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.

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

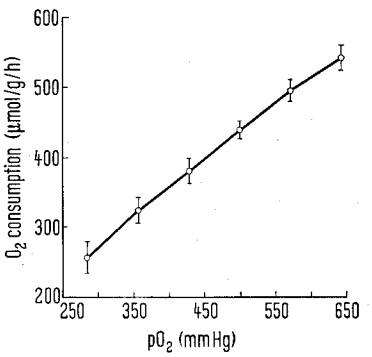
It is known that glucose transport in the everted sacs of rat small intestine[1] is accompanied by the production of a considerable amount of lactic acid[2–4]. NEWEY et al.[4] believe that this lactic acid production may be an artifact due to inadequate O_2 availability in the intestinal wall, when this 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.

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function of the decreasing pO_2. O_2 consumption was then related to the dry weight of the preparation.

The results of our experiments (Figure) show that at no pO_2 between 40% and 90% of the saturation point (285÷642 mm Hg) it is possible to evidence a critical pO_2 level in the incubating medium above that at which O_2 consumption of the sacs remains at a steady state: in fact, O_2 consumption always varied along with pO_2.

It is therefore clear that O_2 requirements of the preparation are never completely satisfied; the large amount of lactic acid produced by the everted sacs of rat small intestine during incubation in a medium containing glucose should consequently be considered, at least partially, as a consequence of anaerobic glycolysis resulting from inadequate O_2 availability.

Riassunto. Misurando il consumo di O_2 in funzione della pO_2 nel mezzo di incubazione è stato dimostrato che i sacchetti di intestino tenue rovesciato di ratto si trovano in condizione di parziale anaerobiosi nel corso dell'incubazione in liquido fisiologico contenente glucoso. Ciò viene posto in relazione con la notevole produzione di acido lattico da parte dell'intestino isolato mantenuto in tali condizioni.

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Significance of Cyclic AMP in the Regulation of Exocrine Pancreas Secretion

Since its discovery[1], adenosine-3′,5′-monophosphate (cAMP) has been implicated as an important regulatory mechanism in the control of a wide variety of divergent processes[2–4]. Early investigators have provided evidence that cAMP is closely linked to the endocrine system: ACTH, vasopressin, luteinizing hormone, TSH, MSH, and glucagon activities appear to be related to cAMP formation[5–10]. More recently, questions regarding the influence of cAMP on the exocrine systems have been raised. Alonso and Harris[11] have demonstrated that cAMP stimulates acid secretion by frog gastric mucosa; Kulka and Sternlicht[12] have shown that cAMP stimulates the secretion of amylase by mouse pancreas, and Case et al.[13] have postulated that cAMP mediates the action of secretin on the exocrine cat pancreas. We have examined the effects of cAMP on the secretion of the exocrine rabbit pancreas.

Materials and methods. New Zealand white male rabbits weighing 2.6–3.6 kg were anesthetized with 0.7 ml/kg Dial-Urethane (CIBA Pharmaceutical Co.) given i.v. The pancreas was removed and mounted according to the method of Rothman and Brooks[14,15]. Krebs-Hanseleit bicarbonate solution gassed with 95% O_2 and 5% CO_2 and 95 mg/100 ml added glucose was used as the bathing medium; pH was maintained in the range 7.2–7.4. Pancreatic secretion was collected at $^1/_2$ h intervals for a period of 5 h; collection periods 1 and 2 were allowed for equilibration and washout of the secretion already present in the main duct. N^6-2-*O*-dibutyryl cyclic adenosine-3′,5′-monophosphate (Schwarz BioResearch Inc.), $1\times10^{-5}M$, and theophylline (Cal BioChem), $1\times10^{-3}M$, and $1\times10^{-2}M$, were added to the bath singularly and in combination after collection period 4; effect on enzyme concentration, enzyme output, and volume were determined. After activation with enterokinase (Cal BioChem), esterase activity of trypsin and chymotrypsin was determined from the initial reaction velocities of their respective hydrolysis of TAMe[16] (*p*-toluenesulfonyl-L-arginine methyl ester) and ATEe[17] (acetyl-L-tyrosine ethyl ester) with a radiometer titrator. Levels of significance were determined employing the Student *t*-test for paired data comparison.

Results. In our control animals, and in previous controls done in this laboratory[18], there has been a constant downward progression of enzyme concentration and output with volume remaining fairly constant over a 5 h period (Figure 1). When dibutyryl cyclic AMP (DcAMP), $1\times10^{-5}M$, was added to the bath, enzyme concentration and output markedly increased as compared to controls while volume remained stable (Figure 2). Theophylline, $1\times10^{-3}M$, caused a volume increase and a rise in trypsin-chymotrypsin concentration and output, although only the trypsin output was significantly increased. Addition of theophylline, $1\times10^{-2}M$, produced a volume rise and a statistically significant increase in trypsin and chymotrypsin concentration and output. DcAMP, $1\times10^{-5}M$, and theophylline, $1\times10^{-3}M$, combined resulted in volume, trypsin and chymotrypsin concentration similar to those seen with DcAMP alone and a slight increase in enzyme output over that observed in DcAMP-only experiments. Summation of these results and statistical comparison is shown in the Table.

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