found that irradiation of fats, otherwise inactive in preventing rickets, caused them to become active and that rations which ordinarily produced wide rachitic metaphysis in the shaft bones of rats became antirachitic and promptly effected a rapid and complete healing of the lesion.

These facts have now been correlated with what is known of the properties of the antirachitic vitamine and found in substantial agreement. As a result of this experimental work, the action of direct irradiation and the reported antirachitic action of irradiated air has also become understandable to us from a different point of view.

These experiments, which have been in progress since November, 1923, will be reported shortly in the *Journal of Biological Chemistry*. In the meantime, to protect the interest of the public in the possible commercial use of these findings, applications for Letters Patent, both as to processes and products, have been filed with the U. S. Patent Office and will be handled through the University of Wisconsin.

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ON THE EFFECTS OF VARIATION IN FREQUENCY OF STIMULATION ON STRIATED, CARDIAC AND SMOOTH MUSCLE[1]

During the course of an investigation carried out by one of us on the effects of variation in frequency and intensity of stimulation of the vagus nerve on the lower end of the esophagus, the cardia and the fundus et corpus ventriculi of the cat, concerning which a preliminary note has been published,[2] it became desirable to extend experiments of this kind to direct stimulation of the different types of muscle. Accordingly, we have chosen for investigation the m. gastrocnemius of the frog, the m. omohyoideus of the turtle, the apex of the turtle's ventricle, portions of the alimentary canal of the cat and the siphon muscle of the clam. The results, which have corroborated those obtained in the vagus experiments, are here reported in a second preliminary communication.

Considering first striated muscle, frequencies of interruption of the primary current of about 40 per second cause pronounced and well-maintained tetanus of the frog's gastrocnemius and the omohyoid of the turtle, but an increase in frequency to 100 per second or more causes more or less complete relaxation. If the higher frequencies are employed at the outset, the muscle responds with a rather brief initial tetanus, relaxation taking place thereafter. The effects are most clearly obtained from the omohyoid of the turtle, for it has much less tendency to enter into a state of contracture than the gastrocnemius. These results are obtained from the curarized as well as the non-curarized muscle.

In case the stimulation is long continued, the gastrocnemius begins to contract rhythmically. This occurs best with a frequency of about 40 per second. The contractions are slowed in frequency and increased in strength as the stimulation is maintained. An increase in frequency to 120 per second or more stops the rhythm and causes the muscle to relax to its contracture level. On decreasing the frequency to its excitatory value, the rhythmicity is resumed, often after a considerable latent period. These results, likewise, are given by the curarized and the non-curarized muscle.

Injection of atropine sulphate into the dorsal lymph sac greatly increases the tendency of the gastrocnemius to contract rhythmically in response to the tetanizing current, and accordingly a much higher frequency is required to stop the rhythm in the atropinized preparation. In one experiment, in which the muscle was both curarized and atropinized, a frequency of 560 per second was hardly sufficient to suppress it. The gastrocnemius of the other leg, which had been atropinized only, exhibited a strong and quite regular rhythm in response to a frequency of 640 per second. Atropine has shown repeatedly this ability to counteract the inhibitory effects of high frequency stimulation.

The results from the apex of the turtle's ventricle have been even more striking. A frequency of interruption of 2.5 per second usually establishes a regular rhythm of contraction. A moderate increase in frequency slows the rhythm and increases the magnitude of the contractions. With a further increase in frequency, the contractions cease and the muscle relaxes almost completely. In this relaxed state, the contractile forces of the muscle are recovered, as indicated by the character of the response obtained when the frequency is lowered again to its excitatory value. Surprisingly low frequencies are inhibitory. Ten interruptions or fewer per second are often sufficient to suppress the rhythm entirely. Atropinization, however, changes the results in a significant manner. Rhythmic contractions are set up by stimulation as before, but extraordinarily high frequencies are required to suppress them—760 interruptions per second often leave the rhythm in progress. It is of interest to note also that atropinization often leads to spontaneous rhythmicity of the apex of the ventricle, which is difficult to check by high frequency stimulation. Pilocarpine, as would be expected, counteracts the effects of atropine. By its application the relations of frequency to effect produced can be made

[1] From the Laboratory of Physiology in the Harvard Medical School.

[2] Veach, H. O., Science, 1924, LIX, 260.

to revert to those holding for the non-atropinized preparation.

