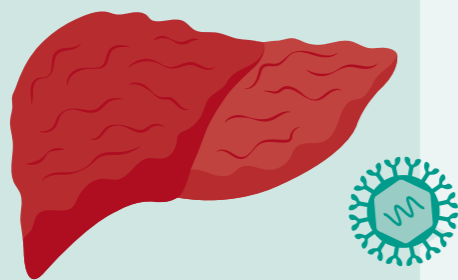


➔ Drug-induced liver injury (DILI) is a disorder whereby drugs (including pharmacological therapies, traditional medicines, and herbal or dietary supplements) cause liver damage. Two forms of DILI exist: intrinsic DILI, which is dose-related and occurs shortly after exposure, and idiosyncratic DILI, which is unpredictable, is driven by host factors and can occur after several weeks.

MECHANISMS

Drugs are taken up from the circulation into hepatocytes, where they are metabolized by phase I and phase II enzymatic reactions. These reactions can produce reactive metabolites of the drugs that can covalently bind to cellular proteins, altering their function, or form haptens, which can initiate an immune response in genetically susceptible patients. Both of these processes might contribute to liver injury. In addition, some drugs or their metabolites block the export of bile from hepatocytes, leading to increased intracellular concentrations of toxic bile salts and mitochondrial damage. Ultimately, the drug-induced cellular changes lead to hepatocyte death or promote an immune response, leading to liver injury.

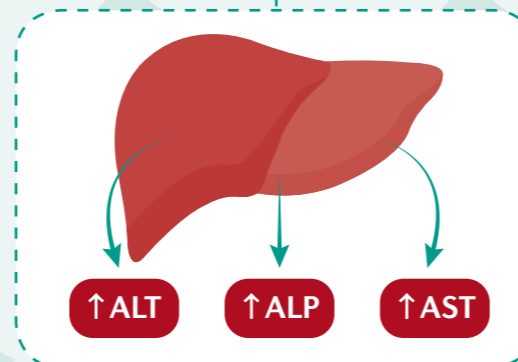


DIAGNOSIS



Symptoms of DILI include fever, nausea, vomiting, jaundice, dark urine and right upper quadrant pain

DILI should be suspected in those with increased aminotransferases during investigation for non-specific symptoms or in those with acute viral hepatitis-like syndrome



Implicated drugs should be stopped when DILI is suspected

Individuals with suspected DILI should provide a detailed history of prescription medication and other substance use



Competing aetiologies — such as viral or autoimmune hepatitis — should be ruled out before a diagnosis of DILI is made



OUTLOOK

DILI-specific biomarkers are required to improve the diagnosis of DILI in clinical practice and to inform prognosis. Candidate biomarkers include molecules that are released from damaged hepatocytes (such as miR-122) or markers of immune function (such as osteopontin).

EPIDEMIOLOGY

Estimating the incidence of DILI worldwide is difficult owing to diverse cultures, health-care systems and lack of consistent reporting. In South Korea, the

incidence of DILI-related hospitalization is 12 cases per 100,000 persons per year, whereas in the UK, the incidence of non-fatal DILI is

! The proportion of DILI cases that are caused by dietary and herbal supplements is increasing

2.4 cases per 100,000 individuals. Epidemiological data from Latin American or African countries are scarce.

Rx MANAGEMENT

After diagnosis of DILI, the causative agent should be immediately stopped and patients should undergo frequent monitoring to ensure their liver function does not worsen. Therapeutic options for DILI are limited. Many patients are prescribed corticosteroids, although there is little evidence supporting their use. Individuals with acute liver failure should be referred for liver transplantation.



! Most patients with DILI fully recover, although a proportion of patients can develop acute liver failure or chronic DILI

QUALITY OF LIFE

Many patients develop fear and anxiety towards the use of medications after a severe drug-related adverse event. These feelings can include worries about recurrence, re-exposure to the drug, effects on fertility and developing adverse reactions with other drugs. Ultimately, these feelings can affect treatment adherence and might increase discontinuation of needed therapies.

