choline, accumulating in excess, might have a depressing effect, although this action of acetyl choline is said to be reversed under curare.[3, 4] The delayed recovery here is evidently not so caused, for acetyl choline (1 mg. in 1 cc.) injected intra-arterially during the rising phase of the recovery curve, has an immediate potentiating, not a depressing, effect.

Nevertheless repetitive stimulation of the nerve, under curare, does appear to leave some kind of after-depression which is not found with Mg. No muscular response was ever obtained *during* tetanization of the nerve, even with frequencies as low as 14 per second (*Cf.* Bremer and Titeca[5]). The recovery curve may be determined by 2 factors, the changing concentration of a decurarizing chemical and gradual recovery from a depression which varies in depth and duration according to the previous activity of the nerve. Unless the latter factor is assumed to exist, the decurarizing agent appears to be too slowly mobilized to be concerned in the normal excitation of muscle.

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Chemical Transmission from Nerve to Muscle, in Animals "Curarized" with Magnesium Sulphate.

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Lubinska[1] has described a type of peripheral summation or facilitation in cats. Following the administration of sufficient $MgSO_4$ intraperitoneally, the muscular response to single stimuli applied to a motor nerve is lost. Repetitive stimuli, however, evoke a tetanus, and temporarily thereafter single stimuli are again effective.

It seems to us that such effects might be due to local accumulation of some decurarizing chemical agent released at the nerve endings. Acetyl choline[2] and potassium[3] are temporarily effective antagonists

[3] Rosenblueth, A., Lindsley, D. B., and Morison, R. S., *Am. J. Physiol.*, 1936, **115**, 53.

[4] Briscoe, Grace, *J. Physiol.*, 1936, **87**, 425.

[5] Bremer, F., and Titeca, J., *Arch. Int. Physiol.*, 1935, **42**, 223.

[1] Lubinska, L., *Arch. Int. de Physiol.*, 1935, **41**, 456.

[2] Rosenblueth, A., Lindsley, D. B., and Morison, R. S., *Am. J. Physiol.*, 1936, **115**, 53.

[3] Wilson, A. T., and Wright, S., *Quart. J. Exp. Physiol.*, 1936, **26**, 127.

to curare, and it has been inferred that both substances are released at the endings of cholinergic nerves.[4, 5]

We have used cats and dogs, anesthetized with nembutal. Contractions were recorded from the tibialis anticus muscle, the lever allowing 1.1 mm. of shortening per kilogram of tension. The sciatic trunk was sectioned and shielded electrodes placed on the peroneal branch. Single test stimuli, from a neon-tube circuit, were applied at intervals of 4 to 6 seconds. For tetanizing we used a photocell stimulator with a rotating disc interrupter. Both circuits were adjusted so that the shocks were barely strong enough to give a maximum normal twitch. $MgSO_4$ (7.7% solution of the heptahydrated salt) was administered intravenously in small repeated doses.

When response to single shocks had failed, it was always restored following a period of tetanic stimulation of the nerve. The higher the frequency of tetanic stimuli (up to 120 per second) the greater the degree of recovery after a short tetanus. The "physiological" frequency of 27 per second, used by Lubinska, is therefore not an optimum for this effect. The duration of the recovery varies both with the frequency and with the duration of the preceding tetanus. Following a tetanus of 30 seconds at 120 per second, the restored twitches may take 8 minutes or more in sinking to zero or to a new base level. If this recovery is due to accumulated acetyl choline, the local mechanism for its removal is obviously slow in action.

Recovery of the response to single shocks is at a maximum immediately after cessation of the tetanus. The twitches fall away rapidly at first and then more slowly, describing a smooth curve. Such a curve would be expected if the diminishing concentration of a chemical activator were plotted against time, but it is not apparent why the twitch-tension should follow the same type of curve. An entirely different form of recovery curve is obtained in animals under curare.[6]

$CaCl_2$ (2 cc. of isotonic solution) or physostigmin (0.5 to 1 mg. per kilo) injected into the iliac artery, induce a gradual but sustained recovery. Acetyl choline (0.2 to 2 mg. in 2 cc.) and KCl (1 to 3 cc. of 2 to 4% solution) give recovery curves which more nearly resemble those following brief tetani.

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[4] Dale, H. H., Feldberg, W., and Vogt, M., *J. Physiol.*, 1936, **86**, 353.

[5] Feldberg, W., and Guimarais, J. A., *J. Physiol.*, 1936, **86**, 306.

[6] Boyd, T. E., and Brosnan, J. J., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 404.