STANFORD UNIVERSITY
ENGINEERING IN MEDICINE AND BIOLOGY

EXPERIMENTAL STUDIES OF THE VARIATIONS IN THE MECHANICAL PROPERTIES OF THE CANINE ABDOMINAL VENA CAVA

PH. D. DISSERTATION

BY

WILLIAM G. YATES

BIOMECHANICS LABORATORY

DEPARTMENT OF AERONAUTICS AND ASTRONAUTICS

NOVEMBER 1969

This work was carried out at the Ames Research Center of NASA under a collaborative research arrangement with Stanford University (NASA Grant NGR 05-020-223) and was supported in part by NIH Predoctoral Fellowship F1-GM-25,574.

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Department of Aeronautics and Astronautics
Stanford University
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This work was carried out at the Ames Research Center of NASA under a collaborative research arrangement with Stanford University (NASA Grant NGR 05-020-223) and was supported in part by NIH Predoctoral Fellowship F1-GM-25,574. Dr. Eric Ogden of the Ames Research Center has been closely associated with this research work and has made many valuable suggestions; Mr. Leonard Q. Chan has assisted ably in the laboratory; and fellow students in the Stanford Biomechanics Group have provided an intellectually stimulating environment. Miss Kathleen Hunt has typed the final manuscript.

ABSTRACT

The objective of this work was to acquire quantitative data which will aid the development of a mathematical model for the mechanical behavior of large veins, including the associated control mechanisms.

Techniques for assessing the mechanical properties of blood vessels have been the subject of intensive study for many years. Much attention has been given to the evaluation of elastic and viscoelastic properties of large vessels from their wave transmission characteristics. If an appropriate mathematical model for the mechanical behavior of a blood vessel is available, the mechanical properties of its wall can be determined from the vessel geometry and the manner in which waves are propagated by the vessel. The speed of waves traveling in a vessel, the dependence of this speed on wave frequency, and the wave attenuation with distance are all important transmission characteristics.

A method for determining the speed and attenuation of artificially-induced pressure waves propagating in the abdominal vena cavae of anesthetized dogs is described. Short trains of small-amplitude, sinusoidal pressure waves are generated by a vibrating piston placed in the left common iliac vein. The volumetric displacements generated by the piston movement create small pressure waves which propagate into the vena cava. The amplitude and frequency of the piston movement can be accurately controlled. Two catheter-tip manometers, which are placed a few centimeters apart in the segment of abdominal vena cava between the bifurcation and the renal branches, detect the propagating pressure waves; the outputs from the manometers are amplified and recorded on a high-speed oscillograph. The wave speed is calculated by dividing the distance between the catheter-tip manometers by the time required for a particular wave to travel from one manometer to the other. The attenuation is obtained by

comparing the wave amplitudes recorded by the two transducers.

The wave speeds in the abdominal vena cava were found to range from 100 to 350 cm/sec for wave frequencies from 20 to 110 Hz. There were relatively small changes in wave speed with frequency. Therefore, the vena cava can be described as being mildly dispersive. The wave amplitudes were attenuated exponentially with distance traveled, and the attenuation per wave length was independent of frequency from 20 to 110 Hz. Values of the logarithmic decrement for amplitude decay ranged from 0.6 to 3.3.

The wave speed was found to increase markedly with increasing venous pressure. A catheter-tip balloon was placed in the inferior vena cava just caudal to the heart; when it was inflated, the venous pressure increased from control values of about 100 mm H_2O to a level between 200 and 300 mm H_2O within 10 to 20 seconds. Values of $\Delta c/\Delta P_V$, the change in wave speed c resulting from a change in venous pressure P_V, were between 1 and 5 cm/sec/mm H_2O.

Transmural pressure versus diameter relationships (P_T versus D) for the vena cava were determined during the balloon inflations. The internal diameter of the vessel was measured by a Pieper catheter-tip gage.

Values for the effective Young's modulus E of the vessel wall were calculated utilizing the Moens-Korteweg equation, the wave speed, and the vessel geometry and were plotted as a function of the circumferential stress σ. E versus σ curves were obtained during the balloon inflations and show that E can increase from about 1×10^6 dynes/cm^2 at $\sigma = 2 \times 10^5$ dynes/cm^2 to as much as 200×10^6 dynes/cm^2 at $\sigma = 12 \times 10^5$ dynes/cm^2.

Active changes in the mechanical behavior of the abdominal vena

cava produced by greater splanchnic nerve stimulation and by epinephrine injection (0.5-30 μg/kg) were demonstrated by changes in the P_T versus D and E versus σ relationships induced by these stimuli. Particularly for $\sigma > 8 \times 10^5$ dynes/cm^2, the E values were less in the stimulated cases than for the controls.

Diameter, wall thickness, and in situ strain for the abdominal vena cavae of 16 dogs are included.

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CHAPTER 1

GENERAL INTRODUCTION

"Always both the stimulus and the goal of this effort have been the same: to find what verifiable and agreed-upon factors determine the normal activity or malfunction of the system, so that human cardiovascular disease can be understood and handled, and perhaps prevented." These words of Chauncey D. Leake[1] describing the historical development of cardiovascular physiology provide a meaningful introduction to the work described herein.

Methods for ascertaining the mechanical properties of blood vessels have been the subject of intensive study for years. This interest is a result of desires to understand normal cardiovascular function, including the control mechanisms involved in maintaining and regulating circulation, as well as to understand circulatory changes occurring with age and as a result of disease. The determination of mechanical properties of living tissue such as blood vessels can be complicated by relatively rapid changes in mechanical behavior mediated by neural or humoral stimuli. Thus for accurate evaluation of in vivo mechanical properties it is advisable to utilize methods which provide nearly instantaneous data.

Evaluating the elastic and viscoelastic properties of large blood vessels from their wave transmission characteristics has received significant attention. Comprehensive reviews of theoretical and experimental investigations of wave transmission in blood vessels and general hemodynamic problems have been made by McDonald[2,7], Fox and Saibel[3], Rudinger[4], Skalak[5], Fung[6] and Cox[8]. Significant theoretical contributions have been made by Iberall[9], Morgan and Kiely[10], Womersley[11], Hardung[12], Klip[13], and many other investigators.

The work described here is part of a systematic theoretical[14-18] and experimental[17, 19, 20] study of the transmission characteristics of blood vessels for the purpose of developing a noninvasive, nontraumatic technique for determining the elastic and viscoelastic properties of blood vessels in man.

The transmission characteristics of small signals in a given medium are customarily described by the dispersion and attenuation of infinitely long trains of sinusoidal waves propagating in the medium. The dispersion describes the variations in wave speed as a function of wave frequency, and the attenuation is an expression of the degree to which the wave amplitude decreases with distance traveled. Therefore, in this work the transmission characteristics of blood vessels refer to the dispersion and attenuation of small signals propagating in the vessels.

The transmission characteristics of a blood vessel lead to the determination of the mechanical properties of the vessel in the following manner. If the transmission characteristics and the geometry of a vessel can be evaluated experimentally and if an appropriate mathematical model for the mechanical behavior of the vessel is available, the mechanical properties can be determined. However, the accuracy and relevance of quantitative values for mechanical properties of vessels so derived will be no better than the experimentally determined transmission characteristics and geometry and will be no better than the associated mathematical model.

Clinical applications for a noninvasive, nontraumatic technique for assessing quantitative values of mechanical properties of large blood vessels in man are obvious, for example in detecting and investigating vascular disease such as atherosclerosis and in evaluating the aging process. Applications to space flight are also evident; these techniques could be adapted to monitor the

mechanical properties of major vessels in astronauts during prolonged exposure to weightlessness in attempts to assess the state of the cardiovascular system in general and to evaluate the results of cardiovascular conditioning programs the astronauts will undertake.

This dissertation documents experimental studies on the abdominal vena cavae of large, anesthetized dogs. Dispersion and attenuation data have been collected (Chapter 2), and the effects of increasing the intraluminal pressure have been evaluated (Chapter 3). Values of effective Young's modulus in the circumferential direction have been determined for a variety of conditions, including varying transmural pressure (Chapters 4 and 5), sympathetic stimulation (Chapter 5), and epinephrine injection (Chapter 5).

It should be emphasized that the determination of quantitative values for elastic properties of the canine abdominal vena cava is not in itself the primary goal of these studies; more important is the effect this work will have on the development and improvement of the mathematical model of large veins, including the role of the associated control mechanisms.

As the mathematical model for large blood vessel behavior evolves and as continuous-wave and pulsed-wave ultrasound sensors for determining transmission characteristics and vessel geometry are developed, the attainment of a noninvasive, nontraumatic technique for determining the elastic and viscoelastic properties of blood vessels in man will become a reality[21].

CHAPTER 2

THE DISPERSION AND ATTENUATION OF SMALL PRESSURE WAVES IN THE ABDOMINAL VENA CAVA

2.1 INTRODUCTION

The propagation of naturally occurring or artificially induced pressure waves in large arteries has been studied by Peterson[22], Landowne[23,24], McDonald and Taylor[25], McDonald[26], Anliker, Histand and Ogden[19], Moritz[27], and others. Large veins have received less attention than arteries at least in part because of greater difficulties in obtaining accurate data on venous distensibility. Veins are thin-walled, highly distensible vessels and can be in a state of partial collapse when subjected to low transmural pressures. Even small variations in transmural pressure resulting from breathing, muscular contraction, postural changes, or alteration in pressure-flow relationships in other portions of the cardiovascular system may cause relatively large changes in the geometry of some of the vessels and in their mechanical properties, all of which affect the distensibility.

For the most part, veins do not exhibit well-defined, naturally occurring pressure waves of appreciable amplitude. Propagation of artificially induced pressure waves in large veins has been studied by Peterson[22,28], Mackay et. al.[29], and others. In general the complex shapes and the large amplitudes of pressure waves used in these studies do not allow for determination of transmission characteristics and therefore do not allow for detailed evaluation of the accuracy and relevance of various mathematical models developed for the mechanical behavior of blood vessels.

In order to provide experimental information on transmission characteristics of large veins to allow for evaluation of mathematical descriptions of

blood vessels we are presenting here our findings on dispersion and attenuation of short trains of small-amplitude, sinusoidal, pressure waves propagating in the abdominal vena cavae of large anesthetized dogs. This work is an extension of previously reported[17] experimental findings from our laboratory.

2.2 THEORETICAL CONSIDERATIONS

The transmission characteristics of small signals in a given medium are customarily described by the dispersion and attenuation of infinitely long trains of sinusoidal waves propagating in the medium. The dispersion describes the variations in wave speed (phase velocity) as a function of wave frequency, and the attenuation is an expression of the degree to which the wave amplitude decreases with distance traveled. In determining the dispersion and attenuation of waves in blood vessels one is dealing with real systems and thus is limited to finitely long trains of sinusoidal waves propagating in finite media; however, this restriction proves to be surmountable, as described later in this section.

In these studies the speed and attenuation of artificially induced short trains (4 cycles) of small amplitude (less than 20 mm H_2O peak-to-peak), sinusoidal, pressure (distention) waves propagating in the abdominal vena cavae of large anesthetized dogs were determined. Sample tracings of finite trains of sinusoidal pressure waves of different frequencies recorded in the abdominal vena cava by catheter-tip manometers separated by a distance ΔX are shown in Figure 1. The tracings were separated for illustrative purposes; therefore, each has a different baseline.

The rationale for the choice of wave parameters described in the previous paragraph has theoretical and experimental backing and is described below.

In general, naturally occurring waves in the venous system are of

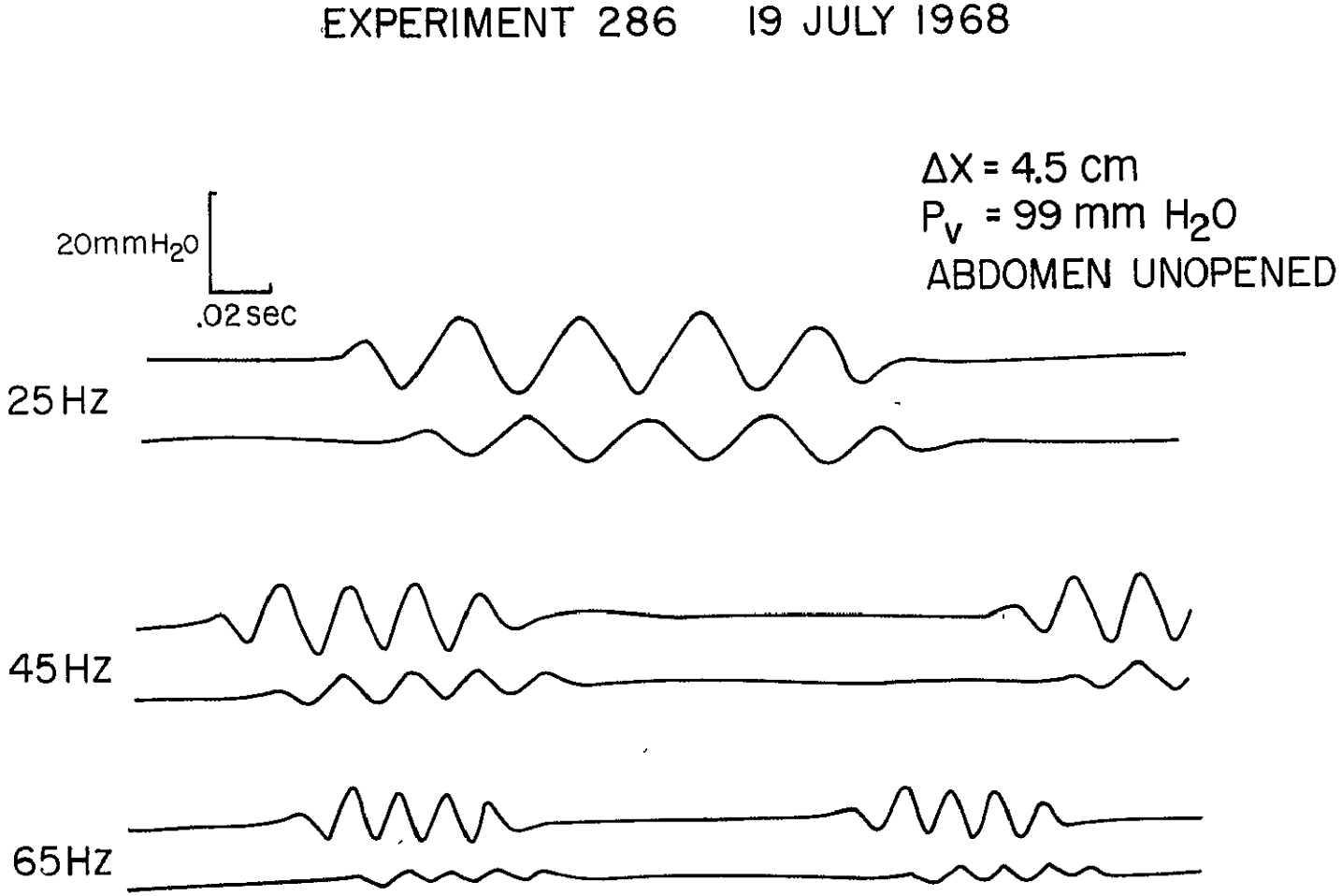


Figure 1. Sample tracings of finite trains of sinusoidal pressure waves of different frequencies recorded in the abdominal vena cava of an anesthetized dog. The tracings have been shifted vertically for illustrative purposes. P_V is venous pressure and ΔX is the distance between the catheter-tip manometers. See also Figure 3. General experimental preparation.

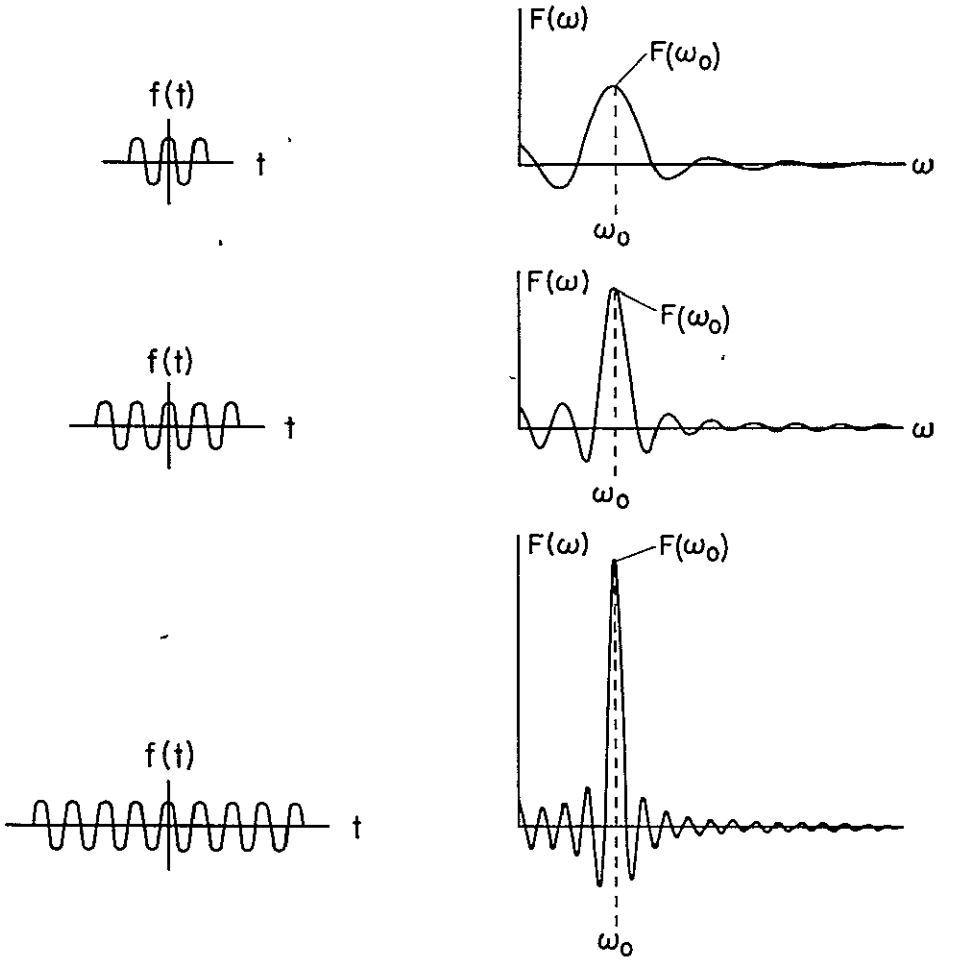
small amplitude and are of sufficiently complex form and origin to preclude their usage in obtaining transmission characteristics; artificially induced waves allow for controlled wave shape, amplitude, frequency, and origin.

Waves traveling in blood vessels can be characterized by intraluminal pressure perturbations, flow fluctuations, or wall displacements. The choice of parameters to be measured depends upon the magnitude of fluctuations which can be produced, the sensitivity and reliability of the measuring instrument, and the compatibility of the measuring instrument with the desired experimental preparation. We chose to place all transducers intraluminally in an attempt to avoid making complete exposure of the blood vessel mandatory. The availability of small-diameter, high-sensitivity, high-frequency-responding, catheter-tip manometers and the lack of appropriately qualified transducers for intraluminal measurement of small-amplitude, high-frequency wall displacements or flow fluctuations led to our choosing pressure waves for transmission characterization.

Large-amplitude waves are difficult to analyze mathematically because they are generally associated with nonlinear phenomena which preclude the resolution of the signal into harmonic components for the purpose of determining the dispersion and attenuation. Therefore, most theoretical studies assume signals of sufficiently small amplitude to allow for linearization and harmonic analysis. Wells[17] has presented experimental evidence which indicates the abdominal vena cava of the anesthetized dog behaves essentially in a linear fashion with respect to propagating sinusoidal pressure waves if their peak-to-peak amplitudes are less than 20 mm H_2O and their frequencies are between 20 and 100 Hz.

As mentioned before, in determining the dispersion and attenuation of waves in blood vessels one must deal with wave trains of finite length propagating in finite media. The dispersion and attenuation data can be obtained from the

transmission properties of finite trains by employing Fourier analysis. However, for mildly dispersive media, that is those in which the phase velocity varies by at most a few percent whenever the frequency is changed by ten percent, the speed of a finite train of sinusoidal waves is a good approximation of the phase velocity corresponding to the frequency of the sinusoidal waves. This is demonstrated by the Fourier transforms of finite trains of sine waves shown in Figure 2. A nonperiodic function $f(t)$ can be mathematically represented by an infinite collection of harmonic functions with circular frequencies assuming all values in the range $-\infty \leq \omega \leq +\infty$. The mathematical representation assumes the form of an integral, called a Fourier integral, which can be written as shown in the Figure; the function $F(\omega)$ is usually referred to as the Fourier transform of $f(t)$. The uppermost pair of graphs illustrates a nonperiodic function $f(t)$ (a train of 2-1/2 sine waves of circular frequency ω_0) (left), and the corresponding Fourier transform $F(\omega)$ (right). The pairs of graphs in the center and at the bottom correspond respectively to trains of 4-1/2 and 8-1/2 sine waves of the same circular frequency ω_0. Note that in each case the Fourier transform $F(\omega)$ has a distinct maximum at $\omega = \omega_0$. As the train length increases, $F(\omega)$ peaks more sharply at $\omega = \omega_0$, and $F(\omega_0)$ dominates the spectrum in increasing proportion. In the limiting case of an infinitely long train $F(\omega)$ would be infinite at $\omega = \omega_0$ and zero everywhere else. The progressive dominance of $F(\omega_0)$ with increasing length of the sine wave train implies that in a mildly dispersive medium such signals should have a speed of propagation which is a close approximation of the phase velocity corresponding to ω_0. Therefore the dispersion can be obtained by determining the speed of finite trains of sinusoidal waves, and performance of extensive computations required by the Fourier analysis can be avoided. Also, the attenuation



$$f(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F(\omega)\, e^{i\omega t}\, d\omega \qquad F(\omega) = \int_{-\infty}^{\infty} f(t)\, e^{-i\omega t}\, dt$$

$$f(t) = \begin{cases} \cos(\omega_0 t), & |t| < \frac{\tau}{2} \\ 0, & |t| > \frac{\tau}{2} \end{cases} \qquad F(\omega) = \frac{\tau}{2} \left[\frac{\sin\left(\frac{\omega-\omega_0}{2}\right)\tau}{\left(\frac{\omega-\omega_0}{2}\right)\tau} + \frac{\sin\left(\frac{\omega+\omega_0}{2}\right)\tau}{\left(\frac{\omega+\omega_0}{2}\right)\tau} \right]$$

Figure 2. Fourier transform of finite trains of sine waves.

characteristics can be obtained directly by comparing the amplitudes of the same wave trains measured at two or more locations.

Real systems may introduce reflection sites sufficiently close to the observation points to appreciably alter the wave shapes recorded. However, if the artificially induced waves have sufficiently high frequencies and short trains, the waves can be recorded before their reflections arrive at the recording site. Also, in the case of strong attenuation, the reflections of small waves will be completely damped out before they reach the recording site.

In dogs weighing 20 to 40 kg the section of abdominal vena cava between the renal veins and the bifurcation into common iliac veins is usually between 10 and 15 cm in length and between 1.0 and 1.5 cm in diameter. Except for minor branches this section is a reasonably straight, cylindrically-shaped vessel which can easily accommodate the catheter-tip transducers available in our laboratory. The experiments described here were limited to this section of the vena cava. With the progressive miniaturization of catheter-tip manometers, smaller vessels, for example the external jugular vein, will become candidates for studies of a similar nature.

2.3 METHODS

The methods and experimental procedures described in this dissertation have evolved in our laboratory during a period of more than three years. Many of the earlier experimental techniques for generating and recording artificial pressure waves in large, canine veins were developed and were first described in detail by Anliker, Wells, and Ogden[30]. Most of the experimental techniques described in Chapters 2 and 3 have been previously reported[17,30], but they are repeated here for completeness. Chapters 4 and 5 contain detailed descriptions of some methodology not previously published. Methods and experimental

procedures common to Chapters 2 through 5 are described in this chapter.

Guided by the considerations discussed in the preceding section we have generated short trains of small amplitude, sinusoidal, pressure waves in the abdominal vena cavae of mature mongrel dogs of uncertain age and origin. The animals usually weighed 20-40 kg and were mostly males. They were anesthetized intravenously with 30 mg/kg sodium pentobarbital (Nembutal). The general experimental preparation is schematically represented in Figure 3.

The small sinusoidal pressure waves were produced by the movement of a 5.5 mm diameter, lightweight aluminum piston vibrating inside a brass tube; the latter prevented direct contact of the moving piston with the vessel wall. The tube and piston were introduced through the right femoral vein, and the tips were positioned in the right common iliac vein near the bifurcation. The other ends of the tube and the piston were attached to the housing and the core, respectively, of the solenoid shown in Figure 4. Finite trains of sinusoidal piston movement were produced by driving the solenoid with a circuit containing a Hewlett-Packard 204B electronic oscillator*, an Electro-Voice Model A50 high fidelity amplifier**, and a General Radio Company Type 1396-A tone burst generator***.

The pressure fluctuations in the abdominal vena cava were monitored by two catheter-tip manometers introduced through the right external jugular vein and positioned 3-5 cm apart approximately midway between the renal veins and the bifurcation. One of these manometers is shown in Figure 5. The transducer is a Bytrex Model HFD-5 silicon semiconductor, strain gage pressure cell**** modified to form a leak-proof flexible catheter for physiological use by

*Hewlett-Packard, 1501 Page Mill Road, Palo Alto, California
**Electro-Voice, Inc., Buchanan, Michigan
***General Radio Company, West Concord, Massachusetts
****Bytrex Division of Tyco, 223 Crescent Street, Waltham, Massachusetts

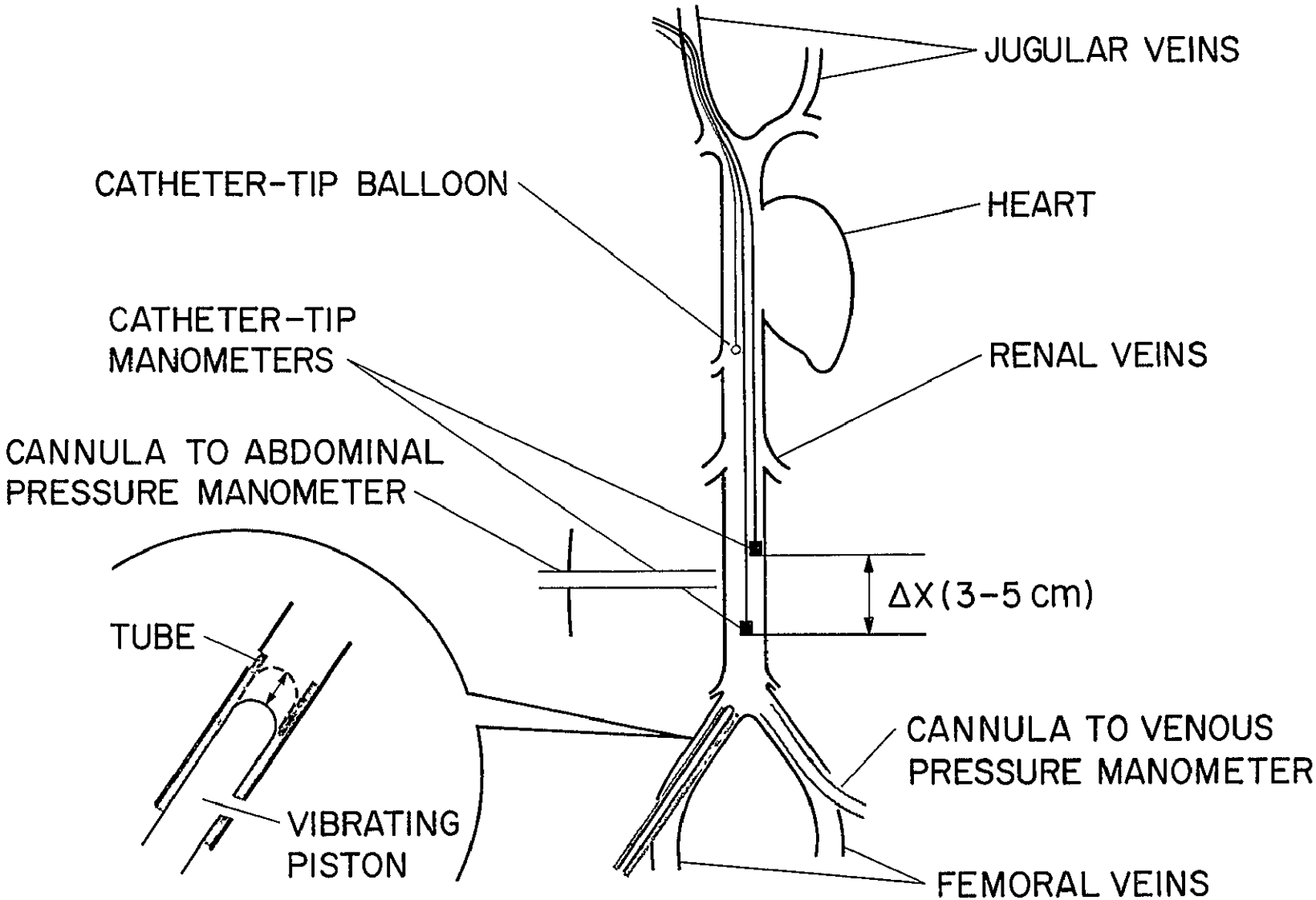


Figure 3. General experimental preparation for studying the dispersion and attenuation of small, artificially-induced pressure waves in the abdominal vena cavae of anesthetized dogs (Chapter 2) and for determining the effect of pressure on the speed of these waves (Chapter 3).

