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Research Article

HISTOPATHOLOGICAL CHANGES IN ERECTILE TISSUE AND TESTIS IN AGEING MALE

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A R T I C L E I N F O

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A B S T R A C T

Epidemiologic studies have shown an association between aging and male ED, demonstrating that thepercentage of potent men decreases from 60% to 33% between 40 and 70 years of age a decrease in elastic fibers in the tunica albuginea and an alteration of microarchitecture may contribute to impotence in some

Until recently we had a poor understanding of the effect of aging on male fertility. It was assumed that male fertility was relatively immortal because so many elderly men have been able to impregnate their wives. However, there has been previous crude data showing a relative decrease in sperm count, and possibly fertility, in a certain percent of aging men.

INTRODUCTION

Ageing and the Erectile Tissues

Cavernosal perivascular smooth muscle cells (SMCs) and sinusoidal lining endothelium build up the vascular component which is embedded in an extracellular matrix (ECM) mostly composed by collagen and elastic fibers. With the advancement of age, several modifications in the composition and organization of these components were reported and suggested to alter elderly erectile capability. [1,2]

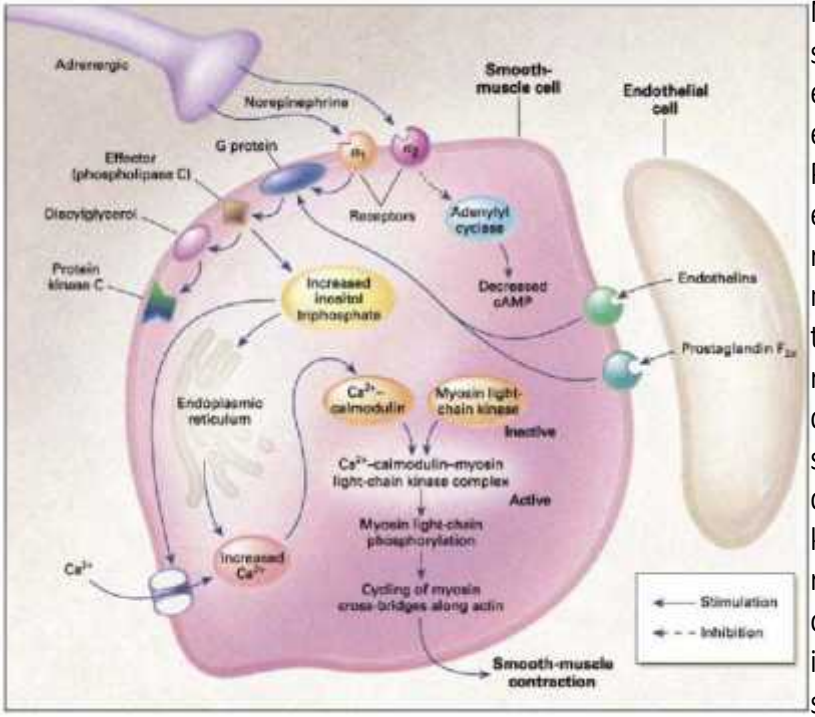
Decreased Spermatogenesis & Fertility of Men Associated with Increasing Age –In Testicle biopsy sections of men in the third and fourth decades of life, 90% of seminiferous tubules contain spermatids. In the fifth to seventh decades of life, only 50% of the seminiferous tubules contain mature spermatids. In men over 80 years of age only 10% of seminiferous tubules contain mature spermatids. Thus, although some seminiferous tubules continue to make sperm sufficient for impregnating the female partner as late as the ninth decade of life, the percentage of seminiferous tubules still functioning and making sperm quite distinctly decline with advancing age. [3]

Mechanisms Involved In Normal Erectile Function [7,8,9]

