A NEW TECHNIQUE FOR CONTINUOUS MONITORING OF SYSTOLIC BLOOD PRESSURE

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ABSTRACT

A new non-invasive method for monitoring changes in arterial systolic blood pressure is presented in this dissertation. This new method avoids certain disadvantages of conventional blood pressure measuring techniques.

Elastic reservoir theory is adopted to show that, under certain conditions and assumptions, the time rate of blood volume change in a part of the microcirculation can be related to the systolic blood pressure. An electronic test circuit was built and a number of experiments were conducted. The results of these experiments show that any errors experienced when using this method are largely due to activity of the sympathetic nervous system at the site of measurement. By using appropriate techniques, these errors can be reduced so that satisfactory indication of blood pressure changes can be achieved.

By an extension of this method, other variables of the systemic circulation could be simultaneously measured, while using the same transducer.

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GLOSSARY [29, 37, 38]

artefact	any unwanted signal.
arteriole	one of the small terminal twigs of an artery that ends in capillaries.
arterio-venous-anastomosis	direct channel between an arteriole and a venule.
artery	a vessel through which the blood is pumped away from the heart.
atrium	an anatomical cavity or passage; especially a main chamber of the heart into which blood returns from circulation.
auscultation	the act of listening for sounds in the body.
autonomic nervous system	part of the nervous system which acts independently of the volition.
bio-feedback	feedback of value of a physiological variable such as blood pressure to subject for purposes of control.
blood	a suspension of cells in a fluid (plasma).
capillary	the finest blood vessels normally about 5 to 6 micrometers in diameter and about 0.5 millimeters long in the systemic circulation.
cardiac catheterization	insertion of catheter into heart cavities for diagnostic purposes.
cardiac output	the product of the heart rate and stroke volume.
catheter	a tubular medical device inserted into canals, vessels, passage ways or body cavities, usually to permit injection or withdrawal of fluids or to keep a passage open.
collagen	an elastic tissue found in the walls of large arteries and other tissues.

diastole	a rhythmically recurrent expansion, especially the dilatation of the cavities of the heart as they fill with blood.
diastolic blood pressure	the lowest pressure in an artery during a heart cycle.
distal	remote; farthest from the centre, origin or head.
distensibility	an ability of a hollow structure to change its volume.
elastin	an elastic tissue found in the walls of arteries.
electrocardiogram (ECG)	a record of the electrical activity of the heart.
essential hypertension	high blood pressure without known cause.
heart	muscular organ that maintains circulation of the blood.
hemodialysis	removal of waste products from the blood by an artificial kidney.
hemoglobin	the oxygen-carrying red pigment of the red blood corpuscles.
hormone	a discrete chemical substance secreted into the body fluids by an endocrine gland which has a specific effect on the activity of other organs.
hypertension	abnormally high arterial blood pressure.
intra-arterial pressure	fluid pressure in an artery.
intraocular pressure	fluid pressure in the interior of the eye.
isobestic point	the wave length of light at which two absorbing substances have the same absorption coefficient.
Korotkoff sounds	sounds produced by sudden pulsation of blood being forced through a partially occluded artery and heard during auscultatory blood pressure determination.

left ventricular ejection time (LVET)	time during which blood is ejected from the heart.
metarteriole	extension from an arteriole which connects to a capillary.
microcirculation (microvasculature)	consisting of smallest blood vessels including capillaries, arterioles, and venules.
neurogenic	originating in the nervous system.
non-invasive technique	physiological measurement technique which does not require puncturing of the skin or entering any organ.
organism	any organized body of living economy.
oxyhemoglobin	a compound of oxygen and hemoglobin formed in the lungs.
parasympathetic nervous system	part of the autonomic nervous system.
peripheral blood vessels	smallest arteries, veins, and blood vessels of the microcirculation.
plasma	the fluid portion of the blood in which the corpuscles are suspended.
platelets (thrombocyte)	one of the small, colourless corpuscles in the blood.
plethysmograph	a device for measuring the volume changes of an organ or part of the body.
pre-ejection period (PEP)	time interval between onset of electrocardiographic S-wave and start of mechanical contraction of the heart.
pressure pulse	pulsation in an artery or vascular bed due to increase of pressure.
protein	any one of a group of complex organic nitrogenous compounds forming an important part of all living things.
pulse pressure	the difference between systolic and diastolic blood pressure.

pulse wave velocity	rate at which pressure pulse travels along an artery.
red blood cell (erythrocyte)	a corpuscle in the blood which carries oxygen to the tissues and removes carbon dioxide from them.
sigmoid	S-shaped
sino-auricular node (S.A. node)	a well-defined collection of cells producing a periodic electrical discharge which initiates contraction of the heart.
smooth muscle	non-striated muscle which is controlled by the autonomic nervous system.
Sphygmomanometer	an instrument for measuring blood pressure.
stroke volume	amount of blood pumped during each heartbeat.
sympathetic nervous system	a part of the autonomic nervous system.
systole	the contraction or period of contraction of the heart, especially that of the ventricles during which blood is ejected from the heart.
systolic blood pressure	highest pressure in the artery during a heart cycle.
tonometry	the measurement of tension.
Valsalva manoeuvre	reduction of arterial blood pressure by increasing the internal pressure on great veins leading to the heart.
vascular bed	any tissue which contains blood vessels.
vasoconstriction	decrease in calibre of blood vessels.
vasodilatation	increase in calibre of blood vessels.
vasodilator	a substance which causes the blood vessels to dilate.
vasomotor	having to do with the musculature that affects the calibre of a blood vessel.
vasomotor activity	changes in calibre of blood vessels due to activity of the autonomic nervous system.

veins	the vessels which carry blood from the tissues back to the heart.
ventricle	a chamber of the heart which receives blood from a corresponding atrium and from which blood is forced into the arteries.
venule	a small vein; especially one of the minute veins connecting the capillary bed with the larger systemic veins.
volume pulse	pulsation in an artery or vascular bed due to injection of blood.

NOMENCLATURE

A	maximum amplitude
A_n	Fourier coefficient
AV	atrio-ventricular valves
AVO	atrio-ventricular valves open
AV●	atrio-ventricular valves closed
A_oV	aortic valve
A_oVO	aortic valve open
A_oV●	aortic valve closed
α	attenuation factor for light passing through tissue plus blood
B	maximum amplitude
B_n	Fourier coefficient
b	arbitrary exponent
C	concentration of absorbant
C_v	pulse wave velocity
D	optical density
E	Young's modulus of elasticity
E_a	Average stiffness (elastance) of aorta and large arteries during diastole
E_i	Average stiffness (elastance) of blood vessels in a microvascular region M_i during diastole
F	proportionality constant
h	thickness of arterial wall
I	transmitted light intensity
I_o	incident light intensity

K_1	arbitrary constant
K_2	arbitrary constant
K_3	arbitrary constant
K_4	arbitrary constant
K_5	arbitrary constant
k_1	arbitrary constant
k_2	arbitrary constant
M	total of all microvascular regions except M_i
M_i	a small microvascular region containing arterioles, capillaries, venules and arterio-venous anastomoses.
MV	mitral valve
P_a	arterial blood pressure at beginning of diastole
$P(t)$, $P_a(t)$	instantaneous value of arterial blood pressure
P_o	reference pressure
P_c	$P_a - P_o$
P_i	blood pressure across a microvascular region M_i
P_s	arterial systolic blood pressure
P_d	arterial diastolic blood pressure
$P_f(t)$	oscillatory part of arterial blood pressure
P_m	mean arterial blood pressure
P_1, P_2	values of arterial blood pressure
ΔP, ΔP_i	change in blood pressure
PV	pulmonary valve
ρ	density of blood
Q_{in}	inflow of blood to region M

$Q_{i\ in}$	inflow of blood to region M_i
Q_t	sum of inflow of blood to regions M and M_i
R	fluid resistance of region M
R_i	fluid resistance of region M_i
R_t	fluid resistance of regions M and M_i together
T, T_k, T^+	arbitrary time intervals
T_p	time of one complete heart cycle
T_c	time constant
t	time variable
t_d	duration of diastole
t_o	start of diastole
t_1, t_2	arbitrary time
TV	tricuspid valve
V	blood volume of region M
V_i	blood volume of region M_i
V_{io}	blood volume of region M_i at $P_i = 0$
V_a	blood volume of aorta and large arteries
V_{ao}	blood volume of aorta and large arteries at $P_a = 0$
V_{i1}	blood volume acting on transducer at a particular location 1
V_{i2}	blood volume acting on transducer at a particular location 2
ΔV, ΔV_i, V_b	change in blood volume
V_T	total volume of blood plus tissue
x	length of path traversed by light
Z	impedance of blood plus tissue traversed by exciting current

CHAPTER I

INTRODUCTION

1.1 Preliminaries

The human body is a complex organism, consisting of many interacting subsystems. One of these subsystems is the circulatory system. The circulatory system comprises a contractile, pulsatile organ, called the heart, which pumps a fluid, blood, through a closed network of tubes known collectively as blood vessels. In a normal human male the blood leaves the heart at a pressure of approximately 120 mm Hg above atmospheric pressure and undergoes pressure drops as it flows through various blood vessels. The blood finally returns to the heart at approximately atmospheric pressure.

Fig. 1.1 shows a simple schematic of the circulatory system. Blood is expelled from the heart in regular pulses (blood flow out of the heart is not continuous) and enters the arteries which are distensible. The resulting pressure in the arteries during one cycle (from one pulse to the next) varies from a highest pressure (systolic) to a lowest pressure (diastolic). The alternation between high and low pressure in the arteries produces the pressure pulse. From the arteries the blood flows through the peripheral blood vessels, which are the smallest vessels. The blood then flows into the low pressure vessels which are called veins and is returned to the heart.

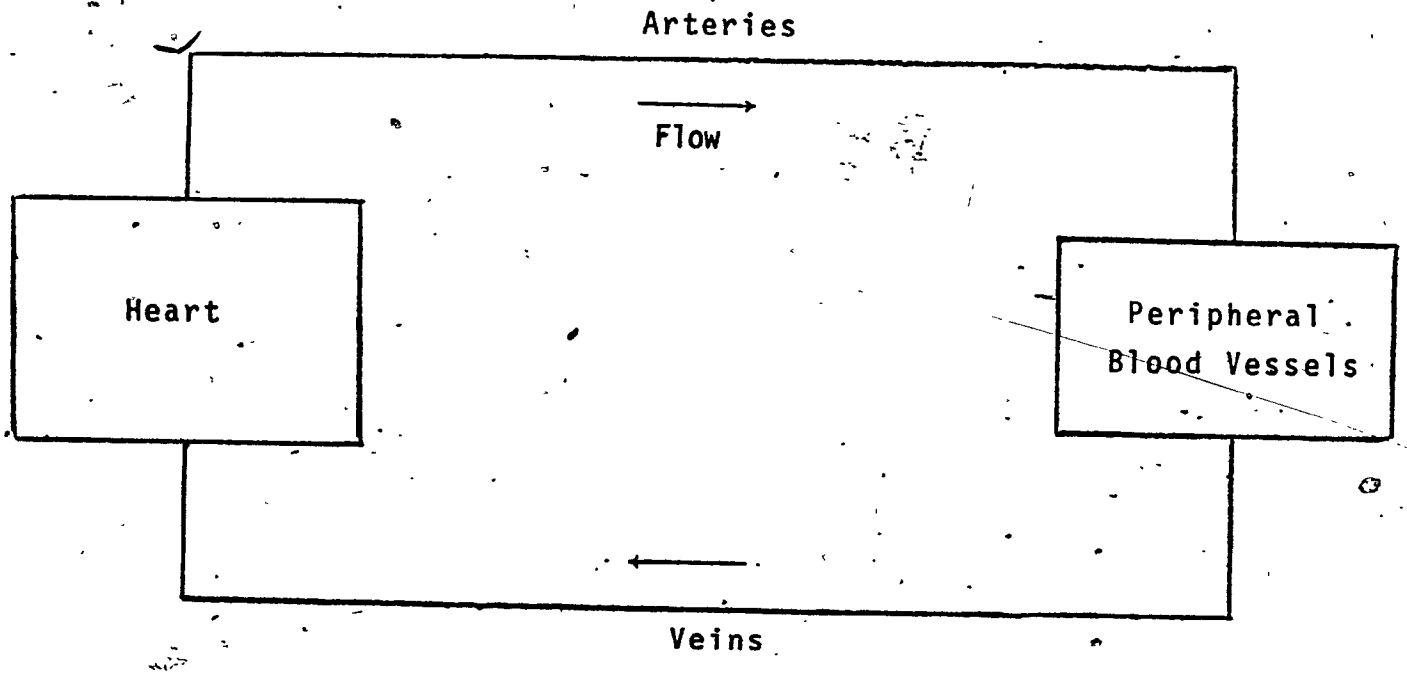


FIG. 1.1 Simple Schematic Diagram of Circulatory System

The measurement of the blood pressure in various parts of the circulatory system is of great importance in physiology and medicine since the level of the blood pressure and its dynamic changes must be known in order to understand the physiology of the circulation and to assess the state of health of the individual.

The blood vessels which carry blood at pressures near those at which it leaves the heart (high pressure) are called arteries. The pressure of blood in the arteries is of particular significance to physicians, and is one of the most frequently measured quantities in medicine and physiology.

The magnitude of arterial blood pressure must be known in the diagnosis and treatment of certain disease states - such as hypertension. In other cases continuous monitoring of the blood pressure may be necessary - as after major heart surgery - since in these cases the blood pressure can fall suddenly.

In some areas of physiological research continuous blood pressure monitoring is also necessary in order to correlate changes in blood pressure with changes in other physiological variables. There is a need for a simple non-traumatic means of continuous arterial blood pressure measurement (or relative measurement) of reasonable accuracy.

Although various methods of arterial blood pressure measurement exist they all have certain disadvantages. A critical review of current methods of blood pressure measurement is given in Chapt. III.

1.2 Characterization of Blood Pressure

The magnitude of the arterial blood pressure is not constant, but varies in a periodic manner between a maximum value called the systolic pressure, P_s and a minimum value known as the diastolic pressure, P_d. This is shown in Fig. 1.2 from which it can be seen that the instantaneous pressure can be represented as the sum of a steady pressure and an alternating pressure in the form

$$P(t) = P_m + P_f(t) \qquad (1.1)$$

where $P(t)$ = instantaneous pressure in mm Hg.

P_m = steady pressure in mm Hg.

$P_f(t)$ = oscillatory pressure in mm Hg.

The oscillatory part $P_f(t)$ is not sinusoidal, as shown in Fig. 1.2, and hence is generally represented through a Fourier series in Eqn. 1.1. [1]

$$P(t) = P_m + \sum_{1}^{\infty} (A_n \cos n\omega t + B_n \sin n\omega t) \qquad (1.2)$$

One of the simplest measurements that can be made on the circulatory system is to measure the blood volume changes in a peripheral vascular bed. Although the shape of the pulsations vary from site to site, in general they are similar to those shown in Fig. 1.2. It is not easy to relate these blood volume changes to the pressure in terms of Equations (1.2) or (1.1).

However, employing the following approach the peripheral blood volume pulse can be related to the arterial pressure producing it:

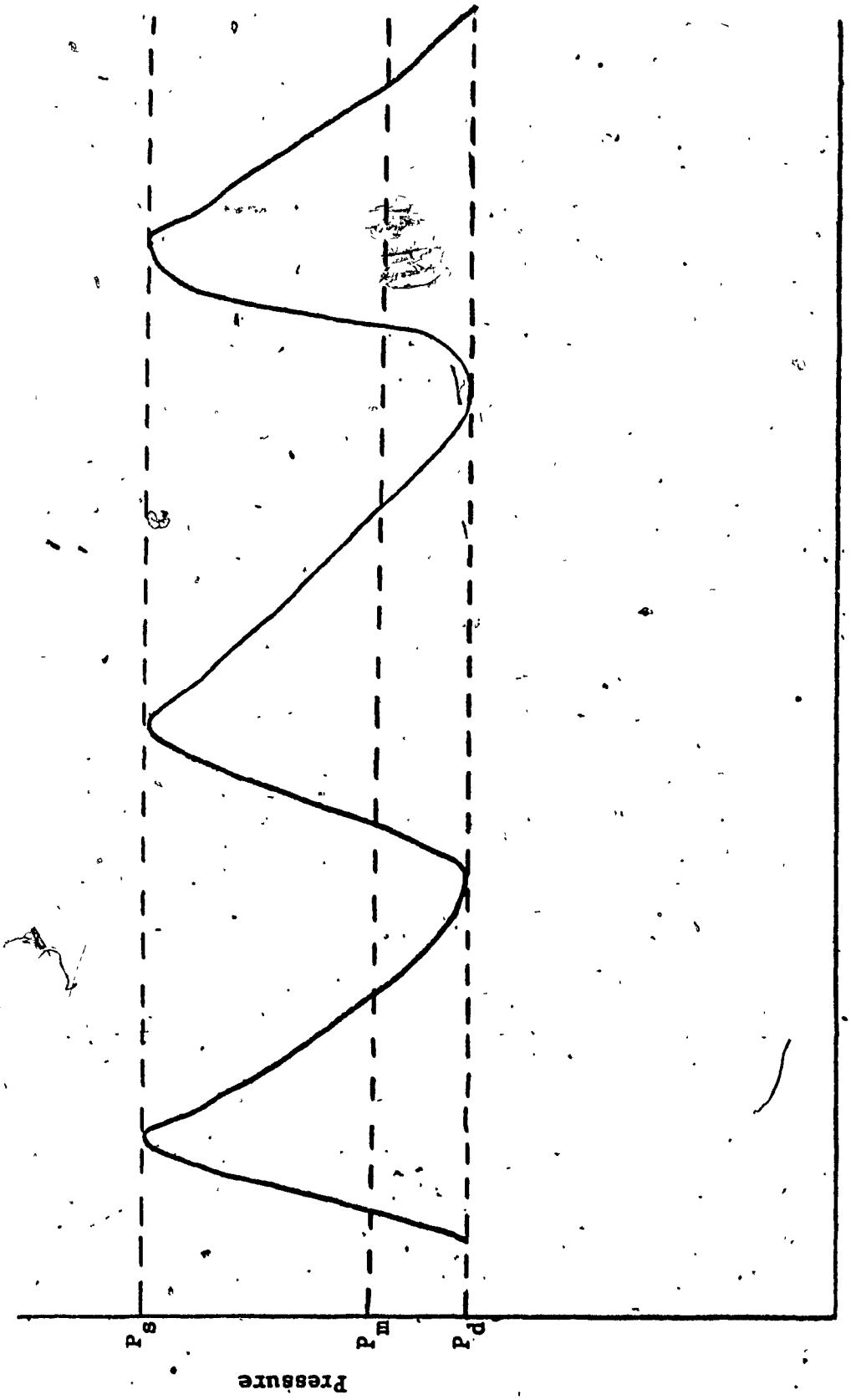


FIG. 1.2 Form of Pulse Wave

i) P(t) and the volume pulse are considered only during diastole, when they are monotonic and when the only forces producing blood flow are those of the stretched arterial walls.

ii) P(t) and the volume pulse during diastole are modelled in a negatively exponential form.

iii) P(t) and the volume pulse are considered only at one specific instant during each cycle, i.e. the start of diastole when their rate of change during diastole is maximum.

By this procedure the peripheral volume pulse can be related to the arterial systolic pressure subject to a number of conditions and assumptions. The arterial systolic blood pressure may then be expressed as:

$$P_s = A \text{ EXP } [-b(T - t_o)] + \frac{d}{dt}[B \text{ EXP } \{-b(t - t_o)]_{max.} \quad (1.3)$$

where

P_s = arterial systolic pressure

A,B = constant

b = measured quantity

t_o = start of diastole

T = arbitrary time $> t_o$

t = time variable $> t_o$

The advantage of this method is that by considering pulsatile arterial blood pressure changes and pulsatile peripheral blood volume changes as being piecewise negatively exponential, a simple, nontraumatic, continuous measurement of relative systolic pressure is possible. This concept

is developed in Chapter IV.

1.3 Scope of the Dissertation

This dissertation deals with a new method of making relative systolic blood pressure measurements. The method does not give the absolute values, and hence a calibration against a standard blood pressure method will be required for each series of measurements on an individual. However, once this calibration is made this new method will follow changes in systolic pressure for as long as the measurements are being made, without any further calibration.

In the second chapter, a short description of the human circulatory system is given in order to provide an appropriate physiological background for the theoretical development which follows. Since the circulatory system is a highly complex entity, only its essential features are outlined. However, all of the terms and functions necessary for a simple understanding of the circulatory system have been defined and explained. For further clarification, all physiological and medical terms used have been included in the glossary.

A critical review of the principal methods of blood pressure measurement is given in Chapter III. This provides a background against which to compare the new method presented in this dissertation. It will be seen that very little work has been done in the area of indirect, non-occlusive blood pressure measurement. The new method to be described lies precisely in this area; and it is in this area that successful development of a new method would be needed.

The theoretical basis for the new method of relative blood pressure measurement is presented in Chapter IV. It is based on a simple form of the elastic reservoir theory of the circulatory system[2]. The topics touched on, in Section 1.2 above, are developed in detail.

There are a number of techniques for measuring pulsatile peripheral blood volume changes. Two of these, the electrical impedance plethysmograph and the photoelectric plethysmograph are discussed in Chapter V. A method of measuring the total peripheral resistance to blood flow is also described.

An experimental test circuit based on the discussions of Chapter IV and Chapter V was built. The operation of this test circuit in its simplest mode is described in Chapter VI. The explanations are given in functional block diagram form. A number of experiments were carried out with the experimental test circuit on two subjects. These experiments were done in order to solve certain problems with the new method. The experiments and their results are discussed in Chapter VII. The principal sources of error, physiological and instrumental, are discussed in Chapter VIII. The most serious error is physiologic but can be made acceptable by appropriate techniques.

The final chapter includes a discussion of the dissertation as a whole, applications of the new method and future work that could be done in this area.

CHAPTER II

THE CIRCULATORY SYSTEM

2.1 Introduction

In this chapter the circulatory system of the normal human body is briefly described. This is presented for providing a proper background for the material to follow. The circulatory system is a closed network of tubes in which a particulate solution known as blood circulates due to the pumping action of the heart. The units of measure used in describing the system are given and the important functions and properties of the blood, heart and blood vessels are described. The pressure relations that exist at different times in the heart and aorta during the heart cycle are explained. Some aspects of the control of the circulation, exercised by parts of the nervous system, are also discussed.

2.2 Units of Measure

2.2.1 Pressure

Arterial blood pressure is universally expressed in mm Hg. This is the difference in height, caused by the differential pressure, between the two levels of mercury in a U-tube manometer. In indirect measurements, if an Aneroid Barometer is used, it is calibrated in terms of mm Hg. When pressure transducers are used in direct measurement, the output of the transducer-amplifier system is also calibrated in terms of mm Hg.

2.2.2 Flow

Blood flow is normally expressed in terms of volume rate of flow. The outflow from the left ventricle, given in liters per minute, is

Called the cardiac output or minute volume. The left ventricular outflow can also be given in terms of the volume of blood expelled with each contraction. This volume is called the stroke volume, and is expressed as milliliters (ml) per stroke or simply milliliters. In various regions of the body, the regional blood flow is given as milliliters per minute.

2.2.3 Flow Resistance

Two units of flow resistance that are in common use, Stacey[3.4], are:

(1) Peripheral Resistance Unit (PRU_m)

The PRU_m is defined as that resistance which requires a pressure difference of 1 mm Hg. to produce a flow of 1 ml/min.

that is: $PRU_m = \frac{\text{mm Hg. min.}}{\text{ml}}$

PRU_s is similar to PRU_m except that it is based on a flow rate of 1 ml/sec., and hence:

$$PRU_s = \frac{PRU_m}{60}$$

(2) Absolute Unit of Resistance (AU)

The AU is defined as that resistance which requires a pressure difference of 1 dyne/cm^2 to produce a flow of 1 cm^3/sec.

that is: $AU = \frac{\text{dyne sec.}}{cm^5}$

The relationship between PRU_s and AU is, then,

$1\ PRU_s = 13.6 \times 980 \times 0.1 \times AU$

$= 1332\ AU$

or 1 mm Hg. = 1332 dynes/cm^2

The PRU_s unit will be used in this dissertation.

2.3 Basic Functions of the Blood

The blood carries out several functions in the human body[4]. It conveys oxygen to the various tissues, enabling them to carry out their metabolic processes. It transports nutrients such as glucose to the tissues and carries away waste products including carbon dioxide, urea etc. Hormones, such as adrenalin, are transported from the glands to the organs and tissues upon which they act. It acts to regulate the temperature of the body core in transporting heat from the interior to the surface (skin), where it is dissipated. The movement of blood throughout the body is effected by the heart and blood vessels. The total blood volume in an adult male is 30 ml per pound of body weight. Thus for a 170 lb. man the total blood volume is about 5.1 liters.

The blood is composed of a mixture of several different particles (cells) suspended in a liquid medium. There are three principal kinds of cells: the red blood cells or erythrocytes, the white blood cells or leucocytes and the platelets or thrombocytes. Each type of cell carries out a special function and their circulation throughout the human body is necessary for the body to survive. The erythrocytes are the most numerous, constituting about 97% of the total cell volume of the blood[5]. The red blood cell is normally a biconcave disc, about 8 microns in diameter and about 2 microns thick. There are about 5 million red blood cells in one cubic millimeter of blood. The red

blood cellular content of the blood ranges from 37% to 54% of the total blood volume[6].

The liquid medium is called plasma with water making up about 90% of its weight. Another 7% of its weight is made up of various proteins, of which albumin is the principal one. The rest of the plasma consists of a large number of substances, such as hormones, antibodies, carbohydrates, electrolytes including sodium, potassium, calcium etc. and other biochemical substances[4,6].

The particulate mixture of cellular bodies in plasma is referred to as whole blood in order to identify it from plasma, which contains only colloidal or molecular particles. The specific gravity of whole blood ranges from 1.052 to 1.061. Although plasma is a colloidal solution it behaves like a Newtonian fluid [7]. Whole blood with its larger cellular particles suspended in the plasma shows deviations from a Newtonian behaviour. However, McDonald [7] has shown that when the internal diameter of the blood vessel is very large compared to the diameter of the red blood cells, whole blood behaves like a Newtonian fluid. This is not valid when the vessel diameters are of the order of 0.5 mm or less.

The apparent viscosity of whole blood is about three times that of water, that is, at 20°C this is about three centipoises. It is a common practice to use the ratio of whole blood viscosity to that of water, known as the relative viscosity. The reference temperature is 37^{o} C, since this is the temperature of the blood in the body core. The viscosity of water at 37° C is 0.695 centipoises. The apparent viscosity varies according to the rate of shear at the vessel wall.

