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Goitrogenic Effect of Dietary Fat.

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Marine¹ believes that thyroid activity may be more necessary for oxidation of fats than of carbohydrates. Harington² suggests that fats, especially unsaturated ones, may interfere with iodine absorption by the thyroid. Chidester³⁻⁶ states that unsaturated fats absorb iodine from the body. Few positive experiments have been reported to support these beliefs. McCarrison⁷ found that diets excessively rich in proteins and fats caused thyroid enlargement in pigeons. The Mellanbys⁸ noticed that puppies receiving cod-liver oil as their only fat had small, normal thyroids, but with other fats there was always some hyperplasia, which was intensified when the amount of dietary fat was increased. Levine and Remington,⁹ in a comprehensive review, do not refer to the goitrogenic action of fats.

White rats, weighing about 50 gm., were kept in cages which prohibited coprophagy. The diets are given in Table I. Olive and cocoanut oils were chosen so that the effects of relatively saturated and unsaturated fats might be compared, olive oil being a typical unsaturated fat, and cocoanut oil, saturated. The salt was the usual Osborne and Mendel¹⁰ mixture, except that the potassium iodide was decreased. The salt mixture of diets A and B contained 13.5 mg. of potassium iodide per 500 gm., as compared with 4.6 mg. in diets C and D. The 2 diets containing olive oil differed only in the content of iodine. Levine, Remington, and von Kolnitz¹¹ have found that 1-2 gammas of iodine per day are sufficient to prevent goiter in the rat. The iodine in our salt mixtures supplied an excess well over the minimum requirement. (Table II.) The iodine content of

² Harington, C. R., Lancet, 1935, 228, 1199.

³ Chidester, F. E., Med. World, 1935, 53, 649.

4 Chidester, F. E., Am. Med., 1934, 40, 162.

- ⁵ Chidester, F. E., Science, 1932, 75, 286.
- ⁶ Chidester, F. E., Med. World, 1935, 58, 167.

7 McCarrison, R., Indian J. Med. Research, 1919, 7, 633.

⁸ Mellanby, E., and Mellanby, M. J., J. Physiol., 1921, 55, Proc. Physiol. Soc., vii.

9 Levine, H., and Remington, R. E., J. Chem. Ed., 1933, 10, 649.

10 Osborne, T. B., and Mendel, L. B., J. Biol. Chem., 1913, 15, 317.

11 Levine, H., Remington, R. E., and von Kolnitz, H., J. Nutrition, 1933, 6, 347.

¹ Marine, D., Physiol. Rev., 1922, 2, 521.

the other dietary constituents was not determined. Vitamins were supplied by brewer's yeast, viosterol, and caritol.* At the end of 50-60 days, the rats were killed and the thyroids were removed, weighed immediately, and then preserved in formalin for histological study.

| Diet | Protein % | Fat % | | Carbohydı % | rate | Salt Mixture % |
|------|---------------|--------------|----|----------------|------|-------------------|
| Α | Casein 18 | Olive oil | 28 | Cornstarch | 50 | 4 |
| в | , , ,, | Cocoanut oil | ,, | ,, | " | 4 |
| С | ,, ,, | Olive oil | ,, | ,, | ,, | 4 |
| D | »» »» | None | | " | 78 | 4 |

TABLE I.

Histological examination[†] revealed no pathology, and showed that the glands were essentially alike regardless of the sex of the rat or the type or amount of fat fed. They showed a cubical acinar epithelium of normal appearance and an abundant storage of colloid, probably near the upper limit of the normal.

