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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TABLE I. Percent Changes from Control of Circulatory and Respiratory Responses to Injections of Epinephrine and Nor-epinephrine, Bilateral Carotid Occlusion and Hypoxic Hypoxia in the Normothermic and Hypothermic Dog.

	Epinephrine		Nor-epinephrine		Carotid occlusion		Hypoxia	
	37°C	28°C	37°C	28°C	37°C	28°C	37°C	28°C
Heart rate	+ 3.3	−19.2	−25.6	− 23.6	+ 3.2	− 1.5	+ 11.4	+ 2.8
Syst. press.	+39.3	+49.5	+64.0	+101.9	+16.9	+ 8.9	+ 13.2	+ 6.3
Diast. "	+28.2	+25.7	+44.2	+ 87.5	+20.2	+11.9	+ 13.1	+16.9
Resp. rate	+ 2.2	−16.7	− 9.7	− 17.1	−10.9	−10.9	+120.0	+69.2
Tidal vol.	+ 7.0	+ 9.4	+ 9.8	+ 7.7	− 1.6	− 1.5	− 2.8	+12.4
Pulm. vent.	+ 9.3	+ .6	− 3.9	+ 6.1	−11.5	−11.2	+134.3	+95.9
Max. insp. flow	+22.9	+25.0	+ 2.6	+ 11.2	− 7.6	+ 2.0	+ 44.4	+27.2
" expir. "	+18.3	+17.8	+ .8	+ 3.8	+ 3.9	− 3.9	—	—
End tidal CO_2	+ 7.0	+ 1.9	+ 1.8	+ 3.8	0	+ 1.9	− 30.8	−16.1

blood pressure returned to control level. Nor-epinephrine response was measured in the same manner. The common carotid arteries were clamped caudad to the carotid sinus for one minute during which time the pressor response had reached a steady state. Hypoxic hypoxia was induced by inhalation of 9% O_2 in N_2 from a Douglas bag connected to the inspiratory side of a low resistance respiratory valve. Recordings were during the 5th minute of inhalation.

Following the observations at normal body temperature the animal was partially immersed in an ice water bath. At a blood temperature of 27-28°C the procedures used as 37° were repeated.

Results and discussion. Control values just prior to drug injection, carotid occlusion or hypoxic hypoxia, were used as unity and the various respiratory and circulatory responses to these conditions were expressed as percent changes from unity for both normothermic and hypothermic conditions (Table I).

Responses to exogenously increased epinephrine and nor-epinephrine. Heart rate in the normothermic animals following injection of epinephrine was 125 as compared with a control level of 121 beats per minute. In the hypothermic animal heart rate fell from 73 to 59 beats per minute as a result of injection of epinephrine. However, in both hypothermic and normothermic animals, systolic and diastolic pressures were increased as a result of the epinephrine infusion. Systolic pressure was elevated approximately 10% more in hypothermic animals than in the normothermic condition. These results would indicate that hypothermia potentiates the response of systolic pressure to increased (exogenously) epinephrine at 28°C. This is especially noticeable when it is considered that the rise in systolic pressure in the hypothermic animal is greater than that in the normothermic animal even though heart rate is decreased in the hypothermic animal during blood pressure rise. Respiratory changes as a result of epinephrine injection were approximately the same under the 2 body temperatures studied. Respiratory rate was decreased from an average of 13.2 breaths per min to 11.0 in the hypothermic animals during the epinephrine-caused blood pressure rise. This is probably related to the interplay between blood pressure rise and respiratory rate changes usually seen as a result of the elevated pressure. End tidal CO_2 was increased from 5.7 to 6.1% in the normothermic animals and from 5.2 to 5.3% in the hypothermic animals following injection of epinephrine.

Quantitatively, 2 major differences were seen between responses to epinephrine and nor-epinephrine. Whereas little change occurred in heart rate in the normothermic animals following epinephrine injection the same dosage of nor-epinephrine decreased the average heart rate from 125 to 93 beats per minute. Approximately the same percentage decrease in heart rate was observed at reduced body temperature. Also, in the normothermic animals nor-epinephrine increased systolic pressure 64% but in the hypothermic state an increase 102% was seen. These increases were of a higher order of magnitude than were observed with epinephrine. Again

(as with epinephrine) the greater increase of systolic pressure was observed in hypothermia in presence of a slower heart rate. These results indicate that the hypothermic animal is more sensitive to exogenously increased nor-epinephrine than is the normothermic animal.

The disagreement between the results of epinephrine administration reported here and those of Koella *et al.*(2) and Mukherjee *et al.*(1) may be related to depth of anesthesia and/or to dosage of the hormones administered. Doses of adrenaline administered by Mukherjee *et al.* varied from 100-200 μg in cats anesthetized (i.m.) with urethane in dosage of 1.5 to 1.8 g/kg. Koella and colleagues administered adrenalin at a dosage of 20 gamma but their animals (cats) were anesthetized with Dial urethane i.p., 25 mg/kg body weight, and immobilized with intocostrin so that artificial respiration was necessary. Our experiments are more closely related to those of Koella *et al.* with respect to dosage of adrenalin used but differ markedly in depth of anesthesia. However, we agree with these two groups on the findings that cardiac slowing induced by the pressor response is more marked in the hypothermic condition than in the normothermic.

