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By

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INTRODUCTION

The work supported by this grant constitutes a part of a systematic effort to study the effects of various parameters and properties of the cardiovascular system on the transmission characteristics of sounds and pressure pulses. The transmission and generation of sounds and pulse waves within the circulatory system are phenomena of great importance in the diagnosis of cardiovascular disorders. These phenomena have so far been utilized mostly on an empirical basis since we lack a satisfactory quantitative understanding of the mechanical behavior of the circulatory system. A reliable interpretation of sound generation and wave transmission data calls for mathematical models of the cardiovascular system or components thereof that have been validated by carefully planned experiments. Our principal incentive to study these phenomena from the physical sciences point of view is their potential usefulness in determining the elastic properties of arteries and veins and the changes of these properties under physical and physiological stresses that may for example be produced by trauma, prolonged weightlessness or acceleration. As additional support of our motivation we can state that the proper elastic behavior of blood vessels in situations of stress is essential to maintaining adequate circulation and is governed by intricate control mechanisms that are not yet fully understood.

GOALS OF PROJECT

1. A better understanding of the mechanical behavior of the circulatory system and its control mechanisms.
2. Development of methods of measuring the changes in the elastic properties of blood vessels in man that do not require the penetration of the skin.

PERSONNEL ASSOCIATED WITH RESEARCH PROJECTS SUPPORTED BY GRANT NGR 05-020-223

Dr. Max Anliker, Principal Investigator	40% time charged to Grant
Dr. Leo Sapirstein, Professor of Physiology and Radiology, School of Medicine, Stanford University, Faculty Associate	5% time charged to Grant
Dr. I-Dee Chang, Associate Professor of Aeronautics and Astronautics, Stanford University, Faculty Associate	25% time charged to Grant
Dr. James A. Maxwell, Part-time Research Associate	No charge to Grant
Mr. W. Astleford, Ph.D. student in Aeronautics and Astronautics, Stanford University, Research Assistant	50% time charged to Grant
Mr. John Bailie, Ph.D. candidate, Department of Aeronautics and Astronautics, Stanford University, Research Assistant	No charge to Grant
Mr. Michael B. Histand, Ph.D. candidate, Department of Aeronautics and Astronautics, Stanford University, Trainee	100% time, no charge to Grant (supported through NSF Training Grant)
Mr. Everett Jones, Ph.D. candidate, Department of Aeronautics and Astronautics, Stanford University, Research Assistant	50% time charged to Grant
Mr. Lane L. Loyko, graduate student, Department of Aeronautics and Astronautics, Stanford University, Laboratory Assistant	50% time charged to Grant
Mr. William Moritz, Ph.D. candidate, Department of Aeronautics and Astronautics, Stanford University, Trainee	100% time, no charge to Grant (supported through NASA Training Grant)
Mr. Robert L. Rockwell, Ph.D. candidate, Department of Aeronautics and Astronautics, Stanford University, Fellow	100% time, no charge to Grant (supported through Fellowship from USN)
Mr. Michael Wells, Ph.D. candidate, Department of Aeronautics and Astronautics, Stanford University, Research Assistant	100% time, 1 month, charged to Grant
Mr. Dean C. Winter, graduate student, Department of Aeronautics and Astronautics, Stanford University, Laboratory Assistant	50% time charged to Grant
Mr. William G. Yates, Ph.D. candidate, Department of Physiology, Stanford University, Fellow	100% time, no charge to Grant (supported through NIH Fellowship)
Dr. Eric Ogden, Grant Monitor, Consultant and Collaborator, Environmental Biology Division, Ames Research Center	No charge to Grant (NASA employee)
Mr. Leonard Chan, Bio Lab Technician, Physiology Branch, Ames Research Center	No charge to Grant (NASA employee)

A. THEORETICAL INVESTIGATIONS

A-1. The second part of Mr. Maxwell's Ph.D. dissertation "Dispersion and Dissipation of Waves in Blood Vessels" has been rewritten for publication under the title "The Dissipation and Dispersion of Small Waves in Arteries and Veins with Viscoelastic Wall Properties." The final form of the manuscript will be available early in January 1968. Dr. Maxwell presented a concise description of our findings at the 20th Annual Conference on Engineering in Medicine and Biology in Boston on November 13, 1967. A reprint of this paper as it appeared in the Proceedings of the Conference is given as Appendix I.

