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To clarify the effects of hyperthyroidism on myocardial oxygen consumption ($V_{O_2}$), a polarographic method was employed to compare the $V_{O_2}$ of isolated papillary muscles from 13 normal euthyroid cats with that of 11 hyperthyroid cats. Basal $V_{O_2}$ was greater in the hyperthyroid group ($3.03 \pm 0.20$ vs. $2.36 \pm 0.19 \text{ SE \mu liter} \cdot \text{mg dry wt}^{-1} \cdot \text{hour}^{-1}, P < 0.05$). In muscles studied under afterloaded isotonic conditions, hyperthyroidism shifted the force-velocity curve upward and to the right, with an increase in both extent and velocity of shortening at equivalent loads. These changes in myocardial behavior in hyperthyroidism were associated with an increase in myocardial


Experiments were carried out on perfused canine kidneys in situ to determine if renal conversion of angiotensin I occurs. Various concentrations of decapptide produced an immediate increase in renal resistance when injected directly into the renal artery. Since the decapptide is biologically inactive, increased renal resistance was interpreted as indicating generation of angiotensin II. The extent of renal conversion of angiotensin I to angiotensin II was estimated to be approximately 19% in the normal dog. This percent conversion was reduced to about 10% in dogs maintained on high salt and DOCA for 7 to 10 days.


Regional flow measurements were made, using the Rudolph and Heymann microsphere technique, before and after 10, 30, and 50% of the previously measured blood volume was withdrawn from five unanesthetized rhesus monkeys restrained in horizontally tilted primate chairs. Measurements at similar time intervals were also made in seven control monkeys. Systemic arterial and central venous pressures, cardiac output, stroke volume, and hematocrit decreased progressively at each level of bleeding. Heart rate (until severe hemorrhage), respiratory rate, and blood levels of $\alpha$-glucosidase rose; bradykinin levels in arterial blood were unchanged. The fraction of cardiac

BEVAN, J. A., AND TÖRÖK, J. Movement of norepinephrine through the media of rabbit aorta. Circ Res 27: 325-331, 1970. (Department of Pharmacology, UCLA School of Medicine, Los Angeles, California 90024.)

The entry and movement of norepinephrine through the media of the isolated rabbit thoracic aorta has been investigated using an isotopic frozen section technique. After 1-minute exposure of the intimal surface of a helical strip to Krebs bicarbonate solution containing tritiated norepinephrine ($^{3}$H-NE), the $^{3}$H material was distributed throughout the thickness of the wall. The highest concentration occurred at the innermost layer of the media and gradually decreased toward the adventitial side. The shape of the tritium distribution curves was not significantly changed by previous treatment of aortic strips with either cocaine, phenoxybenzamine or the MAO and COMT inhibitors, pargyline and tropolone, respectively. Temperature reduction to
output was found to be progressively increased to brain, heart, adrenal gland, and hepatic artery vascular bed at the expense of skin, spleen, and pancreas. The hepatic artery vascular bed was the only one that showed significant vasodilatation at either 30 or 50% hemorrhage.

During acute endotoxin shock in monkeys, we have previously found a similar fall in systemic arterial pressure due to a decrease in total peripheral resistance and a different pattern of regional blood flow changes. The lack of bradykinin production, the integrity of cardioregulatory mechanisms, and the fall of hematocrit levels found during hemorrhage may help account for some of the hemodynamic differences between these two types of shock.

**ADDITIONAL KEY WORDS** microspheres, organ blood flow, peripheral vascular resistance, sympathetic nervous system, blood pressure, cardiac output, α-glucosidase, bradykinin, endotoxin shock

27°C had no significant effect on the tritium distribution curves. The apparent diffusion coefficient for 3H-NE calculated for movement into the extracellular (inulin) space of the media was $7.29 \times 10^{-7}$ cm$^2$/sec. This relatively slow rate of diffusion is probably due to physical barriers such as elastic lamellae within the tunica media.

