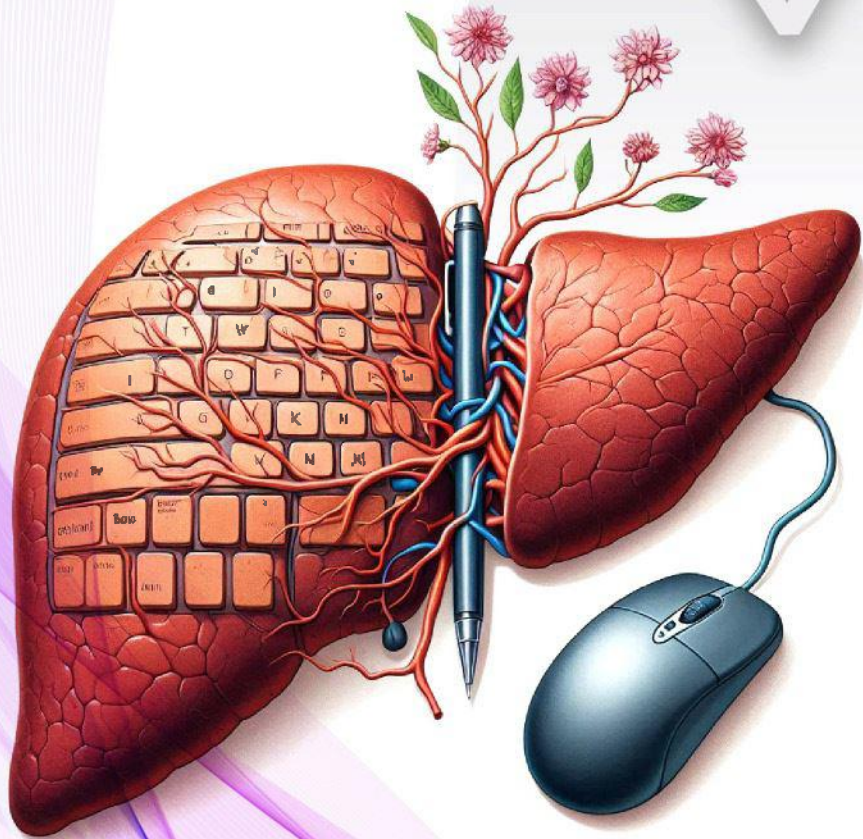


Autoimmune Hepatitis and Biliary Cholangitis:

A Comprehensive Guide for Patients

Authors:

Seyed Moayed Alavian M.D,
Professor in medicine, Hepatologist
SeyedeHoda Alavian M.D,
Internist



Autoimmune Hepatitis and Biliary Cholangitis:

A Comprehensive Guide for Patients

Authors:

**Seyed Moayed Alavian M.D,
Professor in medicine, Hepatologist
SeyedeHoda Alavian M.D,
Internist**

سرشناسنامه

علویان، موید، ۱۳۴۱

عنوان و نام پدیدآور

هپاتیت خود ایمنی و کلانژیت های صفراوی: راهنمای جامع برای بیماران

مشخصات نشر

تهران، شرکت سلامت پویان کوثر، ۱۴۰۰.

مشخصات ظاهری

۱۰۴ ص.: مصور.

شابک

۹۷۸-۶۲۲-۸۷۸۰۸-۰-۱

وضعیت فهرست نویسی

فیبا

یادداشت

نمایه.

موضوع

هپاتیت خود ایمنی-کلانژیت صفراوی

موضوع

Autoimmune Hepatitis-Biliary Cholangitis

رده بندی کنگره

رده بندی دیویی

شماره کتابخانه ملی

هپاتیت خودایمنی

نام کتاب:

و کلانژیت های صفراوی: راهنمای جامع برای بیماران

ناشر:

انتشارات شرکت سلامت پویان کوثر

تألیف:

دکتر سید موید علویان / دکتر سیده هدی علویان

صفحه آرایشی:

راضیه جانباز

طراحی جلد:

راضیه جانباز

نوبت چاپ:

اول

تیراژ:

۱۰۰

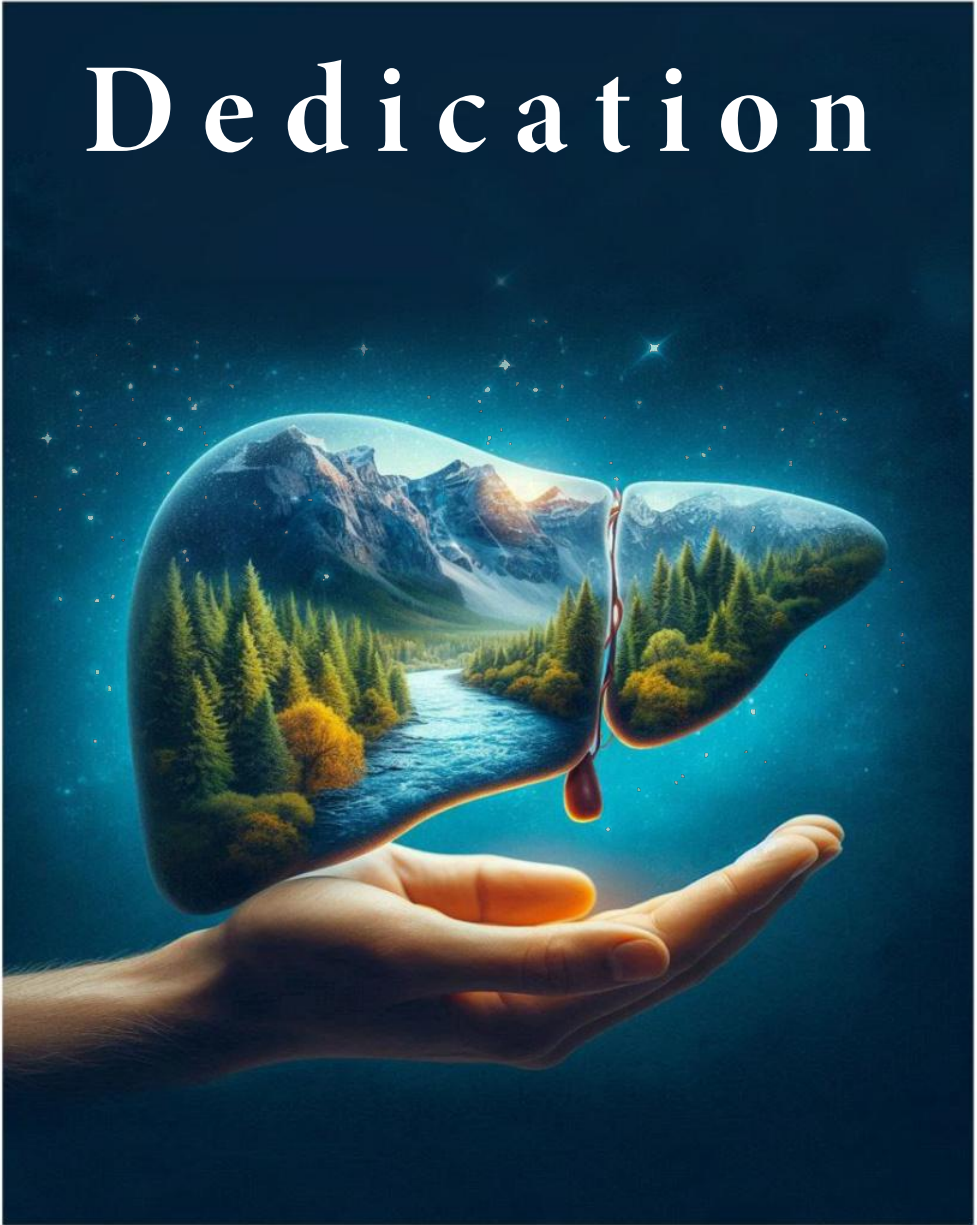
شابک:

۹۷۸-۶۲۲-۸۷۸۰۸-۰-۱

قیمت:

۴۸۰۰۰ ریال

Dedication



Dedicated to autoimmune patients who bear the burden of their illness.

Dr. Seyed Moayed Alavian
SeyedeHoda Alavian M.D,
November 2024

Introduction

In today's world, being aware of various diseases and their impact on our health has become increasingly important. One of the diseases that may be less known to many is **Autoimmune Hepatitis** and related liver diseases such as **Primary Biliary Cholangitis** and **Primary Sclerosing Cholangitis**. These autoimmune liver diseases result from the immune system mistakenly attacking the liver cells or bile ducts. In this book, our goal is to introduce you to these diseases in a simple and understandable way, so that you can take better care of your health, or if a loved one is affected by these conditions, you will have sufficient information to help them.

Autoimmune Hepatitis, Primary Biliary Cholangitis (PBC), and Primary Sclerosing Cholangitis (PSC) are all autoimmune diseases that cause liver damage. In Autoimmune Hepatitis, the immune system mistakenly attacks the liver tissues, leading to inflammation and damage. **Primary Biliary Cholangitis** mainly affects the small bile ducts within the liver, disrupting bile flow and causing liver damage. **Primary Sclerosing Cholangitis**, on the other hand, affects both the intrahepatic and extrahepatic bile ducts, leading to scarring and narrowing of the bile ducts. Without treatment, these diseases can lead to liver failure and cirrhosis. However, with timely diagnosis and proper medical management, it is possible to slow down disease progression and improve the quality of life for patients.

Understanding these diseases can help us make better decisions when faced with them. Autoimmune Hepatitis, Primary Biliary Cholangitis, and Primary Sclerosing Cholangitis are complex conditions that may affect you or a loved one. Knowing the symptoms, diagnosis methods, and treatment options can greatly impact the well-being of those living with these diseases.

This book is written for anyone seeking a better understanding of Autoimmune Hepatitis, Primary Biliary Cholangitis, and Primary Sclerosing Cholangitis. Whether you are affected by these diseases yourself, have a loved one facing them, or are simply interested in expanding your knowledge about autoimmune diseases, this book will serve as a valuable reference. Our goal is to provide scientific information in a simple and accessible way, guiding you in better understanding and managing these conditions.

Finally, it is important to note that the information provided in this book is intended solely to raise awareness among the general public and patients. It should not be used as a basis for individual decision-making, and all medical decisions should be fully followed and guided by your healthcare provider.

Dr. Seyed Moayed Alavian
Professor in Medicine, Hepatologist
SeyedeHoda Alavian M.D,
Internist
November 2024
Tehran, Iran

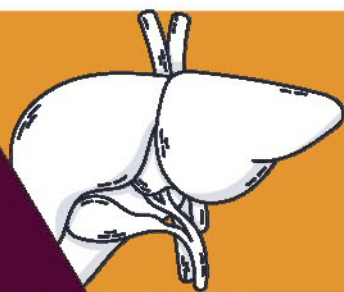


Table of Contents:

Introduction and Basic Principles

Chapter 1: Introduction to Autoimmune Hepatitis and Related Liver Diseases

16

An overview of **autoimmune liver diseases** such as **Autoimmune Hepatitis**, **Primary Biliary Cholangitis**, and **Primary Sclerosing Cholangitis**, and the importance of understanding these conditions.

Chapter 2: Understanding the Liver and Biliary System: Anatomy and Normal Function

18

A detailed look at the normal functions of the **liver** and **bile ducts**, particularly in the digestion of fats and detoxification of the body.

Chapter 3: What is Hepatitis?

26

A definition of **hepatitis** and its various forms, including **viral** and **autoimmune hepatitis**, with explanations of their causes and complications.

Chapter 4: The Immune System and Its Role in Autoimmune Diseases

37

An explanation of how the **immune system** functions in autoimmune diseases like **Autoimmune Hepatitis** and biliary cholangitis, focusing on the immune mechanisms that cause these conditions.

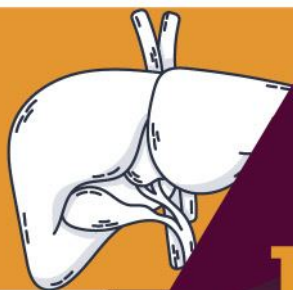


Table of Contents

Book One: Autoimmune Hepatitis

Chapter 1: What is Autoimmune Hepatitis (AIH)? 38

A definition of Autoimmune Hepatitis and the mechanisms behind the development of this disease.

Chapter 2: Types of Autoimmune Hepatitis (Type One and Type Two) 41

An overview of the differences between Type 1 and Type 2 Autoimmune Hepatitis, focusing on aspects such as age, gender, and symptoms.

Chapter 3: Causes and Contributing Factors of Autoimmune Hepatitis 43

An exploration of the various factors that lead to or exacerbate Autoimmune Hepatitis, including genetic predisposition, environmental triggers, infections, and hormonal changes.

Chapter 4: The History of Autoimmune Hepatitis: From the Beginning to Modern Times 53

A historical perspective on the discovery and evolution of Autoimmune Hepatitis, from early diagnoses to modern advancements in its diagnosis and treatment.

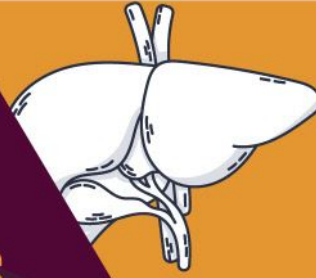
Chapter 5: Autoimmune Hepatitis in Iran 55

An analysis of the prevalence and treatment of Autoimmune Hepatitis in Iran, including references to notable physicians and active medical centers specializing in this field.

Chapter 6: Why Awareness of These Diseases is Important 59

Discussing the importance of early diagnosis and proper care to prevent severe complications related to Autoimmune Hepatitis.

Table of Contents



Book One: Autoimmune Hepatitis

Chapter 7: Symptoms and Signs of Autoimmune Hepatitis 62

Common symptoms of the disease, such as fatigue, jaundice, and abdominal pain.

Chapter 8: Diagnosing Autoimmune Hepatitis: Medical Tests and Evaluations 64

A description of diagnostic methods, including blood tests and liver biopsy for confirming the presence of Autoimmune Hepatitis.

Chapter 9: Drug Treatments for Autoimmune Hepatitis 72

A detailed look at immunosuppressive medications used to treat the disease and how to manage their side effects.

Chapter 10: Non-Drug Treatments for Autoimmune Hepatitis 80

Exploring non-pharmaceutical approaches such as lifestyle changes, proper nutrition, and stress reduction techniques to manage the disease.

Chapter 11: Complications of Autoimmune Hepatitis 83

An overview of complications associated with Autoimmune Hepatitis, such as osteoporosis, diabetes, and other comorbid conditions

Chapter 12: Autoimmune Diseases Associated with Autoimmune Hepatitis 89

A discussion of other autoimmune conditions that may co-occur with Autoimmune Hepatitis, such as Lupus, Rheumatoid Arthritis, and Hashimoto's Thyroiditis.

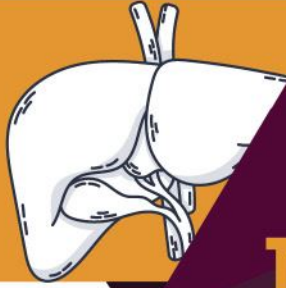


Table of Contents

Book One: Autoimmune Hepatitis

 **Chapter 13: Pregnancy and Autoimmune Hepatitis** 97

Managing the disease during pregnancy, including the challenges and potential effects of immunosuppressive drugs on the fetus.

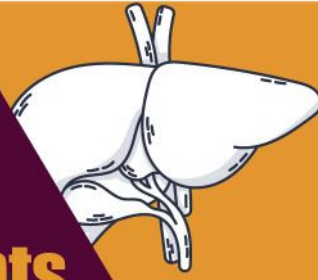
 **Chapter 14: Frequently Asked Questions about Autoimmune Hepatitis** 99

Answers to common questions from patients and their families regarding the disease.

 **Chapter 15: The Future of Autoimmune Hepatitis Treatment** 101

An insight into innovative treatment methods and future research directions for improving outcomes for those with Autoimmune Hepatitis.

Table of Contents



Book Two: Primary Biliary Cholangitis

Chapter 1: What is Primary Biliary Cholangitis? 104

A definition of **Primary Biliary Cholangitis** and an explanation of how the disease develops.

Chapter 2: Primary Biliary Cholangitis in Iran 107

An examination of the prevalence, management, and treatment of **PBC** in **Iran**, with insights into how the healthcare system handles the disease.

Chapter 3: Causes and Risk Factors of Primary Biliary Cholangitis 110

A look at the various risk factors that may contribute to the development or worsening of **PBC**, including genetic predispositions, environmental triggers, and infections.

Chapter 4: Symptoms and Signs of Primary Biliary Cholangitis 118

Common symptoms of **PBC**, such as **fatigue**, **jaundice**, and **itching** of the skin, and how they manifest in patients.

Chapter 5: Diagnosing Primary Biliary Cholangitis: Medical Tests and Evaluations 122

A review of diagnostic methods for **PBC**, including **blood tests** and **liver biopsy**, and how these tests help in confirming the diagnosis.

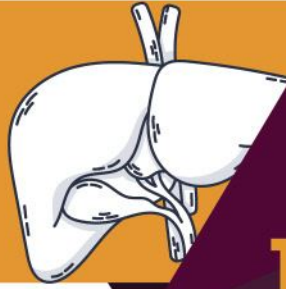


Table of Contents

Book Two: Primary Biliary Cholangitis

Chapter 6: Treatment and Management of Primary Biliary Cholangitis

126

Treatment strategies and methods for managing PBC, focusing on medications that reduce inflammation and prevent disease progression, as well as other therapeutic options.

Chapter 7: Living with Primary Biliary Cholangitis: Management, Care, and Lifestyle Changes

130

Practical approaches to daily life for PBC patients, including managing fatigue, pain, and digestive issues. This section will also cover essential care strategies to prevent disease exacerbation and long-term complications like liver failure and the need for a liver transplant. Additionally, it will provide guidance on improving quality of life through dietary changes and physical activities.

Table of Contents



Book Three: Primary Sclerosing Cholangitis

Chapter 1: What is Primary Sclerosing Cholangitis? 136

A definition of Primary Sclerosing Cholangitis (PSC) and an explanation of how this disease affects the bile ducts, causing scarring and narrowing over time.

Chapter 2: Primary Sclerosing Cholangitis in Iran 139

An examination of studies and the prevalence of PSC in Iran. This section will also cover research efforts and the treatment landscape in specialized centers across the country, highlighting how PSC is managed within the Iranian healthcare system.

Chapter 3: Symptoms and Signs of Primary Sclerosing Cholangitis 142

A review of the common symptoms of PSC, including fatigue and itching (pruritus), and how these symptoms manifest in patients.

Chapter 4: Diagnostic Methods for Primary Sclerosing Cholangitis 144

An exploration of diagnostic techniques used to identify PSC, including imaging tests, blood tests, and liver biopsy to confirm the disease and assess its progression.

Chapter 5: Association of Primary Sclerosing Cholangitis with Bowel Diseases and Other Autoimmune Conditions 148

A discussion of the link between PSC and inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, as well as the relationship between PSC and other autoimmune disorders.

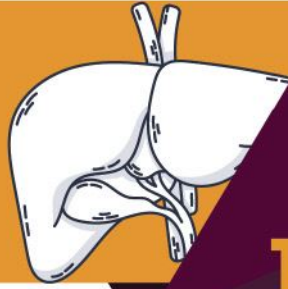


Table of Contents

Book Three: Primary Sclerosing Cholangitis

Chapter 6: Surgical and Non-Surgical Treatment Methods

151

An overview of the various treatment approaches for PSC, including the use of medications, stent placement in the bile ducts, and surgical interventions aimed at reducing inflammation and bile duct obstructions.

Chapter 7: Overlap Syndromes and Autoimmune Cholangiopathy Associated with IGg4

163

An in-depth examination of **Overlap Syndromes**, which involve the coexistence of PSC with other autoimmune liver diseases, and the association of IGg4-related autoimmune cholangiopathy with PSC.



Introduction and Basic Principles

Primary Sclerosing Cholangitis (PSC)

Primary sclerosing cholangitis is another autoimmune liver disease, affecting the larger bile ducts outside the liver. It causes inflammation and narrowing of the bile ducts, which can lead to blockages and eventually severe liver damage. PSC is often seen in patients with inflammatory bowel diseases such as ulcerative colitis. Like primary biliary cholangitis, PSC can also lead to cirrhosis if left untreated.

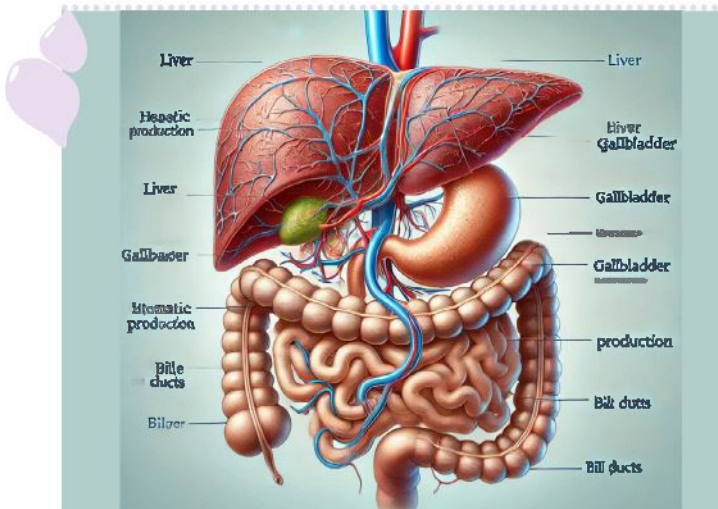
Importance of Understanding These Diseases

Early and accurate recognition of autoimmune liver diseases is crucial, as failing to diagnose these conditions in time can lead to liver failure and the need for a liver transplant. Early diagnosis allows patients to improve their quality of life and prevent disease progression through lifestyle changes and appropriate medical treatments. With advancements in medical research, effective therapies are now available to manage these diseases, including immunosuppressive drugs and supportive treatments.

These diseases share a common mechanism, as they all result from the immune system malfunctioning and attacking the healthy tissues of the liver and bile ducts. However, they differ in clinical symptoms, disease progression, and recommended treatments. Understanding these differences is essential for both physicians and patients.

Understanding the Liver and Biliary System: Anatomy and Function in a Healthy State

The liver and biliary system are two highly important and complex parts of the human body, playing an extensive role in metabolism, detoxification, energy storage, and fat digestion. These two systems work closely with other organs to perform various vital functions that are essential for maintaining health and sustaining life.



The schematic image of the structure of the liver, gallbladder, and digestive system is ready. This image clearly shows the position of the liver, gallbladder, and their connection with the stomach, intestines, and bile ducts.

Chapter 2

Understanding the Liver and Biliary System: Anatomy and Normal Function

Liver: Anatomy and Main Functions

The liver is the largest gland and one of the most vital organs in the body, located in the upper right part of the abdomen, weighing between 1.4 to 1.6 kilograms. Due to its wide range of functions, the liver plays a key role in overall health.

The liver is composed of two main lobes (the right and left lobes). It is protected by a membrane called Glisson's capsule and is divided into smaller units known as lobules. Each lobule contains a network of liver cells called hepatocytes, which are responsible for performing many of the liver's vital functions. Additionally, the liver consists of blood vessels and bile ducts, which are responsible for transporting bile to the gallbladder and then to the intestine.

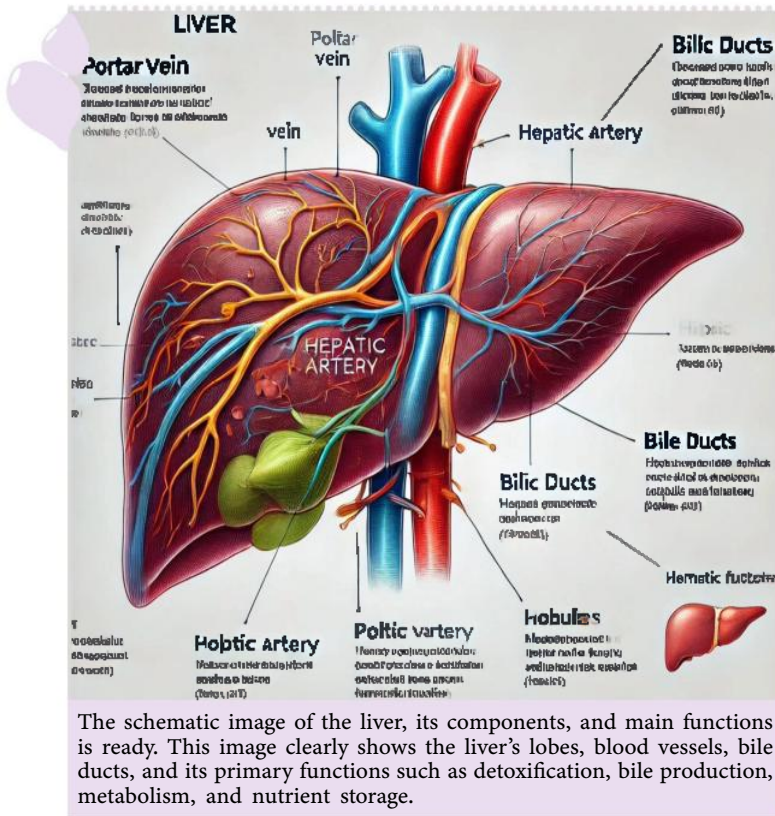
Main Functions of the Liver

Nutrient Metabolism in the Liver

The liver is one of the primary organs involved in the metabolic process and plays a vital role in processing and storing nutrients after their absorption from the digestive system. After digestion and absorption of food in the small intestine, these nutrients are transported to the liver via the hepatic portal vein. In the liver, nutrients are converted and stored in different forms to be used as energy or other essential substances when the body needs them. One of the liver's most important roles is regulating blood sugar levels. After carbohydrates are digested in the intestines, glucose is transported to the liver through the portal vein. Here, the liver converts excess glucose into glycogen, a stored form of glucose. This process allows the liver to store glucose for use when the body needs it. In situations such as fasting or reduced food intake, the liver breaks down glycogen to release glucose into the bloodstream, keeping blood sugar levels stable and providing energy for cells. Additionally, the liver can produce glucose from non-carbohydrate sources like amino acids and glycerol, a process known as gluconeogenesis. This process becomes active during prolonged fasting or intense exercise when the body's glycogen stores are depleted.

The liver also plays a critical role in fat metabolism. After fats are digested in the intestines, free fatty acids and glycerol are transported to the liver via the lymphatic system and the portal vein. The liver forms triglycerides from fatty acids and glycerol, storing them or sending them to other body tissues. The liver converts fats into lipoproteins (VLDL, LDL, and HDL), which play an important role in the transport of fats and cholesterol in the blood. The liver also produces cholesterol, which is essential for building cell membranes, producing hormones, and creating bile. When the body needs energy and there is not enough carbohydrate available, the liver converts fats into ketones, which serve as an energy source for tissues such as the brain and muscles. This process becomes active during prolonged fasting or low-carbohydrate diets and is known as ketogenesis.

The liver also plays a crucial role in protein metabolism. Amino acids derived from the digestion of proteins in the intestine reach the liver via the portal vein, where they are processed. Some of these amino acids are used to produce essential body proteins. Albumin is one of the most important blood proteins, responsible for maintaining the osmotic pressure of the blood and transporting various substances. Additionally, the liver plays a key role in the deamination of amino acids. In this process, amino groups are removed from amino acids and converted into urea, a non-toxic substance excreted by the kidneys. This process helps the body eliminate toxic nitrogenous compounds like ammonia.

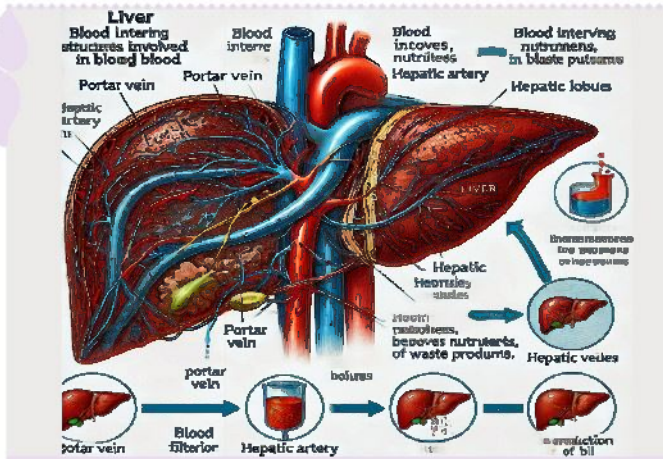


● **Bile Production**

The liver is one of the body's primary organs with many vital functions, including the production of bile. Bile is a yellowish, alkaline fluid that plays a crucial role in digestion, particularly in the digestion and absorption of fats. Without bile, the body would be unable to digest fats and absorb many essential fat-soluble vitamins.

● **Detoxification**

The liver breaks down toxic substances present in the blood (such as ammonia, drugs, and alcohol) through biochemical processes and eliminates them from the body. This process prevents the accumulation of harmful substances in the body.



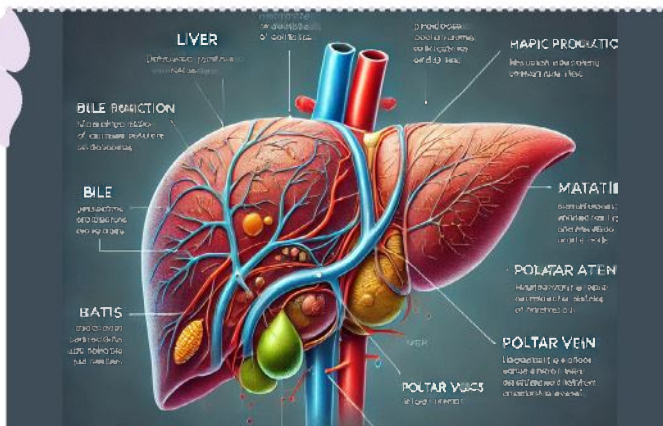
The schematic image of the liver and its role in blood filtration is ready. This image clearly shows the liver's main structures, including the portal vein, hepatic artery, and liver lobules, involved in blood filtration. It also illustrates how toxins are removed, nutrients are processed, and waste products are metabolized.

• Blood Sugar Regulation

The liver stores glucose in the form of glycogen and, when needed, breaks it down into glucose and releases it into the bloodstream. This helps maintain stable blood sugar levels in the body.

• Production of Important Blood Proteins

The liver produces proteins such as albumin, which regulates blood pressure, and clotting factors that play a role in blood coagulation. Without these proteins, the body would be highly vulnerable to bleeding.



The schematic image of the liver and its functions is ready. This image clearly shows the liver's main roles, including detoxification, bile production, the metabolism of carbohydrates, proteins, and fats, the storage of vitamins and minerals, and blood filtration.



Storage of Vitamins and Minerals in the Liver:

The liver is one of the most vital organs in the body, not only for its important roles in metabolism and detoxification but also for storing essential vitamins and minerals. These vitamins and minerals are crucial for various bodily functions, and the liver ensures their availability when needed. This process is particularly important during times of nutrient deficiency from the diet, helping to maintain the balance of essential substances in the body. Fat-soluble vitamins such as vitamins A, D, E, and K cannot easily dissolve in water or blood due to their chemical nature and require fat tissues for transport and storage. The liver is the main organ for storing these vitamins and can retain them for extended periods, releasing them when the body needs them.

- **Vitamin A** is essential for vision, immune system health, cell growth, development, and skin health. It helps in the production of pigments in the retina of the eye and plays an important role in seeing in low light. The liver can store large amounts of vitamin A and release it into the bloodstream when needed. In case of dietary deficiency, liver stores can supply the body's needs for several months to years.

- **Vitamin D** plays a key role in regulating calcium and phosphorus levels in the body and maintaining bone health. It aids in the absorption of calcium from the intestines and helps prevent osteoporosis. The liver stores vitamin D in its inactive form and converts it to its active form when the body needs it. This process is particularly important when the intake of vitamin D from sunlight or diet is limited.

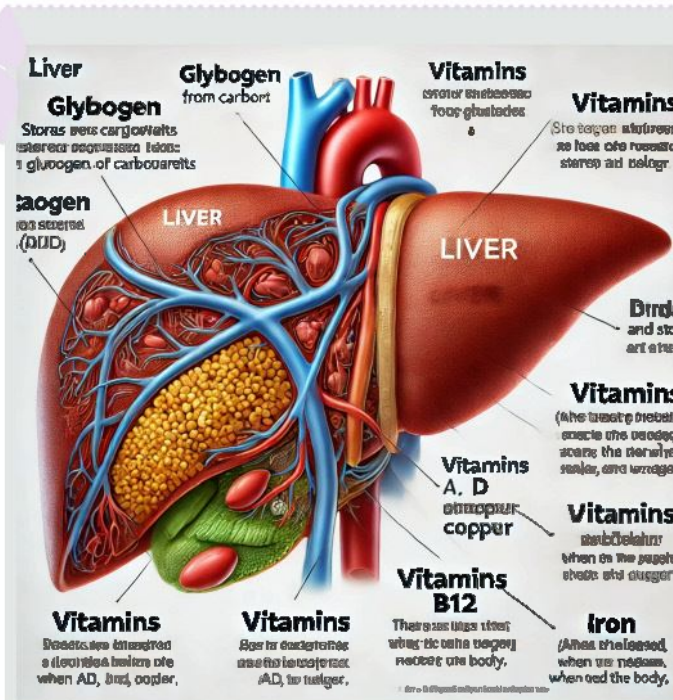
- **Vitamin E** is a powerful antioxidant that protects cells from oxidative damage. It also plays a role in immune system health and reducing inflammation. The liver stores vitamin E and gradually releases it into the bloodstream to protect cells from oxidative damage.

- **Vitamin K** is essential for producing proteins necessary for blood clotting. Without this vitamin, the body would be unable to clot blood, leading to serious bleeding. Vitamin K is also stored in the liver and is released when needed, especially for the production of clotting proteins.

In addition to vitamins, the liver stores important minerals like iron and copper, which are essential for various bodily functions, including the production of blood cells and oxygen transport.

- **Iron** is necessary for producing hemoglobin (a protein in red blood cells that carries oxygen to the body's tissues) and myoglobin (a protein in muscles that stores oxygen). The liver stores iron in the form of ferritin, a protein that allows the liver to safely store and release iron as needed. These iron reserves help the body meet its needs during times of reduced dietary intake or increased demand (e.g., during pregnancy or blood loss).

- **Copper** plays a vital role in energy production, connective tissue formation, and melanin production (skin pigment). It also helps in the production of red blood cells and maintains the health of the nervous system. The liver stores the majority of the body's copper and uses it in metabolic processes such as producing various enzymes. In cases of copper storage and metabolism disorders (such as Wilson's disease), copper accumulates in the liver, potentially leading to liver damage.



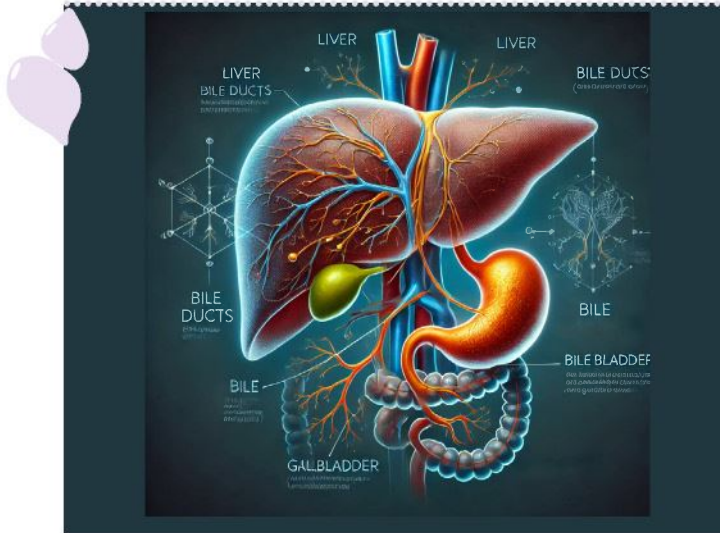
The schematic image of the liver's role in storing nutrients is ready. This image clearly illustrates how essential nutrients such as glycogen (from carbohydrates), vitamins (A, D, B12), and minerals (iron and copper) are stored in the liver.

Biliary System: Structure and Function

The biliary system is a complex network of ducts responsible for transporting bile from the liver to the gallbladder and then to the small intestine. This system includes both intrahepatic (inside the liver) and extrahepatic (outside the liver) bile ducts, as well as the gallbladder. The primary function of this system is to aid in the digestion of fats and the elimination of fat-soluble waste products from the body.

• **Bilirubin**, which is produced from the breakdown of red blood cells, contributes to the yellow color of bile. Bilirubin is transported by bile to the intestines and is excreted through the feces.

Excess cholesterol produced by the body is also eliminated through bile. Any disruption in this process can lead to the formation of gallstones, which are caused by the accumulation of cholesterol in the gallbladder. Bile also helps eliminate certain toxins and waste products resulting from metabolism in the body.



The schematic image of the liver and gallbladder is ready. This image clearly shows the liver's structure, including its lobes and bile ducts, as well as the position of the gallbladder beneath the liver. It also illustrates the connection between the liver, gallbladder, and bile ducts leading to the digestive system, along with the function of bile storage and release by the gallbladder.

Gallbladder

The gallbladder is a small, pear-shaped, and essential organ located beneath the liver. It plays a vital role in fat digestion by storing, concentrating, and secreting bile, a fluid that helps digest and absorb fats in the digestive system. The gallbladder is situated on the lower part of the liver, in the upper right area of the abdomen. It is about 7 to 10 centimeters long and can store approximately 30 to 50 milliliters of bile. Bile is continuously produced by the liver, but it is only needed when food, especially fatty food, is present in the digestive tract. Between meals, bile is transferred from the bile duct to the gallbladder, where it is stored.

One of the gallbladder's primary functions is to concentrate bile. When bile is stored in the gallbladder, water and some electrolytes are absorbed from it, resulting in a thicker fluid containing higher amounts of bile salts, cholesterol, and other compounds. This concentration allows a smaller amount of bile to work more effectively.

When food enters the small intestine, especially the duodenum (the first part of the small intestine), particularly if it contains fat, a hormone called cholecystikinin (CCK) is secreted by cells in the intestinal wall. CCK signals the gallbladder to contract and release bile into the duodenum through the common bile duct.

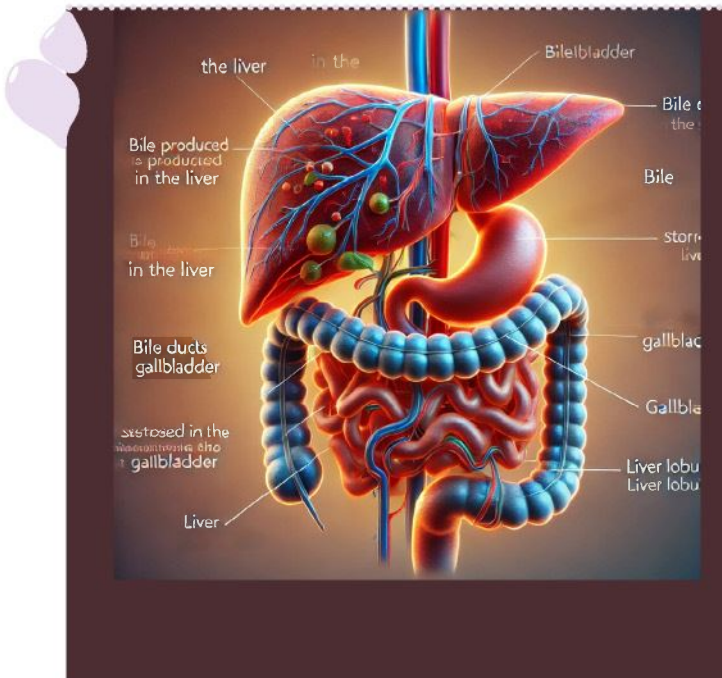
Bile contains bile salts, which play a key role in emulsifying fats. Emulsification is the process by which large fat droplets are broken down into smaller particles, allowing digestive enzymes, particularly lipase (an enzyme that breaks down fats), to act more efficiently. As a result, fats are broken down and then absorbed by the cells lining the small intestine.

■ Bile Ducts

The bile ducts are a network of small and large ducts that transport bile from the liver to the gallbladder and then to the small intestine. Bile ducts are divided into two categories:

Intrahepatic bile ducts: These are smaller ducts that collect bile from inside the liver.

Extrahepatic bile ducts: These are larger ducts that carry bile from the liver and gallbladder to the small intestine.



The schematic image of bile production in the human body is ready. This image clearly shows how bile is produced in the liver, stored in the gallbladder, and secreted into the digestive system. It also displays the bile ducts, gallbladder, and liver lobes involved in this process, along with explanations.

■ Role of Bile in Fat Digestion

Fats, due to their insoluble nature in water, are difficult to break down in the aqueous environment of the small intestine. Bile, through a process called emulsification, breaks fats into smaller droplets, allowing them to be digested and absorbed by digestive enzymes. Bile salts, the most important component of bile, attach to fat droplets and break them into smaller particles. This increases the surface area of fats for contact with lipase (a digestive enzyme produced by the pancreas), speeding up their digestion.

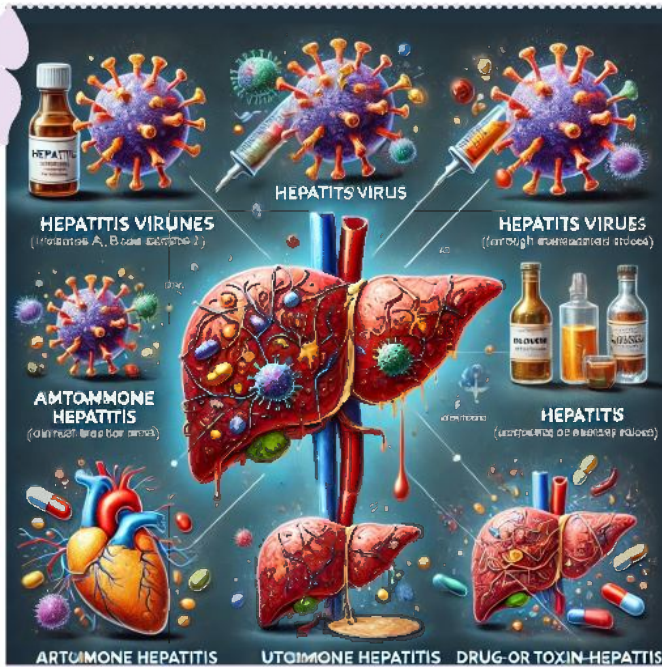
Dietary fats naturally exist as large droplets in the stomach. Bile salts break these droplets into smaller particles, a process known as emulsification, making them more accessible for digestive enzymes to break down. Bile also aids in the absorption of fat-soluble vitamins such as A, D, E, and K. Without bile, the body would be unable to efficiently absorb these essential vitamins.

Chapter 3

What is Hepatitis?

■ Hepatitis and Its Types

Hepatitis refers to inflammation of the liver tissue and can occur due to various reasons, including viral infections, the consumption of toxic substances like alcohol, the use of certain medications, and even autoimmune disorders. The liver, being one of the body's vital organs, plays an important role in metabolism, energy storage, detoxification, and the production of digestive enzymes. Therefore, any damage or inflammation in the liver can lead to serious and widespread health problems. Below, we will explore the different types of hepatitis and provide more details about each of them.



The schematic image related to different types of hepatitis and their effects on the liver is ready. This image clearly shows hepatitis viruses A, B, C, D, and E and how they attack the liver through various routes like contaminated water, blood, and body fluids. It also depicts liver damage caused by alcohol consumption, autoimmune hepatitis, and drug- or toxin-induced hepatitis.

