Erectile Dysfunction

Growth Factors and Gene Therapy for Erectile Dysfunction

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Potential for the future? Investigators are looking at ways to regenerate the cavernous nerve and to affect the aging process in smooth muscle to help patients with erectile dysfunction.

The Role of Growth Factor on Regeneration of Nitric Oxide Synthase (NOS)-Containing Nerves After Cavernous Neurotomy in the Rats

Jung GW, Kwak JY, Kim IH, et al.
Int J Impot Res. 1999;11:227-235.

Erectile dysfunction following radical pelvic surgery occurs as a result of trauma/transection of the cavernous nerves that run along each side of the prostate gland. The nerve-sparing radical prostatectomy introduced by Walsh and colleagues attempts to overcome this recognized complication/side effect of the surgery. However, results of the nerve-sparing procedure, despite improvements and refinements in the technique over the years, are not universally successful, suggesting that the cavernous nerve(s) are still at risk during the procedure. Is there any way the surgeon can minimize this risk? One suggestion has been to better identify the nerves during the procedure, as with the Caver-Map. Yet even when surgical aids such as this are used, erectile dysfunction from nerve injury can still occur.

One experimental paradigm that has been suggested is the "transplantation" of a nerve in the area affected, in order to bridge the gap made by the surgery. In animal studies, there are hints of high promise for such a neural transfer. However, the chemical factors that augment the "acceptance" of such a neural graft in vivo have not been elucidated. In an animal study conducted by Jung et al, the ability of various growth factors known to affect neural growth were investigated following unilateral or bilateral neurotomy of the cavernous nerve. The authors found that the somatomedin, insulin-like growth factor (IGF-1), which is known to affect neurite outgrowth and has been shown to increase nerve regeneration in other neural systems, and transforming growth factor (TGF-ß2) may also have a beneficial effect on regeneration of the cavernous nerve. It remains to be determined whether treatment of patients at risk for neural injury during radical pelvic surgery will be in the form of a neural transfer and/or treatment with these two growth factors.

Intracorporal Injection of hSlo cDNA in Rats Produces Physiologically Relevant Alterations in Penile Function

Christ GJ, Rehman J, Day N, et al.
Am J Physiol. 1998;275:H600-H608.

It is apparent that the most common cause of erectile dysfunction in man is "venous leak," or failure to store blood within the corporal tissue. The reason is that the tissue within the corpora—the corporal smooth muscle—is unable to relax sufficiently enough to allow attainment of an intracorporal pressure high enough to compress the subtunical veins. The defect, therefore, is not in the veins but in the corporal smooth muscle itself. This is evidenced histologically by an increase in defective smooth muscle in impotent men compared with potent men.

This defective smooth muscle is also seen in the rat model of aging, when the corporal tissue becomes more fibrotic as the animal ages. What has also been shown in this aged animal model is a reduction in NOS activity in the corporal tissue.

In an attempt to overcome this dual hit to aged tissue, investigators have searched for ways to either regenerate the relatively noncompliant corporal tissue or to up-regulate the factors that promote smooth muscle relaxation. One of the ways to accomplish this is via the Ca^{+2} sensitive K^{+} channel (maxi-K^{+}) that regulates smooth muscle relaxation. Christ et al used naked DNA that encodes the maxi-K^{+} channel for injection into the penises of aged animals and was able to augment their erectile response in this manner. This gene therapy approach to overcome the processes that fail with certain disease states highlights what can be expected in the future for the treatment of patients who have erectile dysfunction that is refractory to medical therapy. ■