

EXPERIMENTAL INVESTIGATIONS OF THE
HIGHER DYNAMIC FUNCTIONS OF THE
HEART IN THE ALBINO RAT

by

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CHAPTER I

INTRODUCTION

Physiological evaluation of cardiovascular performance, both clinically and experimentally, was until recently restricted to the classical methods e.g. ECG, phonocardiogram and pressure recordings. Though these methods have proved to be useful, they all fail to give reliable information on certain important aspects of the mechanical performance of the heart. Because of the urgent need for reliable procedures, much research effort has recently been directed towards the development of new methods of evaluating cardiac function. A possible method is ballistocardiography (Bcg). The term ballistocardiography was introduced by Starr in 1939 (Starr et al 1939). This marked the beginning of a new era in cardiovascular research. Based on the Newtonian laws of motion, this method is aimed at the evaluation of the higher dynamic myocardial functions by applying relevant mathematical and physical principles.

The classical methods measured basic aspects e.g. pressure, heart rate and duration of systole. The information obtained in the new approach to cardiovascular function gives insight into the higher dynamic functions of myocardial activity. This includes the measurement of the rate of change in arterial pressures, the rate of blood ejection, the rate of tension development in the contracting myocardium and the rate of change in the rate (acceleration) of most of the physical aspects of cardiac

function. The velocity or acceleration (first and second time derivatives) or the first and second time differentiated aspect of cardiac function is therefore measured. By measuring these phenomena a better insight into the heart's performance is permitted.

The basic function of the heart is to supply life-sustaining substances to the tissues. This is accomplished by the heart functioning as a pump. Ballistocardiography measures cardiac forces and provides information about cardiac co-ordination. It may thus provide valuable information on the higher dynamic functioning of the heart. Where the classical methods, for instance, failed to distinguish between the cardiac function in the old and young, the ballistocardiogram reflected changes in cardiovascular performance with age (Starr 1966). Being more sensitive to changes in cardiovascular performance, a more reliable distinction between normal and abnormal function seems possible through this method of evaluating cardiovascular status.

The extensive studies on the physical aspects of the method by Burger et al. (1953, 1956, 1957). Burger and Noordergraaf (1956), Von Wittern (1953, Talbot and Harrison (1955), Rappaport (1956^{a,b,c}) and Noordergraaf (1956,1961), placed this method on a sound basis.

To investigate the value and possibilities offered by this method, experiments with animals are of the utmost importance.

Drastic changes in the cardiovascular performance of animals can be brought about and the measurement of these changes provides valuable information about the haemodynamics of the animal as well as the scope of the method. Animal experiments have also greatly improved the understanding and interpretation of the recordings and of cardiovascular dynamics.

Ballistocardiographic studies concerning the influence of factors such as congenital metabolic, dietetic and cardiovascular anomalies as well as ageing are urgently needed. Small animals provide suitable subjects for the investigation of these factors on an experimental basis.

The relatively short lifespan of rats makes them ideal animals in studying the effects of age. Furthermore it is possible to breed rats with specific congenital cardiovascular or metabolic disorders. In an earlier study (Pretorius et al. 1965, 1966) it was noted that the UF Bcg (a) of rats shows a clear atrial wave complex. As the recordings of other animals have not shown this complex clearly, the rat seems to be an exceptionally suitable animal for experimental ballistocardiography.

Very little experimental ballistocardiographic research has been done on small animals. This may be partly due to the technical problems involved in making a suitable ballistocardiograph, for a physically reliable method to

cope with the usual high heart rates must be used. The rat is the most extensively used laboratory animal but little is known about the higher dynamic function of the heart in rats. Reliable Bcg recordings of white rats would therefore prove valuable in making available a new field of study and at the same time providing a sensitive means of measuring the various aspects of cardiovascular function in small animals.

The aim of this study was to investigate the possibility of obtaining reliable acceleration ballistocardiograms of rats and to establish the genesis and value of the recorded waves. As the UF Bcg method seems to be most suitable for animal experimentation, it was decided to use this type of system in the present study.

The physical aspects and development of the method as such are discussed in Chapter 2. Adoption of the UF Bcg system to meet the requirements for its application to small animals, is described in Chapter 3 and discussed in Chapter 10.

The normal pattern of the UF Bcg (a) of rats is described in Chapter 4. Some changes in cardiovascular function associated with age as measured by the UF Bcg (a) are described in Chapter 5.

In order to establish the genesis and significance of certain waves in the UF Bcg (a) of rats, some changes were induced in cardiac function. Mechanical changes brought

about are discussed in Chapter 6. The changes found in the UF Bcg (a) following administration of certain cardio-active substances are discussed in Chapter 7. Q-time analyses and the relationships in amplitude of different cardiovascular phenomena are discussed in Chapter 8. The results obtained in this study are compared with the results of similar experiments on other animals described in the literature. Some aspects of differences were noted. The possible genesis of the UF Bcg (a) waves of the rat is described in Chapter 9.

Some important features of the UF Bcg system used in the present study and the results obtained with this instrument, are discussed in Chapter 10.

CHAPTER 2

BALLISTOCARDIOGRAPHY

A. Development of the method

The observation that the body moves in sympathy with the beating of the heart was made long ago. The movements were first described by an English physician, Parry, in 1825 in dealing with a case of hyperthyroidism.

Gordon (1877), however, was the first to record graphically these movements. Gordon's idea precipitated from the observation that the indicator needle of a spring balance oscillated synchronously with the beating of his heart.

Gordon (1877) constructed a platform which was suspended by ropes from the ceiling and when a subject was placed in the supine position on the platform, recorded its movement mechanically. This was the first low-frequency system.

Two years later Landios (1880) described a basic instrument which enabled him to show that the amplitude of the records made from patients with aortic insufficiency exceeded the amplitude of records made from healthy subjects. Henderson in 1905, quite unaware of Gordon's work, suspended a wooden board by wires and, through a system of levers, recorded the longitudinal movements of the platform. Henderson was the first to realize that the body movements were caused by recoil action and he suggested that the amplitude of the recording was related to cardiac output. After this, numerous records were obtained by different workers employing

methods as diverse as the investigators themselves.

Satterthwaite (1913) recorded ballistocardiograms by using a weighing machine. A platform suspended from the membrane of a drum was used by Heald and Tucker (1922). The subject had to stand on the platform while his ballistocardiogram was recorded. In 1933 Abramson built a complicated aluminium chair by means of which he recorded body movements. He called the recording a 'Kardiodynamogramm'.

The first really successful recordings, however, were made by Isaac Starr in 1939 (Starr et al. 1939). Starr also coined the term ballistocardiography. In his articles Starr described a simple high-frequency system (10 Hz.) and worked out empirical formulae for the calculation of cardiac output from the ballistocardiogram and compared the values with those obtained by the direct Fick method. In later studies this ballistocardiograph was abandoned after investigating the effects of shock (Gournand et al. 1943). Shortly thereafter Nickerson and Curtis (1944) published the design of a low-frequency ballistocardiograph, basically of the same design as that of Henderson (1905) but with a damping device added. By critical damping, the effect of respiration on the light-weight low-frequency system was practically eliminated. The platform was suspended by weak leaf springs with adjustable clamps to control the natural frequency of the leaves at 1.5 Hz.

Another type of ballistocardiograph developed by Dock and Taubman (1949) is known as the direct body ballistocardiograph (DB Bcg). In essence it consists of a shinbar placed on the legs of a subject reclining on a rigid table. The movement of the bar relative to the table is picked up by a photocell and recorded. This instrument was extensively used for clinical work. The Dock instrument can be regarded as a high-frequency system (Burger et al. 1956).

In 1952 Jonnart constructed a system of yet another type, known as the ultralow-frequency ballistocardiograph, with a natural frequency of about 0.3 to 0.5 Hz. The platform was suspended by four leaf springs and he recorded the acceleration of the platform.

It was now realized that the recordings obtained from the different systems were not alike. Thorough physical studies of the method were done by Burger et al. (1953, 1956, 1957), Von Wittern (1953), Talbot and Harrison (1955), Rappaport 1956^{a,b}) and Noordergraaf (1956, 1961).

These studies revealed that the high-frequency platforms so far in use yielded distorted recordings. It was also found that firm coupling of the platform to its surroundings and the use of heavy platforms gave distorted signals. They suggested the use of lightweight platforms and a system with a very low natural frequency, less than 0.5 Hz.

At this stage a tendency to revert to the older low-frequency

systems of Gordon (1877) and Henderson (1905) developed. Recent investigators, however, recorded acceleration by means of suitable accelerometers as this avoids the distorting effect of respiration. This most important application of accelerometers was first described by Jonnart (1952) and Von Wittern (1953).

The intensive physical studies of ballistocardiography by Burger et al. (1953, 1956, 1957), Von Wittern (1953) and Burger and Noordergraaf (1956) revived interest in the method. Their work resulted in the design of more reliable systems and therefore greatly increased the value of ballistocardiography and enabled different investigators to obtain comparable recordings. The contributions of Burger et al. (1953) and Rappaport (1956^{a,b,c}) in this respect, particularly concerning ultralow-frequency systems, deserve special mention.

Although the earlier interests in ballistocardiography were centered in its application as a method of calculating the cardiac output or stroke volume (Henderson 1905 and Starr et al. 1939), it was soon realized that ballistocardiography was of much more value as a method of obtaining information about the basic physiological function of the heart (Starr 1946-1947).

In 1954 Elsbach described the first extensive clinical study

using the ultralow-frequency system. He made use of a piezo electric crystal transducer and electronically differentiated displacement signals into velocity and acceleration.

Talbot et al. (1954) constructed an aperiodic system. This new type of ultralow-frequency ballistocardiograph consisted of a platform floating on mercury. The acceleration was recorded directly. Thereafter followed several ultralow-frequency systems, like the platform with rollerball support (Klensch 1955) and the platform supported by ball-bearings (Hollis 1956).

Most investigators recorded only the longitudinal (y-axis) body movements. Hamilton et al. (1945) took records in three spatial axes, x, y and z, in an endeavour to increase the amount of information that can be derived from ballistocardiography. Other workers, Scarborough et al. (1950), Franzblau et al. (1950), Brandt et al. (1951) and Braunstein (1953) attempted to record multi-axial and vector ballistocardiograms. According to Scarborough et al. (1958) and Talbot (1958) these were, however, not very reliable and prone to artifacts.

In 1958 Talbot described a differential ballistocardiograph with three degrees of freedom, and made satisfactory three-dimensional Bcg recordings. Knoop et al. (1961^b), Knoop (1962) and Knoop et al. (1962) made two-dimensional

displacement recordings of humans and dogs.

Later studies of vector ballistocardiograms were even more successful. Knoop (1964) and Van der Linde and Knoop (1966) suggested that vector ballistocardiography might be more valuable in giving a complete picture of cardioballistic events. Beischer and Hixon (1966) described the recording of triaxial ballistocardiograms in a weightless environment obtained by performing Keplerian trajectories with a jet aircraft. Franke and Braunstein (1967) described the design of a three-dimensional high-frequency system.

A fairly recent trend in ballistocardiography is the development of air-supported ballistocardiographs. Cunningham and Smiley (1961), Cunningham and Saunders (1967) and Harrison and Talbot (1967) are of the most important investigators in this field.

In 1967 Trefny and Wagner described a quantitative ballistocardiograph, which may be called a very high-frequency ballistocardiograph (VHF Bcg) by virtue of its high natural frequency of about 12 kilocycles.

Since the late fifties ballistocardiography has developed tremendously. Different societies were formed, of which the most important are the Ballistocardiographic Research Society of America and its European equivalent. In April

1965 the First World Congress on Ballistocardiography and Cardiovascular Dynamics met in Amsterdam, with Prof. A. Hoitink as president.

In order to understand the shape and significance of the recordings, it is necessary to consider briefly the general physical background of the method.

B. Basic principle

The method is principally based on Newton's laws of motion, which may be stated as follows:

Law 1: Every body will continue in a state of rest, or of uniform motion in a straight line, unless it is compelled by the action of external force to change that state.

Law 2: The rate of change of momentum is proportional to the impressed force, and takes place in the direction in which the force acts.

Law 3: To every reaction there is an equal and opposite reaction.

The third law explains the principle of the conservation of momentum which may be stated as follows: Action and reaction between the different parts of a system cannot change the TOTAL momentum of that system in any given direction. A typical example of this is a shot fired from a gun. The mass of the bullet times its velocity will equal the momentum of the gun in the opposite direction

(recoil).

Applied to the body it means that the momentum of the mass of blood pumped by the heart will cause a movement of the total body mass. In other words, to maintain the centre of gravity of the body as a whole, the body must move in an opposite direction to the flow of the blood mass.

By suspending the body so that it is free to move and also free from external forces, the body movements caused by the pumping action of the heart can be measured. These periodic positional changes of the body can be recorded as displacement, velocity and/or acceleration, all of which would bear a close relationship to the dynamic action of the cardiovascular system. The ballistocardiogram thus originates mainly from the movement of the blood from the heart to the periphery, during and just after the period of ejection.

C. Mechano-physical considerations.

Though the method is based on simple physical laws, it is not without complications in its application. Under ideal conditions the body should be a rigid mass, the coupling between body and cardiovascular system and between body and platform (support) should be firm, and the body must be suspended free in space. None of these conditions can be fully met in practice, although some can be approximated by careful instrumentation. A recent trend is to minimize

the effects of interference by mechanical or electronic devices. Computers and analog computers were used by Noordergraaf (1966) and Smith et al. (1966).

(i) Free suspension of body: In order to obtain recordings of the movement of the body imparted to it by the pumping action of the heart, it must be suitably suspended. The suspension must be such that the body is unrestricted in its movement and also protected from ambient vibrations. Gordon (1877) and Henderson (1905) apparently realized that suspending the body in space can be approximated by using long ropes or wires. In this pendulum type of system the length and nature of the supports determine the degree of binding to the surroundings which will affect the natural frequency of the system. Thus, the stronger the binding the higher is the natural frequency and vice versa. According to Burger et al. (1953) the natural frequency of the system will, amongst other things, determine what is measured. If the binding is strong, the recorded displacement of the platform measures the internal forces, as in the case of the high-frequency systems (10-15 Hz) used by Starr et al. (1939). If the binding is weaker, as in the Nickerson system with a natural frequency of about 1 Hz (LF_{Bcg}), the recorded displacement will be proportional to the displacement occurring in the system. By using a system that is critically damped, the displacement of the platform will be proportional to the velocity of displacement of the

centre of gravity of the ejected blood. With an ultralow-frequency system, according to Burger et al. (1953), the displacement of the centre of gravity of blood resulting from the cardiac forces can be measured fairly accurately. As the high-frequency systems record force and the low-frequency systems displacement, the once integrated curve of the high-frequency system will give velocity and the twice integrated high-frequency signal will give displacement. Under ideal conditions therefore, the twice differentiated displacement signal of the ultralow-frequency system should approximate the curve obtained from the high-frequency ballistocardiograph.

The natural frequency of the system is also of further importance. In high-frequency systems the binding to the surroundings is usually strong. If a subject is placed on such a platform, the excursions of the platform would not necessarily be that of the body, as the relative movement of the body to the platform cannot be disregarded.

Burger et al. (1953) suggested that in the high-frequency system the body will be less firmly coupled to the platform than in a low-frequency system, with the result that there can be no certainty about the recorded movements of the platform. This unwanted condition is further aggravated in high-frequency systems by the large weight (mass) of the platforms commonly used. Following the line of thought of Burger et al. (1953, 1956) and Rappaport (1956^{a,b,c}) it

seems that suspension of the body in space can be best approximated by using an untralow-frequency system, with a natural frequency of less than 0.5 Hz and with a minimum of damping. It is simplest to achieve this by suspending a lightweight platform from the ceiling or a framework by means of ropes or wires.

In designing a ballistocardiograph the natural frequency should receive special attention. When a high-frequency ballistocardiograph is used, the respiratory movements have little if any effect on the recording. The respiratory frequency (± 0.3 Hz), however, is clearly shown by the ultralow-frequency system. The high-frequency system is thus not suitable for recording phenomena in the low-frequency zone. Burger et al. (1953) have shown that the frequency response of the high-frequency system is inferior to that of the low-frequency system. The interference of respiration and the natural frequency of the system can seriously distort the signal in a low-frequency system. When a low-frequency system is used, the ratio of the applied frequency (heart rate) to the natural frequency should be carefully controlled. If the ratio of natural frequency to applied frequency is unity and no damping is applied to the system, resonance will occur. The natural frequency must therefore differ enough from the applied frequency to minimize this effect. Furthermore, if the natural frequency is nearly the same as that of the applied

frequency, it would be extremely difficult to distinguish between them on the recording. A single impulse (disturbing the resting position of the centre of gravity of the system) at the applied frequency would then result in a train of oscillations at the natural frequency. To prevent undue oscillations occurring in the system, damping of the system seems necessary.

Rappaport (1956^a), studying the dynamic principles of the ultralow-frequency system, concluded that damping should be minimal in order not to interfere with the binding of the system to its surroundings, and to give 100% response at the specific ratio of applied frequency to natural frequency. According to Burger et al. (1953) and Rappaport (1956^a) the degree of damping will also determine the degree of phase shift and therefore also the frequency response of the system. Nickerson et al. (1966) suggested that the phase shift characteristics of a system are the best index of the amount of distortion present in the system.

Consideration should also be given to the amount of ambient or building tremor present when making recordings. In general the frequency spectrum of building vibrations falls together with that found in cardioballistics. Rappaport (1956^b) mentioned that the displacement ballistocardiogram is least affected by ambient vibrations while the acceleration ballistocardiogram is the most susceptible. It is

apparent from this study that the use of low-pass filters is of little practical value and that it is better to use a basement room where building tremor is the least.

By using isolated air beds Cunningham and Saunders (1967) have eliminated the effect of horizontal building vibrations. They encountered difficulties in eliminating vertical floor vibrations and are still working on this problem.

Trefny and Wagner (1967), working on a new type of 'VHF' ballistocardiograph with a natural frequency of 12 kc's and a loaded frequency of 1 kc, reported that their instrument was completely insensitive to floor vibrations.

(ii) Coupling between body and platform: Reporting on intensive studies, Burger et al. (1956) and Talbot and Harrison (1955) concluded that in the ultralow-frequency system, the coupling between body and platform is superior to other ballistocardiographic systems. In their first report on the physical basis of ballistocardiography, Burger et al. (1953) suggested that the relative movement between body and platform may distort the signal obtained from the platform to such an extent in the high-frequency ballistocardiograph, that recordings are of little value. Walker et al. (1953), using a direct ballistocardiograph (Dock type), investigated the effect of various 'coupling media'. They concluded that in the case of the Dock type of instrument, hard, flat surfaces are less desirable for

ballistocardiograph platforms. From this study on the DB Bcg, it was evident that a soft or viscous material like sand or 'putty' which adapts to the contours of the body, is superior in eliminating relative movement between subject and platform.

Von Wittern (1953), using a low-frequency system, made a valuable report on the coupling of the body to the platform. According to Burger et al. (1956), Von Wittern unfortunately used a heavy platform (10^4 grams) and the natural frequency of his system was rather high (0.6 Hz).

It seems therefore that the ultralow-frequency system, using a lightweight platform, offers the best subject to platform coupling. Rappaport (1956^b), using a lightweight platform (4 lbs.) made of Grade A airplane fabric, showed that even doping the fabric caused it to have a drum-like action and resulted in introducing artifacts. In the high-frequency systems including the direct body type (Dock), the tissues between skeleton and platform act as a damping device, resulting in phase shift and unsatisfactory force transmission to the platform. According to Rappaport (1956^a) even the optimal use of clamping devices such as shoulder supports and footplates, render the high-frequency system (Starr) of less practical value. Where there is unsatisfactory coupling between subject and platform, secondary or parasitic oscillations as described by Rappaport (1956^a), may completely mask

the basic cardiovascular complexes. In addition a system of this nature rapidly attenuates the cardioballistic movements in the higher frequency area (5 to 30 Hz).

As the suspension of the body in space can only be approximated, all types of ballistocardiographs so far discussed, share this common deficiency, which is more pronounced in the case of the high-frequency systems.

To summarize, the weight of the platform, the degree of applied and natural damping, and the ratio of natural to applied frequency, are intimately associated with the degree of restraint of the suspended system and thus the accuracy of the registered ballistocardiogram.

(iii) Coupling between cardiovascular system and body:

Although the degree of coupling between the different body structures cannot be altered by instrumental manipulation, it seems fit to mention some of the problems encountered in this respect.

The ballistic movements of the body as a result of the pumping action of the heart can be explained by Newton's third law of motion. The situation is, however, not so simple, because of the anatomical arrangement of the cardiovascular system. The force vector which imparts ballistic movement to the body is of variable magnitude and spatial direction throughout the cardiac cycle. Factors such as the

compliance of the tissues between the heart and skeletal structure, the compliance between the vascular system and skeletal structure, and the compliance of various skeletal appendages, will greatly affect the transmission of the force vector to the body mass, even if the latter is suspended free in space. The movement imparted to the body is further complicated by the compliance between skeletal structure and platform, and the elasticity and resistance in the peripheral vessels (Rappaport 1956^a).

The coupling between the cardiovascular system and skeleton was treated quantitatively by Von Wittern (1953), Grandell (1955), Honig and Tenney (1956^a), Burger et al. (1957) and Nickerson et al. (1966). Although slightly different systems were used and the approach necessarily varied, the importance of tissue distortion in recording ballistocardiograms was stressed. According to Burger et al. (1957) and Nickerson et al. (1966), the latter working on dogs, the ultralow-frequency ballistocardiograph minimizes the distortion.

Nickerson et al. (1966) described the ultralow-frequency system as a simple damped oscillator and this system seems therefore to be the most reliable. From a mathematical point of view it is the least complicated system and fairly accurate calculations can be made by using basic mathematical expressions. As a result of the physical analyses of ballistocardiography by Nickerson and Curtis (1944),

Nickerson et al. (1966), Burger et al. (1953, 1956, 1957), Burger and Noordergraaf (1956), Von Wittern (1953), Noordergraaf (1956) and Rappaport (1956^{a,b,c}), a better understanding of the genesis of wave patterns was possible. These studies placed ballistocardiography on a sound basis, thereby ending a rather confused stage in the development of the method and the interpretation of the waves.

D. Meaning and origin of the ballistocardiogram

The expulsion of blood from the heart applies to the body certain opposing forces approximately equal in force, but with a temporal difference. Although the amount of movement imparted to the body is not a quantitative measure of the forces at the source - by virtue of the transmissional losses - it serves as a valuable indication of the internal forces responsible for the propulsion of blood. If a force of known magnitude is applied to a ballistocardiographic system, the system can be calibrated and the relative magnitude of the forces of cardiac origin can be fairly accurately evaluated.

The normal longitudinal ballistocardiogram consists of a number of headward and footward motions, the most important waves being designated H, I, J, K and L. This system, introduced by Starr, was adopted by the American Heart Association.

It is customary to arrange the polarity of the recording system in such a way that a headward movement of the platform is recorded as a positive wave (above the base line) and a footward movement of the platform as a negative deflection. The flow of blood down the descending aorta of a reclining subject will cause a headward movement of the subject plus platform and result in a positive deflection being recorded. When interpreting records it is important to note that rapid deceleration of blood will cause acceleration of the subject in the same direction. Keeping the various systems and recording methods in mind, the striking similarity of the ballistocardiograms obtained, is surprising.

Starr et al. (1939) was the first to make progress in interpreting the waves of the ballistocardiogram. Starr and Rawson (1941), by carefully studying the various forces associated with the deceleration and acceleration of blood in segments of the circulation, obtained a theoretical ballistocardiogram which differed very little from a recorded ballistocardiogram. Hamilton et al. (1945) obtained similar results. In studies using human cadavers, Starr et al. (1950, 1953), Starr and Schnabel (1954), and Starr (1956) obtained larger ballistocardiographic waves when the velocity of 'ejection' was increased. Their ballistocardiograms lacked the G and H waves, indicating that these waves are associated with heart action or

atrial activity rather than with the flow of blood. The J wave became broad and even notched as they progressively diminished the synchronization between right and left ventricular 'ejection'. Starr (1959^{a,b}) demonstrated a good correlation between the force of 'systole' in cadavers and the amplitude of the I wave of the high frequency ballistocardiogram.

Since the extensive studies of Burger (1953), Noordergraaf (1956), and Noordergraaf and Heynekamp (1958) on the physical aspects of ballistocardiography, it was possible to approach the genesis of the different waves in mathematical terms. They made use of physiological and anatomical data to calculate strictly theoretical ballistocardiograms. They counterchecked their calculations by comparing the difference between calculated and experimental values of plethysmograms obtained from the arms and legs. Working on the total mass displacement of blood in the body, they obtained a very good correlation between predicted and experimentally recorded ballistocardiograms. Again the predicted ballistocardiogram lacked the H wave. They concluded that the normal ballistocardiogram was mainly caused by events taking place in the ventricles and larger arteries.

Klensch and Eger (1956) and Eger and Klensch (1956), working on a model of the circulation, obtained pressure curves and displacement ballistocardiograms which simulated the normal

pattern to a marked extent.

Honig and Tenney (1956^{a,b}, 1957^{a,b,c}) recording ultralow-frequency acceleration ballistocardiograms of humans, dogs, as well as that of a hydrodynamic model, clearly demonstrated the importance of acceleration and deceleration of blood in the genesis of body movements. The latter is of particular importance during and after closure of the aortic valve. The early diastolic vibrations, subsequent to valve closure, are thought to originate mainly from arterial resonance. Arterial resonance may be caused by the aortic standing wave during elevated arterial pressure.

Noordergraaf (1961) compared the contribution of the pulmonary circulation to that of the systemic circulation in the genesis of the waves. He also correlated the effects of heart and associated soft tissue movements, the filling of the heart, and the contribution of the smaller arteries to the shape and amplitude of the ballistocardiographic waves. He confirmed that the I and J waves are indicative of ejection force. Furthermore, the HI segment would be largely due to events in the larger (proximal) arteries while the IJ segment would reflect a larger proportion of events in the smaller arteries. According to this study, the GH segment of the ultralow-frequency acceleration ballistocardiogram is mainly due to isovolumetric contraction of the ventricles. The L, M and N waves are complex and are

caused by cardiac filling and the changes in blood flow in the smaller arteries associated with the arrival of the pulse wave at the periphery.

As the aim of the present study was to secure more information about the ultralow-frequency acceleration ballistocardiogram of the rat, a closer look at the literature relating to animal experiments seems fit. Experiments on animals are of great value in that various drastic experimental alterations can be made to the cardiovascular system and the results so obtained provide useful information about the genesis of the ballistocardiogram.

Using a high-frequency system, Hamilton et al. (1945), recorded dog ballistocardiograms. In 1955 Cossio et al. recorded dog ballistocardiograms with a direct body ballistocardiograph. They found no marked alterations in the ballistocardiogram pattern after occlusion of the venae cavae, although in some cases an increase in amplitude was found. They concluded that heart motion is the most important contributing factor to the ballistocardiogram.

Honig and Tenney (1956^a) recorded acceleration ballistocardiograms of dogs using an ultralow-frequency apparatus. Their findings differed considerably from that of Cossio et al. (1955). Honig and Tenney (1956^a) found that the ballistocardiogram of the dog consists of three main waves. The first wave is associated with atrial contraction and

preceeds ejection. It is not affected by interruption of blood flow and its amplitude varies directly with heart size and force of contraction. The second wave is abolished by interruption of blood flow and it bears a close temporal correlation to cardiac ejection. The amplitude of the second wave was found to correlate with stroke volume and blood acceleration (ejection force) during systole. The third wave was found to be associated with venous flow and after vibrations caused by the aortic standing wave. In a later study Honig and Tenney (1957^a) stressed the importance of the deceleration of blood in the genesis of the diastolic waves in the ballistocardiogram.

Darby et al. (1954, 1957) recorded direct body ballistocardiograms of dogs using transducers firmly coupled to the neural spines of dogs by means of a rod. They were able to prove, by direct strain gauge measurements, that an increase in the force of cardiac contraction was directly proportional to the amplitude of the IJ segment of the acceleration ballistocardiogram. In 1959 the same workers found that the acceleration IJ segment of the ultralow-frequency ballistocardiogram of the dog was reduced in slope with an increase in diastolic pressure. By careful drug administration they found that the IJ segment was increased in slope and amplitude when the cardiac contractile force was increased or the peripheral resistance was lowered. When both factors were increased or lowered,

very little change in the amplitude of the IJ segment could be demonstrated.

Further studies on dog ballistocardiograms were done by Scarborough (1957) and Scarborough et al. (1958). From these studies it was evident that the anatomical arrangement of the aorta and venous factors contribute to the ballistic wave patterns. In 1960 Moreira described an ultralow-frequency system for dogs, employing the U-effect accelerometer.

Hoitink (1955) and Knoop and Hoitink (1955) used HF, LF and UF types of ballistocardiographs in taking recordings from dogs. Since then, these workers have covered an extensive field on the ballistocardiogram of dogs and man. Knoop and Hoitink (1960, 1961) have shown the differences in the displacement ballistocardiogram of dog and man. From these studies it was clear that the anatomical arrangement of the ascending aorta and heart greatly affects the configuration of the HIJ complex. The magnitude of cranial displacement in the dog was found to exceed that in man. This, and the small temporal difference between cranial and caudal directed displacements of the blood mass, account for the rather inconspicuous I wave found in the dog's ballistocardiogram.

The difference between the ultralow-frequency acceleration ballistocardiogram of man and dog was confirmed by Knoop

et al. (1961) and Pretorius (1962^a). In reporting on an intensive study on the ultralow-frequency acceleration ballistocardiogram of the dog, Pretorius (1962^b), also recording the electrokymogram, was able to demonstrate clearly that the ballistocardiogram of the dog is caused by heart vibrations as well as blood flow. In this study it was conclusively proved that the H wave is associated with cardiac activity during the isometric contraction phase. Ventricular ejection is associated with the IJ complex, especially the J wave. Considerable evidence has been obtained showing that the dynamic events during valve closure cause body acceleration, recorded as the LM segment.

Pretorius (1962^b) further suggested that under certain circumstances the forces associated with atrial activity might produce body acceleration recorded as the F wave, and that the H wave may be influenced by atrial contraction. The work on the ballistocardiogram of the dog by Winter et al. (1966, 1967), confirmed these findings. It appears that the acceleration ballistocardiogram is remarkably sensitive to changes in ventricular ejection pattern.

Experiments with animals other than the dog are very limited. Klensch (1960, 1961) recorded the ultralow-frequency displacement ballistocardiogram of the frog. Occlusion of the great veins resulted in an impressive reduction of ballistocardio-

gram amplitude. It seems from this study that the ballistocardiogram in cold blooded animals is largely due to blood flow; the contribution of cardiac movement being very small. Honig and Tenney (1956^a) calculated that the stroke acceleration of the turtle is but $\frac{1}{2500}$ of that of a dog of the same weight, expressed as the rate of change of linear velocity in the proximal segment of the arterial system. They attempted to record the acceleration ballistocardiogram of a 15kg alligator snapping turtle, but were not successful. It also seemed impossible to record the UF Bcg (a) of the clawed-toed frog (Pretorius and Rademeyer 1963).

A method to record the ultralow-frequency acceleration ballistocardiogram of the rat was first published by Pretorius and associates (1966). This study indicated that the rat has a rather complex ballistocardiogram and that it may be a suitable animal for ballistocardiographic studies.

The object of the present study was to evaluate the applicability of ballistocardiography to the rat, and to establish the genesis of the acceleration ballistocardiogram using an undamped system of ultralow natural frequency.

CHAPTER 3

METHODS

From the studies of Von Wittern (1953), Burger (1953, 1956^{a,b}), Rappaport (1956^{a,b,c}), Noordergraaf (1956, 1961), Honig and Tenney (1956^{a,b}, 1957^{a,b,c}) and Nickerson et al. (1966), it is clear that the ultralow-frequency ballistocardiograph is least prone to artifacts and distortion. It was therefore decided to use this system in studying the acceleration ballistocardiogram of the rat. A further advantage of this system is that its low natural frequency differs widely from that of the impressed frequencies associated with the high heart rate in rats. A good ratio of $\frac{f^*}{fN}$ could thus be obtained, minimizing possible resonance or after-vibrations.

As it was not desired to damp the platform, acceleration of the platform was measured directly with the U-effect accelerometer, described by Ueda et al. (1950, 1951), explored for ballistocardiography by Elliott et al. (1954), and modified for use on a small animal platform by Pretorius et al. (1966). This type of accelerometer was also used by Reeves et al. (1957), Malt (1958), Frederick and Eddleman (1958), Pretorius (1962) and Pretorius et al. (1966).

f^* = applied frequency (heart rate),
 fN = Natural frequency of platform.

A. Apparatus

(i) The ballistocardiograph: The general layout of the ballistocardiograph is shown in Fig. 1. The upright supports were $\frac{1}{2}$ inch square solid brass rods welded to the lower section of 1 inch angle brass. The upright supports were braced asymmetrically to minimize resonance. The lower section was screened with copper gauze on three sides and the bottom. The front was hinged as a door and one side was left open for easy manipulation of the experimental animal. Two movable square brass rods were placed on the upright supports and isolated from the surroundings and framework by pieces of $\frac{1}{4}$ inch rubber tubing. By suspending the platform from these rods and by placing the whole ballistocardiograph on four stout rubber bungs, a minimum of ambient vibrations reached the platform. The whole apparatus was placed on a concrete slab separate from the structure of the building and as far as possible from AC-mains lines.

(ii) Platform: The platform (Fig. 2) was constructed of 'perspex foam' (polyesterene foam) and weighed 4 grams with the accelerometer attached. Several types of platforms were constructed in an attempt to improve the subject to platform coupling. In this study a flat piece of 'perspex foam' $8 \times 2\frac{1}{2} \times \frac{1}{4}$ inches was used. Two torso supports were glued onto the platform to contain the rat in the supine

FIG.1.

BALLISTOCARDIOGRAPH. ($\frac{1}{16}$ SCALE)

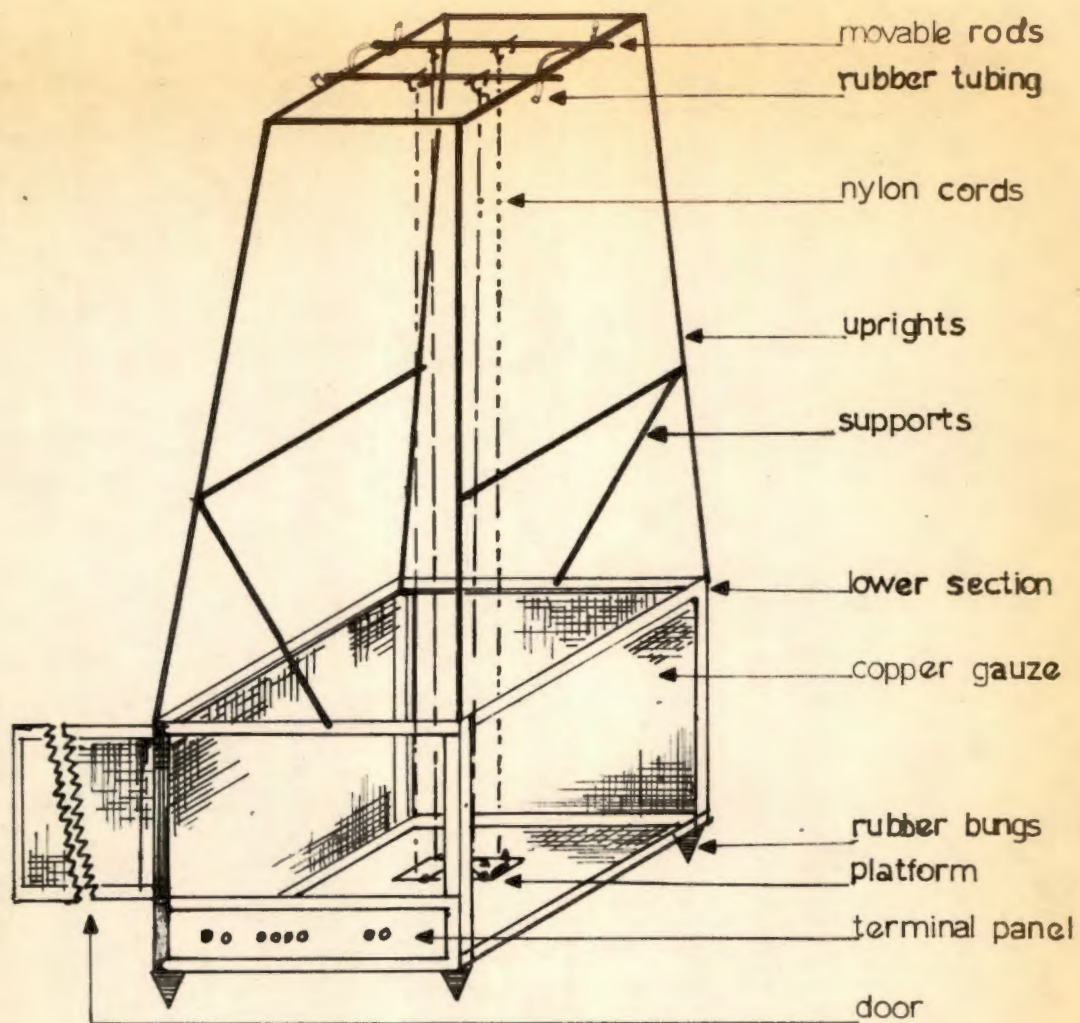
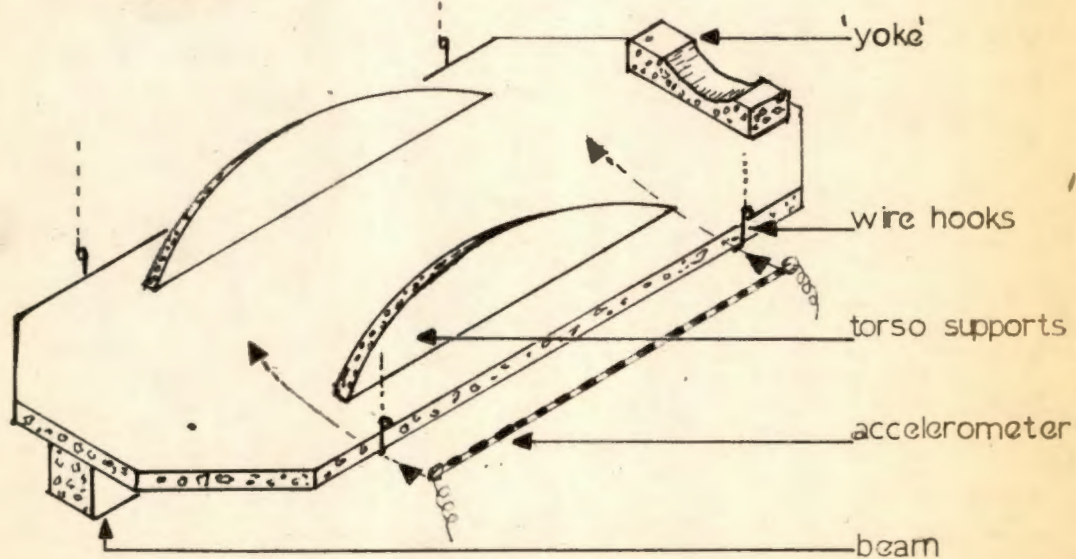


FIG.2.

DETAIL OF PLATFORM ($\frac{1}{2}$ SCALE)



position.

On the one end of the platform a "U-shaped yoke" was glued. The rat was placed so that the yoke fitted between its shoulders and occiput. It was thought that this markedly increased the coupling. The platform was made more rigid by glueing two $\frac{1}{2}$ inch square beams of 'perspex foam' below the platform, along the centre in the y-axis. Thin aluminium wire was embedded across the beams and bent to make contact with the platform. The platform was suspended by means of four braided nylon cords 68 inches long, tied to the aluminium wires and coupled to the buffered brass rods on the ramp by knife-edge riders. The modified accelerometer (Pretorius et al. 1966) was glued to the platform at the intersections of the beams and the aluminium wires only, thus minimizing any bending of the accelerometer in event of sagging of the platform or beam under load. No appreciable bending of the platform, however, was noticed during this study. The natural frequency of the platform was 0.38 Hz.

(iii) Accelerometer: The accelerometers were from 8 to 10 cm. long and had an average of 2.5 to 3 columns of mercury per centimeter. The mercury columns were separated by layers of 0.5N sulphuric acid. Copper or platinum electrodes were introduced and sealed with apoxy resin to the glass capillaries, and connected with guage 38 vinyl acetal insulated copper wire to terminals on the ballisto-

cardiograph. The thin copper wire was spiralled and did not interfere with the movements of the platform. Thin walled capillaries of ± 0.5 mm. internal diameter were drawn to limit the weight of the accelerometer. Several accelerometers were fixed to the platform and checked for phase lag or low sensitivity by mechanical shaking of the platform at 0.4 Hz, 3 Hz and at higher frequencies. Most of the experimental work described in this study was done by using one accelerometer of 'ideal' construction.

