The Role of Urothelium in Regulating Lower Urinary Tract Function

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Originally thought to act only as a barrier, the functions performed by the urothelium are now known to include a primary role in bladder sensation and powerful influences over detrusor contraction. During bladder filling, stretch of urothelial cells induces the release of chemical mediators including ATP, acetylcholine, prostaalandins and nitric oxide. The activation of sensory nerve fibres by ATP and PGE2 is well established, while our understanding of the role of other mediators is less complete.

The urothelium and lamina propria also develop tonic contractions which can be induced by neurotransmitters and drugs acting via a number of receptors including muscarinic, alpha- and beta-adrenergic, tachykinin and serotonergic receptors. These are the same receptors that regulate contractions of the detrusor muscle and thus drugs used clinically to treat overactive bladder will also influence these urothelial/lamina propria responses resulting in altered bladder function. In addition to tonic contractions to drugs, the bladder urothelium/lamina propria also has pacemakers which generate spontaneous contractile activity. This is enhanced during bladder stretch by a mechanism involving acetylcholine release from the urothelium. This finding is particularly interesting when one considers that muscarinic antagonists in the clinical setting act on bladder function during the filling stage of the micturition cycle (ie. during bladder stretch).

These mechanisms involving urothelial mediators and urothelium/lamina propria contractile activity may be necessary for maintaining continence, and changes in function have been observed in a number of conditions including enhanced release of ATP in interstitial cystitis, overactive bladder and ageing. Changes in urothelial function are also found following intravesical drug treatments with cytotoxic drugs or systemic treatment with cyclophosphamide where urinary metabolites cause bladder inflammation and urothelial damage. These urothelial changes may be responsible for the severe urological side effects observed following treatment with cytotoxic drugs.

In conclusion, urothelial functions are regulated by a number of receptors that will be affected during treatment for urinary tract conditions, including anti-cholinergics, alpha-blockers and beta-agonists, whilst cytotoxic drugs directly or indirectly damage the urothelium to cause bladder dysfunction.