TABLE I. Isoefficiency Ratios* for Nitrogen, BAL, Ethanol, and Sodium Hydrosulfite Calculated from Data Presented in Fig. 1 and 2.

	Nitrogen	BAL (0.04 M)	Ethanol (3.5 M)	Sodium hydrosulfite (0.04 M)
Dose ratio ($\rho = 10^{-1}$ survival)	3.2	4.0	3.1	3.7

* Isoefficiency ratio $= \frac{\text{kr required to give } \rho \text{ survival in presence of agent}}{\text{kr required to give } \rho \text{ survival without agent}}$.

However, since the "isoefficiency ratio" for sodium hydrosulfite is higher than that found by saturating the suspension with nitrogen, it seems worth while to further investigate the protective action of sodium hydrosulfite.

Methanol; 2-propanol; 1-butanol; 2-methyl-1-propanol; 2-methyl-2-propanol; 1,2,3-propanetriol; 1,2-propanediol; and 1,2-ethylenedioxydiol are about as effective as ethanol on a molar basis.

The concentration of ethanol necessary to effect the large increase in cell survival of *E. coli* B/r (Fig. 2) is much higher than the concentrations reported to interfere with the X-ray inactivation of trypsin(14). However, ethanol in lower concentrations (0.02-0.1 M) has been found to increase cell survival if the suspensions are incubated in its presence at higher temperatures (25-37°C) prior to irradiation.

Summary The X-ray sensitivity of *E. coli* is reduced if the cells are irradiated in the presence of certain chemical agents. BAL, ethanol, and sodium hydrosulfite increase the dose required to kill a given number of cells in suspensions at 2°C by a factor of 3-4. Other sulfhydryl compounds, glycols, and low-molecular-weight alcohols also increase the survival of *E. coli* suspensions.

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14. Kaufmann, B. P., McDonald, M. R., Gay, H., Belser, N. O., Pennoyer, J. M., Lennihan, M. R., and Judge, J. T., Carnegie Institution of Washington Year Book, 1950, No. 49, 175.

Maintenance of Normal Thyroid Activity after Transplantation of Thyroid Gland into Spleen or Kidney. (18875)

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Shortly after the intravenous injection of thyroxin labelled with radioactive iodine, much of the radioactivity can be demonstrated in the liver, gastrointestinal contents and feces(1,2). Most of the gastrointestinal and fecal iodine is no longer in the form of thyroxin(1). Since thyroid hormone appears to circulate in the form of thyroxin(3) it might be concluded that the liver normally plays an important part in the isolation, destruction and excretion of circulating thyroid hormone. However, the sudden introduction of a test material into the bloodstream may cause a transient elevation in the concentration of the

1. Gross, J., and LeBlond, C. P., *J. Biol. Chem.*, 1947, v171, 309.

2. Gross, J., and LeBlond, C. P., *J. Biol. Chem.*, 1950, v184, 489.

3. Taurog, A., and Chaikoff, I. L., *J. Biol. Chem.*, 1948, v176, 639.

substance, and thus call into play mechanisms of catabolism not ordinarily involved in the metabolism of normal concentrations of the compound. The following experiment was therefore designed to determine whether the liver plays any important role in the catabolism and excretion of endogenous thyroid hormone secreted at a normal rate.

Method. Three groups of Sprague-Dawley rats were thyroidectomized under ether anesthesia. In one group, the right lobe of the excised gland was implanted deep in the spleen. In a second group, the thyroid implant was made in the right kidney. The third group served as a thyroidectomized control. A fourth group was not operated on.

The animals were maintained on Rockland rat ration. The operated animals received drinking water fortified with 9 g calcium lactate and 1 g calcium chloride per liter. The rats were weighed weekly.

After 82 days, the animals were anesthetized with intraperitoneal pentobarbital. The abdomen was opened and as much blood as possible was withdrawn from the inferior vena cava into an oxalated syringe. The oxalated blood was centrifuged, and the protein-bound iodine in the plasma determined by the alkaline ash method of Barker and Humphrey(4).

The thyroid glands were removed from the normal animals and placed in Zenker's fixative. The implants were identified in kidney or spleen and excised in a small tissue block which was similarly fixed. The height of thyroid cells was estimated with an ocular micrometer on the hematoxylin-eosin stained sections. By the use of a mechanical stage, random follicles were selected in a progressive pattern which prevented recounting the same follicle. Four cells were measured in each follicle, the cells selected for measurement being distributed equally about the circumference of the follicle. At least 20 cells were measured in each section.

Observations. Transplantation of the thyroid into the spleen was accompanied by a fairly high immediate operative mortality,

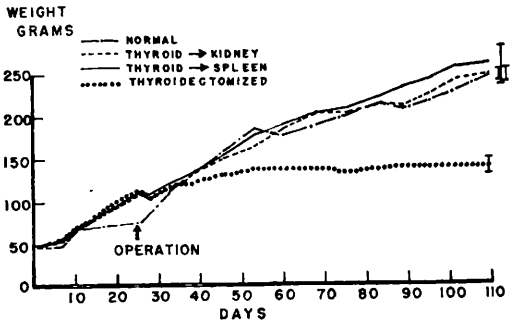

FIG. 1. Comparison of growth curves of normal, thyroidectomized and thyroid-transplanted male rats. Vertical lines at 110 days define standard error of mean of terminal weights.

but all of the animals which survived the immediate postoperative period lived until the end of the experiment. It is unfortunate that only 3 spleen-transplanted animals survived; however, the results obtained were so clear cut that fairly reliable conclusions are possible.

