normal rat portal vein is well characterized[4,5]. Bursts of action potentials appear at a frequency of 2–3 per min, followed by phasic contractions (see figs 1 and 2). In previous studies[3,6,7] it has been shown by mechanical recording that rat portal veins lose their spontaneous contractile activity when subjected to 5 days increased transmural pressure. The present study confirms this (fig. 1). We have also shown that the smooth muscle cells of such hypertensive (H) vessels have a more negative resting potential than cells from normotensive control (C) veins. If the H cells are depolarized by an increase of $[K^+]$ in the bathing media to 15 mM (fig. 2) bursts of action potentials followed by contraction are elicited. This contraction pattern is very similar to that found in C veins at normal (5.9 mM) $[K^+]_o$. Phasic contractions can also be initiated if $Ba^{2+}$ (up to 0.5 mM) is added to the Krebs solution. This ion is known to decrease $K^+$ conductance in the rat portal vein[9]. Figure 3 illustrates that comparable integrated mechanical activity can be recorded from C and H veins if $[K^+]_o$ is increased for the latter. The difference in $K^+$ sensitivity becomes less pronounced in higher $[K^+]_o$, and maximum contractile response is reached at similar concentrations (50 mM $[K^+]_o$). Maximum response was significantly higher in H veins. A tendency to[3] or a clear increase[6,7] in maximum active force in H veins have been reported earlier. This, and also the increased dry weight[3] of the H veins, suggest a considerable synthesis activity during the hypertensive period.

Smooth muscle cells from tail arteries in spontaneously hypertensive rats (SHR) are found to have similar transmembrane potentials[10] (although an increased electrogenic component is suggested) to those of cells from normotensive control animals. The development of hypertension in SHR is, however, slower than in the animal model used in the present study. Rats subjected to normobaric hypoxia (which induces pulmonary hypertension) have already after 10 days[11] an increased membrane polarization in smooth muscle cells of small pulmonary arteries (SPA). The authors of that study proposed that the hyperpolarization in SPA cells may be a result of an increased activity of the electrogenic $Na^+$-$K^+$-pump, possibly caused by an increase in the coupled influx[12] of $Na^+$ and amino acids (the latter necessary for the synthesis activity of the hypertrophying cell). The energy metabolism of the portal vein preparation is well characterized[7,13] and in a previous study[7] an increased basal lactate production was found in H compared to C veins, despite optimum $O_2$ supply. As there are indications[14] of a coupling in smooth muscle between aerobic glycolysis and the $Na^+$-$K^+$-pump, this might well suggest an increased activity of that pump, which then leads to the observed hyperpolarization of the H cells.

1 This work was supported by grants from the Swedish Medical Research Council (B14X-28), and the Medical Faculty, University of Lund. The present address of S.B. Sigurdsson is: Department of Physiology, University of Iceland, Reykjavik (Iceland).
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0014-4754/83/111288-03$1.50 + 0.20/0


## Increased plasma concentration of cyclic GMP in atrial fibrillation

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*Summary.* Plasma concentration of cyclic nucleotides in patients with paroxysmal atrial fibrillation was determined by ultrasensitive radioimmunoassay on the day of attack and also the next day, following recovery to sinus rhythmus. The concentration of cyclic GMP in the plasma of patients with attacks of paroxysmal atrial fibrillation was significantly higher than in those with sinus rhythmus, but no significant difference in plasma concentration of cyclic AMP was observed.

The accurate determination of plasma cyclic nucleotides appears to be very useful for assessing responses to hormones and neurotransmitters in clinical studies. With cyclic AMP, which is the 2nd messenger for $\beta$-adrenergic agents and many hormones, the plasma concentration appears to reflect changes in the tissues[1], because the nucleotide in plasma is in a dynamic steady-state relationship with its intracellular pools[2]. Cyclic GMP, like cyclic AMP, is present in plasma[3], and the plasma concentration of cyclic GMP could serve as a good index for cholinergic activity[4].

*Material and methods.* 100 and 2 normal subjects (48 males, 54 females; mean age, $52.8 \pm 9.1$) and 5 patients with paroxysmal atrial fibrillation, on the day of attack as well as the next day on recovery to sinus rhythmus, were studied. Blood (1–2 ml) was collected into a chilled tube in ice with 2 µl of 0.5 M EDTA and immediately centrifuged at 4 °C. Plasma was separated and frozen at −20 °C until assayed. Cyclic nucleotides were simultaneously measured in duplicate by the radioimmunoassay method of Cailla et al.[5,6], as modified by Honma et al.[7]. The recovery of plasma cyclic AMP was $105 \pm 5.5\%$ with 15 pmoles added, and that of cyclic GMP was $93 \pm 2.0\%$ with 121 pmoles added[7]. All values are expressed as mean ± SEM. Statistical analysis was performed with Student's t-test. Regression lines were fitted by the method of least squares.