A-2. To investigate the effects of blood viscosity on the dispersion and dissipation of waves in arteries and veins, an extensive parametric study has been carried out. A linearized analysis of pressure waves in a cylindrical vessel that contains a viscous fluid and whose wall is thin and isotropically elastic indicates that there are two families of axisymmetric waves--a family of slow waves and one of fast waves. The family of slow waves has been studied earlier by Womersley and others, while the fast waves have only recently been examined theoretically to some extent by Atabek and Lew. Limited experimental evidence of the existence of the two families was given by Van Citters.

This analysis shows that the faster waves are more sensitive to variations in the elastic properties of the medium surrounding the blood vessels and to changes in the wall thickness to radius ratio. At high Reynolds numbers the attenuation due to fluid viscosity over a fixed length is found to be substantially greater for the fast waves than for the slow waves. At very low Reynolds numbers the effects of attenuation are reversed--that is, the family of slow waves is much more strongly attenuated than the family of fast waves.

The radial displacements are generally much larger for the slow waves than for the fast waves, while conversely the axial displacements are much larger for the faster waves than for the slow waves. For the family of slow waves the axial wall displacements are larger than the radial displacements for sufficiently low frequencies. The presence of external constraints modifies these results.

For the slow waves the phase angle between pressure and radial wall displacement is virtually negligible for mild external constraints, while the phase angles between pressure and fluid velocity are at most 45°. The corresponding phase angles for the fast waves exhibit much larger variations with changes in the elastic properties of the surrounding medium.

The analysis was modified to include the effects of a viscoelastic wall for physiologically meaningful parameter values and high frequencies. The results show that the damping due to viscosity is much less than than due to the viscoelasticity of the wall material for both families of waves. Comparing our tneoretical predictions with extrapolated experimental evidence obtained in our laboratory, we find that the attenuation parameter due to the viscoelasticity of the wall is approximately twice that reported by Bergel for frequencies below 15 cycles per second and agrees within limits with the data quoted by McDonald and Gessner.

A-3. To study the influence of the vascular bedding on the elastic behavior of blood vessels we have formulated the equations of motion for axisymmetric waves in a fluid-filled cylindrical shell that is surrounded by a thick elastic continuum. A digital computer program for the determination of the dispersion curves corresponding to various levels of axial stretch and transmural pressure is currently being modified. It was found that the subroutines for the Bessel functions and modified Bessel functions initially utilized in the program are not sufficiently accurate and have to be replaced by improved routines.

A-4. Under certain conditions it must be expected that veins are not fully extended but partially collapsed. We are therefore analyzing the wave transmission properties of fluid-filled tubes with elliptic cross-sections. We also are attempting to obtain stability criteria of such vessels. The equations governing the propagation of small pressure waves have been formulated and a digital computer program has been developed which is presently being checked for errors and accuracy.

A-5. In view of the fact that arteries have a wall thickness to radius ratio of the order of 1 to 5, they can not necessarily be expected to behave mechanically as thin-walled shells. We are therefore studying the effects of wall thickness on the dispersion of pressure waves in arteries by treating the vessel wall as a thick elastic continuum.

A-6. Earlier studies of the phenomenon of Korotkoff sounds at diastole have been extended. It has been shown that propagating disturbances are amplified as they pass through the segment of the brachial artery that is affected by the cuff; this constitutes a theoretical verification of the mechanism of Korotkoff sound generation originally postulated in a recent paper by Anliker and Raman. We are now also investigating the phenomenon of Korotkoff sounds at systolic and intermediate pressure levels.

B. EXPERIMENTAL INVESTIGATIONS

B-1. During the past two years Drs. Anliker and Ogden have developed two new techniques for determining rapid distensibility changes in arteries, veins and the ventricular cavities under in-vivo conditions. Both methods involve the generation of small but accurately controlled sinusoidal pressure perturbations and either the determination of their propagation characteristics or their relationship to volumetric changes. The frequency of these pressure signals, induced by means of an electrically driven piston or a sinusoidal pump, ranges from 10 to 200 cps. Results obtained so far on the aorta and vena cava of anesthetized dogs exhibit a strong pressure dependence of the distensibility and the elastic parameters of the wall and further indicate that the attenuation per wave length is essentially independent of frequency between 20 and 200 cps. It is also shown that the distensibility of the left ventricle of dogs with open chests varies during the cardiac cycle by as much as an order of magnitude and that the effective Young's modulus of the ventricular wall may exceed 10^7 dynes/cm^2 during systole.

