

the blood are of the same magnitude,<sup>7</sup> and that the "lymph comes closer to reflecting the actual environment of the body cells than any other fluid that can be collected" (Drinker

and Joffey<sup>8</sup>).

The well known role played by the lymphatic system in certain infections adds further interest to this observation.

<sup>7</sup> Abel, J. J., Hampil, B., Jonas, A. F. and Chalian, W., *Bull. Johns Hopkins Hosp.*, 1938, **62**, 522.

<sup>8</sup> Drinker, C. K., and Joffey, J. M. *Lymphatics, lymph and lymphoid tissue. Harvard University Press, Cambridge, Mass.* 1941.

16383

### Influence of Sodium Tetrathionate on Rate of Blood Flow to the Digits.

TRAVIS WINSOR.\*

*From the Cardiovascular Laboratory, University of Southern California Medical School, Birmingham Veterans Administration Hospital, and the Nash Cardiovascular Foundation, Hospital of the Good Samaritan, Los Angeles.*

Sodium tetrathionate (Tetrathione) has been used extensively by Theis and Freeland,<sup>1-4</sup> primarily for peripheral vascular disorders characterized by deficient oxygenation of the blood and tissues. Most prominent among these are Buerger's disease.<sup>5</sup> Theis and Freeland<sup>1</sup> show, during the active stages of thromboangiitis obliterans, either a decrease in the oxygen capacity or in the degree of oxygen saturation of the arterial blood, as well as increased sedimentation rates without significant departures from the normal in erythrocyte counts and hemoglobin percentages. In these cases venous blood taken from the involved extremities was abnormally dark, showed an increase in viscosity and sedimentation rate, rapid coagulation without an increase in fibrinogen, increased alkalinity and a low degree of oxygen saturation with a low carbon dioxide content. A subnormal content

of the oxidation catalyst, the reduced form of glutathione, was noted in the venous blood. Sodium tetrathionate administered intravenously was of value in restoring to normal these abnormal blood findings. Since this work, some controversy over the value of sodium tetrathionate in the treatment of peripheral vascular disorders has arisen.

The present studies were carried out to determine whether or not sodium tetrathionate influenced the rate of blood flow, skin temperature, or pulse rate in normal individuals and in patients with peripheral vascular disease.

*Methods and Materials.* The rate of blood flow was determined, using a digital pneumoplethysmograph.<sup>6</sup> The occluding cuff was placed at the ankle or wrist. The venous occlusion was accomplished by inflating a cuff with approximately 60 mm of mercury pressure. The rate of volume change was measured by taking the angle between the base line before and after venous occlusion. The volume of the part was measured using the volumeter, as described by Burch.<sup>6</sup> The rate of flow was then determined after a period of rest, not less than 45 minutes. Tracings were taken after the injection of 10 cc of distilled water intravenously, after injection of 0.6 g of sodium tetrathionate in 10 cc of distilled water, and after placing

\* All opinions held are those of the author and are not necessarily those of the Veterans Administration.

<sup>1</sup> Theis, F. V., and Freeland, M. R., *Arch. Surg.*, 1939, **28**, 191.

<sup>2</sup> Theis, F. V., and Freeland, M. R., *Arch. Surg.*, 1940, **40**, 190.

<sup>3</sup> Theis, F. V., and Freeland, M. R., *Ann. Surg.*, 1941, **113**, 411.

<sup>4</sup> Theis, F. V., and Freeland, M. R., *Surg.*, 1942, **11**, 101.

<sup>5</sup> Robinowitz, H. M., *Am. J. Surg.*, 1933, **21**, 260.

<sup>6</sup> Burch, G. E., *Am. J. Surg.*, 1947, **33**, 48.