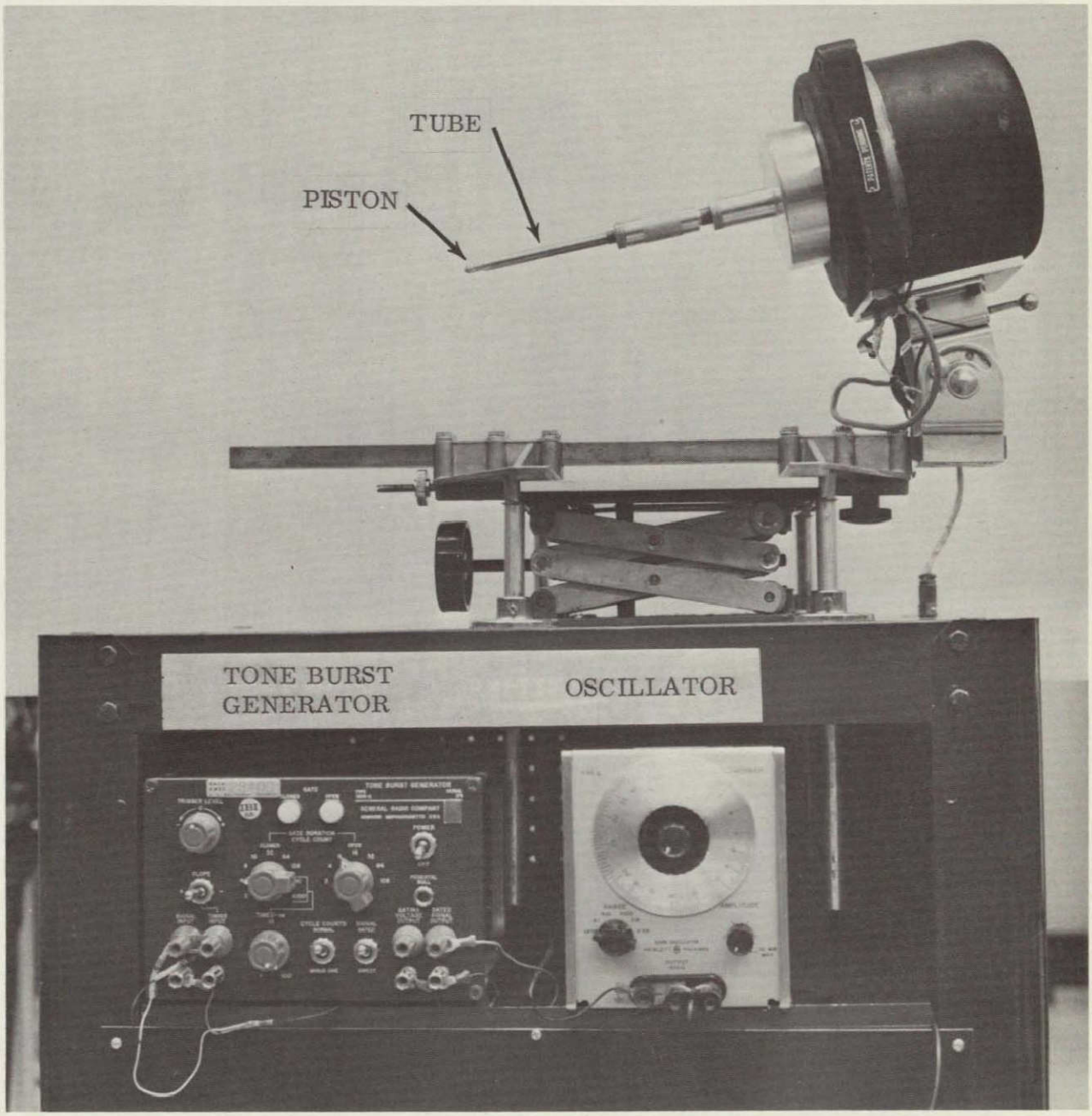


Figure 4. Electrically-driven piston with tone burst generator and oscillator.

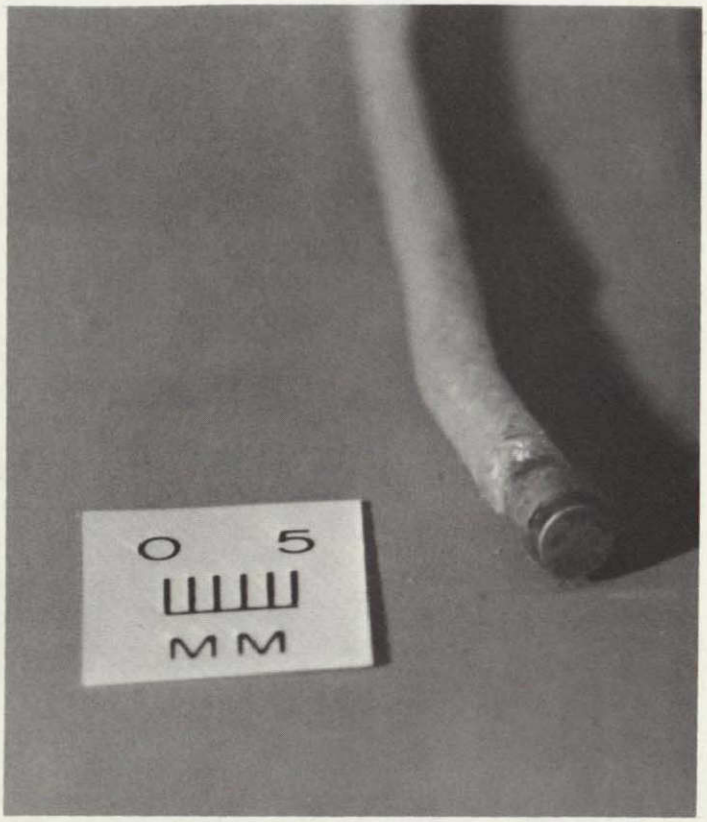


Figure 5. Bytrex Model HFD-5 pressure cell modified for use as a catheter-tip manometer.

gold plating the cell to reduce the corrosive effects of blood and by protecting the shielded leads and the venting tube with heat-shrinkable plastic tubing. The Bytrex pressure cell has a diameter of 3 mm, a natural frequency above 60 kHz in air, a response linear within 1% from 0 to 300 mm Hg, and a sensitivity of 80 to 100 μV/mm Hg with 25 volts excitation. The output from the bridge circuit is amplified by an Astrodata Model 885 amplifier* and recorded on a Honeywell Model 1108 Visicorder oscillograph** equipped with galvanometers having frequency responses flat up to 2000 Hz. This system allows for resolution of pressure fluctuations less than 1 mm H_2O when the maximum amplifier gain of 3000 is employed.

Unfortunately the Bytrex pressure cell and its associated electronics are subject to baseline drift and were therefore not used for absolute venous pressure measurement. Venous pressure was measured continuously by a Statham P23BB manometer attached to a saline-filled polyethylene cannula inserted through the left femoral vein and positioned near the bifurcation; the gage was connected to a Honeywell gage control unit and Model M-104 Accudata d-c amplifier; and the output was recorded on the Honeywell oscillograph. This system provided baseline drift of less than ± 2 mm H_2O during several hours.

The arterial pressure was continuously monitored by a Statham P23Dd manometer attached to a saline-filled metal cannula inserted into the left femoral artery or the left carotid artery. All Statham manometers were excited, amplified, and recorded as described in the preceding paragraph.

The catheter-tip manometers, the Statham gages, the amplifiers, and the recording equipment were calibrated as a system for each experiment.

Respiration was monitored continuously by attaching a mercury-filled

*Astrodata, Inc., 240 East Palais Road, Anaheim, California
**Denver Division of Honeywell, 4800 East Dry Creek Road, Denver, Colorado

silastic tube to the chest. Chest wall movement changed the length of the mercury-filled tube; the resulting variations in electrical resistance were monitored by a bridge circuit, the output of which was amplified by an Astro-data Model 885 amplifier and was recorded on the Honeywell oscillograph.

Theoretically[14,15] and experimentally[17,19,27] the transmission characteristics of blood vessels can be shown to vary with transmural pressure. In some experiments the abdomen was opened by a midline incision from the caudal end of the sternum to the pubis, and the abdominal viscera were displaced into a plastic bag on the dog's left side. This procedure exposed the vena cava to atmospheric pressure and provided for a well-defined transmural pressure.

In other experiments the abdomen was not opened, but an effective transmural pressure was determined by subtracting the intra-abdominal pressure from the intraluminal venous pressure. The intra-abdominal pressure was monitored with a Statham P23BB manometer attached to a saline-filled metal cannula which had been inserted into the abdomen through a small incision in the abdominal wall. The tip of the cannula was positioned near the vena cava test section; saline was dripped slowly through the cannula preventing abdominal viscera from blocking the tip.

In still other experiments the abdomen was not opened; intra-abdominal pressure was not measured; and intraluminal venous pressure was used as an index of transmural pressure.

Variations in intraluminal pressure were artificially produced by inflating a catheter-tip balloon inserted through the left external jugular vein and positioned in the inferior vena cava just caudal to the heart. The effect of pressure on the speed of small pressure waves is discussed in Chapter 3.

The relative positions of the catheter-tip manometers, the vibrating piston, and the pressure-monitoring cannulae were determined fluoroscopically within an accuracy of 1 mm with the aid of an image intensifier and a radio-opaque grid having a mesh size of 1 cm and by taking into account the effects of parallax. The distance between the tip of the vibrating piston and the closest catheter-tip manometer was usually between 4-7 cm. The tip of the cannula for measuring intraluminal venous pressure was positioned as close to the bifurcation as possible without noticeably altering the induced pressure waves. The tip of the cannula for measuring intra-abdominal pressure was positioned within 2 cm of the vena cava, in the horizontal and vertical planes. The distance between the tips of the catheter-tip manometers was usually 3-5 cm and was verified several times during an experiment.

During data acquisition all the transducer signals after having been amplified were recorded simultaneously by the Honeywell oscillograph at paper speeds of 50 or 100 cm/sec.

The speed and attenuation of the artificially induced pressure waves propagating in the vena cava were determined as shown in Figure 6. To avoid the changes in wave transmission characteristics that can occur during the active phase of the respiratory cycle[17] only those waves generated and recorded during the resting phase of the respiratory cycle were analyzed for dispersion and attenuation information.

To evaluate the wave speed c the distance between the tips of the catheter-tip manometers ΔX was divided by the time increment required for a characteristic point in the wave train to traverse that distance. As a characteristic point we chose the intersection of lines tangent to successive inflection points of the sinusoidal pressure wave. This method for determining a

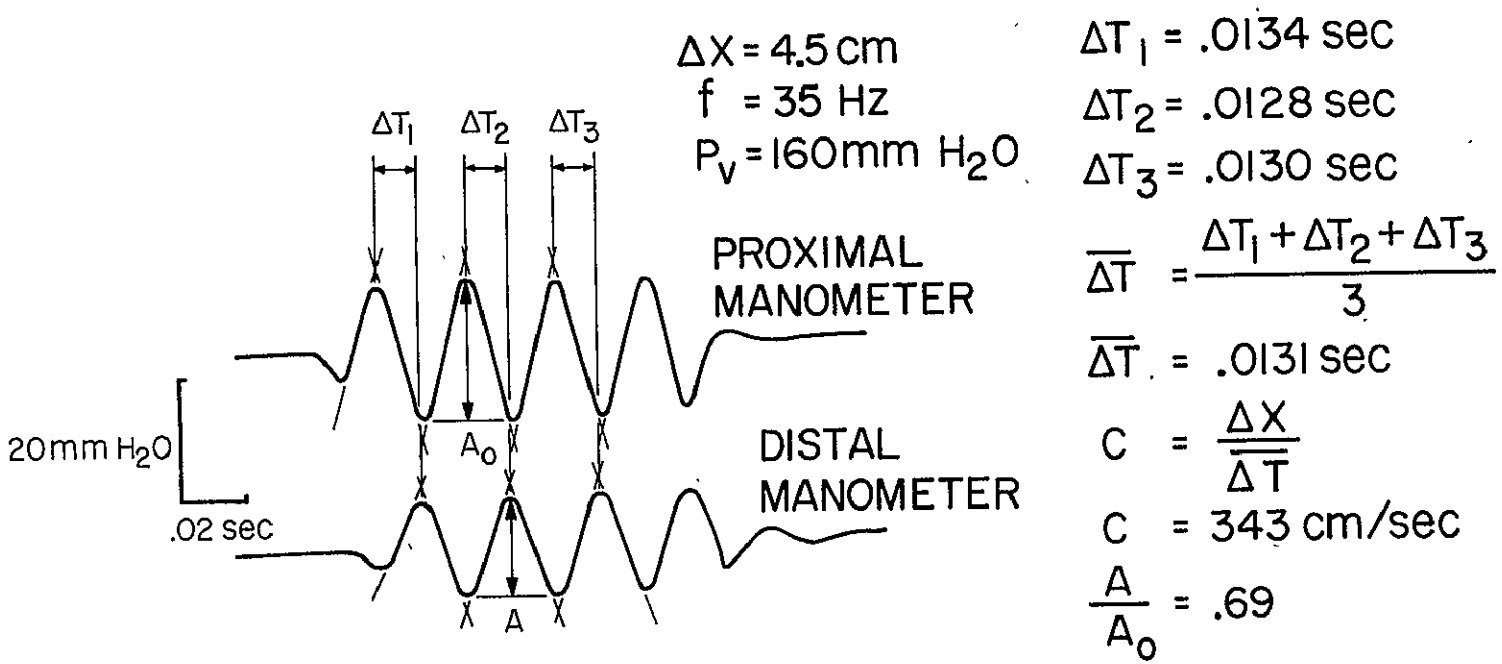


Figure 6. Sample tracing of a finite train of sinusoidal pressure waves illustrating the data analysis.

characteristic point is deemed superior in accuracy and repeatability to other methods we have investigated. Generally, ΔT's for the first three peaks of a wave train were determined; and an average wave speed was calculated using the average $\overline{\Delta T}$ of the three ΔT's. However, for dispersion data presented in this chapter a wave speed was calculated for each ΔT; and the values of wave speeds for the first three waves of several wave trains were averaged. The attenuation was evaluated by dividing the amplitude A of a particular wave recorded by the manometer farthest from the wave generator (distal manometer) by the amplitude A_o of the same wave recorded by the manometer closer to the wave generator (proximal manometer). In general, A/A_o was determined for the second wave of the train.

With paper recording speeds of 50 or 100 cm/sec we were usually able to evaluate ΔT within 0.5 msec and ΔX was determined with the fluoroscope to an accuracy of 1 mm.

The maximum expected relative error in wave speed can be evaluated in the following manner. The wave speed is defined as

$$c = \frac{\Delta X}{\Delta T} .$$

Forming the differential dc and dividing by $c = \frac{\Delta X}{\Delta T}$ we obtain

$$\frac{dc}{c} = \frac{d(\Delta X)}{\Delta X} - \frac{d(\Delta T)}{\Delta T} .$$

The maximum expected relative error in c can therefore be defined as

$$\frac{\delta c}{c} = \frac{\delta(\Delta X)}{\Delta X} + \frac{\delta(\Delta T)}{\Delta T}$$

where δc is the maximum error of the speed and where $\delta(\Delta X)$ and $\delta(\Delta T)$ represent the maximum errors of individual measurements of ΔX and ΔT. The maximum expected error in c will be small when ΔX and ΔT are large. This is, for example, the case when $\Delta X = 5.0$ cm and $\Delta T = 35$ msec. Therefore this leads to

$$\frac{\delta c}{c} = \frac{0.1 \text{ cm}}{5.0 \text{ cm}} + \frac{0.5 \text{ msec}}{35 \text{ msec}} = 0.03 \text{ or } 3\%.$$

The maximum expected relative error will be larger when ΔX and ΔT are small, for example when $\Delta X = 2.5$ cm and $\Delta T = 3$ msec. In such a case

$$\frac{\delta c}{c} = \frac{0.1 \text{ cm}}{2.5 \text{ cm}} + \frac{0.5 \text{ msec}}{3 \text{ msec}} = 0.21 \text{ or } 21\%.$$

In order to minimize the maximum expected error, ΔX was maintained as large as possible. However, ΔX was usually not greater than 5 cm for the following reasons. In order to avoid possible nonlinearities associated with propagation of large-amplitude pressure waves the peak-to-peak amplitudes of the waves recorded by the proximal transducer were usually maintained less than 20 mm H_2O. In addition, at high frequencies the stroke of the vibrating piston was not sufficiently large to produce pressure waves at the proximal transducer of more than 10 to 15 mm H_2O peak-to-peak. Attenuation of the waves was approximately exponential with distance, and high-frequency waves were attenuated to a greater extent than low-frequency waves in the same distance ΔX. The distal transducer was placed sufficiently close to the proximal transducer so that waves recorded on the distal transducer were of large enough amplitude at all frequencies to make their analysis for wave speed possible.

Maximum expected relative errors in wave speed were usually less

than 10% except at highly elevated pressures for which c was large and ΔX and ΔT were small.

In general, the amplitudes A and A_o could be evaluated within 0.3 mm H_2O. The maximum expected relative error in A/A_o can be evaluated in the same manner as was demonstrated for wave speed and will be largest when A, A_o, and A/A_o are small. Usually, the maximum expected relative error in A/A_o was less than 10%; but for very small-amplitude (< 5 mm H_2O), high-frequency (> 60 Hz) waves it was as high as 20%.

2.4 EXPERIMENTAL PROCEDURE

This list of experimental procedures was generally followed in the preparation and performance of experiments.

1. After sufficient warm-up to allow for stability the Statham manometers were calibrated, and the sensitivities of the catheter-tip manometers were set equal and were calibrated.
2. After being anesthetized with 30 mg/kg sodium pentobarbital (Nembutal) and delivered by animal colony personnel and shaved by our laboratory technician, the dog was placed in the supine position on the animal board.
3. In order to aid the dog's breathing, an endotracheal tube was placed, or a tracheotomy was performed and a Y-tube was placed in the trachea.
4. A metal cannula filled with heparinized saline was placed in the left femoral artery or the left carotid artery and was attached to the Statham P23Dd manometer. During the experiment the arterial pressure was used as a general indicator of the physiological state of the animal.
5. A polyethylene cannula filled with heparinized saline was placed in the left femoral vein and was attached to a Statham P23BB manometer.
6. If intra-abdominal pressure was to be measured, an incision was made in the

abdominal wall 5-10 cm right of midline and approximately two-thirds the distance between the caudal end of the sternum and the penis. After the muscles were separated and a small incision was made in the peritoneum, a saline-filled metal cannula was placed into the abdomen and was attached to a Statham P23BB manometer. A purse-string stitch placed in the abdominal wall around the catheter was drawn tight, essentially sealing the abdomen. The cannula was fixed in position by clamps and a ringstand after the tip had been placed near the vena cava.

7. The catheter-tip balloon was inserted through the right external jugular vein and was positioned in the inferior vena cava just caudal to the heart.

8. To avoid clotting on the catheter-tip manometers the dog was given up to 250 units/kg heparin sodium (Panheprin) intra-arterially.

9. The catheter-tip manometers were inserted through the right external jugular vein and were positioned in the vena cava just caudal to the renal branches.

10. The brass tube used to protect the vibrating piston was filled with heparinized saline; the tip was placed in the right femoral vein; and with one smooth, steady movement the tube was inserted about 15 cm into the femoral vein. This insertion was a critical point in the preparation; because if the relatively large tube (6.3 mm diameter) was not inserted the full distance on the first attempt, it was likely that the vein constricted around the tube and prevented further insertion; on occasion this resulted in the tube's and the piston's being so far from the catheter-tip manometers that the recorded pressure waves were too small to analyze, so the experiment was terminated.

11. After the brass tube was in position the aluminum piston connected to the core of the solenoid was inserted into the tube, and the tube was connected to the solenoid housing.

12. In some experiments the abdomen was not opened, and intra-abdominal

pressure was not measured; in others the abdomen was not opened, but intra-abdominal pressure was measured; and in others the abdomen was opened by a midline incision and the abdominal viscera were displaced into a bag on the dog's left side.

13. The catheter-tip manometers were positioned together so their tips were in the same cross section of the vena cava at a location midway between the renal branches and the bifurcation. Minor adjustments in the orientation of the wave generating equipment were made in order to optimize the sinusoidal nature of the waves. Sample waves were induced, recorded, and inspected in order to check that the sensitivities of the manometers were the same and to check for evidence of nonaxisymmetric waves. If necessary, the catheter-tip manometer amplifiers were adjusted so that the recorded signals were of equal amplitude. If the shapes of the same wave were different on the respective manometer recordings, then this difference was considered due to nonaxisymmetric waves. This occurred when the catheter-tip manometers were within 1 or 2 cm of the vibrating piston; therefore, the proximal transducer was always positioned at least 2 cm from the vibrating piston.

14. The catheter-tip manometers were repositioned so that ΔX was about 3-5 cm and so that the waves were of sufficient amplitude to merit analysis. Sample waves were inspected for evidence of reflections. Large differences in the magnitude of ΔT_1, ΔT_2, and ΔT_3 in a single wave train; large differences in shapes of successive waves in a single wave train; or oscillations in the recorded signal immediately following the four induced waves are interpreted as indications of reflections. Occasionally one or more of these phenomena were observed, and generally they could be eliminated by appropriately repositioning the catheter-tip manometers.

15. Data acquisition for wave speed and attenuation information was accomplished by inducing and recording several short trains of pressure waves for each of several wave frequencies. The recording started with waves of 25 or 30 Hz, and the wave frequency was increased in steps of 10 Hz until the waves became too small to analyze (60-120 Hz). Then the wave frequency was decreased by one step of 5 Hz followed by steps of 10 Hz until the waves became significantly nonsinusoidal (10-20 Hz). In order to allow a check on possible changes in transmission characteristics occurring during this period of data acquisition waves of 25 and 30 Hz were recorded again. The maximum frequency range for these studies was about 15-110 Hz, and the minimum was about 25-50 Hz. Usually the data were acquired in five to ten minutes.

16. If the protocol provided for a change in the experimental preparation, for example opening the abdomen or placing the dog on its side, this was done; and recordings for wave speed and attenuation data were obtained for the new condition.

17. The distance between the catheter-tip manometers was checked before and after data acquisition for each condition.

18. At the end of the experiment the animal was sacrificed, generally by administering a saturated solution of potassium chloride into the vascular system.

19. If not already opened, the abdomen was opened, the abdominal viscera were displaced, and the vena cava was surgically exposed to allow measurement of the external diameter and two times the wall thickness using vernier calipers.

2.5 RESULTS

Dispersion and attenuation data for short trains of small-amplitude, artificially-induced, sinusoidal pressure waves propagating in the abdominal vena cava were collected from 25 large anesthetized dogs. Some data were acquired for each of the following conditions:

1. Abdomen unopened
    a. dog supine
    b. dog on left side
2. Abdomen unopened, except for intra-abdominal pressure measurement
    a. dog supine
    b. dog on left side
3. Abdomen opened; viscera displaced
    a. dog supine

Not all conditions were investigated for each dog, and emphasis in this work was placed on conditions 1a and 1b in order to obtain data from an animal that had been exposed to a minimum of surgical trauma.

The experimental procedure is easiest to perform when the dog is in the supine position; this was the first position used in our laboratory. The dog was placed on its left side in some experiments in an attempt to avoid the abdominal viscera's lying directly on the vena cava and in order to study a position which might also be assumed by lightly restrained, unanesthetized animals.

In the course of the studies conducted in our laboratory we became increasingly aware of the effects of the transmural pressure on the wave transmission properties of the vena cava. Therefore, conditions 2a and 2b were developed so that an effective transmural pressure could be estimated in a dog with its abdomen unopened.

Condition 3a has been thoroughly investigated in this laboratory[17]. Although some new information for dogs in this condition has been obtained, discussion here is limited to comparison of conditions 2a and 3a on the same dog in an attempt to evaluate the effects of opening the abdomen and displacing the abdominal viscera.

All data presented are for waves recorded during the resting phase

of the respiratory cycle; the animal was in the supine position unless otherwise noted.

2.5.1 Abdomen unopened

Dispersion and attenuation data were acquired from 11 dogs in the supine position; 7 of these dogs were then placed on their left sides and more dispersion and attenuation data were collected. Representative dispersion curves are given in Figures 7-10. Most points represent the means of 9 to 15 determinations of wave speed at a particular frequency.

A wave speed was calculated for the ΔT acquired from each of the first three waves of 3 to 5 wave trains; these 9 to 15 values of wave speed were averaged; the standard error of the mean was calculated and is shown for each frequency on the dispersion curves. In most cases the data for a particular frequency were acquired within 5 seconds during the resting phase of one respiratory cycle; however, for some wave frequencies the averages represent data acquired from two or more 5 second intervals spaced a few minutes apart within the 5 to 10 minute period usually required to obtain dispersion data; this allowed a check on possible variations in the transmission characteristics occurring during this 5 to 10 minute period. In general the frequency range studied was limited at high frequencies by waves too small to analyze and at low frequencies by waves that became progressively less sinusoidal in shape with decreasing frequency, particularly below 20 Hz.

The dispersion data in Figure 7 show that the wave speed increased with frequency from about 150 to 250 cm/sec between 20 and 110 Hz. Because the wave speed varied by at most a few percent when the frequency was changed by 10 percent, the speed of a finite train of sinusoidal waves is a good approximation of the phase velocity corresponding to the frequency of the

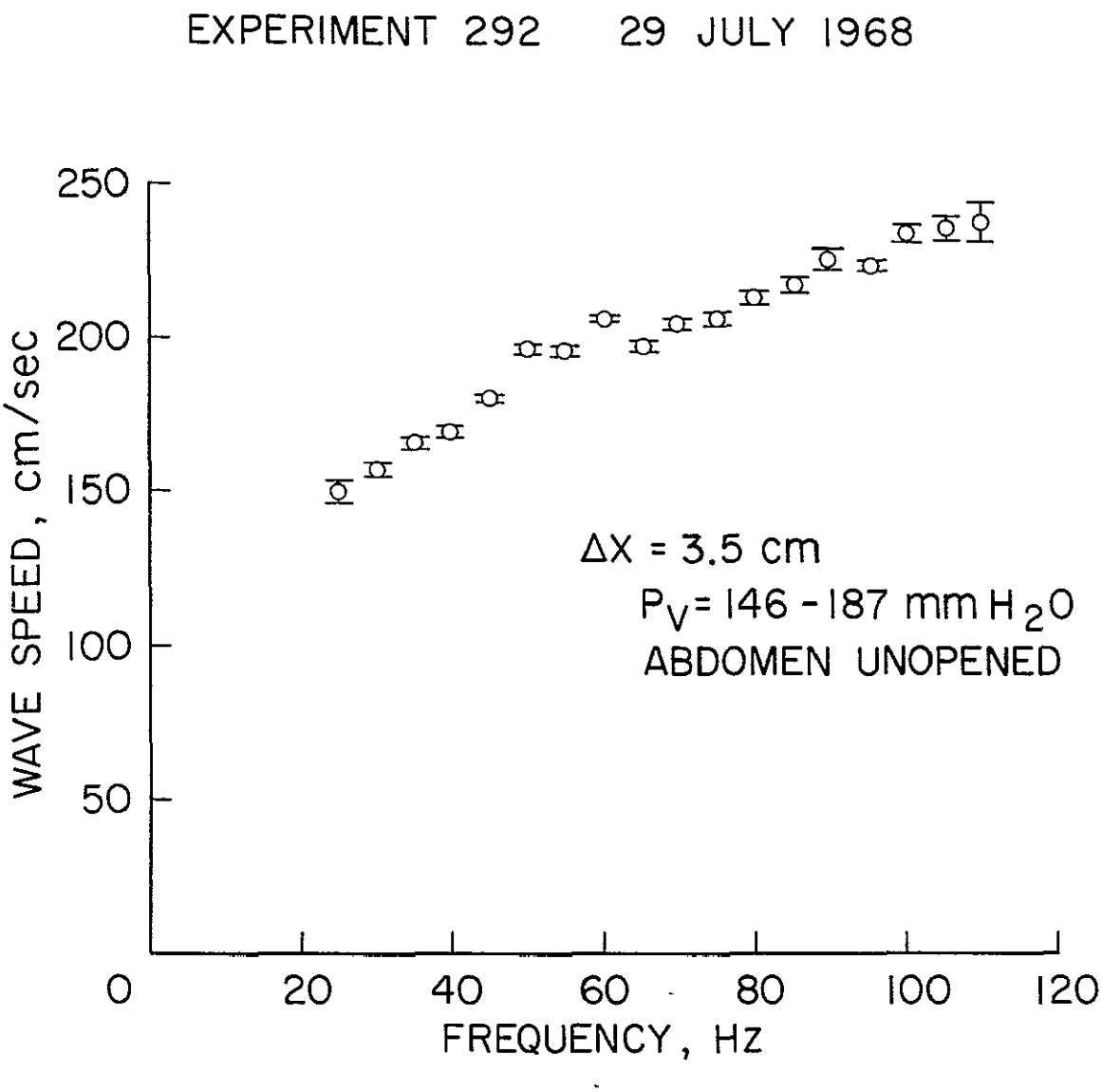


Figure 7. Dispersion of pressure waves in the abdominal vena cava; abdomen unopened.

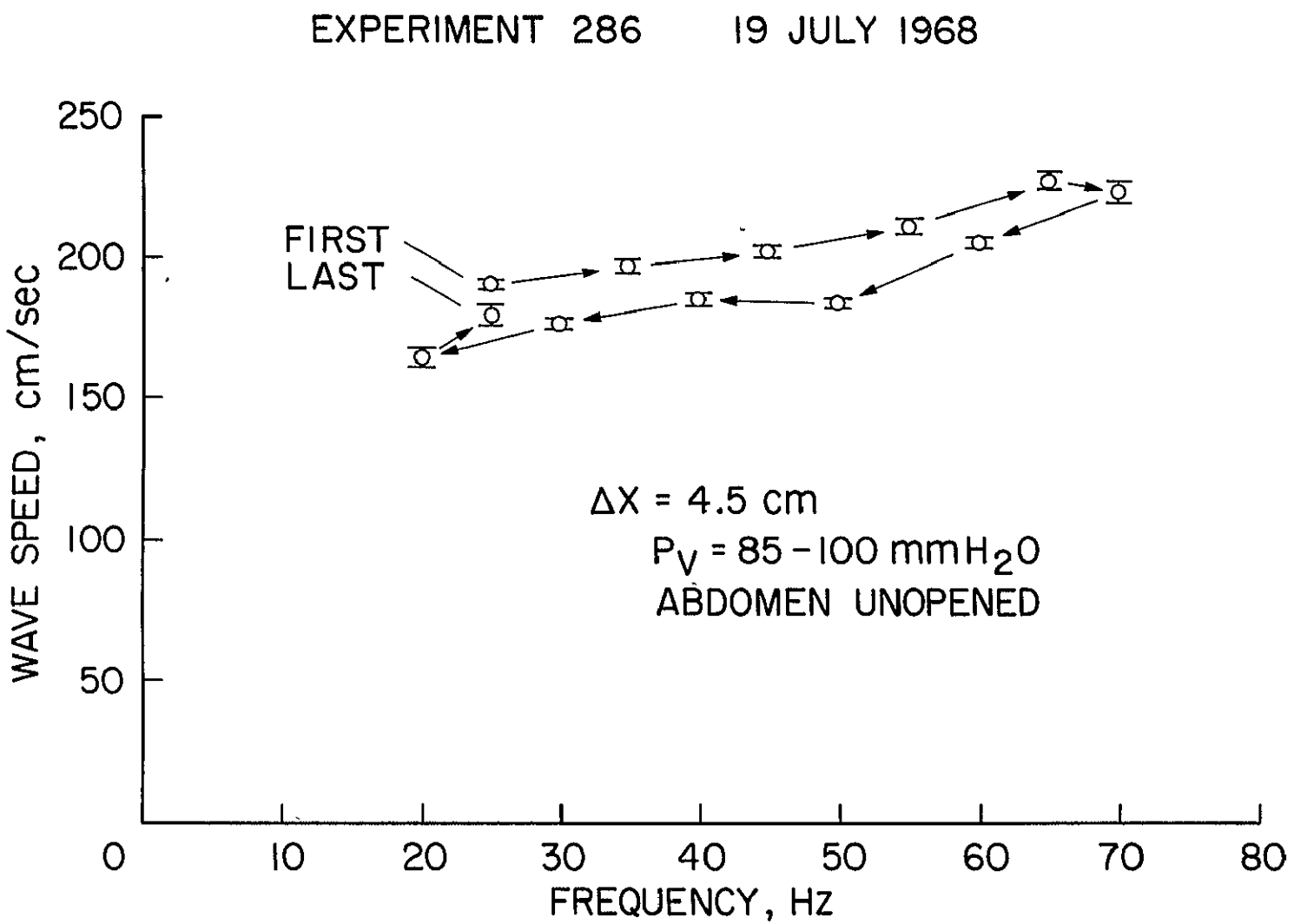


Figure 8. Dispersion of pressure waves in the abdominal vena cava; abdomen unopened.