The results that demonstrate the nonlinear character of the elastic behavior of blood vessels have been reported by Drs. Anliker and Ogden in an invited paper at the 7th International Conference on Medical and Biological Engineering in Stockholm, Sweden, on August 15, 1967. A reprint of the summary as it appeared in the Digest of the Conference is attached as Appendix II.

In response to an invitation, Dr. Anliker has presented a comprehensive paper on these two techniques at the 20th Annual Conference on Engineering in Medicine and Biology at Boston, November 13-16, 1967. A copy of the summary as it appeared in the Proceedings of the Conference is attached as Appendix III.

B-2. Artificial heart sounds of controlled frequency have been induced by placing the electrically-driven piston mentioned under B-1 into the left or right ventricle of anesthetized dogs with open chests. The sinusoidal pressure fluctuations or artificial heart sounds produced by the piston are being propagated into blood vessels leading to and from the heart in the same manner as the natural pulses generated by the heart. We have therefore utilized these signals to determine the distensibility of the ascending aorta and the aortic arch. A paper describing the technique and the initial results has been presented at the 40th Scientific Sessions of the Annual Meeting of the American Heart Association in San Francisco, California, October 20-22, 1967. A copy of the summary as it was printed in Supplement II to Circulation is attached as Appendix IV.

B-3. Since our direct measurements of the distensibility of heart cavities required the emplacement of highly sensitive catheter-tip manometers in the ventricles, we were able to record the naturally-occurring heart sounds as well as artificially induced pressure signals. By utilizing electronic band-pass filters we obtained the frequency spectra of the first and second heart sounds. We have only recently begun compiling these data and shall present the results in a detailed report.

B-4. In an attempt to interrelate the tilt-table tolerance with the distensibility of veins in the lower part of the body, we have measured the speed of artificially induced pressure waves in the abdominal vena cava of anesthetized dogs at various pressure levels and at various time instances. The transmural pressure in the vena cava was systematically varied with the aid of a tilt table and waves were generated by means of a hydraulic pump, an electrically-driven piston or a spring-loaded syringe. The wave speed at first generally increases markedly with increasing pressure indicating a sizable reduction of the distensibility or a substantial increase in the effective Young's modulus of the vena cava wall. The increase in Young's modulus with pressure can be attributed to a combination of active and passive mechanisms. This is substantiated to some extent by the fact that after a prolonged exposure of the vena cava to higher pressure levels the distensibility may substantially increase with increasing pressure, thus suggesting a loss of the ability of the vena cava to adapt to higher pressures. This reversal in the response of the vessel wall to a rise in pressure is particularly pronounced at high angles of tilt. Judging from our experimental results this reversed behavior may serve as an indication of an increase of venous pooling leading to a cardiovascular collapse.

To substantiate the observed indication of venous pooling we are now conducting a series of tilt-table tolerance experiments with anesthetized dogs in which the diameter of the vena cava is continuously measured with the aid of a Pieper gauge. The sensitivity of this transducer allows for the detection of the diameter changes induced by small pressure waves as well as those associated with changes in the mean transmural pressure. Earlier attempts to measure the external vena cava diameter by means of a mercury-filled Sylastic tube were discontinued due to experimental difficulties encountered with the calibration of changes in the vessel circumference and due to excessive distortions of the vessel caused by the stiffness of the strain gauge. The Young's modulus of the vena cava has been computed from the wave speed and from the diameter change produced by a large pressure pulse. The corresponding values ranged from 3 to 4 x 10^6 dynes/cm^2, and in general they differed by less than 20 per cent.

The increase in wave speed with inspiration reported earlier and interpreted initially as a change in distensibility with respiration has been investigated in greater detail. Measurements of the dynamic pressure in the abdominal vena cava reveal high levels (up to 100 cm/sec) of flow during inspiration. Theoretical studies on the effect of a mean flow on the velocity of pressure waves have shown that the wave speed increases by approximately the value of the flow velocity. In the light of these findings the changes in wave speed with respiration can no longer be attributed exclusively to variations in the distensibility of the vena cava with respiration, but appear to be primarily associated with changes in flow. (It may be interesting to note that mean flow velocities up to 80 cm/sec were also observed in the human inferior vena cava by Dr. Bergel at the Hammersmith Postgraduate Medical Center in England, according to an oral communication from Dr. Bergel.)

