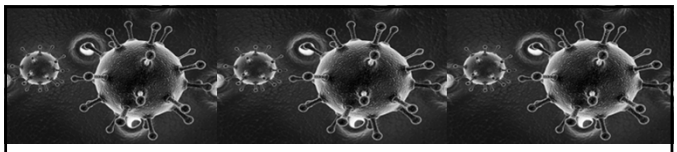

Hepatitis C Virus:
Understanding the epidemic

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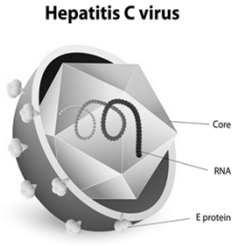
Objectives

1) Describe the Hepatitis C virus (HCV), including transmission, disease progression, risk factors, and clinical significance.
2) Evaluate global and national HCV statistics.
3) Discuss HCV diagnostic testing procedures and treatment regimens.

Definitions

Hepatitis C (HCV) – the basics



- Single stranded RNA virus
- Classified as "non-A, non-B" before 1989
- Seven different genotypes, G1-G7

HCV – transmission

- Exposure to contaminated blood and body fluids
  - IV drug use
  - Blood transfusion and organ transplant (before 1992)
  - Needlestick injury
  - Sexual contact
  - Perinatal
  - Unregulated body piercing and tattooing

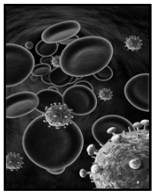
Health Officials Shut Down Unregulated Tattoo Parlor at Magnolia Home

Posted: Feb 27, 2017 11:32 AM CST
Updated: Feb 27, 2017 11:32 AM CST

DOVER, Del. - A Magnolia man has been ordered to stop giving people tattoos out of his home after it was discovered he was doing so without a permit.
According to the Delaware Division of Public Health, 38-year-old **William Smiley** had been conducting tattooing activities out of his home on Grays Lane in Magnolia without a required body art establishment permit. DPH staff say they were also unable to confirm Smiley was using proper sanitary precautions.

http://www.wboc.com/story/34614898/health-officials-shut-down-unregulated-tattoo-parlor-at-magnolia-home

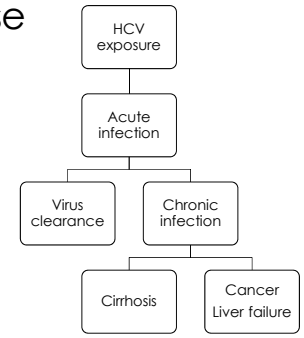
HCV transmission



- **Cannot** be spread through
  - Breast milk
  - Food and water
  - Hugging, kissing
  - Sharing food or drinks with infected person

HCV – the disease

- 15-40% clear virus w/out treatment
- 60-85% will develop chronic HCV
- Of those with chronic HCV, risk of cirrhosis is 15-30%



HCV – acute phase

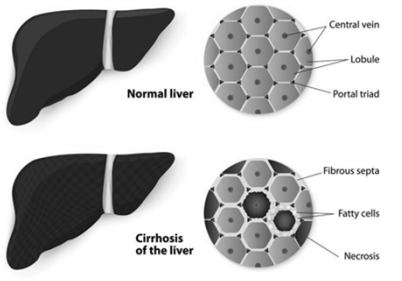
- Acute phase lasting @ 6 mths
- Symptoms appear 6 – 7 weeks
- HCV virus detectable in serum by 1 – 2 weeks
- Antibodies to HCV detectable by 10 – 11 weeks
- Liver enzymes spike, then return to normal

- Symptoms include:
  - Jaundice
  - Fatigue
  - Nausea
  - Fever
  - Muscle aches

HCV – chronic phase

- Viral infection for many years, long enough to damage the liver
- HCV virus persistent in serum
- Antibodies to HCV persistent in serum
- Liver enzymes variable

- Symptoms include:
  - Fatigue
  - Jaundice, dark urine
  - Decreased appetite
  - Weight loss
  - Fluid buildup in abdomen (ascites)
  - Dermatological issues
  - Vasculitis
  - Rheumatoid issues
  - Multi-organ involvement



Liver disease progression

- Fat deposits between hepatocytes, causing enlarged liver
- Inflammation results in scar tissue and fibrosis
- More connective tissue accumulates
- Necrosis of hepatocytes
- Blood flow is obstructed
- Carcinoma develops