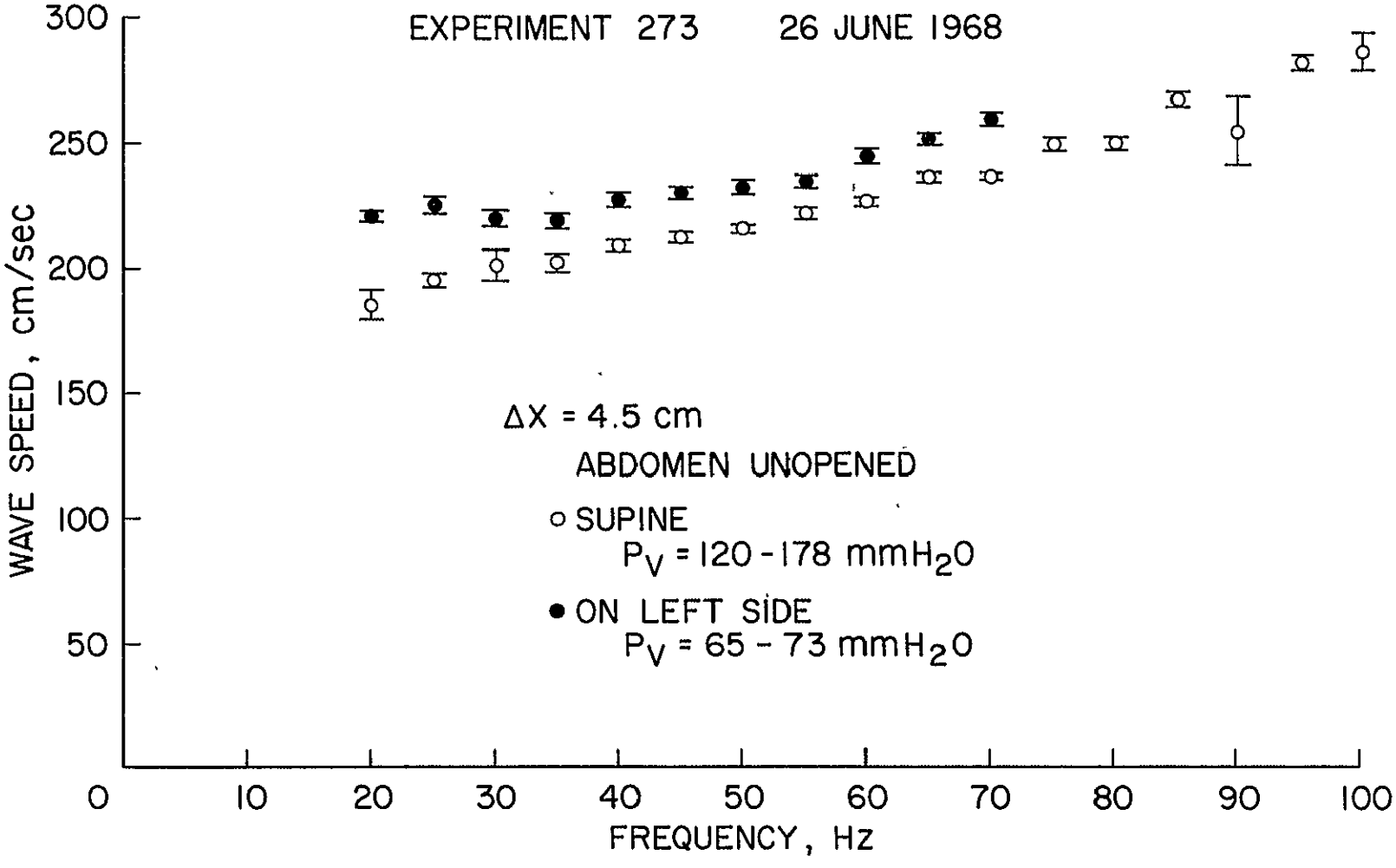


Figure 9. Effect of position on dispersion of pressure waves in the abdominal vena cava; abdomen unopened.

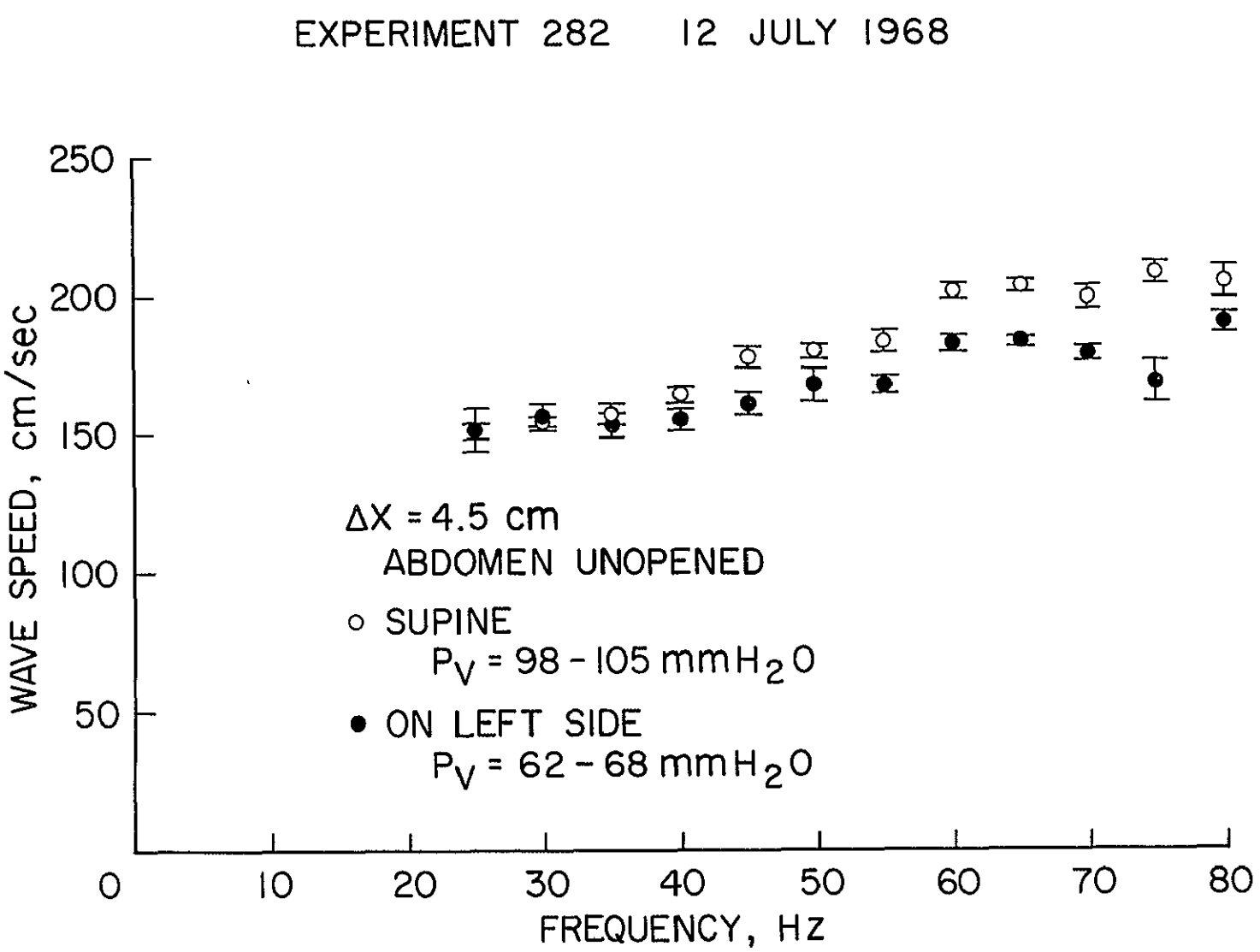


Figure 10. Effect of position on dispersion of pressure waves in the abdominal vena cava; abdomen unopened.

sinusoidal waves; and the vessel can therefore be described as mildly dispersive.

Figure 8 provides an indication of the changes in wave speed that can take place during the 5 to 10 minute data acquisition period. The sequence of data acquisition is indicated by the arrows. The wave speed data obtained when the frequency was increased appear to be significantly different from those collected when the frequency was decreased. This difference is probably the result of physiological changes occurring during the data acquisition period.

The effect of animal position on dispersion of pressure waves in the vena cava is demonstrated in Figures 9 and 10. Data were recorded with the dogs in the supine position and with the dogs on their left sides. Although the differences in mean values of wave speed at a particular frequency for the two positions are statistically significant for most frequencies, in general the differences are small; the dispersive nature of the vessel is essentially unchanged and is at most mild. Note that in Figure 9 the wave speeds are higher for the dog on the left side while in Figure 10, the opposite is true. It should be noted that some of the points in the graphs 9 and 10 have relatively large standard errors of the mean because only a few wave speed measurements were made in those cases.

The venous pressure manometer was calibrated with the dog in the supine position and was not recalibrated after the dog was placed on its left side; therefore, the venous pressure for the dog on its left side may be in error by as much as 20 mm H_2O due to a change in elevation of the vena cava.

Previous work in our laboratory on arteries[19, 27] and veins[17] has demonstrated that to a good approximation the amplitude of small pressure waves propagating in large blood vessels decreases exponentially with the distance

traveled and the attenuation per wave length is independent of frequency. This approximation can be expressed mathematically by

$$\frac{A}{A_o} = e^{-k\frac{\Delta X}{\lambda}}$$

where A/A_o is the amplitude ratio, k the attenuation coefficient or logarithmic decrement, ΔX the distance between the transducers, and λ the wave length.

The attenuation data corresponding to the dispersion curves presented in Figures 7-10 are shown in Figures 11-14. A/A_o has been plotted on the vertical logarithmic scale versus $\Delta X/\lambda$ on the linear horizontal scale; a straight line passing through $A/A_o = 1$, $\Delta X/\lambda = 0$ has been drawn through the points, and a value of k has been determined for each straight line. To the extent that the points lie close to a straight line the data can be said to approximate the mathematical expression we have assumed. For each train of waves that was analyzed only one value of amplitude ratio A/A_o was calculated while three wave speed determinations were made. Therefore, most points on the attenuation curves represent an average of only 3 to 5 values of the amplitude ratio. Because of this limited number of samples for each data point, no standard errors of the mean were calculated. In general the maximum expected relative error for the amplitude ratio was slightly higher than that for the wave speed, and the data scatter for the amplitude ratio was also slightly greater than that for the wave speed.

In Figures 13 and 14 the effect of position on attenuation is shown. In Figure 13 the attenuation is slightly greater for the dog in the supine position and in Figure 14 the attenuation is greater for the dog on its left side. However,

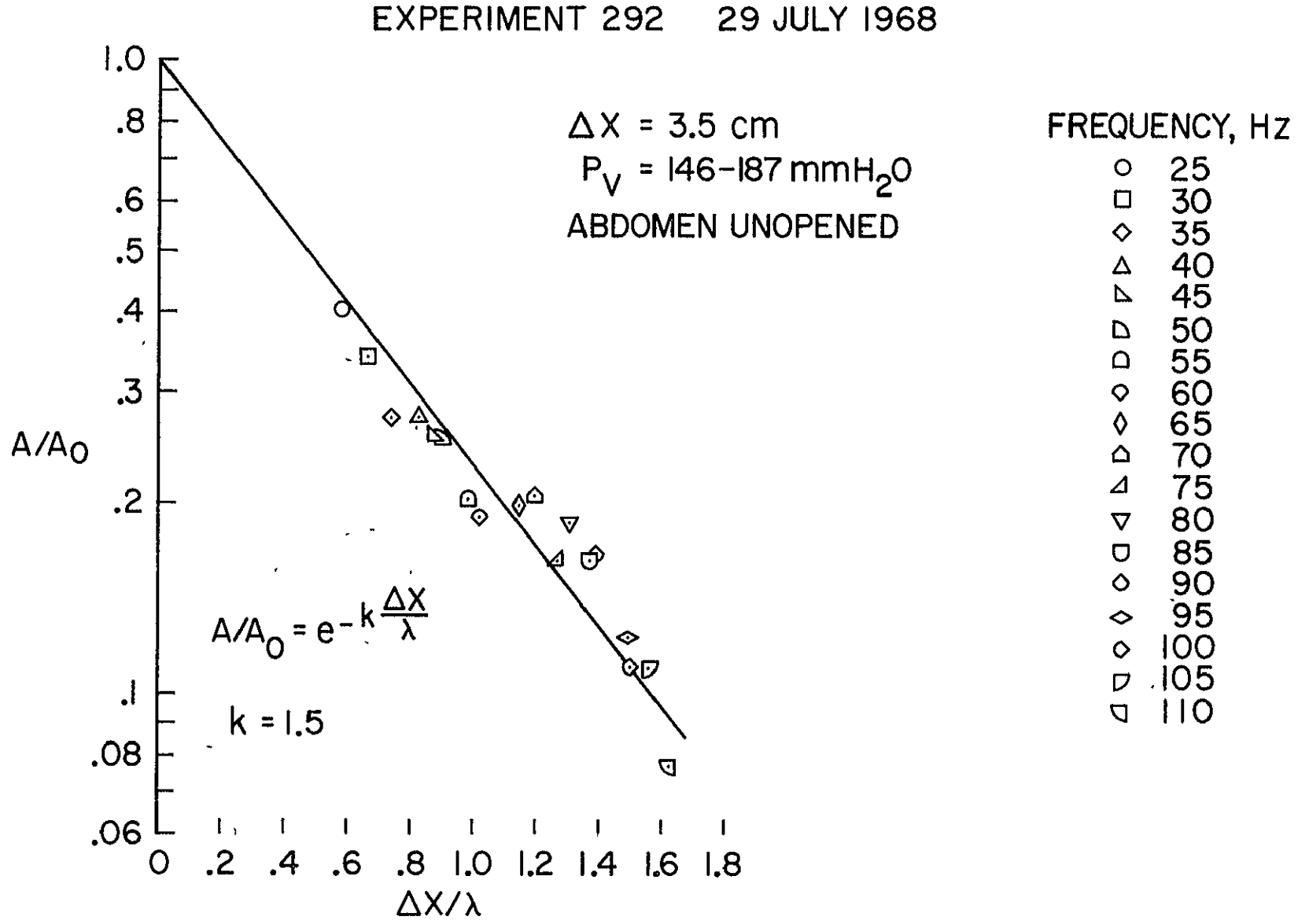


Figure 11. Attenuation of pressure waves in the abdominal vena cava; abdomen unopened.

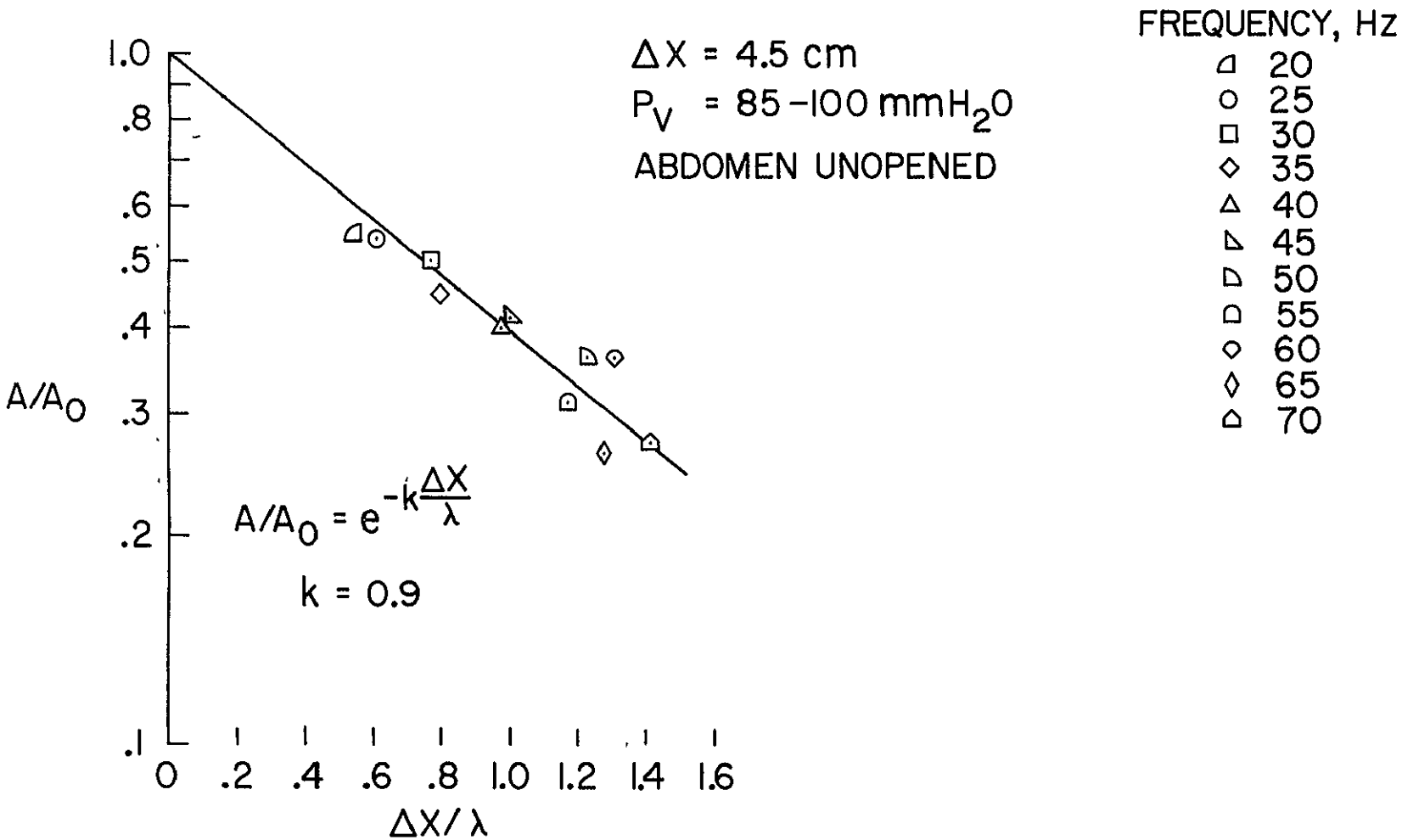


Figure 12. Attenuation of pressure waves in the abdominal vena cava; abdomen unopened.

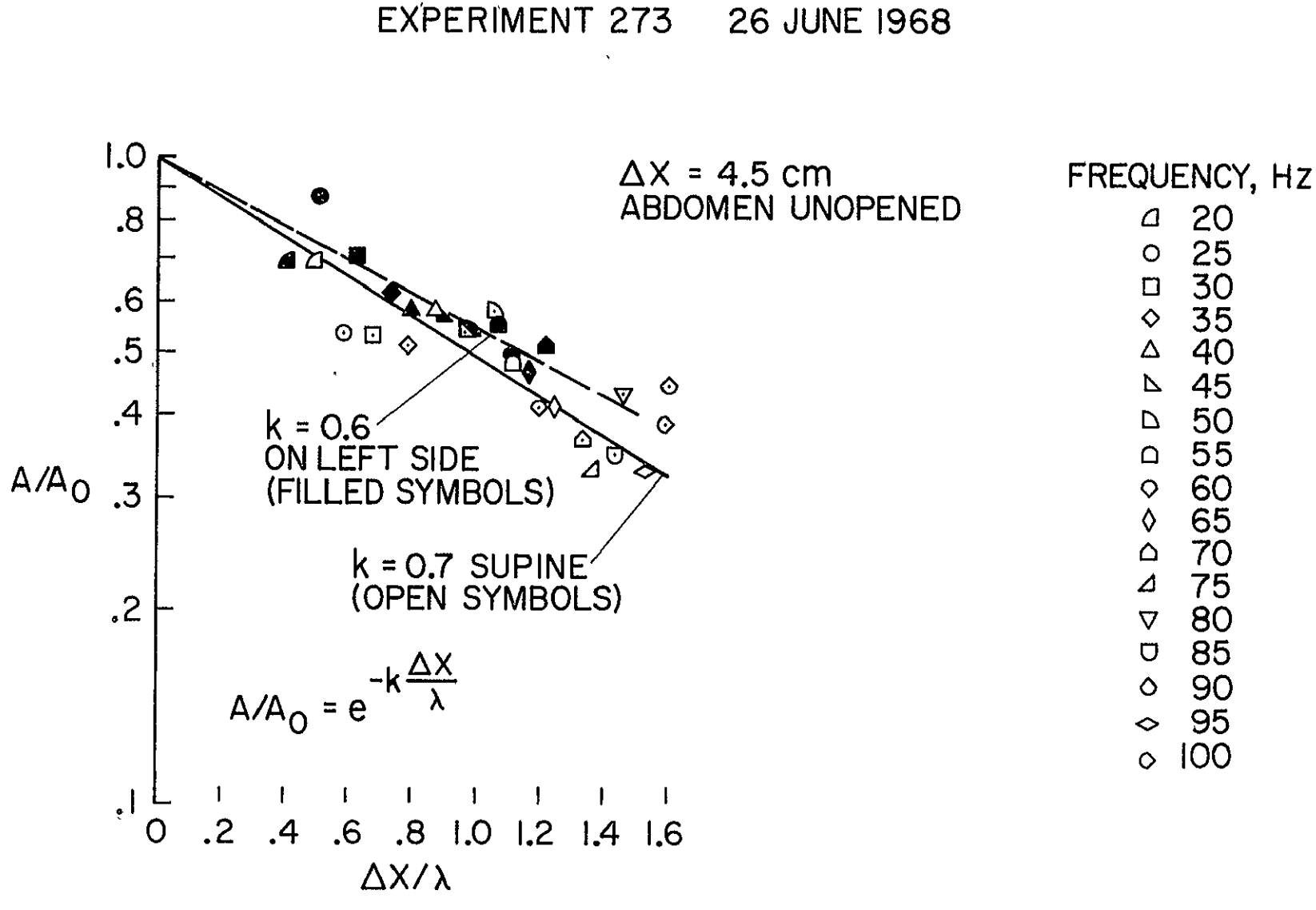


Figure 13. Effect of position on attenuation of pressure waves in the abdominal vena cava; abdomen unopened.

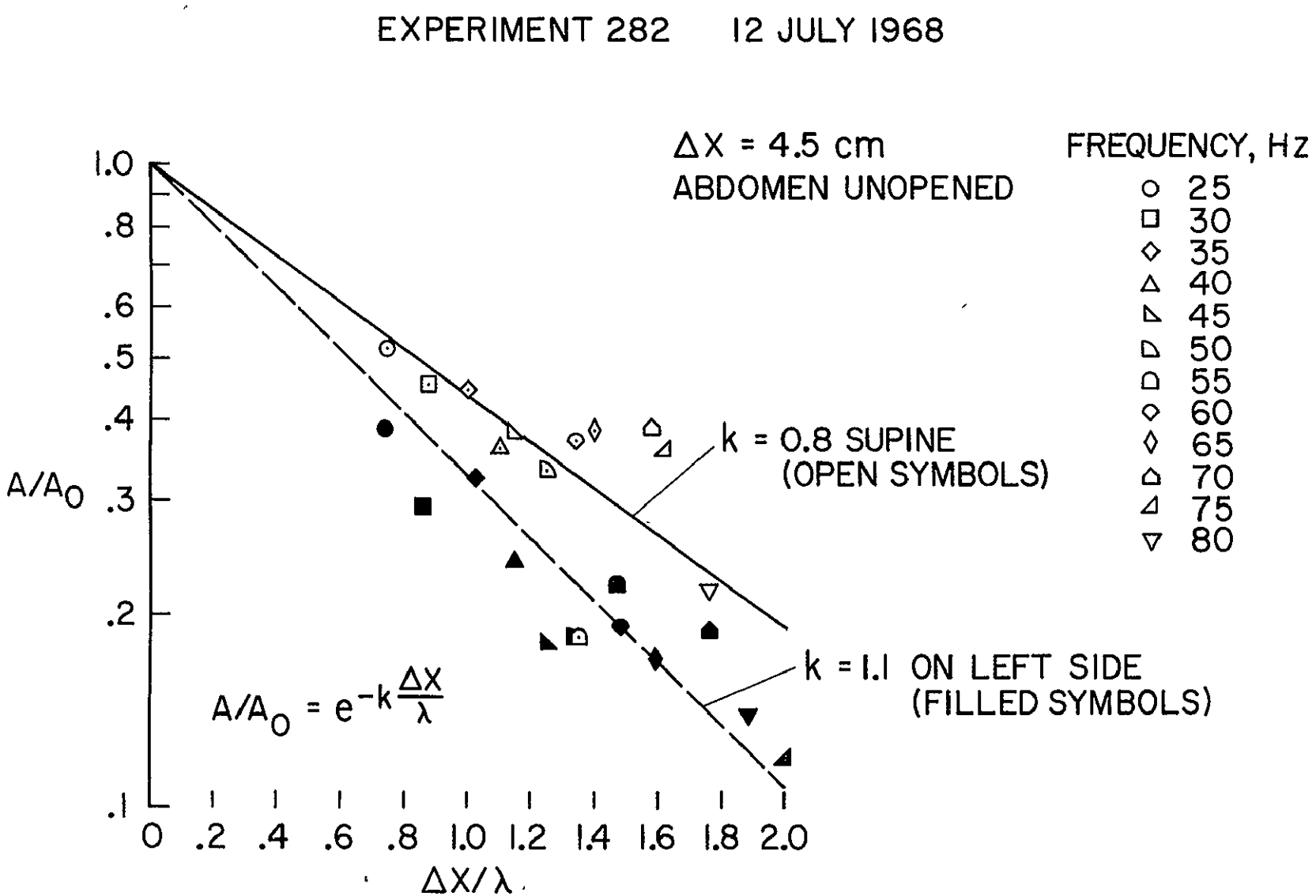


Figure 14. Effect of position on attenuation of pressure waves in the abdominal vena cava; abdomen unopened.

these differences are small, and considering the results from other experiments we conclude that there appears to be no essential predictable difference in attenuation between the supine position and that with the dog on its left side.

In general the dispersion and attenuation data for the 11 dogs with their abdomens unopened is described by wave speeds from 100-300 cm/sec in the frequency range 20-110 Hz, and by logarithmic decrements of 0.6-2.0.

2.5.2 Abdomen unopened, except for intra-abdominal pressure measurement

Dispersion and attenuation data were acquired from 7 dogs in the supine position and from 5 different dogs on their left sides. The comments made in 2.5.1 concerning data analysis, statistical analysis, and data scatter apply here also. Figure 15 illustrates dispersion for a dog in the supine position; the wave speeds vary from 200-260 cm/sec in the frequency range 20-65 Hz. In this experiment the magnitudes of the various pressures were about as follows: $P_V = 140$, $P_{ABD} = 120$, and $P_T = 20$ mmH_2O. Transmural pressure P_T was calculated by subtracting intra-abdominal pressure P_{ABD} from intraluminal pressure P_V. P_{ABD} is difficult to measure (see 2.6 DISCUSSION AND CONCLUSIONS) and is subject to considerably larger errors than is P_V; therefore, the values of P_T are subject to question.

In order to provide an indication of changes in wave speed that can occur within an hour or two during an experiment, dispersion of waves recorded early and late in an experiment are presented in Figure 16. Wave speeds recorded from 1:40-1:48 p.m. are greater than those recorded from 3:15-3:20 p.m., but in general both sets of data indicate the vena cava is at most mildly dispersive with most wave speeds lying between 150 and 250 cm/sec in the frequency range 20-75 Hz.

The attenuation data corresponding to the dispersion shown in

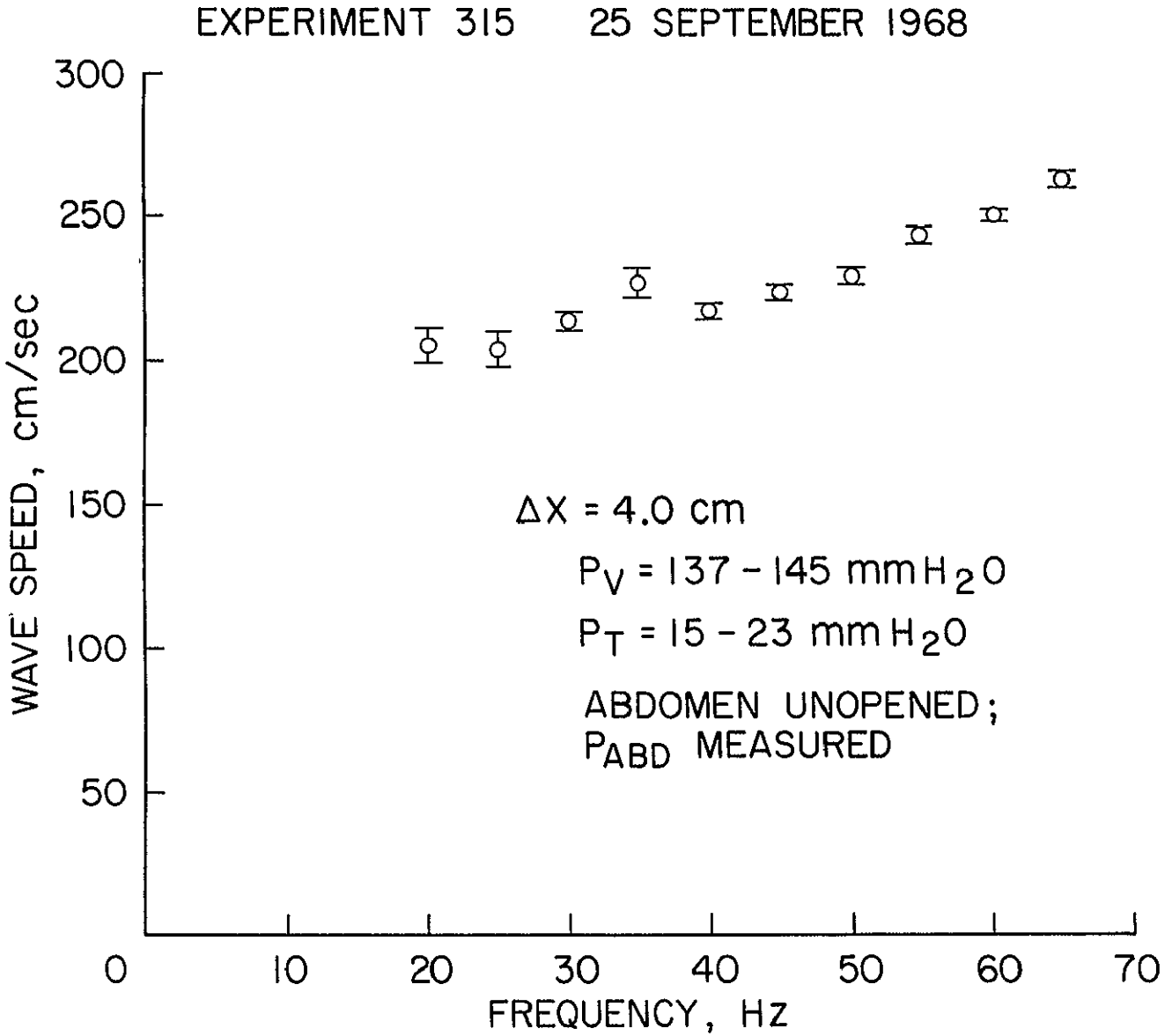


Figure 15. Dispersion of pressure waves in the abdominal vena cava; abdomen unopened, except for intra-abdominal pressure measurement.

