Why do some patients benefit from medications while others do not?

We all differ in how we respond to medications, even if they are taken as prescribed. For the most effective prescription drugs, not everyone will have a favorable response. Those not gaining full benefit from a medication are known as “partial-responders” or “non-responders.” Why is it that people respond differently to the same medication?

**Do expectations play a role?**
Expectations matter. It has been shown that patients with higher expectations or hopes for a positive treatment effect are more likely to have a positive response. One example comes from a study in patients with sore throats, where two groups were randomly selected and treated. Half of the patients were given a prescription for an antibiotic with enthusiasm and encouragement, and the other half were given neutral or factual information with the prescription. The results of this research project were clear: Those patients given the positive, enthusiastic information responded better to the antibiotic.

This theory may extend to popular herbal remedies and supplements, as their reported positive effects could be due to the positive attitude among employees in stores selling such products. This effect is related to the discussion of placebos (inactive sugar pills), which is discussed in Chapter 27.

**Are there medical reasons for differences in response?**
There are several medical reasons for different treatment responses. An important one to rule out is incorrect diagnosis. The same symptom(s) may involve many different underlying conditions, which may require different medications.

Patients who take their medications as prescribed are more likely to benefit than those who skip doses or otherwise fail to take their medications as prescribed.

The stage or phase of your condition may also be important. Some medications are most effective when taken during the early phase of a disease or condition, while others are more effective for the advanced stages of disease. Not surprisingly, medication doses could be another factor. The best, most effective dose for most medications varies a lot among patients, even if ages and body sizes are similar. Why? Due to differences in rates of absorption
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(uptake) of the medication into your blood stream and how fast the medication is metabolized (broken down) and removed (eliminated) from your body, the responses differ. In addition, you may be more sensitive to a drug than someone else. A growing body of evidence suggests that individual responses to medications are genetically determined. Today, there are genetic tests that can help predict whether certain drugs for the treatment of special forms of cancer will be effective. Trastuzumab (Herceptin) is approved for use in the 30 percent of women with breast cancer who have a particular variant of the so-called HER-2 gene.

To whom do clinical trial results apply?
The results of a clinical trial designed to determine the health benefits and potential harm of a medication apply strictly to the group of participants in that trial. A group benefit is what regulatory agencies require for approval of a new medication. Clinicians caring for patients are left to make a judgment call about whether the findings in a clinical trial apply to other groups of subjects or to individual patients.

“At its best a trial shows what can be accomplished with a medicine under careful observation and certain restricted conditions. The same results will not invariably or necessarily be observed when the medicine passes into general practice.” (Austin Bradford Hill)

As discussed in Chapter 48, pre-approval trials have several limitations. In addition to often being small and of short duration, the trial participants are highly selected and typically differ from future users. Older and sicker patients are excluded, and they are the group most likely to suffer adverse medication effects.

As a result, physicians in clinical practice often have difficulty determining if the trial results apply to certain patients. They would consider many factors, including the setting of the trial; patient selection and characteristics; and treatment outcomes, including reported adverse drug effects. As a result, they may underuse effective medications. While benefits are often easier to generalize, determining safety can be a challenge.

Can treatment effect vary within a patient?
In patients with certain chronic conditions, the benefit of a medication may decrease over time, and an initial good effect may weaken. This development of tolerance (see Chapter 31) has been observed in some patients receiving long-term treatment for asthma and Parkinson’s disease.

Another example of varying treatment benefit has been observed in migraine patients. Their symptoms of severe headache are typically episodic (they come and go), and treatment with a class of drugs called triptans should
be started at the first sign of an attack in order to be most effective. Clinical studies have shown that triptan treatment provides symptom relief in about 70 percent of migraine attacks. Initially, this was interpreted as meaning that 70 of every 100 migraine patients benefitted, while 30 did not. A closer review of the findings revealed the results of triptans use was varied. Among patients who had multiple attacks, some always experienced symptom relief with triptans, others got relief only some of the time, and a few did not respond at all. One explanation is that treatment benefit depends on how soon after the onset of an attack the medication is taken, as well as the severity of the attack.

Key messages

✔ No medication is effective in all patients with a given condition.
✔ Effectiveness may be associated with the stage of a disease.
✔ Genetic factors may also influence the response to treatment.
✔ Whether the drug is taken as prescribed influences the benefit.
✔ Lack of benefit may be due to an incorrect diagnosis.