

the spontaneous occurrence of exophthalmos in 2 thyroidectomized young rabbits. The exophthalmos of Graves' disease also appears to depend in part upon a relative thyroid insufficiency, since it may develop after and is frequently made worse by partial thyroidectomy and since the most beneficial treatment^{4, 5, 6} has been with desiccated thyroid or thyroxin and iodine.

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Measurement of the Circulation Time with Saccharin

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Among the methods used for the measurement of the circulation time in man are those in which a foreign substance is injected into a vein and the time of its arrival in the capillaries of the tongue is signalled by a sensation of taste. Winternitz, Deutsch, and Bruell¹ have used the interval between the intravenous injection of sodium dehydrocholate and the appearance of a bitter taste as a measure of the circulation time. Both they and Tarr, Oppenheimer, and Sager (personal communication) have obtained excellent results in the clinical application of the method.

We have found that soluble saccharin (sodium benzosulphinid) is admirably adapted to the estimation of the circulation time between the antecubital veins and the capillaries of the tongue. Soluble saccharine possesses the following advantages: 1. It stimulates the taste buds in very high dilution. 2. It is very soluble, so that only a small volume of solution is needed. This is important because the injection can be performed rapidly and the saccharin is contained in a small blood volume, with resultant sharp definition of both the time of injection and of arrival in the tongue. 3. It is apparently entirely harmless in the quantities used. In over 100 individuals no unpleasant reactions were encountered. Paravenous infiltration causes no necrosis. In several instances the circulation time was measured twice, and once even 3 times within a few min-

⁴ Zimmerman, L. M., *Am. J. Med. Sci.*, 1929, **178**, 92.

⁵ Ruedemann, A. D., *J. Am. Med. Assn.*, 1931, **97**, 1700.

⁶ Benedict, W. L., *Arch. Ophth.*, 1933, **9**, 1.

¹ Winternitz, Deutsch, and Bruell, *Med. Klin.*, 1931, **27**, 986.

utes, but no reactions were observed. 4. The measurement can be repeated as soon as desired. The residual saccharin in the blood does not interfere with perception of the newly injected substance.

The measurement is performed as follows: 2.5 gm. of soluble saccharin is dissolved in 2 cc. of distilled water by heating. The subject reclines in a comfortable position and is told to call out when he experiences a sweet taste. The solution is injected rapidly into a large antecubital vein (less than 0.5 seconds is required). The time that elapses until perception of the sweet taste is measured. The subject usually describes the sweet taste as passing with great rapidity from the base to the tip of the tongue and quickly disappearing. He should be instructed to relax and not to hold his breath following the insertion of the needle, for this slows the venous return to the heart.

One hundred individuals, mostly hospital patients, suffering from a variety of complaints, were tested. In only one of these was the endpoint not definite enough for a reading. In 63 subjects there was no reason to suspect abnormality of circulation. The circulation times in these 63 "normals" were as follows:

Circulation Time sec.	No. Individuals
9-9 $\frac{3}{4}$	8
10-10 $\frac{3}{4}$	18
11-11 $\frac{3}{4}$	6
12-12 $\frac{3}{4}$	11
13-13 $\frac{3}{4}$	12
14-14 $\frac{3}{4}$	3
15-15 $\frac{3}{4}$	5

Repeated injections in the same subject check closely.

In circulatory failure, as found by previous investigators, the circulation time is markedly protracted, in severe cases to over 40 seconds. The circulation time is undoubtedly a very valuable index of circulatory failure. In fact, the slowing of the circulation time in circulatory insufficiency appears to be proportionately greater than the diminution in the cardiac output as revealed by recent investigations with the acetylene method.