Hepatitis C: Hospital Medicine Focus

Overview of Hepatitis C

Hepatitis C (HCV) is a viral infection caused by the hepatitis C virus, primarily affecting the liver and leading to a spectrum of disease ranging from acute infection to chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). It is a major public health concern, with an estimated 2.4 million people in the U.S. living with HCV (CDC, 2023). In the hospital setting, HCV often presents as an acute flare, a complication of chronic disease, or an incidental finding in high-risk patients. Hospitalists play a critical role in diagnosis, initiating treatment, managing complications, and coordinating care. This guide provides a comprehensive overview of HCV, including pathophysiology, risk factors, transmission, diagnostic tests, complications, diagnostic studies, treatment strategies, hospital medicine implications, and includes tables and clinical scenarios for practical application.

Pathophysiology

- **Virus:** HCV is a single-stranded RNA virus (genus Hepacivirus, family Flaviviridae), with 6 major genotypes (1-6). Genotype 1 is most common in the U.S.

Mechanism:

- HCV enters hepatocytes via receptors (e.g., CD81), replicates using RNA-dependent RNA polymerase, and evades immune responses through rapid mutations.
- Chronic inflammation leads to hepatocyte injury, fibrosis (via hepatic stellate cell activation), and eventual cirrhosis.
- Immune-mediated damage (CD8+ T-cell response) contributes to liver injury but often fails to clear the virus (chronic infection in 50-80% of cases).

Progression:

- **Acute Infection:** Often asymptomatic (75%), 20-50% spontaneously clear within 6 months.
- **Chronic Infection:** Persistent viremia, progresses to fibrosis (Metavir F0-F4), cirrhosis (F4) in 20-30% over 20-30 years.

- **End-Stage:** Cirrhosis leads to portal hypertension, decompensation (e.g., ascites, variceal bleeding), and HCC (3-5% annual risk in cirrhosis).

Risk Factors and Transmission

Risk Factors:

- **Injection drug use (IVDU):** 60% of new cases (shared needles).
- **Blood transfusion/organ transplant before 1992** (before HCV screening).
- **Chronic hemodialysis.**
- **Healthcare exposure:** Needlestick injuries, unsafe injection practices.
- **High-risk sexual behavior:** Multiple partners, MSM, HIV co-infection.
- **Incarceration:** Higher prevalence due to IVDU, tattooing.
- **Mother-to-child transmission:** 5-10% risk (higher with HIV co-infection).
- **Tattoos/piercings** with unsterile equipment.

Transmission:

- **Primary Mode:** Bloodborne (direct percutaneous exposure to infected blood).
- **Less Common:** Sexual transmission (low risk, ~1% per year in monogamous couples), perinatal transmission.
- **Not Transmitted:** Casual contact, breastfeeding (unless cracked nipples), food/water.

Clinical Presentation

Acute Hepatitis C:

- Often asymptomatic (75%).
- **Symptomatic:** Fatigue, nausea, jaundice (dark urine, pale stools), right upper quadrant (RUQ) pain, fever.
- **Duration:** 2-12 weeks, may resolve spontaneously (20-50%).

Chronic Hepatitis C:

- **Early:** Often asymptomatic or mild fatigue, vague RUQ discomfort.
- **Advanced (Cirrhosis):** Ascites, variceal bleeding (hematemesis), hepatic encephalopathy (confusion), jaundice, spider angiomas, palmar erythema.

Extrahepatic Manifestations:

- **Cryoglobulinemia:** Vasculitis, purpura, glomerulonephritis.
- **Porphyria Cutanea Tarda (PCT):** Photosensitive rash, blisters.
- Diabetes, lymphoma, thyroiditis (immune-mediated).

Diagnostic Approach

Screening:

- **Who to Screen:** All adults aged 18-79 (USPSTF 2020), pregnant women, high-risk groups (IVDU, HIV, hemodialysis).
- **Initial Test:** Anti-HCV antibody (ELISA, sensitivity >97%).
  - **Positive:** Indicates exposure (past or current infection).
  - **Negative:** Rules out infection (unless acute, retest in 3-6 months).