Transplantation of the thyroid gland to spleen or to kidney had no detectable effect on the rate of growth of the animals (Fig. 1) or on their final weight (Table I). Thyroidectomy, as expected, caused almost complete cessation of growth.

The splenic implants maintained a normal plasma protein-bound iodine concentration. The kidney-implanted animals had a somewhat reduced protein-bound iodine concentration as compared to the unoperated controls ($t = 3.53$; $p < .01$), but it is doubtful whether the degree of depression can be considered physiologically significant. It was impossible to obtain enough blood to do the protein-bound iodine analysis in the case of the thyroidectomized rats because of their small size. In a group of five full-grown rats of the same strain, which had been thyroidectomized three weeks prior to bleeding, the plasma protein-bound iodine was significantly lower than in any of the groups with thyroid tissue present ($p < .01$).

From these data it is apparent that the thyroid transplants in both kidney and spleen were functional, and that they were able to maintain the animals in a euthyroid state, as manifested by normal growth curves and normal plasma protein-bound iodine concentra-

4. Barker, S. B., Humphrey, M. J., and Soley, M. H., *J. Clin. Invest.*, 1951, v30, 55.

TABLE I. Effect of Thyroid Transplant and Thyroidectomy Upon Growth and Plasma Protein-Bound Iodine of Male White Rats.

Procedure	No. rats	Preoperative wt, g	Terminal wt, 82 days post-operative, g	Total gain, g	Plasma protein-bound iodine, μg/100 ml	Mean thyroid cell height, μ
Normal	5	90 ± 18.2*	248 ± 8.6	158 ± 14.2	6.5 ± .37	10.9 ± 1.9
Thyroidectomized	5	104 ± 10.7	140 ± 9.7	36 ± 10.2	3 ± .22†	
Thyroid to spleen	3	114 ± 6.3	263 ± 17.6	149 ± 13.2	6.2 ± .21	11.7 ± .3
Thyroid to kidney	6	109 ± 4.5	249 ± 9.8	140 ± 7.6	4.7 ± .35	12.8 ± .5

* All values given are mean ± standard error of the mean ($\sqrt{d^2/n(n-1)}$).
† PBI determinations were impossible on the thyroidectomized rats of this series because sufficient plasma could not be obtained. The values in the table refer to adult thyroidectomized rats of the same strain.

tions. If the liver were normally concerned with the destruction of thyroxin, one would expect the spleen-implanted animals to show signs of thyroid deficiency. This might not have occurred, however, even in the face of hepatic destruction of thyroid hormone, if the splenic implant were sufficiently active to flood and overwhelm the enzyme systems concerned with thyroxin degradation in the liver. If this were the case, one would expect to see signs of increased secretory activity in the splenic implants. Examination of the implants, however, failed to demonstrate any morphologic abnormality of the thyroid cells; and, the mean follicular cell height was not increased in the thyroid tissue implanted in the spleen (Table I).

Discussion. These observations indicate that when thyroid hormone is secreted directly into the portal vein, and therefore must pass the liver before reaching the general circulation, no significant impairment of effectiveness of the hormone can be detected. This might simply mean that the site of action of the hormone lies in the liver, and that the "detoxification and excretion" previously discussed is a reflection of the normal utilization of the hormone. Since the effects of thyroxin appear to be manifested in all tissues of the body, however, this seems unlikely. If the site of action of thyroxin is in the peripheral tissues, the liver seems not to interfere with the passage of the hormone from spleen to its site of action.

These observations appear to contradict the results obtained when labelled thyroxin is injected. The difference is probably due to the fact that the injection of thyroxin, even in very small quantities, temporarily raises the concentration of thyroxin in the blood. Under these circumstances, the injected thyroxin may be handled in part as a foreign substance. This explanation is favored by the observation of Gross and LeBlond that as the dose of thyroxin was decreased in the labelled-thyroxin experiments, smaller and smaller fractions of the radioiodine were recovered in the liver plus gastrointestinal tract plus feces(2). The fact that orally administered thyroxin is as effective calorigenically as intravenously administered hormone(5) also implies that the thyroid hormone is not destroyed by the liver when the quantities involved are small.

Summary and conclusions. Thyroid fragments implanted into the spleen of thyroidectomized rats are functional and capable of maintaining normal growth and plasma protein-bound iodine concentrations. No morphologic evidence of hyperactivity of the implants could be observed. It therefore appears that the liver does not destroy and excrete the thyroid hormone to a significant extent, when the hormone is present in physiologic quantities.

Statistical analyses were carried out as described by Snedecor, G. W., Statistical Methods. Iowa State College Press, 1946.

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5. Salter, W. T., Lerman, J., and Means, J. H., *J. Clin. Invest.*, 1933, v12, 327.

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