(iv) Recorder: A six channel EMT 81 (Minograf Elema Schönander) was used. The recorder was fitted with six ECG preamplifiers, one universal-preamplifier with compensator (EMT 12, 16 and 17), one phono-preamplifier (EMT 21), an electromanometer (EMT 31) and a heart rate meter (EMT 50). Six standard final amplifiers (EMT 7) fed the signals to the jet galvanometers.

The frequency response of the combined final amplifier and galvanometer is practically linear from dc to 500 Hz. Comparing ballistocardiograms of the same rat on a fast risetime oscilloscope with that of the recorder, showed no difference. The frequency response of the universal-preamplifier (Bcg) was determined. When a rectangular signal was fed to the preamplifier no loss of voltage amplification was found up to 500 Hz. At 600 Hz a voltage loss of 12%, at 700 Hz a loss of 16% and at 800 Hz a loss

of 30% peak to peak was found. This loss can be attributed to the galvanometer as it is specified as 30% down at 700 Hz. The risetime was found to be satisfactory. A phase shift of $\pm 30\%$ ($\pm 108^\circ$) at 400 Hz and $\pm 16\%$ (60°) at 200 Hz was found using a rectangular wave with a risetime of 5 nanoseconds. The response for sine wave was much better.

It was concluded that the frequency response of the preamplifiers and the following stages were sufficient to record ballistocardiograms of rats with high fidelity.

(v) Pressure differentiator: For obtaining the time derivative of the carotid pressure, a Nexus SA2 solid state differential amplifier was passively connected directly between the pressure transducer and a final amplifier. The same undifferentiated signal was looped directly from the transducer to the electromanometer for recording the pressure. The circuit diagram of the differentiator is shown in Fig. 3. In selecting the values of the input and loop R-C circuits, the output impedance of the transducer as well as the input impedance of the final amplifier, were taken into account.

(vi) Pressure stand: The pressure transducer, a mercury manometer and the saline vessel were suspended from a standard 'Elema' telescopic pressure stand. The saline vessel was hung to give a pressure of 55 mm of mercury

FIG. 3 PRESSURE DIFFERENTIATOR

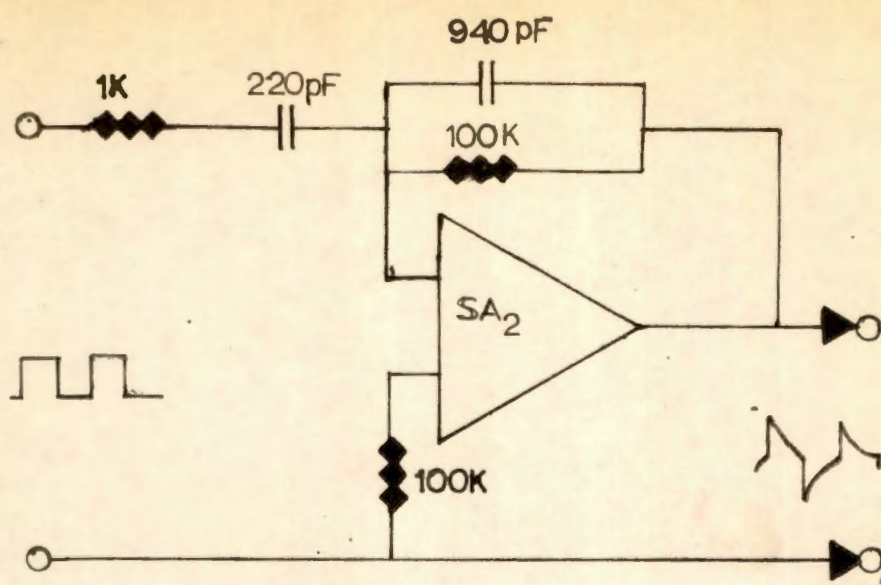


FIG. 4. CALIBRATOR

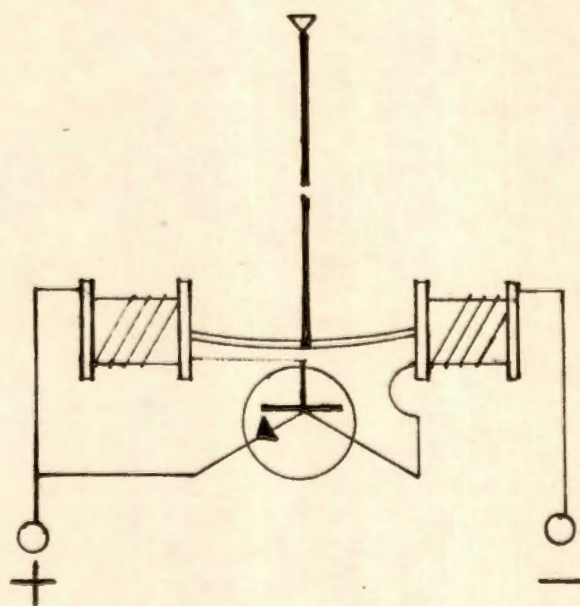
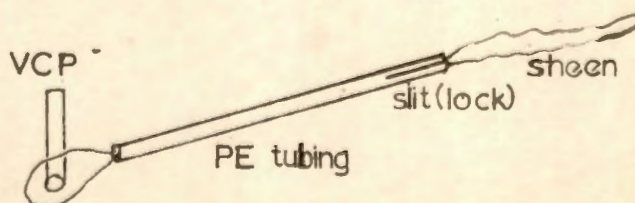


FIG. 5. LIGATION LOOP



at the transducer. The pressure transducer and mercury reference manometer were placed at the same height as the ballistocardiograph platform. The saline vessel was connected to an ordinary sphygmomanometer air pump to control the pressure in the catheter.

B. Calibration of the system

(i) Recorder: With the ECG amplifiers driving all six final amplifiers, the machine was calibrated to give a deflection of 15 mm per mV at a jet length of 35 mm. The sensitivity of the final amplifiers was locked in that position and crosschecked by driving all six final amplifiers by the phono-preamplifier or universal preamplifier. Channel synchronization was checked by a signal generator driving the final amplifiers, or through applying a signal to any of the preamplifiers. The decay time of the universal preamplifier was also tested at regular intervals. The paper speed calibration at 2.5, 10, 100, 125, 250 and 500 mm/sec, was regularly tested.

(ii) Pressure transducer: The pressure transducer was calibrated before every experiment and checked immediately thereafter, by using the mercury manometer on the stand. An ordinary sphygmomanometer was placed at the same height and connected to the catheter by means of a T-piece to test the reference manometer at regular intervals. The transducer and pressure preamplifier were calibrated at 0, 100

and 200 mm/Hg. No filtering was employed. The performance of the pressure differentiator was tested on an oscilloscope by applying square wave signals at 1 kc and by injection of artificial pressure pulses.

(iii) Accelerometer: A transistor driven pendulum was constructed to calibrate acceleration of the platform. The calibrator is shown in Fig. 4. It consists of a driver and collector coil connected through an OC 71 transistor, driving a pendulum at a fixed frequency of 1.3 Hz. The transistor was connected to a Philips PE 4817 dc supply, having separate controls for constant voltage or current regulation.

The acceleration of the platform was calculated as described by Pretorius et al. (1966). Although this method gives a fair approximation of the acceleration of the platform it was found less reliable than was anticipated because of the following reason: The formula for simple harmonic motion was applied to calculate the acceleration, viz.

$$a = \left(\frac{2\pi}{T}\right)^2 A$$

As soon as the pendulum is placed on the platform with a natural frequency of 0.4 Hz, it forms a coupled oscillatory system and the expression does not hold. When the pendulum was oscillating on the platform, the platform was

brought into motion and it was extremely difficult to measure accurately the angle of deflection of the pendulum.

In view of this problem a simpler method was developed. A weight of 100 or 150 grams was placed on the platform. The platform was brought into motion, the displacement was measured optically, while acceleration was recorded. By applying the expression for simple harmonic motion, the maximum acceleration was calculated and the ballistocardiograph calibrated accordingly. When the deflection angle of the platform (which can be considered as a large pendulum) did not exceed 3 degrees consistent results were obtained.

(iv) ECG and phonocardiogram: The ECG- and phonopreamplifiers were locked at a comfortable sensitivity and calibrated as usual by a built-in calibration push-button.

C. Experimental procedures

White rats from a local strain were used. The rats were fed commercial mice cubes, supplemented twice a week by skimmed milk and raw vegetables, ad libitum. Males and females were housed in separate cages after weaning.

For the recording of ECG, Bcg and phonocardiograms rats were anaesthetized by intraperitoneal injection of 30 to 35 mg/kg 'Sagatal' -pentobarbitone Sodium B vet C (Maybaker). This was the minimum dose that resulted in

enough sedation to make the recordings possible. When the carotid pressure was recorded it was essential to increase the anaesthesia to 40-50 mg/kg bodyweight for the necessary surgical procedures. In view of the work of Corbascio and Smith (1966), the minimum dosage of anaesthetic was used (see p. 209). It was shown in earlier studies that an additional 10 to 12 mg/kg pentobarbitone depressed the Bcg (a) and lowered the blood pressure (Pretorius et al. (1966)).

Anaesthetized rats were placed on the platform in the supine position. Small pins, soldered to guage 38 insulated copper wire and to terminals on the Bcg framework, served as ECG connections. An Elema Schönander EMT 25 microphone was placed in the mid-sternal position and kept in place with adhesive tape. Leads I, II, III, aVR, aVL and aVF were recorded. Immediately thereafter lead II, the Bcg (a) and the phonocardiogram were recorded. In some cases catheterization of the carotid was performed, the rats replaced on the platform and the pressure and its time derivative ($\frac{dp}{dt}$) were recorded simultaneously with the other phenomena. For recording the ECG only, a paper speed of 100 mm/sec was used. All other recordings were made at 250 and 500 mm/sec.

Ligation of the vena cava was obtained by making a loop around the vessel with sheen and the latter pulled through

a piece of polyethylene tubing. By adopting this procedure the vessel could be occluded and opened quickly and easily (Fig. 5). Ligation of the inferior vena cava was applied between the liver and the lower surface of the diaphragm. When pressure recordings were made, the catheter was flushed with 100 x diluted heparin to prevent clotting. A 14 inch piece of 'Intramedic' PE 50 or PE 60 polyethylene tubing (O.D. about 0.038 inches) served as a catheter.

To ensure thorough coupling of the rat and to prevent vibrations of the appendages, the hind legs of the rat were 'hooked' to the platform supports while the front legs were tied to the microphone and body by means of adhesive tape. The position of the tail did not interfere with the Bcg or platform movement.

CHAPTER 4

THE GENERAL PATTERN OF THE ULTRALOW-FREQUENCY ACCELERATION BALLISTOCARDIOGRAM OF THE RAT

It is extremely difficult, if not impossible, to obtain good recordings from rats without anaesthesia. Most anaesthetics, however, cause irritation or depress certain physiological functions such as respiration or cardiac contractility. Previous experience proved that rats tolerate 'Sagatal' better than 'Nembutal' (Sodium Nembutal Maybaker). There seemed to be a wider range between the effective and the lethal 'Sagatal' dosage (Rademeyer 1965). In a previous study (Rademeyer 1963) 'Nembutal' was used as anaesthetic. From the recordings obtained in this study it seemed that 'Nembutal' caused a more severe depression of respiration. In a previous study Pretorius et al. (1966) found that pentobarbitone caused a slight decrease in the amplitude of the UF Bcg (a) of rats. Corbascio and Smith (1966) showed that the UF Bcg (a) of dogs is also affected by pentobarbitone. According to Ling (1957), great species differences in the reactions to pentobarbitone exist. The use of succinylcholine followed by nitrous oxide and oxygen (80:20%) as suggested by Corbascio and Smith (1966) is technically difficult in the case of rats. In the first instance the platform used in this study weighed only 4 grams. To make and fit a suitable

mask for rats without seriously affecting the platform weight and restraint seemed to be impossible with the available facilities.

The curves that were considered as normal in this study, were therefore obtained after anaesthesia was induced by intraperitoneal injection of 35 to 40 mg/kg 'Sagatal'.

A. Procedure in studying the recordings

The Q wave of lead II of the ECG was used as a point of reference to calculate the time intervals of the different Bcg waves. The UF Bcg (a) shows well defined and sharp peaks which facilitated accurate time measurements.

It was soon easy to recognise the J or I waves at a glance. Once these waves were identified, it was fairly easy to recognise the other peaks. The ECG and heart sounds were recorded simultaneously in all cases and were most valuable in identifying the isometric and early diastolic waves. No serious difficulties were encountered in recognizing artifacts. As no damping was employed the respiratory forces resulted in well defined, large, irregular and easily identifiable waves. Between respiratory distortions, an average of at least three unaffected heart beats could usually be identified and studied. It was customary to study the beat in the middle

of two successive respiratory cycles. The average values of the amplitudes were derived from all the undistorted Bcg signals of the two respiratory cycles. As the expiratory force in the anaesthetized rat is short and fast, it is also clearly shown in about 65% of the phonocardiograms.

As high heart rates sometimes resulted in a fusing of the atrial and presystolic waves of two successive heart beats, it was decided to divide the rats into four groups according to weight. The four groups were thus classified as follows: The first group consisted of male and female rats ranging in weight from 230 to 320 grams. The second and third groups were males and females ranging in weight from 320 to 520 grams. The fourth group of rats consisted of males weighing less than 200 grams. The differences in heart rates of the various groups with its possible influences on the Bcg pattern were thus treated separately.

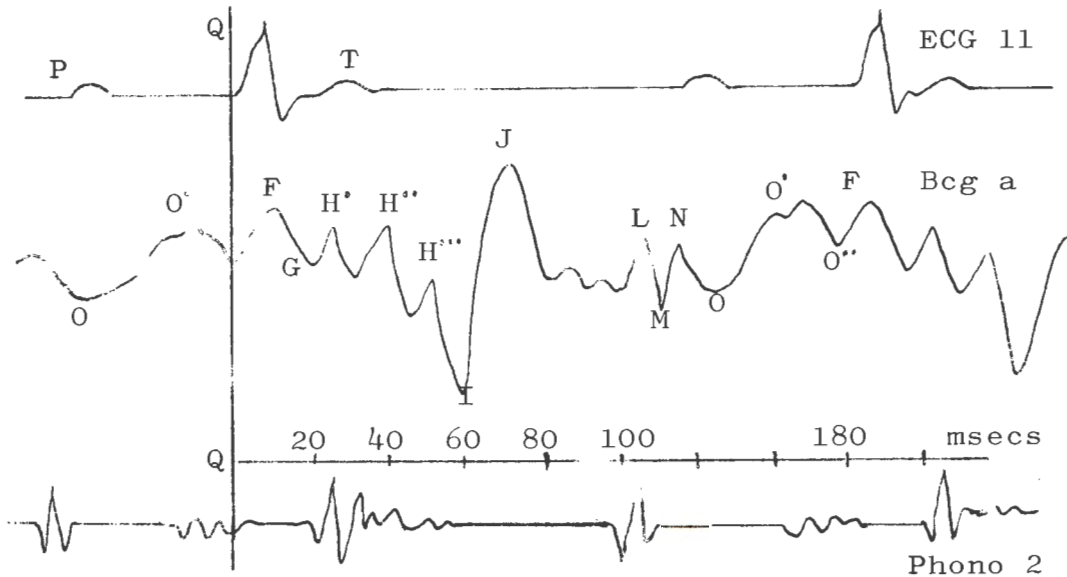
Although some differences in the Bcg pattern and amplitude were found among individuals, it seemed that rats of the same strain and age showed fairly consistent patterns. A group of 5 males with an average weight of 245 grams was used as a separate experimental group. Recordings of these 5 rats were made regularly at 2 to 5 day intervals until their average weight was 270 grams (20 days later). The

recordings showed a great degree of similarity although some differences were noticed.

B. The normal ballistocardiogram of young rats

Rats weighing from 230 to 320 grams were considered as young, fully grown rats. The general pattern of the UF Bcg (a) of rats is shown in Fig. 6.

FIG. 6. GENERAL PATTERN OF RAT UF BCG (a).



The UF Bcg (a) of the rat is more complex than that of the dog or rabbit. Pretorius (1962^{a,b}) recognized three main parts in the recordings of dogs, viz., a pre-ejection complex, ejection complex and a diastolic complex. In rats four phases can be distinguished, the atrial wave

being clearly separated from the diastolic complex. This is in accordance with our earlier study (Pretorius et al. 1966).

The mean times of the different waves for 64 young rats (230 to 320 grams) are shown in Table IA. The amplitudes are shown in Table IB.

(i) The atrium wave complex: The atrium wave complex consisted of at least four waves which were designated the O', O'', F and G waves. The first negative peak following N could usually be identified as the O wave. The O wave followed the preceding Q wave at about 124 msec (min. 118 - max. 142 msec). The O' wave followed after a positive deflection of the O wave and formed a small negative peak or depression. The O' wave was considered as the first atrial wave. It peaked at about 148 msec after Q, and from 16 to 28 msec after P. The O'' wave was negative and peaked shortly before the F wave. The O'' wave followed Q of the preceding beat at an average of 155 msec and P after about 45 msec. It was often fused with the F and G waves and could not be identified with certainty in 8% of the recordings.

The atrial wave showed a considerable amount of variation in amplitude. It was often difficult to identify, the pattern was different at various heart rates and was often

TABLE IA
Q-TIME MEASUREMENTS OF THE UF BCG (a) WAVES
OF 64 'NORMAL' RATS

	RANGE	MEAN
Weight	230 - 320 grams	275 grams
Heart rate	300 - 470 /min.	390 /min.
Systole	72 - 100 msec	79.7 msec
P-F	48 - 58 msec	50.4 msec
Q-F	1 - 9 "	4.6 "
Q-G	12 - 18 "	15.2 "
Q-H'	18 - 26 "	22.4 "
Q-H''	32 - 42 "	36.6 "
Q-H'''	46 - 56 "	49.6 "
Q-I	50 - 62 "	55.9 "
Q-J	64 - 76 "	71.6 "
Q-L	96 - 120 "	110.2 "
Q-M	102 - 128 "	114.0 "
Q-N	114 - 130 "	120.5 "
Q-O	118 - 142 "	124.0 "
Q-O'	$\pm$ 148 "	
Q-O''	$\pm$ 155 "	

TABLE IB

AMPLITUDES OF THE UF BCG (a) WAVES OF 64 'NORMAL'
'NORMAL' RATS

	RANGE		MEAN
Weight	230	- 320 grams	275 grams
F-G	0.2	- 2.1 cm/sec ⁻²	1.2 cm/sec ⁻²
H'	0.183-	1.5 "	1.0 "
H''	0.55 -	3.3 "	1.6 "
H'''	0.185-	2.8 "	1.3 "
H''' I	0.2 -	3.3 "	2.4 "
IJ	3.2 -	6.4 "	4.5 "
O-O'	0.9 -	3.0 "	1.6 "
L	0.55 -	3.1 "	1.65 "
M	WIDE		?
N	WIDE		?

not identical in the same rat after a day or two. Even a change in the heart rate or duration of systole in the same rat markedly affected the pattern of the atrium wave. The O to O' excursion was, however, fairly constant

and the mean headward acceleration from 0 to 0' amounted to 1.6 cm/sec^{-2} (0.9 to 3 cm/sec^{-2}).

The F wave was a positive wave which followed P at a mean of 50.4 msec (48 to 58 msec). It followed from 0 to 9 msec after Q. It was often of small amplitude and partly obscured by the isometric waves. The F wave was absent in 6% of the recordings. In the rat it preceded the first heart sound and was considered to be of atrial origin (Chapters 8 and 9).

The G wave (FG) was negative and followed Q after 12 to 18 msec (mean 15.2 msec). It was of about the same frequency as the F wave, but of a lower frequency than the H waves. The mean amplitude of the G wave was about the same as that of the first H wave (GH). The G wave peaked at the very beginning of the first heart sound in 83% of the rats. It peaked a few msec later in 9% of the recordings.

(ii) The isometric or pre-ejection wave complex: The waves of the isometric contraction phase were indicated by the letters H', H" and H'''.

The first H wave (H') followed the Q wave after 18 to 26 msec (mean 22.4 msec). The amplitude of H' varied from 0.18 to 1.5 cm/sec^{-2} , with a mean value of 1.0 cm/sec^{-2} .

The first H wave (H') peaked during the first third of the first heart sound. It was a positive wave.

The second H wave (H'') followed the Q wave in 32 to 42 msec (mean 36.6 msec). It was absent in one female and one male rat (less than 2%). The H'' wave had a mean amplitude of 1.6 cm/sec^{-2} . It varied between a minimum of 0.55 and a maximum of 3.3 cm/sec^{-2} with a mean value of 1.6 cm/sec^{-2} . The H'' wave was notched in 20% of the females but in only 8% of the males. If notching was present, the time difference between the two peaks was from 10 to 12 msec. In some cases, especially where the left and right ventricles seemed to be slightly desynchronized, the H'' wave showed a deep negative wave before it turned positive to peak as H''' . Most of the cases where notching of the H'' wave occurred showed a slightly longer first heart sound. It was considered as prolonged if its duration was in excess of 44 msec. It should be noted that the least amount of desynchronization between the left and right ventricles could be detected at the high recording speeds used in these experiments. It was therefore not considered as an indication of myocardial malfunctioning.

The H''' wave peaked positively from 46 to 56 msec (mean 49.6 msec) after the Q wave. In about 40% of the recordings the H''' wave peaked at 48 msec, while 40% of

the rest peaked at 52 msec after the Q wave. The H''' wave showed considerable amplitude variation. The minimum amplitude was $0.185 \text{ cm/sec}^{-2}$ and the maximum 2.8 cm/sec^{-2} with a mean of 1.3 cm/sec^{-2} . The H''' wave was sometimes (about 12% of the rats) fused with the I wave and created the impression of a notch in the latter wave (see Chapters 8 and 9).

(iii) Ejection wave complex: The waves forming this complex were designated the I and J waves and were the most conspicuous waves found in the recordings made during this study.

The negative wave following Q at 50 to 62 msec (mean 55.9 msec) was identified and treated as the I wave. The amplitude of the I wave ($H''I$) varied from 0.2 to 3.3 cm/sec^{-2} with a mean of 2.4 cm/sec^{-2} . This large variation, especially the occurrence of very low values, was thought to be due to a 'shift' of the H''' wave to a lower position in relation to the base-line. This was usually found when the H'' and H''' waves were affected by a desynchronized isometric contraction (see H''' wave).

The positive wave following Q at 64 to 76 msec (mean 71.6 msec) was designated as the J wave. In 62% of the recordings the J wave peaked at 70 to 72 msec after the Q wave. The amplitude of the J wave (IJ) varied from

3.2 to 6.4 cm/sec⁻² (mean 4.5 cm/sec⁻²). The J wave showed the least variation in time and amplitude of all the identified waves.

Examples of curves considered as normal from this weight group, are shown in Fig. 7.

(iv) Diastolic wave complex: The normal recordings of rats in this group showed no definite K wave. With the commencement of the second heart sound, however, a fairly clear positive wave could be identified as the L wave. The L wave followed Q in 96 to 120 msec (mean 110.2 msec). The most commonly found peaking values were 108, 110 and 112 msec after Q.

The M wave was identified as the first negative wave following the L wave. The M wave was of approximately the same frequency as the L wave. The M wave followed Q in 102 to 128 msec (mean 114 msec). The majority (52%) of M waves peaked at 112, 114 or 116 msec after Q. It could not be identified in 6% of the recordings. The M wave usually peaked during the second part of the second heart sound.

The positive wave following M was identified as the N wave. It was considered to be of slightly lower frequency than the L and M waves. The N wave followed the Q wave after a mean period of 120.5 msec. The Q-N

FIG. 7 REPRESENTATIVE RECORDINGS OF FOUR 'NORMAL' RATS

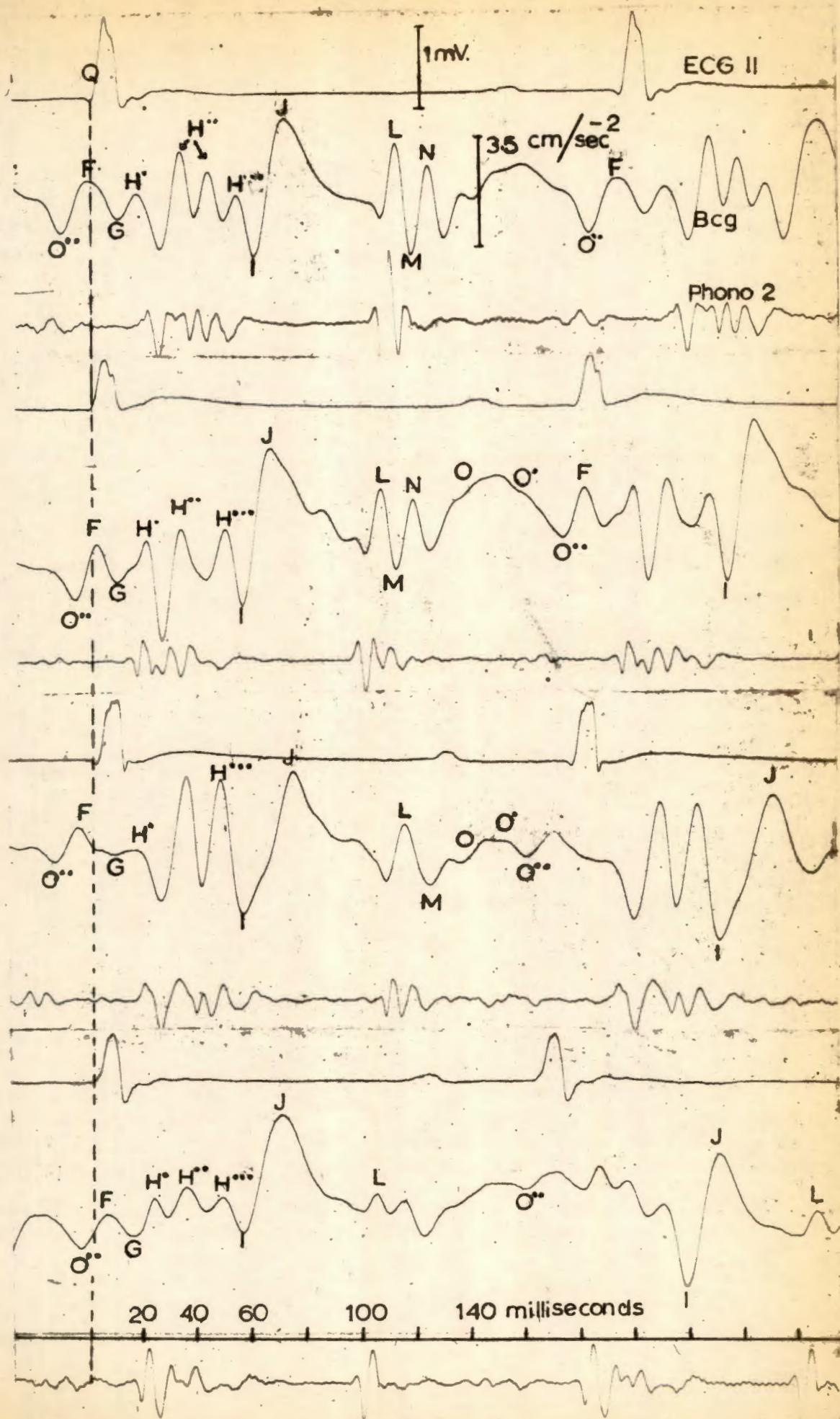
From the top downwards the ECG (lead II), the UF Bcg (a) and the phonocardiogram are shown. Paper speed = 500 mm/sec.

Note the complex isovolumetric waves consisting of three H waves.

The atrial waves O", F and G are clearly visible in the recordings.

The HI wave shows greater variation in amplitude than the IJ wave.

FIG.7. TYPICAL NORMAL UF BCG a OF 'NORMAL' RATS



time varied from 114 to 130 msec. In one instance a Q-N time of 140 msec was recorded.

From the N wave peak a negative acceleration was usually found to form a part of the O wave. The N wave peaked at the cessation of, or a little later than, the second heart sound.

C. Discussion

The group of rats from which these observations were made, consisted of 36 males and 28 females ranging in weight from 230 to 320 grams. Recordings of more rats were made in this weight group but with a different platform and accelerometer. No marked differences in pattern or amplitude were noticed but they were excluded from the calculations because the platform was calibrated by the pendulum calibrator. The recordings of rats included in the study of this group were thus all made with the same accelerometer, at the same calibration (direct natural frequency method) and the same amplifier sensitivity.

In Chapter 5 the variations in Bcg (a) pattern associated with age and weight will be discussed. The recordings of this group of rats (230 to 320 grams) were considered as the basic 'normal' recordings for the following reasons:

(i) It was noted that rats of various mass, that is usually of different age, showed different Bcg (a) patterns. Although the differences were not always consistent, factors such as different heart rates and the ratio of body weight to heart weight were thought to play an important part in the Bcg (a). It was further reasoned that these, perhaps, small variations might obscure some important aspects of the normal Bcg (a).

(ii) Old rats might show abnormal Bcg (a) patterns and if they are included in the calculations of the normal pattern, they may lead to serious error. It was found that most of the rats developed a respiratory disease (bronchiectasis) in our animal room at the age of about eight months. This was confirmed in a histological study (Burger 1967). It was further found that most of the older rats showed signs of hypertension and that rupture of the pulmonary vessels sometimes resulted after arterenol administration (Chapter 7).

(iii) For obvious reasons, e.g. high heart rates, body to heart weight ratio and incomplete growth, the Bcg (a) patterns of rats weighing less than 200 grams were also excluded when calculating the normal pattern.

(iv) As a larger amount of anaesthetic was used to

perform surgical procedures, e.g. vena caval occlusion or catheterization, recordings of these rats were also excluded in the calculations of the normal pattern.

It was shown by Corbascio and Smith (1966), Pretorius (1962^b), Pretorius et al. (1966, 1967) and Green (1967) that intravenous doses of pentobarbitone affects the Bcg (a) pattern of dogs, rats, goats and rabbits. It was further noted that the catheterization of animals resulted in changes of the Bcg (a) pattern. Pretorius et al. (1966) showed a longer P-Q time and an increased Bcg (a) pattern for rats after catheterization. Green (1967) found an increase in the IJ wave amplitude of rabbits after catheterization. In this study the left common carotid artery was used for catheterization. The depressor nerve and the sympathetic cord runs parallel and very close to the common carotid artery. Any surgical procedure involving the carotid arteries may seriously damage or affect the normal functioning of those nerves. As the one nerve is of sympathetic and the other of parasympathetic origin, damage to any or both of them may seriously alter cardiovascular function. Some of these changes are discussed in Chapter 6.

(v) A further possible source of variation kept in mind was the indirect effect of the anaesthetic. A small decline in the IJ wave amplitude was often found in the

recordings 25 to 30 minutes after the anaesthetic was injected. This decrease in Bcg (a) amplitude might be due to a lowered body temperature and a lowered myocardial oxygen uptake (Rushmer 1961). Anaesthesia became effective 5 to 10 minutes after the injection of 'Sagatal'. For calculating the normal Bcg (a) patterns recordings were made as soon as possible after the injection (in less than 20 minutes).

The recordings from this group of rats showed some individual variations but the I and J waves, which were suspected to be caused by the forces of ejection, were remarkably constant. The UF Bcg (a) of rats is, however, fairly complex. From this study it was clear that extremely small variations in cardiovascular dynamics may alter the pattern, amplitude and Q-time measurements of the Bcg (a). Extreme care should therefore be excercised in interpreting the recordings.

It is concluded that most of the confusing variations in the Bcg (a) pattern can be eliminated by careful selection and treatment of the rats.

CHAPTER 5

VARIATIONS OF THE UF BCG (a) PATTERN IN RATS OF DIFFERENT AGE GROUPS

In any certain strain of rats the body weight correlates with age when fed on a fixed diet (Rademeyer 1963). From age and weight graphs the age of rats up to about 400 days can be estimated fairly accurately when the weight is known. In the present study, rats were divided into three age groups, according to weight. Very young rats, viz. 180 to 200 grams (10 to 12 weeks old) constituted the youngest group included in this study. A second group weighing from 230 to 320 grams (18 to 24 weeks old) was included and considered as normal, fully grown rats. The third group was composed of rats weighing from 330 to 500 grams (older than 25 weeks). The young group had a mean weight of 190 grams, the normal group a mean weight of 250 grams and the third group a mean weight of 420 grams. The latter group was classified as old.

A. Results

The mean Q-time measurements for the different groups are shown in Table IIA. The mean UF Bcg (a) amplitudes can be seen in Table IIB.

From these tables it is evident that the amplitudes and

Q-time intervals of the isometric waves, H', H'' and H''' did not change much with age. The Q-I and Q-J times showed a more conspicuous increase with age. This seemed to be true in the case of the Q-O'' time as well.

The only amplitude changes that seemed to be significant were that of the H'''I and the IJ waves. In young rats the mean amplitude of the IJ segment was found to be 4.0 cm/sec^{-2} . It increased to 4.4 cm/sec^{-2} in adult ('normal') rats and it decreased to 3.8 cm/sec^{-2} in old rats. This tendency was more strikingly illustrated when the amplitudes (at the same amplifier sensitivity) were measured in millimeters. Most of the other waves showed changes of less significance.

A further noteworthy feature of variance between the age groups was the range of the time and amplitude of the different waves. Although the mean time and amplitude values did not differ much in the different age groups, the minimum and maximum values did. The smallest IJ amplitudes were observed for the old age group. In young rats less variation existed between maximum and minimum values. In old rats the greatest variance was found, while the normal (adult) rats showed a range of values somewhere in between.

The recordings for old rats showed a general change of pattern, characterised by rounded peaks and decreased

slopes (see point (iii) below).

B. Discussion

(i) Q-time measurements: Starr and Noordergraaf (1967) states that they secured very little help from time measurements in the detection of abnormalities in ballistocardiograms of man. Although it was observed that some of the ballistic waves are retarded in disease, it seems difficult to use time measurements per se as a yardstick for detecting cardiac abnormality. Furthermore, the splitting or 'rounding' of wave peaks commonly found in older age groups and abnormal records, might seriously hamper accurate measurements of wave identification. Scarborough et al. (1958) and Moss (1961) produced several tables giving normal UF Bcg time measurements for man, but such tables for rats could not be found in the literature.

In the present study the duration of mechanical systole, that is from the beginning of the first heart sound to the beginning of the second heart sound, was also measured. As such, the duration of mechanical systole remained essentially the same in the different age groups (see Table IIA). The duration of mechanical systole was decreased in young rats, which correlated with the slightly higher heart rates of this group.

TABLE IIAQ-TIME MEASUREMENTS (MILLISECONDS)

	'OLD'		'NORMAL'		YOUNG	
	Mean	Range	Mean	Range	Mean	Range
Weight (grams)	420	340-510	275	240-310	196	188-198
P-F	54	46- 68	50.4	48- 58	47	42- 50
Q-F	7	4- 11	4	0- 6	2	0- 4
Q-G	15	12- 18	15	11- 16	12.5	10- 14
Q-H'	23	20- 28	22.5	18- 24	20.5	20- 24
Q-H''	38	32- 42	37	32- 42	33	32- 38
Q-H'''	52	40- 56	50	45- 54	44.5	40- 48
Q-I	60	48- 64	56.5	50- 62	50	48- 56
Q-J	76.5	72- 82	71.6	66- 74	64	60- 68
Q-L	104	94-114	104	96-114	100.5	96-112
Q-M	114	104-120	111	98-116	106.5	96-116
Q-N	122	100-128	120	108-132	113.5	100-128
P-O	11	7- 14	16	6- 18	12	8- 14
Q-O	128	116-136	126	118-134	121	118-132
Q-O'	146	130-150	149	138-152	134	138-144
Q-O''	160	150-171	156	148-161	144	140-152
Systole*	78	76- 82	78	74- 80	74	68- 76
Heart rate (per min.)	370		380		412	
No. of Rats	26		39		25	

* Mechanical systole.

TABLE IIB

<u>BCG (a) AMPLITUDE MEASUREMENTS (cm/sec⁻²)</u>						
	'OLD'		'NORMAL'		YOUNG	
	Mean	Range	Mean	Range	Mean	Range
H' (GH)	0.9	0.4-1.4	1.2	0.2-1.0	0.7	0.2-1.1
H"	1.5	0.8-3.6	1.5	0.4-2.6	1.8	1.1-2.5
H'''	1.2	0.4-2.2	1.4	0.4-2.1	1.1	0.4-2.5
H'''I	1.6	0.4-3.3	1.8	0.4-3.1	1.9	0.4-2.5
IJ	3.8	1.3-4.2	4.4	3.0-5.1	4.0	2.9-4.5
L	1.1	-	1.2	-	1.2	-
O-O'	1.6	0.9-3.0	1.4	0.9-3.0	1.9	-
O'	0.8	-	0.4	-	0.6	-
O'-O''	1.0	-	1.1	-	1.3	-
O''-F	0.8	-	1.1	-	1.0	-

The ratio between Q-J time and the duration of mechanical systole, however, correlated significantly with age. In old rats this ratio approached unity and was even above that in 15% of the 'old' rats. In young rats this ratio was in the region of 5:6 and in young adult ('normal') rats in the region of 7:8 (see Chapter 10).

In scrutinizing the recordings it became evident that at least three factors, acting separately or simultaneously might affect the Q-J:mechanical systole time ratio.

The first factor that might partially increase the Q-J time was an increase in the duration of the isometric contraction phase. This is shown by the progressive increase in Q-H''' time with age. Although the mean values for old and 'normal' rats did not show this clearly, it was quite conspicuous in some of the recordings of old rats. The onset of ejection was therefore retarded in the recordings of some old rats (Fig. 8).

The second factor that was thought to increase the Q-J time was a decrease in the H'''I slope. In some old rats the H''' wave was nearly absent or superimposed on the 'H''I' wave. This 'shifting' of the H''' wave created the impression of a much more rounded I wave (Fig. 9).

The last factor that was thought to affect the Q-J time was the decreased IJ slope found in almost all the recordings of the old group. In some recordings of this group the J wave peaked at the very end of systole, with the result that the L wave followed sooner on the J peak. From Table IIA it is evident that the Q-L time increased with only 3.5 msec while the Q-J time increased by a mean value of 12 msec with age.

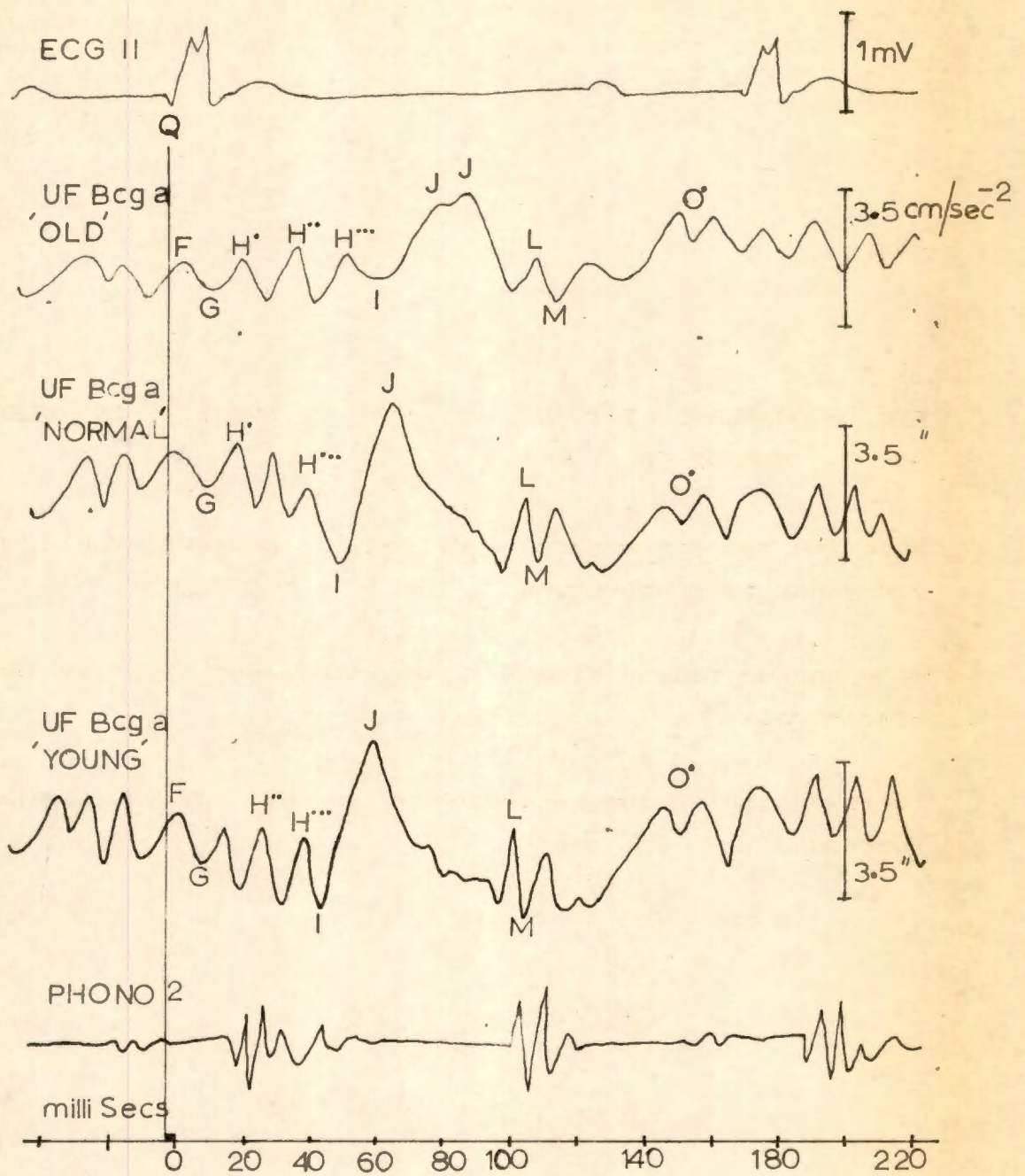
FIG. 8 GENERAL PATTERN OF THE UF BCG (a) IN DIFFERENT AGE GROUPS

From the top downwards the UF Bcg (a) pattern of old, normal and young rats are shown.

