in their early to intermediate stages, and the finding of normocapnia and hypoxemia in a patient with hyperventilation may herald the onset of rapid respiratory failure and should prompt an assessment to determine if the patient is becoming fatigued. Respiratory alkalosis is common during mechanical ventilation.

The hyperventilation syndrome may be disabling. Paresthesia; circumoral numbness; chest wall tightness or pain; dizziness; inability to take an adequate breath; and, rarely, tetany may be sufficiently stressful to perpetuate the disorder. Arterial blood-gas analysis demonstrates an acute or chronic respiratory alkalosis, often with hypocapnia in the range of 15–30 mmHg and no hypoxemia. CNS diseases or injury can produce several patterns of hyperventilation and sustained $Paco_2$ levels of 20–30 mmHg. Hyperthyroidism, high caloric loads, and exercise raise the basal metabolic rate, but ventilation usually rises in proportion so that arterial blood gases are unchanged and respiratory alkalosis does not develop. Salicylates are the most common cause of drug-induced respiratory alkalosis as a result of direct stimulation of the medullary chemoreceptor (Chap. 472e). The methylxanthines, theophylline, and aminophylline stimulate ventilation and increase the ventilatory response to CO_2. Progesterone increases ventilation and lowers arterial $Paco_2$ by as much as 5–10 mmHg. Therefore, chronic respiratory alkalosis is a common feature of pregnancy. Respiratory alkalosis is also prominent in liver failure, and the severity correlates with the degree of hepatic insufficiency. Respiratory alkalosis is often an early finding in gram-negative septicemia, before fever, hypoxemia, or hypotension develops.

The diagnosis of respiratory alkalosis depends on measurement of arterial pH and $Paco_2$. The plasma $[K^+]$ is often reduced and the $[Cl^-]$ increased. In the acute phase, respiratory alkalosis is not associated with increased renal HCO_3^- excretion, but within hours net acid excretion is reduced. In general, the HCO_3^- concentration falls by 2.0 mmol/L for each 10-mmHg decrease in $Paco_2$. Chronic hypocapnia reduces the serum $[HCO_3^-]$ by 4.0 mmol/L for each 10-mmHg decrease in $Paco_2$. It is unusual to observe a plasma HCO_3^- <12 mmol/L as a result of a pure respiratory alkalosis.

When a diagnosis of respiratory alkalosis is made, its cause should be investigated. The diagnosis of hyperventilation syndrome is made by exclusion. In difficult cases, it may be important to rule out other conditions such as pulmonary embolism, coronary artery disease, and hyperthyroidism.

TREATMENT RESPIRATORY ALKALOSIS

The management of respiratory alkalosis is directed toward alleviation of the underlying disorder. If respiratory alkalosis complicates ventilator management, changes in dead space, tidal volume, and frequency can minimize the hypocapnia. Patients with the hyperventilation syndrome may benefit from reassurance, rebreathing from a paper bag during symptomatic attacks, and attention to underlying psychological stress. Antidepressants and sedatives are not recommended. β-Adrenergic blockers may ameliorate peripheral manifestations of the hyperadrenergic state.

SECTION 8 ALTERATIONS IN SEXUAL FUNCTION AND REPRODUCTION

67 Sexual Dysfunction

Kevin T. McVary

Male sexual dysfunction affects 10–25% of middle-aged and elderly men, and female sexual dysfunction occurs with similar frequency. Demographic changes, the popularity of newer treatments, and greater awareness of sexual dysfunction by patients and society have led to increased diagnosis and associated health care expenditures for the management of this common disorder. Because many patients are reluctant to initiate discussion of their sex lives, physicians should address this topic directly to elicit a history of sexual dysfunction.

MALE SEXUAL DYSFUNCTION

PHYSIOLOGY OF MALE SEXUAL RESPONSE

Normal male sexual function requires (1) an intact libido, (2) the ability to achieve and maintain penile erection, (3) ejaculation, and (4) detumescence. *Libido* refers to sexual desire and is influenced by a variety of visual, olfactory, tactile, auditory, imaginative, and hormonal stimuli. Sex steroids, particularly testosterone, act to increase libido. Libido can be diminished by hormonal or psychiatric disorders and by medications.

Penile tumescence leading to erection depends on an increased flow of blood into the lacunar network accompanied by complete relaxation of the arteries and corporal smooth muscle. The microarchitecture of the corpora is composed of a mass of smooth muscle (trabecula) that contains a network of endothelial-lined vessels (lacunar spaces). Subsequent compression of the trabecular smooth muscle against the fibroelastic tunica albuginea causes a passive closure of the emissary veins and accumulation of blood in the corpora. In the presence of a full erection and a competent valve mechanism, the corpora become noncompressible cylinders from which blood does not escape.

The central nervous system (CNS) exerts an important influence by either stimulating or antagonizing spinal pathways that mediate erectile function and ejaculation. The erectile response is mediated by a combination of central (psychogenic) innervation and peripheral (reflexogenic) innervation. Sensory nerves that originate from receptors in the penile skin and glans converge to form the dorsal nerve of the penis, which travels to the S2-S4 dorsal root ganglia via the pudendal nerve. Parasympathetic nerve fibers to the penis arise from neurons in the intermediolateral columns of the S2-S4 sacral spinal segments. Sympathetic innervation originates from the T11 to the L2 spinal segments and descends through the hypogastric plexus.

Neural input to smooth-muscle tone is crucial to the initiation and maintenance of an erection. There is also an intricate interaction between the corporal smooth-muscle cell and its overlying endothelial cell lining (Fig. 67-1). Nitric oxide, which induces vascular relaxation, promotes erection and is opposed by endothelin 1 (ET-1) and Rho kinase, which mediate vascular contraction. Nitric oxide is synthesized from l-arginine by nitric oxide synthase and is released from the nonadrenergic, noncholinergic (NANC) autonomic nerve supply to act postjunctionally on smooth-muscle cells. Nitric oxide increases the production of cyclic 3′,5′-guanosine monophosphate (cyclic GMP), which induces relaxation of smooth muscle (Fig. 67-2). Cyclic GMP is gradually broken down by phosphodiesterase type 5 (PDE-5). Inhibitors of PDE-5, such as the oral medications sildenafil, vardenafil, and tadalafil, maintain erections by reducing the breakdown of cyclic GMP. However, if nitric oxide is not produced at some level, PDE-5 inhibitors are ineffective, as these drugs facilitate, but do not initiate, the initial enzyme cascade. In addition to nitric oxide, vasoactive prostaglandins (PGE_1, $PGF_{2\alpha}$) are synthesized within the cavernosal tissue and increase cyclic AMP levels, also leading to relaxation of cavernosal smooth-muscle cells.