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Effects of Constriction and Release of an Extremity.

HARWELL WILSON AND NORMAN W. ROOME. (Introduced by D. B. Phemister.)

From the Department of Surgery, University of Chicago.

The dangers of prolonged tourniquet application are as follows: 1. Interference with nutrition of the part sufficient to cause gangrene; 2. Paralysis, possibly due to prolonged pressure on the nerves; 3. Circulatory depression which frequently occurs after the release of a constrictor. Paolucci[1] and Fogliani[2] observed in animals that this circulatory depression was followed by death in many cases.

The present study is an attempt to evaluate the possible factors producing this fall of blood pressure and death. The factors considered were: 1. Return of blood to the limb (if this had been expressed before application of the tourniquet); 2. Reactive hyperemia (Bayliss); 3. Absorption of toxic metabolites; 4. Swelling of the limb by transudation.

Experiments were done on 19 dogs anesthetized with sodium barbital. One hind leg was constricted at the level of the hip joint for periods of from 2 to 20 hours. Six animals recovered after tourniquet applications of 2 to 6½ hours while 13 dogs died after constrictions of 3 to 20 hours. Seventeen percent of a control series of dogs died from the prolonged anesthesia.

In the animals dying, the hind quarters were symmetrically removed after the method of Blalock.[3] There was an average increase in weight of the ligated limb of 3.54% of the body weight. Plasma protein estimations showed the edema fluid to resemble diluted blood plasma. Johnson and Blalock[4] found that a loss of plasma equal to 2.4% of the body weight in 28 hours was sufficient to cause the death of dogs. In 3 cases gas was present in the tissues; clostridia were found in a high percentage of cases from both the normal and the ligated leg. These were not tested for exotoxin production and their identity with *B. welchi* was therefore not definitely established (Trusler and Reeves[5]).

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[1] Paolucci, R., *Arch. Ital. Di. Chir.*, 1928, **21**, 229.

[2] Fogliani, U., *Rivista di Patologia Sperimentele*, 1932, **9**, 257.

[3] Blalock, A., *Arch. Surg.*, 1930, **20**, 959.

[4] Johnson, G. S., and Blalock, A., *Arch. Surg.*, 1931, **22**, 626.

[5] Trusler, H. M., and Reeves, J. R., *Arch. Surg.*, 1934, **28**, 479.

Further studies are necessary to definitely determine the rôle of bacterial products in the causation of death; however, since the loss of plasma-like fluid into the ligated leg was adequate to produce death this would seem to be the most likely explanation.

These findings agree with studies in traumatic shock which show the serious consequences of a decrease of the circulating blood volume as a result of local fluid loss into the tissues.[5, 6]

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Effect of Dinitrophenol, Sodium Citrate, Sodium Bicarbonate, and Citric Acid upon Distribution of Cholesterol.

IRWIN C. WINTER, DANIEL HALE AND CHESTER J. FARMER.

From the Department of Chemistry, Northwestern University Medical School, Chicago.

The report of Marie[1] that sodium citrate administered by mouth or intravenously reduced the blood cholesterol of rabbits 60% led us to try its effect upon blood cholesterol of other species. It is of interest in this connection to note that dogs with a hyperpyrexia induced by the administration of 10 mg./kg. dinitrophenol showed an increase in blood cholesterol, the initial value of 161 mg. % being elevated to 285 mg. % 2 hours after injection of the drug. These observations led us to continue the study with albino rats.

Five groups of 5 rats each were placed upon a diet similar to that suggested by Chanutin and Ludewig,[2] in which extracted casein was substituted for extracted dried beef. To this cholesterol deficient diet, cholesterol was then added to the extent of 2%. The first group of rats received no supplement and served as control animals. In the second group, each animal received a daily subcutaneous injection of 1 mg. dinitrophenol per 100 gm. body weight. To the third, 0.2 gm. sodium citrate per 100 gm. body weight was given in aqueous solution by stomach tube. The fourth and fifth groups received $NaHCO_3$ and citric acid solutions, respectively, by stomach tube, in order to determine, if possible, the ion responsible for any change in the distribution of cholesterol. These 2 substances were given in amounts furnishing separately the same quantities of

[6] Roome, N. W., Keith, Wm. S., and Phemister, D. B., *S. G. O.*, 1933, **56**, 161.

[1] Marie, A. C., *Compt. rend. Soc. Biol.*, 1932, **109**, 13.

[2] Chanutin, A., and Ludewig, A., *J. Biol. Chem.*, 1933, **102**, 57.