Confirmatory Tests:

- **HCV RNA (PCR):** Detects active infection (viral load in IU/mL).
  - **Positive:** Confirms current infection (chronic if >6 months).
  - **Undetectable:** Indicates spontaneous clearance or cured infection.
- **Genotype Testing:** Determines genotype (1-6) to guide treatment (e.g., genotype 1: 60% of U.S. cases).

Labs:

- **LFTs:** Elevated ALT/AST (2-10x ULN in acute, mild elevation in chronic), bilirubin (jaundice).
- **CBC:** Thrombocytopenia (cirrhosis, portal hypertension), anemia (GI bleed).
- **PT/INR:** Prolonged in cirrhosis (hepatic synthetic dysfunction).
- **CMP:** Hypoalbuminemia, renal function (cryoglobulinemic glomerulonephritis).
- **HIV Testing:** High co-infection rate (20-30% in IVDU).

Fibrosis Assessment:

- **FIB-4 Score:** Age, AST, ALT, platelets (FIB-4 >3.25 suggests advanced fibrosis).
- **FibroScan:** Transient elastography (stiffness >12.5 kPa indicates cirrhosis).

Diagnostic Studies:

- **Ultrasound Abdomen:** Cirrhosis (nodular liver, splenomegaly), portal hypertension, HCC screening.
- **CT/MRI Liver:** HCC (arterial enhancement, washout), cirrhosis complications.
- **Liver Biopsy:** Rarely needed (gold standard for fibrosis staging, Metavir F0-F4).
- **Esophagogastroduodenoscopy (EGD):** Screen for esophageal varices in cirrhosis.
- **Alpha-Fetoprotein (AFP):** HCC screening (with ultrasound, q6 months in cirrhosis).

Complications

Cirrhosis: 20-30% over 20-30 years.

- **Portal Hypertension:** Ascites, variceal bleeding, splenomegaly.
- **Hepatic Encephalopathy:** Confusion, asterixis, coma (ammonia >100 µmol/L).
- **Hepatorenal Syndrome (HRS):** AKI (Cr >2 mg/dL), poor prognosis without transplant.
- Hepatocellular Carcinoma (HCC): 3-5% annual risk in cirrhosis, presents with weight loss, RUQ mass, worsening liver function.

Extrahepatic:

- **Cryoglobulinemic Vasculitis:** Purpura, neuropathy, glomerulonephritis.
- **Diabetes:** 2-3x increased risk (insulin resistance).
- **B-Cell Lymphoma:** 2x increased risk (chronic immune stimulation).

Hospital Complications:

- **Sepsis:** High risk in cirrhosis (e.g., SBP, 30% mortality).
- **Variceal Bleeding:** Mortality 15-20% per episode.
- **Decompensated Cirrhosis:** Acute-on-chronic liver failure (ACLF), mortality 50% within 90 days.

Treatment Strategies

General Principles:

- **Antiviral Therapy:** Direct-acting antivirals (DAAs) are curative (>95% SVR, sustained virologic response at 12 weeks).
- **Supportive Care:** Manage cirrhosis complications (e.g., diuretics for ascites, lactulose for encephalopathy).
- **Vaccinations:** HAV, HBV (prevent co-infection), pneumococcal/influenza (cirrhosis patients).

Antiviral Treatment (DAAs):

- **Indications:** All patients with detectable HCV RNA (acute or chronic), unless life expectancy <12 months.
  - **Regimens (Genotype 1, Most Common)**:**
    - **Sofosbuvir/Velpatasvir (Epclusa):** 400/100 mg PO daily x 12 weeks (pan-genotypic, first-line).
    - **Glecaprevir/Pibrentasvir (Mavyret):** 300/120 mg PO daily x 8-12 weeks (pan-genotypic, shorter duration).
    - **Sofosbuvir/Ledipasvir (Harvoni):** 400/90 mg PO daily x 12 weeks (genotype 1, 4-6).
- Special Cases:
  - **Cirrhosis:** Extend to 12-24 weeks, add ribavirin if decompensated (Child-Pugh B/C).
  - **HIV Co-Infection:** Same regimens, check ART interactions (e.g., avoid efavirenz with sofosbuvir).
  - **Renal Failure:** Glecaprevir/pibrentasvir safe in CKD (eGFR <30 mL/min).

