Concerning Possible Contractile Mechanisms in the Pancreas – Myoepithelial Cells

It is well established that myoepithelial cells are associated with the acini in many types of exocrine glands, but the literature contains no mention of them with respect to the exocrine pancreas. Recent electron microscopic studies of the cat pancreas[1,2] do not mention myoepithelial cells either positively or negatively.

Myoepithelial cell activity causes pressure changes against a head of pressure in the ducts of salivary glands[3,4]. In the present investigation a similar system has been used to ascertain whether or not such activity exists in the pancreas of the cat, and pancreatic tissue has also been studied morphologically for the presence of myoepithelial cells.

For the physiological studies 3 cats were used. After induction with ether, anaesthesia was maintained using chloralose (80 mg/kg). The abdomen was opened and the main pancreatic duct was carefully dissected and cannulated with a metal cannula of widest possible bore which was connected to a pressure transducer by polyethylene tubing. A closed pressure recording system was arranged as described previously[3]. The pressure in the duct could be set at any desired level through a connection to a pressure bottle. Pressure changes in the duct were registered on a polygraph. The system could also be opened to study secretion. In order to avoid a continuous secretion from the gland, the cats were fasted for 12 h and the pylorus was ligated.

The parasympathetic and sympathetic nerves of salivary glands have been found to contain motor fibres for the myoepithelial cells[3,4] and their effects can be imitated pharmacologically[4]. To study this on the pancreas of the cat vagal stimulation, methacholine and adrenaline were tried; secretin[5] was also used in 2 experiments. The drugs were injected i.v. through a femoral vein and vagal stimulation was achieved by stimulation of the posterior vagal trunk at the lower end of the oesophagus after intrathoracic exposure of the nerve.

Vagal stimulation caused a slow, continuous increase in pressure in the pancreatic duct, but this only became evident at a fairly high frequency of stimulation, about 10/sec, and in the open system this initiated a slow pancreatic secretion. Secretin caused a similar effect on the pressure when given in doses large enough to induce secretion; secretin in lower doses had no perceptible effect on the duct pressure. Methacholine, e.g. 1 µg/kg, was similarly found to give a pressure rise which was slow in onset but of short duration, while adrenaline in doses up to 10 µg/kg did not affect the duct pressure. In the open system, methacholine, in doses affecting the duct pressure, sometimes but not always caused a small secretory response which was not seen after adrenaline. Thus, the effect of the stimuli on the pressure in the pancreatic duct seems to be closely related to secretion.

For the morphological studies separate small pieces from the head, tail and uncinate process from 4 cats were rapidly frozen by liquid nitrogen and cryostat sections were used for studying alkaline phosphatase activity by the method of HUGON and BORGERS[6]. Adjacent pieces of tissue were fixed with a paraform-glutaraldehyde mixture, post fixed with osmium tetroxide, embedded in araldite and ultrathin sections were examined, after lead staining, by electron microscopy.

Salivary myoepithelial cells in the cat show a strong alkaline phosphatase activity[7]. In the pancreas no alkaline phosphatase was found in association with acinar structures (as shown previously by PETKOV[8], using different techniques). Furthermore no myoepithelial cells were found by electron microscopy.

In salivary glands both parasympathetic and sympathetic stimulation cause 2 types of pressure response in the ducts: one type related to myoepithelial activity and another to secretory activity[3,4]. In the pancreas of the cat, the present experiments show only one type of pressure response – that related to secretory activity – thus indicating that myoepithelial cells might not exist in the pancreas; this possibility was confirmed by electron microscopy.

The exact function of myoepithelial cells is not understood. They are found in most salivary glands but do not seem to be indispensible, for they have not been found in the parotid gland of the rat[9]. The present study shows that myoepithelial cells are also absent in the pancreas of the cat.

Zusammenfassung. Aktivität myoepithelialer Zellen in Speicheldrüsen verursacht Druckerhöhungen in den Ausführgängen der Speicheldrüsen[3]. Die Pancreasdrüse der Katze zeigt nichts dergleichen, da keine myoepitheliale Zellen vorhanden sind. Druckerhöhungen erhält man nur, wenn durch vagale Reizung oder bei Verabreichung von Methakolin und Sekretin die Sekretion angeregt wird.

J. R. GARRETT[10], S. LENNINGER and P. OHLIN

Institute of Physiology, University of Lund (Sweden), 28 January 1970.

[1] L. H. HERMODSSON, Thesis (Almqvist and Wiksells, Uppsala 1965).
[2] P. G. LEGG, J. Anat. *103*, 359 (1968).
[3] N. EMMELIN, J. R. GARRETT and P. OHLIN, J. Physiol. *196*, 381 (1968).
[4] N. EMMELIN, P. OHLIN and A. THULIN, Br. J. Pharmac. *37*, 666 (1969).
[5] GIH Research Unit, Chemistry Department, Karolinska Institutet, Stockholm (Sweden).
[6] J. HUGON and M. BORGERS, J. Histochem. Cytochem. *14*, 429 (1966).
[7] J. D. HARRISON and J. R. GARRETT, Proc. R. microsc. Soc., *5*, 71 (1970).
[8] P. E. PETKOV, Histochemie *11*, 305 (1967).
[9] B. N. SCOTT and D. C. PEASE, Am. J. Anat. *104*, 115 (1959).
[10] J.R.G., Department of Oral Pathology, King's College Hospital, London, wishes to acknowledge a travel grant from the Royal Society.

