

Module 2: Gastroenterology

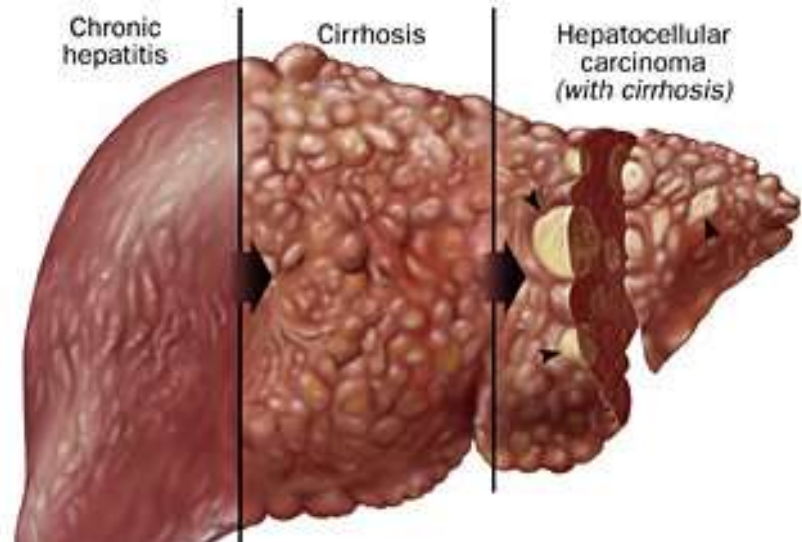
Chronic Hepatitis, 4 hours

NOTES FOR PRACTICAL LESSONS IN INTERNAL MEDICINE FOR STUDENTS OF IV
COURSE OF MEDICAL SCHOOL V.N.KARAZIN KHARKOV NATIONAL UNIVERSITY
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Plan of the Lesson

- Definition
- Classification
- Epidemiology
- Etiology
- Mechanisms
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Clinical cases
- Abbreviations
- Diagnostic guidelines



Definition

- Hepatitis is a **disease or clinical syndrome** in other diseases defined by the **inflammation** of the liver with the presence of inflammatory cells in its tissues and **may occur with limited or no symptoms**, but often leads to jaundice , poor appetite, and malaise
- Hepatitis is **chronic when it persists longer than six months**
- Chronic hepatitis **may progress over time to fibrosis and cirrhosis** (chronic liver failure)

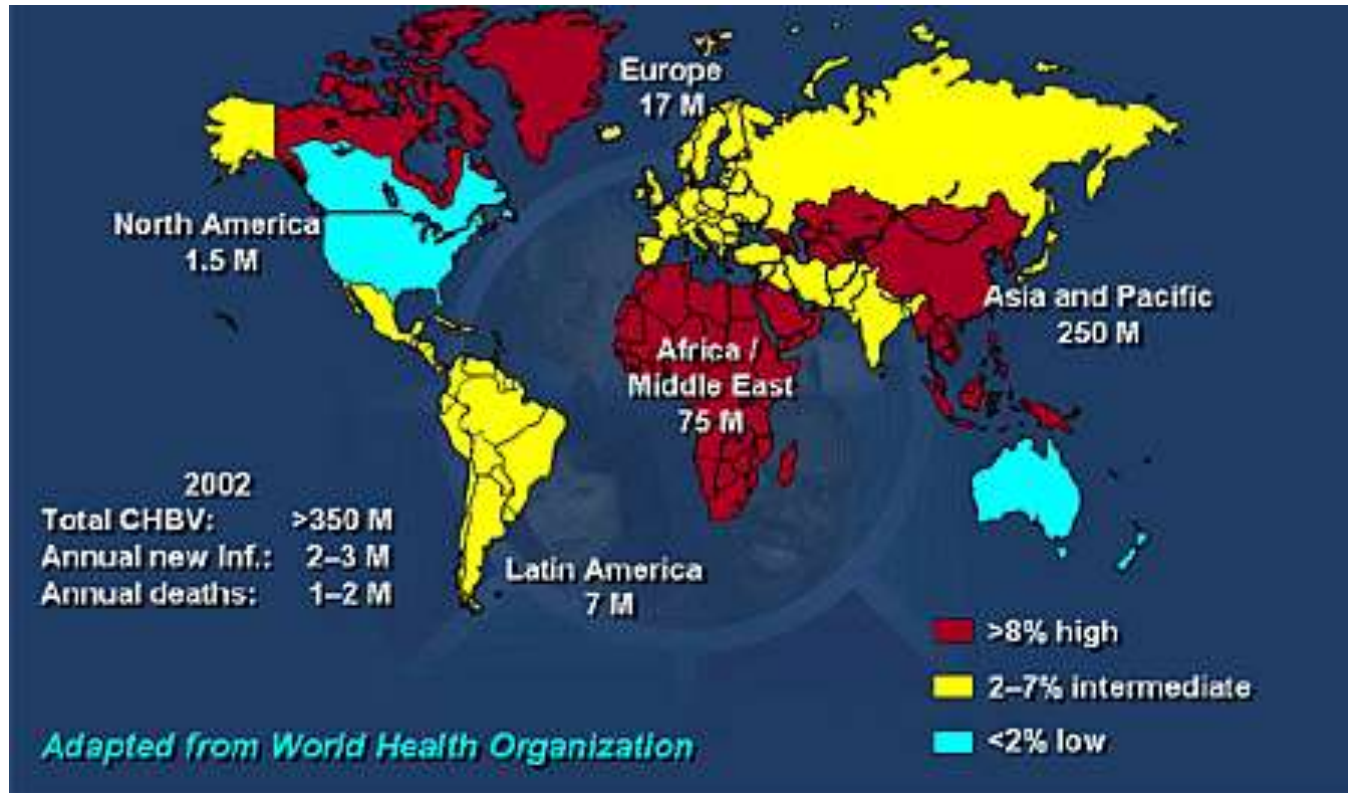
Classification

- Viral hepatitis - B, C, D (requires hepatitis B to cause disease).
- Alcoholic hepatitis (alcohol intake in excess of 80 grams of alcohol a day in men and 40 grams a day in women is associated with development of alcoholic hepatitis).
- Toxic and drug-induced (a large number of medications and other chemical agents can cause hepatitis: acetaminophen, antibiotics, and central nervous system medications) hepatitis.
- Autoimmune (lupoid) hepatitis (caused by an abnormal immune response against liver cells, very often as clinical syndrome in other autoimmune diseases).
- Non-alcoholic fatty liver.
- Ischemic hepatitis (shock liver, is most often associated with heart failure).
- Wilson Disease.

