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A Further Report on the Effect of Thyroparathyroidectomy on the Action of Irradiated Ergosterol.

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In a recent note[1] we reported that calcium in the blood could be raised to abnormal levels in dogs and in monkeys by feeding large amounts of irradiated ergosterol, but that hypercalcemia could not be induced by this means after the parathyroids and thyroids had been extirpated. In these experiments, the amount of ergosterol which was given was usually about 40 times that which is prescribed for infants of equivalent weight.

In the course of subsequent experiments of this kind, we have found that if still larger amounts of irradiated ergosterol are given, it is possible to induce hypercalcemia, after the thyroid and parathyroid glands have been excised. For this series of tests, 100 to 400 times the therapeutic dose has been given; in some instances as much as 800 times this dosage has been fed. Under such conditions, the calcium may rise from 6 or 7 mg. to 17 or even 20 mg. per 100 cc. of blood. That the parathyroids had been completely removed from the body, was shown furthermore by the fact that the inorganic phosphorus in the urine became markedly decreased or even was entirely absent following the operation.

As stated previously[2] we are of the opinion that the source of the marked increase in serum calcium induced by excessive amounts of irradiated ergosterol is the tissues, more particularly the bones, which are the great storehouses of calcium in the body. Subsequent investigations have confirmed this point of view. If dogs are fed, for a period of weeks or even months, on a diet which is almost free of calcium, being composed of cracker meal, dried meat and mazola (corn) oil, the calcium of the blood can be raised to abnormal levels by feeding excessive amounts of irradiated ergosterol, in spite of the deficiency of calcium in the ration. Furthermore, metabolism tests on dogs treated in this way show that there is a lack of retention of calcium, either a definitely diminished or a negative balance. It may be added that in rats which were given excessive amounts

[1] Hess, A. F., Weinstock, M., and Rivkin, H., PROC. SOC. EXP. BIOL. AND MED., 1929, xxvii, 55.

[2] Hess, A. F., Weinstock, M., and Rivkin, H., PROC. SOC. EXP. BIOL. AND MED., 1929, xxvi, 199.

of irradiated ergosterol, the ash of the bones was lower than in those of the control animals which had not received this addition.

It is our opinion, therefore, that very large amounts of activated ergosterol are able to withdraw calcium from the bones and that, if the dose is sufficiently large, they are able to accomplish this after the parathyroid glands have been excised. It should be emphasized, however, that this conclusion does not hold true for therapeutic doses of this drug, for it has been satisfactorily shown[3] that small amounts of irradiated ergosterol bring about a retention of calcium, as is true of cod liver oil and of direct ultra-violet irradiation.

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The "S" and "R" Forms of Hemophilus Influenzae.

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During the course of an experiment with a culture of *Hemophilus influenzae,* transplants were made on a plate of Levinthal's solid transparent medium. It was observed that the culture contained 2 types of colonies. Well defined small transparent colonies resembling the textbook description of the typical Pfeiffer bacillus colony were found but in addition there were larger, slightly opaque iridescent mucoid smooth colonies. Transplants were made from the transparent colonies on Levinthal agar and all the colonies were found to be identical with the mother colony. The same was true of transplants from the opaque iridescent colonies. It was thus possible to separate 2 cultures each of which produced typical colonies. Since the largest transparent colonies were found to have a rough surface the strain producing these colonies has been called an "R" strain; and since the iridescent colonies from the other culture had a smooth surface this strain has been called an "S" strain.

This culture and 2 others from which "S" and "R" forms were subsequently isolated had been seeded many times on blood or chocolate agar and the variation in the colonies had not been noticed. Yet the difference in the colony appearance was marked when transplants were made on the transparent agar plates. Very striking was

[3] Shohl, A. F., Bennett, H. B., and Weed, K. L., PROC. SOC. EXP. BIOL. AND MED., 1928, XXV, 551.