Effect of Antilymphocyte Serum on Experimental Myocardial Infarction

Arrhythmia and conduction disturbances have frequently been observed[1–3] to follow myocardial infarction. It has been shown in earlier experiments[4] that the stasis dermatitis due to temporary ischemia can be prevented by induced lymphopenia and immunosuppression (ALS, Imuran treatment).

In the present work, the effect of antilymphocyte serum (ALS) on the frequency of arrhythmia and con-

duction disturbances, and the histological alteration of the necrotic area in the early stage of experimental myocardial infarction were studied.

Materials and methods. The experiments were performed on 55 white rats, both males and females of inbred strain, ranging from 200–250 g in weight. 30 animals were injected i.p. with 2 ml of ALS 4 h before the operation. The ALS injection, using 2 and 1 ml was repeated 24 and 48 h after the operation, respectively. The ALS was produced in rabbits by the method of GRAY and MONACO[5]. The serum activity was assessed from the decrease in the count of circulating lymphocytes. The counts of lymphocytes decreased, on the average, by 15–20% as compared with those taken before the injection, while the absolute leucocyte counts slightly increased or remained unchanged. No ALS was administered to the control animals.

After thoracotomy the myocardial infarction was induced by ligation of the left anterior coronary artery, verifying its onset also from the electrocardiogram ECG tracings were recorded by a 3-channel Hellige direct writer ECG apparatus. Generally 12 ECG leads (I–III limb leads, unipolar limb and unipolar chest (V_1–V_6) leads) were used. The susceptibility to arrhythmia and conduction disturbances was established from the electrocardiograms recorded for 4 min while the rats inhaled a mixture of 5% oxygen and 95% nitrogen gas.

Results and discussion. Before the operation neither arrhythmia nor conduction disturbances were observed as a result of the inhalation of oxygen-deficient gas mixture. After the ligation of the coronary artery, arrhythmia and conduction disturbances were observed mainly on the rats which had not been treated with ALS (Figures 1 and 2). The frequencies of the disturbances for both the test and the control group are shown in the Table. For histological analysis the animals were sacrificed 48 h after the operation, immediately on termination of the ECG. On the post mortem section of the heart taken from the control animals, the structure of the cardiac muscle is masked by a cellular infiltration containing plasma, leucocytes, lymphocytes and hystiocytes penetrating finger-like in-between the healthy muscle fibres also (Figure 3). On the sections prepared from the heart of the animals injected with ALS, the infarction area appears sharply isolated from the environment. The

Frequency rate of the conduction disturbances and the arrhythmias in the ALS treated and the control groups.

	Antilymphocyte serum	Control
Arrhythmias	5 (16.7%)	8 (32%)
Conduction disturbances	7 (23.3%)	9 (36%)
Negative	18 (60%)	8 (32%)
Summary	30 (100%)	25 (100%)

[1] A. HARTAI, F. SOLTI, M. ISKUM, J. NAGY, E. KOLIN and S. VÁRKONYI, Országos Mentőszolgálat jubileumi emlékkönyve. Budapest (1968).
[2] H. W. DAY, Am. J. Cardiol. *21*, 251 (1968).
[3] T. KILLIG and T. KIMBALL, Am. J. Cardiol. *20*, 457 (1967).
[4] I. FÖLDES, Országos Diákköri Konferencia előadásai 34. Szeged (1969).
[5] J. GRAY, A. P. MONACO, M. L. WOOD and P. S. RUSSEL, J. Immun. *96*, 217 (1966).

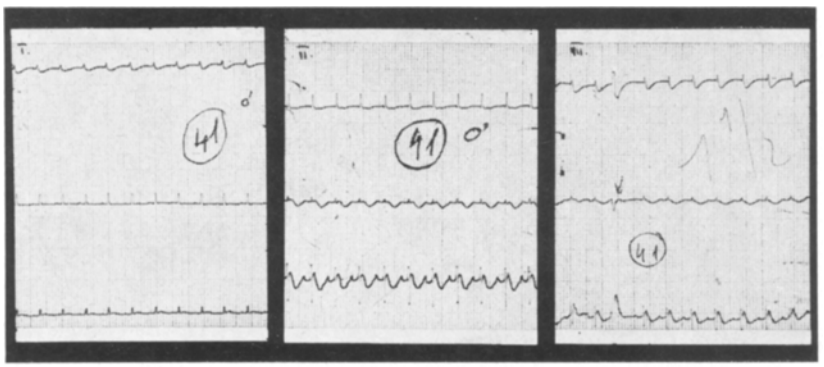

Fig. 1. I. Normal rat electrocardiogram (before coronary ligation). II. Myocardial infarction (electrocardiogram after coronary ligation). III. Atrioventricular block after $2^1/_4$ min of hypoxia (inhalation of oxygen less gas mixture in myocardial infarction).