Epidemiology

- Hepatitis B is the **most common viral hepatitis** worldwide, affecting as much as 10% of the adult population in endemic areas and causing approximately 780,000 deaths per year worldwide.
- Hepatitis C affects an estimated 3.2 million adults living in the United States and roughly 60-70% of HCV-infected adults are unaware of their infection.
- Autoimmune hepatitis has an **incidence of 1-2 per 100,000 per year**, and a prevalence of 10-20/100,000 and affects women much more often than men (70%).

Epidemiology

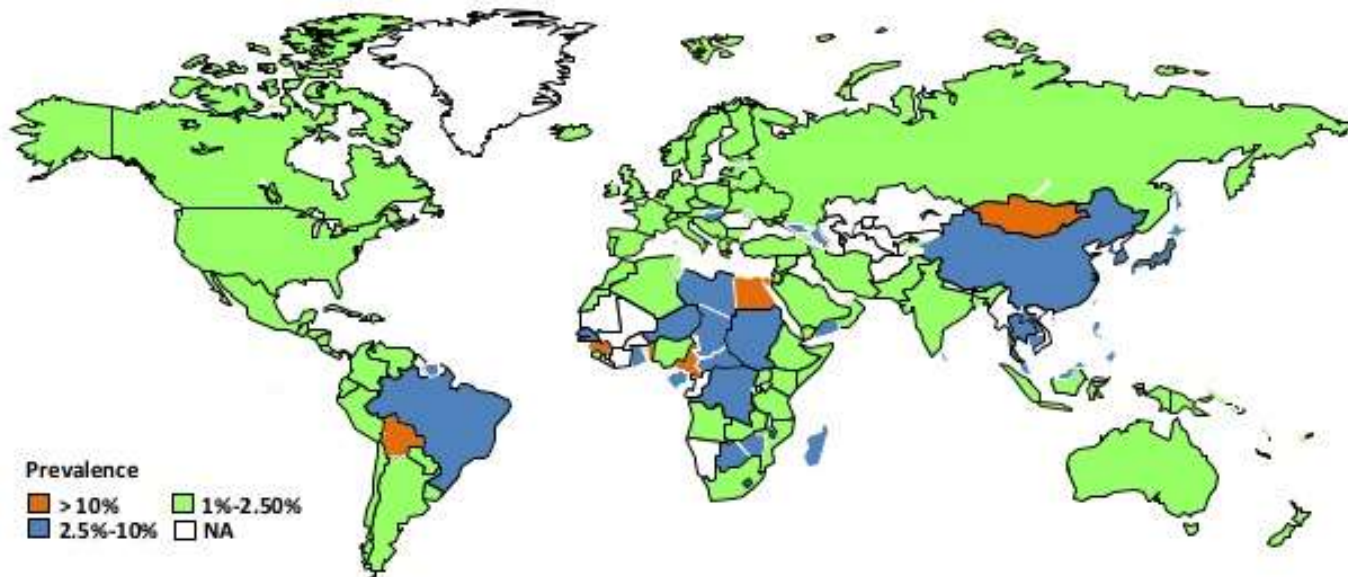


The global prevalence of hepatitis B is not static, either. **Southeast Asia and sub-Saharan Africa** have the highest prevalences.

Epidemiology

About 170 Millions of Hepatitis C Carriers Worldwide

3-4 millions new infections/year



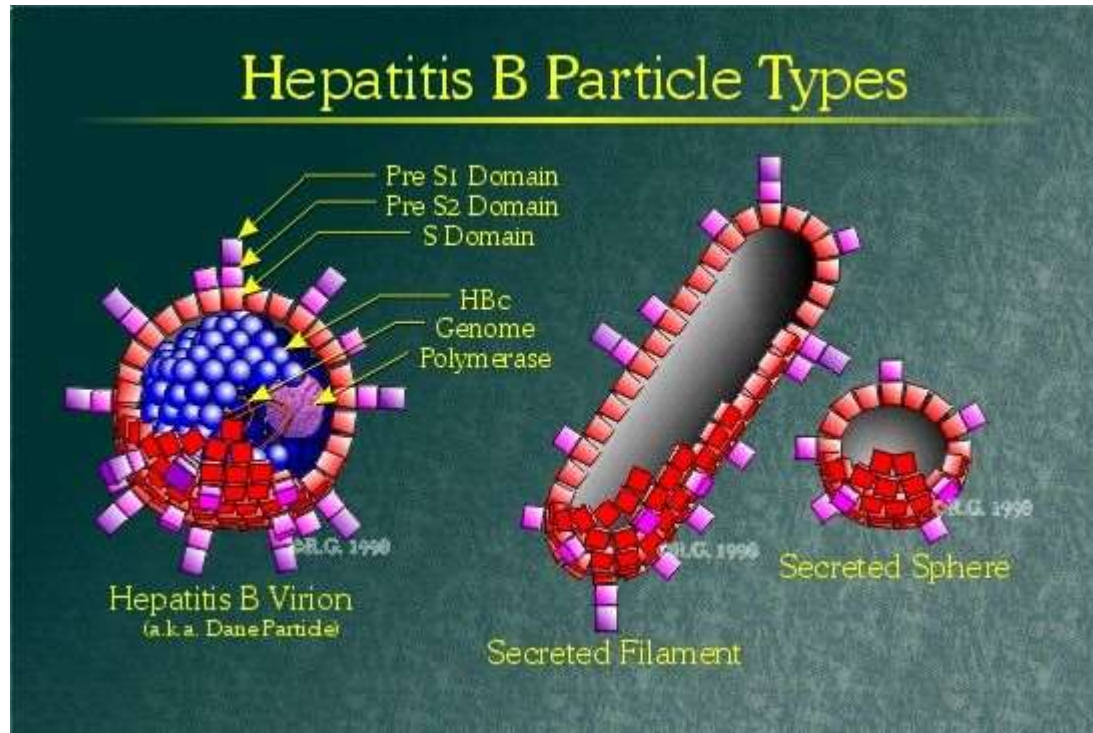
World Health Organization 2008. Available at: <http://www.who.int/ith/es/index.html>