| Diet | No. of rats | Aver. daily gain gm. | Daily iodine intake* gamma | Thyroid wt., mg. | Thyroid per 100 gm. body wt,. mg. | | |
|------|-------------|-------------------------------------|------------------------------------|------------------------------------|---|--|--|
| A | 5 | 2.02 (1.77-2.17)† | 6.55 (5.98-6.60) | 16.3 (11.1-30.9) | 10.3 (7.3-19.5) | | |
| в | 4 | 1. 72 | 6. 90 | ` 15.1 ´ | ` 10.5 | | |
| С | 5 | (1.42-1.87) 2.27 (1.78, 2.62) | (6.60-7.22) 2.43 (2.06-2.68) | (13.7-18.0) 20.6 (17.0-24.0) | (9.7-12.8) 10.6 (9.8-12.4) | | |
| D | 5 | (1.78-2.62) 2.19 (1.73-2.87) | (2.06-2.08) 3.79 (3.51-4.54) | (17.0-24.0) 16.7 (13.5-19.0) | (9.8-12.4) 8.6 (7.0-10.4) | | |

TABLE II.

*This comprises iodine content of salt mixture only.

[†]The figures in parentheses represent the extremes of individual variations in each group.

Table II shows that the degree of saturation of a fat is not a factor in thyroid enlargement. A comparison of the thyroids of animals fed a diet of low iodine and high fat content (Diet C) with those of animals fed a diet low in its iodine content but containing no added fat (Diet D), indicates a slightly increased weight of the thyroids of Group C (an increase of approximately 20%). However, this is hardly significant, since Levine, Remington, and von

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Kolnitz¹² have shown that rat thyroids 400-1000% above the normal weight can be produced by a goitrogenic diet.

Since this work was completed, Remington has reported, at the April, 1937, meeting of the American Chemical Society, that neither saturated nor unsaturated fats, up to a level of 13% of the diet, have any measurable effect upon the size, dry matter, or iodine content of the thyroid gland. Our results are in accordance with his. Under the conditions of our experiments, neither the type nor the amount of fat in the diet had any demonstrable influence upon the weight or histology of the thyroid.

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Observations on the L-Organism of Klieneberger.

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The streptobacillus moniliformis, under various names, has been reported to occur in rats in pulmonary disease,^{1,2,3} otitis media,⁴ and as inhabitant of the nasopharynx;⁵ in mice, as an agent of systemic disease;^{5, 6, 7} in humans, in fevers following the bite of rats or other small animals,⁸⁻¹¹ or as an epidemic¹² or isolated¹³ infection of variable transmission. A similar organism has been observed by Smith¹⁴ in pneumonia of calves. All organisms described in the above reports are characterized morphologically by huge bulbous or

⁶ Levaditi, C., Selbie, R. F., and Schoen, R., Ann. Inst. Pasteur, 1932, 48, 308.

⁷ Mackie, T. J., Van Rooyen, C. E., and Gilroy, E., *Br. J. Exp. Path.*, 1933, 14, 132.

8 Schottmüller, H., Derm. Woch., 1914, 58 (Supp.), 77.

⁹ Blake, F. G., J. Exp. Med., 1916, 23, 39.

10 Dick, G. F., and Tunnicliff, R., J. Inf. Dis., 1917, 23, 183.

11 Scharles, F. H., and Seastone, C. V., New Eng. J. Med., 1934, 211, 711.

12 Parker, F., Jr., and Hudson, N. P., Am. J. Path., 1926, 2, 351.

¹² Levine, H., Remington, R. E., and von Kolnitz, H., J. Nutrition, 1933, 6, 325. ¹ Tunnicliff, R., J. Inf. Dis., 1916, 19, 767.

² Jones, F. S., J. Exp. Med., 1922, 35, 361.

³ Klieneberger, E., and Steabben, D. B., J. Hyg., 1937, 37, 143.

⁴ Nelson, J. B., J. Inf. Dis., 1930, 46, 64.

⁵ Strangeways, W. I., J. Path. and Bact., 1933, 37, 45.

¹³ Levaditi, C., Nicolau, S., and Poincloux, P., Compt. Rend. Acad. Sci., 1925, 130, 1188.

¹⁴ Smith, T., J. Exp. Med., 1918, 28, 333.