Physiology of Penile Erection and Pathophysiology of Erectile Dysfunction

Anthony J. Bella, William O. Brant, and Tom F. Lue

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3.1 Physiology of Erection

Penile erection is primarily a neurovascular event modulated by psychological and hormonal status. Sexual stimulation causes a release of neurotransmitters from the cavernous nerve terminals and relaxing factors from the endothelial cells in the penis, resulting in relaxation of smooth muscle in the arteries and arterioles supplying the erectile tissue.

3.1.1 Vascular Events

As discussed in Chapter 2, a several-fold increase in blood flow occurs with a concomitant increase in compliance of the sinusoids from relaxed cavernous smooth muscle, facilitating rapid filling and expansion of the sinusoidal system against the tunica albuginea. The subtunical venular plexuses are thus compressed between the trabeculae and the tunica albuginea, resulting in almost complete occlusion of venous outflow (Fournier et al. 1987; Banya et al. 1989). Blood is trapped within the corpora cavernosa, which raises the flaccid penis to an erect state. Intracavernous pressures are increased to approximately 100 mmHg (the full erection phase).

During sexual activity, the bulbocavernosus reflex is triggered, thus causing the ischiocavernosus muscles to forcefully compress the base of the blood-filled corpora cavernosa and the penis. The penis becomes very rigid, with an intracavernous pressure reaching several hundred mmHg (the rigid erection phase). During this phase, inflow and outflow temporarily cease. Detumescence can be the result of three separate activities: sympathetic discharge during ejaculation, breakdown of second messengers by phosphodiesterases, or cessation of erectile neurotransmitter release. The venous channels open with contraction of the trabecular smooth muscle, therefore expelling the trapped blood and restoring flaccidity.

3.1.2 Nervous Events

The penis is innervated by autonomic and somatic nerves. The somatic component is controlled by the pudendal nerve, which is responsible for penile sensation and the contraction and relaxation of the bulbocavernosus and ischiocavernosus striated muscles. Blood flow during erection and detumescence is regulated via the cavernous nerves, consisting of sympathetic and parasympathetic nerve fibers, which merge to form these nerves in the pelvis.

The principal neurotransmitter for penile erection is nitric oxide, which is released from nonad-
renergic-noncholinergic neurotransmission of the cavernous nerves and the endothelium (Lue 2000). Nitric oxide activates soluble guanylyl cyclase raising intracellular concentrations of cyclic guanosine monophosphate (cGMP). cGMP in turn activates a cGMP-specific protein kinase, which phosphorylates certain proteins and ion channels, resulting in opening of the potassium channels and hyperpolarization, sequestration of intracellular calcium by the endoplasmic reticulum, and inhibition of calcium channels, blocking calcium influx. The consequence is a drop in cytosolic calcium and smooth muscle relaxation/erection. During the return to the flaccid state, cGMP is hydrolyzed to guanosine monophosphate by phosphodiesterase type 5. Other phosphodiesterases are also found in the corpus cavernosum, but they do not appear to play an important role in detumescence.

3.2 Classification and Epidemiology

Erectile dysfunction may be classified as psychogenic, organic (neurogenic, hormonal, arterial, cavernosal and drug-induced), and mixed. Mixed erectile dysfunction is most commonly encountered having both a psychogenic and organic component (Table 3.1). Several pathophysiologic states, such as diabetes mellitus, may have detrimental effects upon erectile capacity via multiple pathways.

Many epidemiologic studies have described the relationship between erectile dysfunction and increasing age, with a reported prevalence of 40% at age 40, compared to 70% by 70 years of age; for severe erectile dysfunction, rates triple from 5% to 15% for men aged 40 compared to 70 (Feldman et al. 1994).

Table 3.1. Classification and common causes of erectile dysfunction

<table>
<thead>
<tr>
<th>Category of erectile dysfunction</th>
<th>Common disorders</th>
<th>Pathophysiology</th>
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<tbody>
<tr>
<td>Neurogenic</td>
<td>Stroke or Alzheimer's disease, spinal cord injury, radical pelvic surgeries, diabetic neuropathy, pelvic injury</td>
<td>Interrupted neuronal transmission, failure to initiate nerve impulse</td>
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<tr>
<td>Psychogenic</td>
<td>Depression, psychological stress, performance anxiety, relationship problems</td>
<td>Impaired nitric oxide (NO) release, over-inhibition of NO release, loss of libido</td>
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<tr>
<td>Hormonal</td>
<td>Hypogonadism, hyperprolactinemia</td>
<td>Loss of libido, inadequate NO release</td>
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<tr>
<td>Vasculogenic (arterial and venogenic)</td>
<td>Hypertension, atherosclerosis, diabetes mellitus, trauma, Peyronie's disease</td>
<td>Impaired veno-occlusion, inadequate arterial inflow</td>
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<td>Drug-induced</td>
<td>Antihypertensives, antiandrogens, antidepressants, alcohol abuse, cigarette smoking</td>
<td>Central suppression, decreased libido, alcoholic neuropathy, vascular insufficiency</td>
</tr>
<tr>
<td>Systemic diseases</td>
<td>Normal aging, diabetes mellitus, chronic renal failure, coronary heart disease</td>
<td>Multifactorial neuronal and vascular dysfunction</td>
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