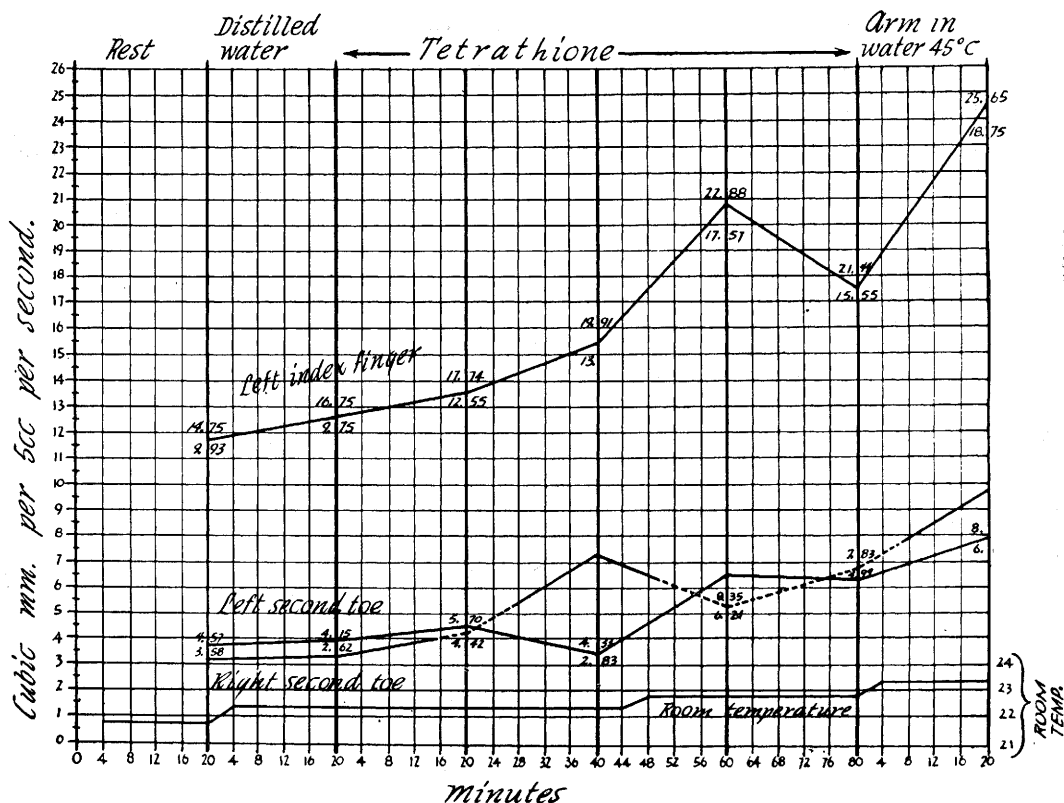


FIG. 1.

Effect of 0.6 g of sodium tetrathionate given intravenously and indirect heat on the rate of blood flow of 10 normal subjects.

one arm in water at 45°C, for a period of 20 minutes. The flow rate was measured at an average room temperature of approximately 22.5°. The room temperature varied less than plus or minus 1.1°C.

Skin temperatures were recorded from the left index finger and from the left and right great toes, using a Micromax automatic recorder. The skin temperature measurements were accurate to within plus or minus 0.5°C. The thermocouple junction was applied with Scotch Tape to prevent evaporation.

Pulse rates were recorded from the plethysmogram.

Skin temperatures and flow rates were determined simultaneously on the above mentioned subjects. The experiments were carried out on 10 normal subjects and 10 patients with arterial arteriosclerotic obliterative disease of the lower extremities who have had a left lumbar sympathectomy.

**Results.** The mean flow rate of 10 normal subjects at rest in the left index finger was 11.6 cu mm, per 5 cc of tissue per second, while in the left second toe and the right second toe it was 3.7 and 3.2, respectively (Fig. 1). Twenty minutes after the injection of 5 cc of distilled water the mean flow rate of the finger had increased to 12.6. The flow rates in the toes were essentially unchanged. The maximum rate of flow in the finger was reached 60 minutes after injection of sodium tetrathionate, at which time the mean flow was 20.8. The maximum flow in the lower extremities was reached in the right second toe at 40 minutes, the maximum being 7.2. Eighty minutes after the injection of sodium tetrathionate the flow rate in the finger was 17.6, while that in the right second toe and left second toe was 6.8 and 6.4, respectively. After placing the arm in water 45°C, for 20 minutes, the

