Because of suggestions that norepinephrine release from cardiac sympathetic nerves contributes to the myocardial action of digitalis, the effect of beta-receptor blockade on these actions was determined. $10^{-4} \text{M}$ propranolol did not alter the basal contractility of isolated kitten papillary muscles or of atrial strips from kittens, guinea pigs, rabbits, dogs, and chickens but decreased by 85% their inotropic response to norepinephrine released by tyramine or high-intensity electrical stimulation. The same concentration of propranolol had no effect on cumulative inotropic concentration-effect curves for ouabain, cetylmyristate, and digoxin in these preparations. Presence of copranolol did not modify the actions of cardiac glycosides on the time course.


The present study was designed to explore the effects of environmental oxygen as a possible regulator of cardiac cell division and growth. Trypsin-dispersed heart cells from the ventricles of chick embryos 8 to 12 days old were grown in culture at 37°C in a nutrient medium (NCI) with 10% fetal bovine serum. They were exposed to constant 5% CO$_2$ gas environments in which the percent of O$_2$ was varied. Net protein synthesis increased progressively as O$_2$ was reduced from 80% to 2 to 5%. After the first 24 hours, little further protein synthesis occurred in plates grown in 80% O$_2$. The rates of cellular incorporation of $^{14}$C-amino acids and uridine-$^3$H increased progressively as the fraction of O$_2$ was reduced. In cells grown at 80% O$_2$, incorporation of...
ad power is only 1 to 51% of total ventricular power. Calculated efficiency varied from 35% with isoproterenol infusion to 100% with norepinephrine, phenylephrine, and open-chest states. Control efficiency was 78%. The concept of impedance matching was investigated; maximal efficiency occurred with isometric matching. Internal resistance was shown to represent an easily measurable quantity which also partially corresponds to the more complex impedance measurement.

**KEY WORDS** ventricular impedance phenylephrine isoproterenol

**EY WORDS**

| ventricular | isometric contraction. Beta-receptor blockade was without effect on increases in active tension and increases in resting tension induced by toxic concentrations of cardioactive steroids. The frequency of digitalis-induced tachycardia in guinea pig atrial strips and kitten papillary muscles was significantly decreased by propranolol, presumably because of its direct electrophysiologic actions. Exposure of cat hearts to digoxin in vivo and to ouabain in vitro had no effect on myocardial norepinephrine concentrations. It is concluded that release of myocardial norepinephrine plays no role in the actions of cardiac glycosides on the heart.

**KEY WORDS** isolated heart muscle propranolol ouabain

**EY WORDS**

| atrial concentration-effect curves acetylstrophanthidin contracture

| ventricular automaticity myocardial norepinephrine rabbits dogs

| tachycardia cats guinea pigs

incorporating the gate. The magnitude of the delay which can develop at coupling intervals just in excess of the functional refractory period tends to be small in healthy tissue and larger in depressed tissue. Suitable delays allowed premature impulses having coupling intervals shorter than the refractory period at the gate to be conducted distally. The refractory period in response to rapid rates of stimulation was discordant in the several false tendons in six of nine preparations studied. Both delayed conduction and 2:1 conduction were shown to occur near the limit of response to rapid stimulation. The data presented suggest certain functional analogies between the A-V node and the gating mechanism.

**KEY WORDS** action potential duration refractory period A-V node

**EY WORDS**

| arrhythmias premature impulses tachycardia aberrant conduction

| functional refractory period functional A-V block
Distribution of cortical blood flow was measured in the dog by a technique based on radionuclide-labeled microspheres. Initially it was necessary to test possible pitfalls of this technique. Completeness of trapping in the kidney, the effect on renal function, and the notion that microsphere distribution reflects blood flow distribution in the kidney cortex were studied. Renal vein blood contained less than 0.2% of the microspheres (16.8 μm diameter) found in the renal artery after an aortic injection. No impairment of $C_{PAH}$ (control 167 ± 4; postinjection 179 ± 31 ml/min), $C_{PA}$ (control 39.3 ± 6; postinjection 37.6 ± 2 ml/min), and $T_{bg}$ glucose (control 90.8 ± 13; postinjection 102 ± 24) was observed.