Note the decreased HI and IJ amplitude and slope in the case of old rats.

The Q-J time in the recording of the old rat is remarkably increased.

FIG.8. GENERAL CHANGE IN PATTERN WITH AGE



(ii) Wave amplitude measurements: A rather wide scatter in the amplitude of the different waves in all three groups was found. Scatter can be decreased by taking the square root of the overall measurement (Starr 1955). In their recent book Starr and Noordergraaf (1967) thoroughly discussed the amplitude of the ballistic waves found by most investigators. Valuable tables are given and the discrepancies discussed. From their discussion it is apparent that it is extremely difficult to tabulate normal human amplitude standards. Technique and apparatus are still far from standard as well as the procedure in measuring the waves.

Accurate placing of a base-line, particularly in an undamped system, is impossible. In the present study the overall amplitudes of waves were therefore measured.

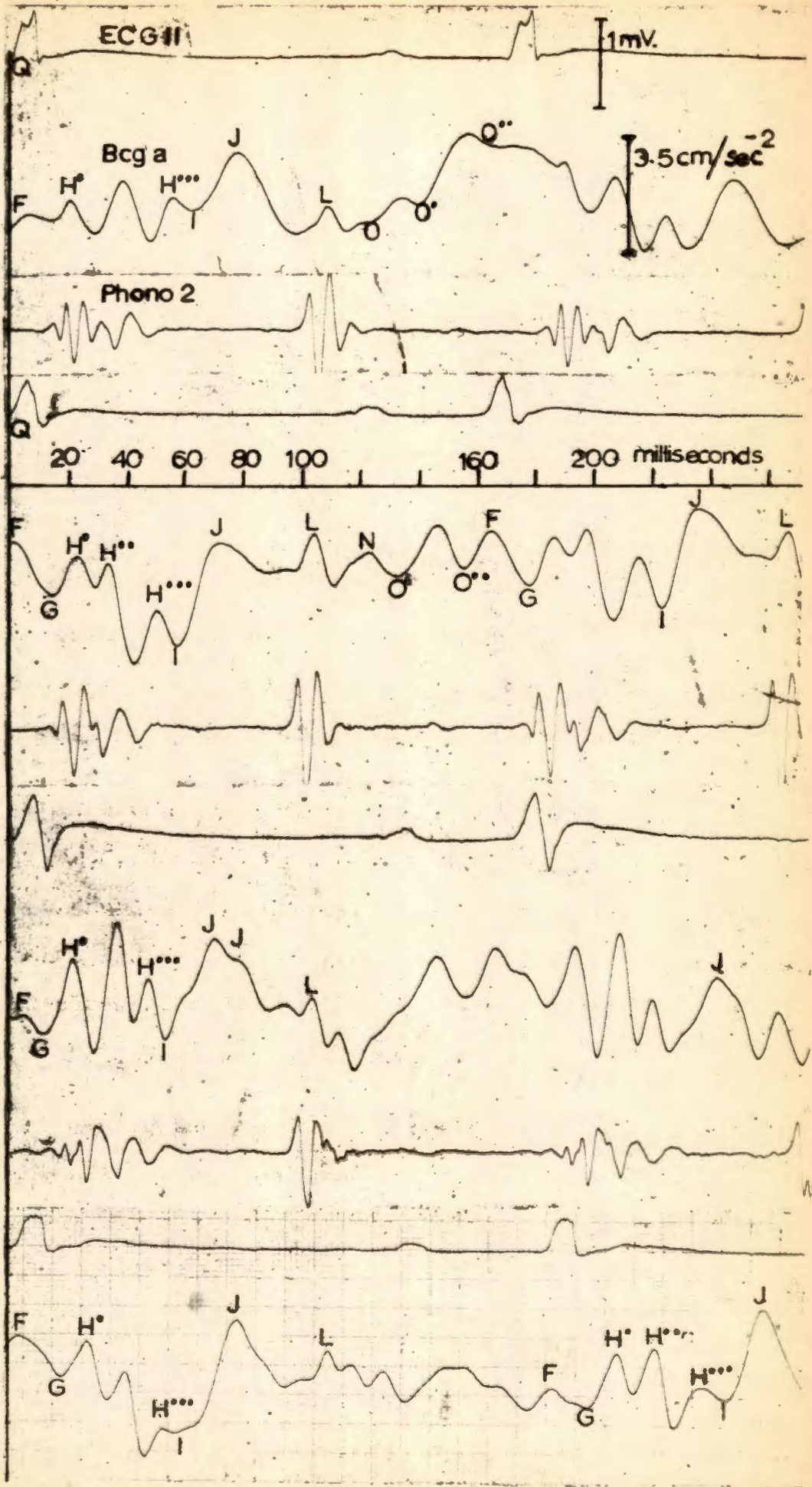
From Table IIB it is evident that most of the waves measured, did not show marked changes with age. Important exceptions, however, were the HI and IJ waves. The H^{III}I wave showed a progressive decrease with age. This was also found to be the case in human recordings made by Moss (1961) and Starr (1966).

The IJ wave had the highest amplitude in the case of 'normal' rats. It was lower in young rats and much lower in the old rats. Values as low as 1.2 cm/sec^{-2} were found in some old rats. The lowest value found in

FIG. 9 A FEW EXAMPLES OF UF BCG (a) RECORDINGS OF
OLD RATS

Note the greater individual differences in the general
pattern and the 'rounded' appearance of the individual waves.

FIG.9. TYPICAL UF BCG a OF 'OLD' RATS



'normal' rats was 3.0 cm/sec^{-2} , which is more than double the lowest amplitude found in some of the old rats.

(iii) Observations not reflected in Tables IIA and IIB:

Looking at the mean values of time and amplitude, the Tables seemed not to reflect conspicuous changes as expected from comparing the recordings. Starr and Noordergraaf (1967) came to the following conclusion: "Unfortunately, differences between normal and abnormal records occur not only in items that are easily measured, like amplitude and timing, but also in conspicuous changes of form which are very difficult to describe simply in quantitative terms Finally there is real doubt that we yet know the measurements most worth making, in either the normals or in our patients

Representative recordings of old rats are shown in Fig. 9. If these recordings are compared to those of 'normal' rats (Fig. 7) or young rats (Fig. 10) the difference in contour of the UF Bcg (a) is immediately realized. In the case of old rats the descending leg of the H'' wave is in most cases more conspicuous than the H''' negative peak. If the H'' wave is the 'real' I wave, H''' could then be identified as a notch in the I wave, in which case the H''' would be absent. The first complex in the third curve (Fig. 9) and the last curve in

Fig. 10 illustrates this point. In most of the other curves shown, the H'' wave seems to be superimposed on the 'IJ' wave, if $H''I$ is taken as the 'real' I wave. During different phases of the respiratory cycle most of the H'' waves could be identified and were considered as such in the calculations. Furthermore, Q-time measurements confirmed that most of the I or J wave notches were in fact H'' waves. This 'shifting' of the H'' wave was also encountered in a few of the recordings of 'normal' and young rats. In recordings discussed in this chapter the $H''I$ wave was taken as the real HI wave and the calculations made accordingly (see Chapters 8 and 9).

A further striking aspect of difference found in the recordings for old and 'normal' rats, is the slope and amplitude of the J wave. In the case of 'normal' rats the IJ and JL segments can clearly be distinguished, while it is not so easy in the case of old rats.

Another possible point of difference is the impression that the waves in old rats are more sluggish and round. This is more evident at a paper speed of 250 mm/sec than at 500 mm/sec as in Figures 7 and 9.

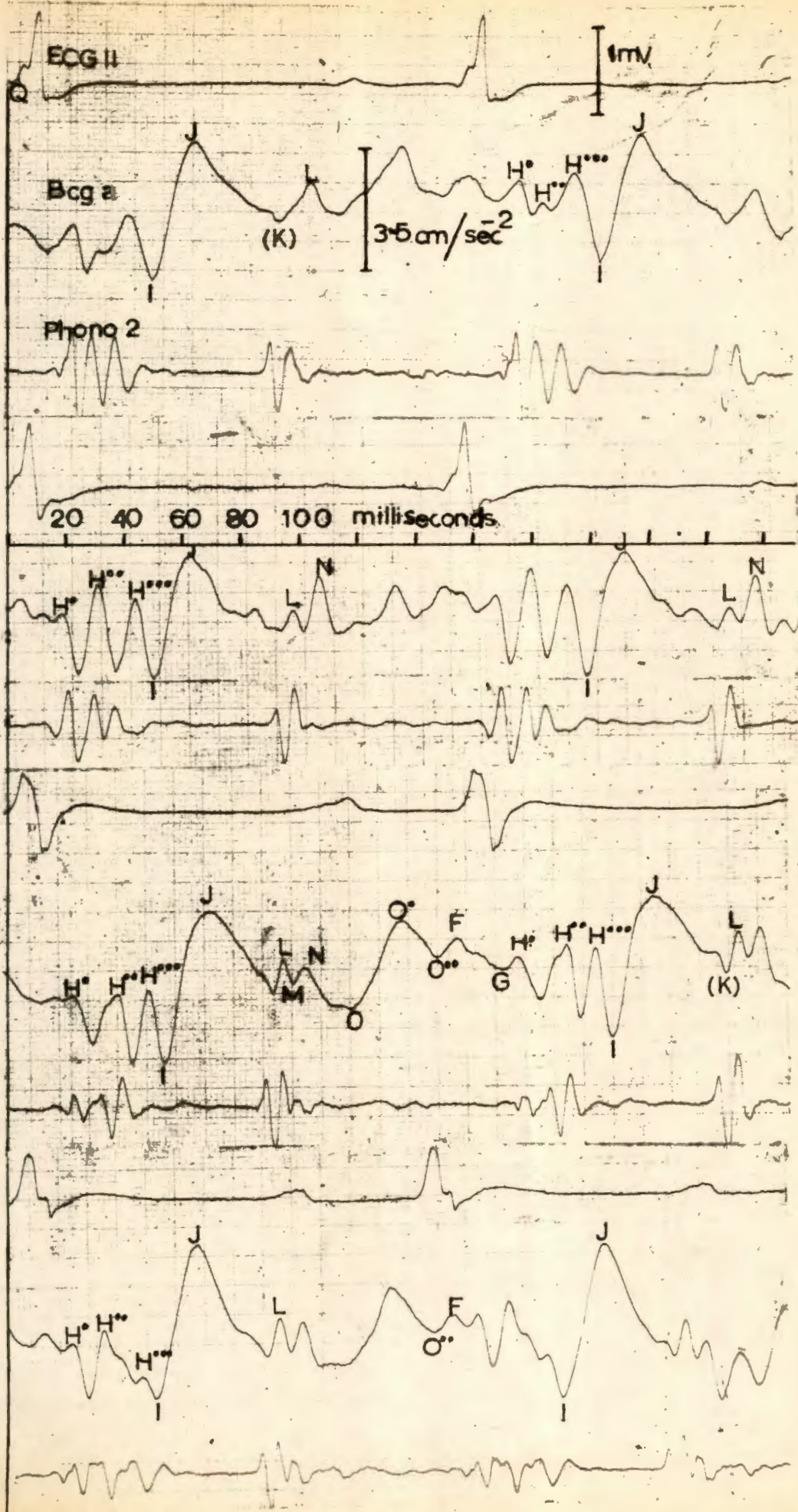
When more complexes of the Bcg were visually inspected, the overall appearance of recordings of old rats showed

FIG. 10 REPRESENTATIVE RECORDINGS OF THE UF BCG (a)
OF YOUNG RATS

Note that the general pattern is very similar to that of
'normal' rats.

The IJ wave shows less individual variation than the other
Bcg waves.

FIG. 10 TYPICAL UF BCG a OF YOUNG RATS



a greater amount of variation in Bcg complexes during a respiratory cycle. This is evident by looking at only the two successive complexes per rat that could be shown in Figures 7 and 9. It seems, therefore, that the criterium of 'normality' proposed by Brown et al. (1952) might apply to the recordings of rats as well.

By comparison, the recordings of young rats hardly differed from those of 'normal' rats. In most young rats, however, the atrium waves (O', O" and F) and pre-ejection waves (H', H" and H''') had a squashed appearance. This was undoubtedly due to the higher heart rates of the young group.

(iv) The ratio of body weight to heart weight: According to Hamilton and Dow (1965) the logarithm of heart weight is directly proportional to the logarithm of body weight. One may then reason that an increase in body weight without a proportional increase in heart weight would result in a decrease in the measured acceleration of the cardiac force.

A strictly hypothetical situation where the increase in body weight with age is logarithmic and the increase in heart weight in rats is linear was visualized. It is suggested that this situation may develop in rats when

the body weight exceeds 300 grams, as the increase in body weight of rats after the attainment of adulthood is largely due to obesity. It was further reasoned that this extra 'dead weight' of the body can, for all practical purposes, be added to the platform weight, if the coupling between platform and body can be kept constant, as the total mass of the body and platform can in any event be regarded as a single mass (Burger et al. 1953, 1956, and Burger and Noordergraaf 1956).

It was decided that an increase in the platform weight might effectively simulate an increase in 'dead weight' of the body, as the total mass of the system (subject plus platform) is of importance. The ratio of the mass of the total system to heart weight might determine the actual amount of measurable force transferred to the platform (accelerometer).

Means of increasing the 'body weight' of rats without it having a profound effect on cardiac function, were investigated. It was reasoned that if the body weight of a young adult rat ($\pm$ 250 grams) could artificially be increased to the body weight of an old rat ($\pm$ 350 grams), the recorded acceleration should resemble recordings obtained from old rats - if the ratio between heart weight and body weight is the most important contributing factor. In a pendulum type of UF ballisto-

cardiograph an increase in platform weight does not alter the natural frequency of the system. Loading of the platform can be done in such a way that the centre of gravity of the system (rat and platform) is not disturbed. It was further reasoned that the only possible change in the system might be in the degree of coupling between rat and platform, as an undamped system was used in this study.

To increase the 'effective' body weight of a rat, two lead bars weighing exactly 45 grams each, were placed symmetrically around the centre of gravity of the system, flush with the torso supports of the platform (fig. 2). The rat was not moved at all. The loading of the platform resulted in changing the ratio of body weight to platform from about 63:1 to 2.5:1.

The result of loading the platform is seen in Fig. 11. The two upper recordings were made at a paper speed of 500 mm/sec, while the lower recordings were made at 250 mm/sec in order to show more cardiac complexes simultaneously.

When the platform was loaded, a decrease of about 40% in HI amplitude resulted. The IJ wave amplitude was reduced by about 25%. Measured by drawing a perpendicular through the I wave peak, a mean decrease of 7

degrees in the HI slope and 5 degrees in the IJ slope was noted. Phase shift resulted in the J peak being recorded about 4 milliseconds late in the loaded system. The atrial and H wave complex (isometric part) were markedly suppressed in the loaded system. Electronic filtering of the Bcg (a) signal through a low pass filter, attenuating signals above 30 Hz critically, produced remarkably similar results. In Fig. 12 the result of passing the Bcg (a) signal through a low pass filter with a cut off frequency of 15 Hz is compared to the same unfiltered Bcg signal. In this case the same tendency is more dramatically manifested. This may well be an interesting situation when dealing with the physical aspects of the method, as it clearly demonstrates that a heavy platform might act as a mechanical or electronic filter.

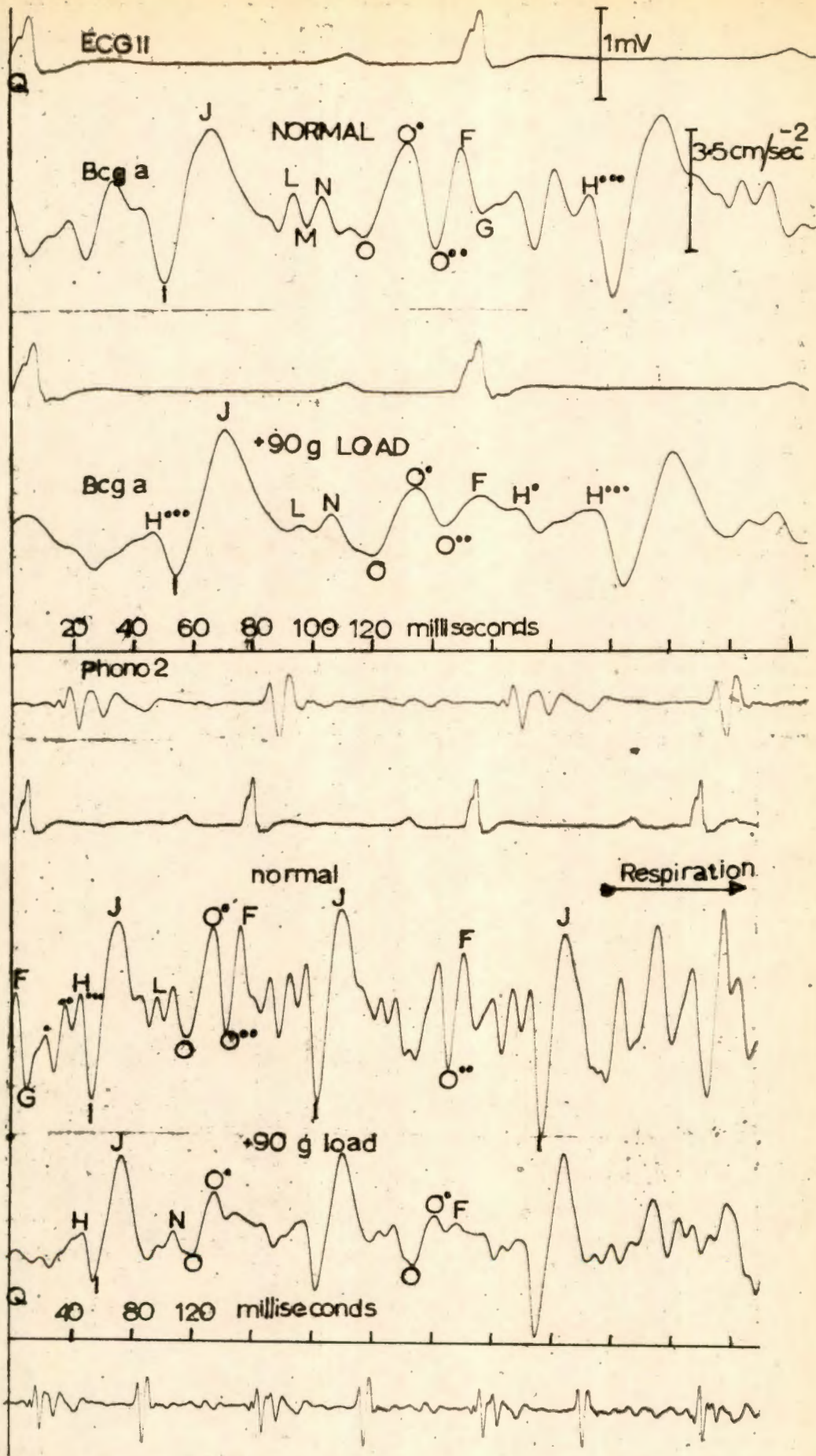
The most conspicuous effect of loading the platform on the UF Bcg (a) is the reduction in amplitude of the isometric and atrial waves. The amplitude of the atrial waves (O', O" and F) was decreased by about 50% (12 mm to 6 mm). The isometric waves (H', H" and H''') could not be identified individually. The commencement of the I wave was therefore considered as the H''' wave. The UF Bcg (a) of rats recorded using a loaded platform seemed to resemble the UF Bcg (a) of man to a remarkable extent.

FIG. 11 THE EFFECT OF LOADING THE PLATFORM ON THE
BCG PATTERN OF 'NORMAL' RATS

The two upper recordings were made at a paper speed of 500 mm/sec while the lower recordings were made at a paper speed of 250 mm/sec.

Note the attenuation of the isometric and atrial wave complexes when the platform is heavy.

FIG. 11. EFFECT OF LOADING ON BCG a



By comparing the recordings obtained from old rats with the 'loaded' recordings of this experiment, it was immediately evident that the differences in amplitude and slope cannot be accounted for by the weight ratios alone. The most striking difference seemed to be the much longer Q-J time and reduced HI slopes found in the recordings of old rats. It was concluded that the differences in the recordings of old rats should rather be explained in terms of difference of cardiovascular dynamics, although the physical aspects of weight could be a contributing factor.

Old rats might therefore show a general lowering of the Bcg (a) amplitude as a result of a less favourable ratio between body weight and heart weight. Although the effect of body weight in adult man seems to be of little importance, while the weight of children is important (Starr and Noordergraaf 1967), it may be concluded that the body weight in small animals is of importance in interpreting Bcg recordings.

(v) Earlier studies: In general the findings of this study confirmed that of an earlier study (Pretorius et al. 1966). There were, however, points of difference.

There were differences in Q-time measurements of the

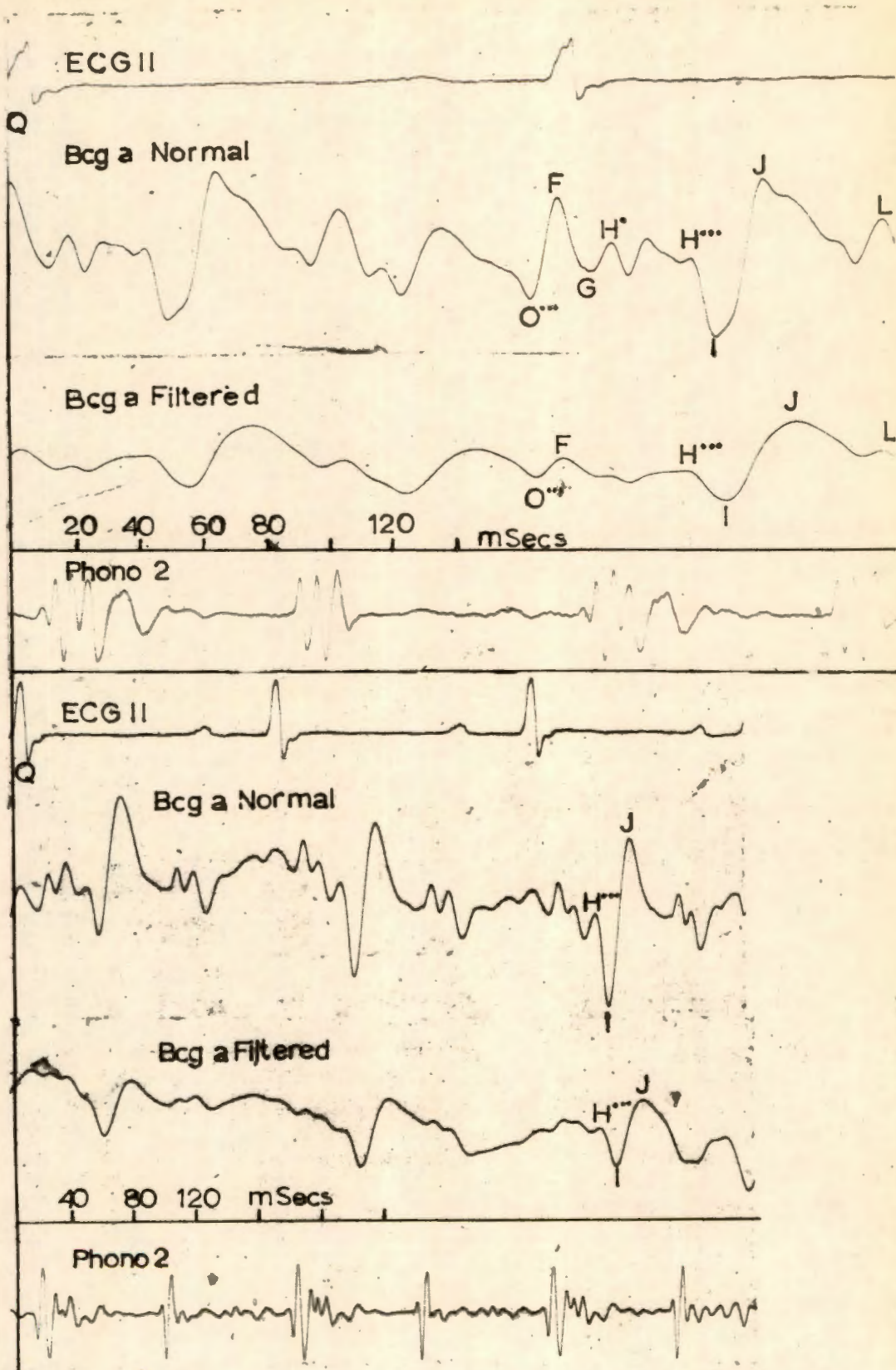
FIG. 12 ELECTRONIC FILTERING OF THE UF BCG (a) SIGNAL

The upper two recordings were made at a paper speed of 500 mm/sec while the two lower recordings were made at a paper speed of 250 mm/sec.

Note the overall phase shift and decreased amplitude of individual waves.

The isometric and atrial waves are dramatically reduced in amplitude when the Bcg (a) signal is filtered.

FIG.12. FILTERING OF BCG a SIGNAL



different waves, the values of the earlier study being slightly higher. (In the earlier study only the values of the H complex (H', H'' and H'''), the I wave and the atrial wave were published.) On the other hand the amplitudes of the different waves expressed in cm/sec^{-2} , were slightly higher. It seems possible, however, to account for most of these differences.

In the first instance a different ballistocardiograph was used. The Potchefstroom system (earlier study) had shorter supporting ropes which resulted in a natural frequency of 0.5 Hz. The Durban system (the present study) had a natural frequency of 0.38 Hz. The platform shape was also modified. In the Potchefstroom study a 'sunken centre' platform was used without any lateral or longitudinal devices to increase coupling. The Durban platform was flat with lateral supports as well as a longitudinal coupling support ('yoke' Fig. 2). As discussed earlier in this chapter, the loading of the platform introduced phase shift. It can also be reasoned (Rappaport 1956^a) that a heavier platform decreases coupling between body and platform. It is believed that most of the Q-time measurement differences can be explained by this phase shift as it is accepted that the coupling between the rat and platform is superior

in the case of the Durban platform. Although believed to be of minor or of very little importance, different types of pre-amplifiers for the Bcg signals were used in the two studies. All these instrumental differences make it difficult to compare the results in detail.

A further instrumental difference was the method of calibrating the amplitudes. In our earlier study (Pretorius et al. 1966) calibration was done by means of a transistor driven pendulum oscillator (Fig. 4). As discussed in Chapter 3, it is prone to difficulty and some error. In this study the platform was loaded with 150 grams at the approximate centre of gravity (balancing). The platform was allowed to oscillate at its natural frequency, covering a distance of 5 millimeters to each side of the resting centre of gravity. The acceleration was calculated by using the formula for simple harmonic motion, which is nearer to truth in this instance. This might explain the difference in amplitude found in the two studies concerned.

Of major importance too is the different strain of the rats. Although both strains were not pure, there might be quite a difference in cardiovascular physiology. This might be further influenced by the topographical and climatic difference between Potchefstroom and Durban.

Potchefstroom is about 5000 feet above sea level, while the laboratory in Durban is about 20 feet above sea level. Furthermore temperature fluctuations are more marked at Potchefstroom, winter temperatures dropping below freezing point and summer temperatures going to over 100°F. At Durban, by comparison, humidity is extremely high. Generally larger rats (old rats) were used in the Potchefstroom study to facilitate catheterization. In calculating normal values in the present study, rats used for pressure recordings were not included as in the case of the Potchefstroom study.

C. Conclusions

It is concluded that:

- (i) Old rats showed slightly lower HI and IJ amplitudes compared to 'normal' rats.
- (ii) The HI and IJ slopes were decreased in old rats.
- (iii) The ratio between Q-J time and the duration of mechanical systole was near unity in old rats.
- (iv) The difference between the Bcg (a) of young and 'normal' rats was small.
- (v) The Bcg (a) of rats of the different age groups showed some aspects of variance in the pattern which are

not readily expressed in numerical terms.

(vi) Differences in technique, instrumentation and the possible cardiovascular differences, explained satisfactorily the higher Q-time and amplitude values of an earlier study with rats as reported by Pretorius et al. (1966).

(vii) It is beneficial to use age or weight classification of small animals in describing normal values of the Bcg (a).

(viii) Small animals (rats) with low body weight and high heart rates and the associated cardiovascular dynamics are extremely suitable for experimental ballistocardiographic research.

(ix) A ballistocardiographic study on rats of a pure strain and of homogenous anatomy to limit scatter, is indicated for future investigation of the relationship between age and cardiovascular function.

CHAPTER 6

EFFECTS OF MECHANICAL CHANGES IN THE CIRCULATION ON THE BCG (a) PATTERN

Although extensively used as an experimental animal, very little research has been done on the circulatory dynamics of the rat. The relatively small size of rats may account for this. Small-sized homiothermous animals usually have high heart rates which demand sensitive apparatus. Furthermore the small size of the arteries and veins make it difficult to implant flowmeters or to use, for instance, balloon catheters. With the available facilities, a few alterations to the circulation, that can be considered mechanical, were brought about.

A. Catheterization of the carotid artery

Carotid catheterization is not considered as a primary mechanical modification of the circulation but the secondary influences are of importance and will now be discussed.

In an earlier study (Pretorius et al. 1966) it was noted that catheterization of the carotid artery caused an increase of the Bcg (a) amplitude in some rats. This was thought to be due to sympathetic stimulation.

Green (1967), working on rabbits, reported that in most cases an increase in IJ amplitude resulted from femoral

artery catheterization. In this study the HI amplitude did not show constant changes, while the heart rate showed an average increase of 26.4%. The response was very similar to that obtained when a small dose of arterenol was administered. It thus resembled sympathetic stimulation.

In the present study a small increase ($\pm 5\%$) in P-Q time was noted after catheterization. The heart rate increased by about 9% (range 5 to 25%) in most cases. Changes in Bcg amplitude were inconsistent. In most cases the IJ amplitude was slightly increased after catheterization. The atrial waves (O" and F) showed a more conspicuous increase. In some cases the amplitude of the atrial wave was increased by nearly 115%. In Fig. 13 an example of the increase in atrial wave amplitude is shown. There is a close resemblance to the changes observed when the myocardium was stimulated by small doses of catecholamines (Chapter 7).

Extreme care was taken in interpreting changes associated with catheterization. The rat has a relatively small blood volume, and it is difficult to heparinize the blood without increasing the immediate circulating volume. The catheters used in this study were all PE 50 polythylene 'Medicon' tubing cut to a precise length. The dead

space in the catheters and their fittings amounted to ± 4.8 minims. If the heparin was contained in 5 minims of fluid, a total of nearly 10 minims ($\frac{5}{8}$ cc.) of fluid had to be displaced in order to get the full dose into the circulation. The addition of fluid to the circulation of the rat in itself may cause a transient increase in Bcg (a) amplitude (see Chapter 8).

The pressure at which the fluid is administered is of importance too. If the saline is injected at a fast rate (high pressure) it may affect the circulation in various ways. The baroreceptors might be stimulated by the high pressure and cause vasodilation and cardiac inhibition. The injected fluid, of a lower viscosity than blood, would return to the right atrium more quickly and might increase central venous pressure and return quite substantially. In interpreting the effects of catheterization in small animals, the exact time after catheterization, the amount of fluid and the pressure at which the fluid is injected, must be taken into account. Some of the more direct effects of accidental mechanical stimulation or damage to the nerves in preparing the carotid artery for cannulation were discussed in Chapter 4.

B. Vena caval occlusion

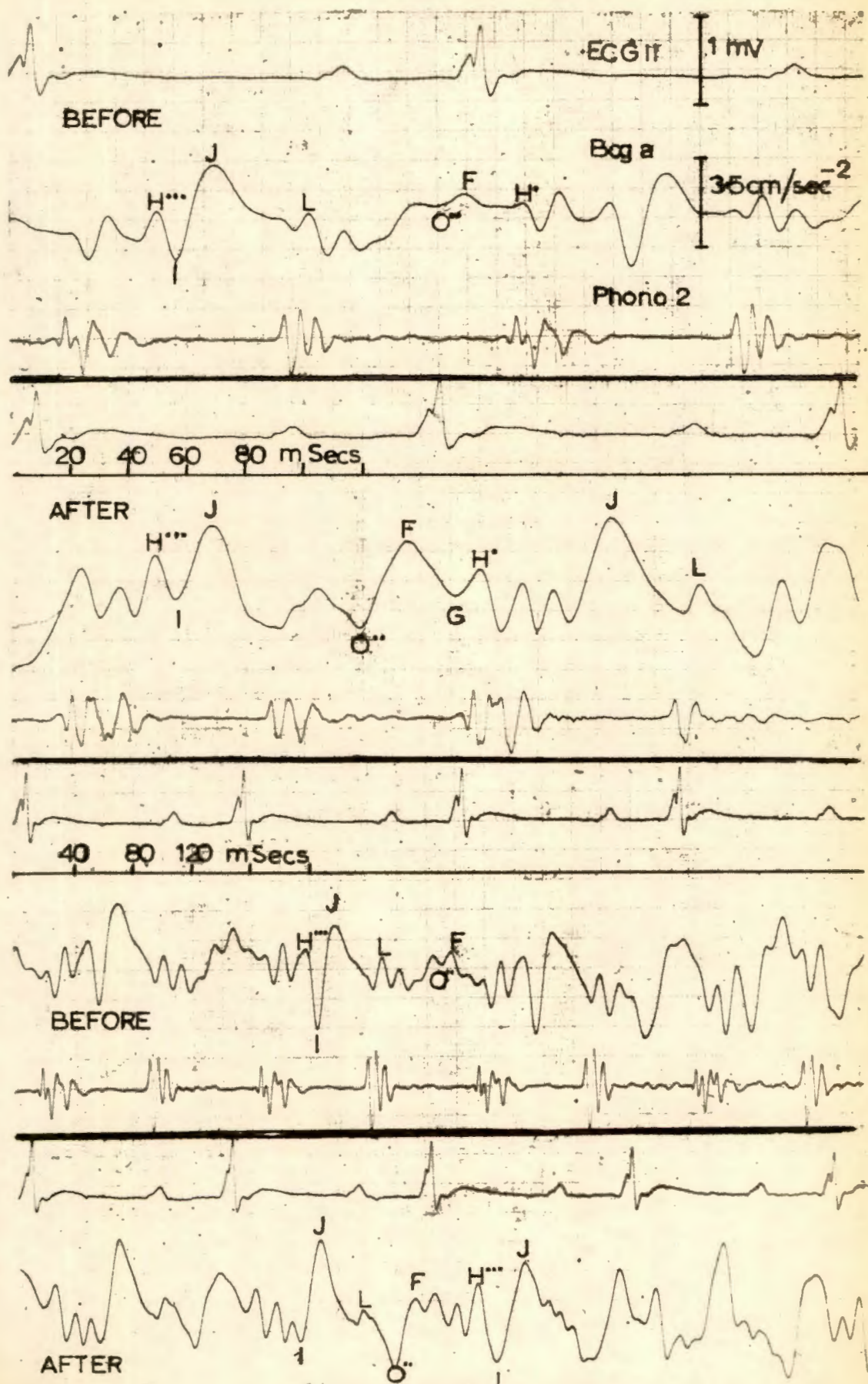
In order to establish the genesis of certain Bcg (a)

FIG. 13 THE EFFECT OF CAROTID CATHETERIZATION ON THE
UF BCG (a) PATTERN

The upper two recordings were made at a paper speed of 500 mm/sec. The lower recordings were made at a paper speed of 250 mm/sec.

Note the increased amplitude of the atrial wave complex after catheterization. The heart rate is also increased after catheterization.

FIG.13. EFFECT OF CAROTID CATHETERIZATION ON BCG a



waves the posterior vena cava was ligated by means of a snare (Fig. 5). Using this type of loop it was easy to occlude and open the vena caval flow. In order to omit the influence of catheterization on the circulation, vena caval loops alone were inserted in twelve rats. The effects of vena caval occlusion on blood pressure are discussed in Chapters 8 and 9.

The effect of posterior vena caval occlusion on the Bcg (a) and phonocardiogram is shown in Fig. 14. The top recording ("open 1") shows the 'normal' Bcg (a) pattern soon after the surgical placing of the loop. The Bcg (a) did not show any marked changes following the abdominal incision. An increase in respiratory rate was noted in most cases after the surgical procedure. Great care was exercised to avoid perforating the diaphragm when the snare was applied.

Occlusion and opening of the posterior vena cava by tightening and releasing the loop is performed with the rat in position on the Bcg platform. Occlusion of the posterior vena cava always resulted in a marked decrease in amplitude of all the Bcg waves except the H' and H" waves. An average decrease of 85 to 90% in both the HI and IJ wave amplitudes was noted. In some recordings the HI and IJ waves could hardly be identified. The dashed

line in the top curves in Fig. 14 shows the position of the I wave. In the lower curves ("open 2" and "closed 2") the possible position of the J peak is shown.

From these recordings it was evident that only the H' and H" waves remained more or less unchanged. In the case of rats it is believed that these waves are associated with isometric contraction. Persistence of the isometric waves in the UF Bcg (a) of dogs during the total vena caval occlusion was demonstrated by Pretorius (1962^b), and also in rats after posterior vena caval occlusion by Pretorius et al. (1966).

Striking changes in the phonocardiogram of the rats after vena caval occlusion resulted. The first heart sound was reduced to lesser components. It seemed that the only component that remained in the first heart sound was caused by vibrations of the myocardium and blood during isometric contraction. The valvular components of the first heart sound were much reduced or practically non-existent. This seems to agree with the persistence of the isometric contraction waves (H wave complex) in the UF Bcg (a).