■ Types of Hepatitis

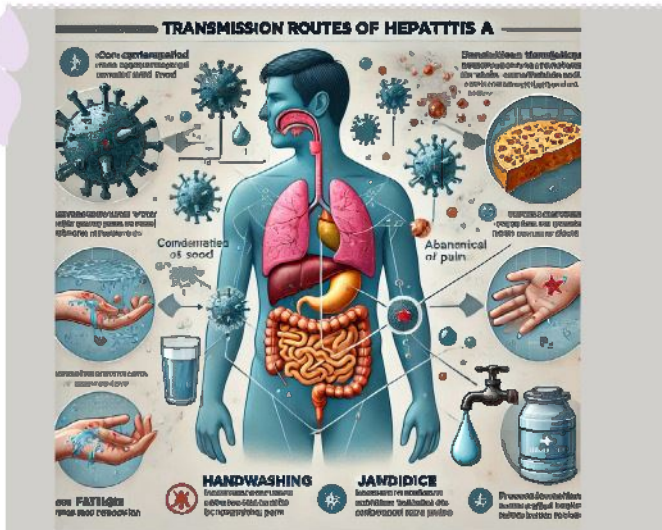
● Viral Hepatitis

Viral hepatitis is the most common type of hepatitis and can be caused by five main types of hepatitis viruses: A, B, C, D, and E. These viruses are

transmitted through different routes, and each has its own symptoms, severity, and outcomes. Below are more details about each of these viruses:

☺☺ Hepatitis A

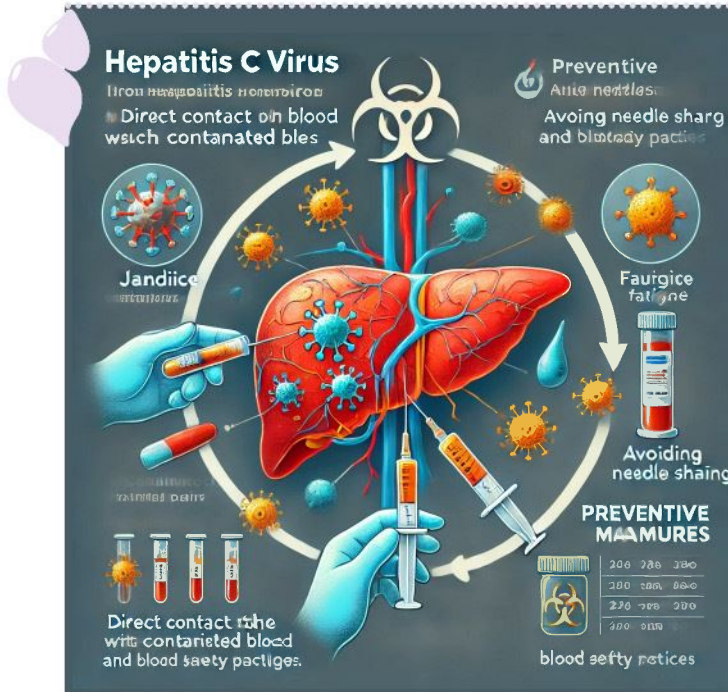
- **Transmission:** Hepatitis A is usually transmitted through the consumption of food or water contaminated with the virus. The virus often enters the environment through the feces of infected individuals and is more common in areas with poor sanitation.
- **Symptoms and Complications:** Hepatitis A is typically an acute and short-term illness, rarely progressing to chronic hepatitis. Symptoms include fatigue, jaundice (yellowing of the skin and eyes), abdominal pain, and nausea. Most people recover without the need for specific treatment.
- **Prevention and Treatment:** A hepatitis A vaccine is available for prevention. Personal hygiene and the consumption of clean water are also effective methods to prevent the virus.



The schematic image related to the transmission routes of Hepatitis A is ready. This image shows the virus being transmitted through contaminated water and food, highlighting handwashing as a preventive measure. It also illustrates symptoms such as fatigue, jaundice (yellowing of the skin), and abdominal pain, emphasizing the importance of prevention through hygiene and vaccination.

☺☺ Hepatitis B

- **Transmission:** Hepatitis B is transmitted through contact with the blood or bodily fluids of an infected person, such as saliva, semen, or vaginal secretions. Transmission can occur through sexual contact, contaminated needles, or from mother to baby during childbirth.
- **Symptoms and Complications:** The virus can lead to either acute or chronic hepatitis. Some individuals develop chronic hepatitis, which increases the risk of cirrhosis and liver cancer.
- **Prevention and Treatment:** The Hepatitis B vaccine is one of the most effective ways to prevent the disease. Antiviral medications are available for infected individuals to control the virus and prevent disease progression.



The schematic image related to the transmission of the Hepatitis C virus through direct contact with infected blood, such as contaminated needles, is ready. This image illustrates the symptoms and signs of the disease, including jaundice, fatigue, abdominal pain, and liver damage, while emphasizing the importance of prevention by avoiding needle sharing and adhering to blood safety measures.

☉☉ Hepatitis D

- **Transmission:** Hepatitis D can only occur in individuals who are already infected with the hepatitis B virus. This virus exacerbates the hepatitis B infection, leading to more severe symptoms.
- **Symptoms and Complications:** Hepatitis D infection can accelerate liver disease progression and increase the risk of cirrhosis.
- **Prevention and Treatment:** The best way to prevent hepatitis D is by getting vaccinated against hepatitis B, as the hepatitis D virus cannot cause infection without the presence of hepatitis B.

☉☉ Hepatitis E

- **Transmission:** Like hepatitis A, hepatitis E is transmitted through the consumption of contaminated water or food. It is especially common in areas with poor sanitation and limited access to clean water.
- **Symptoms and Complications:** Most cases of hepatitis E are acute and resolve on their own. However, the disease can be more severe and dangerous in pregnant women and individuals with weakened immune systems.
- **Prevention and Treatment:** Personal hygiene and the consumption of clean water are effective methods for preventing this virus. A vaccine for hepatitis E is available in some countries, but it is not widely accessible.



The schematic image related to the transmission and prevention of Hepatitis E is ready. This image shows that the virus is mainly transmitted through contaminated water and food, with preventive measures such as handwashing, using clean water, and maintaining hygiene practices. It also highlights the higher prevalence of this disease in areas with poor sanitation and its greater severity in pregnant women and individuals with weakened immune systems.

Alcoholic Hepatitis

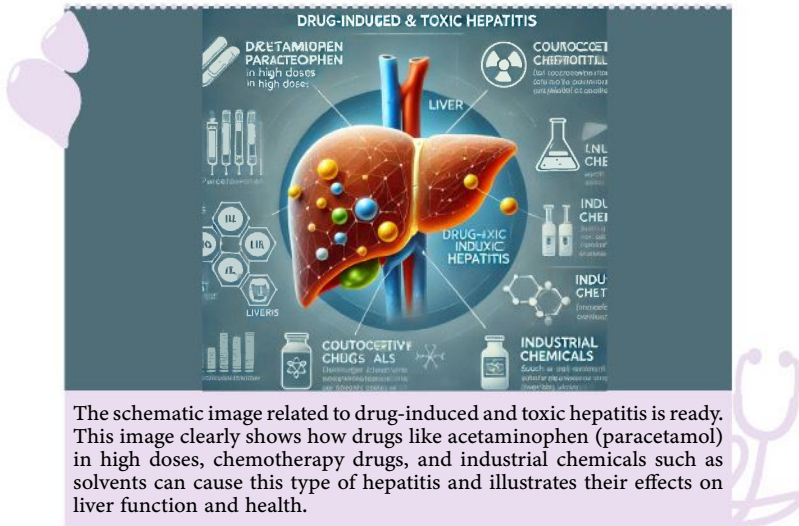
Alcoholic hepatitis is the result of excessive and prolonged alcohol consumption, which leads to damage and inflammation of liver cells. Long-term heavy alcohol use can lead to fibrosis and eventually cirrhosis of the liver. Symptoms of alcoholic hepatitis include severe pain in the upper right abdomen, jaundice (yellowing of the skin and eyes), weakness, and extreme fatigue. In severe cases, alcoholic hepatitis can lead to liver failure and even death. The best way to prevent alcoholic hepatitis is to avoid excessive alcohol consumption. If alcoholic hepatitis is diagnosed, complete abstinence from alcohol and following medical treatment can prevent the disease from worsening.



The schematic image related to alcoholic hepatitis, its causes, symptoms, and prevention methods is ready. This image shows symptoms such as jaundice, pain in the upper right abdomen, and severe fatigue, along with advanced complications like cirrhosis and liver failure. Additionally, a “no alcohol” symbol is clearly displayed to emphasize the prevention of this disease through avoiding excessive alcohol consumption.

Drug-Induced and Toxic Hepatitis:

Drug-induced and toxic hepatitis is caused by the use of medications or exposure to toxic chemicals that damage the liver. Certain chemotherapy drugs, acetaminophen (paracetamol) in high doses, and industrial chemicals such as solvents can lead to liver inflammation. Toxic hepatitis can cause symptoms such as jaundice, abdominal pain, nausea, and vomiting. If left untreated, it can result in severe liver damage. Preventive measures include avoiding the excessive use of medications and limiting exposure to toxic chemicals. In the case of toxic hepatitis, discontinuing the triggering agent (such as a drug or chemical) and seeking immediate treatment can prevent the disease from progressing.



Autoimmune Hepatitis:

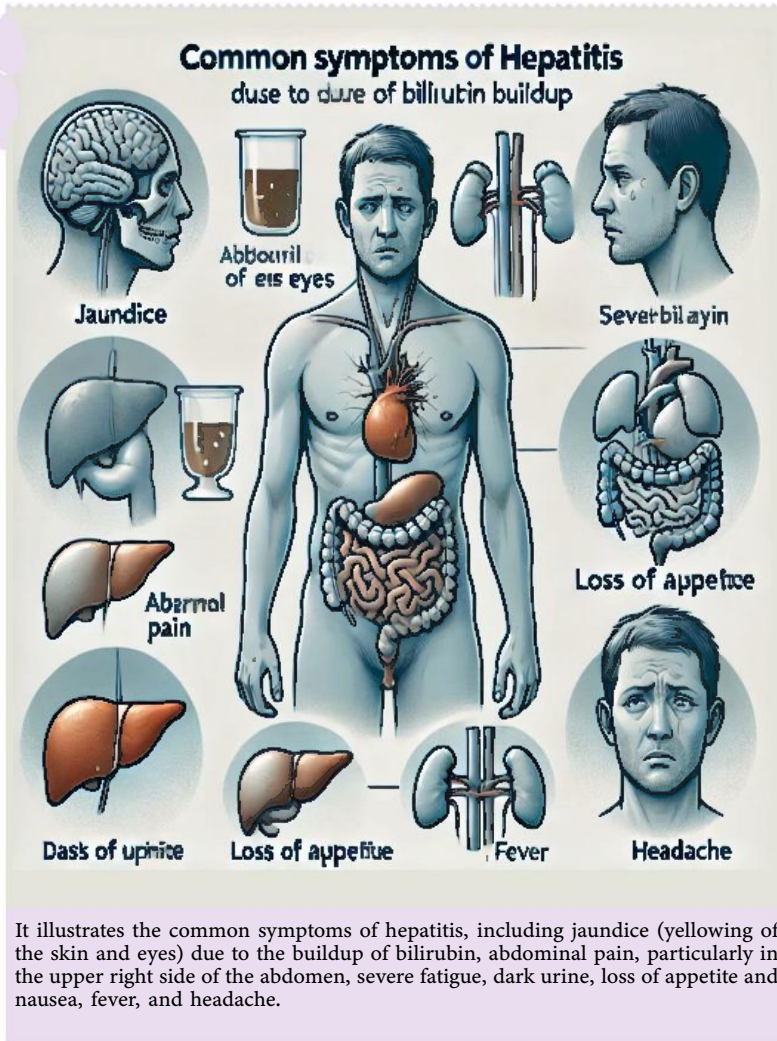
Autoimmune hepatitis is a rare disease in which the body's immune system mistakenly attacks liver cells, causing chronic liver inflammation. The exact cause of this condition is unknown, but genetic and environmental factors may play a role. Autoimmune hepatitis can lead to cirrhosis and liver failure. Symptoms include fatigue, joint pain, jaundice, and other symptoms similar to other types of hepatitis. Treatment typically involves the use of immunosuppressive drugs like corticosteroids and azathioprine. Long-term treatment can help reduce inflammation and prevent disease progression.

Symptoms and Signs of Hepatitis

The symptoms of hepatitis vary depending on its type and severity. In some cases, hepatitis can be asymptomatic. Common symptoms of hepatitis include:

- **Jaundice:** A yellowing of the skin and eyes caused by increased bilirubin in the blood.
- **Severe Fatigue:** A general feeling of weakness and inability to perform normal activities.
- **Abdominal Pain:** Particularly in the upper right side of the abdomen, where the liver is located.
- **Dark Urine:** Caused by the excretion of excess bilirubin through the kidneys.

- Loss of Appetite and Nausea: Accompanied by feelings of nausea and vomiting.
- **Fever and Headache:** Occurring in some cases, especially in viral hepatitis.



Diagnosis of Hepatitis

The diagnosis of hepatitis typically involves a combination of clinical evaluations and laboratory tests. Some common diagnostic methods include:

- **Liver Function Tests:** These tests measure liver enzyme levels and indicate inflammation or liver damage.
- **Serological Tests:** Used to detect the presence of antibodies or antigens for hepatitis viruses.
- **Imaging:** In cases such as chronic hepatitis, ultrasound, CT scan, or MRI may be needed to assess liver damage.
- **Liver Biopsy:** In some cases, a small sample of liver tissue is taken to evaluate the extent of inflammation and liver damage.

Chapter 4

The Immune System and Its Role in Autoimmune Diseases

Function and Abnormalities

Autoimmune hepatitis is a rare and chronic condition where the body's immune system mistakenly attacks healthy liver cells, leading to chronic inflammation and eventually liver tissue damage. To better understand this disease, it is essential to explore how the immune system normally functions and how it becomes disrupted in autoimmune diseases like autoimmune hepatitis.

The immune system is a complex network of cells, tissues, and organs, with its primary function being to protect the body from foreign agents such as viruses, bacteria, fungi, and toxins. The immune system is divided into two main branches: innate immunity and adaptive immunity.

Innate Immunity

Innate immunity is the body's first line of defense and includes nonspecific mechanisms that respond quickly to infections. Some of the key components of innate immunity are:

- **Phagocytic cells:** Including neutrophils and macrophages, which destroy invaders through phagocytosis (engulfing and digesting foreign particles).
- **Complement proteins:** These proteins activate in the presence of pathogens and enhance the immune response by marking invaders for destruction by other immune cells.
- **Natural killer (NK) cells:** These cells identify and destroy virus-infected or cancerous cells.

Adaptive Immunity

Adaptive immunity is more specialized and complex. It can create immune memory, allowing the body to respond more quickly and effectively to subsequent encounters with the same pathogen. This branch includes two key cell types:

- **B cells:** Responsible for producing antibodies, which are proteins that bind to pathogens and mark them for destruction by other immune system components.
- **T cells:** Divided into two main types:
 - **Helper T cells (Th cells):** These cells help other immune cells recognize and respond to invaders.
 - **Cytotoxic T cells:** These cells directly attack and kill infected or cancerous cells.

Autoimmunity: Immune System Dysfunction

Under normal conditions, the immune system can distinguish between the body's own cells and foreign invaders, attacking only external threats. However, in autoimmune diseases, this distinction fails, and the immune system mistakenly attacks healthy cells. In autoimmune hepatitis, the immune system wrongly targets liver cells. The immune system produces antibodies that attack the liver, including:

- **Antinuclear antibodies (ANA):** These antibodies attack specific parts of the body's cells, such as the cell nucleus.
- **Anti-smooth muscle antibodies (SMA):** These antibodies target proteins in smooth muscle and are involved in autoimmune hepatitis.
- **Anti-mitochondrial antibodies (AMA):** Although rare in autoimmune hepatitis, these antibodies can assist in diagnosis.

The Role of T Cells in Autoimmune Hepatitis

T cells play a critical role in the development and progression of autoimmune hepatitis. Normally, T cells are activated to recognize and attack foreign agents such as viruses. However, in autoimmune hepatitis, T cells mistakenly recognize liver cells as foreign and attack them.

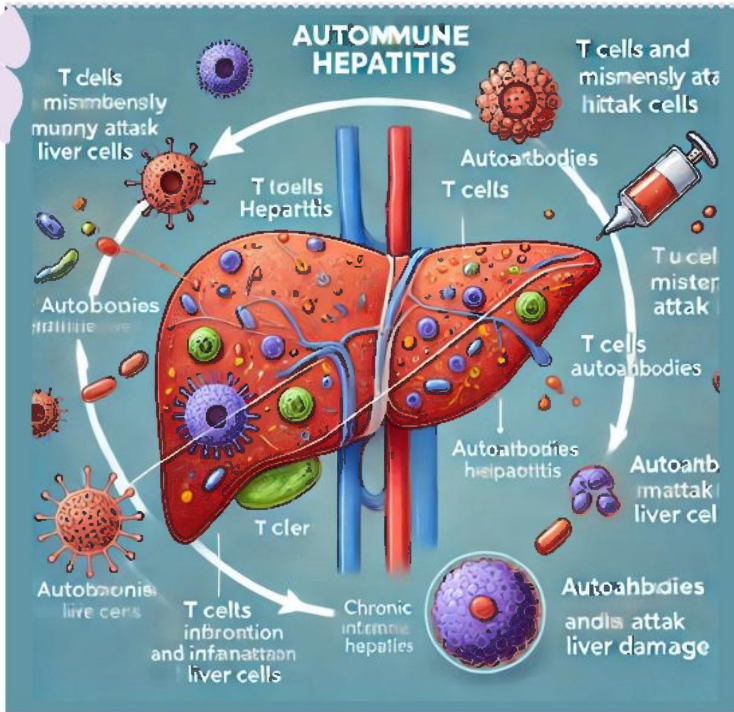
- **Helper T cells Type 1 (Th1):** These cells release cytokines like interferon-gamma (IFN- γ), which trigger inflammation and activate other immune cells in the liver, leading to chronic liver inflammation and tissue damage.
- **Cytotoxic T cells:** These cells directly attack liver cells, leading to their destruction. Continuous attacks result in severe inflammation and tissue damage, which, if unchecked, can progress to liver cirrhosis and even liver failure.

Cytokines and Their Role in Autoimmune Hepatitis

Cytokines are proteins that regulate and coordinate immune responses. In autoimmune hepatitis, certain cytokines play a key role in disease progression, including:

- **Interleukin-2 (IL-2):** Promotes the growth and proliferation of T cells, enhancing the immune response.
- **Interferon-gamma (IFN- γ):** A powerful inflammatory trigger that stimulates other immune cells, increasing chronic inflammation in the liver.
- **TNF- α (Tumor Necrosis Factor-alpha):** A strong inflammatory cytokine that contributes to the destruction of liver cells.

In summary, autoimmune hepatitis results from the immune system's failure to distinguish between healthy liver cells and foreign invaders. T cells and cytokines play critical roles in the inflammation and tissue damage associated with this condition. Understanding the underlying immune dysfunction in autoimmune hepatitis is essential for developing targeted treatments that can help manage and prevent disease progression.



The schematic image of the immune system's role in autoimmune hepatitis is ready. This image shows how T cells and autoantibodies mistakenly attack liver cells, leading to chronic inflammation and liver damage.

Under normal conditions, the immune system has mechanisms that prevent overactivity and attacking the body's own cells. One of these mechanisms involves Regulatory T cells (Tregs), which are responsible for suppressing excessive immune responses and maintaining balance within the immune system. However, in autoimmune diseases such as autoimmune hepatitis, the function of regulatory T cells becomes impaired, allowing the immune system to attack liver cells without proper regulation.

BOOK 1

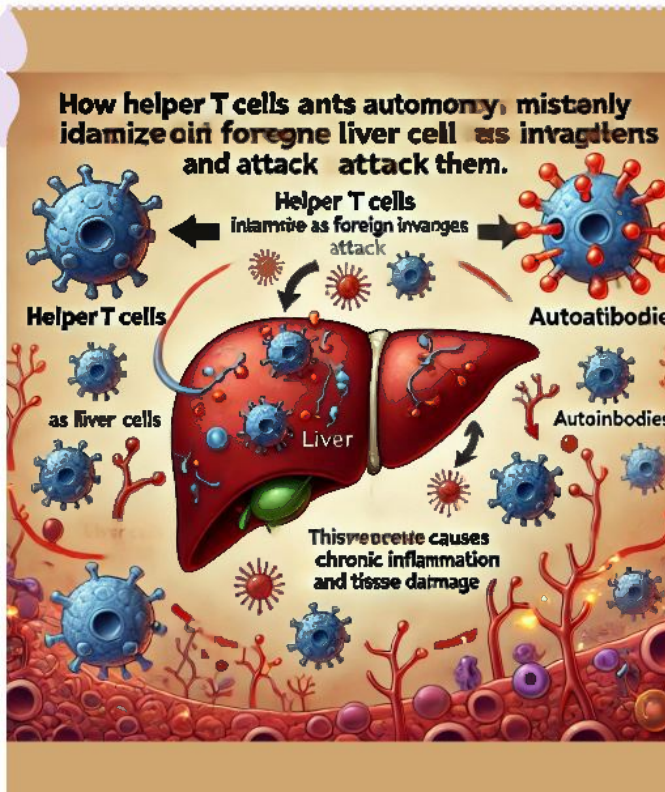


Autoimmune Hepatitis

Chapter 1

What is Autoimmune Hepatitis? Definition and Overview

Autoimmune hepatitis is a chronic liver disease in which the immune system abnormally attacks the liver cells. This attack leads to chronic inflammation in the liver, which, if left untreated, can result in extensive liver tissue damage, fibrosis (formation of scar tissue), and eventually cirrhosis or liver failure. The disease can occur at any age but is more common in young and middle-aged women.

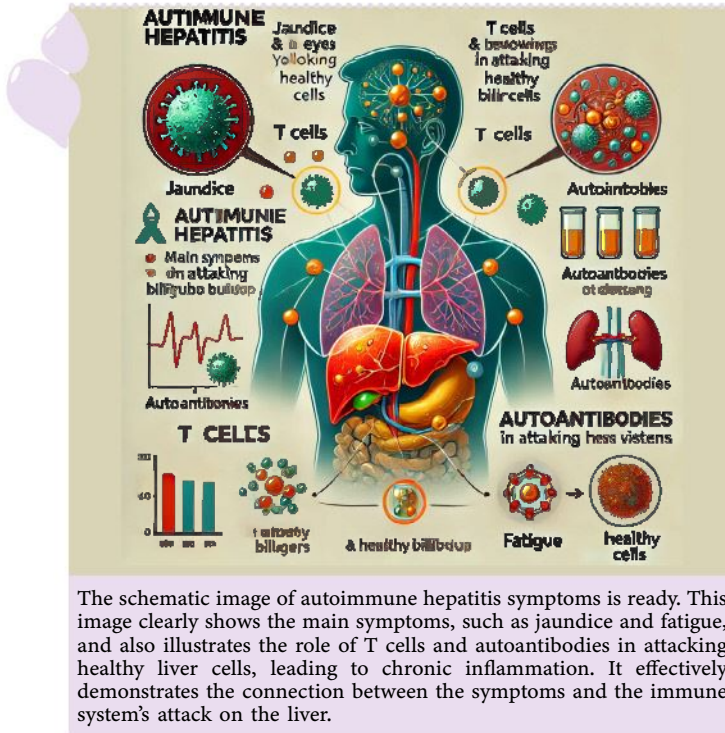


The schematic image illustrating how helper T cells and autoantibodies mistakenly attack liver cells is ready. This image shows how these immune cells identify liver cells as foreign invaders and attack them, leading to chronic inflammation and tissue damage in the liver.

Normal Function of the Immune System

The immune system is typically designed to defend the body against foreign invaders such as viruses, bacteria, and cancer cells. Immune cells, like T cells and antibodies, attack and destroy these external threats, helping protect the

body from infections and diseases. In a healthy state, the immune system can distinguish between the body's own cells and foreign invaders. However, in autoimmune diseases, including autoimmune hepatitis, this distinction is disrupted. The immune system mistakenly identifies healthy cells as invaders and attacks them. In autoimmune hepatitis, liver cells (hepatocytes) become the target of these immune attacks.



■ Disease Process in Autoimmune Hepatitis

In autoimmune hepatitis, the immune system's ongoing attacks on the liver cause chronic inflammation. If this inflammation is not effectively controlled, it leads to the destruction of liver cells, which can result in fibrosis (scar tissue formation) and cirrhosis. Cirrhosis is a stage where the liver becomes severely damaged, reducing its ability to perform its normal functions. Symptoms of cirrhosis may include jaundice, abdominal swelling (ascites), severe fatigue, and loss of appetite. If the disease progresses without proper treatment, cirrhosis can lead to liver failure, and in such cases, a liver transplant may be the only remaining treatment option.

■ Immune Mechanisms and Contributing Factors in Autoimmune Hepatitis

The immune mechanisms involved in autoimmune hepatitis include the abnormal activation of T cells and the production of autoantibodies. These autoantibodies attack liver cells, causing their destruction. The most important antibodies involved in this disease include **antinuclear antibodies (ANA)**

and **anti-smooth muscle antibodies (SMA)**. In addition to genetic factors, certain environmental factors can trigger or exacerbate autoimmune hepatitis. Some viral infections can act as triggers, activating an abnormal immune response. Certain medications may also stimulate the immune system and initiate autoimmune hepatitis. The disease is more commonly seen in women, suggesting that sex hormones may play a role in its development.

■ **Diagnosis of Autoimmune Hepatitis**

Diagnosis is based on a combination of clinical symptoms, blood tests, and liver biopsy. Blood tests are used to detect elevated liver enzymes and the presence of autoantibodies. A liver biopsy is a key diagnostic tool for assessing the extent of inflammation and tissue damage.

■ **Treatment of Autoimmune Hepatitis**

The treatment of autoimmune hepatitis primarily focuses on suppressing the immune system to prevent it from attacking liver cells. The main medications used include:

- **Corticosteroids**, such as prednisone, to reduce inflammation.
- **Azathioprine** and other immunosuppressive drugs, such as mycophenolate mofetil and cyclosporine, to prevent attacks on liver cells.
- In some cases, if the disease does not respond to treatment or progresses to advanced stages like liver failure, a **liver transplant** may be necessary.

In addition to medical treatment, maintaining a healthy lifestyle is crucial for managing autoimmune hepatitis. This includes consuming nutritious foods that support the immune system and liver health. Avoiding alcohol is essential, as it can increase liver inflammation and worsen damage. Regular monitoring through tests to check liver inflammation levels and function is also important.

Autoimmune hepatitis is a serious and chronic disease that requires early diagnosis and ongoing management. With appropriate treatment, many patients can lead normal lives. Early and effective treatment can prevent the disease from progressing and causing severe complications like cirrhosis and liver failure.

Chapter 2

Types of Autoimmune Hepatitis (Type 1 and Type 2)

Autoimmune hepatitis is divided into two main types, Type 1 and Type 2, which differ in terms of age of onset, gender, and symptoms. These differences influence the recognition, diagnosis, and management of each type of the disease.

Autoimmune Hepatitis Type 1

Type 1 is the most common form of autoimmune hepatitis, accounting for approximately 70-80% of cases. This type is more frequently seen in adults, especially in young and middle-aged women, but it can occur at any age. The female-to-male ratio is higher in Type 1 (approximately 4 to 1).

The symptoms of Type 1 can vary and may sometimes be nonspecific. Some patients may be asymptomatic, while others may present with severe symptoms, even progressing to cirrhosis. Common symptoms include extreme fatigue, jaundice (yellowing of the skin and eyes), pain in the liver area, and elevated liver enzymes. In some cases, symptoms of other autoimmune diseases, such as rheumatoid arthritis, Hashimoto's thyroiditis, or ulcerative colitis, may also be present.

Blood tests typically show the presence of **antinuclear antibodies (ANA)** and **anti-smooth muscle antibodies (SMA)**, which are key markers for autoimmune hepatitis Type 1.

The response to treatment in Type 1 is generally good, especially if the disease is diagnosed early. Immunosuppressive treatments, such as corticosteroids (prednisone) and azathioprine, are commonly used to reduce inflammation and prevent disease progression.

Autoimmune Hepatitis Type 2

Type 2 is less common and is primarily seen in children and adolescents, particularly in girls. While more prevalent in childhood and adolescence, Type 2 can also occur in adults, though less frequently. The symptoms of autoimmune hepatitis Type 2 are often more severe than those of Type 1. Patients often present with severe jaundice and acute liver failure.

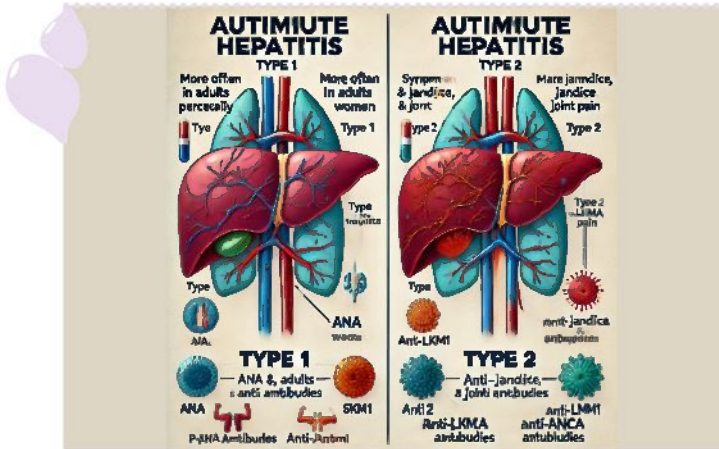
Early symptoms typically include severe fatigue, yellowing of the skin and eyes, abdominal pain, and an enlarged liver and spleen. Other autoimmune symptoms are also common, as many patients with Type 2 have coexisting autoimmune diseases, such as Type 1 diabetes or thyroiditis.

In Type 2, different antibodies are present, including **anti-liver kidney microsomal antibodies (anti-LKM1)** and **anti-neutrophil cytoplasmic antibodies (p-ANCA)**. Patients with Type 2 are less likely to have ANA or SMA, which are commonly seen in Type 1.

Due to the severity of symptoms and rapid disease progression, Type 2 requires more immediate treatment. Unlike Type 1, Type 2 may be less responsive to

treatment, and patients may require higher doses or stronger medications. As with Type 1, treatment includes corticosteroids and azathioprine, but patients with Type 2 typically require longer-term treatment and have a higher risk of disease recurrence.

In conclusion, while both types of autoimmune hepatitis share similar underlying mechanisms, their differences in presentation, severity, and treatment response necessitate tailored approaches for diagnosis and management. Early detection and effective treatment can help manage symptoms and prevent complications, improving the quality of life for patients.



The schematic image of the two types of autoimmune hepatitis is ready. This image clearly shows that Type 1 is more common in adults, particularly women, with symptoms such as fatigue, jaundice, and joint pain, and ANA and SMA antibodies are noted as key markers. Type 2 occurs more frequently in children and adolescents, presenting with symptoms like severe jaundice and liver enlargement, and involves anti-LKM1 and p-ANCA antibodies. The key differences between these two types are well illustrated in this image.

Comparison of Type 1 and Type 2 Autoimmune Hepatitis

Feature	Type 1 (AIH-1)	Type 2 (AIH-2)
Age of Onset	Adults (young and mid-(dle-aged	Children and adolescents (less (common in adults
Gender	More common in women	More common in girls and children
Symptoms	Fatigue, jaundice, liver pain	More severe symptoms: pronounced jaundice, liver failure
Antibodies	ANA and SMA	Anti-LKM1 and p-ANCA
Response to Treatment	Generally good	Typically more complex, often requiring higher doses
Associated Autoimmune Diseases	Hashimoto's thyroiditis, arthritis	Type 1 diabetes, thyroiditis

Chapter 3

Causes and Contributing Factors in Autoimmune Hepatitis

Autoimmune hepatitis is a complex and multifactorial disease resulting from a combination of genetic, environmental, hormonal, and immune system factors. In this section, we will take a closer look at these factors and how they contribute to the onset and progression of the disease.

Genetic Factors and Autoimmune Hepatitis

Genetics and racial background play a significant role in autoimmune liver diseases like autoimmune hepatitis. This complex disease is influenced by a combination of genetic and environmental factors. Studies show that the prevalence of autoimmune hepatitis is higher in certain racial and ethnic groups. For example, the disease is more common among white populations compared to other racial groups. Genetic differences, particularly in certain human leukocyte antigen (HLA) gene variants, may contribute to this. In some ethnicities, there is a higher likelihood of developing specific types of autoimmune hepatitis or experiencing varying disease severity. Genetic factors influence the prevalence, severity of disease manifestations, and response to treatment in different populations. Variations in immune responses driven by genetic differences may lead to significant disparities in the occurrence and presentation of autoimmune hepatitis across individuals and groups.

Prevalence Across Different Populations

Autoimmune hepatitis is more common in certain populations, especially women. Genetic factors, such as HLA genes that play a role in immune system regulation, are key contributors to these prevalence differences among populations. **HLA-DR3** and **HLA-DR4** are two crucial genes that are more prevalent in certain populations and increase the risk of autoimmune hepatitis. For example, **HLA-DR3** is more frequently found in Northern European populations, while **HLA-DR4** is more common in East Asian and Latin American populations. Studies have shown that in regions like Scandinavia, the rate of autoimmune hepatitis is higher compared to other parts of the world. This may be due to the unique genetic makeup of these populations.

Genetic Susceptibility to Autoimmune Hepatitis

Genes play a significant role in the development of autoimmune hepatitis. Some individuals are more susceptible to the disease because they carry specific gene variants. Among these are **HLA genes**, which help regulate the body's immune response. Specific gene variants identified in people with autoimmune hepatitis cause the immune system to attack healthy cells, especially liver cells, instead of foreign invaders. Individuals with certain genetic variants may be at higher risk of developing autoimmune hepatitis. These genes influence how antigens are presented to T cells, and mutations may cause misidentification of



the body's own cells as invaders. Additionally, variants in other genes, such as CTLA4 and FAS, have been associated with autoimmune hepatitis in various populations, including Europeans and Japanese.

Variations in Disease Manifestation

Genetic differences can influence the severity and clinical presentation of autoimmune hepatitis. The disease is classified into two main types. **Type 1** is usually seen in adults and young people and is associated with **HLA-DR3** and **HLA-DR4** genes. **Type 2**, on the other hand, is more common in children and young people and is linked to other genes, such as **HLA-DR7**. This genetic difference makes Type 2 generally more severe in its clinical presentation. In some populations, such as those of African descent, autoimmune hepatitis may present with more severe symptoms and progress faster. These differences could be due to variations in **HLA genes** and other genetic factors.

Differences in Treatment Response

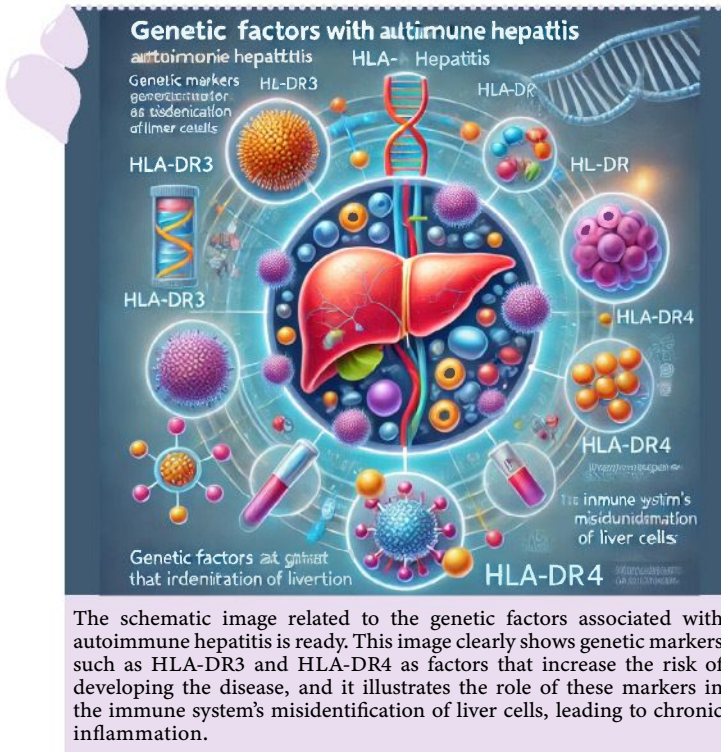
Patient response to treatment may also be affected by genetic factors. Patients with **HLA-DR3** may respond better to standard immunosuppressive therapies, such as corticosteroids. However, patients with certain genetic variants may show a poorer response to treatment or require higher doses of medication. Patients with **HLA-DR7** may not respond as well to standard treatments and may need stronger therapies, such as azathioprine or mycophenolate mofetil.

In different populations, the distribution of **HLA genes** and other genetic factors varies, which can influence the prevalence and severity of the disease. For example, in Northern Europe, autoimmune hepatitis Type 1 is more common and usually responds well to treatment, whereas in Africa and Latin America, the disease may come with more complications due to greater genetic diversity, requiring more complex treatment approaches.

Conclusion

Genetic differences play a significant role in the prevalence, clinical manifestation, and response to treatment in patients with autoimmune hepatitis. Further research into genetic factors and differences between populations can improve treatment strategies, enabling physicians to offer more tailored therapies to patients in different regions of the world.

Recent research in the field of genetics has contributed to a better understanding of the role genes play in the development of autoimmune hepatitis. Advanced techniques such as genome sequencing are now being used to identify genetic differences among patients. This research may lead to the development of new therapeutic approaches that offer personalized treatments based on an individual's genetic makeup.

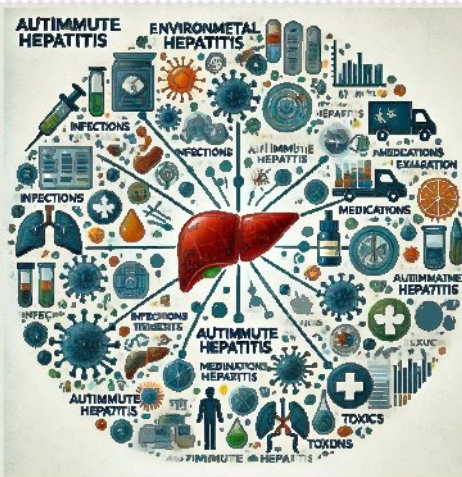


Environmental Factors and Autoimmune Hepatitis

Environmental factors play a significant role as triggers in the development or exacerbation of autoimmune hepatitis. These factors include viral infections, certain medications, and even exposure to specific chemicals. Although the primary cause of autoimmune diseases is often linked to genetics, environmental factors can act as triggers, activating the immune system and causing it to attack liver cells.

Viral Infections

Some viruses can directly stimulate the immune system, leading to autoimmune hepatitis in genetically predisposed individuals. Infections with viruses like Hepatitis A, B, and C can activate abnormal immune responses, eventually resulting in autoimmune hepatitis. These viruses may alter liver cell function and stimulate the immune system to mistakenly attack these cells. Although less common, herpes **simplex viruses** have also been implicated in some studies as potential triggers for autoimmune hepatitis, as they can stimulate immune responses and, in some cases, lead to the onset of the disease.



The schematic image related to environmental factors influencing autoimmune hepatitis is ready. This image clearly illustrates various environmental factors such as infections, medications, and toxins, showing their role in the development or exacerbation of autoimmune hepatitis.

The use of certain medications can also act as an environmental factor in triggering autoimmune hepatitis. These drugs may disrupt the immune system and lead to immune attacks against the liver. **Isotretinoin**, commonly used to treat severe acne, has been identified as a potential trigger for autoimmune hepatitis. By altering immune system regulation, isotretinoin can provoke autoimmune reactions. **Minocycline**, an antibiotic frequently prescribed for bacterial infections, has also been linked to autoimmune hepatitis in some cases. These drugs can cause changes in immune cells and increase liver inflammation.

Exposure to specific chemicals can also serve as an environmental factor that triggers autoimmune hepatitis. Some studies suggest that prolonged exposure to chemical toxins, such as solvents and pesticides, may increase the risk of developing this disease.

In many cases, environmental factors can only lead to autoimmune hepatitis in individuals who are genetically predisposed. These individuals carry genes that cause their immune system to abnormally activate when exposed to external triggers, resulting in attacks on liver cells. This explains why some individuals may never develop autoimmune hepatitis despite exposure to these environmental factors.

Environmental factors can play a significant role in the onset or exacerbation of autoimmune hepatitis. Identifying and avoiding these triggers, especially for individuals with a family history or genetic predisposition, can help reduce the risk of developing this disease.

■ Hormonal Changes and Autoimmune Hepatitis

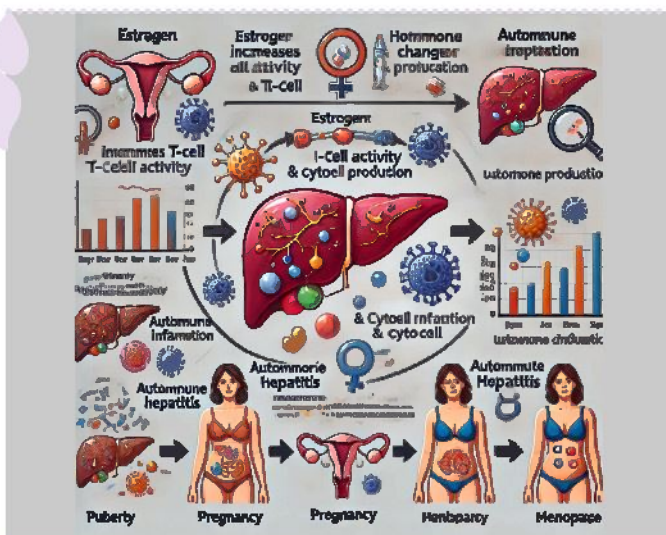
Autoimmune hepatitis is more common in women, particularly during young adulthood and middle age. This suggests that hormonal changes may play a role in the onset and progression of the disease. **Sex hormones** like estrogen can significantly influence immune system regulation and impact the development or

worsening of autoimmune diseases. Estrogen, the primary female sex hormone, has a direct effect on the immune system. It can enhance immune responses, which may explain why autoimmune diseases, including autoimmune hepatitis, are more prevalent in women. By stimulating immune cell activity, estrogen can trigger inflammatory and abnormal immune responses, leading to attacks on healthy cells such as liver cells in autoimmune hepatitis.

Hormonal Changes During Key Phases in Women’s Lives

- **Puberty:** The sudden increase in sex hormones during puberty can activate or worsen autoimmune diseases.
- **Pregnancy:** Hormonal changes during pregnancy can lead to immune system alterations. In some cases, autoimmune diseases may improve during pregnancy, but they often worsen after childbirth.
- **Menopause:** The decline in estrogen levels during menopause may also influence immune responses and affect the severity or onset of autoimmune diseases.

Studies indicate that women are more susceptible to autoimmune diseases due to the presence of sex hormones, particularly estrogen. Estrogen enhances the activity of T cells and increases cytokine production, contributing to inflammation and autoimmune attacks. Hormonal changes, particularly elevated estrogen levels, can play a crucial role in the onset and worsening of autoimmune hepatitis. These changes during key phases of a woman’s life—such as puberty, pregnancy, and menopause—can disrupt immune regulation and increase the risk of developing autoimmune diseases.



The schematic image explaining the role of estrogen and hormonal changes in autoimmune hepatitis is ready. This image clearly shows how estrogen increases T-cell activity and cytokine production, leading to liver inflammation in autoimmune diseases. It also depicts different stages of a woman’s life, such as puberty, pregnancy, and menopause, and illustrates how these hormonal changes can affect the risk of developing autoimmune hepatitis.

Nutritional and Lifestyle Factors

While autoimmune hepatitis is not directly caused by lifestyle or diet, nutritional and lifestyle factors play an important role in managing the symptoms. A proper diet, anti-inflammatory foods, avoiding alcohol, and steering clear of processed foods can help reduce inflammation, lessen the liver's burden, and ease symptoms of the disease.

