

10 - Drug induced hepatic damage

Drug-induced hepatic damage

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Hy's rule is defined as alanine aminotransferase (ALT) more than three times the upper limit of normal combined with serum bilirubin more than two times the upper limit of normal. This is recommended by the US Food and Drug Administration (FDA) to assess the hepatotoxicity of new drugs.⁸⁰ Drug-induced hepatic damage can be due to:

- ■ Direct dose-related hepatotoxicity (type 1 adverse drug reaction). A small number of drugs fall into this category (e.g. paracetamol, alcohol).
- ■ Hypersensitivity reactions (type 2 adverse drug reaction). These can present with rash, fever and eosinophilia. Almost all drugs have been associated with cases of hepatotoxicity; the frequency varies. Almost any type of liver damage can occur, ranging from mild transient asymptomatic increases in LFTs to fulminant hepatic failure. See Tables 8.1–8.6 for details of the hepatotoxic potential of individual drugs. Risk factors for drug-induced hepatotoxicity include:¹⁰⁰

- ■ Increasing age.
- ■ Female gender.
- ■ Alcohol consumption.
- ■ Co-prescription of enzyme-inducing drugs.
- ■ Genetic predisposition.
- ■ Obesity.
- ■ Pre-existing liver disease (small effect).

When interpreting LFTs, remember that:¹⁰¹

- ■ About 12% of the healthy adult population have one LFT outside (above or below) the normal reference range.
- ■ Up to 10% of patients with clinically significant hepatic disease have normal LFTs.
- ■ Individual LFTs lack specificity for the liver, but more than one abnormal test greatly increases the likelihood of liver pathology.
- ■ The absolute values of LFTs are a poor indicator of disease severity. When monitoring LFTs consider the following:

- ■ Ideally LFTs should be measured before treatment starts so that 'baseline' values are available.
- ■ LFT elevations of over two times the upper limit of the normal reference range are rarely clinically significant.
- ■ Most drug-related LFT elevations occur early in treatment (first month) and are transient. They may indicate adaptation of the liver to the drug rather than damage per se. Transient LFT elevations may also occur during periods of weight gain.¹⁰²
- ■ If LFTs are persistently elevated more than threefold, continuing to rise or accompanied by clinical symptoms, the suspected drugs should be withdrawn.
- ■ When tracking change, >20% change in liver enzymes is required to exclude biological or analytical variation.

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