# SCIENCE ON THE MARCH

## THYROPROTEIN FOR INCREASED MILK AND EGG PRODUCTION

WHILE thyroid gland substance has been used for more than half a century for the correction of thyroid deficiency in man, it has been found only recently that thyroidal materials may also be used very effectively to stimulate such processes as milk production in dairy animals and egg production in hens. In the past, research on the possible use of thyroid treatment in animal production has not been undertaken, in part because of the prohibitive cost of the natural hormone for such purposes. The recent development by the authors of a chemical process for producing an inexpensive and highly active "thyroprotein" will, it is believed, lead to rapid progress in this field.

The discovery of iodine in the thyroid in high concentration by Baumann about fifty years ago stimulated considerable research on methods of introducing iodine into the protein molecule.

It was found that protein could be iodinated though the final product, varied according to the conditions employed. During the next 40 years, these various iodinated proteins were tested for thyroidal activity with either negative results or very questionable effects.

In the meantime thyroxine was isolated from hydrolysates of thyroid substance in 1919 and synthesized by Harington and Barger in 1927. This work was extremely important in establishing the constitution of thyroxine, but the synthetic hormone was still far too expensive for extended use with domestic animals.

Returning in the late thirties to further research on iodinated proteins, a Swiss investigator obtained more definite physiological effects by the recovery of an acid-insoluble fraction of iodoprotein after hydrolysis. Later, German chemists reported the isolation of traces of thyroxine from hydrolysates of iodoproteins. Their observations were confirmed by the famous English thyroid chemist, Harington. This work indicated that by suitable means of iodinating protein one step in the synthesis of thyroxine had been made. However, since the iodinated protein as such contained little thyroidal potency, it was thought that the transformation to thyroxine occurred during the process of hydrolysis.

A new interest was aroused by the discovery of Graham in Canada of the marked influence of thyroid feeding and thyroxine injection upon milk and fat secretion of dairy cows. Following the administration of thyroidal substances, the yield of milk and the fat percentage both increased and were sustained at a higher level so long as administration continued. However, since the cost of all thyroidal substances was very high, it seemed desirable to determine if the thyroidal potency of iodinated protein could be increased sufficiently so that it would serve, without preliminary hydrolysis, as a cheap source for animal feeding.

Using the frog tadpole as a test of biolgical activity at first, the various steps in the process of iodinating the milk protein, casein, were checked. Such factors as pH, extent of iodination, temperature, time, catalyzers, agitation, and others were tested. As a result of these studies it has been found possible to produce iodinated casein containing about 3 to 4 per cent thyroxine.

By this process of iodinating casein, or at least as the end result, nonthyroidally active proteins are transformed into biologically active thyroproteins by the synthesis *in vitro* of the thyroxine amino acid as an integral part of the protein. There is every reason to believe that this *in vitro* process is identical to the *in vivo* formation of the thyroid hormone in the gland. In one case any tyrosine-rich protein can be used as a starting material, whereas in the thyroid gland globulin is transformed into thyroglobulin. That the thyroid gland does not always complete the process has been shown by the great variation in thyroidal potency of thyroid globulin and by the further fact that iodination of such thyroglobulin may increase its potency.

It has been shown that the thyroxine recovered from the thyroid gland is in the optically active levo form. We have been

able to isolate l-thyroxine from casein thyroprotein, showing that it is similar to the natural product in this respect.

The use of desiccated thyroid to correct conditions of thyroid insufficiency in man is a well-established therapeutic remedy. The fact that it can be administered orally has greatly contributed to its wide use. In domestic animals its use has been limited by its high cost. In addition to its favorable effect upon the milk secretion process in dairy cattle, preliminary experimental work indicates its favorable effect on the lactation process in other domestic animals where the milk production may be a limiting factor in the rate of growth of the young.

Trials with poultry indicate beneficial effects in promoting more rapid growth and feathering of growing chicks and in stimulating and maintaining a high level of egg production, especially during the summer when the natural thyroid secretion is at a low ebb. Experiments are in progress to determine if the decline in egg production with advancing age may not be partially arrested so that the productive life of the laying hen may be extended.

The experimental work already conducted with thyroprotein indicates the importance of the dosage range to obtain beneficial effects. It is necessary to feed somewhat more than the thyroids produce normally and yet not enough to increase the metabolism beyond the optimum. At the optimum level of feeding, the body weight and productive processes are maintained. If excessive amounts are fed, the well-known signs of hyperthyroidism appear—loss of weight, rough hair, increased heart rate, reduced milk and egg production, etc. In the smaller animals the proper amount of thyroprotein can be added to the grain mixture; in larger animals such as dairy cows the optimum amount to feed can be judged by the animal husbandman as measured by the body weight and condition, and by the production of milk.

That the products, milk and eggs, of animals fed thyroprotein are safe foods has been shown by their freedom from thyroxine. The mammary gland and the oviduct of the hen are nonpermeable to thyroxine.

Although the synthesis of highly active and uniform thyroprotein is now well established, research into its possible uses is just beginning. A few applications have been described. It is believed, however, that many other interesting and possibly useful effects of this substance will come to light as investigations continue.—C. W. Turner and E. P. Reineke, Missouri Agr. Exp. Sta.