induced by acetylcholine in zero-Ca medium remained unchanged for 2 h, in which time 9 successive contractions were induced. It appears therefore that not only different smooth muscles differ in their Ca binding properties but the same muscle from different species may differ in this respect[8,9]. The present results, showing that there was no decline in response in successive contractions induced by acetylcholine in zero-Ca medium, indicate that Ca which is mobilized by acetylcholine is located either intracellularly or on the inner surface of the cell membrane. This Ca, during its mobilization for contraction, does not appear to leak out into the extracellular medium, since in that event the diffused Ca would be captured by EGTA in the external medium (see methods) and would not be available for the consecutive contractions (Figure 3). Alternatively, the cellular calcium pool is enormously greater than the fraction mobilized during a contraction. No information on the precise location of this Ca or the mechanism of its release and re-accumulation can be given. Preliminary experiments on isolated mitochondria and microsomes from this tissue showed that acetylcholine in the concentration used in the present experiment had no effect on Ca binding or release by these fractions[9,10,11].

Zusammenfassung. Im K-depolarisierten Myometrium ist die mechanische Aktivität durch die extrazelluläre Ca-Konzentration graduierbar. Zugabe von Acetylcholin in die Ca-freie, depolarisierende Lösung ergibt mechanische Spannungsentwicklung des Myometriums.

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Temperature Responses of Exercizing Dogs to Infusion of Electrolytes

In man, equilibrium levels of rectal temperature (T_{re}) during exercise are highly correlated ($r = +0.71$) with plasma sodium and osmotic concentrations, but are essentially unrelated ($r = +0.34$) to variations in plasma volume[1-3]. This ion-osmotic factor appears to act by controlling sweat gland function; that is, the rate of sweating is inversely proportional to the plasma ionic-osmotic concentration. It is not clear if the ions act directly on the sweat glands or if the action is primarily on the hypothalamus. Hasama[4] was one of the first to observe the relationship between plasma ionic concentration and body temperature in resting animals and more recently Myers and Yaksh[5] found that solutions of 3 to 5 times normal concentration of sodium injected into the cerebral ventricles of monkeys increased resting temperature and similar concentrations of calcium decreased body temperature. They postulated that the setpoint for body temperature during rest was determined by the Na^+/Ca^{++} ratio. In the present study the effect of infusions with solutions of various ionic and osmotic composition on exercise temperature responses was studied in dogs, who do not regulate their temperature by sweating.

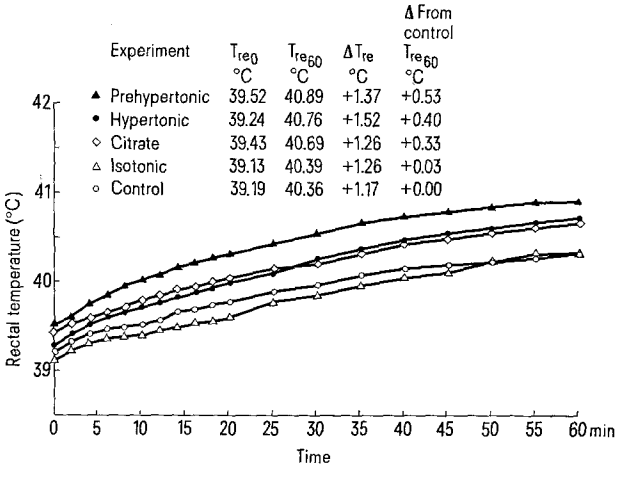

Fig. 1. Average (± S.E.) rectal temperature responses at rest (0-min) and during 60 min of exercise for the 5 experiments.

Material and methods. Six, male, mongrel dogs (11.6 to 27.2 kg) maintained on a standard diet were used. 24 h before each experiment they were deprived of food, but had free access to water. In all experiments the dogs performed 1 h of standard treadmill exercise (1.2 m/sec; 12° slope). Their T_{re} was measured with a thermistor (Electronic) inserted 13 cm. There were 5 different experiments performed on each dog: a) hypertonic: continuous i.v. infusion of NaCl solutions (6.7% to 10.0%, and 110 to 134 ml at a mean rate of 3.6 ml/min (range 2.6 to 4.1) was given for the first 20 min of exercise and 1.1 ml/min (range 0.7 to 1.3) for the final 40 min; the rate was proportional to the size of the estimated extracellular fluid volume designed to raise plasma osmolality to about 320 and 330 mOsm/l; b) isotonic: 0.9% NaCl was infused during the run at the same rate as in (a); c) prehypertonic: the same osmotic load as in (a) was infused during 30-min starting 1 h before exercise; d) control: 1 h of exercise with no infusion; and e) citrate: 3.8% sodium citrate was injected i.v. at a dose of 1.8 ml/kg immediately before exercise.

The infusions were given with a Unipan (Model 304) peristaltic pump. Plasma osmolality (Fiske Osmometer), plasma proteins (Biuret method), plasma sodium (Zeiss flame photometer), and micro-hematocrit (Unipan Model 316) were measured on the 0, 5, 15, 25, 40 and 60 min venous blood samples. The results were analyzed by the *t*-test for paired data with the level of significance ($P \leq 0.05$).

Results and discussion. At the end of one hr of exercise, the highest mean T_{re} was attained following prehyper-

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tonic infusion, the next highest was hypertonic, then citrate, as compared to the isotonic and control T_{re} (Figure 1). The ΔT_{re} in the prehypertonic and citrate experiments were lower than in hypertonic because their 0-min values were elevated 0.2 to 0.3 °C. The prehypertonic T_{re} was higher ($P \leq 0.05$) than isotonic and control T_{re}. Mean T_{re} increases during exercise were higher ($P \leq 0.05$) in the prehypertonic experiment compared with those in the control experiment between 12 and 40 min during the run, but not thereafter due to the increasing variance between dogs.