B-5. Aiming for an understanding of the control mechanisms governing the systemic circulation, we are conducting measurements of the rapid changes in the distensibility of the vena cava in anesthetized dogs produced by means of chemical, nervous and physical stimulation. Since these changes in distensibility must be interpreted as the result of a combination of active and passive responses of the vena cava wall, we have initiated systematic experiments that should hopefully permit a distinction between an active and passive response of the vessel wall. It was found that: (1) the velocity of pressure waves depends strongly on the wave amplitude; (2) the phase velocity of small pressure signals increases by 100 per cent or more when the animal is sacrificed by intravenous injection of saturated potassium chloride solution. The phase velocity of small sinusoidal wave trains in the abdominal vena cava increases 10 to 20 per cent when the right vagus nerve is stimulated for 10 to 20 seconds at the carotid level (heart and breathing stop). The maximum phase velocity usually occurs near the end of vagal stimulation, and then it decreases and reaches control levels about 10 seconds after termination of vagal stimulation. After injection of atropine sulphate the increasesin phase velocity induced by vagal stimulation diminish with increased amounts of the drug. After application of 2 or 4 per cent xylocaine to the abdominal vena cava wall, we still observe a typical 10 to 20 per cent increase in the phase velocity of small sine waves during right vagal stimulation.

B-6. So far all experimental work on wave transmission has been restricted to axisymmetric radial waves (waves of type I) which have associated with themselves strong transmural pressure fluctuations. The results of these experiments do not permit a full verification of any of the mathematical models postulated in recent work. To allow for an incisive indication as to the most appropriate mathematical model for the mechanical behavior of blood vessels, we have embarked on a new experimental program aiming at the determination of the wave transmission characteristics of axial and torsion waves in arteries and veins. The dispersion, mode shapes and attenuation of these waves are measured with the aid of an electro-optical tracking system that has been purchased with funds provided under this grant and that is capable of sensing biaxial displacements of less than 10 microinches 2,500 Å for frequencies up to 200 cycles per second. Axial waves have been generated in the carotid arteries of anesthetized dogs with the help of a collar attached to the vessel and an electrically-driven vibrator. As in the case of the artificially induced pressure waves described under B-1, the device allows for the generation of finite trains of sine waves of a torsional and axial nature with variable frequency and amplitude. A paper describing the method of approach and initial results has been accepted for presentation at the Spring Annual Meeting of the American Society for Experimental Stress Analysis, May 7-10, 1968, in Albany, New York, on the basis of the abstract given as Appendix V.

B-7. The concept of an elasto-optical pressure transducer utilizing fiber optics has been further substantiated with the help of the Instrumentation Division. Pilot tests on such manometers indicate a satisfactory repeatability and a sensitivity of up to 2 mV/mm Hg.

ACKNOWLEDGMENT

The team gratefully acknowledges the help it received from the Instrumentation Division of the Ames Research Center. It also wishes to thank Dr. Oyama, Chief of the Physiology Branch, for providing laboratory space and administrative support.

PUBLICATIONS SINCE JULY 1, 1967

"Effects of Pressure on Dispersion and Attenuation of Waves in the Aorta," by Max Anliker and Eric Ogden, Digest of 7th International Conference on Medical and Biological Engineering, Stockholm, Sweden, August 14-19, 1967, p. 149.

"Intravascular Transmission Characteristics of Artificially Induced Heart Sounds," by Max Anliker and Eric Ogden, Circulation, Vol. XXXVI, No. 4, Supplement No. II, October 1967, pp. 254-55.

"The Dissipation and Dispersion of Waves in Large Arteries and Veins With Visco-elastic Wall Properties," by James A. Maxwell and Max Anliker, Proceedings of the Conference on Engineering in Medicine and Biology, 20th Annual Meeting, Boston, Massachusetts, Nov. 13-16, 1967, p. 6.1.

"New Techniques for the Study of the Elastic Behavior of the Heart and Large Arteries and Veins," by Max Anliker, Eric Ogden and William J. Astleford, Proceedings of the Conference on Engineering in Medicine and Biology, 20th Annual Meeting, Boston, Massachusetts, Nov. 13-16, 1967, p. 11.2.

