

detectable rise in [phage] and consequently the suspension never lysed. This maintenance of a constant titre cannot be ascribed to continuous thermal inactivation of phage just sufficient to balance the production of new phage, for in keeping with earlier work the control solutions held at 42.3°C showed no drop at the end of 2 hours. There remain two alternative explanations for the phenomenon: it may depend upon the thermal inactivation of precursor as it is produced in the growing organisms or it may involve inhibition of the synthetic mechanism. The first possibility appears remote because it has been shown in experiments on activated resting cells that the rate of precursor inactivation is relatively slow. The velocity constant at 42.3°C is 0.031 and it takes almost 1 hour to abolish the store of precursor in fully activated bacteria under the conditions of the present experiment.

Experimentally the fact is that when a mixture of phage and growing susceptible staphylococci is kept at 42.3°C the bacteria grow without inducing the formation of phage. The conclusion seems valid that this result depends upon inhibition of the precursor-producing mechanism of the cell rather than upon thermal destruction of phage or phage-precursor.

11942

Nature of the Blood Iodine. II. Nature of the Plasma Iodine.

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In a previous publication¹ it was indicated that all the iodine normally occurring in the blood is in a form which does not pass through a cellophane membrane when the blood is dialyzed against water.

This study is an attempt to cast further light upon the state in which the iodine exists in the plasma.

It has been known since the early work of Baumann and Oswald that much of the iodine present in the thyroid gland exists in combination with protein, particularly globulin. The presence of a specific iodized globulin—thyroglobulin—has been established. Because of the presence of thyroglobulin as the chief iodine-con-

¹ Silver, S., *J. Mt. Sinai Hosp.*, 1940, **7**, 97.

taining protein in the thyroid gland it has often been assumed that this is the form in which the iodine circulates in the peripheral blood.

As early as 1923 Hektoen² attempted to demonstrate the presence of thyroglobulin in the circulating blood by means of a specific precipitin reaction. Recently these experiments have been repeated by Lerman³ and by Stellar and Olken,⁴ all of whom were unable to detect thyroglobulin either in the peripheral blood, the venous blood from the thyroid gland or in the lymph from the thyroid.

This study is a quantitative estimation of the plasma iodine and its distribution in the albumin and globulin fractions of the plasma.

Method. Sufficient pooled human plasma was obtained to allow for determinations in quadruplicate in each series. The total iodine in the plasma was determined using a modification of the Leipert procedure as modified by Matthews.⁵ The plasma was then divided into albumin and globulin fractions by salting out with half-saturated ammonium sulfate. The globulin fraction was washed with half-saturated ammonium sulfate and these washings were added to the albumin fraction. The iodine content of each fraction was determined separately. All the usual precautions to insure iodine-free reagents were taken. The blank was less than 0.04 gamma iodine per determination.

The total plasma iodine was determined using 25 cc of plasma. For the albumin and globulin determinations 50 cc of plasma was treated with 50 cc of saturated ammonium sulfate.

Discussion. If thyroglobulin is the chief form in which the iodine circulates then most of the plasma iodine should be in the globulin fraction. This, however, is not the case. There is evidence, rather, that the albumin and globulin fractions each contain iodine and that the iodine content of each fraction varies with the protein content of the fraction. There is no evidence to assume that thyroglobulin is the main form in which the blood iodine circulates.

It seems, therefore, that although thyroglobulin may be the form in which the hormone is stored in the thyroid gland it is not the only form in which it circulates. It would, in fact, be difficult to visualize how so large a molecule could pass through the cells of the gland and the blood vessels to reach the circulating blood. It is more likely that the stored thyroglobulin is fragmented, and iodized amino acids, short chain iodized polypeptids or other iodized frag-

² Hektoen, L., Carlson, A. J., and Schulof, K., *J. A. M. A.*, 1923, **81**, 86.

³ Lerman, J., *J. Clin. Invest.*, 1940, **19**, 555.

⁴ Stellar, L. I., and Olken, H. G., *Endocrinology*, 1940, **27**, 614.

⁵ Matthews, N. L., et al., *J. Indust. Chem.*, 1938, **10**, 612.

TABLE I.
Results: Iodine Content of Pooled Plasma and Its Fractions
All iodine values in micrograms.

	Plasma 1	Plasma 2	Plasma 3
Iodine in 50 cc plasma	3.5	2.6	2.6
	3.7	2.6	3.0
	3.5	2.3	3.0
	3.6	2.4	3.1
	—	—	—
Avg	3.6	2.5	2.9
Iodine in albumin fraction derived from 50 cc plasma	2.7	1.9	2.1
	2.4	2.1	2.0
	2.5	1.7	2.2
	2.5	1.9	2.3
	—	—	—
Avg	2.5	1.9	2.1
Iodine in globulin fraction derived from 50 cc plasma	1.2	1.0	1.2
	1.3	1.2	1.0
	1.3	1.1	1.0
	1.3	1.1	0.9
	—	—	—
Avg	1.3	1.1	1.0
% total protein in plasma	6.8	6.3	6.1
Albumin-globulin ratio in plasma	2.1-1	2.0-1	2.2-1
Parts iodine per million in albumin fraction	1.1	0.9	1.0
Parts iodine per million in globulin fraction	1.2	1.0	1.0

ments of thyroglobulin are secreted into the blood stream and that these are then incorporated in the circulating serum proteins without regard to the specific nature of these proteins, but rather in proportion to the concentrations of these proteins in the plasma. Unpublished studies have shown that both albumin and globulin *in vitro* have the ability to fix thyroxine and diiodotyrosine and render them non-dialyzable.

Summary. The plasma iodine is divided between the albumin and the globulin fractions of the plasma in proportion to the relative amounts of albumin and globulin present. There is no chemical evidence for the presence of a preponderant amount of thyroglobulin in the circulating blood.