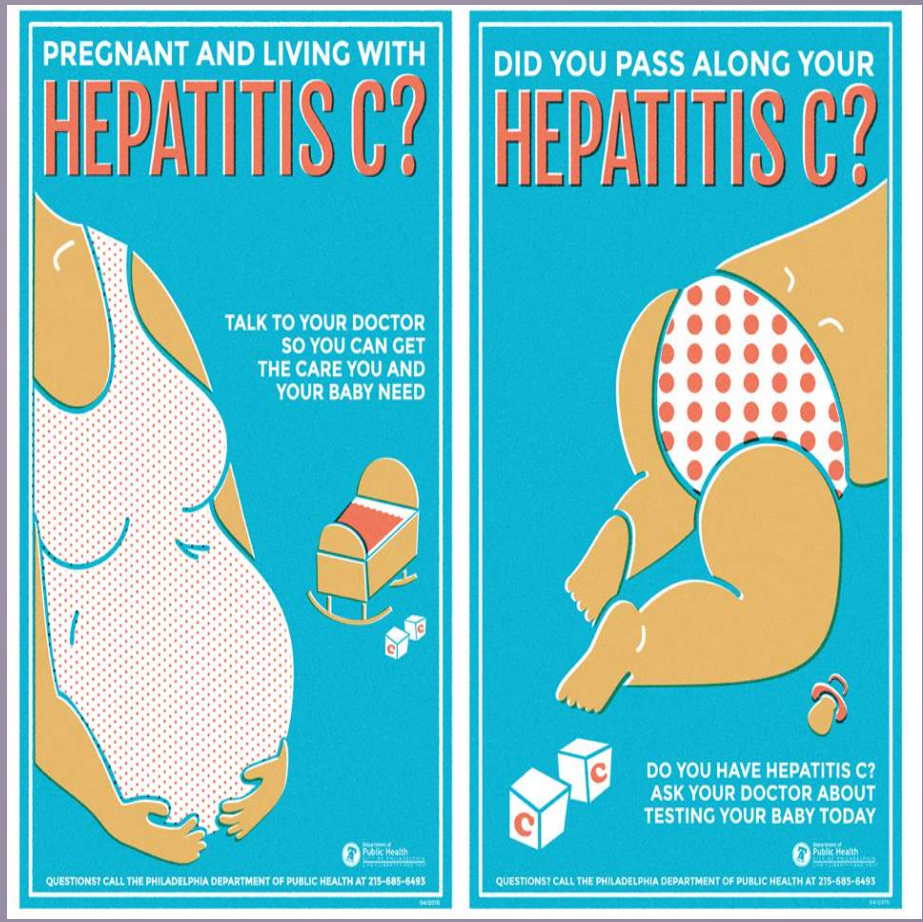
- Exact transmission timing during pregnancy unknown
- Occurs almost exclusively in women with HCV viremia

Major risk factors for perinatal transmission:

- **Maternal HIV co-infection**
- **Detectable HCV viremia during pregnancy/?degree**

Mother-to-child transmission has **NOT** been associated with mode of delivery or breastfeeding*

*Note: mothers with HCV should not breastfeed if damaged, cracked, or bleeding nipples



Natural History of HCV in Children and Adolescents

- Infections acquired in infancy:
  - 20-45% spontaneous clearance before age 2
  - 6-12% after age 2
- Markers of likely chronic infection
  - + HCV RNA after 1-2 years of age; monitoring/assessing for perinatal HCV transmission is an area of active discussion
  - Usually asymptomatic
  - Usually with normal AST/ALT and liver function
- Bridging fibrosis/cirrhosis: 4-6%
- Decompensated cirrhosis: 2%
- Risk factors for progression in pediatric patients not well-defined

- Mohan P et al. Evaluating progression of liver disease from repeat liver biopsies in children with chronic hepatitis C. Hepatology 2013; 58:1580.
- Bortolotti F et al. Long-term course of chronic hepatitis C in children: from viral clearance to end-stage liver disease. Gastroenterology 2008; 134:1900.