The acute effects of 6-hydroxydopamine (6-OH-DA) injected directly into the sinus node artery were studied in 57 dogs. The positive chronotropic effect of 6-OH-DA was intermediate between that of norepinephrine and that of tyramine, when these substances were compared on the basis of their $E_{max}$. The increase in heart rate produced by 6-OH-DA was inhibited by prior intranode injection of propranolol and deaminopyrophenamine. At high doses, injection of 6-OH-DA was often associated with arrhythmias such as periodic slowing of the sinus rate, atrial premature beats, atrial fibrillation, and ventricular extrasystoles. In the 72 hours following injection of 1.5 mg 6-OH-DA, the
Decreases (−16% to −35%) in VR could also be achieved by premixing DZ in the blood perfusion reservoir at concentrations between 40 and 100 ng/mL (which may be achieved clinically); thus albumin binding does not influence the activity of DZ. Decreases in VR by DZ were not related to stimulation of beta-adrenergic receptors, alteration in Na⁺ or K⁺ balance, or changes in venous levels of glucose lactate, pO₂, pCO₂, or pH. When norepinephrine and angiotensin II were infused during diazoxide infusions their vasoconstrictor response was attenuated. Thus DZ has a direct effect in reducing VR which is independent of measurable changes in gracilis muscle metabolism. Moreover, the VR effect of DZ is not dependent on a prolonged arteriolar effect independent of plasma concentrations of the drug.

**KEY WORDS** pharmacokinetics arteriolar receptors norepinephrine angiotensin

and using doses adequate to measure renal blood flow (5 mg/injection X 4 injections). After 4 injections of 50 mg each significant impairment of renal function was observed. Intrarenal blood flow distribution was determined using hemorrhagic hypotension. ¹³¹I-labeled microspheres were injected into the root of the aorta before, and ³²³Tc-labeled microspheres after, acute hemorrhage. Radioactivity was measured in the outer two thirds and inner one third of kidney slices. Tissue blood flow was calculated and expressed as the ratio of outer cortex to inner cortex counts. Renal blood flow was redistributed to the inner cortex after hemorrhage (ratio before, 3.00; after 1.30, P < 0.01). Finally, the results of this technique were compared to a widely used method measuring intrarenal blood flow distribution, ¹³³Xe washout. The first component of the washout technique correlated fairly well with total cortical flow but it was not possible to match the second component with any single anatomical area of the kidney. Limitations of the ¹³³Xe washout are discussed.

**KEY WORDS** shock kidney blood flow radioactive washout renal blood flow distribution yohimbine smooth muscle neuroeffector distance

**KEY WORDS** 6-OH-DA treatment, response to right stellate stimulation was diminished, and the response to vagal stimulation was not altered. It was concluded that the local perfusion of the sinus node with 6-OH-DA produces a marked norepinephrine depletion of the perfused region compatible with a localized degeneration of the sympathetic nerve terminals.

**KEY WORDS** adrenergic nerve terminals cardiac arrhythmia right stellate ganglion stimulation tyramine histofluorescence uptake and release of norepinephrine

**KEY WORDS** adrenergic nerve terminals cardiac arrhythmia right stellate ganglion stimulation tyramine histofluorescence uptake and release of norepinephrine
Depressed excitability and responsiveness were created in excised bundles of canine Purkinje fibers. A segment 8 mm long was depressed by being encased in agar containing 47 mM K⁺, the ends of the bundle outside the agar maintaining normal. Either normal end could be excited through extracellular electrodes. Action potentials were recorded by intracellular microelectrodes at each end and within the depressed segment. Conduction velocity within the depressed segment fell as low as 0.05 m/sec. Abnormalities of impulse transmission through the depressed segment included delay, 2:1 block, higher degrees of block, rate-dependent block, and block showing the Wenckebach phenomenon.


Human plasma converting enzyme activity was investigated by comparing biological with immunological activity of added or generated angiotensin after plasma incubation. Sodium citrate (2 X 10⁻³ M), 2,2'-dipyridyl (1 X 10⁻⁴ M), chromotropic acid (3 X 10⁻³ M and 3 X 10⁻⁴ M), and desferrioxamin (10 and 100 mg/100 ml) did not interfere with converting enzyme. By contrast, EDTA (3 X 10⁻³ M and 3 X 10⁻⁴ M), ECTA (3 X 10⁻³ M), 8 quinolinol (1 X 10⁻³ M), and oxalic acid (3 X 10⁻⁴ M) were shown to interfere with plasma converting enzyme activity. The EDTA inhibition of converting enzyme activity could be partially reversed by molar excess amounts of calcium, zinc and cobalt. The ability of these ions to restore converting enzyme...
summation of excitation in the center of the depressed area resulted in induction of activity out the branch at an interval appropriate to re-excite the aile heart. When one end of the preparation could excite the branch, induction of the other end sometimes inhibited excitation of the branch. The result is important as part of the explanation of phenomena associated with re-entry arrhythmias.

