

syringe (10 ml per animal). Powders were insufflated into the vagina with a small insufflator at the rate of $\frac{1}{2}$ g per rabbit. After treatment the rabbits were examined at various intervals for 3 to 5 weeks and sacrificed

after 6 to 8 weeks. The evaluation was based on one application of a given drug.

Results. Table I indicates the 58 therapeutic agents used for treatment of the vaginal infections produced by *T. foetus*; of these compounds tested, only 3 appeared to reduce the duration of infection in the rabbits; entozon, iodine and sulfomerthiolate. Entozon, iodine and sulfo-merthiolate eliminated the infection, in 1, 4 and 5 days, respectively. The infection in all the other drugs tested persisted for at least 15 days following the treatment. None of the compounds tested at the dosage employed produced any symptoms of toxicity nor was there any apparent damage to the mucous membranes of the vagina on post-mortem examination. The 3 drugs when used on 10 rabbits each appeared to shorten the duration of infection when compared with 10 untreated controls (Fig. 1). The results, however, are considered inconclusive.

Summary. A standardized, controlled *in vivo* technic utilizing female rabbits has been described for testing the trichomonacidal properties of various therapeutic compounds against *Trichomonas foetus*. A total of 58 compounds was tested by this method. Only 3 compounds: entozon, iodine and sulfomerthiolate appeared to reduce the duration of infection.

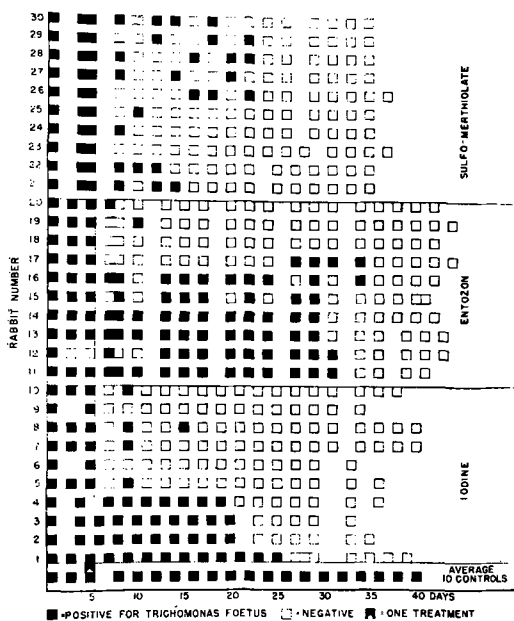


FIG. 1.

Results of *in vivo* tests with sulfo-merthiolate, entozon and iodine on *Trichomonas foetus*; 10 control rabbits.

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Effect of Alpha Naphthylthiourea (ANTU) on Serum Cholesterol in Thyroidectomized Dogs.

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Chronic poisoning of dogs with alpha naphthylthiourea (ANTU) is accompanied by a marked increase of the cholesterol content of the plasma. After discontinuing administration of ANTU the plasma cholesterol diminishes rapidly.¹ ANTU like other thiourea derivatives depresses the function of the thy-

roid gland. This underfunction leads to compensatory enlargement of the gland. Richter² who introduced ANTU as a rodenticide described hyperplasia of the thyroid in rats poisoned with the drug. The antithyroid effect of the drug has also been demonstrated by cytological studies of the thyroid of rats

¹ Chanutin, A., Gjessing, E. C., and Ludewig, S., *Proc. Soc. Exp. Biol. and Med.*, 1947, **64**, 174.

² Richter, C. P., *J. Am. Med. Assn.*, 1945, **129**, 927.

TABLE I.
Total Serum Cholesterol in Mg Per Cent.

Thyroidectomy	Treatment	Minimum	Maximum	Mean	S.E.*	Ratio free: total cholesterol
Before	None	145	210	187	7	.27
After	Thyroid	74	225	165	10	.30
"	Thyroid + ANTU	160	458	288	13	.33
"	Thyroid†	150	294	221	25	.33
"	Thyroid‡	177	210	196	6	.35

* Standard error of the mean.

† One week after discontinuing ANTU.

‡ Two weeks after discontinuing ANTU.

treated with ANTU.³ Hypothyroidism is known to be accompanied by a rise in plasma cholesterol. The increase in plasma cholesterol in dogs chronically poisoned with ANTU could therefore possibly be due to the "chemical thyroidectomy", caused by ANTU.¹

In order to determine the possible role of the thyroid, it was necessary to study the effect of ANTU poisoning on the serum cholesterol of thyroidectomized dogs. The thyroid deficiency due to removal of the thyroid had to be compensated by administration of desiccated thyroid by mouth. From studies in hypothyroid children⁴ and thyroidectomized rabbits⁵ it was known that the elevated serum cholesterol due to thyroid deficiency decreases rapidly to normal values under treatment with the thyroid hormone.

