(Fig. 71-1). NO activates guanylyl cyclase, which converts guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). Protein kinase G is activated by cGMP and in turn activates several proteins that decrease the intracellular concentration of calcium ions (Ca^{2+}). Decreased Ca^{2+} concentration in the smooth muscle causes muscular relaxation, cavernosal artery dilation, increased blood flow, and subsequent penile erection. The control of blood flow on the venous outflow side is less well understood.

CAUSES OF ERECTILE DYSFUNCTION

Psychogenic ED was once thought to be the most common type of ED. However, advances in understanding of the mechanics and neurophysiology of erectile function have identified other more common causes. Psychogenic ED is now thought to account for fewer than 15% of patients seen by ED specialists. The anatomic site now believed to be the most common cause of ED is the neuromuscular junction. This is the place where the cavernosal nerves meet the smooth muscle and endothelium of the deep cavernous penile arteries. The decreased release of NO by cavernosal nerves and the impaired response by smooth muscle cells that occurs at the neuromuscular junction is termed *endothelial dysfunction*. Other common causes of ED include certain endocrine disorders, vascular diseases, central and peripheral nerve disorders, and medications.

Cardiovascular Disease

In the United States, atherosclerotic vascular disease, hyperlipidemia, smoking, and hypertension are frequent causes of ED. These relationships are expected because erection is achieved by a combination of relaxation of arteriolar smooth muscle and increased venous resistance of channels penetrating the wall of the corpora cavernosa. Cardiovascular disease may decrease erectile ability by decreasing blood flow to the penile arteries, by mechanical obstruction of the vascular lumen, or, more commonly, by endothelial dysfunction. Endothelial dysfunction is the most common cause of ED. It results from interruption of the neural control mechanism of vascular smooth muscle function and leads to decreased blood flow and pressure in the corpora cavernosa.

The principal blood vessels supplying the corpora cavernosa are the cavernosal arteries, which are terminal branches of the internal pudendal artery. Diseases of large and small arteries may decrease corporal blood pressure and lead to decreased penile lengthening and rigidity. Veno-occlusive disease in the penis is also a significant cause of ED. These patients often experience normal initial rigidity, but quickly lose their erection before ejaculation occurs.

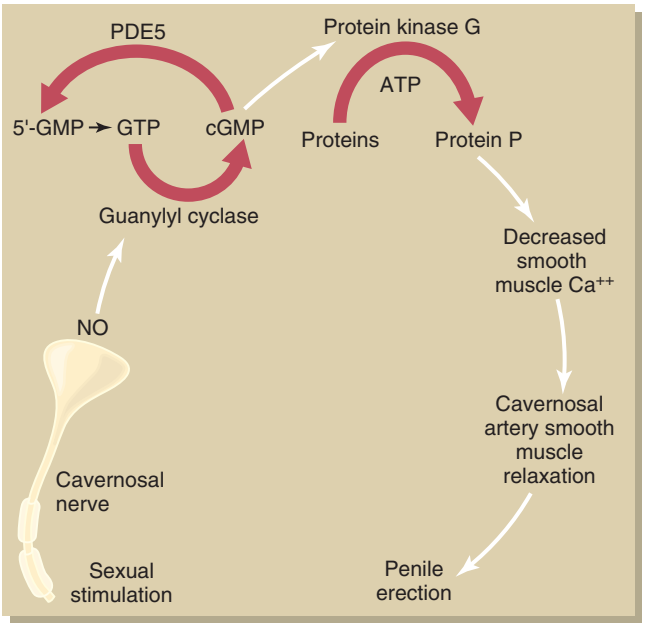

FIGURE 71-1 Sexual stimulation causes the release of nitric oxide (NO) by the cavernous nerve into the neuromuscular junction. ATP, Adenosine triphosphate; cGMP, cyclic guanosine monophosphate; GMP, guanosine monophosphate; GTP, guanosine triphosphate; PDE5, phosphodiesterase type 5.

Neurogenic Erectile Dysfunction

Because the nervous system plays an integral part in the physiology of an erection, any disease process that affects the brain, the spinal cord, or the peripheral nerves can cause ED. For example, dementia, Parkinson's disease, and stroke are diseases of the brain associated with ED. Patients with spinal cord injury commonly have ED. Because of an intact reflex pathway, most patients with spinal cord injury respond to tactile sensation, but they usually require medical therapy to maintain the erection through intercourse. Iatrogenic injury to nerves during surgery (e.g., prostatectomy, rectal surgery) is also a common cause of neurogenic ED. Neurogenic ED due to decreases in penile tactile sensation can occur with increasing age.

Endocrine Disorders

Testosterone plays a permissive role in erectile function, and many endocrine disorders can directly or indirectly decrease plasma free or bound testosterone. However, androgen deficiency is an uncommon primary cause of ED because erectile ability is only partially androgen dependent. Patients with androgen deficiency typically have decreased or absent libido in addition to loss of erectile rigidity. Androgen replacement may induce return of erectile function in patients with very low or undetectable serum testosterone concentrations. More commonly, however, the impotent patient has normal or mildly decreased levels of circulating androgens. Testosterone replacement rarely restores erectile function in men with mildly decreased serum testosterone. Testosterone supplementation is never indicated for patients with normal circulating androgen levels.

The most common endocrine disorder affecting erectile ability is diabetes mellitus. In addition to causing atherosclerotic and microvascular disease, diabetes affects both the autonomic and the somatic nervous system, including loss of function of long autonomic nerves. The loss of long cholinergic neurons results in interruption of the efferent side of the erectile reflex arc. Diabetes also appears to produce dysfunction of the neuromuscular junction at the level of arterial smooth muscle in the penile corpora cavernosa. Studies have indicated markedly decreased acetylcholine and NO concentrations in the trabeculae of the corpora cavernosa in diabetic patients. These findings probably represent a combination of neural loss and