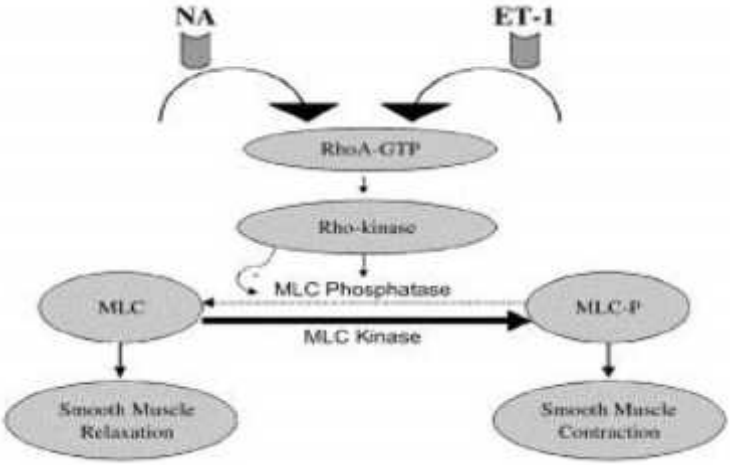
Erection thus involves sinusoidal relaxation, arterial dilatation, and venous compression. The importance of smooth muscle relaxation has been demonstrated in animal and human studies.

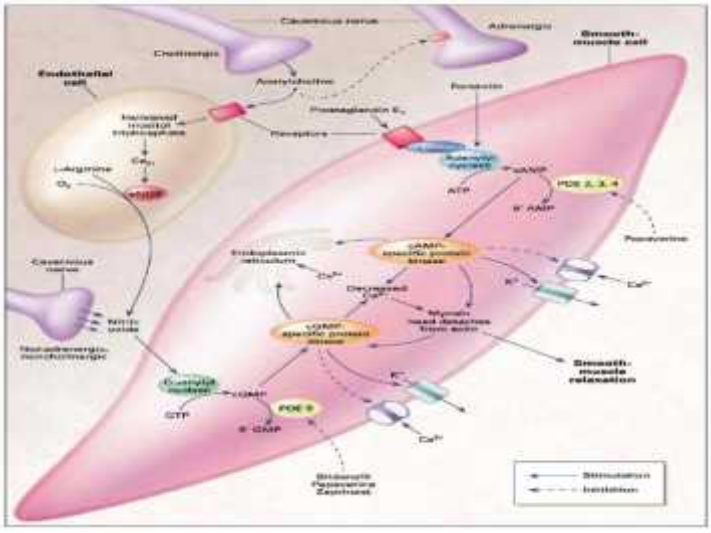
What Happens In Ageing- Degenerative changes (Peyronie's disease, old age, and diabetes) or traumatic injury to the tunica albuginea (penile fracture) resulting in inadequate compression of the subtunical and emissary veins. A decrease in elastic fibers in the tunica albuginea and an alteration of microarchitecture may contribute to impotence in some. Structural alterations in the fibroelastic components of the trabeculae, cavernous smooth muscle, and endothelium may result in venous leak. Cavernosal perivascular smooth muscle cells (SMCs) and sinusoidal lining endothelium build up the vascular component which is embedded in an extracellular matrix (ECM) mostly composed by collagen and elastic fibers. With the advancement of age, several modifications in the composition and organization of these components were reported and suggested to alter elderly erectile capability. Aged cavernosal tissue presents variations in SMC content and function, changes in vascular angioarchitecture, increase in collagen production and degeneration of elastic fibers. These modifications affect penile hemodynamics by impairing cavernosal SMC relaxation, reducing penile elasticity, compliance, and promoting fibrosis.[4,5,6]

