lipides are involved in cellular growth.

Summary. 1) The influence of age upon radioactive turnover and chromatographic separation of the individual phospholipides was studied in female mice. 2) There was an increase in concentration of μg phospholipide P/mg liver N for the 8 to 60 day old mice after which the concentration remained unchanged with age. There was little change in % of total lipide phosphorus for the various phospholipide fractions with respect to age. However, the relative specific activities of each phospholipide fraction were greater in the younger mice.

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Ionic Alterations Associated with Resuscitation of the Isolated Rabbit Heart.* (26284)

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Resuscitation of the heart after chemically-induced arrest produced by potassium chloride, potassium citrate or acetylcholine has been accomplished experimentally(1,4,8), and also clinically in cardiac surgery. The isolated perfused rabbit heart may be subjected to as many as 10 successive periods of potassium ion-induced arrest with complete resuscitation in all cases(1). Furthermore, a close correlation has been found between resuscitability of the heart and temperature at which arrest was induced as well as duration of arrest. The importance of the electrolyte composition of the perfusion media employed in resuscitation procedures was stressed by all investigators. However, specific requirements for the optimum compositions are unknown. Hence the effects of cardiac arrest *per se* on electrolyte content of myocardium was of interest since it might shed some light on the significance of electrolyte distribution in reinitiation of the heart beat following arrest. Therefore, the alterations in heart muscle electrolytes incident to prolonged periods of cardiac arrest were determined.

Methods. Isolated rabbit hearts were perfused by the Langendorff technic in air at an ambient room temperature of 22-24°C. Three groups of hearts were studied: 1. *Control Group* consisted of 18 isolated hearts perfused with aerated Ringer-Locke solution at 36°C for a period of 25 minutes. After this period of stabilization, 30 ml of 5% dextrose in demineralized water were perfused through the hearts to flush excess electrolytes from the vascular system. Determinations on these tissues served to establish electrolyte and water content of normal isolated heart

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TABLE I. Electrolyte and Water Content of Rabbit Heart before and after Arrest and Following Complete Resuscitation.

	Mean values in mg % ± S.E.				Water in g %
	Chloride	Sodium	Potassium	Calcium	(mean ± S.E.)
Control	413.6 ± 9.6	110.8 ± 6.7	1050.7 ± 20.6	24.3 ± 1.6	81.2 ±.26
Arrested group	304.9 ± 21.3	126,3 ± 6.8	666.3 ± 20.3	19.0 ± .7	80.9 ±.4
P (arrested *vs* control)	<.001	>.15	<.001	<.01	>.45
Resuscitated group	473.5 ± 25.6	248.6 ±14.6	549.1 ± 13.8	35.6 ± 1.8	83.6 ±.2
P (resuscitated *vs* control)	<.02	<.001	<.001	<.001	<.001
P (resuscitated *vs* arrested)	<.001	<.001	<.01	<.001	<.001

muscle. 2. *Arrested Group* consisted of 14 isolated hearts perfused similarly to the control group for a period of 25 minutes. The perfusion solution was discontinued abruptly after this period and the hearts were allowed to come to complete ventricular and auricular arrest; this process required from 15 to 24 minutes. The isolated organs remained mechanically inactive for 2 hours in air at room temperature with no provisions to prevent surface drying. At that time 30 ml of 5% dextrose-demineralized water solution were perfused through the hearts; they were analyzed prior to the appearance of any mechanical contractions. These tissue samples were used for determining the effect of cardiac arrest *per se* on concentration of electrolytes of the myocardium. 3. *Resuscitated Group* consisted of 14 hearts perfused and arrested in a manner identical to the Arrested Group. After 2 hours ventricular and auricular contractions were reinitiated by perfusing with normal Ringer-Locke solution. Resuscitations were generally complete within 2-5 minutes even though several hearts displayed spontaneous irregularities in the pattern of ventricular contractions and in co-ordination of the atrial and ventricular beats. After 15 minutes of activity, 30 ml of 5% dextrose wash solution were introduced into the system and the tissues were analyzed.

For preparation of tissue samples, each of the 4 chambers of the heart was incised and rinsed thoroughly 3 times with cold demineralized water. Extraneous fat was trimmed from the myocardium and water was removed from the surfaces by blotting with gauze. Two samples of heart tissue of 4 to 8 g, each containing portions of atrium and ventricle, were used for determination of chloride and of water, sodium, potassium and calcium, respectively. Water content was determined by drying to constant weight at 105°C. The dried sample was transferred to an electric furnace and ashed at 525°C for 16 hours. The ash was dissolved in 5 ml of boiling 0.5 N hydrochloric acid and diluted to 50 ml with demineralized water. Calcium was determined by a flame photometric adaption of the Kramer-Tisdall method(2). Potassium and sodium were quantified by flame photometry using the method of Mosher *et al.*(9) which was modified by employment of standards appropriate for tissue electrolytes. Chloride content was measured on fresh tissue by the Volhard technic as used by Van Slyke and Sendroy(10).

All electrolyte concentrations were calculated on a dry weight basis.

Results. The results of quantitative determinations for sodium, potassium, calcium, chloride and water are summarized in Table I. *Water content* of the Resuscitated Group was significantly increased over both those of the Control and Arrested Groups. Water content of the Arrested Group did not differ significantly from the Control Group. *Chloride content* of the Arrested Group was significantly lower than that of Control Group. However, after resuscitation the chloride content of the hearts returned to control levels. *Sodium content* of the Arrested Group did not differ significantly from that of Control Group. On the other hand, following resuscitation, the sodium content of the hearts was twice that of either Control or Arrested

Group. *Potassium content* in the arrested hearts was significantly decreased from Control Group while potassium in the Resuscitated Group of hearts was only half of control level. A significant difference was also noted between potassium content of arrested and resuscitated hearts. Cardiac arrest resulted in a significant loss of *calcium* from heart muscle; however, following resuscitation calcium content rose markedly and exceeded both arrested and control values.