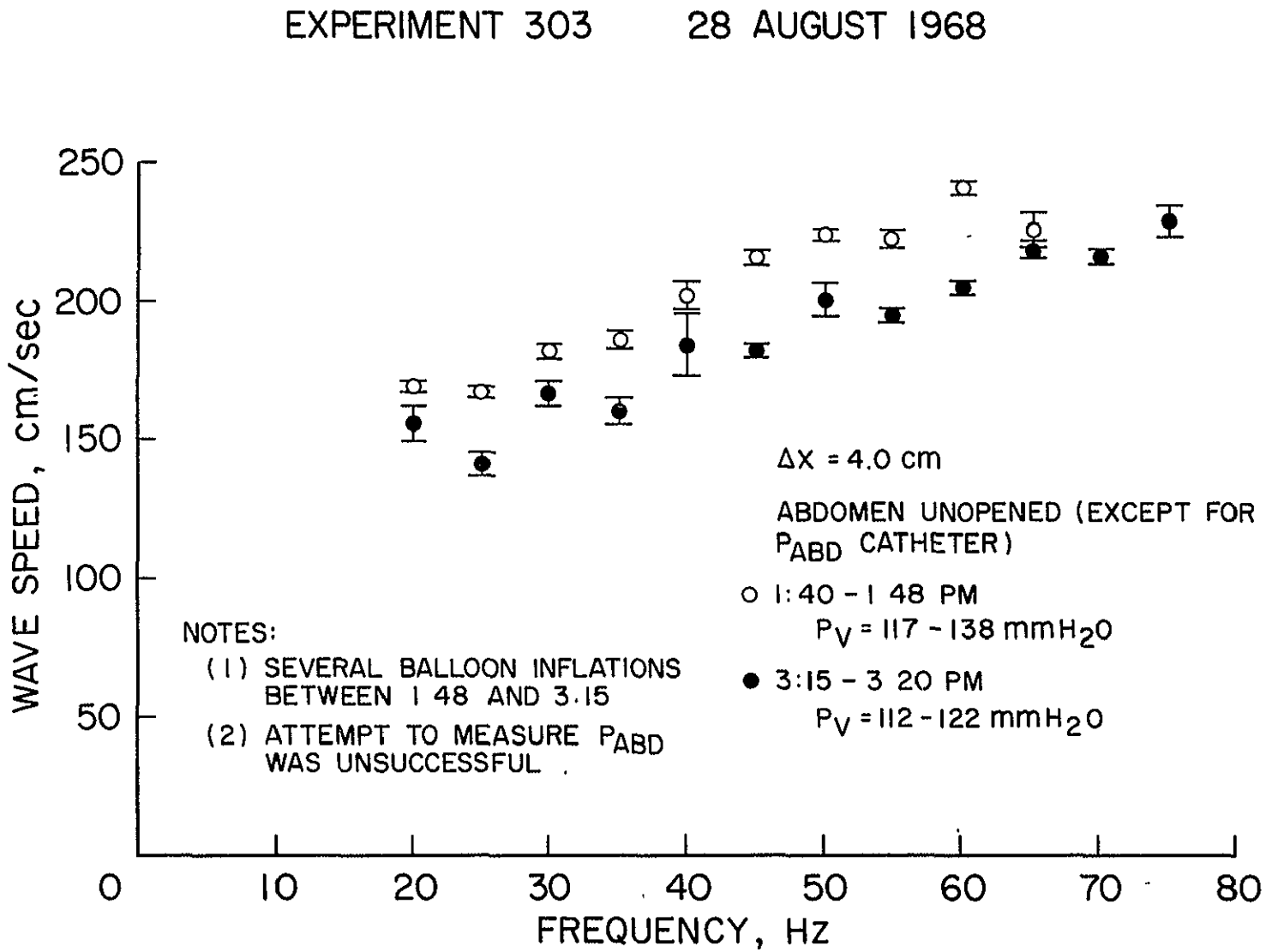


Figure 16. Dispersion of pressure waves in the abdominal vena cava recorded early and late in the experiment; abdomen unopened, except for intra-abdominal pressure measurement.

Figures 15 and 16 are plotted in Figures 17 and 18. In Figure 17, $k = 0.9$; and in Figure 18, the values of k for the data acquired early and late in the experiment are the same to the first significant figure (0.6).

In general the dispersion and attenuation data for the 12 dogs with their abdomens unopened, except for intra-abdominal pressure measurement, is described by wave speeds from 100-300 cm/sec in the frequency range 20-90 Hz and by logarithmic decrements of 0.6-3.2.

2.5.3 Abdomen unopened, except for intra-abdominal pressure measurement; compared with abdomen opened, viscera displaced

Two experiments were specifically designed to evaluate possible changes in transmission characteristics resulting from opening the abdomen and displacing the abdominal viscera. Dispersion and attenuation data were collected for three conditions on each of the two animals in the following order:

1. Abdomen unopened, except for intra-abdominal pressure measurement
2. Abdomen opened (viscera not displaced)
3. Abdomen opened; viscera displaced.

In addition, to evaluate the effects of variations in venous pressure on the wave speed (Chapter 3), balloon inflations were performed for each of these conditions. In an attempt to avoid possible changes in wave speed resulting from axial movement of the catheter-tip manometers in the vena cava[17] which might have occurred during the opening of the abdomen and the displacement of the abdominal viscera, the manometer tips were repositioned in the axial direction after each change in condition, if necessary, using the lumbar vertebrae as references.

The dispersion data for these two experiments are shown in Figures 19 and 20. Values of standard error of the mean are shown for only two of the three

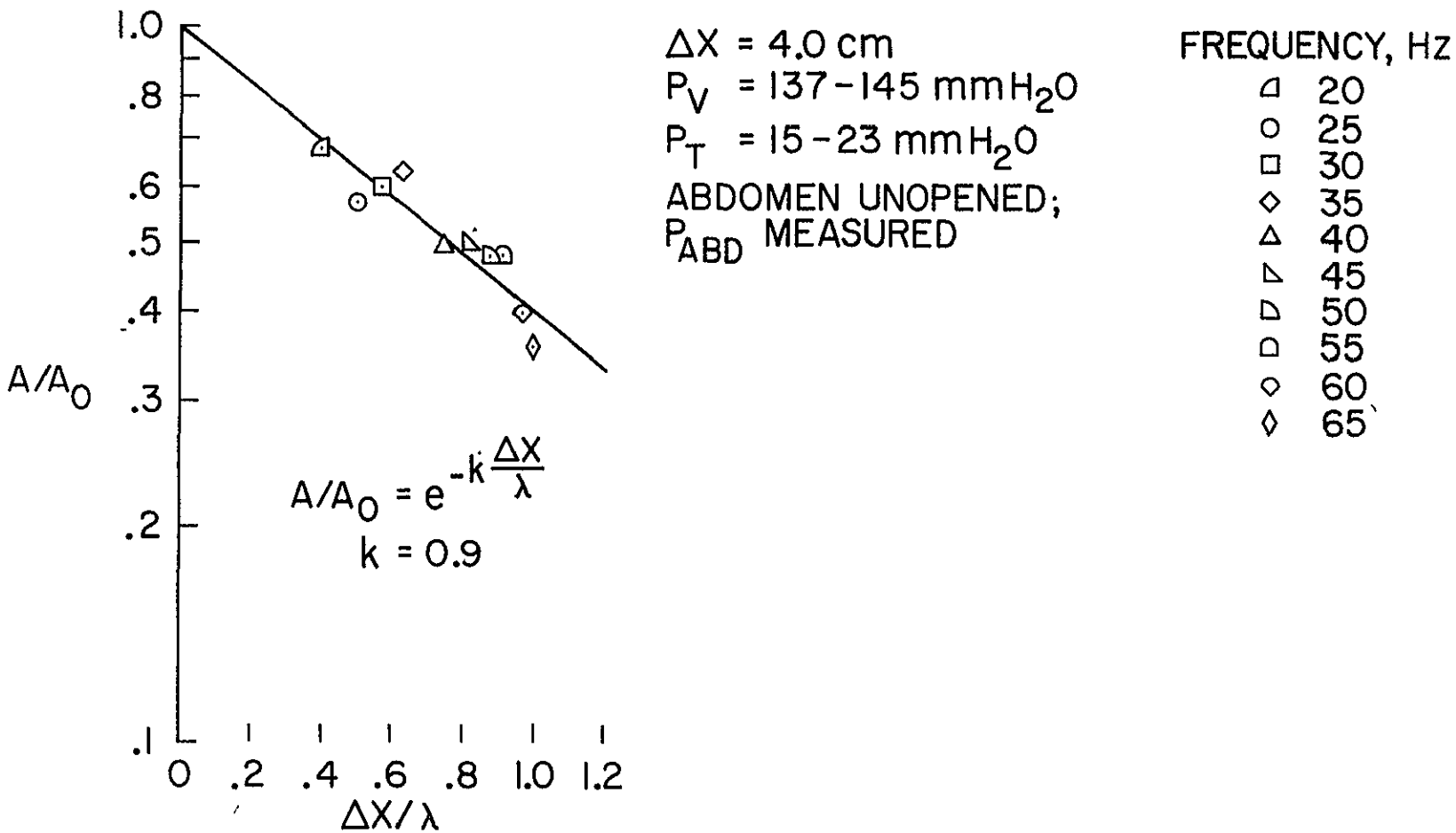


Figure 17. Attenuation of pressure waves in the abdominal vena cava; abdomen unopened, except for intra-abdominal pressure measurement.

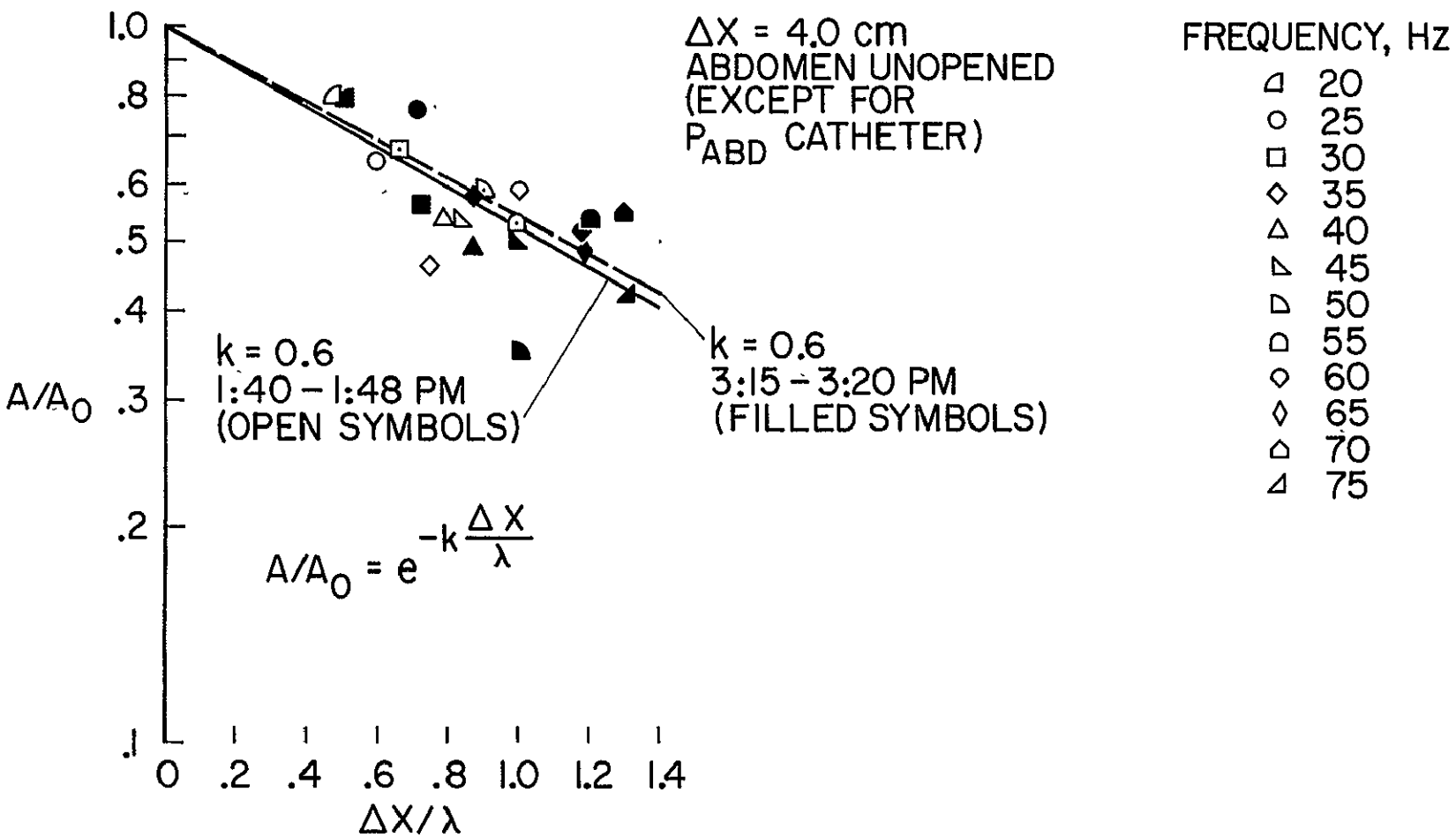


Figure 18. Attenuation of pressure waves in the abdominal vena cava recorded early and late in the experiment; abdomen unopened, except for intra-abdominal pressure measurement.

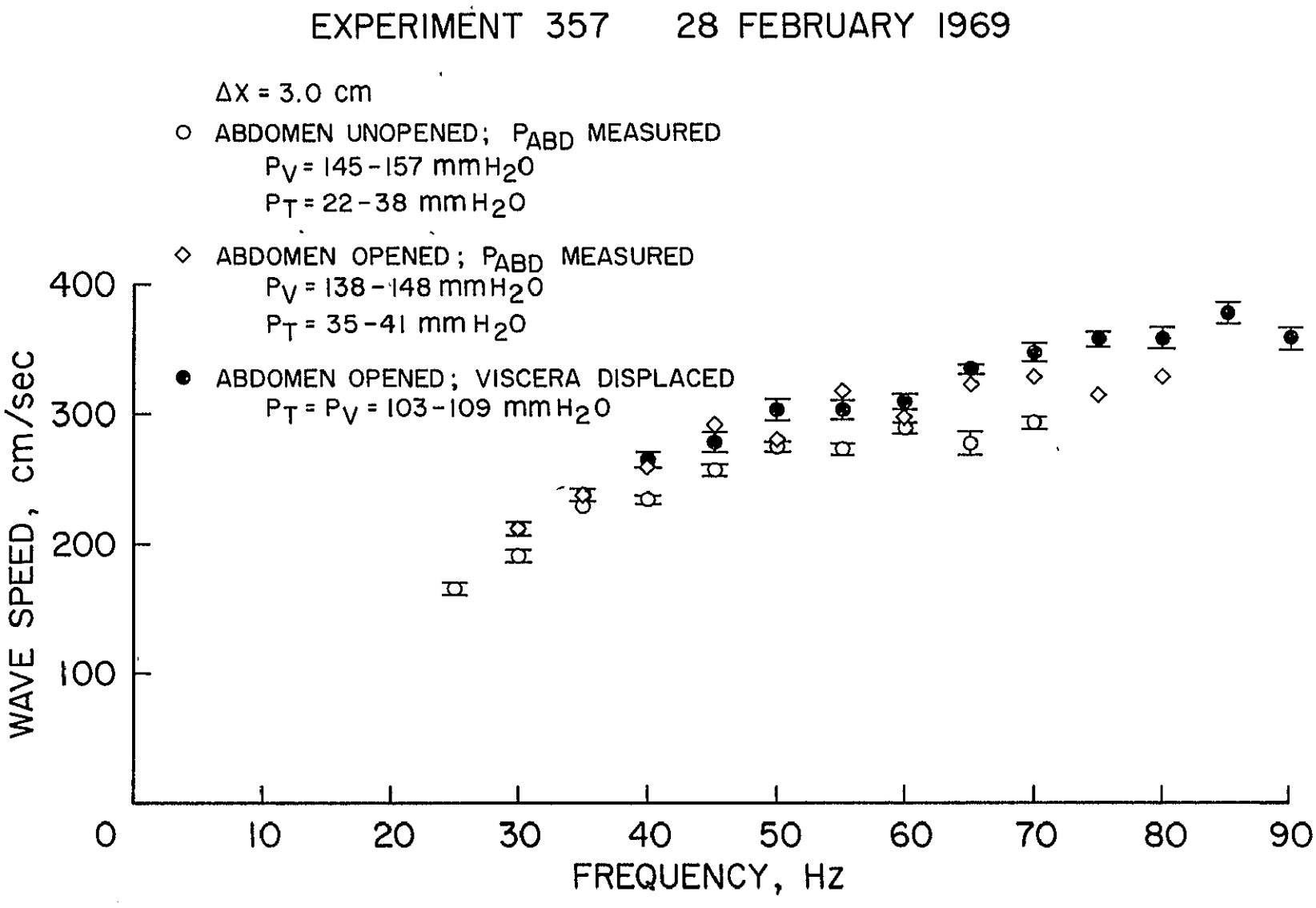


Figure 19. Effect of opening the abdomen and displacing the abdominal viscera on dispersion of pressure waves in the abdominal vena cava.

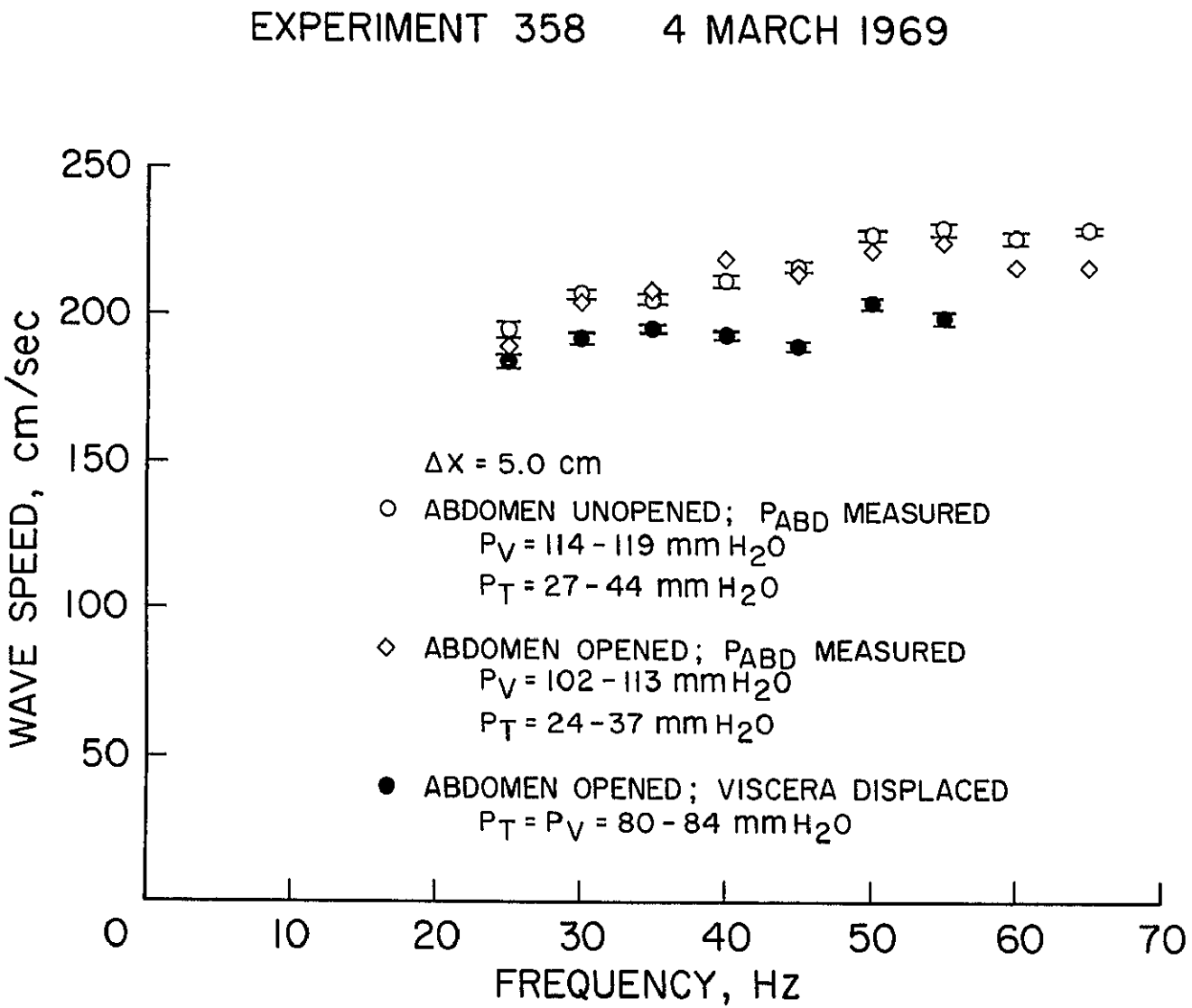


Figure 20. Effect of opening the abdomen and displacing the abdominal viscera on dispersion of pressure waves in the abdominal vena cava.

conditions. In Figure 19 the wave speeds are higher for the condition with the abdomen opened and the viscera displaced, and in Figure 20 the opposite is true. The corresponding attenuation data are presented in Figures 21 and 22. The values of k (2.8-3.3) shown in Figure 21 are larger than we usually observe them. In this experiment k was lowest for the condition with the abdomen opened and the viscera displaced, and in the experiment described in Figure 22 the opposite is true.

In general the results of these two experiments indicate that both opening the abdomen and displacing the abdominal viscera may have changed the wave speeds and attenuation coefficients; however, the direction and magnitude of the changes that occurred were not predictable and did not greatly alter the general dispersive and attenuating nature of the vessels.

2.6 DISCUSSION AND CONCLUSIONS

Dispersion and attenuation data for small pressure waves were acquired from 25 dogs in a variety of surgical states and animal positions. Differences in transmission characteristics from dog to dog and between conditions in a particular dog, although in many cases statistically significant, were usually not excessively large. In general for all the conditions studied the wave speeds were between 100 and 350 cm/sec in the frequency range 20-110 Hz. Typical results for a single experiment showed wave speeds increasing from about 150 cm/sec at 20 Hz to approximately 250 cm/sec at 80 Hz. Thus the vena cavae exhibited mild dispersion of small-amplitude pressure waves, which is in agreement with theoretical predictions[14,16]. Usually, the waves were attenuated exponentially with distance traveled, and the attenuation per wave length was independent of frequency. Values of the logarithmic decrement k ranged from 0.6 to 3.3 and generally were in the range 0.8 to 2.0. The values

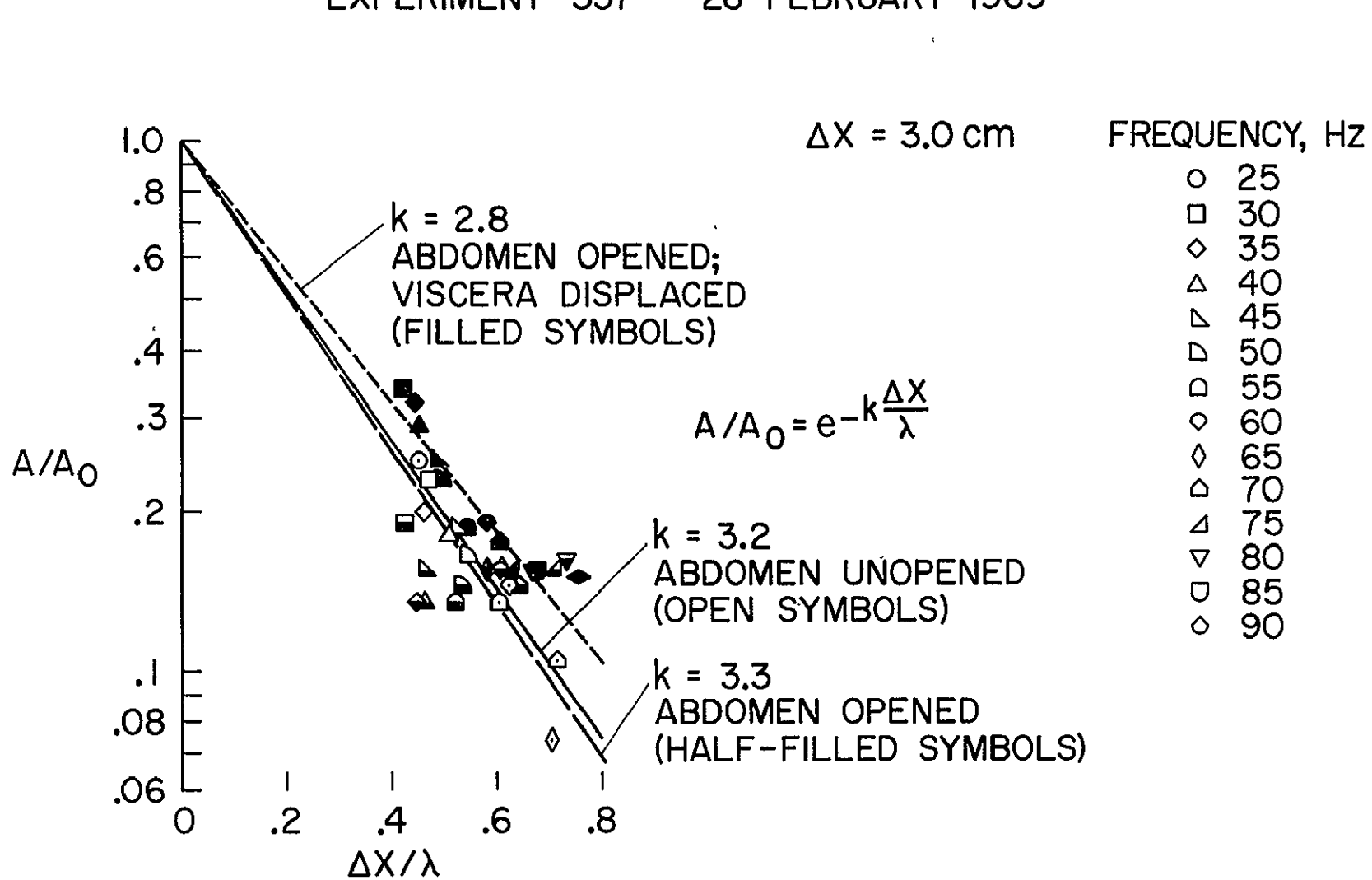


Figure 21. Effect of opening the abdomen and displacing the abdominal viscera on attenuation of pressure waves in the abdominal vena cava.

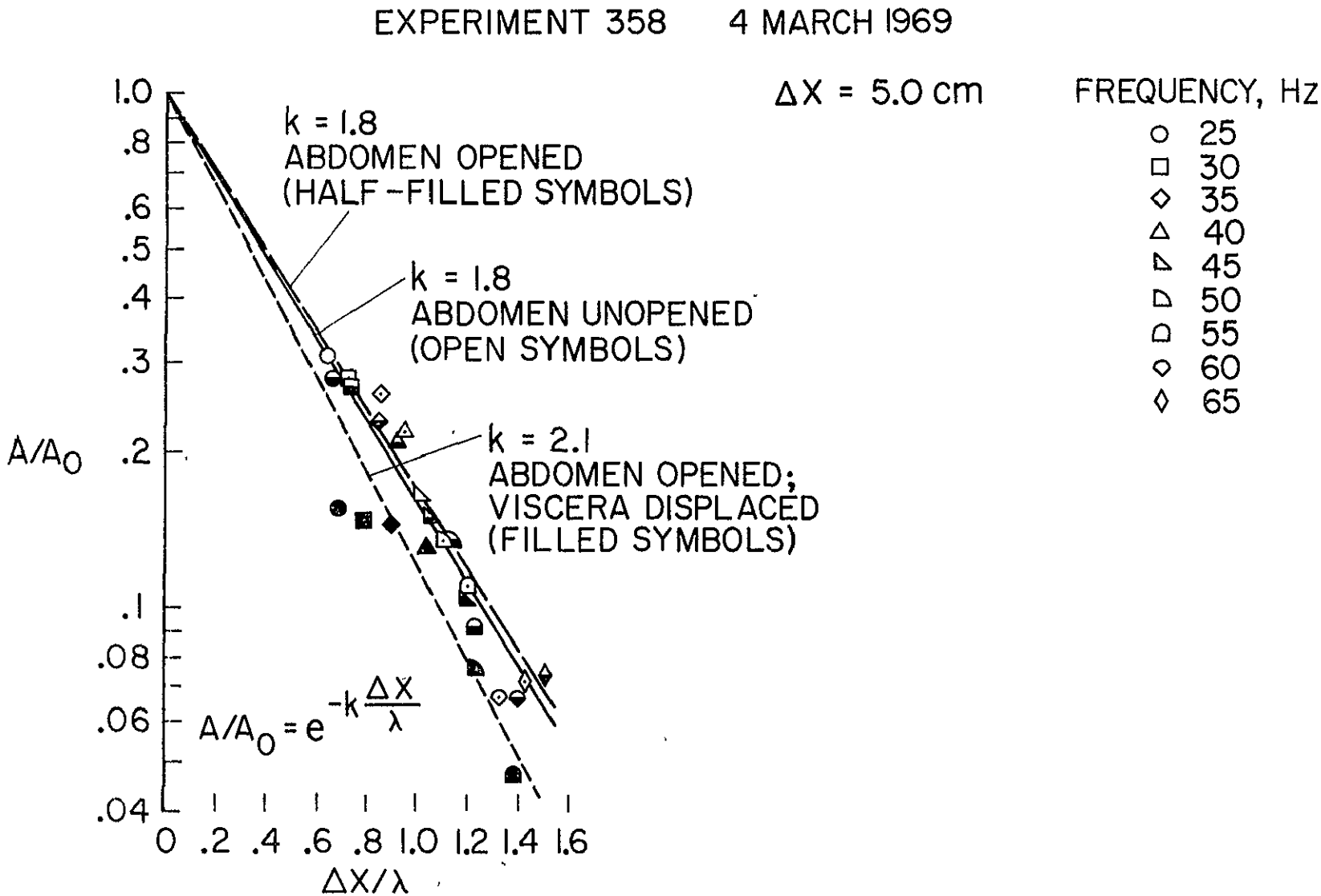


Figure 22. Effect of opening the abdomen and displacing the abdominal viscera on attenuation of pressure waves in the abdominal vena cava.

for the wave speed c and the logarithmic decrement k found in these experiments compare favorably with those previously reported from our laboratory for the abdominal vena cavae of large, anesthetized dogs with their abdomens opened and abdominal viscera displaced[17]. Values for c and k in the thoracic aorta during diastole are 400-600 cm/sec and 0.7-1.0[19] and in the carotid artery about 1100 cm/sec and 1.0[27].

The reader is again referred to sample tracings of finite trains of sinusoidal pressure waves of different frequencies recorded in the vena cava shown in Figure 1. Although the waves are attenuated with distance, they retain their sinusoidal character; this absence of obvious distortion is further evidence that the vena cava is not strongly dispersive to pressure waves in the amplitude and frequency ranges considered here, and that effects of reflections, if any, are small. For pressure waves less than 20 mm H_2O peak-to-peak the value of ΔT did not depend appreciably on the choice of a characteristic point in a particular wave train; this is further evidence that the sinusoidal character of the propagating waves is not distorted by the vena cava.

In each experiment, sample recordings were inspected for evidence of reflections. Large differences in the magnitude of ΔT_1, ΔT_2, and ΔT_3 in a single wave train; large differences in the shapes of successive waves in a single wave train; or oscillations in the recorded signal immediately following the four induced waves are considered as evidence of important reflections. If any of this evidence was seen and could not be eliminated by appropriately repositioning the catheter-tip manometers, the experiment was terminated; this occurred for about 5% of the dogs studied.

