Journal of Andrology, Vol 20, Issue 4 509-518, Copyright © 1999 by The American Society of Andrology

JOURNAL ARTICLE

Reproductive aging in the Brown Norway rat is characterized by accelerated germ cell apoptosis and is not altered by luteinizing hormone replacement

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Reproductive aging in the male Brown Norway (BN) rat is characterized by decreased Leydig cell steroidogenesis associated with seminiferous tubule dysfunction. This could be a result of a combination of a primary testicular defect and a secondary hypothalamic pituitary dysfunction. In the present study, we determined in the BN rat whether germ cell loss occurred via apoptosis. We then defined the age of onset of Leydig cell dysfunction and germ cell loss and examined whether chronic luteinizing hormone (LH) replacement would delay or prevent reproductive aging. Plasma hormone levels, testicular sperm concentrations, and germ cell apoptosis were studied in 6, 9, 12, 15, 18, and 21-month-old BN rats. Beginning at 15 months, testicular weight, sperm concentration, total sperm counts, plasma testosterone, LH, and inhibin decreased, whereas the proportion of regressed testes and plasma follicle-stimulating hormone (FSH) levels increased with aging. Accelerated germ cell apoptosis involving spermatogonia, preleptotene and pachytene spermatocytes, and spermatids was evident in some tubules of the relatively normal testes from 21-month-old rats. In the regressed testes, complete cessation of spermatogenesis occurred. The apoptotic index was higher in the testes of old (21-month-old) rats in particular at stages XII-XIV when compared with younger animals. Chronic LH replacement (0.5 microg i.p. twice per day) administered to 15-month-old BN rats for 6 months did not alter plasma hormone levels, testes weight, sperm concentration or content, or the germ cell apoptotic index. In the control group, 3 out of 10 testes were regressed, whereas in the LH-replaced group, only 1 out of 12 testes was regressed. We show in this study that early reproductive aging in the BN rat began at around 15 months. Germ cell loss associated with aging occurs via apoptosis. Replacement therapy with LH for 6 months does not decrease or delay the testicular dysfunction associated with aging. It is unlikely that hypothalamic-pituitary dysregulation is the major cause of testicular aging.

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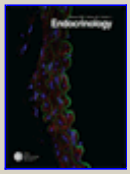

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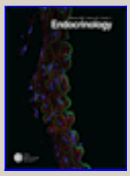

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