Hospital Medicine Implications:

- Acute Hepatitis C:
  - Often asymptomatic, diagnose via HCV RNA if recent exposure (e.g., needlestick).
  - Start DAAs early (within 12 weeks) to prevent chronicity (SVR >95%).
- Chronic Hepatitis C:
  - **Cirrhosis Complications:**
    - **Ascites:** Spironolactone 100 mg PO daily + furosemide 40 mg PO daily, paracentesis if tense.

        - **Variceal Bleeding:** Octreotide 50 µg IV bolus, then 50 µg/h, EGD with banding, non-selective beta-blocker (propranolol 20 mg PO BID).
        - **Hepatic Encephalopathy:** Lactulose 30 mL PO q2-4h (titrate to 2-3 stools/day), rifaximin 550 mg PO BID.
        - **SBP:** Cefotaxime 2 g IV q8h, albumin 1.5 g/kg IV day 1 (if Cr >1 mg/dL).
        - **HCC Screening:** Ultrasound + AFP q6 months in cirrhosis.
- Inpatient DAA Initiation: (also frequently started outpatient if patient is stable)
    - Start DAAs in admitted patients with HCV RNA (e.g., sofosbuvir/velpatasvir 400/100 mg PO daily).
    - **Consult hepatology:** Ensure outpatient follow-up for SVR12 (HCV RNA at 12 weeks).
    - Monitor LFTs qweek, Cr (ribavirin-induced hemolysis risk).
- Co-Infections:
    - **HIV:** Coordinate with ID for ART, avoid DAA-ART interactions.
    - **HBV:** Screen for HBV (HBsAg, anti-HBc); risk of HBV reactivation with DAAs (start tenofovir if co-infected).

Supportive Care:

- **Nutrition:** High-protein diet (1.2-1.5 g/kg/day) in cirrhosis, avoid alcohol.
- **Vaccinations:** HAV, HBV, pneumococcal (PPSV23), influenza.
- **Social Work:** Address barriers to care (e.g., IVDU, housing, insurance for DAAs).

Table: Diagnostic Findings in Hepatitis C

Clinical Stage	Features	Labs	Diagnostic Studies	Complications
Acute HCV	Fatigue, jaundice, RUQ pain	ALT/AST 2-10x ULN, HCV RNA+	Anti-HCV Ab, HCV RNA PCR	Fulminant hepatitis (rare, <1%)
Chronic HCV	Mild ALT/AST Fatigue, RUQ discomfort	elevation, HCV RNA+	FibroScan (fibrosis), MRI (HCC)	Cirrhosis, HCC, cryoglobulinemia
Cirrhosis	Ascites, variceal bleeding, jaundice	Thrombocytopenia, INR >1.5, low albumin	Ultrasound (nodular liver), EGD (varices)	HRS, encephalopathy, HCC
Extrahepatic	Purpura, neuropathy, rash (PCT)	Cryoglobulins+, RF+, low C4	Kidney biopsy (glomerulonephritis)	Diabetes, lymphoma

Table: Hospitalist Management Checklist for Hepatitis C

Task	Acute HCV	Chronic HCV (No Cirrhosis)	Cirrhosis (Compensated)	Cirrhosis (Decompensated)
Diagnosis	HCV RNA, anti-HCV Ab	HCV RNA, genotype, FIB-4	Ultrasound, EGD, ultrasound, AFP	MELD score
Treatment	Sofosbuvir/ velpatasvir x 12 weeks	Sofosbuvir/ velpatasvir x 12 weeks	Sofosbuvir/ velpatasvir x 12 weeks	Glecaprevir/ pibrentasvir + ribavirin x 12-24 weeks
Complications	Monitor LFTs, watch for fulminant hepatitis	Screen for HCC if fibrosis	Manage varices, HCC screen q6 months	Ascites (diuretics), variceal bleed (octreotide)
Consult	Hepatology, ID (if HIV)	Hepatology, social work	Hepatology, gastroenterology	Hepatology, transplant team
Monitoring	LFTs qweek, HCV RNA at 12 weeks	LFTs qweek, SVR12	Ultrasound/AFP q6 months, INR	MELD score, Cr q12h, ammonia

