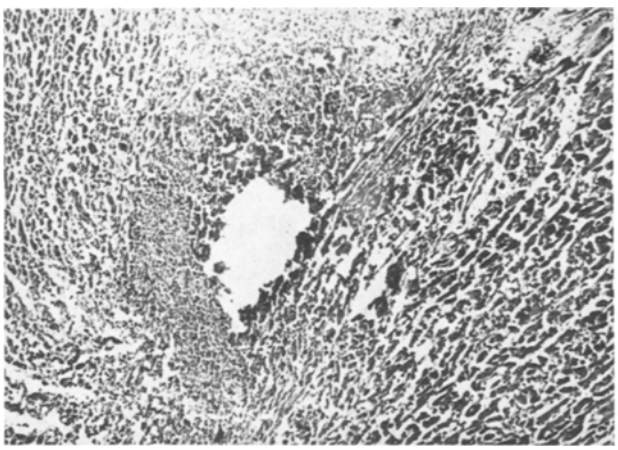

Fig. 3. Histological structure of necrotized cardiac muscle of the control animals.

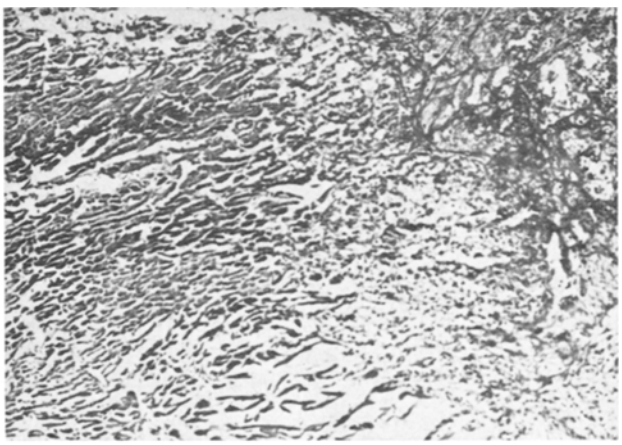

Fig. 4. Histological structure of necrotized cardiac muscle of the ALS treated animals.

cellular infiltration is visible only at the boundary of the necrotic area and it contains very few lymphocytes. Plasma effusion is not appreciable (Figure 4).

The present experiments indicate that the frequency of the arrhythmia and conduction deterioration in the initial stage of myocardial infarction is reduced by the administration of ALS. Considering that the inflammation zone, the trigger zone – is known to be largely responsible for the rhythm disturbances, this effect can be attributed to the depletion of the inflammation, i.e. plasma effusion and lymphocyte infiltration around the necrotic area. It was observed by Ono et al.[6] that the administration of ALS leads to the prolongation of rat heart allograft function and to the reduction of rhythm disturbances and low voltage, reflecting early rejection.

The present experiment, along with the findings of other authors[7–9], suggests that the immunomechanism of the organism reacts to the necrotized tissue in the same way as to any allograft. The inflammation around the cardiac muscle necrotized due to ischemia seems thus to be comparable with the rejection of the allograft heart.

Zusammenfassung. Bei mit Antilymphozyten-Serum behandelten Ratten wird die Entzündungsreaktion der durch Ischämie hervorgerufenen Nekrose des Myokardiums bedeutend vermindert. Ausserdem werden dadurch Rhythmus- und Leitungsstörungen, welche im Anfangsstadium des Herzinfarktes häufig sind, seltener.

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Mechanism of the Fall in Blood Pressure After 'Unclamping' in Rats with Goldblatt-type Hypertension

In dogs, constriction of one renal artery consistently induces hypertension only if the contralateral kidney is removed ('Goldblatt-type' of hypertension). In the rat, hypertension may be induced by constricting one renal artery with or without removing the opposite kidney; the 'Goldblatt-type' of hypertension is more severe than hypertension after clamping without contralateral nephrectomy. There are, furthermore, major functional differences between these 2 types of experimental renal hypertension. In the type induced by clamping without nephrectomy, there are changes in the renin activity of the kidneys[1], while the renin activity of peripheral blood increases considerably[2]. In the 'Goldblatt-type' of hypertension there is no increase in renin activity in the 'clamped' kidney and blood renin activity does not increase[2]. Removal of the clamped kidney later than 1 week after the beginning of hypertension induces a fall of blood pressure in animals which did not undergo contralateral nephrectomy[3,4], but not in the 'Goldblatt-type' of hypertension[4]. In the latter condition, hypertension persists in spite of a fall of the blood renin activity to extremely low levels[5]. In contrast to removal of the whole 'ischemic' kidney, surgical removal of the constricting clamp on the renal artery causes a rapid and permanent fall of blood pressure[6]. The data summarized in Table I confirm these observations and show, furthermore, that ligation of the ureter before removing the clamp on the renal artery completely suppresses the fall in blood pressure after un-

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clamping. The animals used in these experiments were male rats of the Wistar type whose left kidney was removed under ether anaesthesia while the right renal artery was constricted by a clamp of 0.2 mm[7] I.D. when they weighed between 120 and 150 g. Most of them became hypertensive (B.P. >150 mm Hg, measured plethysmographically according to [6]) within 3–6 weeks. In animals hypertensive for 1–2 weeks, the clamp was surgically removed under ether anaesthesia.