**ADDITIONAL KEY WORDS** catecholamine, smooth muscle, cocaine, isotopic frozen section technique, MAO and COMT inhibitors, phenoxybenzamine, distribution curves, diffusion coefficient, reduced temperature

$\dot{V}O_2$. Isometrically contracting muscles from hyperthyroid animals demonstrated significant increases in both developed tension ($6.3 \pm 0.7$ vs. $4.7 \pm 0.4$ g/mm$^2$, $P < 0.05$) and rate of tension development ($32.6 \pm 3.5$ vs. $19.4 \pm 1.5$ g/mm$^2$•second$^{-1}$, $P < 0.01$), as compared to the euthyroid group. Myocardial $\dot{V}O_2$, expressed per g/mm$^2$ isometric developed tension, was significantly greater in the hyperthyroid group ($0.64 \pm 0.09$ vs. $0.42 \pm 0.04$ mliter • mg dry wt$^{-1}$ • beat$^{-1}$, $P < 0.02$). Thus, experimental hyperthyroidism augments myocardial $\dot{V}O_2$ whether measured in resting or contracting cardiac muscle. This increase can be attributed, at least in part, to the altered contractile function of the heart in hyperthyroidism.

**ADDITIONAL KEY WORDS** cat papillary muscle, muscle mechanics, contractile state, external work, force-velocity relations, myocardial metabolism, tension development, 1-thyroxine

**ADDITIONAL KEY WORDS** converting enzyme, angiotensin II
After recovery from acetylstrophanthin-induced ventricular tachycardia, a repetitive ventricular response (RVR) following a single diastolic stimulus could be elicited for 22 minutes. With atrial pacing at the maximum ventricular follow rate, RVR was obtainable for 70 minutes. A pause in pacing also evoked a ventricular ectopic beat; however, this persisted for only 27 minutes. The minimum heart rate required for RVR was always less than the minimum rate required for pause-induced ectopic beats. Extrasystoles following a pause during pacing, RVR in sinus rhythm, and RVR during rapid heart rates represent decreasing levels of ventricular automaticity corresponding to...
conduction system with block occurring in several instances in the latter. In the type 3 response there was also a progressive delay in A-V nodal conduction time, and a sudden marked delay in conduction in the ventricular specialized conduction system. Conduction block occurred distal to the His bundle depolarization. The relevance of conduction delay and block in the different regions of the A-V conduction system to the full recovery time and the relative, functional, and effective refractory periods of A-V conduction is indicated.

ADDITIONAL KEY WORDS  
His bundle electrogram  conduction block  
premature atrial impulses  conduction delay  full recovery time  
functional refractory period  relative refractory period  
effective refractory period

catecholamines, the divalent cations Ba^{2+}, Sr^{2+}, and Ca^{2+} restored action potentials to atrial muscle fibers depolarized by elevated K^+. The effectiveness of the divalent ions in allowing action potentials was inversely related to the estimated hydrated ionic radii. Like the action potentials observed in the presence of isoproterenol, those permitted by Ba^{2+}, Sr^{2+}, and Ca^{2+} were prevented by Mn^{2+} but insensitive to blockade by tetrodotoxin.

ADDITIONAL KEY WORDS  
acetylstrophanthidin digitalis toxicity  
atrial pacing ventricular premature beats ventricular tachycardia  
calcium electrode properties tetrodotoxin epinephrine isoproterenol  
norepinephrine

progressive dissipation of digitalis intoxication. The underlying mechanism for RVR probably is due to net loss of intracellular potassium, which can be induced both by digitalization and by rate acceleration.

ADDITIONAL KEY WORDS  
acetylstrophanthidin digitalis toxicity  
atrial pacing ventricular premature beats ventricular tachycardia  
subsided gradually over a period of 2 to 5 minutes. At higher [K]_o, the effect of overdrive on membrane potential was reduced. Substitution of Na^+ with Li^+ or exposure to 2,4-dinitrophenol abolished the late hyperpolarization during overdrive. The membrane resistance was not altered after an overdrive period. The results suggest that driving ventricular Purkinje fibers at a rate higher than their intrinsic rate causes an initial loss of K^+ and the activation of an electrogenic Na^+ pump. The activation of the electrogenic pump is the major mechanism responsible for overdrive suppression.

