the effect of electrical stimulation of the preganglionic parasympathetic nerves more easily than that of stimulation of the postganglionic nerves in the submandibular glands of cats[7]. The enzyme activity in the toxin-treated submandibulars, expressed as a percentage of the contralateral glands, is of the same magnitude as that reported by Nordenfelt[5] in these glands of cats after previous section of the preganglionic parasympathetic nerves; the mean percentage figure in his study was 60, 2–5 weeks after the surgical procedure. The reduction obtained after the nerve section has been attributed both to degeneration of the preganglionic nerves within the gland and to a fall in the enzyme activity of the postganglionic nerves. Section of the preganglionic parasympathetic nerves to parotids, which have their relay outside the glands, caused the enzyme activity to fall by about 25% in the postganglionic nerves in cats[8] and dogs[9]. In addition, prolonged treatment with a ganglion-blocking drug was followed by a decrease in the enzyme activity also of about 25% in rat parotids[10]. From his finding of a decreased choline acetyltransferase activity in the parotids of cats after cutting the preganglionic parasympathetic nerves, Nordenfelt[8] suggested that the enzyme activity in the postganglionic nerves was dependent on the traffic of impulses in these nerves. This concept is supported by the outcome of a series of experiments, mainly on salivary glands[11]. The profound fall in the choline acetyltransferase activity of the submandibular glands after treatment with botulinum toxin may thus be explained by a decrease of the enzyme activity in both the pre- and postganglionic parasympathetic nerves of the glands; the decrease in the postganglionic nerves being partly a consequence of a reduction or loss of the propagation of impulses along these nerves resulting from the toxin interfering with the transmission at the ganglia. Morphological examination of the postganglionic nerves within the glands treated with the toxin showed no obvious differences from those in the contralateral glands, except that the density of cholinesterase positive nerves appeared to be greater in those glands showing most atrophy. No clear evidence of axonal sprouting, as previously found in somatic motor nerves after botulinum toxin treatment of skeletal muscles in mice[12,13], has so far been observed. Conversely, in the same sort of skeletal muscle preparation, no change in choline acetyltransferase activity was noticed[14].

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Reproductive consequences of mega vitamin E supplements in female rats[1]

N. Y. J. Yang and I. D. Desai

Division of Human Nutrition, University of British Columbia, Vancouver, B.C. (Canada V6T 1W5), 3 March 1977

Summary. Female rats fed 0, 25, 2500 and 10,000 IU vitamin E/kg diet for 3 months were examined for reproductive performance. On 10,000 IU vitamin E/kg diet, the fertility of inseminated rats was significantly reduced as compared to rats given normal or nutritional levels of vitamin E.

Vitamin E supplementation has been proclaimed by some medical practitioners and popular press to be beneficial for health and for protection against numerous ailments. Vitamin E has been advertised widely for self-medication and is available freely without prescription. Even though vitamin E has been established as an essential factor for successful reproduction in the female rat[2], potential hazards of hypervitaminosis E warrant thorough investigation. The study presented in this report demonstrates the harmful effects of excess vitamin E on the fertility of female rats.

Methods and materials. Female weanling rats of Wistar strain weighing approximately 50 g were randomly divided into 4 groups with 5 rats in each group. The rats were housed in individual hanging wire-meshed cages in a room which was lighted from 6.00 h to 18.00 h daily and thermostatically maintained at 23 °C. Food and water were provided ad libitum. The basal vitamin E deficient diet of Draper et al.[3], with different levels of vitamin E supplements was fed to the 4 groups of rats for 3 months. 1 group of rats was fed only the basal diet without any vitamin E supplements. 2 of the 4 groups of rats were treated with excess vitamin E, the levels being 2500 and 10,000 IU vitamin E (dl-α-tocopheryl acetate)/kg diet respectively. The rats in the control group were fed 250 IU/kg diet for the first month and then 25 IU/kg diet for the rest of the experimental period. At the end of 3 months, female rats were mated with males of the same age which were maintained on commercial laboratory chow. The fertility rate of males and females on control diets was between 90 and 100% at this stage of life. The mating was carried out by exposing each female rat to a different male rat during each day until insemination occurred or up to a maximum of 10 days (2 estrus cycles). Vaginal swab technique was used to examine estrus. The day of insemination was determined by the appearance of sperms in the vaginal smear. After insemination, all females were housed individually and were killed 19 days post-insemination. The uteri were examined for the number of live, dead and resorbed fetuses and for the implantation sites. All fetuses were examined for possible external malformations.