Etiology

- Viral hepatitis is the most common cause of chronic hepatitis (B, C, D) and is a **systemic viral infection** that predominantly involves the liver.
- Other common causes of **non-viral hepatitis** include toxic (notably alcohol, some industrial organic solvents, and plants) and drug-induced (such as paracetamol), alcoholic, autoimmune, fatty liver, and metabolic disorders (autosomal recessive inherited disorder of copper metabolism - Wilson Disease)
- **Less commonly** some bacterial, parasitic, fungal, mycobacterial and protozoal infections can cause hepatitis
- Additionally, certain **complications of pregnancy** and decreased blood flow to the liver can induce hepatitis
- Cholestasis (**obstruction of bile flow**) due to hepatocellular dysfunction, biliary tract obstruction, or biliary atresia can result in liver damage and hepatitis.

Etiology

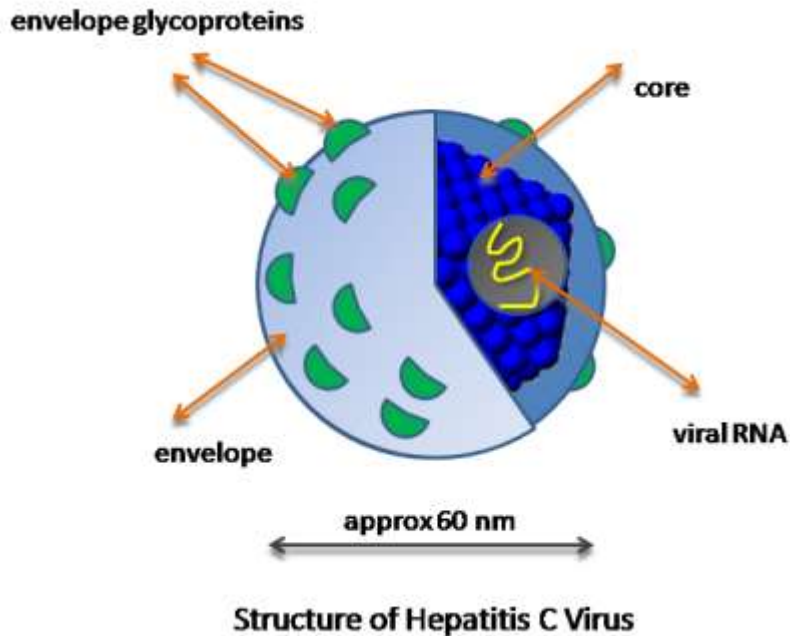
Hepatitis B Particle Types



- The hepatitis B virion (HBV, the Dane particle) has a diameter around 42nm
- The outer envelope contains high amounts of hepatitis B surface proteins
- The envelope surrounds the inner nucleocapsid which is comprised of 180 hepatitis B core proteins arranged in an icosahedral arrangement with T=3 and T=4 symmetry
- The nucleocapsid also contains at least one hepatitis B polymerase protein as well as the HBV genome
- Two other subviral particles can be found in an infected individual's serum, namely the hepatitis B filament and hepatitis B sphere (a diameter of 22nm) that are composed solely of hepatitis B surface proteins without infectious nature

Etiology

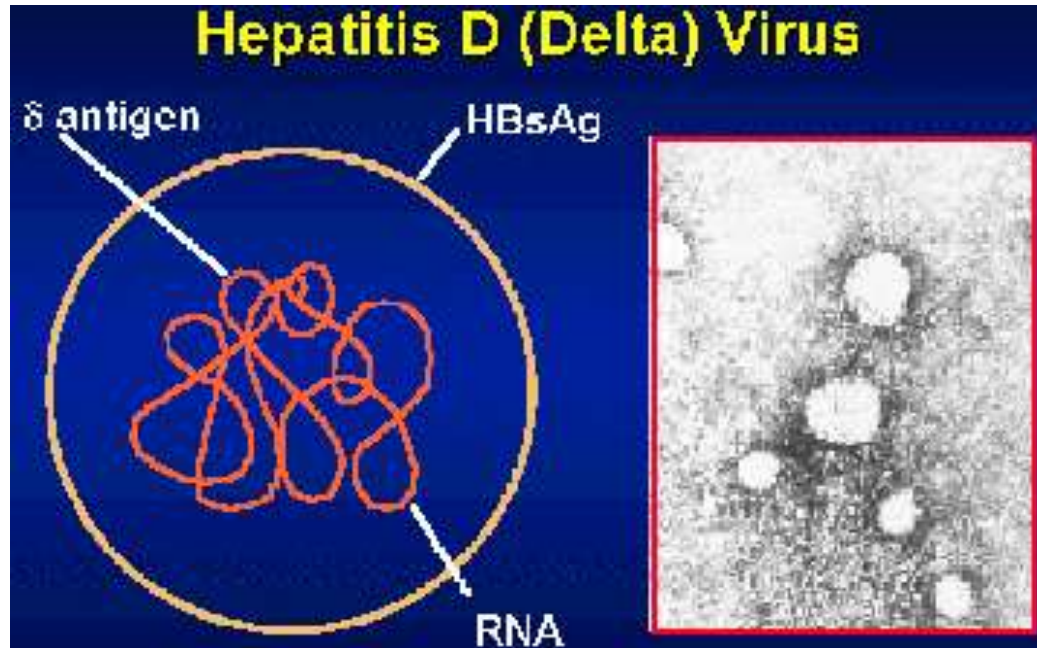
Hepatitis C Particle Types



- The hepatitis C virus (HCV) particle consists of a core of genetic material (RNA), surrounded by an icosahedral protective shell of protein, and further encased in a lipid (fatty) envelope of cellular origin
- Two viral envelope glycoproteins, E1 and E2, are embedded in the lipid envelope
- The virus replicates mainly in the hepatocytes of the liver, where it is estimated that daily each infected cell produces approximately fifty virions with a calculated total of one trillion virions generated
- The virus may also replicate in peripheral blood mononuclear cells, potentially accounting for the high levels of immunological disorders found in chronically infected HCV patients