Clinical Scenarios

Scenario 1: Middle-Aged Male with Acute HCV from Needlestick

- Presentation: A 45-year-old male healthcare worker presents 8 weeks after a needlestick injury with fatigue, nausea, and dark urine. Exam shows T 37.5°C, BP 120/80 mmHg, HR 80 bpm, RR 16/min, mild RUQ tenderness, no jaundice.
- Diagnostic Workup: **Labs:** ALT 500 U/L, AST 400 U/L, anti-HCV Ab+, HCV RNA 1 million IU/mL (genotype 1a), normal INR, FibroScan: F0, HIV negative.
- Diagnosis: Acute HCV → Recent exposure, elevated LFTs, HCV RNA+.
- Management: Admit to medicine (acute hepatitis). Start sofosbuvir/ velpatasvir 400/100 mg PO daily x 12 weeks. Monitor LFTs qweek (ALT decreases to 100 U/L by week 2). Consult hepatology: Confirm SVR12. Educate on transmission prevention (e.g., safe sex, no needle sharing). After 3 days, discharged with hepatology follow-up.

Scenario 2: Elderly Female with Chronic HCV and Cirrhosis

- Presentation: A 70-year-old female with a history of IVDU (1970s) presents with abdominal distension and fatigue. Exam shows T 37°C, BP 110/70 mmHg, HR 90 bpm, RR 18/min, ascites, spider angiomas, palmar erythema, no encephalopathy.

- Diagnostic Workup: **Labs:** HCV RNA 500,000 IU/mL (genotype 3), ALT 80 U/L, INR 1.4, albumin 3.0 g/dL, platelets 90,000/µL, FibroScan: F4 (cirrhosis), ultrasound: Nodular liver, no HCC, AFP 5 ng/mL.
- Diagnosis: Chronic HCV with compensated cirrhosis → HCV RNA+, F4 fibrosis, ascites.
- Management: Admit to medicine (cirrhosis). Start glecaprevir/pibrentasvir 300/120 mg PO daily x 12 weeks. Spironolactone 100 mg PO daily + furosemide 40 mg PO daily for ascites. Consult hepatology: HCC screening (ultrasound/AFP q6 months), EGD (no varices). Monitor LFTs, INR qweek. After 5 days, ascites improved, discharged with hepatology follow-up.

Scenario 3: Young Male with HCV and Decompensated Cirrhosis

- Presentation: A 35-year-old male with HCV (IVDU history) presents with confusion, hematemesis, and jaundice. Exam shows T 37°C, BP 90/60 mmHg, HR 110 bpm, RR 20/min, GCS 14, jaundice, ascites, asterixis, melena on rectal exam.
- Diagnostic Workup: **Labs:** HCV RNA 2 million IU/mL (genotype 1b), ALT 150 U/L, INR 2.0, albumin 2.5 g/dL, ammonia 120 µmol/L, Cr 2.2 mg/dL, MELD score 25, EGD: Bleeding esophageal varices, ultrasound: Cirrhosis, no HCC.
- Diagnosis: Decompensated HCV cirrhosis with variceal bleeding → HCV RNA+, variceal bleed, encephalopathy, HRS.
- Management: Admit to ICU (bleeding, shock). Octreotide 50 µg IV bolus, then 50 µg/h, EGD with banding. Transfuse PRBCs (Hgb 6 g/dL), FFP (INR 2.0). Lactulose 30 mL PO q2h (encephalopathy). Start sofosbuvir/velpatasvir 400/100 mg PO daily + ribavirin 600 mg PO daily x 24 weeks. Consult hepatology/transplant: HRS (albumin 1.5 g/kg IV), transplant evaluation. Monitor MELD, Cr q12h. After 7 days, bleeding controlled, GCS 15, discharged with transplant follow-up.