The relative effect of impulses in the low and high threshold afferent fibers on the excitability changes in the tooth primary afferent terminals was examined by varying the strength of the conditioning stimuli applied to the infraorbital nerve and by stimulating the δ fibers of another tooth pulp. The threshold for the infraorbital nerve was estimated from responses recorded by a monopolar electrode placed on the surface of the medulla 3 mm below the obex. Increased excitability was already apparent when the strength of conditioning stimulus was 1.2 × treshold and it increased rapidly, reaching approximately 90% of its maximum at the 5 × threshold strength. Figure 2, B shows the optimum interval of the increased excitability of the tooth pulp primary afferent terminals produced by a conditioning volley in the infraorbital nerve at 3.7 × threshold. When conditioning stimuli were applied to the tooth pulp of the other ipsilateral canine tooth a similar increase in the antidromic potential evoked by the test shock was seen. This is shown by Figure 2, D only for the optimum interval, but the time course and magnitude of changes of the excitability were similar to that observed after a preceding volley to the infraorbital nerve. It can, therefore, be concluded that impulses in both fast-conducting A α- and β-fibers as well as slow-conducting A δ fibers contribute to the depolarization of tooth pulp primary afferent terminals in the medulla oblongata[9].

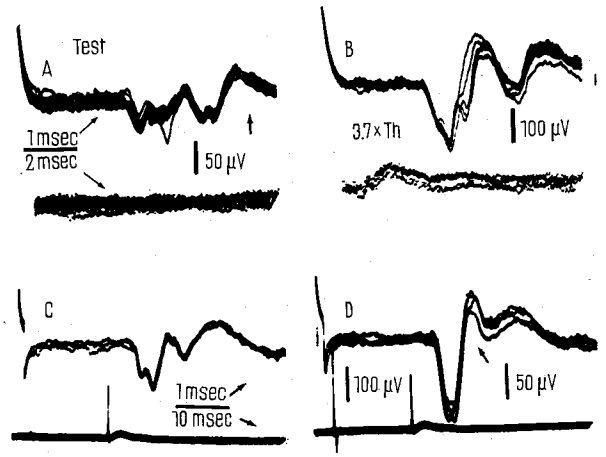


Fig. 2. (A–B) Excitability changes of the tooth pulp primary afferent terminals evoked by an impulse in low threshold trigeminal afferent fibres. Upper traces, antidromic action potentials recorded from the upper canine; lower traces, monopolar recordings from the surface of the oblongata 3 mm below obex. (A) Control, (B) the same preceded in the interval of 20 msec by a stimulus to a branch of the infraorbital nerve at a strength 3.7 times threshold. (C–D) Excitability changes of the tooth pulp afferent terminals evoked by an impulse in δ fibres of another tooth. Upper traces, antidromic action potential from the tooth pulp of the upper canine; lower traces, monopolar recordings from the surface of the oblongata at lower speed. (C) Control, (D) the same preceded by a volley in the tooth pulp of lower canine.

Zusammenfassung. Die zentralen Endigungen der primären afferenten Fasern der Zahnpulpa, welche ausschliesslich der A-δ-Gruppe angehören, können sowohl durch Impulse in A-α-und β-Trigeminus-Fasern als auch in A δ afferenten Fasern der Pulpa eines anderen Zahnes depolarisiert werden.

L. VYKLICKÝ[10], W. I. R. DAVIES, K. VESTERSTRØM and D. SCOTT JR.

Department of Physiology, University of Pennsylvania, Philadelphia (Pennsylvania, USA), 17 November 1969.

[9] Supported in part by Center for Oral Health Research, University of Pennsylvania, U.S.P.H.S. Grants No. De-02623-03.

[10] Present address: Institute of Physiology, Czechoslovak Academy of Sciences, Praha 4-Krc (CSSR).

Spontaneous Sympathetic Activity in Experimental Heart-Failure

The marked decrease in catecholamine levels in clinical and experimentally produced congestive heart failure (CHF) is a well-documented finding[1–3]. The exact mechanism whereby the noradrenaline content is reduced in the sympathetic nerve terminals at the heart is not completely understood. It has been suggested[4] that the defect lies in the synthesis or binding of norepinephrine. CHIDSEY and BRAUNWALD[1] later presented evidence which supported the view that depletion of cardiac norepinephrine was a consequence of a reduction in the number of nerve endings. It has also been reported[5] that postganglionic sympathetic nerve stimulation elicits a reduced cardiac response in dogs with experimentally produced heart-failure. Cardiac muscle from cats in experimental heart-failure has been shown to be in a depressed contractile state[7]. SIEGEL and SONNENBLICK[6] suggested that animals in CHF may maintain or increase their cardiac contractility by an increase in the spontaneous sympathetic activity due to vasomotor reflex mechanisms. Pharmacological evidence has been presented[1] which suggests that there is an increased sympathetic nervous discharge in patients with heart-failure. In this study we directly measured spontaneous sympathetic nerve activity to the normal and failing heart in order to determine whether the failing heart is supported to any degree by increased sympathetic activity.