Etiology

Hepatitis D Particle Types



- In 1977, an Italian doctor named Mario Rizzetto discovered a new nuclear antigen in the liver cells of patients infected with Hepatitis B Virus (HBV)
- The antigen was thought to be a new protein encoded by HBV, and it was labeled as the delta antigen
- Subsequent research on chimpanzees, however, indicated that this antigen was derived from a new virus, named the Hepatitis Delta Virus (HDV)
- **HDV is not classified into a viral family** because it is a unique virus dependent on HBV

Etiology

Hepatitis viruses

	<u>HAV</u>	<u>HBV</u>	<u>HCV</u>	<u>HDV</u>	<u>HEV</u>
Transmission	Enteral	Parenteral	Parenteral	Parenteral	Enteral
Classification	<i>Picornavirus</i>	<i>Orthohepadnavirus</i>	<i>Hepacivirus</i>	<i>Deltavirus</i>	<i>Hepevirus</i>
Genome	+ssRNA	dsDNA-RT	+ssRNA	–ssRNA	+ssRNA
Antigens		HBsAg, HBeAg	Core antigen	Delta antigen	
Incubation period	20–40 days	45–160 days	15–150 days	30–60 days	15–60 days
Severity/Chronicity	mild; acute	occasionally severe; 5–10% chronic	subclinical; 70% chronic	exacerbates symptoms of HBV; chronic w/ HBV	normal patients, mild; pregnant women, severe; acute
Vaccine	10 year protection	3 injections, lifetime protection	None available	None available	Investigational (approved in China)

Etiology

Chronic viral hepatitis

- Hepatitis B transmitted **vertically** in areas of high incidence (perinatally) from mother to baby during birth) or **horizontally** by being exposed to infected blood or blood products or less common through exposure to mucous membranes
- Hepatitis C transmitted **in same ways** and has become the most common viral hepatitis since widespread vaccination for Hepatitis B in the mid-1980s

Epidemiology and etiology

Understanding Chronic Hepatitis B

Mechanisms

- The **specific mechanism varies** and depends on the underlying cause for the condition.
- In viral hepatitis, the presence of the virus in the liver cells causes the immune system to attack the liver, resulting in inflammation and impaired function.
- In autoimmune hepatitis, the immune system attacks the liver due to the autoimmune disease.
- In some hepatitis, often including hepatitis caused by alcoholism, fat deposits accumulate in the liver, resulting in fatty liver disease (steatohepatitis).
- Chronic hepatitis **in severe cases** is occurring with portal based inflammation, fibrosis, disruption of the terminal plate, and piecemeal necrosis.
- Chronic hepatitis without piecemeal necrosis (formerly called chronic persistent hepatitis) has no significant periportal necrosis or regeneration with a fairly dense mononuclear portal infiltrate.

Mechanisms

Hepatitis A, B, C, D

Clinical investigation

- Chronic hepatitis may **cause nonspecific symptoms** such as malaise, tiredness, and weakness, and often leads to no symptoms at all.
- It is commonly **identified on blood tests** performed either for screening or to evaluate nonspecific symptoms.
- The presence of **jaundice indicates advanced liver damage**.
- On physical examination there may be enlargement of the liver.
- Extensive damage leads to weight loss, easy bruising and bleeding, peripheral edema (swelling of the legs), and accumulation of ascites (fluid in the abdomen).
- Acne, abnormal menstruation, lung scarring, and inflammation of the thyroid gland and kidneys may be present in women with autoimmune hepatitis.
- Hepatitis **associated aplastic anemia** may occur 2–3 months after an acute attack of hepatitis.
- Superinfection and coinfection with **HDV** results in more severe complications compared to infection with HBV alone.

Clinical investigation

Alcoholic hepatitis

- Alcoholic hepatitis is characterized by a **myriad of symptoms**, which may include feeling unwell, enlargement of the liver, development of fluid in the abdomen (ascites), and modest elevation of liver enzyme levels (as determined by liver function tests).
- Alcoholic hepatitis can vary from mild with only liver enzyme elevation to severe liver inflammation with development of jaundice, prolonged prothrombin time, and even liver failure. Severe cases are characterized by either obtundation (dulled consciousness) or the combination of elevated bilirubin levels and prolonged prothrombin time; the mortality rate in both severe categories is 50% within 30 days of onset.
- Alcoholic hepatitis is distinct from cirrhosis caused by long-term alcohol consumption.
- Alcoholic hepatitis by itself does not lead to cirrhosis, but cirrhosis is more common in patients with long term alcohol consumption.
- Some alcoholics develop acute hepatitis as an inflammatory reaction to the cells affected by fatty change (alcoholic steatonecrosis) .
- **Neuropsychiatric features**: asymmetric tremor, clumsiness with the hands, personality changes, dystonia, spasticity, rigidity, emotional lability, impulsiveness, disinhibition, self-injurious behavior, cognitive.

Clinical investigation

Autoimmune hepatitis

- Individuals with autoimmune hepatitis often have **no initial symptoms** and the disease is detected by abnormal liver function tests.
- Common initial symptoms include fatigue or muscle aches or signs of acute liver inflammation including fever, jaundice, and right upper quadrant abdominal pain, and occasionally systemic symptoms such as arthralgias, myalgias, polyserositis and thrombocytopenia.
- Patients usually present with evidence of moderate to severe hepatitis with elevated serum ALT and AST activities in the setting of normal to marginally elevated alkaline phosphatase and gamma-glutamyltranspeptidase activities.
- The disease may occur in any ethnic group and at any age, but is most often diagnosed in patients between age 40 and 50.
- Though there is a strong female predominance, men are also at risk for the disease.

