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Effect of Temperature Change on Heart Performance (Heart-Lung Preparation). (32564)

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In 1912 Knowlton and Starling(1) reported that within wide limits the output of the heart is independent of temperature in isolated heart-lung preparations. Since then many papers have been published on the cardiovascular effects of hypothermia, most of them on intact animals(2-6).

In an isolated heart-lung preparation, Reissmann and Kapoor(7) reported that lowering the temperature diminished the ratio of work to filling pressure. On the other hand, both Covino(8) and Goldberg(9) demonstrated a marked increase in myocardial contractile force, by attaching a strain gage arch to the myocardium of anesthetized, artificially ventilated, hypothermic, but otherwise "intact" dogs.

In this study of the influence of temperature on cardiac performance, an isolated heart-lung preparation was chosen in preference to an intact animal. This preparation excludes nervous and humoral influences; thus the changes observed may be ascribed to the direct action of temperature *per se* on myocardium. By reporting the effects on a stroke work basis, we are avoiding some of the complications of the chronotropic effects of temperature.

Method. Mongrel dogs (7.7-10.0 kg body weight) were anesthetized intravenously with sodium pentobarbital (30 mg/kg). The method of Knowlton and Starling(1) was followed with some modifications. The preparations were ventilated either with room air or with a mixture of 40% O_2, 4% CO_2, and 56% N_2. The preparations were supported by a continuous infusion of 5% glucose (10 mg/min) containing insulin (0.008 units/min) (10). Five mg heparin per 100 ml blood was used as an anticoagulant.

The blood reservoir was a polythylene bag 4 inches in diameter immersed in a water bath 9 inches in diameter to maintain a constant pressure head in spite of changes in volume of blood in the reservoir (Fig. 1). The inflow and the aortic pressure were adjusted with 2 screw clamps. The water bath was maintained thermostatically and altered rapidly by heating or adding ice. The blood temperature was read from a thermometer in the cannula in the superior vena cava through which the blood was delivered from the reservoir to the heart.

Arterial pressure was recorded through a polyethylene catheter inserted into the left subclavian artery and connected to a Statham P 23 Dd transducer and a Brush 8-channel oscillograph recorder. Left atrial pressure was recorded through a rubber tube inserted through the left appendage and connected both to a Statham PR 23 transducer and to a saline manometer; the latter was used for calibration and direct reading.

In some experiments right atrial pressure was measured by a saline manometer through a polyethylene tube inserted *via* the inferior vena cava.

The systemic flow was recorded with a rotameter(11). The pulmonary flow was measured with a pulsed field electromagnetic flowmeter (Medicon Division of Statham In-

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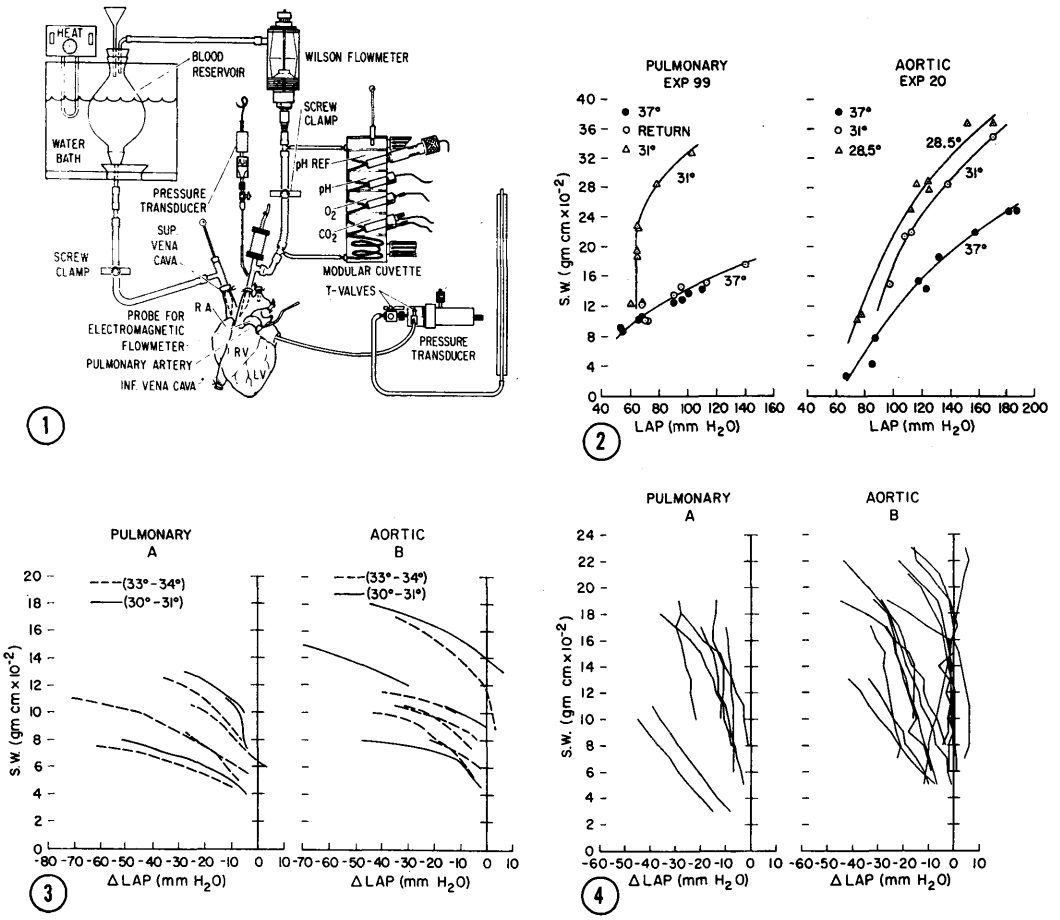


