than the loss of lethal homozygotes. In any given generation the frequency of homozygotes is defined by p^2—the square of the frequency, p, of the gene in the population—whereas that of the heterozygous carriers is $2p(1-p)$. For a rare gene (p being small and $1-p$ close to 1) the number of carriers may become hundreds of times as large as that of the homozygotes, so that a decrease in vigor of the carriers by, for instance, 5% will have a far greater effect than the complete elimination of the much rarer homozygotes.

The data presented here are of a preliminary nature. Retests of lethals may result in some changes in the specific figures given but will hardly lead to fundamental alterations in the conclusion.

In Vivo Iodination of Tissue Protein Following Injection of Elemental Iodine[1]

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The work of Dvoskin (*2*) indicated that subcutaneous injection of elemental iodine into rats resulted in the synthesis of thyroxin-like material. This conclusion was reached from a study of the effects of the injected iodine on the histological appearance of thyroids of thiouracil-treated animals as well as on the growth curves of thyroidectomized young rats. It seemed reasonable to expect that this treatment would result in the formation of protein-bound iodine (PI) very probably due to the direct iodination of protein, similar to the purely *in vitro* production of iodinated protein.

TABLE 1

Effect of Subcutaneous Injection of Elemental Iodine in Propylene Glycol Solution on Plasma Protein-bound Iodine of Rats

Treatment	Plasma PI
	γ/100 cc
Unoperated + propylene glycol for 30 days	4.6
" + 4 mg of I_2/kg/day for 1 day	34.8
" + 4 mg of I_2/kg/day for 30 days	86.3
" + 16 mg of I_2/kg/day for 30 days	260.7
Thiouracil + propylene glycol for 30 days	1.3
" + 4 mg of I_2/kg/day for 30 days	60.0
" + 16 mg of I_2/kg/day for 30 days	338.0
Thyroidectomized + propylene glycol for 30 days	1.1
" + 16 mg of I_2/kg/day for 30 days	251.0

In order to test this hypothesis, albino rats of the Sprague-Dawley strain were injected subcutaneously with either 4 or 16 mg of elemental iodine (I_2)/kg of body weight, dissolved in propylene glycol (PG); the solvent alone was injected into controls. The use of propylene glycol eliminated the complications arising from the NaI required to dissolve I_2 in water or alcohol. The procedure for determination of PI was that recently described from this laboratory (*1*), with the modification that 0.5 ml of 1.5% As_2O_3 solution in 1N NaOH is used in the trap of the iodine-distilling apparatus instead of the Na_2SO_3 originally described. This alteration eliminates the aeration step, since there is no SO_2 present. It should be unnecessary to emphasize that every precaution must be taken to avoid contamination of the PI fraction being studied with elemental or inorganic iodine.

Table 1 shows the considerable increase in plasma PI after several different periods of injection. Even a single injection at the 4-mg level produced a considerable elevation in plasma PI by 24 hrs, and the values reached remarkable heights when 16 mg/kg was injected each day for 30 days.

TABLE 2

Tissue Protein-bound Iodine in Rats 24 Hrs After Single Injection of Propylene Glycol or Elemental Iodine in PG

Tissue analyzed		Protein-bound iodine after	
		propylene glycol (PG)	16 mg of I_2/kg in PG
Plasma	(γ/100 cc)	2,75	96.0
Thyroid	(γ/gland)	8.2	8.3
Kidney	(γ/100 gm)	11.7	86.8
Liver	(γ/100 gm)	17.9	46.7
Heart	(γ/100 gm)	10.4	25.6
Skeletal muscle	(γ/100 gm)	8.9	19.8
Injection site	(γ/100 gm)	0.0	36,230

Parallel determinations of oxygen consumption were performed on the animals shown in Table 1. These results indicate that the thiouracil-treated and thyroidectomized groups given the 16-mg/kg/day dose were the only ones to show increased metabolic rates. This finding suggests that a large proportion of the iodine combined with the plasma proteins must have been in a form other than thyroxin.

The possible role of the various organs of the animal body in the elaboration of the PI was investigated by comparing the tissue PI levels for kidney, liver, muscle, heart, and thyroid with that found at the site of injection. As can be seen from the results of one such experiment (Table 2), there can be little doubt that iodination of the tissue protein occurred primarily directly where the I_2 injection was made, since this PI value was so extremely high. Indeed, it would seem quite unlikely that free elemental iodine could exist in sufficient quantities in the blood plasma or in the lymph to be carried as such to liver or kidney for synthesis purposes. It is apparent from the thyroid results that this gland is not a major factor in the formation, and probably not in the breakdown, of the PI. On the other hand, the elevated kidney PI most likely denotes some excretory or "detoxifying" function of this organ.

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