[1] C. A. CHIDSEY and E. BRAUNWALD, Pharmac. Rev. *18*, 685 (1966).
[2] E. T. ANGELAKOS, M. P. KING and R. W. MILLARD, Ann. N.Y. Acad. Sci. *156*, 219 (1969).
[3] J. H. K. VOGEL, D. JACOBOWITZ and C. A. CHIDSEY, Circulation Res. *24*, 71 (1969).
[4] J. F. SPANN JR., C. A. CHIDSEY and E. BRAUNWALD, Science *145*, 1439 (1964).
[5] J. W. COVELL, C. A. CHIDSEY and E. BRAUNWALD, Circulation Res. *19*, 51 (1966).
[6] J. H. SIEGEL and E. H. SONNENBLICK, Arch. Surgery *89*, 1026 (1964).
[7] J. F. SPANN JR., R. A. BUCCINO, E. H. SONNENBLICK and E. BRAUNWALD, Circulation Res. *21*, 341 (1967).

Methods. Cardiac sympathetic nerve activity was recorded in normal cats and in those with acute and chronic experimentally-induced heart-failure.

In the control experiments, cats were anaesthetized with chloralose (70 mg/kg i.v.) following induction of anaesthesia with halothane, nitrous oxide and oxygen mixture. The left stellate ganglion was carefully exposed after a midline incision, and pre- and post-ganglionic nerves dissected free. Recordings of neural activity were measured at preganglionic sites by placing teased fibres of the thoracic sympathetic nerve on to a pair of platinum electrodes (Figure 1). Post-ganglionic recordings were obtained in a similar manner from fibres of the inferior cardiac nerve (Figure 1). Nerve activity was amplified and displayed conventionally on a cathode follower, preamplifier and Tektronix 565 oscilloscope, and photographic records obtained. Left ventricular pressures were recorded with a polythene catheter inserted into the left ventricle via the common carotid artery.

In 3 acutely failed cats, the aorta was constricted with a polythene-coated wire and the diameter was constricted progressively until the heart failed.

Under halothane anaesthesia and after an incision into the 3rd intercostal space, experimentally-induced chronic heart-failure was produced in 6 cats by partial constriction of the aorta (75%–85%) and sympathetic nervous activity recorded 1–3 months later by the same techniques as described above.

Results. Three criteria were used to assess the degree of heart-failure induced in cats by aortic constriction. Left ventricular end-diastolic pressures were measured and found to be elevated above normal in all cases, averaging 13.2 ± 2.4 mm Hg compared with control values of 3.4 ± 0.7 mm Hg ($p = 0.03$). The second criterion of failure was the reduction of catecholamine levels[1–3]. In all chronically failed cats catecholamine levels were decreased below control values. Thirdly, several enzymes whose activities are altered in CHF were measured histochemically. A decreased level of succinic and lactic dehydrogenase, diminished myosin ATPase and a rise in isocitrate dehydrogenase were observed. These observations support the view that the cats used were in a moderate state of heart-failure.

The values obtained in normal preparations for spontaneous pre- and post-ganglionic sympathetic discharge were 70.5 ± 4.6 impulses/min (18 fibres) and 68.8 ± 5.9 impulses/min (315 fibres) respectively, and thus are not significantly different. The mean post-ganglionic discharge rate obtained from chronically failed cats was 59.3 ± 4.8 impulses/min (14 fibres) which was also not significantly different from the control values. Representative records of sympathetic activity from normal and chronically failed cats are illustrated in Figure 2. The mean arterial pressure of the 6 failed cats was 128.3 mm Hg, and the mean for normal cats was 127.5 mm Hg.

