Although our series is too short to be conclusive, there is no evidence of a difference in bromide distribution in paretic and non-paretic individuals. The total halide distribution ratio $(Br+Cl)_s$: $(Br+Cl)_{csf}$ was practically constant, 0.85-0.89 in the 5 cases in which it was determined. It should be noted that this is lower than that observed for the system, serum: edema fluid, and that predicted for the system by the Gibbs-Donnan distribution law. This agrees with the values for the ratio $(Cl)_s:(Cl)_{csf}$ found in the absence of bromide by others,[3, 4]

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The Effect of High Doses of Irradiated and Non-Irradiated Ergosterol on the Albino Rat.*

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There have been many conflicting reports concerning the toxicity of irradiated products. This report covers the work of 4 years throughout which we endeavored to follow procedures which closely resemble the clinical administration of these irradiated products. We used a commercial product prepared and furnished to us by Mead Johnson and Company.

All materials were reassayed by us for vitamin D potency by the McCollum line-test. We also studied the blood calcium and phosphorus of representative animals at various stages. Our high dosages of irradiated ergosterol varied from 100 X to 465,000 X the therapeutic dose. All animals were carefully weighed and observed for their behavior. A record of the matings and condition of all litters was kept. All animals sacrificed or found dead were carefully autopsied and microscopic sections made of the thyroid, thymus, aorta, heart, lungs, liver, stomach, duodenum, spleen, kidneys, and gonads.

In summarizing our results we can say that: 1. Special, very potent commercial preparations of irradiated ergosterol were stan-

[3] Fremont-Smith, F., Dailey, M. E., Merritt, H. H., Carroll, M. P., Thomas, G. W., *Arch. Neur. and Psych.*, 1931, **25**, 1271.

[4] Muntrogler, E., Way, C. T., Pomerene, E., *J. Biol. Chem.*, 1931, **92**, 733.

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dardized by the McCollum line-test and found to possess the claimed activity. 2. Ten adult albino rats on stock diet plus 100 to 800 X the therapeutic dose for 36 weeks were without observable harmful effects. 3. The progeny, consisting of 48 second, 35 third, 4 fourth, 18 fifth, and 12 sixth generation rats, were placed on the same stock diet plus doses up to 50,000 X the curative dose without observing harmful effects. The sixth generation animals were treated for 18 weeks, all the others for longer periods. 4. Pure ergosterol was irradiated in the solid form by a Cooper-Hewitt mercury arc lamp and fed to albino rats and their offspring in amounts up to 25,000 X the curative dose for 10 to 23 weeks without harmful effects. 5. Albino rats were placed on the McCollum 3143 diet with and without the commercial preparation in amounts up to 10,000 X the therapeutic dose. Although most of the animals died in less than 30 weeks, no true hypervitaminosis could be detected. 6. Young albino rats on a stock diet including bread and milk plus 93,000 X the curative dose for 12 months showed a loss of weight in some cases. Adult animals under the same conditions showed an immediate loss of weight and in some cases died with pathological findings similar to those indicated below. 7. Young and adult albino rats on a stock diet including bread and milk plus 465,000 X the therapeutic dose showed immediate toxic effects. These were immediate loss of appetite and weight, bloody discharge from the nose, diarrhea, marked muscular flabbiness, and gross pathological changes involving enlarged adrenals, atrophied thymus, and abnormal appearance of the heart and kidneys. The adult animals were again more susceptible than the young ones. 8. Rachitic diet was substituted for the stock diet on the 46,500, 93,000, and 465,000 dosage experiments on young animals. This change made the animals more susceptible. 9. Potassium iodide was added to the dosage of 93,000 X the curative amount without changing the picture. 10. Young from mothers on 10,000 X the therapeutic dose were weaned and placed on a rachitic diet. Only very slight rickets developed. Similar young nursed by stock diet foster mothers developed typical rickets. 11. These results indicate that the toxic effects observed by others on relatively low dosages are due to the presence of a toxic substance other than the true antirachitic agent in appreciable amounts in the preparation tested. Whether the toxic effects observed by us on our commercial preparation when given in very high doses are due to a trace of this hypothetical by-product or to the vitamin D substitute remains to be determined. 12. Our results when compared with others again indicate

that the toxicity of a given irradiated ergosterol preparation is also determined in part by the character of the diet. In general the more complete and better balanced diets, act in a more protective manner.