🍴 Anti-Inflammatory Foods

Consuming anti-inflammatory foods can be effective in managing the inflammation caused by autoimmune hepatitis. Some beneficial foods include:

- **Fatty fish** like salmon and tuna, which are rich in omega-3 fatty acids with anti-inflammatory properties.
- **Antioxidant-rich fruits and vegetables** such as berries, leafy greens, and tomatoes that help protect liver cells.
- **Turmeric and ginger**, known for their strong anti-inflammatory effects, may help reduce liver inflammation.

🍴 Avoiding Alcohol

Alcohol directly damages the liver and can worsen autoimmune hepatitis symptoms. Complete abstinence from alcohol is essential for individuals with autoimmune hepatitis, as their liver is already vulnerable due to chronic inflammation, and alcohol can accelerate disease progression.

🍴 Avoiding Processed Foods

Processed foods high in saturated fats, added sugars, and salt can exacerbate inflammation in the body and negatively affect liver function. Opting for fresh, natural foods instead of processed ones can improve immune system function and overall liver health.

🍴 Maintaining a Healthy Weight

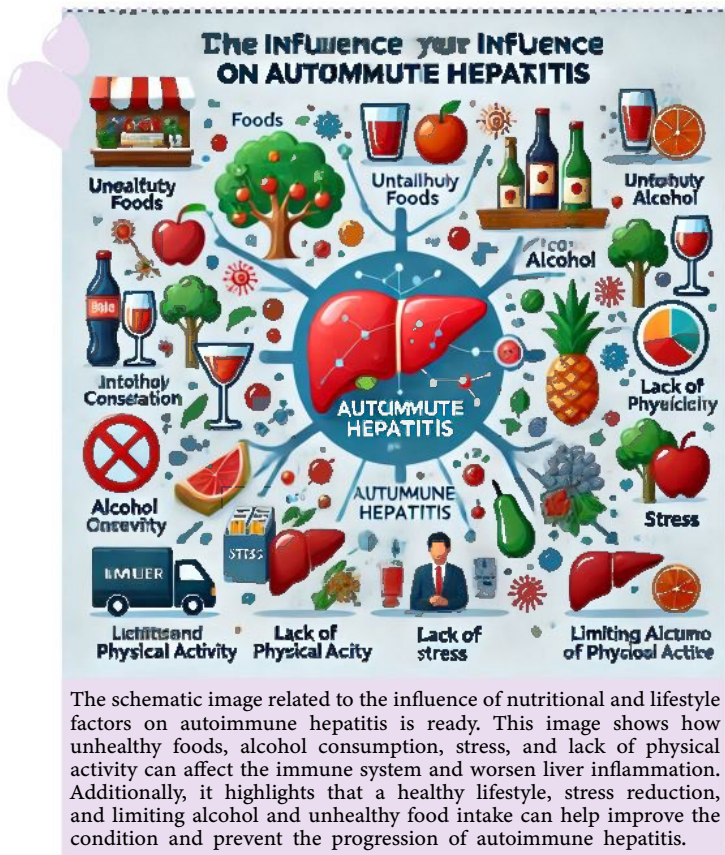
Excess weight can negatively impact liver function, leading to the progression of fatty liver disease or liver inflammation. Losing weight and maintaining a healthy weight can reduce the liver's workload and improve autoimmune hepatitis symptoms.

🍴 Lifestyle Factors and Their Impact on Autoimmune Hepatitis

- **Regular Exercise:** Engaging in regular physical activity can reduce inflammation and improve immune function. Activities like walking, yoga, and swimming can enhance circulation, strengthen the immune system, and reduce stress, all of which contribute to managing autoimmune hepatitis.
- **Stress Reduction:** Chronic stress can stimulate the immune system and worsen autoimmune diseases like autoimmune hepatitis. Techniques such as meditation, deep breathing, and mindfulness can help reduce stress, improve quality of life, and alleviate disease symptoms.

Though autoimmune hepatitis is not directly linked to lifestyle or diet, following a healthy, balanced diet and incorporating light physical activity can help reduce inflammatory load and manage symptoms. Avoiding alcohol, steering

clear of processed foods, maintaining a healthy weight, and managing stress can significantly improve the quality of life for those with autoimmune hepatitis.



■ The Role of the Immune System and Inflammatory Mechanisms

In autoimmune hepatitis, the immune system mistakenly attacks hepatocytes (liver cells), leading to severe liver inflammation. This autoimmune process involves the activation of T cells and the production of autoantibodies such as **antinuclear antibodies (ANA)** and **anti-smooth muscle antibodies (SMA)**. The key mechanisms involved in this disease include the activation of T cells and the production of autoantibodies that directly contribute to the attack on liver cells.

Under normal circumstances, the immune system functions to recognize and eliminate pathogens such as viruses and bacteria. However, in autoimmune diseases like autoimmune hepatitis, the immune system incorrectly targets the body's healthy cells. In this case, **T cells** are abnormally activated and attack liver cells, resulting in inflammation and liver damage.

The inflammatory process in autoimmune hepatitis consists of several stages:

- **Activation of T Cells:** T cells, which act as the immune system's soldiers, mistakenly become activated against liver cells. These cells attack hepatocytes,



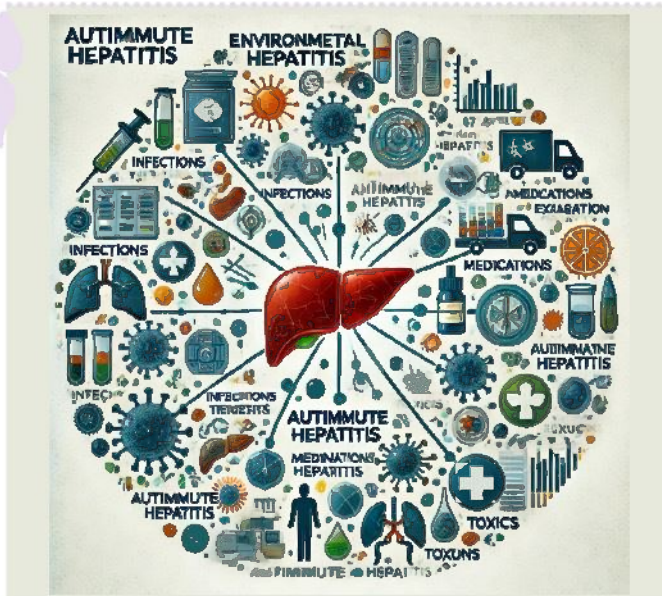
causing inflammation in the liver tissue.

● **Production of Autoantibodies:** The immune system also begins producing autoantibodies that attack the body's own cells. In autoimmune hepatitis, the most significant autoantibodies are:

- **Antinuclear antibodies (ANA):** These attack proteins within the cell nucleus.
- **Anti-smooth muscle antibodies (SMA):** These attack proteins found in smooth muscle cells.

These autoantibodies, along with the activated T cells, cause the gradual destruction of liver cells and lead to scarring of the liver tissue. If untreated, this process can progress to fibrosis and cirrhosis, which are advanced stages of liver damage.

In summary, in autoimmune hepatitis, the immune system mistakenly targets liver cells, causing severe inflammation and damage to the liver. This attack involves the activation of T cells and the production of autoantibodies like ANA and SMA, which play a crucial role in liver destruction. Treatments for autoimmune hepatitis are usually focused on **suppressing the immune system** to reduce inflammation and prevent further liver damage.



The schematic image illustrating the role of the immune system in autoimmune hepatitis is ready. This image clearly shows how the immune system mistakenly identifies healthy liver cells as foreign invaders and attacks them, leading to liver inflammation.

● **Autoimmune hepatitis is significantly more common in women, and while the exact reasons for this gender difference are not fully understood, several key factors may explain this pattern.**

● Hormonal Differences

Estrogen, a primary hormone in women, has a direct impact on the immune system. Estrogen may enhance immune responses, which can sometimes lead

to autoimmune reactions. This is why autoimmune diseases like autoimmune hepatitis, lupus, and rheumatoid arthritis are more prevalent in women. Estrogen's role in boosting immune activity may also increase the risk of immune system malfunction, leading to the immune system attacking healthy liver cells in autoimmune hepatitis.

● Genetic Factors

Women have two X chromosomes (XX), while men have one X and one Y chromosome (XY). The X chromosome carries genes that are involved in immune system regulation. Since women have two X chromosomes, they have a higher likelihood of experiencing genetic abnormalities related to the immune system, increasing their susceptibility to autoimmune diseases. Certain autoimmune-related genes, such as **HLA-DR3** and **HLA-DR4**, which play a role in autoimmune hepatitis, tend to be more active in women.

● Pregnancy and Hormonal Fluctuations

Pregnancy introduces significant changes to the immune system, as the body must balance protecting the mother while tolerating the presence of the fetus. These immune changes can trigger or worsen autoimmune diseases like autoimmune hepatitis. After pregnancy or during periods of hormonal shifts, such as menopause, the disease may become more active, contributing to its higher prevalence in women.

● Stronger Immune Responses in Women

Women generally have a stronger immune system compared to men and exhibit more robust immune responses to infections. While this is advantageous for fighting infections, it also raises the risk of developing autoimmune diseases. The heightened immune activity can lead to a greater chance of the immune system mistakenly attacking the body's own tissues, including liver cells in autoimmune hepatitis.

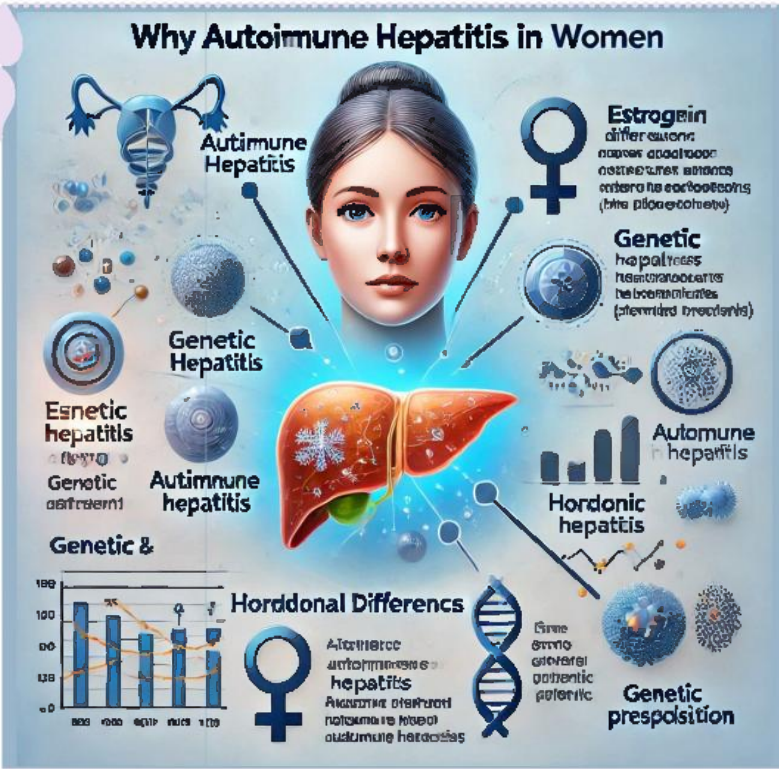
● Environmental and Lifestyle Factors

Environmental triggers, such as viral infections, certain medications, or exposure to chemicals, can also influence the onset of autoimmune hepatitis. Women may be more sensitive to these environmental factors due to their hormonal and genetic differences, making them more prone to developing autoimmune diseases.

● Conclusion

Autoimmune hepatitis is more common in women due to a combination of hormonal, genetic, and immune system differences. Hormonal changes throughout life, such as during pregnancy and menopause, can have a greater impact on the female immune system and increase the risk of developing autoimmune diseases. While more research is needed to fully understand these differences, hormonal fluctuations, genetic predisposition, and stronger immune responses play a significant role in the higher incidence of autoimmune hepatitis in women.





The schematic image illustrating why autoimmune hepatitis is more common in women is ready. This image clearly shows the genetic and hormonal differences that increase the likelihood of developing this disease in women, explaining the role of estrogen and genetic predisposition.

Chapter 4

The History of Autoimmune Hepatitis from the Beginning to Today

Autoimmune hepatitis was first identified in the 1950s, and since then, significant advancements have been made in diagnosing and treating this chronic liver disease. The journey from initially recognizing this condition as a form of unknown liver inflammation to the modern advances in immunology and genetics has been a complex one. Here, we review the key milestones in the development of autoimmune hepatitis research.

📌 Early Discoveries: 1950s

The first reports of a specific type of liver inflammation, later known as autoimmune hepatitis, date back to the 1940s. At that time, liver inflammation was identified by symptoms like jaundice, fatigue, and an enlarged liver. Initially, these symptoms were believed to be caused by viral infections or other factors. However, in 1950, Swedish physician Jan Waldenström was one of the first to identify that some of these cases were due to an autoimmune condition. He described this disease as “lupoid hepatitis,” as patients not only had liver inflammation but also elevated levels of immune-related antibodies in their blood, distinguishing it from other types of hepatitis.

📌 Progress in Immunology: 1960s and 1970s

In the 1960s and 1970s, advancements in immunology and blood testing led to the identification of **autoantibodies**, such as **antinuclear antibodies (ANA)** and **anti-smooth muscle antibodies (SMA)**. These became key markers in diagnosing autoimmune hepatitis. Researchers gradually recognized that autoimmune hepatitis was a disease in which the immune system attacked the liver cells (hepatocytes). During this period, **corticosteroids**, particularly **prednisone**, were introduced as effective treatments to control inflammation and suppress the immune system. These drugs dramatically improved the condition of autoimmune hepatitis patients and marked the beginning of widespread use of immunosuppressive drugs to treat this disease.

📌 Classification into Types: 1980s and 1990s

In the 1980s and 1990s, researchers classified autoimmune hepatitis into two main types:

- **Type 1 Autoimmune Hepatitis:** More common in adults, especially women, and associated with ANA and SMA autoantibodies.
- **Type 2 Autoimmune Hepatitis:** More common in children and adolescents and associated with anti-LKM1 and p-ANCA autoantibodies.

This classification allowed for more accurate diagnosis and treatment. **Azathioprine** was added as a complementary drug to corticosteroids to further suppress the immune system and prevent the progression of inflammation and



fibrosis. These treatments played an effective role in controlling symptoms and preventing the disease from advancing.

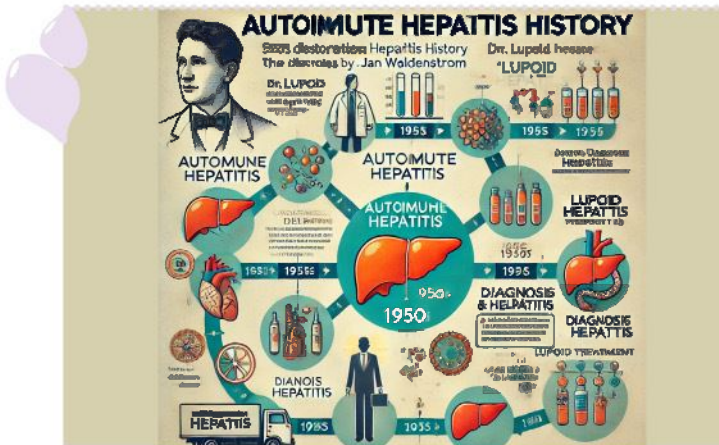
■ Genetic and Immunological Advances: 2000s Onward

Since the early 2000s, progress in genetics and immunology has helped better understand the molecular and genetic mechanisms involved in autoimmune hepatitis. Today, it is known that certain **HLA genes**, such as **HLA-DR3** and **HLA-DR4**, are linked to an increased risk of developing autoimmune hepatitis. These discoveries highlighted the significant role of genetic factors in the disease's development, showing that individuals with a genetic predisposition might develop autoimmune hepatitis after viral infections or exposure to certain medications.

Advancements in diagnostic techniques, such as **liver biopsy**, advanced blood tests, and **genetic testing**, have enabled doctors to diagnose the disease more accurately and quickly. Since the 2010s, new treatments, alongside traditional medications, have been introduced. These include **biologic drugs** that specifically target molecules involved in inflammation and have fewer side effects than traditional drugs. Patients who are resistant to conventional treatments have benefited from these newer therapies, leading to more effective disease control and improved quality of life.

■ Conclusion

From the first descriptions of autoimmune hepatitis in the 1950s to modern advancements in diagnosis and treatment, this disease has undergone significant transformations. With the use of immunosuppressive drugs and precise diagnostic methods, autoimmune hepatitis is now managed more effectively. With recent advancements in genetics and biologic therapies, the future looks brighter for patients with autoimmune hepatitis, with greater chances of achieving better disease control than ever before.



The schematic image illustrating the history of autoimmune hepatitis is ready. This image starts from the 1950s with the initial description of the disease by Dr. Jan Waldenström and highlights key milestones in the diagnosis and treatment of the disease, including its initial name as "lupoid hepatitis" and developments up to the present day.

Chapter 5

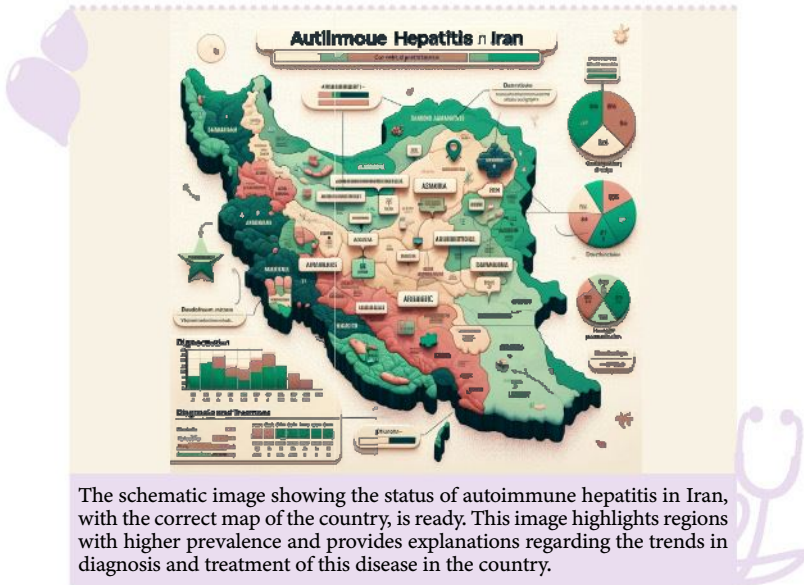
Autoimmune Hepatitis in Iran

In recent years, autoimmune hepatitis has gained more attention in Iran. Although exact statistics on the prevalence of the disease in the country are limited, existing data indicate that it is more common in women, as seen globally. In some regions of Iran, due to a lack of awareness, delayed diagnoses are more frequent, leading to worsening symptoms and the development of serious complications such as liver cirrhosis.

Healthcare professionals in Iran have increasingly focused on improving diagnostic capabilities and raising awareness about autoimmune hepatitis. However, challenges remain, particularly in rural areas where access to advanced medical care and awareness about autoimmune conditions can be limited. This delay in diagnosis and treatment often results in the disease progressing to more severe stages.

Efforts to address this issue include better training for healthcare providers in recognizing the symptoms of autoimmune hepatitis, as well as educating the public about the importance of early diagnosis and treatment. In recent years, more advanced diagnostic techniques, such as liver biopsies and autoantibody testing, have become more accessible in major medical centers across Iran, helping to improve outcomes for patients.

Although significant strides have been made in managing autoimmune hepatitis in Iran, there is still room for improvement, especially in terms of public health awareness and access to treatment in underserved areas. Continued efforts to educate both healthcare professionals and the general public will be crucial in reducing the long-term impacts of this disease on the Iranian population.



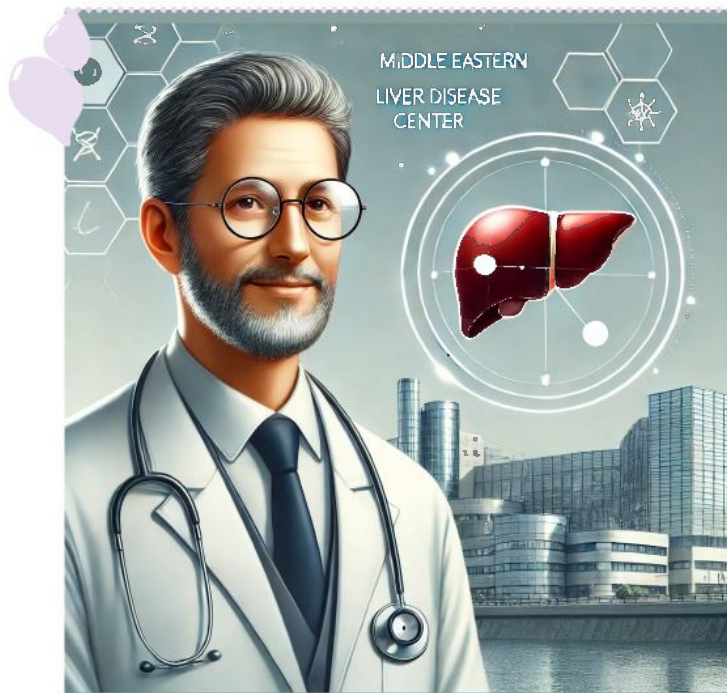
Autoimmune hepatitis type 1 is more common in Iran, particularly among young and middle-aged women. As in other parts of the world, the exact cause of autoimmune hepatitis remains largely unknown. Recent studies in Iran indicate that autoimmune hepatitis is increasingly being diagnosed; however, delayed diagnosis remains one of the main challenges, primarily due to a lack of public awareness and insufficient medical education. This delay in diagnosis can lead to liver cirrhosis and even liver failure in patients. Additionally, genetic factors such as **HLA-DR3** and **HLA-DR4** genes have been identified in Iran as contributing factors to the increased risk of this disease. Environmental factors, including viral infections and the use of certain medications, also play a role in exacerbating the disease. Studies have shown that autoimmune hepatitis is often associated with other autoimmune diseases such as **Hashimoto's thyroiditis**, **type 1 diabetes**, and **rheumatologic diseases**.

Public awareness about this disease and the importance of early diagnosis remains limited. In Iran, as in many developing countries, one of the biggest challenges in treating autoimmune hepatitis is the delayed diagnosis. Many general practitioners may mistake the symptoms of this disease for other liver conditions such as viral hepatitis or gastrointestinal disorders. This misdiagnosis can result in delays in treatment and increased risks associated with disease progression.

Another challenge is the limited access to newer biologic drugs and advanced treatment methods. Currently, drugs like **prednisone** and **azathioprine**, which are the standard treatment for autoimmune hepatitis, are widely available. However, some of the newer drugs used in advanced countries for treating patients who are resistant to treatment or who suffer from serious side effects from traditional drugs are not easily accessible in Iran.

In recent years, there have been more efforts to raise awareness and conduct scientific research on autoimmune hepatitis in Iran. Several research and medical centers in the country are actively working in this field. **Dr. Seyed Moein Alavian**, a pioneer in liver diseases in Iran, has played a crucial role in raising public awareness and introducing new treatments for autoimmune hepatitis. Through the **Iranian Liver Research Society** and by organizing scientific and educational conferences for general practitioners and specialists, he has worked to provide more accurate information about early diagnosis and treatment methods for this disease.

One of the main problems in Iran is the delayed diagnosis of the disease, which can lead to its progression and the development of cirrhosis. It is predicted that with increased awareness and better education for doctors, early diagnosis and access to modern treatments will improve. The use of new technologies in genetic testing and the use of immunological biomarkers may help in faster diagnosis and more effective treatment. Additionally, access to modern biologic drugs may increase in the near future, offering new treatment options for patients who are resistant to traditional therapies.



The schematic image of the professor with glasses, a kind smile, and an expression full of experience and knowledge at the Middle Eastern Liver Disease Center is ready.

In recent years, scientific conferences related to autoimmune hepatitis and other liver diseases have been consistently held in Iran. One of the most important events in this field is the **Tehran International Hepatitis Conference**, which is held annually. This conference is one of the largest scientific gatherings on hepatitis and liver diseases in the Middle East.

During the **8th and 9th editions of the conference**, held in **2021 and 2022**, more than **2,000 researchers and specialists** from around the world participated, including from countries such as the **United States, United Kingdom, Germany, France**, as well as regional countries like **Turkey and Iraq**. The event aimed to present the latest scientific advancements in the diagnosis and treatment of viral hepatitis and liver diseases, including autoimmune hepatitis, and provided a platform for the exchange of information and experiences among physicians and researchers.

Moreover, live streaming platforms made these conferences accessible to individuals both inside and outside Iran, allowing a larger number of specialists to participate and benefit from the latest knowledge on autoimmune and viral hepatitis. This widespread access has enhanced the reach of these conferences, helping more professionals stay updated on advancements in the field.



The schematic image illustrates the International Hepatitis Conference in Tehran, where a gathering of medical professionals is present. This image highlights the importance of international events in Iran for knowledge exchange and advancements in medical fields like hepatitis. Such conferences provide an opportunity for specialists from around the world to share and collaborate on research, new treatments, and developments related to liver diseases.

Chapter 6

Why Awareness of These Diseases Is Important

Awareness of autoimmune hepatitis and similar diseases is crucial because, when diagnosed early and managed properly, these conditions can be effectively controlled, preventing serious complications such as liver cirrhosis and liver failure.

Importance of Early Detection of Autoimmune Hepatitis

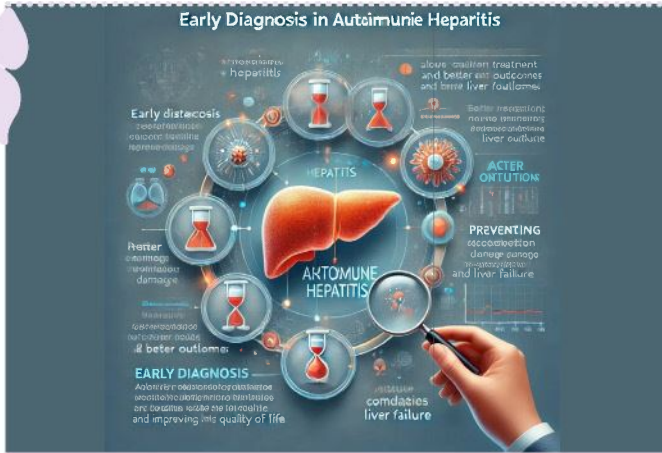
Recognizing autoimmune hepatitis early is vital, as the disease, if not diagnosed in time, can lead to severe complications like cirrhosis and even liver failure. Early detection not only helps in better disease management but also increases the chances of a positive response to initial treatments, preventing the progression of the disease. Below are key reasons why early detection is important:

- o Preventing Permanent Liver Damage:** Autoimmune hepatitis is a chronic, progressive disease that, if not diagnosed early, can gradually affect the liver. Continued inflammation leads to the destruction of liver cells, which are replaced by scar tissue (fibrosis). If this process continues, cirrhosis—a usually irreversible condition—develops. In advanced stages, a liver transplant might be the only way to save the patient. Early diagnosis allows for timely initiation of immunosuppressive treatments, preventing further damage to the liver.
- o Increasing the Chances of Recovery and Disease Control:** Patients diagnosed with autoimmune hepatitis at an early stage generally respond better to initial treatments. Immunosuppressive drugs like prednisone and azathioprine are effective in controlling inflammation and preventing disease progression. However, if the disease is diagnosed at an advanced stage, the body may not respond adequately to these drugs. Starting treatment early can slow disease progression and reduce the need for more intense treatments.
- o Preventing Severe and Fatal Complications:** Without early diagnosis, autoimmune hepatitis can lead to liver failure, one of the most serious complications. In such cases, liver function significantly deteriorates, making it difficult for the body to detoxify or process essential nutrients. This can lead to severe symptoms such as intense jaundice, extreme fatigue, and ultimately the need for a liver transplant. Early detection can prevent these life-threatening complications.
- o Improving Quality of Life:** Patients diagnosed early with autoimmune hepatitis can manage the disease more effectively and maintain a better quality of life. Early treatment not only helps control symptoms but also prevents the physical and mental challenges that come with advanced stages of the disease. With lifestyle changes and adherence to medical recommendations, patients can continue with their daily activities.

◦ **Reducing Treatment Costs:** Early detection often requires less complex and less expensive treatments. In cases of late diagnosis and progression to cirrhosis or liver failure, treatment costs rise significantly, and patients may require surgeries or liver transplants. Early treatment using simpler medications and better disease management can greatly reduce healthcare costs.

Conclusion

Early recognition and diagnosis of autoimmune hepatitis not only improve the chances of recovery and prevent disease progression but also enhance the quality of life for patients and prevent serious and fatal complications. Public awareness and physician education play a key role in timely diagnosis and better management of the disease.



The schematic image illustrating the importance of early diagnosis in autoimmune hepatitis is ready. This image shows how early diagnosis allows for quicker treatment and better outcomes, preventing more severe liver damage and liver failure. It also clearly demonstrates the benefits of early intervention in avoiding acute complications and improving the patient's quality of life.

Proper care for preventing serious complications in autoimmune hepatitis is essential for effective disease management and reducing associated risks. These measures are critical for preventing disease progression and improving the quality of life for patients. Below are some important and key steps for proper care:

◦ **Regular Medical Monitoring:** Patients with autoimmune hepatitis should undergo continuous medical monitoring. This often includes periodic blood tests to assess liver function, liver enzyme tests (ALT and AST), and autoimmune antibody tests. Regular monitoring allows doctors to detect any changes in the disease at an early stage and adjust treatments accordingly. This is especially important in preventing complications like cirrhosis and liver failure.

◦ **Consistent and Accurate Medication Use:** One of the most important actions for controlling autoimmune hepatitis is taking prescribed medications regularly. Medications include:

- **Corticosteroids** (like prednisone), which reduce inflammation.
- **Azathioprine**, an immunosuppressant that helps reduce the activity of the immune system and prevents it from attacking liver cells. Patients must take these medications as prescribed to prevent worsening inflammation and further liver damage. Stopping medications suddenly or taking them inconsistently can lead to a flare-up of the disease and serious complications.
- **Avoiding Risk Factors:** To prevent further liver damage, patients should avoid risk factors such as alcohol, which can exacerbate liver damage. Alcohol accelerates liver inflammation and can worsen the condition. Additionally, processed foods and saturated fats can increase inflammation in the body, so patients should avoid these as well.

Lifestyle Modifications:

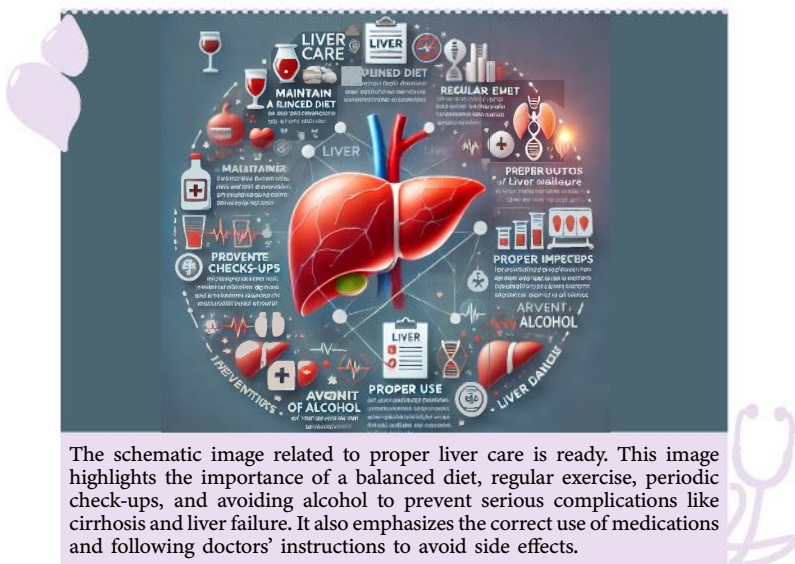
Eating anti-inflammatory foods like fruits, vegetables, and fatty fish (such as salmon, rich in omega-3) can reduce inflammation.

Reducing stress is crucial, as it can play a significant role in lowering inflammation and improving immune function.

Regular physical activity and exercise can help maintain overall health.

- **Stress Management and Psychological Support:** Patients with autoimmune hepatitis may experience psychological stress and anxiety due to the chronic nature of the disease. Stress management through yoga, meditation, and deep breathing techniques can enhance immune function and reduce inflammation. Additionally, receiving social and psychological support from family, friends, and professional counselors can be highly beneficial for patients.

Early detection, regular and diligent care can help patients with autoimmune hepatitis maintain their quality of life and prevent serious complications. Regular medical check-ups, proper medication adherence, and avoiding risk factors are key to successfully managing the disease and keeping patients from reaching advanced stages, such as liver failure.



The schematic image related to proper liver care is ready. This image highlights the importance of a balanced diet, regular exercise, periodic check-ups, and avoiding alcohol to prevent serious complications like cirrhosis and liver failure. It also emphasizes the correct use of medications and following doctors' instructions to avoid side effects.

Chapter 7

Symptoms and Signs of Autoimmune Hepatitis

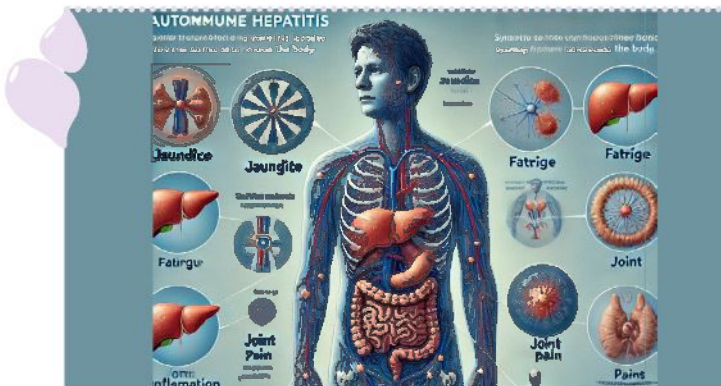
The symptoms and signs of autoimmune hepatitis can vary depending on the severity and stage of the disease. Some patients may experience mild symptoms that are difficult to diagnose, while others may present with more severe and concerning signs. One of the most common and early symptoms of autoimmune hepatitis is **extreme fatigue**. This fatigue tends to persist and does not improve with physical activity. Patients may feel weak, lethargic, and experience a lack of energy. Chronic fatigue is common in autoimmune diseases and, specifically in autoimmune hepatitis, can be linked to improper immune system function and chronic liver inflammation.

Another key symptom of autoimmune hepatitis is **jaundice**. Jaundice refers to the yellowing of the skin and the whites of the eyes, caused by an increase in bilirubin levels in the blood. A damaged liver cannot effectively process bilirubin, leading to its accumulation in the bloodstream. Jaundice is usually accompanied by darkening of the urine and light-colored stools.

Many patients with autoimmune hepatitis experience **abdominal pain** or discomfort, typically felt in the upper right part of the abdomen where the liver is located. Liver inflammation or enlargement (hepatomegaly) can lead to this pain, which may be intermittent or constant and can worsen when pressure is applied to the liver area.

Patients may also experience **unexplained weight loss** and a **loss of appetite**. Inflammation and liver damage can disrupt the body's metabolic processes, impairing its ability to process food, which leads to weight loss and a feeling of fullness even after eating small amounts.

By recognizing these symptoms early, it is possible to manage autoimmune hepatitis more effectively and prevent further liver damage. Proper treatment and monitoring are crucial for improving patient outcomes and quality of life.



The schematic image showing the symptoms and signs of autoimmune hepatitis is ready. This image clearly illustrates how autoimmune hepatitis can affect various parts of the body, leading to symptoms throughout the body.

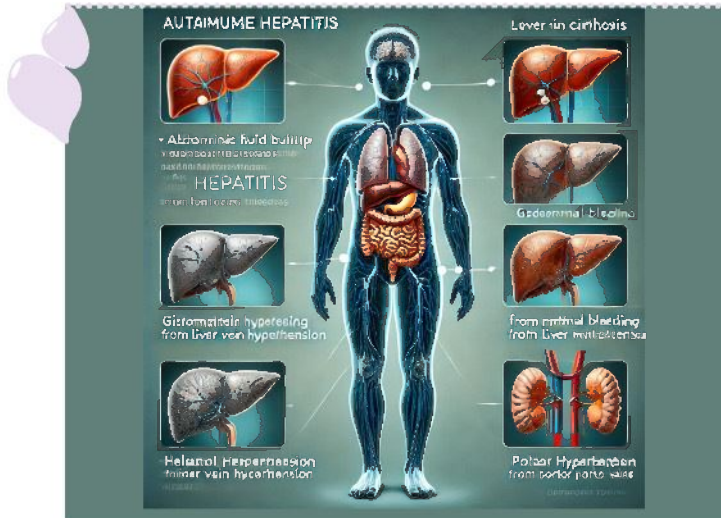
Many patients with autoimmune hepatitis experience flu-like symptoms in the early stages of the disease. These symptoms may include mild fever, joint pain, muscle aches, and headaches. These symptoms occur due to chronic inflammation and abnormal immune system activity. In some cases, patients with autoimmune hepatitis may experience skin itching. This symptom may result from an increase in bile salts in the blood, which occurs due to impaired liver function and obstruction of the bile ducts.

Patients may also experience an enlarged liver or spleen. These symptoms are typically observed in the more advanced stages of the disease and may be accompanied by abdominal pain and a sense of pressure in the liver area. Changes in the color of stool and urine are another significant symptom in patients with autoimmune hepatitis. Dark urine and pale stool are signs of liver dysfunction and the inability to properly break down bilirubin.

Many patients with chronic autoimmune diseases, such as autoimmune hepatitis, may experience psychological issues such as anxiety and depression. These issues are often due to the constant stress of the disease and its impact on daily life.

If autoimmune hepatitis progresses to more advanced stages and leads to cirrhosis of the liver, the following symptoms may appear: abdominal swelling (ascites), swelling in the hands and feet, gastrointestinal bleeding (due to high blood pressure in the liver veins), and confusion or mental changes (symptoms of hepatic encephalopathy).

Autoimmune hepatitis has a wide range of symptoms that can vary from mild to severe. Early diagnosis and appropriate treatment can prevent the progression of the disease and serious complications like cirrhosis and liver failure. Paying attention to early symptoms, such as extreme fatigue, jaundice, and abdominal pain, and consulting a doctor for evaluation and liver function tests can help better manage the disease and prevent dangerous complications.



The new image related to the advanced symptoms of autoimmune hepatitis and cirrhosis is ready. This image clearly illustrates the advanced symptoms of the disease and its effects on the body.

Chapter 8

Diagnosis of Autoimmune Hepatitis: Tests and Medical Examinations

The diagnosis of autoimmune hepatitis is a multi-step process involving clinical evaluations, blood tests, and imaging techniques. Given that the symptoms of this disease may resemble other liver disorders, precise and early diagnosis is essential to initiate timely treatment. Below is a detailed examination of the common diagnostic tools for autoimmune hepatitis:

■ Clinical Examination and Symptom Evaluation

The first step in diagnosing autoimmune hepatitis is a thorough clinical examination and evaluation of the patient's symptoms. This stage helps the physician gather initial clues about the disease's presence, allowing them to proceed with additional testing. Here's a more detailed explanation of the clinical examination and symptom evaluation process:

● Comprehensive Clinical Interview and Patient History

A detailed patient history is one of the first steps in the clinical examination. During this process, the physician asks specific questions to assess the symptoms and conditions accurately. These questions may include:

- **Family history of autoimmune diseases:** Autoimmune hepatitis may be more common in individuals with a family history of autoimmune disorders.
- **Previous or coexisting illnesses:** Patients with other autoimmune conditions, such as Hashimoto's thyroiditis, rheumatoid arthritis, or type 1 diabetes, are at a higher risk of developing autoimmune hepatitis.
- **Medication usage:** Some medications may contribute to liver inflammation. It's essential to inquire about specific drug usage.
- **Symptom patterns:** The physician will ask when symptoms began and how they have progressed. For example, is fatigue constant or intermittent? Has jaundice appeared gradually?

● Evaluation of Physical Symptoms

After the interview, the physician examines the patient's physical symptoms. Jaundice, or the yellowing of the skin and the whites of the eyes, is a key sign of liver problems and is commonly seen in patients with autoimmune hepatitis. This symptom occurs when the liver cannot process bilirubin properly, causing it to accumulate in the body. The physician can detect this through close observation of the skin and eyes. Persistent fatigue reported by the patient is also a critical sign, often stemming from systemic inflammation and the liver's inability to perform metabolic functions properly. The physician must assess the degree and severity of the patient's fatigue. Many patients may report pain or discomfort in the upper right side of the abdomen, where the liver is located.

This pain can result from liver inflammation or enlargement (hepatomegaly). The physician can detect tenderness or pain in this area through palpation, indicating liver inflammation.

● Full Physical Examination

A full physical examination helps detect other possible symptoms, such as:

- **Liver or spleen enlargement (hepatomegaly or splenomegaly):** The physician may detect enlarged organs by palpating the abdomen.
- **Changes in urine and stool color:** Dark urine and pale stools are signs of liver dysfunction. The physician inquires about changes in urine and stool color.
- **Swelling or ascites:** Swelling in the legs and abdomen, caused by fluid retention due to liver failure, is examined.

● Systemic Symptom Review

Autoimmune hepatitis may be accompanied by other systemic immune symptoms or autoimmune diseases, such as joint pain, skin rashes, or flu-like symptoms. By examining the skin, joints, and general health, the physician gathers information about the presence of co-occurring conditions.

● Weight and Appetite Changes

Unexplained weight loss and decreased appetite may be signs of autoimmune hepatitis. The physician will pay attention to any sudden, unexplained weight loss, which can indicate liver dysfunction and metabolic problems.

📖 Medical Tests for Confirming Diagnosis

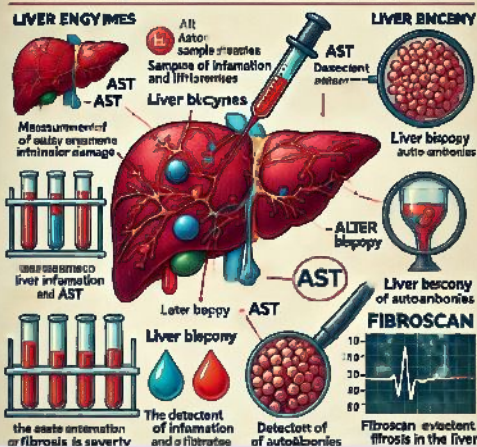
After the initial clinical evaluation, various laboratory tests are performed to confirm the diagnosis of autoimmune hepatitis, including:

- **Liver Function Tests:** To measure liver enzymes (ALT, AST), bilirubin levels, and albumin, helping assess liver inflammation and damage.
- **Immunological Tests:** To detect the presence of autoantibodies like ANA (antinuclear antibodies), SMA (smooth muscle antibodies), and anti-LKM1 (anti-liver kidney microsomal antibodies), which are crucial markers of autoimmune hepatitis.
- **Imaging (Ultrasound, CT, MRI):** These imaging tests help assess the liver's structure, detect enlargement, and rule out other causes of liver damage.
- **Liver Biopsy:** In some cases, a liver biopsy is performed to directly examine liver tissue for signs of inflammation, fibrosis, or cirrhosis, confirming the extent of liver damage.

📖 Importance of Early Detection

A thorough clinical examination and symptom assessment are key steps in diagnosing autoimmune hepatitis. The physician uses the information from the physical exam, patient history, and symptom evaluation to form an initial diagnosis, followed by confirmatory tests. Early recognition of clinical symptoms can facilitate faster diagnosis and treatment, preventing severe complications like cirrhosis and liver failure.

AUTOMUTE HEPATTIS



The educational schematic image related to medical tests and evaluations for diagnosing autoimmune hepatitis is ready. This image clearly shows the measurement of liver enzymes like ALT and AST, liver biopsy, detection of autoantibodies, and the use of FibroScan to assess liver fibrosis.

Blood tests play a crucial role in diagnosing autoimmune hepatitis and help physicians assess the patient's liver function and immune system status by analyzing specific markers. Below is a detailed explanation of the blood tests commonly used in diagnosing this disease:

A. Liver Enzymes

Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST): These are key enzymes found in liver cells. Elevated levels of these enzymes in blood tests can indicate liver cell damage. In autoimmune hepatitis, liver inflammation leads to the destruction of liver cells, which causes these enzymes to leak into the blood, raising their levels.