This effect is most pronounced when the vessel diameter is 0.5 mm or less.

2.4 The Heart

The circulation of blood in humans and other animals is effected by the rythmic contractions and relaxations of the heart [4]. A schematic diagram of the heart is shown in Fig. 2.1. There are four chambers;two on the left side and two on the right side. Blood which has circulated in the body enters the right atrium from the superior vena cava and the inferior vena cava during the relaxation phase of the heart, and passes through to fill the right ventricle. At the same time blood from the lungs enters the left atrium and passes through it to fill the left ventricle. When the heart contracts blood is forced from the left ventricle into the aorta and from the right ventricle into the lungs.

The S-A node (Sino-Auricular node) is a specialized part of the heart which periodically produces an electrical discharge which causes first the atria, then the ventricles to contract. The rate of contraction of the heart and the force of the contractions are partly controlled by the heart itself and partly by the nervous system.

2.5 Circulation

The heart actually consists of two pumps which operate synchronously and which pump blood through two separate circuits connected in series [4]. A schematic diagram of this circulatory system is shown in Fig. 2.2. Blood enters the right atrium and right ventricle at a pressure of about 2 to 3 mm Hg. from the superior vena cava and the inferior vena cava. This blood has passed through the body and has

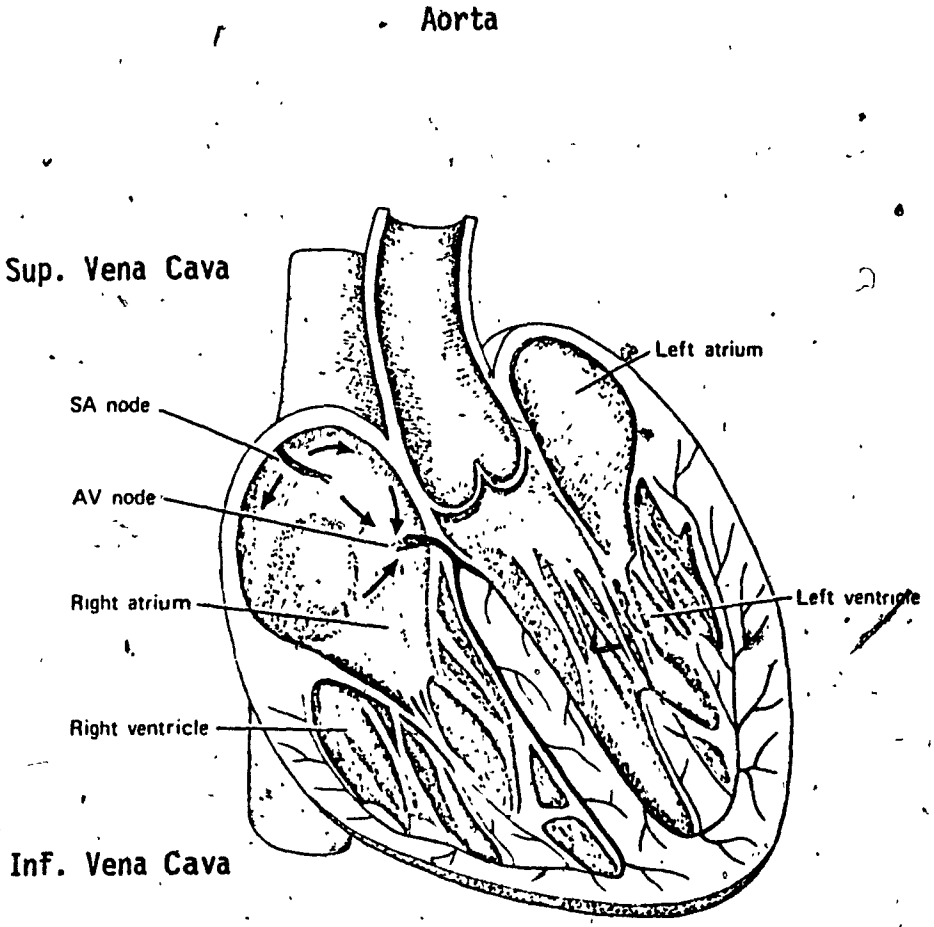


FIG. 2.1 Schematic Diagram of Heart [36]

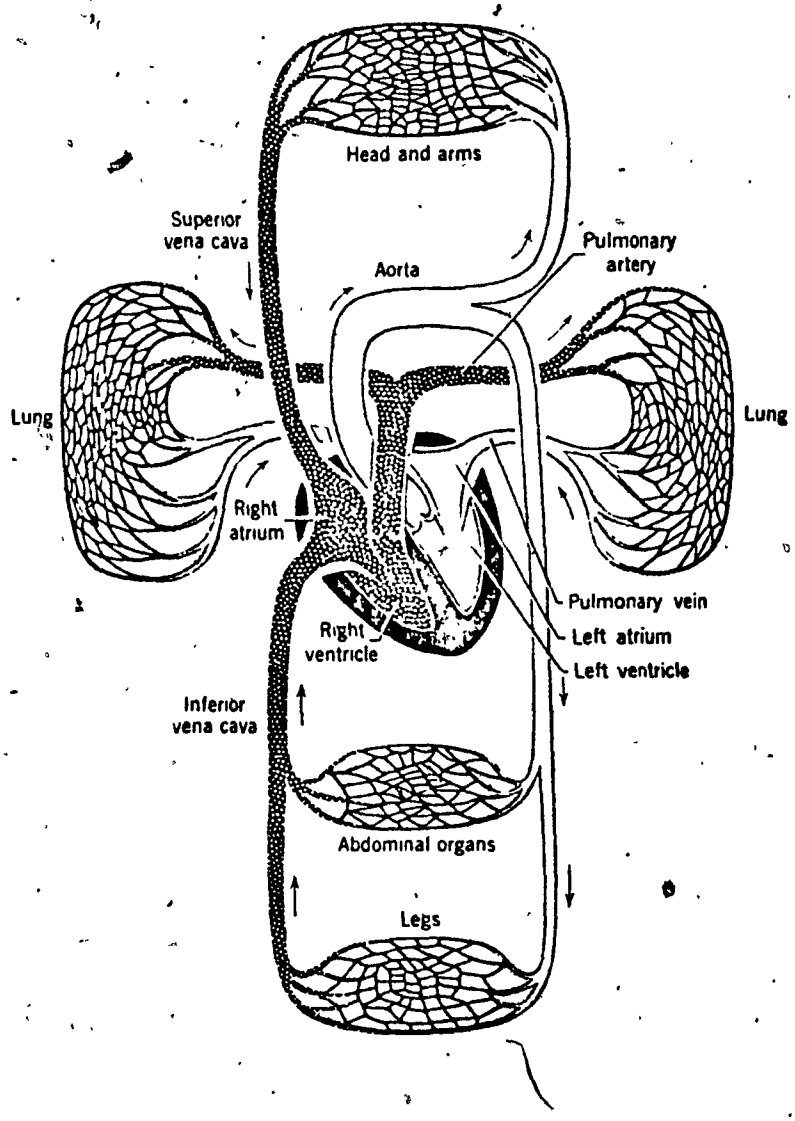


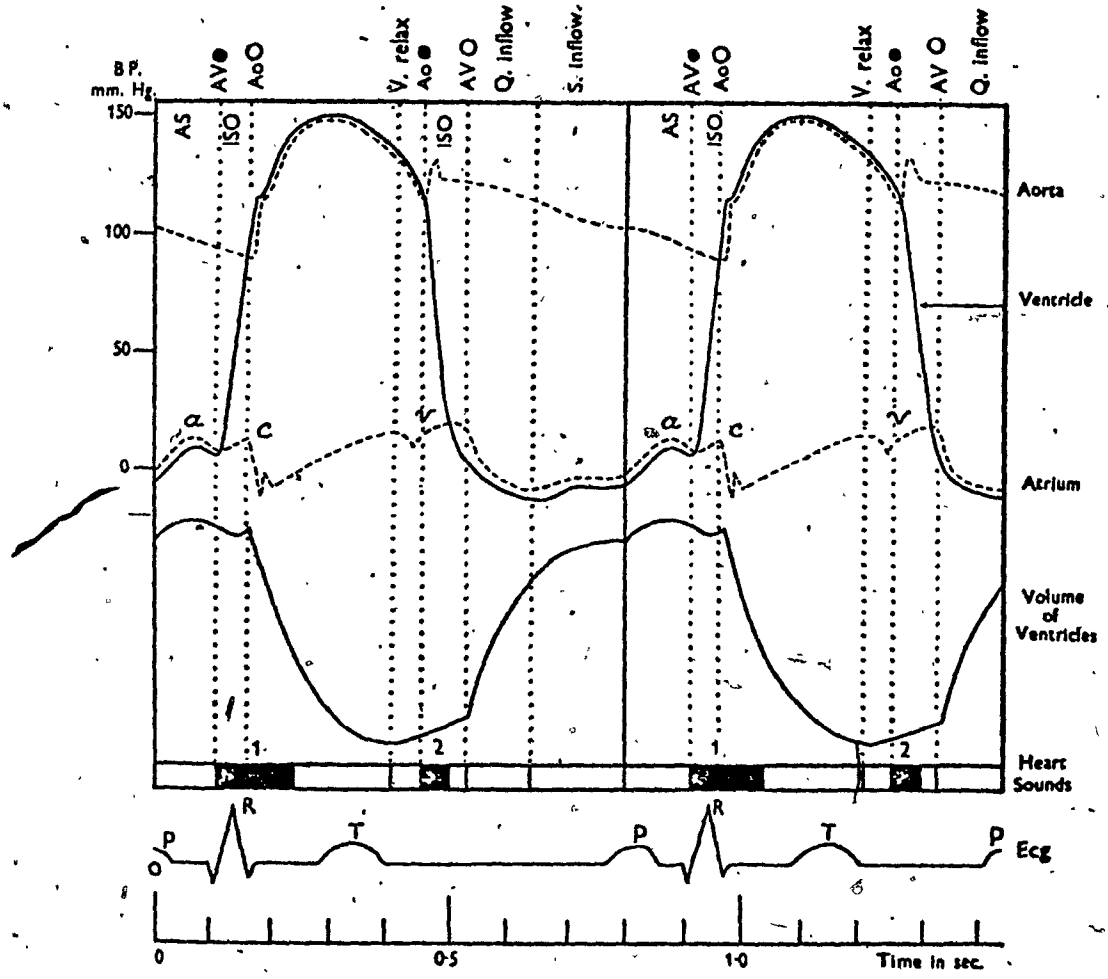
FIG. 2.2 Schematic Diagram of Circulation [36]

had oxygen removed from and carbon dioxide added to it. The right heart pumps this blood through the right and left pulmonary arteries to the right and left lungs. This is called the pulmonary circulation. The maximum pressure is about 25 mm Hg. in the pulmonary artery. In the lungs, oxygen is added to the blood and carbon dioxide removed. The oxygenated blood leaves the lungs via the pulmonary veins and enters the left atrium and left ventricle during the relaxation phase of the cycle. The next contraction of the heart sends a part of this blood through the aorta into the vessels serving the head, arms, legs and abdominal organs as shown in the figure. ~~This~~ is known as the systemic circulation. As the blood flows through the small blood vessels of the systemic circulation, oxygen and nutrients are taken up from the blood by the tissue and waste products given off. After passing through the various body organs the blood enters the superior and inferior vena cava near zero pressure and on the next relaxation of the heart, enters the right atrium, thus completing one cycle.

A system of four one-way valves in the heart keeps the blood flowing unidirectionally. When the heart is relaxed, the mitral valve (MV) and the tricuspid valve (TV) are open, permitting flow from the atria to the ventricles. The aortic valve (AoV) and the pulmonary valve (PV) are closed, preventing backflow across them. When the heart contracts, the mitral and tricuspid valves close, preventing backflow from the ventricles to the auricles. The aortic valve and the pulmonary valve are open permitting flow into the aortic and pulmonary arteries respectively.

2.6 Pressure Relations

The fluid pressure in the circulatory system is not constant, but varies regularly during each cycle [4]. The pressure relations in the heart and aorta are shown in Fig. 2.3. The cycle starts at the left at time 0.1 seconds. The mitral valve between the left atrium and left ventricle, and the tricuspid valve between the right atrium and right ventricle, are known collectively as the atrio-ventricular valves - AV valves. At time 0.1 seconds, the left ventricle has just started to contract and the AV valves are closed. The pressure in the left ventricle is low, near zero mm Hg. and the volume is at a maximum. The pressure in the aorta is about 90 mm Hg. As the contraction continues, the pressure in the left ventricle rises rapidly until its pressure exceeds that in the aorta. At this point, the aortic valve opens (A_oVO), and blood leaves the ventricle and enters the aorta. The pressure in the aorta remains slightly less than that in the left ventricle, due to a small pressure drop across the aortic valve. The pressure reaches a maximum, as much of the blood is expelled from the ventricle, then begins to fall, slowly at first, then more rapidly. The fall of pressure becomes more rapid in the ventricle than in the aorta and eventually it is less than that in the aorta, and the aortic valve closes (A_oVC). The period during which the aortic valve is open is called systole. The aortic valve closes at about time 0.45 seconds. The volume of the left ventricle is now near a minimum. The pressure in the ventricle continues to drop rapidly until its pressure drops below that of the left atrium. At this point, at time 0.45 seconds, the AV valves open (AVO) and blood from the left atrium flows into



Curve of the pressure in the aorta, left ventricle, and left atrium constructed from data by Wiggers for a heart rate of 75 beats per minute. The volume curve of the ventricles, obtained by a cardiometer, rises when the volume increases. The timing of the occurrence of the first and second heart sounds is indicated by the black rectangles.

AS = atrial systole. V. relax. = ventricle relaxes.
ISO = isometric phase—both AV valves and aortic valves closed.
AV● = AV valves closed. AV O = AV valves open.
Ao● = aortic valves closed. Ao O = aortic valves open.
Q. inflow = quick inflow into ventricles.
S. inflow = slow inflow into ventricles.

FIG. 2.3 Pressures in the Heart and Aorta [8]

the left ventricle, increasing its volume. This starts the relaxation or filling period known as diastole. At time 0.9 seconds, ventricular contraction starts again.

Each contraction is initiated by an electrical discharge. The spread of the electrical discharge across the heart produces a voltage-time pattern known as the electrocardiogram (ECG). This is shown on the line labelled ECG in Fig. 2.3. The onset of the triangular wave labelled R (R-wave) coincides with the beginning of contraction.

Heart sounds are produced when the heart valves close. The principal sounds are those made when the AV valves close (first heart sound) and when the aortic valve closes (second heart sound). The maximum pressure reached in the aorta during a cycle is called the systolic pressure. In the figure this pressure is about 150 mm Hg. The lowest pressure in the aorta during a cycle is called the diastolic pressure. This is about 90 mm Hg in the figure. The systolic and diastolic pressures do not remain constant but vary from beat to beat.

The average pressure in the arteries during a cycle depends on the shape of the pressure pulse wave shown in Fig. 1.2. This is called the mean arterial pressure and is used for calculating the total peripheral resistance (TPR) from the cardiac output. The total peripheral resistance is given by:

$$TPR = R_t = \frac{\text{Mean arterial pressure in mm Hg}}{\text{Cardiac output in ml/sec.}} \qquad [4]$$

The difference between systolic pressure and diastolic pressure is known as the pulse pressure. Only a small pressure drop occurs with

blood flow in the large blood vessels whereas most of the pressure losses occur in the micro-circulation.

2.7 Blood Vessels

A schematic flow diagram of the blood vessels is shown in Fig. 2.4. When the heart contracts, blood is expelled into the aorta. Other vessels or arteries branch from the aorta. As the branching continues, the arteries become smaller in diameter and larger in number. There are millions of capillaries, although there is only a relatively small number of large arteries. While the diameter of the aorta is approximately 1 cm in an average-sized man, the diameter of a capillary is only about 0.0008 cm and is approximately 0.4 cm long.

It is in the capillaries that exchange of nutrients and waste materials take place. When the blood leaves the capillaries, they enter another set of vessels known as veins. Veins converge as they conduct the blood back until only two large veins, the superior vena cava and the inferior vena cava, enter the heart, as shown in the figure.

The pressure and the rate of flow of blood in the arteries are not constants but pulsate due to the periodic pumping action of the heart and the elastic properties of the arteries. The large arteries have a considerable amount of elastic tissue, known as elastin and collagen, in their walls. The capillaries are not generally considered to have any elastic material present in their walls whereas the arterioles have a small amount of elastic tissue.

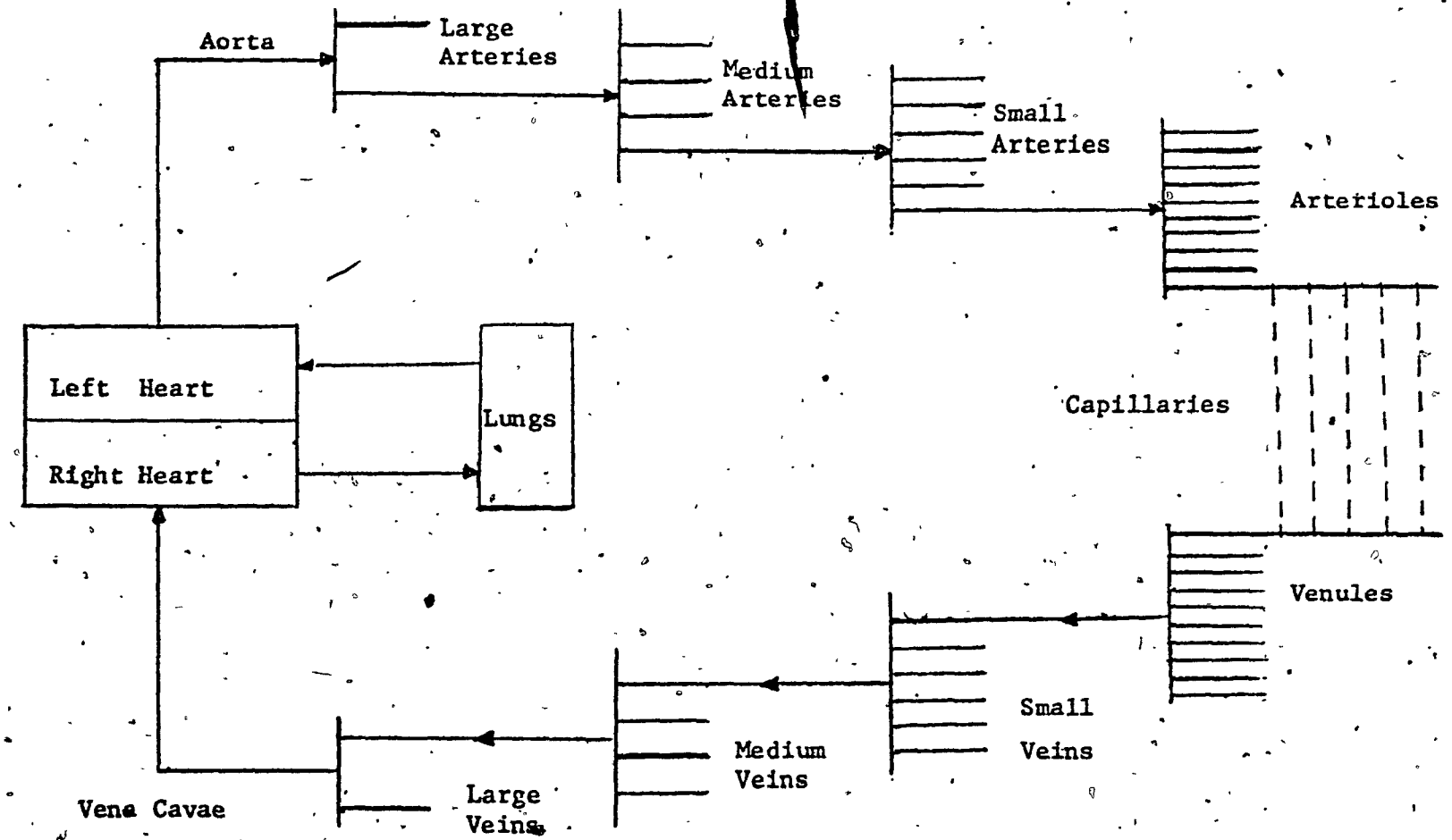


FIG. 2.4 Branching of Blood Vessels

Arterioles, capillaries, and venules comprise the microcirculation (or peripheral circulation) system. Some expansion of blood vessels takes place in the microcirculation, as the existence of the volume pulse in these areas indicates. A diagram of the microcirculation is shown in Fig. 2.5. It consists of a network of arterioles, metarterioles, capillaries and collecting venules. Not shown are the small arteries which feed the arterioles. In place of elastic tissue, the arteriole walls contain smooth muscle cells. The precapillary sphincter is at the junction of the capillary with the metarteriole. One path for the flow of blood is from small artery to arteriole to metarteriole to capillary to collecting venule and on to larger veins. The precapillary sphincter consists of smooth muscle cells and, when contracted, can effectively shut off blood flow through the capillaries.

Other channels bypass the capillaries and go directly from metarteriole to collecting venule. These are called arteriovenous anastamoses (AVA) or shunts and although no exchange takes place in them, the opening and closing of these paths affects blood flow in the area. Contraction or relaxation of the smooth muscle in the microcirculation can alter the calibre and distensibility of the muscle coated blood vessels, and thus can alter the resistance to the flow of blood. These vessels are known as the resistance vessels and play a major role in controlling the flow of blood in the body. As the arteries get larger they contain less smooth muscle and more elastic tissue.

All of the blood ejected from the heart during a beat cannot immediately flow through the microcirculation. Some of it dilates the larger

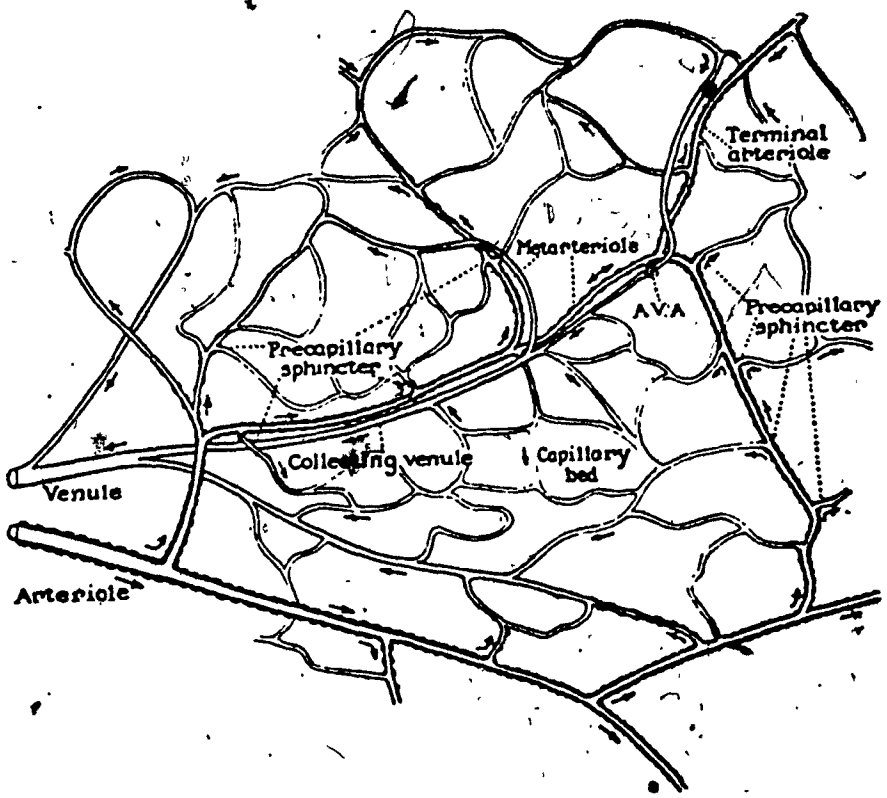


FIG. 2.5. Schematic Drawing of Microcirculation [4]

arteries. This happens because the flow rate through the microcirculation is not large enough to take away all of the stroke volume during ejection. In fact, most of the blood vessels are distended. However, most of the increase of volume takes place in the larger arteries. The excess stroke volume is stored in the dilated arteries. This is the reservoir function of the arteries.

Due to the dilatation of the arteries, there is some potential energy stored in them. When ejection is completed, and the heart is shut off from the aorta by closure of the aortic valve, the dilated arteries return the potential energy (elastic recoil) which is converted to kinetic energy as the stored blood flows through the microcirculation during diastole. The combined action of the heart, arteries and microcirculation produce periodic variations of pressure and volume in the systemic circulation. A typical pressure pulse is shown in Fig. 2.6 and a volume pulse in Fig. 2.7. The pressure pulse and the volume pulse can have similar shapes. However, the shape of each of them varies considerably according to the site at which they are measured.

2.8 Nervous Control of Blood Vessels

It was pointed out in the previous section that the small blood vessels, including small arteries, arterioles and metarterioles, have smooth muscle in their walls. This smooth muscle is under the control of a part of the nervous system known as the autonomic nervous system[4]. The autonomic nervous system is not normally under conscious control, but responds automatically to various physiological factors and conditions.

Activity of the autonomic nervous system causes the smooth muscle of the small blood vessels to contract or relax, thus altering their calibre, distensibility and flow resistance. The autonomic nervous system has two parts: the sympathetic and the parasympathetic branches. The sympathetic branch is particularly active in skin areas of the fingers, toes, ears and some other regions. In other areas sympathetic innervation is less widely distributed or may be absent, such as in the skin of the forehead [9].

The autonomic nervous system activity is increased (or decreased) by emotions and conditions such as heat, cold and pain. Such change in activity produces, among other things, changes in the distensibility and flow resistance of the small blood vessels.

2.9 Heart Rate and Cardiac Output

The number of times the heart contracts per minute is called the heart rate. The heart rate may vary from a low of about 30 beats per minute to a high of about 180 - 200. Very low rates and very high rates are abnormal, and cannot in general be sustained by the body for long periods of time. Normal heart rate at rest is about 72 beats per minute for an adult male. This gives a cycle length, or period, of about 830 milliseconds. Even at rest, the heart rate is not constant but varies slightly with respiration.

The left heart pumps about 5 liters of blood per minute through the circulation of a normal man at rest. If the heart rate is 72 beats per minute, the stroke volume is about 70 ml. The stroke

volume and heart rate vary from beat to beat, but for a fixed set of physiological conditions the cardiac output is fairly constant. The resistance to the flow of this blood occurs mainly in the small blood vessels as previously pointed out.

2.10 Conclusion

A brief outline of the essential features of the circulatory system has been given in this chapter. This should provide a useful background for the material which is presented in the following chapter.

