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Instructions to Authors

Information about suitability of manuscripts for Circulation Research and their preparation, submission, review and editing now appears in the first number of each volume (July and January).
Burns, J.W., Covell, J.W., Myers, R., and Ross, J., Jr. Comparison of directly measured left ventricular wall stress and stress calculated from geometric reference figures. Circ Res 28: 611-621, 1971. (Department of Medicine, School of Medicine, University of California San Diego, La Jolla, California 92037.)

Mean left ventricular wall force was determined with a calibrated transmural auxotonic strain gauge in the left ventricle of six anesthetized, open-chest dogs with intact circulation. The gauge was oriented in the plane of the minor left ventricular equator, midway between the papillary muscles. Left ventricular internal volume was derived from the passive pressure-volume curve of the arrested heart and calculated mean wall stress was derived both from spherical and ellipsoidal reference figures for the left ventricle and compared with measured forces. Control left ventricular end-diastolic pressure averaged 38 ± 4 torr.

Peterson, D.F., and Brown, A.M. Pressor reflexes produced by stimulation of afferent fibers in the cardiac sympathetic nerves of the cat. Circ Res 28: 605-610, 1971. (From Departments of Physiology and Medicine, University of Utah Medical Center, Salt Lake City, Utah 84112.)

Afferent fibers in cardiac sympathetic nerves were stimulated electrically in an attempt to evoke circulatory reflexes. A pressor response was always elicited during stimulation of the central end of the cut left inferior cardiac or pericoronary nerve in vagotomized intact-brain or spinal cats. The maximum blood pressure rise was 21.5 mm Hg during inferior cardiac nerve stimulation and 14.1 mm Hg during pericoronary nerve stimulation. Heart rate and respiration were unaffected by stimulation. The alpha-receptor-blocking agent phenoxybenzamine hydrochloride abolished the pressor response. Sequential

Wolinsky, H. Effects of hypertension and its reversal on the thoracic aorta of male and female rats: Morphological and chemical studies. Circ Res 28: 622-637, 1971. (From the Departments of Medicine and Pathology and the Unit for Research in Aging, Albert Einstein College of Medicine, Bronx, New York.)

Effects of hypertension and its reversal on the wall of the thoracic aorta of male and female rats were studied. Hypertension for 10 weeks caused increased diameter, wall thickness, tangential tension, wall stress, and medial area in both sexes. In addition, absolute amounts of elastin, collagen, and noncollagenous, alkali-soluble protein were significantly increased in the walls of all hypertensive vessels. Associated with the decrease of calculated tension and wall stress to normotensive levels after reversal of hypertension, wall thickness and medial area in males remained significantly greater than in
sectioning of cardiac nerves arising from either the stellate ganglion or the thoracic sympathetic trunk, or of white rami 1 through 4, indicated that each branch carried afferents contributing to the pressor response. Evoked potentials revealed that excitation of Aδ fibers in the inferior cardiac nerve elicited a weak pressor response, and excitation of C fibers provoked a much stronger response. C fiber continuity between the pericoronary nerve and the inferior cardiac nerve was demonstrated.

KEY WORDS pericoronary nerve sympathetic reflex vagotomy evoked potential phenoxybenzamine hydrochloride inferior cardiac nerve

controls and similar to the values found in hypertensive vessels, whereas in females these parameters returned fully to control levels. Absolute amounts of noncollagenous, alkali-soluble proteins did return to control levels after hypertension reversal, but elastin and collagen remained elevated in amounts similar to those in vessels with sustained hypertension; in females, this resulted in an above-normal concentration of these fibrous elements in the vessel wall. Compositional changes of the female vessel wall after reversal of hypertension were thus similar to but more clearcut and complete than those found in the male aorta. Recognition of irreversible changes in vessels subjected to hypertension may have implications for the benefits to be gained from blood pressure reduction on the progression of cardiovascular disease.