FDA-Approved Treatment Regimens for HCV in Adolescents

- **•Ledipasvir 90mg/sofosbuvir 400mg (Harvoni®) Genotype 1, 4, 5, 6**
  - ≥12 years of age, ≥35 kg
  - Non-cirrhotic, or compensated cirrhosis
  - Treatment-naïve or experienced
- **•Sofosbuvir 400mg (Sovaldi®) + Ribavirin Genotype 2 or 3**
- https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm551407.htm

Coffee, Herbs & Supplements

- **Coffee**
  - **HALT-C trial: 766 patients with bridging fibrosis/cirrhosis with food intake diary**
  - **Coffee consumption (>3 cups/day) was associated with lower risk of disease progression**
- **Herbs and Supplements**
  - **No established role in liver disease.**
  - **St. John's Wort known to interact with HCV medications**

Counseling Messages:

Coffee seems to be hepato-protective
Beware of potential hepatotoxicity of herbs & supplements
Advise patients to stop all herbs & supplements during HCV treatment

- **Livertox.nlm.nih.gov**

- *Freedman, N. D., Everhart, J. E., Lindsay, K. L., et al.*
- *Hepatology. 2009; 50: 1360–1369.*

Milk Thistle (Silymarin)

- **Animal model data suggest hepatoprotection during varying liver insults**
- **SyNCH trial (2012): double-blind, placebo-controlled**
- **No change in serum ALT or HCV RNA during 24 weeks of silymarin**
- **HALT-C study (2008)**
- **No difference in anti-HCV efficacy or ALT, but somewhat better quality of life**

Counseling Message:
Insufficient evidence to support milk thistle use, but appears to be safe.
Milk thistle should be stopped during HCV treatment

- *Fried MW, Navarro VJ, Afdhal N, et al. JAMA. 2012;308:274-282.*
- *Seef LB, Curto TM, Szabo G, et al. Hepatology. 2008.*
- *Feld JJ, Modi AA, El-Diwany R, et al. Gastroenterology. 2011;140(3): 830-9.*

Alcohol Use

- **Safe level for those with underlying liver disease is unknown**
- **Harmful drinking levels; strongly counsel against**
  - **≥ 2 drinks per day for women**
  - **≥ 4 drinks per day for men**
- **Abstinence is recommended for all patients with significant fibrosis (F2 or higher)**
- **Reduce to non-harmful levels in all**

- *Thun, MJ, Peto R, Lopez AD, et al. NEJM. 1997.*
- *Poynard T, Bedossa P, Opolon P. Lancet. 1997.*
- *Monto A, Patel K, Bostrom A, et al. Hepatology, 2004.*

Cannabis Use

- **Daily cannabis use associated with progression of advanced liver disease and an independent risk factor for moderate to severe fibrosis**
  - Associated with a sevenfold higher odds of moderate to severe fibrosis compared to non-daily users
  - Recommend non-daily use in those with advanced fibrosis who use

Not a requirement to stop using marijuana or alcohol before treating for HCV

- *Ishida JH. Clin Gastroenterol Hep. 2008.*
- *Hezode C. Gastroenterology. 2008.*
- *Freedman, N. Hepatology. 2009.*

Summary

- U.S. prevalence of HCV: ~3.5-5.2 million
- Transmission mainly via IDU
- Many extra-hepatic manifestations can improve with cure
- Interferon-free treatment for adolescents
- HCC screening every 6 months if F3-4
- The good, the bad and the borderline:
  - Good: Coffee, Acetaminophen
  - Bad: Herbs, Ibuprofen, Alcohol
  - Borderline: Cannabis

LOVE IS LIKE A VIRUS
IT CAN HAPPEN TO
ANYBODY AT ANY TIME

Maya Angelou

Resources

- www.hcvguidelines.org
- www.hepatitisc.uw.edu
- Hep-druginteractions.org
- www.hcvdruginfo.ca/tables.html
- HCVECHO@ucsf.edu
- Livertox.nlh.nih.gov
- nccc.ucsf.edu: UCSF Clinical Consultation Center for HIV/HCV/substance use

Comparison of various fibrosis assessment tools

	APRI or FIB-4	FibroSure™ FibroTest™	Transient elastography	Liver biopsy
Methodology	Uses indirect biochemical markers of fibrosis	Measures indirect serum markers of fibrosis, based on age, gender, serum haptoglobin, α2 macroglobulin, apolipoprotein A1, GGT, bilirubin	Measures liver stiffness by detection of ultrasound-propagated shear waves. [MR elastography clinically superior to TE but may be cost-prohibitive, also may not be widely available]	Direct observation of fibrosis
Accuracy for detecting cirrhosis	Moderate	High	High	High
Accuracy for detecting intermediate fibrosis	Low	Moderate	Moderate to high	High
Complication risk	Minimal	Minimal	Minimal	Risk of pain/bleeding
Disadvantages	Minimal (see limitations below)	Minimal (see limitations below)	Decreased accuracy if obesity and/or narrow rib spaces	Invasive; contraindicated if coagulopathy
Limitations	Falsely elevated if acute hepatitis (of any etiology). Not good for detecting intermediate fibrosis.	Falsely elevated if hemolysis, inflammation, Gilbert's, atazanavir use. Not good for detecting intermediate fibrosis	False-positives with inflammation, congestion	Sampling error; observer variation; not suitable for longitudinal monitoring
Cost	Low per-test cost	Moderate	High initial equipment cost	Highest per-test cost