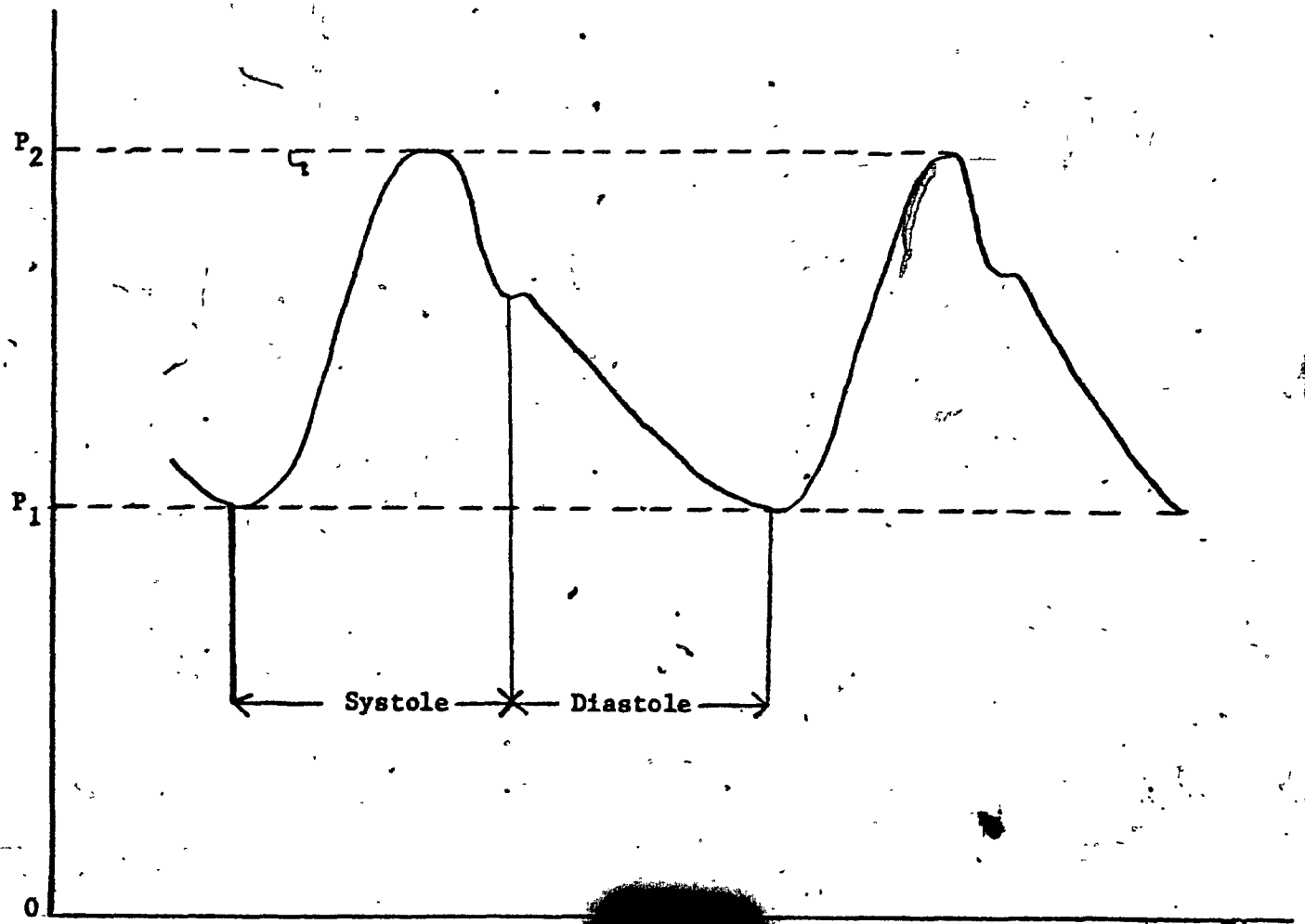


FIG. 2.6 Fo[redacted]sure Pulse

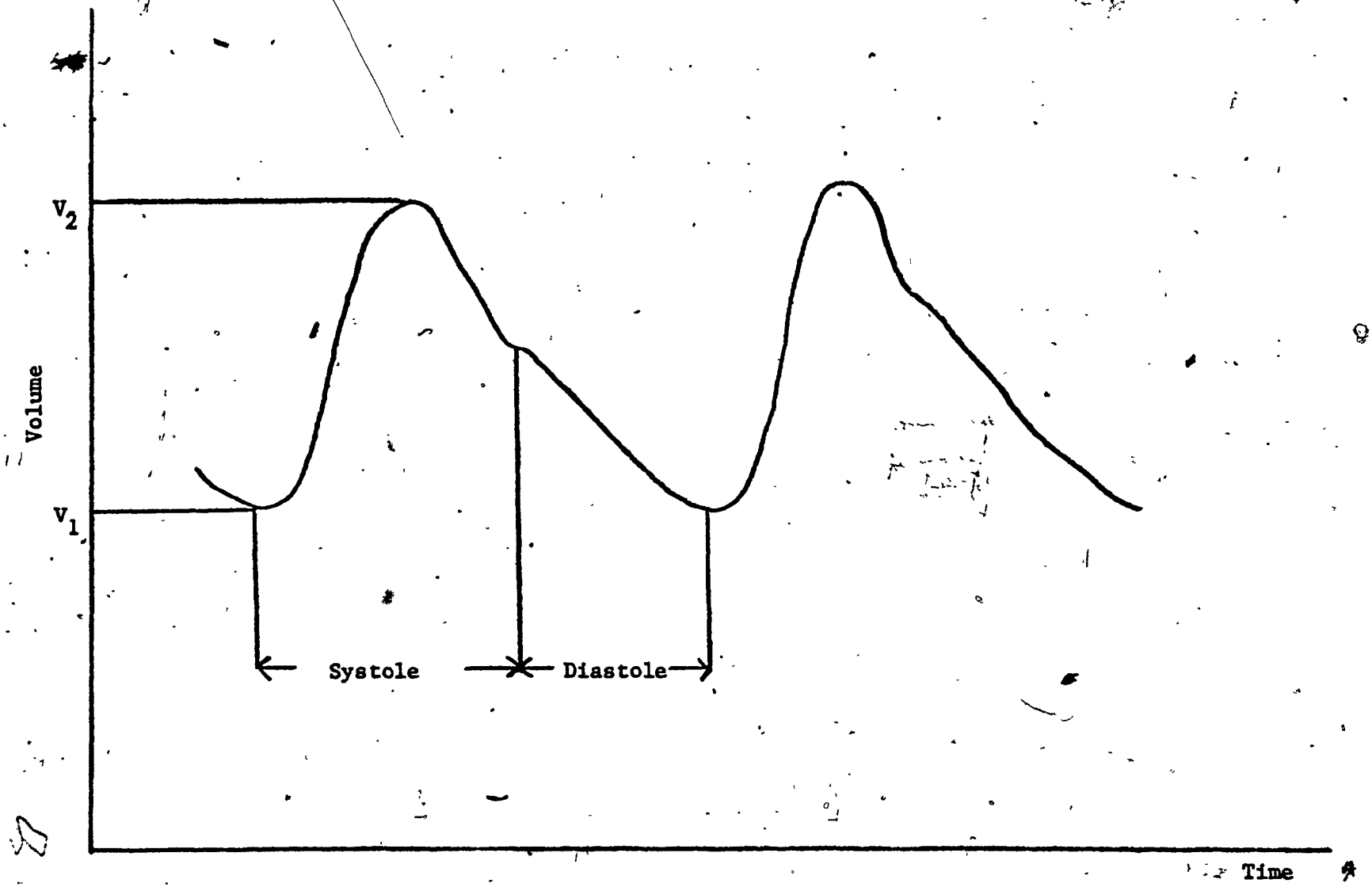


FIG. 2.7 Form of Volume Pulse

CHAPTER III

CURRENT METHODS OF ARTERIAL BLOOD PRESSURE MEASUREMENT

3.1 Introduction

Geddes[10] has published an interesting and informative survey of blood pressure measurement methods. In this survey, the principle of operation of the various methods are given and their advantages and disadvantages are discussed. Based on this work, a brief outline of the principal blood pressure measuring methods is given in this chapter. Direct and indirect methods of measurement are explained and their advantages and limitations discussed.

Although the strength or force of the pressure pulse has long been taken as a crude estimate of the blood pressure, it was not until 1733 that Hales[10] made the first arterial blood pressure measurement on a horse using a manometer attached directly into the femoral artery. Since then many developments on the instrumentation for measuring arterial blood pressure have been made.

3.2 Direct Measurement

3.2.1. Transducer Outside Artery

In this type of measurement, one end of a fluid filled tube or catheter is introduced into an artery and the other end is attached to a pressure transducer. The pressure transducer is most often a strain gauge, a linear voltage differential transformer (LVDT) or a capacitative type[11]. The signal from the transducer is conditioned, amplified, and then traced out on a recorder or displayed on a meter.

Although the electronic equipment following the transducer is subject to its own errors and limitations it is assumed that the equipment can accurately reproduce the signal from the transducer. Here we are concerned only with the effectiveness of the interface system, for example, the catheter and transducer between the subject and the amplifier.

One of the advantages of this method of measuring arterial blood pressure is that it gives a continuous record of the waveform or variation of blood pressure with time. The fluid filled catheter may introduce distortions in the waveform and amplitude which have to be corrected.[12] In addition clots can form at the opening of the catheter, degrading the amplitude-frequency response or sometimes blocking it completely. The transducer may also cause distortion of the variable being measured due to excessive damping.

3.2.2 Transducer Inside Artery

Instead of placing the transducer at the outside end of a fluid-filled catheter, it may be miniaturized and placed directly into an artery at the end of a non-fluid filled catheter [13]. The fluid-filled catheter is dispensed with, and because of this, the resonant frequency of the miniature (intracardiac) manometer can remain quite high, thus ensuring high fidelity reproduction. The disadvantages of this type are that it is difficult to check the calibration and impossible to determine the zero-pressure baseline of this transducer in situ.

A major disadvantage of the direct method of measuring blood pressure is that it requires arterial puncture. This involves a

risk of blood clot formation to the patient. Inserting the cannula or needle into an artery is sometimes difficult and requires the services of a physician. Further, long term in-dwelling of the needle or cannula provides a route for infection to enter the body. This technique has only restricted use, during and after certain surgical operations and during cardiac catheterizations.

3.3 Indirect Occlusive Measurement

3.3.1 Manual Methods.

In indirect methods, no puncturing of an artery is required. The flow of blood in a convenient artery (one near the surface of the skin) is arrested by compressing it with an externally applied measurable pressure. Then the external pressure is slowly released while observing its magnitude. When the applied pressure is just below the maximum periodic pressure in the artery, a small quantity of blood flows (spurts) during the time that the systolic pressure exceeds the external pressure. The external pressure at the time such spurting occurs is taken to be equal to the systolic pressure.

In practice the brachial artery in the arm is most often chosen for this type of measurement. An inflatable cuff, attached to a mercury or aneroid manometer, is wrapped around an arm, and inflated to a pressure beyond what the actual systolic pressure might be (say 200 mm Hg.). This occludes the brachial artery. The pressure is then slowly released from the cuff and the indication of the manometer observed. It is now necessary to determine when the first spurt of blood occurs in the brachial artery. The criteria for determining this give rise to a number of variations of this method.

The most widely used technique uses the Korotkoff sounds [14]. Here, a stethoscope is placed over the brachial artery. When the first spurt occurs as the occluding pressure falls, a tapping sound (Korotkoff sound) is heard through the stethoscope. This signals the beginning of partial blood flow and the pressure indicated by the manometer is taken to be the systolic pressure. As the occluding pressure falls the quality of the Korotkoff sounds changes. In the last stage they become muffled and may finally disappear. The manometer pressure at which muffling occurs is usually taken as the diastolic pressure. Some physicians feel that the disappearance of the sounds gives a better criterion, although they do not always disappear.

3.3.2 Automatic Methods

In the previous technique, the cuff can be inflated and deflated automatically and the stethoscope replaced with a microphone. This gives an automatic blood pressure measuring system. Many automatic blood pressure measuring systems have been devised, using various criteria for detecting flow in the artery [15].

Both manual and automatic indirect methods suffer from a number of disadvantages. They are:

i) Errors in the measured value of systolic pressure and/or diastolic pressure will occur due to the width of the occluding cuff in relation to the circumference of the arm it is placed on. Effective occlusion of the arterial segment being compressed depends on the width of the occluding cuff and the amount of tissue between the artery and the cuff, i.e. the

circumference of the arm. The corrections to be applied to compensate for these errors are given in Fig. 3.1 in relation to the arm circumference for a cuff width of 13 cms. For an arm circumference of about 28 cms, the systolic pressure is correct but the diastolic pressure is overestimated by about 10 mm Hg. For a normal diastolic pressure of about 80 mm Hg, this gives a reading 12.5 percent too high. When the measured diastolic pressure is correct--at an arm circumference of 17 cms--the measured systolic pressure is too low by about 15 mm Hg. If this error is referred to a normal systolic pressure of 120 mm Hg, the reading will be 12.5 percent less. For arm circumferences above 28 cms, the measured values of both systolic and diastolic pressures are too high. In order to minimize these errors, different cuff widths must be used for infants, children, normal size adults and obese adults.

ii) It was explained that when the cuff pressure is decreasing and falls just below the systolic pressure, the first Korotkoff sound is heard. As the cuff pressure continues to fall, the Korotkoff sounds are supposed to continue. Sometimes after one or two taps, the sounds disappear and resume after an additional fall in cuff pressure. This disappearance of sound is known as the auscultatory gap. If the cuff is inflated too slowly, the auscultatory gap may occur causing errors in the systolic pressure reading, due to uncertainty of the start of the Korotkoff sounds. The auscultatory gap has been related to pooling of venous blood in the arm during cuff inflation, Geddes[10]. Generally, a rapid inflation of the cuff minimizes the occurrence of the auscultatory gap.

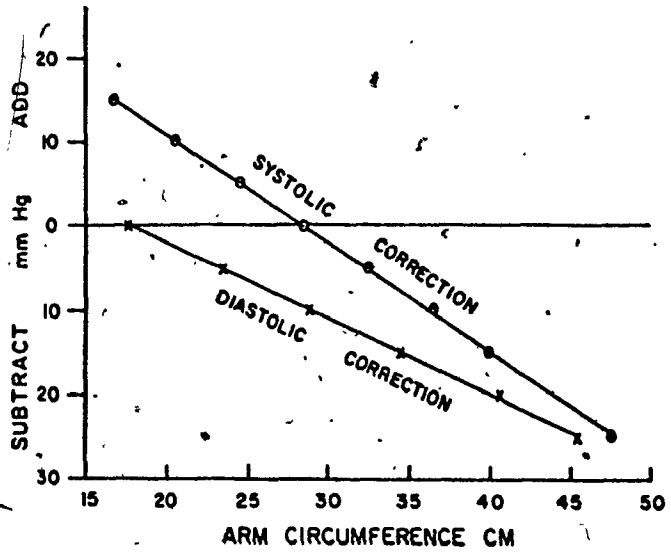


FIG. 3.1 Error in Blood Pressure Measurement with Cuff [10]

iii) Repeated inflation and deflation of the cuff cannot be carried on for long periods of time without causing discomfort to the patient. Sudden, rapid inflation of a cuff is particularly discomforting to a relaxed patient.

iv) If the cuff is deflated too quickly, errors in both systolic and diastolic pressure readings may occur due to the fact that the change in manometer reading may be too rapid between sounds.

v) Indirect occlusive methods do not give a continuous beat by beat indication of arterial blood pressure.

3.4 Indirect Non-occlusive Methods

3.4.1 Arterial Tonometry

Non-occlusive methods have not achieved any significant clinical adaptation and are largely restricted to research use. A number of attempts have been made to measure arterial pressure by placing a pressure transducer (arterial tonometry) on an accessible artery[16,17]. Such arteries are few in number. In this technique, a structural element of the transducer in the form of a ring bears on the artery in such a way as to reduce tension to zero in the part of the arterial wall under measurement. A pressure sensing element, passing through the ring, rests on the arterial wall and reproduces its movements due to the pressure variations within it.

This technique is being used successfully to measure intraocular pressures routinely. But it has met with little success in blood pressure measurements. Besides difficulties of calibration, its overriding

weakness is the great difficulty in stabilizing the transducer on the artery. The slightest movement not only produces an artefact, but may also alter the calibration. In order to have reasonable readings, the patient has to be very cooperative and must remain virtually motionless.

3.4.2 Peri-arterial Transducer

Another indirect blood pressure measuring technique is to place a pressure transducer around the artery (peri-arterial)[18]. This method requires surgical techniques and is not generally suitable for humans, certainly not for continuous monitoring, although this is what they are used for in animals.

3.4.3 Pulse Wave Velocity

It has long been known that a relationship exists between the arterial pulse wave velocity and the mean pressure within the artery. In 1878, Moens[3] presented the following formula relating pulse wave velocity and the Young's modulus of elasticity of the arterial wall.

$$C_v = F\left[\frac{E\,h}{2R\rho}\right]^{1/2} \qquad (3.1)$$

where

C_v = pulse wave velocity in meters per second

E = Young's modulus of elasticity in dynes/cm^2

h = Arterial wall thickness in cms

R = Radius of artery in cms

ρ = Density of blood in grams per ml

F = Proportionality constant

This formula is derived by considering the artery as a thin-walled tube filled with an incompressible fluid. No reflections are considered to exist in the artery in which the wave is travelling. In an artery, Young's elastic modulus varies with the state of tension of the vessel wall (17). Since the tension of the wall is related to the intramural pressure, the pulse wave velocity varies with the blood pressure. Equation (3.1) can also be expressed[3] as:

$$C_v = 0.357\left[\frac{V\Delta P}{\Delta V}\right]^{1/2} \qquad (3.2)$$

where

C_v = pulse wave velocity in meters/second

ΔP = change in pressure in mm Hg

ΔV = change in volume accompanying change in pressure, ΔP, in ml

V = original volume in ml

In 1964, Wickham and Salisbury[19] suggested using the pulse wave velocity to monitor the arterial blood pressure. Weltman[20] and Warner[21] have built instruments to measure the apparent pulse wave velocity and the apparent pulse wave transmission time respectively. Unfortunately, this method is not entirely satisfactory. True pulse wave velocity depends not only on the intra-arterial pressure, but also on the vasomotor tone of the arterial wall. Vasomotor activity (vasoconstriction or vasodilation) of the arterial wall can change the pulse wave velocity in the absence of pressure changes.

The apparent transmission time of the pulse can be measured from the onset of the electrical R-wave of the heart to the time of arrival

of the pulse at the pick-up site. The pulse wave transmission time, measured in this way, contains the pre-ejection period (PEP) of the heart, in addition to the true pulse wave transmission time. PEP contains interesting information about the state of the heart; therefore, the measurement of pulse wave transmission time (PWTT) can be useful to the clinician. This quantity can be monitored continuously without discomfort to the patient and is capable of signalling inadequate cardiac performance on the part of the patient. Nevertheless, it is not possible to correlate accurately the instrument reading with arterial blood pressure. It is only possible to indicate that the blood pressure is somewhere within a rather wide tolerance band and the instrument may indicate erroneously low or high pressures.

3.5 Summary

The principal methods of arterial blood pressure measurement have been briefly outlined in the above paragraphs and their main advantages and faults discussed. It is clear that a simple, easy-to-use, non-invasive pressure monitor is not available. Such a monitor would be useful in many medical and physiological research situations. Evidently, the higher the accuracy of such an instrument, the more useful it would be. But an accuracy within 10 percent to 15 percent of the true value would still prove useful in certain situations, such as blood pressure monitoring on coronary patients and hemodialysis patients.

CHAPTER IV

THEORETICAL MODEL

4.1 Introduction

The circulatory system consists of a network of viscoelastic tubes through which blood is pumped by the heart. Like any other fluid dynamic system, it is characterized by pressure, flow, and resistance. The systolic pressure P_s is one of the most important characteristic pressures in the system. The systolic pressure can be measured by various methods explained in Chapter III or it can be calculated from the mean pressure P_m and the pulse pressure P_p. A new approach to follow changes in P_s through measurement of a different variable is given.

4.2 Characteristic Pressures of the Circulatory System

The essential features of the circulatory system were explained in Chapter II. It was seen that at periodic intervals, the heart ejects a quantity of blood (stroke volume) into the circulation, raising its pressure. During ejection, some of it dilates the blood vessels; the rest flows directly through the microcirculation. After ejection ceases, i.e. during diastole, blood continues to flow in the circulation due to the elastic recoil of the arteries and is accompanied by a decrease in pressure.

A typical pressure-time relation in a major artery is shown in Figure 4.1. The pressure alternates between 120 mm Hg (systolic) and 80 mm Hg (diastolic). The mean pressure is about 93 mm Hg. The

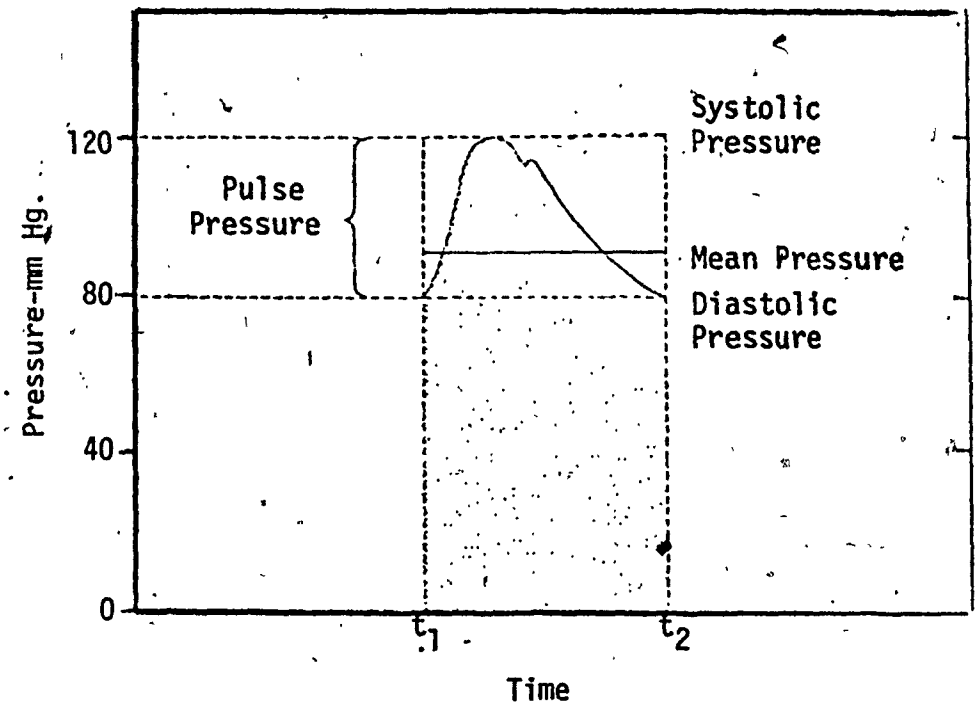


FIG. 4.1 Arterial Systolic, Diastolic, Pulse and Mean Pressures [23]

exact mean pressure P_m over a cycle is given by the area under the curve divided by the period of the cycle. That is,

$$P_m = \frac{\int_{t_1}^{t_2} P_a(t)dt}{t_2 - t_1}$$

where P_m = mean arterial pressure in mm Hg

$P_a(t)$ = instantaneous arterial pressure in mm Hg

t_1 = beginning of heart cycle

t_2 = end of heart cycle

The mean pressure is usually averaged over several cycles for better accuracy. A good approximation to the mean pressure is found by the formula given by Catton[22] and is,

$$P_m = \frac{P_s + 2P_d}{3} \tag{4.1}$$

where

P_s = arterial systolic blood pressure in mm Hg

P_d = arterial diastolic blood pressure in mm Hg

The pulse pressure P_p is defined as the difference between the systolic and diastolic blood pressures in a cycle, i.e.

$$P_p = P_s - P_d \tag{4.2}$$

The simultaneous Equations (4.1) and (4.2) may be solved to give,

$$P_s = P_m + 2/3\ P_p \tag{4.3a}$$

$$P_d = P_m - 1/3\ P_p \tag{4.3b}$$

The non-oscillatory part of the arterial blood pressure is the weighted average P_m of the systolic and diastolic pressures. The four pressures—systolic, diastolic, pulse, and mean—are the standard pressures used for characterizing the pressure aspects of the circulatory system.

4.3 New Pressure Relations

4.3.1 Preliminary Considerations

New pressure relations in the circulatory system can be used to give P_s by writing the right-hand side of Equation (4.3a) differently. Figure 2.2 is redrawn schematically to show the microcirculation more clearly, as in Figure 4.2, for the period of diastole, i.e. when the aortic valve is closed. The pulmonary circulation is not shown as it is not relevant to this discussion. The regions M_1, M_2, ...M_n are microvascular areas containing arterioles, metarterioles, capillaries, A-V anastamoses, and venules. Each is fed by a small artery and drained by a small vein. The instantaneous volume of blood in each region M_i, is V_i where i=1, 2, 3....n. The blood flow through each region is Q_i and is due to the elastic recoil of the arterial system. P_c is the pressure in the large arteries referred not to a datum of zero but to a pressure P_o. That is,

$$P_c = P_a - P_o \tag{4.4}$$

where P_a = arterial pressure in mm Hg

P_o = reference pressure in mm Hg

In the discussion to follow, P_a will be referred to as the pressure in the large arteries but is not to be taken as systolic pressure. V_a is the volume of the large arteries at pressure P_a. V_{ao} is the volume at zero pressure, i.e. $P_a = 0$.