The second heart sound was reduced to a barely visible vibration. This indicated that little blood was ejected and that small forces were responsible for closure

FIG. 14 OCCLUSION OF THE POSTERIOR VENA CAVA

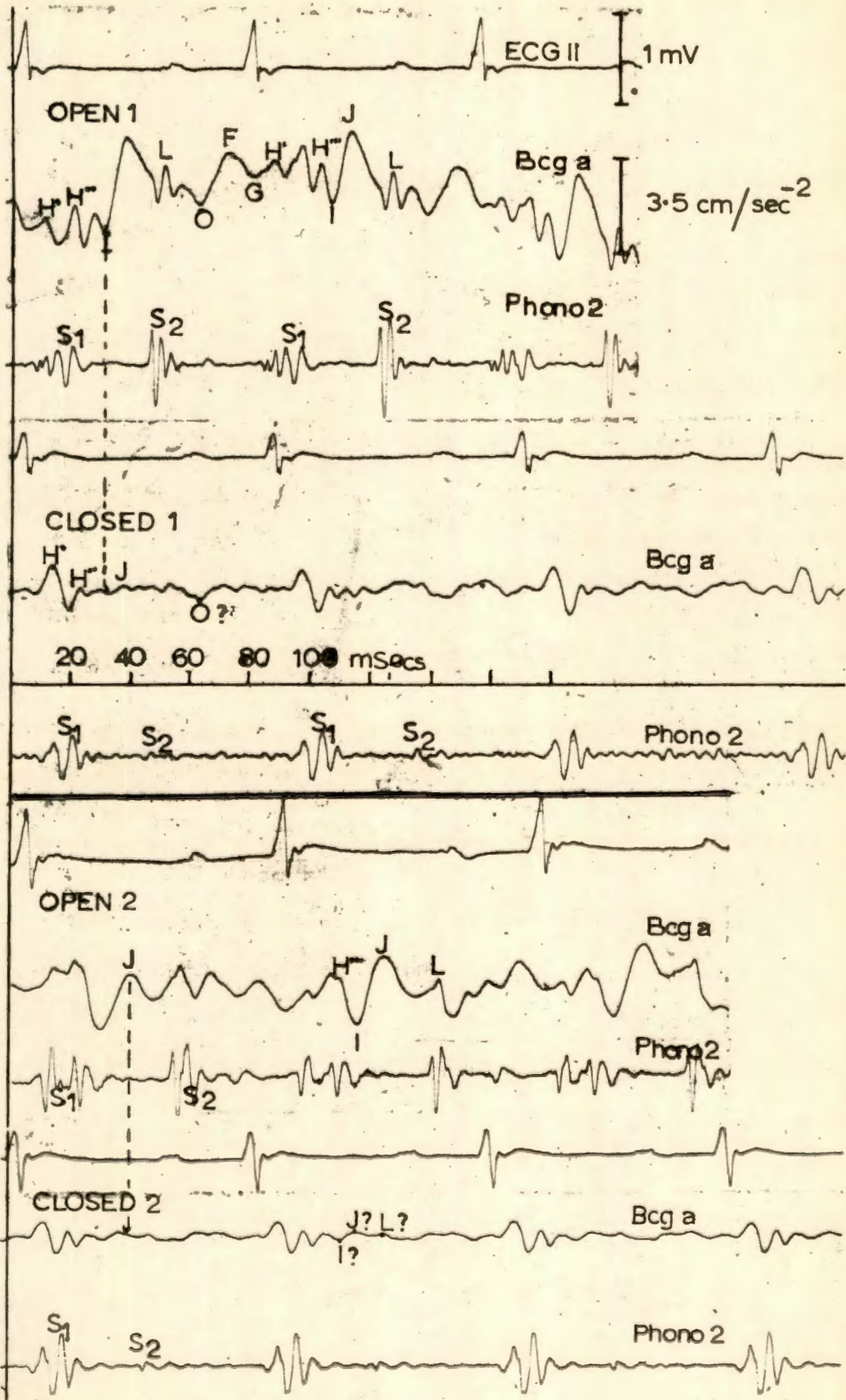
'Open 1' and 'open 2' show the UF Bcg (a) pattern of two different rats after sugrical placing of the snare around the posterior vena cava.

'Closed 1' and 'closed 2' show the UF Bcg (a) pattern after complete ligation of the posterior vena cava.

Note that all the Bcg waves except the H' and H" waves are practically abolished during closure of the vena cava.

The second heart sound (S2) is much decreased in amplitude.

FIG.14. OCCLUSION OF POSTERIOR VENA CAVA



of the aortic and pulmonary valves. It correlated with the extremely low amplitudes of the I and J waves in the Bcg (a). The L wave, usually associated with closure of the arterial valves, could not be identified with confidence.

From these experiments it is evident that, in rats, the posterior vena cava transports the major part of the venous return. The contribution of the azygos and anterior caval veins towards venous return seems to be of little importance in rats. In dogs (Corbascio and West 1961 and Pretorius 1962^b) and in rabbits (Green 1967) the contribution of the anterior vena cava to the end diastolic volume seemed to be more substantial. When both venae cavae were occluded by balloon catheters, Knoop (1965) noted a marked decrease in the UF displacement Bcg amplitude of dogs. Comparable results on the UF Bcg (a) were also demonstrated by Pretorius (1962^{a,b}).

The waves (O', O" and F), thought to originate from atrial activity, were markedly reduced in amplitude 15 secs after posterior vena caval occlusion by an estimated value of about 90%. It seems, therefore, as if posterior vena caval occlusion in rats results in a very much reduced stroke volume. This was confirmed when the arterial pressure and its time derivative were recorded simultaneously (Chapters 8 and 9).

Changes in heart rate after posterior vena caval occlusion were not consistent. Most rats showed an increase in heart rate while in some cases a decrease resulted. These inconsistent changes in heart rates following ligation of the posterior vena cava were also observed in rabbits (Green 1967).

Respiratory arrest developed in rats within 30 seconds after ligation of the posterior vena cava. To prevent severe ischaemia, the ligature was usually released within one minute. After the effects on the Bcg were noted, the ligation was sustained for a longer period in a few rats. In some rats respiration was resumed after 2 minutes - when it was more forceful but at a lower rate. It is of interest to note that in dogs (Pretorius 1962^b) and rabbits (Green 1967) a reflex hypernoea resulted after vena caval occlusion. It seems, therefore, that in the rat greater physiological respiratory impairment results from occlusion of the posterior vena cava.

From these occlusion-experiments it is evident that the major proportion of the UF Bcg (a) waves are due to the ejection and flow of blood and not to heart movement or heart filling as described by Cossio et al. (1955). The H wave complex prior to the I wave peak in rats, can be

considered as waves originating from myocardial vibrations associated with isometric contraction (pre-ejection waves).

C. Slight alterations in the aortic flow direction in relation to the recording axis

In an earlier study on rats (Pretorius et al. 1966) it was noted that the ascending aorta follows the longitudinal body axis (y-axis) closely. The proximal part of the aorta follows the longitudinal body axis in the Y-Z plane (lateral view) closely.

In the X-Y plane (ventral view) the proximal aorta shows a small deviation from the longitudinal (y) axis. It extends slightly towards the right before the aortic arch is formed. From the Röntgenograms shown in Fig. 15 it is clear that the descending aorta follows the longitudinal body axis more closely in the X-Y plane than in the Y-Z plane.

In order to obtain a more parallel spatial relationship between the descending aorta and the longitudinal body axis, a half inch square wedge of perspex foam was inserted between the rat and the Bcg platform.

By placing the wedge more or less in line with the diaphragm, the descending aorta was straightened and

followed the y-axis more closely. After taking recordings with and without the wedge, the rats were sacrificed by exsanguination and BaSO_4 was injected through the cannulated carotid artery. The wedge was kept in place and radiographs were taken. After removal of the wedge another radiograph was taken in the Y-Z plane (lateral view). Representative radiographs are shown in Fig. 15. Recordings obtained from these experiments are shown in Fig. 16. Recordings as well as X-ray exposures were made while the rats were in a supine position.

Changes brought about by 'straightening' the descending aorta by means of the perspex wedge were not consistent. The descending aorta was more closely parallel to the longitudinal body axis in some rats under normal as well as experimental conditions. It was not possible to place the wedge at exactly the same position, as the rats were of different lengths. The precise positioning of the wedge could at the best be approximated only. Insertion of the wedge might also change the degree of coupling between platform and rat and the tilting of the rat during and after insertion could provoke cardiovascular changes that would be difficult to evaluate. Slight anatomical differences in the vascular system of rats might result in the wedge bringing about divergent

FIG. 15 RÖNTGENOGRAMS OF THE AORTA OF RATS

The first exposure shows the spatial relationship of the aorta to the longitudinal body (y) axis.

Note that the ascending and descending aorta are more or less parallel to the recording axis (y-axis).

The second and fourth exposures (Rat A and B normal) show the course of the aorta in the saggital (Y-Z) plane.

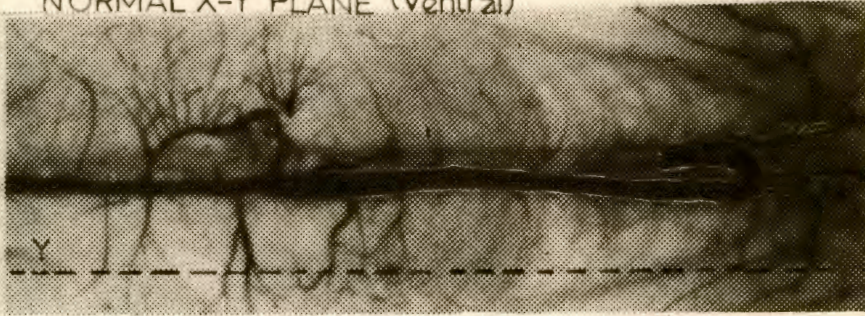
The third and fifth exposures show the alterations in the course of the aorta in rat A and B after insertion of the wedge.

Note the improved alignment of the proximal aorta with the recording axis obtained in the case of rat A.

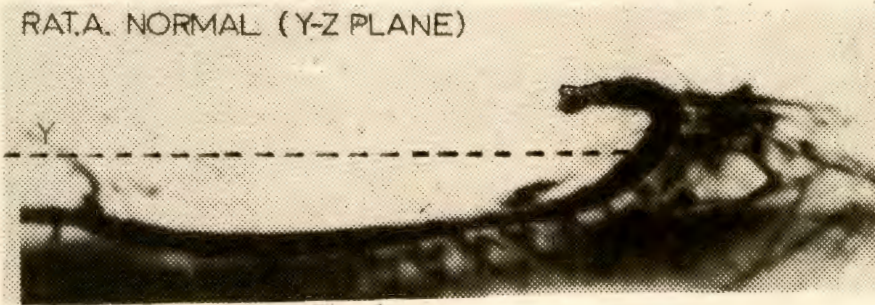
In the case of rat B the course of the aorta is not as parallel to the recording axis as in rat A.

FIG.15. AORTIC FLOW DIRECTION.

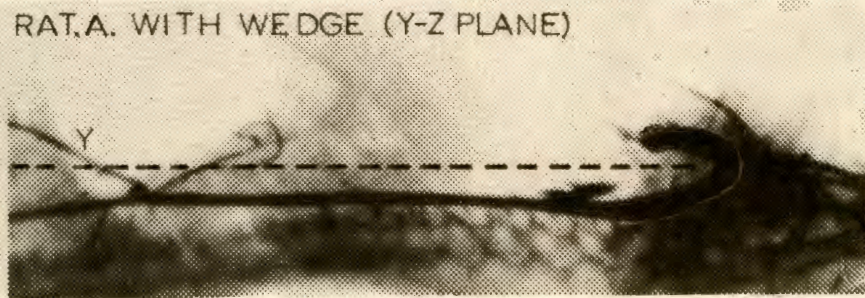
NORMAL X-Y PLANE (ventral)



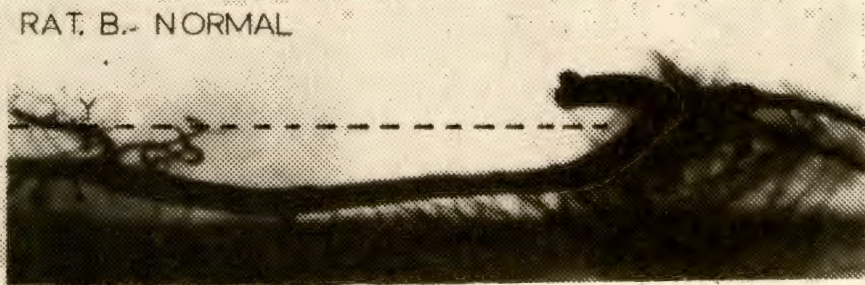
RAT.A. NORMAL (Y-Z PLANE)



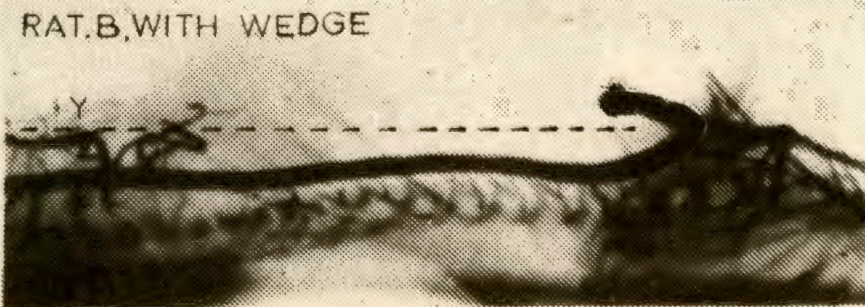
RAT.A. WITH WEDGE (Y-Z PLANE)



RAT. B.- NORMAL



RAT.B,WITH WEDGE



changes. If the proximal aorta is, for instance 100% parallel to the y-axis in the normal position in a rat, the insertion of the wedge could direct the proximal aorta to form an angle with the y-axis. This was the case in some rats (see Rat B Figures 15 and 16). On the other hand, the proximal aorta may follow a line forming a small angle with the y-axis in the Y-Z plane. Bending of the rat by insertion of the wedge would then result in a reduction or an increase in this angle depending on the anatomy of the rat concerned.

Although these anatomical differences were very slight, they were reflected in the UF Bcg (a). Examples of the most divergent Bcg (a) results are shown in Fig. 16. In rat A a much better alignment of the descending as well as the ascending aorta with the y-axis was obtained by lifting the posterior part of the thorax with the wedge. This was confirmed by the X-ray observations shown in Fig. 15. The UF Bcg (a) of this rat showed the most conspicuous changes which agreed with the anatomical changes. The HI wave amplitude was increased by about 60% while the J wave amplitude was increased by about 16%. There was, however, a general increase in Bcg amplitude of about 16% which could have been due to secondary physiological reactions (tilting, venous return, pressor receptor, reflexes, etc.). The only change of

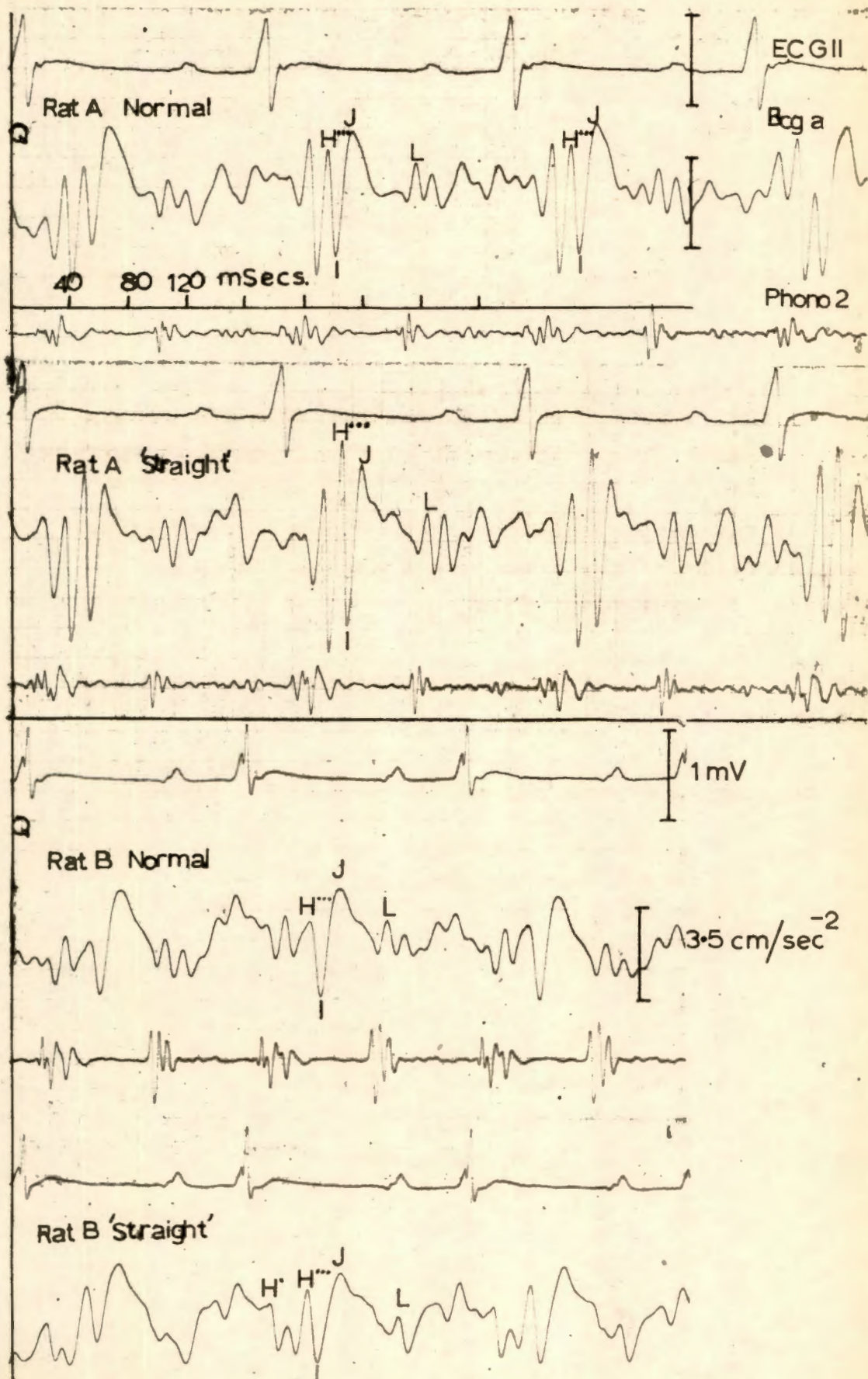
FIG. 16 THE EFFECTS OF 'STRAINGTHENING' THE AORTA BY
MEANS OF A WEDGE ON THE UF BCG (a) PATTERN

Note that rat A shows an increased UF Bcg (a) amplitude after insertion of the wedge which agrees with the anatomical changes (Fig. 15).

In the recordings of both rats a conspicuous change in the J-L segment slope is noted.

Note the sharper J peak and the decreased J-L slope.

FIG.16. EFFECT OF CHANGING DIRECTION OF THE AORTA



significant magnitude was therefore the increase in HI amplitude (44%).

In rat B the least amount of anatomical change was brought about by insertion of the wedge (see Fig. 15). The Bcg (a) changes (Rat B Fig. 16) were also less conspicuous. The HI wave remained essentially unchanged. The IJ wave amplitude showed a slight decrease amounting to about 12%. The heart rate remained constant in rat B while it decreased in rat A. Changes in the IJ slope were also inconsistent. The J-L time was increased in 30% of the rats (e.g. Rat B Fig. 16).

Consistent changes were, however, observed in the late systolic waves. Most of these changes are difficult to express in numerical terms. The J peak was sharper after the insertion of the wedge. The recording for rat A (Fig. 16) showed this most conspicuously, while that for rat B showed it to a lesser extent. The Bcgs for other rats showed intermediate changes. The JL segment showed an alteration in contour which was difficult to describe or to interpret. If rats had a clear K wave, it seems likely that its amplitude would have been decreased by insertion of the wedge. The proximal descending segment of the J wave seemed to be more vertical. The later part of the descending leg of the J wave (JL segment) was

decreased in slope. The latter change was observed in all six rats used in this experiment.

It seems therefore that slight changes in the anatomical arrangements in the ascending and descending aorta might be reflected in the Bcg (a). It was, however, suggested that the displacement Bcg is more sensitive to anatomical changes (Elsbach and Rodrigo 1964; and Starr and Noordergraaf 1967).

D. Anatomical relationships and Ballistocardiographic variations in the supine and prone positions

Stimulated by the results of the previous section, it was decided to investigate whether anatomical and cardio-ballistic changes could be demonstrated with rats in the supine and prone positions. Furthermore, differences between recordings made of rats in the supine and prone positions were noticed in an earlier study (Rademeyer and Pretorius 1963). The relationship of the aorta to the longitudinal body axis (y-axis) in the prone and supine positions is shown in Fig. 17. In the supine position the ascending (proximal) aorta ran parallel to the y-axis. In the prone position this segment deviated from the y-axis in the lateral plane by about 10° to 12° . It also seemed that this segment of the aorta was slightly

increased in functional length in the prone position. This might be due to a larger proportion of the aortic arch being incorporated in the functional ascending aorta in the prone position.

If the H^{III}I wave is representative of initial left ventricular ejection, a slight decrease of the H^{III}I segment recorded in the y-axis should result from this angular deflection of the proximal aorta. Theoretically a decrease of about 4% in the measured acceleration in the y-axis should result from the first 10° of deviation of the force vector from the y-axis. The recordings in Fig. 18 show the results obtained from one of the rats in this experiment. The X-ray photographs shown in Fig. 17 are from the same rat. A mean decrease of 6.5% in the HI amplitude was found. Although this value was higher than the theoretical value, the latter did not include the force vector within the ventricle, but was calculated from the aortic valves only. In any event it seems that the HI wave of the UF Bcg (a) reflected the change in direction of the acceleration of blood in the ascending aorta with great accuracy. It further seems to confirm that blood acceleration in the proximal aorta is reflected by the HI wave of the UF Bcg (a).

The angle between the y-axis (recording axis) and the

FIG. 17 THE COURSE OF THE AORTA AND ITS SPATIAL
RELATIONSHIP TO THE RECORDING AXIS IN THE
SUPINE AND PRONE POSITIONS

Fig. 17B shows the angles between various aortic segments and the recording axis.

Note the increased angles of all the aortic segments with the recording axis in the prone position.

FIG.17. COURSE OF THE AORTA

PRONE



SUPINE

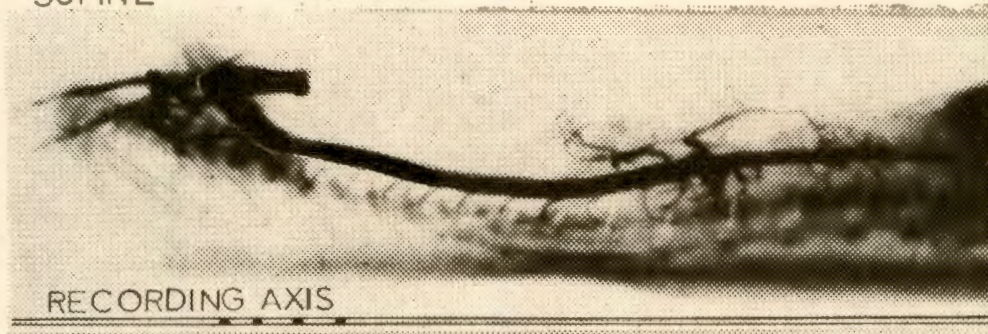
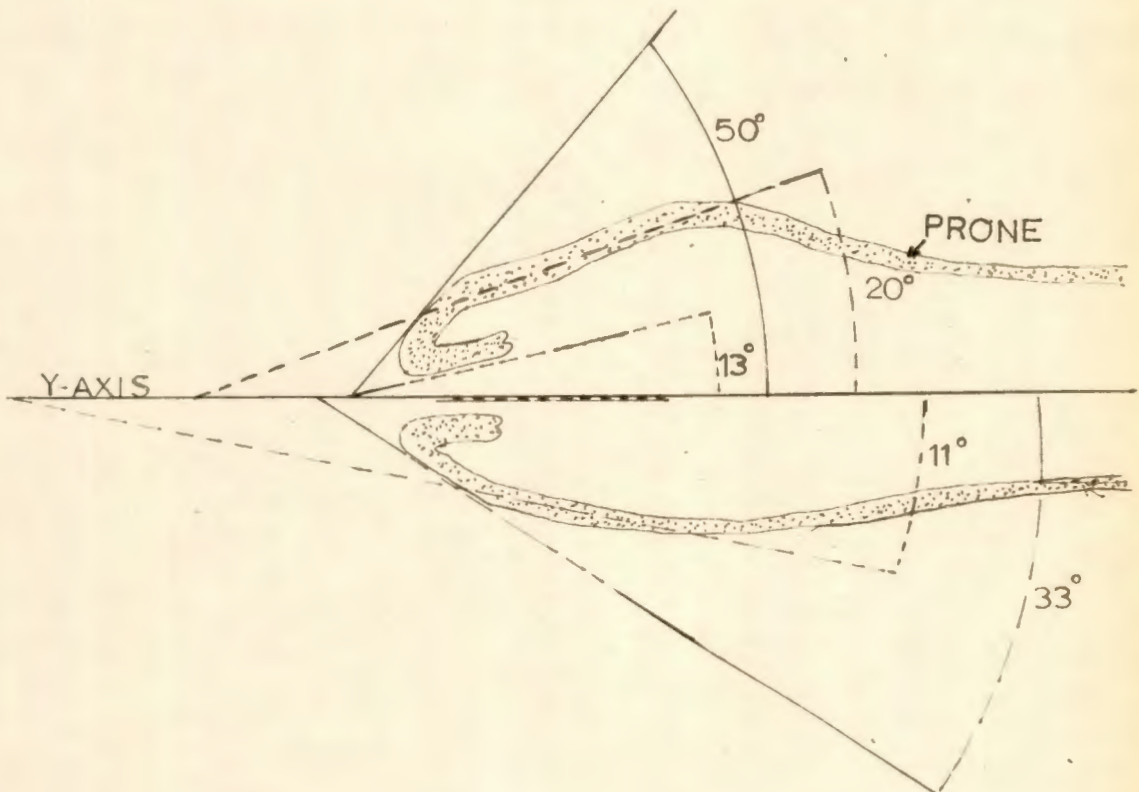


FIG.17B. ANGLES BETWEEN Y-AXIS AND AORTIC SEGMENTS,



first part of the descending aorta (Y-Z plane) was increased from 33° to 50° by changing the rats from a supine to a prone position (Fig. 17). Theoretically a decrease of the acceleration vector in this segment of about 8% in the y-axis, should result if rats are placed in the prone position. For the major part of the descending aorta the angle between the y-axis and the aorta is increased by a further 9° in the prone position.

It is difficult to determine the change of direction on the aortic arch brought about by placing the rats in a prone position. If the IJ wave in the UF Bcg (a) of rats is caused by acceleration in the first and subsequent parts of the descending aorta, a theoretical decrease of about 14% ($8\% + 6\%$) of the force vector of the aorta in the longitudinal axis should result from placing rats in the prone position. A mean decrease of 45%, however, was noted in the IJ amplitude of the UF Bcg (a) (see Fig. 18). The IJ wave in rats probably also includes forces of deceleration, or a greater amount of force in the aortic arch which cannot be readily accounted for in the calculations made from the X-ray photographs.

The Q-I time was decreased by about 8% and the Q-J time about 4% in the prone position.

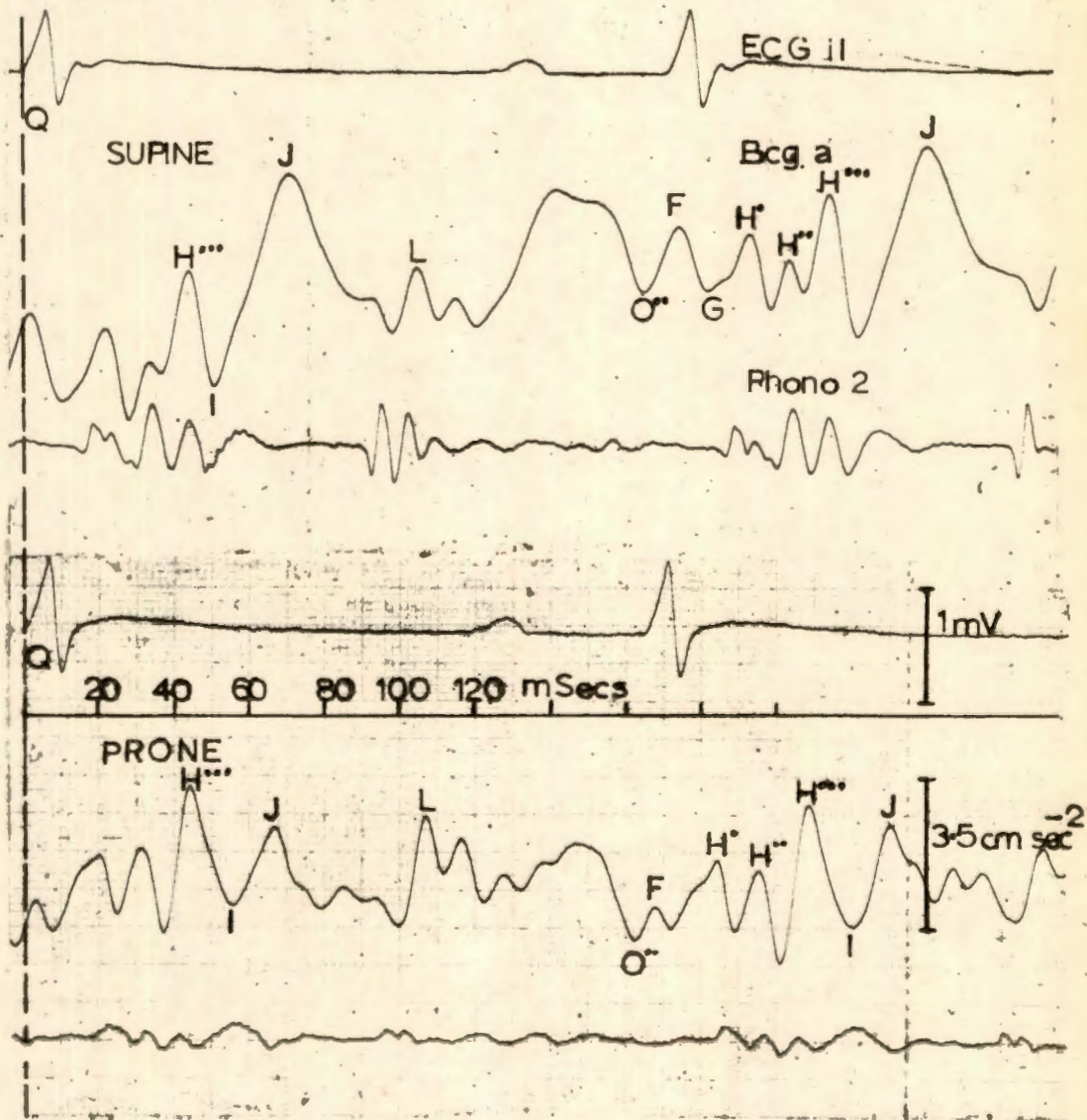
These experiments described under C and D are of a similar nature to experiments performed on dogs by Pretorius (1962^b). The main difference is that the recording axis (y-axis) was not changed in the present study while the relative position of the aorta in the Y-Z plane was. Pretorius (1962^b), on the other hand, kept the aorta in a fixed position with his dogs reclining on their sides (Y-Z plane now in the X-Y plane), while the recording axis was changed.

Pretorius (1962^b) found a conspicuous increase in the HI wave of the UF Bcg (a) of dogs when the recording axis was more closely aligned to the proximal aorta, e.g. from 0° to 45° . The most conspicuous HI wave in dogs was recorded when the recording axis was at 90° (x-axis) to the longitudinal (y) axis. The most conspicuous IJ amplitude in the study was recorded at a 45° angle relative to the y-axis.

The difference in anatomical arrangement and possible cardiovascular dynamics of the dog and rat might account for the numerical differences. In general these experiments confirmed the following results of Pretorius (1962^b):

(i) The HI wave (real I wave) in the dog and rat was recorded with a greater amplitude if the recording axis

FIG.18. PRONE AND SUPINE BCG a



THE UP BCG (a) OF THE SAME RAT IN THE PRONE
AND SUPINE POSITIONS.

Note the decrease in HI slope and IJ amplitude in the
prone position.

was aligned practically parallel to the proximal ascending aorta.

(ii) A slight increase in Q-I and Q-J time in the dog and rat was noted when the recording axis was optimal in relation to the course of the aorta.

It seems likely that the UF Bcg (a) of rats and dogs reflects to a certain extent the contour of the aorta.

It is further indicated that anatomical differences in the cardiovascular systems and recording axes should be considered in comparing UF Bcg (a) of different species.

This view is also held by Pretorius and associates (1968^b).

CHAPTER 7

EFFECTS OF ARTERENOL AND LEVARTERENOL

The cardiovascular effects of arterenol (adrenaline) and levarterenol (noradrenaline) are different. The precise action of these hormones on the coronary circulation has not yet been established because of the divergent results described in the literature. The well known secondary effects of these hormones in intact subjects further complicate the interpretation of their primary effects.

From the work of Goldenberg et al. (1948), Wakim and Essex (1952) and Von Euler (1958) it is clear that arterenol and levarterenol cause an increase in blood pressure, but in different ways. Arterenol causes an increase in cardiac performance, vasodilation, and a decrease in peripheral resistance. The increase in blood pressure caused by arterenol is due to an over-compensation of the depression of the peripheral circulation by an increase in heart rate and stroke volume. Levarterenol acts more directly on the peripheral circulation. It causes vasoconstriction and increases peripheral resistance and mean arterial pressure. Cardiac performance is unchanged or slightly inhibited.

Arterenol caused a consistent increase in Bcg (a) I and J wave amplitudes (Darby et al. 1955, Honig and Tenney 1956^a, Corbascio and West 1961, Moreira and de Azevedo 1962, Knoop 1965 and Pretorius et al. 1966). This initial increase

in I and J wave amplitude may diminish with increased blood pressure as the effect of arterenol passes off.

The effects of levarterenol are less consistent. Hoitink and Knoop (1964) and Knoop (1965) reported an increase in UF displacement Bcg amplitude following administration of this drug. Moreira (1960, 1964) and Pretorius (1962^b) found a transient increase in UF acceleration Bcg when levarterenol was injected. Secondary effects caused by reflex action probably obscured the primary effects of this drug.

In this study small (2 to 5 gamma/kg) and large ($\pm$ 8 to 12 gamma/kg) doses of arterenol were administered intra-arterially. The immediate effects (5 to 20 seconds) after injection were treated separately from the over-all effects. In the case of levarterenol only fixed doses of 8 gamma/kg were administered through the carotid cannula. The immediate and subsequent effects were again treated separately.

A. Effects of small doses of arterenol

The immediate (direct) effects of a small (2.3 gamma/kg) dose of arterenol are shown in Fig. 19. The recording was made six seconds after the injection of arterenol.

(i) Heart rate: The heart rate was slightly increased

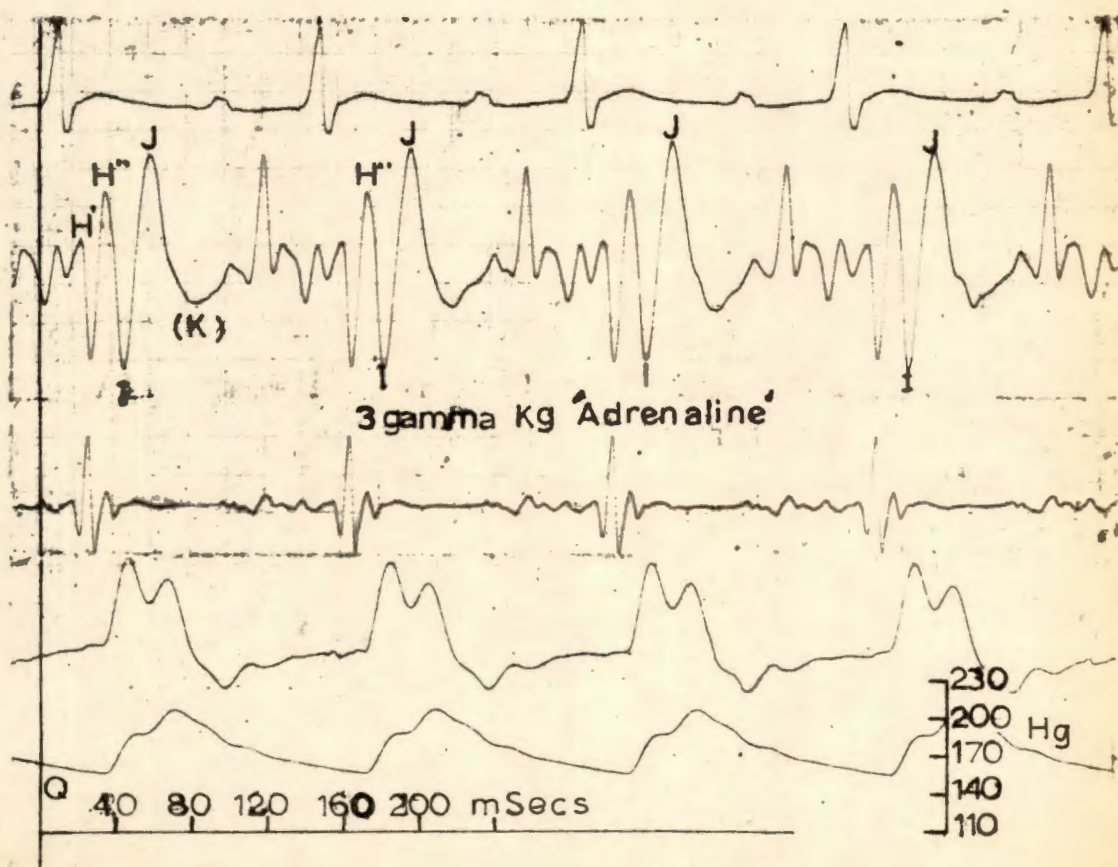
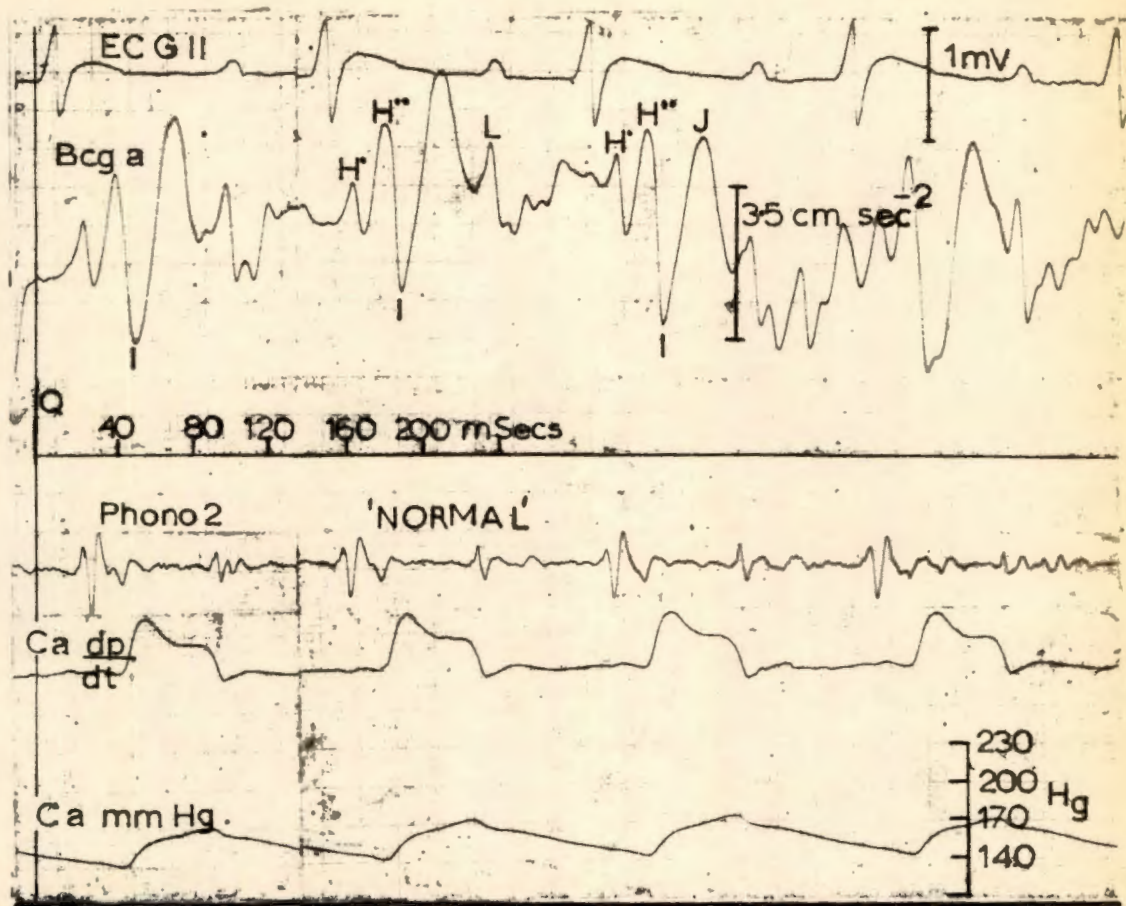
FIG. 19 THE IMMEDIATE EFFECTS OF A SMALL DOSE OF
ARTERENOL (ADRENALINE) ON MYOCARDIAL FUNCTION

The EGC (lead II), the UF Bcg (a), the phonocardiogram (2), the carotid pressure pulse derivative ($Ca \frac{dp}{dt}$) and the carotid pressure (Ca mmHg) are shown from the top downwards before and after arterenol administration.

The lower recording was made 6 seconds after the arterenol injection.

Note the slight increase in heart rate and the decrease in Q-I' and Q-J time intervals.

FIG. 19. EFFECT OF 'ADRENALINE' (small dose)



($\pm 10\%$) in five rats. In six rats the heart rate remained the same. The P-Q time was increased by about 10%. Twenty seconds after the injection a slight decrease in heart rate resulted. This was probably due to a reflex increase in vagal tone in response to the elevated blood pressure.

(ii) Bcg (a) changes:

(a) Q time measurements: The Q-H' time was not affected by small doses of arterenol. The Q-H" time was decreased by a mean value of 10% (22 to 20 msec), the Q-I time by 8%, and the Q-J time by a mean of 12%. The Q-L time was increased by a mean of 15%.