FIG. 1. Modified Starling heart-lung preparation and monitoring systems.

FIG. 2. Effect of cooling on left ventricular performance. The performance of the heart was evaluated by the relationship between left atrial pressure (LAP) and stroke work (SW). (a) SW calculated from pulmonary flow—varying stroke work with change in aortic pressure—flow constant. (b) SW calculated from aortic (systemic) flow—varying stroke work with change in aortic flow—aortic pressure constant.

FIG. 3. Effect of cooling of blood on LAP at any fixed SW. ΔLAP represents the difference in LAP at 37° and lower temperature at corresponding levels of SW. Stroke work was varied with change in aortic pressure—flow constant, (a) Stroke work calculated from pulmonary flow and mean aortic pressure. (b) Stroke work calculated from aortic flow and mean aortic pressure.

FIG. 4. Same as Fig. 3. Shows effect of cooling from 37° to 30°C on LAP at any fixed SW. In these experiments, SW was varied with change in flow—aortic pressure constant. (a) Stroke work calculated from pulmonary flow and mean aortic pressure. (b) Stroke work calculated from arotic flow and mean arotic pressure.

struments). A portion of systemic flow was shunted through a modular cuvette† with a multiple electrode assembly for continuously measuring pCO_2, pO_2, and pH of blood (Beckman-Spinco Severinghaus-type pCO_2 electrode, oxygen macro electrode, micro blood pH electrode).

† Fabricated by Instrument Research Division, Ames Research Center.

The systemic flowmeter was calibrated with graduate cylinder and stopwatch; the pulmonary flowmeter was similarly calibrated after the experiment by allowing blood to flow at a constant pressure head through the pulmonary artery and one of its main branches; pressure in the system was maintained by a screw clamp on the outflow. The other branch was ligated.

Left ventricular function curves were obtained by plotting the left atrial pressure against the stroke work (pulmonary or systemic flow $\times$ mean aortic pressure/heart rate). Ejection (ml) $\times$ arterial pressure (mm Hg) was converted to gram centimeters. Performance was evaluated by a comparison of stroke work curves obtained with a change of temperature in the same dog heart.

Experimental design. Approximately half an hour after the preparation was completed, a "normal" work curve was established at 37°C. This was used to verify recovery from the procedures and to evaluate any subsequent spontaneous deterioration of the preparation. This served as a control for the data obtained at other temperatures. In most experiments the extreme upper end of the work curve was not explored, since atrial pressures of over 150 mm H_2O tend to impair performance irreversibly.

Work curves were measured at temperatures above and below 37°C. The temperature range explored was 28.5° to 44°C. The lower limit was determined by the appearance of irregularities of heart beat; the upper limit by the tendency toward the rapid onset of pulmonary edema. A final work curve at 37°C was obtained at the conclusion of each experiment.

