found to be supraminimal and at times even maximal. A similar result was obtained with lactic acid, which was administered to the muscle in an isotonic solution of various salts. When lactic acid in a strength of 1/3200, or even 1/6400, gram-molecular solution, was injected into the muscle, a stimulus heretofore subminimal immediately elicited contractions. Thus both carbon dioxide and lactic acid in small quantity are capable of increasing the irritability of protoplasm. Gotschlich found that continued subminimal stimulation of muscle renders it acid in reaction, even though no contractions occurred. The conclusion therefore seems to be justified that summation of stimuli may be explained as due to a rise in irritability, brought about by the action on the living substance of small quantities of certain products of metabolism, especially carbon dioxide and lactic acid, the same substances which, in larger quantity, are important factors in fatigue.

24 (434)

The action of magnesium salts: A. In relation to motor nerve impulses; B. In relation to sensory stimulation.

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Since 1869 it has been generally held that magnesium salts have a curare-like action (Jolyet and Cahours, *Arch. de physiol.*, 1869, ii, 113; Binet, *Rev. méd. de la Suisse romande*, 1892, xii, 523, 593; Wiki, *Jour. de physiol. et de path. gén.*, 1906, viii, 794–803; Bardier, *ibid.*, 1907, ix, 611, and others). As this point is of interest in connection with the behavior of animals after the subcutaneous injection of magnesium salts, we have re-investigated this phase of their action.

A. In Relation to Motor Nerve Impulses.

Frogs have for the most part been used, though some observations have been made on mammals (rabbits, dogs, cats, rats, etc.). As the results are in agreement for all animals so far tried, only those on frogs and rabbits will be mentioned here.

In the frog the femoral blood vessels in one leg were ligated and the two gastrocnemius muscles connected with levers. Stationary electrodes were placed beneath the sciatic nerves and by a suitable arrangement of keys an induced current could be led into either nerve at will. After establishing the control response in both muscles from 1.0 to 1.5 c.c. of the salt in saturated solution was introduced into the dorsal lymph sac. The nerves were stimulated at intervals and the results recorded.[1]

Results. — 1. Injection of 1.0 to 1.5 c.c. saturated solution of magnesium sulphate into the dorsal lymph sac of a 20 to 30 gram unpithed frog is soon followed by a loss of muscular response to nerve stimulation while direct stimulation of the muscle remains as effective as before the injection.

2. The limb whose blood vessels were previously ligated showed no such loss of response to nerve stimulation.

It may be remarked that it is known that other salts, *e. g.*, sodium chloride also have a curare-like action.

B. IN RELATION TO SENSORY STIMULATION.

After ligating the femoral blood vessels to one leg in frogs, the response to sensory stimulation, *e. g.*, thermal, electrical, chemical (acid) and mechanical stimulation of the skin of the fore and hind limbs was recorded by contraction of the gastrocnemius muscles. Magnesium salts, 1.0 to 1.5 c.c. saturated solution, were then injected into the dorsal lymph sac. After a time no response in the unligated leg could be elicited by stimulating as before, but the muscles in the ligated limb responded strongly. At this stage the muscles in the unligated leg responded strongly to direct stimulation, but not at all to nerve stimulation. In such an experiment at this stage the animal is still breathing well and there are no indications of insensibility.

A rabbit was poisoned with magnesium salt solution administered subcutaneously. After a time one sciatic nerve was exposed and stimulated with an induced current. Upon stimulation of the sciatic nerve, reflex contraction of the muscles of the trunk occurred while only slight or no response of the muscles supplied by this nerve was observed. Direct stimulation of the muscles

[1] Detailed descriptions of the apparatus and technique employed will be included with the complete account of these experiments.

with a current of the same strength brought a good response. At this time the animal was breathing well and there were none of the symptoms of asphyxia which appeared later.

Results. — 1. The behavior of an animal in response to sensory stimulation is notably altered after the subcutaneous injection of magnesium salts in large amounts. Motor response may even entirely disappear but a disappearance of sensitiveness is not concomitant with motor paralysis. But if previous to the administration of the salt in frog, the blood vessels to a hind limb be ligated, the muscles of such a limb show good response to stimulation of the skin of the fore limbs.

2. A rabbit poisoned with magnesium sulphate shows a loss of muscular response to indirect stimulation, while at this time the muscular response to direct stimulation is good. At this stage the reflex mechanism is still capable of functioning as shown by the contraction of trunk muscles on stimulating the central end of the sciatic nerve. The more peripheral muscles seem first to be paralyzed. The muscles of respiration appear to be the last to become paralyzed.

25 (435)

The effects of direct application of magnesium salts: A. To motor and sensory nerves; B. To cardio-inhibitory nerves.

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A. The sciatic nerves in both legs of frogs were exposed and three pairs of stationary electrodes placed beneath each. The wiring was such that an induced current could be switched to any of the six pairs of electrodes at will. After recording the control, direct and reflex response of the gastrocnemius muscles, the solution to be tested was applied to the nerve trunk at the site of one of the middle pairs of electrodes. Stimulation of the nerves was continued and the result recorded. After a time the solution on the nerve (or on both nerves, when two substances were being tested at the same time) was removed and return of function