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In reply:—Oeseburg and Kwant emphasize that many sources of error exist in the determination of blood P_{O_2} and that these may be related to blood sampling, sample handling, and the measuring system. However, even with the most meticulous sampling and handling techniques, there will be differences between observed and actual P_{O_2} values. Therefore, the purpose of our report[1] was twofold: first, to point out that the measuring system introduces errors specific to each particular system; second, to show how it is possible to eliminate these errors of a measuring system by applying a standardized reference method based on blood tonometry using a well-defined reference system, and transforming the results onto a nomogram. We did not intend to produce a complete record of possible errors.

As can be seen from our nomogram, the inaccuracy of the oxygen analyzer increases with increasing blood P_{O_2} values, reaching deviations of more than 20 per cent at P_{O_2} levels of more than 500 torr. This is to a certain extent dictated by the shape of the oxyhemoglobin-dissociation curve. The remarks of Oeseburg and Kwant concerning the different slopes and intercepts of such nomograms suggest that they will be linear, but in fact the ABL 1 nomogram is nonlinear.

An additional topic of current interest should be mentioned to complete the subject. It is of particular concern to anesthesiologists that halothane may have a considerable effect on the stability of the P_{O_2} electrode due to the polarographic reduction of halogenated hydrocarbons.[2] It appears that with the ABL 1 system even a single exposure to blood containing halothane, 1 per cent, results in a gradual upward drift in the electrode calibration, and that this effect may persist for several hours.[3]

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Hypothermia and Neuromuscular Blockade

To the Editor:—Like Ham *et al.*,[1] we have observed and reported the prolongation of nondepolarizing neuromuscular blockade when the temperature of muscle is decreased.[2,3] In control experiments we have also demonstrated, in both man[4] and dog,[5] that hypothermia alone will produce a decrease in the indirectly elicited twitch response (fig. 1), an effect that is antagonized by edrophonium. This clearly demonstrated that hypothermia to less than 32 C in man and 29 C in the dog critically decreased acetylcholine mobilization and release, which is fundamental to neuromuscular transmission. The effect of cold on acetylcholine mobilization has been demonstrated to be biphasic, with a transient initial increase followed by a marked diminution.[6] Temperatures at which this failure occurs vary according to the species studied, being lower in hibernating animals and amphibians than in the higher species of mammals.[7] It is probable that this failure of acetylcholine mobilization is the cause of the increased synaptic delay time that occurs during hypothermia.[8] It is most probable, therefore, that it is this critical decrease in the margin of safety of neuromuscular transmission that results in the prolongation of the effect of the nondepolarizing relaxants during hypothermia, an effect that will be exacerbated by the decrease in renal clearance observed by Ham *et al.*, but was unlikely to have contributed to the prolongation of block observed in our

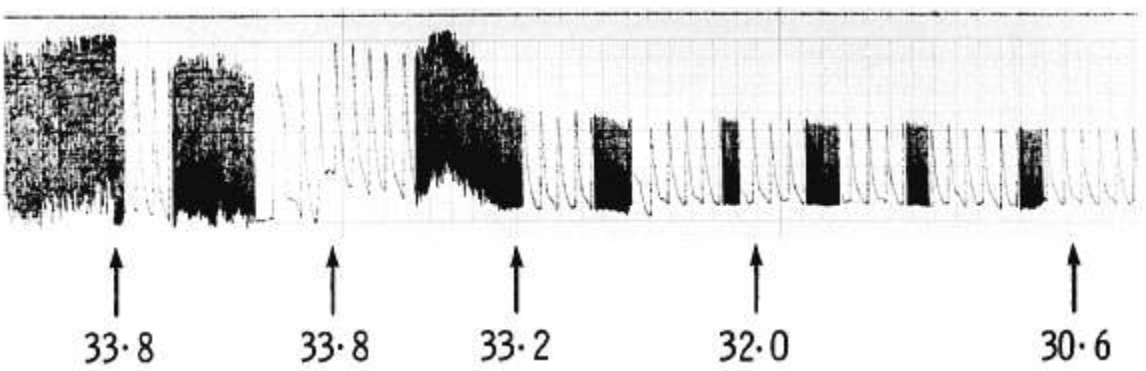

FIG. 1. Adductor twitch response to stimulation of the ulnar nerve during hypothermia from 33.8 to 30.6 C in a 6-year-old patient (no muscle relaxant administered).

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