Why do medications have adverse effects?

In spite of efforts to develop medications with only beneficial actions, there is no medication totally free of adverse effects. We have to accept that all medications have unfavorable or unwanted actions -- some mild, some just annoying -- while others have risks that may be more serious and troubling.

Is the problem their broad actions?
Most medications have many different effects on the body. The human body is very complex, so it comes as no surprise that medications can interfere with many normal functions and lead to adverse reactions. The hope is that drug development will yield therapeutic agents with beneficial effects that clearly outweigh the harmful ones.

Is medication dose another problem?
The dose is often a major factor. If the dose is too low, you may not benefit at all, or only to a limited extent. If the dose is too high, the risk of adverse effects is increasingly higher. One type of adverse effect may be unrelated to the intended use of the medication, while another results from a greater-than-hoped-for treatment response. Overtreatment of high blood pressure may lead to hypotension (low blood pressure), which is associated with dizziness and falls. Overtreatment of diabetes (high level of blood sugar) may lead to hypoglycemia (low level of blood sugar), which may be associated with weakness and, ultimately, unconsciousness. For many medications, it is critical to find the right dose: neither too low nor too high.

Is targeted treatment possible?
One objective of treatment of asthma is to dilate (widen) the constricted (narrowed) airways to the lung. This can be accomplished by stimulation of beta-2 receptors in the lungs. To increase exposure to medications such as terbutaline and albuterol (Bricanyl and Ventolin), these beta-2 receptor stimulants are inhaled using aerosol sprays or dry powder inhalers to reach high concentrations in the lungs while maintaining low levels in the rest of the body. When these agents are inhaled, the effects on the airways include reduced shortness of breath and less wheezing. Even with this type of administration, however, the medication still reaches the blood and is distributed throughout the body. Since other organs and tissues, like the heart and skeletal muscles,
have beta-2 receptors, stimulation of these receptors can lead to undesirable effects such as increased heart rate and muscle tremor.

Some types of cancer treatments are targeted. Cancer cells differ from normal cells because they have more frequent cell divisions and need a greater blood supply. Thus, several targeted treatments interfere with cell divisions while a few newer ones inhibit development of new blood vessels.

Although some targeting is possible, all organs in the body are exposed to at least some dose of all medications after they reach the blood. This is a common cause of adverse effects.

Are all patients equally susceptible to adverse effects?

This susceptibility can vary substantially, since the body’s ability to break down and eliminate medications is based, in great part, on our genetic make-up. For this reason, our sensitivities can be very different.

The field of genetics is a major focus of medical research, and efforts are under way to identify genes which influence whether, and to what extent, individuals respond to specific medications. The hope is that by determining the presence of specific genes, researchers will be able to identify patients most
likely to benefit from a medication and those who are most likely to be harmed (and would, therefore, not be treated).

A recent review summarized the findings for seven genetic markers which identify patients who have a delayed breakdown of certain medications and, as a result, they have more serious adverse reactions. Five of the seven markers are present in 10 percent or fewer of patients. These genetic markers are more common in patients of Asian origin.

The FDA urges genetic prescreening before prescribing the AIDS drug abacavir. A recent study reported that 61 percent of people with a genetic variant suffered a hypersensitivity reaction compared to four percent of those without the variant.

Key messages

✓ Medications typically have several mechanisms of action, some of which may be harmful.
✓ Finding the right dose is critical, since overtreatment may cause adverse effects.
✓ Chemical receptors in the body that are targeted by a medication may be present in other organs as well.
✓ Genetic make-up is emerging as a determining factor when considering which patients will respond adversely to specific medications.