4.3.2 Conditions and Assumptions

1) The model is chosen to be effective only at the beginning of diastole. At this time, the aortic valve

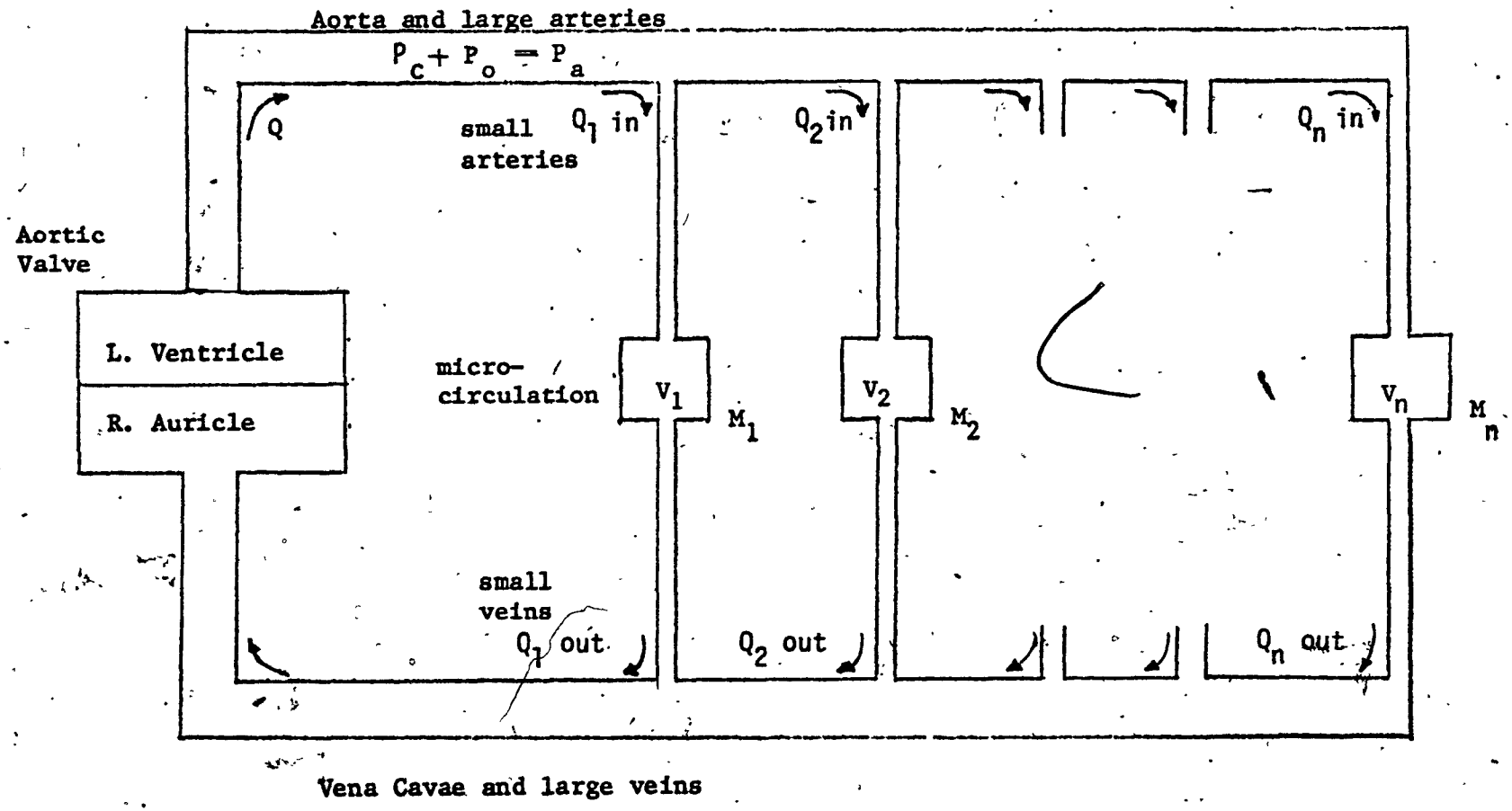


FIG. 4.2 Schematic Representation of Microcirculation during diastole

is closed and all blood flow is due to the elastic recoil of the large arteries—mainly the aorta. The fall of pressure is monotonic and the pulsatile nature of the arterial blood pressure need not be considered.

2) The blood vessels of a particular microvascular region, M_i, are assumed to be maximally dilated and to remain so.

3) The blood viscosity in the microvascular region is assumed to be constant.

4) The blood is assumed to be incompressible.

5) Assumptions 2 and 3 above mean that the fluid resistance in the particular microvascular region M_i is constant.

6) The pressure in the aorta at closure of the aortic valve is a constant fraction of the systolic pressure.

7) No pressure drop is assumed to occur in the aorta and large arteries. The pressure in the vena cavae and large veins is assumed to be zero.

8) A region M_i is taken to include the part of the small artery feeding it and the part of the small vein draining it.

9) It is assumed that the pressure across the microvascular region M_i is a constant fraction of the arterial pressure P_a. This is justified because it is assumed that no pressure drop occurs in the large arteries and that the small arteries in the vicinity of M_i which feed it and

the small veins which drain it are maximally dilated.

10) The stiffness of the microvascular region M_i is constant.

11) The walls of the aorta and large arteries are assumed to be elastic rather than viscoelastic.

12) It is assumed that at pressure P_0 the flow in the systemic circulation is very small.

4.4 Analysis for Pressure Relations

4.4.1 Variable Component of the Pressure

In this section, the pressure P_a in the large arteries is shown to be proportional to the rate at which the blood volume of a microvascular region changes plus a variable factor P_0, employing the conditions and assumption described in Section 4.3. A modified form of Fig. 4.2 is illustrated in Fig. 4.3. The aorta and large arteries are lumped and drawn as a balloon with volume V_a, to emphasize their distensibility. The left ventricle is not shown because it is not a functional part of the outflow circuit when the aortic valve is closed. M_i is a particular microvascular region within the dashed rectangular area. It is divided into two parts: a resistance R_i and a dintensible volume V_i. M represents all the rest of the body's microvasculature lumped together. R_i is the fluid resistance of M_i and R is the fluid resistance of M. The part of the heart cycle considered is just after closure of the aortic valve and the instantaneous values of the variable quantities are taken at this time. Blood is being squeezed out of volume V_a due to its elastic recoil and the pressure P_a is falling. The pressure P_i in volume V_i is:

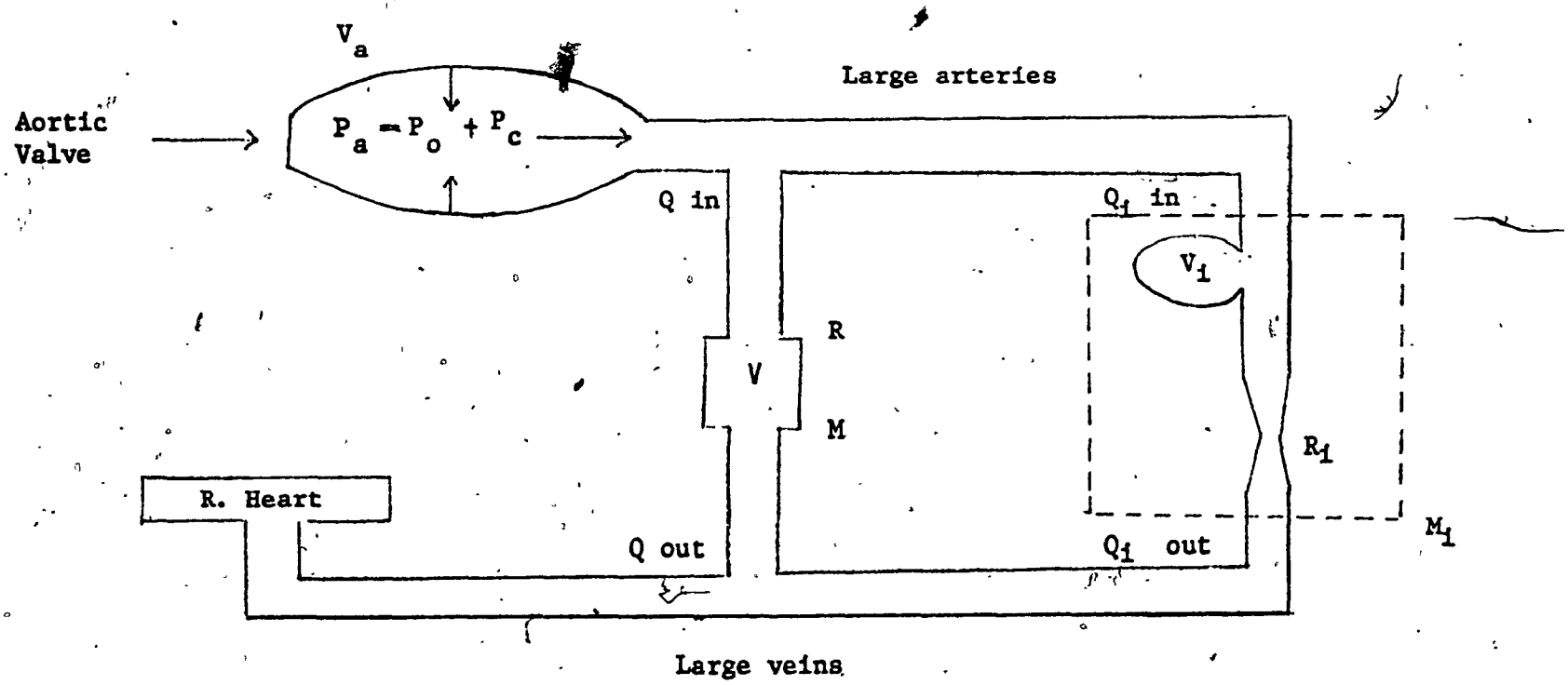


FIG. 4.3 Lumped Circulation during Diastole

$$P_i = \frac{\Delta P_i}{\Delta V_i} (V_i - V_{io})$$

$$= E_i (V_i - V_{io}) \qquad (4.5)$$

where

P_i = Pressure in volume V_i in mm Hg

E_i = Stiffness of volume V_i in mm Hg/ml

V_i = Volume of microvascular region M_i in ml at pressure $P_i > 0$

V_{io} = Volume of microvascular region M_i in ml at pressure $P_i = 0$

= Constant

ΔP_i = Change of pressure P_i

ΔV_i = Change of volume V_i due to ΔP_i

since the pressure P_i is proportional to P_a by assumption

$$P_i = k_1 P_a = k_1 (P_c + P_o) \qquad (4.6)$$

where

k_1 = Proportionality constant

substituting Equation (4.6) in Equation (4.5)

$$k_1 (P_c + P_o) = E_i (V_i - V_{io})$$

or

$$P_c = \frac{E_i}{k_1} (V_i - V_{io}) - P_o \qquad (4.7)$$

Since P_c is decreasing, volume $(V_i - V_{io})$ must also be decreasing at

the same rate since $\frac{E_i}{k_1}$ is a constant.

thus differentiating Equation (4.7)

$$\frac{dP_c}{dt} = \frac{E_i}{k_1}\frac{dV_i}{dt} \tag{4.8}$$

The rate at which the volume of V_a is decreasing is equal to the rate of outflow from it. That is,

$$\frac{dV_a}{dt} = -(Q_{in} + Q_{i\ in}) = -Q_t \tag{4.9}$$

where

$\frac{dV_a}{dt}$ = volume rate of change of V_a in ml/sec.

Q_{in} = inflow to region M in ml/sec.

$Q_{i\ in}$ = inflow to region M_i in ml/sec.

$Q_t = Q_{in} + Q_{i\ in}$

but also

$$Q_t = \frac{P_a}{R_t} = P_a\left(\frac{1}{R} + \frac{1}{R_i}\right) \tag{4.10}$$

$$= \frac{P_a RR_i}{R + R_i}$$

where

R_t = Total fluid resistance in PRU_s

R = Fluid resistance of M in PRU_s

R_i = Fluid resistance of M_i in PRU_s

Substituting Equation (4.10) in Equation (4.9)

$$\frac{dV_a}{dt} = -\frac{P_a}{R_t} = -\left(\frac{P_c}{R_t} + \frac{P_o}{R_t}\right) \tag{4.11}$$

The pressure P_a in the distended volume V_a is given by

$$P_a = P_c + P_o = E_a (V_a - V_{ao}) \tag{4.12}$$

where

E_a = stiffness of volume V_a in mm Hg/ml

V_{ao} = volume of V_a in ml at P_a equals zero

= constant

Differentiating Equation (4.12) gives

$$\frac{dP_c}{dt} = E_a \frac{dV_a}{dt} \tag{4.13}$$

or

$$\frac{dV_a}{dt} = \frac{1}{E_a} \frac{dP_c}{dt} \tag{4.14}$$

Now substituting Equation (4.14) in Equation (4.11) and neglecting $\frac{P_o}{R_t}$ which is very small,

$$\frac{1}{E_a} \frac{dP_c}{dt} = -\frac{P_c}{R_t}$$

or

$$\frac{dP_c}{dt} = -\frac{E_a P_c}{R_t} \tag{4.15}$$

Finally substituting Equation (4.15) in Equation (4.8)

$$\frac{E_a P_c}{R_t} = - \frac{E_i}{k_1} \frac{dV_i}{dt}$$

or

$$P_c = - \frac{E_i}{k_1} \frac{R_t}{E_a} \frac{dV_i}{dt} \qquad (4.15a)$$

Since only the absolute value of P_c is required, the negative sign in Equation (4.15a) can be dropped, giving

$$P_c = \left| \frac{E_i R_t}{k_1 E_a} \frac{dV_i}{dt} \right| \qquad (4.16)$$

In this equation, E_i and k_1 are constants. The total fluid resistance R_t and the stiffness may vary over a number of heart cycles but are constant during any one cycle. They determine the rate at which V_a and therefore P_c decrease. $\frac{dV_i}{dt}$ has its maximum value at the beginning of diastole and hence Equation (4.16) is only valid at the start of diastole.

From Equations (4.4) and (4.16)

$$P_c = P_a - P_o = \left| \frac{E_i}{k_1} \frac{R_t}{E_a} \frac{dV_i}{dt} \right| \qquad (4.17)$$

or

$$P_a = P_o + \left| \frac{E_i}{k_1} \frac{R_t}{E_a} \frac{dV_i}{dt} \right|$$

It was assumed in Subsection 4.3.2 that the arterial pressure at closure of the aortic valve is a constant fraction of the systolic pressure

of the same cycle. Then

$$P_a = k_2 P_s \tag{4.18a}$$

where

k_2 = constant

Substituting Equation (4.18a) in Equation (4.17)

$$P_s = \frac{P_o}{k_2} + \left| \frac{E_i}{k_1 k_2} \frac{R_t}{E_a} \frac{dV_i}{dt} \right| \tag{4.18b}$$

The significance of the datum or "steady" pressure P_o will be discussed in the following subsection.

4.4.2 The "Steady" Component P_o

In the previous subsection, the pressure P_c was defined as $(P_a - P_o)$. This pressure P_c was shown in Equation (4.16) to be proportional to the time rate of change of a microvascular volume V_i at the beginning of diastole and an expression for the arterial pressure P_a was given in Equation (4.17). The origin and significance of pressure P_o is explained in this subsection.

Consider Equation (4.15) without a restriction on the time interval and with the datum level equal to zero.

$$\frac{dP_a(t)}{dt} = -\frac{E_a P_a(t)}{R_t} \tag{4.15b}$$

solving for $P_a(t)$

$$\int \frac{dP_a(t)}{P_a(t)} = \int \frac{E_a}{R_t} dt$$

$$\ln P_a(t) = \frac{E_a t}{R_t} + \ln P_a^*$$

$$\frac{P_a(t)}{P_a^*} = \text{EXP}\left[-\frac{E_a}{R_t} t\right]$$

Since $P_a(t)$ is a decreasing function of time during diastole, the exponent of the exponential term is negative.

$$P_a(t) = P_a^* \text{ EXP}\left[-\frac{E_a}{R_t} t\right] \qquad (4.19)$$

where

$P_a^* = P_a\text{max.}$ = value of $P_a(t)$ at $t = 0$ (i.e. beginning of diastole.)

The fall of pressure in the large arteries is exponential and depends on the values of stiffness E_a and the total peripheral resistance R_t. This is illustrated in Fig. 4.4a. A dog's femoral artery is occluded some time after systole and the pressure in the distal portion (away from the heart) is plotted versus time. The graphs are drawn for different hematocrit values. The hematocrit values are given in the top right corner of each graph. Only the solid-circle graphs are relevant to our discussion. The plots ought to be straight lines since

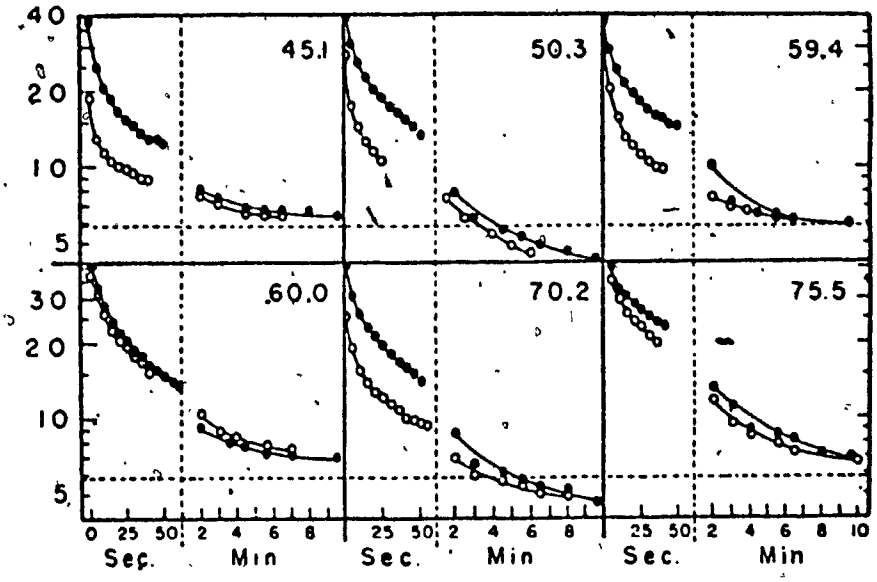


FIG. 4.4a Fall of Pressure in Occluded Dog Artery [34]

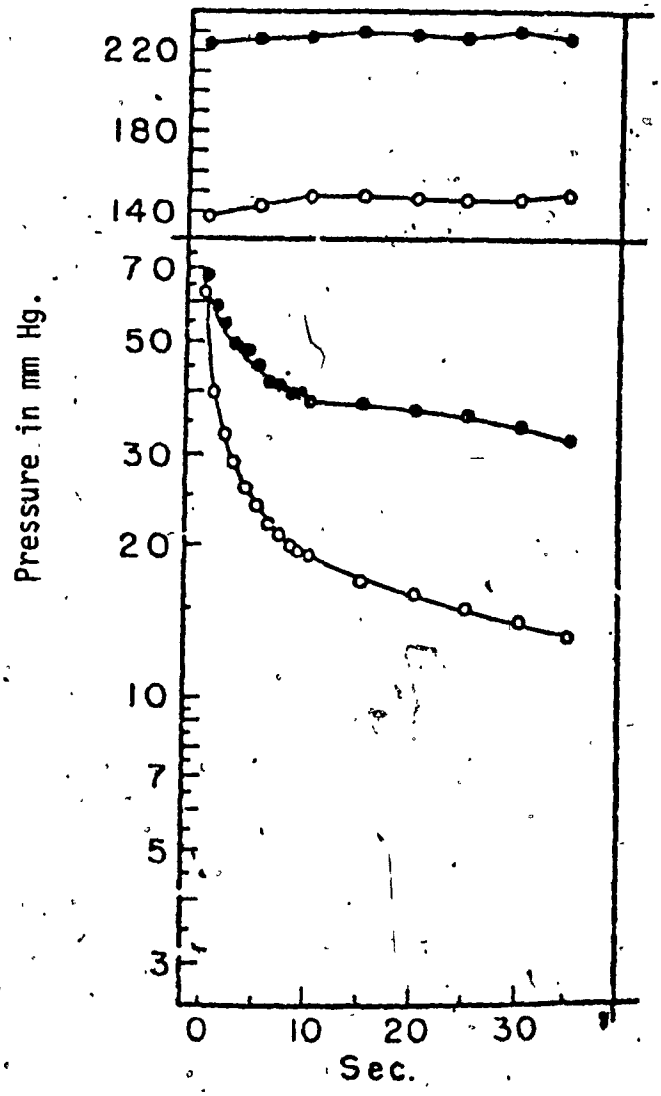


FIG. 4.4b Fall of Pressure in Occluded Dog Artery Before and After Vasoconstriction [34]

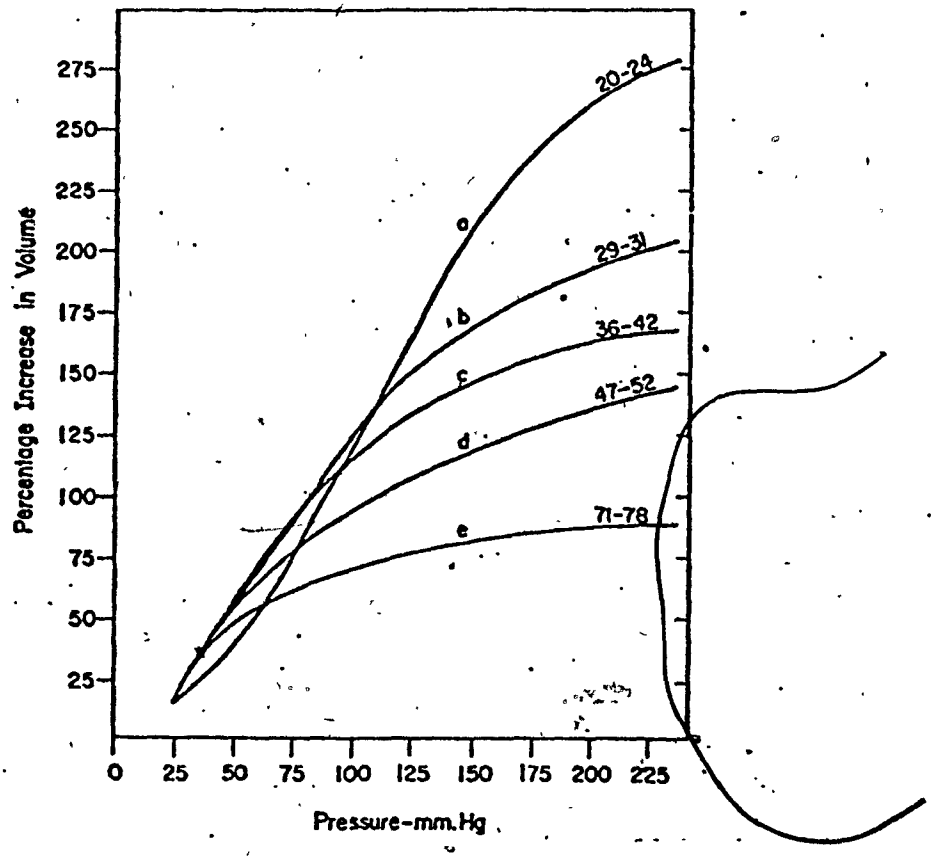


FIG. 4.5 Percentage Change of Volume of Aorta with Increase of Pressure [23]

the pressure scale is logarithmic. The plots show some curvature, particularly in the early parts of the graphs. This may be assigned to the fact that the stiffness E_a is not constant but increases as the distending pressure P_a enlarges the artery[24].

This may be further explained by the relationship between aortic pressure and aortic volume which is shown in Fig. 4.5. Pressure is plotted versus the percentage increase of volume with reference to the volume at zero pressure. The measurements are made on aortas removed from humans at autopsy. Five different age groups are represented. For the youngest age group, aged 20 to 24 years old, the curve is slightly sigmoid, but is fairly linear in the middle range. The stiffness $\frac{\Delta P}{\Delta V}$ decreases slightly as the pressure increases from zero but increases again at high pressures.

In all the other age groups, the stiffness increases as the pressure increases. At high intra-arterial pressures, E_a will be larger and the time constant $\frac{R_t}{E_a}$ will be smaller, permitting a more rapid fall of pressure. As the pressure falls, E_a diminishes, approaching a constant value at some lower pressure and the rate of fall of pressure also decreases. The blood viscosity rises as the hematocrit value increases, thus increasing the fluid resistance and reducing the rate of fall as shown in the figure.

The fall of pressure in the occluded dog femoral artery is shown more clearly in Fig. 4.4b. Here again, the femoral artery is occluded and the fall of pressure plotted against time. The pressure scale is logarithmic. The open circle curves are for pressure fall without drugs

and the closed circle curve is for pressure fall after injection of 7.5 mg of Wyamine sulphate, which constricts the blood vessels. The rate of pressure fall after administration of Wyamine sulphate is clearly smaller than the rate before. After about eight seconds, both curves become reasonably straight, indicating that the time constants are no longer varying.

For the normal situation with no drugs (curves with open circles), in Fig. 4.4b, the pressure drop in the first 8 seconds is about 64 mm Hg. This gives an average rate of change of $\frac{64}{8}$ or 8 mm Hg/sec. The fall of pressure in the next 27 seconds is about 7 mm Hg, giving an average rate of pressure drop of 0.26 mm Hg/sec. Since 0.26 is much smaller than 8.0, the average rate of change after 8 seconds can be taken as zero and the pressure at this time may be considered to vary very little from beat to beat. Then the pressure at the end of the initial 8-second period is:

$$P_o = P_a^* \text{ EXP } \left[- \frac{E_a}{R_t} T^+ \right] \qquad (4.20)$$

where T^+ = value of t in Equation (4.19) when $\frac{dP_a(t)}{dt}$ is very small.

= 8 seconds for above example.

The assumption of zero flow at a pressure P_o is justified since in the dog flow is small at an arterial pressure of about 20 mm Hg.[39] Therefore, the two pressures, P_c and P_o, can be derived from Fig. 4.4b, using Equations (4.15) and (4.19).

From Equation (4.15) valid at start of diastole,

$$\frac{dP_c}{dt} = -\frac{E_a}{R_t} P_c$$

or

$$P_c = \left| \frac{R_t}{E_a} \frac{dP_c}{dt} \right| = \left| \frac{E_i}{k_1} \frac{R_t}{E_a} \frac{dV_i}{dt} \right| \qquad (4.21a)$$

From Equation (4.19) at $t = T^+$, $\frac{dP_a(t)}{dt} \simeq 0$ and

$$P_o = P_a^* \, EXP \left[- \frac{E_a}{R_t} T^+ \right] \qquad (4.21b)$$

P_o is termed "steady" because it is not truly constant as Equation (4.21b) indicates, where P_a^* and $\frac{E_a}{R_t}$ are variables. However, P_o is nearly constant. An increase in P_a^* causes E_a to become larger, and may be accompanied by a reduction of R_t. Some decrease in the time constant $\frac{R_t}{E_a}$ will take place, allowing the higher pressure to decay faster. This interaction between the various quantities tends to maintain P_o constant in a particular individual.

4.5 Comparison Between the Standard and the New Pressure Relations

The relationship between P_s, P_c, P_a, and P_o is shown in Fig. 4.6a. The systolic pressure is the sum of a variable component $\frac{P_c}{k_2}$ and a "steady" component $\frac{P_o}{k_2}$. If E_a or R_t changes, $\frac{P_o}{k_2}$ will take on a new value. However, the changes in P_o will be small compared to those that can occur in P_c from beat to beat.

In Fig. 4.6b, the relationships between the standard pressures P_s, P_d, P_m, and P_p are shown. Here the systolic pressure P_s is also the sum of a "steady" component P_m and the variable part P_p. P_m is seen to be greater than P_o and reciprocally P_p is less than P_a.