Sample recordings were also inspected for nonaxisymmetric pressure

waves by placing the catheter-tip manometers side by side so their tips were in the same cross section. If the shapes of the same wave were different on the respective manometer recordings, then nonaxisymmetric waves were considered important. This occurred if the catheter-tip manometers were within 1 or 2 cm of the vibrating piston; therefore, this positioning was avoided.

Attenuation of pressure waves can be attributed to three major causes:

1. Viscosity of the blood
2. Radiation of energy into the surrounding medium
3. Viscoelastic damping in the vessel wall.

Theoretically[16] the effects of blood viscosity are small for the small-amplitude, low-frequency pressure waves investigated here. Radiation of energy into the surrounding medium probably plays a minor role, because the logarithmic decrement did not decrease appreciably when the abdomen was opened and the viscera were displaced, a procedure which exposes a significant portion of the vena cava to the atmosphere. In the case of the thoracic aorta[19] the complete surgical exposure of the segment in which the waves were studied did not cause a noticeable change in the dissipation of the waves observed prior to exposure. An investigation of dissipation before and after complete surgical exposure of the abdominal vena cava was not attempted here. Because of the minor effects attributed to blood viscosity and radiation of energy into the surrounding medium, we conclude the major dissipative factors are viscoelastic elements in the vessel wall.

The significant differences in wave speeds from animal to animal observed in our experiments can be attributed to differences in vessel elastic properties and geometry, and to differences of the physiological state in the animal including transmural pressure, flow, axial stretch, surgical trauma, and depth of anesthesia.

The effects of a mean flow are predicted to increase the velocity of a wave propagating in the direction of the mean flow by an amount approximately equal to the average stream velocity[31]. In order to minimize the effects of increased flow[17] and variations in transmural pressure and axial stretch which can occur during inspiration, only waves recorded during the resting phase of the respiratory cycle were reported here. No systematic study of the effects of inspiration on wave speed was made; however, both increases and decreases in wave speed as well as increases and decreases in venous pressure were observed during the active phase of the respiratory cycle (not in the same animal).

Intra-abdominal pressure is difficult to measure and is subject to considerably more error than venous pressure. Positioning the metal catheter tip near the vena cava test section while avoiding blockage of the tip by the omentum or other intra-abdominal tissue was not always successful. In an attempt to avoid tip blockage by abdominal viscera, saline was dripped slowly through the cannula. In some experiments a short section of rubber tubing having several holes in its walls was attached to the end of the metal cannula before its insertion into the abdomen; this made likely the possibility that at least one or more holes were open allowing pressure communication between the abdominal cavity and the fluid inside the cannula. Movement of abdominal viscera during the active phase of the respiratory cycle added further complications to measuring intra-abdominal pressure. Considering these problems, the values of intra-abdominal pressure are subject to question, as are the values of transmural pressure obtained by subtracting intra-abdominal pressure from intraluminal (venous) pressure.

It is hoped that the dispersion and attenuation data reported here will aid theoreticians in checking and formulating their mathematical models of the mechanical behavior of blood vessels. Although this study was limited to

pressure waves in the vena cava, investigation of the transmission characteristics of axial and torsional waves propagating in the vena cava or other veins would allow the degree of anisotropy in the elastic and viscoelastic behavior of the vessel walls to be evaluated.

CHAPTER 3

THE EFFECT OF PRESSURE ON THE SPEED OF SMALL PRESSURE WAVES IN THE ABDOMINAL VENA CAVA

3.1 INTRODUCTION

It has been shown theoretically[14,15] and demonstrated experimentally[17,19,27] that the transmission characteristics of blood vessels can be altered by changing the transmural pressure. Results obtained during the initial phases of the experimental studies described here indicate that large increases in wave speed following heart block by vagal stimulation and following death are generally accompanied by major increases in venous pressure.

In order to evaluate the effects of venous pressure on the speed of pressure waves propagating in the abdominal vena cava a catheter-tip balloon, inserted through the external jugular vein and positioned in the inferior vena cava just caudal to the heart, was inflated to obstruct the vessel lumen and, thus, to induce an increased venous pressure in the test section. These studies are ground work for future investigations of control of venomotor tone and distensibility.

3.2 EXPERIMENTAL PROCEDURE

The methods and experimental procedures used in these experiments were the same as those described in Chapter 2; in fact, most of the data documenting the influence of pressure on wave speed was acquired from some of the dogs discussed in Chapter 2.

The usual procedure was to obtain dispersion and attenuation data from a dog in a particular condition and then to determine the effects of increased venous pressure on the wave speed for the same condition by inflating the balloon

one or more times. In an attempt to avoid possible baroreceptor reflexes mediated by a fall in arterial blood pressure associated with the decreased venous return during balloon inflation, the balloon was inflated quickly, allowing acquisition of wave speeds for a wide range of venous pressures within a few seconds. The balloon was allowed to deflate quickly, immediately after data acquisition.

3.3 RESULTS

The effect of venous pressure on the speed of small-amplitude, artificially-induced, sinusoidal pressure waves propagating in the abdominal vena cava was determined for 10 of the 25 anesthetized dogs described in Chapter 2. The effect of pressure on wave speed in the vena cava of dogs with their abdomens opened and viscera displaced has been previously studied in our laboratory[17]; emphasis in the work described here was placed on a preparation with the abdomen unopened, in order to provide the ground work for future investigations, such as those on unanesthetized animals. In an attempt to evaluate the wave speed in terms of transmural pressure, as well as venous pressure, intra-abdominal pressure was measured in 8 of the 10 dogs discussed in this chapter. Transmural pressure was calculated by subtracting intra-abdominal pressure from venous pressure.

Typical results of wave speed variations during one balloon inflation plotted as a function of venous pressure (open symbols) and transmural pressure (filled symbols) are shown in Figure 23. Before the balloon was inflated the wave speeds were about 200 cm/sec; as the balloon was inflated, venous pressure P_V, transmural pressure P_T, and wave speed c increased to maximum values of about 260 mmH_2O, 200 mmH_2O, and 800 cm/sec, respectively, in less than 14 seconds. Note that both the c vs P_V and the c vs P_T curves

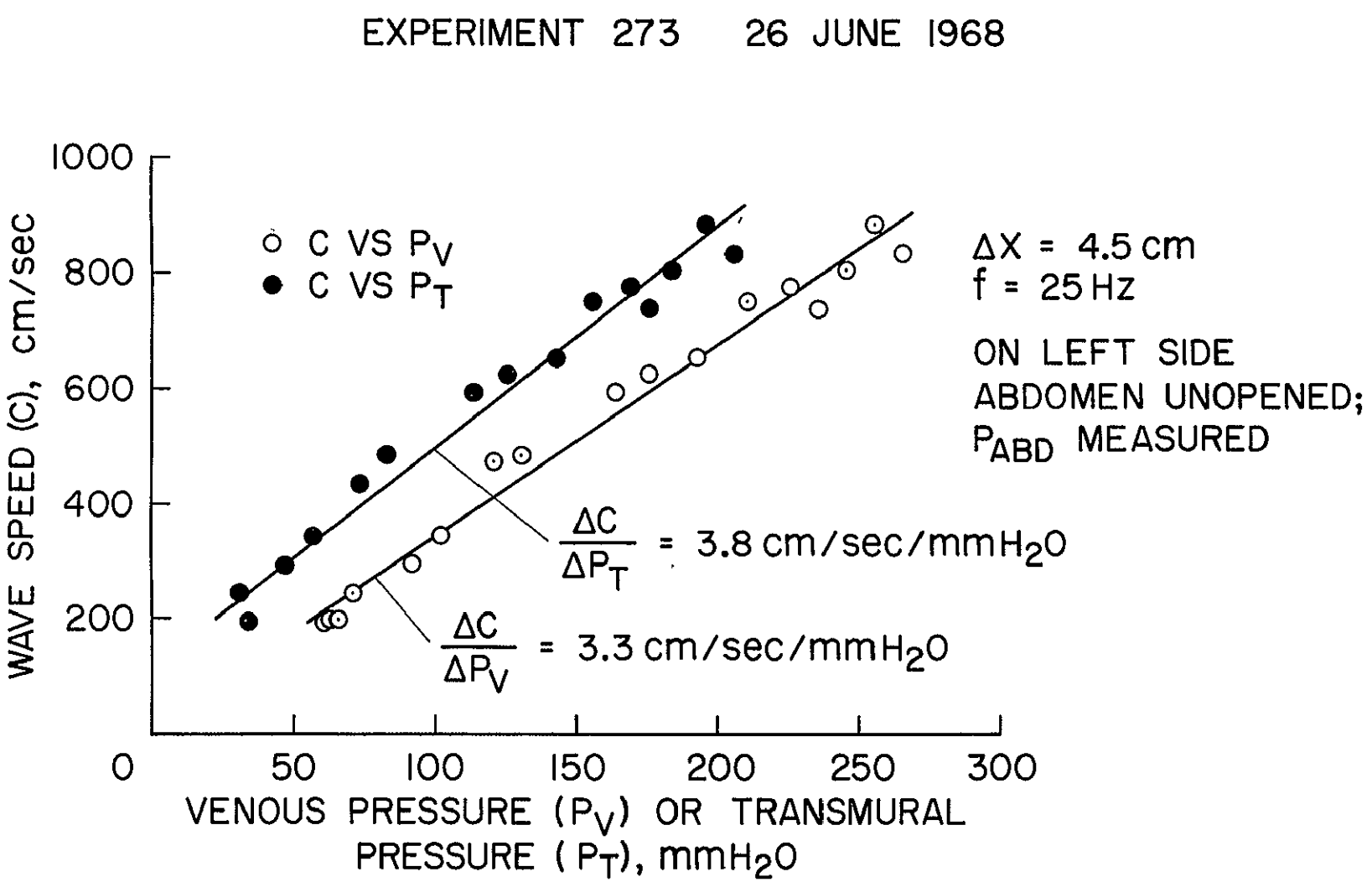


Figure 23. Speed of pressure waves in the abdominal vena cava plotted as a function of intraluminal (venous) pressure and transmural pressure.

are reasonably linear. Each point on the curve represents a single average wave speed determined from the average ΔT for the first three waves in a single wave train. All points shown were acquired while the pressure was increasing and within 14 seconds after balloon inflation was initiated. Linear regression lines using the method of least squares were calculated and are shown in the figure. The slopes of these lines are

$$\frac{\Delta c}{\Delta P_V} = 3.3 \text{ cm/sec/mm } H_2O \quad \text{and} \quad \frac{\Delta c}{\Delta P_T} = 3.8 \text{ cm/sec/mm } H_2O.$$

$\frac{\Delta c}{\Delta P_T}$ is larger than $\frac{\Delta c}{\Delta P_V}$ because the intraluminal (venous) pressure increased more than the transmural pressure.

Although arterial blood pressure decreased from a control of 163/120 mm Hg to 110/90 five seconds after inflation and to 84/68 fourteen seconds after inflation, the average heart rate for the first 5 seconds of balloon inflation was the same as control (2.3/sec) and increased to only 2.45/sec in the period 10-15 seconds after inflation was started. Apparently baroreceptor reflexes were not effective in increasing the heart rate (somewhat high already) during the first few seconds of balloon inflation even though the arterial pressure had decreased significantly following the decrease in venous return. In general the average heart rate did not increase from control levels by more than 5% until 10-15 seconds after balloon inflation was initiated. We consider this as an indication that arterial baroreceptor reflexes could not have mediated appreciable changes in the mechanical behavior of the vena cava wall during the first few seconds following initiation of balloon inflation.

Figure 24 illustrates representative wave speeds and venous pressures acquired during 5 balloon inflations, separated by at least 2 minutes and performed

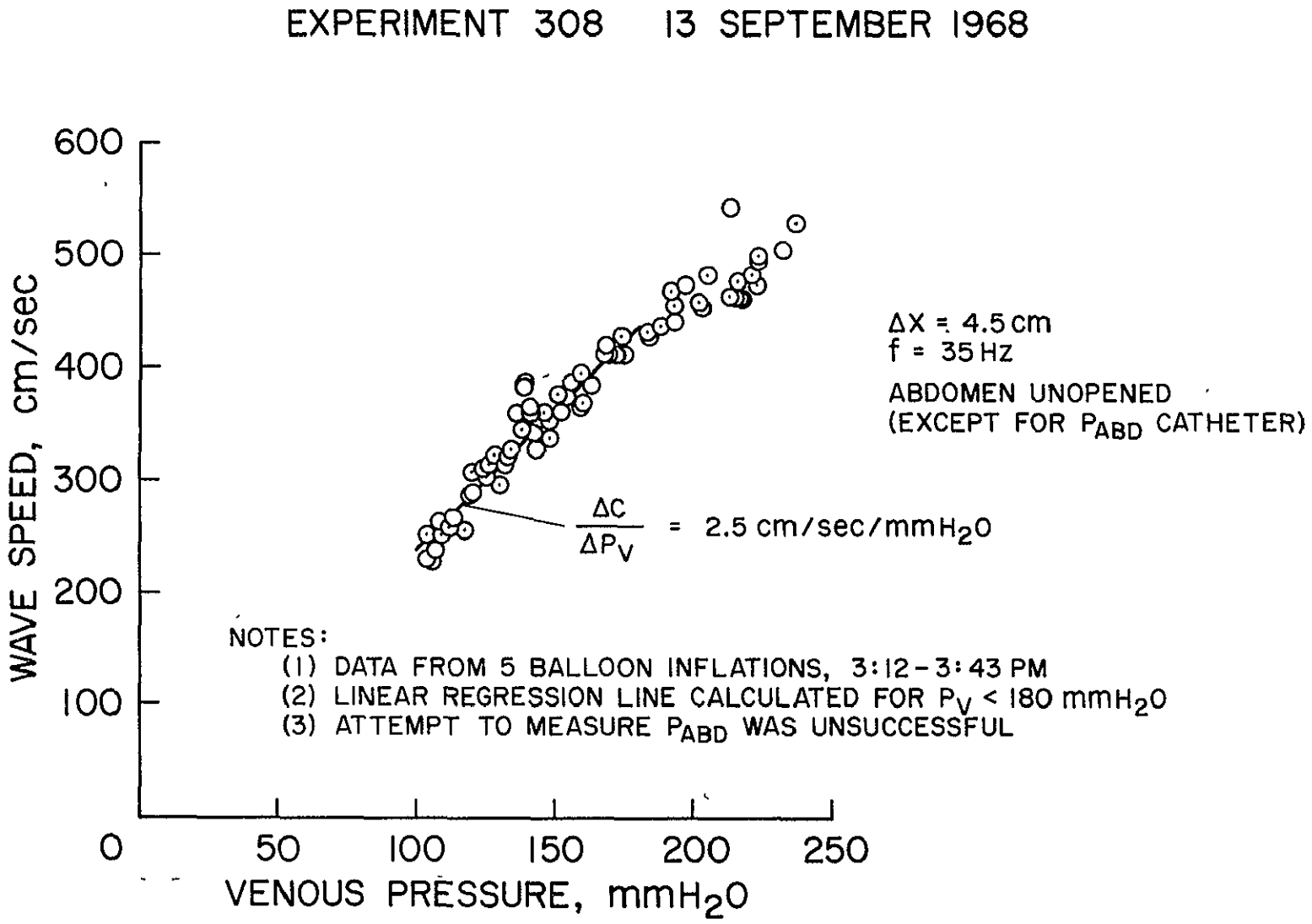


Figure 24. Speed of pressure waves in the abdominal vena cava plotted as a function of intraluminal (venous) pressure.

within a 30 minute interval. Wave speeds increased from 230 cm/sec at venous pressures of 110 mm H_2O to 500 cm/sec at 230 mm H_2O. To aid the reader in ascertaining an approximate slope for the lower portion of the curve, a linear regression line has been calculated for all points with $P_V < 180$ mm H_2O; the resulting slope is $\frac{\Delta c}{\Delta P_V} = 2.5$ cm/sec/mm H_2O.

The results of 6 balloon inflation studies performed on a single dog utilizing wave frequencies of 25, 35, 40 and 50 Hz are presented in Figure 25. The wave speed is again plotted versus venous pressure P_V and versus transmural pressure P_T. As expected, the wave speed increased quite consistently with pressure. Linear regression lines have been calculated and plotted for points corresponding to $P_V < 235$ mm H_2O. For all frequencies the wave speeds lie near these lines at low pressures; however, a marked frequency dependence is evident for values of $P_V > 235$ mm H_2O. The slopes of the linear regression lines are

$$\frac{\Delta c}{\Delta P_V} = 2.4 \text{ cm/sec/mm } H_2O \quad \text{and} \quad \frac{\Delta c}{\Delta P_T} = 2.7 \text{ cm/sec/mm } H_2O.$$

Generally speaking, for venous pressures up to about 200 mm H_2O the wave speed increased nearly linearly with venous pressure and with transmural pressure for the 10 dogs studied; the corresponding values of $\frac{\Delta c}{\Delta P_V}$ ranged from 1 to 5 cm/sec/mm H_2O and were mostly in the range of 2 to 4 cm/sec/mm H_2O. At higher pressures the slopes were usually less than initial slopes, and a marked dependence on wave frequency was noted in some cases. Inflating the balloon several times for 15 seconds did not appear to alter the wave speed-pressure relationships or the physiological state of the animal. However, in at least one experiment the balloon could not be deflated following

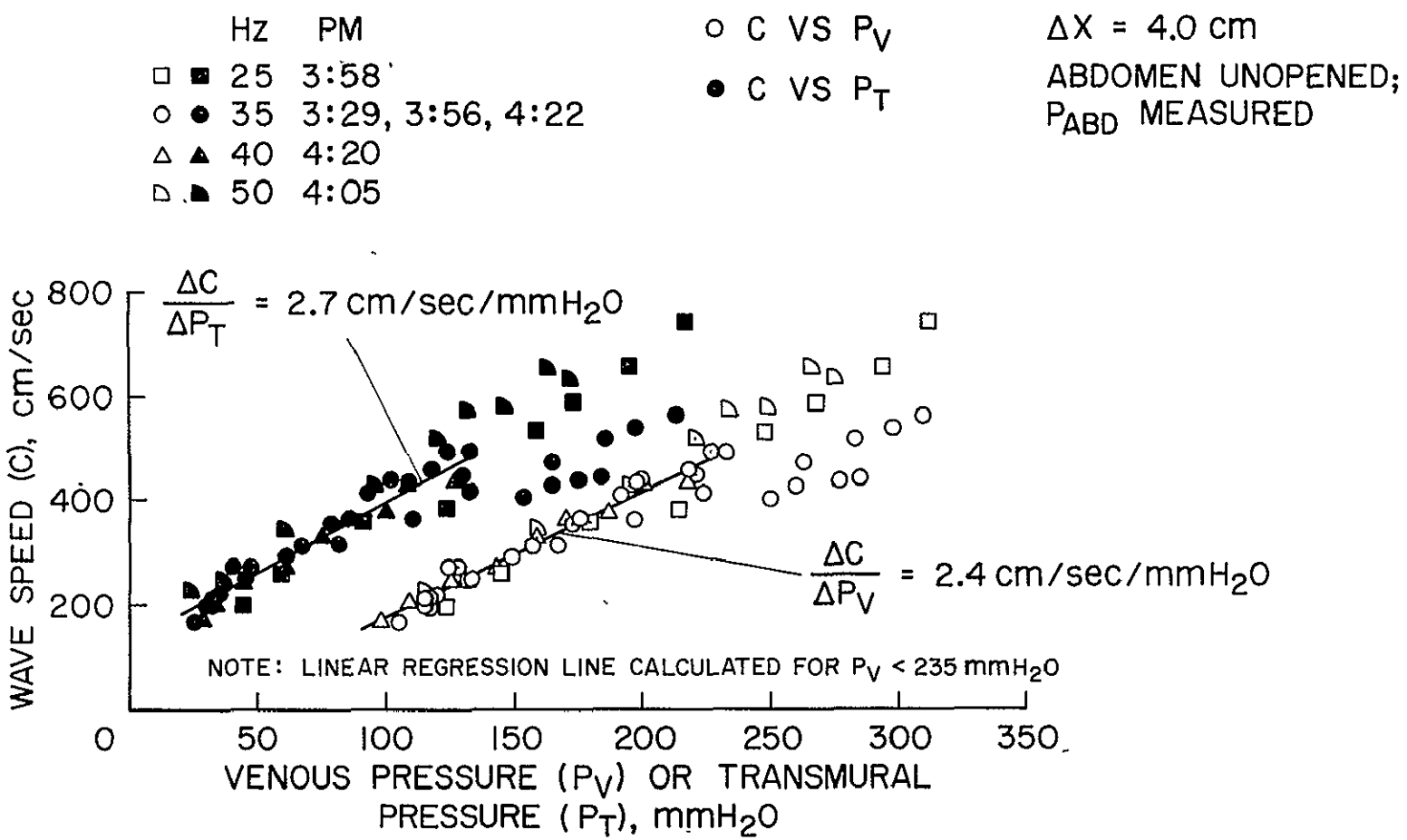


Figure 25. Speed of pressure waves in the abdominal vena cava plotted as a function of intraluminal (venous) pressure and transmural pressure.

an inflation, and the animal deteriorated significantly in a matter of minutes as evidenced by a steady fall in arterial blood pressure. Five dogs were studied in the supine position and five while lying on their left side; no significant differences in wave speed-venous pressure relationships resulting from animal position were noted.

3.4 DISCUSSION AND CONCLUSIONS

It is apparent from these studies that the speed of small-amplitude pressure waves propagating in the abdominal vena cavae of large anesthetized dogs is strongly dependent on venous pressure and transmural pressure. The slopes of the wave speed-venous pressure curves correspond well to values determined in our laboratory for anesthetized dogs with their abdomens opened and their abdominal viscera displaced: 1.5 to 2.5 cm/sec/mm H_2O[17]. Studies in our laboratory designed to determine the wave speed-pressure relationship in the thoracic aortas of anesthetized dogs have yielded values of $\frac{\Delta c}{\Delta P}$ from 3 to 6 cm/sec/mm Hg[19]. These values are approximately an order of magnitude smaller than we find for the abdominal vena cava; differences in vessel geometry, particularly wall thickness, and wall properties including histological differences explain much of the order of magnitude discrepancy.

The large increase of wave speed seen with increasing venous pressure apparently is the result of significant increases in the elastic and/or viscoelastic moduli of the vessel wall. It should be noted that the peak-to-peak amplitude of the small, artificial pressure waves usually increased sizeably with increasing pressure even though the stroke volume of the vibrating piston was constant during any one balloon inflation. Therefore, a constant change in volume produced a larger and larger change in pressure as venous pressure increased. This behavior may be interpreted as a decrease in the distensibility

of the vessel which is usually defined as $\frac{dV}{dP}$, where dV is the change in volume associated with a small change in pressure dP.

Theoretically[14] the predicted increase in wave speed with increasing transmural pressure is very much smaller than the values of $\frac{\Delta c}{\Delta P_T}$ we observed experimentally; however, the theory does not account for changes in elastic modulus of the vessel wall, which are quite apparent in our experimental studies.

The fact that the heart rate did not increase by more than 5% during the first 10 to 15 seconds of balloon inflation is interpreted as an indication that arterial baroreceptor reflexes did not mediate appreciable changes in the abdominal vena cava wall properties during this time interval. Further support for this hypothesis is found in our preliminary studies of the control of venomotor tone. In experiments designed to evoke changes in the mechanical behavior of the abdominal vena cava no consistent increases or decreases in the wave speed or in venous pressure could be elicited by occluding both common carotid arteries for periods up to a minute. Probably the anesthetized state of the animal significantly depresses the centrally routed baroreflexes.

Although arterial baroreceptor reflexes do not appear to have played a major role in mediating the changes of the elastic and viscoelastic properties evident in these studies, at this time we can not attribute these changes solely to the variations in transmural pressure. Other reflexes might have been influential, for example, those associated with responses of right atrial receptors to the decrease in venous return occurring during a balloon inflation.

The problems associated with measuring intra-abdominal pressure and with interpreting the associated calculated transmural pressure were thoroughly discussed in Chapter 2. Although the values of transmural pressure

are subject to question, changes in transmural pressure occurring during any one balloon inflation are more reliable. Because values of $\frac{\Delta c}{\Delta P_V}$ during a balloon inflation were generally no more than 15% less than values of $\frac{\Delta c}{\Delta P_T}$, $\frac{\Delta c}{\Delta P_V}$ may be used as a reasonable approximation to $\frac{\Delta c}{\Delta P_T}$ in future investigations on animals exposed to a minimum of surgical trauma; therefore, measurement of intra-abdominal pressure can be avoided. However, if absolute values of transmural pressure are required, intra-abdominal pressure measurement will be necessary.

CHAPTER 4

THE EFFECTS OF TRANSMURAL PRESSURE ON THE QUASI-STATIC AND DYNAMIC BEHAVIOR OF THE ABDOMINAL VENA CAVA

4.1 INTRODUCTION

Because of their ability to accommodate large changes in blood volume with relatively small variations in transmural pressure, the veins have traditionally been described as the capacitance elements of the cardiovascular system. It has been assumed that control of the venous reservoir is no less important in maintaining a functional circulation than regulation of the arterial tree; therefore, significant effort has been devoted to studying the factors which maintain and control venomotor activity.

Alexander[32] has provided a comprehensive review of the peripheral venous system and has summarized various methods for the assessment of venomotor activity, including in vitro studies, direct observation, inferences from venous pressure, measurements of pressure gradients, pressure measurements in an occluded venous segment, pulse methods, and venous distensibility patterns. Pulse methods are of particular interest, because the pulse speed in a blood vessel can be ascertained in a relatively short time interval and yields quantitative information about the changes in the elastic properties of the vessel wall, which may occur as a result of muscular activity within the time span of one second or less.

Assessment of changes in the elastic and viscoelastic properties of blood vessel walls elicited by neural and/or humoral stimuli is of major importance in the development of mathematical models which accurately predict the mechanical behavior of blood vessels. Therefore, we have initiated an experimental program to evaluate changes in large blood vessel behavior which

can occur as a result of neural and/or humoral stimuli.

In order to provide experimental information to serve as controls in the evaluation of changes in mechanical properties of the abdominal vena cava resulting from sympathetic stimulation and epinephrine injection (Chapter 5), we are presenting here our findings on the quasi-static and the dynamic behavior obtained as the transmural pressure increased during balloon inflation studies.

4.2 THEORETICAL CONSIDERATIONS

The speed of a small-amplitude pressure wave propagating in a fluid-filled, circular, cylindrical, elastic vessel can be related to the circumferential Young's modulus by the Moens-Korteweg equation:

$$c^2 = \frac{Eh}{2\rho_f a}$$

where c is the wave speed, E the circumferential Young's modulus, h the vessel wall thickness, ρ_f the density of the fluid, and a the mean radius of the vessel. Theoretical studies[16] indicate that the Moens-Korteweg equation provides a reasonable approximation for the speed of low-frequency pressure waves propagating in a vessel with the geometry of the abdominal vena cava.

The abdominal vena cava of a 20 to 40 kg dog is thin-walled (~ 0.15 mm) with a mean radius of about 7 mm. It has a wall which can be assumed as incompressible[2] and therefore, to a very good approximation, the radius and wall thickness are related by

$$ah = K$$

where K is a constant that can be evaluated by one simultaneous measurement

of radius and wall thickness, $a_o h_o = K$. These expressions, combined with the Moens-Korteweg equation, yield the following relation for the effective Young's modulus in the circumferential direction:

$$E = \frac{2\rho_f a c^2}{h} = \frac{2\rho_f a^2 c^2}{K} = \frac{2\rho_f a^2 c^2}{a_o h_o} .$$

We have added the adjective "effective" because here "E" includes effects of viscoelastic properties of the vessel in addition to the elastic properties and also represents the combined effects of the various histologic components (smooth muscle, collagen, elastic tissue, and endothelium) of the wall. Therefore the effective Young's modulus for the vena cava can be calculated by knowing the density of blood, the mean radius of the vessel, the speed of small pressure waves propagating in the vessel, and the value of K which can be determined by one simultaneous measurement of a and h. This expression allows the calculation of variations in the effective Young's modulus with time, provided that the radius and the wave speed can be measured with time. Note that by utilizing the relationship $ah = K = a_o h_o$, we have avoided the continuous measurement of h.

The speeds of small sinusoidal pressure waves propagating in the abdominal vena cava can be determined from recordings acquired in less than 0.1 second, and the radius can be measured continuously; therefore, an effective Young's modulus can be determined nearly instantaneously and also as a function of the frequency of the sine waves. As such, it reflects the dynamic behavior of the vessel wall material in two ways: (1) It portrays the frequency dependence of the quasi-instantaneous elastic modulus of the vessel wall and (2) It exhibits the

variations of this quasi-instantaneous elastic modulus over time intervals that are long compared with the period of the sine waves. Hence, we can determine the variations in the effective Young's modulus which occur during balloon inflation studies where the transmural pressure increases gradually over a period of 10 to 20 seconds.

An alternative expression for the circumferential Young's modulus E of a fluid-filled, circular, cylindrical, elastic vessel can be derived by considering the variation in diameter dD produced by a small change in pressure dP

$$E = \frac{D^3}{4K}\frac{dP}{dD}$$

where $D = 2a$ is the diameter of the vessel and $K = ah = a_o h_o$ as above.

In this equation E also represents an effective Young's modulus which would reflect the dynamic behavior of the vessel wall material if we could measure the small changes in diameter produced by the small sinusoidal pressure waves generated in our wave speed experiments. The value of E obtained in this fashion could then be compared with that E calculated from the Moens-Korteweg equation. This comparison would allow a check on the latter method which constitutes a less direct determination of E. However, the diameter measuring transducer (see 4.3 METHODS) utilized in our experiments does not have a sufficient frequency response to faithfully follow the changes in diameter produced by our small sinusoidal pressure waves. Unfortunately, we do not yet have available ultrasonic echo ranging devices which allow for accurate measurements of rapidly occurring vessel diameter variations and therefore this valuable check on the applicability of the Moens-Korteweg equation can not be

made at this time.

Nevertheless our diameter gage yields useful quasi-static measurements of the diameter. By recording it together with the venous pressure during balloon inflation studies we can plot the traditional pressure-diameter curves. We have designated these pressure-diameter relationships as the quasi-static behavior of the vena cava, since the balloon inflations take place during time intervals of 10 to 20 seconds.

The slope of a pressure-diameter curve $\frac{dP}{dD}$ and the vessel distensibility $\frac{dV}{dP}$ are related by a geometrical factor. For a circular, cylindrical vessel of unit length

$$V = \frac{\pi D^2}{4} \cdot 1$$

and

$$dV = \frac{2\pi D}{4} dD = \frac{\pi D}{2} dD.$$

Therefore

$$\frac{dV}{dP} = \frac{\frac{\pi D}{2} dD}{dP} = \frac{\pi D}{2} \frac{1}{\frac{dP}{dD}}.$$

By using the previously derived equation

$$E = \frac{D^3}{4K} \frac{dP}{dD}$$

and by evaluating $\frac{dP}{dD}$ from the pressure-diameter curve, a quasi-static value of effective Young's modulus can be calculated. It should be stressed, however, that values of E obtained in this manner must be designated as quasi-static, for they are calculated from slopes of pressure-diameter curves obtained during balloon inflations, and the time required to generate sufficient changes in pressure

and diameter to allow an accurate determination of the slope is at least 1 second in our experiments. This is in contrast to an effective Young's modulus determined from the speeds of propagating pressure waves which are recorded in less than 0.1 second. In addition, changes in the contractile state of the smooth muscle occurring during the recording of one train of propagating waves will be small, but changes occurring during the time interval required to produce a well defined $\frac{dP}{dD}$ may be significant. Therefore, the values of effective Young's modulus calculated from wave speeds should more accurately represent the purely passive dynamic behavior of the vessel than would the effective Young's moduli derived from slopes of our pressure-diameter curves. The ability to separate active and passive behaviors is particularly necessary in studying the importance of control mechanisms on the mechanical behavior of the vessel wall.