PAPERS ACCEPTED FOR PRESENTATION

"Transmission Characteristics of Axial Waves in Blood Vessels," by Max Anliker, William E. Moritz and Eric Ogden, to be presented at the Meeting of the Society for Experimental Stress Analysis in Albany, New York, May 7-10, 1968.

The Dissipation and Dispersion of Waves in Large Arteries and Veins with Viscoelastic Wall Properties

20th Annual Conference on
Engineering in Medicine and Biology
November 13, 14, 15, 16, 1967
Statler-Hilton Hotel, Boston, Mass.

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The dissipation of waves in blood vessels can be attributed to three main causes: viscosity of the blood, viscoelastic behavior of the vessel wall, and radiation of energy into the surrounding medium. The combined effect of these dissipative mechanisms has been assessed in the past by means of an indirect technique making use of simultaneous recordings of the natural pulse wave at various points along the aorta and other arteries of anesthetized dogs. 1) It has also been measured directly by a recently developed method based on artificially induced perturbations, in the form of trains of sinusoidal pressure waves. This direct technique has been applied to large arteries and veins of anesthetized dogs. 2) The results obtained with this method reveal a strong frequency dependence of the dissipation per cm at frequencies between 12 and 200 cps, while the dissipation per wave length is essentially independent of frequency within this range. The dissipation per cm of these sine waves exceeds by far the value that could be attributed to the viscosity of the blood alone. Considering in addition that the dissipation of waves is essentially the same when the vessels are partially exposed, we conclude that at higher frequencies the primary cause for the attenuation must be the viscoelastic behavior of the vessel walls.

Therefore, in this theoretical investigation we neglect effects of blood viscosity and of the surrounding medium. Besides this, we assume the vessels to behave like thin-walled circular cylindrical shells whose walls have isotropic and homogeneous viscoelastic properties. The perturbations are described by small three-dimensional sinusoidal displacements of the middle surface of the shell measured from an equilibrium configuration which is defined by a mean transmural pressure and an initial axial strain. The fluid motion associated with the waves is considered as irrotational, and the linearized differential equations of motion are based on the shell equations derived by Flügge.

In addition to axisymmetric waves we include in our consideration waves which exhibit a circumferential dependence of the corresponding displacements of the vessel wall. For each circumferential wave number we find infinitely many waves with individual speeds of propagation, of which only the three slowest waves are not due to the compressibility of the fluid. In this study we disregard all but the three slowest waves, and denote these as waves of type I, II and III. In waves of type I the radial displacement component is dominant at high frequencies, while in waves of type II the circumferential and in waves of type III the axial displacement component dominate at high frequencies. Of these three types of waves, those of type II and III are less important from the practical point of view, since only type I waves are associated with significant internal pressure fluctuations.

Several mathematical models have been postulated in the literature which take into consideration the viscosity of the fluid and the viscoelastic properties of the vessel wall, but largely adhere to a membrane analysis, and exclusively consider only axisymmetric waves of type I. Also, these models have neglected the presence of an axial stretch and a transmural pressure, both of which play a significant role.

The results of our parametric analysis indicate that in the limiting case of an elastic model for the vessel wall the axisymmetric waves are only mildly dispersive, while the non-axisymmetric waves are highly dispersive and exhibit cut-off phenomena. Also, the transmural pressure and the initial axial stretch can have a marked effect on phase velocities, mode shapes and cut-off frequencies of waves of all three types.

The viscoelastic properties of the vessel wall are treated by assuming that the wall material is incompressible but behaves as a Voigt solid in shear. Using such a viscoelastic model it is found that the theoretically predicted decrease in wave amplitude per wave length is essentially independent of frequency over a wide range of high frequencies. This result is in qualitative agreement with recent experiments on the dissipation of high frequency waves in the thoracic aorta of anesthetized dogs. 2) Axisymmetric waves of type II and type III exhibit stronger dispersion as compared with the elastic case, while those of type I remain only slightly dispersive. In contrast to the elastic case, non-axisymmetric waves are propagated at all frequencies, although the damping per wave length of such waves is very strong at frequencies below the elastic cut-off point. For a viscoelastic wall behavior the dissipation exhibits a high sensitivity to changes in the transmural pressure and initial axial stretch. Consequently, the reliable estimation of the viscoelastic parameters of the vessel wall from experiments involving high frequency wave propagation should take into consideration the effects of axial stretch and transmural pressure.

