



Choices, health and wellness for people with
long-term disease.

HCV Diagnosis

The key to case finding with HCV is a high index of suspicion.



HCV Risk Factors

- received blood, blood products, or an organ transplant prior to 1992
- ever, even once, shared drug paraphernalia
- ever been stuck by a used blood needle
- been on kidney dialysis
- had a tattoo or body piercing in an unsterile setting
- had multiple sex partners, or sexual activity that involved contact with blood
- shared personal care items (razors, toothbrushes, etc.) with other people
- been incarcerated
- combat veteran



Clinical Presentation of Chronic Hepatitis C

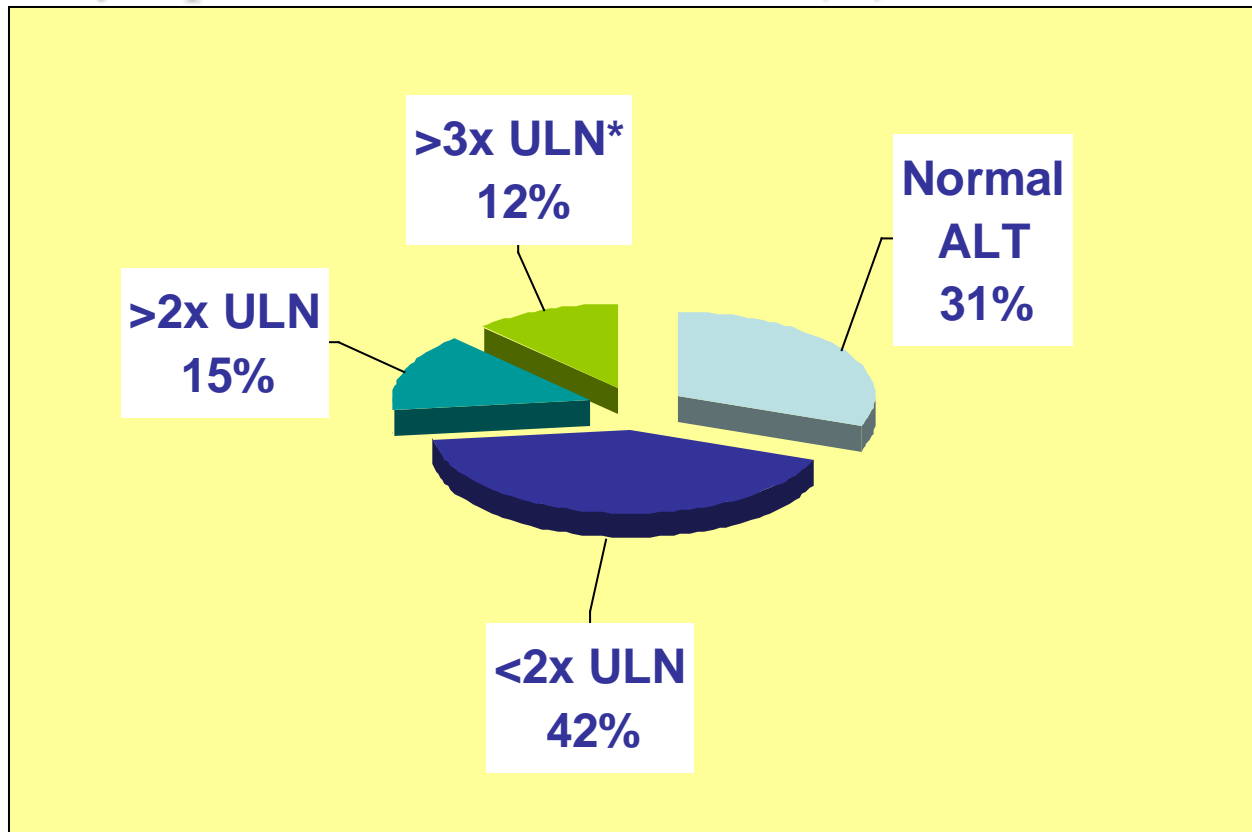
- Patient are often asymptomatic or have nonspecific symptoms such as fatigue, malaise, abdominal discomfort.
 - **mild-to-moderate elevations of ALT (SGPT) or AST (SGOT) or risk factors are the tip-off**
- Some asymptomatic patients have normal liver enzymes.
 - **as many as 44% have normal levels at initial evaluation**
 - **may have positive hepatitis C antibody test despite normal liver enzymes**
- Any degree of abnormality in liver enzymes should be evaluated further!

Clinical Presentation of Chronic Hepatitis C

- Any degree of **abnormality in liver enzymes** should be evaluated further.
- Any **positive HCV antibody test** should be evaluated with subsequent testing.

Pattern of ALT Elevation in Chronic Hepatitis C

Asymptomatic HCV RNA (+) Individuals



Diagnosis of Chronic Viral Hepatitis: Serologic Testing

- Patients should be tested for HCV and HBV if they:
 - have known risk factors for viral hepatitis
 - indicate possible risk factors for hepatitis
 - have elevated liver enzymes
 - express a desire to know their HCV and/or HBV status

Diagnosis of Viral Hepatitis in the Primary Care Setting: Patients with Risk Factors

- A single normal ALT level does not rule out chronic viral hepatitis.
- ALT levels may be intermittently normal in a significant number of patients who have chronic hepatitis C.
- If risk factors are present or HCV is suspected, screen for anti-HCV antibodies even if liver enzymes are normal.
- The definition of normal ALT continues to evolve.
 - a normal ALT is probably ~20-27 for a female and ~ 25-30 for a male
 - depends on iron status, BMI (presence of fatty liver), as well as use of alcohol



Diagnosing Chronic HCV

Elevated ALT

All persons with chronic ALT elevation should undergo HCV testing.