ADDITIONAL KEY WORDS  
overdrive suppression high potassium  
substitution of sodium with lithium dinitrophenol ionic pump  
diastolic depolarization and electrogenic pump

Fresh tissues were taken for light microscopy from the trabeculae carneae at the right ventricular base, apex, left ventricular base, and apex of four normal canine hearts and nine whose pulmonary artery had been banded for 7 to 48 weeks. After banding, the width of the intercalated disc at the right base, 1.34 ± 0.10 μ (mean ± SE), was greater than at the right apex, 1.02 ± 0.09 μ (P < 0.002); both were greater than the normals (P < 0.005 and P < 0.001). The intercalated discs were wider than corresponding normals in only three

Matsushita, S., and Fanburg, B. L. Pyrimidine nucleotide synthesis in the normal and hypertrophying rat heart: Relative importance of the de novo and "salvage" pathways. Circ Res 27: 415-428, 1970. (New England Medical Center Hospitals, Boston, Massachusetts 02111.)

Radioactive orotic acid incorporation into RNA (de novo pathway of pyrimidine nucleotide synthesis) was considerably lower for rat heart than for rat liver in vivo and in vitro. 3H uridine ("salvage" pathway) was incorporated into heart RNA to a greater extent than 3H orotic acid, and the labeling with uridine in the heart exceeded that in the liver. Extracts of heart showed little enzymatic conversion of orotic acid to pyrimidine nucleotides in the presence of ATP and ribose-5-phosphate, a condition under which there was good activity in other tissues such as the liver, spleen, and kidney. Addition of phosphoribosylpyrophosphate (PRPP) markedly enhanced orotic acid conver-

Kjekshus, J. K., and Sobel, B. E. Depressed myocardial creatine phosphokinase activity following experimental myocardial infarction in rabbit. Circ Res 27: 403-414, 1970. (Department of Medicine, School of Medicine, University of California, San Diego, La Jolla, California 92037.)

Since creatine phosphokinase (CPK) is found predominantly in myocardial and skeletal muscle cells, in contrast to cells participating in the inflammatory response, it was considered likely that measurement of activity of this enzyme in the heart would provide a sensitive and relatively specific index of the extent of ischemic injury following acute coronary artery occlusion. Accordingly, CPK activity was measured serially following coronary artery occlusion in extracts from rabbit myocardium with gross infarction and from normal rabbit left ventricle. In addition, myocardial CPK activity was assayed in extracts from various portions of dog hearts 24 hours after ligation of the coronary artery.


Third degree heart block was produced in anesthetized dogs by injecting 95% ethanol into the region of the A-V node. When the ventricles were paced artificially at a constant rate near the spontaneous rate of the S-A node, then the atria and ventricles became synchronized. During synchronization, the P wave oscillated rhythmically around the QRS. When the P preceded the QRS, the arterial blood pressure increased, whereas when the P wave followed the QRS, the blood pressure fell. Synchronization depended on such rhythmical fluctuations in blood pressure because (1) when the blood pressure changes were severely attenuated, synchronization ceased, and (2) simulation of the
CPK activity of rabbit myocardium with infarction was uniformly depressed within 6 hours following coronary occlusion. After 24 hours, activity declined from 15.5 ± 0.9 (mean ± SE) to 3.4 ± 0.3. CPK activity in whole left ventricular extracts was depressed, and in general, the extent of depression was proportional to the size of the gross infarct. CPK depression in various regions of the dog heart 24 hours after coronary occlusion correlated with the extent of reduction of blood flow determined with the use of radioactively labeled microspheres. Results suggest that depression of myocardial CPK activity may be useful in estimating the extent of tissue damage following experimental coronary artery occlusion and the effect of prophylactic and therapeutic measures on the survival of myocardium in this setting.

**ADDITIONAL KEY WORDS**
- myocardial enzymes
- myocardial ischemia
- coronary artery occlusion
- myocardial necrosis
- infarct size
- myocardial enzymes
- coronary artery occlusion
- infarct size
- myocardial necrosis

Hearts at the left base and six at the left apex. The mean widths of the discs correlated positively with both ventricular wall thickness and weight in the right ventricle but not in the left. Structures characterized by two, three, or four transverse segments of discs lying along the same myofibrils, each two of which are separated by 1 to 10 sarcomeres, have been named multiple intercalated discs. In six of the nine hearts whose pulmonary artery was banded, there were more multiple discs per mm² at the right base and right apex than in the corresponding normals (P < 0.02). In five of these, the number of multiple discs per mm² was greater at the right base than in the corresponding apex (P < 0.001). There was no significant increase in the number of multiple discs per mm² in either the left base or left apex of the experimental animals compared to controls. After banding the pulmonary artery, tension increases in the right ventricle and this stimulates a broadening of the folds of the discs and then triggers a mechanism for the formation of new sarcomeres, perhaps involving multiple intercalated discs.

