Why are dose adjustments important in patients with liver or kidney disease?

The liver and kidneys are important for the body’s ability to break down and excrete medication. Diseases of the liver or the kidneys, in addition to aging (Chapter 12), often require doses to be lowered in order to avoid adverse drug reactions.

What is the role of the liver?
The liver is the body’s “chemical factory,” responsible for the breakdown and conversion of many substances in the body -- including medications. The liver has the ability to make fat-soluble medications more water-soluble so they can be excreted through the kidneys. Another route of excretion is through the bile, which is produced in the liver and excreted to the intestines.

The ability of the liver to break down medications is genetically determined and varies among individuals. Some subjects break down medications quickly (rapid metabolizers), while others break down medications more slowly (slow metabolizers), possibly leading to more adverse drug reactions. Through genetic testing, it is possible to determine whether a person is a fast or slow metabolizer. Such testing, available for more than 50 medications, is seldom used in clinical practice.

What type of dose adjustment ought to be done in patients with liver disease?
Reduced liver function due to liver disease impairs the breakdown of medications. This is the case with inflammation (hepatitis) and liver damage (cirrhosis). Patients suffering from these conditions should consult with their physicians prior to taking any medication, prescribed or over-the-counter, or dietary supplements. Some fat-soluble medications should be avoided totally. Water-soluble medications are preferred since they are excreted through the kidneys without involving the liver.

What’s the role of the kidneys?
Most medications are excreted in the urine through the kidneys, with exceptions including fat-soluble medications that have to be converted to water-soluble breakdown products by the liver.

In addition to increasing age, the kidney function declines as a result
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of specific diseases of the kidneys. Among these are kidney problems due to diabetes.

**What type of dose adjustments are called for in patients with kidney disease?**
If kidney function is only modestly declined, it is usually sufficient to lower to doses of medications excreted through the kidneys. In case of severely reduced kidney function, certain medications ought to be avoided while others can be given in a reduced dose. Alternatively, water-soluble medications should be replaced by fat-soluble medications. A clinical problem is the limitation of kidney function tests in elderly subjects. They tend to overestimate function, which leads to insufficient adjustments of medication doses.

**Key messages**

✔️ The liver is important since it converts fat-soluble medications into water-soluble products that can be excreted in the urine.
✔️ This conversion by the liver varies among subjects and is genetically determined.
✔️ Patients with markedly reduced liver function should avoid certain medications and dietary supplements.
✔️ Most medications are excreted in the urine by the kidneys.
✔️ Moderately impaired kidney function may require lower medication doses; severely impaired function requires avoidance of certain medications.