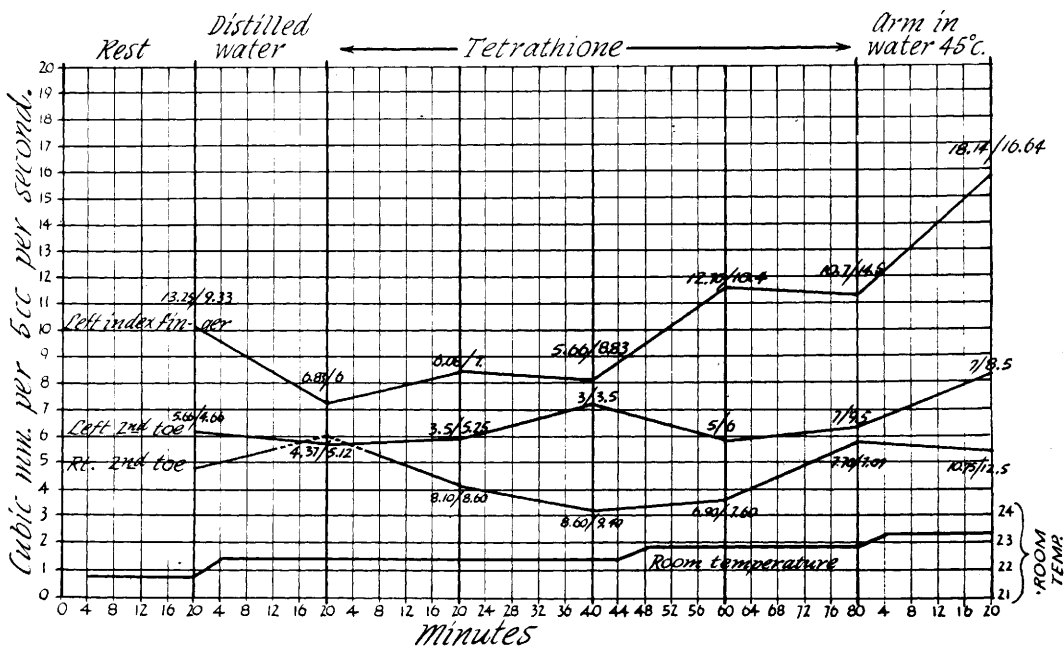


FIG. 2.

Effect of 0.6 g of sodium tetrathionate given intravenously and indirect heat on the rate of blood flow of patients with arteriosclerotic obliterative disease who have had a left lumbar sympathectomy.

mean flow rate of the finger increased to 24.5, in the right second toe to 9.8, and in the left second toe to 7.9.

Fig. 2 shows the rate of blood flow in 10 patients with arteriosclerotic obliterative disease who have had a left lumbar sympathectomy. After 45 minutes of rest the mean rate of flow in the left index finger was 10.2, in the left second toe 6.1, and in the right second toe 4.8 cu mm, per 5 cc per second. The flow rates twenty minutes after the intravenous injection of 5 cc of distilled water were 7.2, 5.8 and 5.9, respectively. The intravenous injection of 0.6 g of sodium tetrathionate produced a gradual increase in flow rate in the finger, with maximum at 60 minutes, the average being 11.6 cu mm, per 5 cc per second. The maximum flow rate in the left second toe was reached at 40 minutes, the average being 7.2 cu mm, per 5 cc per second. At this time the poorest rate of flow was detected through the right second toe, the average being 3.2 cu mm, per 5 cc per second. Eighty minutes after the injection of sodium tetrathionate the flow rates in the left index finger, the left second toe and

right second toe were 11.2, 6.4, and 5.8, respectively. Twenty minutes after placing the arm in hot water at 45°C, the average flow in the finger was 15.8, in the left second toe 8.2 and in the right, 5.4.

Skin temperature measurements from the left index finger, the left great toe and right great toe were made simultaneously with the recording of flow rates (Fig. 3). After 45 minutes of rest the mean skin temperature for 10 normal subjects was 30°, 27.2° and 26.6°C, respectively. Twenty minutes after the injection of distilled water these values were 30.6, 27.2 and 26.6°C, respectively. Maximum sodium tetrathionate effect in fingers and toes was noted at 80 minutes after injection, at which time the values were 31.7, 28.8 and 27.2, respectively. Twenty minutes after placing the right arm in water up to the elbow 45°C, these values were 33.4, 31.4 and 30.5, respectively. During the course of these experiments, the room temperature increased approximately 2°C.

Skin temperatures were carried out on 10 patients with arteriosclerotic obliterative disease who have had a left lumbar sympathectomy.