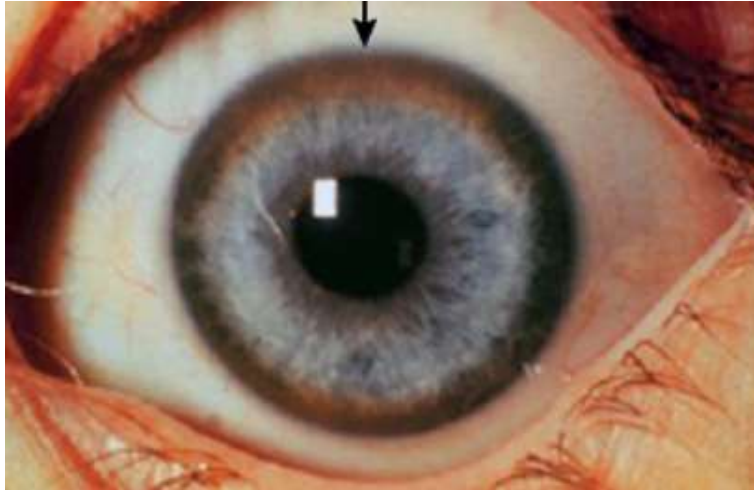
Clinical investigation

Wilson Disease 1

- The major patterns of hepatic involvement: chronic active hepatitis, cirrhosis (the most common initial presentation) and fulminant hepatic failure.
- **Neuropsychiatric features:** asymmetric tremor, difficulty speaking, excessive salivation, ataxia, masklike facies, clumsiness with the hands, personality changes, dystonia, spasticity, grand mal seizures, rigidity, flexion contractures, emotional lability, impulsiveness, disinhibition, self-injurious behavior, cognitive.
- **Musculoskeletal manifestations:** osteoarthritis, osteoporosis, osteomalacia, rickets, spontaneous fractures.
- **Hematologic and renal manifestations:** intravascular hemolysis, urolithiasis, hematuria.
- **Kayser-Fleischer rings:** the deposition of copper in the Descemet membrane in the limbus of the cornea with the color from greenish gold to brown.
- Skin pigmentation and a bluish discoloration at the base of the fingernails (azure lunulae).

Clinical investigation

Wilson Disease 2



Kayser-Fleischer rings.



Skin pigmentation and a bluish discoloration at the base of the fingernails (azure lunulae).

Clinical investigation

The natural history of chronic hepatitis B virus infection

- Stage 1: **high viral loads and immune tolerance**. In acute infection, this corresponds to the incubation period, but with neonatal chronic infection, this period often lasts for decades.
- Stage 2: **an immunologic response develops leading to hepatocyte necrosis**. In patients with chronic infection, stage 2 may persist for 10-20 years and lead to cirrhosis and its complications.
- Stage 3: **the immune response decreases the number of infected cells with beginning of low viral replication**, referred to as the inactive carrier state. In this stage, **HBeAg** is no longer detectable, a marked decrease in HBV viral load is observed, and aminotransferase levels become normal. Some patients continue to have high levels of serum HBV DNA and amino-transferases (referred to as HBeAg-negative chronic hepatitis), because of HBV variants that prevent the production of HBeAg.
- Stage 4: **patients become negative for HBeAg and positive for anti-HBs, and HBV DNA** is usually no longer detectable in serum, although still present in liver tissue. Immune clearance occurs at a rate of about 1% per year in chronic carriers of HBV. Some patients can reactivate their hepatitis B when given chemotherapy or immuno-suppressive treatment. Patients with active HBV replication are at increased risk for cirrhosis, hepatic decompensation and hepatocellular carcinoma compared to inactive carriers.

Clinical investigation

Activity

- Grade 0: No significant inflammation or necrosis.
- Grade 1 (minimal activity): Portal inflammation with predominantly mononuclear cells almost entirely confined to the portal areas, no interface hepatitis or lobular inflammatory foci.
- Grade 2 (mild activity): Mild portal inflammation, interface hepatitis, and scant lobular spotty necrosis.
- Grade 3 (moderate activity): Moderate portal inflammation, interface hepatitis, and lobular spotty necrosis.
- Grade 4 (severe activity): Marked portal inflammation, interface hepatitis, and lobular necrosis, including bridging necrosis.

Clinical investigation

Fibrosis

Stage 0: No fibrosis

Stage 1: Fibrous portal expansion

Stage 2: Periportal fibrous extension

Stage 3: Fibrous septa formation, including portal-to-central bridging fibrosis

Stage 4: Cirrhosis

Diagnosis

- Diagnosis is made by assessing an individual's symptoms, physical exam, and medical history, in conjunction with blood tests, liver biopsy, and imaging.
- Blood testing includes blood chemistry, liver enzymes, serology and nucleic acid testing.
- Abnormalities in blood chemistry and enzyme results may be indicative of certain causes or stages of hepatitis.
- Imaging can identify steatosis of the liver but liver biopsy is required to demonstrate fibrosis and cirrhosis.
- A **biopsy is unnecessary** if the clinical, laboratory, and radiologic data suggests hepatitis.

Diagnosis

Special blood testing

- Hepatitis B: surface antigen (*HBsAg*), hepatitis B core antigen (*HBcAg*), IgM antibodies specific to the hepatitis B core antigen (*anti-HBc IgM*), hepatitis B e (a viral protein that is secreted by hepatitis B infected cells) antigen (*HBeAg*). The presence of HBeAg in a host's serum is associated with much higher rates of viral replication and enhanced infectivity; however, variants of the hepatitis B virus do not produce the 'e' antigen, so this rule does not always hold true.
- Hepatitis C: *HCV antibody* enzyme immunoassay or ELISA, recombinant immunoblot assay, and quantitative HCV RNA polymerase chain reaction (PCR). HCV RNA can be detected by PCR typically one to two weeks after infection, while antibodies can take substantially longer to form and thus be detected.
- Hepatitis D: HDAg in two forms; a large (L)-HDAg, and a small (S)-HDAg of 24kDa. *HDag-S* is produced in the early stages of an infection and enters the nucleus and supports viral replication. *HDag-L*, in contrast, is produced during the later stages of an infection, acts as an inhibitor of viral replication, and is required for assembly of viral particles.
- Autoimmune hepatitis: antinuclear antibody (*ANA*), anti-smooth muscle antibody (*SMA*), liver/kidney microsomal antibody (*LKM-1, LKM-2, LKM-3*), anti soluble liver antigen and liver–pancreas antigen (*SLA/LP*) and anti-mitochondrial antibody (AMA)), increased Immunoglobulin G level. The diagnosis always requires a liver biopsy.