Molecular Basis- In fact, with aging, events controlling tissue remodeling, such as the ratio apoptosis/proliferation, become unbalanced ensuing in loss of homeostasis. Molecularly, alterations in the serine/threonine protein kinase, mitogen-activated protein p42/44 kinase (p42/44 MAPK), has been suggested to occur in aged tissues affecting remodeling status. This important downstream effector kinase regulates a multitude of cellular activities, including cell proliferation, survival, and ECM expansion .In fact, in younger versus elderly human CC, there seems to occur a differential activation of the p42/44 kinase, suggesting a distinct function for this protein during adulthood .Differential activation of p42/44 in human young and aged erectile tissue. In younger CC, p42/44 is mostly phosphorylated in SMCs In certain vascular spaces; activated p42/44 was clearly identified lining the sinusoids. Elderly erectile tissue presented increased phospho-p42/44 expression in areas of collagen deposition.[10,11,12,13]



Norepinephrine from sympathetic nerve endings and endothelins and PGF2a from the endothelium activate receptors on smooth muscle cells to initiate the reactions that result in elevation of calcium concn and smooth muscle contraction. Protein kinase C is a regulatory component of the Ca2+-independent, sustained phase of agonist-induced contractile responses





The intracellular messengers mediating smooth muscle relaxation, cAMP and cGMP, activate specific protein kinases, which cause opening of potassium channels, closing of calcium channels. The fall in intracellular calcium leads to smooth muscle relaxation

Decreased Spermatogenesis & Fertility of Men Associated with Increasing Age

It is widely viewed that although the female gradually becomes less fertile with age and eventually undergoes menopause between the ages of 45 and 55 years, the male retains his fertility well into old age and does not go through an endocrinological menopause. This point of view is in general accurate. Men at middle age do not have hot flashes and dramatic elevations of FSH and LH associated with gonadal atrophy as women do. In fact, men have been documented in the scientific literature to retain their fertility to as old an age as 94. Similarly in animals, bulls have been known to retain their fertility to as old as 19 Years of age (quite aged for cattle). Abundant spermatozoa have been found in the testes of men undergoing orchiectomy at an extremely old age. Thus, it is clear that men do not undergo a menopause similar to women, and men in general can be expected to retain their fertility well into advanced old age.[14]

Until recently we had a poor understanding of the effect of aging on male fertility. It was assumed that male fertility was relatively immortal because so many elderly men have been able to impregnate their wives. However, there has been previous crude data showing a relative decrease in sperm count, and possibly fertility, in a certain percent of aging men.Thus, although some seminiferous tubules continue to make sperm sufficient for impregnating the female partner as late as the ninth decade of life, the percentage of seminiferous tubules still functioning and making sperm quite distinctly decline with advancing age. [15]

When the sperm count is reduced in young infertile men, as mentioned before, it is usually closely related to the percentage of cell loss during postprophase of meiosis (i.e., the second meiotic division). With careful, quantitative evaluations of testicular histology, sperm production rates in humans are usually closely related to the percentage of cell loss during the later stages of meiosis both in infertile as well as fertile men.[16,17]

However, in the aging testicle the situation is different. In aging men, the reduction in average daily sperm production occurs during meiosis also, but it does not occur in the late stage of meiosis. Rather, the age-related decline in daily sperm production results largely from a block to further meiosis in the early prophase stage of meiosis. To explain this in a different fashion, there is no difference between older men and younger men in the number of early primary spermatocytes per gram of testicular tissue. However, there is a vast difference between older and younger men in the number of late spermatocytes. This is what causes the mean reduction in numbers of spermatozoa seen in a population of older men versus a similarly random population of younger men. Older men have a significant reduction 'in potential daily sperm production between the early and the late primary spermatocyte stage, not late in meiosis as occurs more commonly in infertile men. [18]

For example, a man who in his youth had a sperm count of 50 million per cc might perhaps in his 80s have a sperm count of 10 million per cc. If there is no specific pathological process other than aging, it is possible that his only problem is a reduction in the number of spermatozoa and not a reduction in fertility The answer to this question awaits the type of massive clinical study in men of varying ages

Regardless of this present lack of clarity on the issue of fertility in older men, at least it can be said with certainty that there is an age-related decline in spermatogenesis that might possibly result in a moderate decline in male fertility.

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