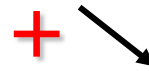
elevated ALT level + risk factor(s) for hepatitis C



anti-HCV (EIA) testing



<5% chance of
hepatitis C



diagnosis of hepatitis C
>95% certain

Confirm with HCV RNA testing.

Refer to specialist for evaluation and treatment.



Diagnosing Chronic HCV

Normal ALT

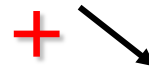
normal ALT + positive anti-HCV test



HCV RNA testing



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Laboratory Tests for Evaluation of the Liver

Liver enzymes are not the same
as liver function tests (LFTs).

Liver Enzymes versus LFTs

- liver enzymes
 - ALT (formerly SGPT), AST (formerly SGOT), GGT, others
 - elevations indicate inflammation and hepatocyte damage
 - provide no information about the presence or absence of fibrosis, cirrhosis, or functional hepatic impairment

Liver Enzymes versus LFTs

- Liver Function Tests (LFTs)
 - – indirect measures of liver function
 - **platelet count, bilirubin, albumin, PT/INR, cholesterol, and others**
 - **provide information about the functionality of the liver**
 - **sensitivity in detecting changes in liver function is limited until decompensation begins**
- Surrogate markers of advanced fibrosis include low platelet count, splenomegaly, and varices

HCV Viral Load Testing*

What it does tell you

- Viral load testing commonly confirms HCV viremia.
- Viral load influences likelihood of response to interferon-based therapy
 - People with low viral loads (<2 million copies/mL or 500,000 IU/mL) have a better response rate than those with high viral loads (> 2 million copies/mL or 500,000 IU/mL).
- Definitive tests such as TMA are more sensitive and are sometimes employed when viremia is not detected by standard viral load tests such as bDNA assays.

*using nucleic acid tests or molecular testing



HCV Viral Load Testing*

What It Does Not Tell You

- Viral load does not correlate with disease severity (inflammation and fibrosis).
- Viral load does not predict nor correlate with disease progression.
- Changes of less than 2 logs are within the normal variation of HCV infection (viral fluctuations and test variability).

*using nucleic acid tests or molecular testing



HCV Viral Testing

- three types are commonly used: PCR, TMA, bDNA
- quantitative viral load is measured in IU/mL (the current standard); old records may report copies/mL
- viral load is “high” when it is $> 800,000$ IU/mL
- with PCR: convert IU/mL to copies/mL
 - multiply by 2.7
- with TMA: convert IU/mL to copies/mL
 - multiply by 5.2

HCV Genotype Distribution, U.S.

1a/1b: 70%

2a/2b: 15%

3a: 6-7%

4, 5, 6: 8-9%



Why Determine HCV Genotype?

- genotype 3a associated with higher degrees of steatosis
- genotype 1a/1b and 4 less likely to respond to interferon-based therapy:
 - **45% sustained response to peg- interferon + ribavirin**
- genotype 2/3 more likely to respond to interferon-based therapy and may have a shorter duration of therapy:
 - **70-80% sustained response to peg- interferon + ribavirin**

Standard Lab Tests Predictive of Cirrhosis

- **decreased platelet count and WBC** due to splenic enlargement and sequestration
- **increased bilirubin** as hepatic function declines
- **increased INR** as synthetic function declines
- **decreased albumin** as synthetic function declines
- **increased AST/ALT ratio** as hepatocellular death increases

Predictors of Advanced Fibrosis with Chronic Hepatitis C

- splenomegaly and thrombocytopenia - most sensitive and specific predictor of advanced liver disease
 - AST/ALT ratio > 1
 - platelet count $< 150,000/\text{mm}^2$

¹Pohl et al. Am J Gastroenterol 2001;96:3142

²Imbert-Bismut et al. Lancet 2001;357:1069



Lab Tests to Monitor for Complications of HCV

Hepatocellular carcinoma (HCC)

- alpha-fetoprotein is a marker for HCC
 - elevations less than 1000 ng/mL – serious concern for increased risk of developing HCC; warrants follow-up testing including baseline ultrasound
 - >1000 ng/mL = HCC until proven otherwise; refer for specialty consultation and possible liver transplant evaluation

Lab Tests to Monitor for Complications of HCV

Essential Mixed Cryoglobulinemia

- markers – rheumatoid factor, cryoglobulins
- symptoms – rash, neuropathy, arthralgias, Sicca syndrome, vasculitis
- low levels of cryoglobulins (<3%) are normal in HCV
 - **elevations are diagnostic if they occur with signs and symptoms**
- can lead to lymphoma and glomerulonephritis
- responds to interferon

Lab Tests to Monitor for Complications of HCV

Autoimmune Complications

- autoimmune thyroiditis, lichen planus, Raynaud's syndrome, diabetes, Sicca syndrome, others
- markers – ANA, thyroid panels, anti-mitochondrial antibodies, elevated fasting blood glucose
- symptoms
 - arthralgia, paresthesia, myalgia, pruritis, or dry eyes and mouth
 - occur in at least 10% of HCV patients



Lab Tests to Monitor for Complications of HCV

Iron Overload

- hepatic iron levels ↑ in 10-36% of HCV patients
- markers (iron studies)
 - **ferritin***, transferrin, Fe saturation, serum Fe
- iron is hepatotoxic and accelerates fibrosis

*ferritin –also an acute phase protein; may not be a reliable indicator in acute hepatitis