



# Chemical Hepatitis

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## Definition

Chemical hepatitis is hepatocellular dysfunction or injury related to the direct and acute effects of parent medications or their metabolites. The effect of toxicity can range from mild, transient changes of the liver to fulminant hepatic failure leading to death.

Drug-induced reactions generally are classified as hepatocellular, cholestatic, or mixed. Drug-induced disease can mimic viral hepatitis or biliary tract obstruction. Generally, drug-induced liver disease is reversible with drug withdrawal. Recovery of liver function depends on the amount and length of exposure to the offending drug.

## Incidence

No specific data are available about the incidence of chemical hepatitis because it has numerous potential causes.

## Risk Factors

A. Direct and acute effects of either parent medications or their metabolites on the liver

1. Antitumor agents

- a) High potential for causing chemical hepatitis
  - (1) L-asparaginase
  - (2) Cytarabine
  - (3) Etoposide
  - (4) Intra-arterial fluorodeoxyuridine
- (5) Methotrexate
  - (a) Long-term, low-dose use, such as in the management of rheumatoid arthritis and psoriasis
  - (b) High-dose treatment
  - (c) Complication occurs more commonly with

long-term oral methotrexate than with intermittent IV methotrexate

- (6) Plicamycin
- (7) Streptozocin
- (8) Vincristine
- (9) Combination of 5-fluorouracil and levamisole
- b) High potential to cause chemical hepatitis when given in high doses
  - (1) Busulfan
  - (2) Carmustine
  - (3) Cisplatin
  - (4) Cyclophosphamide
  - (5) Cytarabine
  - (6) Dactinomycin
  - (7) Etoposide
  - (8) Interferons
  - (9) Lomustine
  - (10) Methotrexate
  - (11) 6-mercaptopurine
  - (12) Mitomycin
- 2. Therapeutic agents used in cancer care
  - a) Acetaminophen
  - b) Allopurinol
  - c) Antibiotics
    - (1) Amoxicillin and clavulanate
    - (2) Erythromycin
    - (3) Isoniazid
    - (4) Nitrofurantoin
    - (5) Tetracycline
    - (6) Trimethoprim-sulfamethoxazole
  - d) Anticonvulsants
    - (1) Phenytoin
    - (2) Valproic acid
  - e) Antifungals
    - (1) Fluconazole
    - (2) Itraconazole
    - (3) Ketoconazole
  - f) Azathioprine
  - g) Halothane (usually develops after multiple exposures)

- h) Hormonal agents
  - (1) Tamoxifen
  - (2) Testosterone
- i) Methyldopa (Toxicity may develop over years without any symptoms or evidence of hepatitis.)
- j) Nonsteroidal anti-inflammatory agents (NSAIDs)
- k) Phenothiazine antiemetics, especially chlorpromazine
- l) Vitamin A (Toxicity may develop over years without any symptoms or evidence of hepatitis.)
- 3. Miscellaneous agents
  - a) Alcohol (Toxicity generally is greatest in people with a history of alcohol abuse.)
  - b) Herbal remedies
    - (1) Hepatotoxicity may be one of the most frequent adverse reactions to herbal remedies.
    - (2) Frequently transient effects seen, but can result in acute liver failure and chronic liver disease
    - (3) Types of herbal remedies with most frequent reports of hepatotoxicity
      - (a) Pyrrolizidine alkaloids (found in more than 350 plant species)
        - i) Comfrey
        - ii) Brush teas
      - (b) Germander

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