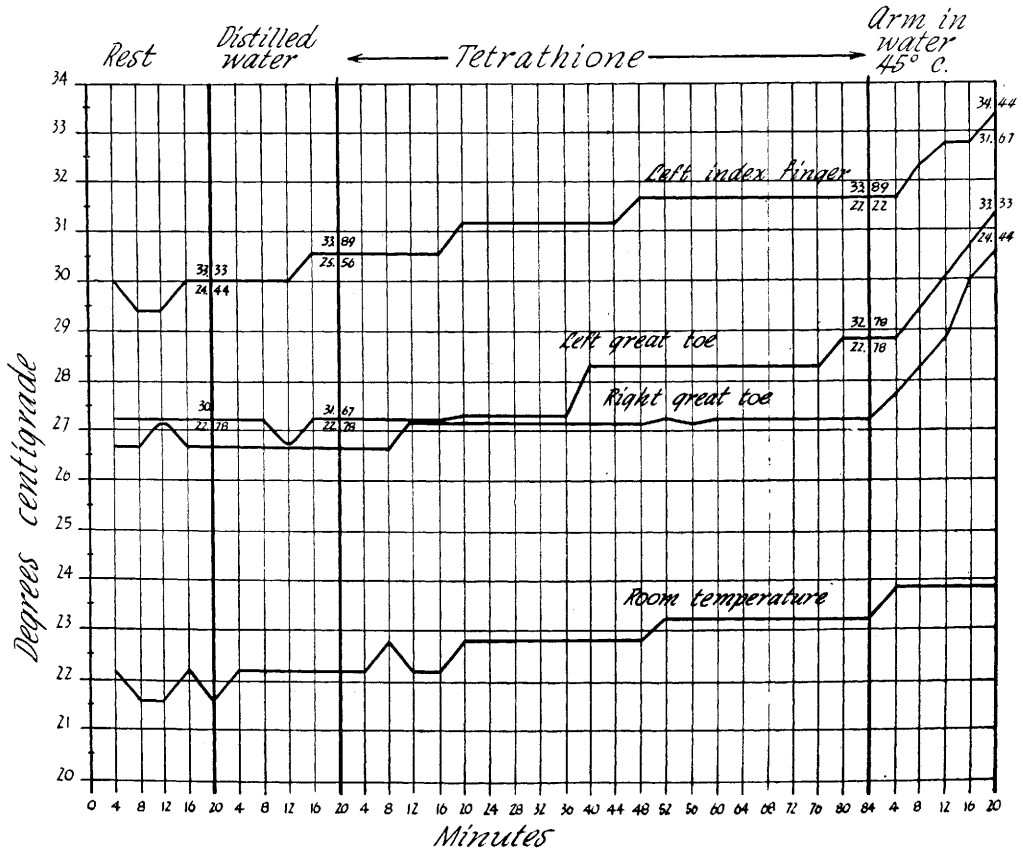


FIG. 3.

Effect of 0.6 g of sodium tetrathionate given intravenously and indirect heat on skin temperatures of 10 normal subjects.

tomy (Fig. 4). Temperature readings were made from the left index finger, left great toe and right great toe. At the end of a 45-minute rest period the temperatures were 28.8, 27.7 and 25.6°C, respectively. Twenty minutes after the injection of distilled water these values were 28.8, 27.7 and 24.4. Sodium tetrathionate produced no significant rise in skin temperature throughout an 80-minute period on the unsympathectomized lower extremity. On the sympathectomized lower extremity the rise was less than 0.5°C. Maximum skin temperature on the left index finger was reached at 68 minutes after the injection of sodium tetrathionate, at which time the temperature was 29.4°C. Eighty-four minutes after the injection of sodium tetrathionate these values were 28.3, 28.2 and 23.8, respectively. Twenty minutes after placing the right arm in water up to the elbow

45°C, these values were 32.4, 29.4 and 26.6, respectively. The room temperature increased less than 2°C, during this experiment.

The effect of the intravenous injection of 0.6 g of sodium tetrathionate in 10 cc of distilled water on the pulse rate of 10 normal subjects, is shown in Fig. 5. Ten cc of distilled water produced a fall in the pulse rate of 2 beats per minute. The lowest average pulse rate reached, after injection of sodium tetrathionate, occurred at the end of a 40-minute period, at which time the pulse rate had fallen 2 beats per minute. At the end of 60 minutes, after injection, the pulse rate returned to the pre-injection level. After placing the arm in hot water for 20 minutes there was an increase in pulse rate of one beat per minute.