4.3 METHODS

Guided by the theoretical considerations discussed in the preceding section we have added to the wave generating and recording equipment described in Chapter 2 a transducer for measuring the internal diameter of the abdominal vena cava. It is shown schematically in the general experimental preparation illustrated in Figure 26 and photographically in Figure 27. The transducer is a catheter-tip device developed and built by Heinz Pieper and has the capability of measuring both diameter and pressure; however, the pressure transducer was not used in these experiments. The diameter measuring capability is described by Pieper and Paul[33]. Both the diameter transducer and the pressure transducer use the principle of a linear variable differential transformer. The coupling of the diameter gage transformer is determined by the position of a ferromagnetic sleeve that slides over the transformer coils which are housed in the central tube. This sleeve is mechanically linked to three spring-loaded braces spaced

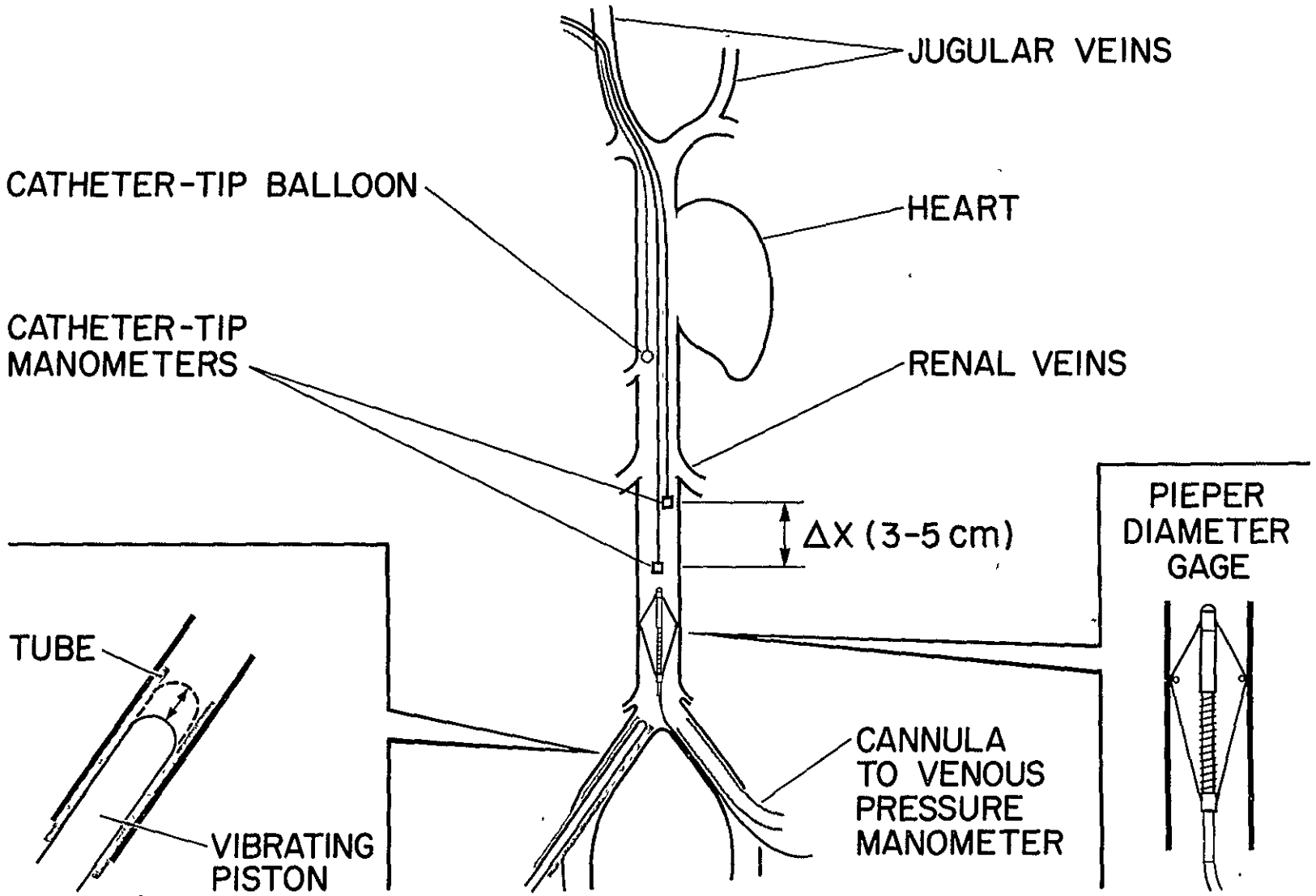


Figure 26. General experimental preparation for studying the effects of transmural pressure on the quasi-static behavior and the dynamic behavior of the abdominal vena cava (Chapter 4) and for investigating the active changes in the mechanical behavior of the vena cava produced by sympathetic stimulation and by epinephrine (Chapter 5).

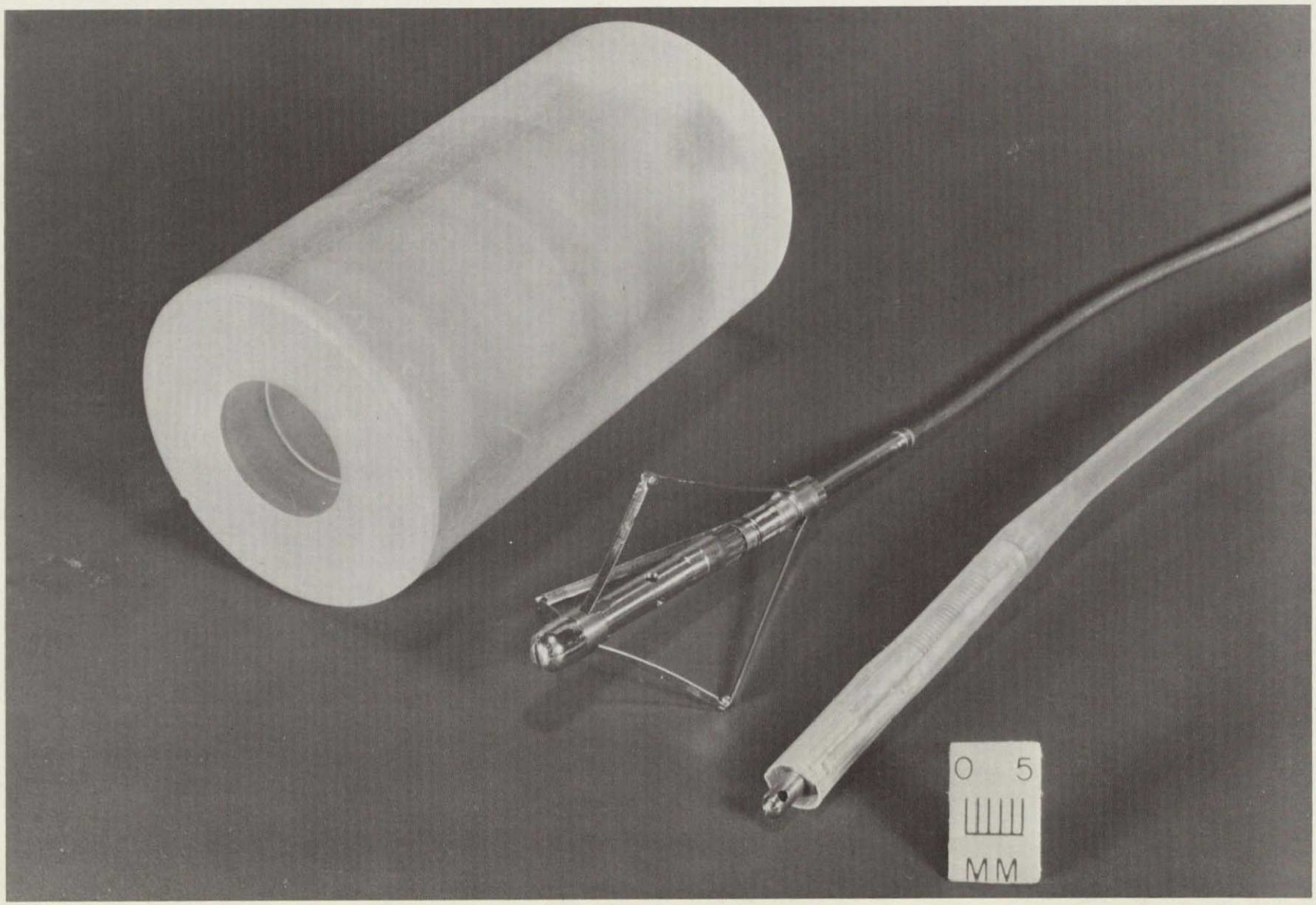


Figure 27. Pieper pressure-diameter gages, sheathed and unsheathed, with plastic calibrating cylinder.

120° apart around the instrument. The spring loading tends to maintain the braces in an open position; any change in the position of the braces causes the sleeve to move over the transformer coupling, yielding a signal proportional to the change in the spread of the braces. The transformer is operated by a Plug-In Instruments Model SOP oscillator-power supply and a Model SCA carrier amplifier* with excitation frequency of 20 kHz. The amplifier output was recorded on the Honeywell oscillograph.

For insertion of the gage the tip, with the braces collapsed, is withdrawn into a Teflon sheath having an external diameter of 5 mm (Figure 27). When the gage is appropriately positioned in the vessel lumen, the Teflon sheath is withdrawn allowing the braces to distend until they touch the vessel wall. There is no indication of a smooth muscle response to the brace pressure on the wall of the aorta[33].

The gage was designed for large arteries and in its original condition distorted the abdominal vena cava into a triangular cross section. By replacing the spring which spread the braces with a much weaker one this distortion was effectively eliminated; however, the frequency response of the gage was thereby considerably reduced. The modified, weak-spring gage was used in all experiments described here and is shown with its Teflon sheath removed and its braces open in Figure 27; included in the photograph are a sheathed pressure-diameter gage and a Plexiglas calibrating cylinder.

The diameter gage was calibrated statically before and after a series of measurements by placing the gage in a 37°C water bath and slowly drawing it through a plastic cylinder with bore increments of 0.5 mm between 7 and 15 mm. Accuracy of the calibration for diameters less than 9 mm is marginal. With

* Plug-In Instruments, Inc., 1416 Lebanon Road, Nashville, Tennessee

sufficient warm up, the gage exhibited little drift or change in sensitivity.

In our experiments the diameter gage was inserted through the left femoral vein, and the tip was positioned in the abdominal vena cava near the bifurcation before the Teflon sheath was removed. To avoid damage of the delicate diameter gage or of the catheter-tip manometers the latter were positioned slightly more cephalic in the vena cava, but always at least 2 cm caudal to the renal branches.

The general experimental methodology was similar to that described in Chapters 2 and 3; however, one notable exception is that in order to provide a well-defined transmural pressure the abdomen was opened by a midline incision and the abdominal viscera were displaced into a plastic bag on the dog's left side in all the experiments. This allowed us to equate intraluminal (venous) pressure with transmural pressure, to a good approximation.

The speeds of the artificially induced, small-amplitude pressure waves propagating in the abdominal vena cava were determined as shown in Figure 6; an average wave speed was calculated using the average ΔT of the first three waves in a single wave train.

A value of the effective Young's modulus was calculated for each wave train analyzed, utilizing the previously discussed equation

$$E = \frac{2\rho_f a^2 c^2}{a_o h_o} .$$

The density of the blood ρ_f was taken to be 1.0 gm/cm^3 and the radius of the vena cava a was assumed to be one-half the diameter registered by the diameter gage. The average wave speed c was derived from one wave train while a_o and h_o, the radius and wall thickness of the vena cava, were

obtained simultaneously at one time in the experiment, usually at autopsy.

For each point in time that E was determined a value of circumferential stress σ was calculated from the well-known hoop stress equation which was modified to include the relation $ah = K = a_o h_o$:

$$\sigma = \frac{P_T a}{h} = \frac{P_T a^2}{K} = \frac{P_T a^2}{a_o h_o} .$$

Since the abdomen was open and the viscera were displaced, P_T is assumed to be the same as intraluminal (venous) pressure.

The maximum expected relative error in E can be evaluated by forming the differential of E, dividing it by E, and evaluating the resulting terms as follows:

$$E = \frac{2\rho_f a^2 c^2}{a_o h_o}$$

$$dE = 2\rho_f \left(\frac{2ac^2}{a_o h_o} da + \frac{2a^2 c}{a_o h_o} dc - \frac{a^2 c^2}{a_o^2 h_o} da_o - \frac{a^2 c^2}{a_o h_o^2} dh_o \right)$$

$$\frac{dE}{E} = 2\frac{da}{a} + 2\frac{dc}{c} - \frac{da_o}{a_o} - \frac{dh_o}{h_o} ;$$

the maximum expected relative error in E can be defined as

$$\frac{\delta E}{E} = 2\frac{\delta a}{a} + 2\frac{\delta c}{c} + \frac{\delta a_o}{a_o} + \frac{\delta h_o}{h_o}$$

where $\frac{\delta()}{()}$ represents the relative accuracy to which we can measure each of

the quantities represented by the parentheses. To a good approximation we can evaluate the radius a within 5%, the wave speed c within 10%, autopsy radius a_o within 2%, and autopsy wall thickness h_o within 10%. Therefore, the maximum expected relative error in effective Young's modulus is approximately

$$\frac{\delta E}{E} = 2(.05) + 2(.10) + .02 + .10 = .42 \text{ or } 42\%.$$

Note that the blood density ρ_f is assumed to be a known constant.

If for the same section of vena cava in one experimental animal, values of effective Young's modulus are compared for possible significant differences, then a_o and h_o can be assumed known constants; and the maximum expected relative error for E is decreased to about 30%.

In the same manner as above the maximum expected relative error for circumferential stress σ can be evaluated:

$$\sigma = \frac{P_T a^2}{a_o h_o}$$

$$\frac{d\sigma}{\sigma} = \frac{dP_T}{P_T} + 2\frac{da}{a} - \frac{da_o}{a_o} - \frac{dh_o}{h_o}$$

$$\frac{\delta\sigma}{\sigma} = \frac{\delta P_T}{P_T} + 2\frac{\delta a}{a} + \frac{\delta a_o}{a_o} + \frac{\delta h_o}{h_o}$$

$$\frac{\delta\sigma}{\sigma} = .03 + 2(.05) + .02 + .10 = .25 \text{ or } 25\%$$

where we have assumed P_T can be measured within 3%.

However, for comparative purposes in the same section of vena cava

in one animal the maximum expected relative error in circumferential stress is only 13%.

As noted in the previous section a quasi-static expression for effective Young's modulus can be calculated from

$$E = \frac{D^3}{4K}\frac{dP}{dD} = \frac{D^3}{4a_o h_o}\frac{dP}{dD}$$

where D is the vessel diameter and $\frac{dP}{dD}$ is the slope at a particular point on a pressure-diameter curve obtained during a balloon inflation study. Assuming the change in pressure dP and the change in diameter dD necessary to evaluate the slope of a pressure-diameter curve can be determined within 15%, the maximum expected relative error for the quasi-static expression for effective Young's modulus is 57%.

4.4 EXPERIMENTAL PROCEDURE

The general experimental procedures were the same as those described in Chapters 2 and 3; however, there were slight modifications, for example those necessitated by utilization of the Pieper diameter gage.

1. The diameter gage was calibrated in a 37°C water bath at least twice before its insertion in order to check for baseline drift and sensitivity changes.
2. To avoid clotting of blood on the diameter-gage springs and braces, additional heparin, up to a total of 500 units/kg, was administered i.a.; and the diameter gage was inserted during the latter part of the experimental preparation.
3. After the diameter gage was positioned in the abdominal vena cava and the protective sheath was removed, the venous-pressure cannula was inserted into the left femoral vein adjacent to the diameter-gage catheter, and the tip was positioned near the bifurcation as shown in Figure 26.

4. Data were acquired as venous pressure increased following inflation of the catheter-tip balloon. Usually several balloon inflations were performed, at intervals as short as 2 minutes.

5. Following data acquisition the diameter gage was removed and the calibration was checked.

6. In order to provide a well-defined transmural pressure the abdomen was opened and the abdominal viscera were displaced in all experiments.

7. The objective of these experiments was to obtain transmural pressure-diameter and effective Young's modulus-stress relationships; therefore, recordings were generally not acquired for the purpose of obtaining dispersion and attenuation data.

4.5 RESULTS

In conjunction with the study of active changes in the mechanical behavior of the abdominal vena cava described in Chapter 5, the abdominal venous pressure was caused to increase, then decrease, several times in 18 dogs by inflating, then deflating, a catheter-tip balloon placed in the inferior vena cava just caudal to the heart. Experiments performed early in this investigation were of a preliminary nature and utilized the diameter gage and venous pressure manometer, but not the wave generating and recording equipment; these experiments yielded transmural pressure-diameter relationships. Later experiments involved use of the diameter gage, the venous pressure manometer, and the wave generating and recording equipment; and, therefore, allowed the determination of the quasi-instantaneous effective Young's modulus as a function of the circumferential stress in addition to the pressure-diameter relationships. Figure 28 illustrates the effect of the transmural pressure on the diameter of the abdominal vena cava during the period of increasing transmural pressure following a single balloon

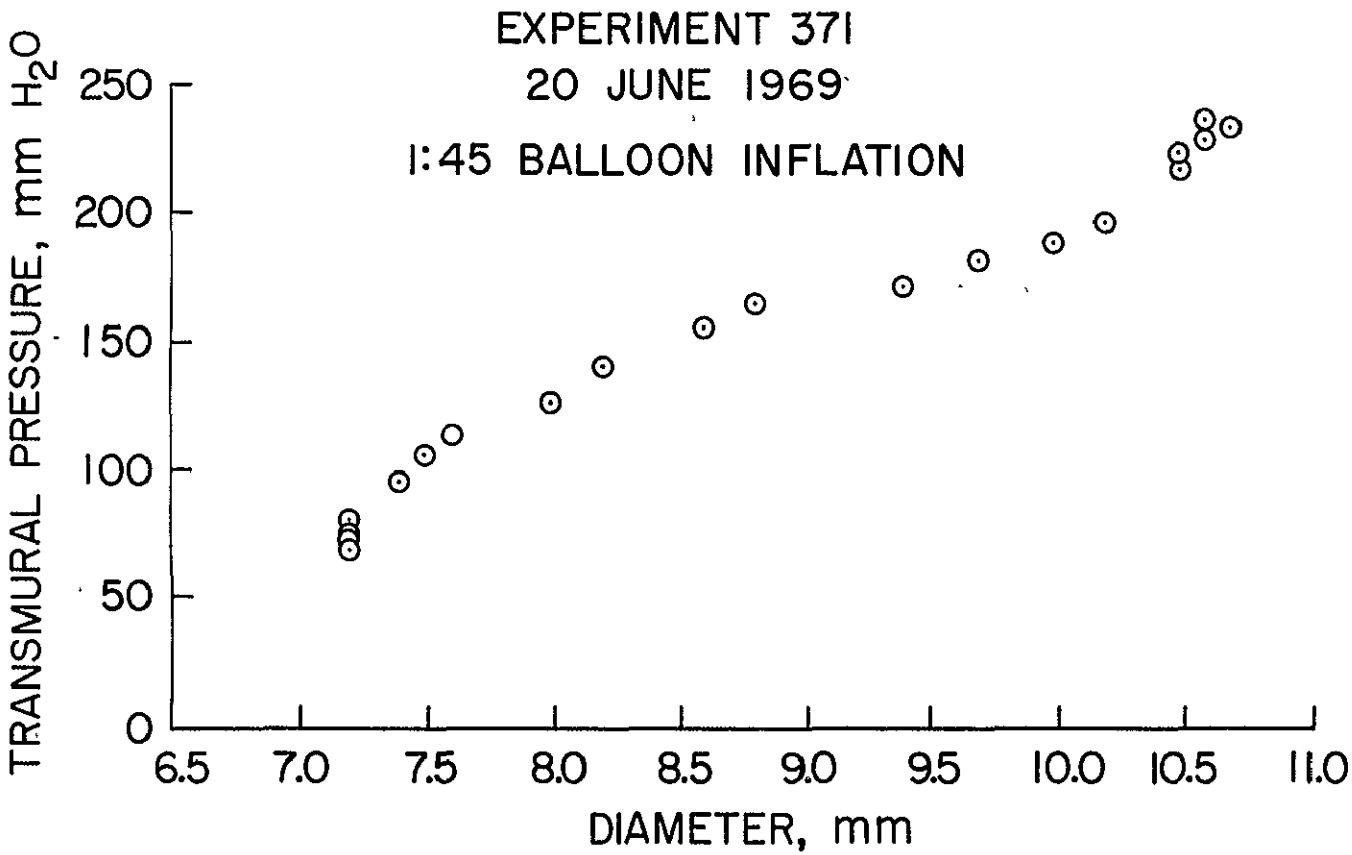


Figure 28. Effect of transmural pressure on the diameter of the abdominal vena cava.

inflation. As the transmural pressure increased from its pre-inflation value of about 70 mm H_2O to 220 mm H_2O, the diameter increased from 7.2 mm to 10.7 mm. Note the sigmoid shape of the curve. All points on the curve were recorded as the pressure increased and were acquired within 20 seconds after balloon inflation was initiated. This curve illustrates one of the maximum changes in diameter that was observed during a single balloon inflation in the course of our experiments. Although vena cava diameter was recorded continuously, the recordings were digitized and the results were plotted only for those points for which wave speed and effective Young's modulus calculations were made.

The effective Young's modulus E versus stress σ curve corresponding to the same balloon inflation described in the preceding paragraph is shown in Figure 29. Each point represents a value of effective Young's modulus calculated from an average wave speed determined from the average ΔT of the first three waves in a single wave train. Therefore each E is based on data which took less than 0.1 seconds to record. Before balloon inflation was initiated, E was 1×10^6 dynes/cm^2 and σ was 1×10^5 dynes/cm^2. While transmural pressure increased during balloon inflation, E increased slowly at first then more rapidly and reached 100×10^6 dynes/cm^2 at a σ of 8×10^5 dynes/cm^2. Except at low values of σ where the points are very close together and where an occasional value of E was not plotted for sake of clarity, each point on the E versus σ plot corresponds to the same instant of time as one point on the P_T versus D curve in Figure 28.

After the experiment described in the preceding paragraphs the bladder was emptied and the diameter gage was positioned in a different location. A new series of balloon inflations was performed and the transmural pressure versus diameter curves which resulted are shown in Figure 30. In each case the

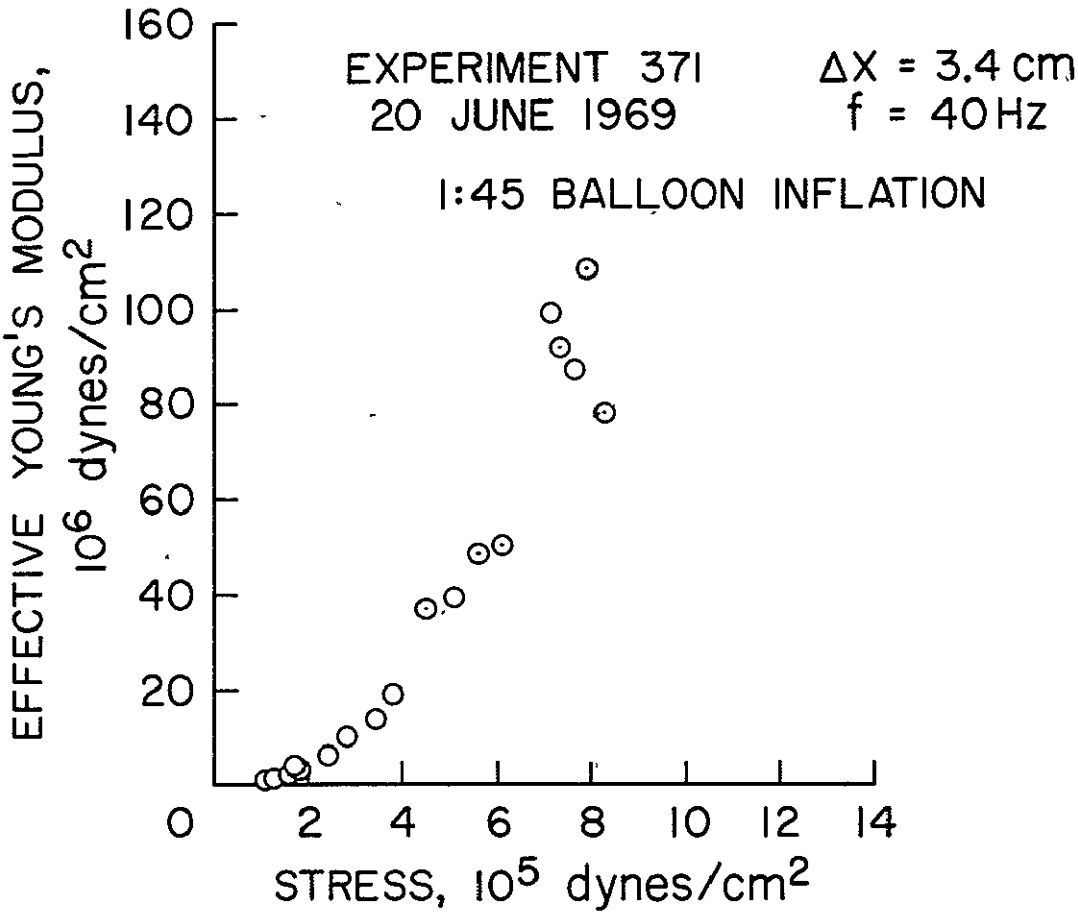


Figure 29. Effect of transmural pressure on the effective Young's modulus of the abdominal vena cava.

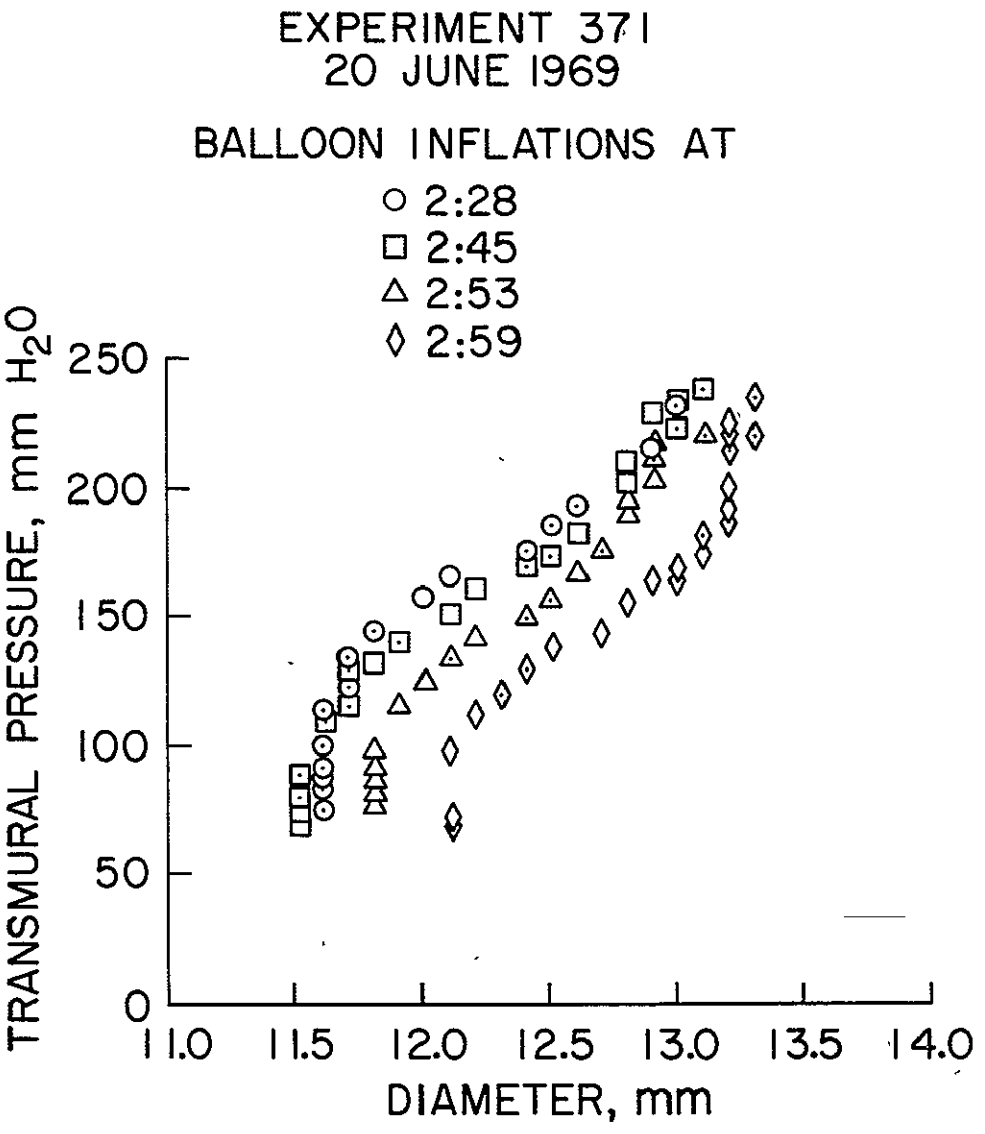


Figure 30. Effect of transmural pressure on the diameter of the abdominal vena cava.

transmural pressure and the diameter increased during balloon inflation from pre-inflation values of P_T = 60-70 mm H_2O and D = 11.5-12.1 mm to about 225 mm H_2O and 13.0-13.3 mm. The four balloon inflations illustrated were performed between 2:28 and 2:59 p.m. and during this time interval the diameter gage, the venous manometer, and the wave generating and recording equipment were not adjusted; in fact the animal was not touched. However, two sympathetic nerve stimulation studies (2:33, 2:37) and one epinephrine injection study (2:49) described in Chapter 5 were conducted during this interval in addition to the four balloon inflation experiments. Although slightly displaced from each other, the curves are very similar in shape and provide an indication that a reasonably stable preparation can be maintained, if the pharmacological studies are spaced a few minutes from the nonpharmacological balloon inflations illustrated here.

The corresponding effective Young's modulus data are plotted versus circumferential stress in Figure 31. Most of the points fall near a hypothetical curve starting from pre-inflation E values of 2×10^6 dynes/cm^2 and a σ of 3×10^5 dynes/cm^2 and ending at 150×10^6 dynes/cm^2 where σ is 12×10^5 dynes/cm^2. The frequency of the propagating pressure waves was 40 Hz and ΔX varied between 3.3 and 3.4 cm.