**ADDITIONAL KEY WORDS**
- right ventricular hypertrophy
- banded pulmonary artery

Blood pressure changes by means of a servo-controlled pump also produced synchronization. A biological control system operates in such a way that (1) the P-R interval affects blood pressure by virtue of changes in the atrial contribution to ventricular filling; (2) the blood pressure has an inverse effect on atrial frequency through the baroreceptor reflex, and perhaps other mechanisms; and (3) changes in atrial frequency alter the P-R interval, to complete the control loop.

**ADDITIONAL KEY WORDS**
- control system
- heart rate
- arrhythmia
- complete heart block
- artificial pacemaker
- baroreceptor reflex
- cardiac nerves
- atrial contraction

Enzymes in liver and skeletal muscle

Uridine kinase activity in the heart was similar to that in the liver. Uridine kinase appeared to be rate limiting in the "salvage" pathway. Aortic constriction produced an increase in uridine kinase activity at 24 hours with a peak at 2 to 6 days (50 to 60% stimulation) after operation, while uridylate kinase, uridine phosphorylase, and orotidine monophosphate pyrophosphorylase activities remained unchanged. The "salvage" pathway appears to play an important role in pyrimidine nucleotide synthesis in the heart, and uridine kinase may be regulatory in this pathway during cardiac hypertrophy.
The amino acid analog, alpha-aminoisobutyric acid (AIB) has been used to study myocardial amino acid transport in the isolated rabbit right ventricular papillary muscle. Intracellular AIB accumulation is linear for 2 hours and reaches a plateau at 3 hours at an intracellular/extracellular concentration gradient of 3.4. Anoxia does not inhibit this process whereas simultaneous inhibition of aerobic and anaerobic metabolism inhibits AIB accumulation.

The exchanges of $^{125}$I-labeled 4-iodoantipyrine (I-Ap), $^{14}$C-labeled antipyrine ($^{14}$C-Ap), and tritiated water (THO) were studied in isolated blood-perfused, beating, nonworking dog hearts. From a first set of experiments, analysis of externally monitored myocardial clearance curves of I-Ap after its injection into coronary artery blood showed its washout to be flow limited at flows ranging from 0.8 to 3.8 ml • g$^{-1}$ • min$^{-1}$. Therefore, these curves can be used for estimating coronary blood flow. In a second set of experiments, coronary sinus dilution curves of simultaneously injected I-Ap and THO were found to be indistinguishable in shape at high coronary flows. At low...
flows (<1.8 ml • g⁻¹ • min⁻¹), THO curves showed an earlier upslope and higher peak than antipyrine, indicating either a diffusional shunt for water or a larger volume of distribution for antipyrine. ^14C-Ap had a slightly faster washout than I-Ap. The differences are partially attributable either to differences in solubility of I-Ap, ^14C-Ap, and THO in erythrocytes or to differences in their volumes of distribution, and partially to diffusional shunting of water.

ADDITIONAL KEY WORDS indicator dilution isotopic labeling tritium iodine coronary blood flow capillary permeability diffusible indicators intratissue diffusion volume of distribution compartmental analysis

Intracellular AIB accumulation follows Michaelis-Menten kinetics with a Km of 6.8 x 10⁻³ M and a V_max of 6.6 μmoles • ml intracellular fluid⁻¹ • hour⁻¹. Sodium ion is obligatory for the transport process whereas no absolute potassium or calcium requirement exists. Ouabain, 10⁻⁸ M, inhibits AIB uptake. Myograph techniques were utilized to determine the effect on AIB accumulation of subjecting unstimulated papillary muscles to various degrees of passive stretch. Muscles incubated at any tension above zero developed a greater intracellular/extracellular fluid AIB concentration ratio than muscles incubated at zero tension. These data suggest that increased myocardial wall tension may be a mechanical stimulus capable of inducing adaptive changes in myocardial metabolism.

ADDITIONAL KEY WORDS hypertrophy tension ouabain extracellular fluid space cellular volume
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