DIFERENT CAUSES OF HEPATITIS

- Infections
- Autoimmune
- Ischemic
- Congestive
- Drugs
- Toxins
- Miscellaneous
Asymptomatic hepatitis
(10 to 30 times more common)
In general, the younger the patient, the milder the clinical form of hepatitis.

Symptomatic hepatitis:
1. The incubation period
2. The preicteric phase
3. The icteric phase
4. The convalescent phase
The incubation period is the time immediately after acquisition of infection to the time of first symptoms.

It varies from a few weeks to as long as 6 months, depending on the type of the viral infection.

During this time, the patient is well and without symptoms.
Symptoms include malaise, joint pain, myalgia, fatigue, anorexia, nausea and vomiting, and abdominal or right upper quadrant discomfort.

Approximately 25% of patients describe their initial symptoms as an “influenza-like” illness.

The symptoms of pharyngitis, cough, coryza, and photophobia generally last only 1 to 3 days and are replaced by the more typical symptoms of malaise and anorexia.

Patients may give a history of distaste for alcohol and tobacco smoke.

Nausea and vomiting are common, are rarely severe, and can increase in severity as the day continues.
The prodromal symptoms usually last a few days but can persist for 2 or 3 weeks. In the absence of jaundice, these symptoms may be passed off as an influenza-like illness unless a specific exposure or risk is elicited in the history.

Jaundice may occur with varying severity and last from a few days to several weeks.

It is usually preceded by dark urine reflecting bilirubinuria caused by the rising concentrations of conjugated serum bilirubin.

Jaundice is first noted in the sclera and is usually accompanied by pale stool, reflecting the absence of bile pigment in the stool.

Pruritus, which is reported by 40% of jaundiced patients, is usually mild and transient unless a cholestatic illness is present, as is sometimes the case with HAV infection.

Pruritus associated with jaundice may lead to excoriations.

Lymphadenopathy is found in 5%, splenomegaly in approximately 15%, and hepatomegaly in 85%
FHF

- Fulminant hepatic failure, defined as severe liver failure that develops within 8 weeks of the onset of symptoms.
- The term “acute liver failure” is used to describe the onset of encephalopathy within 12 weeks of the onset of jaundice.
- “Hyperacute” refers to the development within 7 days, and “subacute” refers to an onset between 5 and 12 weeks.
- It occurs in only 0.14% to 0.35% of hospitalized cases of HAV infection.
- The incidence of fulminant hepatic failure in acute HBV infection is 1% to 4% of hospitalized patients, and the risk increases when there is associated HDV infection.
- The risk of acute liver failure as a consequence of acute hepatitis C appears to be very low, but it may be more common in patients with underlying chronic HBV infection.
- Acute liver failure secondary to HEV infection varies from 0.5% to 3% in nonpregnant pt. to 25% in pregnant women.
HAV infection is spread predominantly by direct person-to-person contact by the orofecal route or by the ingestion of contaminated food or water.

HAV has an incubation period of 15 to 50 days, with a mean period of 30 days.

Jaundice is very unusual in children younger than 4 years, and in the age group from 4 to 6 years, 90% are anicteric. In contrast, jaundice is present in 40% to 70% of those older than 15 years.

Prolonged Cholestasis (8%) & Chronic Relapsing coarse (1.5% to 11.9%)
HBV is transmitted by cutaneous and mucosal exposure to infectious blood or bodily fluids.

- Serum Sickness Syndrom
- Fibrosing Cholestatic Hepatitis
- FHF
- Symptomatic versus Asymptomatic
- Chronicity
- HDV Co- & Superinfection
The clinical symptoms resemble those of other forms of viral hepatitis, and the disease can be distinguished only by serologic testing.

Fewer than 15% to 25% of cases of acute HCV infection result in the development of jaundice, and therefore there is a high rate of subclinical infection.

The mean incubation period is 50 days.

Symptomatic versus Asymptomatic

As with HBV, some patients develop a serum sickness-like syndrome characterized by rash, urticaria, and arthralgias resolving with the onset of jaundice or within a few days.
HEV is transmitted by the fecal-oral route, and most reported epidemics have been related to the consumption of contaminated drinking water.

Person-to-person contact does not appear to be an efficient mode of transmission, and secondary attack rates among household contacts are only 0.7% to 2.2%, in contrast to the rate of 15% to 20% seen with HAV.

Hepatitis E causes disease that is indistinguishable from HAV without serological testing.

A cholestatic variant similar to that in HAV infection has been described with HEV infection and usually resolves within 2 to 6 months.

The incubation period of HEV infection ranges from 15 to 45 days and is on average 10 days longer than that for HAV infection.