References:

1. D. A. McDonald and Urs Gessner, "Wave Attenuation in Viscoelastic Arteries," Proc. First Intl. Conf. on Hemorheology, Pergamon Press, Oxford, 1966.

2. Max Anliker, M. Histand, E. Ogden and R. M. Westbrook, "Direct Measurement of Dissipation of Waves in Arteries and Veins," Proc. 19th Annual Conf. on Engineering in Medicine and Biology, Vol. 8, 1966.

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8–3 Effects of Pressure on Dispersion and Attenuation of Waves in the Aorta

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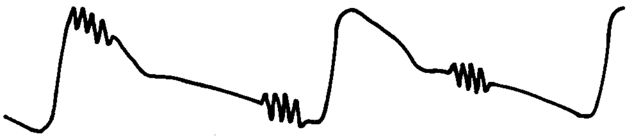
The study of the mechanical properties of blood vessels in vivo by examining wave transmission has been attempted for 50 years with limited success. Most of the data available in the literature on the dispersion and attenuation of pressure waves in arteries are restricted to frequencies below 20 cps and are obtained from recordings of the natural pulse wave of anesthetized dogs. As such, the data are based on the assumption that the propagation of the pressure pulses generated by the heart is governed by linear laws that allow a harmonic analysis. While the presence of reflected waves has been taken into consideration (1), this was done by assuming that the outgoing wave and the reflected wave are propagated at the same speed. A recently developed method, described in part in reference (2), has made it possible to extend the frequency range to 200 cps. More significantly, it avoids the need for the assumption of linearity and for the laborious computations associated with a harmonic analysis of pressure recordings. This method is based on pressure signals of the form of short trains of sine waves that are superimposed on the natural pulse wave as illustrated in Figure 1.



The sine waves are generated by an electrically driven impactor placed over the artery and producing small indentations of the vessel. For sufficiently high frequencies and short trains the effects of reflections can be completely disregarded because the transient signals are recorded before their reflections arrive at the sites of the pressure transducers. For mildly dispersive media, the velocities of such signals are good approximations to the corresponding phase velocities. This follows from the Fourier spectrum of a finite train of sine waves, which is dominated by the frequency of the sine wave in increasing proportion to the length of the train.

The pulse wave and signals are recorded with the aid of Bytrex Model HD5 pressure cells which have been adapted for use as catheter-tip manometers. While the wave generator was emplaced in the upper segment of the thoracic aorta of an anesthetized dog, a Bytrex pressure cell was inserted through each of the femoral arteries. By placing one of the Bytrex transducers a few cm distal of the impactor, and the other at various points farther downstream, one can observe directly the speed and attenuation of the sinusoidal pressure signals as a function of distance. The location of the catheter-tip manometers was determined with a fluoroscope and the distances between them ranged from 2 cm to 15 cm. To allow for the continuous calibration of the catheter-tip manometers, the cannula of a Statham transducer was inserted through one of the carotid arteries into the aorta. Since the indentations of the aorta produced by the impactor are not axisymmetric, it is to be expected that the ensuing pressure fluctuations have non-axisymmetric components. However, such components were observed only within a distance of less than 6 cm from the wave generator, where the pressure records exhibited a variation of the signal amplitude with position of the pressure cell in relation to the cross-section. From the fact that at distances greater than 6 cm from the impactor no such variation was noticed, one concludes that for frequencies ranging from 50 to 200 cps the non-axisymmetric pressure waves must be strongly damped if they are being propagated (3).

The results of experiments conducted on several dogs anesthetized with Nembutal indicate that pressure waves with frequencies from 50 to 200 cps and amplitudes of the order of 5 mm Hg exhibit phase velocities that are about 20 to 30% higher at systolic pressures than at diastolic pressures. The attenuation of these waves does not show such a marked variation with pressure. The observed changes during the cardiac cycle may be directly due to the variations in pressure or to an active response by the tissue. The present technique facilitates more refined studies of variations in vessel properties.

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1. McDonald, D. A. and Gessner, Urs, "Wave Attenuation in Viscoelastic Arteries," Proc. First Intl. Conf. on Hemorheology, Pergamon Press, Oxford 1966.