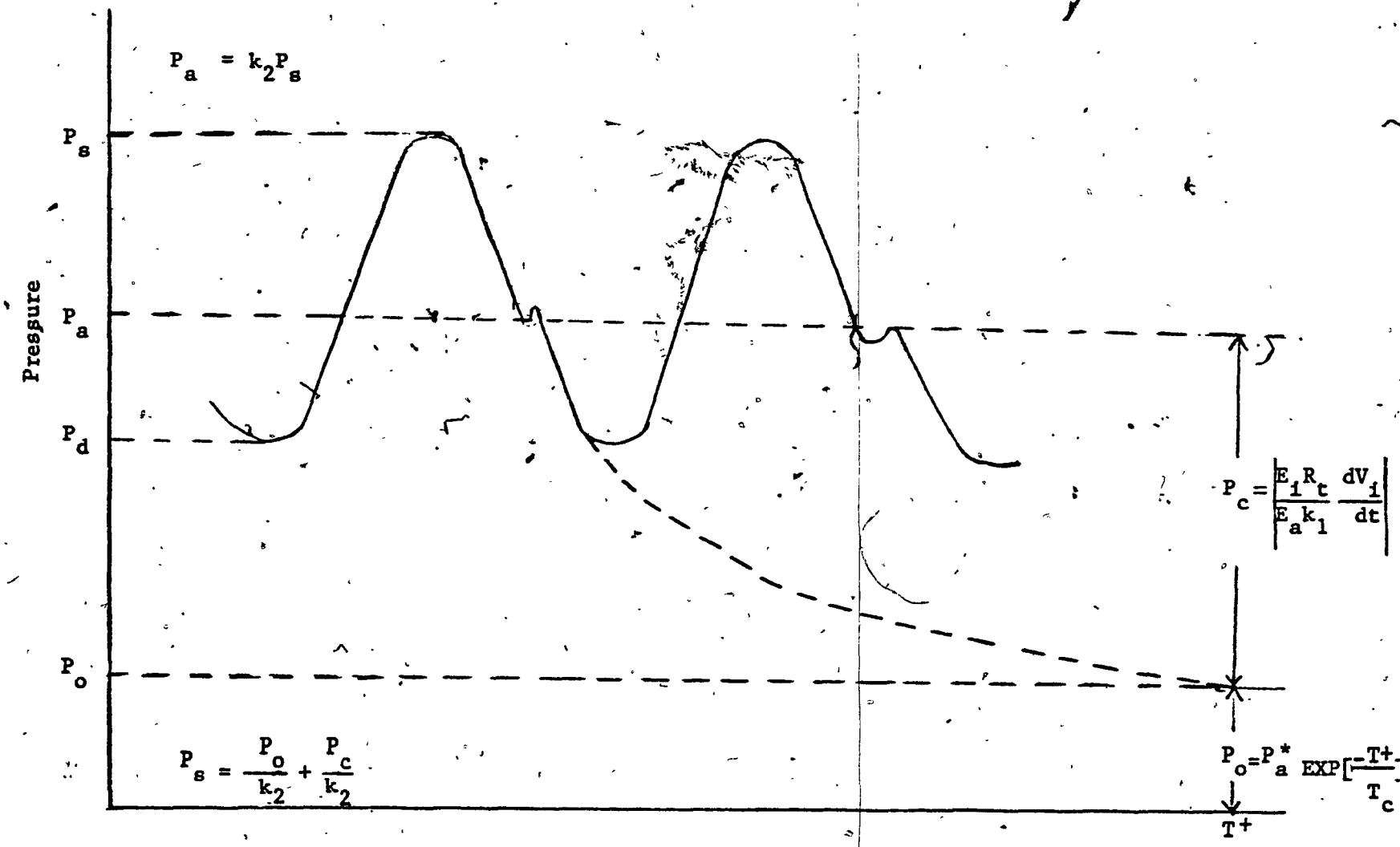


FIG. 4.6a Relationship between P_s, P_c, P_a and P_o.

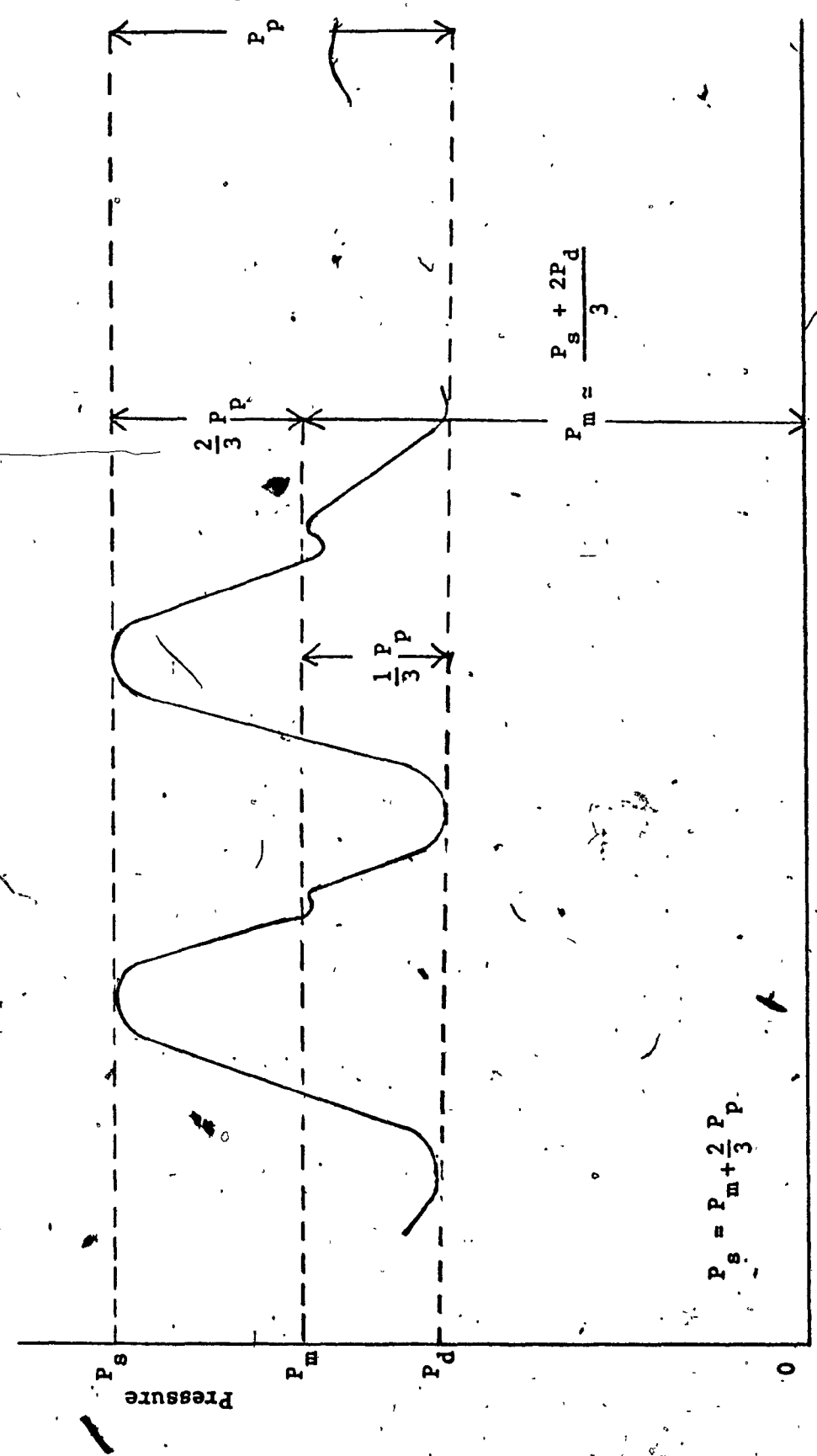


FIG. 4.6b Relationship beteeen P_s, P_d, P_m and P_p.

With a systolic pressure of 125 mm Hg and a diastolic pressure of 80 mm Hg, the mean pressure is:

$$P_m = \frac{P_s + 2P_d}{3} = \frac{125 + 160}{3}$$

$$= 95 \text{ mm Hg.}$$

In a normal male, to find P_o one needs to know the values of P_s, E_a, R_t, and T^+. Let T^+ be 3 seconds, corresponding to a heart rate of 20 beats per minute. E_a could be determined by referring to Fig. 4.5 and using Curve b. At a mean pressure of 95 mm Hg, the change in volume due to a 50 mm Hg pressure change is about 65 ml. This gives:

$$E_a = \frac{\Delta P}{\Delta V} = \frac{50 \text{ mm Hg}}{65 \text{ ml}} = 0.77 \text{ mm Hg/ml}$$

In Chapter II, the blood flow rate for a normal male was given as about 83 ml/sec. Then the total peripheral resistance R_t is given by $\frac{P_m}{Q_t} = \frac{95 \text{ mm Hg}}{83 \text{ ml/sec.}} = 1.14 \text{ PRU}_s$.

For a systolic pressure of 125 mm Hg,

$$P_o \simeq 125 \text{ EXP}\left[\frac{-0.77 \times 3}{1.14}\right] \simeq 125 \times 0.135$$

$$\simeq 17 \text{ mm Hg.}$$

4.6 Diastolic Pressure

It should be possible to find the diastolic pressure P_d from Equation (4.21b) by replacing the constant time interval T^+ with a variable time interval t_d, equal to the time interval between the start and end of diastole [2].

$$P_d \simeq P_a \, EXP\left[-\frac{E_a}{R_t} t_d\right] \qquad (4.21c)$$

where

$$P_a = k_2 P_s$$

Equation (4.22) can be checked for rough accuracy with data taken from the literature.

E_a can be calculated from Fig. 4.5. Using Curve b, a change of pressure from 75 mm Hg to 125 mm Hg produces a percentage increase in volume of 85 percent at 75 mm Hg and 150 percent at 125 mm Hg. If the aortic volume at zero pressure is taken as 100 ml [4], then the change in volume accompanying a pressure change from 75 mm Hg to 125 mm Hg is 250 ml - 185 ml = 65 ml.

The stiffness $E_a = \frac{\Delta P}{\Delta V} = \frac{50}{65} \simeq 0.77$ ml/mm Hg.

A table of pulse measurements taken from Neuman [35] is given in Table I. The measurements were taken on patients with renal hypertension. Consider the first subject No. 39. The subject's systolic pressure is 200 mm Hg and the diastolic pressure is 120 mm Hg. His

TABLE 1

Measurements of the Pulse and Alpha Waves in Patients with Renal Hypertension [35]

SUBJECT NO.	AGE	SEX	BLOOD PRESSURE	PART	VOLUME OF PART STUDIED	VOLUME OF THE DEFLECTIONS OF THE ALPHA WAVES		FREQUENCY OF THE DEFLECTIONS OF THE ALPHA WAVES			VOLUME OF THE PULSE WAVES		
						Mean	Maximum	Mean	Maximum	Minimum	Mean	Maximum	Minimum
	years		mm. Hg		cc.	cu.mm./5 cc. of part		No. per minute			cu.mm./5 cc. of part		
39	46	M	200/120	F*	4.2	14.0	38.2	7.8	10	5	12.5	15.0	7.7
				T*	4.0	7.1	22.2	11.0	13	10	5.2	6.2	4.5
				P*	2.0	5.2	17.3	10.0	17	7	9.5	9.7	9.0
40	38	F	220/148	F	3.9	19.8	54.5	11.6	12	6	6.8	7.6	6.4
				T	3.1	5.1	36.9	11.2	12	5	2.9	3.0	2.9
				P	1.2	4.5	20.0	9.8	15	6	1.6	1.6	0.8
44	[illegible]	M	198/140	F	7.1	12.3	37.3	8.0	9	6	4.0	4[illegible]	3.5
				T	6.1	5.2	13.8	8.4	10	5	2.1	2.4	1.1
				P	3.0	4.1	10.1	10.2	14	7	8.4	10.0	0.5
57	40	F	190/138	F	3.2	12.4	47.4	7.8	10	6	5.7	7.0	4.7
72	27	F	200/140	F	3.2	14.3	50.8	14.2	18	12	9.1	10.2	6.9
				T	3.9	5.4	19.5	10.2	13	7	2.7	3.9	2.5
74	28	F	184/124	F	3.5	11.1	38.2	9.8	10	9	3.3	5.6	2.2
				T	3.3	7.7	23.0	11.2	14	10	3.3	9.7	6.8
Mean, maximum and minimum for the group				F		14.0	54.5	9.9	18	5	8.2	15.0	2.2
				T		5.1	36.9	10.4	13	5	4.2	9.7	1.1
				P		4.6	20.0	10.0	17	6	6.5	10.0	0.5

* F = Right index finger tip.
T = Right second toe tip.
P = Postero-superior portion of the right pinna.

mean pressure is:

$$P_m = \frac{P_s + 2P_d}{3} = \frac{200 + 240}{3} = \frac{440}{3} = 147 \text{ mm Hg.}$$

Assume that his cardiac output is normal—about 5 liters/min. or 83 ml/sec. Then the total peripheral resistance, R_t, is

$$R_t = \frac{147}{83} \simeq 1.77 \text{ PRU}_s$$

Let the heart rate be normal, i.e. 72 beats/min. The period T_p is 830 milliseconds. Then $t_d \simeq 0.6T_p \simeq 500$ milliseconds. From Fig. 2.3

$$k_2 = \frac{P_a}{P_s} \simeq \frac{120}{145} \simeq 0.82$$

Finally,

$$P_d \simeq k_2 P_s \text{ EXP}\left[-\frac{E_a}{R_t} t_d\right]$$

$$\simeq 0.82 \times 200 \times \text{EXP}\left[-\frac{0.77}{1.77} \times 0.5\right]$$

$$\simeq 164 \times \text{EXP}[-0.2175]$$

$$\simeq 164 \times 0.80$$

$$\simeq 131 \text{ mm Hg.}$$

The diastolic pressure for Subject No. 39 is 120 mm Hg. The calculated value of 128 mm Hg is just about 9.1 percent greater. This is a reasonably good agreement between measured and calculated values in accordance with elastic reservoir theory.

4.7 Summary

In this chapter a new set of relations have been derived to give the arterial systolic pressure P_s under a number of conditions and assumptions. The expression for systolic pressure is derived as

$$P_s = \frac{P_a}{k_2} \text{EXP}\left[-\frac{E_a}{R_t} T^+\right] + \left|\frac{E_i}{k_1 k_2} \frac{R_t}{E_a} \frac{dV_i}{dt}\right| \tag{4.22}$$

where the quantities to be measured are $\frac{dV_i}{dt}$ and $\frac{R_t}{E_a}$. If $\frac{R_t}{E_a}$ is considered constant (as it is in many situations), Equation (4.22) becomes

$$P_s = P_1 + K_5 \frac{dV_i}{dt} \tag{4.23}$$

where K_5 is a constant to be determined at calibration and P_1 has an almost constant value, since it is small compared to normal values of P_c.

The use of Equations (4.22) and (4.23) permits the estimation of the arterial systolic blood pressure from a single easily measurable primary variable—the change in microvascular volume ΔV_i—after calibration against a standard systolic pressure measurement. The estimation is made with each heart beat so that continuous monitoring is possible.

CHAPTER V

TECHNIQUES OF MEASUREMENT

5.1 Introduction

In the previous chapter an expression (4.22) was derived to give the systolic pressure P_s in terms of a number of constant and variable factors.

$$P_s = \frac{P_a}{k_2} \text{ EXP}\left[-\frac{E_a}{R_t} T^+\right] + \left|\frac{E_i R_t}{E_a k_1 k_2} \frac{dV_i}{dt}\right|$$

where E_i, k_1, k_2, and T^+ are constants and $\frac{R_t}{E_a}$ and $\frac{dV_i}{dt}$ are the variables to be measured.

Since $P_a = k_2 P_s$,

$$P_s = P_s \text{ EXP}\left[-\frac{T^+}{T_c}\right] + \left|\frac{E_i R_t}{E_a k_1 k_2} \frac{dV_i}{dt}\right| \qquad (5.1)$$

$$= P_1 + K_1 T_c \frac{dV_i}{dt} \qquad (5.2)$$

where

$$T_c = \frac{R_t}{E_a} = \text{Time constant in seconds.}$$

$$K_1 = \frac{E_i}{k_1 k_2} = \text{Constant}$$

$$P_1 = P_s \text{ EXP}\left[-\frac{T^+}{T_c}\right]$$

T_c and $\frac{dV_i}{dt}$ are now the two variables to be measured for obtaining P_s. Equation (5.2) can be used for following the changes in the systolic pressure P_s by the following calibration procedure:

1) Determine the systolic pressure P_s by standard means, such as auscultation.

2) Set $P_s \text{ EXP}\left[-\frac{T^+}{T_c}\right] = P_1$ to an initial value using P_s as determined above and an appropriate value of T^+.

3) Adjust K_1 in such a way as to make $P_1 + K_1 T_c \frac{dV_i}{dt}$ equal to P_s.

Now by updating the values of T_c and $\frac{dV_i}{dt}$ in Equation (5.2) for each heart cycle, the changes in P_s can be continuously followed. An electronic instrument may be developed to follow such changes in P_s according to Equation (5.2). The only quantities to be measured are $\frac{dV_i}{dt}$ and T_c. In the following two sections, the techniques of measurement of these variables is explained.

5.2 Measurement of Rate of Change of Microvascular Volume V_i

There are a number of ways of measuring blood volume changes in a vascular bed[25]. Two methods, namely; electrical impedance plethysmography and photoelectric plethysmography are discussed below.

5.2.1 Electrical Impedance Plethysmography

The electrical impedance plethysmograph measures tissue impedance in various parts of the body. A schematic diagram of an impedance plethysmograph applied to an arm is shown in Fig. 5.1. A high frequency constant current generator passes current from electrode No. 1 through the tissue of the arm to electrode No. 4. The frequency of the current usually lies between 20 and 100 kHz and its magnitude somewhere between 100 microamperes and 1 milliampere. The constant current produces a voltage across the tissue it traverses. This voltage is "tapped" off by electrodes No. 2 and No. 3 (receiving electrodes) which lead it to a detector-amplifier. The detector-amplifier produces an output signal which is proportional to the impedance of the tissue between electrodes No. 2 and No. 3.

Changes in tissue impedance between the receiving electrodes is taken to correspond to changes in tissue blood volume [25]. The change in impedance produced by the blood volume pulse in the arm is illustrated in Fig. 5.2. The impedance varies between a minimum and a maximum with a waveform similar to that shown in Fig. 3.4. The rate of change of the blood volume is proportional to the time derivative of the impedance wave Z(t).

$$\frac{dV_T(t)}{dt} \propto \frac{dZ(t)}{dt}$$

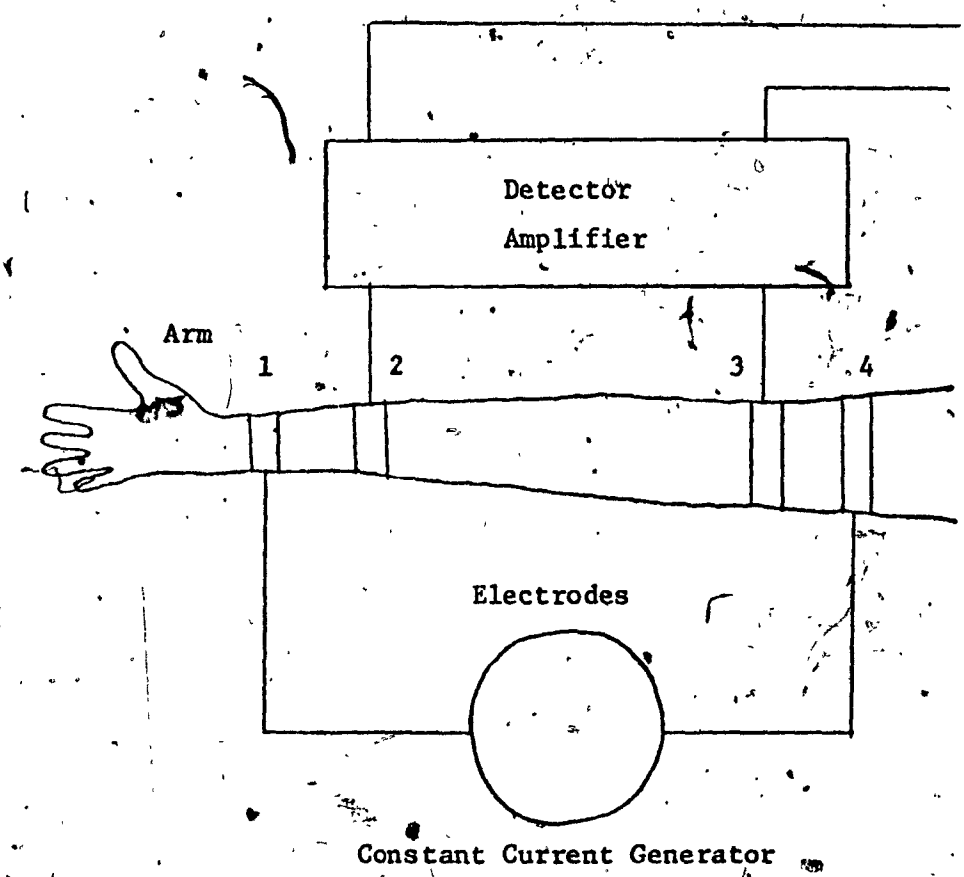


FIG. 5.1 Schematic Diagram of Electrical Impedance Plethysmograph

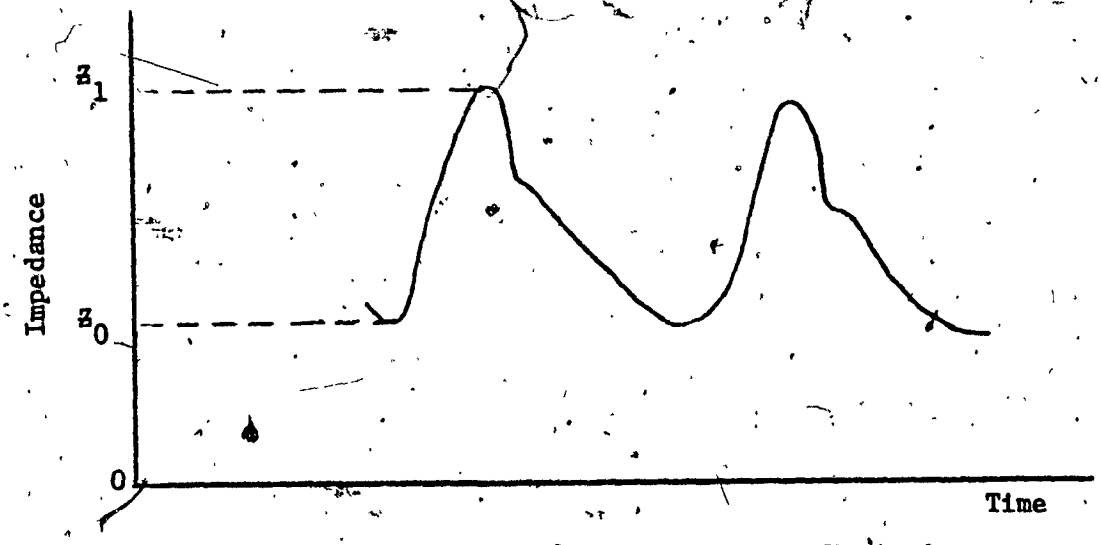


FIG. 5.2 Waveform of Impedance Variations

or

$$\frac{dV_T}{dt} = C_1 \frac{dZ}{dt}$$

where

$Z(t)$ = Tissue impedance in ohms

$V_T(t)$ = Total volume of tissue in ml

C_1 = Proportionality constant

Since the changes in tissue impedance are caused by changes in tissue blood volume, this method can be used to find $\frac{dV_i}{dt}$. However, it is useful only if the patient or subject, whose systolic pressure is being monitored, remains fairly motionless. Movement of the receiving electrodes relative to the skin will produce transient signals (artifacts). Almost any movement of the arm will produce some electrode movement. This method is not suitable in any situation where the subject does not remain quiet.

5.2.2 Photoelectric Plethysmography

The photoelectric plethysmograph is another method used for indicating blood volume changes. This method is based either on the absorption of light as it passes through body tissue and the blood flowing in it, or the reflection of light when it is incident on blood carrying tissue. Both these cases will be described below.

a) Transmission Type Photoelectric Plethysmography

The schematic of a transmission type plethysmograph is shown in

Fig. 5.3a. A low power lamp operating on two or three volts passes light through a suitable portion of body tissue. Since some light must emerge from the tissue, the tissue cannot be too thick. Suitable body tissues are fingers, toes, pinna and lobe of the ear. In the figure, the light is shown passing through the ear lobe tissue. The emergent light falls on a photocell whose output is fed to an amplifier. The intensity of emergent light depends on the optical density of the tissue. Changes in optical density are taken to be proportional to changes in the amount of blood in the optical path. A plot of optical density versus time is shown in Fig. 5.3b. The optical density has a minimum and a maximum within each heart cycle. The waveform is similar to that of the impedance plethysmograph. The slope of the curve will give the rate at which the blood volume is changing. That is:

$$\frac{dV_T(t)}{dt} \propto \frac{dD}{dt}$$

where

D = Optical density of tissue and blood

V_T = Total volume of tissue and blood in optical path

Actually, the transmitted light and its variations are detected by the photocell. Therefore, the optical density must be expressed in terms of light intensity. Or, more precisely, the rate of change of the absorption path is to be expressed as the rate of change of light intensity as shown next.