*Discussion.* Sodium tetrathionate given intravenously to 10 normal subjects produced

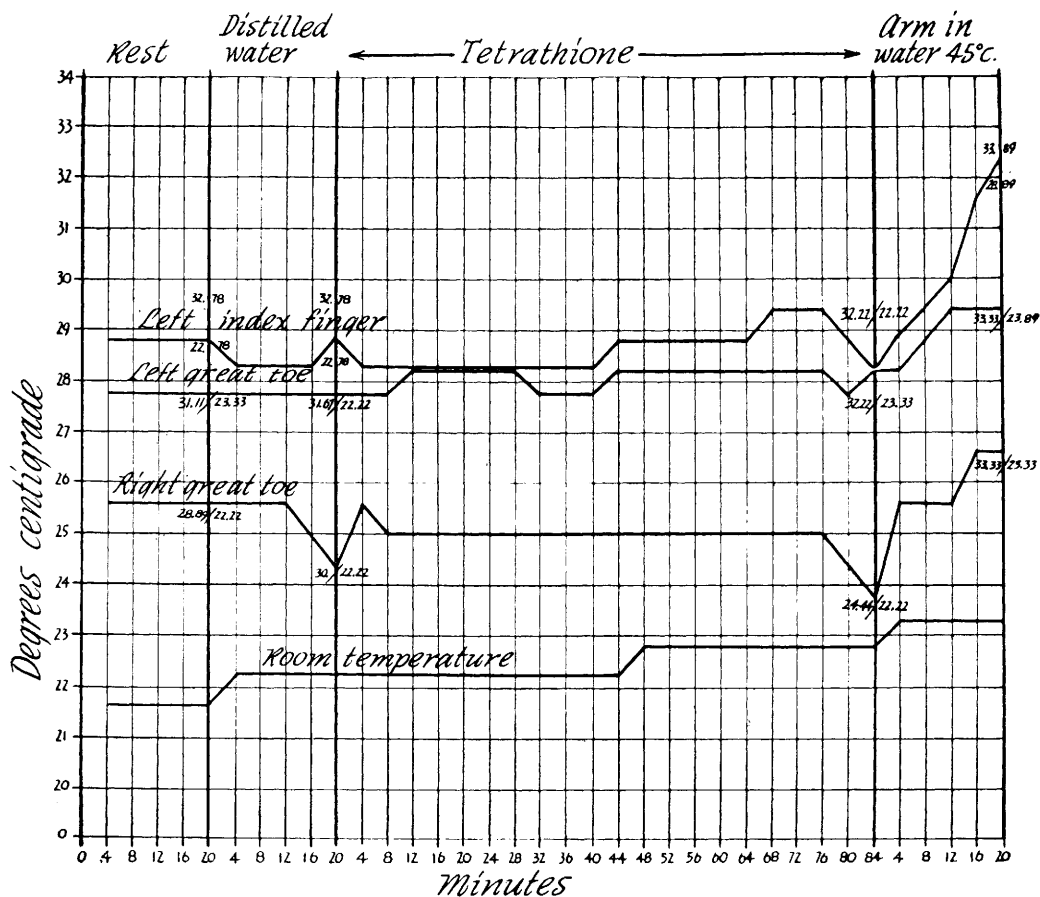


FIG. 4.

Effect of 0.6 g of sodium tetrathionate given intravenously and indirect heat on skin temperatures of 10 patients with arteriosclerotic obliterative disease who have had a left lumbar sympathectomy.

a definite but slight rise in the rate of blood flow in the fingers. In the lower extremities the flow rates were increased to a lesser extent. After placing the arm in water at 45°C, there was an additional increase in the rate of blood flow. It should be noted in these experiments that the room temperature increased slightly during the procedure. Thus, the evidence seems to indicate that sodium tetrathionate may produce a very slight increase in flow rates in normal individuals, particularly to the upper extremities. This increase in rate is not marked, however, as compared to the increased flow rates which resulted from indirect heating by placing one arm in water 45°C. In all instances, the arm was placed in water to a level somewhat below the elbow. Subsequent experiments have

shown that incomplete dilatation is ordinarily produced by this method. The rate of flow can be augmented in individuals by placing the arm in water 45°C, with the level of the water well above the elbow. A still greater rate of flow is recorded when both arms are placed in water above the elbow. This is particularly true when the patient is heavily covered with blankets. Thus, sodium tetrathionate must be considered relatively ineffective in increasing the flow rates in these individuals. The skin temperatures of these 10 normal subjects increased only slightly, approximately 2° after the use of sodium tetrathionate. As the room temperature also increased slightly during these experiments, it is felt that sodium tetrathionate had no definite effect upon the skin temperatures.

