roxine for lactation. This would provide an explanation for the significant increase in thyroid hormone output which occurs during early lactation in rats(16) and sheep(17).

Summary. The effect of various levels of estradiol benzoate (E.B.) upon thyroxine secretion rate (TSR) has been studied in young mature female rats. A dose of 3.6 μg/day E.B. caused significant increase of 35.5% in TSR over average control value of 1.24 μg/100 g/day l-thyroxine while 1, 15 or 50 μg/day had no effect. In another experiment, body weight and thyroid weight/100 g were not affected by injecting 1 or 3.6 μg/day E.B. for 5 days. Thyroid weight/100 g was significantly increased while appetite and body weight were markedly reduced following 15 or 50 μg/day for same period. Pituitary weight/100 g was significantly increased in all but the 1 μg/day group. Adrenal weights/100 g were lower in all groups with significant depression occurring in 50 μg/day group. These data are discussed in relation to stimulation or depression of thyroid activity by estrogen.

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Effect of 2-PAM on Neuromuscular Blockade Induced by Certain Chemicals. (24881)

J. H. WILLS, A. M. KUNKEL, J. F. O'LEARY AND A. H. OIKEMUS
Physiology Division, Medical Research Army Chemical Center, Md.

Holmes and Robins(1) found that 2-formyl-1-methylpyridinium iodide oxime (2-PAM) induces paralysis of isolated phrenic nerve-diaphragm preparation of the rat; the curaremimetic action of this compound has been corroborated for calf muscles of the cat, excited *in situ* through sciatic nerve stimulation by ourselves and for adductor muscle of human little finger, excited by stimulation of ulnar nerve(2). In addition, 2-PAM (5 x 10^{-3} M) decreases rate of shortening of isolated rectus abdominis of the frog in response to acetylcholine, but smaller concentrations of 2-PAM increase this rate(3). Grob and Johns reported also(2) that some patients given 2-PAM intravenously experienced thereafter orthostatic tachycardia and hypotension. These findings, and those that 2-PAM is particularly active in promoting reactivation of inhibited cholinesterase in cholinergic neurons of ganglia(4) and in motor end-plates of skeletal muscle(4,5), suggest that the oxime has a special affinity for nicotinic effectors, where it has a depolarising action of its own and also competes with other quaternary molecules (acetylcholine, for example) for the receptor site. Wagley(6) found, indeed, a reversible increase of about 40% in end-plate potential of frog muscle treated with 2-PAM *in vitro;* this is the type of change expected from a de-

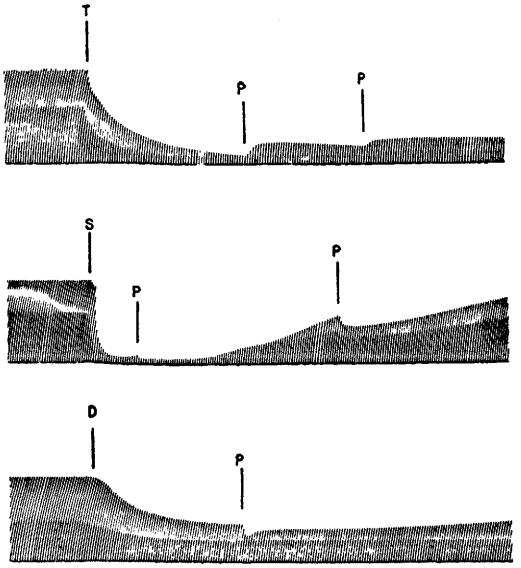

FIG. 1. Effects of 2-PAM (P) on neuromuscular block induced in the cat by d-tubocurarine (T), succinylcholine (S) or decamethonium (D).

polarising agent. Contradictory of the above suggestion is the report of Holmes and Robins (1) that oximes had no effect on transmission blocks induced in isolated phrenic nerve-diaphragm preparation by d-tubocurarine, succinylcholine or decamethonium.

Methods. The present work was undertaken to restudy effects of 2-PAM on acute neuromuscular block. Cats prepared in our usual manner(7) were used, contractions of the gastrocnemius-soleus-tibialis anticus muscle group in response to electrical stimulation (one shock every 2 seconds) of the sciatic nerve being recorded kymographically. Intravenous injections of d-tubocurarine chloride(0.1 mg/kg), of succinylcholine chloride (0.05 mg/kg) or of decamethonium bromide (0.06 mg/kg) were used to produce a marked decrease in response of muscle to just supramaximal nerve stimulation. During period of reduced response, one or 2 intravenous injections of 5 mg/kg of 2-PAM were made.

Typical *results* are shown in the Figure. Injection of 2-PAM into cats treated previously with d-tubocurarine induced some increase in response to motor nerve excitation; similar injections into cats given initially succinylcholine or decamethonium intensified the decrement of response induced by the first compound.

These results, unlike those of Holmes and Robins(1), show that 2-PAM has effects on neuromuscular blocks induced by d-tubocurarine, succinylcholine or decamethonium. That block induced by d-tubocurarine is antagonised by 2-PAM but that those induced by succinylcholine or decamethonium are intensified by oxime supports the idea that 2-PAM has a depolarising action at the neuromuscular junction, antagonising block produced there by competitive blocker d-tubocurarine and intensifying those produced by depolarising blockers succinylcholine and decamethonium.

Summary. In the anesthetized cat, i.v. injection of 2-PAM lessens neuromuscular block induced by d-tubocurarine but intensifies that induced by succinylcholine or decamethonium. In addition to being a reactivator of cholinesterase inhibited by P-containing anticholinesterases, 2-PAM may depolarise the neuromuscular junction.

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