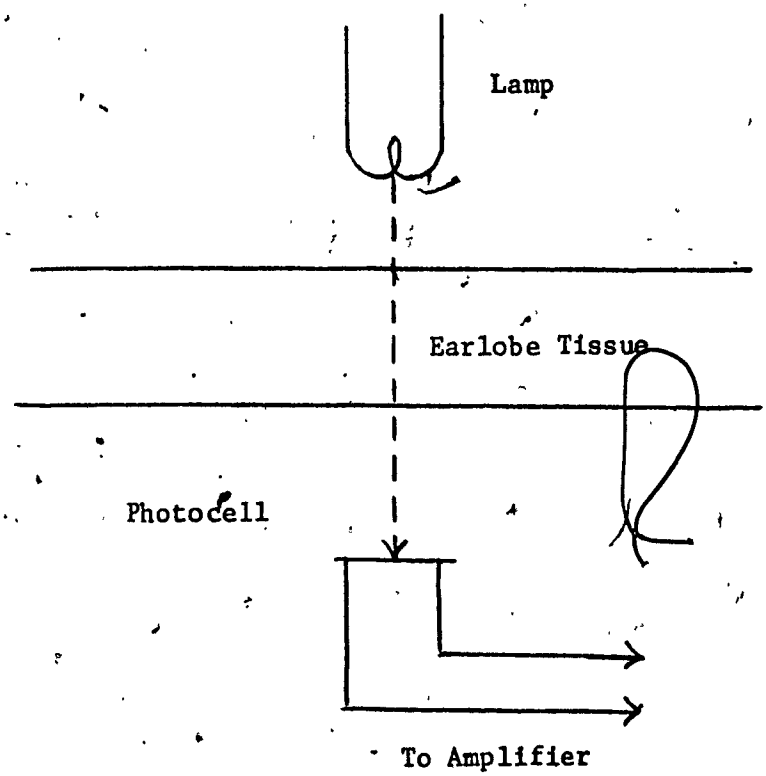


FIG. 5.3a Transmission Type Photoelectric Plethysmograph

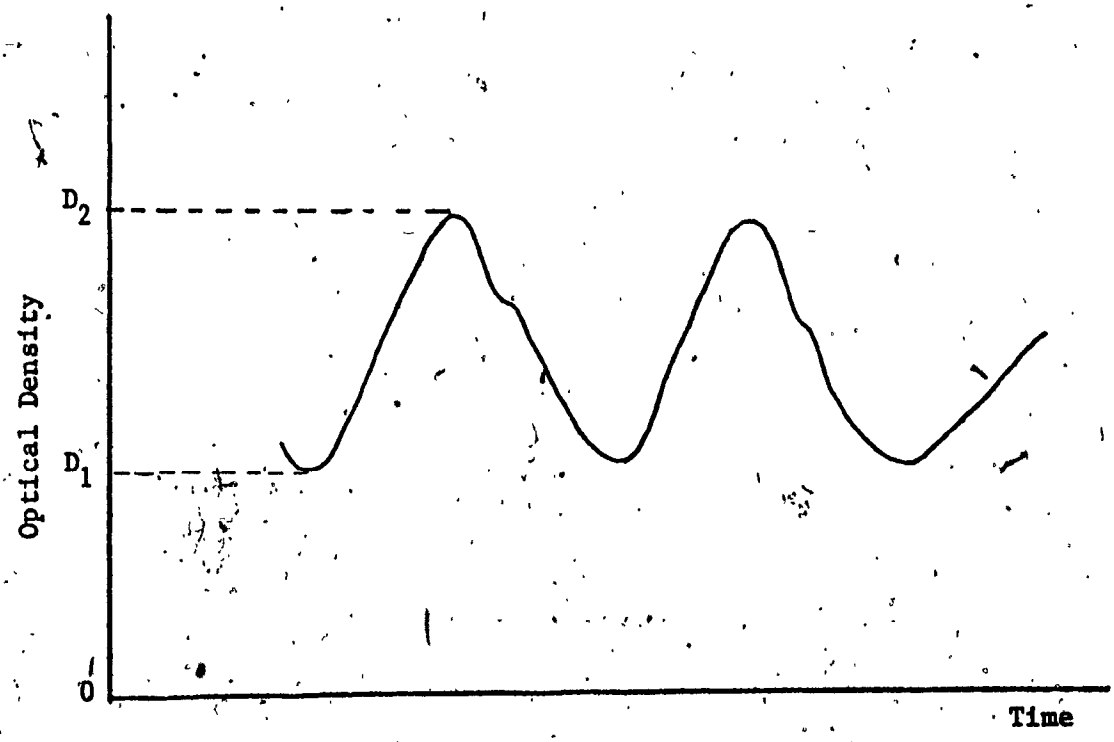


FIG. 5.3b Waveform of Optical Density Variations

The transmission of light through an absorbing medium is governed by the Lambert-Beer Law [26].

$$I = I_0 \text{ EXP } [-\alpha C x] \tag{5.3}$$

where

I = Intensity of transmitted light

I_0 = Incident light

= Constant

α = Attenuation coefficient (light attenuation per unit concentration per unit length)

C = Amount of absorbant per unit volume

x = Length of absorbing path

Taking natural logarithms of both sides of equation (5.3)

$$\ln I = \ln I_0 - \alpha C x$$

or

$$\ln \frac{I}{I_0} = -\alpha C x \tag{5.4}$$

The optical density D is defined as

$$D = -\log_{10} \frac{I}{I_0} = -0.434 \ln \frac{I}{I_0}$$

or

$$\ln \frac{I}{I_0} = 2.304 \log_{10} \frac{I}{I_0} \tag{5.5}$$

Substituting Equation (5.5) in Equation (5.4)

$$2.304 \log_{10} \frac{I}{I_0} = -\alpha C x$$

$$\log_{10} \frac{I}{I_0} = -0.434\ \alpha C x \qquad (5.6)$$

or

$$\log_{10} I = \log_{10} I_0 - 0.434\ \alpha C x \qquad (5.7)$$

Differentiating

$$\frac{d(\log_{10} I)}{dt} = -0.434\ \alpha C \frac{dx}{dt} \qquad (5.8)$$

This means that the time rate of change of the length of the absorbing medium is proportional to the time rate of change of the logarithm of the intensity of the transmitted light. An expression for the rate of change of the light intensity $\frac{dI}{dt}$ can be obtained directly by differentiating Equation (5.3).

$$\frac{dI}{dt} = -\alpha C \frac{dx}{dt} I_0 \ EXP[-\alpha C x]$$

or

$$\frac{dI}{dt} = -\alpha C \frac{dx}{dt} I \qquad (5.9)$$

It will now be shown that in Equation (5.9), I can be considered constant.

Changes in transmitted light intensity are due to changes in the volume of tissue in the path of the light. These changes are due to variations in blood volume in the tissue. Measurements of the blood volume pulse in relation to total tissue volume have been done by Burch[27]. Tests carried out on twelve subjects showed a maximum blood volume pulse of 12.4 cu.mm. in 5 cc of tissue in fingers, toes and ears. The percent volume change is 0.25. The mean volume pulse was 6.9 cu.mm. in 5 cc of tissue or 0.14 percent change.

The optical density of well dilated ear tissue is about 0.8[28]. At this optical density the percent change in light intensity I will be about 1.8 times the percent change in optical path length (tissue volume seen by transducer). Thus for a 0.25 percent change in tissue volume the transmitted light intensity will change by 0.46 percent. Since this is less than 1.0 percent, I can be considered constant. Equation (5.9) can now be written as

$$\frac{dI}{dt} = -\alpha C I \frac{dx}{dt} \qquad (5.10)$$

where

$$I = \text{Constant}$$

Changes in the linear dimensions x are assumed to be proportional to changes in tissue volume[40]. Since the photoelectric plethysmograph is used to detect changes in blood volume, this assumption is implicit in its use. Now $\frac{dV_i}{dt}$ can be substituted for $\frac{dx}{dt}$ in Equation (5.10) giving:

$$\frac{dI}{dt} = K_2 \frac{dV_i}{dt} \tag{5.11}$$

or

$$\frac{dV_i}{dt} = K_3 \frac{dI}{dt} \tag{5.12}$$

where

K_2, K_3 = Constants

b) Reflection Type Photoelectric Plethysmography

The schematic of a reflectance type plethysmograph is shown in Fig. 5.4a. In this case, the lamp and photocell are on the same side of the skin and can be placed almost anywhere on the body. Light from the lamp is reflected partly from the skin and partly from the vascular bed immediately beneath the skin. Some of the reflected light falls on the photocell producing a signal.

As in the case of the transmission type photoelectric plethysmograph, the changes in reflected light intensity are taken to be proportional to blood volume changes.[31, 40] That is,

$$\frac{dV}{dt} = K_4 \frac{dI_r}{dt} \tag{5.13}$$

where

I_r = Reflected light intensity

K_4 = Constant

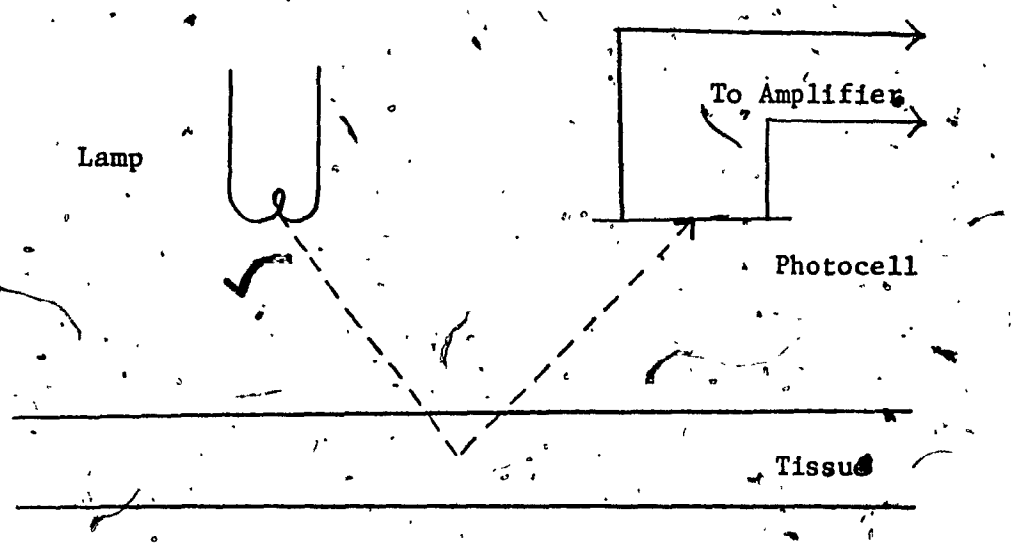


FIG. 5.4a Reflection Type Photoelectric Plethysmograph

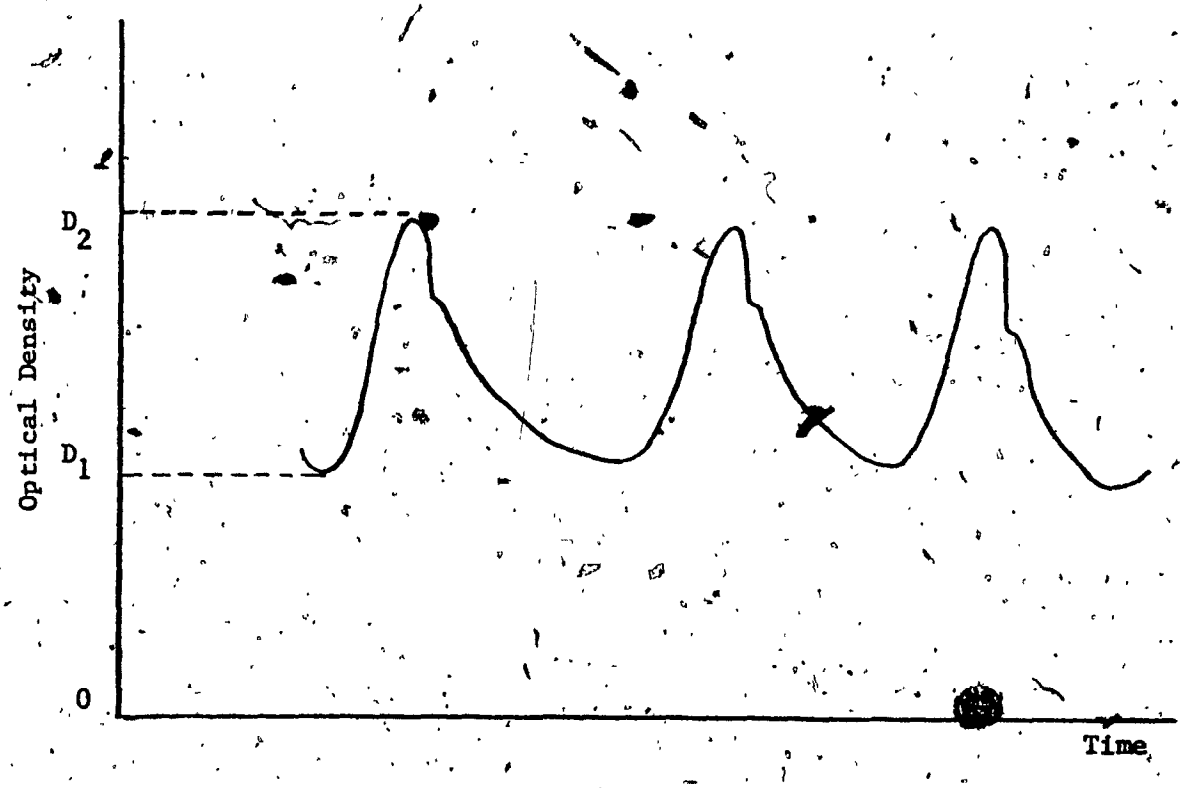


FIG. 5.4b Waveform of Optical Density Variations

The photoelectric plethysmograph is simple and inexpensive to use. Its electronic circuitry is less complex than that of the impedance plethysmograph. It is easy to apply the transducer to the body. Body movement produces artefacts in this case also but these are not as severe as those experienced with the impedance method. Therefore, the photoelectric plethysmograph is well suited to measure $\frac{dV_i}{dt}$.

5.3 Measurement of Time Constant of Large Arteries.

The time Constant of the large arteries is:

$$T_c = \frac{R_t}{E_a}$$

From Equation (4.5)

$$P_i^* = k_1 P_a^* = E_i (V_i^* - V_{io}) = E_i \Delta V_i^* = E_i V_b^*$$

where V_i^* = value of V_i at start of diastole in a particular heart cycle.

$$P_a^* = \frac{E_i}{k_1} V_b^*$$

According to Equation (4.19)

$$P_a(t) = P_a^* EXP\left[-\frac{t}{T_c}\right]$$

substituting $\frac{E_i V_b}{k_1}$ for P_a

$$V_b(t) = V_b^* EXP\left[-\frac{t}{T_c}\right]$$

By measuring $V_b(t)$ at two instants T_1 and T_2, T_c may be determined.

Suppose $T_2 - T_1 = T_k$ = Constant; if starting time $T_1 = 0$

$T_k = T_2$

then

$$V_b^* \text{ EXP}[0] - V_b^* \text{ EXP}\left[-\frac{t_2}{T_c}\right] = \Delta V_b^* \tag{5.14}$$

or

$$V_b^*\left[1 - \text{EXP}\left[-\frac{t_2}{T_c}\right]\right] = \Delta V_b^*$$

$$-\text{EXP}\left[-\frac{t_2}{T_c}\right] = \frac{\Delta V_b^*}{V_b^*} - 1$$

Taking logarithms of both sides,

$$\frac{t_2}{T_c} = \ln\left(\frac{\Delta V_b^*}{V_b^*} - 1\right)$$

or

$$T_c = \frac{t_2}{\ln\left(\frac{\Delta V_b^*}{V_b^*} - 1\right)} \tag{5.15}$$

In order to measure time constant T_c it is only necessary to measure ΔV_b^* and V_b^* and make the calculation using a suitable value of T_k—say, 100 milliseconds.

In addition to being used in Equation (5.2), T_c could be used as an indicator of the state of the arterial system.

5.4 Summary

In some situations, as when the subject is sitting or lying down, the arterial stiffness E_a and total peripheral resistance R_t vary very little. In these cases T_c can be considered to be constant. Since $P_s \text{ EXP}\left[-\frac{T}{T_c}\right]$ is of the order of 20 mm Hg, (Chap. IV, Subsection 4.4.2) an error of 20 percent in its value will cause an error of only about 3 percent when the systolic pressure is 125 mm Hg. If in addition the variations in P_s do not exceed ± 25 percent, $P_s \text{ EXP}\left[-\frac{t}{T_c}\right]$ can be considered constant, since an accuracy of ± 5 percent is considered quite adequate for most blood pressure measurements.

Therefore, Equation (5.2) can now be written

$$P_s = P_2 + K_5 \frac{dV_i}{dt} \tag{5.16}$$

This leaves only one variable to be measured, $\frac{dV_i}{dt}$, and simplifies considerably the instrumentation.

In this chapter the techniques of measuring the variable quantities $\frac{dV_i}{dt}$ and T_c have been discussed, thus laying the groundwork for the development of appropriate instrumentation.

CHAPTER VI

PROPOSED BLOOD PRESSURE FOLLOWER

6.1 Introduction

In Chapter V techniques for measuring $\frac{dV_i}{dt}$ and T_c were presented and the use of Equation (5.2) for following the variations in systolic pressure, after calibration using a known value of P_s, was discussed. In this chapter the electronic implementation of Equation (5.2) is dealt with. The general features of a Blood Pressure Follower (BPF) are discussed in relation to a block diagram.

6.2 Blood Pressure Follower (BPF)

A functional block diagram of a Blood Pressure Follower is shown in Fig. 6.1. By following the blocks and signal flow the operation of the Blood Pressure Follower can be understood.

At the left, X_1 is a photoelectric plethysmograph, similar to that described in the previous chapter. Transmitted light, I, from the tissue under test falls on the photoconductive cell in the transducer and produces voltage variations across it, proportional to the variations in I. These voltage variations are small, usually only a few millivolts, and must be amplified. This is done in amplifier A_1 where the signal level is raised to several volts. The waveforms give the waveshapes at the various designated points. The output of X_1 is coupled to A_1 through capacitor C in order to remove the DC component or datum of the input signal, which is not needed.

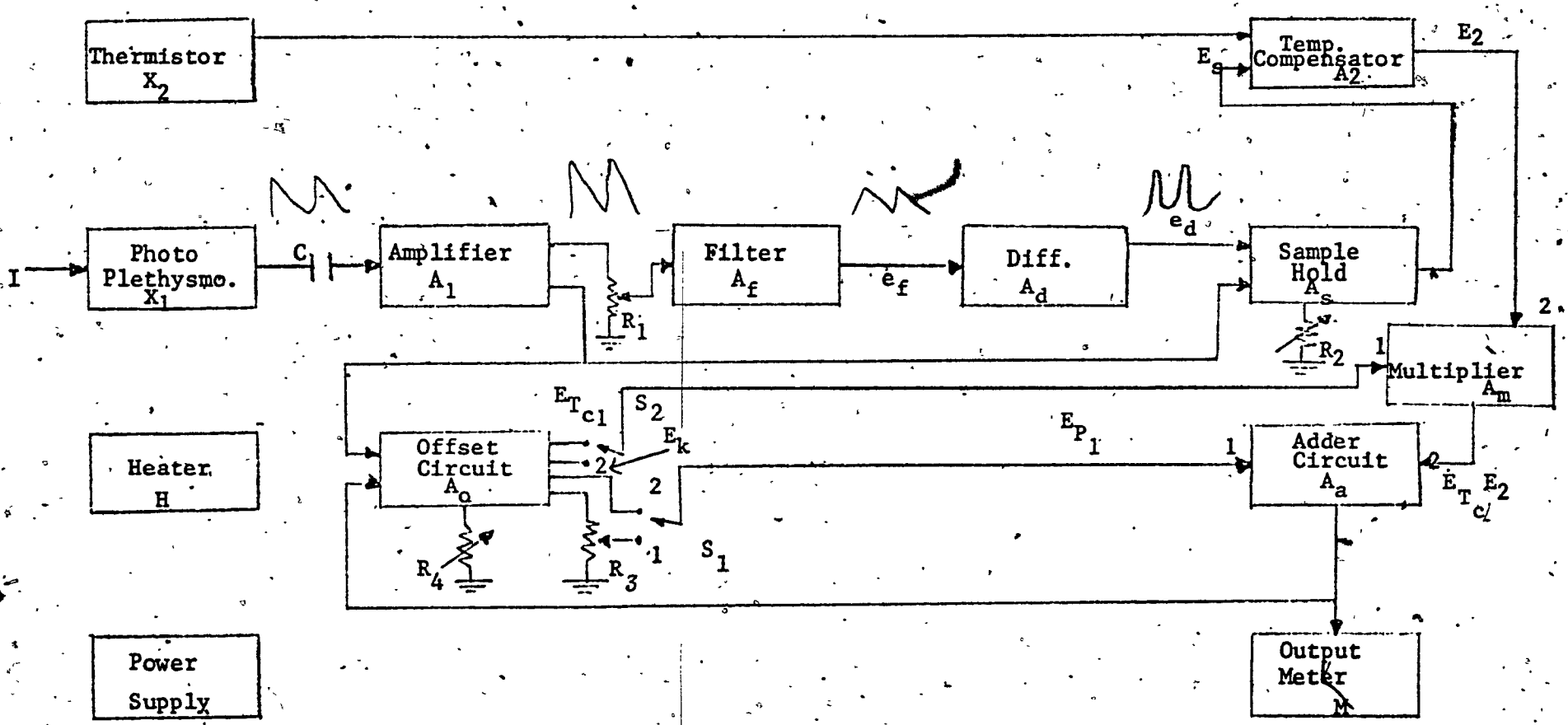


FIG. 6.1 Block Diagram of Blood Pressure Follower

The output of A_1 now passes through a bandpass filter A_f, which limits the bandpass to between 1/2 HZ and 12 HZ, approximately. The filter is needed to remove the 60 HZ interference and the high and low frequency transients above and below the bandpass. A voltage divider R_1 between A_1 and A_f adjusts the overall gain of the circuit. Next the signal from A_f is differentiated in differentiator A_d so that the output signal of A_d is proportional to the rate at which its input is changing. Then during diastole

$$e_d \propto \frac{de_f}{dt} \propto \frac{dI}{dt} \propto \frac{dV_i}{dt}$$

where e_d = output voltage of A_d, in volts

e_f = output voltage of A_f, in volts.

The maximum value of e_d during diastole is sampled and held by sample and hold circuit A_s. Sampling is done once per heart cycle, initiated by a signal from A_1. The output of the sample and hold circuit is a DC voltage E_s which is updated once per heart cycle. By means of variable resistor R_2 the sample and hold circuit may be adjusted so that its output follows changes in the input quickly or slowly. The output of A_s is fed to temperature compensator A_2. A_2 is an amplifier whose gain depends on the resistance of Thermistor X_2.

It was pointed out in Chapter II that activity of the sympathetic nervous system alters the calibre, and thus the volume, of the blood vessels in the microvasculature - except the capillaries. The change in calibre alters the fluid resistance R_i and volume V_i. This causes

changes in $\frac{dV_i}{dt}$ unrelated to changes in systolic pressure and consequently errors in indicated pressure. (This phenomenon is discussed in greater detail in Chapter VIII under Sources of Error).

Changes in the volume of the blood vessels of the skin produce changes in the rate of heat transfer from the blood, through the skin, to the air or surface in contact with the skin. The skin temperature thus depends on the rate of heat transfer across it and the temperature of the air in contact with it. For constant air temperature (room temperature ≈ 22°C), the skin temperature depends on its blood volume, increasing when the volume increases and vice versa.

Changes in skin temperature under transducer X_1 can be used to compensate $\frac{dV_i}{dt}$ for errors in it due to slow changes in skin blood volume, caused by activity of the sympathetic nervous system. Amplifier A_2 is the compensating circuit, with thermistor X_2 contacting the skin under X_1.

The output of A_2, which is E_2, is proportional to $\frac{dV_i}{dt}$ and is fed to input #2 of Multiplier A_m. The #1 input of A_m is connected to Offset circuit A_o. A_o receives inputs from A_1 and adder A_a and computes voltages E_{T_c} and E_p, which are proportional to T_c and P_1 respectively. E_{T_c} is fed to A_m, and E_{P_1} to the #1 input of A_a. The product $E_{T_c}E_2$ is formed by A_m and fed to the #2 input of A_a. $E_{T_c}E_2$ is proportional to $T_c\frac{dV_i}{dt}$. The output of A_a is applied to the output meter M, which is calibrated in mm Hg. The Offset circuit finds T_c according to Equation (5.15) and forms a voltage proportional to P_s EXP $[-\frac{T^+}{T_c}] = E_{P_1}$. R_3 and R_4 are controls whose function will

be described in the next section on Calibration.

A small electrical heater, H, may be applied to the tissue under transducer X_1, in order to produce and sustain a high degree of dilatation.

A suitable power supply provides power for the various electrical and electronic circuits.

6.3 Calibration of Blood Pressure Follower

6.3.1 Calibration with T_c Variable (S_2 in Position 1)

In operation, the instrument is turned on and allowed to warm up for a few minutes with the photoelectric plethysmograph attached to the subject. Next voltage divider R_1 is rotated to zero and switch S_1 is set at position 1. In this position the #1 input to adder A_a is connected to the wiper of voltage divider R_3. R_3 is supplied with a fixed voltage E_{P_1} max, from which E_{P_1} is derived. The diastolic pressure is measured with a sphygmomanometer, and R_3 adjusted to make E_{P_1} equal to 1/3 the diastolic pressure on Meter M. Now the systolic pressure is measured and R_1 is adjusted to make Meter M indicate the systolic pressure, P_s. S_1 is next set to position 2 and control R_4 is adjusted to make Meter M read P_s again if it has changed. R_4 determines the value of T^+ in the computation of the voltage proportional to P_s EXP $[-\frac{T^+}{T_c}]$. The BPF is now calibrated and should follow changes in the systolic pressure P_s.

6.3.2 Calibration with T_c Constant (S_2 in Position 2)

When T_c can be considered constant and P_s does not vary by more than about ± 25%, Equation (5.16) can be used as the basis of instru-

mentation as discussed in section 5.4. In this case,

$$P_s = P_2 + K_5 \frac{dVi}{dt} \qquad (5.16)$$

Now Switch S_2 is set to position 2 at the start of calibration. This applies a fixed voltage E_k to input #1 of multiplier A_m. Calibration is now carried on as in sub-section 6.3.1 above, except that Switch S_1 remains at position 1 and no adjustment of R_4 is required.

6.4 Summary

The general features of an instrument to follow changes in systolic pressure have been described. This instrument is based on Equation (5.2) but has not actually been built. However a test circuit based on Equation (5.16) has been built and various tests have been carried out with it. The results of these tests are given in the next chapter.

In an actual instrument the implementation of Equation (5.1) (or Equation 5.2) is in a recursive form

$$P_{s_{n+1}} = P_{s_n} \text{EXP}\left[-\frac{T^+}{T_{c_{n+1}}}\right] + \left|\frac{E_i}{k_1 k_2} T_{c_{n+1}} \frac{dV_{i_{n+1}}}{dt}\right|$$

where the calculated value P_{s_n} from the previous heart cycle is used to help calculate the new value $P_{s_{n+1}}$ for the current heart cycle.

CHAPTER VII

EXPERIMENTAL RESULTS

7.1 Introduction

In Chapter V a simplified relationship between P_s and $\frac{dV_i}{dt}$ was given in Equation (5.16) as

$$P_s = P_2 + K_5 \frac{dV_i}{dt} \qquad (5.16)$$

An experimental electronic circuit based on this equation was built and used for testing whether changes in systolic pressure could be followed in this way. In order to establish its feasibility, a number of tests were carried out on two subjects. These are reported in this chapter.

7.2 Experimental Procedure

7.2.1 Preliminary

The experimental procedure followed was to simultaneously measure blood pressure in a subject by a standard means (auscultation) and by the new test circuit. Two middle-aged subjects, R.G. and S.M. were used. In practice the test instrument was turned on and the photo-electric plethysmograph (earpiece) was attached to an earlobe of the patient and allowed to "warm up" for 15 minutes. This permitted heat from the small earpiece lamp to produce a vasodilatation of the blood vessels of the ear. A sphygmomanometer cuff was placed on the contra-lateral arm (arm opposite to ear with earpiece attached). After 15 minutes of warm up, the test circuit was calibrated to give the same indication as the standard means.