KEY WORDS vascular disease elastin aortic wall thickness aortic wall tension aortic wall stress aortic diameter aging collagen

3.0 ± 0.6 mm Hg (SE). At this level of end-diastolic pressure, measured peak wall stress averaged 97.2 ± 14.4 g/cm², whereas calculated peak wall stress averaged 79.3 ± 9.9 and 118.6 ± 12.9 g/cm² for the spherical and ellipsoidal models, respectively. Measured end-diastolic wall force values averaged 9.4 ± 4.5 and 29.2 ± 8.1 g/cm² at an end-diastolic pressure of 3.0 and 12.3 mm Hg, respectively. In all cases, stress values calculated from spherical reference figures for the left ventricle were significantly lower than those measured directly. In four other experiments, using right heart bypass, the ventricular septum was exposed and active wall force was determined at two or more sites on the left ventricular minor equator. Wall stress at these sites differed by an average of 15.3%, indicating that stresses around the minor equator are relatively uniform. These studies lend validity to the application of geometric models in the calculation of mean wall stress and favor the application of an ellipsoid for the geometric reference figure.

KEY WORDS auxotonic force gauge average left ventricular wall force Laplace relationship major axis stress ellipsoid of revolution
Higgins, C.B., VATNER, S.F., Franklin, D., Patrick, T., and Braunwald, E. Effects of prostaglandin A\textsubscript{1} on the systemic and coronary circulations in the conscious dog. Circ Res 28: 638-648, 1971. (From the Department of Medicine, School of Medicine, University of California San Diego, La Jolla, California.)

The effects of intravenous prostaglandin A\textsubscript{1} (PGA\textsubscript{1}) on systemic and coronary hemodynamics were studied in 13 intact, conscious dogs after recovery from operation for implantation of Doppler ultrasonic flow probes on the ascending aorta and left circumflex coronary artery. Graded doses of PGA\textsubscript{1} (0.01 to 1.0 \(\mu\)g/kg) caused arterial pressure and total systemic resistance to decrease progressively and heart rate and cardiac output to increase progressively. At the maximum dose administered (1.0 \(\mu\)g/kg), arterial pressure and systemic resistance decreased by averages of 30\% and 51\% below...

Whayne, T.F., Jr., and Felts, J.M. Activation of lipoprotein lipase: Evaluation of calcium, magnesium, and ammonium as cofactors. Circ Res 28: 649-654, 1971. (From the Banting and Best Department of Medical Research, University of Toronto, Toronto 5, Ontario, Canada.)

Lipoprotein lipase (LPL) from rat heart acetone powders has been reported to depend on the presence of NH\textsubscript{4}\textsuperscript{+}, calcium, or other divalent cations for optimal activity. In addition, the enzyme will not hydrolyze an artificial triglyceride emulsion unless it is converted to an active substrate by the addition of very low density lipoproteins, high density lipoproteins (HDL), or certain peptides contained in these complexes. We observed earlier that HDL that had been extensively dialyzed against 0.005M ethylenediaminetetraacetic acid (EDTA), which probably removed most of the divalent cations, produced little lipolytic activity in LPL from rat heart acetone powders. This observation led us to evaluate the cation requirements for LPL. LPL was prepared in...


The perfused rabbit ear artery shows a biphasic contractile response to intraluminal norepinephrine and sympathetic nerve stimulation. The peak of the first phase occurs after approximately 10 seconds of exposure to NE, and the second, after 1\% to 2 minutes. The magnitudes of the two responses are similar. The time course of the second phase of contraction is similar to the rate of saturation of the vessel's extracellular space as measured by tissue uptake of tritiated norepinephrine. On the other hand, the first phase of contraction occurs when norepinephrine has penetrated only partly into the media. It is proposed that the two phases of contraction are due to different mechanisms of excitation and that the first phase is associated with excitation of the surface layer...