Acute infection during pregnancy is associated with an inordinately high mortality rate for reasons that are unclear.
DIAGNOSIS

- HAV Ab IgM Type
- HBs Ag
- HBc Ab IgM Type
- HCV Ab
TREATMENT OF ACUTE VIRAL HEPATITIS

- Bed rest
- Dietary manipulation
- Parenteral vitamin K
- Drugs

**Special Treatment:**
- HAV
- HBV
- HCV
- HDV
- HEV
CHRONIC VIRAL HEPATITIS
CHRONIC VIRAL HEPATITIS

- HBV
- HBV+HDV
- HCV
- HEV?
- CMV & HSV & CMV & .....
Among inactive hepatitis B carriers and persons with mild to moderate chronic hepatitis B, symptoms are usually absent, although some with mild to moderate chronic hepatitis B report fatigue and, less commonly, right upper quadrant discomfort or “fullness.”

More severe and advanced cases can be associated with fatigue and jaundice, but persons with compensated cirrhosis may have no symptoms at all.

Decompensated cirrhosis may be accompanied by fatigue, jaundice, loss of muscle mass (weight loss), ascites, edema, bruising (coagulopathy), gastrointestinal bleeding (gastroesophageal varices or portal hypertensive gastropathy), and hepatic encephalopathy.
Management of Chronic HBV Infection*

HBsAg +

HBeAg

Positive

ALT < 1 X ULN
- Q 3-6 mo ALT
- Q 6-12 mo HBeAg

ALT 1-2 X ULN
- Q 3 mo ALT
- Q 6 mo HBeAg
  Consider biopsy if persistent or age > 40, Rx as needed

ALT >2 X ULN
- Q 1-3 mo ALT, HBeAg
  Treat if persistent
  Liver bx optional
  Immediate Rx if jaundice or decompensated

* HCC surveillance if indicated
Management of Chronic HBV Infection*

HBsAg +

- HBeAg

  - Negative
    - ALT ≥ 2X ULN
      - HBV DNA ≥ 20,000 IU/mL
        - Treat if persistent, Liver biopsy optional
    - ALT 1-2X ULN
      - HBV DNA 2,000-20,000 IU/mL
        - Q 3 mo ALT & HBV DNA
          - Consider biopsy if persistent
          - Rx as needed
    - ALT < 1X ULN
      - HBV DNA < 2,000 IU/mL
        - Q 3 mo ALT X 3, Then Q 6-12 mo
          - If ALT still <1x ULN

* HCC surveillance if indicated
<table>
<thead>
<tr>
<th>HBeAg</th>
<th>HBV DNA (PCR)</th>
<th>ALT</th>
<th>Treatment Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>&gt;20,000 IU/mL</td>
<td>≤2 × ULN</td>
<td>Low efficacy with current treatment. Observe; consider treatment when ALT becomes elevated. Consider biopsy in persons &gt; 40 years, ALT persistently high normal-2x ULN, or with family history of HCC. Consider treatment if HBV DNA &gt;20,000 IU/mL and biopsy shows moderate/severe inflammation or significant fibrosis.</td>
</tr>
<tr>
<td>+</td>
<td>&gt;20,000 IU/mL</td>
<td>&gt;2 × ULN</td>
<td>Observe for 3-6 months and treat if no spontaneous HBeAg loss. Consider liver biopsy prior to treatment if compensated. Immediate treatment if icteric or clinical decompensation. IFNa/pegIFNa, LAM, ADV, ETV, TDF or LdT may be used as initial therapy. ADV not preferred due to weak antiviral activity and high rate of resistance after 1st year. LAM and LdT not preferred due to high rate of drug resistance. End-point of treatment – Seroconversion from HBeAg to anti-HBe. Duration of therapy: • IFNa: 16 weeks • PegIFNa: 48 weeks • LAM/ADV/ETV/LdT/TDF: minimum 1 year, continue for at least 6 months after HBeAg seroconversion.</td>
</tr>
<tr>
<td>−</td>
<td>&gt;2,000 IU/mL</td>
<td>&gt; 2 x ULN</td>
<td>IFNa/peg IFNa, LAM, ADV, ETV, TDF or LdT may be used as initial therapy. LAM and LdT not preferred due to high rate of drug resistance ADV not preferred due to weak antiviral activity and high risk of resistance after 1st year. End-point of treatment – not defined. Duration of therapy: • IFNa/peg IFNa: 1 year • LAM/ADV/ETV/LdT/TDF: &gt; 1 year • IFNa non-responders / contraindications to IFNa → TDF/ETV.</td>
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<tr>
<td>−</td>
<td>&gt;2,000 IU/mL</td>
<td>1-2 × ULN</td>
<td>Consider liver biopsy and treat if liver biopsy shows moderate/severe necroinflammation or significant fibrosis.</td>
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<tr>
<td>−</td>
<td>≤2,000 IU/mL</td>
<td>≤ULN</td>
<td>Observe, treat if HBV DNA or ALT becomes higher. Compensated: HBV DNA &gt;2,000 IU/mL—Treat, LAM/ADV/ETV/LdT/TDF may be used as initial therapy. LAM and LdT not preferred due to high rate of drug resistance; ADV not preferred due to weak antiviral activity and high risk of resistance after 1st year. HBV DNA &lt;2,000 IU/mL—Consider treatment if ALT elevated. Decompenated: Coordinate treatment with transplant center, LAM (or LdT) + ADV, TDF or ETV preferred. Refer for liver transplant.</td>
</tr>
<tr>
<td>+/-</td>
<td>detectable</td>
<td>Cirrhosis</td>
<td>Compensated: Observe. Decompenated: Refer for liver transplant.</td>
</tr>
<tr>
<td>+/-</td>
<td>undetectable</td>
<td>Cirrhosis</td>
<td></td>
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</table>
Interferon Alfa
Pegylated Interferon Alfa
Lamivudine
Adefovir Dipivoxil
Entecavir
Telbivudine
Tenofovir
Other Agents
The most typical patient with recently discovered hepatitis C is asymptomatic, but fatigue is one of the more common clinical feature in symptomatic persons.