Diagnosis

Liver chemistry test

Liver chemistry test	Clinical implication of abnormality
Alanine transaminase (ALT)	Hepatocellular damage
Aspartate transaminase (AST)	
Lactate dehydrogenase	
Bilirubin	Cholestasis
Alkaline phosphatase	
Gamma-glutamyl transpeptidase (GGT)	
Bile acids	
Prothrombin time	Impaired synthetic function
Albumin (ALB)	

Diagnosis

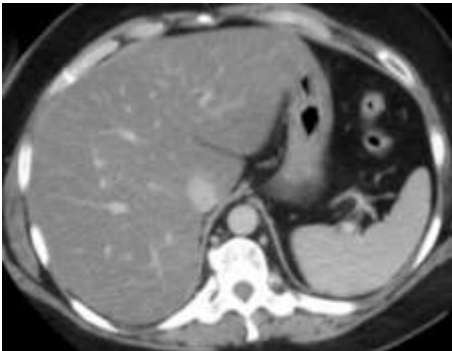
Imaging studies



Echocardiogram of
parenchyma
is increased and
heterogeneous.

The following radiologic
studies may be used to
evaluate patients with
hepatitis B disease:

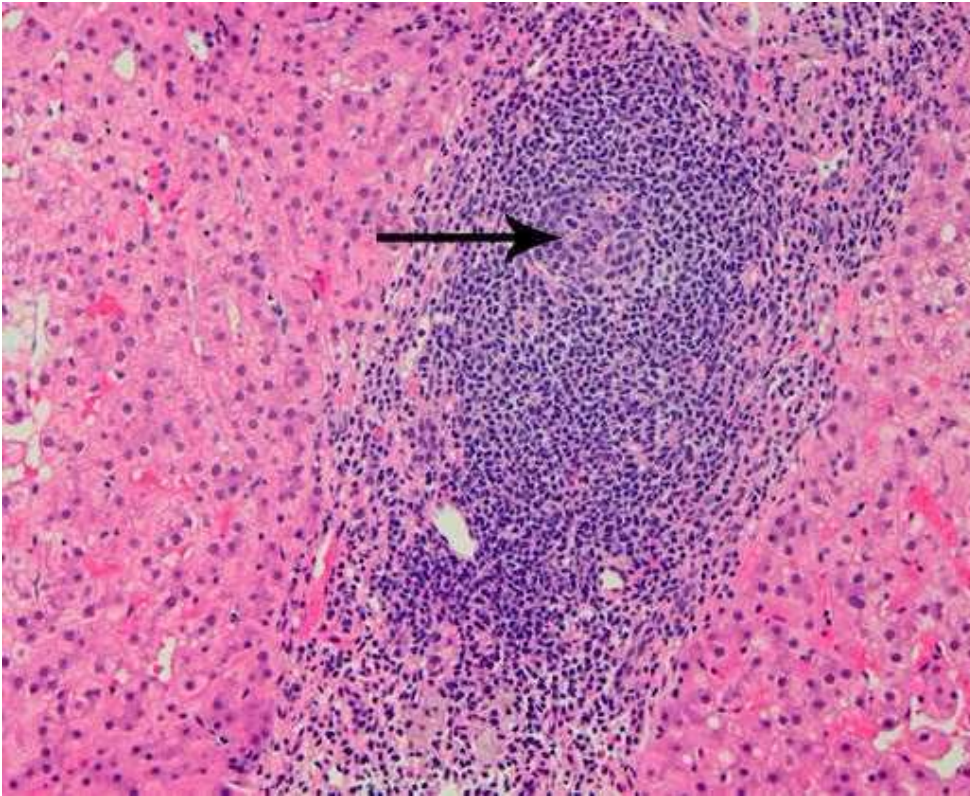
- Abdominal
ultrasonography
- Abdominal computed
tomography (CT) scanning
- Abdominal magnetic
resonance imaging (MRI).



Fatty liver
disease as seen
on CT.

Diagnosis

The histopathologic features



- The histopathologic features of chronic hepatitis from any cause **are very similar** and do not distinguish one disease from another.
- The portal tracts show variable number of mononuclear cells, principally small lymphocytes with a variable population of plasma cells and macrophages.
- Eosinophils may also be present. The inflammation in cases with little or no activity is largely limited to portal tracts.

Diagnosis

Wilson Disease

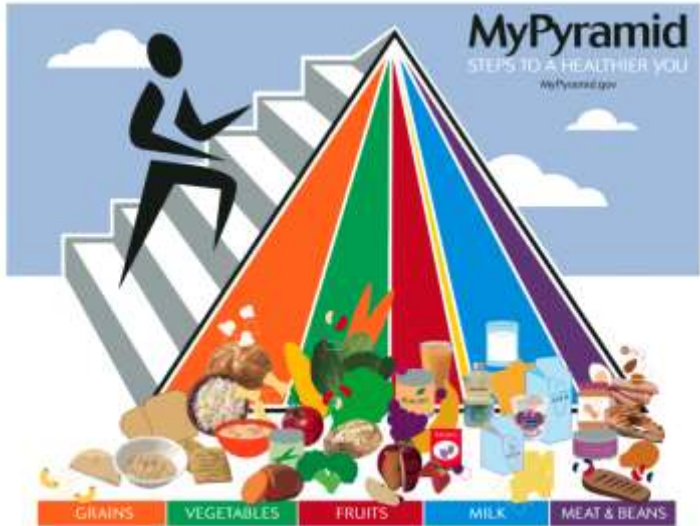
- Serum ceruloplasmin levels are less than 20 mg/dL (reference range, 20-40 mg/dL) in approximately 90% of all patients.
- The urinary copper excretion rate is greater than 100 mcg/day (reference range, < 40 mcg/day) in most patients.
- In a patient with Kayser-Fleischer rings, a serum ceruloplasmin level < 0 mg/dL and 24-hoyn urine copper excretion >40 mcg/day establish the diagnosis.
- Hepatic **copper** concentration (criterion standard) on a liver biopsy specimen is >250 mcg/g of dry weight even in asymptomatic patients.
- Radiolabeled copper testing directly assays hepatic copper metabolism.
- Genetic testing is limited to screening of family members for an identified mutation detected in the index patient.
- Brain imaging shows characteristic findings; MRI appears to be more sensitive than CT in detecting early lesions..
- Resting ECG abnormalities include left ventricular or biventricular hypertrophy, early repolarization, ST segment depression, T-wave inversion, and various arrhythmias.

