edematous fluid passes by way of the abdominal and thoracic chains of nodes into the thoracic duct and subclavian vein, lymphadenitis is seen in these other nodes, varying in severity in direct proportion to their proximity to the primary lesion.

Clinical observations and the autopsy findings of widespread vascular dilatation, hemorrhage, and edema led Taube and Essex to conclude that their animals died in shock. Whereas shock seems the most probable major factor in the death of animals subjected to venom intravenously, the evidence is not so clear for this assumption following the subcutaneous administration. Our animals showed none of the generalized vascular lesions which Moon[5] has suggested as the pathologic basis of shock. There was only a subcutaneous loss of blood and fluid, which was so extensive, however, that it might be considered capable of causing shock.

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Cerebral Blood Flow Changes During Insulin and Metrazol (Pentamethylenetetrazol) Shock.

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The use of insulin and metrazol in shock therapy for schizophrenia is now well known.

Using a greatly modified, flexible thermoströmuhr simultaneous records of blood flows in carotid artery and meningeal branch of the jugular vein were made in rabbits throughout the course of 128 shock experiments.

Normal venous and arterial blood flows were recorded for one hour. Blood was taken for initial glucose determination.* Insulin was injected subcutaneously (2 units per kilo). Blood sugars were estimated at half-hour intervals for 1½ hours, after which 15-

[5] Moon, V. H., *Arch. Path.*, 1937, **24**, 642, 794.

* True glucose was determined on 0.3 cc blood precipitated by the method of Herbert and Bourne[1] and glucose determined by a modified Shafer-Hartman reagent (Harding and Downs[2]).

[1] Herbert, F. K., and Bourne, M. C., *Biochem. J.*, 1930, **24**, 299.

[2] Harding, V. J., and Downs, C. E., *Can. Chem. Met.*, 1932, **16**, 12.

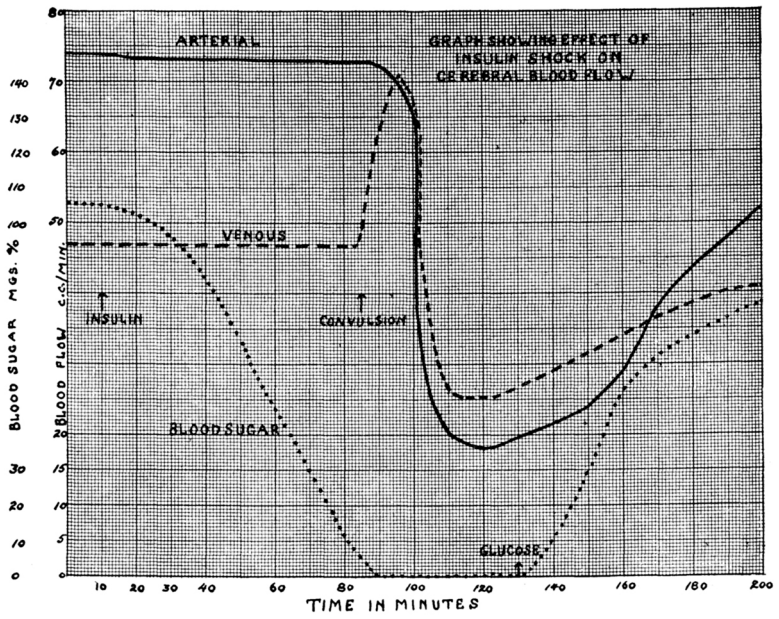

FIG. 1.

minute samples were taken. Blood flow readings were taken at intervals of 2 minutes or less.

The animals usually developed convulsions within 1½-2 hours (Fig. 1). At the onset of the convulsions the blood sugar was always 6 mg % or less. During the convulsions the blood sugar was always undetectable. In the coma stage, following the initial convulsion, the blood sugar fluctuated from 6 mg % to 8 mg %. Spontaneous secondary convulsions frequently occurred, during which time the blood sugar was again undetectable.

At the onset of the primary convulsion the blood flow (Fig. 1) in the cerebral branch of the jugular vein increased very markedly, even up to 50%, while at the same time the arterial blood flow remained constant. This initial phase was followed by a simultaneous decrease in both arterial and venous flow to as low as 25% of the normal level.

In cases where the animals did not go into convulsions there were no significant changes in blood flow, even though the blood sugar had decreased from 95 mg % to 6 mg %.

Shock was induced by metrazol injections in another series of animals prepared in a manner similar to that already described. It has been found that typical convulsions are produced in rabbits (2-3 kilo) by the intravenous injection of 0.75 cc of a 4 % solution of metrazol in distilled water.

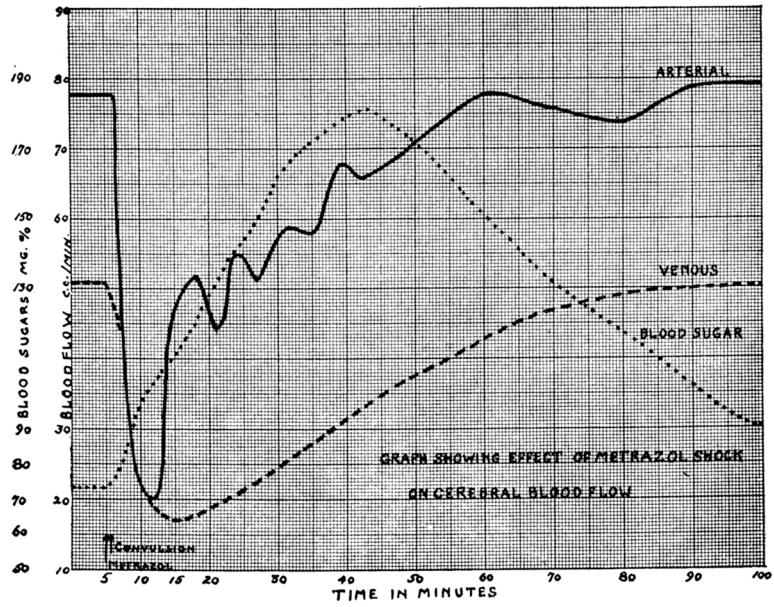

FIG. 2.

Following the injection of an effective dose of metrazol (Fig. 2) the animal almost immediately went into a very typical convulsion which lasted about 2 minutes. This was followed by a semi-comatose state which persisted for several hours. Coincident with the beginning of the convulsive state the arterial and venous blood flows decreased rapidly to one-half or even one-fifth of the normal flows. The blood flow rates returned to normal in an irregular fashion, suggesting the widespread cerebral arteriolar effects brought about by the metrazol injections.

The tremendous fall in blood pressure during the actual convulsion made it impossible to obtain blood samples from the ear for sugar estimations. However, in the post-convulsion state there was a definite hyperglycemia which persisted for several hours. (Fig. 2.)

Thus in insulin shock there was an initial increase in venous return from the brain, suggesting a decrease in size of the brain, while the arterial flow remained constant. This phase was promptly followed by a simultaneous decrease in blood flow in both the arterial and venous sides to such an extent that cerebral anemia was inevitable.

The blood flow changes during metrazol shock were even more rapid. The decrease in cerebral blood flow, both arterial and venous, was sufficient to produce a severe and prolonged cerebral anemia.