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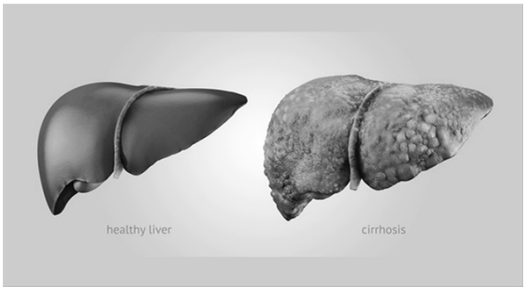
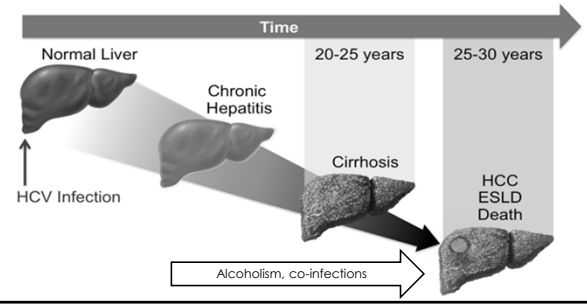
HCV – disease progression



HCV – disease progression



Who is most at risk?

- Current or past injection or intranasal drug users
- Anyone who has had sexual contact with an HCV+ person
- Anyone born between 1945 – 1960
- Children born to HCV+ mothers
- Long-term hemodialysis patient
- Healthcare and emergency workers
- People exposed to unsanitary piercing or tattoo equipment
- Hemophiliacs treated with clotting factors before 1987
- Blood and organ recipients before 1992
- People with HIV
- People who are/were in jail or prison
- People who have shared personal care items with known HCV+ person
- Anyone with unexplained liver problems or inflammation, including abnormal liver tests

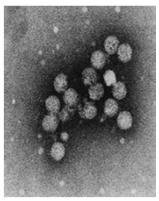
HCV – clinical significance

- Most common bloodborne infection in US
- Most frequent cause of liver disease and liver cancer
- Leading indicator for liver transplant
- No vaccine available; research ongoing
- No marker to predict when/if acute becomes chronic
- Current epidemic correlated to injection drug use epidemic (opioid)

Statistics

HCV by the numbers, worldwide

- 71 million people infected
- 1.8 million new infections in 2015
- 339,000 deaths each year



http://www.who.int/mediacentre/factsheets/fs164/en/

World Health Organization

HCV by the numbers, United States

- 3.5 million people infected (chronic)
- 2436 new cases per year (reported)
- 33, 900 new cases (estimated)
- 20,000 deaths each year

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

https://www.cdc.gov/hepatitis/statistics/index.htm

Why do we have an HCV epidemic?

- Because we have an opioid epidemic
- IDU is primary risk factor for HCV transmission
- IDU is now the leading cause of HCV incidence in the US
- Virus can circulate quickly through networks of PWID
- POAs are major influence

IDU	• injection drug use
PWID	• person who injects drugs
POA	• prescription opioid analgesic

Per CDC: https://ajph.aphapublications.org/doi/pdf/10.2105/AJPH.2017.304132

What are opioids?

- Narcotic pain medication
- Bind opioid receptors in brain, spinal cord
- Interfere with pain message signaling to the brain
- Incurs tolerance, dependence, and addiction

Generic name	Brand name
Codeine	
Fentanyl	Actiq, Duragesic, Fentora
Hydrocodone	Hysingla ER, Zohydro ER
Hydrocodone/ acetaminophen	Lorfab, Norco, Vicodin
Hydromorphone	Dilaudid
Meperidine	Demerol
Methadone	Dolophine, Methadose
Morphine	Kadian, MS Contin
Oxycodone	OxyContin, Oxaydo
Oxycodone/ acetaminophen	Percocet, Roxicet
Oxycodone/ naloxone	Targin, Targiniq, Targinact

The HCV/opioid epidemic

- Report published by CDC in *American Journal of Public Health (AJPH)*:

HCV incidence

↑ 400% in persons aged 18 to 29

↑ 325% in persons aged 30 to 39

2004 – 2014

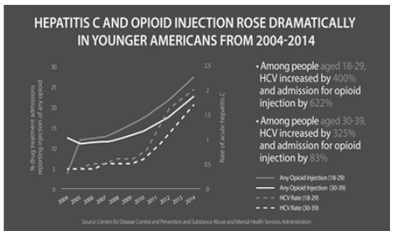
Treatment admission for IDU, age 18 to 29