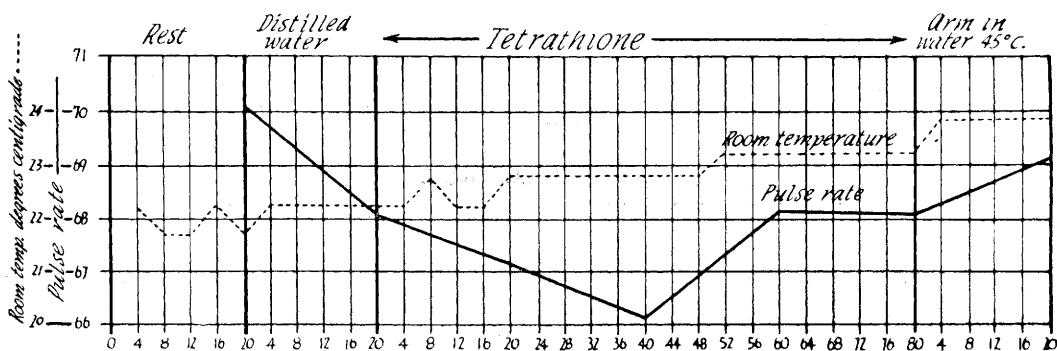


FIG. 5.

Effect of 0.6 g of sodium tetrathionate given intravenously and indirect heat on the pulse rate of 10 normal subjects.

Again placing the arm in water 45° C, below the elbow produced a greater increase in the skin temperatures than that produced by sodium tetrathionate. Here again, placing both arms in water at this temperature above the elbow often produces a greater degree of temperature rise than that following the insertion of a single arm in water below the elbow. The 10 patients with arteriosclerotic obliterative disease showed essentially no significant increase in flow rates to the lower extremities following the injection of sodium tetrathionate. The rate of flow in the finger increased somewhat after the use of intravenous sodium tetrathionate. The increase was less than that seen in the normal group. Here again, indirect heating increased the flow rates more markedly than did sodium tetrathionate. Skin temperature measurements showed a slight increase in skin temperature of the left index finger after sodium tetrathionate. There was no significant increase in skin temperature of the toes. After the indirect heating the skin temperatures of the fingers and toes increased. This would indicate that sodium tetrathionate is not useful in increasing the rate of blood flow nor in raising the skin temperature in the lower extremities in individuals with arteriosclerotic obliterative disease in either an unsympathectomized lower extremity or in a sympathectomized lower extremity.

It should be pointed out that in determining the rate of blood flow, the occluding cuff was placed at the wrist or ankle. If the cuff had been placed at the base of the finger or at the base of the toe, the flow rates would

have been approximately 3 times greater.<sup>7</sup>

Lastly, it appears that sodium tetrathionate produces a very slight slowing of the pulse rate which occurs approximately 40 minutes after injection. During these injections no toxic effects were encountered. In all instances the drug was injected very slowly. Thus, it seems that if sodium tetrathionate is of value in the treatment of peripheral vascular disease, it must act by mechanisms other than by increasing the rate of blood flow.

*Summary.* The rate of blood flow, skin temperature, and pulse rates were determined after the intravenous injection of 0.6 g of sodium tetrathionate. In 10 normal subjects the rate of blood flow and skin temperature increased slightly in the left index finger. In the lower extremities the rates of flow increased to a lesser extent. Indirect heating produced a greater rate of flow in the upper and lower extremities and increased the temperature in the upper and lower extremities to a greater degree. In 10 subjects with arteriosclerotic obliterative disease who have had a left lumbar sympathectomy, the rate of flow and skin temperatures through the upper extremities were increased slightly. However, there was no significant change in the lower extremities. Indirect heating was more efficacious in increasing the flow rate and skin temperature than was the sodium tetrathionate. The pulse rate was slowed slightly, the maximum slowing occurring 40 minutes after injection.

<sup>7</sup> Goetz, Robert H., *Am. Ht. J.*, 1946, **31**, 146.