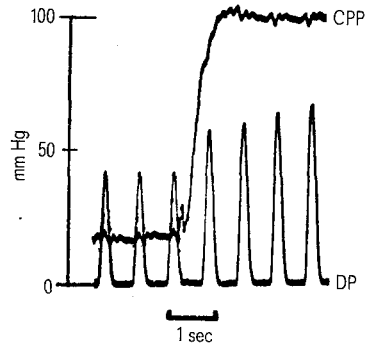
ejection of the balloon through the aortic valve during the fall of perfusion pressure due to clamping. Ejection was identified by a wide pulse of the perfusion pressure induced by the volume change in the small capacitance segment of the remainder aorta provoked by the herniation of the balloon; experiments in which this occurred were discarded. The table shows the data of 7 analysed experiments: DP of the systole following coronary release was $27.4 \pm 7.8\%$ higher than the underperfused beat and this effect was observed 0.61 ± 0.18 sec after coronary release. The figure illustrates a representative example.

Our results strengthen the view that a physical factor must be considered in determining ventricular performance when coronary perfusion pressure changes, regardless of the intervening myocardial nourishment.



Effect of sudden elevation of coronary perfusion pressure (CPP) on developed pressure (DP) of isovolumetric canine left ventricle.

The mechanism by which perfusion pressure can affect cardiac performance is not yet established. Some of the postulated hypotheses imply an improvement of the metabolic cardiac support by modifications of myocardial blood flow[3–5]. It seems reasonable to assume that these mechanisms cannot account for the change in ventricular performance observed in our experiments, since the time which elapsed from the increase of coronary perfusion pressure to the improvement of cardiac performance was certainly not sufficient to permit metabolic accomodation. Our results can be understood only on the basis of a mechanism involved in beat-to-beat regulation. The sole theory in accordance with our data is that proposed by Arnold et al.[6], namely the 'garden hose effect'. According to this proposal, increase in intravascular pressure distends myocardial vessels resulting in stretching of surrounding myocardial fibres. Improvement of contractile function in this way must be related to the Frank-Starling mechanism.

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Effect of potassium on isolated bovine facial and human saphenous veins

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Summary. A moderate elevation of external (K_0^+) (5–10 mM) induces relaxation in bovine facial and human saphenous veins. A further increase of (K_0^+) leads to biphasic reactions (relaxation followed by contraction). Concentrations of (K_0^+) higher than about 15 mM cause contractions only. The potassium-induced relaxation may be explained by the stimulation of an electrogenic sodium pump.

Recently, the multiple physical and chemical factors that affect vascular responsiveness were reviewed by Altura and Altura[1]. Referring to earlier work from our laboratory[2], they wrote that our 'studies with bovine facial veins failed to demonstrate an alteration in resting tension when (K_0^+) was changed from 2.6 to 15 mM'. In some experiments with animal and human veins performed since then, we found, however, that upon elevation of external potassium (K_0^+) a relaxation, a biphasic reaction (relaxation followed by constriction) or merely constriction may result. The statement given above was based on results obtained with large veins (diameter from 5–10 mm). In our more recent experiments, veins of a smaller size (2–3 mm) were used.

Methods. The experiments were performed on helical strips of 50 isolated bovine facial veins and 5 human saphenous veins. The human vessels were obtained from patients undergoing surgery. The vessels were mounted in a double-walled chamber in which the ambient air was kept at 37.5 °C by circulating warm water and rinsed continuously by physiological salt solution having the following composition (in mM): KCl, 2.68; NaCl, 136.88; $MgCl_2$, 0.49; $CaCl_2$, 1.36; $NaHCO_3$, 11.88; NaH_2PO_4, 0.32; Glucose 8. All solutions were aerated with 95% O_2 and 5% CO_2. The potassium content was increased or decreased by replacing NaCl with KCl on an equimolar basis. After applying a resting tension to the strips, an equilibration period of 1–2 h was allowed to elapse before starting the experiments. The tension of the strips was recorded isometrically. The drug used was β-methyldigoxin (Boehringer Mannheim).

Results. The effect of potassium on bovine facial veins is shown in figure 1. It can be seen that an elevation of the potassium concentration in the bathing medium initially produced a relaxation with a maximum at about 7.5 mM. The amplitude of the relaxation decreased when the potassium concentration was augmented and at about 15 mM K^+ the response became biphasic. The exposure of the bovine facial veins to 30 mM K^+ caused a rapid contraction preceded by a small, initial relaxation. In most preparations spontaneous mechanical activity was observed (figures 1–3). On account of our own results[2–4] and of those of other investigators[5] it has been suggested that potassium-induced vasodilation results from stimulation of membrane Na-K-

ATPase which activates an electrogenic sodium pump leading consequently to hyperpolarization and to relaxation of the vascular smooth muscle cells. When the Na-K-activated ATPase was inhibited by β-methyldigoxin (1.22×10^{-5} M) the relaxation induced by 10 mM potassium was reversed to a constriction (figure 2).

Experiments were also done with human saphenous veins. A representative tracing is given in figure 3. In the absence of β-methyldigoxin a marked relaxation of the veins was observed when 8 or 10 mM potassium was applied. Following the addition of 10^{-7} M β-methyldigoxin, biphasic responses (relaxation followed by contraction) were observed; after prolonged exposure to the drug only contractions were caused by elevated (K_0^+).