↑ 622% for any opioid injection

↑ 603% for heroin injection

↑ 817% for POA injection

https://ajph.aphapublications.org/doi/pdf/10.2105/AJPH.2017.304132

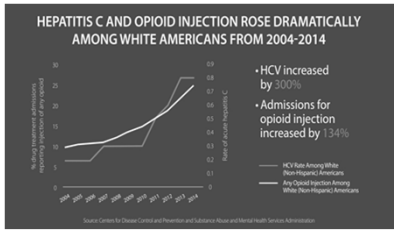


The dual epidemic

Young Americans,

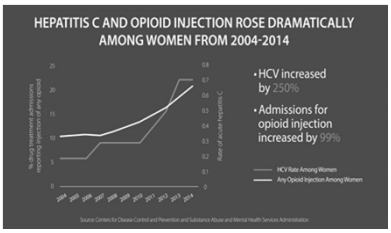
age 18-29

age 30-39



The dual epidemic

Non-Hispanic Whites represent largest increases

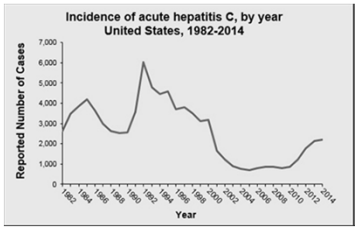


The dual epidemic

Women,
age 18-39

Infants born to HCV+ mothers ↑ 68% from 2011-2014

HCV incidence, United States



Diagnosis

Liver profile

Alanine aminotransferase (ALT)

- Enzyme found in cells of liver and kidney
- Converts alanine into pyruvate (required for cellular energy production)
- Released into blood when liver cells are damaged/dying

- Most specific to hepatitis
- Acute: sharp increase, gradual decrease
- Chronic: persistently increased

Test	Ref. range
ALT	7 – 55 U/L
AST	8 – 48 U/L
ALP	40 – 140 U/L
Total protein	6.3 – 7.9 g/dL
Bilirubin(total)	≤ 1.2 mg/dL
Albumin	3.5 – 5.0 g/dL
GGT	
Lactate dehydrogenase	
Prothrombin time (PT)	
Alpha-feto protein (AFP)	

Hepatitis panel

May be ordered when:

- Patient has abnormal liver panel results
- Patient presents with symptoms of liver damage
- High risk patients
- Known exposure

Hepatitis A antibody, IgM

Hepatitis B core antibody, IgM

Hepatitis B surface antigen

Hepatitis C antibody

HCV screening test

Anti-HCV
- EIA
- CLIA
- Rapid tests

Antibodies to HCV

- Anti-HCV IgG
- Detectable 10 – 11 weeks after exposure
- Remain positive for lifetime

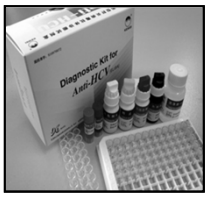
- Acts as a screen only
- Positives should be confirmed with molecular testing

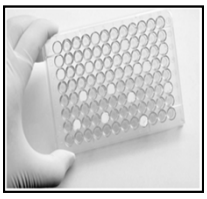
- Reactive
  - Current HCV infection
  - Past infection resolved
- Nonreactive
  - No infection

HCV screening test

Anti-HCV
- EIA
- CLIA
- Rapid tests

- Detect presence of antibodies to HCV





HCV molecular testing

HCV RNA

Nucleic acid amplification test (NAT)

- per CDC guidelines if anti-HCV(+)
- RNA detectable within 1-2 weeks after exposure
- Remains positive for chronic infections

- Detected
  - current HCV infection
- Not detected
  - past HCV infection
  - false(+) Ab screen

RT-PCR

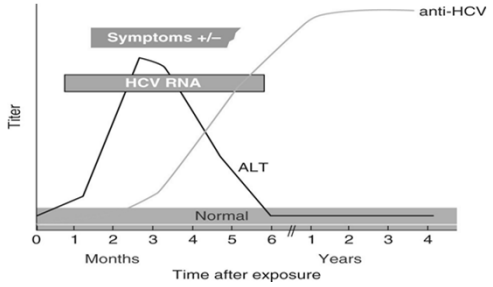
- Qualitative
- Quantitative
  - Confirm (+)Ab screens
  - Detect suspected infection
  - Screen blood/organ donors
  - Detect perinatal transmission
  - Monitor viral load
  - Maintain therapeutic goals

HCV molecular testing

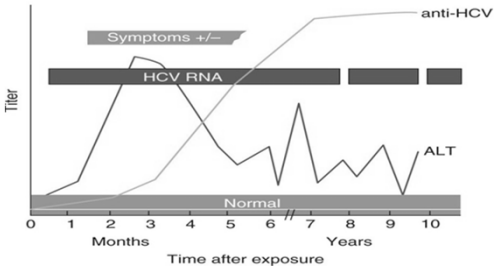
HCV RNA

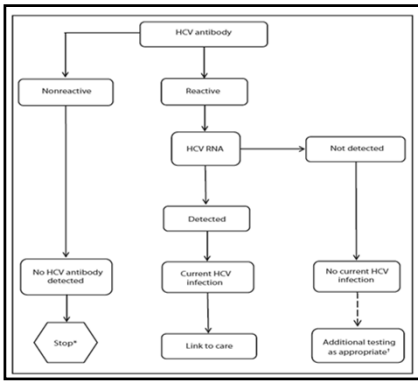
- Roche Diagnostics COBAS® TaqMan® Analyzer; Cobas® 4800 System
- Siemens ADVIA Centaur® Systems