The influence of various enzyme inhibitors on the cardiovascular effects of L-dopa (methylester) has been studied to determine the sites of action of the drug or a responsible metabolite. L-Dopa, 10 mg/kg, iv, had minor early effects on heart rate and blood pressure in normal dogs, but in animals with inhibition of monoamine oxidase (MAO), it caused tachycardia and severe hypotension of gradual onset. When MAO was inhibited, earlier doses of a dopamine \(\beta\)-oxidase inhibitor (FLA 63) did not significantly modify the effects of L-dopa; prior administration of a decarboxylase inhibitor, NSD 1055 or Ro 4-4602, prevented...
soluble form from rat heart acetone powders. HDL was isolated from rat serum by ultracentrifugation. The assay system contained a phospholipid-stabilized triglyceride emulsion as substrate. The addition of the whole rat serum to the LPL assay system produced high LPL activity. The addition of dialyzed HDL isolated from the same volume of serum produced low LPL activity. The addition of calcium in physiological concentration to the assay containing HDL increased LPL activity markedly. The high enzyme activity produced by both serum and HDL plus calcium was inhibited by ethyleneglycol bis(β-aminoethylether)-N,N'-tetraacetic acid (EGTA), a specific calcium chelating agent. The addition of NH₄⁺ or magnesium at several concentrations did not replace calcium in stimulating LPL activity. We conclude that calcium has a cofactor function in the LPL lipolytic reaction and that the optimal enzyme reaction rate is attained in the presence of calcium concentrations found in serum.

KEY WORDS postheparin lipolytic activity enzyme activation heparin cofactor triglycerides lipoproteins heart rat lipolysis albumin

control, respectively, and heart rate and cardiac output rose 64% and 47%, respectively. After beta-receptor blockade with propranolol, PGA₁ still caused a similar increase in cardiac output. In spite of arterial hypotension, PGA₁ produced a progressive increase in coronary flow, with a peak increase of 74% above control with 1.0 µg/kg and a corresponding graded decrease in coronary resistance, with a decrease of 61% below control with 1.0 µg/kg. Marked increases occurred in systolic as well as diastolic coronary flow. The coronary vasodilation was not abolished by preventing the PGA₁-induced tachycardia with electrical pacing, by beta-receptor blockade, or by combined blockade of beta receptors and cholinergic nerve fibers. While arterial Po₂ remained constant, coronary sinus Po₂ rose when coronary flow was increased by PGA₁. Thus PGA₁ is both a primary and secondary coronary vasodilator which increases cardiac output and decreases total systemic resistance.

KEY WORDS blood pressure coronary flow cardiac output cholinergic blockade beta-receptor blockade heart rate

tall but the initial effects; selective extracerebral decarboxylase inhibition with MK 486 (L-α-hydrazino-α-methyl dopa) prevented the tachycardia but not the hypotension. DL-threo-Dihydroxyphenylserine caused an initial rise in blood pressure in dogs with MAO inhibition, had less pressor activity when peripheral decarboxylase was also inhibited, and in both cases did not cause the hypotension characteristic of L-dopa. L-Dopa enhanced pressor responses and especially associated bradycardic responses to norepinephrine in dogs with MAO inhibition. This action was prevented by all decarboxylase inhibitors but not FLA 63. Responses to angiotensin were similarly augmented. Thus, MAO inhibition enabled L-dopa to induce severe hypotension, which appeared to rely on a central conversion to dopamine; the other effects were probably mediated by peripherally formed dopamine.

KEY WORDS heart rate angiotensin dopamine β-oxidase inhibition blood pressure DL-threo-dihydroxyphenylserine norepinephrine MAO inhibition decarboxylase inhibition

of smooth muscle cells with subsequent myogenic propagation of excitation through the thickness of the vessel wall. The second may be related to the local concentration of norepinephrine in the extracellular space of the vessel.