Removal of the clamp in the 'Goldblatt-type' of renal hypertension in the rat thus induces a fall in blood pressure which is obviated by ligating the ureter and, therefore, could be related to some change in the excretory function of the kidney after unclamping. Unclamping, under these circumstances, induces an impressive diuretic response which had been observed previously by LEDINGHAM and COHEN[8].

In order to investigate the relationship between this diuretic response and the fall in blood pressure, the following experiment was done: 12 of 22 rats with 'Goldblatt-type' hypertension (group A) were anaesthetized with ether and the clamp on the renal artery was removed; 10 of these 22 rats (group B) were sham-operated, i.e. their renal arteries were dissected free and the clamp was isolated from the surrounding tissue, but not removed. Simultaneously, 6 rats which, after nephrectomy and clamping of the remaining renal artery, had not become hypertensive (B.P. <150 mmttg, group C), were also unclamped. Immediately after the operation all rats were placed in restriction cages and their urine was collected for 6 h. The urinary concentrations of sodium and potassium were measured by flame photometry. The blood pressure of the animals was measured before and 24 h after operation. It proved difficult to measure blood pressure, by tail plethysmography, when the animals were taken out of the restriction cages 6 h after the operation. The results of these experiments are summarized in Table II.

Comparing groups A and B shows that unclamping causes an additional excretion of 38 ml/kg body wt. of water, of 4.6 mEq/kg of sodium and of 0.9 mEq/kg of potassium; comparison of groups B and C shows that unclamping causes a smaller loss of water and of sodium in animals which had not become hypertensive. The excretion of sodium, potassium, and water in the animals of group B did not differ significantly from values observed by ourselves and by others[9] in normal rats. In group A, the additional sodium and water excreted after unclamping amounted to approximately 10% of the total body sodium[10] and 12% of the extracellular volume of normal rats[9]. In groups A and C, the fall in blood pressure within 24 h after unclamping was highly significantly correlated to sodium excretion in the 6 h following the operation.

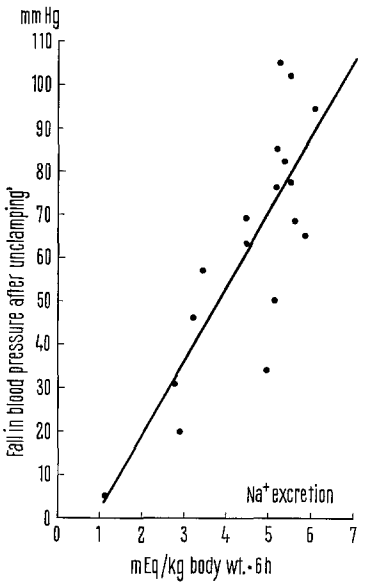
Table I. Blood pressure (BP) before and after unclamping the renal artery in rats with Goldblatt hypertension

	Unclamping			Unclamping + ligation of ureter
No. of animals	9	12	7	9
BP before operation	170 ± 7	170 ± 6	175 ± 9	171 ± 5
BP after operation:				
6 h	139 ± 6			
24 h		120 ± 6		170 ± 5
5 days			94 ± 5	
30 days			96 ± 3	

Blood pressure measured plethysmographically[6] before and 5 or 30 days after unclamping, and by cannulating a carotid artery under pentobarbital anaesthesia 6 and 24 h after unclamping. Values are means $\pm$ S.E. The blood pressure of normal rats of this strain, measured plethysmographically, was 104 ± 1 mm Hg ($n = 100$); when measured in a carotid artery it was 124 ± 2 mm Hg ($n = 77$).

Table II. Fall in blood pressure and diuretic response after unlamping in 'Goldblatt-type' hypertensive rats (group A) or in animals which did not become hypertensive after the same operation (group C), as well as in sham-unclamped 'Goldblatt-type' hypertensive rats (group B)

	Group A	Group B	Group C
No. of experiments	12	10	6
Blood pressure mm Hg:			
Before operation	176 ± 6	178 ± 5	110 ± 6
24 h after operation	97 ± 3	168 ± 6	79 ± 5
Fall	79 ± 5	–	31 ± 7
Renal excretion of:			
Water (ml/kg. 6 h)	54 ± 4	16 ± 4	37 ± 7
Sodium (mEq/kg. 6 h)	5.3 ± 0.2	0.6 ± 0.1	3.2 ± 0.7
Potassium (mEq/kg. 6 h)	2.4 ± 0.2	1.6 ± 0.2	1.5 ± 0.1
Urinary concentration of:			
Sodium (mEq/l)	111 ± 16	48 ± 8	98 ± 9
Potassium (mEq/l)	47 ± 3	133 ± 26	57 ± 19



Regression of the fall in blood pressure, observed within 24 h after 'unclamping' the constricted renal artery, in rats of the 'Goldblatt-type', on sodium excretion within 6 h after unclamping. Regression line calculated according to the method of least squares. Each point represents one experimental animal of groups A and C.

