

# Drugs & Liver Damage

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## **DRUGS THAT MAY CAUSE LIVER DYSFUNCTION DAMAGE**

The liver is the principal organ that is capable of converting drugs into forms that can be readily eliminated from the body.

Given the diversity in use today and the complex burden they impose upon the liver, it is not surprising that a broad spectrum of adverse drug's effects on liver functions and structures has been documented.

The reactions range from mild and transient changes in the results of liver function tests to complete liver failure with death of the host.

Many drugs may affect the liver adversely in more than one way, as cited below in several listings.

# DRUGS THAT MAY CAUSE LIVER DYSFUNCTION DAMAGE

The use of the following drugs requires careful monitoring of their effects on the liver during the entire course of treatment.

This list is just a general guideline.

Many drugs affect the liver to one degree or another and we can't list all of them here; new drugs are always being approved for general use.

Read the accompanying literature with your prescriptions and always consult with your doctor or pharmacist about any new medication if you have liver disease!

When drugs injure the liver and disrupt its normal function, symptoms, signs, and abnormal blood tests of [liver disease](#) develop.

# DRUGS THAT MAY CAUSE LIVER DYSFUNCTION DAMAGE

Abnormalities of drug-induced liver diseases are similar to those of liver diseases caused by other agents such as viruses and immunologic diseases.

For example, drug-induced hepatitis (inflammation of the liver cells) is similar to viral hepatitis; they both can cause elevations (AST) and (ALT) as well as anorexia, fatigue, and nausea.

Drug-induced cholestasis can mimic the cholestasis of autoimmune liver disease (e.g., primary biliary cirrhosis or PBC) and can lead to elevations in blood levels of bilirubin (causing jaundice, alkaline phosphatase and itching).

**What are some important examples of drug-induced liver disease?**

**Drugs that may cause ACUTE DOSE-DEPENDENT LIVER DAMAGE (resembling acute viral hepatitis)**

- acetaminophen
- salicylates (doses over grams d2 aily)

## **Drugs that may cause ACUTE DOSE-INDEPENDENT LIVER DAMAGE (resembling acute viral hepatitis)**

- acebutolol
- indomethacin
- phenylbutazone
- allopurinol
- isoniazid
- phenytoin
- atenolol
- ketoconazole
- piroxicam
- carbamazepine
- labetalol

# Drugs that may cause ACUTE FATTY INFILTRATION OF THE LIVER

- adrenocortical steroids
- phenothiazines
- sulfonamides
- antithyroid drugs
- phenytoin
- tetracyclines
- isoniazid
- salicylates
- valproic acid
- methotrexate

## Drugs that may cause CHOLESTATIC JAUNDICE

- actinomycin D
- chlorpropamide
- erythromycin
- amoxicillin/clavulanate
- cloxacillin flecainide
- azathioprine
- cyclophosphamide
- flurazepam
- captopril
- cyclosporine
- flutamide
- carbamazepine
- danazol



## **Drugs that may cause LIVER GRANULOMAS (chronic inflammatory nodules)**

- allopurinol
- gold
- phenytoin
- aspirin
- hydralazine
- procainamide
- carbamazepine
- isoniazid
- quinidine
- chlorpromazine
- isoniazid
- quinidine

## Drugs that may cause active chronic hepatitis

- acetaminophen (chronic use, large doses)
- dantrolene
- methyldopa
- isoniazid
- nitrofurantoin

## **Drugs that may cause liver cirrhosis or fibrosis (scarring)**

- methotrexate
- terbinafine HCl (Lamisil, Sporanox)
- nicotinic acid

## **Drugs that may cause chronic cholestasis (resembling primary biliary cirrhosis)**

- chlorpromazine/valproic acid (combination)
- imipramine
- thiabendazole
- phenothiazines
- tolbutamide
- chlorpropamide/erythro-mycin (combination)
- phenytoin

## **Drugs that may cause LIVER TUMORS** (benign and malignant)

- anabolic steroids
- oral contraceptives
- thorotrast
- danazol
- testosterone

## Drugs that may cause DAMAGE TO LIVER BLOOD VESSELS

- adriamycin
- dacarbazine
- thioquanine
- anabolic steroids
- mercaptopurine
- vincristine
- azathioprine
- methotrexate
- vitamin A (excessive doses)
- carmustine
- cyclophosphamide/cyclo-sporine (combination)
- oral contraceptives

## What are the symptoms of liver disease?

- Patients with mild liver disease may have few or no symptoms or signs.
- Patients with more serious disease develop symptoms and signs that may be nonspecific or specific.
- Nonspecific symptoms, that is, symptoms that don't suggest that the liver is their cause, include:
  1. fatigue,
  2. weakness,
  3. vague abdominal pain
  4. loss of appetite.