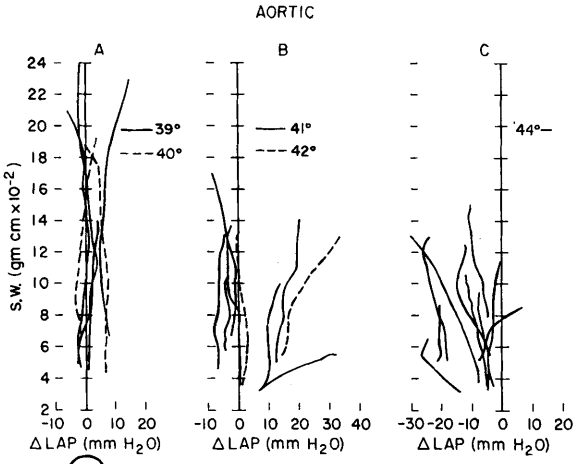
Results. The effect of cold on stroke work. Representative curves from 2 experiments are presented in Fig. 2. On the left hand graph, the work load was varied by keeping the flow constant and changing the aortic pressure. On the right, the work load was varied by changing the flow and keeping the aortic pressure constant. Stroke work was plotted against its simultaneous left atrial pressure. It is clearly demonstrated here that the work per beat of the myocardium at any filling pressure within the ranges presented is increased with cooling.

Because of variability in the performance of different hearts, it is not feasible to average the results of various experiments. Fig. 3 presents deviations of left atrial pressures of ventricles at 33°-34°C and 30°-31°C from the left atrial pressures of tests at 37°C at the corresponding levels of stroke work. The stroke work was varied by keeping the flow constant and changing the aortic pressure. These experiments indicate that at temperatures lower than 37°C, a lower LAP was found with the same amount of stroke work. Moreover, the higher the work per beat, the greater is this improvement in cardiac performance.

The data presented in Fig. 4 were obtained in a manner similar to that presented in Fig. 3 and in the same temperature range; however, in these experiments the work per beat was varied by changing the flow and keeping the aortic pressure constant. Essentially, the findings are the same, though the improvement is less pronounced.

In Figs. 2, 3, and 4, the left hand graphs show the left ventricular stroke work computed from the mean aortic pressure and pulmonary flow. The right hand graphs represent the data of the left ventricular stroke work computed from the mean aortic pressure and the aortic systemic flow. Since the stroke work, computed on the base of systemic flow only, neglects the variable flow in the coronary system, it is therefore more difficult to interpret rigidly. The "systemic" information serves to indicate the effective circulating capacity of the ventricle above its conorary needs.

The effect of elevated temperature on stroke work. Fig. 5(a,b,c) present data similar to those of Fig. 3 for hearts subjected to 37°, 39°, 40°, 41°, 42°, and 44°C. The work load was varied by changing the flow and keeping the aortic pressure constant. The stroke work was computed from the systemic flow and the mean aortic pressure. Whenever possible, the entire temperature range from 37°C upward was examined in each dog. This was done in the above order with a final trial at 37°C as an added control. In general, it is shown that warming the heart to 42°C produces inconsistent results (Figs. 5a and b). In some cases the work per beat was reduced. We consider that this reduction in stroke work (as compared with its control at 37°C) might be due to the gradual and slight deterioration of the heart. However, in all but one experiment at 44°C there was an improvement in cardiac performance (Fig. 5c). This improvement may be greater than



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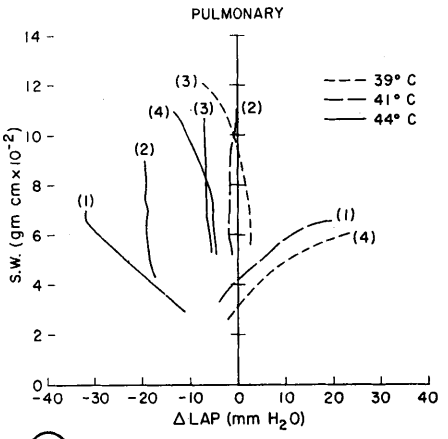

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FIG. 5. Effect of warming of blood on LAP at any fixed SW. ΔLAP represents the difference in LAP at 37°C and another temperature at corresponding levels of SW. Stroke work calculated from aortic flow and mean aortic pressure. Varying stroke with change in flow — pressure constant.

FIG. 6. Effect on LAP of warming at fixed SW, calculated from pulmonary flow (of Fig. 5). Each line represents a series of consecutive measurements at the temperature indicated. 2 work curves were carried out on each dog heart as indicated by the numbers.

it appears, since the curve constructed at 44°C was near the termination of the experiment. The improvement at 44°C becomes more evident as we compare it with the work performance at 39° to 42°C (Figs. 5a and b).