Effect of hypothermia on carotid sinus reflex. Heart rate was essentially unchanged as a result of this maneuver at both normal and reduced body temperatures. Systolic pressure was increased from 130 to 152 mm Hg at normal body temperature and from 112 to 122 mm Hg at 27°C, increases of 17% and 9% respectively. Diastolic pressure was affected in essentially the same manner. Reduction in body temperature did not grossly change respiratory responses except for maximum inspiratory flow rate which decreased 7.6% in normothermia and increased 2% at 28°C as a result of carotid occlusion. These data show that the hypothermic animal retains reflex activity when body temperature is reduced 9-10°C. These findings are in agreement with Nashat and Neil(4) who elicited carotid sinus reflexes by raising the static pressure in one isolated carotid bifurcation. They found that respiratory and circulatory reflex responses were invariably present in cats at 26°C although the reflex fall of blood pressure produced by sinus hypertension was of less extent than at normal temperatures.

Effect of hypothermia on respiratory and cardiovascular responses to hypoxic hypoxia. Heart rate was increased 11% during the 5th min of exposure to the low oxygen gas mixture at normal body temperature: at reduced body temperature an increase of 3% was recorded. Systolic pressure increased 13.2% and diastolic pressure 13.1% at 37° as a result of the hypoxic hypoxia. These values were 6.3% and 16.9%, respectively at 28°C.

More pronounced differences between the warm and cold conditions occurred in respiratory responses to hypoxic hypoxia. Respiratory rate was more than doubled (37.6 to 82.7 breaths per min) during normothermia but increased only 69% (12.0 to 20.3) in hypothermia. Tidal volumes were relatively unchanged at the 2 levels of body temperature so that pulmonary minute volume was not as greatly elevated in hypothermia as at normal temperature. Maximum inspiratory air flow rates were different at the different body temperatures and are related to the changes in respiratory rates. The normothermic animal hyperventilates relatively more than the hypothermic animal exposed to hypoxic hypoxia as evidenced by the differences in end tidal CO_2. Hypoxic hypoxia produced a decrease of 31% in end tidal CO_2 at normal body temperatures whereas a fall of 16% was recorded at the lowered body temperature. These results indicate that the hypothermic animal maintains the capacity to respond to hypoxic hypoxia *via* stimulation of the peripheral chemoreceptors.

Kilmore and Chase(5) reported the response of arterial pressure to inhalation of 15% O_2 was essentially the same under normothermic and hypothermic conditions in dogs. Systemic circulatory and respiratory responses of cats at 26°C to anoxia (produced by inhalation of 10% O_2 in N_2) were reported as very feeble by Nashat and Neil (4). The differences in results obtained by

the various groups again may be attributed to depth of anesthesia or perhaps an inherent difference between hypothermic responses of cats and dogs.

Summary. Evidence is presented which indicates that pressor response to injections (2 μg/kg) of epinephrine and nor-ephinephrine is potentiated in the anesthetized dog at blood temperatures of 27-28°C. The augmented response to nor-epinephrine was greater than that for epinephrine. Evaluation of respiratory and circulatory responses to bilateral carotid occlusion and hypoxic hypoxia indicates that the hypothermic dog retains reflex activity but magnitude of the responses is less than that at normal body temperature.

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Plasma Free Fatty Acids and the Rare-Earth Fatty Liver.* (26286)

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Some of the lanthanide elements when injected intravenously into rats and other species can produce a fatty liver cycle that is affected by certain endocrines(1,2). The influence of endocrines on release of free fatty acids (FFA) from adipose tissue and the implied significance of FFA in lipid transport (3-6) suggested to us that mobilized extrahepatic lipids might be the source of at least part of the increased liver glyceride level caused by cerium. The experiments described here have tested this possibility; the data demonstrate that cerium does cause an increase in free fatty acids of the plasma and that substances which bind cerium or aggregate it prevent the FFA response and the fatty liver.

Method. Female Carworth-Farms-Nelson (CFN) albino rats weighing 150-200 g were used in all of the experiments except for one group of 7-male CFN rats (136-160 g) and another group of Charles River hypophysectomized female rats (139-170 g). Cerous chloride† (2 mg Ce/kg) was injected intravenously into the tail vein. All animals were maintained on a Dietrich and Gambrill‡ laboratory chow before the cerium injection; some animals were fasted 24 hr before death and others were fed *ad libitum.* Water was available at all times. At 24, 30, 48, and 72 hr after cerium injection, the animals were anesthetized with ether and blood was drawn in a heparinized syringe from the abdominal aorta. The plasma free fatty acids were extracted and determined in duplicate by the procedure of Dole(3). An Ultra Micro-Buret, model 200, obtained from Scientific Industries, Inc., was used for all titrations. In a few rats, glucose was measured(7) in serum obtained from blood after decapitation.

Cerium in combination with versene, albumin, adenosine triphosphate, plasma, phosphate, hydroxide, adenine, adenosine, cytidine, citric acid, and heparin was injected into rats to see whether these compounds protected the animal from the fatty liver degeneration. The method for extraction and measurement of total liver lipids has been described(1).

Results and discussion. A significant in-

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† Cerous chloride, Fisher, C-252, dissolved in saline.

‡ Dietrich & Gambrill, Inc., Laboratory Animal Food Division, Frederick, Md.