From these results it is evident that the time lag between electrical and mechanical systole is shortened by the administration of arterenol. This was also found in rabbits by Green (1967). The Q-H" time was decreased indicating a reduction in the duration of the isometric contraction. The slightly greater increase in Q-J time compared to the increase in Q-I time, suggests that peak acceleration of blood is reached sooner after arterenol administration. This means that an increase in the slope of the IJ wave (which is also evident in Fig. 19) follows the injection of arterenol. The increased Q-L time coincided with an increased duration of mechanical systole. As the commencement of the pressure waves and heart rate remained constant, a decrease in diastolic time was indicated. As a result

of this the beginning of the atrial wave was fused with the L wave. The P wave of the electrocardiogram did in fact precede the L wave and the second heart sound, in most of the rats, immediately after arterenol administration.

(b) Bcg (a) amplitude: The amplitude of the H' wave was increased by about 20%, while the H'' wave amplitude increased by $\pm 25\%$ twenty seconds after the injection. It is possible that this increase in the amplitude of the isometric contraction waves was caused by augmented vibrations of the myocardium and blood as a result of the more vigorous onset of contraction. The Q-time measurements showed a decrease in the case of the second isometric (H'') wave which further supports this view.

The I wave and the J wave amplitude showed a small increase of about 5%. The overall amplitudes of the I and J waves were, however, much more constant after arterenol administration. A better synchronization or co-ordination of the heart resulting from the sympathomimetic action of arterenol, could explain this improvement in Bcg (a) pattern. This important aspect of sympathetic stimulation was also mentioned by Pretorius (1962^b). A contributing factor in the case of rats might also be the decrease in respiratory rate after arterenol injection. As the phases of respiration and the lung pressure and volume are known to affect

the amplitude of the Bcg, a lower respiratory rate will increase the number of heart beats which can be recorded under the same conditions during a respiratory cycle. The stimulatory effect of catheterization (see Chapter 6) might to some extent obscure the effects of small doses of arterenol. In comparing the results, the 'normal' recording after catheterization was taken as the control curve.

Part of the atrial wave (O" and F) was more conspicuously increased by small doses of arterenol. In some cases an increase of 100% was noted in the atrial wave amplitude. An increase in atrial wave amplitude was also noted after catheterization (Chapter 6), indicating that the atria might be more sensitive to mild sympathetic stimulation than the ventricles in rats, or that the higher diastolic pressure might mask the ventricular waves to some extent.

(iii) Changes in the Phonocardiogram and ECG: Small doses of arterenol initially increased the heart rate slightly in some cases only. The heart rate remained unchanged in 60% of the rats used in this experiment. An increase in P-Q time was noted in all cases. This was also noted in rats by Pretorius et al. (1966).

The phonocardiogram showed a first heart sound of increased intensity (amplitude) and of decreased duration. The

increased intensity of the first heart sound coincided with an increased amplitude of some of the isometric waves, particularly the H" wave. The decreased duration of the first heart sound correlated with the decreased Q-I time, further supporting the view that synchronization or co-ordination was improved. The increased time between the first and second heart sound (mechanical systole) correlated with the increased Q-L time. Mechanical diastole (second to first heart sound) was decreased. Amplitude changes of the second heart sound were not consistent but were usually increased.

(iv) Pressure changes: Soon (5 to 10 seconds) after the administration of a small dose of arterenol the systolic and diastolic pressures (carotid) were increased. The systolic pressure was increased by a mean value of 15%. The diastolic pressure was elevated by a mean value of 12%. The pulse pressure was therefore slightly higher immediately after arterenol was injected. The time derivative of the carotid pressure pulse ($Ca \frac{dp}{dt}$) was increased by about 30% in most cases. This increase in the pressure derivative correlated with the increased Q-I and Q-J times and amplitudes. The $Ca \frac{dp}{dt}$ showed a closer correlation with the IJ slope than with the HI slope. This might be due to the fact that the HI segment contains an isometric component (Pretorius 1962^b), or an atrial component (West and Corbascio 1959). In the rat

it is unlikely that the latter is the case. The atrium wave is usually more clearly defined and its effects would at the most penetrate to the level of the H' wave (see Chapter 9).

In Fig. 20 the effects of a slightly larger dose of arterenol in the same rat as in Fig. 19, is shown. Although the dose of arterenol was doubled, it could still be considered as a small dose. Doses of more than 5 gamma/kg were considered as large in this study, by virtue of the magnitude of the secondary manifestations such as reflex bradycardia, ectopic beats, etc. The striking effect of doubling the dose can be seen by comparing the recordings of Figures 19 and 20. The IJ amplitude was doubled while the HI amplitude increased by a further 30%. The systolic pressure was elevated to 230 mmHg. This was a further increase of 30 mmHg, or about 15%. The diastolic pressure remained more or less the same with the result that the pulse pressure was increased by about 15%. The amplitude of the pressure derivative was increased by a further 30%. P-Q time remained essentially the same but the heart rate decreased by 10%. The Q-L time was reduced which means that the ratio between systolic and diastolic time was near to 'normal'. This was also evident in the lowered amplitude of the O" F (atrial) wave.

The lower curve in Fig. 20 shows the recovery from arterenol.

FIG. 20 THE EFFECTS OF A DOSE OF 5 GAMMA/KG BODY
WEIGHT ARTERENOL

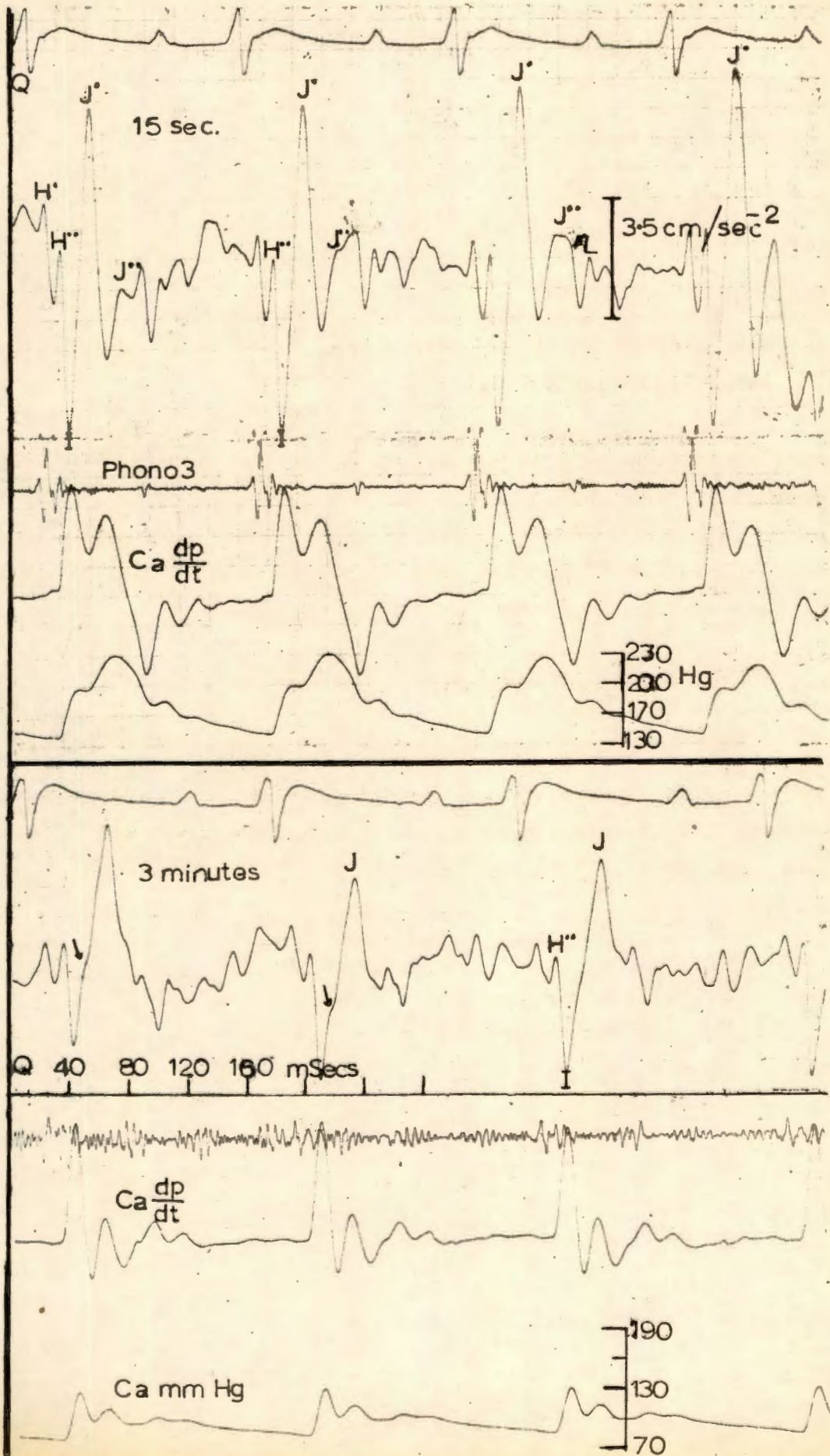
The upper recording was made 15 sec after the administration of 5 gamma/kg arterenol.

Note the increased HI and IJ amplitude, the splitting of the J wave and the decreased Q-J time interval.

The lower recording was made 3 minutes later.

Note the decrease in HI and IJ amplitude and the re-establishment of a single J wave. The arrows indicate a slur in the J wave coinciding in Q time measurement with the peak of the J' wave in the upper recording.

FIG.20. RECOVERY AFTER 'ADRENALINE' (5 gamma/Kg)



The recording was made three minutes after arterenol was administered. As the action of arterenol passed off, a reduction of the carotid pressure resulted. P-Q time was still increased, but the heart rate was even further decreased. IJ amplitude and the carotid pressure derivative were still increased compared to the normal curve. The HI amplitude, however, was lower than in the control recording (top Fig. 19). A slur (indicated by arrows in Fig. 20) developed in the IJ wave three minutes after the administration of arterenol. The slur in the J wave and the reduced HI amplitude might indicate that the heart was slightly overtaxed during the period of forceful contraction against a high pressure head.

Of further importance was the splitting of the J wave as a result of the increased amount of arterenol injected. It seemed as if only a certain component of the IJ wave was increased in amplitude during stimulation. In the top recording of Fig. 20 this was labelled the J wave. The real J wave, as seen in the normal and recovery recordings, remained as the J" wave in the top recording in Fig. 20. The slur appearing in the recovery recording (Fig. 20) bears the same Q time relationship as the J wave in the upper recording. It is obvious from these results that the IJ wave in the UF Bcg (a) of rats is caused by different haemodynamic events (see Chapter 9).

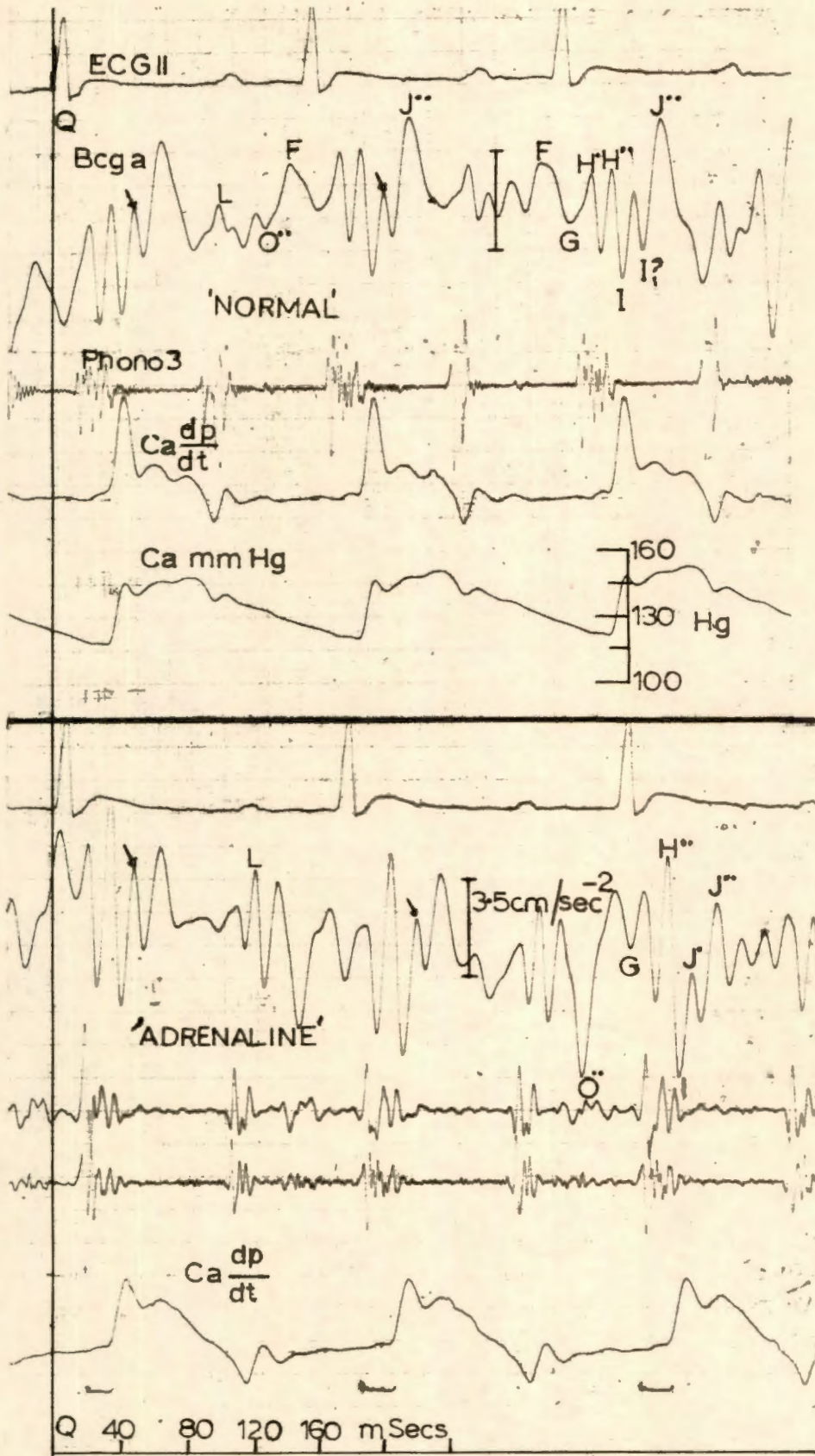
FIG. 21 THE IMMEDIATE EFFECTS OF A LARGE DOSE OF
ARTERENOL (ADRENALINE)

Note the increase in HI wave amplitude.

The arrows in the upper recording indicate J' waves that might be confused with the H'''I waves.

In the lower recording the arrows indicate more pronounced J' waves.

FIG 21 IMMEDIATE EFFECT OF 10 GAMMA/KG 'ADRENALINE'



B. Immediate effects of a large dose of arterenol

As mentioned in chapters 4 and 5, it was sometimes difficult to distinguish between a notch in the J wave and the H''' wave. In most cases the H'''I wave was the most conspicuous footward wave during normal conditions, and was considered to be the real HI wave (Figures 7 and 8). In 'old' rats (Fig. 9) it was more difficult to decide whether the H''I or the H'''I wave should be considered as the real HI wave. The same difficulty was encountered when the carotid artery was cannulated (Figures 13 and 21). It seemed as if sympathetic stimulation decreased the isometric contraction time and resulted in the real HI wave following from the H'' wave because the onset of ejection followed sooner after the Q wave. It is further probable that this might decrease the H''' wave amplitude, or abolish the H''' wave amplitude to such an extent that the events usually causing the H''' wave now cause a slur or notch in the early IJ wave. This 'shift' of the H''' wave is discussed in Chapter 9.

Large doses of arterenol were administered to eleven rats. The recordings listed in the figures were chosen because they showed the nearest resemblance to the calculated mean values. To avoid confusion, the results described are based on these figures and the range of values found in these experiments is given in brackets in the text.

The immediate effects (after 5 seconds) of a large dose (10 gamma/kg) of arterenol are shown in Fig. 21. The heart rate was decreased by 20% (range 15 to 40%). P-Q time was decreased by about 25%. Duration of mechanical systole and Q-L time was increased by about 25%. Of these changes the initial decrease in heart rate was the only one found to differ strikingly from the changes brought about by the injection of small doses of arterenol. If the decrease in heart rate was due to secondary actions, a large dose of arterenol might therefore accelerate the commencement of these secondary (reflex) actions. If this is the case, the difference in reaction of the heart rate to a large and a small dose of arterenol can be accounted for satisfactorily.

The arterial pressure showed a more marked increase after the injection of a large dose of arterenol. After five seconds an increase in the systolic pressure of 60% (40 to 70%) resulted. Half the dose of arterenol (5 gamma/kg) resulted in an increase of 15% (10 to 24%) in systolic pressure. This might further explain the earlier reduction in heart rate mentioned in the previous paragraph.

The diastolic time, as measured in the phonocardiogram, remained essentially the same. The lower heart rate thus coincided with a longer systolic time. The atrial wave

complex in the Bcg (a) was increased by about 66% (30 to 70%). A marked increase in the atrial wave complex also followed after small doses of arterenol when the diastolic time was not decreased.

Large doses of arterenol also resulted in a more conspicuous increase in the HI wave amplitude. The HI amplitude was usually increased by about 50%. This increase was about ten times greater than the increase found when small doses (2 to 5 gamma/kg) of arterenol were injected.

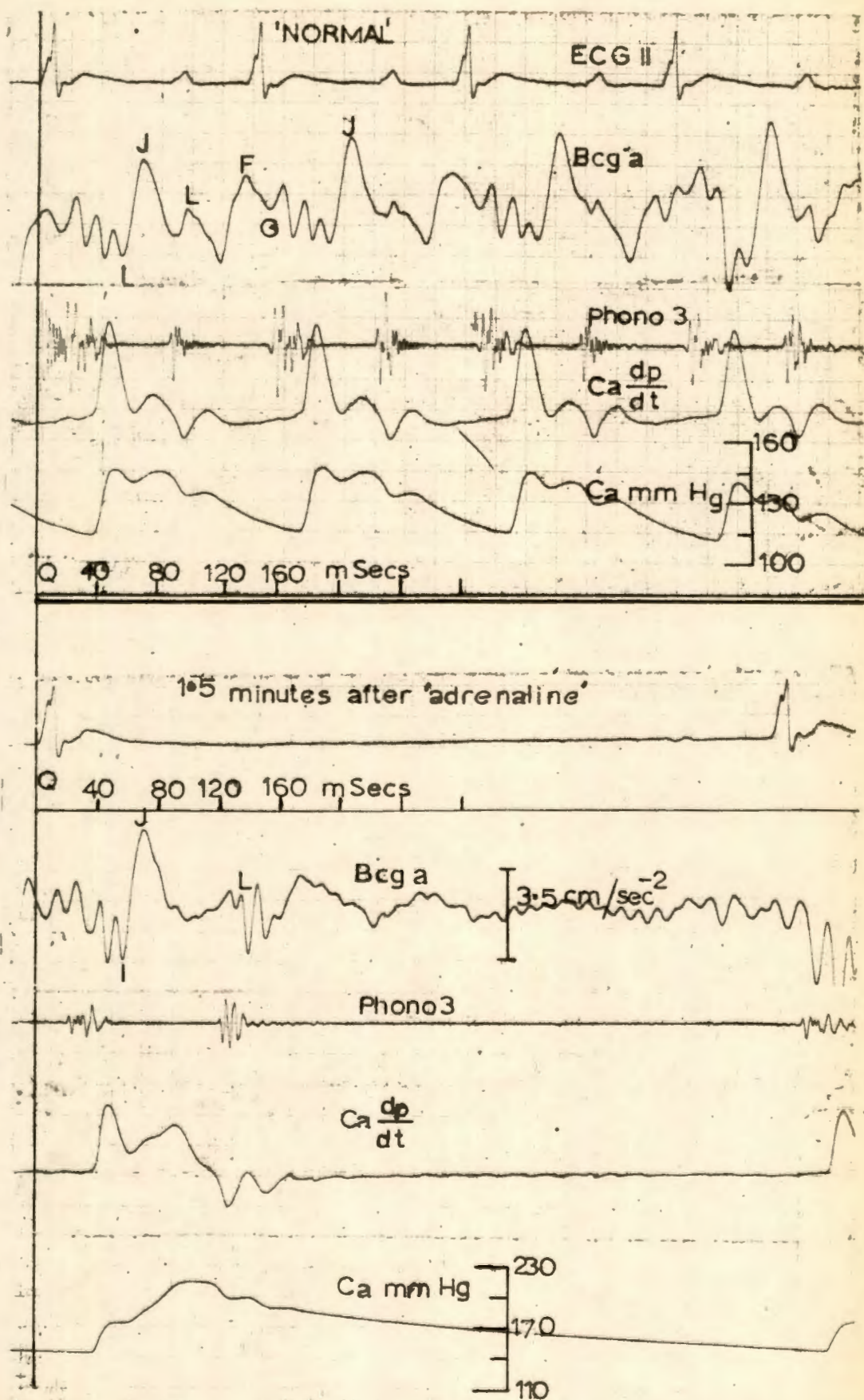
The first J wave (J') amplitude was increased by about 35% (5 to 40%). When 2 to 3 gamma/kg of arterenol was injected, a mean increase of only 5% in IJ amplitude resulted. Five gamma/kg of arterenol, however, increased the IJ amplitude by 150% (80 to 150%). The contour of the J" wave was more markedly changed by the large dose (10 gamma/kg) of arterenol.

From the latter observations it follows that the HI wave amplitude is not affected by an increase in blood pressure to the same extent as the IJ amplitude. When the blood pressure was lower (after 5 gamma/kg arterenol) a more marked increase in IJ wave amplitude resulted. A large dose of arterenol (10 gamma/kg) resulted in a higher HI amplitude and blood pressure, but a relatively smaller IJ amplitude. The smaller increase in IJ amplitude coincided

FIG. 22 LATER EFFECTS OF A LARGE DOSE OF ARTERENOL

Note the similarity of the systolic UF Bcg (a) waves 1.5 minutes after arterenol administration in spite of the marked reflex bradycardia.

FIG. 22. LATER EFFECTS OF 'ADRENALINE' (10 gamma/Kg)



with a smaller amplitude in the carotid pressure derivative (fig. 21). It seems that the greater stimulation of the heart by a large dose of arterenol increased initial ventricular ejection (HI), while the increased mean arterial pressure or higher diastolic pressure impeded the acceleration of blood in the distal segment of the proximal aorta (IJ).

C. The later effects of arterenol

About 20 seconds after a large dose of arterenol (6 to 10 gamma/kg) was administered, marked changes occurred in the recorded events. The most striking was the change in heart rate and P-Q time. Heart rates in the region of 360 beats per minute were decreased to 60 or 70 beats per minute. In some cases the P-Q time was increased by 100% and resulted in 2:1 or 3:1 rhythm. Ectopic beats, extra systoles and isolated P waves appeared in the ECG. These changes will be discussed in Chapter 8.

In Fig. 22 the effects of arterenol (10 gamma/kg) are shown one and a half minutes after its injection. The P-Q time was increased from 48 to 68 milliseconds. Heart rate was decreased from 440 to about 125 beats per minute. Pulse pressure was increased from 30 to about 75 mmHg. This was probably due to the lower heart rate. The slope of the pressure pulse showed signs of deterioration

and the pressure derivative showed a lowered amplitude. The HI wave showed an elevated amplitude of about 40%. The IJ wave amplitude was increased by about 40%. The increased IJ amplitude did not show the same relationship to the pressure derivative amplitude as in the earlier stages of arterenol administration. The amplitude of the L wave and the duration of systole was increased. The increase in L wave amplitude might indicate that the forces associated with closure of the aortic and pulmonary valves are of greater magnitude during elevated arterial pressures.

D. Immediate effects of levarterenol

Levarterenol ('Levophed' Winthrop) was injected in doses of 8 gamma/kg through the carotid catheter used for pressure recordings.

In Fig. 23 the immediate effects of levarterenol on the recorded phenomena, are shown. A slight increase in P-Q time (mean 10%) was noted. In two rats (20%) the P-Q time was increased by about 18%. The heart rate showed an average increase of $\pm 6\%$ during the first 10 seconds after injection.

The first heart sound was more markedly increased in amplitude than the increase found after arterenol administration. This coincided with a more conspicuous

FIG. 23 THE DIRECT EFFECTS OF LEVARTERENOL (NORADRENALINE) RECORDED 7 SECONDS AFTER ITS ADMINISTRATION

Recording A shows the normal pattern.

Recording B shows a marked increase in the amplitude of the atrial wave (O", G and G) complex.

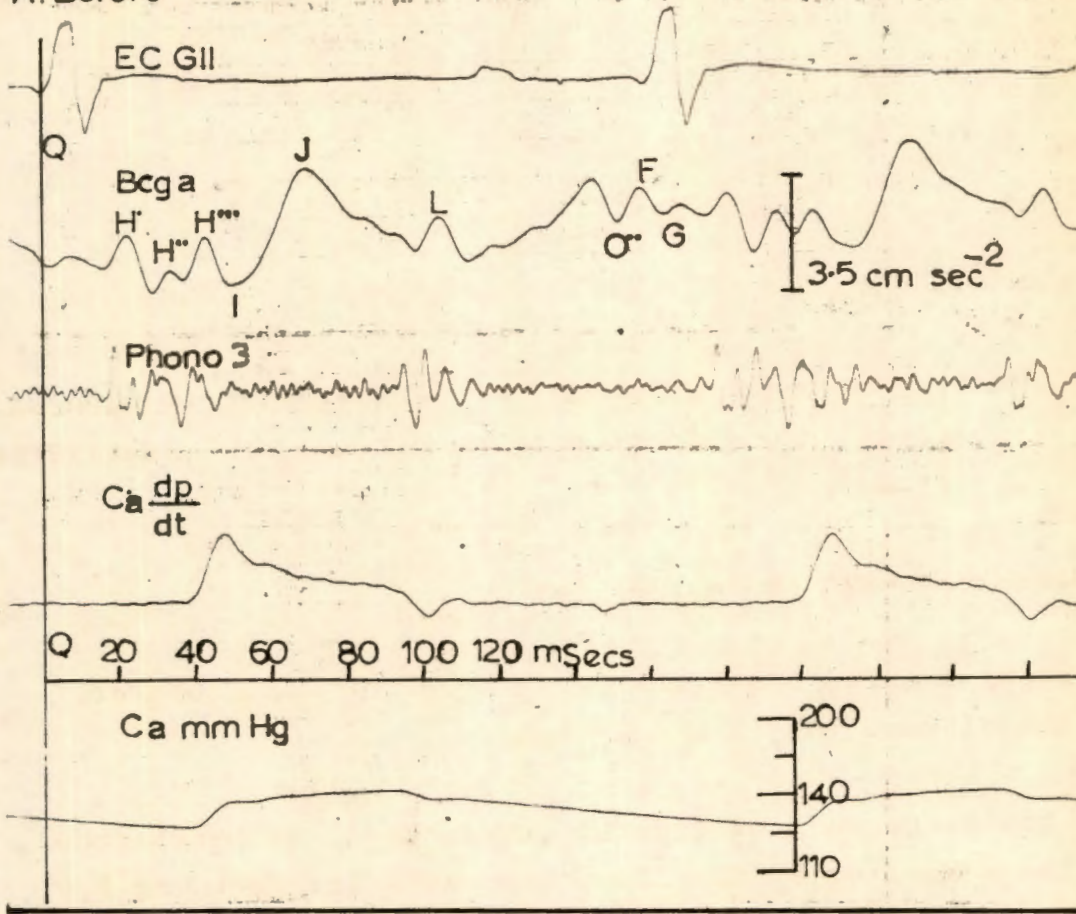
Note the decrease in the duration of the first heart sound and the summation of the isometric waves in recording B.

The increase in HI amplitude was less marked than after arterenol administration.

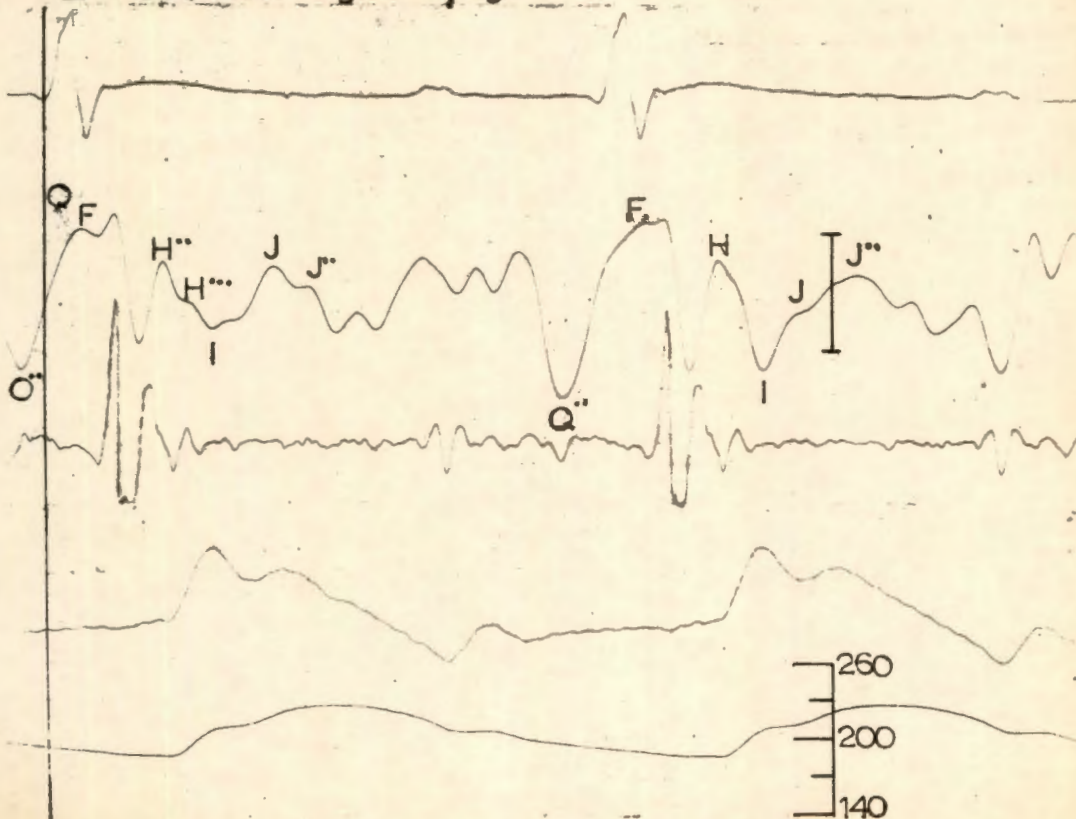
The IJ wave shows a general deterioration in slope and amplitude.

FIG. 23. IMMEDIATE EFFECTS OF 'NORADRENALINE'

A. Before



B. 7 Sec after 8 gamma/Kg.



increase in the isometric H waves of the UF Bcg (a). The Q-L time and mechanical systole were increased by about 10%. The systolic pressure was increased from 145 to 230 mmHg in the recording shown in Fig. 23. The mean increase in systolic pressure in 10 rats amounted to 50%. Diastolic pressure was increased by a mean percentage of 40. A slight increase of the pulse pressure was thus indicated.

The HI wave amplitude was not increased to the same extent as that noted after arterenol injection. On the average an increase of only 3% in HI amplitude could be demonstrated. The Q-H" and Q-I times were, however, decreased as in the case of arterenol administration. The IJ wave showed a deterioration in contour and a slightly lowered amplitude. These changes were in contrast to the changes noted after arterenol injection. It is, however, in accordance with the now accepted view that arterenol stimulates the heart more directly while levarterenol stimulates the peripheral circulation.

The arterial pressure wave and its derivative showed less sharp peaks. The rate of change of pressure, as indicated by the ascending leg of the arterial pressure pulse and the time derivative, was lowered. When arterenol was injected, a faster rate of change of pressure was noted. The rate of change of pressure showed some correlation

with the IJ amplitude and slope, particularly with the latter. The HI wave amplitude and slope also showed some correlation with the rate of change of pressure but to a lesser extent. The correlation between the time derivative and the UF Bcg (a) was noted by various workers e.g., Reeves et al. (1957), Starr and Ogawa (1961), 1962^{a,b}, 1963), Ambrosi and Starr (1965), Starr (1965), Corbascio and Smith (1966), Corbascio et al. (1966), Deuchar (1966) and Pretorius et al. (1966).

As in the case of arterenol, a marked increase in part of the atrial wave (O" F) was noted where the diastolic time was not reduced. A decrease in diastolic time might obscure this increase, as the beginning of the atrial wave was then partly obscured by the L wave and the later phases of the atrial wave were fused with the pre-ejection waves.

The L wave and the second heart sound were decreased in amplitude. This decrease in amplitude coincided with the reduced amplitude of the HI and IJ waves and could be due to the less forceful deceleration of blood association with the decreased force of ejection earlier in the cycle. This further supports the view that lev-arterenol does not stimulate the myocardium to the same extent as arterenol. It may be concluded that the forces responsible for the acceleration and deceleration

of the centre of gravity, are changing at a slower rate after levarterenol injection. Heart action may thus be slightly impaired as was also noted in some other studies (Goldenberg et al. 1948, Drill 1958 and Von Euler 1958).

E. Later effects of levarterenol

The lower recording shown in Fig. 24 was made 80 seconds after levarterenol (8 gamma/kg) was administered. Heart rate was decreased from 390 to ± 70 beats per minute. The P-Q interval was irregular as many isolated P waves occurred (Chapter 8).

The main points of difference between the control recording (top Fig. 24) and the lower recording is the improvement in the UF Bcg (a) pattern. The HI amplitude was increased by about 60%. The IJ amplitude was increased by about 50%. The HI and IJ slopes were also increased. This coincided with an 'improved' or more vigorous pulse pressure and a more 'dynamic' time derivative of the pressure. The amplitude of the pressure derivative was increased by about 35%. The Q-H" time was decreased by about 30%. This indicated a shorter isometric phase. This was also demonstrated in dogs by Pretorius (1962^b).

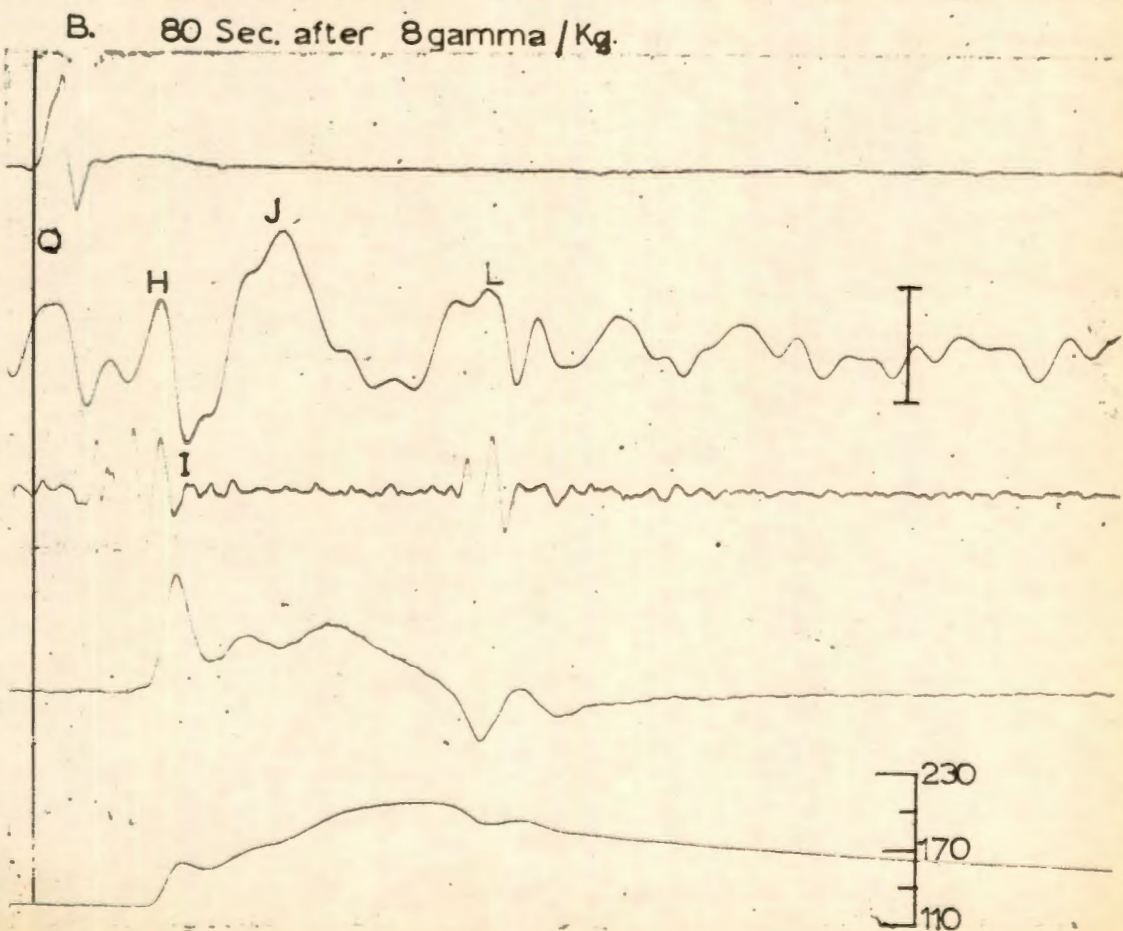
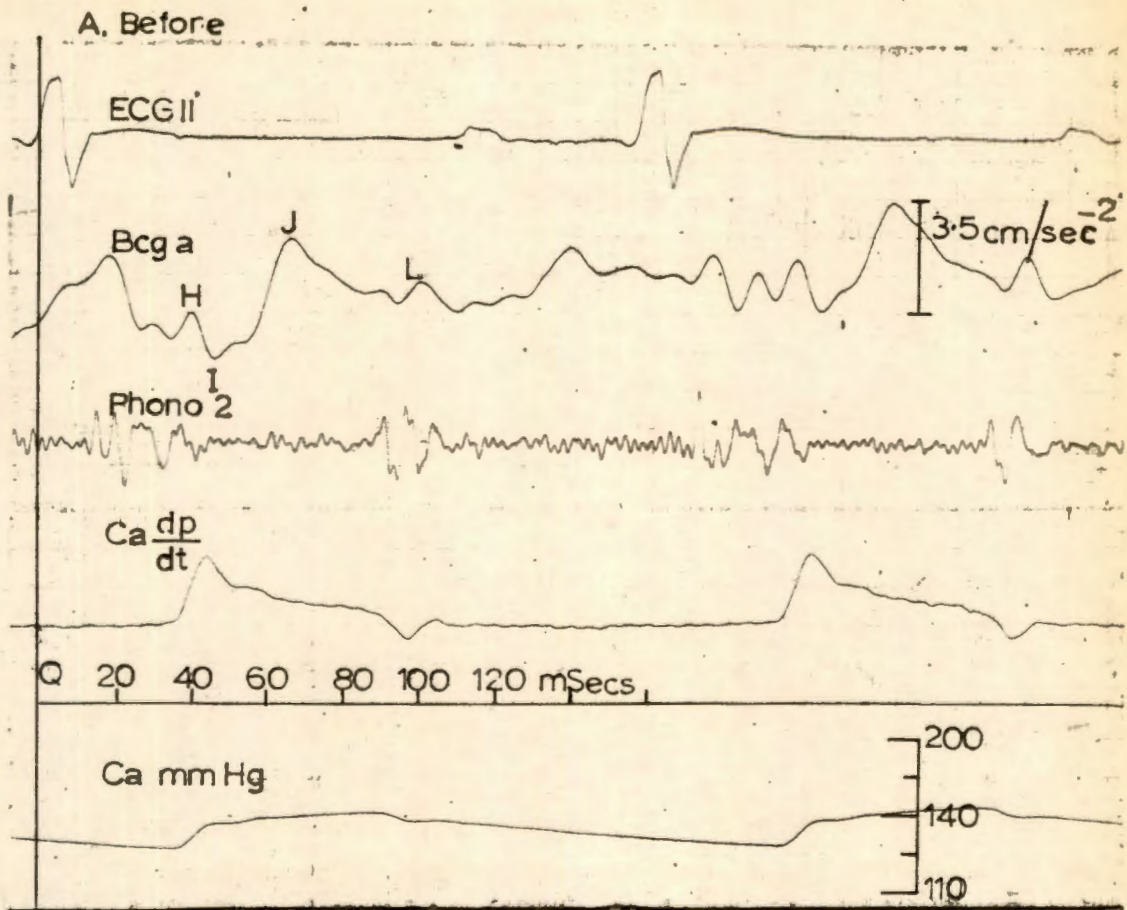
The duration of mechanical systole was increased. The Q-L time (first to second heart sound) and the time from the beginning of the pressure pulse to the closing notch,

FIG. 24 THE LATER EFFECTS OF LEVARTERENOL

The recordings are of the same rat shown in Fig. 23.

Note the reflex bradycardia and the improvement in the systolic wave (HIJ) amplitude and slope. The pulse pressure and amplitude of the time derivative of the pressure pulse also show an increase.