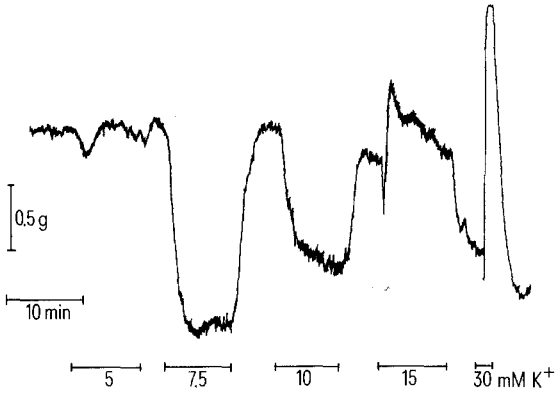

Fig. 1. Effect of increased (K_0^+) on mechanical tension of a bovine facial vein preparation. Isometric recording.

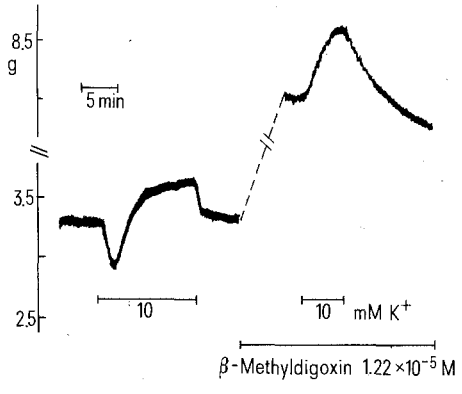

Fig. 2. Inhibitory effect of β-methyldigoxin on potassium-induced relaxation of a bovine facial vein preparation.

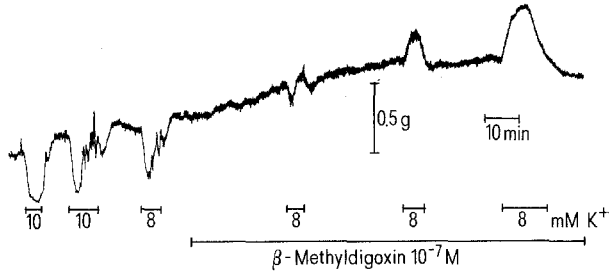

Fig. 3. Inhibitory effect of β-methyldigoxin on potassium-induced relaxation of a human saphenous vein preparation. Note the relaxent effect of 10 and 8 mM (K_0^+) before the application of β-methyldigoxin and the reversal of the effect following the application of the drug.

Discussion. According to an earlier report from this laboratory[2], bovine facial veins contract when potassium is elevated from 2.6 to 15 mM in the bathing media. In numerous more recent experiments we observed that peripheral branches of the venous system having a diameter less than 2–3 mm relax under the effect of an increased concentration of (K_0) (up to 10 mM). A greater increase of (K_0) (10–30 mM) produces a biphasic effect (a relaxation followed by a contraction) and the highest (K_0^+) used produced mainly a contraction. These results suggest that the response of a vein to elevated (K_0^+) is a function of its caliber. While the reactivity of veins to vasoactive drugs seems to be qualitatively uniform, and independent of vessel size, the sensitivity to ionic variations may change considerably from segment to segment of the same branch.

As shown for bovine facial arteries[3,4] and for the perfused dog gracilis muscle[5] cardiac glycosides may convert the potassium-induced relaxation of the bovine facial vein into a constriction. The present work shows that similar effects are also obtained in veins (figure 2). These results support the hypothesis that the potassium-induced vascular relaxation is caused by the stimulation of an electrogenic sodium pump, energized by a Na-K-ATPase system[3,5,6].

Bohr has suggested that the amplitude of the potassium-induced relaxation may be taken as a measure of the Na-K-ATPase activity in the vessel wall[7]. The variable extent of the potassium-induced relaxation seems to indicate that the Na-K-ATPase activity decreases as the diameter of the vein increases. Furthermore, while the distal portions of the bovine facial vein (with diameter smaller than 2–3 mm) contain mainly dilating β-adrenoceptors[8], in the more proximal regions the β-adrenoceptors seem to be masked by constricting α-adrenoceptors. The pharmacology of the proximal regions is now under investigation.

The considerations mentioned above seem to hold true not only for animal but also for human vessels, as we have been able to show with some human saphenous veins (figure 3). There is thus compelling evidence that no great difference exists between human and animal vessels.

It has been shown with microelectrodes that the interstitial (K^+) activity can rise during muscular work to 8–10 mM[9]. In the arterial side of the vascular system this elevation may be important for the induction of functional hyperemia.

On the venous side the biphasic reaction, observed with isolated veins in the present work, could have the following hemodynamic significance: the first response to an elevation of plasma K during muscular work is a dilation, whereby the capacity of the veins is increased. After a brief time interval, the elevated K^+ causes the veins to constrict. This process might have the role of promoting the venous return. Because of the functional heterogeneity of the vascular wall, the threshold of the contraction component of the biphasic venous effect may be variable.

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