ALT: Mainly produced in the liver, and its elevation directly indicates liver damage.

AST: Found in other organs like the heart and muscles as well as the liver, but its increase also signals liver inflammation and damage.

Elevated levels of ALT and AST are common in autoimmune hepatitis and can reflect the severity of liver inflammation and damage.

B. Autoimmune Antibodies

The presence of specific antibodies in the blood is one of the primary indicators for diagnosing autoimmune hepatitis. These antibodies indicate that the immune system is mistakenly attacking the body's own tissues, particularly the liver.

Anti-Nuclear Antibodies (ANA): ANA is a major marker in many autoimmune diseases and targets the nuclei of cells. In autoimmune hepatitis type 1, ANA is commonly found and signifies autoimmune activity in the body. ANA is also seen in other autoimmune diseases like lupus.

Anti-Smooth Muscle Antibodies (SMA): These antibodies target smooth

muscle cells and are specifically found in autoimmune hepatitis type 1. Their presence in blood indicates active autoimmunity against the liver and serves as a key marker for diagnosing type 1 autoimmune hepatitis.

Anti-Liver/Kidney Microsomal Antibodies (anti-LKM1): Found in patients with autoimmune hepatitis type 2, these antibodies indicate autoimmune inflammation of the liver and kidneys. Autoimmune hepatitis type 2 is more common in children and adolescents and is less frequent than type 1.

Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (p-ANCA): These antibodies may be observed in patients with autoimmune hepatitis, especially in those who also have other conditions like primary sclerosing cholangitis or inflammatory bowel disease. Their presence helps in differential diagnosis and identifying coexisting diseases.

C. Immunoglobulin Levels

Increased levels of immunoglobulin G (IgG) are another key indicator in autoimmune hepatitis. This protein is produced in response to immune system activity, and elevated IgG levels in the blood signify an overactive immune system and chronic inflammation. Measuring IgG levels helps confirm the diagnosis and assess disease activity. Many autoimmune hepatitis patients have significantly elevated IgG levels, which can also indicate the severity of the disease.

Other Complementary Blood Tests

In addition to the above tests, physicians may request other tests to assess liver function and differentiate diagnoses:

Bilirubin Test: This test evaluates liver function and measures the amount of bilirubin in the blood, which can indicate jaundice.

Albumin Test: Since the liver produces albumin, a low level of this protein suggests liver failure or advanced liver damage.

Prothrombin Time (PT) Test: This assesses blood clotting ability, as the liver plays a vital role in producing clotting factors.

Liver Imaging

Imaging techniques play a crucial role in diagnosing and managing autoimmune hepatitis by allowing physicians to examine the structural and functional status of the liver. Here's an overview of the key imaging methods used:

Liver Ultrasound

Liver ultrasound is one of the most common and non-invasive imaging methods. It uses sound waves to create images of internal tissues and helps doctors evaluate the size and shape of the liver, detect abnormalities such as enlargement (hepatomegaly), and identify tumors, cysts, or gallstones. It can also detect early signs of cirrhosis.

Elastography (FibroScan)

Elastography is a non-invasive, advanced imaging technique used to measure the stiffness of liver tissue. It's widely employed to detect liver fibrosis and



cirrhosis. This technique works by sending sound waves into the liver and measuring how quickly these waves travel through different tissues. Fibrotic tissue transmits sound waves faster than healthy tissue, allowing physicians to determine the severity of liver fibrosis without needing a biopsy.

- **FibroScan:** A well-known elastography technique specifically designed to measure liver stiffness and assess fibrosis. FibroScan is fast, non-invasive, and reduces the need for biopsies.
- **Advantages:**
 - Non-invasive and quick.
 - Provides accurate information on liver stiffness and the degree of fibrosis.
 - Useful for tracking disease progression and response to treatment.

● Liver Biopsy

A liver biopsy involves taking a small sample of liver tissue with a needle for microscopic examination. Although it provides detailed information about liver histology, it is an invasive procedure with potential risks, including bleeding and infection. Biopsies are typically used when non-invasive tests are inconclusive or if more detailed information about the liver is needed.

■ Limitations of Elastography and FibroScan

- **Difficulty in detecting focal liver lesions:** Elastography cannot pinpoint tumors or specific areas of liver damage. Other imaging modalities like MRI or CT may be required.
- **Reduced accuracy in obese patients:** In patients with extreme obesity, the accuracy of FibroScan may be compromised, and additional imaging techniques may be needed.

■ Conclusion

Blood tests, including liver enzymes, autoantibodies, and immunoglobulin G levels, are critical tools for diagnosing autoimmune hepatitis. These tests help physicians detect liver inflammation and immune system abnormalities while determining the type of autoimmune hepatitis. Early diagnosis through these tests allows for better management and prevents the progression to serious complications like cirrhosis. Additionally, imaging techniques such as ultrasound and FibroScan are essential for evaluating liver structure, detecting fibrosis, and monitoring treatment progress without invasive procedures.

Use FibroScan, measure Liver stiffness and diagnose liver fibrosis

The schematic image related to the use of FibroScan for measuring liver stiffness and diagnosing fibrosis is ready. This image clearly shows the benefits of FibroScan, such as being non-invasive, fast, and a suitable alternative to liver biopsy.



CT Scan

A CT scan (Computed Tomography) is an advanced imaging technique that uses X-rays to create three-dimensional images of the liver and surrounding structures. This method helps physicians view detailed aspects of the liver's structure, including any tissue damage or suspicious masses. The main applications of CT scans in diagnosing autoimmune hepatitis and its complications include:

- Identifying cirrhosis and assessing the size and shape of the liver
- Evaluating liver blood vessels and detecting portal hypertension or thrombosis in the portal vein
- Detecting liver tumors or metastases

Since CT scans use X-rays, they are considered more intensive than ultrasounds but are extremely useful for detecting finer details in the liver's structure and more complex diagnoses.

MRI (Magnetic Resonance Imaging)

MRI is another advanced imaging method that uses magnetic fields and radio waves to generate highly detailed images of the liver tissue. MRI of the liver is especially useful for:

- Detecting and assessing soft tissue changes and minor alterations in liver structure
- Identifying advanced-stage fibrosis or cirrhosis
- Detecting liver tumors or suspicious masses
- Examining bile ducts for any obstructions or narrowing

MRI, due to its high-resolution imaging and ability to accurately identify structural and functional changes in the liver, is one of the key tools in diagnosing and managing liver diseases, including autoimmune hepatitis. Unlike CT scans, MRI does not involve radiation, making it more suitable for patients who need repeated imaging.

Liver imaging is a crucial tool in diagnosing and evaluating autoimmune hepatitis and its complications. Each imaging method, such as ultrasound, elastography, CT scan, and MRI, has its unique benefits and can assist physicians in precisely assessing the structural and functional status of the liver, allowing for appropriate treatment. Combining these methods provides more accurate diagnoses and better management of liver diseases.

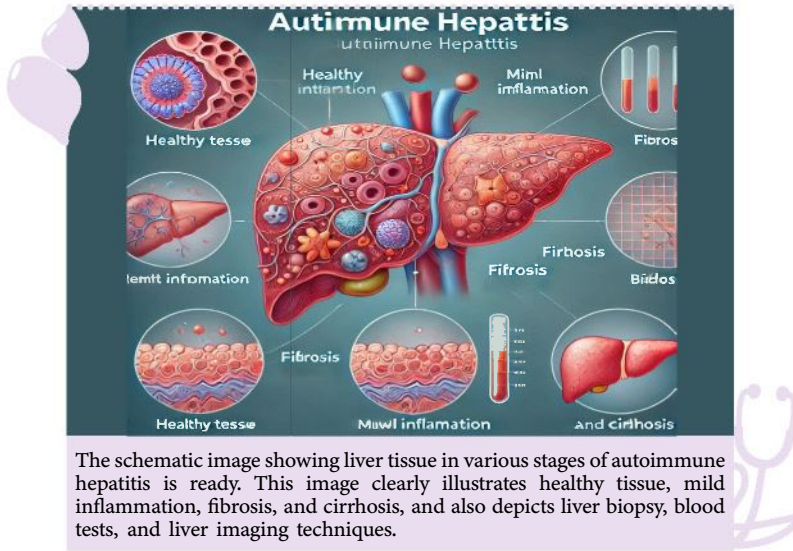
Liver Biopsy: A Precise Diagnostic Procedure in Autoimmune Hepatitis

Liver biopsy is one of the most accurate and essential diagnostic methods for liver diseases, including autoimmune hepatitis. In this procedure, a small sample of liver tissue is taken using a needle and examined under a microscope. It provides critical information about the level of inflammation, fibrosis, and cellular damage in the liver, helping doctors assess the severity and progression of the disease accurately.

How a Liver Biopsy Is Performed

- **Preparing the Patient:** Before the biopsy, the doctor ensures the patient is in proper condition, and blood tests are conducted to check blood clotting to prevent any complications during the procedure.
- **Local Anesthesia:** To minimize pain and discomfort, local anesthesia is applied to the area where the needle will be inserted.
- **Sample Collection:** Using a thin needle, a small sample of liver tissue is extracted. This process usually takes only a few minutes, after which the patient may need to rest for a short time.
- **Microscopic Examination:** The sample is sent to a laboratory where it is closely examined by a pathologist. This examination reveals the extent of inflammation, fibrosis (scarring), and liver cell damage.

Liver biopsy is crucial in determining the exact stage and severity of autoimmune hepatitis, allowing for a more targeted and effective treatment plan.



Applications of Biopsy in Autoimmune Hepatitis

- **Definitive Diagnosis:** When blood tests and imaging do not provide a conclusive diagnosis, a liver biopsy helps confirm the presence and severity of autoimmune hepatitis.
- **Assessment of Liver Damage:** A biopsy enables doctors to determine if the liver has developed fibrosis or cirrhosis, which are critical indicators of advanced and more severe stages of the disease.
- **Distinguishing Types of Autoimmune Hepatitis:** In some cases, a biopsy can help differentiate between various forms of autoimmune hepatitis.

Autoimmune hepatitis can be challenging to diagnose due to the similarity of its symptoms with other liver diseases, particularly viral hepatitis, non-alcoholic fatty liver disease (NAFLD), and primary sclerosing cholangitis (PSC). Therefore, physicians rely on a combination of diagnostic tools such as blood tests, imaging, and biopsy to distinguish between these conditions. For example:

In viral hepatitis, blood tests often show positive results for hepatitis viruses A, B, or C.

In NAFLD, ultrasound or imaging typically reveals signs of fat in the liver, while autoimmune hepatitis is more associated with inflammation and fibrosis.

PSC is usually accompanied by inflammation of the bile ducts, visible in ultrasound or MRI imaging.

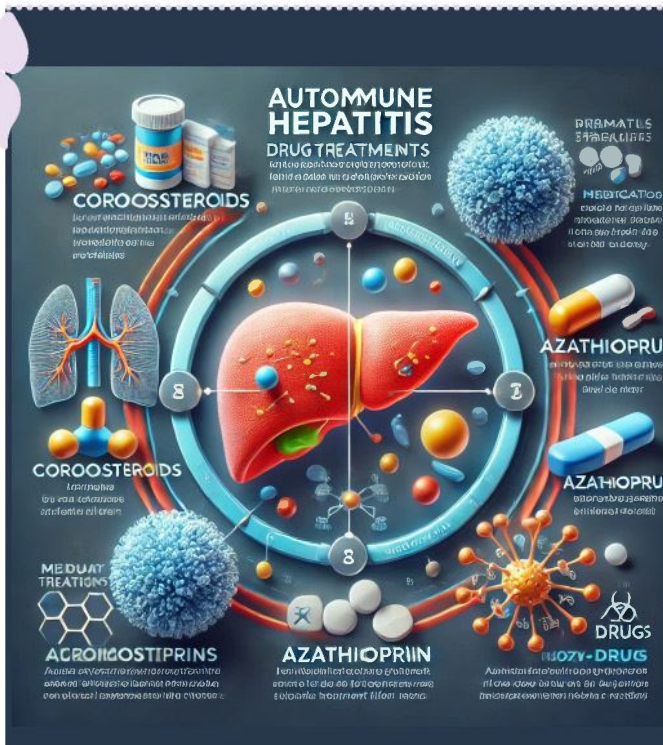
Diagnosing autoimmune hepatitis requires a multi-step approach and the use of precise diagnostic tools. Blood tests for autoimmune antibodies, liver imaging to assess liver structure, and liver biopsy help physicians arrive at a definitive diagnosis. These steps are crucial in determining the severity of the disease and selecting the best treatment plan for the patient. Early diagnosis plays a critical role in improving treatment outcomes and preventing disease progression to cirrhosis or liver failure. Sometimes, all autoimmune blood tests return negative, and only a liver biopsy provides clarity.

Chapter 9

Drug Treatments for Autoimmune Hepatitis - Immunosuppressive Medications and Managing Side Effects

Autoimmune hepatitis is a chronic disease where the immune system mistakenly attacks liver cells, causing inflammation. The primary treatment for this condition is based on drugs that suppress immune system activity to prevent further liver damage. Below is an overview of commonly used medications and strategies for managing their side effects.

Attention Attention: This information is for awareness purposes only and should not cause any changes to your medication regimen.



The schematic image related to drug treatments for autoimmune hepatitis is ready. This image shows how medications like corticosteroids and azathioprine are used as the primary treatment options to reduce liver inflammation and suppress the immune system.

Corticosteroids

Corticosteroids, such as prednisolone, are the main drugs used to treat autoimmune hepatitis. These medications quickly reduce liver inflammation

and suppress the body's immune response. In autoimmune hepatitis, the immune system mistakenly attacks liver cells, and corticosteroids help control inflammation by suppressing cytokine production and reducing the activity of T cells that attack the liver. Commonly, these drugs are referred to as “cortone” or “cortisone” in everyday language.

How Corticosteroids Are Used

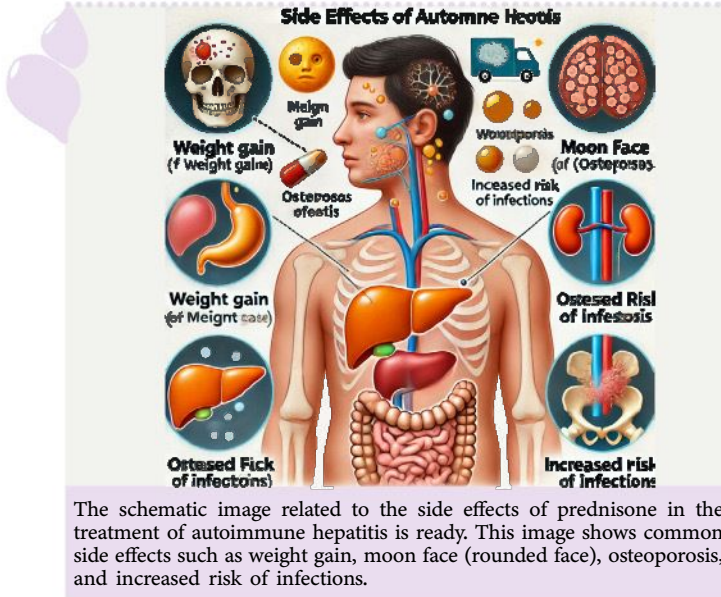
At the start of treatment, doctors usually prescribe a high dose of prednisolone to rapidly control inflammation. This high dose helps reduce inflammation quickly and prevents further liver damage. Once the initial inflammation is under control, the dosage is gradually reduced to minimize side effects.

Side Effects of Corticosteroids

Long-term use of corticosteroids can lead to several side effects, which require careful monitoring and prevention. Some of the key side effects include:

- **Osteoporosis:** Prednisolone can reduce bone density, leading to osteoporosis. To prevent this, calcium and vitamin D supplements are often prescribed alongside corticosteroids. These supplements help maintain bone health and reduce the risk of fractures.
- **Weight Gain and Swelling:** Prolonged use of corticosteroids may cause weight gain and fluid retention, leading to swelling in the hands and feet. Patients can manage these effects by following a low-sodium diet and maintaining regular physical activity, which helps reduce swelling and keep weight in check.
- **Increased Blood Sugar and Diabetes:** Corticosteroids can raise blood sugar levels, potentially causing diabetes in some patients. To manage this risk, patients should regularly monitor their blood sugar and follow a diet low in sugar and simple carbohydrates. In some cases, medication may be needed to control blood sugar levels.
- **High Blood Pressure:** Long-term corticosteroid use can lead to high blood pressure. Doctors may recommend blood pressure medications, and patients should maintain a low-sodium diet and regularly monitor their blood pressure to manage this side effect.
- **Other Potential Side Effects:**
 - **Muscle Weakness:** Prolonged use of prednisolone may cause muscle weakness.
 - **Mood Swings:** Some patients may experience mood changes, depression, or anxiety.
 - **Immune Suppression:** Corticosteroids may lower the body's resistance to infections, so patients should avoid contact with sick individuals and stay up to date with vaccinations.

Corticosteroids are highly effective as the first line of treatment for autoimmune hepatitis and can quickly control liver inflammation. However, due to the potential side effects, regular patient monitoring and careful management of dosage are essential. Using necessary supplements and making lifestyle changes can help reduce side effects and improve the quality of life for patients.



The schematic image related to the side effects of prednisone in the treatment of autoimmune hepatitis is ready. This image shows common side effects such as weight gain, moon face (rounded face), osteoporosis, and increased risk of infections.

■ Budesonide

Budesonide is one of the medications used in the treatment of autoimmune hepatitis. It belongs to the group of corticosteroids but has some differences compared to traditional corticosteroid drugs like prednisone. Budesonide is considered an option for patients with autoimmune hepatitis due to its stronger effects on the liver and fewer systemic side effects. Budesonide, compared to prednisone, is primarily metabolized in the liver, with its effects mostly confined to the liver, which helps reduce systemic side effects. Because of its rapid metabolism by the liver, less of the drug reaches the rest of the body. This characteristic reduces the long-term side effects commonly associated with corticosteroids, such as osteoporosis, weight gain, and diabetes.

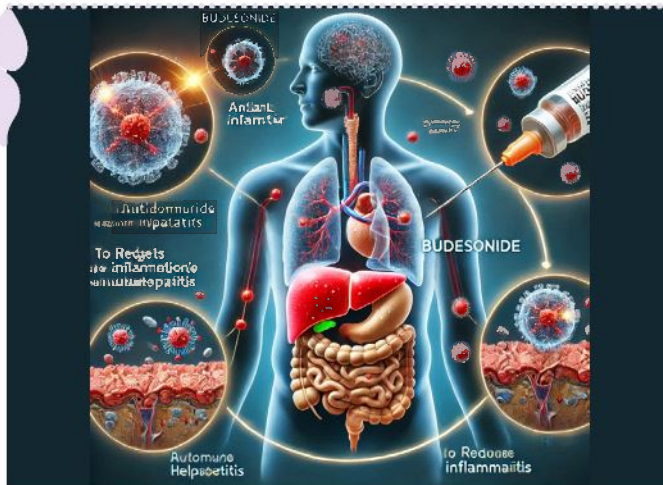
Budesonide is usually prescribed to patients with autoimmune hepatitis who have experienced side effects from prednisone or are looking for a treatment with fewer side effects. It is typically prescribed at a specific daily dose, which is gradually adjusted. The usual dose ranges from 9 mg per day during the initial phase, with a gradual reduction as the disease is controlled. Budesonide is often used in combination with other immunosuppressive drugs like azathioprine. However, its use is not recommended in cases of advanced liver cirrhosis.

Studies have shown that budesonide is effective in patients with mild to moderate autoimmune hepatitis and can improve symptoms in these cases. Additionally, budesonide helps reduce the long-term side effects of corticosteroids. However, in severe or advanced cases of autoimmune hepatitis, budesonide may be less effective, and stronger drugs like prednisone may still be needed.

Although budesonide has fewer side effects than other corticosteroids, it may still cause gastrointestinal disturbances such as nausea and bloating, dizziness or fatigue, and, in rare cases, increased blood sugar levels.

Budesonide is a suitable alternative for patients who need long-term cortico-

steroid treatment but wish to avoid systemic side effects. However, it should be prescribed based on the severity of the disease and under medical supervision to achieve the best therapeutic outcomes.



The schematic image illustrating how budesonide works in the body is ready. This image shows the mechanism of action, highlighting its anti-inflammatory effects and how it targets the liver to reduce inflammation in autoimmune hepatitis or other liver-related conditions.

■ Azathioprine

Azathioprine is an immunosuppressive drug commonly used in the treatment of autoimmune hepatitis, often in combination with corticosteroids. It helps reduce liver inflammation and can lower the required doses of corticosteroids, thereby minimizing the long-term side effects associated with high-dose steroid use. Azathioprine works by inhibiting DNA production in T and B cells of the immune system, which reduces the number of these cells and suppresses the immune response. This suppression prevents the immune system from attacking liver cells, reducing inflammation and liver damage.

Azathioprine helps reduce the need for prolonged high-dose corticosteroids, preventing side effects like osteoporosis, weight gain, and diabetes. It is highly beneficial for long-term disease control and can help patients achieve sustained remission.

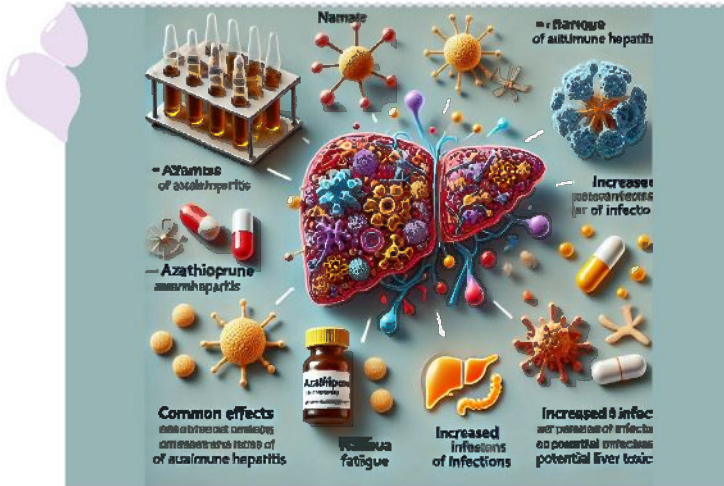
The starting dose is typically 50 mg per day, which is gradually increased based on the patient's response and blood test results. The doctor adjusts the dosage to minimize side effects while ensuring effective disease control.

Azathioprine is a potent drug and, like other immunosuppressants, can cause side effects that require close monitoring and care. Some possible side effects include:

● Bone marrow suppression, which can lead to

- **Anemia** (low red blood cell count), causing fatigue, weakness, and dizziness.
- **Leukopenia** (low white blood cell count), increasing the risk of infections.
- **Thrombocytopenia** (low platelet count), increasing the risk of bleeding.

However, these side effects are usually manageable with proper medical supervision and patient cooperation.



The schematic image illustrating the side effects of azathioprine in the treatment of autoimmune hepatitis is ready. This image shows side effects such as nausea, fatigue, increased risk of infections, and potential liver toxicity.

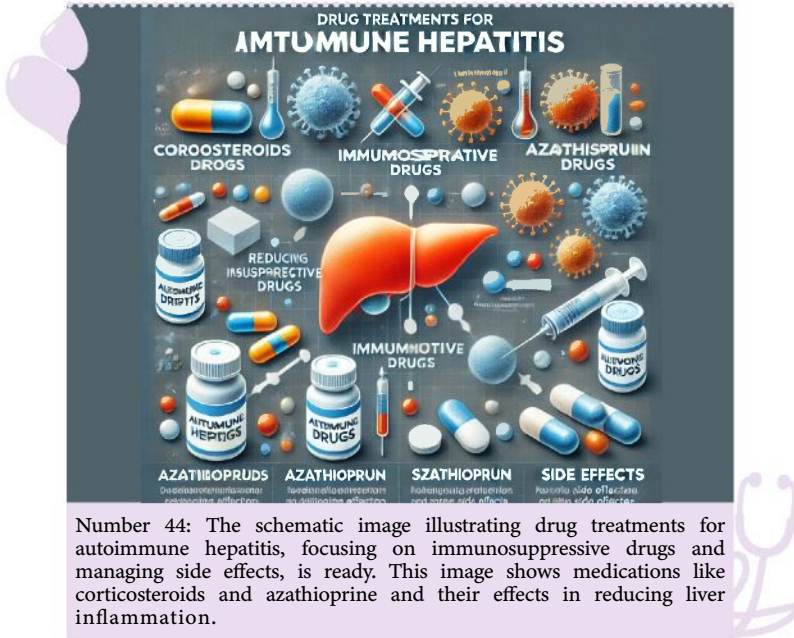
Immunosuppression caused by azathioprine increases the body's vulnerability to viral, bacterial, and fungal infections. Patients should avoid contact with sick individuals and promptly report early signs of infection to their doctor. This drug may cause nausea, vomiting, and diarrhea in some patients. Physicians typically adjust the dosage based on the severity of symptoms. Long-term use of azathioprine can increase the risk of skin and blood cancers. Patients should avoid direct sun exposure and undergo regular skin examinations.

■ Important Considerations and Care for Azathioprine Users:

- **Regular Blood Tests:** Azathioprine can suppress blood cell production, so patients should undergo regular blood tests to monitor blood cell levels, helping the doctor adjust the dosage as needed.
- **Infection Prevention:** To reduce infection risk, patients should maintain good personal hygiene, avoid contact with sick individuals, and report signs of infection like fever or sore throat to their doctor immediately.
- **Timely Vaccination:** Patients should use inactivated vaccines and avoid live vaccines to prevent infection risk.
- **Sun Protection:** Use high-SPF sunscreens and avoid direct sunlight exposure to reduce skin cancer risk.
- **Dietary Adjustments:** For managing gastrointestinal side effects, it is recommended to eat healthy, non-fatty foods and avoid spicy dishes. Smaller, more frequent meals may also help.
- **Cancer Prevention:** Long-term use of azathioprine may increase the risk of certain blood and skin cancers, so regular medical check-ups are essential.
- **Adhering to Medication Schedule and Doctor's Advice:** Patients should

take azathioprine as prescribed and consult their doctor for any side effects or necessary dosage adjustments.

Azathioprine is effective for long-term management of autoimmune hepatitis by reducing the need for corticosteroids and improving disease control. However, due to its potential side effects, patients must be regularly monitored and undergo routine blood tests to prevent complications.



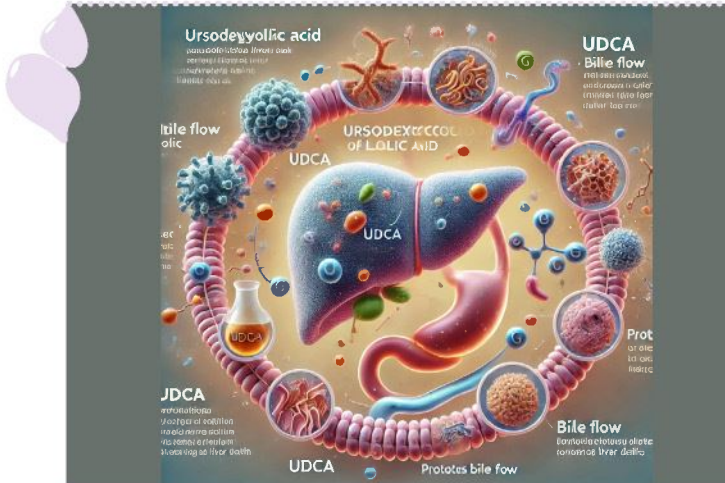
Number 44: The schematic image illustrating drug treatments for autoimmune hepatitis, focusing on immunosuppressive drugs and managing side effects, is ready. This image shows medications like corticosteroids and azathioprine and their effects in reducing liver inflammation.

Ursodeoxycholic acid is primarily used to treat cholestatic liver diseases such as primary biliary cholangitis and primary sclerosing cholangitis, but it is also prescribed in some cases for patients with autoimmune hepatitis (AIH) who experience cholestasis or bile duct issues. This drug is a naturally occurring bile acid produced in small amounts in the body, and it helps improve bile flow while reducing the buildup of toxic substances in the liver.

For autoimmune hepatitis patients who also suffer from cholestasis (blockage or reduction of bile flow), ursodeoxycholic acid can improve bile flow and reduce inflammation. It helps protect liver cells from bile-related damage and can alleviate clinical symptoms such as itching. While ursodeoxycholic acid does not directly affect the autoimmune process, it indirectly helps by safeguarding liver cells against bile-induced injury, thus aiding in the management of autoimmune hepatitis. This medication is particularly useful for patients with concurrent bile duct diseases. Research has shown that using ursodeoxycholic acid can help lower liver enzyme levels, such as ALT and AST, in some autoimmune hepatitis patients, indicating reduced inflammation and liver damage.

Ursodeoxycholic acid is typically used in combination with immunosuppressive medications like corticosteroids and azathioprine. It is generally well-tolerated, but some patients may experience mild side effects like diarrhea or gastrointestinal issues.

While ursodeoxycholic acid is not directly effective in treating autoimmune hepatitis, it can improve liver health and reduce symptoms of cholestasis in patients who experience bile flow issues. Its use should be based on a physician's recommendation and combined with other primary medications for autoimmune hepatitis.



The schematic image illustrating the mechanism of action of Ursodeoxycholic Acid (UDCA) is ready. This image clearly explains bile flow and the protection of liver cells.

Importance of Regular Medical Follow-ups

In patients with autoimmune hepatitis and related diseases, regular medical follow-ups play a crucial role in preventing disease progression and avoiding serious complications. Since AIH can lead to liver damage, cirrhosis, and, in some cases, liver failure over time, it is essential for patients to undergo regular tests and be closely monitored by specialists to assess liver function and overall health.

Regular Tests

- **Liver Function Tests:** These tests measure liver enzymes such as Alanine Aminotransferase and Aspartate Aminotransferase, which indicate liver inflammation and damage. Elevated enzyme levels may signal a disease flare or worsening inflammation.
- **Autoimmune Antibody Tests:** Measuring the levels of autoantibodies like antinuclear antibodies, smooth muscle antibodies, and antimitochondrial antibodies can indicate autoimmune activity in the body.
- **Liver Ultrasound and FibroScan:** In some cases, doctors may use ultrasound and periodic FibroScan tests to assess liver structure and check for fibrosis or cirrhosis.

Prevention of Serious Complications

To prevent serious complications such as liver failure or cirrhosis, patients should follow these recommendations:

- **Adherence to Prescribed Medications:** Patients should take immunosuppressive drugs like corticosteroids and azathioprine exactly as prescribed. Discontinuing or altering doses without a doctor's advice can lead to disease relapse and further liver damage.
- **Avoid Alcohol and Toxic Substances:** Alcohol can directly harm the liver, and in AIH patients, it may worsen inflammation and cause more severe liver damage.
- **Management of Other Coexisting Conditions:** Patients with AIH may also have other autoimmune diseases. Proper management of these conditions can reduce the overall burden of disease and prevent complications.

🕒 Psychological and Social Care

In addition to medical follow-ups, psychological and social support is crucial for AIH patients. Chronic illness can present mental health challenges. Seeking help from a psychologist or counselor and participating in support groups can improve patients' mental well-being.

🕒 Duration of AIH Treatment

The duration of AIH treatment depends on the severity of the disease and the patient's response to therapy. Generally, treatment with immunosuppressive drugs is long-term and may last several years or even a lifetime. AIH treatment consists of two main stages:

- **Initial Phase:** This phase focuses on reducing inflammation and controlling symptoms. Treatment usually begins with corticosteroids like prednisone. In this phase, higher doses of medication are prescribed to rapidly decrease inflammation and improve liver function. This phase may last several weeks to months, depending on the patient's response to treatment. Immunosuppressive drugs like azathioprine are also introduced during this stage.
- **Maintenance Phase:** After initial disease control, the dosage of medications is gradually reduced, and drugs like azathioprine are started or continued to prevent disease relapse. This phase may last for years, and in some cases, lifelong treatment may be necessary to prevent flare-ups of the disease.

🕒 Overall Treatment Duration

Most patients need to continue treatment for several years, with doctors adjusting the medication dosages over time based on the patient's response. Stopping treatment may be considered after at least 2 to 3 years of complete disease control and no liver inflammation (as determined by blood tests, liver biopsy, and recently, FibroScan results). However, this decision depends on the patient's condition, and in some cases, stopping treatment may lead to disease recurrence. For some patients, AIH becomes a chronic condition requiring life-long treatment with low doses of medication.

Patients should regularly follow up with their doctor to adjust medication dosages as needed and to prevent potential side effects from the medications.

Chapter 10

Non-Pharmaceutical Treatments for Autoimmune Hepatitis

Non-pharmaceutical treatments play an essential role in managing autoimmune hepatitis symptoms and improving patients' quality of life. These treatments can complement drug therapies by reducing the side effects of immunosuppressive medications and helping patients better manage their condition.

● Healthy and Balanced Diet

A healthy and balanced diet is fundamental for reducing inflammation and preventing further liver damage. Dietary recommendations for AIH patients include:

- **Anti-inflammatory foods:** Eating fruits, vegetables, fatty fish (like salmon), and nuts can help reduce inflammation in the body.
- **Avoiding processed and fatty foods:** These foods can exacerbate inflammation and are harmful to the liver.
- **Avoiding alcohol:** Alcohol is highly damaging to the liver and should be completely avoided.
- **Limiting salt intake:** Especially important for patients taking corticosteroids, as these medications can cause fluid retention and increase blood pressure.
- **Nutritional supplements:** Supplements like vitamin D and calcium can help prevent osteoporosis, particularly in patients at risk due to long-term corticosteroid use.

● Regular Exercise

Regular physical activity improves both physical and mental well-being. It can reduce stress and strengthen the immune system. Recommended activities for AIH patients include:

- **Walking:** One of the easiest and most beneficial activities for improving cardiovascular health.
- **Yoga and breathing exercises:** These help reduce stress and strengthen muscles.
- **Light stretching exercises:** Beneficial for increasing flexibility and muscle strength.

● Stress Management

Stress is a known factor that can worsen AIH symptoms, and managing it is critical for patients. There are several techniques to help reduce stress:

- **Meditation and breathing exercises:** Focusing on deep breathing and mindfulness can promote mental relaxation and reduce tension.
- **Yoga:** In addition to its physical benefits, yoga helps reduce stress and improve mental well-being.
- **Regular and sufficient sleep:** Adequate and regular sleep improves overall health and reduces fatigue.

Family and Social Support

Emotional support from family and loved ones is vital in managing chronic diseases like AIH. Participating in support groups can also provide patients with the opportunity to share their experiences and receive emotional support. In cases of severe stress, psychotherapy and professional counseling are recommended.

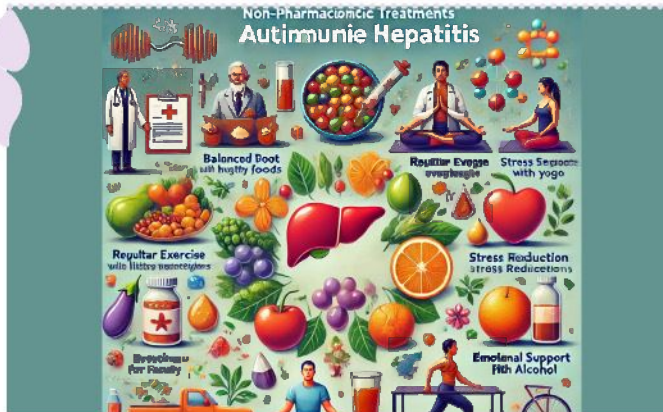
AIH is a chronic and often challenging disease that requires continuous monitoring and care. Family and friends play a crucial role as a strong support network, helping patients manage the disease and improve their quality of life. Ways family and loved ones can assist:

- **Emotional support:** Listening to the patient's concerns and sympathizing can reduce feelings of isolation and anxiety.
- **Helping with medical care:** Family members can help patients keep track of medication schedules and doctor appointments and accompany them to medical visits.
- **Encouraging a healthy lifestyle:** Family can promote a nutritious diet, regular exercise, and stress management to improve the patient's physical and mental well-being.
- **Educational support:** Families should educate themselves about the disease, its symptoms, and its management to offer better care and understanding.

Preventing Complications

To prevent AIH symptoms from worsening, patients must have regular medical check-ups and report any changes in symptoms, such as jaundice, severe fatigue, or abdominal pain, to their doctor. Early detection of changes can prevent serious complications like cirrhosis or liver failure.

Family members can have a significant role in providing emotional, physical, and medical support to AIH patients. This support helps patients better cope with the disease and adhere to their treatments. A strong support network from loved ones can motivate patients to follow medical advice and ensure consistent treatment follow-up.



This image illustrates the non-pharmaceutical treatments for autoimmune hepatitis, which include a healthy diet, regular exercise, stress reduction techniques, emotional support, and avoiding harmful factors. It portrays non-drug treatments for autoimmune hepatitis, including proper nutrition, regular physical activity, stress management techniques, and abstaining from alcohol and harmful substances.

Living with Autoimmune Hepatitis

Patients with autoimmune hepatitis require regular follow-up and care. Although this is a chronic condition, adopting a healthy lifestyle and appropriate care can significantly improve the quality of life for these patients. The following tips are recommended for daily living with this disease:

Maintaining a Proper Diet

Increase consumption of fresh fruits and vegetables: These are rich in antioxidants and nutrients that help strengthen the immune system and reduce inflammation.

Avoid processed and fatty foods: These can exacerbate symptoms and potentially worsen the condition.

Lean protein sources: Skinless chicken, fish, and eggs are good sources of protein that help maintain energy and strengthen muscles.

Patients with autoimmune hepatitis should regularly undergo blood tests to monitor liver function and antibody levels, ensuring any changes in the disease are identified promptly.

Non-pharmaceutical treatments, such as proper nutrition, regular exercise, stress reduction, and avoiding harmful triggers, play a crucial role in improving the quality of life for patients with autoimmune hepatitis. These methods help patients better manage their condition and prevent the progression of severe complications. Regular medical follow-ups and adherence to health and dietary recommendations are essential factors in managing this disease.

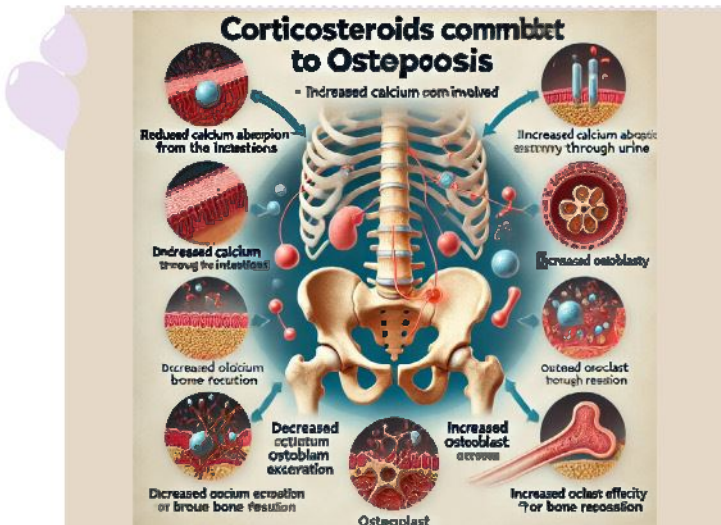
Chapter 11

Complications of Autoimmune Hepatitis

Autoimmune hepatitis is a chronic inflammatory disease where the immune system mistakenly attacks liver cells, leading to liver tissue damage. If not properly managed, this disease can lead to numerous complications, affecting not only the liver but also other parts of the body. These complications may arise from the progression of the disease itself or from the side effects of immunosuppressive medications. Below, we will explore some of the most significant complications of autoimmune hepatitis and how to manage them.

■ Osteoporosis and Corticosteroid Use: Complications and Prevention Strategies

Osteoporosis is one of the most common complications associated with the long-term use of corticosteroid medications, such as prednisone. These drugs are widely used to control inflammation in various autoimmune diseases, including autoimmune hepatitis, asthma, rheumatoid arthritis, and lupus. While these medications are highly effective in controlling inflammation and reducing autoimmune damage, prolonged use can lead to serious side effects, with one of the most significant being decreased bone density, which increases the risk of fractures.



The schematic image illustrating how corticosteroids affect osteoporosis is ready. This image depicts the various mechanisms that lead to reduced bone density, including decreased calcium absorption, increased calcium excretion through urine, decreased osteoblast activity, and increased osteoclast activity. It also highlights the long-term effects of corticosteroid use and the increased risk of fractures in sensitive areas such as the spine, pelvis, and wrist.



How Do Corticosteroids Cause Osteoporosis?

Corticosteroids negatively affect bone metabolism and structure through several mechanisms. These drugs:

- **Decrease Calcium Absorption:** Corticosteroids reduce calcium absorption from the intestines, which lowers the amount of calcium available in the body and bones.
- **Increase Calcium Excretion:** They cause increased calcium excretion through urine, which can deplete calcium reserves in bones.
- **Inhibit Osteoblast Activity:** Corticosteroids reduce the activity of osteoblasts (cells responsible for bone formation), thereby inhibiting new bone production.
- **Increase Osteoclast Activity:** These drugs increase the activity of osteoclasts (cells responsible for breaking down bone), leading to faster bone breakdown.

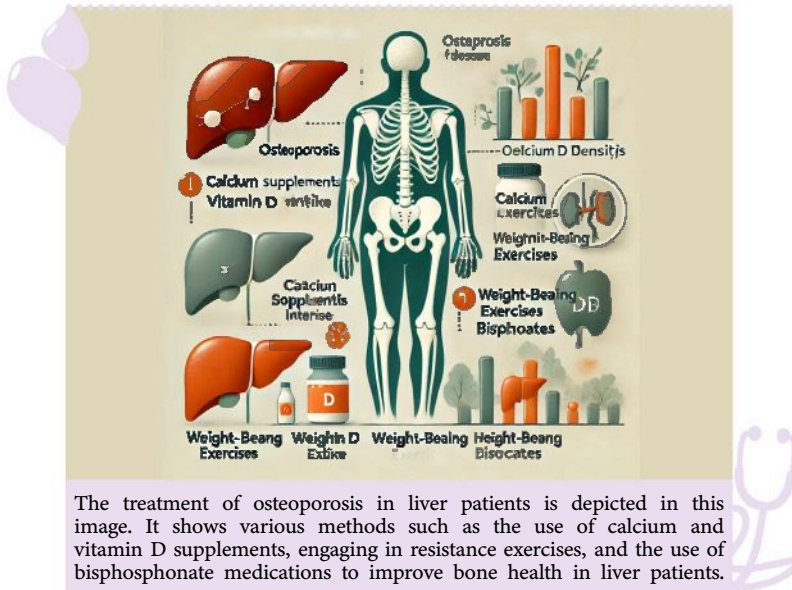
As a result of these mechanisms, long-term use of corticosteroids can reduce bone density and increase the risk of osteoporosis and bone fractures, particularly in sensitive areas like the spine, hips, and wrists.

While corticosteroids are essential for managing autoimmune diseases, understanding their side effects and adopting preventive strategies to reduce the risk of osteoporosis is crucial. Although controlling inflammation with these drugs is necessary, their side effects should not be ignored. Since osteoporosis can lead to a decreased quality of life and serious issues like bone fractures, patients should work with their doctors to develop a plan for preventing and managing this condition.

