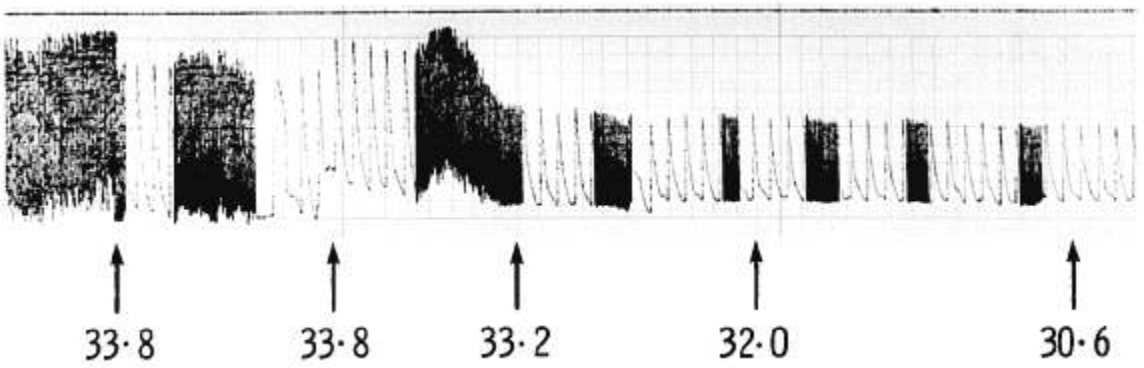

FIG. 1. Adductor twitch response to stimulation of the ulnar nerve during hypothermia from 33.8 to 30.6 C in a 6-year-old patient (no muscle relaxant administered).

experiments when the whole animal, with the exception of the limb studied, was normothermic.

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In reply:—Feldman's observations in man and animal that hypothermia is associated with a diminished amplitude of indirectly elicited twitch tension may explain in part the prolonged duration of neuromuscular blockade during hypothermia from nondepolarizing muscle relaxants.[1,2] We believe the temptation to attribute the effect of hypothermia on the neuromuscular junction to a single mechanism should be resisted. Hypothermia may affect several sites that could alter neuromuscular function, which include: nerve conduction, transmitter release, sensitivity of the cholinergic receptors, cholinesterase activity and mechanical properties of the muscle. A further complicating factor is that the effect of hypothermia appears to be species-dependent. For example, the conduction velocity in the nerve axon during hypothermia increases in the squid axon[3] and is unchanged in the frog sartorius preparation.[4] Transmitter output from the nerve terminal is diminished during hypothermia in the mouse intercostal[5] and frog sartorius.[6] In the rat diaphragm, a more complex effect occurs. In one study a diminished transmitter output was observed.[7] Yet Hubbard *et al.*[8] found a biphasic response, with initial increase and peak at 20 C and subsequent diminution. Ward *et al.*[9] also found a biphasic response, but with an initial decrease in output to 27 C and subsequent increase at less than 20 C. The sensitivity of the postjunctional membrane to transmitter (as measured by miniature end-plate potential amplitude[6,10,11] or response to iontophoretic acetylcholine[4,6,12,13]) is decreased, unchanged, or increased, in different species. Cholinesterase activities of the erythrocytes and plasma are both depressed by hypothermia.[14] The response of directly stimulated muscle

during hypothermia is also variable in different species[12,15,16] and with different rates of stimulation.[17]

In addition, we believe Feldman's observation of diminished indirectly elicited twitch tension in patients during cooling deserves additional study. During our completed studies in cats, as well as ongoing studies in man, we have observed decreases, increases, and biphasic responses of twitch tension to hypothermia without muscle relaxants. The mechanism of hypothermia's effect on the interaction of muscle relaxants with the neuromuscular function obviously is complex. In spite of these problems concerning mechanism of action, there appears to be little doubt that hypothermia prolongs a nondepolarizing neuromuscular blockade.

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