HCV serology – acute infection



HCV serology – chronic infection





CDC Hepatitis C testing algorithm

https://youtu.be/WyVQbJ0JUvI

HCV screening – much room for improvement

Current guidelines:

- One-time screen for persons born between 1945-1965
- Targeted screening for high risk patients

- Risk based practice may be limited and not include actual testing
- Screening disparities exist for women, African Americans, and Hispanics
- Linkage to care and treatment referral widely varies among providers
- Interest in screening still lacking in many age cohorts

Vaccines and treatments

HCV – vaccine research

- Began 25 years ago
- Progress is slow because:
  - Variability of genotype distribution
  - Virus can mutate rapidly within the host
  - Limited animal models

HCV vaccine – clinical trials

1) Therapeutic vaccine trial
   - people who already have chronic hepatitis C
   - purpose is to determine whether each vaccine is safe and successful at reducing evidence of HCV RNA in participants' blood
   - 32 participants
   - Mayo Clinic (Florida, Minnesota), Temple University (Philadelphia), University of Puerto Rico
   - Completion of this trial is expected in 2020

ClinicalTrials.gov Identifier: NCT02772003

HCV vaccine – clinical trials

2) Prophylactic (preventive) vaccine trial
   - people at high risk of infection, i.e. PWID
   - purpose is to determine the safety of the two vaccines
   - find out whether participants receiving either vaccine are less likely to become infected with HCV
   - 548 participants
   - San Francisco, Maryland, New Mexico
   - Completion of this trial is expected in July 2018

ClinicalTrials.gov Identifier: NCT01436357

HCV vaccine – clinical trials

3) Vaccine efficacy trial
   - people with chronic HCV and healthy people
   - purpose is to investigate the effects of chronic HCV infection on the immune response to HBV vaccination
   - understand reasons for vaccine success vs failure
   - 130 participants
   - Rockefeller University Hospital, NY
   - Completion of this trial is expected in May 2019

ClinicalTrials.gov Identifier: NCT02429583

HCV – treatment

Direct acting antiviral (DAA)

- Acute HCV infection: monitor and only consider for treatment if HCV RNA persists after 6 months

- Chronic HCV infection: new highly effective HCV protease inhibitors, oral dose for 8-12 weeks
  - ➢ Achieve sustained virologic response (SVR)
  - ➢ Absence of detectable virus 12 weeks after completion of treatment
  - ➢ 90% cure rate

HCV – treatment

Direct acting antiviral (DAA)

Mechanisms of action:
- ➢ Inhibit viral replication
- ➢ Interfere with protein synthesis
- ➢ Prevent virion assembly
- ➢ Enhance T-cell activity

- Oral pill/capsule forms and injections
- Many require combo therapy
- Cost prohibitive

Name	Action	Cost
Daclatasvir	Inhibits replication	$63,000 (12 weeks)
Elbasvir-grazoprevir	Inhibits replication	$54,600, $72,800
Glecaprevir – pibrentasvir	Inhibits replication	$26,400, $36,400, $52,600
Ledipasvir – sofosbuvir	Inhibits replication	$64,000, $94,500, $189,000
Ombitasvir-paritaprevir-retionavir	Inhibits replication	$76,653 (12 weeks)
Peginterferon alfa-2a	Interferes with protein synthesis	$9,250, $18,500, $37,000
Peginterferon alfa-2b	Interferes with protein synthesis	$8,400, $16,800, $33,600
Ribavirin	Inhibits replication, protein synthesis, enhances T-cell activity	$550 - $850 (12 weeks) $110 - $1700 (48 weeks)
Simeprevir	Inhibits viral replication	$66,360, $85,000, $150,000
Sofosbuvir	Terminates viral replication	$84,000, $168,000
Sofosbuvir – velpatasvir	Inhibits viral replication	$74,760 (12 weeks)
Sofosbuvir – velpatasvir - voxilaprevir	Inhibits and terminates viral replication	$74,760 (12 weeks)

FDA approved treatment options
https://www.hepatitisc.uw.edu/page/treatment/drugs

HCV – in summary

- Single-strand RNA virus, genotypes 1-3 prevalent in US
- Transmission via blood
- Leading cause of liver disease, liver cancer, and liver transplant
- Highest risk in PWID, baby boomers, children born to HCV+ mom
- Dual epidemic with opioid IV drug use
- Anti-HCV screen first, then molecular testing for HCV RNA

HCV – in summary

- Vaccine research ongoing
- 3 current vaccine clinical trials in US
- Treatments available with 90-95% cure rate
- High cost and healthcare access prohibit many for receiving treatment
- Need for intensive testing plans nationwide, continued needle exchange programs, public health education

Thank you for listening!

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