Cremaster muscle spasticity and retractile or undescended testes

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EDITOR–In his interesting commentary, Van Laecke describes the descent of a testis utilizing the Hutson hypothesis.[1] According to Hutson, there are three main ideas to explain the descent of testes.[2] His explanations on the descent of testes are somewhat controversial. Evidence exists that individuals who experienced undescended testes present excess of calcitonin gene-related peptide.[3] If the descent was guided by calcitonin gene-related peptide, undescended testes should be associated with *less* neuropeptide. Furthermore, this explanation does not link the descent of testes and cremaster muscle spasticity. Hutson et al. have recently written that etiology is multifactorial, and/or are they looking in the wrong place.[3] Clinicians should be broadly informed on the subject, with special attention given to the explanations that link the contractility of cremaster muscle, retraction, and ascent.

Gubernaculum is a primitive mesenchymal tissue that gives rise to smooth muscle and striated cremaster muscle. Smooth muscle surrounds the processus vaginalis at 27 weeks' gestation. Cremaster muscle transdifferentiates from the vascular smooth muscle. After the development of muscles, gubernaculum no longer exists. Testes are then descended via propulsive activity through the processus vaginalis. After propelling the testes, the smooth

muscle should undergo programmed cell death for the closure of processus vaginalis. Programmed cell death is achieved through a shift in autonomic tone in favor of parasympathetic tone to activate the intrinsic pathway via calcium signaling.

The key point is the regulation of shift in the autonomic tone. Disturbances in timing, intensity, and duration during the regulation of shift form the basis for pathological consequences.

If the shift takes place before the descent, the amount of smooth muscle decreases. Remaining smooth muscle may not suffice to propel the testis, and results in an undescended testis.

An early shift in autonomic tonus persists during childhood. While parasympathetic tonus acts through generating phospholipase C, sympathetic tonus acts by generating cyclic adenosine monophosphate (cAMP). Continuous stimulation of phospholipase C pathway by phorbol esters results in the development of tumours. On the other hand, the cAMP pathway is important for spermatogenesis. Differences in signaling pathways with dominance of phospholipase C and decrease in cAMP pathways explain the increase in the risk of malignancy and decrease in fertility. Persistence of signaling towards inducing programmed cell death may also play a role in the reduction of number of germ cells associated with undescended testes.

The gubernaculum also supports the muscular layer of vaso-epididymal structures. Signals towards inducing programmed cell death in smooth muscle explains both the reason for vaso-epididymal anomalies and their association with undescended testes.

Despite descent, the persistence of shifted signaling increases cytosolic calcium. Activation of phospholipase C generates inositol 1,4,5-trisphosphate. Inositol 1,4,5-trisphosphate releases Ca^{2+} from internal stores. Increase in cytosolic calcium initiates contraction in striated

muscle. Contracted cremaster muscle may subsequently undergo spasticity and contracture formation. Retraction is not due to a hyperactive reflex, but an increase in contractility results in spasticity, retraction, and ascent.

Central catecholaminergic activity also takes place in the regulation of the hypothalamic-pituitary-gonadal axis. The easing of central catecholaminergic activity establishes the association between undescended testis and hormonal disturbances.

If the intensity or duration of shift in autonomic tone is not at required levels, smooth muscle does not undergo programmed cell death and persists. Persistence of smooth muscle inhibits the obliteration of processus vaginalis to give rise to hernia or hydrocele, depending upon the amount of the remaining smooth muscle.[4,5]

The proposed mechanism satisfactorily explains the descent and links all the occurrences related to failed or fulfilled descent.

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