Tolerance

A person may develop tolerance to a drug when the drug is used repeatedly. For instance, when morphine or alcohol is used for a long time, larger and larger doses must be taken to produce the same effect. Usually, tolerance develops because metabolism of the drug speeds up (often because the liver enzymes involved in metabolizing drugs become more active) and because the number of sites (cell receptors) that the drug attaches to or the strength of the bond (affinity) between the receptor and drug decreases.

Tolerance is not the same as [dependence](https://www.msdmanuals.com/home/mental-health-disorders/substance-related-disorders/overview-of-substance-related-disorders#v26305450) or addiction.

## Resistance

Strains of microorganisms (bacteria or viruses) are said to develop resistance when they are no longer killed or inhibited by the antibiotics and antiviral drugs that are usually effective against them (or, in practice, when significantly higher than normal doses are required to have an effect). Similarly, cancer cells may develop resistance to chemotherapy drugs.

Resistance appears because of the mutations that take place spontaneously in any group of growing cells, whether exposed to drugs or not. Most such mutations change the cell's structure or biochemical pathways in a harmful way. But some mutations change the parts of the cell that are affected by drugs, decreasing the drug's ability to work (that is, causing resistance). Because such mutations are very rare, there are normally only a few such resistant cells in any group. However, if all or many of the “normal” cells are killed by a drug, a much higher proportion of the survivors are likely to be resistant. If the resistant survivors are not killed by the body's natural defenses, which is more likely when drugs are stopped too soon or not taken in the proper manner, they may reproduce and pass on the resistant trait to their descendants.

## Prevention and Treatment

To prevent the development of resistance, doctors try to use antibiotics only when necessary (not for viral infections such as a cold) and have people take them for a full course of treatment. In the treatment of certain serious infections, such as HIV, doctors usually give two or more different drugs at the same time because it is very unlikely that a cell would spontaneously be resistant to two drugs at the same time. However, giving one drug for a short time followed by another can produce resistance to multiple drugs—this has become a problem with tuberculosis in particular.

Once tolerance or resistance has developed to a drug, doctors may increase the dose or use a different drug

### Dependence

It’s possible to be dependent on drugs without being addicted. Dependence can be a bodily response to a substance. This often occurs if you rely on medications to control a chronic medical condition. These conditions may include:

* high blood pressure
* diabetes
* glaucoma

Dependence may involve:

* some or all the symptoms of addiction
* development of a high tolerance for the substance as your body adapts to the drug, leading to a desire for larger or more frequent doses
* physical symptoms of withdrawal when you attempt to stop using the drug

## How drug abuse can lead to dependence

The [National Institute on Drug Abuse](https://www.drugabuse.gov/publications/drugfacts/nationwide-trends) estimates 22.7 million Americans need help treating a drug or alcohol problem. In some cases, people may take a prescription medication for pain or another medical condition. This kind of use can sometimes develop into a substance use disorder.

The following are known triggers for substance use disorders:

* having a family history of addiction
* living in an environment where illegal drugs are often used and easy to access
* having a history of [anxiety](https://www.healthline.com/health/anxiety)
* having a history of [depression](https://www.healthline.com/health/depression)
* having a history of other [mental health conditions](https://www.healthline.com/health/mental-health)