atropine. A part of the stimulatory action of gastrin appears to be of a histaminergic nature, since acid responses to pentagastrin were antagonized by a histamine H_2-antagonist, cimetidine, as shown in this and previous studies[8]. A further possibility for the gastrin-induced stimulation consists of a cholinergic pathway. Goto and Watanabe[9] reported that the tetragastrin-induced acid secretion was inhibited by atropine in the isolated amphibian gastric mucosa preparation. Similar results were found in our study. Direct evidence of the release of acetylcholine by gastrin in the stomach is still absent; however, the possibility should not be considered to be completely excluded. Benneth[10] found that in the guinea-pig ileum the contraction produced by gastrin is caused by the release of acetylcholine and that it could be abolished by hyoscine. Gregory and Tracy[11] demonstrated that atropine reduced the motor effect of gastrin on the stomach and jejunum of the dog. Vizi et al.[12,13] showed that gastrin released acetylcholine from the myenteric plexus in the guinea-pig ileum. The structure of the parasympathetic autonomic innervation (Auerbach's and Meissner's plexi) is almost uniform in the alimentary tract. As shown in in vivo and in vitro studies, atropine inhibits pentagastrin-stimulated acid secretion[14,15]. In the isolated whole stomach of the mouse, gastrin-induced acid secretion was also inhibited by atropine but not by hexamethonium, suggesting that the acid stimulatory effect of gastrin on the stomach is partly mediated via acetylcholine which is released from the postganglionic parasympathetic nerves.

1 Acknowledgments. I am indebted to Miss G.B. Bishop for her help with the English translation.
2 C.F. Code, in: CIBA Foundation Symposium on Histamine, p. 189. Ed. G.E.W. Wolstenholme and C.M.O'Connor. Little, Brown and Co., Boston 1956.
3 A. Soumarmon, A.M. Cheret and M.J.M. Lewin, Gastroenterology *73*, 900 (1977).
4 M.I. Grossmann and S.J. Konturek, Gastroenterology *66*, 517 (1974).
5 J.A. Angus and J.W. Black, Br. J. Pharmac. *62*, 460P (1978).
6 I. Szelenyi and K. Thiemer, Pharmacology *19*, 315 (1979).
7 L. Cavalli-Sforza, Biometrie. Fischer, Stuttgart 1974.
8 K.T. Bunce and M.E. Parsons, Agents Actions *7*, 507 (1977).
9 Y. Goto and K. Watanabe, Japan. J. Pharmac. *25*, 790 (1975).
10 A. Bennett, Nature *208*, 170 (1965).
11 R.A. Gregory and H.J. Tracy, Gut *5*, 103 (1964).
12 E.S. Vizi, G. Bertaccini, M. Impicciatore and J. Knoll, Eur. J. Pharmac. *17*, 175 (1972).
13 E.S. Vizi, Br. J. Pharmac. *47*, 765 (1973).
14 Y. Goto and K. Watanabe, Experientia *32*, 946 (1976).
15 R.F. Lick, W.L. Brückner and W. Hart, Z. Gastroenterol. *5*, 275 (1967).

Coronary perfusion pressure as a determinant of ventricular performance[1]

P.J.F. Tucci, J. Spadaro, A.C. Cicogna and E.A. Bregagnollo

Hemodynamic Research Laboratory, Department of Medicine, Faculdade de Medicina de Botucatu, 18.610 Botucatu, S.P. (Brasil), 5 November 1979

Summary. The results observed in this work support the view that coronary perfusion pressure affects ventricular performance independently of metabolic effects; a mechanism operating in beat-to-beat regulation is proposed.

The depressant effect on contractile force produced by myocardial undernourishment secondary to ischemia or hypoxia is well known. Effects of coronary perfusion pressure on ventricular performance apart from those due to unfulfilled myocardial metabolic requirements are not as well established. Therefore, we investigated the influence of perfusion pressure on ventricular performance and our results seem to confirm that coronary perfusion pressure by itself does affect ventricular contractile function.

Methods. Studies were performed in the isolated metabolically supported canine heart preparation described by others[2]. The heart was perfused with blood derived from the femoral artery of a support dog to a reservoir whose height was adjusted to maintain a perfusion pressure of 100 mm Hg. Coronary venous outflow returned from pulmonary artery to the support dog and a catheter was inserted through the apex of left ventricle to drain thebesian flow. Through a small right atrial incision a total atrioventricular blockade was induced by injecting 0.3–0.5 ml of formalin 10% in the region of the A-V node and ventricular pacing was maintained at the lowest frequency attainable (mean $\pm$ SD = 65 ± 11 beats/min). The mitral apparatus was excized and a soft distensible latex balloon attached to a coupling cannula was maintained in the left ventricle. The cannula was connected to a P23Db pressure transducer and the balloon was filled with saline until a systolic pressure of 70–80 mm Hg was obtained. To test the influence of perfusion pressure on myocardial performance, the line of coronary perfusion was occluded during 10–30 sec and, thereafter, suddenly released. The sole influence of perfusion pressure on cardiac performance was analyzed by comparing pressure developed (DP) by 2 successive beats: the last one that occurred during underperfusion and the first one following the release of the coronary line.

Results and discussion. In order to prevent misinterpretation of the results strict attention was paid to the possible

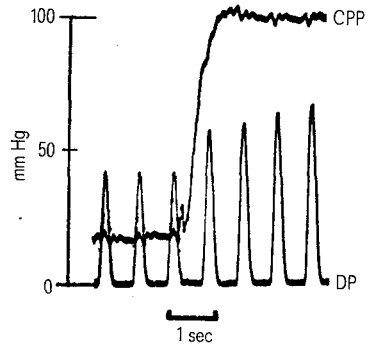
Effect of coronary perfusion pressure on ventricular performance

Experiment	Δt (sec)	A (mm Hg)	B (mm Hg)	Percent*
1	0.5	34	46	+35
2	0.4	54	67	+24
3	0.5	42	58	+38
4	0.5	46	53	+15
5	0.9	49	62	+26
6	0.7	30	37	+23
7	0.8	39	51	+31
Mean $\pm$ SD	0.61 ± 0.18	42.0 ± 8.4	53.4 ± 10.0	$+27.4 \pm 7.8$

Δt: time elapsed from the relief of coronary perfusion line to the onset of the next ventricular contraction; A: developed pressure of the last contraction occurred during occlusion of coronary line; B: developed pressure of the 1st beat occurred after relief of coronary perfusion; * percentual difference between B and A.

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.

1 This work was carried out during the tenure of grants in aid from the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP médicas 78/1392) and from the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 2222, 1608/78).

2 J.W. Covell, E. Braunwald, J. Ross, Jr and E.H. Sonnenblick, J. clin. Invest. *45*, 1535 (1966).
3 M.F. Bacaner, F. Lioy and M. Visscher, J. Physiol., Lond. *216*, 111 (1971).
4 R.M. Abel and R.L. Reis, Circulation Res. *27*, 961 (1970).
5 M. Weisfeldt and N. Shock, Am. J. Physiol. *218*, 95 (1970).
6 G. Arnold, F. Kosche, E. Miessner, A. Neitzert and W. Lochner, Pflügers Arch. ges. Physiol. *299*, 339 (1968).

Effect of potassium on isolated bovine facial and human saphenous veins

H. Nguyen Duong, U. Voss and K. Brecht

Departments of Physiology and Surgery, University of Ulm, D-7900 Ulm (Federal Republic of Germany), 26 September 1979

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-