7.2.2 Calibration Procedure

The calibration procedure consisted of adjusting P_2 and K_5 in the electrical equivalent of Equation (5.16), and was as follows:

1. P_2 and K_5 were set to zero.
2. The arterial diastolic pressure was measured by the sphygmomanometer.
3. P_2 was set to indicate 1/2 the diastolic pressure on the pressure meter.
4. The arterial systolic pressure was measured by the sphygmomanometer.
5. K_5 was adjusted to make the pressure meter indicate the same reading as obtained in step (4) above.

This completed the calibration of the test circuit.

7.2.3 Operational Procedure

Simultaneous pressure readings were periodically made from the test circuit and the sphygmomanometer. Pressure was monitored during three different physiological states.

i) at rest
ii) at lowered pressure produced by Valsalva manoeuvre
iii) at increased pressures produced by exercise.

Pressures were also monitored.

a) with and without compensation for activity of the sympathetic nervous system (as described in Chapter VI).
b) with and without heating of the earlobe in addition to that produced by the earpiece lamp.

7.3 Experimental Results

A) First Test, Fig. 7.1

The results of the first test made are shown in Fig. 7.1. In this test the earlobe was well rubbed, before installation of the earpiece, in order to promote vasodilatation. For the first fifteen minutes the correspondence (after calibration) between test circuit (Test) reading and sphygmomanometer (Sphygmo) readings were fairly good, but show a gradually increasing divergence. The divergence becomes larger with time and is considerable after forty-four minutes. In spite of this divergence it is to be noted that the Test circuit follows rises of pressure (after exercise) and falls of pressure (during Valsalva manoeuvre). The fall of test circuit pressure relative to Sphygmo pressure is due to a progressive loss of vasodilatation (or progressive constriction) in the earlobe. That is, the initial vasodilatation produced by rubbing the earlobe was gradually lost and only that produced by earpiece heat remained thereafter. Obviously earpiece heat did not produce as much dilatation as earlobe rubbing.

This implies that the fluid resistance, R_i and stiffness E_i, did not remain constant, or, referring to Equation (5.16), K_5 did not remain a constant, and changes in $\frac{dV_i}{dt}$ were not always due to changes in pressure P_s.

B) Second Test, Fig. 7.2

The results of the next test are shown in Fig. 7.2. In this test the earlobe was not rubbed. Again there is a progressive decrease in test circuit readings. But then there is a reversal, and the test circuit readings go much higher than the Sphygmo readings. The fluid

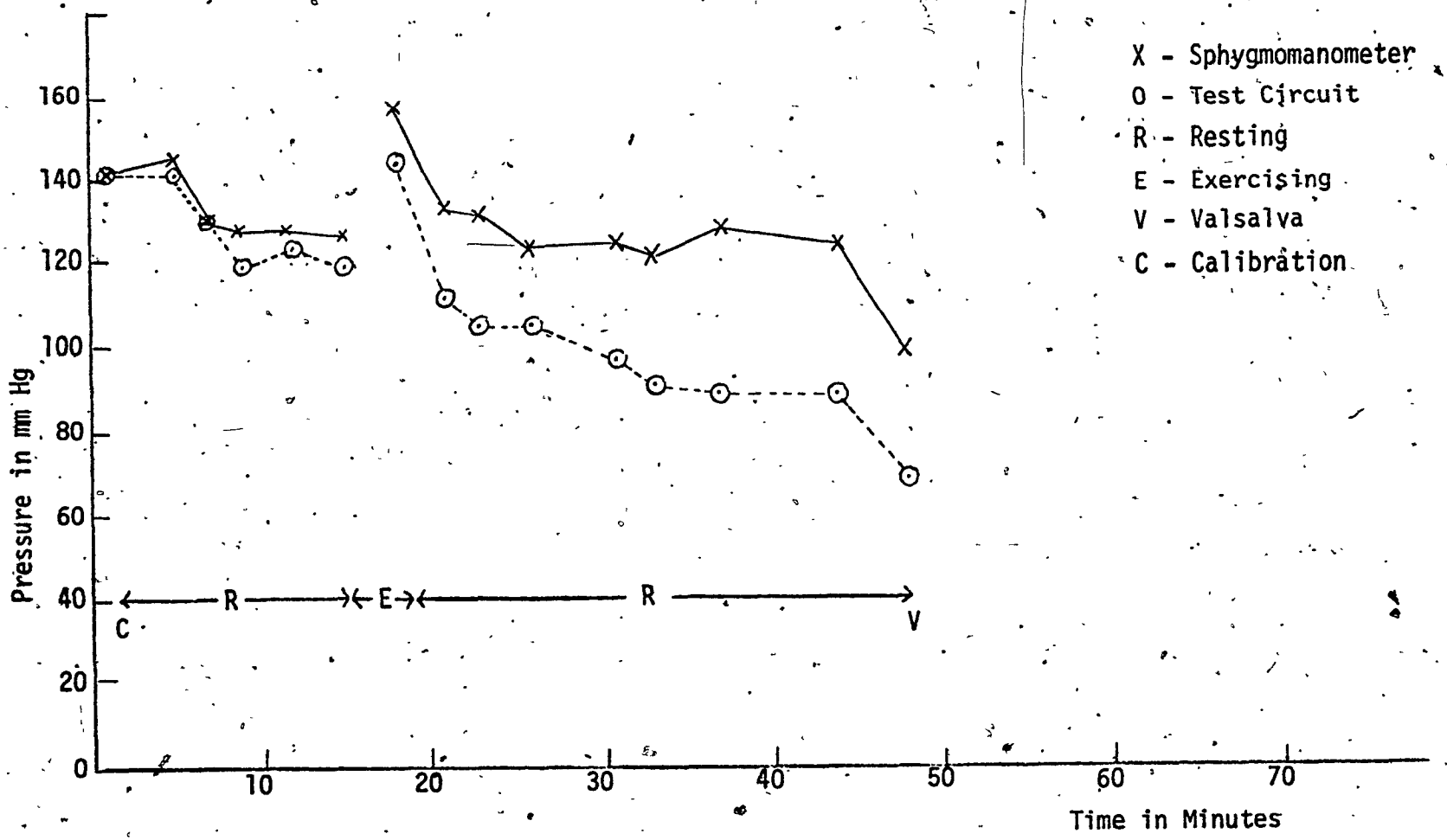


FIG. 7.1 Simultaneous Test and Sphygmo Pressure Reading for Subject R.G., Oct. 11, 1973

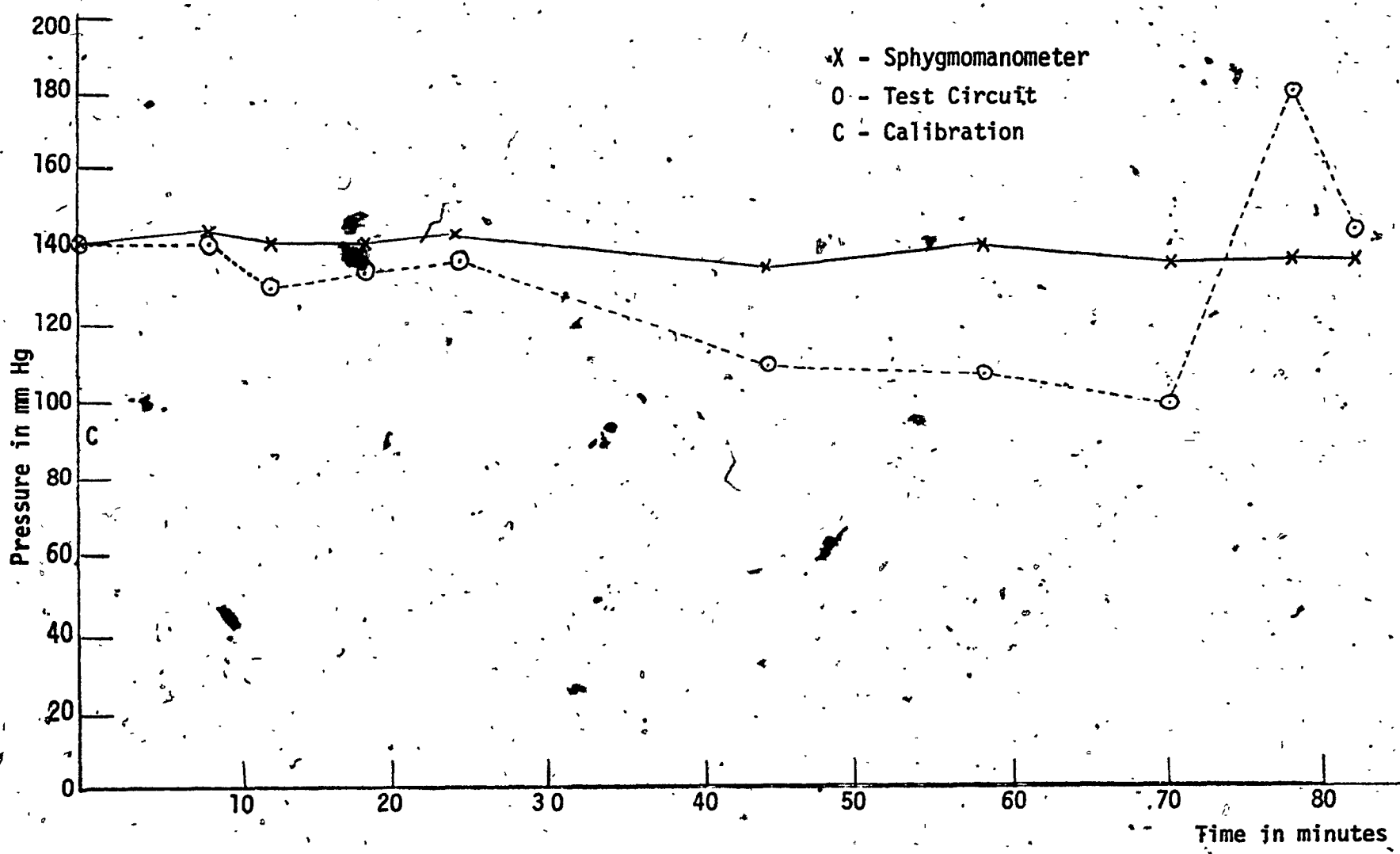


FIG. 7.2 Simultaneous Test and Sphygmo Pressure Reading for Subject R.G., Oct. 29, 1973

resistance and stiffness must be changing again, since the Sphygmo readings are fairly constant throughout the test period. Fluid resistance and stiffness changes are brought about by activity of the sympathetic nervous system which acts on the smooth muscle of the smaller blood vessels (except capillaries) to change their calibre, and thus their resistance.

C) Third Test, Fig. 7.3

In Fig. 7.3 the temperature compensating circuit described in Chapter V was used. Although the temperature compensating circuit was not optimally adjusted, it was still able to reduce the large variations seen in Figs.7.1 and 7.2. Although observations were not taken continuously throughout the test period, the earpiece was in place and all circuits were functioning. However, it is not known how the indications were varying during the time that no observations were being made. This test does indicate, nevertheless, that a significant reduction in the error due to variations of earlobe fluid resistance R_i and stiffness E_i can be achieved by using the earlobe skin temperature to compensate for changes in R_i and E_i.

D) Fourth Test, Fig. 7.4

In another test a vasodilator substance, Finalgon, was applied to the earlobe. The Finalgon was applied to the earlobe thirty-two minutes before calibration because about twenty-five minutes are required for it to produce a large vasodilation. The results of this test are shown in Fig.7.4. For about thirty minutes after calibration, the Finalgon maintained a good vasodilatation. This is indicated by

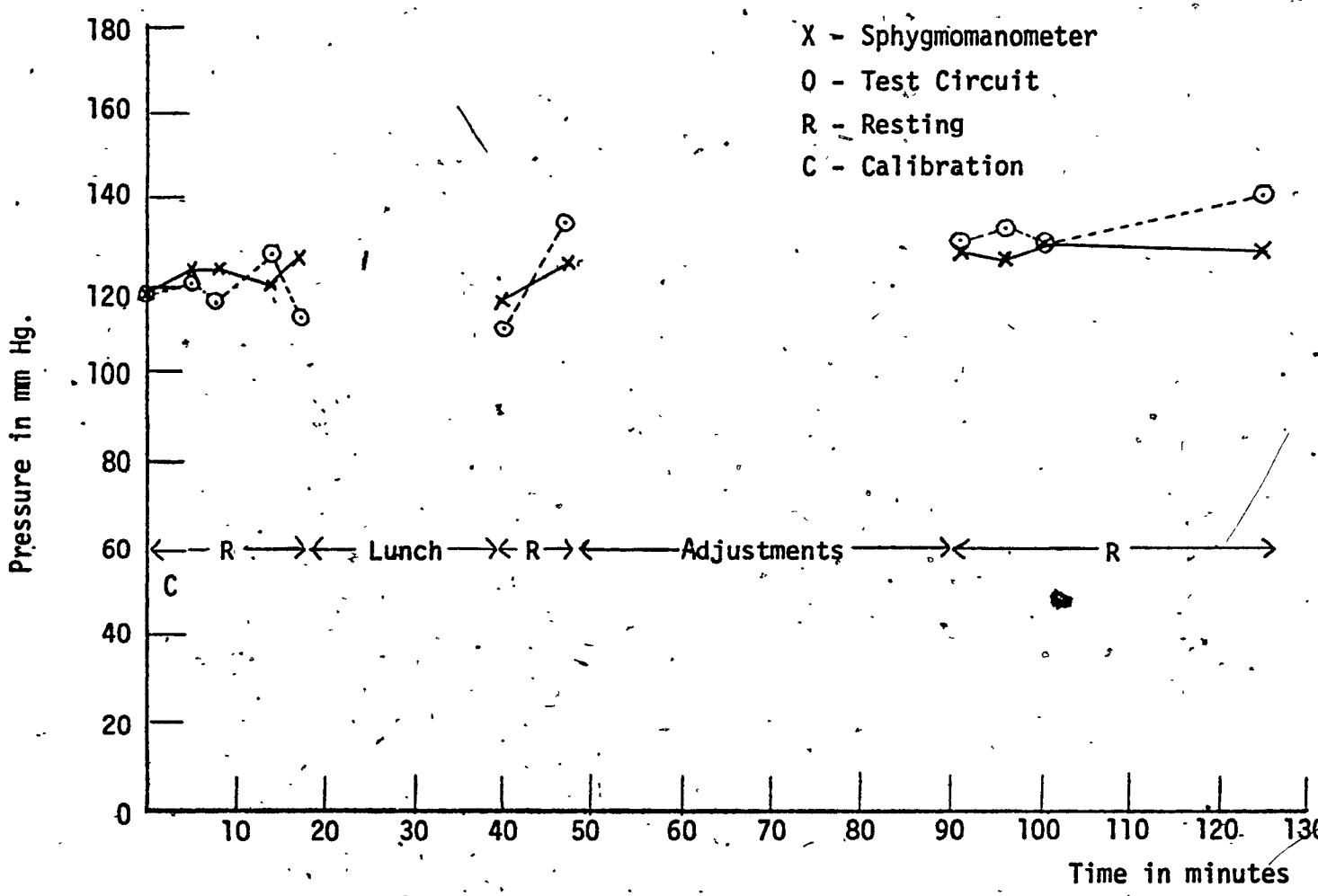


FIG. 7.3 Simultaneous Test and Sphygmo Pressure Reading for Subject S.M., Nov. 28, 1973

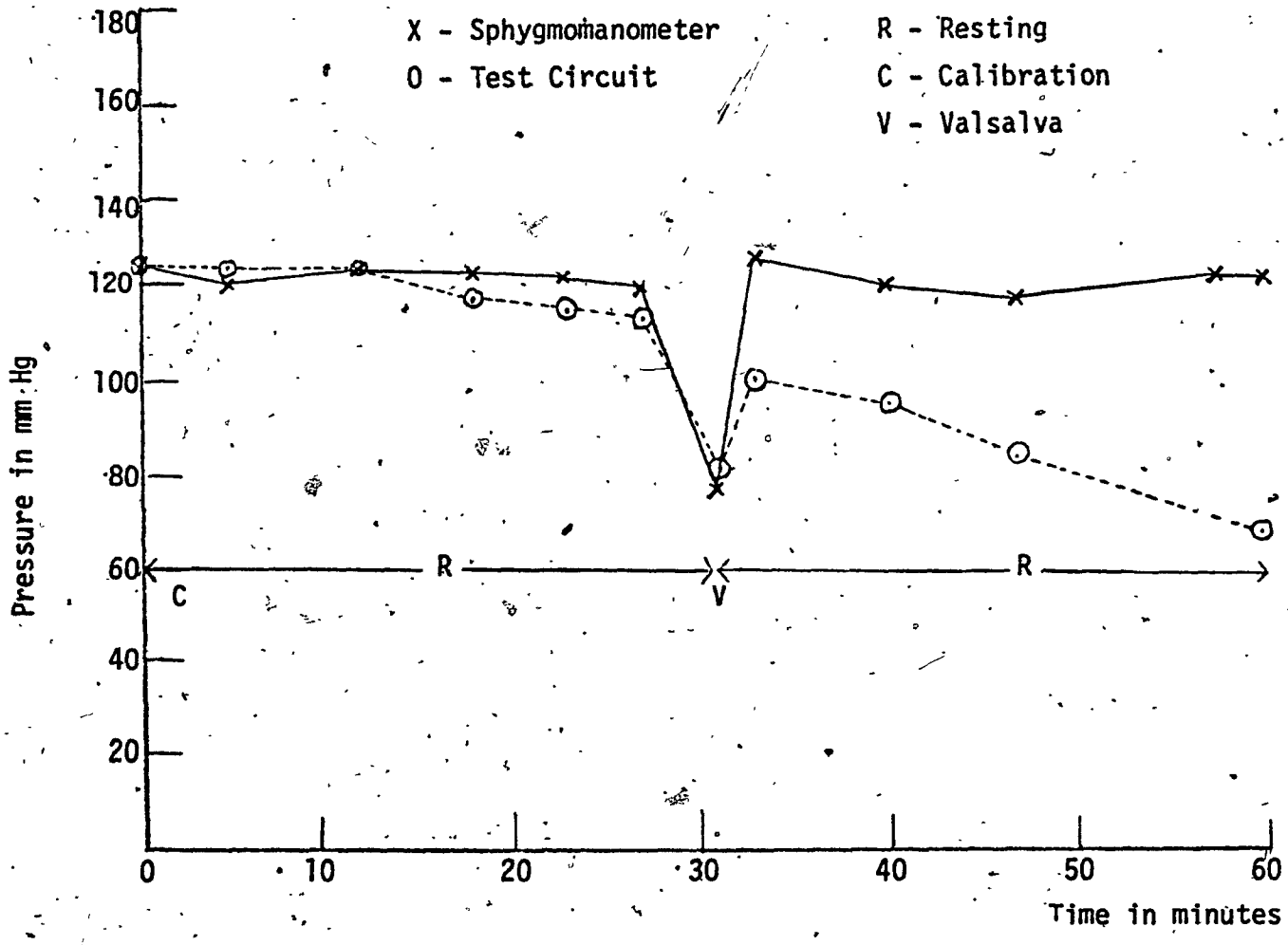


FIG. 7.4 Simultaneous Test and Sphygmo Pressure Reading for Subject S.M., Jan.2, 1974

the good agreement between Test and Sphygmo readings during this time. After the Valsalva manoeuver the test circuit readings dropped greatly indicating a loss of vasodilatation. This test result is similar to that of Fig. 7.1, except that, for a time, the Finalgon apparently maintained a more constant vasodilatation (probably approaching a maximum) than earlobe rubbing did.

E) Fifth Test, Fig. 7.5

In the last test cited, a small electric heater was applied to the earlobe on the same side as the earpiece lamp. The maximum amount of heat that the subject could tolerate without feeling discomfort was applied to the earlobe, in order to promote vasodilatation. The results of this test are shown in Fig. 7.5. After an initial divergence the readings remain relatively constant up to forty minutes. The indicated pressures rise together after exercise and fall together during the Valsalva manoeuvre. There is no progressive increase of divergence with time. The constant heat appears to maintain a more constant vasodilatation over the test period.

7.4 Discussion

It was assumed in Chapter IV subsection 4.2.2, that the fluid resistance and stiffness of microvascular region M_i remains constant. This assumption is crucial for the validity of Equation (5.16). Changes in the stiffness of the blood vessels of the microvasculature alter the amount of dilatation they undergo for a given increase in pressure. For example, if the stiffness increases, i.e., if the increase in volume ΔV_i of region M_i is smaller for the same increase

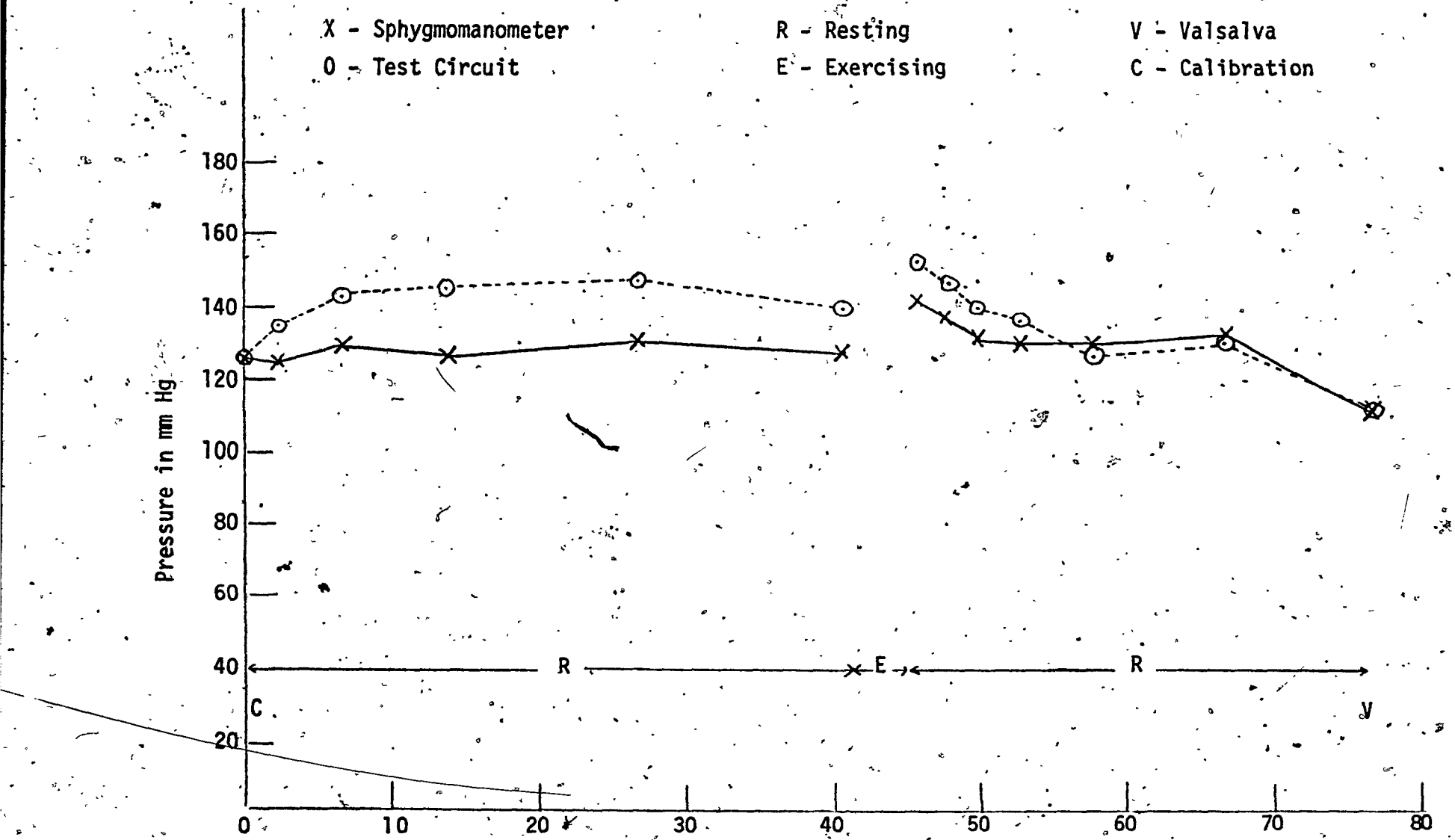


FIG. 7.5 Simultaneous Test and Sphygmo Pressure Reading for Subject S.M., Jan. 16, 1974

in pressure ΔP_i, $\frac{dV_i}{dt}$ will decrease. Such a change in $\frac{dV_i}{dt}$ will produce a change in the value of P_s indicated by the test circuit, even though the true value of P_s remains constant. This is clearly shown in Fig.7.2, where although the sphygmomanometer readings are quite constant, the test circuit readings vary greatly.

These changes in test circuit readings are due to variations in the degree of vasodilatation in the earlobe. This shows up clearly in all of the figures except Fig.7.3, where the electronic circuit is being manipulated in order to correct the test circuit readings. Whenever measures were taken to promote vasodilatation, the test circuit readings agreed well with the Sphygmo readings after calibration. When the effect of the measures diminished, the test circuit readings generally fell below the Sphygmo readings, indicating a decrease in $\frac{dV_i}{dt}$ relative to the true pressure.

The above effect is seen in Fig.7.1. The ear was rubbed prior to the start of the test. After calibration the test circuit readings remained in good agreement with the Sphygmo readings for 15 minutes, then gradually became smaller, with the passage of time. After 18 minutes the difference was 13 mm Hg., after 25 minutes it was 23 mm Hg., and after 44 minutes it was 36 mm Hg. The same effect is seen in Fig.7.2, where the test circuit readings steadily decrease, except that after 77 minutes the test circuit reading showed a sudden large increase over the Sphygmo reading. This was not an instrumental artifact, but was an increase of vasodilatation, indicating that under the condition of measurement, the blood vessels of the earlobe can dilate as well as constrict.

When Finalgon was applied to the earlobe it maintained an effective vasodilatation for 30 minutes after calibration. During this time the test circuit and Sphygmo readings were in good agreement. As the effect of the Finalgon wore off, the test circuit reading showed a steady decrease.

From the above results it would be expected that if the blood vessels of the earlobe could be maintained well dilated indefinitely, the test circuit and Sphygmo readings should show consistently good agreement. This was the case when constant heat was applied to the earlobe. The results for this condition are shown in Fig. 7.5. After calibration the test circuit readings become larger than those of the sphygmomanometer. This is probably due to carrying out the calibration procedure before the blood vessels of the earlobe were sufficiently close to maximal dilatation. After about 7 minutes the variations in the two readings are about the same. In this case the good agreement between test circuit and Sphygmo readings continue throughout the duration of the test - 77 minutes.