Overall, clinical features of chronic hepatitis C, and of decompensated cirrhosis associated with hepatitis C, are similar to those of chronic hepatitis B. Similarly, laboratory test abnormalities in chronic hepatitis B and C are similar; the principal abnormality is an elevation of serum aminotransferase activity, usually (ALT) exceeding (AST), until cirrhosis supervenes, when generally, AST exceeds ALT.

More characteristic of chronic hepatitis C than other forms of chronic liver disease are episodic fluctuations in aminotransferase activity, postulated to result from bursts of hepatic necroinflammatory activity accompanying the emergence of new quasispecies that overcome host immunologic containment of HCV.
Chronic Hepatitis C

- Definition
- Genotype 2,3
- Genotype 1,4
- Biopsy
- Interferon Alfa
- Pegylated Interferon Alfa
- Ribaverin
- Protease Inhibitors (Telaprevir, Boceprevir)
### Table 8. Virological Responses During Therapy and Definitions

<table>
<thead>
<tr>
<th>Virological Response</th>
<th>Definition</th>
<th>Clinical Utility</th>
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<tbody>
<tr>
<td>Rapid virological response (RVR)</td>
<td>HCV RNA negative at treatment week 4 by a sensitive PCR-based quantitative assay</td>
<td>May allow shortening of course for genotypes 2&amp;3 and possibly genotype 1 with low viral load</td>
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<tr>
<td>Early virological response (EVR)</td>
<td>≥ 2 log reduction in HCV RNA level compared to baseline HCV RNA level (partial EVR) or HCV RNA negative at treatment week 12 (complete EVR)</td>
<td>Predicts lack of SVR</td>
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<td>End-of-treatment response (ETR)</td>
<td>HCV RNA negative by a sensitive test at the end of 24 or 48 weeks of treatment</td>
<td></td>
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<tr>
<td>Sustained virological response (SVR)</td>
<td>HCV RNA negative 24 weeks after cessation of treatment</td>
<td>Best predictor of a long-term response to treatment</td>
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<tr>
<td>Breakthrough</td>
<td>Reappearance of HCV RNA in serum while still on therapy</td>
<td></td>
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<tr>
<td>Relapse</td>
<td>Reappearance of HCV RNA in serum after therapy is discontinued</td>
<td></td>
</tr>
<tr>
<td>Nonresponder</td>
<td>Failure to clear HCV RNA from serum after 24 weeks of therapy</td>
<td></td>
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<tr>
<td>Null responder</td>
<td>Failure to decrease HCV RNA by &lt; 2 logs after 24 weeks of therapy</td>
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<tr>
<td>Partial responder</td>
<td>Two log decrease in HCV RNA but still HCV RNA positive at week 24</td>
<td></td>
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</tbody>
</table>
TREATMENT ALGORITHM

A

1. Detectable HCV RNA?
   - Yes: Rapid virological response
   - No: HCV RNA
      - Yes: >2 log₁₀ drop in HCV RNA?
        - Yes: 24 weeks of treatment
        - No: 48 weeks of treatment
      - No: Stop treatment

B

1. Detectable HCV RNA?
   - Yes: Rapid virological response
   - No: Early virological response
      - No: Detectable HCV RNA?
        - Yes: Stop treatment
        - No: 72 weeks of treatment
      - Yes: >2 log₁₀ drop in HCV RNA?
        - Yes: 48 weeks of treatment
        - No: Stop treatment
THANK YOU