Preventive Measures and Management of Osteoporosis with Corticosteroids:

- **Calcium and Vitamin D Supplements:** Since corticosteroids reduce calcium absorption, taking calcium supplements under medical supervision is recommended for many patients. Vitamin D supplements also help improve calcium absorption and play a vital role in bone health, reducing the risk of osteoporosis.
- **Weight-Bearing and Resistance Exercises:** Activities like weight training, walking, running, or strength exercises help strengthen muscles and bones, increasing bone density and reducing the risk of fractures. Regular exercise also improves balance, lowering the risk of falls and injuries.
- **Bisphosphonate Medications:** For patients at high risk of osteoporosis, doctors may prescribe bisphosphonates like alendronate or risedronate. These drugs decrease osteoclast activity and prevent rapid bone breakdown. By slowing bone loss, bisphosphonates help maintain bone density and significantly reduce the risk of fractures.
- **Bone Density Testing:** Bone density tests can assess bone health and help doctors evaluate a patient's risk of osteoporosis. These tests are particularly recommended for patients who have been on long-term corticosteroid therapy.
- **Calcium-Rich Diet:** Consuming calcium-rich foods such as dairy products (milk, cheese, yogurt), dark leafy greens (spinach, broccoli), fatty fish (salmon, sardines), and nuts can help meet daily calcium needs. Foods rich in vitamin D, such as fish, eggs, and fortified milk, also support bone health.

These strategies can help prevent the side effects of long-term corticosteroid use and maintain healthy bones.



Although corticosteroids are powerful drugs in controlling inflammation and autoimmune diseases like autoimmune hepatitis, their long-term use can lead to serious side effects such as osteoporosis. To reduce the risk of this condition and maintain bone health, preventive measures such as taking calcium and vitamin D supplements, engaging in regular exercise, using bisphosphonate medications, and regularly monitoring bone density with diagnostic tests should be implemented. With proper management and collaboration with a healthcare provider, patients can minimize the side effects of these medications and improve their quality of life.

Diabetes Mellitus and Corticosteroid Use: Side Effects and Prevention Strategies

Long-term use of corticosteroids is an effective method for controlling inflammation in many autoimmune diseases, including autoimmune hepatitis, asthma, rheumatoid arthritis, and lupus. However, along with their beneficial effects, these drugs can also have serious side effects. One such side effect is an increase in blood sugar levels, which in some patients can lead to type 2 diabetes. In this section, we will discuss the mechanisms by which corticosteroids raise blood sugar levels and how to manage them.

How Corticosteroids Increase Blood Sugar Levels

Corticosteroids like prednisone affect the metabolism of carbohydrates, fats, and proteins, which can lead to elevated blood sugar levels. These drugs make the body's cells more resistant to insulin. As a result, insulin, which is responsible for lowering blood sugar levels, cannot work effectively, causing blood sugar to rise. They also stimulate the liver to produce more glucose, which can increase blood sugar levels even during fasting. Corticosteroids reduce the absorption of glucose by body tissues, such as muscles, leading to more sugar accumulating in the bloodstream.

With long-term corticosteroid use, blood sugar levels increase steadily, and the body must produce more insulin to compensate. Over time, this constant demand on the pancreas (the organ that produces insulin) and ongoing insulin resistance can lead to type 2 diabetes. Patients with diabetes or those at risk of developing diabetes are particularly vulnerable to high blood sugar levels due to corticosteroid use.

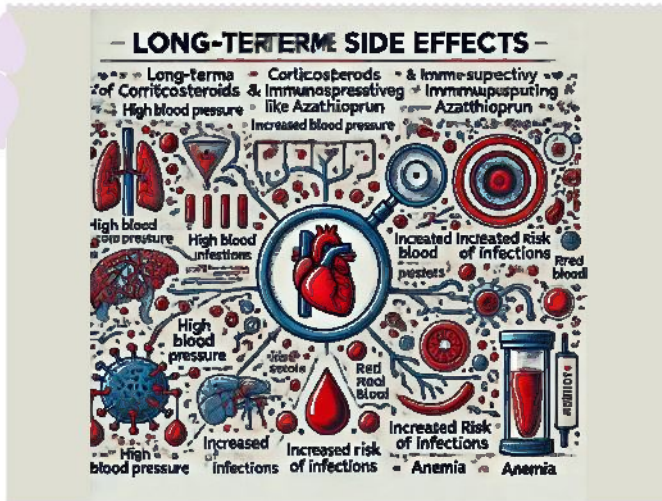
Prevention and Management Strategies for Blood Sugar Control in Patients on Corticosteroids

- **Follow a low-sugar, balanced diet:** One of the most important factors in controlling blood sugar levels is healthy nutrition. A balanced diet that includes low-sugar and low-carbohydrate foods can help prevent sudden spikes in blood sugar. The following strategies can aid in better blood sugar management:
 - **Increase non-starchy vegetables:** Vegetables like spinach, broccoli, and kale are low in sugar and high in fiber, which helps control blood sugar.
 - **Consume lean proteins:** Foods like white meat, fish, and eggs help stabilize blood sugar levels.
 - **Avoid simple sugars and processed foods:** Foods like white bread, sweets, and sugary drinks should be limited, as they cause rapid increases in blood sugar.
 - **Choose complex carbohydrates:** Whole grain breads and cereals help raise blood sugar levels gradually.
- **Engage in regular physical activity:** Exercise is one of the most effective ways to reduce blood sugar and increase insulin sensitivity. Aerobic exercises such as walking, cycling, and swimming help the body use more glucose, reducing blood sugar levels. Resistance training, such as weight lifting, can strengthen muscles and increase glucose uptake by muscle cells.
- **Monitor blood sugar levels regularly:** For patients on corticosteroids, regular monitoring of blood sugar is essential. Checking fasting blood sugar and post-meal levels can help doctors track changes in blood sugar throughout treatment with corticosteroids. Any abnormal increases can be addressed promptly with appropriate treatment.
- **Use blood sugar-lowering medications:** In cases where diet and exercise alone are not sufficient to control blood sugar, doctors may prescribe blood sugar-lowering medications. Some of these medications include:
 - **Metformin:** This drug helps reduce insulin resistance and decreases glucose production in the liver.
 - **Insulin:** In more severe cases, insulin injections may be prescribed for more precise blood sugar control.
 - **Sulfonylureas:** These drugs help stimulate insulin production from the pancreas.
- **Reduce corticosteroid dosage if possible:** In some cases, doctors may reduce the dosage of corticosteroids to minimize side effects such as high blood sugar. Additionally, alternatives to corticosteroids or combining them with other drugs that have less impact on blood sugar may be considered.

By adopting these strategies, patients can better manage blood sugar levels while on corticosteroid treatment, minimizing the risk of developing diabetes and maintaining their overall health.

Top of Form

pneumococcal vaccines) and practicing good personal hygiene can help reduce infection risks. Additionally, patients should promptly consult a doctor if they experience infection symptoms like fever, cough, or sore throat.



The illustration addresses the long-term side effects of corticosteroids and immunosuppressive drugs like azathioprine. The image clearly depicts complications such as high blood pressure, increased risk of infections, and anemia.

Patients with autoimmune hepatitis may develop anemia due to bone marrow suppression or liver-related issues. A reduction in red blood cell count can lead to severe fatigue, dizziness, and general weakness. To prevent anemia, it is recommended to undergo regular blood tests to monitor red blood cell levels and to take iron and folic acid supplements as prescribed by a doctor.

Autoimmune hepatitis is a chronic and complex condition that can lead to serious complications such as osteoporosis, diabetes, cirrhosis, and liver failure. Careful management of the disease, including regular medication intake, consistent medical monitoring, and lifestyle changes, can help prevent the progression of these complications. Comprehensive care, involving drug management, a balanced diet, regular exercise, and stress reduction, enables patients to improve their quality of life and maintain better overall health while managing their illness.

Chapter 12

Co-occurrence of Other Autoimmune Diseases

Patients with autoimmune hepatitis often experience additional autoimmune diseases, a condition known as **overlap syndromes**. These are various disorders that can occur simultaneously with AIH, complicating the clinical management and requiring a multidisciplinary approach to diagnosis and treatment. Some of the most common autoimmune diseases associated with AIH include:

Hashimoto's Thyroiditis

Hashimoto's thyroiditis and autoimmune hepatitis are both autoimmune conditions that can occur together. Hashimoto's thyroiditis, also known as autoimmune hypothyroidism, is one of the most frequently observed autoimmune disorders accompanying AIH. This condition occurs when the immune system attacks the thyroid gland, leading to inflammation and gradual destruction of thyroid tissue, which reduces the production of thyroid hormones. As a result, the patient develops hypothyroidism, presenting symptoms such as extreme fatigue, weight gain, depression, dry skin and hair, and sensitivity to cold.

There are several shared characteristics between patients with Hashimoto's thyroiditis and AIH:

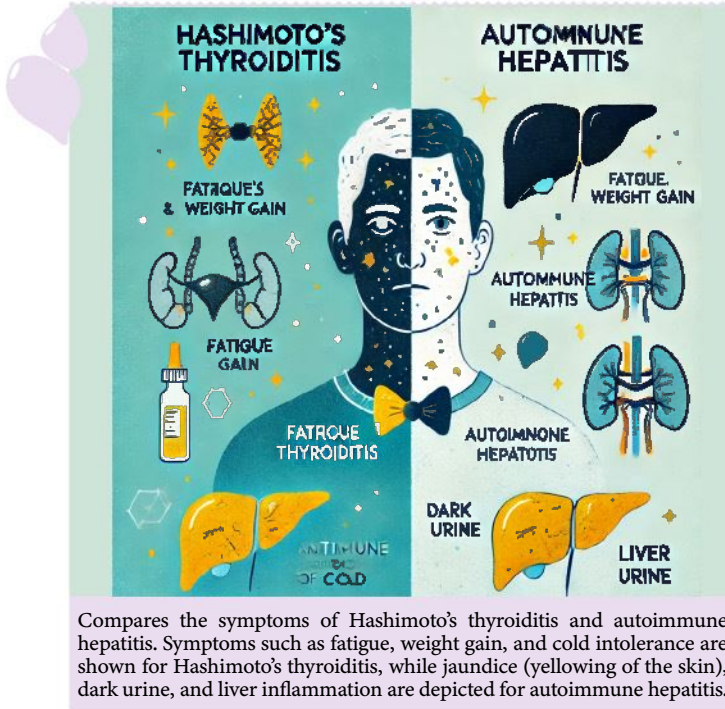
- **Genetic Predisposition:** Certain genes linked to autoimmune diseases, especially HLA-DR genes, are found in both diseases. These genes play a crucial role in regulating immune responses, and defects in them may cause the immune system to attack various body tissues.
- **Chronic Inflammation:** Both conditions result in chronic inflammation in different organs. AIH causes liver inflammation, while Hashimoto's thyroiditis involves the thyroid gland.

Diagnosis of both diseases is typically made through clinical evaluation and blood tests. In patients with both conditions, doctors monitor thyroid and liver function simultaneously. Common tests include **T3, T4, and TSH** to assess thyroid function, and liver enzymes like **aminotransferases** to evaluate liver function.

For treating Hashimoto's thyroiditis, **levothyroxine** is usually prescribed. This medication helps to replace the deficient thyroid hormones in the body. Managing both AIH and Hashimoto's requires careful monitoring and coordination by specialized physicians. Changes in one disease may impact the other. Some specific challenges include:

- **Medication Interactions:** Immunosuppressive drugs used in AIH may interact with thyroid medications, requiring precise dosage adjustments and continuous monitoring.
- **Increased Risk of Infections:** Immunosuppressive drugs reduce the body's ability to fight infections, so patients must be closely monitored to prevent complications.

Collaboration between thyroid and liver specialists is essential to ensure the best therapeutic outcomes for these patients, as the management of one condition may influence the progression and treatment of the other.



Compares the symptoms of Hashimoto's thyroiditis and autoimmune hepatitis. Symptoms such as fatigue, weight gain, and cold intolerance are shown for Hashimoto's thyroiditis, while jaundice (yellowing of the skin), dark urine, and liver inflammation are depicted for autoimmune hepatitis.

■ Rheumatoid Arthritis

Rheumatoid arthritis (RA) and autoimmune hepatitis are both chronic autoimmune diseases that may occur simultaneously in a patient. These conditions result from dysfunction in the immune system, where the body mistakenly attacks its own healthy tissues. The coexistence of these two diseases can complicate the clinical condition of the patient, requiring more precise care and simultaneous drug management.

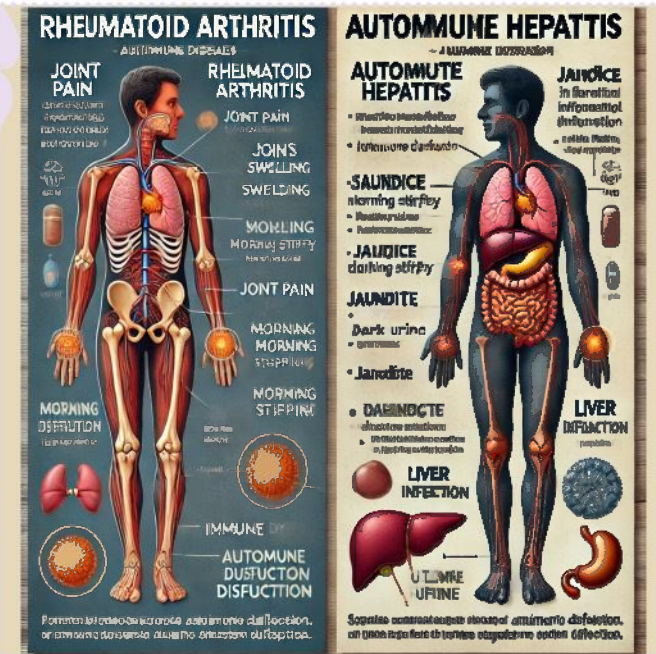
Rheumatoid arthritis is an autoimmune disease that causes chronic inflammation in the joints. Symptoms of RA include joint pain (especially in the morning), extreme fatigue, swelling, and joint destruction, which can eventually lead to permanent joint deformities. While RA and AIH are distinct diseases, due to shared immune system dysfunction, patients can be affected by both conditions at the same time.

Autoimmune genes, particularly the human leukocyte antigen (HLA) genes that are active in both diseases, play an important role in regulating the immune response. Dysfunction in these genes can lead to inappropriate immune activation, causing attacks on both the joints and the liver. In RA, inflammation occurs in the joints, while in AIH, the inflammation is localized to the liver.

To diagnose the coexistence of both diseases, separate tests are needed to evaluate joint and liver function. In RA, common tests include rheumatoid factor (RF) and anti-citrullinated protein antibodies (anti-CCP), which are key indicators of the disease. In AIH, liver tests include aminotransferases to assess liver damage, and autoimmune antibody tests such as antinuclear antibodies (ANA) and anti-smooth muscle antibodies (ASMA) are performed.

The primary treatment for RA includes immunosuppressive drugs like methotrexate, hydroxychloroquine, and nonsteroidal anti-inflammatory drugs (NSAIDs). The treatment for AIH typically involves corticosteroids (such as prednisone) and drugs like azathioprine that suppress the immune system.

Managing both diseases simultaneously can present challenges. Some drugs used for RA may interact with the immunosuppressive drugs used in AIH, requiring precise dose adjustments and regular monitoring. Immunosuppressive drugs may reduce the body's ability to fight infections, so patients need close monitoring to prevent infections. The coexistence of RA and AIH poses a clinical challenge that requires careful care and management. Early detection of both diseases and regular follow-up treatment can improve patients' quality of life and prevent serious complications.



The illustration provides a comparison between rheumatoid arthritis and autoimmune hepatitis, focusing on the symptoms of rheumatoid arthritis such as joint pain, swelling, and morning stiffness, and the symptoms of autoimmune hepatitis such as jaundice, dark urine, and liver inflammation.

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) and autoimmune hepatitis are both autoimmune diseases in which the immune system mistakenly attacks healthy tissues in the body. SLE is a complex condition that can affect many organs and tissues, including the skin, kidneys, heart, joints, and even the liver. In some cases, patients with autoimmune hepatitis may also develop lupus, which complicates the management of their condition.

Lupus is a multisystem autoimmune disease, meaning it can involve several organs simultaneously. The symptoms of lupus vary depending on the organs affected, but the most common include:

- oo Skin rashes (usually in a butterfly shape across the nose and cheeks)
- oo Joint pain and inflammation
- oo Sensitivity to sunlight
- oo Heart and lung issues
- oo Kidney problems
- oo Extreme fatigue
- oo Hair loss

Although autoimmune hepatitis primarily affects the liver, overlap between these two conditions may cause inflammation in both the liver and other organs. In patients with lupus, the liver can also be affected, leading to autoimmune-induced liver inflammation (hepatitis).

There are common symptoms shared by patients with both lupus and autoimmune hepatitis. Both diseases cause severe fatigue, which can significantly impact the patient's quality of life, and both can lead to joint pain and inflammation.

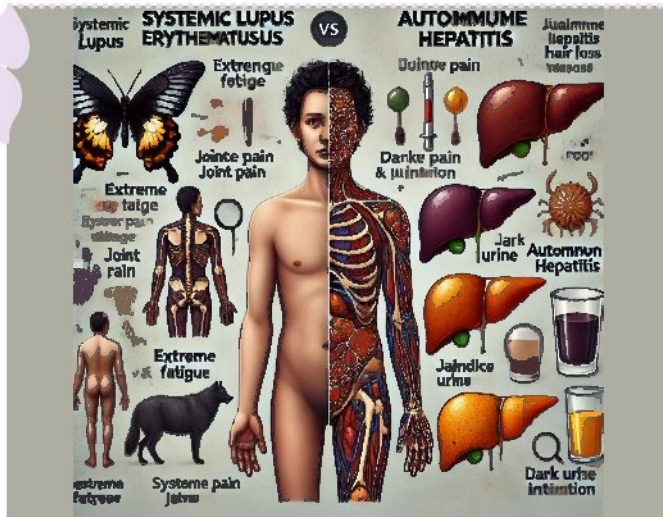
Diagnosis of both conditions is done through clinical evaluation and blood tests. Some of the common tests include:

- o **Antinuclear antibodies (ANA):** This antibody is present in patients with both conditions and is one of the diagnostic criteria.
- o **Anti-double-stranded DNA (Anti-dsDNA):** This is specifically found in patients with systemic lupus erythematosus.
- o **Liver-specific antibodies:** Such as anti-smooth muscle antibodies, which are found in autoimmune hepatitis.

Simultaneous treatment of lupus and autoimmune hepatitis involves:

- o **Prednisone:** To reduce inflammation and control symptoms of both diseases.
- o **Azathioprine and mycophenolate mofetil:** To reduce immune system activity.
- o **Hydroxychloroquine:** Prescribed to manage lupus-related skin and joint symptoms.

The coexistence of systemic lupus erythematosus and autoimmune hepatitis is a complex and challenging condition that requires careful and simultaneous management. Early identification of both diseases and regular follow-up can help reduce complications and improve patients' quality of life.



The image presents a comparison between systemic lupus erythematosus (SLE) and autoimmune hepatitis. Symptoms such as severe fatigue, joint pain, butterfly-shaped rashes on the face, and hair loss are shown for lupus, while symptoms like jaundice (yellowing of the skin), dark urine, and liver inflammation are depicted for autoimmune hepatitis.

■ Ulcerative Colitis and Crohn's Disease

Inflammatory bowel diseases like ulcerative colitis and Crohn's disease are also common in patients with autoimmune hepatitis. These diseases cause severe inflammation in the digestive tract and can lead to symptoms such as bloody diarrhea, abdominal pain, and weight loss.

Both IBD and AIH are autoimmune diseases that may occur simultaneously in some patients. The overlap between these conditions can present challenges in diagnosis and treatment, requiring careful management. This overlap, referred to as "autoimmune overlap syndrome," can lead to concurrent inflammation in both the digestive system and the liver.

Inflammatory bowel diseases are divided into two main types:

- **Crohn's Disease:** This can affect any part of the digestive tract, though it is most commonly seen in the small and large intestines. It causes deep inflammation in the walls of the intestines.
- **Ulcerative Colitis:** This condition is limited to the large intestine (colon) and causes inflammation and superficial ulcers in the inner lining of the colon.

Although AIH primarily affects the liver, patients with IBD may also develop autoimmune liver diseases. In these patients, liver inflammation may occur due to abnormal immune system responses. The connection between IBD and AIH is significant for several reasons:

Shared immune response abnormalities: In both diseases, the immune system mistakenly attacks the body's own tissues, leading to inflammation.

Genetic overlap: Certain immune response genes, such as the human leukocyte antigen (HLA) genes, may be active in both conditions and contribute to their co-occurrence.

Patients with both conditions may experience a combination of gastrointesti-

nal and liver-related symptoms, including:

Gastrointestinal symptoms: Bloody diarrhea, abdominal pain, weight loss, and malabsorption of nutrients in IBD patients.

Liver-related symptoms: Severe fatigue, jaundice (yellowing of the skin), and pain in the liver area caused by AIH.

For diagnosing IBD, colonoscopy and imaging tests are used. Blood tests to assess inflammation and C-reactive protein (CRP) levels may also be ordered.

Treating both conditions simultaneously is often challenging and requires the use of immunosuppressive medications.

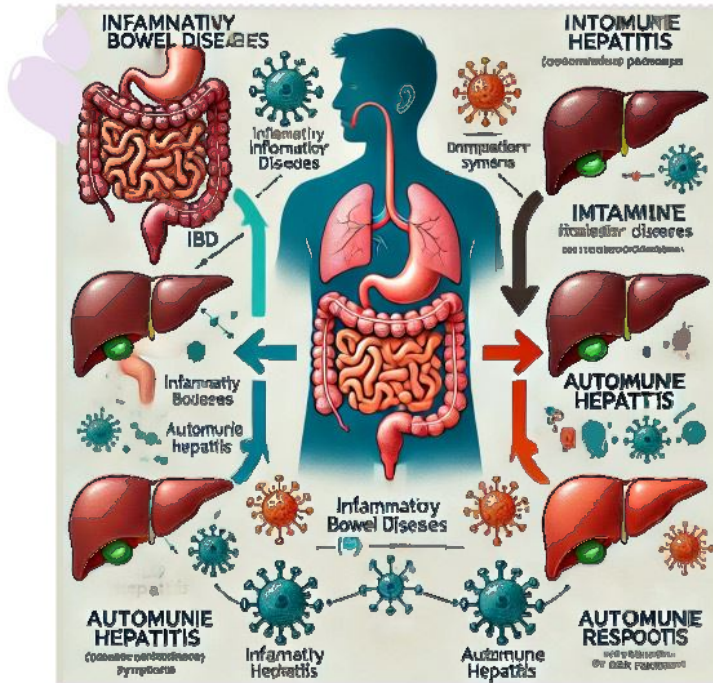
Corticosteroids, such as prednisone, are used to control inflammation.

Immunosuppressive drugs like azathioprine and mycophenolate mofetil are used to suppress abnormal immune activity in both diseases.

Some biological drugs used to treat IBD, such as infliximab, may also help reduce liver inflammation.

Close monitoring is required, as some drugs used to treat IBD may interact with medications for AIH. Precise dosage adjustments and regular monitoring are crucial. Additionally, immunosuppressive medications can lower the body's resistance to infections, so patients need careful supervision to prevent infections.

The coexistence of IBD and AIH is a complex condition that requires careful and coordinated management. Early diagnosis and treatment can help reduce complications and improve the quality of life for patients.



The schematic image related to inflammatory bowel diseases (IBD) alongside autoimmune hepatitis is ready. This image illustrates how these two conditions can coexist, highlighting common inflammatory pathways, symptoms, and potential overlapping risk factors.

Type 1 diabetes

Type 1 diabetes, in which the immune system attacks the insulin-producing cells in the pancreas, is also seen in some patients with autoimmune hepatitis. This combination can complicate blood sugar management and the treatment of autoimmune disorders. Both diseases are more common in individuals with certain autoimmune genes, such as HLA-DR3 and HLA-DR4, indicating a genetic overlap. These genes may trigger an abnormal immune response, leading to the simultaneous development of type 1 diabetes and autoimmune hepatitis. Environmental factors, such as viral infections and hormonal changes, can also stimulate the immune system, potentially worsening autoimmune reactions, causing damage to both the pancreas and the liver.

Both diseases arise from abnormal immune responses. In type 1 diabetes, the immune system attacks the beta cells, reducing insulin production. In autoimmune hepatitis, the immune system targets liver cells, causing chronic inflammation. The similarities in immune system behavior may explain their coexistence. If symptoms such as excessive thirst, frequent urination, unexpected weight loss, fatigue, and increased appetite appear, diabetes should be considered.

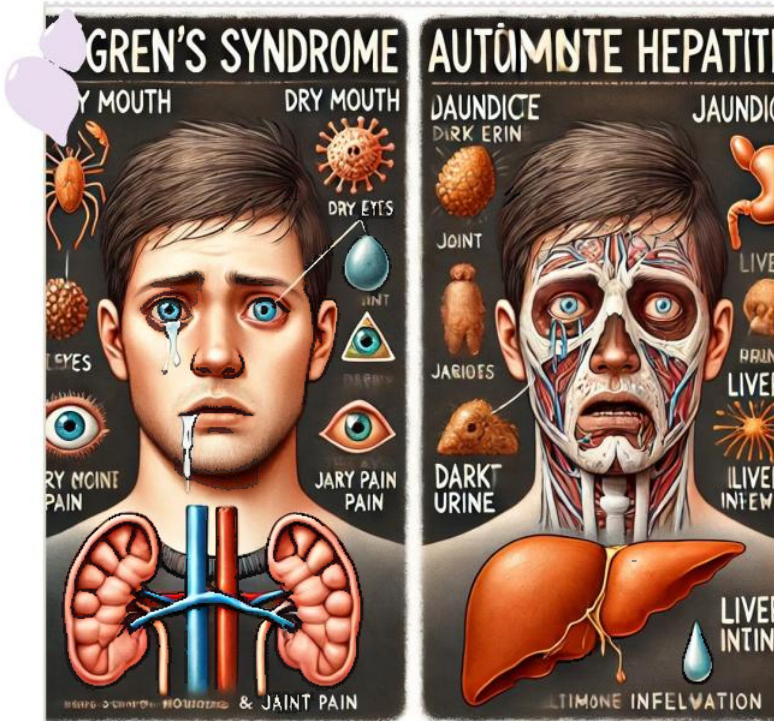
Some immunosuppressive drugs used to treat autoimmune hepatitis may interfere with diabetes management. The coexistence of type 1 diabetes and autoimmune hepatitis can lead to more complex clinical management. Early diagnosis and appropriate treatment of both conditions can improve the patient's quality of life and help prevent complications from progressing.

Sjögren's syndrome

Sjögren's syndrome and autoimmune hepatitis are both autoimmune diseases that may occur simultaneously in a patient. In Sjögren's syndrome, the immune system attacks the glands that produce saliva and tears, leading to dry mouth and eyes. Sjögren's syndrome is typically associated with dryness of the eyes and mouth but can also affect other organs, such as joints, kidneys, and the liver. It can occur on its own or alongside other autoimmune diseases like lupus, rheumatoid arthritis, and autoimmune hepatitis. In addition to affecting the salivary and tear glands, Sjögren's can also involve other parts of the body, including joints, kidneys, and the liver.

For the diagnosis of Sjögren's syndrome, tests for SSA and SSB antibodies (anti-Sjögren's antibodies) are used. In some cases, a biopsy of the salivary glands or liver may be required to confirm the diagnosis. In the treatment of Sjögren's syndrome, in addition to immunosuppressive medications, artificial tear drops and medications like pilocarpine, which stimulate saliva production, are used to relieve symptoms of dryness.

The coexistence of Sjögren's syndrome and autoimmune hepatitis can make medical management more complex. Early diagnosis and treatment of these conditions can improve patients' quality of life and help prevent serious complications from developing.



The image compares the symptoms of Sjögren's syndrome, such as dry mouth, dry eyes, and joint pain, with those of autoimmune hepatitis, including jaundice, dark urine, and liver inflammation. The illustration highlights the organs affected by each condition, emphasizing the differences in their impact on the body.

The diagnosis of autoimmune diseases that occur alongside autoimmune hepatitis is carried out through clinical evaluations and blood tests. In these cases, doctors may use a combination of immunosuppressive drugs, corticosteroids, and medications specific to each condition to manage the associated diseases. As a result, treating these patients requires precise coordination between various specialists, including hepatologists, rheumatologists, and endocrinologists.

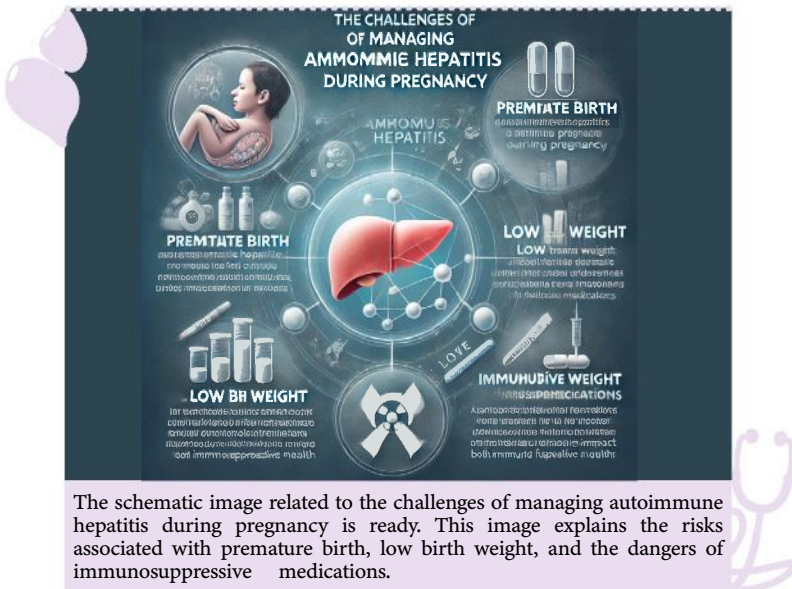
Chapter 13

Challenges of Autoimmune Hepatitis During Pregnancy

Managing autoimmune hepatitis during pregnancy presents several challenges due to the specific immune and hormonal changes that occur. However, with careful monitoring and follow-up, many women with AIH can have successful pregnancies. This section explores the challenges, management strategies, and the effects of immunosuppressive drugs on the fetus.

Pregnancy causes significant changes in the immune system and hormone levels, which can impact the control of AIH. Hormonal increases, such as estrogen and progesterone, during pregnancy can either exacerbate or alleviate symptoms of the disease. Typically, immune changes during pregnancy may lead to a reduction in symptom severity for some patients, while for others, the disease may flare up. A major concern for patients with AIH is the recurrence of symptoms after childbirth. Due to the immune system's shifts during this period, many women experience worsening of their condition postpartum, requiring increased doses of immunosuppressive drugs and close monitoring.

The selection and adjustment of immunosuppressive medications during pregnancy are particularly sensitive. Many of these drugs help control the disease's symptoms, but some may pose risks to the fetus. Corticosteroids are generally considered relatively safe during pregnancy and aid in controlling liver inflammation. Prednisone is one of the common drugs used during pregnancy. However, taking high doses of this medication may pose small risks, such as reduced fetal weight, preterm delivery, and delayed fetal growth. Doctors usually adjust the dosage to ensure both disease control and minimized side effects.



The schematic image related to the challenges of managing autoimmune hepatitis during pregnancy is ready. This image explains the risks associated with premature birth, low birth weight, and the dangers of immunosuppressive medications.



Azathioprine is one of the immunosuppressive drugs widely used in the management of autoimmune hepatitis. Studies have shown that this drug is relatively safe for use during pregnancy and does not have serious negative effects on the fetus. However, it may be associated with low birth weight. Patients using azathioprine should be under close medical supervision, and dosage adjustments may be made if necessary.

Mycophenolate mofetil and methotrexate are generally contraindicated during pregnancy due to their high risks for the fetus. These drugs can lead to severe birth defects and miscarriage. If pregnancy is planned, these medications should be replaced with safer alternatives before pregnancy begins.

Managing autoimmune hepatitis during pregnancy requires close collaboration between gastroenterologists and hepatologists, as well as obstetricians. Key steps in managing the disease include:

- **Regular drug control:** Doctors need to carefully adjust immunosuppressive medications to ensure both maternal and fetal health. Some drugs may be prohibited or restricted during pregnancy.
- **Regular liver monitoring:** Frequent liver function tests are essential to monitor inflammation and assess liver enzyme levels. These tests help doctors make treatment adjustments when necessary.
- **Postpartum care:** After childbirth, patients require special care as the disease symptoms may return strongly. Doctors should be prepared to quickly adjust medication dosages after delivery to prevent serious complications.

Many women with autoimmune hepatitis can have successful pregnancies with close follow-up and proper management. However, some common challenges faced by these patients include:

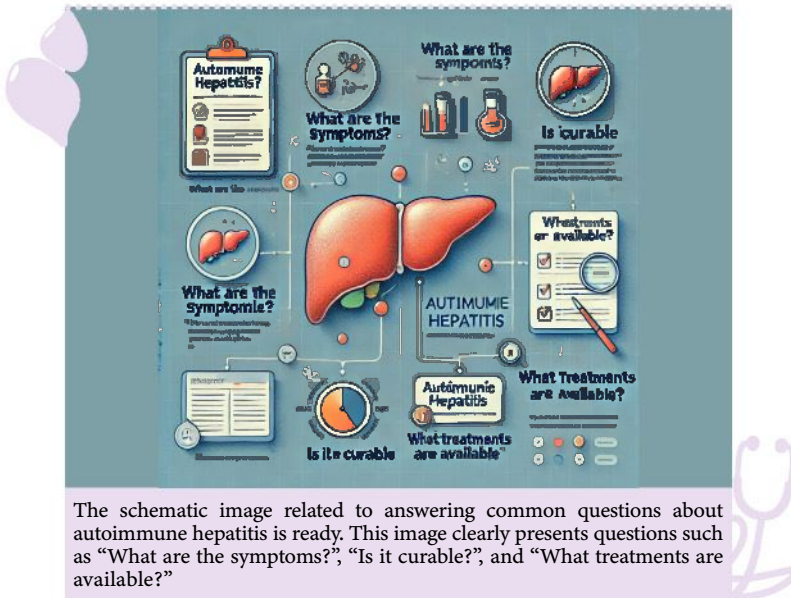
- **Preterm birth:** Women with autoimmune hepatitis may be at risk for preterm delivery, which could be influenced by the effects of immunosuppressive drugs or the disease itself.
- **Low birth weight:** Immunosuppressive drugs like corticosteroids and azathioprine may lead to lower birth weights in newborns.
- **Disease control during pregnancy:** In most cases, with careful management, the disease symptoms are well-controlled during pregnancy, and there are no severe complications for the mother or baby.

Pregnancy in women with autoimmune hepatitis can be challenging, but with close monitoring and appropriate management, many women can have successful pregnancies. Immunosuppressive medications such as corticosteroids and azathioprine should be carefully adjusted to ensure the health of both the mother and fetus. Close cooperation between the medical team and frequent monitoring of the patient and fetus are key to achieving a successful pregnancy.

Chapter 14

Common Questions About Autoimmune Hepatitis

In this chapter, we address some of the most common questions that patients with autoimmune hepatitis and their families have about the disease. These questions cover topics related to symptoms, diagnosis, treatment, and the long-term effects of the condition on patients' lives.



❖ Is autoimmune hepatitis contagious?

No, autoimmune hepatitis is not contagious. Unlike viral hepatitis types B or C, this condition is not transmitted through blood, bodily fluids, or other methods of infection.

❖ How is autoimmune hepatitis diagnosed?

Autoimmune hepatitis is typically diagnosed through the following assessments:

Blood tests to measure liver enzyme levels and detect autoimmune antibodies.

Liver imaging (such as ultrasound, MRI, and CT scan) and FibroScan to assess liver structure and damage.

Liver biopsy, which involves removing a small sample of liver tissue to check for inflammation and damage. This is essential for most patients and provides guidance for future treatment and follow-up.

❖ Can autoimmune hepatitis lead to liver cirrhosis?

If autoimmune hepatitis is not diagnosed and treated in time, it can progress

to liver cirrhosis. Cirrhosis is the final stage of liver disease, where liver tissue is replaced by scar tissue, significantly impairing liver function. Regular treatment can prevent the disease from progressing to cirrhosis.

❖ Can patients with autoimmune hepatitis become pregnant?

Yes, many women with autoimmune hepatitis can have successful pregnancies. However, managing the disease during pregnancy requires special care, as hormonal changes may worsen symptoms. Additionally, some immunosuppressive drugs may affect the fetus, so doctors must carefully adjust treatments.

❖ Do patients with autoimmune hepatitis need a special diet?

Although there is no specific diet recommended for autoimmune hepatitis, patients should follow a healthy and balanced diet. It is recommended that patients:

- Avoid alcohol, as it can further damage the liver.
- Reduce consumption of processed and fatty foods.
- Eat fiber-rich foods such as fruits and vegetables.
- Take calcium and vitamin D supplements if they are on corticosteroids.

❖ Does autoimmune hepatitis affect quality of life?

Autoimmune hepatitis is a chronic condition that may significantly impact patients' quality of life. Some patients may experience extreme fatigue or chronic pain. However, with proper treatment and regular monitoring, many patients can lead normal, high-quality lives. Emotional and social support from family and support groups also plays a vital role in improving quality of life.

❖ Is there a risk of disease recurrence after stopping treatment?

Autoimmune hepatitis, as a chronic disease, may relapse. Even in cases where the disease is controlled through treatment, symptoms may return after stopping or reducing medications. For this reason, patients should remain under regular medical supervision and continue their treatment.

Autoimmune hepatitis is a chronic disease that can be well-managed with timely follow-up and treatment. By answering common patient and family questions, this chapter helps them gain more knowledge about the disease and better cope with it. Ultimately, awareness and ongoing monitoring are crucial to improving patients' quality of life.

Chapter 15

The Future of Autoimmune Hepatitis Treatment - Therapeutic Innovations and Future Research

Autoimmune hepatitis is a chronic condition where the immune system mistakenly attacks liver cells. While current treatments, such as corticosteroids and immunosuppressive drugs like azathioprine, are effective in managing the disease, they still pose challenges, including long-term side effects and relapse after reducing or stopping treatment. With ongoing advancements in medical science and research on autoimmune diseases, the future of autoimmune hepatitis treatment looks promising. Below are some innovations and research areas that may shape the future of treatment for this condition.

Biotechnology and Targeted Drugs

A significant development in autoimmune hepatitis treatment is the rise of biologic drugs, which specifically target immune pathways and molecules. Biologic drugs are already used for other autoimmune diseases like rheumatoid arthritis and psoriasis and could also be effective in treating autoimmune hepatitis. Some biologics, known as targeted drugs, may block specific immune pathways to prevent the immune system from attacking the liver. Cytokines, molecules key to regulating inflammation and immune responses, are targeted by cytokine inhibitors like TNF-alpha or IL-6 inhibitors. These drugs, successful in treating other autoimmune diseases, could be future options for controlling inflammation in autoimmune hepatitis. Additionally, drugs that specifically target T and B cells, which are responsible for attacking liver cells, are a promising research area. These drugs may control the disease without causing the severe side effects common with general immunosuppressants.

Immunotherapy and Immune System Regulators Alongside biologics, immunotherapy is a hopeful approach for autoimmune hepatitis treatment. The goal of immunotherapy is to restore balance in the immune system so that it reduces its attack on liver cells without impairing normal immune function. One novel immunotherapy technique involves immune checkpoint inhibitors that control the activity of destructive immune cells. These drugs have been used in cancer treatments, and researchers are now exploring their potential in autoimmune hepatitis. New research suggests that regulatory T cells (Tregs), which naturally help control the body's immune responses, could help reduce inflammation in autoimmune hepatitis. These cells could be used as a cellular therapy to manage autoimmune diseases.

Gene Therapy and Genetic Editing

Gene therapy is an emerging research area that could potentially impact the treatment of autoimmune diseases, including autoimmune hepatitis. In gene therapy, defective genes responsible for improper protein production or immune regulation are corrected or replaced. CRISPR technology, which enables precise gene editing, may one day be used to correct genetic abnormalities leading to



autoimmune diseases like autoimmune hepatitis. This approach could provide a permanent solution for controlling or even curing the disease.

Stem Cell Transplantation

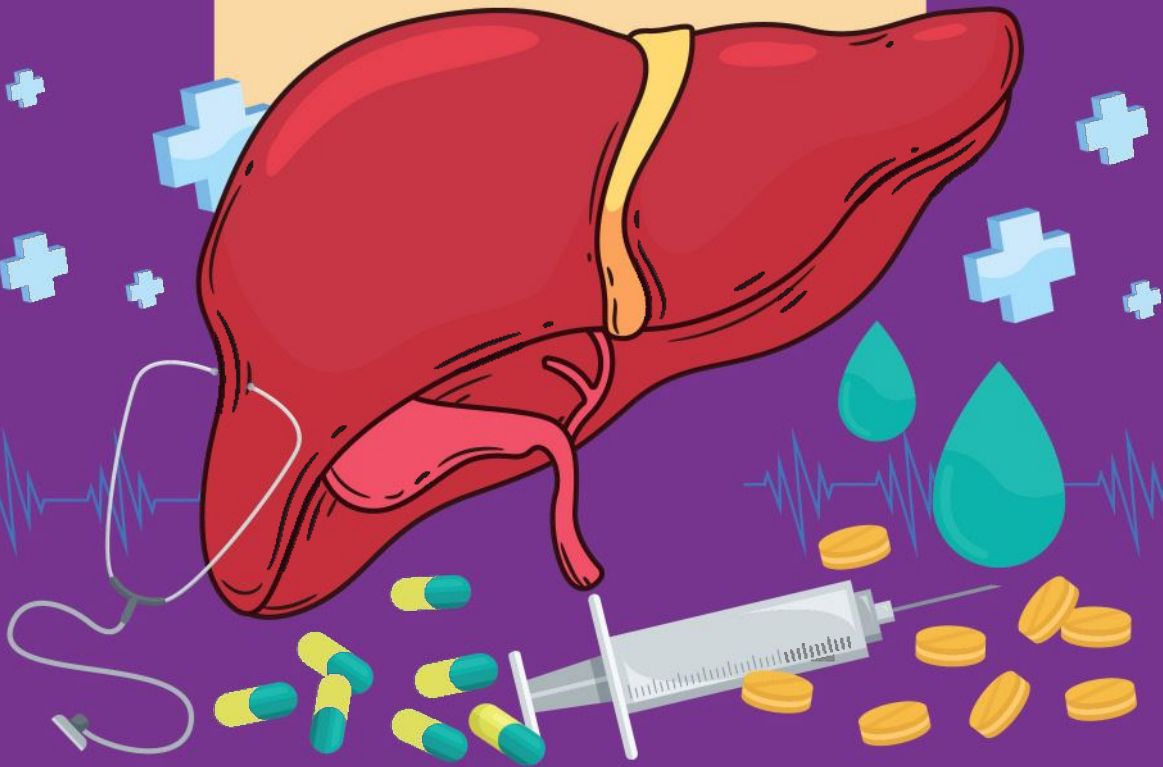
Stem cell transplantation is gaining attention in autoimmune disease treatment. This method involves replacing damaged cells with healthy ones to restore normal tissue function. Early research suggests that stem cell transplants may be effective in patients with severe autoimmune hepatitis who do not respond to conventional treatments.

Future Research and Potential Breakthroughs

Research into autoimmune hepatitis continues to progress, with scientists investigating the genetic and molecular causes of the disease to develop more precise treatments. Since autoimmune hepatitis is a complex condition with various causes, it is expected that a combination of drug therapies, immunotherapies, and gene therapies will lead to more effective treatments in the future.

The future of autoimmune hepatitis treatment is promising, thanks to scientific advancements in biotechnology, immunotherapy, gene therapy, and stem cell transplantation. These innovative methods could lead to better disease control and fewer side effects compared to current medications. With continued research and the development of new therapies, patients with autoimmune hepatitis may soon have access to more effective treatment options with fewer side effects.

