

TABLE I.
Effect of Gold Therapy on Liver Function.

Dog	Alkaline phosphatase, units %	Rose Bengal clearance, %	van den Bergh reaction	
			Direct, mg %	Indirect, mg %
Control Values.				
1	6.2	119	0.0	0.2
2	4.4	109	0.0	0.1
Following 1 wk of daily administration of 25 mg of gold (sodium auro thiomalate).				
1	6.4	94	0.1	0.0
2	5.8	96	0.0	0.0
Following 1 wk of daily administration of 75 mg of gold (sodium auro thiomalate).				
1	7.2	111	0.1	0.0
2	8.2	111	0.1	0.0
Two wks later. No gold given during this interval.				
1	6.3	96	0.0	0.1
2	6.4	—	0.0	0.0
Following 1 wk of daily administration of 100 mg of gold thio glucose.				
1	7.0	115	0.0	0.0
2	6.4	95	0.0	0.0

In this study on dogs, the doses used, in terms of human therapy, were large, and a course of treatment which would require weeks in man is compressed into one week.

Summary. 1. Two dogs received gold in the form of sodium auro thiomalate and of thioglucose daily for a total of 3 weeks.

2. Determinations of Rose Bengal Clear-

ance, alkaline phosphatase, and direct and indirect quantitative van den Bergh revealed no pathological changes in liver function.

3. These observations do not support the view that the ameliorating effect of gold therapy in rheumatoid arthritis is due to the effect of the gold on the liver.

17015

Failure of Thyroidectomy and Thiouracil to Protect Rat Liver from Acute Carbon Tetrachloride Injury.

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(Introduced by K. M. Endicott.)

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Leach and Forbes¹ have reported that sulfanilamide administered to rats protected the liver from inhaled carbon tetrachloride. In a subsequent experiment Forbes, Leach and Williams² found that sulfanilamide also retarded the development of hepatic cirrhosis induced by CCl₄. They suggested that the

protective action might be related to the inhibition of thyroid activity known to be induced by sulfanilamide. György and Goldblatt³ and György, Rose and Goldblatt⁴ have shown that thiouracil and propylthiouracil exert a marked preventive effect on the incidence and degree of dietary cirrhosis in rats. These authors also suggested that the pre-

¹ Leach, B. E., and Forbes, J. C., *Proc. Soc. Exp. Biol. and Med.*, 1941, **48**, 361.

² Forbes, J. C., Leach, B. E., and Williams, G. Z., *Proc. Soc. Exp. Biol. and Med.*, 1942, **51**, 47.

³ György, P., and Goldblatt, H., *Science*, 1945, **102**, 451.

⁴ György, P., Rose, C. S., and Goldblatt, H., *Proc. Soc. Exp. Biol. and Med.*, 1948, **67**, 67.

TABLE I.
Comparison of Liver Damage Produced by Carbon Tetrachloride in Thyroidectomized and Thiouracil-fed Rats and in the Pair-fed and *ad lib.* Controls.

Rat group	No. of rats	Extent of lesion*	Hydropic degeneration†	Necrosis‡	Fatty metamorphosis*
Thyroidectomized	13	++	+++	±	+
Pair-fed controls	13	++	+++	+	++
<i>Ad lib.</i> controls	11	±	+	±	+
Thiouracil-fed	8	++	++	+	+
Pair-fed controls	8	++	++	+	+

* Extent of lesion, fatty metamorphosis—graded on a + to ++++ basis.

† Hydropic degeneration—plus values represent proportion of cells in involved areas showing this type of alteration.

‡ Necrosis —, ± rare cell, ± occasional cell, + a few cells.

ventive effect was mediated through the thyroid gland. Handler and Follis⁵ in experiments with rats concluded "A decreased level of thyroid activity induced by thyroidectomy, thiouracil or p-aminobenzoic acid feeding prevents or retards the development of hepatic necrosis or fibrosis associated with choline and cystine deficiencies."

The experiments reported here show the failure of reduced thyroid activity in the rat to protect the liver against subcutaneously administered carbon tetrachloride.

Materials and Methods. The animals used were male rats of the Sprague-Dawley strain and weighed, at the beginning of the experiments, between 84 and 120 g. In one experiment 13 rats were thyroidectomized. An equal number of pair-fed rats served as one control group. A second control group of 11 rats were allowed diet *ad libitum*. The diet consisted of ground pellets (Purina laboratory chow) in which calcium carbonate was incorporated at a 2% level. The thyroidectomized rats were started on this diet 7 days before operation, and after operation were given 0.25 cc of 10% calcium gluconate intramuscularly for a few days, not exceeding 5 days for any rat. After 44 days all rats were injected subcutaneously with 0.05 cc CCl₄ (in equal parts of mineral oil) per 100 g of body weight, and killed and autopsied 24 hours later. The "thyroid area" in the operated rats was examined under 4X magnification for the presence of thyroid tissue; none was found.