Diagnosis

People With Chronic Hepatitis B Often Do Not
Know It

Treatment

Lifestyle modifications



[MyPyramid](http://www.MyPyramid.gov)

- Lifestyle modifications are **strongly recommended** for patients with chronic hepatitis.
- Even when efficacious pharmacologic interventions are identified, lifestyle changes will likely represent an adjuvant treatment because new drugs are inevitably expensive and may have unanticipated adverse effects after prolonged use.
- Lifestyle modifications typically encompass both **dietary intervention and physical activity** goals.

Treatment

Hepatitis B, D

- Patients with **persistently elevated serum alanine aminotransferase, and HBV DNA levels** are candidates for therapy.
- Treatment lasts **from six months to a year**, depending on medication and genotype.
- Although none of the available drugs can clear the infection, they can stop the virus from replicating, thus minimizing liver damage.
- There are seven medications licensed for treatment of hepatitis: **antiviral drugs** (lamivudine, adefovir, tenofovir, telbivudine and entecavir, and the two **immune system modulators** interferon alpha-2a and PEGylated interferon alpha-2a. The World Health Organization recommended a combination of tenofovir and entecavir as first line agents.
- Interferon treatment may produce an e antigen seroconversion rate of 37% in genotype A but only a 6% seroconversion in type D.
- The drug **myrcludex B, which inhibits virus entry into hepatocytes, is in clinical trials** as of October 2015.

Treatment

Hepatitis C

- HCV induces chronic infection in 50–80% of infected persons.
- Approximately 40–80% of these clear with treatment.
- In rare cases, infection can clear without treatment.
- Those with chronic hepatitis C are advised to avoid alcohol and medications toxic to the liver, and to be vaccinated for hepatitis A and hepatitis B.
- Ultrasound surveillance for hepatocellular carcinoma is recommended in those with accompanying cirrhosis.

Treatment

Alcoholic hepatitis

- Clinical practice guidelines by the American College of Gastroenterology have recommended **corticosteroid** treatment with prednisolone 40 mg daily for four weeks followed by a taper. Prednisolone gave a small reduction in mortality at 28 days but this did not reach significance, and there were no improvements in outcomes at 90 days or 1 year.
- Pentoxifylline (**a xanthine derivative**) is used to improve blood flow for 4 weeks to prevent one patient from dying. Pentoxifylline did not improve survival alone or in combination.

Treatment

Autoimmune hepatitis

- Treatment may involve the prescription of **immunosuppressive glucocorticoids**, with or without **azathioprine**, and remission can be achieved in up to 60–80% of cases, although many will eventually experience a relapse. Budesonide has been shown to be more effective in inducing remission than prednisone, and result in fewer adverse effects.
- Patients who do not respond to glucocorticoids and azathioprine may be given **other immunosuppressives** like mycophenolate, cyclosporin, tacrolimus, methotrexate, etc.
- **Liver transplantation** may be required if patients do not respond to drug therapy or when patients present with fulminant liver failure.

Treatment

Wilson Disease

- The mainstay of therapy is lifelong use of **chelating agents** (e.g., penicillamine, trientine).
- Symptoms, particularly neurologic ones, may worsen with initiation of chelation.
- Surgical decompression or transjugular intrahepatic shunting (TIPS) is reserved for recurrent or uncontrolled variceal bleeding unresponsive to standard conservative measures.
- Orthotopic liver transplantation is curative.
- Other treatments (anticholinergics, baclofen, GABA antagonists, levodopa, antiepileptics, neuroleptics)
- Protein restriction, lactulose, or both to treat hepatic encephalopathy

Treatment

[How to Treat Chronic Hepatitis B](#)

Prognosis

- Prognosis depends heavily on the disease or condition that is causing the symptoms.
- Chronic damage to the liver can result in the formation of scar tissue (**fibrosis**) and can result in nodules that block the liver from functioning properly (**cirrhosis**).
- Another complication of chronic hepatitis is liver cancer, specifically hepatocellular **carcinoma**.
- Some cases can require a liver transplant.

Prophylaxis 1

- **Vaccines** are available to prevent hepatitis B.
- Vaccines to prevent hepatitis B have been available since 1986 and have been incorporated into at least 177 national immunization programs for children.
- Immunity is achieved in greater than 95% of children and young adults receiving the three-dose recombinant virus vaccine.
- Vaccination within 24 hours of birth can prevent transmission from an infected mother.
- Adults **over 40 years of age have decreased immune response** to the vaccine.
- The vaccine for hepatitis B **protects against hepatitis D virus** because of the latter's dependence on the presence of hepatitis B virus for it to replicate.

Prophylaxis 2

- HBV, HCV transmission can be prevented by screening of donated blood, plasma, organ tissue and semen, by viruses inactivation in plasma-derived products, by risk-reduction counselling and by implementation of infection control practices.
- For HBV the single most effective prevention measure is routine immunization for infants.
- Immunization should also be offered to high-risk individuals including healthcare workers, persons with multiple sex partners, intravenous drug users, patients with chronic diseases who are likely to undergo multiple percutaneous procedures and contacts of HBV-infected persons.
- Babies born to HBsAg carrier mothers should be protected against perinatal transmission by administration of hepatitis B immunoglobulin and HBV vaccine.

Clinical cases, 1a

Hepatitis C and Alcohol Abuse - What is the Treatment Plan?

A 57-year-old African American male (AAM) with a past medical history (PMH) of hepatitis C, alcohol (EtOH) abuse, and hypertension (HTN) is referred to the GI clinic because of elevated liver function tests (LFTs). He has no complaints.

Past medical history (PMH)

Intravenous drug abuse (IVDA) with heroin and cocaine abuse 30 years ago, hepatitis C, heavy alcohol abuse, HTN. Rectal bleeding for 2 months - a colonoscopy showed 9 benign polyps (one tubular adenoma and 8 hyperplastic polyps).

Medications

Tenormin (atenolol), lisinopril.

Social history (SH)

Drug abuse as described above. He told his PCP that he is "in remission" from alcohol. On closer questioning, the patient admitted to long term alcohol abuse in binging sprees, drinking 3-5 bottles of wine whenever he can afford it. The last binge was just 2 weeks ago. He finances his EtOH abuse with the money he receives for disability because of his liver disease.

Clinical cases, 1b

Physical examination

WD/WN in NAD (well-developed, well-nourished, no apparent distress).

No signs of chronic liver disease.

HEENT (Head, Eye, Ear, Nose and Throat Exam): no teeth (lost in brawls as per patient).

