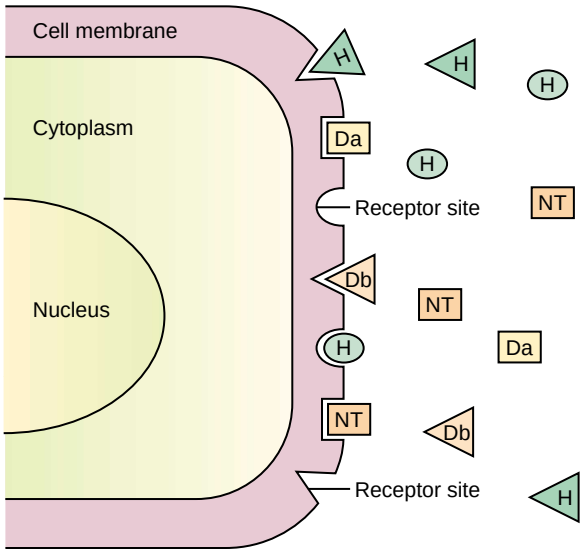

Figure 2–6 Cell membrane contains receptors for physiologic substances such as hormones (H) and neurotransmitters (NT). These substances stimulate or inhibit cellular function. Drug molecules (Da and Db) also interact with receptors to stimulate or inhibit cellular function.

monophosphate (cAMP). cAMP, in turn, can initiate any one of many different intracellular actions, the exact effect depending on the type of cell.

A second type of reaction involves changes in the permeability of cell membranes to one or more ions. The receptor protein is a structural component of the cell membrane, and its binding to a drug molecule may open or close ion channels. In nerve cells, for example, sodium or calcium ion channels may open and allow movement of ions into the cell. This usually causes the cell membrane to depolarize and excite the cell. At other times, potassium channels may open and allow movement of potassium ions out of the cell. This action inhibits neuronal excitability and function. In muscle cells, movement of the ions into the cells may alter intracellular functions, such as the direct effect of calcium ions in stimulating muscle contraction.

A third reaction may modify the synthesis, release, or inactivation of the neurohormones (eg, acetylcholine, norepinephrine, serotonin) that regulate many physiologic processes.

Additional elements and characteristics of the receptor theory include the following:

1. The site and extent of drug action on body cells are determined primarily by specific characteristics of receptors and drugs. Receptors vary in type, location, number, and functional capacity. For example, many different types of receptors have been identified. Most types occur in most body tissues, such as receptors for epinephrine and norepinephrine (whether received from stimulation of the sympathetic nervous system or administration of drug formulations) and receptors for hormones, including growth hormone, thyroid hormone, and insulin. Some occur in fewer body tissues, such as receptors for opiates and benzodiazepines in the brain and subgroups of receptors for epinephrine in the heart ($beta_1$-adrenergic receptors) and lungs ($beta_2$-adrenergic receptors). Receptor type and location influence drug action. The receptor is often described as a lock into which the drug molecule fits as a key, and only those drugs able to bond chemically to the receptors in a particular body tissue can exert pharmacologic effects on that tissue. Thus, all body cells do not respond to all drugs, even though virtually all cell receptors are exposed to any drug molecules circulating in the bloodstream.

   The number of receptor sites available to interact with drug molecules also affects the extent of drug action. Presumably, a minimal number of receptors must be occupied by drug molecules to produce pharmacologic effects. Thus, if many receptors are available but only a few are occupied by drug molecules, few drug effects occur. In this instance, increasing the drug dosage increases the pharmacologic effects. Conversely, if only a few receptors are available for many drug molecules, receptors may be saturated. In this instance, if most receptor sites are occupied, increasing the drug dosage produces no additional pharmacologic effect.

   Drugs vary even more widely than receptors. Because all drugs are chemical substances, chemical characteristics determine drug actions and pharmacologic effects. For example, a drug's chemical structure affects its ability to reach tissue fluids around a cell and bind with its cell receptors. Minor changes in drug structure may produce major changes in pharmacologic effects. Another major factor is the concentration of drug molecules that reach receptor sites in body tissues. Drug- and client-related variables that affect drug actions are further described below.
2. When drug molecules chemically bind with cell receptors, the pharmacologic effects are those due to either agonism or antagonism. *Agonists* are drugs that produce effects similar to those produced by naturally occurring hormones, neurotransmitters, and other substances. Agonists may accelerate or slow normal cellular processes, depending on the type of receptor activated. For example, epinephrine-like drugs act on the heart to increase the heart rate, and acetylcholine-like drugs act on the heart to slow the heart rate; both are agonists. *Antagonists* are drugs that inhibit cell function by occupying receptor sites. This prevents natural body substances or other drugs from occupying the receptor sites and activating cell functions. Once drug action occurs, drug molecules may detach from receptor molecules (ie, the chemical binding is reversible), return to the bloodstream, and circulate to the liver for metabolism and the kidneys for excretion.
3. Receptors are dynamic cellular components that can be synthesized by body cells and altered by endogenous substances and exogenous drugs. For example, prolonged stimulation of body cells with an excitatory agonist usually reduces the number or sensitivity of receptors. As a result, the cell becomes less responsive to the agonist (a process called receptor desensitization