In another experiment conducted at the

same time, 8 rats were fed the ground pellet diet (without calcium carbonate) in which thiouracil was incorporated at a 0.1% level for 38 days and at a 0.2% level for another 45 days. The source of fluid for these rats was a saturated aqueous solution of thiouracil. A group of 8 pair-fed control rats received the same diet without thiouracil; water without thiouracil was the source of fluid. At the end of the 83 day period, all rats were injected with CCl₄ and killed as in the first experiment.

In each experiment the liver and thyroid gland or "thyroid area" of all rats were removed at autopsy and fixed in 10% formalin and prepared for microscopic study by paraffin embedding, and staining with azure eosinate. Frozen sections of the fixed livers were stained with oil red O.

Results. On microscopic examination the extent and type of liver cell damage were graded on a one plus to four plus basis. The liver cell injury, which was characteristically centrilobular in location, comprised loss of diffuse and granular cytoplasmic basophilia, irregular and inconstant slight cytoplasmic hyalinization, cytoplasmic oxyphilia, necrosis, hydropic degeneration and fatty metamorphosis. Of these changes only the last 3 listed, together with the extent of the lesion, were used as a basis of comparison. The results are shown in the accompanying table.

It is evident that the extent of the lesions and the degree of hydropic degeneration were not suppressed by thyroidectomy or thiouracil feeding. It is felt that the slight difference in amount of necrosis between the thyroidec-

⁵ Handler, P., and Follis, R. H., Jr., *J. Nutrition*, 1948, **35**, 669.

tomized rats and their pair-fed controls is within the range of error inherent in the system of grading. Thyroidectomized rats showed less fatty metamorphosis; the difference is not great but may be significant. The livers of rats fed *ad libitum* showed extremely little damage except the one plus fatty metamorphosis. The only known differences between these rats and the pair-fed controls of this experiment were the greater amount of food consumed and a faster growth rate.

The few sections made through the "thyroid area" of each operated rat failed to reveal any thyroid tissue. The thyroid gland of all thiouracil fed rats showed marked epithelial hypertrophy with severe depletion of colloid. The thyroid glands of all other rats were histologically normal.

Discussion. The inhibition of thyroid activity suggested by Forbes *et al.*² as a possible explanation for the liver protective effect of sulfanilamide is not supported by our findings. It should be pointed out, how-

ever, that in their experiment the CCl_4 was administered by inhalation.

György *et al.*³ and Handler *et al.*⁵ found that a decreased level of thyroid activity protected the livers of rats against parenchymal necrosis in dietary cirrhosis studies. In view of the findings in the present study it would seem that the mechanism of protection against carbon tetrachloride necrosis² and the necrosis occurring in dietary cirrhosis is different. In this connection Handler *et al.*⁵ found that sulfasuxidine lessened the tendency of the livers of choline-deficient rats to become necrotic and scarred even though the thyroid glands of these animals were essentially normal.

Summary. The lowering of thyroid activity by (1) thyroidectomy and (2) the feeding of thiouracil in a stock diet, failed to prevent or suppress hydropic degeneration or necrosis of the rat liver induced by subcutaneous administration of carbon tetrachloride.

17016

Effect of Temperature on Transmission of Light by Cell Free Body Fluid in *Phascolosoma gouldii*.

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The biological fluids of higher animals have been studied intensively and extensively from the point of view of chemical, physical, and physiological characteristics. The physical nature of the serum of mammals, for example, has been investigated with great thoroughness by Du Noüy who showed that at 56°C "profound modifications in the structure of the proteins and of the lipoprotidic complex" become evident.¹

On the other hand, very little is known about the physical behavior of invertebrate

body fluids. In order to ascertain the relationship of invertebrate fluids to those of higher animals, a series of experiments was made to test the effect of heating on the transmission of light by the cell free body fluid in *Phascolosoma gouldii*.

Material and methods. In general the procedure was similar to that followed by Du Noüy in studies on horse serum. Body fluid was carefully removed from 10 phascolosomas, using a 5 cc hypodermic syringe fitted with an 18 gauge needle. Approximately 1 to 3 cc of pink fluid were obtained from each worm. The pooled fluid was then centrifuged for about 10 minutes in an ordinary clinical cen-

¹ Du Noüy, L., *Studies in biophysics. The critical temperature of serum (56°)*. New York, 180 pp. 1945.