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INFLUENCE OF AGE ON PEAK FREQUENCY OF LH AND TESTOSTERONE IN A HEALTHY POPULATION

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Aging influences the hypothalamic-pituitary-testicular axis in a complex fashion. Although the primary lesion is essentially at the testicular level, the delayed pituitary response to GnRH suggests the existence of discrete change in hypothalamo-pituitary function. We studied peak frequency of LH and T secretion in young and elderly males. Blood samples were taken every 20 minutes for 24 hrs in 20 young (<60 yrs) and 13 elderly (>70 yrs) monks living together in a monastery. Mean T was significantly lower in the elderly (402±181 ng/dl) than in the young monks (535±134), while the opposite was true for LH (2.8±2.1 ng/ml and 1.7±0.3 respectively) (P<0.05). Peak frequency, analysed by pulsar, of T and LH was significantly higher in 20-40 yrs old monks (n=10) than in elderly monks (LH :3.9±1.0 and 3.0±0.7; T :3.7±0.8 and 1.7±1.0 pulses/12 hrs) (P<0.01). No differences could be found in peak amplitude for both hormones between young and old monks. Percutaneous 5 $\alpha$ -androstanoone (DHT) administration resulted in a more important decrease of LH and T levels in elderly than in young males (T : $\Delta$ post-pre young 123±123 ng/dl -  $\Delta$ old 204±78; LH : $\Delta$ young 1.1±1.5 ng/ml -  $\Delta$ old 2.0±1.6) (P < 0.01) indicating a greater sensitivity to feedback in elderly males in comparison to young males.

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ADRENAL STEROIDS STIMULATE THE GROWTH OF DIMETHYLBENZANTHRACENE (DMBA)- INDUCED RAT MAMMARY TUMORS. Spinola, P.G., Marchetti, B. and Labrie, F., MRC Group in Molecular Endocrinology, Laval University Medical Center, Quebec, G1V 4G2 - Canada.

There is convincing evidence that adrenal steroids, especially androst-5-ene-3 $\beta$ ,17 $\beta$ -diol ( $\Delta^5$ -diol), play a role in the etiology of breast cancer. Dehydroepiandrosterone (DHEA) and DHEA-sulfate (DHEA-S) have been postulated as being involved in the development of breast cancer through the formation of their metabolite  $\Delta^5$ -diol. In order to further investigate the role of adrenal steroids in hormone-sensitive cancer growth, we have studied the effect of treatment with  $\Delta^5$ -diol (2 mg, twice daily) or DHEA (2 mg, twice daily) on the growth of DMBA-induced mammary tumors in the rat. From 3 to 4 months after DMBA administration, at a time when tumors had an average area of 3.76 ± .87 to 4.51 ± 0.89 cm<sup>2</sup>, groups of animals were kept as intact controls or were ovariectomized (OVX) and received either  $\Delta^5$ -diol or DHEA for 24 days. While very few new tumors developed in OVX animals (average = 0.07 ± 0.07 per animal), an average of 0.40 ± 0.24 new tumor appeared in intact rats. In OVX animals treated with  $\Delta^5$ -diol or DHEA, the numbers were 1.85 ± 0.82 and 0.39 ± 0.17, respectively. An even more striking effect was observed on average tumor area that decreased from 4.70 ± 0.95 cm<sup>2</sup> in intact animals to 0.75 ± 0.27 cm<sup>2</sup> in OVX rats. Values of 9.79 ± 2.25 and 3.93 ± 0.86 cm<sup>2</sup> were found in  $\Delta^5$ -diol- and DHEA-treated animals, respectively.  $\Delta^5$ -diol and DHEA led to stimulation of the level of progesterone receptors in both the uteri and DMBA-induced tumors. The present data show that the two C<sub>19</sub> steroids  $\Delta^5$ -diol and DHEA can exert stimulatory effects analogous to those of estrogens on DMBA-induced tumor growth in the rat, thus suggesting a role of these adrenal steroids in breast cancer and other estrogen-sensitive diseases in the human.