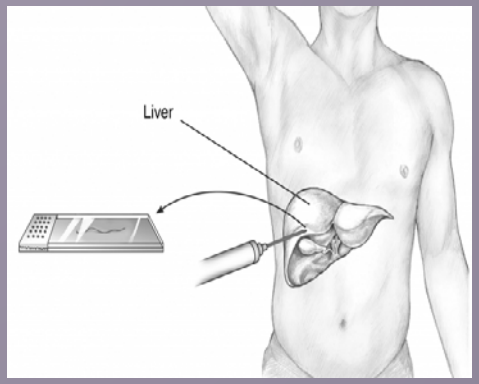
Non-invasive staging:

	Performance	Notes
APRI - AST - Platelets - AST ULN	> 1.0: up to 76% sens and 72% spec for predicting cirrhosis. > 1-1.5: assoc. with advanced fibrosis (METAVIR F3) > 2.0: assoc. with cirrhosis (METAVIR F4): 46% sens, 91% spec	Good utility for predicting severe fibrosis/cirrhosis or low risk of significant fibrosis *Doesn't differentiate well between intermediate and either mild or severe fibrosis*
FIB-4 - Age - AST - ALT - Platelets	< 1.45: 74% sens and 80% spec in excluding significant fibrosis > 3.25: 98% spec in confirming cirrhosis	Good at excluding or confirming cirrhosis *If between 1.45 and 3.25, need another method to assess/predict fibrosis*
FibroSure - Age - Gender - 6 bio-marker composite	Estimates grade and stage in report < 0.31: 91% NPV for absence of clinically significant fibrosis > 0.48: 61% PPV for presence of significant fibrosis (76% if use cutoff of 0.72)	Good at excluding or confirming cirrhosis; *indeterminate for mid-range* *Cost; not widely available* *Not accurate if certain conditions (i.e. Gilbert's, acute hemolysis, renal insufficiency, post-transplant)*

Invasive assessment: liver biopsy

- Still gold standard, but obvious drawbacks! Provides objective, semi-quantitative info regarding amount and pattern of collagen or scar tissue
- Report gives grade *(degree of inflammation reflecting ongoing liver disease injury)* and stage *(amount of currently established fibrosis)*
  - Metavir (F0-F4) and Ishak (0-6) fibrosis scores commonly used to describe the amount of hepatic collagen.

When to consider? If 2 non-invasive markers discordant; when concurrent liver disease suspected (i.e. indirect markers or imaging shows more significant fibrosis than expected); can be considered when indirect, direct, and TE testing unavailable; also-- to help confirm if HCC surveillance indicated



Non-invasive staging:Imaging

Table 13. Diagnosis of Compensated Cirrhosis for the Purpose of Identifying Treatment Candidates

Method	Comment
Clinical Findings	• Physical exam findings (palpable left lobe, splenomegaly, palmar erythema) AND • Low platelet count (<100,000/mm^3)* AND • Abdominal imaging findings (see below)
Abdominal Imaging • Ultrasound • Computed tomography (CT) • Magnetic resonance imaging (MRI)	• Surface abnormalities (e.g., nodularity, and left lobe/caudate lobe hypertrophy) are suggestive of cirrhosis. • Features of portal hypertension (e.g., splenomegaly, recanalization of umbilical vein, collaterals) and ascites also are suggestive of cirrhosis.
Liver Fibrosis Imaging • Vibration-controlled transient elastography (Fibroscan®) • Acoustic radiation force impulse imaging (ARFI)	• Both elastography and ARFI are FDA-approved, ultrasound-based techniques for estimating the extent of liver fibrosis. • Fibroscan value of >12.5 kilopascals has been associated with histologic cirrhosis. • ARFI value of >1.75 meters/second has been associated with histologic cirrhosis.

[www.hepatitis.va.gov/pdf/treatment-considerations-2015-02.pdf]