BOOK 2



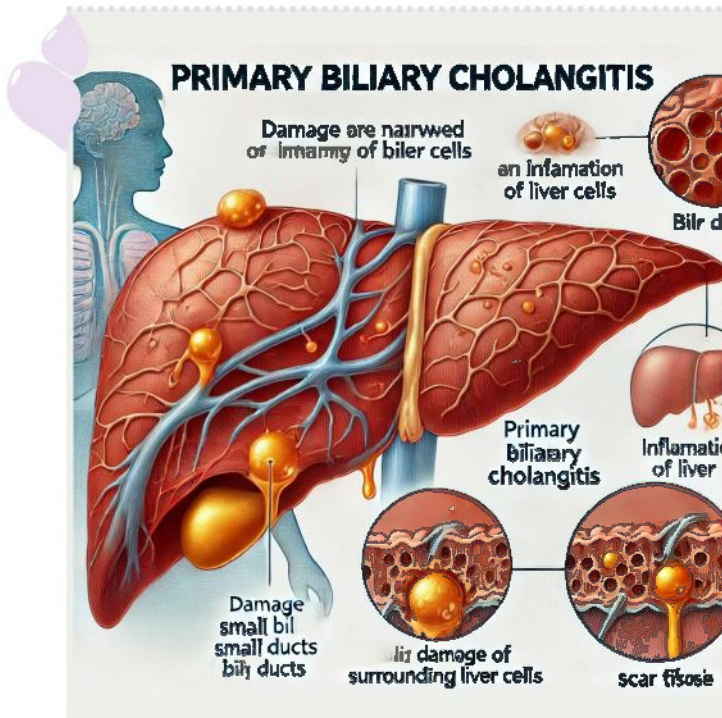
Primary Biliary Cholangitis

Chapter 1

What is Primary Biliary Cholangitis?

Primary biliary cholangitis (PBC) is a chronic and progressive autoimmune disease that gradually causes damage to the liver. In this condition, the immune system mistakenly attacks the cells lining the small bile ducts within the liver. Bile ducts play a crucial role in transporting bile, a substance essential for digesting and absorbing fats in the small intestine.

As these bile ducts are progressively destroyed, the flow of bile from the liver becomes impaired. The buildup of bile in the liver can lead to chronic inflammation, which damages liver cells and disrupts the organ's normal function. In advanced stages of the disease, the damage can lead to cirrhosis (the formation of fibrotic tissue, where healthy liver cells are replaced by scar tissue). Cirrhosis is one of the serious consequences of PBC, significantly reducing liver function and potentially leading to liver failure, portal hypertension (high blood pressure in the liver's veins), and other complications like jaundice (yellowing of the skin and eyes) and severe itching (pruritus).



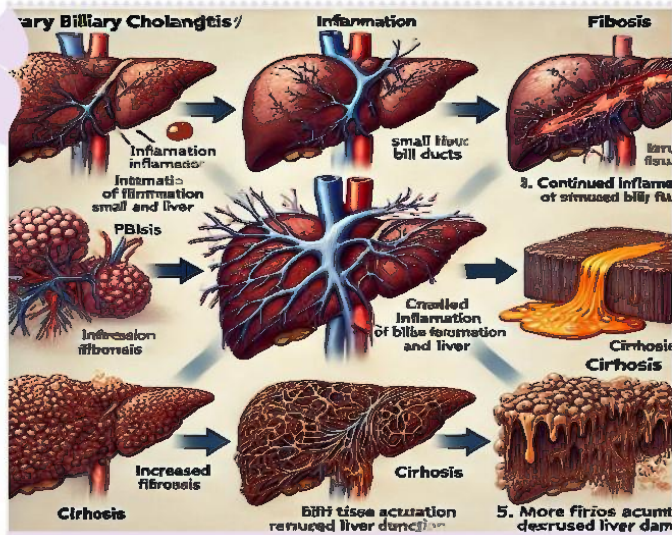
The schematic illustration addresses primary biliary cholangitis, showing damage to the small bile ducts, inflammation of liver cells, and fibrosis.

Both genetic and environmental factors play a role in the development of this disease, although the exact cause of the immune system attacking the bile ducts is not yet fully understood. Current treatments focus on controlling the disease with medications to reduce inflammation and improve bile flow. However, in advanced cases, a liver transplant may be the only treatment option.

Stages of Liver Damage in Primary Biliary Cholangitis (PBC):

In autoimmune diseases like primary biliary cholangitis (PBC), the immune system mistakenly attacks healthy tissues. In PBC, the cells lining the small bile ducts within the liver are the target of this immune attack. These bile ducts are responsible for transporting bile from the liver to the digestive system. Bile plays a crucial role in digesting fats and eliminating waste products like cholesterol and bilirubin. The exact cause of this immune attack is unknown, but researchers believe that genetic and environmental factors (such as viral or bacterial infections, exposure to toxins, or hormonal factors) may trigger the immune system. As a result, the immune system mistakenly identifies the bile duct cells as a “threat” and attacks them.

The immune system’s attack on the bile ducts leads to inflammation. Chronic inflammation causes the walls of the bile ducts to swell, gradually narrowing the ducts. This ongoing inflammation can destroy the cells lining the bile ducts. As the inflammation progresses, the bile ducts become narrower and may eventually become blocked. This blockage prevents bile from properly leaving the liver and reaching the small intestine. Consequently, bile accumulates in the liver. Bile accumulation damages the liver because bile is an irritant, and if it builds up in large amounts in the liver, it can cause serious harm to liver tissue. The buildup of bile damages liver cells (hepatocytes) and leads to cell death. Additionally, the toxic and irritating components of bile cause increased inflammation in the liver tissues. Continuous inflammation results in scarring of the liver tissue (fibrosis). Over time, fibrosis spreads to larger areas of the liver, gradually replacing healthy liver tissue with scar tissue.



The schematic image illustrating the stages of liver damage in Primary Biliary Cholangitis is ready. This image shows the following stages:

- **Inflammation:** Initial inflammation of the small bile ducts and liver.
- **Fibrosis:** With ongoing inflammation, fibrous tissue forms, leading to reduced liver function.
- **Cirrhosis:** In advanced stages, fibrosis progresses to cirrhosis, causing severe liver damage.
- **Bile Accumulation:** Impaired bile drainage leads to accumulation, further damaging the liver.
- **Increased Fibrosis:** More fibrous tissue formation disrupts liver structure and function.

These stages represent the gradual progression of liver damage.

As liver cell damage and bile duct obstruction continue, fibrosis progresses. Fibrosis refers to the formation of scar-like tissue in the liver, which disrupts the liver's normal function. This process can eventually lead to cirrhosis. Cirrhosis is a stage where the liver becomes extensively scarred and loses its ability to perform vital functions.

In the advanced stages of primary biliary cholangitis (PBC), cirrhosis can lead to serious complications. The liver loses its ability to filter toxins, produce essential proteins, and regulate the body's chemical balance. Blocked blood flow through the liver increases pressure in the portal vein (the vein that carries blood from the intestines to the liver), which can cause swelling in the abdomen (ascites) and swelling in the legs and hands. Due to the liver's inability to eliminate bilirubin (a waste product from the breakdown of red blood cells), the skin and eyes turn yellow (jaundice). Additionally, impaired bile production reduces the absorption of fat-soluble vitamins such as vitamins A, D, E, and K.

Although primary biliary cholangitis is a chronic and progressive disease, early diagnosis and appropriate treatment can slow its progression and manage symptoms. Current treatments, such as ursodeoxycholic acid (UDCA) and obeticholic acid, help improve bile flow and reduce inflammation. Moreover, with regular monitoring of liver function and adherence to medical guidelines, many patients can maintain a good quality of life and prevent severe complications of the disease.

Chapter 2

Primary Biliary Cholangitis in Iran

Overview of the Disease in Iran

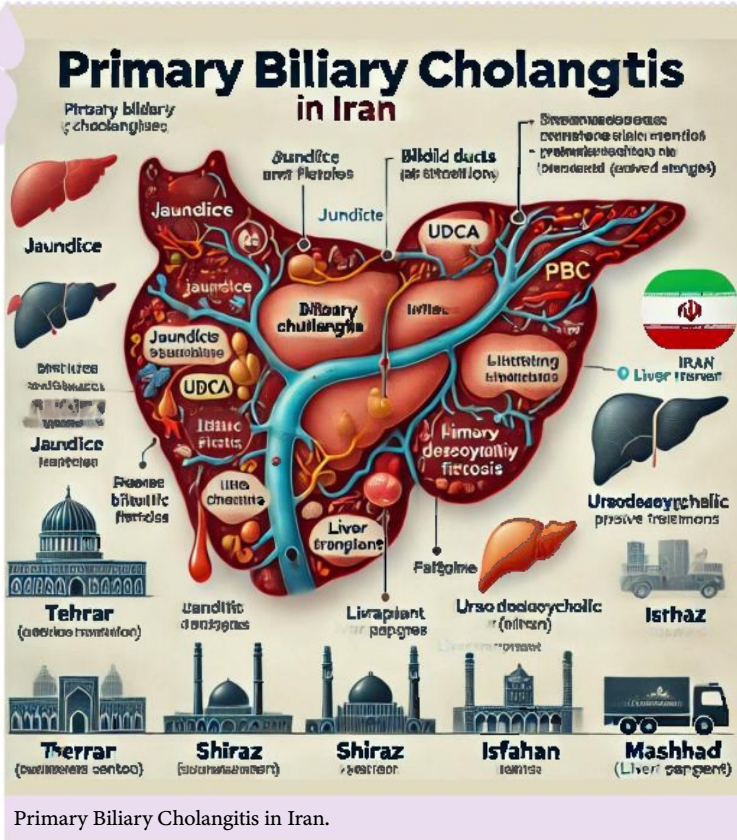
Primary biliary cholangitis (PBC) is a relatively rare disease worldwide, and in Iran, it appears to have a lower prevalence compared to Western countries due to limited official statistics. However, reports and research indicate that the incidence of the disease is increasing in Iran, possibly due to greater awareness and improved diagnostic methods, leading to more cases being identified. PBC is more commonly seen in middle-aged women, a pattern observed in Iran as well. Many cases are diagnosed late due to the absence of specific symptoms in the early stages, which complicates treatment management.

Prevalence of the Disease

There are no precise statistics on the prevalence of PBC in Iran, but studies conducted in specialized gastroenterology and hepatology centers suggest that while the disease is less common than in some Western countries, it is of significant importance among autoimmune liver diseases in Iran. According to scattered studies, the average age of onset is between 40 and 60 years, predominantly affecting women.

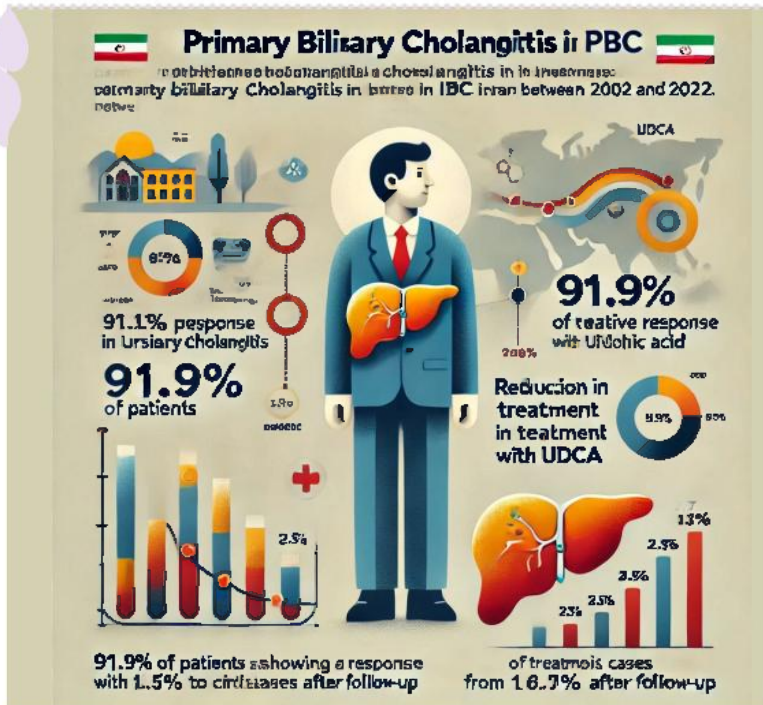
Management of the Disease in Iran's Healthcare System

In Iran, PBC is recognized as a chronic liver disease, and its management follows international and national protocols. Most patients are treated with medications such as ursodeoxycholic acid (UDCA), which helps improve bile flow and reduce inflammation. In more advanced cases, other drugs like obeticholic acid are used. Treatment for PBC in Iran is typically provided in specialized gastroenterology and liver centers, primarily located in major cities such as Tehran, Shiraz, Isfahan, and Mashhad. These centers, often housed in university hospitals, offer specialized consultations and monitor patients regularly through liver function tests and ultrasounds. In advanced cases where complications arise, patients may require liver transplants, which are performed at specialized liver transplant centers in Iran.



Primary Biliary Cholangitis in Iran.

In a study conducted at the Middle East Liver Diseases Center under the supervision of Dr. Alavian in Tehran, patients with Primary Biliary Cholangitis were evaluated over a period from 2002 to 2022. Among 37 PBC patients, 91.9% responded positively to treatment with Ursodeoxycholic Acid (UDCA). Additionally, 16.5% of the patients had cirrhosis at the beginning of the study, but by the end of the follow-up, only 2.7% still had cirrhosis, indicating the reversibility of cirrhosis in some patients.



This is based on a study about Primary Biliary Cholangitis (PBC) in Iran between the years 2002 and 2022. It displays key information, such as a positive response from 91.9% of patients to treatment with Ursodeoxycholic Acid and a reduction in cirrhosis cases from 16.5% to 2.7% after follow-up.

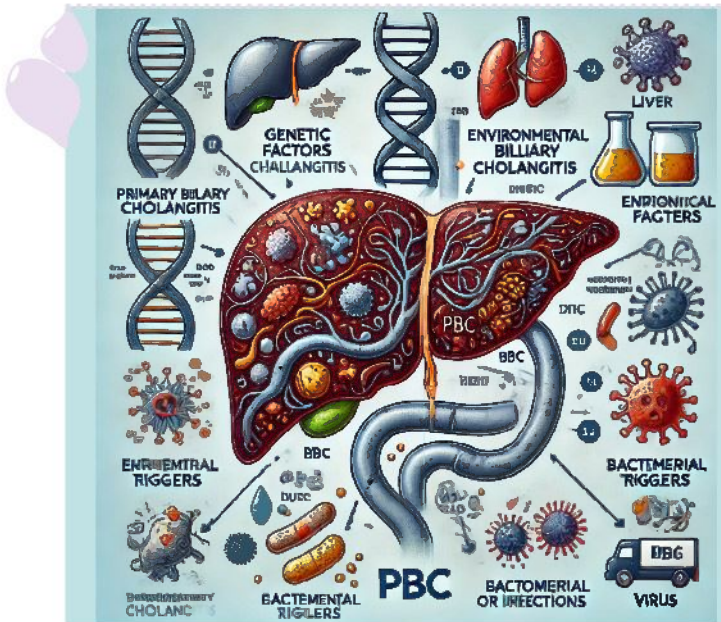
One of the main challenges in managing Primary Biliary Cholangitis (PBC) in Iran is the early diagnosis of the disease. Since the initial symptoms are often vague and mild, patients may not seek medical attention until the disease has progressed to more advanced stages. This delay impacts timely diagnosis and the initiation of treatment. Additionally, access to advanced medications like Obeticholic Acid (OCA) may be limited in some parts of the country. However, raising awareness among the medical community and the general public about autoimmune liver diseases and implementing screening programs can help improve the diagnosis and management of the disease in Iran.

Chapter 3

Causes and Risk Factors of Primary Biliary Cholangitis

Primary biliary cholangitis is a rare autoimmune disease that primarily affects the small bile ducts within the liver. In this condition, the immune system mistakenly attacks healthy cells in the bile ducts, leading to inflammation, destruction, and blockage of these ducts. This disruption reduces or halts bile flow from the liver to the intestines, causing a buildup of waste products in the liver, tissue damage, and eventually liver cirrhosis.

This chapter examines the causes and risk factors of PBC. While the exact cause is not fully understood, researchers have concluded that genetic and environmental factors play significant roles in its development. A combination of genetic predisposition and exposure to certain environmental triggers, such as infections or chemicals, may stimulate the immune system to mistakenly attack the body's own cells, resulting in the disease.



Schematic illustration number 63 highlights the causes and risk factors of PBC, including genetic factors, environmental triggers (such as pollution or chemicals), and bacterial or viral infections that might contribute to or exacerbate the disease.

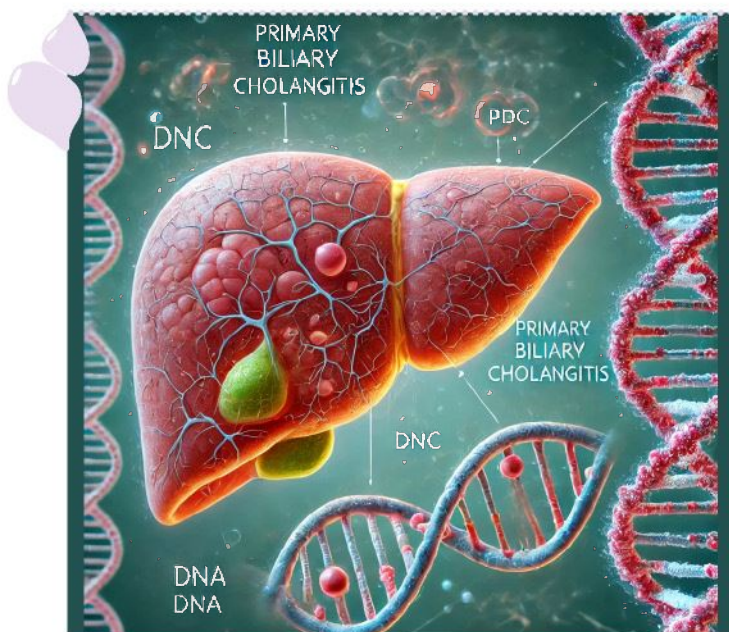
Genetic Factors

One of the primary causes of PBC is genetic factors. Studies have shown that individuals with a family history of autoimmune diseases are more likely to develop PBC. Certain genes can also increase the risk of the disease. Genes associated

with the immune system, particularly those related to human leukocyte antigen (HLA), have been identified in many PBC patients. This suggests that genetic defects in the immune response may play a role in initiating immune attacks on the bile ducts.

Further research into genetic risk factors for PBC highlights the significant role of immune-related genes in its onset. Specifically, genes linked to the human leukocyte antigen (HLA) system, especially HLA-DRB1 and HLA-DQB1, have been identified as influential. These genes regulate the immune system's responses, and defects in them can lead to abnormal immune activity and attacks on the bile ducts. Studies conducted on twins and families with a history of PBC also suggest that genetics plays a role in disease occurrence. These studies reveal that individuals with a family member affected by PBC have a significantly higher chance of developing the disease compared to the general population. These findings indicate that immune response genes, particularly those related to the HLA system, are critical in disease development.

In addition to HLA system genes, research also points to non-HLA genes that may influence disease progression. For example, genes involved in regulating immune cell activity and inflammation, such as IL12A and IL12RB2, have been identified as contributing factors in the progression of PBC. These genes impact immune signaling pathways and influence the severity of immune responses in the body.



The schematic illustration shows the role of genetic factors as one of the primary causes of Primary Biliary Cholangitis. Genetic symbols like DNA strands are depicted alongside an inflamed and fibrotic liver.

Additionally, genetic polymorphisms in certain genes have been identified as risk factors for Primary Biliary Cholangitis. For example, studies have shown that specific polymorphisms in genes related to cytokine production, which are immune signaling molecules, can increase the risk of developing the disease. Cytokines such

as TNF- α and IFN- γ , which play key roles in regulating immune responses, are significantly more active in individuals with PBC compared to healthy individuals.

This combination of genetic factors, especially the involvement of human leukocyte antigen (HLA) genes and other immune-related genes, suggests that PBC is a multifactorial disease with both genetic and environmental influences. In other words, the presence of susceptibility genes alone does not cause the disease; environmental factors or immune triggers, such as infections or toxins, may activate these genes and lead to the onset of the disease.

Environmental Factors

Environmental factors play a significant role in the onset and progression of Primary Biliary Cholangitis. Studies have shown that exposure to certain chemicals and environmental toxins may trigger the immune system and increase the risk of developing the disease. These factors include household chemicals, organic solvents, and certain industrial pollutants, which can enter the body through the skin or respiratory system and cause damage to the bile ducts in the liver, prompting the immune system to attack the body's own tissues.

One of the key chemical risks associated with PBC is organic solvents. These substances are frequently found in industrial and workshop environments, and exposure to them may lead to inappropriate immune responses. Several studies have demonstrated that prolonged exposure to these chemicals, particularly for individuals working in environments with high solvent exposure, is linked to an increased risk of developing PBC.

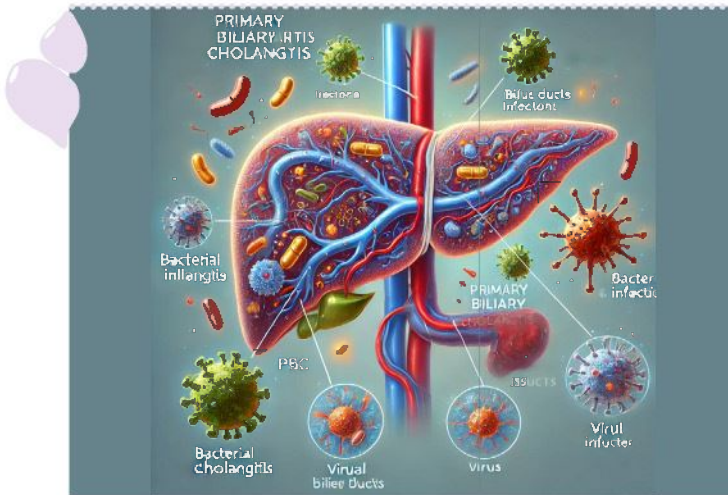
Additionally, air pollution and toxic substances found in urban environments are recognized as another significant environmental factor for PBC. Pollutants such as particulate matter, toxic gases, and heavy metals can cause long-term harm to the body and act as inflammatory triggers. These substances may alter immune cell function and contribute to autoimmune reactions.

Another potential environmental factor related to PBC is the use of cosmetic and hygiene products. Some chemicals found in cosmetics and cleaning products may, with prolonged exposure, stimulate the immune system. Research suggests that certain chemical ingredients in these products could trigger immune system changes that contribute to autoimmune diseases like PBC.

In summary, various environmental factors, including chemicals, air pollutants, and toxins found in household and industrial products, can increase the risk of developing PBC. These factors can stimulate the immune system and alter immune cell function, playing a crucial role in the onset and progression of this disease.

those found in the body's own cells. When the immune system responds to these foreign antigens, it may mistakenly attack the body's own cells with similar structures. This mechanism might explain how infections can trigger the immune system and lead to autoimmune diseases like PBC.

Although viral and bacterial infections are recognized as potential triggers of PBC, no definitive link between specific infections and the disease has been conclusively established. However, the role of chronic infections in stimulating the immune system as a potential factor has been supported by several studies, indicating the need for further investigation.



Highlights the potential role of bacterial and viral infections in triggering or exacerbating primary biliary cholangitis. In this image, the bile ducts of the liver are shown as being affected by chronic infections and immune system attacks

■ Hormonal factors

Hormonal factors play a significant role in the onset and progression of primary biliary cholangitis, particularly given the higher prevalence of this disease in women, especially middle-aged women. This gender difference suggests that sex hormones, especially estrogen, may influence the immune system and its function.

■ Estrogen and its effects on the immune system:

Estrogen is one of the most important female sex hormones and has wide-ranging effects on the immune system. Research has shown that estrogen can enhance immune responses, particularly inflammatory responses. This may explain why women are more prone to autoimmune diseases like PBC than men. Estrogen can increase the activity of immune cells such as T cells and promote the production of inflammatory cytokines, which can trigger autoimmune attacks on the bile ducts.

■ Hormonal fluctuations

Different stages of a woman's life, such as menopause and pregnancy, involve significant changes in hormone levels. Studies have indicated that during menopause, when estrogen levels drop significantly, the risk of developing PBC increases. This suggests that hormonal fluctuations may affect the onset and

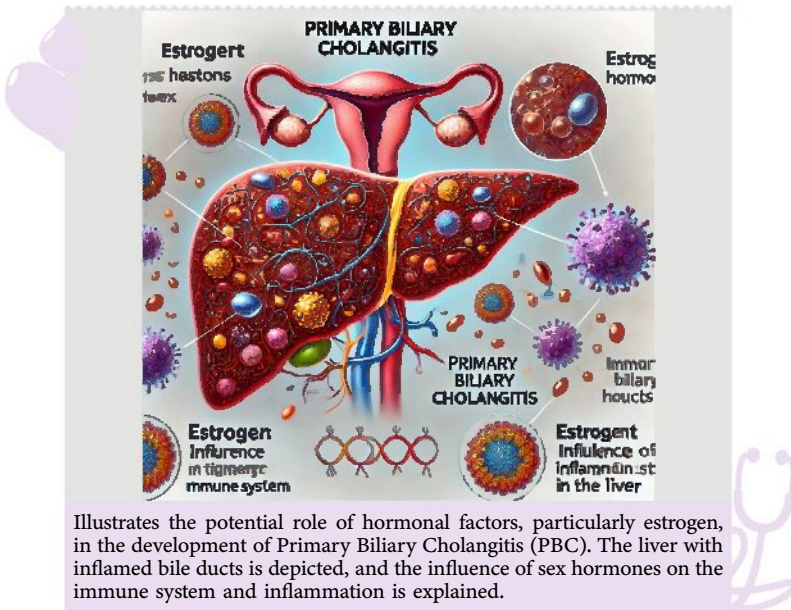
severity of the disease.

Effects of progesterone and other hormones:

In addition to estrogen, other hormones like progesterone may also play a role in the development of PBC. Although the exact role of progesterone is not fully understood, some studies suggest that it may have immunosuppressive effects. Therefore, a decrease in progesterone levels could lead to the activation of autoimmune responses.

The role of genetics and hormones

Research also indicates that the interaction between genetic and hormonal factors can increase the risk of developing PBC. Women with a family history of autoimmune diseases may be more sensitive to the hormonal effects on the immune system, which could be another reason for the higher prevalence of PBC in women. In conclusion, while more research is needed on the role of hormonal factors in the development of PBC, current evidence suggests that sex hormones, especially estrogen, have important effects on the immune system and may be key factors in the higher incidence of this disease in women.



Illustrates the potential role of hormonal factors, particularly estrogen, in the development of Primary Biliary Cholangitis (PBC). The liver with inflamed bile ducts is depicted, and the influence of sex hormones on the immune system and inflammation is explained.

Immune-related factors

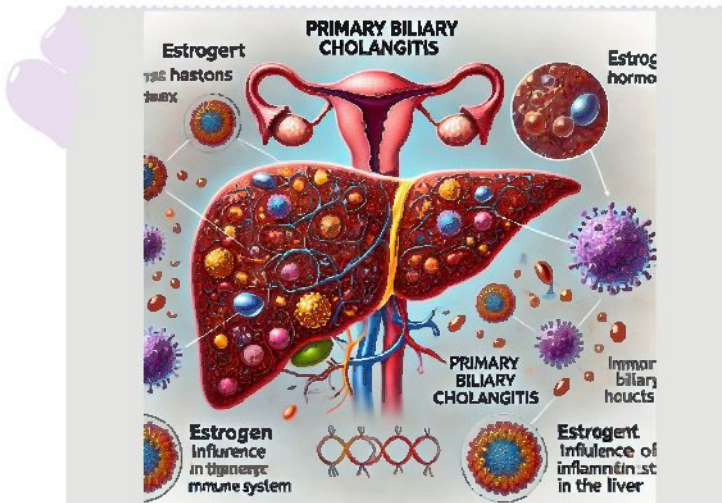
Immune-related factors play a crucial role in the development of Primary Biliary Cholangitis, as it is an autoimmune disease. In autoimmune conditions, the immune system mistakenly identifies healthy cells and tissues as threats and attacks them. In PBC, the immune system targets the epithelial cells lining the small bile ducts within the liver, leading to inflammation and destruction of these ducts. Immune dysfunction is considered a primary factor in the onset of PBC. This dysfunction may involve abnormal regulation of immune responses, overactivity of immune cells such as T-cells and B-cells, and excessive production of autoantibodies. These autoantibodies attack the body's tissues, causing inflammation. Many patients

with PBC have anti-mitochondrial antibodies (AMAs) in their blood, which are key markers of the disease. These antibodies attack the mitochondria of bile duct cells, playing a significant role in the disease's progression.

PBC is often associated with other autoimmune diseases, such as Sjögren's syndrome and Hashimoto's thyroiditis. Sjögren's syndrome, which causes dry mouth and eyes, is frequently seen alongside PBC. This association suggests that these diseases share similar immune mechanisms, with the immune system being broadly dysregulated.

Research has shown that patients with PBC often have specific defects in immune signaling pathways, especially in genes involved in regulating inflammation and immune responses. For instance, genes related to the interleukin-12 (IL-12) and interferon-gamma (IFN- γ) signaling pathways are abnormally active in many PBC patients, enhancing immune responses. These genetic abnormalities, combined with environmental factors, contribute to the onset of the disease.

In summary, PBC is a multifactorial disease caused by immune system dysfunction interacting with genetic and environmental factors. Its connection to other autoimmune disorders highlights shared immune mechanisms in the development and progression of PBC.



This schematic illustration shows the role of immune-related factors in Primary Biliary Cholangitis (PBC). The immune system mistakenly attacks healthy bile ducts, causing inflammation. Additionally, the image depicts the connection with other autoimmune diseases such as thyroid disease and Sjögren's syndrome.

Other Factors

Various factors can play a significant role in the onset and progression of Primary Biliary Cholangitis (PBC). These include concurrent diseases, certain medications, and chronic stress, each of which can influence the immune system and the course of the disease.

Co-occurring diseases such as secondary biliary cirrhosis, rheumatic diseases, and chronic inflammatory bowel diseases are known risk factors. Rheumatic conditions like rheumatoid arthritis and lupus are commonly seen in PBC patients. These autoimmune diseases may heighten inflammatory activity in the

Chapter 4

Symptoms and Signs of Primary Biliary Cholangitis

Primary Biliary Cholangitis is a chronic autoimmune liver disease that may be asymptomatic in its early stages. However, as the disease progresses, several common symptoms can emerge, significantly affecting the patient's quality of life. The most important symptoms include:

Chronic Fatigue: This is one of the earliest and most common symptoms of PBC, greatly impacting patients' daily lives. Fatigue can appear suddenly, making patients feel like they have lost the ability to carry out their regular activities. The main characteristic of this fatigue is that it is not directly related to physical activity and does not improve even after rest or adequate sleep.

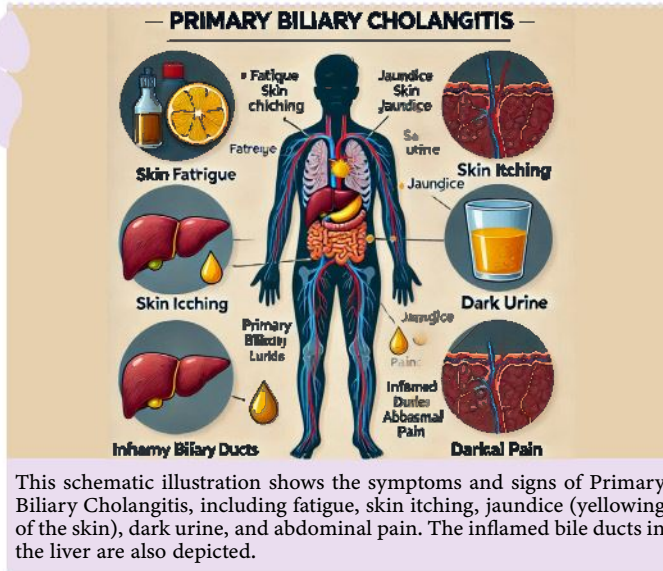
Research indicates that this fatigue may be linked to chronic inflammation caused by immune system activity. When the body is dealing with long-term inflammation, it consumes more energy, leading to severe fatigue. Additionally, nervous system disruptions may also play a role in the onset of fatigue. Some PBC patients experience decreased energy levels due to disruptions in nerve signaling and the malfunction of cellular mitochondria, which are responsible for energy production.

Another possible factor contributing to fatigue in PBC patients is sleep disturbances. Many patients report having trouble sleeping due to other symptoms, such as severe skin itching or joint pain, which in turn worsens fatigue during the day.

Factors Related to Fatigue in Primary Biliary Cholangitis:

- **Metabolic Changes:** Liver dysfunction can result in reduced energy production and irregular metabolism, leading to increased fatigue.
- **Hormonal Imbalance:** Some studies have suggested that imbalances in stress-related hormones, such as cortisol, may contribute to the onset and worsening of chronic fatigue in PBC patients.

Ultimately, fatigue is a complex and multifactorial symptom in PBC that requires comprehensive management. Treatment options for fatigue in these patients include lifestyle changes, improving sleep quality, and, in some cases, the use of specific medications to enhance nervous system function and metabolism.



Severe itching (pruritus) is a prominent and bothersome symptom in Primary Biliary Cholangitis, experienced by most patients. It can appear in the early stages of the disease, even before other symptoms like jaundice develop. The itching often begins in the palms of the hands and soles of the feet, later spreading to other parts of the body. It tends to be more intense at night and can severely affect sleep and daily life.

The exact cause of itching in PBC patients is not fully understood, but one leading theory suggests it results from the buildup of bile-related waste products in the liver and bloodstream. In PBC, bile duct blockages prevent proper bile drainage from the liver. Substances in bile, such as bile salts, can accumulate in the skin, stimulating nerve receptors and causing intense itching.

Some studies suggest that changes in steroid hormone levels, particularly estrogen, might increase skin sensitivity to itching. This theory has been explored, especially in women with PBC, who are more likely to experience hormonal changes. Evidence also points to disruptions in the central nervous system playing a role in the itching experienced by PBC patients. This theory proposes that certain bile components may trigger skin nerve receptors, leading to itching. Additionally, some patients may have heightened sensitivity due to increased activity of chemical receptors in the skin.

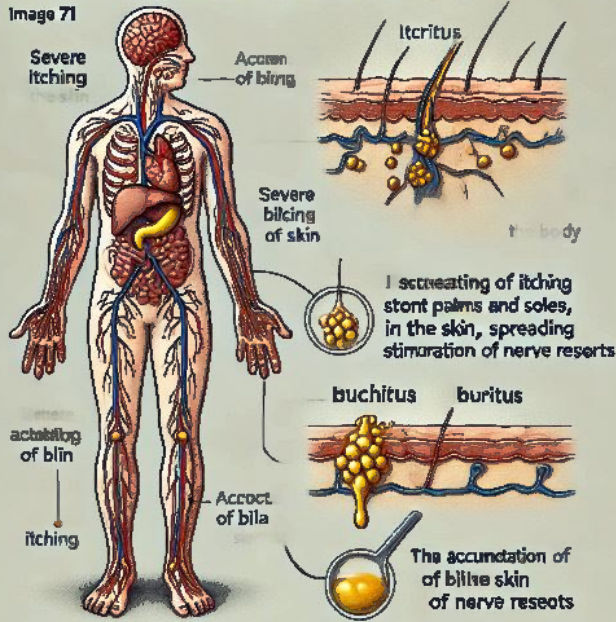
The immune system is abnormally active in PBC, which can lead to increased production of inflammatory cytokines. These cytokines, which are immune signaling molecules, may directly or indirectly stimulate itching receptors in the skin. Managing itching in PBC patients is crucial due to its chronic and debilitating nature. Several approaches exist for controlling this symptom:

- **Anti-itch medications** like cholestyramine, which reduce bile salt absorption in the intestines and lower their levels in the blood.
- **Antihistamines and topical treatments** may also be used to alleviate the severity of itching.
- In severe cases, **opioid antagonists** such as naltrexone can be prescribed to reduce the sensation of itching.

In conclusion, itching in PBC is a complex and multifactorial symptom requiring specialized care and treatment to improve patients' quality of life.

of Primary Biliary Cholangitis

Image 71



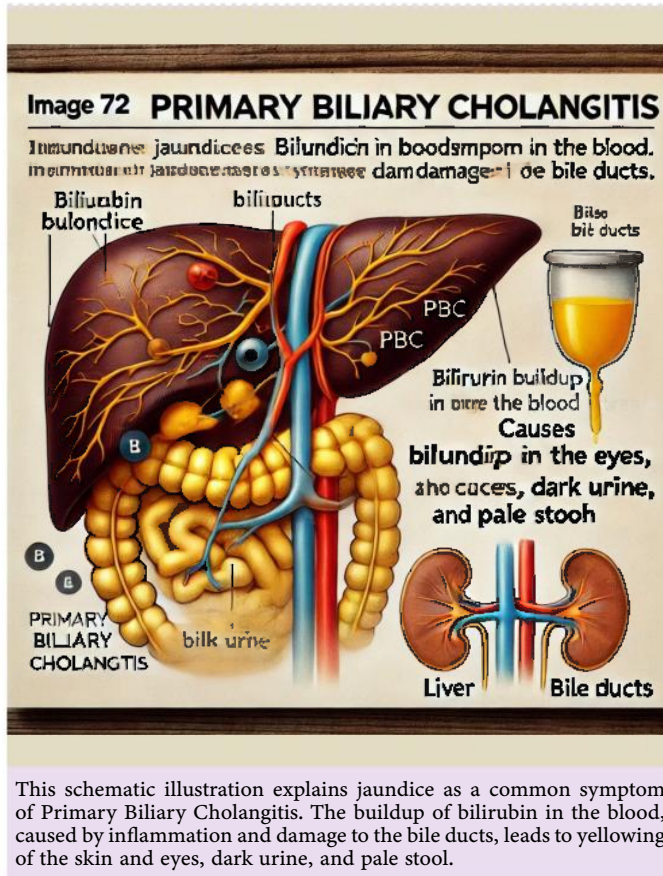
This schematic illustration highlights severe itching (Pruritus) as one of the prominent symptoms of Primary Biliary Cholangitis. The itching typically starts on the palms of the hands and soles of the feet, spreading to other parts of the body. The buildup of bile in the skin and the stimulation of nerve receptors are shown as the possible causes of the itching in the image.

Jaundice, or icterus, is a common symptom in advanced stages of Primary Biliary Cholangitis. It occurs due to the buildup of bilirubin in the body. Bilirubin is a byproduct of the breakdown of red blood cells, which is normally processed and excreted by the liver. In healthy individuals, bilirubin is transported from the liver to the intestines via the bile ducts and is then expelled from the body. However, in PBC, inflammation and damage to the small bile ducts inside the liver prevent bile and waste products from exiting the liver properly. This leads to the accumulation of bilirubin in the bloodstream, resulting in jaundice, or the yellowing of the skin and the whites of the eyes.

Along with this yellow discoloration, the color of urine also changes. As bilirubin is excreted through the kidneys, urine becomes darker, taking on a yellow-brown or orange tint. Additionally, stools may become pale because bile is not reaching the intestines as it should.

Jaundice is typically a sign of the advanced stage of PBC, indicating that liver function is severely compromised and may progress to liver cirrhosis. In this stage, the liver is unable to process and eliminate toxins effectively, leading to further liver damage.

Treatment for jaundice in PBC patients usually involves managing the underlying causes, such as reducing inflammation and improving bile flow. Medical treatments and, in severe cases, liver transplantation may be necessary to preserve liver function and prevent further complications.



Pain in the Upper Abdomen

Some patients with Primary Biliary Cholangitis may experience pain or discomfort in the upper right area of the abdomen. This pain is usually mild but can be more severe in some cases and may be associated with liver inflammation or bile duct issues. In addition to the main symptoms, some patients may also experience other symptoms such as dry eyes and mouth (linked to Sjögren's syndrome), unexplained weight loss, and joint pain. These symptoms can be due to other autoimmune issues often associated with PBC.

In advanced stages of the disease, patients may face complications such as liver cirrhosis, liver failure, and additional complications due to impaired liver function. These complications include abdominal swelling (ascites), swelling in the legs, and internal bleeding, which require urgent medical attention. Early diagnosis and symptom management can help slow the progression of the disease and improve the patient's quality of life.

Chapter 5

Diagnosis of Primary Biliary Cholangitis (PBC): Tests and Medical Examinations

Primary Biliary Cholangitis (PBC) is usually diagnosed through a combination of blood tests, imaging studies, and liver biopsy. These diagnostic methods help physicians not only confirm the disease but also assess liver damage and disease severity.

Blood Tests

Blood tests are one of the most important diagnostic tools for PBC, providing significant information about liver function and the immune system. The most critical blood tests for diagnosing PBC include:

Anti-Mitochondrial Antibodies (AMA)

The presence of AMAs in the blood is a key diagnostic marker for PBC, found in about 90-95% of patients. This test is considered the gold standard for diagnosing PBC.

Liver Enzyme Tests

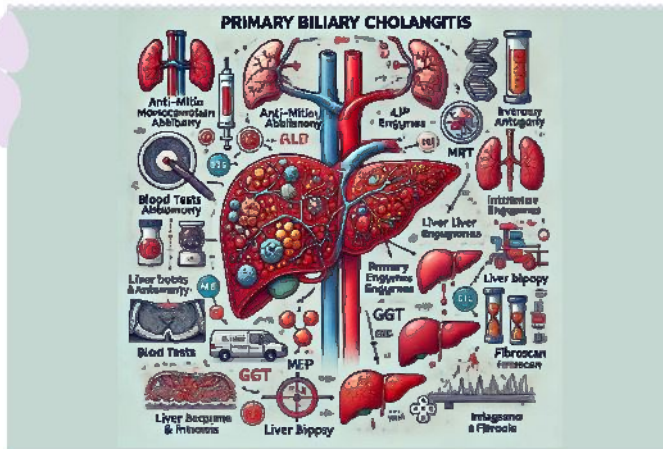
Elevated levels of liver enzymes, especially **alkaline phosphatase (ALP)** and **gamma-glutamyl transferase (GGT)**, indicate damage to the bile ducts. These tests often provide the first clinical signs of liver issues.

Bilirubin

Increased bilirubin levels in the blood indicate that the liver is unable to properly eliminate waste. This may be observed in more advanced stages of the disease.

Immune Tests

In addition to AMAs, anti-nuclear antibodies (ANA) and anti-smooth muscle antibodies (ASMA) may also be positive in PBC patients. These antibodies indicate the presence of autoimmune disorders.



This schematic illustration shows the diagnostic methods for Primary Biliary Cholangitis. It depicts blood tests such as Anti-Mitochondrial Antibodies (AMA), liver enzymes (ALP and GGT), liver biopsy for assessing inflammation and fibrosis, and imaging techniques such as ultrasound, MRI, and FibroScan.

Liver biopsy is one of the most important diagnostic tools for confirming Primary Biliary Cholangitis and assessing the extent of liver damage accurately. A liver biopsy is particularly useful when blood test results are insufficient for a definitive diagnosis, or when doctors need to determine the stage of disease progression. This method provides detailed information about the degree of inflammation, fibrosis, and other damage to the bile ducts.