Generally, both pressure and diameter increased during balloon inflation studies; however, in some cases, particularly when the pre-inflation diameter was large, the diameter measured by our gage did not increase as much as expected and in some cases decreased slightly as the transmural pressures increased. This apparent failure of the vessel to expand appreciably when faced with large increases in transmural pressure was observed in more than one experiment, and when present could be reproduced at will by successive inflations, and deflations, of the balloon. In those experiments in which this

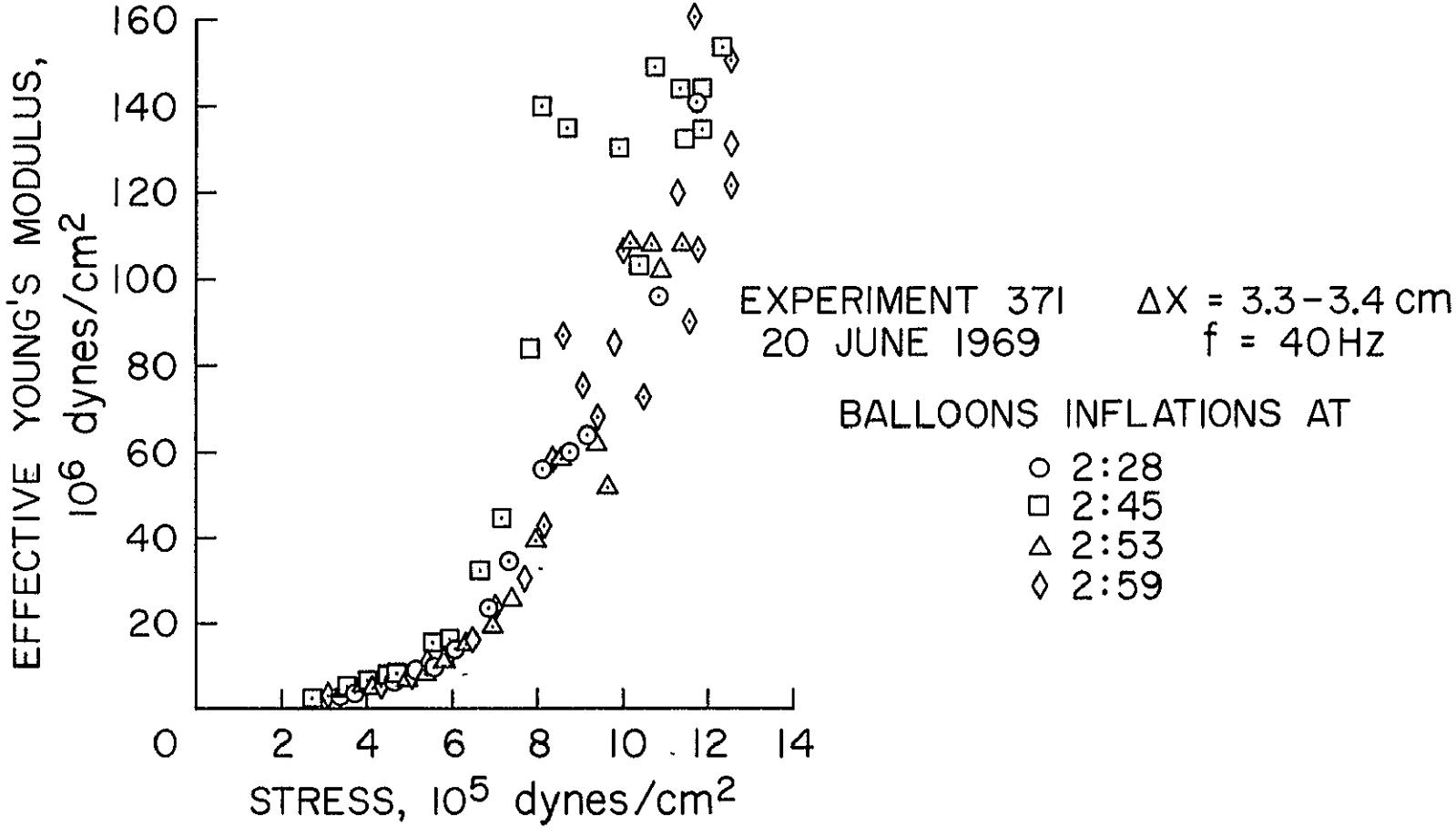


Figure 31. Effect of transmural pressure on the effective Young's modulus of the abdominal vena cava.

phenomenon was observed, the diameter gage was inspected closely after termination of the measurements for evidence of malfunction resulting from excessive blood clotting or other factors, but none was found. Although it is possible that the diameter gage may have changed its orientation in the vena cava during balloon inflations and therefore may have yielded faulty diameter recordings, at this time we feel the small increases or slight decreases in diameter seen during some balloon inflations are not artifacts but represent the response of a dilated vessel. Transmural pressure versus diameter curves for such a response are shown in Figure 32 for two balloon inflations separated by 13 minutes. Note that the diameter increased by at most 0.3 mm (from 13 mm) even though the transmural pressure increased by a factor of 4. The corresponding effective Young's modulus data are plotted versus circumferential stress in Figure 33. The points fall near a smooth curve increasing from less than 5×10^6 dynes/cm^2 at stresses of 2.5×10^5 dynes/cm^2 to nearly 200×10^6 dynes/cm^2 at stresses of 9×10^5 dynes/cm^2.

4.6 DISCUSSION AND CONCLUSIONS

We have obtained both transmural pressure versus diameter and quasi-instantaneous effective Young's modulus versus circumferential stress relationships for the abdominal vena cavae of seven anesthetized dogs.

In general, as the transmural pressure increased during balloon inflation studies, the diameter of the abdominal vena cava increased, sometimes by 50%. Although the shapes of the pressure-diameter curves resulting from repeated balloon inflations in a single animal were usually similar, large variations in shape were seen from dog to dog and, in some cases, for different conditions in the same animal.

Alexander[34,35] has investigated the distensibility of the splanchnic

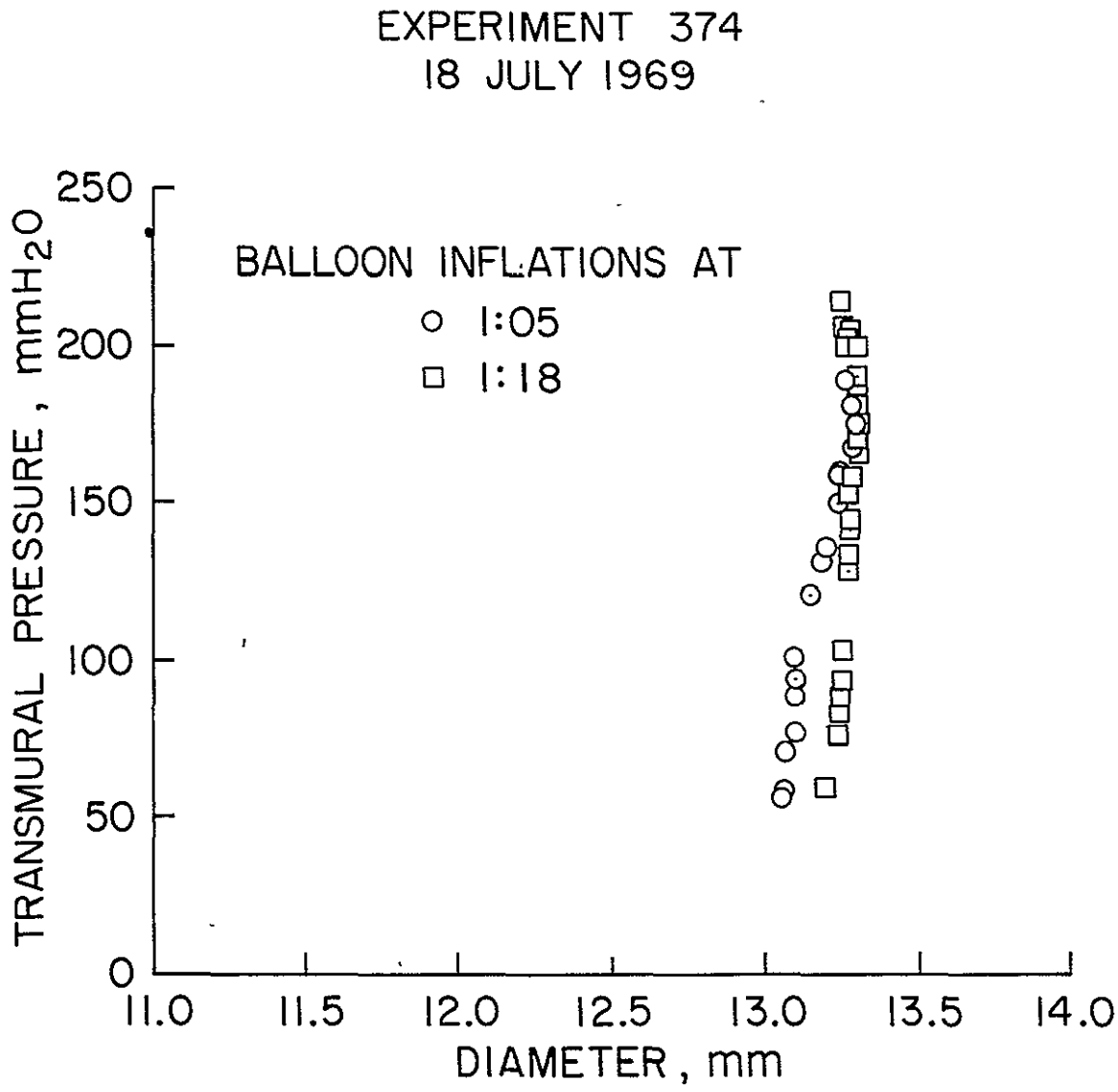


Figure 32. Effect of transmural pressure on the diameter of the abdominal vena cava.

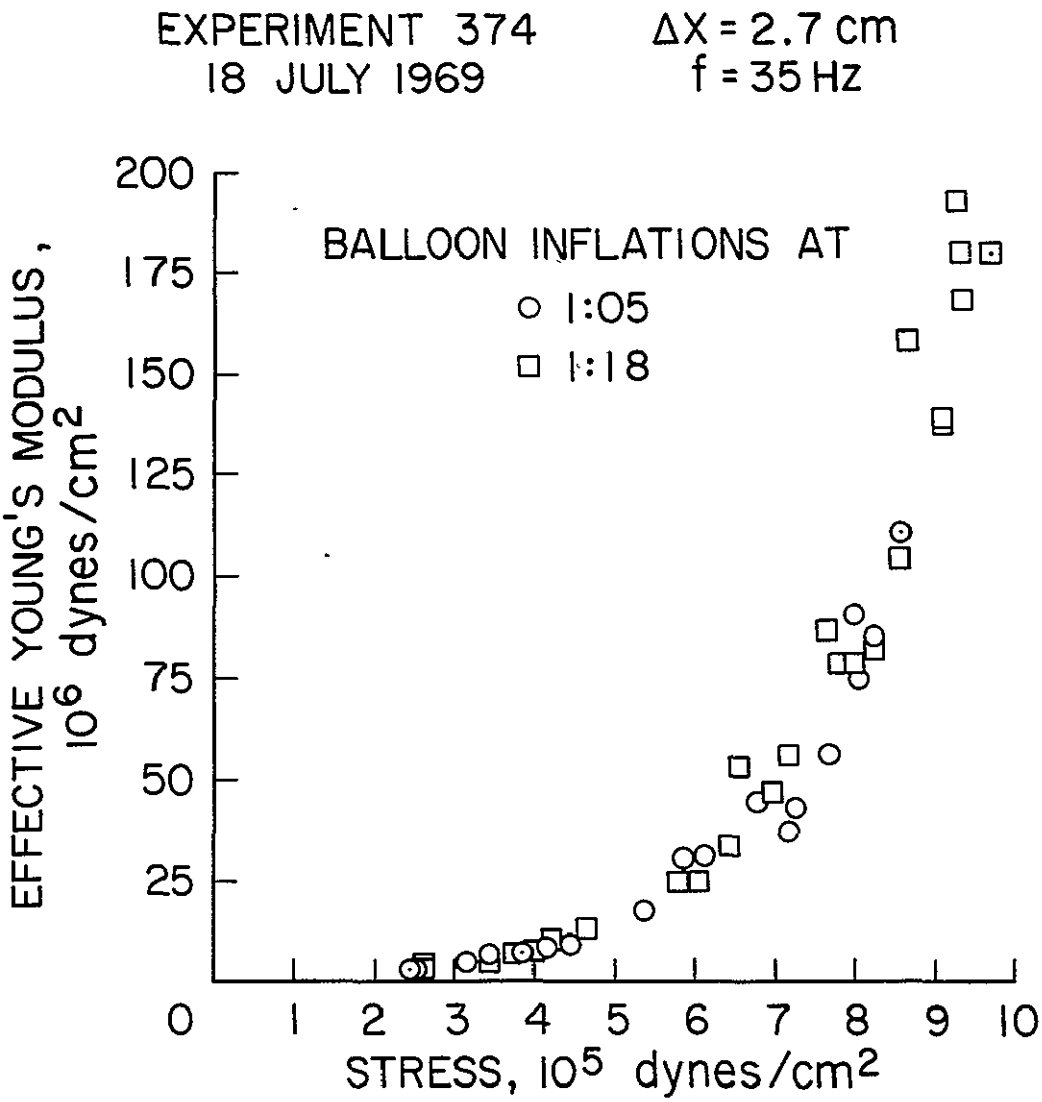


Figure 33. Effect of transmural pressure on the effective Young's modulus of the abdominal vena cava.

venous system by injecting blood at constant rates into the venous side of isolated loops of ileum, which were perfused with arterial blood except when the flow was interrupted to allow a distensibility measurement. The influences of constrictor drugs on the distensibility of this preparation are summarized schematically in Figure 34. The curves labeled "DILATED" and "CONSTRICTED" were respectively obtained before and after administration of adrenaline into the isolated intestinal loop. Note the sigmoidal shape of the "CONSTRICTED" curve and the resemblance of these pressure-volume curves to our pressure-diameter plots. Although there are obvious differences between the splanchnic venous bed and the abdominal vena cava, in the light of Alexander's work we attribute the major variations in the shapes of our pressure-diameter relationships to differences in the contractile states of the abdominal vena cavae. It appears that we have seen the responses to increased transmural pressure of constricted, as well as maximally dilated vessels.

In general, the quasi-instantaneous effective Young's modulus increased markedly with circumferential stress, and in some experiments it increased by two orders of magnitude while the stress increased by only one order of magnitude or less. This large variability of the effective Young's modulus with stress is an important relationship which should be considered in the development of mathematical models for the mechanical behavior of major veins.

In order to compare the effective Young's moduli calculated from wave speed measurements with the E's that could be obtained from the slope of pressure-diameter curves, we drew smooth curves through the points plotted in Figures 28 and 29 and determined a slope and an E at four points on the pressure-diameter curve in Figure 28. These E's are compared below with values for effective Young's moduli obtained from corresponding points on the

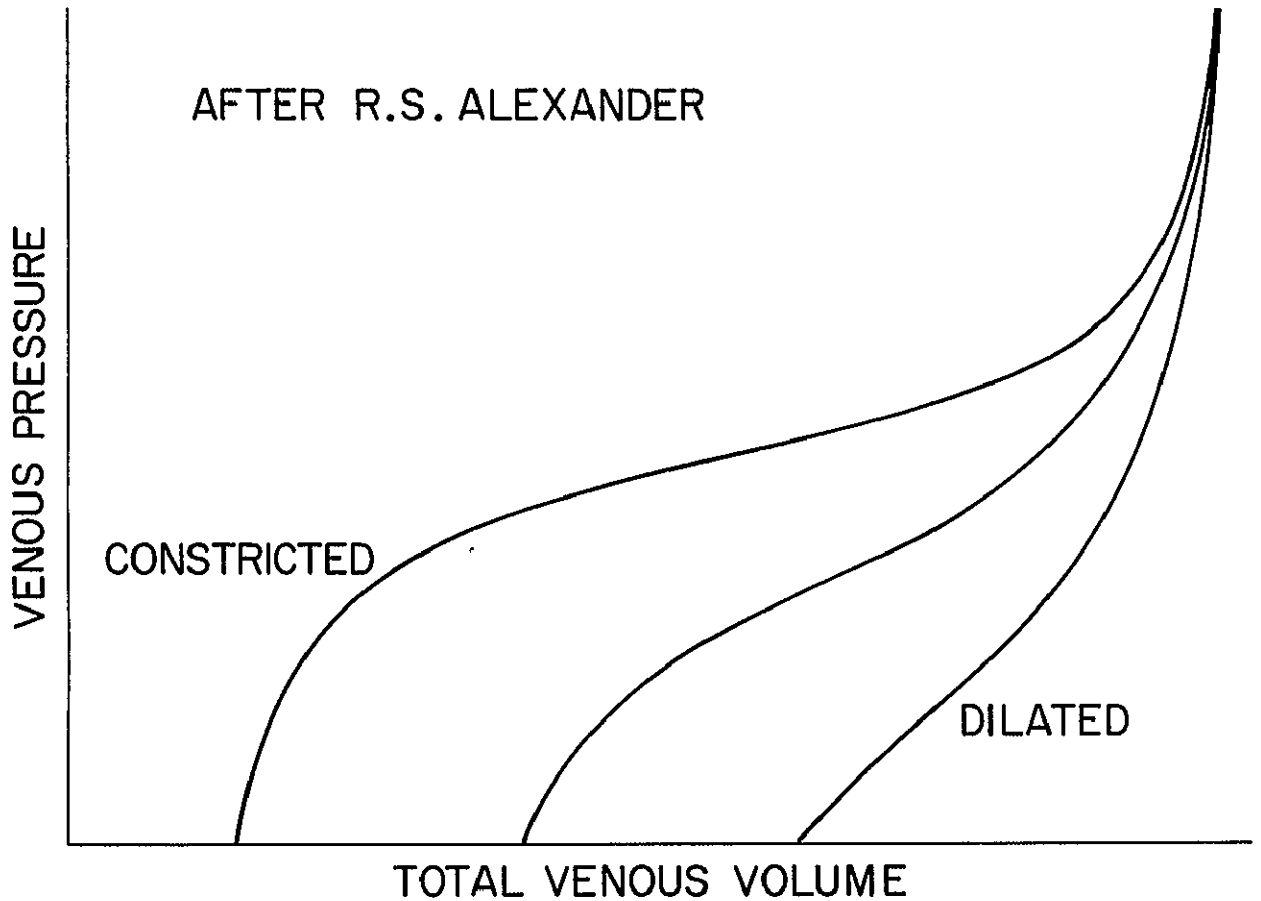


Figure 34. Distensibility patterns recorded from veins in vivo[34,35].

E vs σ curve in Figure 29.

D diameter mm	σ stress 10^5 dynes/cm^2	E from dP/dD 10^6 dynes/cm^2	E from wave speed 10^6 dynes/cm^2
7.5	1.7	1.1	3
8.5	3.3	.7	13
9.8	5.5	.9	45
10.5	7.8	3.9	90

Note that in all cases the E determined from wave speed measurements was substantially larger than that determined from a slope of the pressure-diameter curve. The differences are particularly great at larger values of diameter and stress.

These discrepancies may be a consequence of

1) Errors resulting from approximations in developing the mathematical expressions for the two E's
2) Experimental errors in data acquisition
3) Differences in the importance of the viscoelastic parameters of the vessel wall
4) The occurrence of significant changes in the mechanical behavior of the vessel during the time interval necessary to record enough data to determine a pressure-diameter slope
5) Differences in axial location in the vena cava of the catheter-tip manometers and the diameter gage.

Although we believe that an effective Young's modulus calculated from wave speed measurements may very well be a more accurate indication of the abdominal vena cava mechanical behavior, we cannot prove this definitively at present. When a transducer capable of measuring high-frequency, small-amplitude changes in the diameter of this vessel becomes available, a check on the accuracy of these two methods for determining E can be made by measuring

$\frac{dP}{dD}$ for the small sinusoidal pressure waves. In any event, as shown in Chapter 5 we have used both pressure-diameter relationships and effective Young's moduli calculated from wave speeds to demonstrate active changes in the mechanical behavior of the vena cava.

As noted above, the diameter gage is in a different segment of the abdominal vena cava than are the catheter-tip manometers. Because both wave speed and diameter are required to calculate E from the Moens-Korteweg equation and because the vessel diameter is not constant between the renal branches and the bifurcation, this difference in transducer location can introduce errors. To avoid possible damage to the delicate transducers which might have resulted from their striking each other, the diameter gage was not placed between the catheter-tip manometers.

The effects of the diameter gage on wave transmission characteristics were determined in preliminary experiments. Although the artificially induced pressure waves were sometimes slightly less sinusoidal in shape and smaller in amplitude in the presence of the diameter gage, their dispersion and attenuation were not markedly modified.

The evaluation of the constant K requires a simultaneous measurement of vessel radius a and wall thickness h. Usually at autopsy the abdominal vena cava was surgically exposed and the external diameter was measured with vernier calipers. Then the vessel was placed between the calipers and two times the wall thickness was measured. No doubt there were some variations in circumference and h resulting from collapsing the vessel between the caliper jaws.

CHAPTER 5

ACTIVE CHANGES IN THE MECHANICAL BEHAVIOR OF THE ABDOMINAL VENA CAVA PRODUCED BY SYMPATHETIC STIMULATION AND BY EPINEPHRINE

5.1 INTRODUCTION

The venous system is assumed to play a major role in the adjustment of vascular volume because it comprises about seventy-five percent of vascular capacity[36] and because it actively responds to a broad spectrum of stimuli[32].

Veins are abundantly supplied with nerves which are capable of inducing constriction. Alexander[32] reviews venous innervation and concludes there is clear evidence for tonic sympathetic constrictor activity, apparently without any dilator component; there seems to be no evidence of parasympathetic innervation of veins.

Franklin[37,38] and others have developed and described an appreciable literature on the pharmacology of veins.

The responses of the abdominal vena cava to splanchnic stimulation in the cat and rabbit and to adrenaline in the cat, rabbit, and dog have been studied by Franklin and McLachlin[39,40]. In the cat they found that faradic stimulation of the distal end of the cut splanchnic nerve produced a contraction of the abdominal vena cava between the iliac and renal vein entries and caused a rise of fluid in a vertical glass tube tied into a tributary. Constriction resulting from splanchnic stimulation also occurred following effective exclusion of the adrenals from the circulation. Adrenaline was found to contract the abdominal vena cava in situ, especially its ilio-renal portion.

Guided by this evidence of abdominal vena cava constriction induced by splanchnic stimulation and adrenaline, we began an investigation of the response

of the abdominal vena cava of the anesthetized dog to neural and humoral stimuli in order to further explore the control of large capacitance vessels and in an attempt to quantify changes in the mechanical properties occurring during vessel constriction.

5.2 THEORETICAL CONSIDERATIONS

After considering many possible definitions for an active response to physiological or pharmacological stimuli, we have concluded that active changes in the mechanical behavior of a blood vessel have occurred if

1) the vessel exhibits a different transmural pressure-diameter relationship after the stimulus, or
2) the vessel exhibits a different effective Young's modulus-circumferential stress relationship after the stimulus.

In light of the importance of rates of change of volume and pressure produced during distensibility studies[32], it is assumed that the magnitude of the balloon inflation used to obtain the data for 1) and 2) above is adjusted, if necessary, to provide approximately the same rate of increase in transmural pressure after the stimulus as was induced before.

5.3 METHODS

We have investigated active changes in the mechanical behavior of the abdominal vena cava by determining both pressure-diameter and effective Young's modulus-stress relationships a few minutes before, at the same time as, and a few minutes after the vessel was stimulated by injection of epinephrine or by electrical excitation of the distal end of the cut, right greater splanchnic nerve. The $P_T - D$ and $E - \sigma$ curves were obtained from balloon inflation studies as described in Chapter 4.

In all experiments reported here the abdomen was opened and the abdominal viscera were displaced.

Epinephrine (Adrenalin chloride solution) 0.5 μg/kg to 30 μg/kg was diluted in saline to yield 10 cc of solution and was administered by injection through the venous manometer cannula. A 10 cc saline flush was used. The introduction of this volume of fluid did not appreciably increase the pressure of the venous system as evidenced by the very slight increase in venous pressure, except for the injection transient, when 20 cc of saline were given through the same cannula.

The right greater splanchnic nerve was located in the abdomen just caudal to its passage through the diaphragm. It was surgically exposed as much as possible without disturbing the nearby vena cava. After the nerve was tied with a thread, it was cut cephalicly to the tie and was allowed to lie in the abdominal cavity until the stimulation experiments. In some animals the right kidney was removed in order to increase the working space and to facilitate the search for the nerve. A plastic-shielded, bipolar, palladium electrode was placed around the nerve caudal to the tie and electrical stimulation was achieved with a Grass Instrument Co. Model S4C stimulator*. During the preliminary experiments the stimulus parameters were varied, and it was determined that biphasic electrical pulses of 20 Hz, 5 msec duration, and 10 volts were sufficient to provide up to a 15% decrease in the abdominal vena cava diameter. Increasing the frequency, duration, or voltage above these values did not appreciably add to the change in diameter.

Usually in the first 75 seconds following injection of epinephrine or after initiating splanchnic stimulation there was up to a 15% decrease in vena cava diameter and up to a 40% increase in venous pressure. These changes occurred as a result of the stimulus, for no balloon inflation was performed during this

*Grass Instrument Co., 101 Old Colony Avenue, Quincy, Massachusetts

time. Slopes of pressure-diameter curves resulting from measurements taken during this period of decreasing diameter and increasing pressure are negative and therefore cannot be used to calculate meaningful values of effective Young's modulus; however, effective Young's moduli obtained from wave speed measurements should reflect the mechanical behavior of the vessel wall during this contraction period. Changes in pressure and diameter following initiation of the stimulus were monitored; when they appeared to be extremal, the balloon was inflated causing the venous pressure to increase. The pressure-diameter and quasi-instantaneous effective Young's modulus-stress relationships obtained during this balloon inflation were compared with those data obtained during balloon inflations a few minutes before and a few minutes after the stimulation. Significant differences in these relationships were interpreted as evidence of active changes in the mechanical behavior of the vena cava induced by stimulation.

5.4 EXPERIMENTAL PROCEDURE

The surgical and instrumental preparation was nearly the same as those previously described.

1. The abdomen was opened and the abdominal viscera were displaced early in the experimental preparation before most of the transducers were inserted. If the protocol included stimulating the splanchnic nerve, it was located, exposed, tied, and cut soon after the abdomen was opened. Following this the transducers and wave-generating equipment were introduced into the animal.
2. Sample recordings were checked for evidence of reflections and nonaxisymmetric waves.
3. Usually at least two balloon inflations were performed before a neural or humoral stimulus was administered. Additional balloon inflations followed each of the stimulation experiments. Pressure-diameter and quasi-instantaneous

effective Young's modulus-stress relationships were determined for all balloon inflation studies.

5.5 RESULTS

Eighteen 20-40 kg dogs anesthetized with sodium pentobarbital (Nembutal) were studied.

Preliminary experiments demonstrated that the vena cava diameter could decrease while the venous (transmural) pressure increased.

The observed responses of the abdominal vena cava to stimulation of the distal end of the cut, right greater splanchnic nerve for 60 seconds with biphasic electrical pulses of 20 Hz, 5 msec duration, 10 volts were:

1. The vena cava diameter decreased by 0 to 15%.
2. The venous pressure increased by 5 to 30% in 15 to 20 seconds then decreased to about 0 to 15% above the control value.
3. The arterial pressure increased by 10 to 50%.
4. The breathing rate slowed markedly during the first 10 to 15 seconds of stimulation.

Stimulation of the distal end of the cut, lesser and least splanchnic nerves did not appear to consistently affect the vena cava or its transmural pressure.

The observed responses to 5 μg/kg epinephrine injected through the venous pressure cannula were:

1. The diameter decreased by 5 to 20%.
2. The venous pressure increased by 10 to 40%.
3. The arterial pressure increased by 30 to 80%.
4. The breathing rate increased.

The ability of the vena cava to decrease its diameter while the

transmural pressure increases is a clear indication that the vessel can actively respond, and it encouraged us to perform balloon inflation studies during these active responses.

The transmural pressure-diameter and effective Young's modulus-stress relationships were obtained from 7 dogs for balloon inflations before, during, and after epinephrine injection or splanchnic stimulation. Typical results for one epinephrine injection are shown in Figures 35 and 36. Figure 35 illustrates the transmural pressure-diameter curves for control balloon inflations before (3:13 p.m.) and after (4:03) the epinephrine study of 3:40. Note that there is very little change in diameter with increasing transmural pressures in the control inflations; we interpret this as the response of a maximally-dilated vessel. The values of transmural pressure and diameter just before 2.3 μg/kg epinephrine were injected i.v. are represented by the open squares, $P_T = 85$ mm H_2O and $D = 15.2$ mm. The half-filled squares demonstrate the changes in pressure and diameter occurring during the 45 seconds after epinephrine injection; the vessel decreased in diameter from 15.2 mm to 12.5 mm and the transmural pressure increased from 85 to 110 mm H_2O. Although diameter was measured continuously it was digitized and plotted only for those points on the records at which wave speeds were analyzed. The data obtained during the balloon inflation which was initiated 45 seconds after epinephrine are shown by filled squares. The pressure increased from 110 mm H_2O to 210 mm H_2O while the diameter increased from 12.5 to 15.2 mm, the latter being the same diameter as that just before epinephrine was injected. The shape of this curve resembles Alexander's "CONSTRICTED" vessel shown in Figure 34.

The corresponding effective Young's moduli calculated from wave speeds are shown in Figure 36. Each point on the plot represents the same point

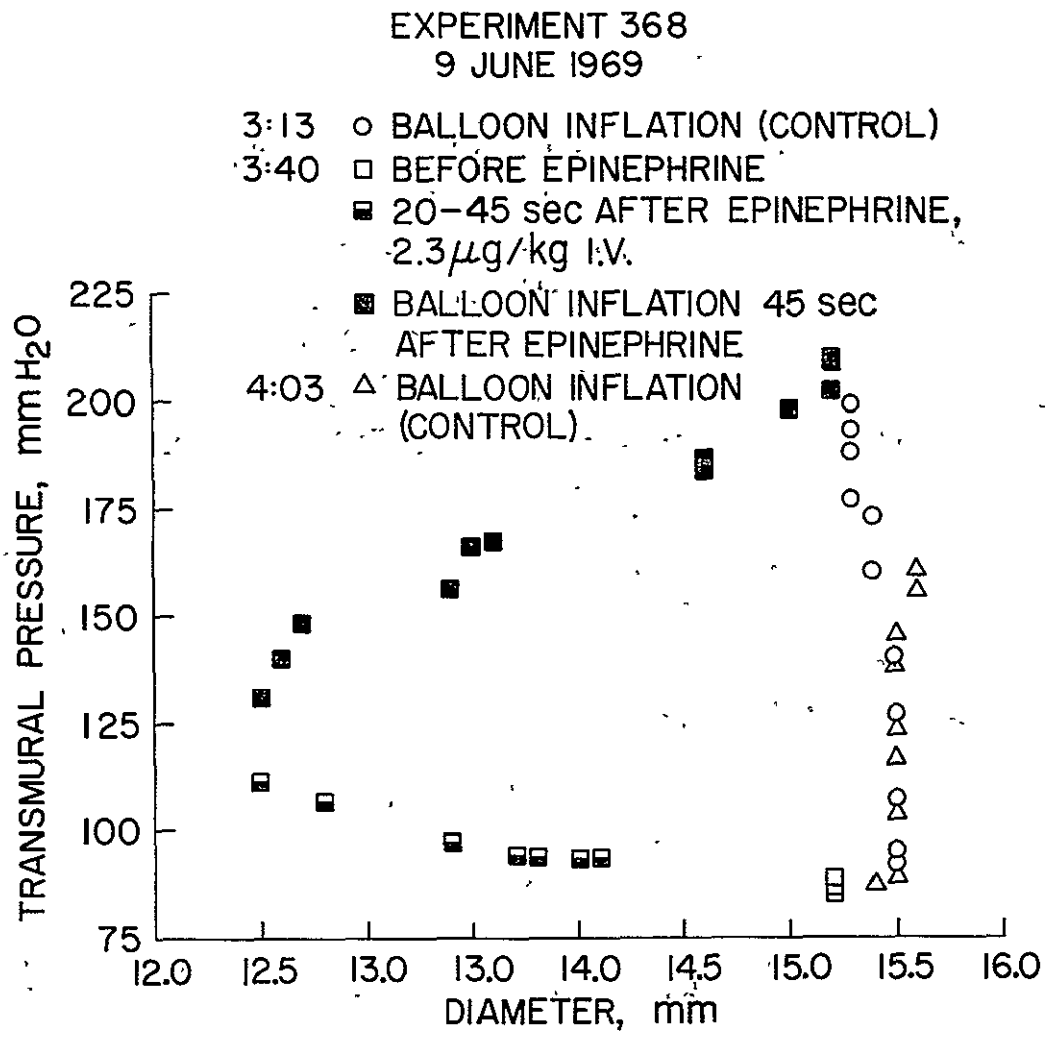


Figure 35. Effects of transmural pressure and epinephrine on the diameter of the abdominal vena cava.

