increasing to 2 cc. twice daily intramuscularly, was given to 22 rabbits over a period of 2 months without producing, or modifying existing, exophthalmos.

Summary. Male rabbits develop exophthalmos more frequently than females. This difference is independent of the thyroid gland. Exophthalmos develops most frequently in rabbits about the age of puberty (4-5 months). Gonadectomy greatly reduces the incidence even in thyroidectomized rabbits. Oestrone (menformon, theelin), pituitrin-S and adrenalin in the dosages and method of administration used neither produce, nor modify existing, exophthalmos.

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Prevention of Atherosclerosis in Rabbits. I. Administration of Potassium Thiocyanate.

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Many efforts have been made to counteract the atherosclerosis produced in rabbits by the feeding of cholesterol or cholesterol-containing foods with or without thyroidectomy.[1] These efforts have converged on a demonstration that iodides may to an extent replace the loss of thyroid in retarding the development of atheromata.[2-4] Completely negative results were reported for bromides. Otherwise attempts to get effects with organic compounds, *e. g.*, chlorophyll and alcohol, have either been unsubstantiated when reported positive, or gave no conclusive results.

Good evidence exists as to the serious changes in permeability of arterial walls following both thyroidectomy and the feeding of cholesterol.[5] It seemed reasonable, therefore, to follow out the investigations suggested by the use of ions. The Hofmeister series, although inaccurate in detail, unmistakably points to an ion which would be expected to be more effective than iodide, namely thiocyanate. At the same time it explains the ineffectiveness of the bromide ion. The relatively low toxicity of thiocyanates, coupled

1 Anitschkow, N., in *Arteriosclerosis*, Macmillan, New York, 1933.

2 Ungar, H., *Arch. Exp. Path.*, 1934, **175**, 536.

3 Turner, K. B., *J. Exp. Med.*, 1933, **58**, 115.

4 Turner, K. B., and Khayat, G. B., *J. Exp. Med.*, 1933, **58**, 127.

5 Duff, G. L., *Arch. Path.*, 1935, **20**, 81, 259.

with the fact that they are to an extent normal constituents of body fluids, led to the following procedure.

Twelve unselected young adult female rabbits from a strain which has been used in this laboratory for 12 years were thyroidectomized. A group of 4, which served as controls, were fed approximately 0.3 gm. cholesterol per kg. per day; a second group of 4 received the same plus 20 mg. per kg. per day of potassium thiocyanate; a third group received the same plus 60 mg. per kg. per day of potassium thiocyanate. All rabbits were given a 2.5% solution of calcium lactate as drinking water for 5 days.

The cholesterol was a very pure product of the Wilson Co., Chicago. The KCNS was recrystallized 2 times from an initially pure product to ensure freedom from traces of impurities, such as iodides. The diet consisted of alfalfa hay and oats with occasional greens.

Examinations were made of the principal organs, especially the aorta and the kidneys. Some blood cholesterols were determined.

Table I shows the results with respect to the appearance of cholesterol in the aorta and kidneys.

TABLE I.

Changes in Rabbits' Aortas and Kidneys on Feeding Cholesterol with and without Potassium Thiocyanate.

Wt.		KCNS mg. per kg. per day	No. of Days	Aorta	Kidneys	Thyroid at Autopsy	Blood Cholesterol
Start	Finish						
2261	2777	0	66	+	+	—	.254
1735	2032	0	59	+++	+++	—	
2036	2371	0	61	+++	+++	—	.530
1765	1800	0	52	+++	+++	tiny fragment	
1776	2096	20	61	+	++	—	
1972	2183	20	52	—	+	—	
1712	1754	20	59	++	+++	—	
2133	2580	20	66	—	+	2 x 2 mm.	.894
2067	2653	60	66	—	—	two 2 x 2 mm.	.387
2110	2354	60	61	—	—	tiny fragment	
1803	2165	60	56	—	—	—	
1946	1581	60	49	—	—	tiny fragment	

The amount deposited is judged as +, ++, +++, and absence as —.

The data present a picture of protection of the aorta by moderate amounts of potassium thiocyanate. Under the conditions the minimal dose must lie somewhere between 20 and 60 mg. of thiocyanate per kilogram body weight for a period of approximately 2 months. Grossly considered the protection seems to extend to the kidneys as well, but is only clear-cut in the case of the larger dosage of potassium thiocyanate.

The presence of tiny fragments of thyroid in 3 cases is considered irrelevant to the results. In 2 cases larger amounts of thyroid tissue, but still very small, were found, but they too are deemed insufficient to affect the results (*Cf.* Turner and Khayat, *loc. cit.*). Besides, the rabbits involved had a high cholesterolemia.

In the case of the control animals the largest rabbit showed slight deposition only. This may be attributed to some extent to the fact that it was receiving relatively about 2/3 of the dosage of cholesterol of the other animals. An analysis of its blood cholesterol showed only 0.254 as against 0.894, 0.530, and 0.387 in other animals. Nevertheless there may be other factors at play.

Whether the protection would break down in a longer period of time, or whether the administration of potassium thiocyanate following the development of atheromata would remove them, are problems reserved for further study. The thiocyanate ion may serve to heighten the degree of dispersion of the cholesterol colloids and it may have a distinct effect on the permeability of the arterial walls, or both. These possibilities, however, are to be investigated separately. Similarly further progress is visioned along the lines of extending the findings to other animals, closer to man in their dietary habits.

Conclusions. Potassium thiocyanate exercises a protective action against the development of cholesterol atherosclerosis in thyroidectomized rabbits.