KEY WORDS entry block exit block parasyystole enkelehach phenomenon ventricular bigeminy ventricular tachycardia ventricular fibrillation transmembrane potentials concealed conduction

14 and 25 days. When alterations in muscle mechanics due to changes in muscle thickness were taken into consideration, muscles from hypertrophied hearts demonstrated a depressed maximum velocity of shortening ($P < 0.001$), while development of isometric tension was unaltered. The latter appeared to be maintained at least in part by a prolonged contraction time, as reflected by increases in the time to peak isometric tension ($P < 0.05$) and the time to peak "unloaded" isotonic shortening ($P < 0.001$). Resting tension was increased in trabecular muscles from hypertrophied hearts. Tissue hydroxyproline concentration was elevated with hypertrophy. The observed depression in muscle shortening velocity at light loads may be explained by altered contractile state or by increased stiffness of the parallel elastic element.

KEY WORDS isolated muscle studies force-velocity relationships aortic constriction hydroxyproline lactate dehydrogenase

The possible role of aortic smooth muscle in the regulation of aortic diameter and activity in the aortic baroreceptors was investigated in anesthetized rabbits. Aortic diameter was measured with ultrasonic technique within the intact thorax, and activity recorded in the whole left aortic nerve was quantified by rectification and integration. Blood pressure was changed by bleeding and reinfusion. At comparable blood pressures, norepinephrine (1 to 6 ng/kg-min) produced a 1% to 10% constriction of the aorta, without affecting the pressure-strain elastic modulus ($E_p$). After phenoxybenzamine, maximum increases in diameter and $E_p$ were 17% and 280%, respectively. When related

LIPSON, M.J., NAIF, S., AND PROGER, S. Synergistic effect of propranolol and nicotinic acid on the inhibition of plasma free fatty acid release in the dog. Circ Res 28: 270-276, 1971. (Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts 02111.)

Fatty acid mobilization was effected in 24 anesthetized dogs by infusion of norepinephrine over a four-hour period. Infusions of propranolol and nicotinic acid at various doses, individually and in combination, were added and free fatty acid levels were serially determined. Synergistic action of the two agents was apparent in that minimally effective concentrations of the two agents when used in combination suppressed the release of free fatty acids to 29 percent of levels achieved with norepinephrine, 1,186 μEq/L and 70 percent of levels in saline control animals (501 μEq/L). Large individual doses were no more effective than low doses used in combination. The synergistic action of propranolol

ECKER, L.C., FORTUN, N.J., AND PITT, B. Effect of ischemia and antianginal drugs on the distribution of radioactive microspheres in the mine left ventricle. Circ Res 28: 263-269, 1971. (Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.)

Radioactive microspheres were used to estimate the changes in regional myocardial blood flow occurring during acute myocardial ischemia. Carbonized 3-μm spheres were injected into the left atrium of 28 open-chest dogs and the radioactivity of selected areas determined after sacrifice. Acute occlusion of the left circumflex coronary artery produced a significant diminution in the proportion of microspheres reaching the circumflex area. In addition, there was disproportionate decrease in endocardial radioactivity in the ischemic area with epicardial radioactivity ratio falling from 1.17 to 0.76,

SHOUKAS, A.A., AND SAGAWA, K. Total systemic vascular compliance measured as incremental volume-pressure ratio. Circ Res 28: 277-285, 1971. (Department of Biomedical Engineering, Case Western Reserve University, University Circle, Cleveland, Ohio 44106.)

We developed a method to measure the compliance, defined as $\Delta V/\Delta P$, of the total systemic vascular bed ($C_v$) without stopping systemic flow. In 11 open-chest dogs, venous return (and cardiac output) was maintained at a constant level by inserting a perfusion pump (with no reservoir) between the caval veins and the right atrium. About 5% of the estimated total blood volume was withdrawn from the dog within 45 seconds. Resultant changes in central venous pressure were measured 10, 30, 60, 120, and 180 seconds after the volume change. The bled volume was then reinfluenced to repeat similar venous pressure measurements for another 180 seconds. The measurements were
<0.001) but not in the nonischemic area. Both nitroglycerin (0.4 mg) and propranolol (1 mg/kg) failed to cause a significant change in the ratio of circumflex to descendens radioactivity during ischemia. They did, however, use a significant increase in the ratio of endocardial to epicardial radioactivity in both ischemic and nonischemic areas.