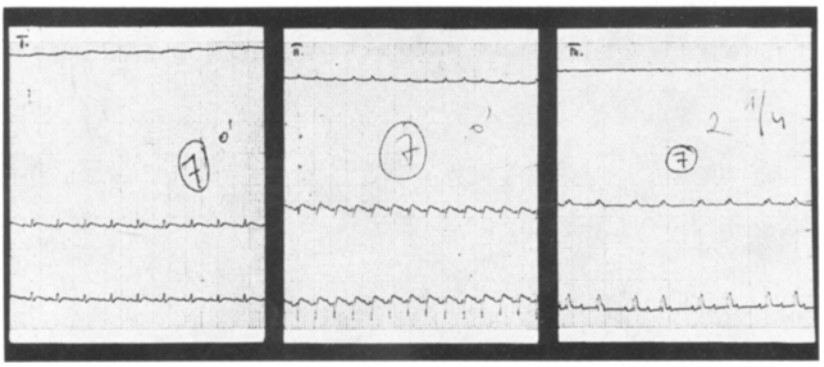

Fig. 2. I. Normal rat electrocardiogram (before coronary ligation). II. Myocardial infarction (electrocardiogram after coronary ligation). III. Ventricular eytrasystole after $1^1/_2$ min of hypoxia.

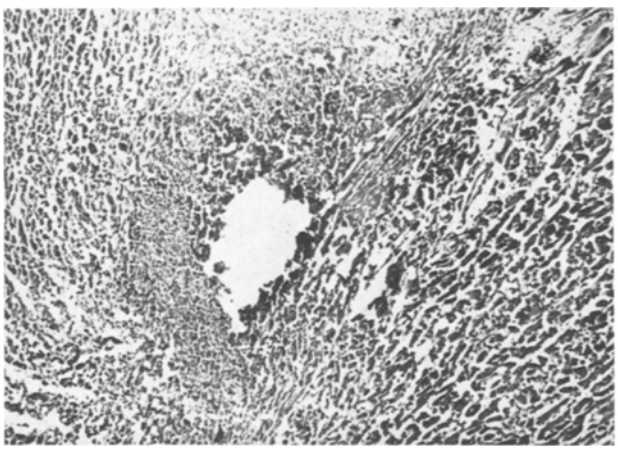

Fig. 3. Histological structure of necrotized cardiac muscle of the control animals.

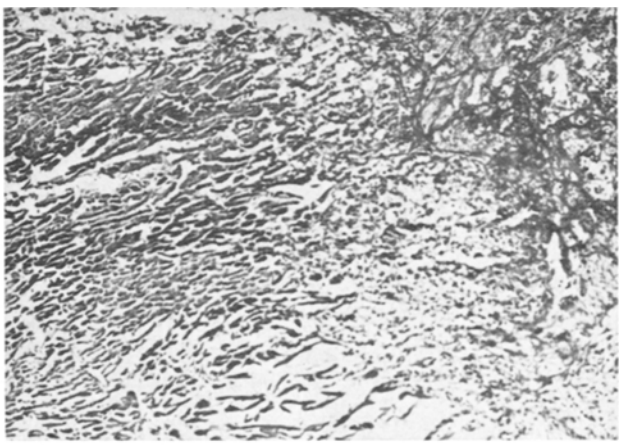

Fig. 4. Histological structure of necrotized cardiac muscle of the ALS treated animals.

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.

I. Földes, S. Várkonyi, F. Solti and A. Kóczé

Institute of Microbiology, First Department of Medicine, and Second Institute of Pathology, University Medical School Budapest (Hungary), 13 January 1970.

[6] K. Ono, E. S. Lindsey, C. W. de Witt and J. H. Walace, Circulation *39*, suppl. 1, 27 (1969).
[7] I. Strausz and Gy. Dobiás, Orvosi Hetilap *107*, 2457 (1966).
[8] H. V. Geld, Lancet *11*, 617 (1964).
[9] H. Kleinsorge and S. Dornbusch, Klin. Wschr. *38*, 970 (1960).

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-

[1] D. Regoli, H. Brunner, G. Peters and F. Gross, Proc. Soc. exp. Biol. Med. *109*, 142 (1962).
[2] G. Schaechtelin, D. Regoli and F. Gross, Am. J. Physiol. *205*, 303 (1963).
[3] F. Gross, H. Brunner and M. Ziegler, Recent Prog. Horm. Res. *21*, 119 (1965).
[4] J. F. Liard, Experientia *25*, 934 (1969).
[5] G. Schaechtelin, D. Regoli and F. Gross, Am. J. Physiol. *206*, 1361 (1964).
[6] F. B. Byrom and L. F. Dodson, Clin. Sci. *8*, 1 (1949).