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Comparative Toxicity of Three Forms of Vitamin D for Albino Rats.

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There are two views as to the nature of the toxic action of Vitamin D.¹ One is that toxication is a function of the antirachitic unitage, while the other holds that this result depends either on toxic by-products of activation or on end products of metabolism of the vitamin in the body.

In the course of some studies on the al-

at ages ranging from 242 to 601 days. One of 3 preparations of Vitamin D was administered to each group in daily doses of 75 units per g of body weight.

Group 1, comprising 4 males and 5 females received Vitamin D₃ (activated 7 dehydrocholesterol in sesame oil),* by stomach tube.

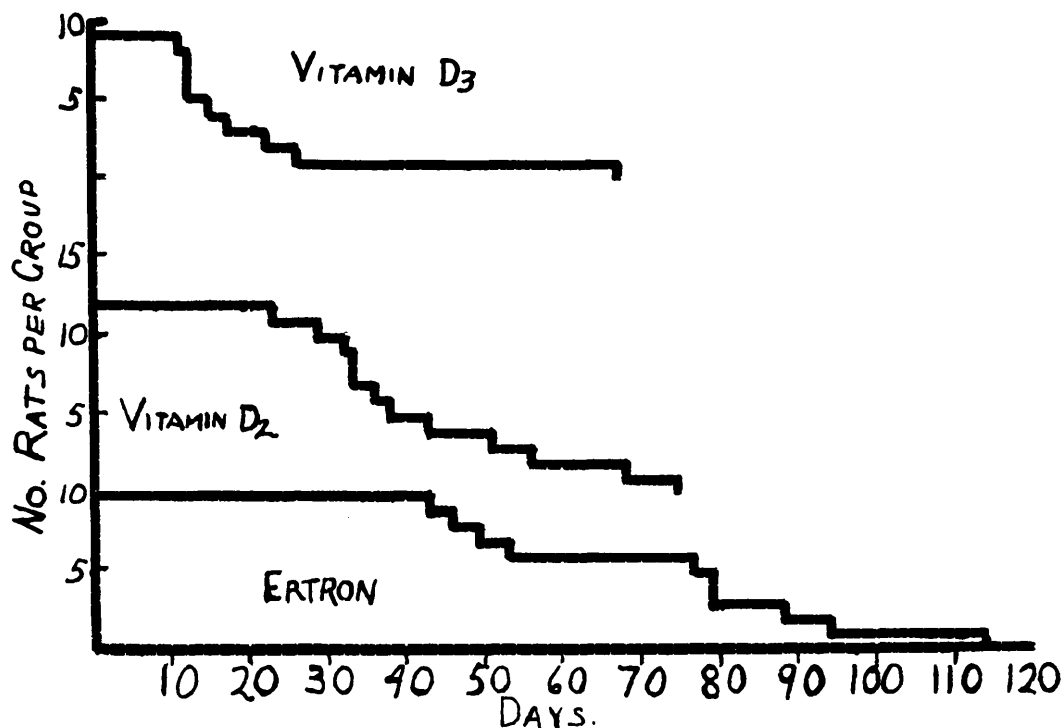


FIG. 1.

Survival rates of comparable groups of rats receiving identical antirachitic unitage of three different preparations of Vitamin D.

leged hypertensive action of Vitamin D in rats² it appeared that different preparations of the vitamin gave different degrees of toxication. Consequently, 3 groups of rats were selected from our standardized stock colony

Group 2, six males and 6 females received Vitamin D₂† (calciferol in corn oil) by stomach tube.

Group 3, seven males and 4 females, received Vitamin D in the form of ertron, an electrically activated ergosterol.‡ This ma-

¹ Reed, C. I., Struck, H. C., and Steek, I. E., *Vitamin D*, 1939, University of Chicago Press.

² Mrazek, R., Novak, C. G., and Reed, C. I., *Proc. Am. Physiol. Soc.*, April, 1942.

* Courtesy of Dr. J. Waddell, DuPont Co.

† Courtesy, Winthrop Chemical Co.

‡ Courtesy, Nutrition Research Laboratories.

terial was not purified, but the activated stock mix was dissolved in corn oil and given by stomach tube.

It is emphasized again that the dose of each preparation was 75 international antirachitic units per g of body weight. There was no standardization of toxic factors, if such exist.

The duration of life in each group is shown graphically in Fig. 1, each unit space representing one rat and each fall, therefore, represents the death of one animal.

In Group 1, the first rat was found dead on the 11th day, and the 8th on the 26th day: the 9th rat survived to the 67th day. This last survivor was a male, but ordinarily no distinction could be made between the two sexes in survival time. The average period of survival was 29.5 days and 15.4 days respectively.

In Group 2, the first rat, (m), died on the 23rd day, while the last (f) died on the 75th day. The average survival period for males was 43.3 days, for the females, 42.3 days.

In Group 3, the first rat (f) died on the 43rd day, the 10th (f) on the 94th day, and the 11th (m) on the 114th day. The mean survival time was 68.4 days for males, 71 for females.

Despite the small numbers of animals in each group it appears that the differences in toxic responses to the different preparations may be specific. Since the antirachitic dose of each preparation was the same, it must be concluded that the fatal outcome of toxication was conditioned, at least, by some other factor not expressed by antirachitic units. Post mortem examination did not reveal any differences of significance in the type of lesions.

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Effects of Various Chemical Agents on Survival of Primitive Respiratory Mechanism.

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That young animals are much less susceptible to anoxia than are adults has been well established.¹⁻³ Selle and Witten⁴ have shown that the respiratory center of rats, rabbits, cats and dogs is itself much more tenacious and viable in the young than in the adult, and that until approximately 6 weeks of age the survival of the respiratory mechanism of the rat is inversely proportional to age. Following decapitation or ligation of the cerebral

vessels, the isolated ischemic head of a full grown rat gasps 5 to 8 times over a period of 10 or 20 sec and thereafter remains motionless; in a week old animal the phenomenon continues for 30 min or more.

Unlike adults, rats under 6 weeks of age display 2 periods of respiratory movements: an initial series which consists of 6 to 12 gasps and lasts 20 to 30 sec, and a second series which begins 30 to 50 sec after cessation of the initial or first series and lasts for a variable time depending upon the age. The total number of gasps in both series, as well as the total duration of gasping, is greater the younger the animal. The second series, which is influenced most by age, lasts 30 to 40 min in new-born animals. As age increases, the number of gasps, as well as duration of gasping, diminishes uniformly. Similar observations have been made on

¹ Reiss, M., and Haurowitz, F., *Klin. Wchnschr.*, 1929, **8**, 743.

² Avery, R. C., and Johlin, J. M., *Proc. Soc. Exp. Biol. and Med.*, 1932, **29**, 1184.

³ Kabat, H., and Dennis, C., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 534.

⁴ Selle, W. A., and Witten, G. A., *Proc. Soc. Exp. Biol. and Med.*, 1941, **47**, 495.

⁵ Himwich, H. E., Alexander, F. A. D., and Fazekas, J. F., *Am. J. Physiology*, 1941, **134**, 281.