FIG. 24. LATER EFFECTS OF 'NORADRENALINE'



were all increased to the same extent.

The Q-J time was decreased 1.5 minutes after levarterenol administration in spite of the longer duration of systole. This might indicate that blood acceleration reached its peak value sooner. Rushmer (1961) noted that peak contraction force was reached sooner when the heart was stimulated by levarterenol.

The increase in IJ wave slope and amplitude, the decrease in Q-H, Q-I and Q-J times and the increase in amplitude of the pressure derivative, all indicated that the heart was accelerating blood more forcefully 1.5 minutes after levarterenol injection. Opposite effects were demonstrated seven seconds after levarterenol administration. This clearly indicates that the immediate (direct) effects of levarterenol were later (after 80 seconds) obscured by secondary effects. From the recordings made soon after levarterenol (Fig. 23) and soon after arterenol (Fig. 21) administration, it is evident that arterenol stimulated the myocardium to a greater extent. (Note the greater increase in the HI segment in the case of arterenol administration and the 'deterioration' of the J wave in the case of levarterenol administration.)

If the immediate effects of levarterenol (Fig. 23) are compared to the later effects (Fig. 24), an increase in HI and IJ slope and amplitude 80 seconds after levarterenol administration, is clearly shown. The heart thus showed

an increased force of contraction which could be ascribed to secondary sympathetic (reflex) action. This secondary sympathetic stimulation might be initiated by the primary vasoconstriction and peripheral ischaemia caused by levarterenol administration.

The results concerning the later effects of arterenol and levarterenol were based on 'normal' beats that could be isolated in the recordings. The Bcg changes during ectopic beats, Wenckebach's phenomena, and other manifestations caused by catecholamine treatment, will be discussed in the next chapter.

F. Discussion and conclusions

The major action of arterenol and levarterenol can be divided into an inotropic and a chronotropic action. The chronotropic effects of catecholamine can be assessed by Q time measurements. From experiments described in this chapter it was concluded that the slope and amplitude of the UF Bcg (a) waves may be used to investigate the inotropic action of cardiac stimulants. It was further observed that the injection of cardio-active substances is of great value in assessing the genesis and significance of the different Bcg waves (see Chapter 9).

(i) The chronotropic action: Administration of arterenol and levarterenol resulted in a decreased Q-I time. The

duration of the isometric contraction phase was therefore decreased. The Q-ejection time (from Q to the initial segment of the pressure pulse) was also decreased, which supports this view. The same results were obtained by catacholamine administration in dogs (Pretorius 1962^b), in rats (Pretorius et al. 1966) and in rabbits (Green 1967 and Pretorius et al. 1968^a).

Immediately after (up to 10 seconds) levarterenol and small doses of arterenol were administered, the heart rate was usually increased. The duration of mechanical systole was increased. Although levarterenol is of higher potency according to Rushmer (1961) and Wislicki (1964), and the amounts injected varied in the present experiments, it was concluded that both arterenol and levarterenol showed a positive chronotropic action on the myocardium of the intact rat. This chronotropic effect of the catecholamines was most conspicuously demonstrated by the UF Bcg (a).

(ii) The inotropic effect: Five to 10 seconds after arterenol was injected, the HI and IJ wave amplitudes were markedly increased. When levarterenol was injected, a marked increase in amplitude of the atrial wave complex resulted. This increase was even greater than that of the HI and IJ segments. These experiments proved that the HI and IJ waves are of importance in measuring the

force of contraction.

The increased peripheral resistance which followed levarterenol injection may have partially masked the inotropic effects of this drug. This means that the higher peripheral resistance might impede the flow of blood in spite of increased cardiac effort. The acceleration Bcg measures mass acceleration of the centre of gravity of the body and is therefore sensitive to alterations in blood flow, which is of vital importance for the maintenance of tissue. The Bcg thus provides information about this essential function of the cardiovascular system.

It was further evident that it is essential to consider the direct (immediate) effects and the indirect (later) effects of cardiac stimulants or depressants separately because the primary effects of the drugs might be masked, reversed or altered by secondary reflex action. As the magnitude of the reflex sympathetic or parasympathetic action is not readily evaluated, it might lead to serious error in the interpretation of the effects of the administered drugs.

From these experiments it was concluded that arterenol shows a more dramatic direct inotropic action than levarterenol on the myocardium of the intact rat. Again the UF Bcg (a) measured this action accurately.

CHAPTER 8

RELATIONSHIPS OF THE UF BCG (a) TO THE CLASSICAL METHODS AND SOME ASPECTS OF HAEMODYNAMICS

When moderate to large doses of arterenol or levarterenol were given to rats, bradycardia, amongst other conditions, developed. With the heart beating at a lower rate and perhaps more efficiently in some respects, the different phases of the cardiac cycle were better defined. Identification and interpretation of the UF Bcg (a) waves could therefore be done with more confidence. It further aided in establishing the genesis of the different wave complexes.

A. Normal time relationships between ECG, UF Bcg (a) and phonocardiogram

Although electrocardiography and ballistocardiography measure totally different aspects of cardiac activity, they show a certain relationship. The electrocardiogram measures the electrical phenomena preceeding and during the mechanical activities of the myocardium, while the Bcg measures mechanical activities. Under normal conditions a fixed time relationship exists between the electrical and mechanical events of cardiac activity. As the electrical events of cardiac activity are fairly well defined, the electrocardiogram serves as a valuable reference point in calculating the relative time intervals of other aspects of cardiac activity.

The Q wave of the ECG is regarded as the onset of electrical ventricular systole. The termination of the T wave, and therefore the end of electrical activity, is not clear in rats.

In the UF Bcg (a) of rats, systole can be subdivided into the latent phase, isometric contraction (pre-ejection) phase, initial ejection phase, maximal ejection phase and the reduced ejection phase followed by the end of mechanical systole. The Q wave of the ECG is therefore useful in providing a reference point from which the time relations of these phases can be calculated.

The information yielded by the UF Bcg (a) is, however, of a higher order than straightforward mechanical data. It is therefore difficult to interpret the time relationship between the ECG and the UF Bcg (a) alone. For this reason the phonocardiogram which provides pure vibrational mechanical information, thereby bridging the gap to a certain extent, will be discussed concurrently.

(i) The Q wave and ventricular systolic events: In Fig. 25 the normal time relations between the UF Bcg (a), ECG and phonocardiogram are shown. The curves were redrawn from the recording of a 'normal' anaesthetized rat weighing 315 grams with a heart rate of 385 beats per minute.

'Normal' Q time measurements were given in Chapter 3 (Table I). The measured Q time intervals were accepted as the true figures, as only a negligible time lag between the different measured aspects could be demonstrated (see Chapter 10).

From Fig. 25A it is evident that electrical systole (Q wave, ECG) preceded mechanical systole (Phono) by about 14 msec. The duration of mechanical systole as measured by the phonocardiogram amounted to 76 msec. This indicated that mechanical systole ended 90 msec after the commencement of electrical systole (Q wave).

In the UF Bcg (a) recording of the rat, systole can be subdivided into at least six phases. These six phases of systole are lettered a, b, c, d, e and f in Fig. 25.

Phase 'a' represents the time difference between the beginning of electrical systole and ballistic ventricular systole. In normal Q time measurements this is the Q-H' time. The duration of this phase was 18 msec, which was 4 msec longer than the same phase in the phonocardiogram. Phase 'a' can thus be named the latent or energizing period. This phase reflects the time between initial depolarization and the onset of the mechanical response in the ventricles. This phase of ballistic quiescence can be prolonged, e.g. by lowering the body temperature

FIG. 25 THE TIME RELATIONSHIPS OF DIFFERENT WAVE
COMPLEXES IN THE UF BCG (a) WITH THE ECG
AND PHONOCARDIOGRAM

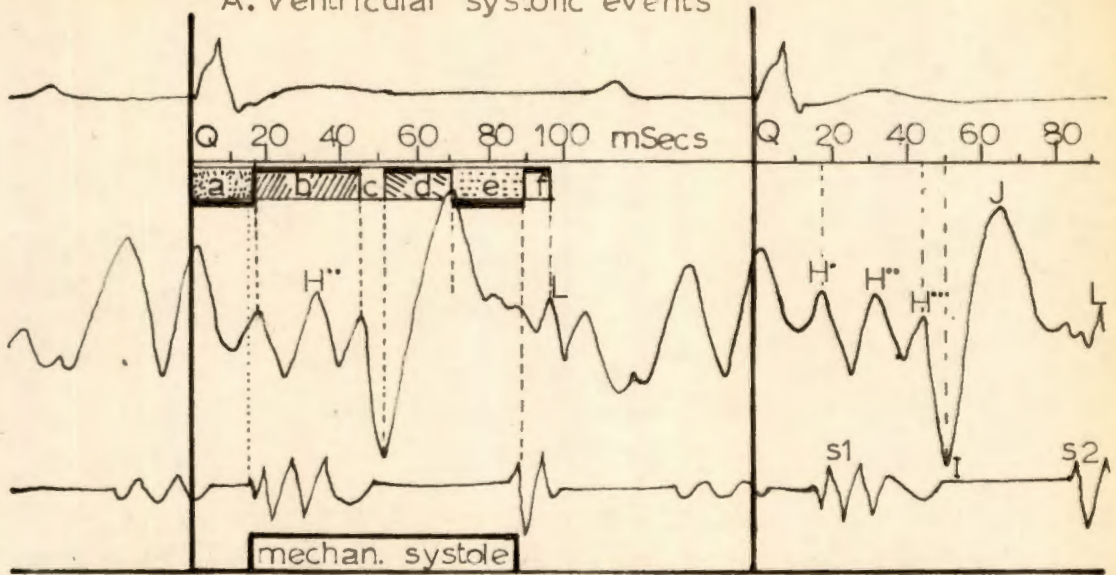
Fig. 25A shows the different phases identifiable in the UF Bcg (a) during ventricular systole. The solid vertical lines indicate the Q wave reference point.

Fig. 25B shows the suggested phases in the UF Bcg (a) during atrial systole. Solid vertical lines mark the P wave reference point.

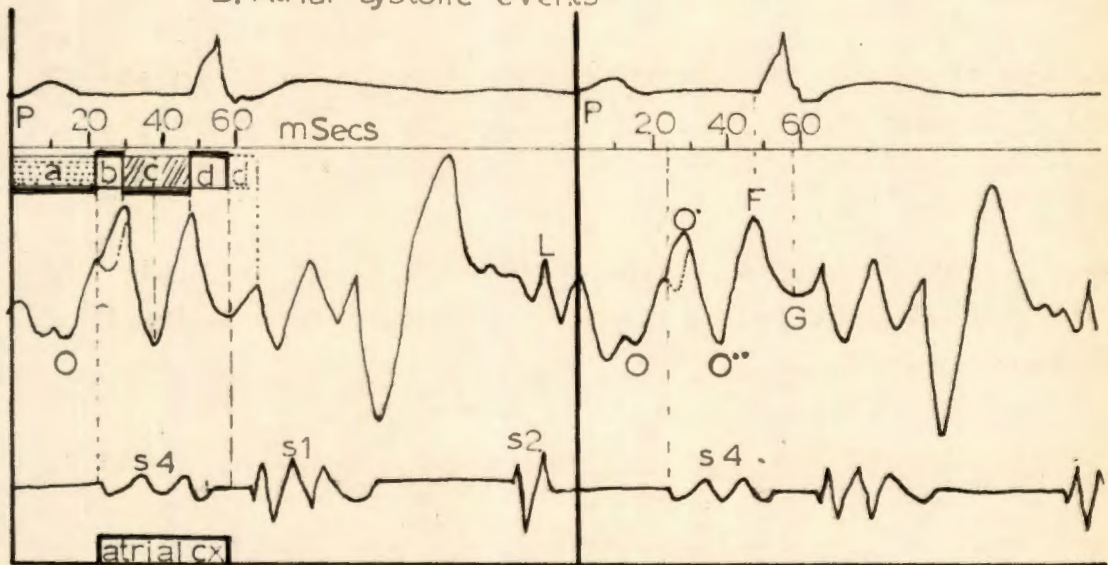
Fig. 25C depicts the diastolic wave complex L, M, N and O.

FIG. 25. ECG, PHONO AND BCG TIME RELATIONS

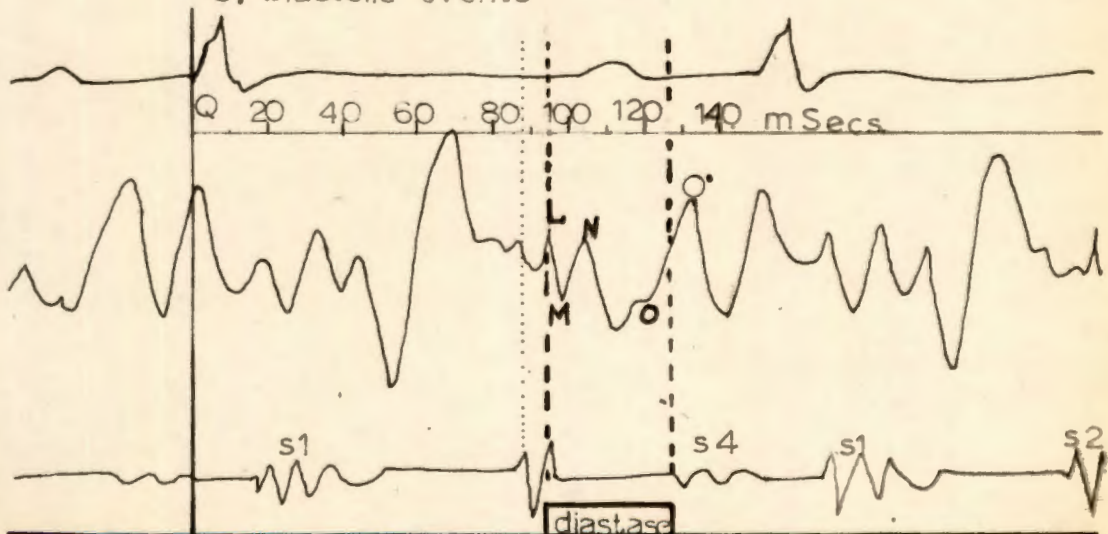
A. Ventricular systolic events



B. Atrial 'systolic' events



C. Diastolic events



(Pretorius et al. 1966).

Phase b starts with the H' wave in the UF Bcg (a) and represents the isovolumetric or pre-ejection (Pretorius 1962^b, Pretorius et al. 1966) period of systole. It terminates at the beginning of the HI wave. Under normal conditions in rats this is indicated as the H''I wave. This phase starts about 18 msec and terminates about 45 msec after the Q wave. Its mean duration is about 30 msec. It coincides with the major part of the first heart sound. In dogs Pretorius (1962) also noticed that the H wave is inscribed during the first heart sound.

Phase c probably represents initial ventricular ejection into the ascending aorta which is, as shown in Chapter 6, directed mainly headward in the rat. This phase commences as the main HI wave about 45 msec after the Q wave (Q-H''' in rats). It ends as the peak of the I wave in the UF Bcg (a) about 50 msec after Q. It is assumed that blood is ejected into the most proximal part of the ascending aorta during this phase. (Chapter 9).

Phase d was termed the period of maximal acceleration (ejection) of blood. It starts at the I wave (Q-I = 50 ± 5 msec) and ends at the J wave peak (Q-J = 68 ± 6 msec). It is believed that the major part of ejection takes place during this phase. This phase lasts for about 18 to 20 msec

and thus represents about 30% of the time of mechanical systole as measured by the phonocardiogram. It is indicated by the most conspicuous positive UF Bcg (a) wave (IJ wave). It is believed that acceleration of blood in the proximal part of the descending aorta is the dominant force being recorded in the UF Bcg (a) as a headward acceleration of the centre of gravity of the body during this phase (Chapter 9).

Phase e starts at the peak of the J wave in the UF Bcg (a). In rats no clear K wave could be identified under normal conditions. This phase would normally include the K wave and terminates shortly before the L wave. This period was called the period of reduced ejection and was normally void of significant Bcg waves, except for the initial fall from the J peak to the baseline. It is believed that blood acceleration slowly diminishes during this period accounting for the lack of large Bcg waves. The phonocardiogram shows the second heart sound during the termination of this phase. A small negative (K?) wave preceeding the L wave is inscribed simultaneously with the second heart sound. This small negative wave might indicate retrograde acceleration of blood associated with closure of the aortic valves. The L wave of the UF Bcg (a) is inscribed immediately after this small negative wave and might be caused by blood recoil immediately after valve closure (Chapter 9).

Phase f indicates the time difference between the termination of mechanical (phono) and ballistic systole. The L wave of the UF Bcg (a) which was taken as the end of ballistic systole was inscribed about 8 to 12 msec after the beginning of the second heart sound and coincided with the last part of the second heart sound. The temporal relationship found between the phonocardiogram and the UF Bcg (a) in rats, is in general very similar to that found in the dog (Pretorius 1962^b) and man (Schuman 1954, Rosa et al. 1955 and Scarborough and Talbot 1956).

(ii) The P wave and the normal atrial wave complex: In rats the cardioballistic waves associated with atrial activity are usually clearly identifiable. In literature very little information could be found on atrial ballistic waves. Pretorius (1962^b) demonstrated atrial waves in dogs when the PQ interval was increased after catecholamine administration. West and Corbascio (1959) obtained isolation of the atrial wave(s) in dogs by selective drug administration. Most rats showed a clear biphasic atrial wave in an earlier study (Pretorius et al, 1966). In the present study atrial waves were identified in all the recordings of 'normal' rats. Considerable variation in amplitude, which sometimes made it difficult to identify the atrial wave, was, however, encountered. High heart rates or a very much increased systolic time

also tended to obscure the atrial waves. Under 'normal' conditions the UF Bcg (a) of rats, however, consistently showed atrial waves.

The atrial wave complex in the UF Bcg (a) of rats is shown in Fig. 25B. The atrial wave was assumed to commence with the wave indicated as the O' wave. The O' wave was inscribed as a positive wave showing a notch or a depression in the UF Bcg (a) in the O-O' segment about 30 to 40 msec after the L wave. The O' wave coincided with the commencement of the atrial sound (S₄) in the phonocardiogram. It followed the P wave of the ECG within 20 to 35 msec. The depression or notch in the UF Bcg (a) denoted as the O' wave, is shown by the dotted curve in Fig. 25B. The atrial sound (S₄) was inscribed during the major part of the atrial wave complex.

The atrial wave complex was divided into four phases (see Fig. 25B). It is believed that the electrical and mechanical events during atrial activity should follow a basic pattern more or less similar to that of ventricular activities.

Phase a was taken as the latent period in the same way as Q-H', and the Q to first heart sound interval was taken as the latent period in the case of ventricular systole. The P-O' interval (Phase a Fig. 25B) lasted 22 msec,

which is slightly longer than the latent period in the case of the ventricles (Q-H').

Phase b was assumed to be the 'isometric' contraction phase' of the atria. It started 22 msec after the beginning of the P wave of the ECG and lasted about 16 msec.

Phase c is postulated to be representative of atrial ejection. It commenced shortly after the O' wave and terminated as the F wave in the UF Bcg (a). It started about 30 msec and terminated about 50 msec after the P wave of the ECG. The major part of this phase was identifiable as a deep negative peak denoted the O" wave (see Chapter 10). The O'O" segment was negative (below the baseline) while the O"F segment was positive (headward acceleration of centre of gravity).

Phase d was taken to commence at the F wave, about 45 to 50 msec after the P wave of the ECG. The exact termination of the atrial events could not be determined. It might end at the G wave or the H' wave of the UF Bcg (a). This phase is postulated to represent late atrial systolic events (Chapter 9).

(iii) The diastolic waves under 'normal' conditions: The only remaining section of the UF Bcg (a) is the diastolic wave complex. The waves believed to be associated with

ventricular diastole are shown in Fig. 225C. The waves are inscribed between the end of the second heart sound (S2) and the beginning of the atrial sound (S4).

The first diastolic waves were designated as the L, M and N waves. The last wave was lettered the O wave. This period started about 95 msec after the Q wave and terminated about 125 msec later probably indicating the period of diastasis.

Variations in Q time measurements were found during changes in heart rate and sympathetic stimulation. The mean time relationships of Bcgs for 'normal' rats as discussed earlier, were, however, remarkably constant.

B. Time relationship between ECG, UF Bcg (a) and phonocardiogram after sympathetic stimulation

(1) Q time relationships: In Fig. 26 recordings after different phases of sympathetic stimulation are shown. The recordings were chosen because they showed the sympathetic stimulation believed to be associated with carotid catheterization most conspicuously. Arterenol is thought to cause sympathetic stimulation. The effects of arterenol, the later effects of levarterenol and the effects of catheterization were therefore regarded as effects of sympathetic stimulation.

A progressive decrease in Q-I time was noted after

FIG. 26 THE Q TIME RELATIONSHIPS DURING DIFFERENT
DEGREES OF SYMPATHETIC STIMULATION

Solid horizontal lines show the Q-J time. The Q-I time intervals are indicated by dotted horizontal lines.

Fig. 26A shows the normal pattern.

Note that the isometric phase shows three H waves.

Fig. 26B shows the UF Bcg (a) of the same rat after catheterization of the carotid artery.

Note the decreased heart rate and the decreased Q-I time. The third H wave is abolished.

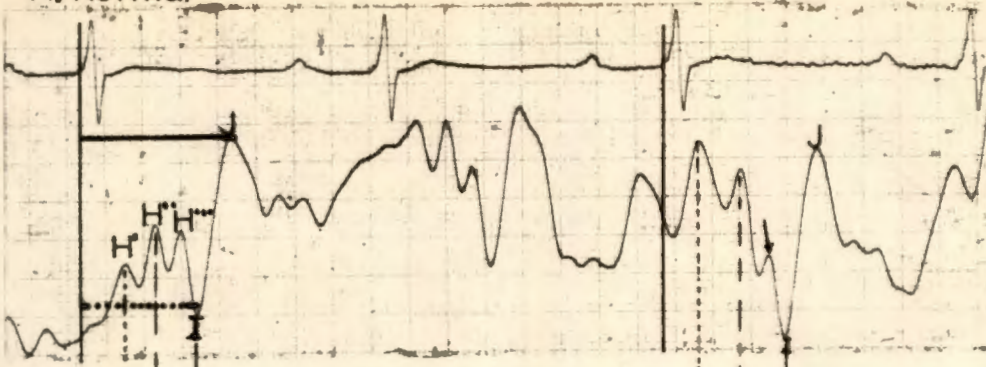
Fig. 26C shows the recording of the same rat 30 seconds after arterenol administration.

Note the decreased Q-I and Q-J time intervals. The arrow in Fig. 26A shows the H''' wave. In the lower recording (Fig. 26C) the arrow indicates a slur in the J wave, having more or less the same Q-time interval.

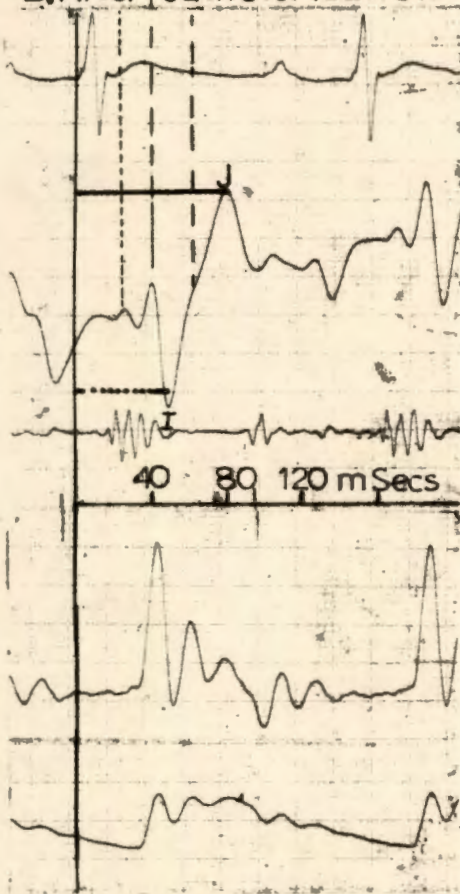
Fig. 26D. The recording was made 80 seconds after the arterenol injection. Bradycardia and partial recovery of the isometric and IJ waves can be noted.

FIG. 26. Q TIME RELATIONS WITH UF BCG a

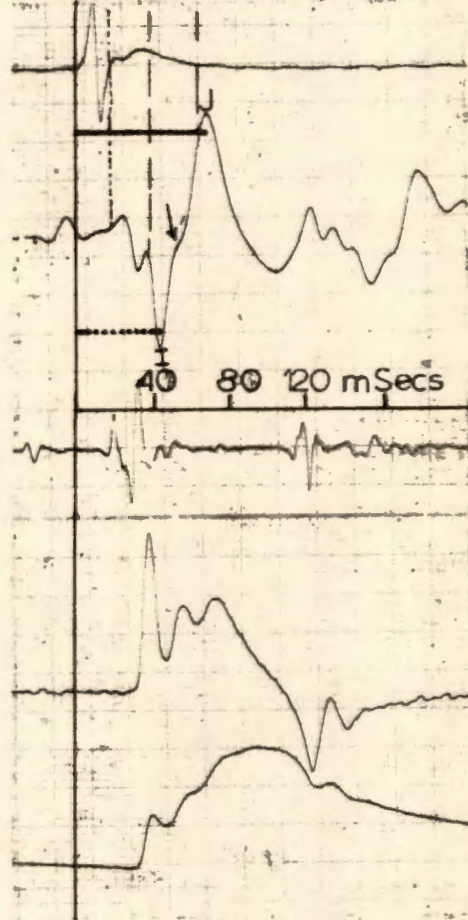
A. Normal



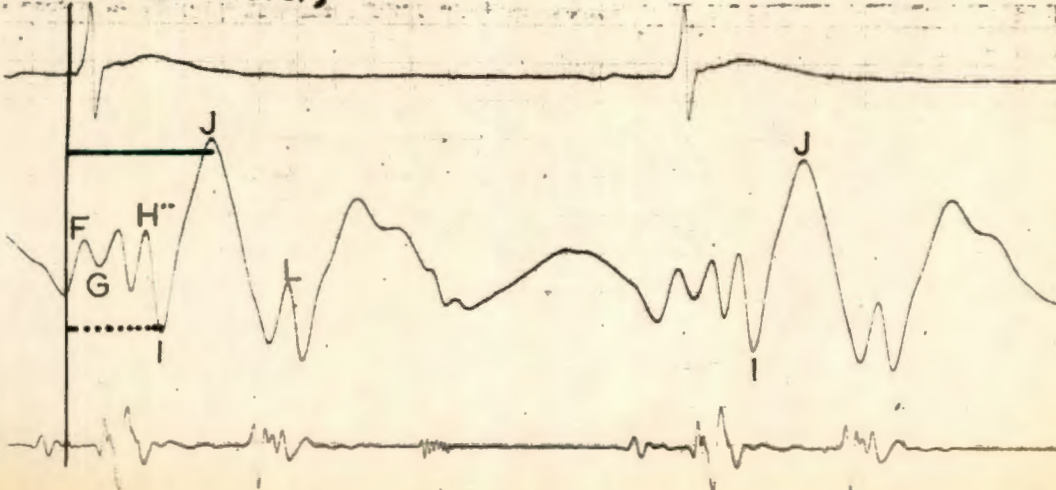
B. After catheterization



C. After adrenaline



D. Partial recovery



sympathetic stimulation (see Fig. 26). The results are summarized in Table III.

TABLE III (Time intervals in milliseconds)

	Q-H'	Q-H''	Q-H'''	Q-I	Q-J
Normal	24	38	54	60	80
After Catheterization	24	36	A	52	78
After Arterenol	24	36	A	46	68
During Recovery	24	38	A	50	76

A = Absent

It is obvious from the results that the decrease in Q-I time after sympathetic stimulation was greater than the decrease in Q-J time. After catheterization the Q-I time was decreased by 14% while the Q-J time was decreased by only 2.5%. After arterenol the Q-I time was decreased by 23% while the Q-J time was decreased by only 15%. It is possible that this difference in response to sympathetic stimulation might indicate a different genesis of the I and J waves.

Of further importance is the disappearance of the H''' wave after sympathetic stimulation. This 'shift' or abolishment of the H''' wave will be discussed in Chapter 9.

In Fig. 27 the effects of sympathetic stimulation are shown at a paper speed of 500 mm/sec.

The Q-H', Q-I, Q-J and Q-L times are shown for recordings A, B and C. It is evident that the Q-H' time was not markedly altered by induced sympathetic activity. A pronounced decrease in the Q-I time was noted which was more conspicuous than the Q-J time decrease. A progressive increase of Q-L time demonstrated an increase in the duration of systole.

(ii) UF Bcg (a) and P-Q time intervals: The longer duration of systole coupled with a slight increase in P-Q time following sympathetic stimulation, resulted in the main atrial wave (O"F) being inscribed shortly after the L wave (Fig. 27C). The shape of the H' wave was sometimes slightly altered by this 'isolation' of the atrial wave but it could still be identified. It is evident that in the case of rats the H' wave is caused by isometric events but it may be influenced by atrial events. In dogs Pretorius (1962^b) noted that the H (H') wave is mainly caused by isometric events but that it might contain some atrial components. West and Corbascio (1959) concluded that the FGH wave complex is mainly caused by atrial events. Noordergraaf's theory indicates a contribution of both atrial and ventricular events. The latter theory seems to be valid in the case of rats also. The fact that the H'

FIG. 27 Q TIME RELATIONSHIPS OF THE UF BCG (a) WAVES
DURING INCREASED CARDIAC EFFORT RESULTING
FROM INDUCED SYMPATHETIC ACTIVITY BY ARTERENOL
ADMINISTRATION

A. The normal pattern.

Note the three H waves during isometric contraction.

B. The Bcg pattern obtained after a small dose of arterenol was administered.

Note the abolishment of the third H wave. A split J wave developed where the J" wave is most prominent.

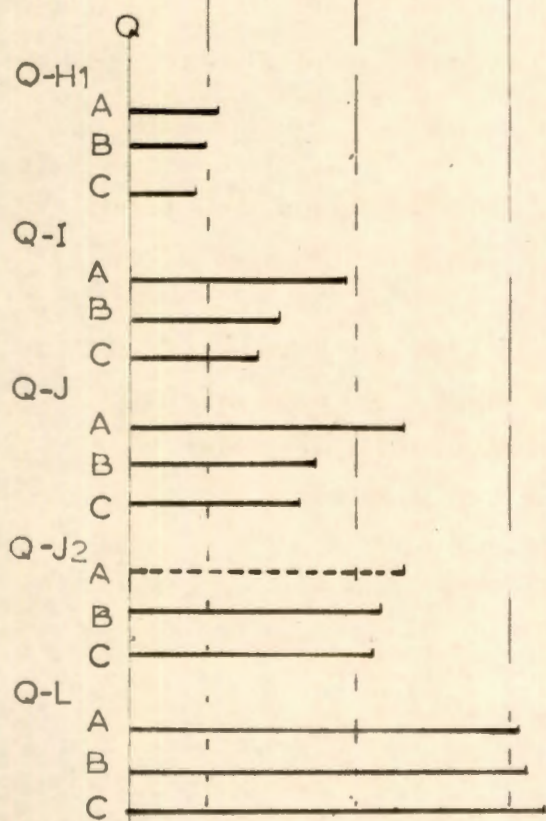
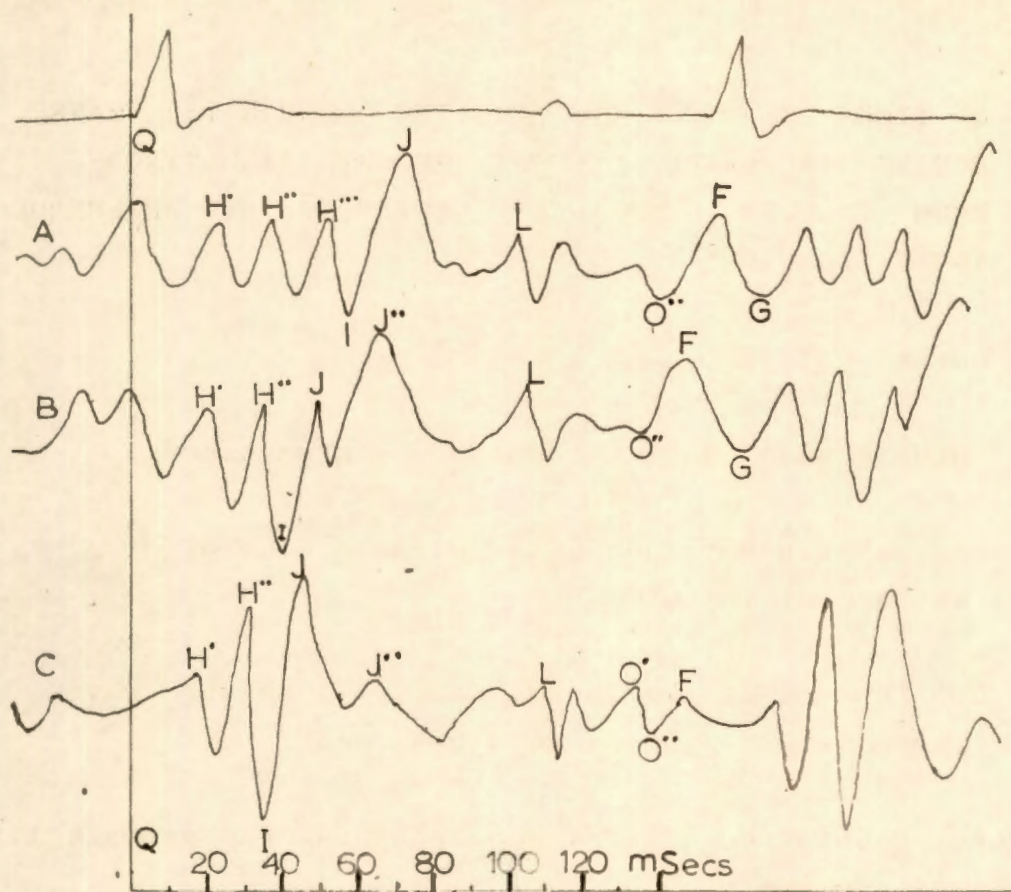
C. Recording obtained after a moderate dose (10 gamma/kg) arterenol was administered.

Note the increased HI and IJ amplitudes. The J" wave is less prominent.

The diagram shows the Q-H', Q-I, Q-J, Q-J" and Q-L times of the three recordings.

Note the progressive decrease in Q time intervals of all the waves except the L wave which shows an increased Q time interval. Decreased Q time intervals are most conspicuous in the cases of the I and J waves.

FIG. 27. Q TIME RELATIONS DURING SYMPATHETIC STIMULATION



wave was, however, present during rat experiments where the atrial effects were completely isolated, confirms the view held by Pretorius (1962^b). The atrial events might affect the amplitude and shape of the H' wave but they cannot be considered as the main cause of the H' wave in rats (see Chapter 9).

The isolation of atrial effects is shown in Figures 28 and 29. In Fig. 28A the normal atrial wave (O"F) associated with a normal P-Q time (46 msec) is shown. It should be noted that the atrial wave can be clearly identified in the Bcg of rats under 'normal' conditions. A normal P-O" time of 35 msec was noted in the normal recording. The F wave was inscribed 38 msec after the P wave. It followed about 2 msec after the Q wave. A Q-F time of up to 8 msec was found in some 'normal' rats. In a few rats the F wave preceded the Q wave by a maximum of 4 msec. A mean Q-F time of about 1.5 msec was noted in 'normal' rats. During normal conditions (before catheterization or drug administration) the influence of the atrial Q", F and G waves, especially the latter on the H' wave cannot be determined accurately.

In Fig. 28B the P-Q interval was increased from 46 msec to about 52 msec. The F wave now preceded the Q wave and the distance between the F and the H' wave was increased. The O" wave was less conspicuous, but the G wave increased

FIG. 28 INCREASED P-Q TIME INTERVAL AND PARTIAL ISOLATION OF THE ATRIAL WAVES.

Double horizontal lines show the P-Q time intervals. Solid vertical lines show the Q reference point. The ECG (lead II), the UF Bcg (a) and the phonocardiogram are shown from the top downwards.

Recording A shows a normal P-Q time interval of about 46 msec.

Note that the first H wave follows directly from the G wave of the atrial wave complex.

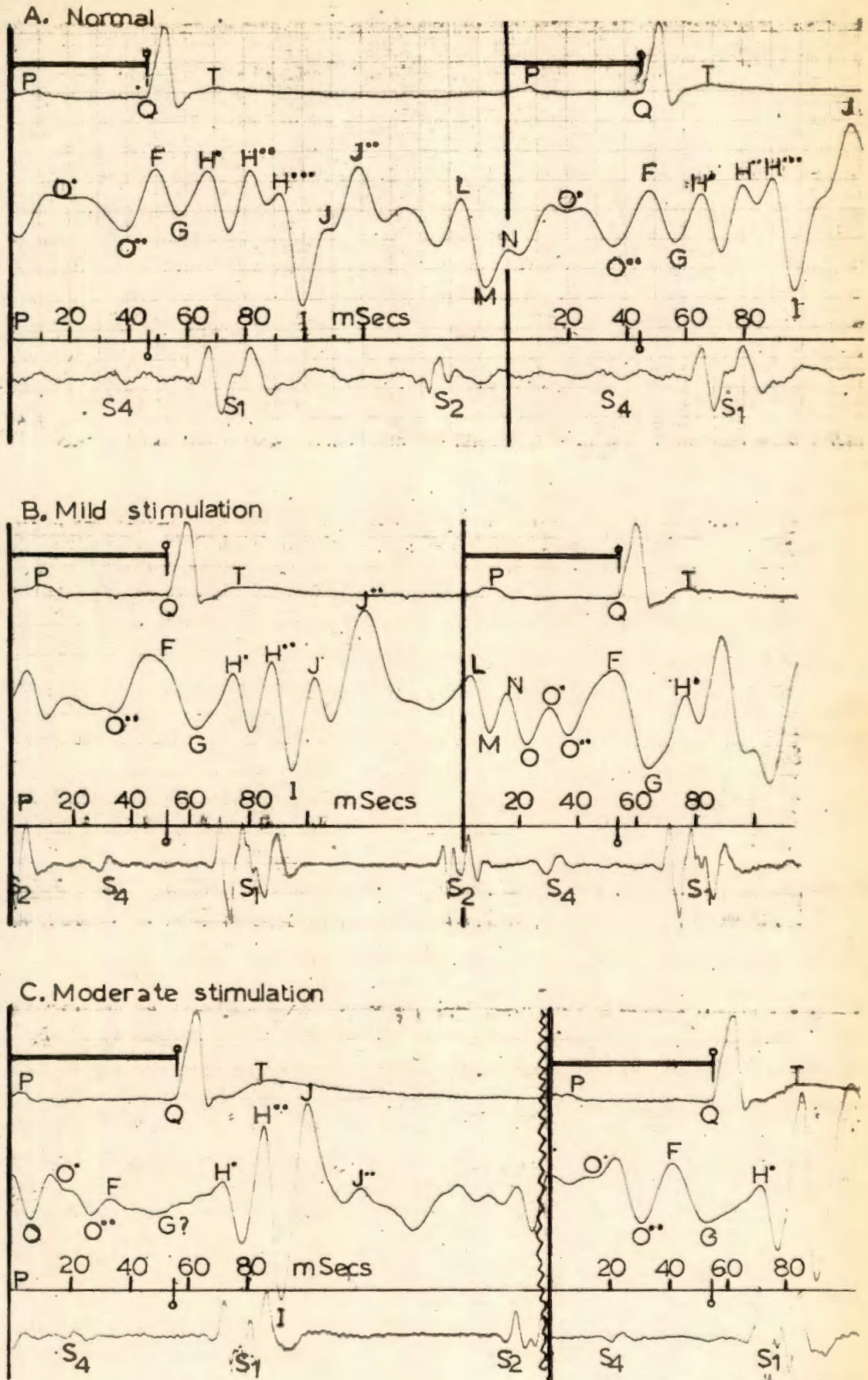
Recording B shows a P-Q time interval of 52 msec.

Note the slur in the GH segment.

Recording C shows a P-Q time interval of about 56 msec.

Note the decreased slope of the GH segment and the decreased amplitude of the G and H waves resulting from the increased G-H time. Bradycardia existed and a piece of quiescent recording was removed in order to show two successive beats.

FIG. 28. INCREASED P-Q TIME AND THE ATRIAL WAVE S.



in amplitude. The H' wave seemed to contain a part of the ascending segment of the G wave.

In Fig. 28C the P-Q interval was prolonged to about 56 msec. The contour of the O', O" and F waves was again very similar to that of the normal recording. The atrial sound (S4) in the phonocardiogram always kept a constant time relation with the atrial waves. During a short P-Q interval the O" wave and the atrial heart sound (S4) were always recorded close to the first heart sound. When the P-Q interval was progressively increased, the O" wave and the atrial sound were inscribed long before the first heart sound and the H' wave.