In 4 preparations the pulmonary flow was recorded and used for the computation of the stroke work. The hearts were subjected to 37°, 39°, 41°, and 44°C (Fig. 6). The results obtained here are essentially similar to those shown in Fig. 5, where the systemic flow was recorded to determine the stroke work.

At elevated temperatures increasing the work load by raising the aortic pressure produced no consistent results. The data for this series of experiments are not presented since they serve only to show that the combination of high temperature and high aortic pressure leads to rapid destruction of the heart.

The effect of temperature on heart rate. Fig. 7 shows relation between the heart rate and temperature on 40 dog hearts. It is shown that there is a variable and significant change in heart rate with change of temperature. This is a well-known fact that temperature affects the heart rate by its direct action on the sinus

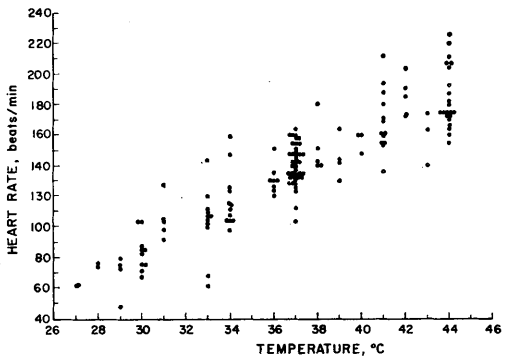

FIG. 7. Effect of temperature on heart rate. The heart rates at various temperatures in 40 heart-lung preparations. Each heart was exposed to 2 or more different temperatures. Each point represents the heart rate at temperatures shown on abscissa.

node. Cooling slows and warming speeds the heart rate.

In monitored experiments, pCO_2 changed less than 5 mm Hg and pH less than 0.04 unit. Small changes such as these have been shown to have no significant inotropic effects. The absolute value for arterial pO_2 was 200 to 250 mm Hg in these experiments.

Discussion. In general, lowering the temperature from 37° to 28.5°C improved the performance of the heart. This held true

whether the systemic or the pulmonary flow was used for the computation of the stroke work.

The degree of improvement appears to be greater when the work load is altered by changing the arterial pressure. Since cold improves the performance of the heart, the question arises why the improvement is more pronounced when a high work load is imposed by increasing the arterial pressure rather than the flow. Cold is known to depress oxyhemoglobin dissociation and therefore might reduce the oxygen available. On the other hand, increasing the arterial pressure, by increasing the coronary flow, would tend to compensate for the possible oxygen shortage due to depressed oxygen dissociation. Therefore, at a lower temperature, increasing the work load by raising the arterial pressure would be more favorable than increasing the flow load. Such a difference might be expected to be more evident at higher work loads, as our findings show.

The degree of improvement also appears to be greater when computed on the basis of the pulmonary flow rather than upon the aortic flow. This is likely to be due to an increased coronary flow since work done in producing coronary flow is measured in the pulmonary computation, but escapes the systemic computations. The change of the relationship between stroke work and left atrial pressure observed with change of temperature is not mainly, if at all, due to the change in heart rate for the following reason.

The increased stroke work for a given atrial pressure at lower temperature is evidence of a positive inotropic effect caused either directly by cooling the myocardium or conceivably by some inotropic result of the changed rhythm. Naturally in heart-lung preparations the longer diastole increases filling and stroke work, but the fact that this should occur without corresponding increase in atrial pressure indicates the positive inotropic activity.

Temperatures ranging from 39° to 42°C in a heart-lung preparation produced inconsistent results. In most cases the work per beat was unchanged or reduced, and only in a few cases was a slight improvement in the performance noted. However, in the temperature range from 43° to 44°C, a consistent and marked improvement in the performance occurred. It is noteworthy that the left ventricular performance increases at both the extremes of temperature which the heart can tolerate. Although such a high temperature is detrimental to the organism, as far as the heart alone is concerned this improvement in the heart performance has a possible survival value.

Summary. The relationship between left ventricular stroke work and left atrial pressure was studied in the Starling heart-lung preparation at various temperatures.

Cooling from 37° to 28.5°C consistently improved the performance. Warming from 37° to 42°C produced variable effects, but all hearts warmed to 44°C performed better than at 37°C.

We conclude that over a temperature range which is detrimental to the total physiology of most mammals the myocardium is not a limiting factor.

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