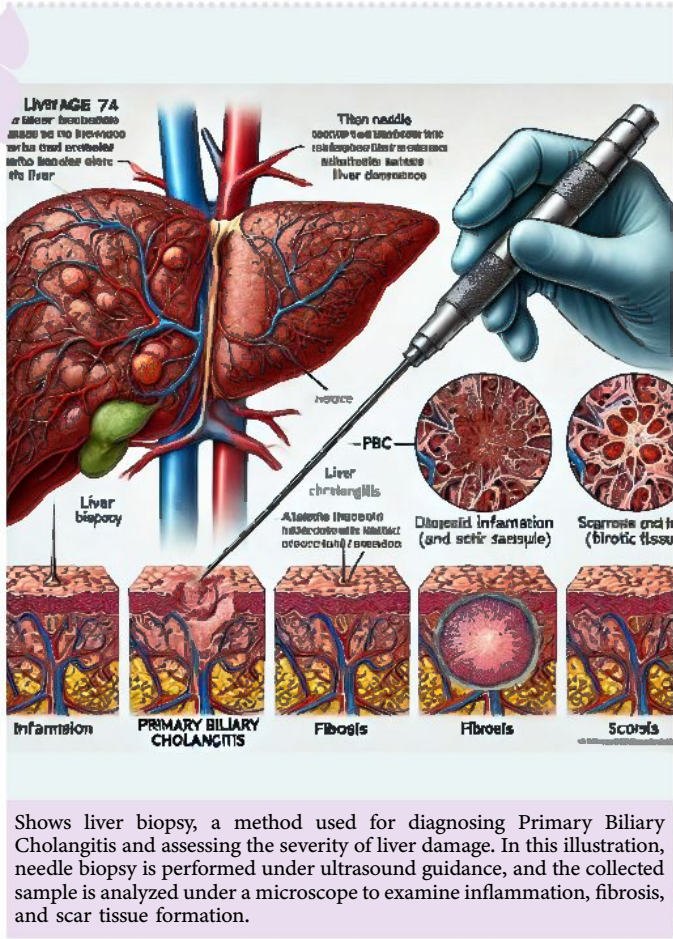
During a liver biopsy, a small sample of liver tissue is taken using a very fine needle. This sample is then examined under a microscope to evaluate tissue changes related to PBC, such as inflammation in the small bile ducts, fibrosis, and the presence of scar tissue (fibrotic tissue formation). Doctors often use imaging guidance (such as ultrasound) to ensure precise targeting during the biopsy.

Liver biopsy plays a crucial role in determining the stage of disease progression. Although the initial diagnosis of PBC is usually made through blood tests, such as Anti-Mitochondrial Antibody (AMA) and liver enzyme tests, a biopsy provides a more detailed assessment of the degree of fibrosis or the likelihood of progression to cirrhosis. In fact, the biopsy can help doctors create a more tailored treatment plan for the patient.

A biopsy helps assess the severity of inflammation and fibrosis in the bile ducts. This information allows doctors to gauge how far the disease has progressed. It can also detect early signs of cirrhosis, which is critical for predicting future complications and making treatment decisions. If doctors suspect other conditions alongside PBC, such as fatty liver disease or hepatitis, the biopsy can also aid in diagnosing these issues.

Liver biopsy is an invasive procedure and may be associated with certain risks, including pain at the biopsy site, bleeding, or infection. However, it is generally considered a safe procedure, and serious complications are rare. For this reason, liver biopsy is typically performed only in cases where blood tests alone cannot provide a definitive diagnosis, or when a more detailed assessment of liver damage is required.

While liver biopsy is not always the first option for diagnosing Primary Biliary Cholangitis, it serves as a critical diagnostic tool in specific cases where confirmation of the diagnosis or evaluation of disease progression is necessary. This procedure provides valuable insights into the extent of liver damage, inflammation, and fibrosis, helping guide treatment decisions for better disease management.

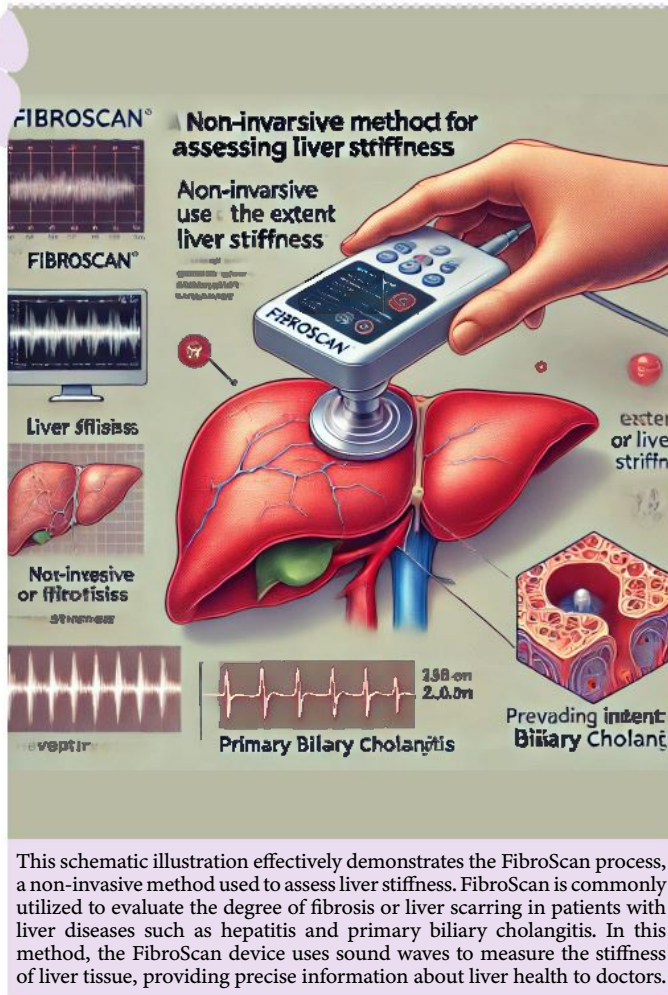


Ultrasound is a non-invasive method that can be used to examine the liver and bile ducts. This technique helps detect blockages in the bile ducts and liver enlargement. In cases requiring more detailed evaluation, MRI or MRCP (Magnetic Resonance Cholangiopancreatography) may be used. These imaging techniques provide a clear picture of the bile ducts and their condition.

FibroScan or transient elastography is a non-invasive and quick method for assessing liver stiffness or fibrosis, often used in patients with Primary Biliary Cholangitis. This technique helps physicians measure the amount of scar tissue (fibrosis) in the liver without needing a biopsy, determining whether the liver has progressed toward cirrhosis. However, this method is more commonly used for patient follow-up rather than definitive diagnosis.

FibroScan uses elastic waves and ultrasound to measure liver stiffness. When the

liver becomes stiffer due to inflammation and fibrosis, the waves pass through the tissue at a faster rate. The speed of the waves indicates the extent of fibrosis—the stiffer the liver, the more severe the fibrosis. In PBC patients, FibroScan helps determine the progression of fibrosis and can guide doctors in making treatment decisions. If fibrosis progresses, the patient may be moving toward cirrhosis, requiring treatment adjustments or even liver transplantation. FibroScan is recognized as an effective tool for evaluating and monitoring PBC patients, but it should be used alongside other clinical tests and imaging for a comprehensive diagnosis.



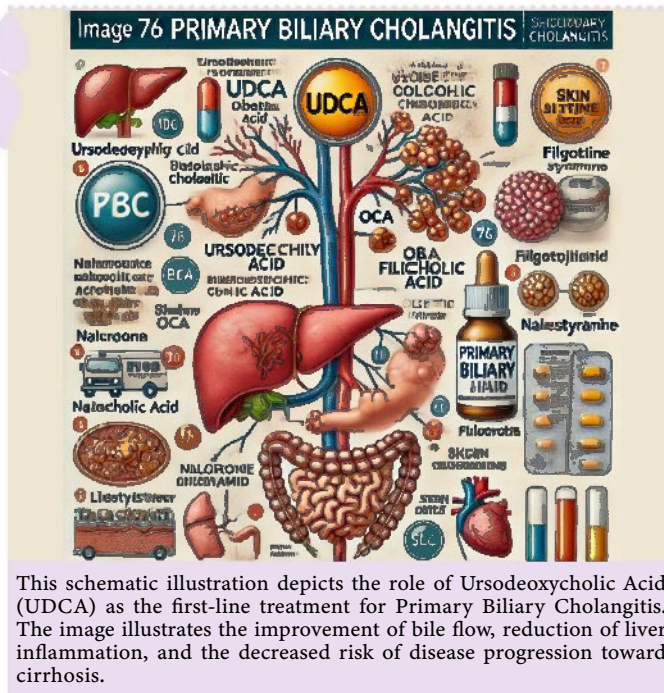
The diagnosis of primary biliary cholangitis is usually made through blood tests, especially the anti-mitochondrial antibody (AMA) test. Liver biopsy and imaging techniques can also be used to confirm the diagnosis and assess the severity of the disease. Early diagnosis of PBC can help in more effective management of the condition and prevent its progression towards more serious complications.

liver function. It also helps by preventing programmed cell death (apoptosis) in liver cells, supporting the health of these cells.

The use of ursodeoxycholic acid leads to improvements in liver enzymes, such as alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT), which indicates a reduction in liver inflammation and damage. For many patients, continued use of ursodeoxycholic acid helps decrease the likelihood of progression to cirrhosis, a serious complication where liver tissue becomes scarred, reducing its function. Studies show that ursodeoxycholic acid can extend the lifespan of PBC patients, especially those who respond well to initial treatment. Most patients taking ursodeoxycholic acid experience significant improvement in their liver condition. However, some patients may not respond to this medication, and in such cases, alternative drugs like obeticholic acid may be prescribed.

The side effects of ursodeoxycholic acid are generally mild, including diarrhea, nausea, and abdominal pain, which usually subside after a few weeks.

Patients on ursodeoxycholic acid treatment should have regular blood tests to monitor liver enzyme levels and other indicators of liver health. If necessary, the doctor can adjust the dosage or add complementary treatments to prevent complications.



New research is underway to enhance the therapeutic effects of Ursodeoxycholic Acid (UDCA) and find ways to improve its efficacy. Combining this drug with newer treatments like Obeticholic Acid (OCA) and Filgotinib may offer additional treatment options for patients with Primary Biliary Cholangitis.

UDCA is an important and effective drug for treating PBC, as it reduces bile toxicity, improves bile flow, and decreases liver inflammation and fibrosis, thus helping to prevent disease progression and improving patients' quality of life.

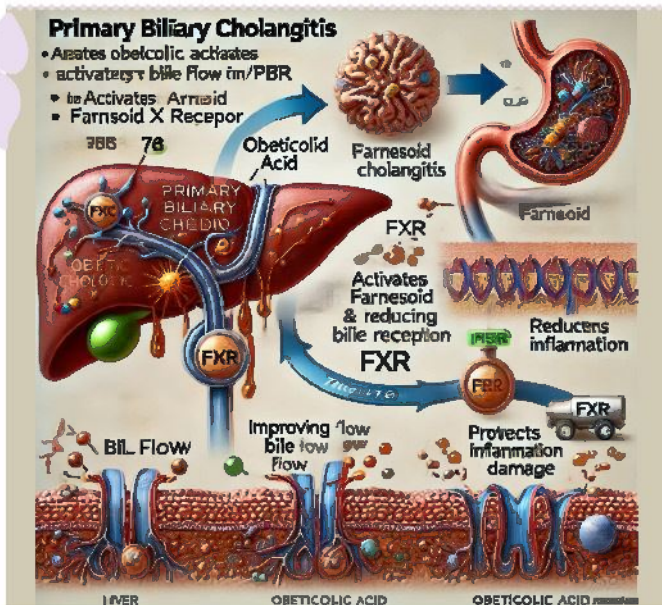
Long-term, regular use of UDCA can help maintain liver health and prevent progression to cirrhosis.

For patients who do not respond to or cannot tolerate UDCA, Obeticholic Acid (OCA) is used as an alternative. OCA is a Farnesoid X Receptor (FXR) agonist that helps reduce inflammation and improve bile flow. It is usually prescribed in more severe cases or when initial treatments are ineffective and has shown positive results in controlling the disease.

OCA works by activating FXR receptors in liver cells, which play a key role in regulating bile flow, fat metabolism, and inflammation. By activating these receptors, OCA reduces bile accumulation in the liver and enhances bile flow from the bile ducts to the intestines. It also helps reduce inflammation and prevents further damage to liver tissue.

Studies have shown that OCA is highly effective in patients who have not responded to UDCA. It is especially helpful for patients with more advanced disease or those nearing cirrhosis. Clinical trials have demonstrated that OCA reduces liver enzyme levels, such as Alkaline Phosphatase (ALP) and Gamma-Glutamyl Transferase (GGT), indicating reduced inflammation and liver damage. OCA may also help delay disease progression toward cirrhosis.

OCA treatment usually begins with a low dose, which is gradually increased. The medication is taken as a pill, and patients may need to use it long-term. In more severe or UDCA-resistant cases, a combination of OCA and UDCA may be prescribed. Although OCA is generally well-tolerated, some patients may experience side effects. Severe itching (pruritus) is one of the most common side effects, which may cause discomfort. Elevated blood cholesterol levels are another potential side effect that requires monitoring.



This schematic illustration shows the role of obeticholic acid in the treatment of Primary Biliary Cholangitis (PBC). The medication works by activating the Farnesoid X receptor (FXR), which helps improve bile flow, reduce inflammation, and prevent liver damage.

Obeticholic acid is specifically prescribed for patients in advanced stages of Primary Biliary Cholangitis (PBC) when treatment with ursodeoxycholic acid (UDCA) is insufficient. This medication helps reduce the progression of fibrosis and cirrhosis and is considered an effective treatment option for patients resistant to initial therapies.

Obeticholic acid is an important option for treating PBC, particularly for patients who have not responded well to conventional treatments. It improves bile flow, reduces inflammation, and slows the progression of fibrosis and cirrhosis, thus improving the quality of life for patients. The use of this medication should be closely monitored by a physician to manage its effectiveness and potential side effects.

Filgotinib is a newer medication used in treating PBC, particularly for patients who have not responded to previous treatments. It helps lower alkaline phosphatase (ALP) levels, which is an important marker of liver inflammation and damage.

Filgotinib acts as a chitinase inhibitor, blocking enzymes responsible for inflammation in the liver and bile ducts. This helps reduce inflammation, preventing the progression of fibrosis and damage to liver tissue. Additionally, filgotinib can reduce the risk of cirrhosis in PBC patients who do not respond to standard treatments. Clinical studies have shown that filgotinib effectively lowers ALP levels in PBC patients, indicating reduced inflammation and improved liver function.

Although filgotinib is generally well-tolerated, some patients may experience mild side effects such as skin itching, headaches, or nausea. Since this drug affects the immune system, there is an increased risk of infection, which requires careful monitoring by a physician. Filgotinib is particularly beneficial for patients with high inflammation levels and disease progression, helping reduce the risk of liver failure and progression to cirrhosis. Filgotinib is considered a promising new drug for PBC treatment, and its role in managing the disease may increase in the future.

Filgotinib is a new and effective treatment option for patients who have not responded to previous therapies but is unfortunately not widely available. It helps reduce ALP levels and liver inflammation, improving disease management and preventing progression to cirrhosis, ultimately improving the quality of life for PBC patients.

To manage symptoms like skin itching, medications such as opioid antagonists (naltrexone) or cholestyramine may be prescribed. Antihistamines can also help relieve itching. In advanced cases, cholesterol-lowering treatments may be used to manage symptoms.

In cases where the disease has progressed to cirrhosis, liver transplantation may be the only treatment option. Liver transplantation is recommended for patients with liver failure, severe complications, or advanced disease that does not respond to medication. The outcomes of liver transplants in PBC patients are generally positive and can significantly improve their quality of life.

Regular monitoring with blood tests to check liver function, measure liver enzymes, and bilirubin is essential. Physicians may also use Fibroscan to assess fibrosis levels and disease progression. PBC treatment focuses on symptom control, slowing disease progression, and preventing complications. Key medications such as ursodeoxycholic acid and obeticholic acid play a crucial role in managing the disease. Early diagnosis, regular follow-ups, and supportive treatments are essential to improving patients' quality of life.

Chapter 7

Living with Primary Biliary Cholangitis: Management, Care, and Lifestyle Changes

Primary Biliary Cholangitis is a chronic autoimmune disease that affects the liver. Living with this condition may present multiple challenges, but with proper management and lifestyle changes, it is possible to improve quality of life and reduce the symptoms of the disease. In this chapter, we explore practical strategies for managing symptoms, basic care, preventing long-term complications, and making dietary and lifestyle changes.

Symptom Management

Fatigue, Pain, and Digestive Issues

Fatigue is one of the most common and debilitating symptoms in patients with PBC, which can significantly limit their daily activities. This fatigue may persist even after rest and continually affect the patient's life. To cope with fatigue and improve energy levels, different approaches can be applied.

Managing Energy Throughout the Day

Patients with PBC should manage their energy throughout the day. Breaking down tasks into smaller parts and planning for regular rest breaks can help prevent extreme fatigue. Completing important tasks that require focus during times of higher energy can be beneficial. It's recommended to schedule short breaks between daily activities to avoid severe fatigue.

Engaging in Light Physical Activities

Light physical activities such as walking, yoga, and stretching exercises can help boost energy levels. These activities not only strengthen the body but also improve mood and reduce stress. Gentle exercises improve blood circulation, oxygenation, and reduce inflammation. A short daily walk can help improve blood flow and increase energy. Yoga and stretching exercises not only calm the mind but also help reduce muscle and mental tension.

Managing Stress

Stress is a major factor in worsening fatigue in PBC patients. Reducing stress through relaxation techniques can improve energy levels and reduce fatigue. Meditation and mindfulness promote mental calmness, reduce anxiety, and help improve focus and energy. Breathing exercises can help relax the body and reduce nervous tension, which in turn reduces fatigue.

Maintaining a Proper Diet

A suitable diet plays a crucial role in boosting energy and reducing fatigue. Foods rich in protein, vitamins, and fiber help maintain energy levels throughout the day. High-fat, high-calorie meals can cause sluggishness and fatigue, so it's best to avoid heavy foods.

● Ensuring Quality Sleep

Getting sufficient, quality sleep is a key factor in reducing fatigue. PBC patients should prioritize good sleep hygiene and establish a regular nighttime routine.

Adopting a regular sleep pattern helps improve sleep quality, thereby reducing fatigue.

Reducing the use of electronic devices: Limiting exposure to electronics before bed can improve sleep quality.

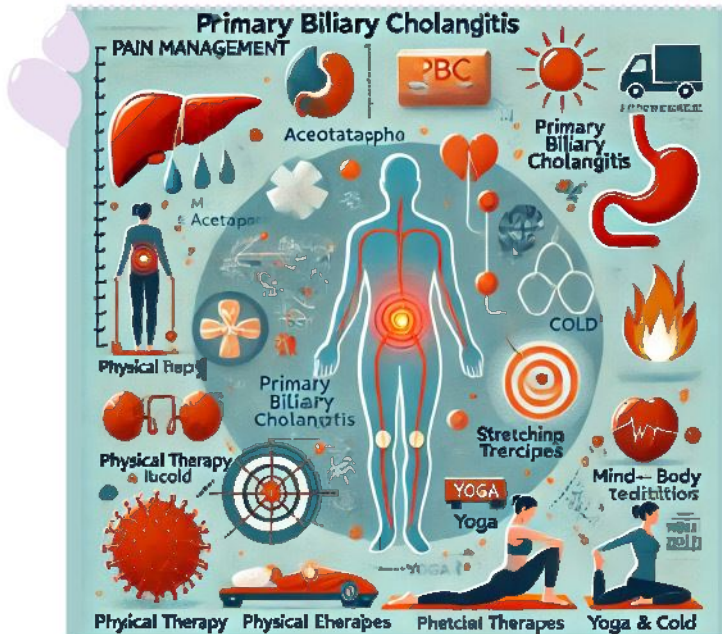
● Emotional Support

PBC patients may face psychological challenges due to ongoing fatigue. Receiving support from family, friends, or participating in support groups can reduce feelings of isolation and improve mental well-being.

By adopting these lifestyle changes, managing energy levels, reducing stress, following a nutritious diet, and ensuring adequate rest, PBC patients can better manage fatigue and improve their quality of life.

To cope with fatigue caused by primary biliary cholangitis, a combination of proper activity planning, mild exercise, stress management, healthy nutrition, and sufficient sleep can help improve energy levels and reduce fatigue. Patients should remember that fatigue may persist, but by using these strategies, they can manage it and improve their quality of life.

Managing pain in patients with primary biliary cholangitis is a key issue in improving their quality of life. These patients may experience chronic joint and abdominal pain due to inflammation, fibrosis, and involvement of joints and muscles. A combination of pharmaceutical and non-pharmaceutical methods can be effective in reducing this pain. Over-the-counter pain relievers such as acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) are recommended to relieve pain. These medications can help reduce inflammation and pain but should be used under medical supervision to prevent side effects. Acetaminophen is usually prescribed for mild to moderate pain and is effective in pain control without causing additional liver damage. Ibuprofen and naproxen can help reduce inflammation and pain but should be used cautiously, especially in patients with liver disease, as long-term or excessive use of these medications may increase the risk of stomach and liver damage.



This infographic illustrates pain management strategies for patients with Primary Biliary Cholangitis. It includes pharmaceutical methods like acetaminophen and ibuprofen, physical therapy, stretching exercises, the use of heat and cold, and mind-body techniques such as yoga and meditation.

Physical therapy can help reduce muscle and joint pain. By performing specialized exercises under the supervision of a physiotherapist, muscles and joints are strengthened, and pain from pressure and inflammation is reduced. Stretching exercises help alleviate muscle tension and increase joint flexibility, allowing patients to relieve recurrent pain caused by stiffness and inflammation. Massage therapy can also improve blood circulation in the muscles and reduce pain and inflammation. Applying heat and cold to painful areas can provide pain relief. Heat packs can enhance blood flow and reduce muscle stiffness, while cold application can reduce inflammation and pain. These methods are especially useful for muscle and joint pain.

Mind-body techniques, such as yoga, meditation, and breathing exercises, can improve mental health and reduce pain. These techniques help alleviate stress and provide relaxation, contributing to better chronic pain control. Patients with Primary Biliary Cholangitis can also benefit from complementary treatments like acupuncture, aromatherapy, or massage techniques to reduce pain and inflammation. Although these methods may require further research, many patients have reported pain relief and overall improvement.

Managing pain in patients with PBC requires a combination of medical and non-medical approaches. Taking pain relievers cautiously under medical supervision, combined with physical therapy, stretching exercises, and relaxation techniques, can reduce pain and improve quality of life.

Digestive issues such as bloating, diarrhea, and nausea are other common symptoms in PBC. Suggested strategies for reducing these problems include eating smaller,

more frequent meals to reduce bloating and improve digestion. Reducing the intake of saturated fats and fried foods can also help alleviate digestive issues. Adding fiber to the diet can improve digestion and prevent constipation.

Primary care and prevention of long-term complications in patients with PBC: PBC is a chronic autoimmune disease that, if not properly managed, can lead to serious complications like cirrhosis and liver failure. Primary care and regular follow-ups are essential to prevent disease progression and improve the quality of life for patients. The most important care and preventive measures for long-term complications in PBC patients are outlined.

PBC patients should undergo regular medical check-ups to monitor potential changes in liver function. These follow-ups include periodic blood tests and imaging studies. Elevated levels of alkaline phosphatase are one of the main markers of PBC and should be regularly measured. A decrease in this enzyme indicates improved bile flow and reduced inflammation. The accumulation of bilirubin in the blood is a sign of bile duct obstruction, which can lead to jaundice (yellowing of the skin) and disease progression. Fibroscan and ultrasound are used to assess fibrosis and liver damage and can aid in the early diagnosis of cirrhosis.

Effective medications for controlling PBC help improve bile flow, reduce inflammation, and prevent disease progression. Regular use of these medications under medical supervision is essential.

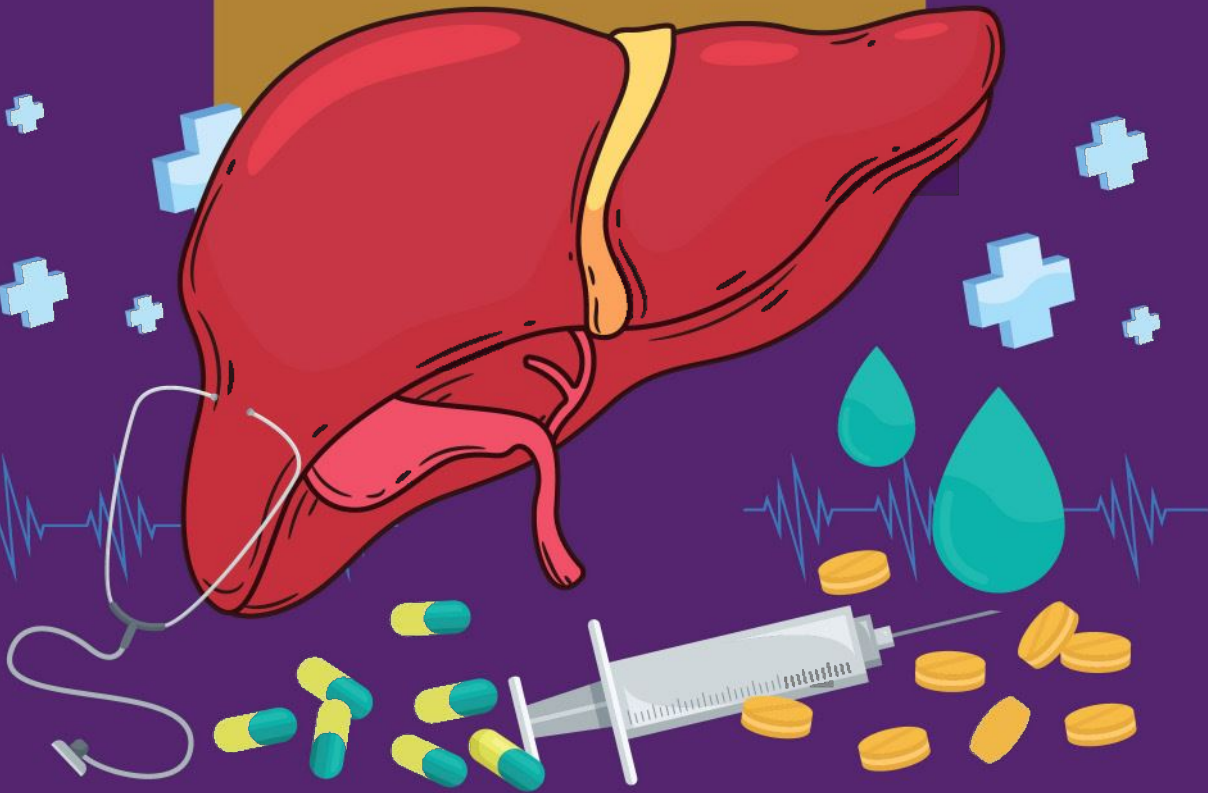
Cirrhosis is a stage where the liver is severely damaged, and healthy liver tissue is replaced with fibrotic tissue. This condition can lead to liver failure and the need for a liver transplant. If the disease progresses to cirrhosis, the doctor may require further evaluations, such as elastography (Fibroscan) or liver biopsy, to assess the extent of fibrosis and liver damage more precisely. In advanced stages of cirrhosis, a liver transplant may be the only treatment option. A liver transplant can save the patient's life and improve their quality of life.

A proper diet, such as consuming foods rich in fiber and vitamins while avoiding saturated fats, can improve liver function. Excessive fat intake can worsen symptoms. Alcohol consumption can severely damage the liver and accelerate disease progression. PBC patients should completely avoid alcohol. Engaging in mild, regular physical activity such as walking and yoga can enhance overall health and reduce stress, preventing symptom exacerbation.

Itching of the skin is a common symptom in PBC that may require medication. The doctor may prescribe drugs such as cholestyramine or naltrexone. In advanced stages of the disease, patients may need supportive treatment for complications related to cirrhosis, such as abdominal swelling (ascites). These treatments include the use of diuretics and reduced salt intake.

Managing PBC requires regular medical follow-ups, adherence to prescribed medications, and maintaining a healthy lifestyle. Preventive measures, timely diagnosis, and regular medication use can prevent the disease from progressing to more dangerous stages, such as cirrhosis. Following these guidelines will increase longevity and improve the quality of life for patients.

BOOK 3

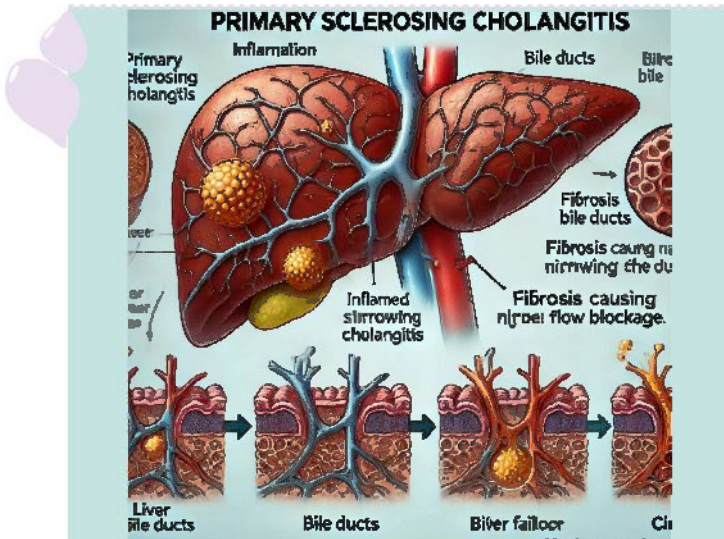


Primary Sclerosing Cholangitis

Chapter 1

What is Primary Sclerosing Cholangitis?

Primary Sclerosing Cholangitis (PSC) is a rare, chronic disease that gradually causes inflammation and damage to the bile ducts both inside and outside the liver. These ducts are responsible for transporting bile from the liver to the small intestine, where bile aids in the digestion of fats. In PSC, ongoing inflammation leads to the formation of scar tissue (fibrosis) in the bile ducts. This scarring narrows the ducts, causing blockages and ultimately disrupting the normal flow of bile. As a result, bile builds up in the liver, leading to liver damage, which may progress to cirrhosis (severe scarring of the liver) and liver failure.



This schematic illustration clearly depicts the progression of Primary Sclerosing Cholangitis (PSC). The image shows the inflammation of bile ducts, fibrosis, obstruction of bile flow, and the progression towards cirrhosis and liver failure.

Pathogenesis of Primary Sclerosing Cholangitis (PSC)

In the early stages of PSC, chronic inflammation of the bile ducts leads to the formation of fibrous tissue (scarring) around the ducts. Over time, this scarring narrows the ducts, causing reduced or complete blockage of bile flow. The reduced bile flow can result in bile accumulation in the liver, leading to damage to liver cells and further inflammation. This damage gradually transforms healthy liver tissue into fibrous tissue, leading to cirrhosis. In cirrhosis, healthy liver tissue is replaced by scar tissue, severely impairing liver function. In severe cases, this disease may lead to liver failure.

Complications and Associated Issues of PSC

As a chronic condition, PSC can lead to various complications, some of which are directly related to liver and bile duct damage, while others involve non-liver-related issues. Here is more information on common complications of the disease and how they manifest:

- **Cirrhosis and Liver Failure:** PSC gradually causes severe damage to the liver tissue. With narrowing and obstruction of the bile ducts, bile cannot properly flow from the liver to the intestines. The accumulation of bile in the liver leads to damage to liver cells and further inflammation. This chronic inflammation and fibrosis bring the liver closer to cirrhosis, a condition characterized by extensive scarring of the liver, which impairs its ability to function. In advanced cirrhosis, the liver can no longer perform essential functions such as detoxifying the blood, producing necessary proteins, and producing bile. Patients with advanced cirrhosis may require a liver transplant.

- **Cholangiocarcinoma:** PSC increases the risk of developing cholangiocarcinoma, a type of bile duct cancer. This cancer originates in the bile ducts and is usually very aggressive. PSC patients should undergo regular monitoring to detect early signs of cholangiocarcinoma, as this cancer can progress rapidly if not diagnosed early. Diagnostic methods such as imaging and tumor marker assessments can help in early detection.

- **Recurrent Bile Duct Infections (Bacterial Cholangitis):** The narrowing and blockage of bile ducts lead to bile accumulation, creating an environment conducive to bacterial growth. This condition can cause recurrent infections in the bile ducts, known as bacterial cholangitis. These infections may present with fever, abdominal pain, and jaundice and require immediate treatment with antibiotics. In severe cases, drainage of the bile ducts through surgery or other methods may be necessary.

- **Gallbladder Failure:** Prolonged obstruction of the bile ducts can also disrupt bile flow to the gallbladder. This disruption may lead to the formation of gallstones or inflammation of the gallbladder. Symptoms may include severe abdominal pain, nausea, and vomiting, and in some cases, gallbladder removal (cholecystectomy) may be required.

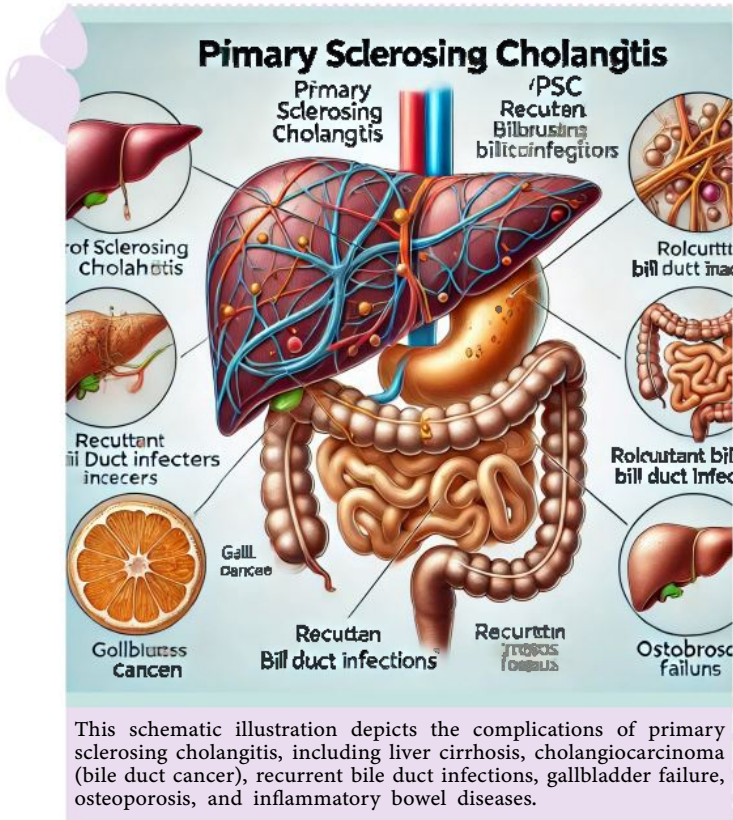
- **Osteoporosis (Osteopenia and Osteoporosis):** A common complication of PSC is reduced bone density. This issue arises due to impaired fat absorption and deficiency of fat-soluble vitamins (such as vitamins D and K), which are critical for calcium absorption and bone health. A deficiency in these vitamins can lead to osteopenia (mild bone loss) and, eventually, osteoporosis (severe bone loss), increasing the risk of fractures. Patients may need vitamin D and calcium supplements, with regular monitoring of bone density under medical supervision.

- **Inflammatory Bowel Disease (IBD):** PSC is often associated with inflammatory bowel diseases such as ulcerative colitis. In some studies, up to 75% of individuals with PSC have some form of IBD. These conditions cause inflammation and ulcers in the intestines, leading to symptoms such as abdominal pain, bloody diarrhea, and weight loss. Additionally, the presence of IBD can increase the risk of colorectal cancer in these patients.

- **Severe Itching (Pruritus):** A relatively common complication of PSC is severe and widespread itching. This itching is caused by the accumulation of bile in the liver and bile ducts and the body's inability to properly excrete bile waste. Itching can be highly debilitating and significantly affect the quality of life of

patients. Treatment for itching usually involves medications that help increase bile excretion.

• **Bile Duct Failure:** Prolonged narrowing and blockage of the bile ducts can lead to complete bile duct failure. This condition causes a reduction or complete cessation of bile flow to the small intestine, leading to malabsorption of nutrients, especially fats and fat-soluble vitamins (A, D, E, and K). This can result in severe nutritional deficiencies and associated complications.



Extrahepatic Complications

Patients with primary sclerosing cholangitis may experience extrahepatic complications, affecting various parts of the body beyond the liver. These complications include gastrointestinal issues, skin conditions, and even involvement of the nervous and cardiovascular systems. Additionally, some patients may develop other autoimmune disorders, such as hypothyroidism or type 1 diabetes.

PSC, as a chronic and complex disease, can lead to numerous complications, ranging from cirrhosis and liver failure to bile duct cancer and extrahepatic problems. Early diagnosis and proper management of symptoms and complications can improve the quality of life for patients and help prevent the progression of the disease. In advanced cases of PSC, liver transplantation is considered the final treatment for patients who develop liver failure.

Chapter 2

Primary Sclerosing Cholangitis in Iran

This chapter focuses on the research efforts and the prevalence of primary sclerosing cholangitis in Iran, as well as the treatment efforts in specialized centers. PSC is a rare and chronic disease, and although it is not widely recognized in Iran, there has been increasing attention toward it in recent years. Significant research and medical efforts are being made to better understand and improve the condition of PSC patients in the country.

Prevalence and Research in Iran

Accurately estimating the prevalence of PSC in Iran is challenging due to the rarity of the disease and the lack of comprehensive national epidemiological studies. However, some studies conducted in large medical centers and universities, particularly in Tehran, Shiraz, Mashhad, and Isfahan, have shown that PSC is often observed alongside inflammatory bowel diseases, such as ulcerative colitis, in patients.

One of the key characteristics of PSC in Iran is its strong association with ulcerative colitis. Many Iranian patients diagnosed with PSC also suffer from some form of IBD. This co-occurrence plays a crucial role in the timely diagnosis and treatment of PSC. Additionally, studies indicate that PSC tends to affect young to middle-aged men more frequently, although women can also develop the disease.

Genetic and Diagnostic Research

In Iran, numerous studies are being conducted to improve the understanding of PSC. Researchers are focusing on various aspects of the disease, including genetic factors, innovative diagnostic methods, and effective treatments. One of the key studies in this field is the investigation of genetic factors contributing to the development of PSC in the Iranian population. The aim is to identify hereditary factors and their connection to PSC. Some studies have found that specific genetic mutations may increase the risk of PSC in certain individuals. This research could aid in better understanding the genetic roots of PSC and the development of targeted treatments for Iranian patients.

Additionally, advanced imaging techniques such as MRCP (magnetic resonance cholangiopancreatography) are widely used in Iran's specialized centers to diagnose and monitor the progression of PSC. MRCP is one of the main diagnostic tools that allows physicians to identify strictures in the bile ducts, helping them determine the best treatment options for patients.

Treatment Approaches in Iran

Research in Iran has also focused on evaluating the effectiveness of new drugs in controlling the progression of PSC and alleviating symptoms. These studies have examined the use of immune-modulating and anti-inflammatory drugs to reduce the severity of the disease and improve patients' quality of life.

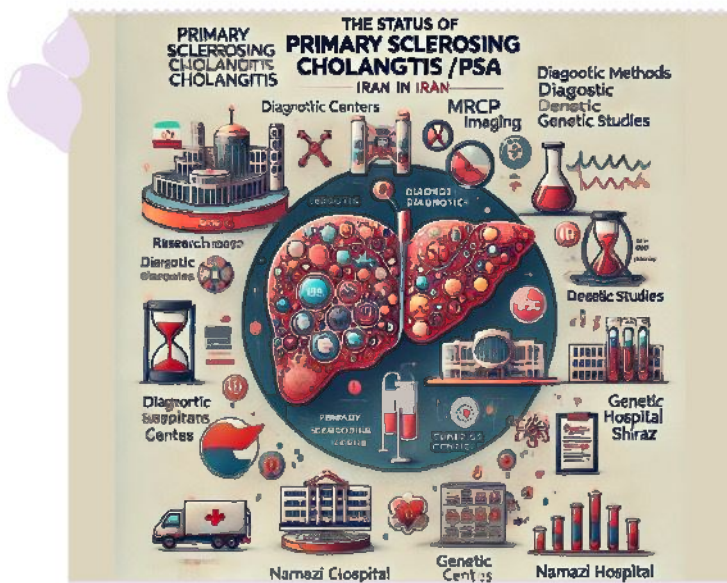


Standard treatment for PSC in Iran, as in other countries, includes anti-inflammatory drugs and immune system modulators. Ursodeoxycholic acid is one commonly prescribed medication that helps improve bile flow and alleviate symptoms, although it does not necessarily extend life expectancy or prevent disease progression.

In advanced cases where PSC leads to cirrhosis and liver failure, liver transplantation becomes the only treatment option. Iran is a leader in liver transplantation in the region, with Namazi Hospital in Shiraz recognized as one of the main liver transplant centers in the Middle East. Patients with end-stage PSC can undergo liver transplantation at these specialized centers. Liver transplants have been highly successful for many PSC patients in Iran, though access to transplants remains a significant challenge due to a limited number of organ donors.

Challenges and Awareness

While considerable progress has been made in the diagnosis and treatment of PSC in Iran, there are still challenges to overcome. One of the major challenges is the lack of public and even medical awareness about PSC. Due to its rarity, many general practitioners and even some specialists may face difficulties in diagnosing the disease early.



This infographic depicts the status of Primary Sclerosing Cholangitis in Iran. It clearly illustrates important research centers, diagnostic methods such as MRCP imaging, genetic studies, and liver transplant centers like Namazi Hospital in Shiraz.

There is also a need for further development of scientific research on Primary Sclerosing Cholangitis in Iran. So far, most studies have been conducted in major specialized centers, and data on the prevalence of the disease and risk factors in other regions of the country are limited. Educational and awareness programs for

doctors and medical staff, along with investment in broader research, can help improve the diagnosis and treatment of PSC in Iran.

PSC in Iran remains a rare and challenging disease, but significant progress has been made in diagnosis and management through research and treatment efforts. Liver transplantation, as the last resort for patients with liver failure due to PSC, is successfully performed in Iran. However, there is a need for greater awareness, more epidemiological studies, and further research on PSC so that Iranian patients can benefit from the best available treatment and disease management methods.



Chapter 3

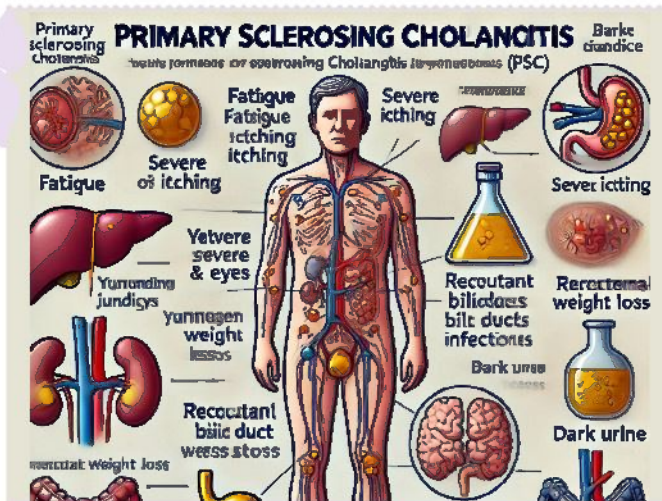
Symptoms and Signs of Primary Sclerosing Cholangitis

Primary Sclerosing Cholangitis presents a range of symptoms that can vary from person to person. In the early stages, the disease may be asymptomatic, but as it progresses, its signs and symptoms gradually become apparent. In this section, we will examine the common symptoms of PSC, particularly fatigue and itching, which are among the most prominent and frequent symptoms of the disease.

Fatigue is one of the most common and debilitating symptoms experienced by patients with PSC. Many patients feel they lack the energy to perform daily activities and, even after sufficient rest, still suffer from overwhelming fatigue. This fatigue can be caused by various factors such as:

- **Liver dysfunction:** The liver's inability to properly detoxify the blood and the accumulation of toxins lead to a general decrease in energy levels in the body.
- **Chronic inflammation:** Persistent inflammation of the bile ducts and liver triggers the release of inflammatory chemicals, which can exacerbate the sensation of continuous fatigue.
- **Vitamin deficiency:** Reduced absorption of fat-soluble vitamins (A, D, E, and K) due to impaired bile secretion can contribute to feelings of fatigue.

Fatigue associated with PSC often develops gradually and may worsen as the disease progresses. Managing fatigue can be challenging due to its multiple causes, and doctors usually focus on controlling symptoms and improving the patient's quality of life.