KEY WORDS nonpropagated response muscular artery diffusion norepinephrine neurogenetic response vasoconstriction sympathetic transmitter propagated response
DNA synthesis and mitotic activity in coronary collateral arterioles was assessed in dogs at different time intervals after gradual ameroid constriction of the left circumflex coronary artery. Labeling of nuclei and the mitotic index were highest at 3 weeks after implantation of the constrictor and gradually declined thereafter. Labeling persisted for at least 8 weeks but radioactive DNA was not found 12 months after coronary artery constriction nor in controls or animals with sham operations. Proliferative activity was, at any time interval, highest at the level of the smallest diameters of the collateral vessels. Labeled nuclei and mitoses were found in endothelial, medial, and adventitial


Excursions of the semiaxes were used to define the distortion and shape of the vessel cross section considered for conic and almost conic models. Some describing functions and mensuration expressions closely approximate, yet greatly simplify, calculations of perimeter and cross sections. Theory and experiments with models were in good agreement, but preliminary experiments showed the real case to be more complicated. Physical properties of the pulmonary trunk varied along its axis, growing stiffer toward the periphery. Furthermore, the dimension variations with transmural loading alter concepts of properties derived from measurements of a single diameter. The influence of


The efficiency of aortic valve closure was studied in five experiments on three normal dogs by simultaneous roentgen videodensitometry, upstream sampling of dye dilution and recording of flow velocity and direction in the ascending aorta using a chronically implanted electromagnetic flowmeter. The aortic valve closed effectively during regular ventricular contractions. However, aortic reflux was observed whenever a weak ventricular contraction produced an opening of the aortic valve that was barely detectable, as evidenced by a minimal aortic pressure pulse and stroke volume. This type of aortic regurgitation was mild and invariably occurred at the end of ventricular ejection, coincident with the
the pericardium on the deformation of the main pulmonary artery under transmural stress was also explored. It was seen that the pericardium exerts significant restraint on the distortion and volume variations of this vessel. Over normal pressure ranges, removal of the pericardium can result in trunk volumes up to 100% greater than realized with the pericardium intact.

**KEY WORDS** pulmonary trunk semiaxes cross-section distortion mensuration inextensional and extensional deformation pericardial restraint

... such regurgitation may be clinically significant in some instances of bigeminal rhythm or rapid atrial fibrillation, and is especially important for the evaluation of aortic angiograms. It further supports the concept that competent aortic valve closure depends on vortex formation in the sinus of Valsalva of sufficient degree to keep the aortic valve leaflets in partial apposition during ejection of blood from the ventricle across the aortic valve.

**KEY WORDS** cardiac arrhythmias and aortic valve closure stroke volume aortic flow and pressure pulses regurgitation across normal aortic valve mechanism of aortic valve closure electromagnetic flowmeter roentgen videodensitometry

cells. Myocardial mesenchymal cells also incorporated tritiated thymidine. The data provide evidence that after constriction of a major coronary artery, the coronary collateral vessels enlarge by an active growth process that follows the basic laws of cell kinetics.

**KEY WORDS** autoradiography DNA synthesis ischemia cell division coronary collateral circulation ameroid constriction vessel wall growth

coefficients were quite small. It was concluded that geometric and elastic inhomogeneities in the thoracic aorta tend to balance one another, keeping the reflection coefficient quite low and helping to “decouple” the oscillatory left ventricular pump from the static peripheral vasculature. Since the aortic pulse contour is reflection-free during the first 50 msec following the onset of ventricular ejection, it may reliably indicate left ventricular properties and their changes with stress. In several animals, norepinephrine infusion was used to elevate the aortic pressure to hypertensive levels. When compared to hypertension induced by carotid reflex stimulation or mechanical occlusion of the aorta, however, aortic wall properties were essentially the same, suggesting that this agent has no important direct effect on the aortic wall.

**KEY WORDS** vascular impedance cats aorta norepinephrine viscoelastic properties of blood vessels biomechanics hypertension
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