as high as those following intramuscular injections of 500,000 units suspended in peanut oil and beeswax.

References

1. Atcheson, D. W., and Edmeades, D. T. *Science*, 1945, **102**, 199.
2. Callomon, F. T., Kolmer, J. A., Rule, A. M., and Paul, A. J. *Proc. Soc. exp. Biol. Med.*, in press.
3. Freund, J., and Thomson, K. J. *Science*, 1945, **101**, 468; *Proc. Soc. exp. Biol. Med.*, 1945, **59**, 145.
4. Kirby, W. M. M., *et al. J. Amer. med. Ass.*, 1945, **129**, 940.
5. Kolmer, J. A., Bondi, A., Jr., Warner, H. F., and Dietz, C. (To be published.)
6. Nichols, D. R., and Haunz, E. A. *Proc. Staff Meet., Mayo Clin.*, 1945, **20**, 403.
7. Romansky, M. J., and Rittman, G. E. *Science*, 1944, **100**, 196; *Bull. U. S. Army med. Dept.*, 1944, **43**, No. 81.
8. Stebbins, R. B., and Robinson, H. J. *Proc. Soc. exp. Biol. Med.*, 1945, **59**, 255.
9. Zinnamon, B. L., and Seeberg, V. P. *Ven. Dis. Inf.*, 1945, **31**, 26.

Effect of Di-Isopropyl Fluorophosphate (DFP) on the Action Potential of Muscle

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Di-isopropyl fluorophosphate (DFP) abolishes the nerve action potential, but this effect is reversible for a limited period of time. DFP is a strong inhibitor of cholinesterase. A striking parallelism between the reappearance of the action potential and cholinesterase activity in nerve can be demonstrated during the recovery from DFP poisoning. The inhibition of cholinesterase by DFP can also be reversed *in vitro* during a period of time comparable to that in the experiments on nerves (*1*). These observations are consistent with the concept that cholinesterase activity and, consequently, the release of acetylcholine are essential events in the conduction of the nerve impulse.

It is generally considered that the mechanisms of the axonal and end-plate potentials are basically identical (*4*). The role of acetylcholine in the end-plate potential is supported by the relation between the activity of cholinesterase and the action potential of the electric organ, which may be considered analogous to the end-plate potential (*5*). Further support is found in the persistence of the high cholinesterase concentration at the motor end plate after complete degeneration of the axon (soleplate) (*2, 3*).

No facts are available concerning the chemical mechanism involved in the action potential of muscle, although many physiologists believe that the electrical manifestations of nerve and muscle are fundamentally identical. Muscle fibers and nerves are the only tissues which contain specific cholinesterase (*6*). This makes possible the assumption that acetylcholine plays a role in both tissues. However, the presence of an enzyme alone does not permit an interpretation of its function. We have therefore tested whether DFP abolishes the action potential of muscle as it does that of nerve.

Frogs (*Rana pipiens*) were curarized with crystalline *d*-tubocurarine chloride (Squibb). After curarization, the sartorius muscle was excised and mounted in a specially constructed chamber. The action potentials evoked by single electrical stimuli were recorded by means of a cathode-ray oscillograph. When not stimulated, the muscle was kept immersed in a Ringer solution containing 0.1 mg./cc. of curarine. This solution was then replaced by an identical solution containing DFP. Under the effect of DFP the action potential of the muscle rapidly disappears. With a concentration of 2 mg. of DFP/cc., the action potential is abolished in as little as 8 minutes. With a concentration of 1 mg. of DFP/cc., the abolition takes longer (20–30 minutes). After washing with the curarine Ringer solution (without DFP) the reappearance of the response is observed.

These experiments present the first evidence that acetylcholine may play a role in the muscle action potential. They are consistent with the idea that the natures of axon, end-plate, and muscle action potentials are basically identical.

References

1. Bullock, T. H., Grundfest, H., Nachmansohn, D., Rothenberg, M. A., and Sterling, K. *J. Neurophysiol.*, 1946, **9**, 253.
2. Couteaux, R. *Bull. Biol.*, 1942, **76**, 14.
3. Couteaux, R., and Nachmansohn, D. *Proc. Soc. exp. Biol., N. Y.*, 1940, **43**, 177.
4. Eccles, J. C. *Trans. N. Y. Acad. Sci.*, in press.
5. Nachmansohn, D., Coates, C. W., and Rothenberg, M. A. *J. biol. Chem.*, 1946, **163**, 39.
6. Nachmansohn, D., and John, H. M. *J. biol. Chem.*, 1945, **158**, 157.

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Derivation, Interpretation, and Application of the Second Law of Thermodynamics

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The second law of thermodynamics is commonly derived by means of an extended series of differential equations not easy to follow and involving so many assumptions and limitations that the result is not altogether convincing. Its physical interpretation is given in a wide variety of statements. That a number of the fundamental relations of thermodynamics may be simply and directly derived from it appears to have been entirely overlooked. It is here derived as a by-