In the hypertonic and citrate experiments T_{re} increases during exercise were distinctly higher than those in the control and isotonic experiments in 4 out of 6 dogs, however, the mean differences were not statistically significant.

The plasma protein concentrations and hematocrit (Hct) reflect the changes in plasma volume (PV): with a constant red-cell volume, a one-unit change in Hct is equivalent to approximately a 4% change in PV[6]. Prehypertonic Hct was low ($P \leq 0.05$) due to the prior infusion and indicated an expanded PV that decreased as the exercise progressed. Hypertonic Hct at 0-min was at the normal level and dropped with infusion during exercise to the prehypertonic level; this also indicated an increase in PV. The citrate and isotonic Hct were essentially constant during exercise, while the control Hct rose slightly (Figure 2). At 0-min the prehypertonic protein concentration was depressed ($P \leq 0.05$) but was not different from those found in the other four conditions at 25 min (Figure 2). Hypertonic proteins were significantly lower than those in the other 4 experiments at 25 min. There was no significant difference in proteins among the 5 groups between 40 and 60 min. In agreement with the Hct data, these results indicate that following prehypertonic infusion, plasma volume was elevated initially and declined progressively during exercise, while with hypertonic infusion PV increased during the first 25 min of exercise and then began to decrease during the last 35 min when the rate of infusion was reduced. It appears that T_{re} was not influenced by these variations in PV (Figure 1).

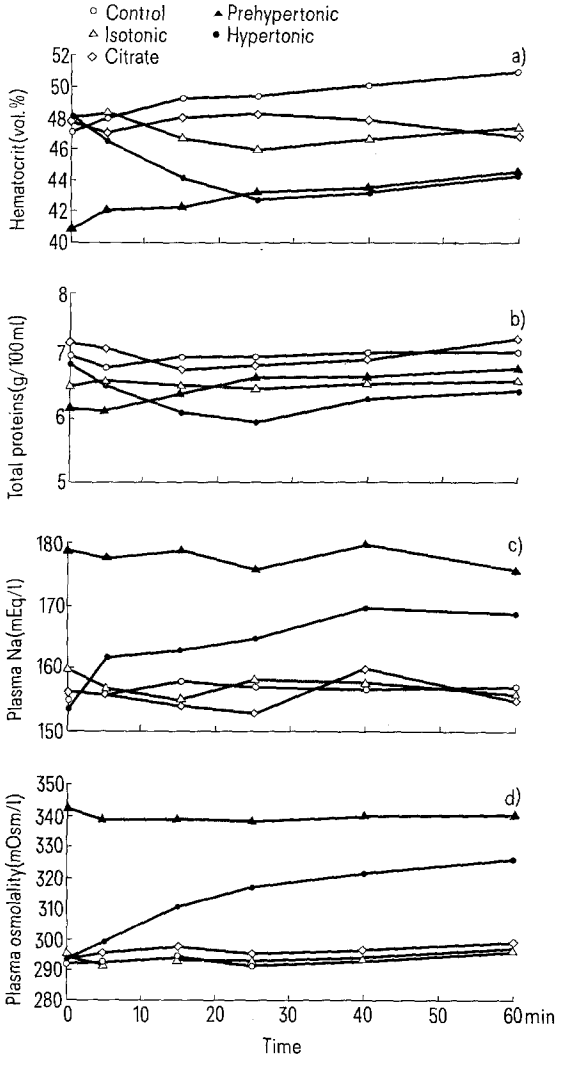

Fig. 2. Average (± S.E.) values for hematocrit and plasma sodium, osmolality and total proteins a rest (0-min) and during 60 min of exercise for the 5 experiments.

During exercise, plasma Na concentrations (Figure 2) followed the changes in plasma osmolality in all 5 experiments. The higher T_{re} in the prehypertonic and hypertonic experiments were associated with higher plasma Na and osmolality. Since a constant exercise load results in a constant heat production for each animal, the proposed explanation is that the ion-osmols act to vary heat dissipation. That is, the higher the plasma osmotic concentration, or cellular dehydration, the greater the inhibition of heat dissipation, and the higher the core temperature. It remains to be determined if hyperosmolality inhibits peripheral blood flow, the panting response, or both. It is clear that the ability to sweat is not a necessary component of the ion-osmotic mechanism.

In the citrate experiment Na and osmotic concentrations during exercise were constant and at the same level as the isotonic and control values. Therefore, the higher T_{re} in these experiments are due to factors other than the Na or osmotic concentrations, perhaps to a decrease in the Ca^{2+} concentration and subsequent increase in the Na^+/Ca^{2+} ratio. These results suggest an association between plasma Na^+ and Ca^{++} within the *normal physiological range* and the control of body temperature during exercise.

Zusammenfassung. Bei Hunden im Training steigt nach Infusion hypotonischer Salzlösungen die mittlere Mastdarmtemperatur stärker an als bei unbehandelten Tieren. Gleichzeitig wird ein starker Anstieg des Plasmanatriums und damit verbunden eine erhöhte Osmolalität des Plasmas gefunden. Wieweit diese beiden Faktoren oder einer von ihnen für die Erhöhung der Rectaltemperatur verantwortlich sind, wird versucht aufzuzeigen.

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