2. Max Anliker, M. Histand, E. Ogden and R. M. Westbrook, "Direct Measurement of Dissipation of Waves in Arteries and Veins," Proc. 19th Annual Conf. on Engineering in Medicine and Biology, Vol. 8, 1966.

3. Max Anliker and J. A. Maxwell, "The Dispersion of Waves in Blood Vessels," Proc. of a Symposium on Biomechanics, sponsored by the Applied Mechanics Div. of ASME, Nov. 1966.

*Hemodynamics
A.M., Tuesday
14 November

New Techniques for the Study of the Elastic Behavior of the Heart and Large Arteries and Veins

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Engineering in Medicine and Biology
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The distensibility of any blood vessel is defined by its geometry and the elastic behavior of the vessel wall. Under in-vivo conditions the distensibility is in general a dynamic variable. Rapid fluctuations in its value are shown to follow nervous and humoral stimuli and changes in pressure or geometry. In the case of the ventricles of the heart the distensibility can be expected to undergo not only fast but also large fluctuations during each heartbeat, considering the sizable geometric changes and the likely variations in the elastic properties of the ventricular walls with each phase of the cardiac cycle. Therefore the distensibility of blood vessels should be determined by a technique that yields essentially instantaneous values. Guided by theoretical considerations, two such techniques have been developed and employed in the measurement of the elastic parameters of arteries, veins and the heart. Both methods involve the generation of small, but accurately controlled sinusoidal pressure perturbations and either the determination of their propagation characteristics or their relationship to volumetric changes. These methods are an improvement on earlier techniques.[1)2)]

Sinusoidal pressure signals with frequencies ranging from 10 to 200 cps are induced by means of an electrically driven piston or a sinusoidal pump. For the generation of very low frequency pressure fluctuations a cannula from the sinusoidal pump is inserted through a major branch into the artery or vein of interest or into the ventricle. For higher frequency pressure signals a vibrating piston is placed over the vessel of interest in the case of arteries, inserted into a major branch in the case of veins and emplaced in the ventricle in the case of the heart. The artificial pressure perturbations induced by the pump or piston are recorded with the aid of Bytrex manometers adapted for physiological use as catheter-tip manometers or capacitance-type pressure transducers recently developed by the Ames Research Center. Since both types of transducers are capable of resolving pressure fluctuations of less than 1 mm Hg within the frequency range of interest, the amplitudes of the artificial pressure signals can be made sufficiently small to justify the interpretation of the experimental results on the basis of a linear theoretical analysis. Also, by generating sufficiently short trains of sine waves in arteries and veins by gating the pump or vibrating piston, it is possible to eliminate the effects of reflection interferences at higher frequencies. Besides this, for mildly dispersive media the signal speeds are close approximations of the phase velocities corresponding to the frequencies of the sine waves; this eliminates the need for Fourier transform computations of the pressure recordings.

Initial results obtained on the aorta of anesthetized dogs have been reported earlier.[3)4)] For the sake of clarity it should be mentioned that these results were obtained with pressure waves induced by placing the piston over the vessel in such a manner as to produce small indentations of its wall. Even though such displacements lead to pressure fluctuations that have non-axisymmetric components whose propagation characteristics are vastly different from the axisymmetric disturbances,[5)] these seem to be completely attenuated within a distance of a few vessel radii from the wave generator. Results obtained so far on the aorta and the vena cava exhibit a strong pressure dependence of the distensibility and the elastic parameters of the wall and indicate that the attenuation per wave length is essentially independent of frequency between 20 and 200 cps. Considering that within the pressure changes induced by the cardiac cycle the wave speeds can vary by more than 30%, the aorta does not behave like a linear system and results derived from a harmonic analysis of the natural pulse wave are doubtful.

Earlier attempts made in our laboratory to determine the distensibility of ventricles by measuring the pressure changes generated by rapidly injecting into the left ventricle of anesthetized dogs with open chests a known volume of saline or blood from a spring-loaded syringe did not lead to well-defined results that could be repeated to a satisfactory degree. However, by inserting the vibrating piston through the atrium into the left ventricle, it is possible to produce controlled sinusoidal pressure perturbations of less than 10 mm Hg amplitude that can be related directly to the volumetric displacements generated by the piston. For a given ventricular configuration and assuming a linear elastic behavior with respect to these small pressure fluctuations, we can interpret them as direct measures of an effective Young's modulus of the ventricular walls. Our results indicate that the distensibility of the left ventricle can vary during the cardiac cycle by an order of magnitude. Specifically we find through simple theoretical considerations that the effective Young's modulus of the ventricular wall is less than 10^6 dynes/cm^2 during diastole when the filling pressure is low. At filling pressures of about 15 mm Hg it may be of the order of 2×10^6 dynes/cm^2 and finally, if resonance phenomena can be ruled out, it increases with cardiac contraction and may reach a level of more than 10^7 dynes/cm^2. The pressure fluctuations produced by the piston are propagated into blood vessels leading to and from the heart and can therefore be used to determine the distensibility of the pulmonary artery, the ascending aorta and the aortic arch.

