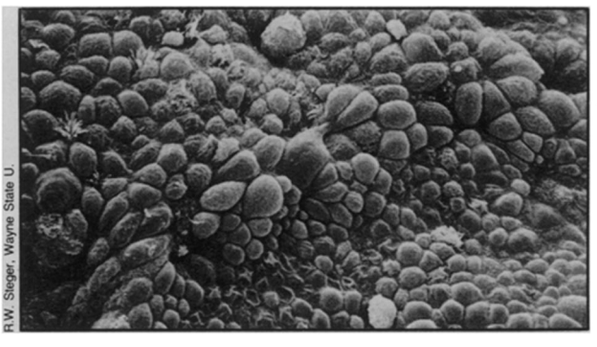
Human Reproduction and Aging

Perhaps aging of the human reproductive system could be due to neurochemicals in the brain



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Surface of an aged human uterus. The cells show very few microvilli, or tiny finger-like projections, indicating decreased secretions in the uterus. Decreased secretions in turn may explain why a fertilized egg fails to implant in the aged uterus.

BY JOAN AREHART-TREICHEL

Although there are documented instances of men reproducing as late in life as age 94, and women as late as age 57, the reproductive abilities of both men and women generally decline in later years. This decline is precipitated by various changes in reproductive functions, the recent annual meeting of the American Aging Association revealed. But what triggers these changes in the first place? The answer, intriguingly, may ultimately lie not with sex hormones but with neurochemicals that convey messages from nerves in the brain to hormone-secreting cells in the brain.

While men and women are in their reproductive prime, their sex hormone activity is similar. The hypothalamus of the brain releases tiny peptides that serve as the master sex hormones of the brain and body. These peptides act on glycoprotein sex hormones in the nearby pituitary gland. The pituitary gland hormones in turn send messages to the ovaries of the woman and to the testes of the man. The ovaries then release an egg for fertilization as well as estrogen and other steroid hormones, which act on the uterus and other tissues to produce female sexual characteristics. The testes then make sperm and produce testosterone and other steroid hormones, which act on spermatogenic cells, the prostate gland and seminal vesicles, as well as on skin, bone, muscle and brain to produce male sexual characteristics.

As men and women age, their steroid sex hormone levels decline—suddenly at the menopause in women and more gradually in men. Pituitary sex hormone levels, on the other hand, rise with age in both men and women. Men and women also share other aspects of reproductive aging. A woman's reproductive capacity, for example, sharply declines between ages 45 and 50 as eggs are no longer regularly released from the ovaries or as the ovarian follicle fails to form a corpus luteum after ovulation. The vagina loses fat content, and there is diminished pubic hair. Although aging does not appear to alter the fallopian tubes, through which eggs used to pass on their way to the uterus, the uterine wall loses muscle protein. Whereas a man can usually reproduce to a later age than a woman can, his testes still shrink with age. He produces fewer sperm and less ejaculate fluids. His sperm become less active and their fertility decreases.

Like other aspects of bodily aging, the origins of sexual aging may be at the cellular, tissue, organ or even system level, or perhaps at more than one of these levels. There is ample evidence for cellular aging of the reproductive system. In prostate gland cells RNA synthesis diminishes with age, and inert material gathers in these cells and in other cells of male sex organs, David Brandes of Johns Hopkins University has found. Progesterone receptors in the uterus decline in number with age, according to Alice Soriero of the University of Texas at Galveston, and testosterone receptors in prostate cells decrease with age, according to Sidney A. Shain of the Southwest Foundation in San Antonio. The immune system may also bring about reproductive aging. Autoantibodies to sperm have been found to increase with age. There is likewise evidence that hormones trigger reproductive aging—for example, the decline in steroid sex hormone levels with age. Which of these changes are the cause of aging and which are the effects of a more basic cause, however, remains to be shown.

Take the case of the decline in sex hormones that comes with age. At first examination one might blame reproductive aging on the decrease in gonadal sex hormones—estrogen and testosterone. There is evidence to support this contention, according to S. Mitchell Harman of the National Institute of Aging. Male sex steroid hormone levels, for instance, decrease at about the same time that sexual performance decreases, and there have been a few anecdotal reports of injections of male steroid sex hormones increasing older men's sex drives. Still other evidence, however, suggests that the gonadal sex hormones are not responsible for aging. Giving steroid sex hormones to older women does not increase their reproductive years, says G.B. Talbert of the State University of New York at Buffalo.

Further evidence suggests that the pituitary sex hormones might be the cause of reproductive aging—at least in rats, and possibly in humans as well. Gail D. Riegle of Michigan State University gave a pituitary sex hormone—luteinizing hormone—to both old and young male rats. After receiving it, the old rats reproduced just as much testosterone as did the young rats, suggesting that a lack of pituitary sex hormones is the cause of reproductive aging. Another Riegle study, in contrast, implies that hypothalamic sex hormones are at the heart of reproductive aging. When he gave a hypothalamic sex hormone—luteinizing releasing hormone—to old male rats, they produced just as much luteinizing hormone as did young rats.

But can one even safely blame reproductive aging on a decline in hypothalamic sex hormones? Apparently not. The hypothalamus of aged rats contains only half the amount of the nerve transmitter norepinephrine that the hypothalamus of young rats produces, Riegle has found. Norepinephrine appears to be intimately involved in the release of pituitary sex hormones from the hypothalamus. Similarly, injecting L-Dopa, a precursor of the nerve transmitter dopamine, into old female rats increased their fertility, suggesting that a defect in neurotransmitters in the hypothalamus might be at the core of reproductive aging.

In other words, reproductive aging may be due not to mishaps in sex hormones per se, but rather to defects in the production of nerve transmitters that help release sex hormones from the hypothalamus. This implication puts the onus for reproductive aging on the central nervous system, or even more specifically, on individual nerve cells, and brings us back to a cellular theory of reproductive aging.

But then there is the ever-nettling question: What elementary blunder in the cell is responsible for reproductive aging, or for any aspect of bodily aging for that matter? □