Results and discussion. The effects of dietary vitamin E supplements on reproductive performance of female rats are presented in the table. 4 out of 5 rats in vitamin E-deficient and control groups, and all 5 rats in 2 groups

1 This work was supported by research grants from the National Research Council of Canada and the Research Committee of The University of British Columbia. We thank Mrs Virginia Green for her help in statistical analysis. Reprint requests should be addressed to Dr I. D. Desai, Professor of Nutrition.
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The effects of dietary vitamin E supplements on reproductive performance of female rats

Dietary vitamin E (IU/kg diet)	No. of animals	Fertility test		Fetus Score[d]		
		Insemination[a] index (%)	Implantation[b] index (%)	Live (%)	Malformed (%)	Resorbed (%)
0	5	80	100	20[e]	0	80[e]
25	5	80	100	91	0	9
2500	5	100	100	90	0	10
10000	5	100	20[e]	100	0	0

[a] Insemination index is 100 × number of rats inseminated/number of rats used for mating. [b] Implantation index is 100 × number of rats with at least one implantation site/number of rats inseminated. [c] Significantly lower than other groups, probability ≤ 0.004 by Freeman and Halton's exact probability test[5]. [d] Fetus score is expressed as 100 × number of live or malformed or resorbed fetuses/number of implantation sites. [e] Significantly different from other groups in the same column, probability ≤ 0.004 by Mann-Whitney U-test[4].

with excess vitamin E supplements were found to be inseminated during the mating period. At necropsy, all inseminated rats fed dietary vitamin E from 0 to 2500 IU/kg diet for 3 months were pregnant. However, only 1 out of the 5 inseminated rats fed 10,000 IU vitamin E/kg diet was pregnant. The low level of fertility in rats fed 10,000 IU vitamin E/kg diet was significantly different from the other 3 groups ($p < 0.004$) using Freeman and Halton's exact probability test[5] for statistical analysis. Fetuses from normal and high vitamin E supplemented rats were otherwise quite normal and no signs of malformations were observed.

In an earlier study, hypervitaminosis E has been reported to disturb ovarian activity in rats[6]. After administration of 3.3 IU vitamin E daily for more than 4 months, it was found that the number of corpora lutea decreased, the weight of ovaries reduced, fewer follicles ripened and the length of estrous cycle altered. The results of our fertility test have demonstrated the possibility of serious reproductive consequences of ovary malfunction induced by hypervitaminosis E. Increased intake of dietary vitamin E has been demonstrated to reduce the serum concentrations of prostaglandins in rats[7]. Since prostaglandins have been shown to play a role in regulating many reproductive processes including ovulation and corpus luteum function[8], the effect of hypervitaminosis E on fertility is quite probably due to its influence on prostaglandins.

Our preliminary results indicate that excess dietary vitamin E, as well as vitamin E deficiency[9], for a prolonged period of time, can interfere with normal reproductive functions in female rats, although the mechanisms may be quite different. Further investigations into the adverse effects of hypervitaminosis E on reproductive functions of female rats are presently being carried out in our laboratory.

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On the mechanism of the amphetamine induced vasodilatation at the rat's cerebral cortex[1]

A. A. Rovere, A. C. Raynald and O. U. Scremin[2]

Catedra de Farmacologia, Facultad de Ciencias Medicas, Universidad de Rosario, Rosario (Argentina), 30 March 1977

Summary. Cerebral cortical blood flow was measured with the hydrogen clearance technique. It was found that the increase in CoBF induced by amphetamine is blocked by atropine or chlorpromazine.

Amphetamine has been reported to increase cerebral blood flow in the rat by a mechanism not dependent on metabolic activation, as the increase in cerebral blood flow is severalfold greater than the change in cerebral metabolic rate of oxygen[3].

The increase in cerebral cortex blood flow (CoBF) associated with electrocortical desynchronization in the urethanized rat has been adscribed to a cholinergic mechanism as it can be blocked by atropine and potentiated by eserine[4]. Also a cholinergic mechanism has been found responsible for the cerebrovascular effect of CO_2 in rats[5]. In order to determine the possible participation of a neurogenic mechanism of the same sort in the action of amphetamine, the present experiments were performed in which drugs affecting synaptic transmission in the central nervous system were assessed on their ability to modify the cerebrovascular effect of amphetamine. As amphetamine is known to release adrenergic transmitters, the effect on CoBF of noradrenaline, adrenaline, isoproterenol and amphetamine itself when topically applied to the cortex was also assessed.

1 This work was supported by grants from Consejo Nacional de Investigaciones Científicas y Tecnicas and Consejo de Investigaciones de la Provincia de Santa Fé, Argentina.
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