This schematic illustration shows the common symptoms of Primary Sclerosing Cholangitis (PSC). Symptoms such as fatigue, severe itching, jaundice (yellowing of the skin and eyes), abdominal pain, unintended weight loss, recurrent bile duct infections, dark urine, and pale stools are clearly depicted in the image. Fatigue and itching are emphasized as prominent symptoms.

Itching

Itching is another common symptom in primary sclerosing cholangitis and can be very debilitating. This itching usually occurs due to the accumulation of bile in the body, which happens because of narrowing and obstruction of the bile ducts, preventing bile from being properly transferred to the intestine. Over time, bile waste materials enter the bloodstream, causing skin irritation and itching. Itching can appear in different forms; it may be widespread or localized, but it often starts in the hands and feet. It may be severe and debilitating, significantly affecting the patient's quality of life. It worsens at night and causes sleep disturbances for the patient.

Itching in primary sclerosing cholangitis can range from mild to severe, and in some cases, it is so severe that it prevents patients from performing daily activities. To control this symptom, doctors usually use medications such as cholestyramine, which helps excrete bile. In more severe cases, advanced treatments like ursodeoxycholic acid and, in some cases, bile drainage methods using surgery or bile duct ballooning are used.

In addition to fatigue and itching, other symptoms are also observed in patients with primary sclerosing cholangitis. Yellowing of the skin and the whites of the eyes is another common symptom of primary sclerosing cholangitis, which occurs due to the accumulation of bilirubin (a bile waste product) in the blood. Yellowing may increase with disease progression and indicates severe narrowing of the bile ducts. Patients with primary sclerosing cholangitis may experience abdominal pain, especially in the upper right part of the abdomen. This pain occurs due to inflammation of the bile ducts and liver and may be exacerbated by bile duct obstruction or recurrent infections.

Unintentional weight loss and loss of appetite are other symptoms associated with primary sclerosing cholangitis. These symptoms may be due to persistent inflammation, insufficient nutrient absorption, and impaired fat digestion.

Patients with primary sclerosing cholangitis are prone to recurrent bile duct infections due to bile duct obstruction. These infections, known as bacterial cholangitis, can present with symptoms such as fever, abdominal pain, and jaundice and require immediate treatment with antibiotics. The accumulation of bile and bilirubin in the blood can lead to pale stool and dark urine, indicating disruption of the normal bile flow.

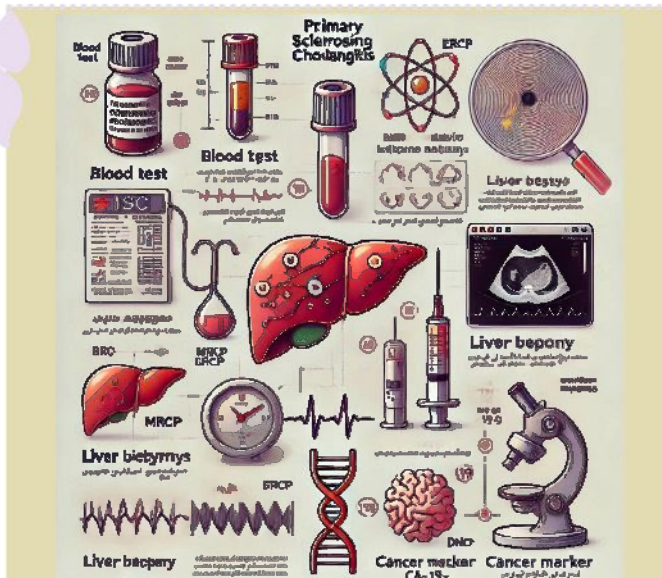
Symptoms of primary sclerosing cholangitis may gradually appear over time, and in some cases, remain asymptomatic until the disease reaches advanced stages. Fatigue and itching are among the prominent and common symptoms of this disease that can significantly affect the patients' quality of life. In addition, other symptoms such as yellowing, abdominal pain, weight loss, and recurrent bile duct infections may also be seen in patients. Early diagnosis and management of these symptoms can help improve the patient's condition and reduce disease progression.



Chapter 4

Diagnostic Methods for Primary Sclerosing Cholangitis

Diagnosing primary sclerosing cholangitis (PSC) is challenging due to its rarity and complex nature. In many cases, patients may not exhibit clear symptoms for a long time, and the disease is usually diagnosed in more advanced stages. To confirm the diagnosis and assess the extent of liver and bile duct damage, a combination of laboratory tests, imaging techniques, and biopsies are used. In this section, we will explore the various diagnostic methods for PSC.



This schematic illustration depicts the diagnostic methods for Primary Sclerosing Cholangitis (PSC), including blood tests (liver enzymes, bilirubin, autoimmune antibodies), imaging techniques (MRCP, ERCP, ultrasound), liver biopsy, genetic testing, and tumor marker screening (CA 19-9). Each method is clearly represented with symbols and simple explanations.

📌 Blood Tests

The first step in diagnosing Primary Sclerosing Cholangitis (PSC) often involves blood tests to assess liver function, bilirubin levels, and related enzymes. These tests help doctors identify early signs of liver damage or bile duct obstruction.

📍 A. Liver Enzyme Tests

• **Alkaline Phosphatase (ALP):** In patients with PSC, the ALP enzyme level is typically elevated. This enzyme is an indicator of bile duct damage, and its increase can be used as a marker for bile duct obstruction.

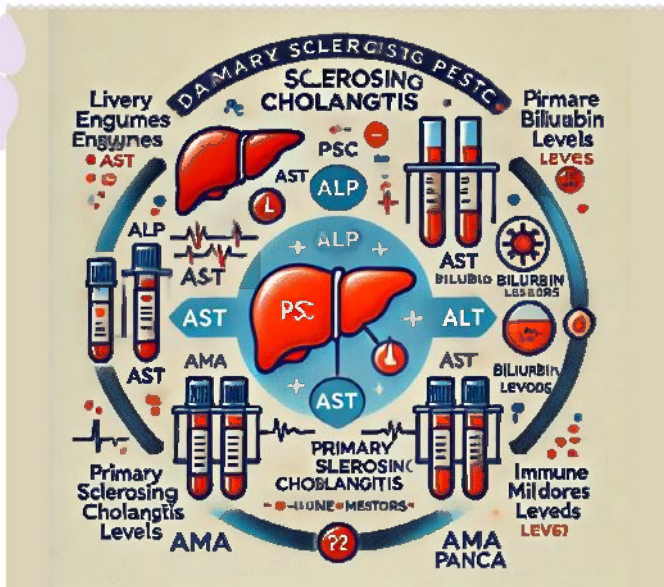
• **Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT):** These enzymes are usually used as indicators of liver cell damage. In PSC patients, their levels may increase, but typically not as much as ALP.

• **B. Bilirubin Test**

• **Bilirubin:** Elevated bilirubin in the blood can occur due to bile duct obstruction and the buildup of bile in the liver. Yellowing of the skin and eyes (jaundice) is often associated with increased bilirubin levels in the blood.

• **C. Immune Markers**

• In some patients, **Anti-Mitochondrial Antibodies (AMA)** or **Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (pANCA)** may be present, which can be identified in blood tests. Although these markers are not specific to PSC, they can aid in diagnosis.



This schematic illustration depicts the blood tests used for diagnosing Primary Sclerosing Cholangitis (PSC), including tests for liver enzymes (ALP, AST, ALT), bilirubin levels, and immune markers (AMA and pANCA). Each test is represented with simple symbols and explanations of its role in diagnosing PSC.

Imaging Techniques Imaging is one of the most important tools in diagnosing Primary Sclerosing Cholangitis (PSC). These methods help doctors examine the bile ducts and identify any blockages or strictures.

• **A. Ultrasound**

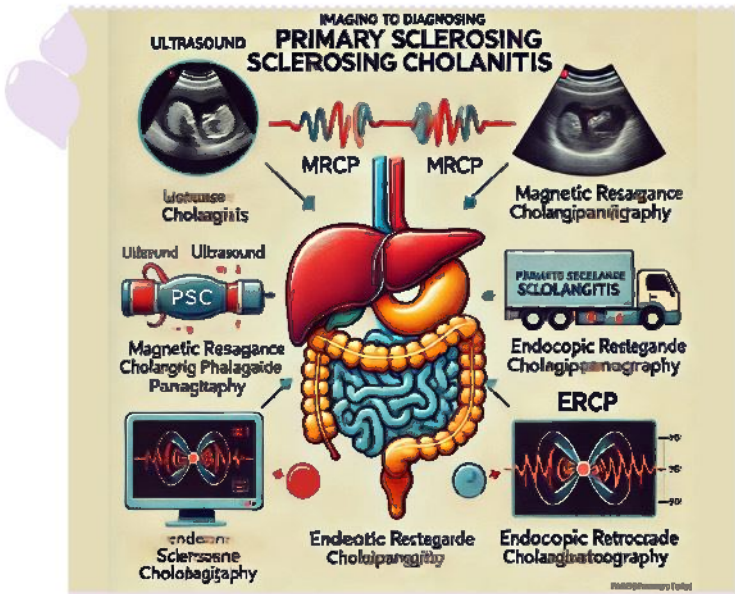
Ultrasound is widely used as a non-invasive method to assess the condition of the liver and bile ducts. Although it can help detect bile duct obstructions, it is generally not sufficient for a definitive diagnosis of PSC. Ultrasound is more commonly used to rule out other bile-related problems such as gallstones.

B. Magnetic Resonance Cholangiopancreatography (MRCP)

MRCP is one of the best non-invasive imaging techniques for diagnosing PSC. It uses magnetic resonance imaging (MRI) to provide a detailed view of the intrahepatic and extrahepatic bile ducts and can show areas of narrowing, blockage, or dilation. MRCP is recommended as the first-line imaging option for PSC due to its high accuracy and non-invasive nature, without the need for invasive tools.

C. Endoscopic Retrograde Cholangiopancreatography (ERCP)

ERCP is an invasive procedure that involves inserting an endoscope into the bile ducts and injecting a contrast dye to provide a precise image of the bile ducts. ERCP can be used for both diagnosis and treatment, such as relieving bile duct blockages. Although highly accurate, ERCP carries risks and potential side effects, so it is usually reserved for specific cases and after non-invasive methods like MRCP have been used.



This schematic illustration depicts the imaging techniques used for diagnosing Primary Sclerosing Cholangitis (PSC), including ultrasound, MRCP (Magnetic Resonance Cholangiopancreatography), and ERCP (Endoscopic Retrograde Cholangiopancreatography). Each method is visually presented along with explanations regarding its role in diagnosing PSC.

Liver Biopsy (Biopsy)

A liver biopsy is a diagnostic procedure in which a small sample of liver tissue is obtained and examined under a microscope. Although a biopsy is not usually necessary for the direct diagnosis of Primary Sclerosing Cholangitis (PSC), it may be used in certain cases where a definitive diagnosis cannot be made through imaging, or when an assessment of liver fibrosis (scarring) is needed.

A. Diagnosis of Fibrosis and Cirrhosis

A liver biopsy can reveal the extent of fibrosis or cirrhosis in the liver. In advanced stages of PSC, the liver tissue may be replaced by widespread scars, a condition referred to as cirrhosis.

B. Evaluation of Other Liver Diseases

In some cases, a biopsy may be performed to rule out other liver diseases such as autoimmune cholangitis or chronic hepatitis.

Other Diagnostic Tests

Depending on the patient's condition, additional tests may be used for better diagnosis or to rule out other similar diseases.

A. Liver Elastography

Elastography is a non-invasive method that uses sound waves to measure liver stiffness. This method can help determine the degree of fibrosis in the liver and may be used as an alternative to biopsy in some patients.

Genetic Tests

Although primary sclerosing cholangitis (PSC) is typically considered an autoimmune disease, some studies have shown that genetic factors may also play a role in its development. In specific cases, genetic testing may be suggested to investigate hereditary risk factors.

The diagnosis of PSC is a complex process that requires a combination of blood tests, imaging, and in some cases, biopsy. MRCP (magnetic resonance cholangiopancreatography) is one of the best non-invasive imaging tools for diagnosing this disease, while ERCP (endoscopic retrograde cholangiopancreatography), due to its invasive nature, is used as both a diagnostic and therapeutic tool in specific cases. Blood tests can indicate early signs of liver damage and bile duct obstruction, and liver biopsy helps assess fibrosis and cirrhosis. Early diagnosis and the use of appropriate imaging methods can improve treatment outcomes and slow disease progression.

Chapter 5

The Association of Primary Sclerosing Cholangitis (PSC) with Inflammatory Bowel Disease and Other Autoimmune Diseases

Primary sclerosing cholangitis (PSC) is an autoimmune disease often associated with other autoimmune disorders, particularly inflammatory bowel diseases (IBD). Understanding these associations can offer insights into the mechanisms of PSC pathogenesis and aid in more effective management. This section explores the connection between PSC and inflammatory bowel diseases, such as ulcerative colitis and Crohn's disease, as well as other autoimmune diseases.

One of the most well-known associations in patients with PSC is the strong link to inflammatory bowel diseases. It is estimated that around 70-80% of PSC patients have some form of IBD. In most cases, this association is seen with ulcerative colitis, though some patients may also have Crohn's disease.

- **Ulcerative Colitis** is the most common inflammatory bowel disease linked to PSC. This chronic condition leads to persistent inflammation and ulcers in the inner lining of the colon. Patients with ulcerative colitis often experience symptoms such as bloody diarrhea, abdominal pain, and weight loss. In some cases, ulcerative colitis may remain mild, and patients with PSC may not show significant symptoms. However, studies have shown a particularly strong connection between PSC and ulcerative colitis, putting PSC patients at a higher risk for colon cancer. As a result, doctors typically recommend regular colonoscopies for PSC patients to monitor colon health.

- **Crohn's Disease** is another type of inflammatory bowel disease that may be associated with PSC. Unlike ulcerative colitis, which affects only the colon, Crohn's disease can impact any part of the digestive tract, from the mouth to the anus. Symptoms of Crohn's include chronic diarrhea, abdominal pain, and weight loss. The link between PSC and Crohn's disease is less common than with ulcerative colitis, but it is still observed in some patients. These cases can present more severe inflammation in both the intestines and bile ducts, making management more challenging.

In addition to its association with inflammatory bowel diseases, PSC is also linked to other autoimmune disorders. Many PSC patients may develop additional autoimmune conditions, complicating the management of their health.

- **Autoimmune Hepatitis** is a disease that leads to chronic liver inflammation due to the immune system attacking liver cells. In some cases, PSC and autoimmune hepatitis can coexist in what is known as overlap syndrome. This condition can lead to more severe liver damage and increase the likelihood of needing a liver transplant.

- **Rheumatoid Arthritis** is an autoimmune disease that causes inflammation and destruction of the joints. Some PSC patients may also develop rheumatoid arthritis, experiencing symptoms like joint pain and inflammation.

- **Ankylosing Spondylitis** is a chronic inflammatory disease that leads to inflammation of the spinal joints and has also been observed in PSC patients. Those affected by both ankylosing spondylitis and PSC may experience back



inflammation and damage. Similarly, in inflammatory bowel diseases, the immune response to the cells lining the intestines leads to chronic inflammation. This commonality in immune mechanisms may explain the coexistence of these diseases.

The coexistence of PSC with inflammatory bowel diseases and other autoimmune diseases can complicate disease management. It requires multi-faceted treatment and coordination between specialists such as gastroenterologists, rheumatologists, immunologists, and endocrinologists. The treatment of these patients often involves anti-inflammatory and immunosuppressive drugs, which can help manage multiple conditions simultaneously.

PSC, as an autoimmune disease, is often associated with inflammatory bowel diseases like ulcerative colitis and Crohn's disease, as well as other autoimmune conditions such as autoimmune hepatitis, rheumatoid arthritis, and type 1 diabetes. The connection between these diseases lies in shared immune response mechanisms that lead to inflammation and tissue damage. Understanding these associations can improve diagnostic and therapeutic approaches, enhancing patients' quality of life.



itching (pruritus) in PSC patients, studies suggest that it has limited effectiveness in slowing disease progression or extending life expectancy. Its primary role is symptom control rather than disease modification.

■ How Ursodeoxycholic Acid Works in PSC

● Improving Bile Flow

UDCA stimulates bile secretion and facilitates its movement from the liver to the intestines, which helps reduce bile accumulation in the bile ducts and liver.

● Anti-inflammatory Effects

UDCA may reduce inflammation in the bile ducts, helping to prevent further damage to liver and bile duct cells.

● Protecting Liver Cells

It protects liver cells from toxic bile acids by reducing their presence, thus helping preserve liver function.

● Symptom Relief

UDCA can alleviate the common symptom of itching (pruritus) caused by bile buildup, significantly improving the quality of life for PSC patients.

● Improving Liver Enzymes

UDCA has been shown to improve liver enzyme levels, such as alkaline phosphatase (ALP), which may indicate reduced stress on the liver and bile ducts.

Limitations of UDCA in PSC

● Limited Disease Progression Impact

Although UDCA improves some clinical markers, it does not significantly slow the progression of fibrosis or bile duct blockages.

● No Impact on Survival

UDCA does not increase life expectancy or prevent complications like liver failure or cirrhosis. Even with its use, patients may still progress to advanced stages of the disease.

In conclusion, while UDCA can help manage symptoms and improve liver enzyme levels in PSC, it does not prevent the disease's progression or extend the patient's lifespan, and advanced stages like cirrhosis may still develop despite treatment.



in the body, thereby decreasing its accumulation in the liver and blood. As bile levels drop, the severe itching caused by bile deposition in tissues and skin is relieved. This mechanism reduces skin irritation and alleviates itching, one of the most bothersome symptoms in PSC patients.

Cholestyramine is prescribed as a primary medication for relieving itching in PSC patients. It is particularly useful for patients who experience itching due to bile buildup. Relieving the itch can significantly improve the quality of life for these patients. In many cases, cholestyramine can quickly relieve itching. Patients suffering from severe and disabling itching may see symptom improvement within a few days of starting treatment with cholestyramine.

Although cholestyramine helps relieve itching, it does not affect the progression of PSC or prevent bile duct fibrosis and narrowing. Cholestyramine is solely used for symptom control and cannot change the course of the disease.

One issue with cholestyramine is its gastrointestinal side effects. Patients may experience constipation or bloating after taking this drug. In some cases, these side effects can be disabling, and dose adjustment or the use of supplemental medications to reduce these effects may be required. Cholestyramine can also reduce the absorption of fat-soluble vitamins A, D, E, and K. These vitamins are essential for overall health, and reduced absorption can lead to problems such as osteoporosis (due to vitamin D deficiency) and bleeding disorders (due to vitamin K deficiency). Therefore, patients taking cholestyramine may need vitamin supplements.

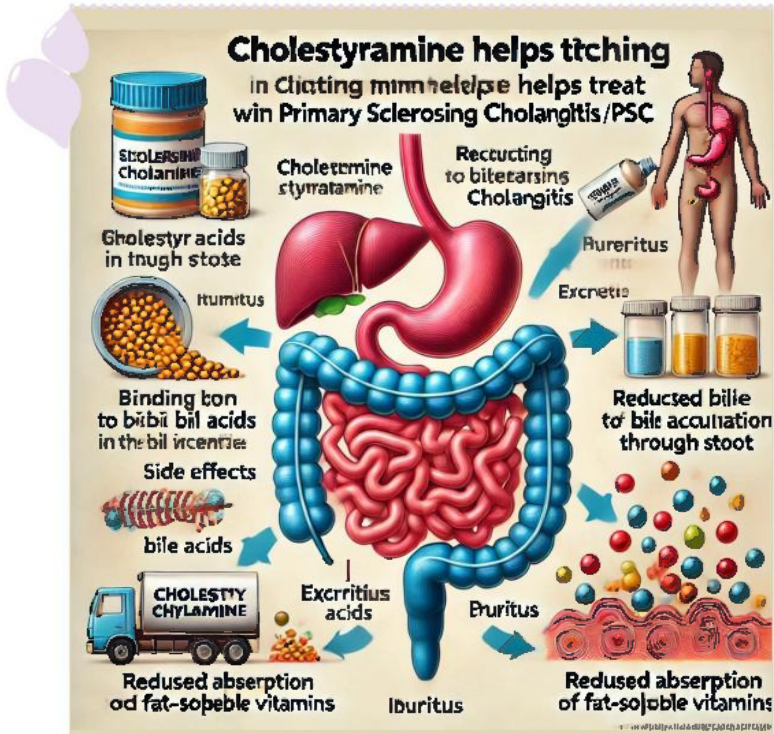
Cholestyramine is used as a symptomatic treatment to relieve itching in PSC patients. Although it does not cure the disease, it is highly effective for controlling one of the main symptoms of PSC. Using cholestyramine improves the quality of life for patients suffering from severe itching. In many cases, cholestyramine is used as adjunct therapy alongside other medications and treatments such as UDCA or immunosuppressive drugs. Combining these therapies can help better control symptoms and manage the disease.

The usual dose of cholestyramine for treating itching in patients with Primary Sclerosing Cholangitis (PSC) ranges from 4 to 16 grams per day, taken as an oral powder. This powder should be dissolved in liquids such as water or juice and then consumed. It is best to take cholestyramine after meals to maximize its bile-binding effect. Additionally, to prevent reduced vitamin absorption, a time gap should be maintained between taking cholestyramine and vitamin supplements.

One of the common side effects of cholestyramine is constipation, which can occur due to the reduced absorption of water and bile in the intestine. To mitigate this side effect, patients may need to consume more fluids and fiber-rich foods. Gastrointestinal symptoms can also occur in some patients and are usually managed by adjusting the dose of the medication or using additional treatments.

As mentioned, cholestyramine can reduce the absorption of fat-soluble vitamins. Therefore, patients may need to take vitamin supplements. Cholestyramine is an effective bile acid sequestrant that is widely used to treat severe itching in PSC patients. By reducing bile levels in the body, it helps relieve itching and improves the quality of life for patients. Although cholestyramine cannot stop the progression of the disease, it plays a significant role in controlling the symptoms

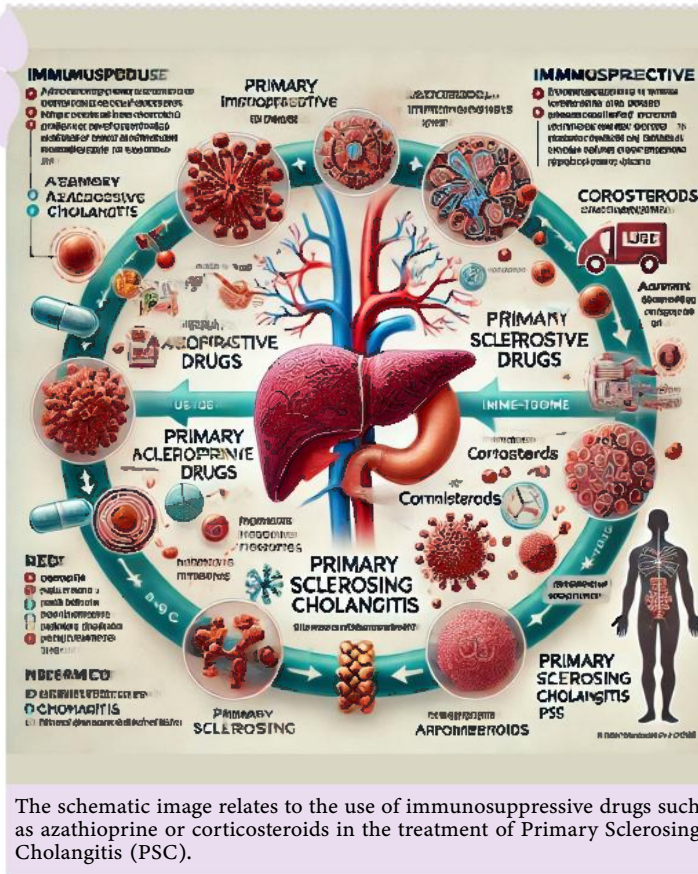
of PSC. However, patients should be aware of gastrointestinal side effects and reduced vitamin absorption, and take vitamin supplements as needed.



This schematic image shows how cholestyramine helps treat itching (pruritus) in patients with Primary Sclerosing Cholangitis (PSC). The image illustrates the process of cholestyramine binding to bile acids in the intestine and their excretion through stool, which reduces bile accumulation and relieves itching. It also highlights side effects such as gastrointestinal issues and reduced absorption of fat-soluble vitamins.

C. Immunosuppressive drugs

In some cases, doctors may use immunosuppressive drugs such as azathioprine or corticosteroids to reduce inflammation and control the body's immune responses in patients with Primary Sclerosing Cholangitis (PSC). These drugs directly affect the reduction of immune system inflammation and are widely used in managing various autoimmune diseases. However, their effectiveness in treating PSC is generally limited and is mostly prescribed for patients who, in addition to PSC, also suffer from other autoimmune conditions like autoimmune hepatitis.



The schematic image relates to the use of immunosuppressive drugs such as azathioprine or corticosteroids in the treatment of Primary Sclerosing Cholangitis (PSC).

C. Immunosuppressive Drugs

• **Azathioprine** is an immunosuppressive drug that reduces the activity of immune cells (such as lymphocytes), leading to decreased inflammation and tissue damage in the body. It is widely used to treat autoimmune diseases such as autoimmune hepatitis and inflammatory bowel diseases. Azathioprine works by inhibiting the production of DNA in immune cells, reducing their activity. This helps decrease inflammation and the body's immune response to its own tissues. However, azathioprine alone does not significantly prevent the progression of Primary Sclerosing Cholangitis (PSC). It is mainly prescribed for patients with PSC who also have autoimmune hepatitis or other autoimmune diseases. In these patients, azathioprine can help reduce liver and bile duct inflammation but has no direct impact on the long-term improvement of PSC. In patients with overlap syndrome (PSC and autoimmune hepatitis), azathioprine can help control liver inflammation and reduce the need for corticosteroids.

Corticosteroids like prednisone are widely used to reduce immune system inflammation in autoimmune diseases. These drugs work by suppressing immune cell activity and inflammatory cytokine production, which reduces inflammation in the body. Corticosteroids are particularly effective in reducing acute inflammation. They are effective in treating severe liver and bile duct

inflammation caused by autoimmune diseases like autoimmune hepatitis. In patients with PSC and autoimmune hepatitis, these drugs can help reduce inflammation and prevent further liver damage. However, research shows that corticosteroids do not significantly prevent the progression of PSC and are not generally recommended for treating PSC alone. They are usually prescribed for patients who have other autoimmune diseases along with PSC.

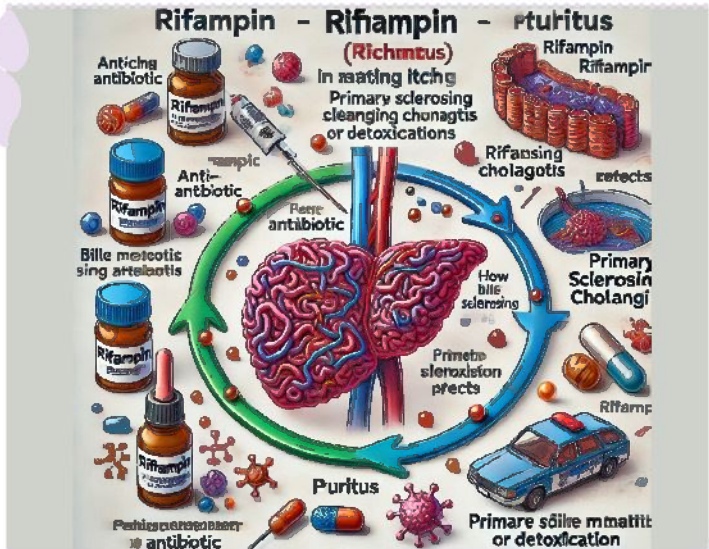
A common side effect of corticosteroids is weight gain and fluid retention, which may lead to swelling and high blood pressure. Long-term use of corticosteroids can also reduce bone density, increasing the risk of osteoporosis. These drugs weaken the immune system and increase the risk of infections, and prolonged use may lead to increased blood sugar levels and steroid-induced diabetes.

Immunosuppressive drugs like azathioprine and corticosteroids can help reduce inflammation and control immune responses in patients with PSC, especially when PSC is accompanied by other autoimmune diseases. However, their impact on the long-term improvement of PSC is limited, and they are typically prescribed for patients with PSC who also have autoimmune hepatitis or other autoimmune disorders. These drugs are generally used for symptom management and inflammation control, and careful monitoring is needed to minimize side effects.

D. Rifampin

Rifampin is an antibiotic widely used to treat bacterial infections such as tuberculosis. However, it is also used to treat certain non-infectious symptoms, such as severe itching in patients with PSC. Due to its unique properties, rifampin may be prescribed for PSC patients suffering from severe itching caused by bile accumulation in the body. Rifampin works by inhibiting hepatic microsomal enzymes, especially cytochrome P450 enzymes, altering the metabolism of certain bilirubin and bile compounds. This change can reduce the accumulation of bile substances that cause itching. In other words, rifampin changes bile metabolism, reducing skin-irritating substances in the body and relieving itching. Although rifampin is mainly known as an antibiotic, it may also have anti-inflammatory effects. This effect can help reduce bile duct inflammation and relieve symptoms related to bile accumulation.

Rifampin is recognized as an adjunct treatment for itching caused by PSC. Patients with PSC suffering from severe, disabling itching may experience symptom relief after taking this drug. In many cases, rifampin can quickly reduce itching, with patients seeing significant relief within a few days to a few weeks of starting treatment. The duration of rifampin use depends on the severity of the itching and the patient's response to treatment. Typically, the drug is prescribed for a few weeks to a few months, and if symptoms are controlled, its use may be reduced or discontinued.



The schematic image related to the use of rifampin (Rifampin) in treating itching in patients with Primary Sclerosing Cholangitis (PSC) is ready. This image clearly shows how rifampin affects bile metabolism and its role in reducing itching symptoms.

E. Antibiotics

In patients with Primary Sclerosing Cholangitis (PSC), one of the common complications is bacterial infection of the bile ducts, known as bacterial cholangitis. These infections occur due to bile duct obstruction and bile accumulation, and they can be very serious and dangerous. The use of antibiotics in such cases is essential, and prompt and effective treatment can prevent more severe complications and even death.



The schematic image related to the use of antibiotics for treating bacterial cholangitis in patients with Primary Sclerosing Cholangitis (PSC) is ready. This image clearly illustrates how infections occur and the use of antibiotics and interventional methods.

◦ **In Primary Sclerosing Cholangitis (PSC)**, ongoing inflammation and the formation of fibrosis in the bile ducts lead to narrowing and obstruction. These blockages prevent bile from flowing properly, causing it to accumulate in the liver and bile ducts. The buildup of bile and increased pressure in these ducts create an environment conducive to bacterial growth. Bacteria can enter the bile ducts through the bloodstream or intestines, causing bacterial infections in the bile ducts and liver.

Bacterial Cholangitis

When a bacterial infection occurs in the bile ducts, it is referred to as bacterial cholangitis. These infections usually spread quickly and can lead to serious complications such as systemic infections (sepsis), liver abscesses, and liver failure.

◦ **Fever** is one of the first symptoms of a bacterial infection in the bile ducts, usually accompanied by chills.

◦ **Pain** in the upper right abdomen (liver area) may occur due to inflammation and infection in the bile ducts and liver.

Bile duct obstruction and bacterial infection can cause **jaundice** (yellowing of the skin and eyes).

◦ **Nausea and vomiting** often occur as the infection progresses and inflammation increases.

Treatment

Treating bacterial cholangitis in patients with PSC is a medical emergency and requires prompt and aggressive treatment with antibiotics. The antibiotics used should cover a broad spectrum of bacteria, especially those commonly causing infections in the biliary system.

◦ **Ciprofloxacin** is commonly used to treat bile duct infections, as it covers a wide range of bacteria and penetrates bile tissues well.

◦ **Ceftriaxone** or **Cefotaxime** are also frequently used to treat bacterial infections of the bile ducts and can help rapidly alleviate infection symptoms.

In some patients with severe infection or severe bile duct obstruction, surgical or interventional procedures may be required, in addition to antibiotics, to open the bile ducts and drain the bile.

Surgical and Interventional Methods

Bacterial infections of the bile ducts (bacterial cholangitis) are a serious complication of PSC, requiring immediate and effective treatment with antibiotics. These infections arise from bile duct obstruction and bile buildup, and if not treated in time, they can lead to severe complications such as sepsis and liver failure. The use of broad-spectrum antibiotics such as fluoroquinolones, cephalosporins, and broad-spectrum penicillins is recommended as the main treatment. In some cases, surgical interventions or **ERCP** (Endoscopic Retrograde Cholangiopancreatography) are necessary to open the bile ducts. Regular follow-up after treatment is essential to prevent infection recurrence and improve the patient's overall condition.

Vancomycin

Vancomycin is an effective antibiotic that, besides its primary role in treating

◦ **Balloon Dilation** is another method used to widen narrowed bile ducts. Like stent placement, this procedure is performed via endoscopy, but instead of placing a permanent stent, a small balloon is sent to the site of the narrowing. The balloon is then inflated to widen the bile duct. Balloon dilation is a temporary treatment and often needs to be repeated. Bile duct strictures may recur over time.

◦ **Endoscopic Retrograde Cholangiopancreatography (ERCP)** is a widely used procedure for patients with Primary Sclerosing Cholangitis (PSC). This method allows doctors to visualize the bile ducts and use special tools to open obstructions or place stents.

In more severe cases, where bile duct strictures are complex and resistant to interventional treatments like stenting or balloon dilation, **biliary surgery** may be required. These surgeries are usually performed when non-surgical methods are ineffective.

Surgical and interventional methods for opening bile duct obstructions in PSC patients are of great importance. Stent placement and balloon dilation are minimally invasive methods that can quickly relieve obstructions, improve bile flow, and reduce symptoms. ERCP is also an important diagnostic and therapeutic tool that helps doctors evaluate and relieve obstructions in the bile ducts. In more severe cases, biliary surgery is the final option for treating complex strictures.

Liver Transplantation

In advanced cases of PSC that lead to cirrhosis or liver failure, liver transplantation is considered the only definitive treatment. Liver transplants are usually performed when liver function is severely impaired and the patient is at risk of death from liver failure. In PSC patients, a chronic and progressive disease, liver failure or cirrhosis may occur in the advanced stages. In these stages, liver function is severely compromised, and the patient is at risk of death due to liver failure. In such cases, liver transplantation is considered the only definitive treatment to save the patient's life. A liver transplant can improve liver function and enhance the quality of life for patients.

Patients with liver failure who experience symptoms such as severe jaundice, ascites (fluid buildup in the abdomen), gastrointestinal bleeding, and brain disorders (hepatic encephalopathy) are prioritized for liver transplantation. Liver failure means the liver can no longer maintain the body's metabolic balance. In many liver transplant centers, the **MELD score** (Model for End-Stage Liver Disease) is used to assess the severity of liver failure and prioritize patients. This score is calculated based on bilirubin levels, creatinine, and the international normalized ratio (INR). Patients with a high MELD score are prioritized for a transplant due to the severity of their liver failure.

Outcomes of liver transplantation in PSC patients are generally positive and successful. Many patients experience significant improvements in quality of life and liver function after the transplant. Following liver transplantation, most patients recover from symptoms related to liver failure and bile duct obstructions. Problems such as jaundice, severe itching, and extreme weakness caused by poor liver function typically improve after the transplant. Patients can often return to a normal life and perform daily activities without the previous limitations.



Although liver transplantation can be a definitive treatment for PSC, in some cases, PSC may recur after the transplant. This recurrence usually happens in the new bile ducts (i.e., in the transplanted liver) and may require additional treatments. However, the likelihood of PSC recurrence after transplantation is relatively low, occurring in about 20-25% of patients.

Liver transplantation is considered the only definitive treatment for PSC in the advanced stages of the disease. Patients at serious risk due to liver failure, cirrhosis, or severe bile duct complications can benefit from this treatment. The results of liver transplantation are generally successful, with most patients experiencing significant improvements in quality of life. Although PSC may recur after transplantation in some cases, the likelihood is relatively low, and the benefits of liver transplantation generally outweigh the risks.

flammation. Liver enzymes such as alkaline phosphatase and transaminases are usually elevated in these patients. They may experience jaundice, itching, fatigue, and abdominal pain.

The diagnosis of overlap syndromes is based on clinical symptoms, blood tests, liver biopsy, and autoimmune antibodies. Management usually involves multi-faceted treatment, including corticosteroids and immunosuppressive drugs to control inflammation, as well as disease-specific medications like Ursodeoxycholic Acid (UDCA) to improve bile flow.

■ IgG4-Related Sclerosing Cholangitis (IgG4-SC)

IgG4-related sclerosing cholangitis is an inflammatory disease characterized by elevated levels of IgG4 (a subclass of Immunoglobulin G) in the blood and fibrotic inflammation in the bile ducts. It is part of the spectrum of IgG4-related diseases, which can affect the bile ducts, pancreas, liver, and other organs.

IgG4-SC shares similarities with other biliary diseases such as PSC but has important differences in diagnosis, clinical features, and treatment. It is commonly associated with autoimmune pancreatitis (inflammation of the pancreas).

- **Jaundice** due to bile duct obstruction is one of the most common symptoms.
- **General fatigue and weakness** may occur due to chronic inflammation and poor liver function.
- **Pain** in the upper right abdomen (liver and bile duct area) is a common symptom.
- **Unintentional weight loss** may occur due to chronic inflammation and systemic effects of the disease. Many patients have autoimmune pancreatitis, which can present with symptoms like abdominal pain, weight loss, and elevated pancreatic enzymes.
- **Widespread inflammation** may affect multiple organs, including the salivary glands, tear glands, lungs, kidneys, and lymph nodes. Therefore, patients may experience inflammation in other tissues in addition to liver and bile duct symptoms.

Suggested Resources

This comprehensive book has been created using a combination of scientifically verified sources, expert insights, and the advanced capabilities of ChatGPT for text creation and DALL·E for visualization. Below are the details of these resources:

Scientific References

American Liver Foundation (ALF)

Provides detailed information on autoimmune liver diseases, including autoimmune hepatitis (AIH), Primary Biliary Cholangitis (PBC), and Primary Sclerosing Cholangitis (PSC).

- Website: liverfoundation.org

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Offers reliable details about the causes, symptoms, and treatment of autoimmune and other liver diseases.

- Website: niddk.nih.gov

Mayo Clinic

A trusted source for up-to-date and evidence-based information on autoimmune liver diseases and their management.

- Website: mayoclinic.org

European Association for the Study of the Liver (EASL)

Publishes clinical guidelines and research papers on liver diseases, including autoimmune hepatitis and cholangiopathies.

- Website: easl.eu

PubMed (National Library of Medicine)

A leading database for scientific articles and reviews on autoimmune hepatitis, PBC, and PSC. Provides access to peer-reviewed research papers.

- Website: pubmed.ncbi.nlm.nih.gov

European Association for the Study of the Liver (EASL)

EASL publishes updated guidelines and research papers on the diagnosis and treatment of liver diseases.

Website: easl.eu

Johns Hopkins Medicine

Trusted insights into autoimmune liver diseases, their symptoms, and management strategies.

- Website: hopkinsmedicine.org

Hepatology Textbooks and Research Papers:

Specialized references such as "Zakim and Boyer's Hepatology" and

"*Autoimmune Liver Diseases*" from renowned publishers like Springer and Elsevier.

Contributions of ChatGPT and DALL·E

- **Text Content:** The text for all chapters has been developed and curated using ChatGPT, integrating up-to-date knowledge of liver diseases, diagnostic methods, and treatment options. The AI ensured the information aligns with clinical guidelines and scientific literature.
- **Visualization:** DALL·E was employed to create educational images illustrating complex medical concepts, such as autoimmune liver disease mechanisms, treatment pathways, and lifestyle adaptations for patients.

Role of AI in Book Development

1. **Content Creation:** ChatGPT served as a tool to draft and refine the chapters, ensuring clarity, accessibility, and scientific accuracy for English-speaking audiences.
2. **Image Generation:** DALL·E provided custom visuals to accompany the text, helping readers visualize topics like liver anatomy, disease mechanisms, and treatment processes.

Acknowledgment of Contributions

This book has been created with a focus on blending advanced AI technologies, scientific research, and user-friendly explanations. The integration of ChatGPT and DALL·E, alongside the utilization of established medical resources, ensures the content is accurate, relevant, and visually engaging.

These resources and methodologies collectively provide a robust foundation for understanding autoimmune liver diseases and their management.



About The Author

Seyed Moayed Alavian, MD

Professor of Gastroenterology and Hepatology

President of the Iranian Association for the Study of Liver Diseases

Director of the Middle East Liver Disease Center, Tehran, Iran

Founder of Hepatitis Monthly Journal

Phone: +9821 88945186-8

Dr. Seyed Moayed Alavian, a prominent physician and researcher in liver diseases, is recognized not only in Iran but across the Middle East and globally. He has established several medical centers in Iran and other regional countries. He is the founder of the **Tehran Hepatitis Conferences** and has chaired 10 international conferences while hosting numerous meetings on hepatitis across the country.

Prof. Alavian has published more than 600 articles in PubMed and ISI indexed journals, with over 50,000 citations and an H-Index of 75. He was born in 1963 and graduated from **Tehran University of Medical Sciences** in general medicine and internal medicine. He ranked second in the national subspecialty board examination and worked as a fellow at the **Digestive Disease Research Center (DDRC)** of Shariati Hospital from 1993 to 1995.

In 1996, he established Iran's first **Hepatitis Clinic** at the Iranian Blood Transfusion Organization in Tehran, which has since registered 25,000 cases of hepatitis B and C infections. That same year, with the help of social and artistic figures, he co-founded a charity to support liver disease patients. Dr. Alavian has also been the founder and **Editor-in-Chief** of **Hepatitis Monthly** since 2006 and served as **Editor-in-Chief** of the **Journal of Clinical Virology (European Virology Journal)** for 10 years. He has been a member of Iran's **National Hepatitis Committee** at the Ministry of Health since 1996, and he served as the **Deputy Minister of Health** from 2005 to 2009.

Dr. Alavian has been a consultant on national hepatitis control projects in Iran and remains an active member of the **National Hepatitis Committee**. He is currently a retired **Professor of Gastroenterology and Hepatology**.

Over the past 30 years, Prof. Alavian has actively participated in **multicenter clinical trials** and **scientific projects** related to viral hepatitis. He has been recognized as a **top researcher** multiple times, including as the best researcher in **gastroenterology and hepatology** and as the **second-best clinical scientist** in Iran during the **Razi Festival**.

According to **Scopus**, based on the keyword "hepatitis," he ranked **first** in the world in the number of published articles between 2010 and 2020. He has authored or co-authored more than 850 papers, with over 600 indexed in **ISI** and **Medline**, garnering more than 50,000 citations. He has also written 75 books and pamphlets for doctors and patients.

Dr. Alavian's main interests include **health policy**, the **epidemiological aspects** of viral hepatitis, and integrating new protocols to control these infections and raise public awareness. He is particularly interested in **clinical trials** of emerging drugs for **hepatitis B** and **hepatitis C**, especially in specific populations like **thalassemia** and **hemophilia** patients.

In the last 30 years, he has been responsible for controlling **hepatitis C** in special patient groups, with more than 18,000 specialized patients treated under his guidance. For the past 15 years, he has chaired both the scientific and executive teams of the **Tehran International Hepatitis Conferences**, each attended by more than 2,000 specialists.

One of his major contributions was founding and managing the **Hepatitis Monthly** journal in 2006, which was indexed in **ISI** in 2007 and has been published monthly in English since 2011. In 2010, the journal was awarded **Best English-Language Journal** at the **16th Razi Medical Science Research Festival**.

In 2015, he was recognized as the **Top Scientist of the Decade** in the field of hepatitis by the **Academy of Sciences**, based on the number of published papers indexed in **Scopus**, and he received the **Fereydoon Azizi Award**.

Another significant achievement of his was founding and presiding over the **Iran Hepatitis Network** from 2004 to 2017. Currently, he serves as the **President of the Iranian Association for the Study of Liver Diseases**.