*Results and discussion.* The mean plasma concentrations of cyclic AMP and cyclic GMP in 102 normal subjects were $17.0 \pm 0.8$ pmoles/ml, and $4.2 \pm 0.2$ pmoles/ml, respectively.

As shown in the table, the plasma concentration of cyclic GMP was 25.7±3.4 pmoles/ml at the onset of atrial fibrillation, which was significantly higher than the 7.8±1.0 pmoles/ml measured the next day after recovery to sinus rhythmus ($p < 0.02$). Thus, under normal conditions cyclic GMP levels are low and increase during fibrillation. However, no significant difference in plasma concentration of cyclic AMP was observed; the concentration of cyclic AMP in plasma changed from 23.8±1.5 pmoles/ml with the onset of atrial fibrillation to 18.0±2.1 pmoles/ml on recovery to sinus rhythmus.

Mean concentration of plasma cyclic GMP and cyclic AMP in patients with paroxysmal atrial fibrillation on the day of attack as well as the next day on recovery to sinus rhythmus

| | No. | Atrial fibrillation | Sinus rhythmus |
|---|---|---|---|
| Cyclic GMP | 5 | 25.7±3.4* | 7.8±1.0 |
| Cyclic AMP | 5 | 23.8±1.5 | 18.0±2.1 |

* Significantly elevated compared with that on the day of sinus rhythmus ($p < 0.02$).

Experimental studies have emphasized the importance of cholinergic stimulation in initiating and sustaining atrial fibrillation[8,9]. Acetylcholine increases the concentration of cyclic GMP by activating the muscarinic receptor[10-11]. The injection of cholinergic agents caused sharp increases in plasma cyclic GMP in fasted rats[12]. The increase in plasma cyclic GMP induced by cholinergic agents was completely abolished by atropine but not affected by hexamethonium, which shows that the increase was due to stimulation of the muscarinic receptor[13]. In our recent study, the plasma cyclic GMP concentration of dogs with electrically induced atrial fibrillation was significantly elevated after the onset of the arrhythmia, whereas the concentration of cyclic AMP showed no significant changes[14]. Thus, the present results indicate that atrial fibrillations may cause an increased stimulation of the parasympathetic nervous system.


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0014-4754/83/111290-02$1.50+0.20/0


## Effects of temperature on anion distribution in perfused rat, guinea-pig and hamster ventricle

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*Summary.* Ventricular tissue from rats, guinea-pigs and hamsters were found to be more anion permeable when perfused and superfused with Ringer's solution at 22 °C rather than 36 °C. When the perfusate temperature was 36 °C the anion permeability of the in vitro rat and guinea-pig ventricle approximated that found in situ. Further, the anion permeability of the rat and guinea-pig heart was found not to be influenced by the absence of plasma proteins in the perfusate.

The isolated perfused heart preparation is used extensively to investigate the effects of various chemical and physical perturbations on cardiac function and metabolism[2-4]. Presently, the preparation is gaining popularity as a mean of investigating cellular ion fluxes under conditions where the tissues are not subject to dissection and interruption of the normal electrophysiological activity of the whole heart[5]. The reliability of this model for estimating in situ ion fluxes rests on the assumptions that the heart tissue is adequately perfused so as to avoid ischemic conditions and the solutions used to perfuse the heart do not alter the ionic permeability properties of the cellular membranes. Recently, it has been shown by Macchia and colleagues[6,7], that isolated skeletal muscles of toad incubated in oxygenated Ringer's solution have anion permeability properties which are significantly larger than in situ muscles or muscles incubated in toad plasma. Further, it has been shown that the plasma fraction responsible for maintaining anion permeabilities in vitro similar to those found in situ is plasma albumin. Since recent studies by Polimeni and Page[5], using isolated rat hearts perfused with a protein-free Ringer's solution, have reported cellular Cl efflux values significantly larger than reported by other investigators using isolated dissected heart preparations[8], anion permeability changes in the perfused heart due to the absence of plasma albumin or other plasma fractions could possibly explain these rapid Cl fluxes. Additionally, the integrity of the heart vasculature may be affected by perfusion with non-blood solutions. Isolated heart preparations perfused with Ringer's solution may therefore be subject to changes in cellular membrane permeability which could possibly yield ion flux measurements which are far from that which