In Fig. 29A the normal positions of the O", F and G waves are shown at a lower paper speed.

In Fig. 29B an isolated P wave and the ballistic atrial waves associated with it are shown. It is followed by an ectopic ventricular beat, probably originating from the A-V node, where the P wave is actually superimposed on the Q wave. In spite of this short P-Q time interval, some of the atrial waves can still be identified, e.g. the O', O" and F waves.

In Fig. 29C an isolated P wave followed by a supra ventricular ectopic beat is shown. Note the persistence of the H' wave and the absence of the G wave in the ectopic

FIG. 29 COMPLETE ISOLATION OF THE ATRIAL WAVE COMPLEX
OBTAINED BY ADMINISTRATION OF A DOSE OF 8
GAMMA/KG LEVARTERENOL

Paper speed = 250 mm/sec.

Fig. 29A shows the normal atrial wave (O', O'', F and G) and its temporal relationship to the H' wave.

Fig. 29B. In this recording an isolated atrial wave complex is shown. The O', O'', F and G waves are associated with atrial systole and coincide with the fourth heart sound. The 'a' wave is probably associated with atrial relaxation. An atrial wave, practically superimposed on the ventricular wave complex, is shown in the second complex.

Note that most of the systolic atrial waves except the G wave can be identified.

Fig. 29C shows another isolated atrial wave complex and a ventricular wave complex not immediately preceded by an atrial wave.

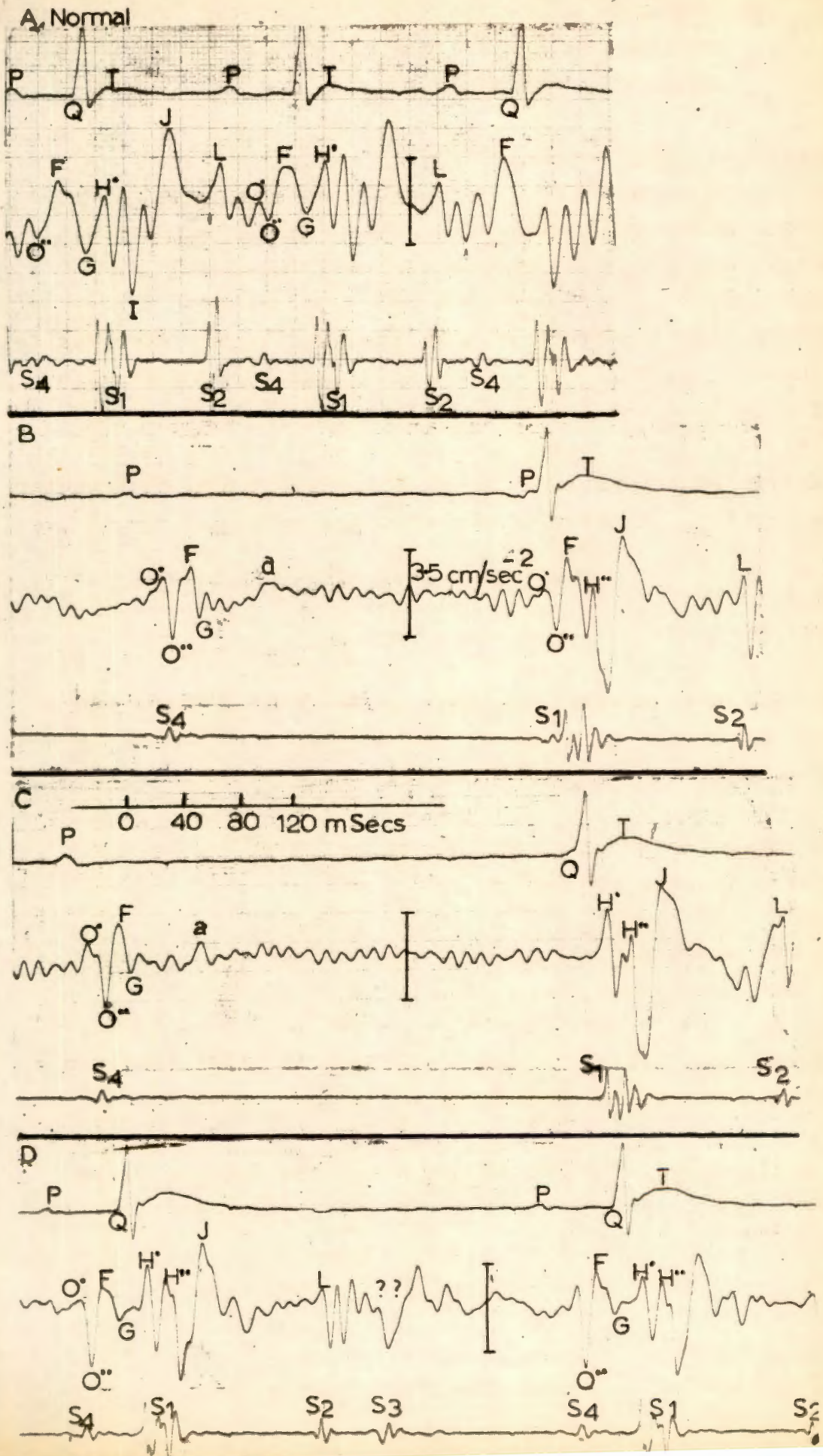
Note the persistence of the H' and H'' waves in the ventricular wave complex.

Fig. 29D shows partial recovery of the Bcg pattern and P-Q time intervals.

Note that the G wave is again starting to participate in the formation of the H' wave.

The beats shown in Figs. 29B to D were successive beats recorded 70 seconds after the levarterenol was administered.

FIG. 29. ISOLATION OF ATRIAL EVENTS.



beat.

In Fig. 29D two more or less normal beats are shown. The time relationships between the F, G and H' waves were nearly re-established.

C. Relationship between UF Bcg (a), carotid pressure pulse and its time derivative

(i) During 'normal' conditions: Most of the time and amplitude relationships between the recorded phenomena were pointed out in the previous chapter in dealing with the effects of catecholamines.

In Fig. 30 the relationships between the UF Bcg (a) and the pulse pressure with its time derivative are shown. Fig. 30A shows the recording obtained from an old rat (390 grams). This recording is compared to that of a young rat (280 grams) with more or less the same blood pressure. Conditions were taken as normal because nothing but pentobarbitone (45 mg/kg) was administered and the effects of catheterization were minimal.

The H''' wave, assumed to indicate the commencement of blood acceleration, was inscribed two msec after the beginning of the ascending limb of the carotid pressure pulse (Ca mmHg) in the old rat (Fig. 30A). In the young

FIG. 30 NORMAL TIME AND AMPLITUDE RELATIONSHIPS
BETWEEN THE BCG AND OTHER CARDIOVASCULAR
PHENOMENA IN RATS

Paper speed = 500 mm/sec.

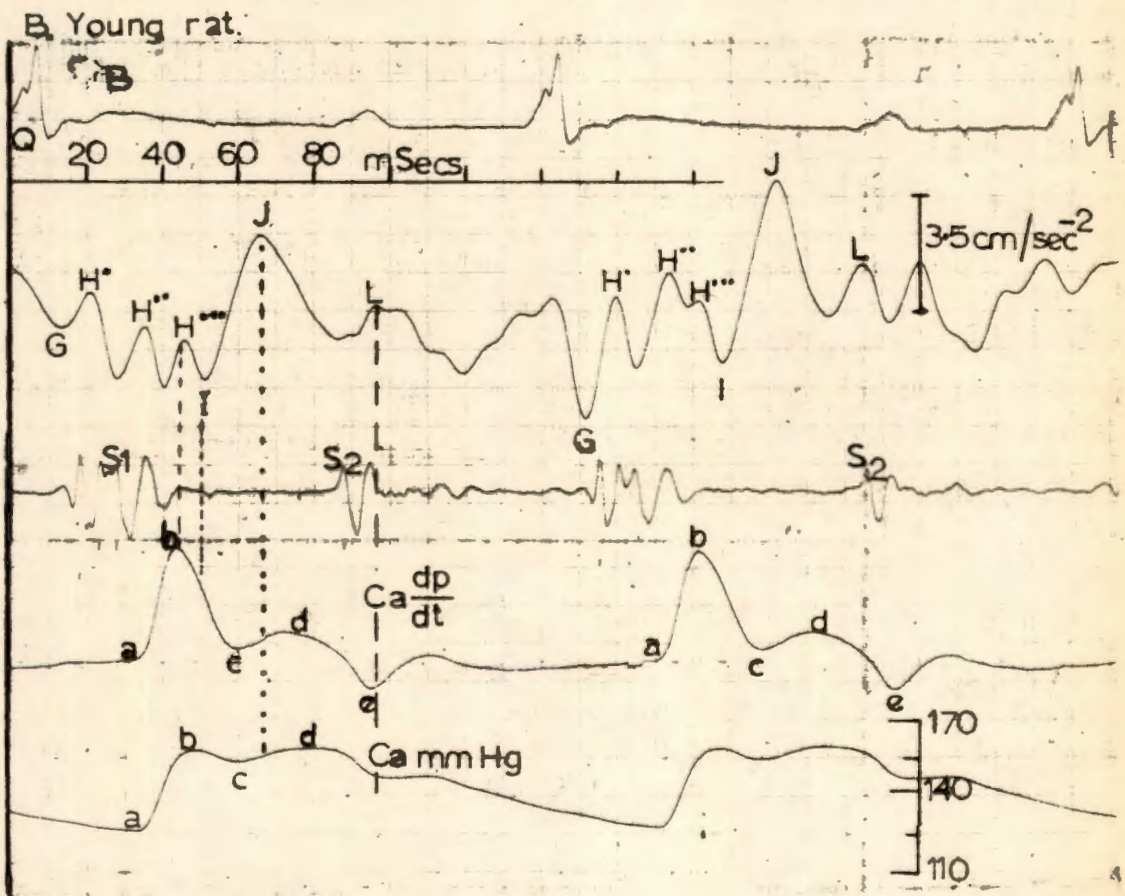
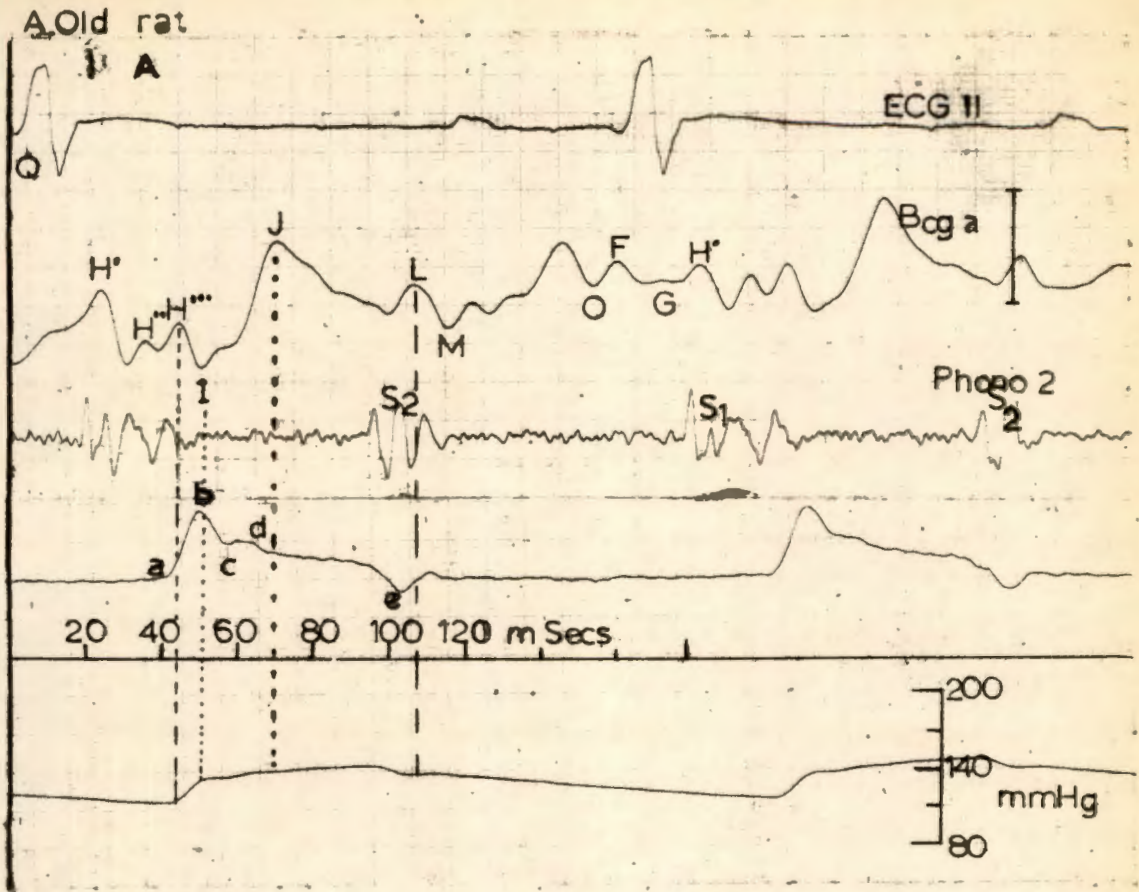
Fig. 30A. Recording obtained from an old rat.

Note the temporal relationship between the H^{III}I wave and the 'ab' segment of the pressure pulse derivative, and the temporal relationship between the L wave and the closing notch (e) in the pressure pulse derivative. Note also the similarity in pattern of the IJL segment in the Bcg and the 'bcde' segment of the pressure pulse derivative.

Fig. 30B. Recording obtained from a young rat.

Note that the H^{III}I wave bears a close time relationship to the 'ab' segment of the pressure pulse derivative. This relationship is comparable to the relationship of the H^{III}I segment in the old rat. Note the more dynamic nature of the pressure pulse derivative and the IJL segment of the Bcg in comparison to the pattern of the old rat.

FIG.30. NORMAL TIME AND AMPLITUDE RELATIONS.



rat (Fig. 30B) the H''' wave peaked 10 msec after the initial segment of the carotid pressure pulse. The H'' wave, however, peaked at the beginning of the pressure pulse in the young rat. Where the H''' wave in the old rat peaked early during the initial ascending segment of the time derivative of the carotid pressure pulse ($C\alpha \frac{dp}{dt}$), the H''' wave in the young rat peaked at the same time as the pressure time derivative.

Inconsistent time relationships were also noted in rats during 'normal' conditions although the same catheter, placed at the same position in the artery, was used. It was concluded that these inconsistent time relationships between the H''' wave and the pressure pulse might be due to physiological differences in cardiac functioning.

When arterenol was injected, a more constant time relationship between the H'' wave and the pressure pulse was demonstrated (see Chapter 7). Before and after catheterization, in the same rat, changes in the time relationship between the H''' wave and the pressure pulse resulted (see Chapter 6). In the same rat this time relationship also varied with the different phases of respiration. Differences in vessel elasticity, length of the vessels, blood pressure and pulse wave velocity might contribute to the different time relationships found in young and old rats. The synchronization between the left and right

ventricle might, however, be of major importance, as experiments have shown that the H''' wave might contain a contribution from right ventricular ejection (see Chapter 9). Sympathetic stimulation or arterenol injection affect the synchrony and would therefore alter the H''' wave (Chapter 7). From these time measurements and experiments it was concluded that the H''' wave in the UF Bcg (a) of rats did not always indicate the beginning of left ventricular ejection. This might be partly due to different degrees of cardiac co-ordination.

The I wave peaked at the top of the initial segment of the carotid pressure pulse in both the old and the young rat. The I wave peak thus showed a more constant relation to the pressure pulse during 'normal' conditions. The I wave peaked from three to six msec after the peak of the time derivative of the pressure pulse.

The slope and general contour of the HI wave seemed to agree with the slope of the initial segment of both the carotid pressure and its time derivative. In most cases a fast rate of change of pressure, indicated by a more vertical initial rising in the pressure pulse and an increased amplitude and slope of the time derivative, was associated with a more vertical HI segment. The HI amplitude was usually increased when the amplitude of the $Ca \frac{dp}{dt}$ was increased but this correlation was less striking

than the slope relationship.

The J wave peaked approximately during the middle of mechanical systole in 'normal' rats and slightly later in old rats. In the pulse pressure recording and its time derivative this period was usually indicated by the beginning of a second peak. The initial segment (ab) of the pressure pulse and its time derivative showed a fast rate of change of pressure which was associated with the I wave. The inertia of the 'stationary' blood in the proximal aorta would impede the acceleration of blood during initial ventricular ejection. Kinetic energy might thus largely be converted to pressure energy which might explain why the recorded initial (ab) increase in carotid pressure is not associated with a large ballistic wave. This might further be due to the small distance travelled by the blood in the proximal aorta, while kinetic energy is converted to pressure energy.

When pressure is 'established' and the inertia is partly overcome, less kinetic energy (energy of ejection supplied by the heart) will be converted to pressure energy. The increased displacement and velocity of the blood (mass acceleration) which results, will cause a greater acceleration of the centre of gravity of the body. An increase in pressure possibly results from this acceleration of the blood as the more peripheral acceleration would still be

less and the same sequence of events is repeated. These events might explain the genesis of the above mentioned second peak (cd) in the carotid pressure pulse and its time derivative. The increased acceleration of blood and the mass displacement of blood might explain why a conspicuous ballistic wave (IJ) is inscribed at this stage of ejection. The J wave peak thus seems to indicate the period of ejection where maximum blood acceleration is reached.

The J(K)L segment of the UF Bcg (a) follows the contour of the carotid pressure and especially that of its time derivative to a remarkable degree. In Fig. 30A the slow rate of change in the pressure derivative (decreased slope) coincides with a decreased slope in the J(K)L segment of the UF Bcg (a). In Fig. 30B the faster rate of change of pressure coincides with an increased slope in the JL segment.

The L wave was inscribed more or less during the middle of the dicrotic notch in the pressure pulse. It followed the same event (e) in the time derivative of the pressure pulse within two to four msec. The contour, slope, and amplitude of the L wave did not seem to show a fixed relationship with the corresponding aspects in the pressure pulse or pressure pulse derivative.

(iii) During sympathetic stimulation: Changes in time

FIG. 31 TIME RELATIONSHIPS BETWEEN THE BCG WAVES AND
DIFFERENT SEGMENTS OF THE PRESSURE PULSE
DERIVATIVE BEFORE AND AFTER INDUCED SYMPATHETIC
STIMULATION

Single horizontal lines show the Q-H time intervals, double horizontal lines depict the Q-H" time intervals and triple horizontal lines show the Q-ejection times.

The temporal relationships of the H, I, J and L waves to the pressure pulse derivative are indicated by broken vertical lines.

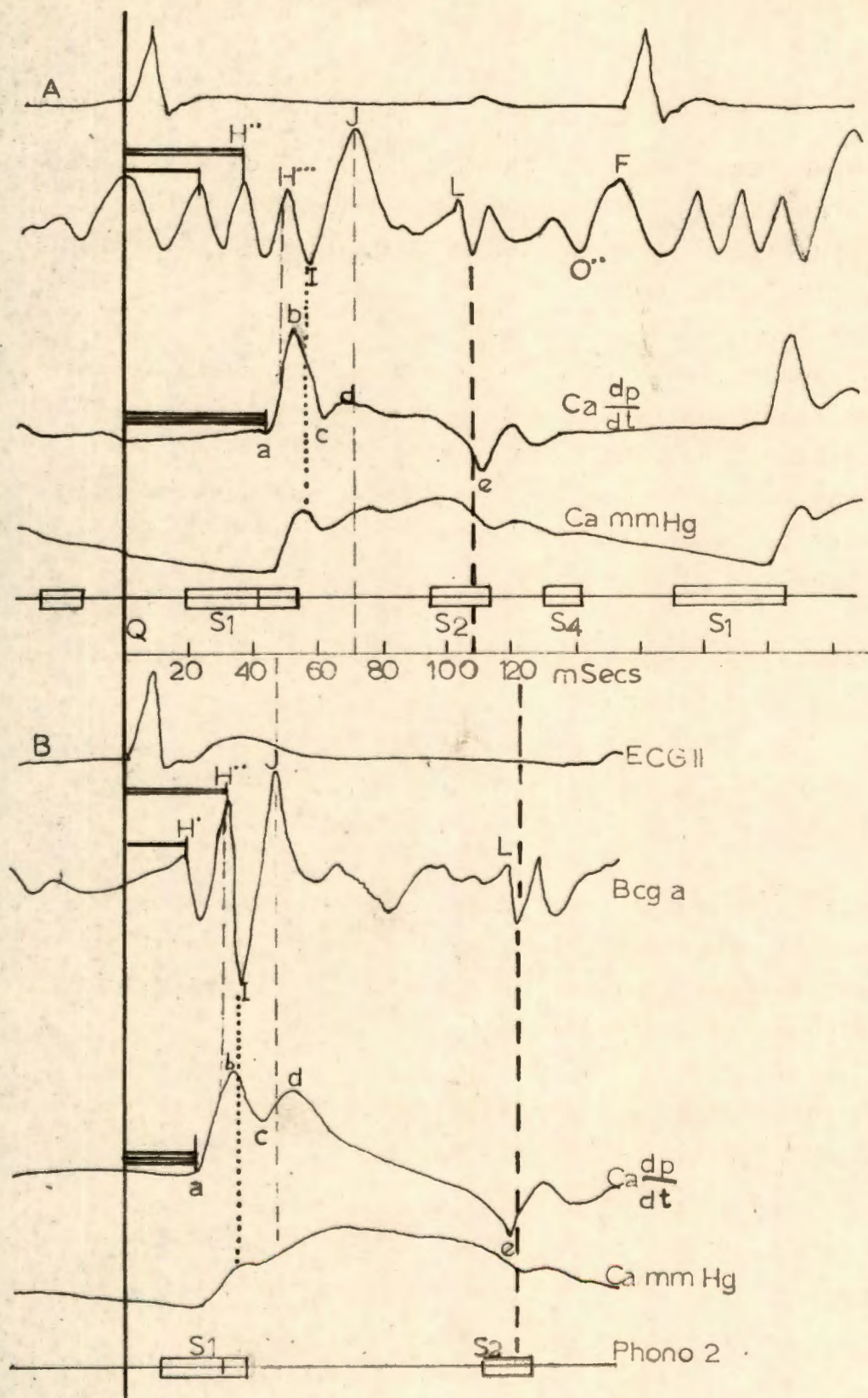
Fig. 31A shows the general normal pattern before sympathetic 'stimulation'.

Fig. 31B shows the general pattern after sympathetic 'stimulation'.

Note the close temporal relationship between the HI (H"^{III}I before the H"^{II}I after sympathetic stimulation) segment of the Bcg and initial ventricular ejection ('ab' segment of the pressure pulse derivative).

Note also the decreased Q-ejection and Q-I time intervals following sympathetic 'stimulation'.

FIG. 31. TIME RELATIONS OF UF BCG AND PRESSURE PULSE.



relationship of the UF Bcg (a) and the pressure pulse are shown in Fig. 31. In the normal recording (Fig. 31A) initial ventricular ejection ($H'''I$) commenced about 52 msec after the Q wave. The time interval from the Q wave to the initial ascending segment of the pressure pulse derivative amounted to about 45 msec. After sympathetic stimulation the initial ventricular ejection ($H''I$) wave was inscribed 32 msec after the Q wave. The pressure derivative started 22 msec after the Q wave.

It is evident that a very close relationship exists between the initial ventricular wave (HI) and the initial excursion of the pressure pulse and its time derivative. This further demonstrated that the isometric phase is much reduced in time by sympathetic stimulation induced by arterenol injection. Sympathetic stimulation also decreased the latent or energizing period by about 16%. This was clearly demonstrated by the decrease in $Q-H'$ time in the UF Bcg (a) and also by the time from Q to the beginning of the first heart sound. The onset of myocardial tension development therefore followed sooner after the electrical impulse, and the rate of tension development was also increased by sympathetic stimulation. The latter was also demonstrated by the $Q-J$ time of the UF Bcg (a) which was decreased by about 33%, reflecting that the maximal acceleration of blood was achieved much sooner. As the other phenomena measured

FIG. 32 THE EFFECTS OF MODERATE CHANGES IN BLOOD
VOLUME ON THE HAEMODYNAMICS OF THE RAT

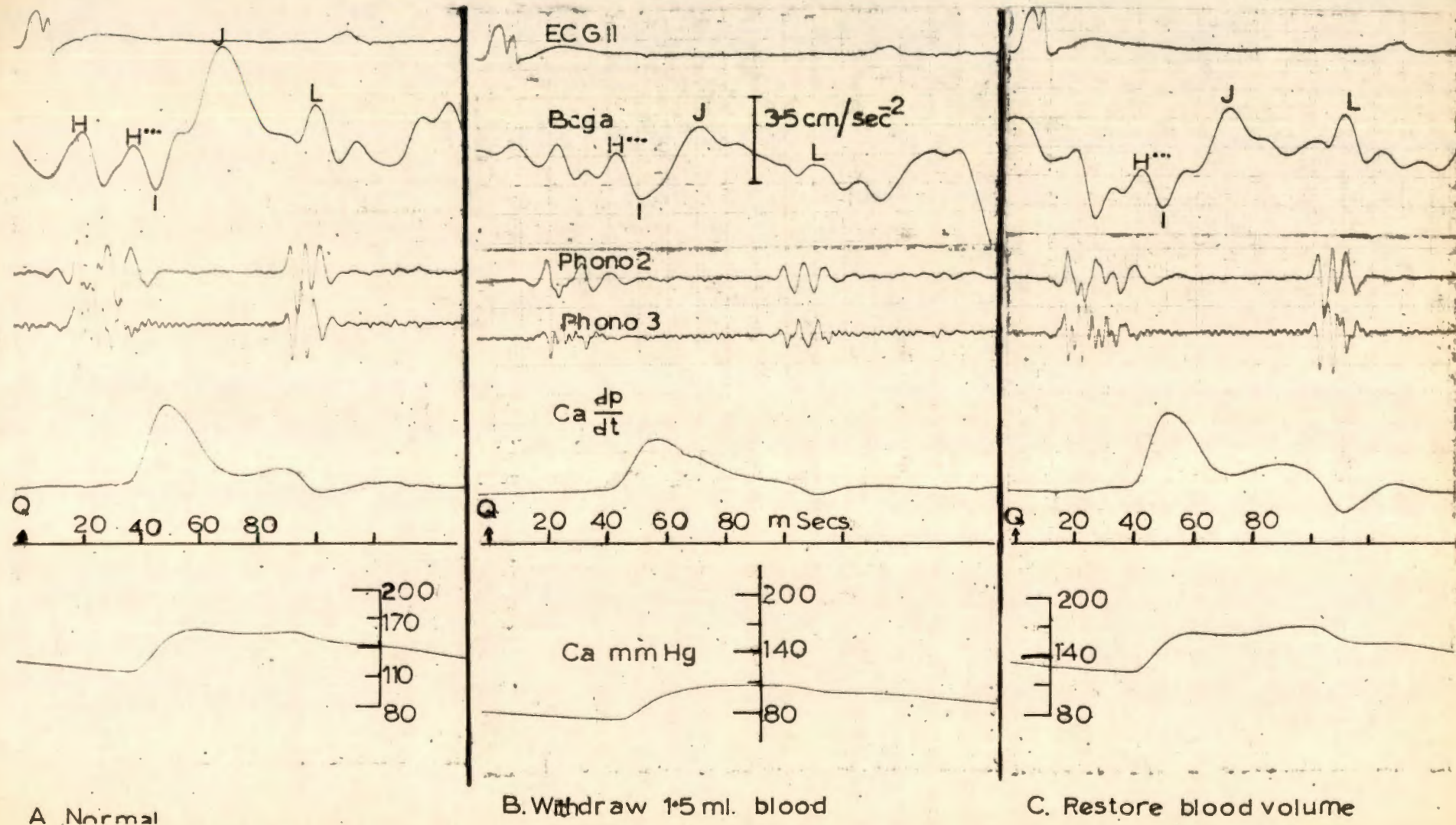
Lead II of the ECG, the UF Bcg (a), the second and third phonocardiograms, the pressure pulse derivative and the carotid pressure are shown from the top downwards.

Fig. 32A shows the normal pattern.

Fig. 32B shows the effect of a moderate decrease in blood volume on the recorded phenomena.

Note the reduction in IJ slope and amplitude. The hypodynamic pressure pulse derivative coincides with a hypodynamic UF Bcg (a) pattern.

Fig. 32C is the recording obtained after the blood volume was restored.



did not show this increase in the rate of change of pressure clearly, it demonstrates the value of the UF Bcg (a) in detecting the rate of change in velocity and force of blood ejection.

The duration of systole was increased by about 35%. This was demonstrated by the H-L time, the phonocardiogram the pressure pulse and its time derivative. During late systole the UF Bcg (a) showed no conspicuous waves (K-L segment). The rate of change in acceleration of blood was therefore not markedly altered. This agreed with the more or less steady state in the pressure pulse and its time derivative.

D. Blood volume and the UF Bcg (a)

If the UF Bcg (a) measures dynamic functioning of the cardiovascular system, changes in the blood volume must be reflected in the recordings.

(i) Moderate changes in blood volume: Changes brought about by moderate alterations in blood volume are shown in Fig. 32. When 1.5 ml of blood was withdrawn from the circulation, a marked decrease in the IJ amplitude resulted. This coincided with a reduction of the blood pressure and the amplitude of the pressure pulse time derivative. The IJ amplitude was decreased by about 50%, the systolic arterial pressure by 30% and the time

FIG. 33 THE EFFECTS OF A DRASTIC REDUCTION IN BLOOD
VOLUME ON THE RECORDED PHENOMENA

Paper speed = 250 mm/sec.

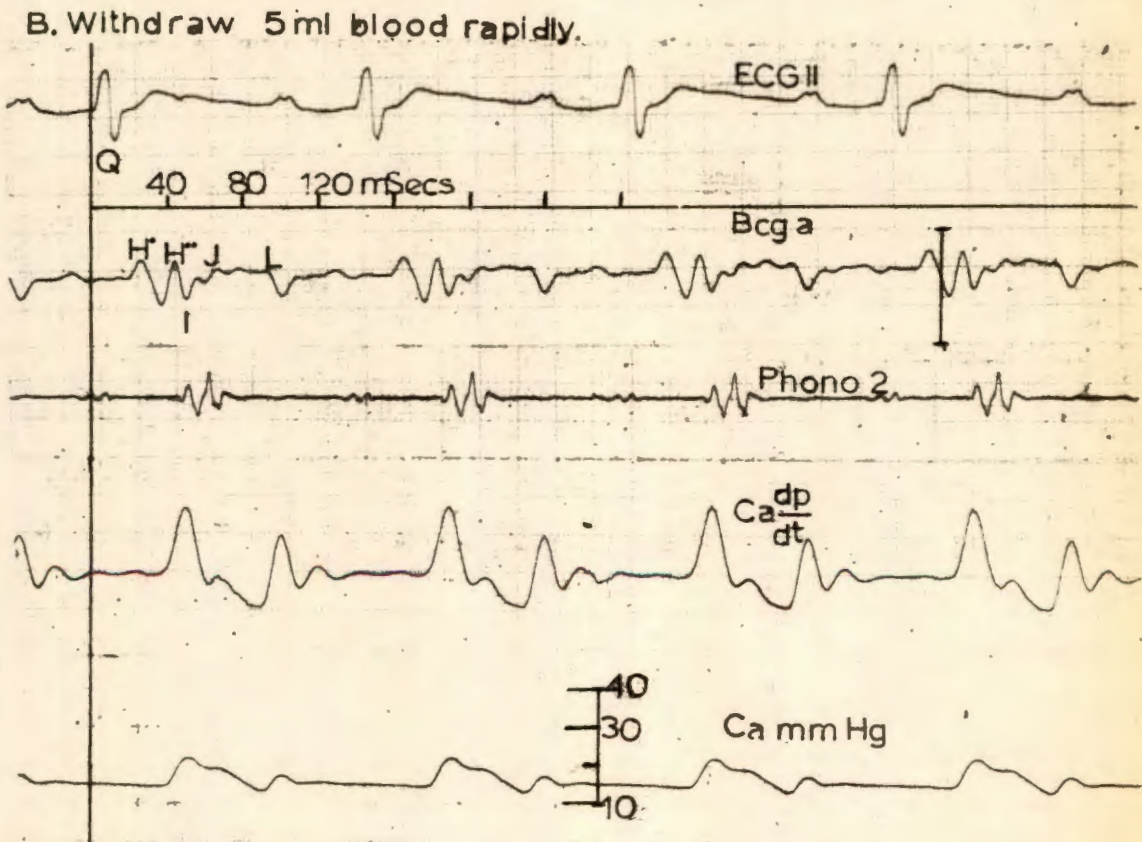
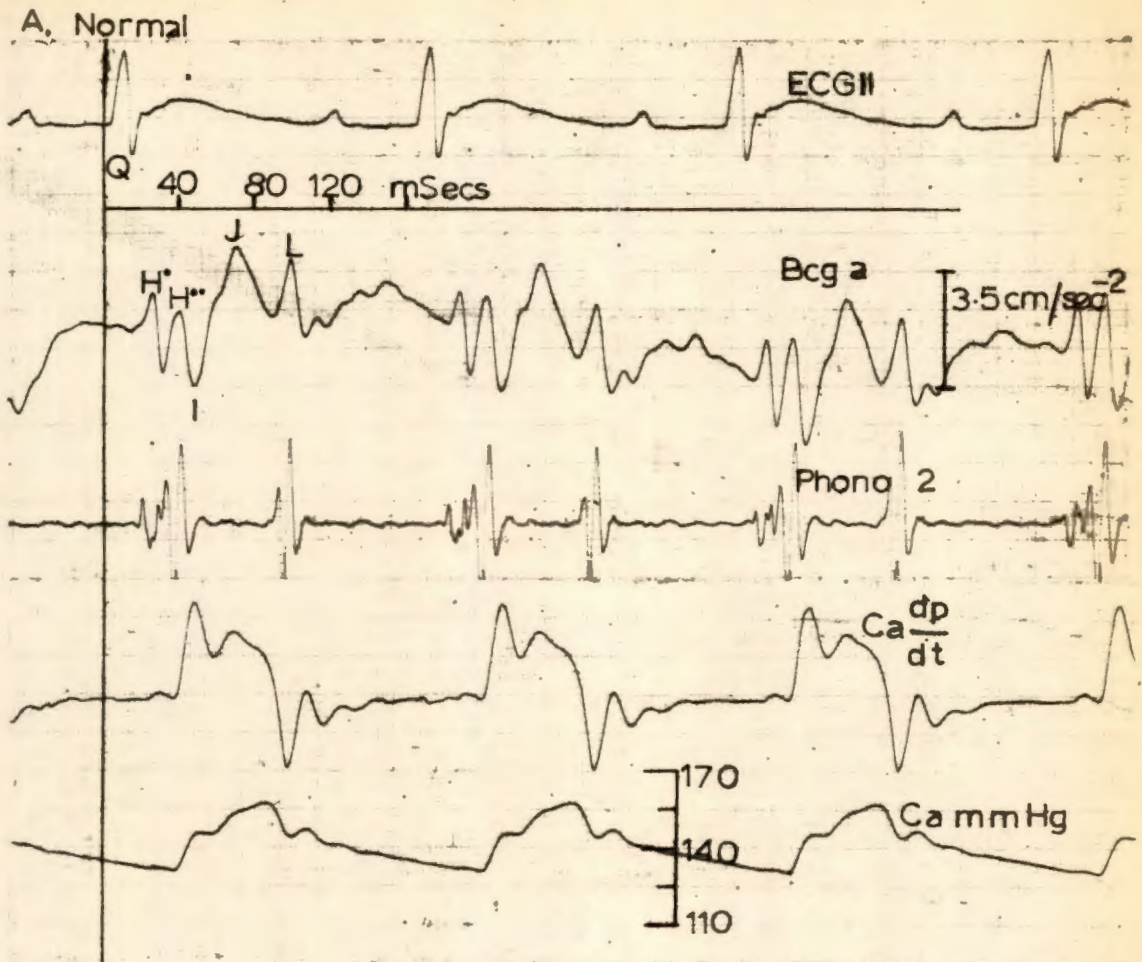
Fig. 33A shows the normal pattern.

Fig. 33B shows the recording obtained immediately after
5 ml of blood had been withdrawn from the circulation.

Note the decreased amplitude of the systolic ballistic
waves, while the H' and H" waves are not dramatically
decreased in amplitude.

Note also the abolishment of the second heart sound and
the decrease of blood pressure to shock level.

FIG.33, DRASTIC REDUCTION OF BLOOD VOLUME



derivative by about 33%. The slope of the IJ wave was also decreased. The first heart sound was slightly reduced in amplitude and the lower intensity of the second heart sound coincided with a marked reduction of the L wave in the UF Bcg (a). It is again evident that the UF Bcg (a) showed the most conspicuous changes.

When the blood volume was restored, the normal picture (Fig. 32A) was almost completely re-established. This experiment also demonstrated Starling's law of the heart. The decrease in blood volume probably resulted in a lowered mean circulatory pressure, a decreased venous return and therefore in a reduced filling of the ventricle. It seems possible that the sarcomere length (Sonnenblick et al. 1964) was decreased within physiological limits and the resulting sarcomere-length:tension development ratio was reduced. This might explain the less forceful acceleration noted in the UF Bcg (a).

(ii) Drastic reduction in blood volume: An example of the effects of a severe reduction in blood volume is shown in Fig. 33. The recording was made soon after five ml of blood was removed from the circulation of a rat. All the Bcg (a) waves except the isometric (H' and H'') waves were almost completely abolished. The HI amplitude was reduced by about 60%. The IJ amplitude was decreased by about 90%. The mean arterial pressure was reduced from 140 to about 12

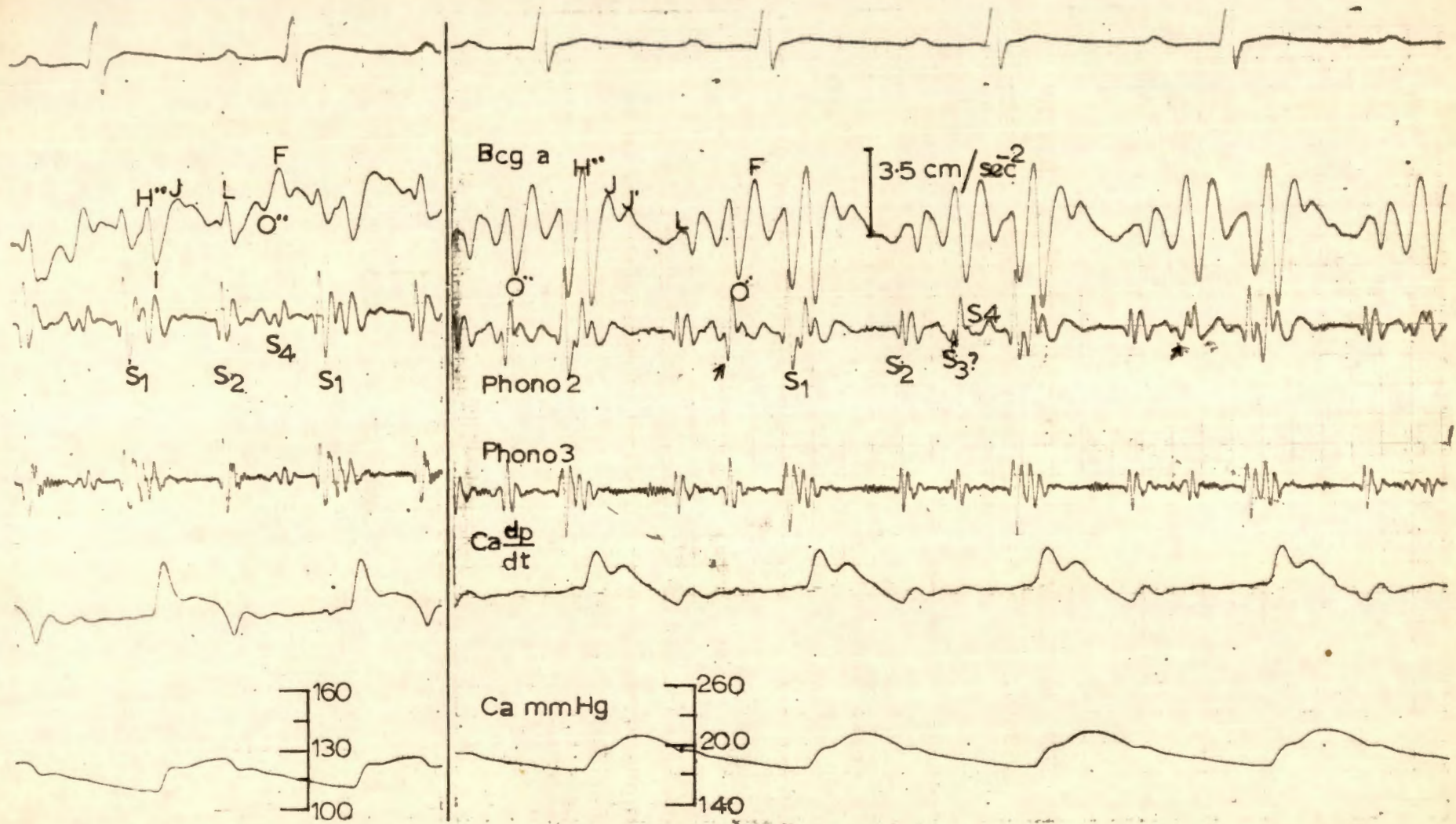
FIG. 34 THE DEVELOPMENT OF GALLOP (TRIPLE) RHYTHM
ASSOCIATED WITH AN ELEVATED BLOOD PRESSURE

Paper speed = 250 mm/sec.