**KEY WORDS** nitroglycerin endocardial/epicardial flow propranolol acute coronary artery occlusion regional myocardial blood flow bilateral flow

---

Diastolic diameter, however, \( E_p \) was mostly increased by norepinephrine and reduced by phenoxybenzamine. Baroreceptor activity at comparable pressures maintained normal during infusion of norepinephrine, but increased after phenoxybenzamine. However, when compared at equal diastolic diameters, the sensitivity of the receptors to aortic distention was found to be increased by norepinephrine and unaltered by phenoxybenzamine. Increased smooth muscle tone therefore served to maintain a normal relationship between blood pressure \( P \) and baroreceptor activity, in spite of the simultaneous reduction in aortic ammeter. Reduction of smooth muscle tone markedly increased activity in the aortic baroreceptors, due to dilatation of the receptor area.

**KEY WORDS** vascular smooth muscle norepinephrine phenoxybenzamine modulus of elasticity

---

Repeated after slightly increasing the blood volume or sectioning the vagi. The mean value of \( C_t \) measured 10 seconds after hemorrhage or reinfusion was \( 1.96 \pm 0.10 \) (SE) ml/mm Hg/kg body weight before vagotomy. Paired t-test indicated no significant difference between measurements of bleeding and reinfusion, measurements with different initial venous pressures or blood volume, or measurements before and after vagotomy. However, \( C_t \) increased with time during the 2-minute period by about 25% of the initial 10-second value (\( P < 0.001 \)) and remained constant thereafter.

**KEY WORDS** capacitance distensibility systemic venous tone pressure-volume relationship dogs

---

And nicotinic acid in the suppression of free fatty acid mobilization may be explained by the action of these two agents on the inhibition of the adenyl cyclase system of the adipose tissue cell. This synergistic action in reducing plasma free fatty acids and their effect on lipid synthesis would allow the use of smaller doses that could reduce the risk of side effects.

**KEY WORDS** lipid synthesis atherosclerosis plasma lipoprotein norepinephrine adenyl cyclase inhibition
ROSSMAN, W., BROOKS, H., MEISTER, S., SHERMAN, H., AND DEXTER, L.

A new technique is described for the instantaneous determination of myocardial force-velocity relationships. The method employs electronic differentiation of the logarithm of intraventricular pressure, which yields a continuous on-line record of \( \frac{dP}{dt} P^{-1} \) (the ratio of the rate of rise of ventricular pressure \( dP/dt \) to the simultaneous ventricular pressure \( P \)). A further technique is described for the automatic projection of force-velocity vector pops, displaying \( \frac{dP}{dt} P^{-1} \) on the ordinate against ventricular pressure on the abscissa in a beat-to-beat fashion. An excellent correlation \( r = 0.982 \) was
demonstrated between \((dP/dt)P^{-1}\) determined by conventional methods and \((dP/dt)P^{-1}\) derived electronically by use of the logarithmic amplifier circuit. Experimental studies are described which document the responsiveness of \((dP/dt)P^{-1}\) determined by the present method to interventions known to affect myocardial contractility. An increase in \((dP/dt)P^{-1}\) was observed following infusions of \(\Delta Cl\), norepinephrine, and glucagon, and a decrease following pentobarbital. 

isofar as \((dP/dt)P^{-1}\) is a valid index of myocardial contractility, the present method permits on-line, beat-to-beat evaluation of changes in ventricular function under a variety of circumstances.

**KEY WORDS**

- \((dP/dt)P^{-1}\)
- logarithmic amplifier
- myocardial contractility
- dog heart
- force-velocity relations
3M Brand Tracer Microspheres are small, uniformly-sized spherical particles labeled with a trace amount of a radioactive isotope. Injected into laboratory animals, the spheres make it possible to measure regional blood flow distribution without disturbing natural flow or moving individual organs. 3M Tracer Microspheres labeled with a choice of four different isotopes, including both GAMMA and BETA emitters, are readily available. All have a shelf life that enables experiments to be completed without significant loss in isotope activity. For detailed information about 3M Tracer Microspheres, and a bibliography of the current literature concerning their use, arranged by body organ, just complete and mail the form.

Mail to: 3M Nuclear Products
3M Company, 3M Center
Saint Paul, Minnesota 55101

Please send me further information on 3M Brand Tracer Microspheres.
My current research objective is______________________________

Name_____________________________________________________
Address____________________________________________________
City, State, Zip_____________________________________________

Or for immediate assistance telephone collect:
612-633-9420