Note: Funded by NASA Research Grant NGR 05-020-223.

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4) M. Anliker and E. Ogden, Proc. 7th Intl. Conf. on Medical and Biol. Engr., Stockholm, 1967, p. 149.
5) M. Anliker and J. A. Maxwell, Proc. of ASME Symposium on Biomechanics, Nov. 1966, pp. 47-67.

INTRAVASCULAR TRANSMISSION CHARACTERISTICS OF ARTIFICIALLY INDUCED HEART SOUNDS

by

Max Anliker*) and Eric Ogden**)

ABSTRACT

Artificial heart sounds of controlled frequency have been induced by placing an electrically driven piston into the left or right ventricle of anesthetized dogs with open chests. The piston, or vibrator, consists of a lightweight rod attached to the core of a solenoid driven harmonically by an electronic oscillator via a high-fidelity amplifier. It was inserted through the atrium and located with the aid of an X-ray fluoroscope. The amplitudes of the volumetric displacements enforced by the piston were less than 0.05 ml, and the frequencies ranged from 30 to 200 cycle/sec. To allow for a decisive identification of the sounds, the oscillator was "gated" by means of a tone-burst generator which gave the sounds the form of finite trains of sine waves. The corresponding pressure waves were recorded by means of pressure cells adapted for use as catheter-tip manometers. These transducers were placed in the ventricles and at various points of the vena cava, the ascending aorta, the aortic arch, and the descending aorta. The amplitudes of the sounds varied with ventricular pressure and cardiac cycle, but were generally comparable with those of the natural heart sounds. To increase the resolution of the transducers, their signals were conditioned with the aid of bandpass filters. For known relative locations of the manometers, the speed and attenuation of the sound waves were determined. The average speed from the aortic valves to the left subclavian branch was approximately 400 cm/sec.

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APPENDIX V

TRANSMISSION CHARACTERISTICS OF AXIAL WAVES IN BLOOD VESSELS

by

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ABSTRACT

The transmission velocity of the natural pulse wave in an artery has been used in the past as an approximate measure of the elasticity of the artery. The effective Young's modulus of the vessel wall can be estimated with the aid of the Moens-Korteweg equation if the wave speed, radius of the vessel, wall thickness and blood density are known.

The Moens-Korteweg equation is based on an extremely simple mathematical model of the elastic behavior of blood vessels. More advanced models have been introduced recently that include the effects of axial stretch, transmural pressure, viscosity and compressibility of the blood and assume the wall material to be viscoelastic. By allowing for wall displacements in the axial and circumferential directions, in addition to the radial direction, it was shown that there exist basically three types of waves.[1)] These waves are distinguished by the dominant component of the wall displacement at high frequencies. We denote as waves of type I those in which the radial component dominates, while in waves of type II and III the circumferential and axial components, respectively, dominate.

So far all experimental studies of wave transmission in blood vessels have been restricted to waves of type I which have associated with themselves strong transmural pressure fluctuations. The results of these experiments do not, therefore, permit a full verification of any of the mathematical models postulated in recent work. For a thorough evaluation of these models it is necessary to measure also the transmission characteristics of waves of type II and III.

To this end, a series of experiments have been devised to determine the dispersion and attenuation of waves of type III in the carotid arteries of anesthetized dogs. Transient signals in the form of finite trains of sine waves are generated with the aid of a vibrating collar. The wall displacements associated with these artificially induced waves are then recorded by means of an electro-optical tracking system whose resolution is of the order of 1000 Å.

Reference

1) Maxwell, James A. and Anliker, Max, Dispersion and Dissipation of Waves in Blood Vessels, SUDAAR Report No. 312, Stanford University, May 1967.

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