The rest of the examination was normal.

What is your diagnosis?

Hepatitis and alcohol abuse.

What laboratory work-up would you order?

CBC, CMP, AFP (complete blood count, comprehensive metabolic panel, alpha-fetoprotein).

Liver ultrasound (U/S).

What about hepatitis C genotype?

The treatment response in hepatitis C depends on the genotype. The response in HCV type 1 is only 40% with interferon (INF) plus ribavirin for 12 months. HCV type 2 and 3 have a better response rate of 80% after 60 months. The patient's genotype was 1a.

Clinical cases, 1c

Would you recommend antiviral treatment with INF and ribavirin?

No. EtOH abuse is a contraindication to the antiviral treatment of hepatitis C.

What happened?

The patient was referred to a drug abuse counseling center and a follow-up (F/U) appointment was made in 1 month to monitor the progress. Liver U/S and repeat LFT were ordered. All patients with chronic hepatitis C need AFP and liver U/S every 6 months to screen for hepatocellular CA.

What did we learn from this case?

Take a careful history of drug abuse. **You cannot treat hepatitis C patients** if the patient is still drinking heavily. EtOH abuse has a detrimental effect on hepatitis C liver disease (interestingly, this is not typically the case with hepatitis B).

Even if you decide to treat this patient, his chance of response would be virtually zero because of the genotype and EtOH abuse. The studies show that African American patients also have a lower response rate. In conclusion, we should first help this patient stop drinking before treating his hepatitis C.

Clinical cases, 2

Use of infliximab in a patient with rheumatoid arthritis and chronic hepatitis B.

Anti-TNF- α agents have emerged as a potent treatment for patients with rheumatoid arthritis unresponsive to conventional disease-modifying antirheumatic drugs. Increased susceptibility to infections induced by these drugs is the main complication of their use.

Reactivation of hepatitis B virus (HBV) is one of the most worrisome side effects in patients with HBV infection receiving anti-TNF- α .

Doubrawa E with colleagues from Hospital de Clínicas, Universidade Federal do Paraná, Rua Nilo Cairo 36/105, Curitiba, PR, Brazil report the case of a 56-year-old male patient with stable hepatitis B and **good response** to the antiviral combination of lamivudine and tenofovir when infliximab was started.

The patient went into remission.

During the 30-month treatment with the biologic, his liver function remained stable, with no HBV reactivation.

Clinical cases, 3

Chronic hepatitis B with type I diabetes mellitus and autoimmune thyroiditis development during interferon alpha therapy.

Interferon alpha is a molecule frequently used in the treatment of chronic hepatitis B, C, and D, with immunomodulatory and antiviral activity. It has been widely claimed that **interferon alpha triggers autoimmunity, with its broad adverse effect profile**. Kose S from Education and Research Hospital Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey present the case of a 29-year-old male patient with chronic hepatitis B diagnosis who developed type 1 diabetes mellitus and autoimmune thyroiditis during treatment with interferon alfa-2b. Within four months of initiation of treatment, the patient presented to clinic with dry mouth, urinary frequency (8 to 10 times per day), drinking plenty of water, night time urination, and tiredness. He was admitted to the clinic when his fasting blood glucose level was detected to be high. After examinations, the patient was diagnosed with type 1 diabetes and autoimmune thyroiditis and began to receive treatment with insulin and propranolol.

Clinical cases, 4

Successful kidney transplantation from a hepatitis B surface antigen-positive donor to an antigen-negative recipient using a novel vaccination regimen.

Transplanting a kidney from a hepatitis B surface antigen (HBsAg)-positive donor to an HBsAg-negative recipient who is naturally immune has been successful in countries endemic for hepatitis B virus (HBV). However, in most of these cases, the donors were deceased. Singh G present a report of a successful HBsAg-discordant kidney transplantation in the United States; in this case, a living donor kidney was transplanted to a vaccinated recipient. The wife of a 58-year-old HBsAg-negative man volunteered to donate a kidney to her husband. She had chronic hepatitis B but undetectable HBV DNA. She tested positive for HBsAg and antibody to hepatitis B core antigen, but hepatitis B e antigen was undetectable. The recipient failed to develop an antibody response to 3 doses of intramuscular recombinant HBV vaccine given in consecutive months. Immunity was induced by using biweekly intradermal vaccine. However, antibody titer tapered to <10 mIU/mL over 14 months. An intramuscular booster vaccine resulted in a prolonged anamnestic response, allowing for successful living unrelated donor transplantation. During the 10 years since transplantation, the patient has continued to have normal liver function, with undetectable HBsAg and HBV DNA.

Clinical cases, 5

Telbivudine myopathy in a patient with chronic hepatitis B.

A 25-year-old man with hepatitis B virus (HBV) infection received antiviral treatment with telbivudine 600 mg daily. Six months after starting treatment, the patient developed progressive weakness and myalgia. Physical examination showed symmetrical proximal weakness. Blood tests at admission revealed positive hepatitis b surface antigen (HBs Ag), and, elevated creatine kinase (CK) level (1,614 U/L, normal range: 38-174 U/L). Aspartate aminotransferase was 64.7 U/L (normal range: 8-40 U/L), and LDH (lactate dehydrogenase) was 293 U/L (normal range: 80-285 U/L). Electrodiagnostic studies indicated myopathic changes. A muscle biopsy revealed myositis and no mitochondrial changes were found. Drug-induced myopathy was suspected and **telbivudine was changed to entecavir**. The muscle weakness and laboratory findings improved. A patient developed drug-induced myopathy during long-term treatment with telbivudine for chronic HBV. To promptly detect this reversible adverse event, monitoring of serum CK level and recognition of myopathic signs and symptoms are necessary. Further investigations are needed to clarify the possible mechanism of telbivudine-induced myopathy.

Diagnostic and treatment guidelines

- [Treatment of Chronic Hepatitis B: 2015](#)
- [Recommendations for Testing, Managing, and Treating Hepatitis: 2014](#)
- [Diagnosis and Management of Autoimmune Hepatitis: 2014](#)
- [The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: 2012](#)
- [Diagnosis and Treatment of Wilson Disease: An Update: 2014](#)
- [Liver Biopsy: 2014](#)
- [Evaluation for Liver Transplantation in Adults: 2013](#)

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