## What are the symptoms of liver disease?

- Symptoms and signs that are specific for liver disease include:
  1. yellowing of the skin (jaundice) due to the accumulation of bilirubin in the blood,
  2. itching, and
  3. easy bruising due to decreased production of blood clotting factors by the diseased liver.



## What are the symptoms of liver disease?

- Severe, advanced liver disease with cirrhosis can produce symptoms and signs related to cirrhosis; these symptoms include:
  1. fluid accumulation in the legs (edema) and abdomen (ascites),
  2. mental confusion or coma,
  3. kidney failure,
  4. vulnerability to bacterial infections, and
  5. gastrointestinal bleeding.

## How do drugs cause liver disease?

- Drugs can cause liver disease in several ways. Some drugs are directly injurious to the liver; others are transformed by the liver into chemicals that can be injurious to the liver directly or indirectly. (This may seem strange in light of the liver's important role in transforming toxic chemicals into nontoxic chemicals, but it happens.)

There are three types of liver toxicity;

1. Dose-dependent toxicity
  2. Idiosyncratic toxicity
  3. Drug allergy.
- Drugs that cause **dose-dependent toxicity** can cause liver disease in most people if enough of the drug is taken.
  - The most important example of dose-dependent toxicity is acetaminophen (Tylenol) overdose .

## How do drugs cause liver disease?

- Drugs that cause **idiosyncratic toxicity** cause disease in only those few patients who have inherited specific genes that control the chemical transformation of that specific drug, causing accumulation of the drug or products of their transformation (metabolites) that are injurious to the liver.
- These inherited idiosyncratic toxicities usually are rare, and depending on the drug, typically occur in less than 1 to 10 per 100,000 patients who are taking that drug; however, with some drugs the prevalence of toxicity is much higher.

## What types of liver disease do drugs cause?

1. **Mild elevations in blood levels of liver enzymes** without symptoms or signs of liver disease
2. **Hepatitis**
3. **Necrosis** that often is caused by more severe hepatitis
4. **Cholestasis**
5. **Steatosis**
6. **Cirrhosis** as a result of chronic hepatitis, cholestasis, or fatty liver
7. **Fulminant hepatitis** with severe, life threatening liver failure
8. **Blood Clots** in the veins of the liver

## How is drug-induced liver disease diagnosed?

- The diagnosis of drug-induced liver diseases often is difficult. Patients may not have symptoms of liver disease or may have only mild, nonspecific symptoms.
- Patients may be taking multiple drugs, which makes it difficult to identify the offending drug.
- Patients also may have other potential causes of liver diseases such as non-alcoholic fatty liver disease (NAFLD) and alcoholism.
- The diagnosis of liver disease is based on a patient's symptoms (such as loss of appetite, nausea, fatigue, itching, and dark urine), findings on the physical examination (such as jaundice, enlarged liver), and abnormal laboratory tests (such as blood levels of liver enzymes or bilirubin and blood clotting times).

## How is drug-induced liver disease diagnosed?

- If a patient has symptoms, signs, and abnormal liver tests, doctors then try to decide whether drug(s) are causing the liver disease by:
  1. Taking a careful history of alcohol consumption to exclude alcoholic liver disease.
  2. Performing blood tests to exclude viral hepatitis B and hepatitis C , and to exclude chronic liver diseases such as autoimmune hepatitis and primary biliary cirrhosis (PBC).
  3. Performing abdominal ultrasound or computerized tomography (CT) scan of the liver to exclude gallbladder disease and tumors of the liver.
  4. Taking a careful history of ingestion-particularly recent initiation--of drugs that are commonly associated with liver disease.

## What is the treatment for drug-induced liver diseases?

- The most important treatment for drug-induced liver disease is stopping the drug that is causing the liver disease.
- In most patients, signs and symptoms of liver disease will resolve and blood tests will become normal and there will be no long-term liver damage.
- There are exceptions, however. For example, Tylenol overdoses are treated with oral N-acetylcysteine to prevent severe liver necrosis and failure.
- Liver transplantation may be necessary for some patients with acute liver failure.
- Some drugs also can cause irreversible liver damage and cirrhosis.

Thank you