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The coefficient of correlation was $r = +0.82$ ($p < 0.001$). Sodium excretion within 6 h after unclamping was also correlated with the mean blood pressure before unclamping; the coefficient of correlation was, however, lower ($r = +0.73$). The Figure shows the fall in blood pressure as a regression on sodium excretion; the slope of the regression line was $b = 16.6$ mm Hg/mEq/kg body wt. of sodium excreted in 6 h and differed highly significantly ($p < 0.001$) from 0.

These data suggest, but do not prove, that the fall in blood pressure after unclamping is related to a loss of sodium and extracellular fluid. TOBIAN et al.[11] found that the total exchangeable sodium in the 'Goldblatt-type' hypertension in rats is increased by 3.9 mEq/kg when compared to that of normal rats, or of animals with hypertension induced by constricting one renal artery without removing the opposite kidney. This amount is nearly the same as the additional sodium excreted within 6 h after unclamping. Thus it is possible that the 'Goldblatt-type' of hypertension is causally related to retention of sodium and water. The possible role of sodium retention in the pathogenesis of different types of hypertension has recently been stressed by GUYTON and COLEMAN[12]. However, it should be pointed out that, in the experiments of LEDINGHAM and COHEN[7], a fall in blood pressure occurred after unclamping 'Gold-blatt-type' hypertensive rats, even when they were thought to have a positive water balance, and in 3 animals in spite of the fact that the urine excreted was reinjected. It appears unlikely that suppression of the fall in blood pressure after unclamping by ligating the ureter could be due to the additional secretion of renin induced by this operation[13].

Résumé. Chez le rat hypertendu par constriction partielle d'une artère rénale et néphrectomie controlatérale, la suppression chirurgicale de la constriction entraîne une normalisation de la pression artérielle et une excrétion urinaire importante d'eau et de sodium; la ligature préalable de l'uretère empêche la normalisation de la pression.

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Mast Cells and Hibernation: Observations in the Indiana Bat, *Myotis sodalis*

An increase in the number of mast cells has been reported as occurring in tissues of hibernating hedgehogs (*Erinaceus europaeus*)[1]. The clotting time of the blood of hedgehogs, hamsters and bats is apparently also increased during hibernation[2–4]. These observations have been used to support the contention that heparin, which is one of the main pharmacologically active substances produced by the mast cell[5,6], is of physiological significance for the circulatory system by decreasing the coagulability of the blood and thus preventing spontaneous thrombosis[2,4].

The evidence for an increase in the blood clotting time in hibernating animals seems conclusive, whereas the existence of a corresponding general increase in the number of mast cells – which is mainly based on studies in a few specimens of a single species[1] – needs confirmation. We have therefore re-investigated the matter of possible changes in the mast cell population during hibernation by studying the mast cells in the interfemoral membrane of the Indiana bat, *Myotis sodalis*, in the autumn and throughout the winter. Prior to and at the end of the hibernating period, tissue levels of histamine in this bat were also determined. Considering that mammalian mast cells in addition to heparin also store the bulk of tissue histamine, and that variations in mast cell number in a particular tissue are usually paralleled by variations in its histamine content[7,8], the histamine determinations may serve as an additional indicator of changes in the mast cell population.

Once every month, from October to April, 6 specimens of *Myotis sodalis* (equal numbers of either sex) were collected from a common hibernating place in Carter Cave (Kentucky). The first collection (October) was made while the bats were gathering in increasing numbers in the cave, and they were still leaving the cave for flights at night-time. Transient arousals from the dormant state were noticed occasionally during the winter months (November to March). Cave temperatures in the winter averages about 5 °C. The last collection (April) was made when bats started to leave their hibernating place for the summer.

Upon capture, the bats were taken to the laboratory and killed with ethyl ether. The interfemoral membrane was then removed and its 2 layers of skin partially split from each other by insertion of a hypodermic needle, followed by injection of methyl alcohol into the tissue between these layers. Subsequently, the whole tissue sample was placed in jars with methyl alcohol for additional fixation. After 2–3 days some of the samples were completely split into 2 layers, stained with alcoholic thionin (0.1%), and studied under the microscope. Other samples were stored in the fixative until April when the mast cell density of samples obtained on all collection trips was compared. Notwithstanding that tissues from the intestinal tract have been included in earlier studies on the mast cells during hibernation[1,4], we avoided such tissues because hibernation is accompanied by fasting which per se may fundamentally affect tissues directly involved in the digestive process.

Judging from the single-layered skin preparations, the interfemoral membranes were always rich in mast cells. We performed both general observations of mast cells

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