



Phenotypes Of Drug Induced Liver Injury

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Drug induced liver injury can be categorized by phenotype or overall clinical characteristics based upon symptoms, signs and laboratory findings. The phenotype describes the specific form of liver disease that the hepatotoxicity resembles. Twelve phenotypes of drug induced liver injury are given below. Not all cases fit neatly into a specific phenotype and some fulfill criteria for two or more different phenotypes. Nevertheless, characterization by phenotype can be helpful in the diagnosis of drug induced liver injury and in assigning causality, particularly when multiple potential injurious agents are being taken or an herbal or unconventional, alternative medication is used. Grouping cases by phenotype may also help to define the pathogenesis of the injury and categorization of cases for genetic and immunological analyses.

1. Acute hepatic necrosis
2. Acute hepatitis
3. Cholestatic hepatitis
4. Mixed hepatocellular-cholestatic hepatitis
5. Enzyme elevations without jaundice
 - a. Hepatocellular
 - b. Cholestatic
 - c. Mixed
6. Bland cholestasis
7. Hepatic steatosis and lactic acidosis
8. Nonalcoholic fatty liver
9. Chronic hepatitis
10. Sinusoidal obstruction syndrome (veno-occlusive disease)
11. Nodular regenerative hyperplasia
12. Hepatic adenoma and hepatocellular carcinoma

The 12 phenotypes can have distinctive immunological features:

1. Immunoallergic
2. Autoimmune

The 12 phenotypes also have adverse outcomes:

1. Acute liver failure
2. Vanishing bile duct syndrome
3. Cirrhosis

Thus, a complete phenotype might be cholestatic hepatitis with immunoallergic features leading to vanishing bile duct syndrome and cirrhosis; or acute hepatitis with autoimmune features (possibly leading to acute liver failure); or chronic hepatitis with autoimmune features (possibly leading to cirrhosis).

Several of the 12 phenotypes are named for and best defined by histological features (bland cholestasis, hepatic steatosis, cirrhosis). In most instances, liver histology can help define the clinical phenotype and can be pathognomonic. Nevertheless, the diagnosis and phenotyping can usually be made using clinical features, laboratory tests and noninvasive imaging.

Descriptions of the 12 phenotypes of drug induced liver injury are given in LiverTox along with clinical case histories, typical histological features and, when appropriate, selected references.