In 3 experiments, the aortae of normal cats were acutely constricted by 80% and a mean reduction of 13.6% in

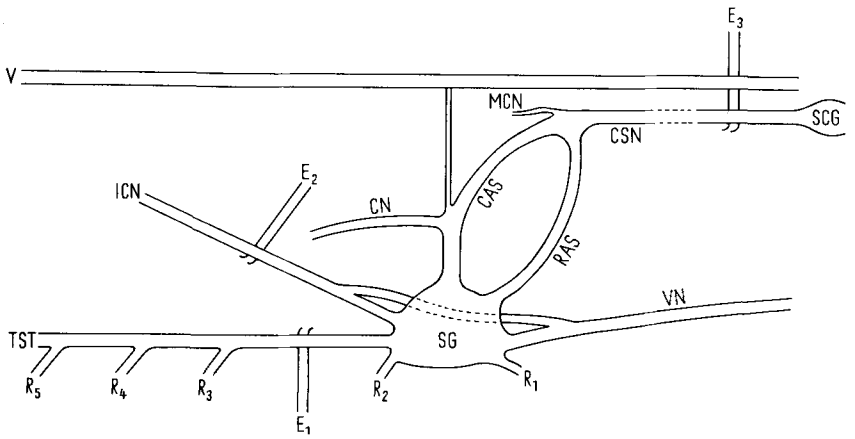


Fig. 1. Diagrammatic representation of pre- and post-ganglionic recording sites. CAS, caudal ansa subclavia; CN, cardiac nerve; CSN, cervical sympathetic nerve; E_1, preganglionic electrode; E_2, postganglionic electrode; E_3, preganglionic electrode; ICN, inferior cardiac nerve; MCN, middle cardiac nerve; R_1–R_5, rami communicantes; RAS, rostral ansa subclavia; SCG, superior cervical ganglion; SG, stellate ganglion; TST, thoracic sympathetic trunk; V, vagus nerve; VN, vertebral nerve.

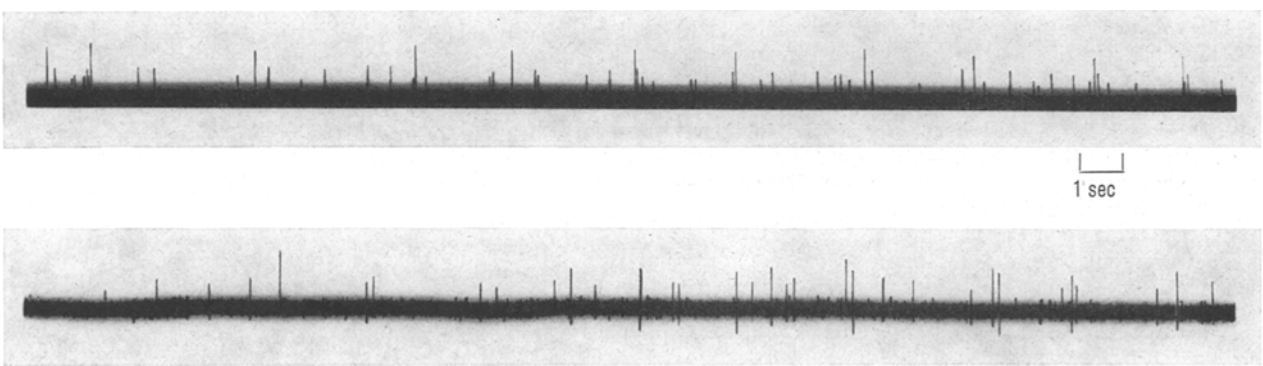


Fig. 2. The upper recording represents the spontaneous postganglionic nerve discharge from a normal preparation. The bottom postganglionic recording was obtained from a chronically failed preparation.

post-ganglionic sympathetic discharge frequency was observed with 1 h of constriction. This decrease can be explained on the basis of a generalized increase in mean arterial pressure of 20 mm Hg and subsequent reflex baroreceptor inhibition of sympathetic outflow.

Discussion. Our experiments did not disclose any significant difference in the spontaneous post-ganglionic sympathetic nerve discharge rate between normal or acutely and chronically failed cats. Our results therefore do not support the possibility raised by SIEGEL and SONNENBLICK[6], that the failing heart increases the frequency of its spontaneous sympathetic discharge rate. Our values for normal sympathetic discharge rates are in agreement with those reported by other workers in this field[8–11].

It has been shown[5] that sympathetic nerve stimulation caused a reduced contractile response in the failed heart, so that even if the spontaneous sympathetic rate were increased in failed animals, this mechanism might not be beneficial towards improving the depressed myocardium.

The present results indicate that a compensatory reflex increase in sympathetic discharge frequency does not occur in experimental heart-failure. In our opinion the decreased contractility in failing hearts is not the result of a neuronal event proximal to the sympathetic nerve terminal in the heart, but occurs at, or beyond that point. This hypothesis is supported by the results of SPILKER and CERVONI[12] who have shown that chronic bilateral stellate ganglionectomy as well as reserpine-pretreatment of cats does not significantly alter myocardial contractility. All of these observations indicate that the catecholamine depletion present in CHF occurs independently of a change in the spontaneous activity of the sympathetic nervous system.