Discussion. The significant loss of potassium from the hearts following arrest and the further loss occurring after resuscitation may be responsible for the arrhythmias noted in some hearts following revival. The loss of potassium from arrested and resuscitated rabbit hearts paralleled the potassium loss observed by Harrison *et al.*(5) in congestive heart failure in man. Post-mortem examinations of ventricular muscle revealed that congestive heart failure was associated with significantly lower potassium levels (30% lower) than were noted in tissue samples from individuals with fatal non-cardiac diseases. Cummings and Clark(3) pointed out that the potassium content of infarcted cardiac muscle of dogs may be diminished to as low as 48% of that of non-infarcted tissue.

The efflux of potassium from heart muscle during cardiac arrest was accompanied by a slight sodium retention. This change could be expected since perfusion was terminated during arrest, and hence, there was no source from which sodium could be drawn to compensate for potassium outflow. After resuscitation, however, a significant influx of sodium occurred which was more than adequate to compensate the potassium loss. Cummings and Clark(3) demonstrated that sodium content of infarcted myocardial tissue averaged 71% higher than in non-infarcted tissue. It would appear that a sodium gain in excess of potassium loss is another indication of the general hypoxia persisting in the myocardium during the period of reinitiated activity after 2 hours of arrest. Leaf(7) reported a similar shift of ionic gradients between potassium and sodium in non-metabolizing heart tissue. Slices of rat heart incubated at 0°C for 50 minutes in an isotonic medium displayed a marked gain of sodium and concomitant loss of potassium. Since maintenance of ionic gradients by tissues is considered to be an active process requiring the expenditure of energy, energy required for the transport process may no longer be sufficient when metabolism is depressed. Sodium that diffuses into the cells according to its concentration gradient can no longer be extruded and potassium can leak out of the cells in absence of active transport.

The low oncotic pressure of the perfusion medium could lead to enhanced water retention in the isolated heart; however, addition of dextran to the perfusion media failed to prevent water accumulation. The net increase in intracellular sodium may be responsible for the increased water content of resuscitated hearts. As sodium enters the cell a net gain in chloride can be expected in addition to water accumulation(7); this did in fact obtain in the resuscitated hearts. However, the role of chloride and other anionic groups, such as phosphate, bicarbonate and sulfate which were not measured in these experiments, still remains to be determined.

Tissue calcium was markedly increased in the isolated heart subsequent to resuscitation. Cummings and Clark(3) noted a 10% increase in heart muscle calcium following infarcts compared to the normal content. Thus, their results on anoxic myocardium of dogs are in general agreement with the results obtained in the isolated rabbit heart after resuscitation.

This accumulation of calcium, in combination with the excess loss of potassium after resuscitation significantly increased the tissue calcium potassium (Ca/K) ratio. This imbalance could be responsible for the varied pattern of resuscitation observed with perfusion media which would aid in sustaining the altered tissue Ca/K ratio in favor of calcium. Kolff and his associates(6) noted that resuscitation was accomplished without arrhythmias when potassium citrate was substituted for potassium chloride in elective cardiac arrest. Since citrate binds calcium, it is postulated that citrate abolishes irregularities incident to resuscitation by diminish-

ing the increased Ca/K ratio of the reperfused myocardium.

Summary. Concentrations of calcium, potassium, sodium, chloride and water have been determined following complete cardiac arrest and after cardiac resuscitation in isolated rabbit hearts. Following 2 hours of arrest both calcium and potassium were decreased significantly whereas water and sodium levels were not altered. After resuscitation following 2 hours of arrest additional potassium was lost; calcium, sodium and water content were increased significantly above control values.

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Effect of Hypothermia on Reflex Activity in the Anesthetized Dog.* (26285)

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The extent of the pressor response to exogenously increased adrenalin seems to be critically dependent on the temperature of the recipient animal. Mukherjee *et al.*(1) reported that administration of adrenalin produced a much less rise of systemic blood pressure at 29°C as compared to pressor response evoked at prehypothermic temperatures. Pressor response was further diminished at 27°C. Koella *et al.*(2) also found that magnitude of the pressor response was dependent on temperature of the animal, but at 29.9°C they showed pressor response remained unchanged from that at 37°C. At 25°C it was as little as 1/5 of that produced by the same amount of adrenalin at 37°C.

To learn more about the influence of temperature on magnitude of pressor response to exogenously increased levels of epinephrine and nor-epinephrine the following experiments were performed at normal and at reduced body temperature (28°C). Circulatory and respiratory responses to hypoxic hypoxia and to bilateral carotid occlusion were also studied in the same animals at normothermic and hypothermic levels to assay the reflex activity of the hypothermic animal.

Methods. Eight mongrel dogs averaging 19.6 kg were used. Dial in Urethane (Ciba), 55 mg/kg i.p., was administered before surgical procedures and was not supplemented. Observations were made at blood temperatures of 37-38°C and repeated at 27-28°C. All observations were recorded during a steady state of body temperature.

Recordings. Respiratory variables were measured from gas flow patterns, as previously described(3). Recordings were made on a Miller oscillograph. Rectal and right heart blood temperatures were measured with copper-constantin thermocouples. Systemic arterial pressure was measured from a Statham pressure transducer connected to a catheter located in a femoral artery.

Epinephrine, 2 μg/kg, was injected into the superior vena cava from a catheter in an external jugular vein. Recordings were started prior to injection and continued until

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