After exercise the test circuit readings approach closer to those of the sphygmomanometer. This indicates some loss of vasodilatation, probably due to the exercise. The same effect can be seen in Fig.7.1 and in Fig.7.4, after the Valsalva manoeuvre. This is probably due to changes in sympathetic nervous system activity brought on by exercise and the Valsalva manoeuvre.

The reduction of the discrepancy between test circuit and Sphygmo readings by electronic compensation also confirms that the major source of error is changes in the degree of vasodilatation of

the earlobe. In Chapter VI it was shown that the skin temperature of the earlobe varies with the degree of vasodilation of its blood vessels. An increase of skin temperature thus indicates an increase of vasodilatation. One should then be able to use some function of the earlobe skin temperature to compensate the amplifier circuits for changes in vasodilatation. When a simple linear function of the earlobe skin temperature was used to compensate the electronic circuitry, the result was as shown in Fig. 7.3. The divergence between test circuit and Sphygmo readings are much smaller than those of Figs.7.1, 7.2 and 7.4. Compensation of this kind, however, will only be effective for slow changes in vasodilatation, due to thermal lags in the earlobe and temperature measuring circuit.

The results show clearly that the major cause of discrepancies between test circuit and Sphygmo readings is changes in the degree of vasodilatation of the earlobe blood vessels. When these blood vessels are kept well dilated agreement between test circuit and Sphygmo readings is good.

7.5 Summary

A test electronic circuit, based on Equation (5.16), was built in order to test the validity of this equation. A number of tests were carried out on two middle-aged men. The results of the tests indicate that the discrepancies between test circuit reading and standard (sphygmomanometer) are largely due to changes in the state of vasodilatation of the vascular bed of the earlobe. When essentially constant vasodilatation of the vascular bed is maintained, good agreement between test circuit measurement and standard measurement is achieved.

CHAPTER VIII

SOURCES OF ERROR

8.1 Introduction

There are a number of sources of error in the blood pressure follower. In Chapter V, Equation (5.1) and Equation (5.16) were given as equations on which a blood pressure following instrument could be built. They are:

$$P_s = P_s \, EXP\left[\frac{-T}{T_c}\right] + \left|\frac{E_i R_t}{E_a k_1 k_2} \frac{dV_i}{dt}\right| \qquad (5.1)$$

or

$$P_s = P_2 + K_5 \frac{dV_i}{dt} \qquad (5.16)$$

In Equation (5.1), $\frac{R_t}{E_a} = T_c$ and $\frac{dV_i}{dt}$ are measured variables and micro-vascular stiffness E_i, k_1, and k_2 are constants. Apart from inaccuracies in measuring T_c and $\frac{dV_i}{dt}$, a major source of error may be due to variations in the value of E_i. Any variations in k_1 and k_2 will of course contribute to errors.

In Equation (5.16), T_c is considered constant. If this equation is used as the basis for measurement, variations in T_c may produce errors.

These errors are physiologic in nature and will be discussed

in the following section along with sources of error due to instrumentation.

8.2 Physiologic Errors

8.2.1 Errors Due to Variations in Microvascular Stiffness E_i

In the derivation of Equation (5.1) the fluid resistance of the microcirculation, R_i, was assumed to be constant. If this were not so $(P_s - P_o)$ would vary not only with $\left(\frac{dV_i}{dt}\right)_{max.}$ but also with R_i. Inasmuch as only $\left(\frac{dV_i}{dt}\right)_{max.}$ is measured, variations in R_i will invalidate Equation (5.1), i.e. $(P_s - P_o)$ will not be directly proportional to $\frac{dV_i}{dt}$ alone, and large errors can result.

Changes in fluid resistance R_i are caused by changes in the calibre of the blood vessels due to contraction or relaxation of the smooth muscle of the blood vessel walls. The state of contraction or relaxation of the smooth muscle determines the stiffness E_i, and volume V_i of the blood vessels of a microvascular region M_i. Fluid resistance R_i and volume V_i, therefore, depend on the stiffness E_i of the blood vessels.

When a transmission type photoelectric plethysmograph is placed on the ear (or toe or finger), variations in pulse (blood volume) unrelated to blood pressure changes are noted, Burch[27]. In addition to a volume variation correlated with respiration (which also correlates with blood pressure change), Burch noted three other kinds of volume changes unrelated to pressure changes, which he designated as alpha,

beta, and gamma.

The alpha waves occurred at a mean rate of about 8 per minute. The mean frequency of the beta waves was about 1 to 2 per minute and their amplitudes were on the average about twice as large as the alpha. The gamma wave variations were from 1 to 8 per hour and their amplitudes were considerably larger than the beta waves. The alpha waves were superimposed on the beta waves, which in turn were superimposed on the gamma waves. The alpha, beta and gamma waves are shown in Fig. 8.1. The waves in A are the desired cardiac waves, whereas the other waves are undesirable and produce errors.

These phenomena were present during the testing of the breadboard circuit mentioned in the previous chapter. Errors in the indicated pressure were sometimes as great as 30 to 40 percent of the blood pressure measured with a sphygmomanometer. These spontaneous volume changes are attributed to the neurogenic vasoconstrictor activity on the smooth muscle of the vascular bed. Heating of the vascular area under measurement with a special heater reduced these spontaneous volume variations considerably, but did not entirely eliminate them. Heating reduces the vasoconstrictor activity allowing the vascular bed to dilate. The amount of heat not causing discomfort to the subject was sufficient to maintain a dilatation which permitted good tracking between test circuit and Sphygmo readings, as seen in Fig. 7.5.

The application of Finalgon, a vasodilator substance, to the vascular bed eliminated the spontaneous volume variation. During the the period of effective action of the Finalgon, blood pressure was

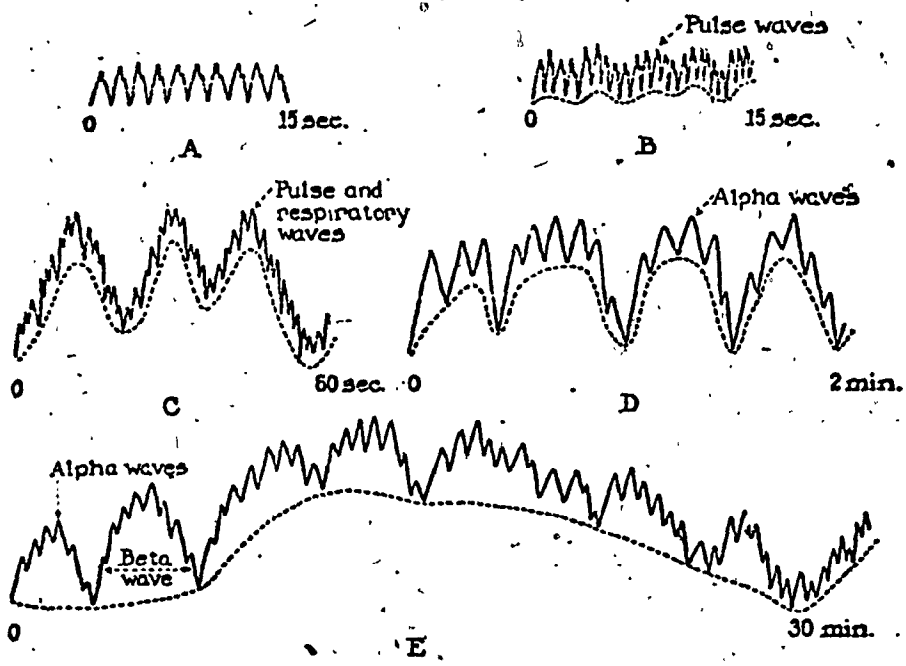


FIG. 8.1 Various Constituents of the Volume Pulse [27]

followed accurately by the breadboard circuit. Unfortunately, an application of Finalgon is effective for only about one hour and, in addition, is somewhat noxious to use (produces a burning sensation in the area to which it is applied). Some compensation for vasoconstriction and vasodilatation can be obtained by measuring the skin temperature of the area under measurement as described in the previous chapter. But this is only effective with slow volume changes and least effective with rapid volume changes.

There is much evidence that the forehead is not supplied with vasoconstrictor nerves. Hertzman[9] investigated this and found that simultaneous application of photoelectric transducers to the finger tip and forehead showed spontaneous volume changes taking place in the finger but none in the forehead. Use of a reflectance photoelectric transducer on the forehead with the breadboard circuit resulted in vastly improved results. The error between experimental circuit pressure readings and sphygmomanometer pressure readings averaged about 5 percent and rarely exceeded 10 percent. No heating or temperature compensation was needed. Extreme cold can produce some vasoconstriction and vasodilatation can occur as it is believed that the forehead is supplied with vasodilator innervation. However, these mechanisms are brought into play only in extreme situations at this site.

8.2.2 Errors Due to Variations in Arterial Time Constant T_c

If $T_c = \left(\frac{R_t}{E_a}\right)$ is not measured but is considered constant, as in

Equation (5.16), then changes in T_c can cause errors in measurement of P_s. When a normal subject is at rest, R_t and E_a remain constant. When the subject exercises, R_t decreases and E_a may increase. Therefore, T_c decreases. Under conditions of light exercise, Equation (5.16) probably holds but with heavy exercise, there could be a significant error in P_s.

8.2.3 Errors due to Variations in k_1 and k_2

a) In Chapter IV, Section 4.2.2, it was assumed that the pressure P_i, in a microvascular region M_i, is a constant fraction of the pressure P_c in the large arteries. That is, $P_1 = k_1 P_c$.

It was also assumed that the region M_i was maximally dilated. Changes in the degree of dilatation of M_i, i.e. changes in stiffness E_i, can produce variations in P_i and thus in k_1. Constant k_1 is thus really a function of E_i and the errors due to it can be considered as part of those due to E_i.

b) Constant k_2 was defined as relating P_a to P_s in the form,

$$P_a = k_2 P_s$$

where

P_a is the arterial pressure at the beginning of diastole.

Changes in the difference between inflow to and outflow from the large arteries can produce variations in P_a and thus in k_2. Inflow to and outflow from the large arteries depend partly on arterial time

constant T_c. Constant k_2 is thus a function of T_c and the errors due to it can be considered as due, in part, to changes in T_c.

8.2.4 Errors due to Changes in Blood Optical Density

Errors can also be caused by changes in percentage oxygen saturation of the arterial blood [26]. This, in turn, would cause changes in the attenuation of light passing through the blood and thus in the optical density. This effect should not be large but can be considerably reduced or eliminated by using light of an isobestic wavelength for oxyhemoglobin and hemoglobin. One such wavelength is 805 milli-microns. By using an appropriate infra-red filter, this operational wavelength can be attained.

In addition, errors can occur due to changes in the hematocrit value of the blood. The hematocrit value is a measure of the concentration of red blood cells per unit of volume of blood. Changes in concentration of red blood cells also cause changes in the attenuation of light passing through the blood. It is expected that the hematocrit value will be constant in each patient under normal conditions. In other circumstances, as during parenteral infusions of liquids, the hematocrit value may change.

8.3 Instrumental Errors

8.3.1 Errors due to Amplitude Distortion

a) The principle source of error in the instrument is a bandpass

filter which filters the amplified transducer signal before it is differentiated. Its main function is to eliminate 60 Hz interference and limit the low frequency response of the amplifier. It should have a passband from 0.5 to 10 or 12 Hz within -3 db. This means that the third harmonic of the highest frequency of interest (3 Hz or 180 beats or pulses per minute) should pass without attenuation. The lowest frequency of interest is 1 Hz. If the gain is not constant over this passband, waveform distortions can result and the $\frac{dV_i}{dt}$ measured will have an error. This will also happen if too much signal below 0.5 Hz passes through the filter. By using an Analog Devices two-pole low pass Butterworth Filter Model 704L2B, and properly proportioning the amplifier interstage coupling, a satisfactory performance was obtained.

b) Another source of amplitude distortion is the photodetector. Photoconductive cells are used extensively in photoplethysmographs. They are small, cheap, highly sensitive and easy to use. However, they have a temperature and light-history dependence which can affect their dynamic characteristics, Fine [30]. The frequency response depends on the cell resistance, i.e. the light level at which the cell is operating. The cell resistance also depends on the previous light history, i.e. the intensity of light and the length of time it has been exposed to it. According to Fine, a cadmium selenide cell, after being stored in the dark and suddenly exposed to a light level which produced a resistance of 70 Kohm at time zero, exhibited a long term drift to

above 160 Kohms in over 100 minutes. Fine also shows that an increase of temperature improved the high frequency response. Since the bandwidth required for the BPF is not large—0.5 Hz to 10 Hz—no particular difficulty was experienced with the photocell used.

8.3.2 Errors due to Shifting of Transducer on Skin

Shifting of the position of the transducer on the skin changes the volume V_{i1} sampled and can produce errors in $\frac{dV_i}{dt}$ if the volume V_{i2} in the new position is significantly different from V_{i1} in the old position. The transducer can be stabilized to a satisfactory degree on the ear and to a high degree on the forehead. Although the errors produced can be significant, they are not likely to occur, particularly at the forehead.

8.4 Summary

A number of sources of error, physiologic and instrumental, are discussed in this chapter. The major source of error is spontaneous blood volume changes produced by changes in the degree of vasoconstriction or vasodilatation of the blood vessels. Changes in vasoconstriction produce variations in the stiffness, E_i, of the blood vessels and are caused by activity of the sympathetic nervous system. Heating of the tissue greatly reduces the activity of the sympathetic nervous system. The forehead is not supplied with sympathetic vasoconstrictor nerves and is an ideal site for the BPF transducer.

CHAPTER IX

CONCLUSIONS

9.1 Preliminary

A new method of measuring relative arterial systolic blood pressure changes is presented in this investigation. The essence of the method is, that the rate of pulsatile blood volume change in a peripheral site such as the earlobe, is used for indicating the magnitude of the arterial systolic blood pressure after calibration against a standard blood pressure measuring means. The correlation between rate of peripheral pulsatile blood volume change and arterial systolic blood pressure is facilitated by considering these quantities only during a portion of each cardiac cycle, i.e. the period of diastole - and for just one instant during this period. Further, these quantities are considered to vary exponentially during this period.

A number of conditions were specified and assumptions made in order to develop the theory behind this new technique. Discussion on these are provided in this chapter with remarks on experimental work done, as well as the practical applications of this method.

9.2 Discussion of Theory and Results

In Chapter IV, an equation was derived to give the arterial systolic blood pressure as

$$P_s = \frac{P_a}{k_2} \text{ EXP } \left[\frac{-E_a}{R_t} T^+ \right] + \left| \frac{E_i R_t}{E_a k_1 k_2} \frac{dVi}{dt} \right| \quad (4.22)$$

Certain assumptions and conditions were made in deriving this equation (Chapter IV, section 4.2.2). The quantities in Equation (4.22) will now be discussed in relation to these assumptions and conditions.

9.2.1 Arterial Time Constant T_c

E_a is the stiffness of the large arteries and R_t is the total peripheral resistance to blood flow from the heart. $\frac{R_t}{E_a}$ is the time constant, T_c, of the arterial system and is a quantity to be measured. There are no assumptions in relation to this quantity in Equation (4.22). However, a simple version of Equation (4.22) was also given in Chapter IV as

$$P_s = P_2 + K_5 \frac{dVi}{dt} \qquad (4.23)$$

In this equation the arterial time constant T_c is considered to be a constant. If T_c is considered constant, as discussed in Chapter VIII, section 8.2.2, Equation (4.23) can be used, otherwise Equation (4.22) must be used. The experimental work done was based on Equation (4.23). As was pointed out in Chapter VII, when the earlobe blood vessels were maintained well dilated the results were good. This indicated that in these experiments, the assumption of T_c to be a constant did not produce any significant error.

9.2.2 Decay Time T^+

In Equation (4.22) the decay time T^+ is the time for the pressure or volume wave to decay from its maximum value, where its rate of change is large, to a value, where its rate of change is small and

and can be considered to be zero. If T^+ is taken to be sufficiently long, the rate of change can be neglected, as seen in Fig. 4.4b. From empirical considerations the value of T^+ should be such as to make P_1 equal to about one-third of the diastolic pressure. Since the instrument is calibrated on each patient with standard blood pressure measuring means, the exact value of P_1 is not very important.

9.2.3 Stiffness E_i of Blood Vessels in Microvascular Region Under Measurement

The usefulness of Equation (4.22) depends on the microvascular stiffness E_i being constant. Variations of this factor can produce large errors as was described in Chapter VII and Chapter VIII. Variations of E_i are due to activity of the sympathetic nervous system as previously discussed. Vasoactive changes due to activity of the sympathetic nervous system can be abolished by producing a near maximal dilatation of the vascular bed -- by the use of drugs or by heating. In the experiments continuous heating of the ear was found to promote good agreement between Sphygmomanometer and Test Circuit readings. This would indicate that E_i remained fairly constant due to the heating. Heating of the vascular area under measurement is therefore a sound and dependable means for maintaining E_i constant.

Another approach to maintaining E_i constant is to find a vascular area which is not subject to sympathetic nervous system activity. One such area is the skin of the forehead. Hertzman[9] found that in the presence of stimuli that produce vasoconstriction in the fingers, no vasoconstriction occurs in the skin of the forehead. This site therefore is potentially a useful one and would require little or no heating.

9.2.4 Constant k_1

Constant k_1 relates the blood pressure across the microvascular bed to the pressure in the main arteries, given by

$$P_i = k_1 P_c \tag{4.6}$$

Since the microvascular region is maintained well dilated, keeping E_i constant, k_1 should also remain constant. The experimental results indicate that this is so.

9.2.5 Constant k_2

The constant k_2 relates the arterial pressure at the start of diastole to the maximum arterial pressure during the cycle, i.e. the systolic pressure and is related by

$$P_a = k_2 P_s \tag{4.18a}$$

During diastole, the only pressure acting in the arterial system is that due to the elastic recoil energy of the distended arteries -- the reservoir arteries. In systole, however, blood is expelled at high pressure from the heart into the aorta. There is an additional pressure in the arteries due to contraction of the heart. Pressure reflections occur at relatively distant parts of the arterial system due to bifurcations and changes of diameter in the arterial tree. These reflected pressure waves travel back toward the heart and add to the instantaneous pressure at various points in the large arteries. This is shown in Fig. 9.1. As the observation point is moved along the aorta away from the heart, the peak pressure increases.

It is obvious that k_2 will be different for different positions in the aorta. In addition, Equation (4.18a) implies that if P_a decays

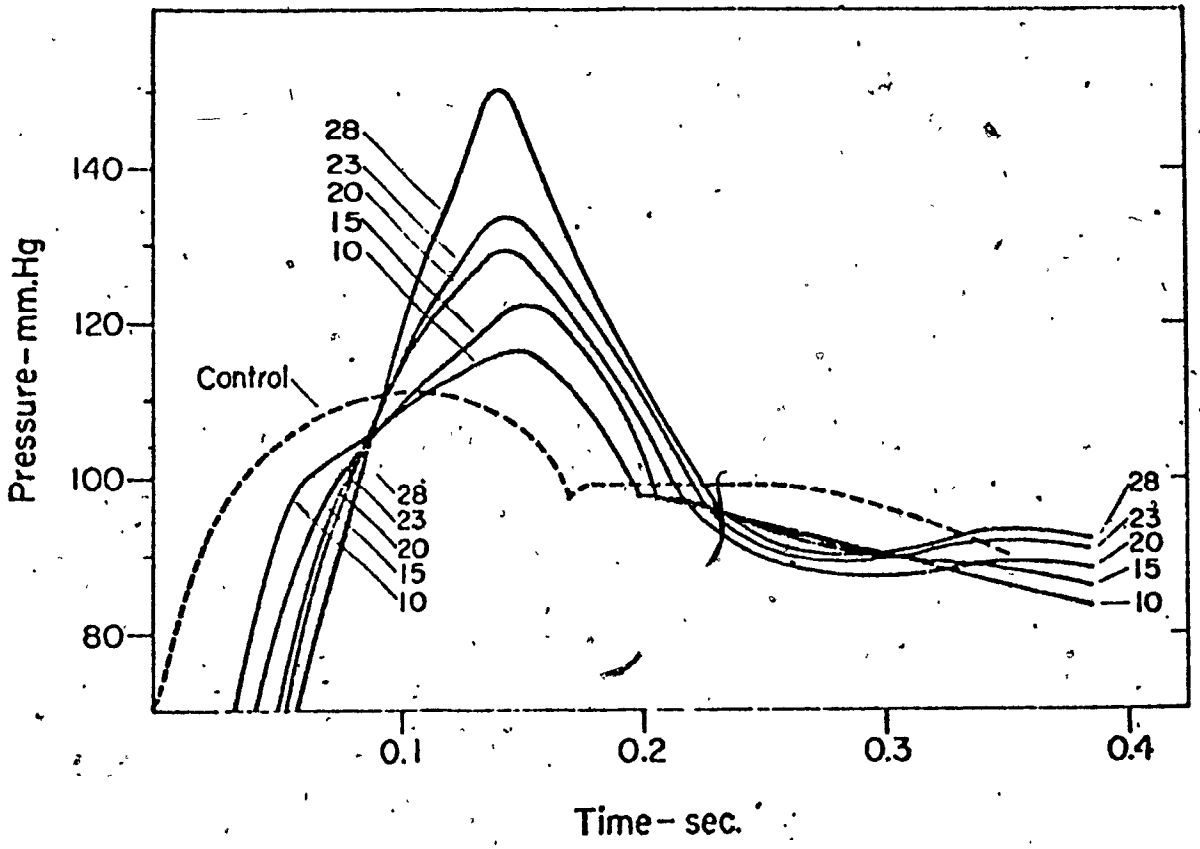


FIG. 9.1 Changes in Configuration of the Arterial Pressure Pulse of the Dog as a Function of the Distance Along the Aorta [23]

exponentially - which it does - then so does P_s. However, the arterial pressure cannot decay exponentially from its peak value to the start of diastole because of the pressure supplied by the heart during this period. It was pointed out in Chapter VIII that k_2 also depends on the arterial time constant T_c. From these considerations Equation (4.18a) can only be an approximation. It can be assumed that the systolic pressure P_s in Equations (4.22) and (4.23) refers to a point in the aorta where the pressure curve is least affected by reflection and the decaying portion approximates best to an exponential curve. Such a point will be somewhere in the upper part of the aorta.

The experimental results indicate that variation of microvascular stiffness E_i is the major source of error. Therefore the approximation of Equation (4.18a) does not introduce any significant error under the conditions of the experiments.

9.2.6 Time Rate of Change of Microvascular Volume V_i

As shown in Equation (4.16), the time rate of change of the microvascular volume V_i depends on the stiffness E_i, the constant k_1 the arterial time constant T_c and the pressure P_c. If all but P_c are constant, then $\frac{dVi}{dt}$ will be directly proportional to P_c. In the absence of artifacts $\frac{dVi}{dt}$ will always give an accurate proportional value for P_c.

From the above considerations it is concluded that Equation (4.22) and Equation (4.23) (where applicable) model the physiological conditions to which they apply with a reasonable degree of accuracy, i.e. indicate

changes in arterial systolic blood pressure with reasonable accuracy.

The standard blood pressure measurement means used in the experiments was a sphygmomanometer. The more accurate direct means of blood pressure measurement (as described in Chapter III) would have been preferable. However it was not possible to use such an invasive method at the time the experiments were made. In any case good agreement with sphygmomanometer readings assures the usefulness of the new method.

9.3 Applications

Knowledge of the state of the arterial blood pressure at frequent intervals is crucial for certain classes of hospital patients. People who have had heart surgery often need to have their arterial blood pressure monitored continuously. Some patients who have suffered heart attacks may have sudden circulatory collapses. These patients need to have their blood pressure continuously monitored. Patients undergoing hemodialysis may also have sudden drops in blood pressure. Such patients may have their blood pressure checked every hour, or more often, during dialysis.

Physicians dealing with these patients have expressed an interest in having a simple, easy-to-operate, blood pressure monitor to use on these patients. In recent years physicians are becoming more and more concerned about the existence of undiagnosed and untreated hypertension in the population. It has been suggested that each home be equipped with a sphygmomanometer and that people routinely check their own arterial blood pressures [32], just as they check their

temperatures with a clinical thermometer. When the blood pressure does not fall in the normal range, a physician should be consulted. However, use of the sphygmomanometer, even by trained personnel, such as physicians and nurses, is not always simple. This points up the need for a simple, relatively inexpensive device that could be used to check blood pressure.

Another field that needs a simple, fairly accurate noninvasive continuous blood pressure monitoring device is biofeedback training. People with essential hypertension are being trained by this method to lower their arterial blood pressure by 10 - 15 mm Hg. mercury and more [33]. Available blood pressure measuring techniques are unsatisfactory for this field.

In spite of the fact that some hospital patients may need to have continuous blood pressure monitoring, it is not always possible to do so because the available instrumentation is not suitable. In these cases, a reliable non-invasive, non-occlusive, continuous, beat by beat blood pressure monitor is needed. At the time of writing, such an instrument does not exist commercially. However, there is a great need for such an instrument. It would not only be useful in the cases outlined above but also in such other fields as;

a) Intensive Care Monitoring
b) Physical Education Research
c) Sports Training
d) Physical Medicine and Rehabilitation
e) Physiological and Medical Research
f) Psychological Research

9.4 Future Work

The beat-by-beat measurement of arterial systolic and diastolic blood pressure by non-invasive, non-occlusive means would be an important addition in the field of non-invasive physiological measurements. A thorough evaluation of this method in a hospital with adequate facilities, e.g. means for direct blood pressure measurement, is necessary for proper validation. A catheterization laboratory would be a suitable place.

The technique described in this work measures relative systolic blood pressure changes. It would be an important advance to develop it into an absolute method, i.e. no calibration necessary between patients. In order to do this, more precise knowledge of the quantity E_i and the constants k_1 and k_2 would be required.

If it were possible to measure the total peripheral resistance R_t separately from the arterial stiffness E_a, the cardiac output could be computed beat-by-beat. The mean arterial blood pressure can be computed from the systolic and diastolic pressures. The cardiac output is then given by

$$\text{Cardiac output} = \frac{\text{Mean Arterial Blood Pressure in mm Hg.}}{\text{Total Peripheral Resistance in PRU}_s \text{ Units}}$$

This instrumentation would then be able to measure systolic and diastolic pressure, cardiac output, heart rate (from the volume pulses), total peripheral resistance, left ventricular ejection time (LVET) (from the volume pulse), and the arterial stiffness. All of this would be done from a simple measurement of the peripheral blood volume pulse. An instrument with these capabilities would be of considerable value in clinical medicine and in physiological and medical research.

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