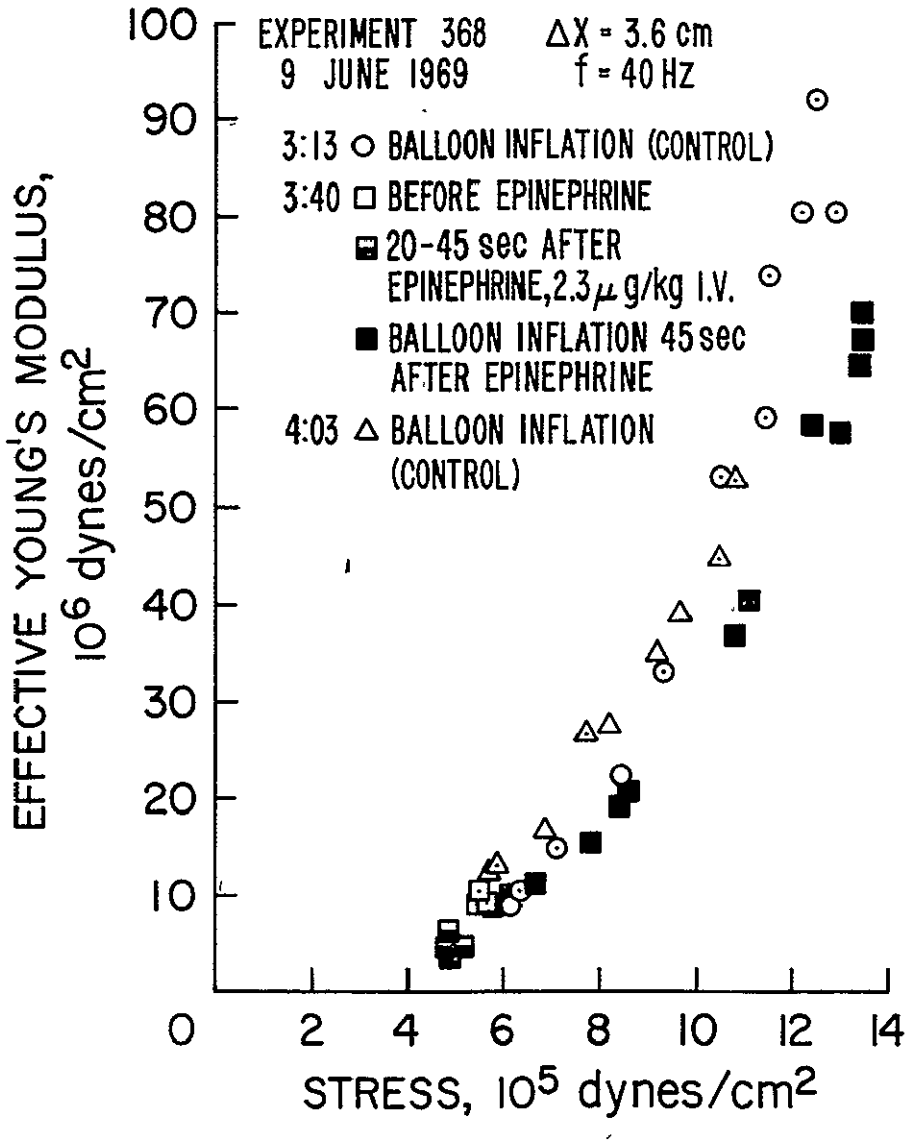


Figure 36. Effects of transmural pressure and epinephrine on the effective Young's modulus of the abdominal vena cava.

in time as one point in Figure 35. Values of E for the control balloon inflations before (3:13 p. m.) and after (4:03) the epinephrine injection of 3:40 increased from about 10×10^6 dynes/cm^2 at $\sigma = 6 \times 10^5$ dynes/cm^2 to 90×10^6 dynes/cm^2 at $\sigma = 13 \times 10^5$ dynes/cm^2. For any given stress greater than 7×10^5 dynes/cm^2 the value of E obtained during the balloon inflation which was initiated 45 seconds after epinephrine is lower than those for the control balloon inflations. This we interpret as demonstrating an active change in the mechanical behavior of the vessel induced by epinephrine. The E's obtained just prior to epinephrine injection (open squares) are twice the magnitude of some of those obtained during the 45 seconds of contraction (half-filled squares, some omitted for clarity).

In general we have observed that $P_T - D$ and $E - \sigma$ curves obtained about 60 seconds after epinephrine injection are different from those obtained during control balloon inflations performed a few minutes before and after the injection. The diameter of the constricted vessel increases more during the balloon inflation, and at any value of transmural pressure the diameter of the constricted vessel is less than that of the unstimulated vessel. For any given stress on the curve the value of effective Young's modulus is less during the balloon inflation following epinephrine than it is for the same stress on the control balloon inflation curves. In one animal we twice observed values of E during balloon inflations following epinephrine that were greater than those obtained for control balloon inflations. However, this was only for stresses less than 5×10^5 dynes/cm^2; at higher stresses E was consistently smaller following epinephrine.

Pressure-diameter and effective Young's modulus curves for a balloon inflation performed 20 seconds after initiating stimulation of the right

greater splanchnic nerve are illustrated together with their respective control curves in Figures 37 and 38. In Figure 37 we see that during control balloon inflations (circles and triangles) the vessel diameter increased from about 10 mm at a transmural pressure of 75 mm H_2O to 12.5-13.0 mm at 115-125 mm H_2O. Just before splanchnic stimulation (open squares tilted) the diameter was 9.5 mm and the pressure was 75 mm H_2O; during 20 seconds of splanchnic stimulation (half-filled squares tilted) the diameter decreased to 8.5 mm and in this case the pressure decreased slightly. Splanchnic stimulation was continued while the balloon was inflated (filled squares tilted); and we observed an increase in diameter and pressure to 13.0 mm and 165 mm H_2O, respectively. For any given pressure the diameter is less for the vessel in the stimulated condition. It is also evident that the pressure-diameter curves for the control balloon inflations are not identical.

Figure 38 shows the effective Young's moduli-stress relationships corresponding to the studies described in the preceding paragraph. In this experiment the E values for the stimulated condition were slightly higher than those obtained during control balloon inflations for stresses less than 5×10^5 dynes/cm^2 but were less than control values for stresses greater than 5×10^5 dynes/cm^2.

The results of splanchnic stimulation and epinephrine studies performed on the same animal are shown in Figures 39 and 40 together with their associated control curves. Again we see major differences in the pressure-diameter relationships obtained from balloon inflations performed while the vena cava was in a neurally or humorally stimulated condition, as compared with the control results (Figure 39). For a given value of stress greater than 6×10^5 dynes/cm^2, the effective Young's modulus for the vessel in a stimulated

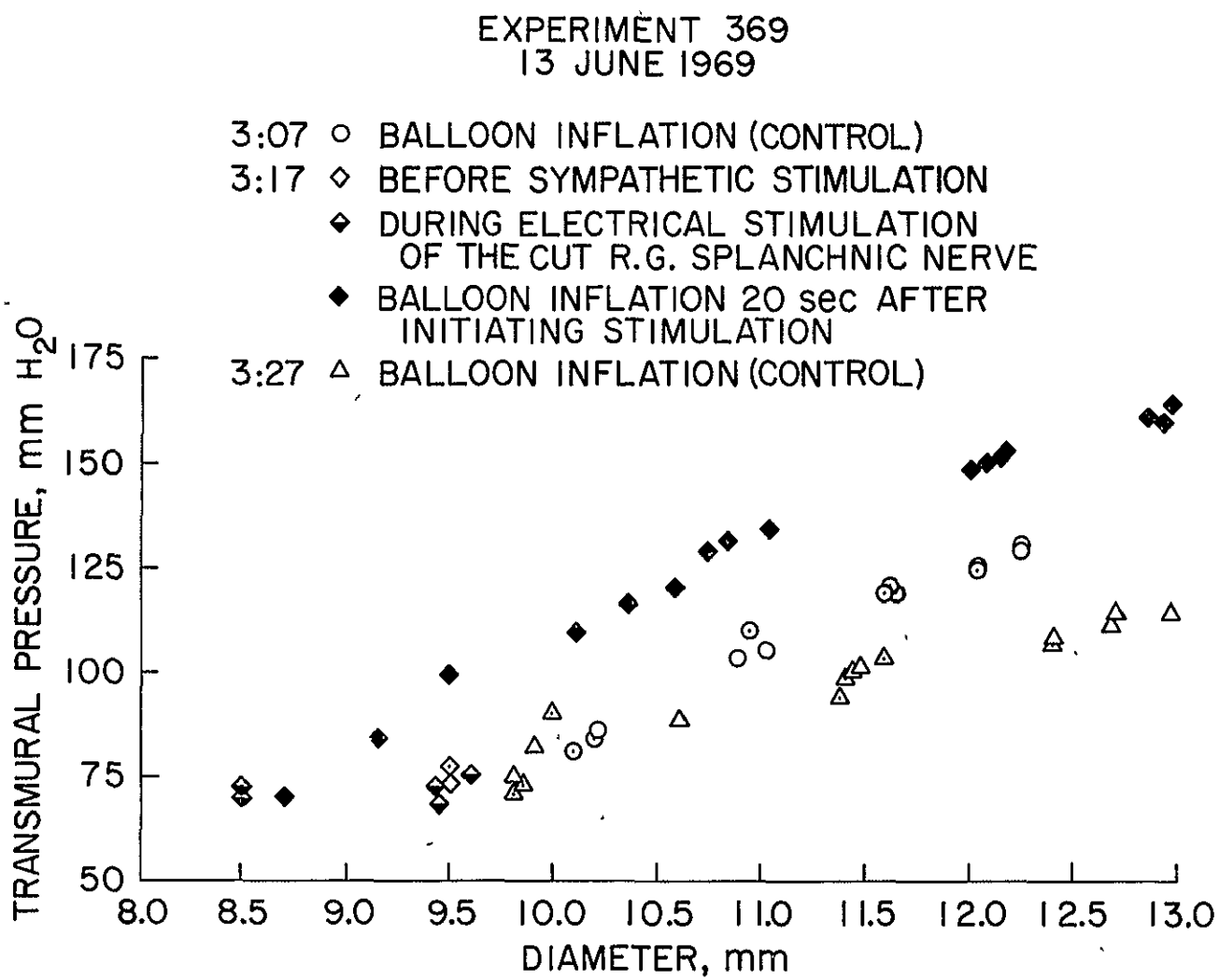


Figure 37. Effects of transmural pressure and sympathetic stimulation on the diameter of the abdominal vena cava.

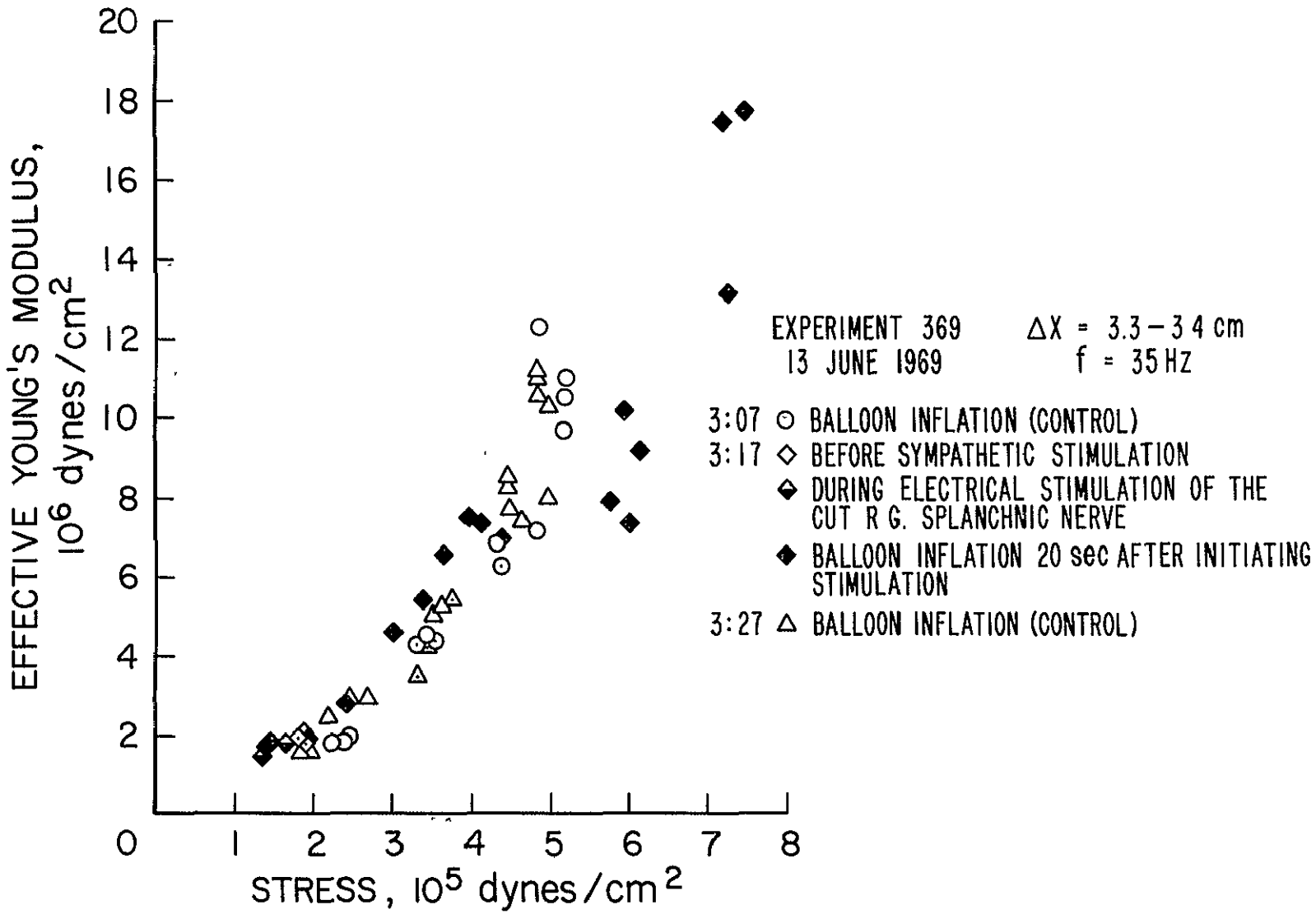


Figure 38. Effects of transmural pressure and sympathetic stimulation on the effective Young's modulus of the abdominal vena cava.

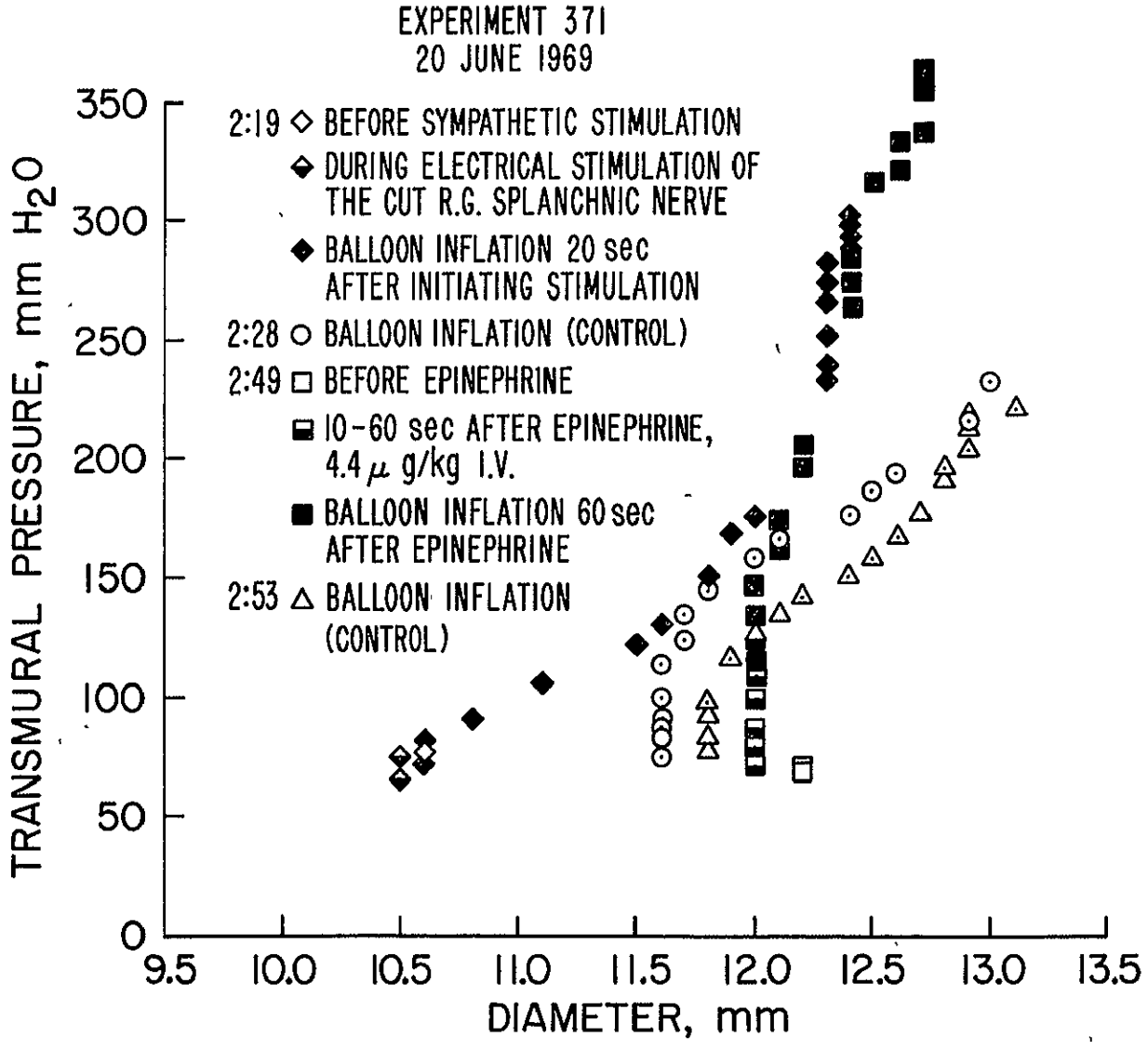


Figure 39. Effects of transmural pressure, sympathetic stimulation, and epinephrine on the diameter of the abdominal vena cava.

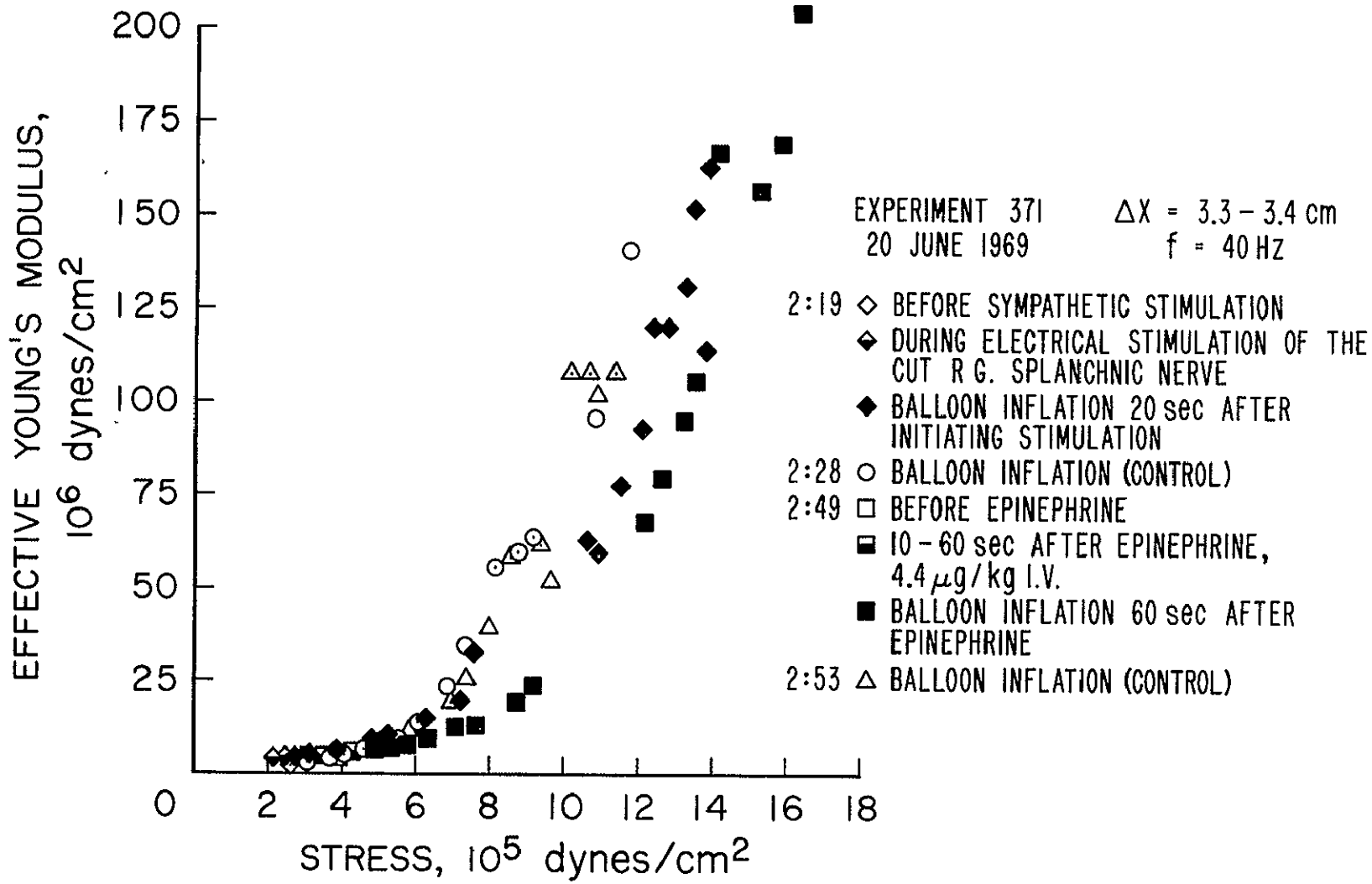


Figure 40. Effects of transmural pressure, sympathetic stimulation, and epinephrine on the effective Young's modulus of the abdominal vena cava.

condition is usually less than that obtained during a control balloon inflation (Figure 40). We again interpret these differences in transmural pressure-diameter and effective Young's modulus-stress relationships as evidence that active changes in the mechanical behavior of the abdominal vena cava occurred as a result of sympathetic stimulation and epinephrine injection.

5.6 DISCUSSION AND CONCLUSIONS

We have presented here the initial results of a systematic study of control mechanisms in the regulation of large capacitance vessels. The mechanical behavior of the abdominal vena cavae of 20-40 kg anesthetized dogs has been demonstrated to actively respond to epinephrine injection and splanchnic stimulation as evidenced by differences in the transmural pressure-diameter and the quasi-instantaneous effective Young's modulus-stress relationships induced by these stimuli. Usually the diameter for a given pressure was less for the stimulated state than for the control, and the effective Young's modulus for a given stress was less during the stimulated state than for the control.

The abdominal vena cava contains smooth muscle, collagen, elastic tissue, and endothelium; its mechanical behavior is the combined responses of these elements. The sigmoid shape of the pressure-diameter curves for constricted veins has been interpreted by Alexander[32] as resulting from the stretch or "pull out" of the muscle at lower transmural pressures with fibrous and elastic tissue governing the distensibility increasingly as the transmural pressure rises. The relatively high distensibility at small diameters is thought to represent primarily the effect of the vascular smooth muscle, while the smaller distensibility at larger diameters is attributed mainly to the stiffer collagen and elastic tissue.

Our effective Young's modulus-stress results indicate that usually

E increases monotonically with σ, and E can increase by two orders of magnitude while σ increases by only one order of magnitude or less. Thus there can be large changes in the mechanical behavior of the vessel as the muscles are "pulled out" and as the collagen and elastic tissue "take over", if indeed this explanation is valid. However, the possibility that reorientation of the vessel wall fibers may play a significant role in altering the mechanical behavior of the vessel wall must also be considered. In addition, it is conceivable that active responses of the vessel may be mediated by local reflexes sensitive to distention or other mechanical factors and may occur during a single balloon inflation study.

It is significant to note that our effective Young's modulus-stress curves indicate that for a given stress, particularly those greater than 8×10^5 dynes/cm^2, E assumes lower values as a result of sympathetic stimulation and epinephrine. If these stimuli mediate changes only in the vascular smooth muscle and not in the collagen or elastic tissue, then we must therefore conclude that the muscle fibers also contribute to E at large diameters or stresses in the stimulated condition. Perhaps, if the vessel were distended by transmural pressures higher than those achieved in our experiments, the muscle fibers might no longer affect E.

The responses to electrical stimulation of the right greater splanchnic nerve may be a result of release of epinephrine from the adrenal medulla and/or direct stimulation of smooth muscle in the vessel wall. Franklin and McLachlin[39] demonstrated in the cat that constriction of the abdominal vena cava resulting from splanchnic stimulation can occur following effective exclusion of the adrenals from the circulation.

The role that reflexly-mediated sympathetic stimulation and the

ensuing catecholamine release may play in anesthetized or unanesthetized laboratory preparations will be a subject of investigation for many years to come. In preliminary experiments we attempted to elicit active responses in the mechanical behavior of the abdominal vena cava by occluding both carotid arteries for a minute or more or by hemorrhaging the animal. We were unable to detect any consistent changes in the vena cava diameter or in the venous pressure when the carotids were occluded. Three experiments were specifically designed to study the effects of hemorrhage on dogs with unopened abdomens. During hemorrhage of up to 1000 ml there were large changes in venous pressure, vessel diameter, arterial pressure, and wave speed; but, the experiments were complicated by many factors including the unopened abdomen and undefined transmural pressure, waves far from sinusoidal shape when the venous pressure was low, and inability to induce large changes in venous pressure by balloon inflation when the dog had been hemorrhaged by 500 to 1000 ml. Because of these complications we abandoned hemorrhage in favor of the type of experiments presented here.

However, in the light of alterations in venomotor tone produced by venous congestion, pressor reflexes, and hemorrhage by Alexander[35,41,42] we feel that experiments can be designed and performed in which active responses in the mechanical behavior of the abdominal vena cava are elicited through reflexes. The likelihood of inducing active responses of the vena cava might be enhanced by using an anesthetic which preserves cardiovascular reflexes to a greater extent than does sodium pentobarbital, for example, a combination of chloralose and urathan.

Early in the experimental studies reported here the right or left vagus was electrically stimulated at the neck in an effort to determine the effects

that this stimulation had on the mechanical behavior of the abdominal vena cava. These experiments were complicated by increases in venous pressure which occurred when the heart was slowed or temporarily arrested. Although the wave speed increased by as much as 25 percent during vagal stimulation, there were no consistent increases in the wave speed or in the effective Young's modulus which could not be accounted for by the associated increases in the venous pressure or in the circumferential stress, respectively. In one experiment the chest was opened and the distal ends of the cut anterior and posterior gastric vagii were electrically stimulated, but no apparent changes in the mechanical behavior of the abdominal vena cava were observed.

At the end of most experiments the animal was sacrificed by injecting a saturated solution of potassium chloride into the cardiovascular system. After the heart stopped, the venous pressure, the wave speed, and the diameter of the vena cava increased; again there were no consistent increases in the wave speed or the effective Young's modulus which could not be accounted for by the associated increases in the venous pressure or the circumferential stress.

In conclusion, we have developed a technique for determining the quasi-instantaneous effective Young's modulus of the abdominal vena cava wall and have demonstrated that this technique is capable of assessing active responses of the vessel to sympathetic stimulation and to epinephrine injection. In either case at a given circumferential stress the value of the effective Young's modulus for the stimulated state was less than that for the control condition.

Additional studies on the abdominal vena cava and other large veins are needed to determine the roles of cardiovascular reflexes in maintaining and regulating the venous capacitance system.

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APPENDIX

DIAMETER, WALL THICKNESS, AND IN SITU STRAIN OF THE ABDOMINAL VENA CAVA

At the conclusion of some experiments the abdominal vena cava was surgically exposed so that the diameter, the wall thickness, and the in situ strain could be determined. The external diameter was measured with vernier calipers at the location where the diameter gage had been. Two times the wall thickness was measured by placing the flattened vessel between the jaws of the calipers. The distance between hemostats placed on the vessel at two points between the renal branches and the bifurcation was determined before and after this section of vessel was excised from the animal; the in situ length is ℓ, and the unstretched length measured after the blood was drained from the excised segment is designated ℓ_o.

The data obtained from 16 dogs are presented in Table 1. It should be noted that the values shown were determined at autopsy, after the animal had been subjected to various experimental procedures including injection into the cardiovascular system of large amounts of various chemicals; therefore, they may not be representative of normal physiological states. Also, the placing of the hemostats on the vessel before the in situ length was measured necessarily altered, at least slightly, the in situ length.

TABLE 1

Diameter, Wall Thickness, and In Situ Strain of the Abdominal Vena Cava

Experiment	Weight	D = 2a	2h	a/h	ℓ	ℓ_o	$\frac{\ell-\ell_o}{\ell_o}$
	kg	mm	mm		cm	cm	
340	22	--	--	--	8.3	5.1*	.63*
342	23	13.2	0.2	66	8.1	6.4	.27
345	23	--	--	--	8.2	5.8	.41
346	25	11.2	--	--	8.6	5.5	.56
351	19	11.6	0.3	39	5.6	3.7	.51
357	33	13.8	0.25	55	7.3	5.2	.40
358	36	14.2	0.3	47	6.3	4.4	.43
362	36	11.8	0.3	39	--	--	--
363	34	9.7	0.35	28	8.6	6.3	.37
367	32	13.5	0.3	45	8.1	5.3	.53
368	45	14.5	0.25	58	8.8	6.3	.40
369	36	10.2**	0.35	29**	7.8	6.3	.24
371	23	13.1	0.25	52	5.2	3.2	.63
373	35	13.8	0.25	55	4.5	3.4	.32
374	26	10.9	0.35	31	6.6	5.1	.29
377	27	10.0**	0.3	33**	7.9	5.9	.34
Average	30			44			.42

D = 2a = the outside diameter

2h = twice the wall thickness

ℓ = the in situ length of the vessel segment

ℓ_o = the excised length of the vessel segment after the blood had drained from the segment

* ℓ_o was obtained with some blood in the vessel segment.

** D = 2a was determined by measuring the width ($\pi D/2$) of the flattened vessel.