Material and methods. Six adult female dogs weighing around 14 kg were used. After a pre-operative control period the thyroid and parathyroid glands were removed surgically and the parathyroid glands reimplanted. Calcium lactate was given intravenously and by mouth during the first few days after operation. Feeding with Desiccated Thyroid U.S.P. 640 mg daily was started a week after operation. As soon as the dogs were stabilized on a normal cholesterol level feeding with ANTU (10 mg per kg bodyweight daily) was started. This was continued for a period of from 3 to 10 weeks. After this period ANTU was dis-

continued but treatment with desiccated thyroid was continued. In one of these dogs the chronic ANTU poisoning was repeated after the cholesterol level had reverted to normal for about 2 months. All dogs were sacrificed after completion of the study. No thyroid tissue or only minute amounts were found at autopsy.

Free and total cholesterol were determined by a modified Schoenheimer-Sperry procedure.⁶ A number of determinations of total cholesterol were made without digitonine precipitation on samples extracted with alcohol-ether. The results for total cholesterol obtained by this method were in good agreement with those obtained by the modified Schoenheimer-Sperry procedure.

Results. A summary of our experiments is given in Table I. Both from this summary and from the individual data on each experiment it can be seen that the thyroidectomized dogs treated with adequate doses of thyroid show normal serum cholesterol levels. The cholesterol levels of the operated dogs treated with thyroid tend to be slightly lower than during the pre-operative period. This is in agreement with the known fact that serum cholesterol levels in the adequately treated hypothyroid patient are in the normal or low normal range. Chronic poisoning with ANTU superimposed on the treatment with thyroid hormone results in a marked rise in serum cholesterol in every experiment. After discontinuing ANTU without changing the dose

³ Jones, R. P., *J. Path. and Bact.*, 1946, **58**, 483.

⁴ Wilkins, L., and Fleischmann, W., *J. Am. Med. Assn.*, 1941, **116**, 2459.

⁵ Fleischmann, W., Shumacker, H. B., Jr., and Wilkins, L., *Am. J. Physiol.*, 1940, **131**, 317.

⁶ Hawk, P. B., Oser, B. L., and Summerson, W. H., *Practical Physiological Chemistry*, 12th Ed. Blakiston Co., Philadelphia, 1945, p. 531.

of thyroid extract given by mouth the serum cholesterol level gradually reverts to normal values in every experiment. The ratio of free to esterified cholesterol stays within normal limits during the whole experiment and seems not to be appreciably changed by chronic ANTU poisoning.

Discussion. The experiments demonstrate that chronic poisoning with ANTU produces a reversible rise in serum cholesterol in thyroidectomized dogs treated with adequate doses of thyroid hormone. From our experiments it cannot be determined whether ANTU influences the metabolism of cholesterol or the distribution of cholesterol between blood and tissues. We can assume therefore, that ANTU produces a direct effect on serum cholesterol quite independent from an indirect effect due to the antithyroid properties of the drug.

The large dose of thyroid hormone used (640 mg daily) without inducing signs or symptoms of hyperthyroidism reflects the tolerance of dogs to large doses of thyroid

hormone. The dog, in proportion to its body weight, has apparently a much greater capacity than does man to inactivate exogenous thyroid hormone. This inactivation seems to take place in the extrathyroid tissues. Therefore both normal and thyroidectomized dogs can tolerate large doses of thyroid hormone without damage.⁷

Summary. Chronic poisoning with alpha naphthylthiourea (ANTU) produces a reversible rise in serum cholesterol in thyroidectomized dogs maintained on a dose of thyroid hormone adequate to prevent thyroid deficiency. This indicates that the effect of ANTU on serum cholesterol is at least partly independent from its property as an antithyroid drug.

We wish to thank Mrs. Aurora Bradford for her assistance in the cholesterol determinations, and Miss Frieda Faïman for statistical analysis of the data.

⁷ Danowski, T. S., Man, E. B., and Winkler, A. W., *Endocrinology*, 1946, **38**, 230.

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On the Chemical Sterilization of Blood and Blood Plasma.*

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The present study was undertaken in a search for a suitable means of chemically sterilizing human plasma and whole blood without so altering the blood components as to make them unsuitable for intravenous injection. The high incidence of homologous serum jaundice (4.5 to 7.2%) resulting from the injection of pooled plasma has become a serious problem in the use of pooled lyophilized plasma. At the present time only those methods involving the irradiation of

plasma with ultraviolet light,¹ x-ray, or high speed electrons² have offered promise of a solution to this problem. Of these methods, only electron bombardment has appeared to offer any promise in the sterilization of whole blood. All of these irradiation technics require the use of highly specialized equipment which precludes the possibility of treating plasma or blood except at specially equipped plants.

The specifications for a chemical sterilizing agent are dictated by the future intra-

* Part of this material was presented at the Regional Meeting of the American College of Physicians, Detroit, Michigan, November 20, 1948.

† The authors are indebted to Dr. Elizabeth M. Yagle for the immunological data in this report.

¹ Wolf, A. M., Mason, J., Fitzpatrick, J., Schwartz, O., and Levinson, O., *J.A.M.A.*, 1947, **136**, 476.

² Trump, J. G., personal communication.