The results obtained from smooth muscle are likewise significant. The siphon muscle of the clam reacts to variation in frequency of stimulation in much the same way as the omohyoid of the turtle, though it relaxes in response to lower frequencies. The frequencies required to cause relaxation of the smooth muscle of the alimentary canal, on the other hand, are extraordinarily high. In one Magnus preparation[3] of the circular coat of the duodenum, taken from a cat anesthetized with urethane, frequencies of 320 and above were required to cause relaxation during stimulation. In a preparation taken from the lower end of the esophagus of a decerebrate cat, and arranged to record the contractions of the longitudinal coat, the myenteric plexus remaining intact, a frequency of 240 per second caused well-maintained, rhythmic contraction. Relaxation took place, however, when the frequency was increased to 400 per second. The latter frequency when applied to the resting preparation, the intensity remaining constant, caused contraction.

These observations tend to establish a definite relation between frequency of stimulation and the response produced in the effector: low frequencies of stimulation are excitatory and high frequencies are inhibitory. The analogy to Wedensky inhibition[4] is close, and we are inclined to account for the results chiefly on the basis of the reduction in magnitude of a propagated disturbance, which travels in the relative refractory phase following its predecessor. This has been shown by Lucas to be true for the sciatic nerve[5] and the sartorius muscle[6] of the frog. We place the seat of reduction of the propagated disturbances to subnormal magnitude in a conducting mechanism of the muscle. The reduced disturbance might be rendered thus subthreshold for the contracting mechanism. Rhythmicity is seen to be explicable on the same basis. Fatigue would lower the threshold of the contracting mechanism and result in relaxation. During relaxation, the contractile forces would be recovered, with a resulting fall in threshold, and the conditions would be established for contraction. The occurrence of contraction, however, would fatigue again the contracting mechanism, and the process might thus be repeated rhythmically. Incidentally, the results indicate that the seat of inhibition for the turtle's heart is within its musculature. They indicate also that the chief cause of the production of Wedensky inhibition may lie in the properties of a conducting mechanism of the muscle fiber.

[3] Magnus, R., *Arch. f. d. ges. Physiol.*, 1904, CII., 349.

[4] Wedensky, N., *Archives d. Physiol.*, 1891, XXIII., 687.

[5] Lucas, K., *Journ. Physiol.*, 1911, XLIII., 46.

[6] Lucas, K., *Journ. Physiol.*, 1909, XXXIX., 331.

A full account of this investigation will appear in the *American Journal of Physiology.*

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A HIGH RESISTANCE FOR USE WITH ELECTROMETERS

A QUADRANT electrometer may be used to measure current by two methods: (1) By measuring the rate of deflection when one pair of quadrants is attached to a system of known capacity which is being charged by the current to be measured; (2) by using the electrometer to measure the potential drop across a high resistance through which the current is flowing. The resistance to be used in the latter method should be high, non-polarizable and it is desirable to have it made of such materials that the magnitude of the resistance may be varied to meet the requirements of the experiment. It was suggested by Professor G. N. Lewis that solutions of iodine in non-conducting solvents such as benzene might meet these conditions.

The benzene used in these experiments was washed successively with concentrated sulfuric acid, sodium carbonate solution and distilled water, dried with phosphorous pentoxide and distilled. The iodine used was purified by resubliming the commercial product. The conductivities of the solutions were measured in a glass cell with platinum electrodes which were four centimeters in area and approximately one millimeter apart. The concentrations of the solutions tested varied from 10.62 to 2.69 grams of iodine in 100 cc of solution and the specific resistances ranged from 1.1×10^{11} to 4.8×10^{11} ohms. At the lower concentrations of iodine the conductivity is very nearly proportional to the concentration of the iodine but at higher concentrations the ratio of conductivity to concentration increases slightly. The temperature coefficient is fairly high, the conductivity increasing approximately one per cent. of the value at 20° C. for each degree rise in temperature.

Several resistances have been made using these solutions and have been tested with a Compton electrometer with satisfactory results. The currents which have been measured with this arrangement are of the order of 10^{-15} ampere, but it is evident that by suitable variation of the resistances or of the sensitivity of the electrometer a wide range of currents may be covered. If the resistance is adjusted so that with the maximum deflection observed the potential drop across the resistance is not more than about one tenth of a volt the system rapidly adjusts itself to a change of current. If actual values of the current are desired the system should be calibrated by one of the usual methods.

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