Zusammenfassung. Es wird bestätigt, dass der Katecholamingehalt des Herzmuskels bei Herzinsuffizienz abnimmt; ein kompensatorischer Anstieg der Reflexaktivität des sympathischen Nervensystems besteht hingegen nicht.

B. A. SPILKER and M. L. HAYDEN

Research Division, The Pfizer Group, Sandwich (Kent, England), 4 December 1969.

[8] D. W. BRONK, L. K. FERGUSON, R. MARGARIA and D. Y. SOLANDT, Am. J. Physiol. *117*, 237 (1936).
[9] B. FOLKOW, Acta phys. scand. *25*, 49 (1952).
[10] A. IGGO and M. VOGT, J. Physiol., Lond. *150*, 114 (1960).
[11] A. MALLIANI, P. J. SCHWARTZ and A. ZANCHETTI, Am. J. Physiol. *217* (1969).
[12] B. SPILKER and P. CERVONI, J. Pharmac. exp. Ther. *168*, 60 (1969).

Evaluation of O_2 Availability During Glucose Transport in Everted Sacs of Rat Small Intestine

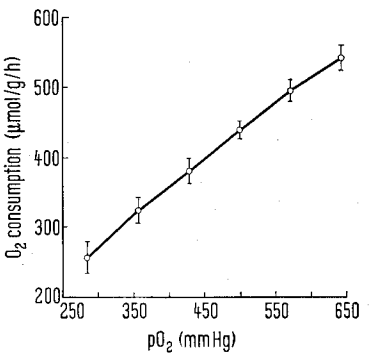
It is known that glucose transport in the everted sacs of rat small intestine[1] is accompanied by the production of a considerable amount of lactic acid[2–4]. NEWEY et al.[4] believe that this lactic acid production may be an artifact due to inadequate O_2 availability in the intestinal wall, when this is incubated in vitro. On the contrary, WILSON[3] thinks that lactic acid is produced even in perfectly aerobic conditions: according to him, a considerable fraction of glucose is likely first to be transformed into lactic acid, and subsequently actively transported by the rat intestine.

In our opinion, a suitable approach to the solution of this problem is to assess whether O_2 availability in everted sacs of rat small intestine, during incubation in a medium containing glucose, is adequate to permit their true aerobic survival.

For this purpose, experiments were carried out in order to study O_2 consumption in everted sacs of rat small intestine as related to O_2 partial pressure (pO_2) in a medium of this kind.

These experiments provide information on the problem, because the survival conditions of the preparation are undoubtedly aerobic only above a certain critical pO_2 level in the incubating medium, which permits complete satisfaction of its O_2 requirements; above this level, O_2 consumption of the preparation does not depend on pO_2. On the contrary, when incubated in a medium at a lower pO_2, the preparation is anaerobic to a varying degree, and its O_2 consumption depends on pO_2.

The experimental procedure was carried out according to a method described by us in a previous paper[5]. A test-tube was filled with 30 ml of Krebs-Henseleit solution[6] containing 15 mM/l of glucose. The solution was equilibrated with a gaseous mixture of 5% CO_2 in O_2 and thermostatically set at 37 °C. An everted sac (4–5 cm in length) of rat small intestine (albino male rats, average weight 140 g) was placed in the test-tube, and the fall of the pO_2 in the incubating medium was continuously checked for a 60 min period using a polarographic device (Beckman 160 Gas Analyzer). Since the quantity of O_2 in the incubating medium was known, it was possible to calculate O_2 consumption at any desired pO_2 level, as a



O_2 consumption of everted sacs of rat small intestine as a function of O_2 partial pressure (pO_2) in the incubating medium. Each point represents the mean of 10 experiments; vertical bars indicate standard error.

[1] T. M. WILSON and G. WISEMAN, J. Physiol. *123*, 116 (1954).
[2] T. M. WILSON and G. WISEMAN, J. Physiol. *123*, 126 (1954).
[3] T. M. WILSON, J. biol. Chem. *222*, 751 (1956).
[4] M. NEWEY, D. M. SMYTH and B. C. WHALER, J. Physiol. *129*, 1 (1955).
[5] P. PIETRA and V. CAPPELLI, Boll. Soc. ital. Biol. sper. *45*, 51 (1968).
[6] M. A. KREBS and K. HENSELEIT, Z. physiol. Chem. *210*, 33 (1932).