80. Temperature Dependence of the Healing-over in Mammalian Cardiac Muscle

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The rapid decrease of the injury potential, or healing-over, is characteristically seen in cardiac muscle.1) The present investigation was undertaken in order to clarify the influence of the temperature on this process. This could give an information of the mechanism of healing-over and also could be a contribution for the treatment of wound healing in medicine. The sucrose-gap technique was applied for the first time for this kind of study. It made possible to record the membrane potential continuously in spite of the movement of muscle.

The guinea-pig's papillary muscles excised from the right ventricle were used. The single sucrose-gap arrangement designed for the voltage-clamp experiment2) was suitable for the recording of membrane potential as well as for the application of electrical stimuli. The membrane potential was measured by two extracellular electrodes placed across the sucrose-gap. The muscle could be stimulated capacitatively through a condenser connected to the electrode in the current pool. This pool was filled with K-Tyrode's solution. The potential pool was perfused with Tyrode's solution3) and its temperature was varied between 19-42°C.

At the beginning of each experiment, action potentials were elicited by the electrical stimulation (Fig. 1 Aa, Ba). Its mean amplitude was 90 mV (range, 64-125 mV). Then, a lesion was produced in the potential pool by cutting the muscle transversely by scissors at about 500 μ from the border of the sucrose-gap. Usually, the lesion was large and the muscle was severed. A sustained depolarization, injury potential, appeared following an action potential (Fig. 1 Ab, Bb). The mean amplitude of the injury potential was 49 mV (range, 32-67 mV). The injury potential declined initially slowly, then relatively steeply and finally most slowly (Fig. 1 A). The slow decay of the initial part could be expected if the relation between the injury potential and the conductance at the lesion was non-linear as the relation between the synaptic potential and its conductance. The rate of

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this healing process was highly dependent on temperature of the solution. As the temperature was lowered, the rate of healing was remarkably depressed (Fig. 1 C, D). It should be mentioned that after the long depolarization, at low temperature, the recovery of action potential was incomplete compared with its rapid recovery at high temperature (Fig. 1 D). To obtain a quantitative relation between the temperature and the rate of healing-over, the half-decay time of the injury potential ($t_{1/2}$) was plotted against temperature on a logarithmic scale (Fig. 2). The figure shows that the representative value of $t_{1/2}$ at 37°C was 30 sec, while it increased to 270 sec at 20°C. The temperature coefficient ($Q_{10}$) was calculated from the slope. It was −3.6 between 19 and 42°C. Similarly, $Q_{10}$s of the decay to 3/4 and 1/4 of the maximal amplitude of injury potential were also about −4.

Recently De Mello and his colleagues have reported that the rate
of healing is depressed by the decrease of temperature in toad heart. They reported the result obtained at the temperature range between 5 and 24°C and Q_{10} was not measured. However, their result coincides qualitatively with ours.

The present investigation has revealed that the rate of healing-over was highly dependent on temperature in mammalian cardiac muscle. The lower the temperature, the slower the recovery of the resting potential. This could be also the case with the rate of healing in situ. Then, in clinical medicine, the rate of isolation of damaged cells in heart could be influenced by the temperature.

In Fig. 1 D, the action potential was heavily depressed after the prolonged injury potential. This change of action potential could be expected if Na ions had diffused into cells from the cut end considerably. Indeed the diffusion through the cut end was not negligible. When the muscle was cut in the solution containing tetraethylammonium ions, the action potential was prolonged by the intracellular action of the drug (Ochi and Nishiye, in preparation).

Ca is essential for the healing-over. The Q_{10} of the diffusion of Ca from the outside of cell to tight junction should be about -1.3. Thus the present value of Q_{10} suggests that the metabolic process
might be implicated in the healing-over. The metabolic process might help calcium to block the junctional coupling near the lesion.6)