Fig. 34A shows the normal pattern.

Fig. 34B was recorded after the administration of 5
gamma/kg arterenol.

Note the appearance of an abnormal fourth (atrial)
heart sound (indicated by arrows), fused with the third
heart sound.



A. NORMAL

B. DEVELOPMENT OF GALLOP RHYTHM

mmHg (about 92%). The amplitude of the initial segment of the pressure derivative was reduced by about 20%. The phonocardiogram amplitude was decreased by about 60%. The heart rate was increased by about 15%. This increase in heart rate could indicate sympathetic stimulation of the heart initiated by the pressoreceptors. In spite of the possible increased cardiac effort associated with sympathetic stimulation, the Bcg (a) amplitude showed a marked decrease. A decrease in pulse pressure from about 30 mmHg to 12 mmHg (60%) was also noted.

From these experiments it was concluded that the HI, IJ, LMN and atrial (O', O" and F) waves of the UF Bcg (a) are mainly caused by forces associated with the flow of blood. The persistence of the H waves pointed to a different genesis of the isometric waves. The effects of a drastic reduction in blood volume showed a close similarity to that of vena caval occlusion (see Chapter 6). Except for the lowering in mean arterial pressure, the HI and IJ waves of the UF Bcg (a) showed the most conspicuous changes when the blood volume was reduced.

E. The dying heart

Doses of 10 to 12 gamma/kg arterenol sometimes caused fatal vascular accidents in some rats. In a few cases severe pulmonary haemorrhage resulted from rupture of the capillaries. This was confirmed at autopsy (see Chapter

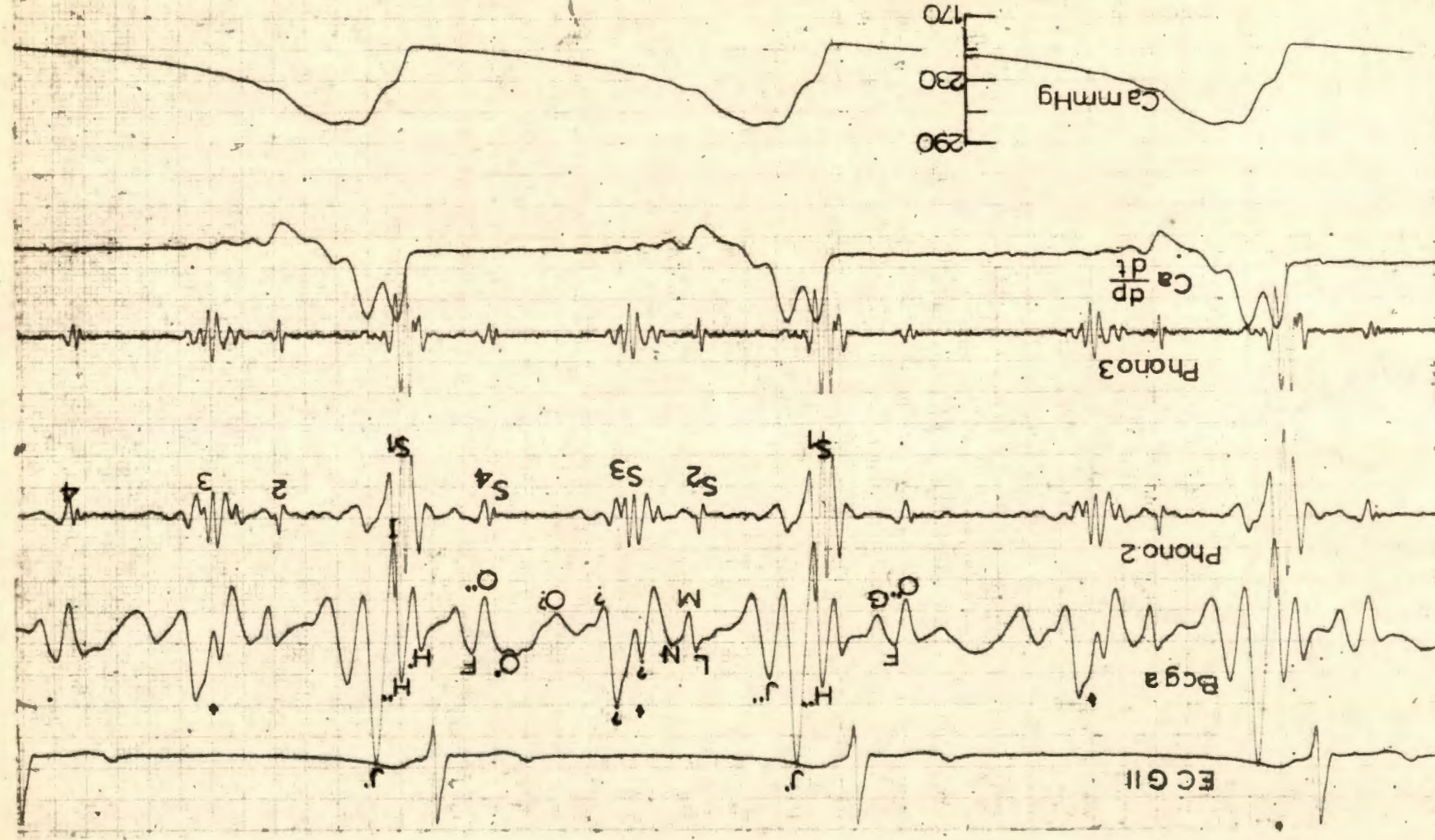
FIG. 35 THE ESTABLISHMENT OF GALLOP RHYTHM IN THE
SAME RAT AS IN FIG. 34

Paper speed = 250 mm/sec.

Note the bradycardia and the conspicuous third (S3) heart sound. The third and fourth heart sounds are now clearly separated.

Note also the abnormal ballistic waves following the N wave and preceding the O wave.

FIG.35. ESTABLISHED GALLOP (TRIPLE) RHYTHM.



9). The ischaemia and hypoxia following pulmonary damage gave rise to hypovolaemia, secondary atrial fibrillation and cardiovascular shock. These changes in cardiovascular dynamics proved valuable in furthering the understanding of the UF Bcg (a) waves.

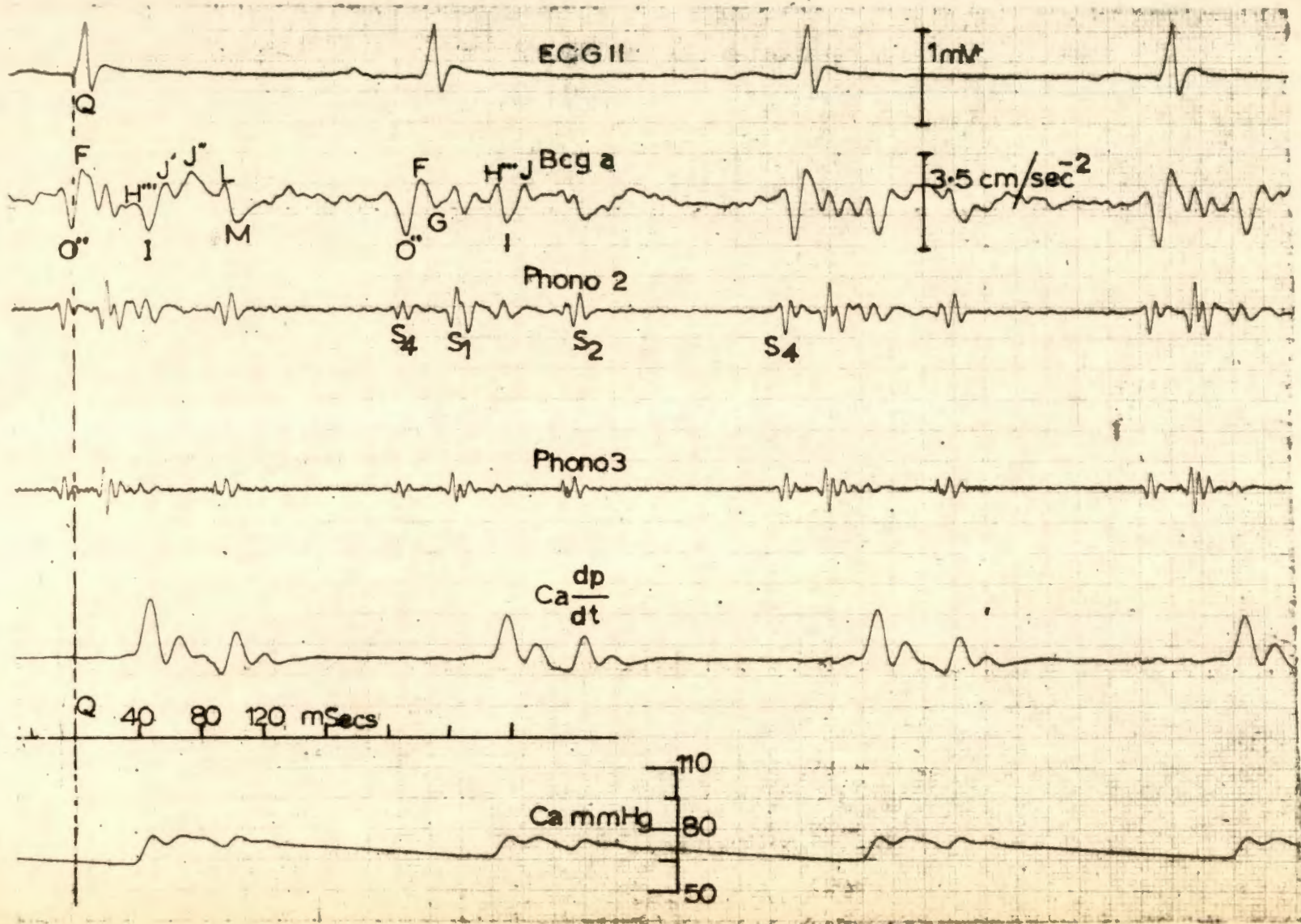
A sign of a failing circulation under these conditions was, for example, the development of a gallop rhythm. In most cases the high blood pressure preceding lung damage coincided with the development of tripple (gallop) rhythm.

In Figures 34 and 35 typical examples of gallop rhythm are shown. Gallop rhythm is characterized by a third heart sound of high intensity and ballistic waves of considerable amplitude following the L wave but preceding the atrial wave. The genesis of the ballistic waves associated with gallop rhythm is not well understood. As these waves are inscribed during the phase after ventricular systole and before atrial systole, they must be at least partially caused by abnormal ventricular relaxation and filling. High arterial pressures were usually associated with the development of gallop rhythm in which cases the aortic standing wave (Honig and Tenney 1957^a) might contribute more conspicuously to the early diastolic waves.

FIG. 36A FURTHER DETERIORATION OF CARDIAC FUNCTION IN
THE SAME RAT AS IN THE PREVIOUS TWO FIGURES

Note the disappearance of the third heart sound, the lowered blood pressure, the abnormal pressure pulse derivative and the lowered amplitude of the HI and IJ wave segments.

FIG. 36A DETERIORATION OF CARDIAC FUNCTION



Ectopic beats and complete A-V block usually followed gallop rhythm.

The progressive deterioration of cardiovascular function (in the same rat) is shown in Fig. 36. In Fig. 36A the third heart sound disappeared as the blood pressure became lower. The P wave showed polarity changes but the Bcg atrial wave (O"F) was still of reasonable amplitude. All other UF Bcg (a) waves were markedly reduced in amplitude. The contour of the JL segment of the UF Bcg (a) became abnormal and coincided with an abnormal contour in the time derivative of the pressure pulse. Pulse pressure was reduced to 12 mmHg. A little later (Fig. 36B) ectopic beats developed.

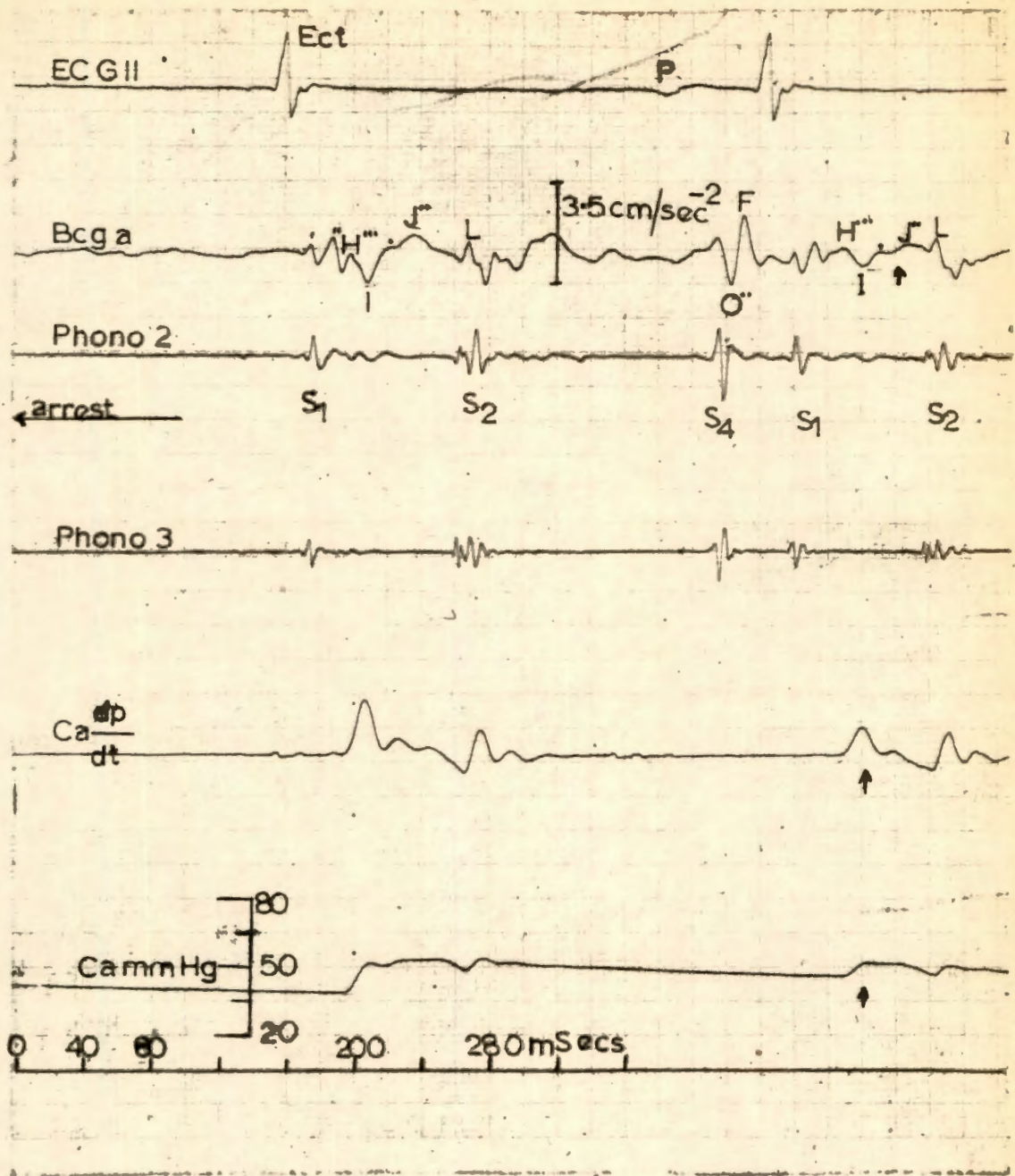
The ectopic beat in Fig. 36B was inscribed after a period of total cardiac arrest. Note the slightly increased pulse pressure, amplitude of the time derivative and the IJ amplitude if compared to the following sinus node beat. This might be due to an increased venous return. The pause before the ectopic beat resulted in better ventricular filling, a slightly improved pulse pressure and IJ amplitude. The contraction following after the ectopic beat probably handled less blood, although it was preceded by atrial contraction, because the end diastolic volume might have been less.

FIG. 36B CARDIAC FUNCTION OF THE DYING HEART

An ectopic beat is shown after a period of cardiac arrest (Ect).

Note that three H waves can still be identified. The pulse pressure and the pressure pulse derivative show a greater ejection of blood than in the second complex although the latter was preceded by atrial contraction.

FIG.36.B. THE DYING HEART.



A progressive increase in the latent period and isometric contraction phase (a and b Fig. 25) coincided with failure of the heart. The waves caused by atrial contraction is clearly visible in the Bcg. The IJ and to a lesser extent the HI wave in the UF Bcg (a) indicates blood flow and is extremely sensitive to changes in the myocardial dynamics associated with blood ejection.

CHAPTER 9

THE GENESIS OF THE UF BCG (a) OF THE RAT

A. The atrial wave complex

The UF Bcg (a) of rats obtained in this study, showed clear atrial waves seldom seen in other species. The different phases of cardiac activity, such as atrial contraction, isometric ventricular contraction, ventricular ejection and the diastolic waves, are reflected clearly in the UF Bcg (a) of rats. The clear separation of the different cardiac phases is surprising as one would not expect it to occur at the high heart rates commonly found in small homothermous animals. Various factors might, however, favour the development of such a situation.

(i) The high heart rates in rats (350 to 420 p/m) result in a relatively short diastolic period. To achieve sufficient ventricular filling in such a short time, the contribution of the atria during normal conditions might be of more importance and therefore incorporate relatively greater forces than in other species with lower heart rates. The greater forces associated with the possible increased contribution of the atria towards ventricular filling might account for the conspicuous Bcg atrial waves found in rats.

(ii) It was imperative to make recordings at high paper

speeds (250 to 500 mm/sec) and to use equipment with an adequate frequency response (Chapter 3). A body to platform weight ratio of about 70:1 was obtained by using the platform described in Chapter 3. When the body to platform weight ratio was decreased to about 3:1, a marked decrease in the atrial wave complex (O', O'', F and G) resulted (Chapter 5). From the results of the platform loading experiments described in Chapter 5 it was concluded that thorough coupling of the rat to the platform was obtained in the present study. Furthermore, no external damping was applied to the system. All the above-mentioned desirable instrumental properties of the system further favoured separation of the different phases and the recording of the atrial waves.

The general pattern and Q-time intervals of the atrial waves were shown in Fig. 25 and discussed in Chapter 8. Figures 28 and 29 showed isolated atrial waves during A-V block. The experiments discussed in Chapter 8 showed that the waves designated as O', O'', F and G in the recordings of rats were indeed waves associated with atrial activity. During three experiments the injection of large doses of arterenol (10 gamma/kg) resulted in severe pulmonary haemorrhage. This was manifested by severe bleeding through the nose and respiratory arrest. At autopsy the lungs were filled with blood and froth. The main pulmonary arteries and veins were intact, indicating

that some of the pulmonary capillaries were ruptured by high blood pressure (in excess of 280 mmHg). A recording made 30 seconds after the vascular accident is shown in Fig.

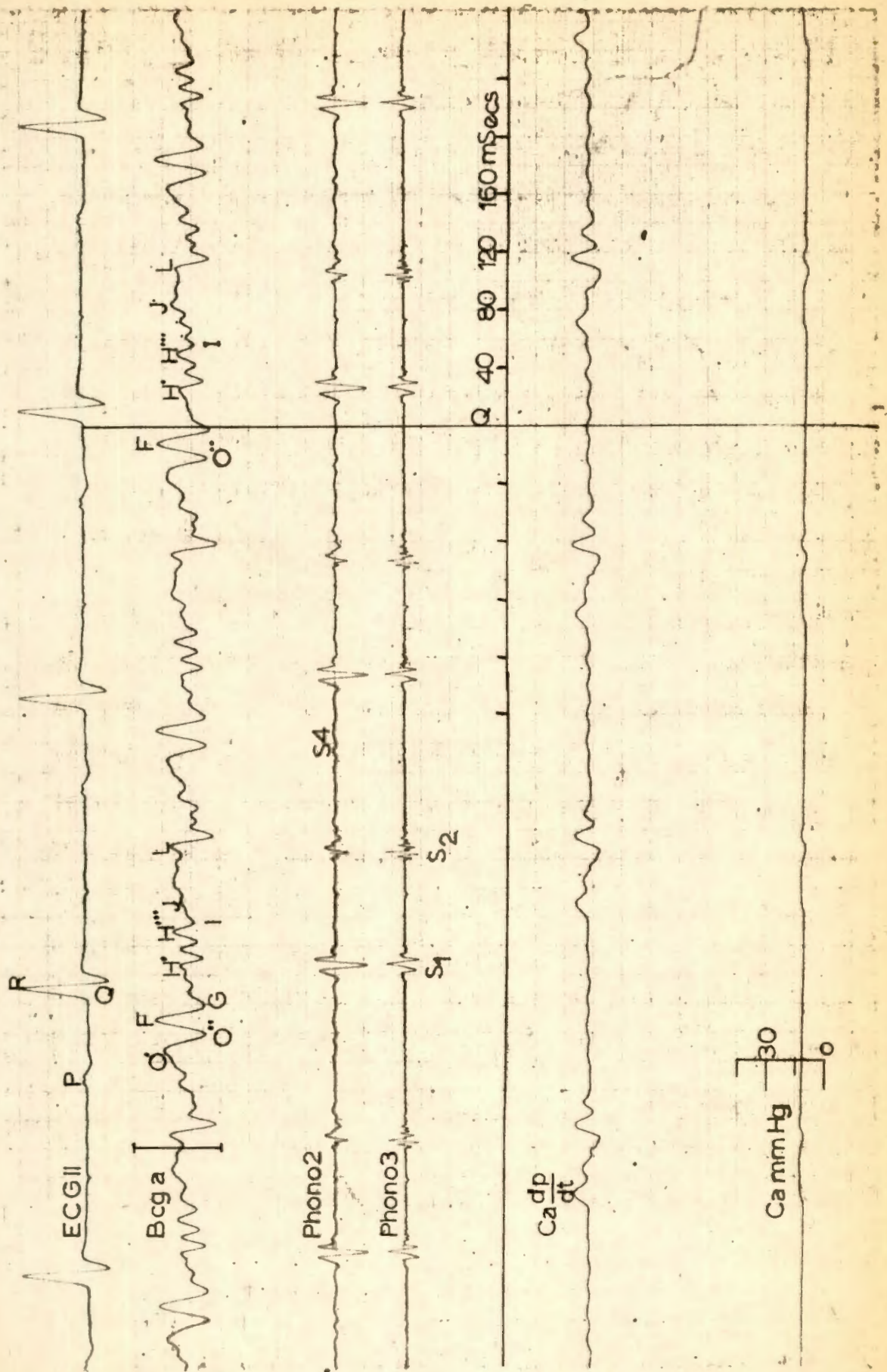
37. The recording showed markedly reduced HI and IJ waves which coincided with a hypodynamic pressure pulse. The practical abolishment of the HI and IJ waves was interpreted as a much reduced ejection of blood from the left ventricle. The same changes in the HI and IJ amplitudes were noted after reduction of the blood volume described in the previous chapter. The atrial waves (O', O'', F and G) were, however, still recorded with more or less the same amplitude.

The right atrium was probably still receiving blood from the venae cavae which was pumped to the lungs resulting in the atrial wave being recorded. As the lung damage was extensive, as proved by post mortem findings, very little blood probably returned to the left ventricle. The resulting weak cardiac ejection forces might explain the low amplitude of the systolic Bcg waves. Although conditions were not normal, the contour of the atrial wave complex showed a remarkably normal pattern if compared to normal and isolated atrial waves described in the previous chapter. The O'O'' segment of the atrial waves in rats as described in this study was negative (footward). As the caval veins are fairly large and valveless, considerable

FIG. 37 RECORDING MADE 30 SECONDS AFTER THE
DETECTION OF PULMONARY HAEMORRHAGE

Note the decreased HI and IJ amplitudes and the hypodynamic pressure pulse. The atrial wave is still clearly recorded.

FIG. 37. SEVERE PULMONARY BLEEDING.



retrograde flow of blood might take place during the commencement of atrial systole. The caval veins are, however, arranged in opposite directions and the reaction forces might largely cancel each other (Honig and Tenney 1957^a). As the openings of the caval veins are fairly near the base (upper margin) of atrium in rats, the displacement of blood towards the caval openings might result in a slight footward acceleration of the body. The contribution of a retrograde flow in the pulmonary veins to the footward segment of the atrial wave might also be conspicuous as the proximal parts of the pulmonary veins are undirectional and more or less parallel to the y-axis (recording axis).

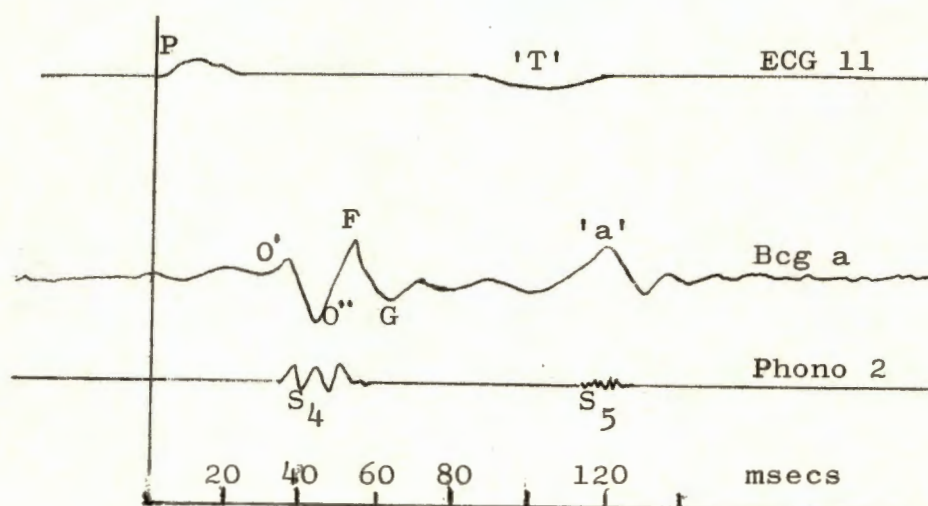
The O''F segment of the atrial wave was recorded as a headward acceleration of the body. This wave might be due to the footward ejection of blood into the ventricles. The ejection of atrial blood through the A-V valves might cause enough force to accelerate the body in a headward direction. The vibrations associated with the rapid ventricular filling in rats were recorded as the fourth (atrial) heart sound and coincided with the recording of the O', O'' and F waves (see Fig. 25 and text in Chapter 8).

The G waves in the recording made during this study were considered to be part of the atrial waves.

When isolation of the atrial wave resulted from complete

A-V block, following catecholamine administration, a late atrial wave not seen in normal recordings could be identified. In some recordings a repolarization wave of the atria in the ECG coincided with the late Bcg atrial wave. A fifth heart sound was sometimes inscribed simultaneously. A typical isolated atrial wave is shown in Fig. 38.

FIG. 38. COMPLETELY ISOLATED ATRIAL WAVE



- Note:
- (i) Atrial repolarization in ECG indicated as 'T'.
 - (ii) Systolic atrial waves O', O'', F and G.
 - (iii) Diastolic atrial wave indicated by 'a'.
 - (iv) Fourth and fifth heart sounds, S4 and S5.

The usual visible atrial wave complex O', O'', F and G is shown. The late or diastolic atrial wave is denoted by the letter 'a'. Note the atrial 'T' wave and sound vibration coinciding with the 'a' wave.

By virtue of its time relationship to the phonocardiogram and ECG it was concluded that the 'a' wave in the atrial wave complex might be due to rapid atrial filling. As evidence exists that retrograde blood flow coincides with atrial ejection (see Chapter 7 and above) it is likely that the veins are distended during atrial ejection and that rapid atrial filling might follow atrial relaxation. Although complete isolation of the atrial wave in the present study was found only after catecholamine administration, it was also noted in an earlier study during hypothermia (Pretorius et al. 1966). In the latter study an 'a' wave in the atrial wave complex was also demonstrated. These experiments indicated that an 'a' wave in the atrial wave complex might be present during normal conditions.

In order to evaluate the possible contribution of the atrial wave complex to other Bcg waves, detailed analyses were made of ectopic beats and beats during different degrees of A-V block. Some of the results were discussed in Chapter 8.

Progressive A-V block and an ectopic beat is shown in Fig. 39. These recordings show that the G wave of the atrial wave complex partakes in the formation of the H' wave in the normal recording. With an increased P-Q time the G wave is separated from the H' wave. The ascending segment (G') of the G wave no longer contributes to the H' wave and the amplitude of the H' wave is consequently reduced by

FIG. 39 THE CONTRIBUTION OF THE ATRIAL WAVE TOWARDS
THE H' WAVE.

The tracings were redrawn from the recording of a rat after the administration of levarterenol.

Fig. 39A shows a 'normal' P-Q time interval and atrial wave.

Note that the G wave of the atrial wave complex (indicated by the arrow) partakes in the formation of the H' wave. The area and amplitude of the H' wave are schematically indicated.

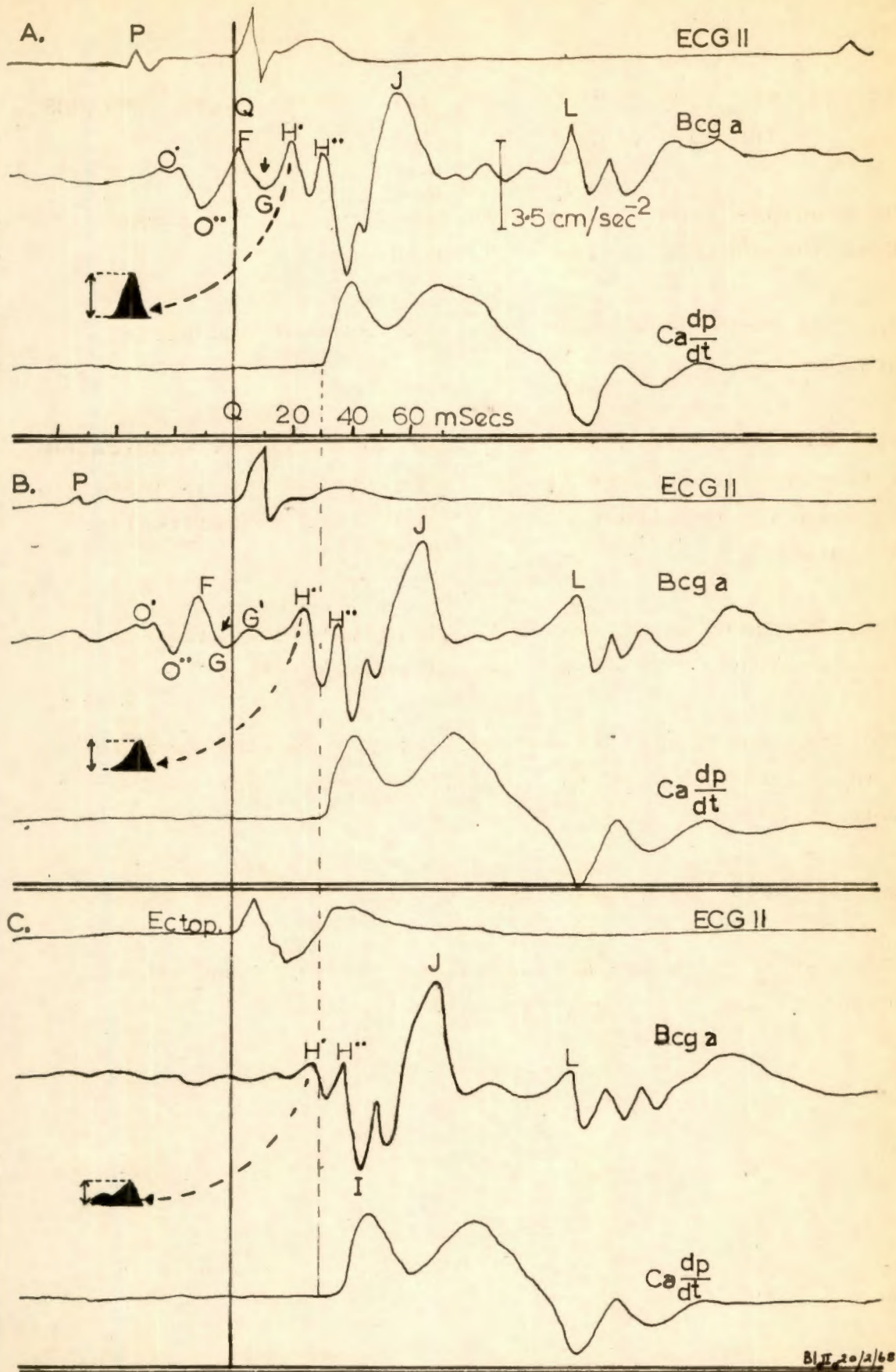
Fig. 39B shows an increased P-Q time interval and a corresponding shift of the atrial wave complex.

Note that the G wave is now spatially separated from the H' wave. The H' wave amplitude is thereby decreased by about 30%.

Fig. 39C shows an ectopic beat recorded 8 seconds later.

Note that the systolic Bcg waves and the pressure pulse derivative are not significantly affected.

FIG. 39. CONTRIBUTION OF ATRIAL WAVE TO THE H* WAVE.



by about 25%. Although arterenol was administered, the recordings showed a remarkable resemblance to normal recordings. The relative amplitudes of the waves seemed to have the same ratio as during normal conditions. The G wave of the atrial wave complex might therefore contribute about 25% of the amplitude of the H' wave under normal conditions.

The H wave complex in the ectopic beat showed a more conspicuous decrease in amplitude. Ectopic beats associated with retrograde atrial stimulation are shown in Fig. 40. The conspicuous decrease in the isometric wave complex during ectopic beats not preceded by atrial waves, might be due to the following factors: Firstly, the direct contribution of the G wave, which might account for about 25% of the H' wave, is lacking. Secondly, the beneficial effect of increasing the sarcomere length and proper ventricular filling by the atria is lacking. The lack of this haemodynamic effect of the atria on the initial tension development of the ventricle might also reduce the amplitude of the isometric waves. In the third instance, the lack of co-ordination of ventricular systole during ectopic beats might seriously affect the isometric contraction phase. During the ectopic beat shown in Fig. 39, the Q-ejection time was, for instance, prolonged by about six msec (about 20%). A longer isometric phase which might be associated with reduced forces (slower rates of

FIG. 40 ECTOPIC BEATS FOLLOWED BY ATRIAL ACTIVITY

The recording was made 40 seconds after levarterenol was administered.

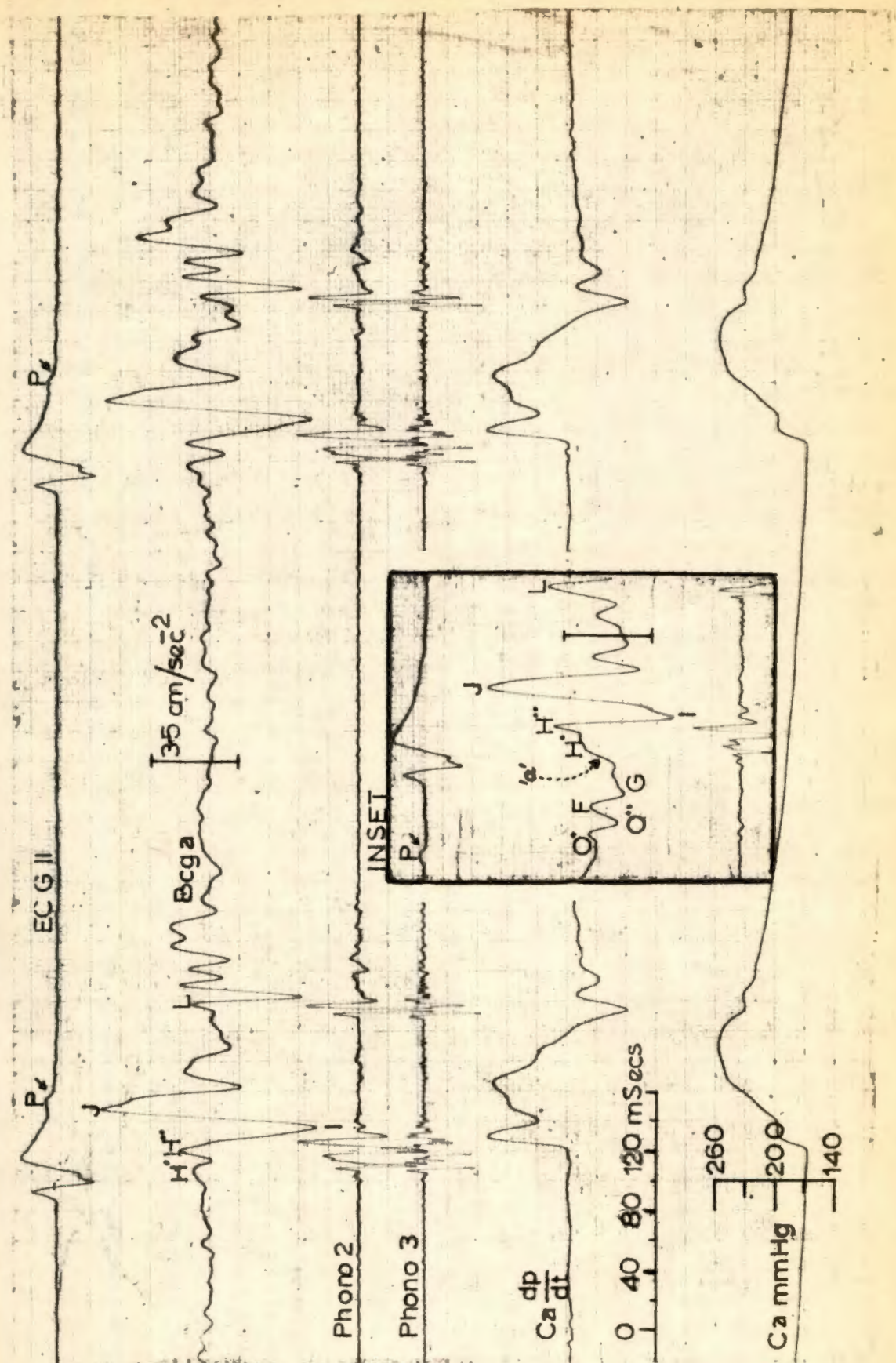
Note that the P waves in the ECG are superimposed on the T wave. In spite of this the ventricular systolic Bcg waves are practically normal. The H' and H'' waves can be identified with confidence.

The inset shows ventricular activity preceded by atrial activity in the same rat.

Note that atrial ballistic waves coincide with the P wave. The atrial diastolic wave ('a' wave) is superimposed on the H' wave because the P-Q time interval is prolonged.

Note that the ventricular systolic Bcg waves (HI and IJ) are similar although the atrial wave coincided with or preceded (inset) ventricular activity.

FIG. 40. RETROGRADE ATRIAL STIMULATION



change) might further explain the lowered amplitude of the H wave complex.

From studying atrial waves which were superimposed on the ventricular waves (see Fig. 40) it was concluded that the forces associated with atrial activity are more or less obscured by the ventricular ballistic waves. When an isolated atrial wave was recorded by the ECG during ventricular systole, no significant effects of the atrial ballistic waves on the Bcg could be demonstrated (Chapter 8).

As the 'a' wave of the atrial Bcg wave complex is of lower magnitude than for instance the O" F wave, it was concluded that the 'a' wave does not affect the ventricular systolic Bcg waves.

It is therefore clear that the atrial systolic waves might contribute to the isometric waves, especially to the H' wave, in the UF Bcg (a) of rats.

Some controversy concerning the influence of the atrial waves on the isometric Bcg waves is, however, indicated by recent investigations.

Pretorius (1962^b) suggested that the 'H' wave is of isometric or pre-ejection origin and that it contains a minimal contribution of atrial origin. West and Corbascio (1959) suggested that the 'H' wave is largely

caused by atrial activity in the dog. As the rat UF Bcg (a) showed at least two H waves and the last H wave (H" or H''') is part of the HI segment, it is very unlikely that the atrial wave contributed towards the last H (H" or H''') wave.

The contribution of the atrial wave to the isometric waves as described earlier in this chapter confirms the findings of Pretorius (1962^{a,b}).

As the Bcg (a) of the rat showed much clearer atrial waves under normal conditions than other species, it is suggested that the rat would be an ideal experimental animal in studying the atrial waves of the UF Bcg (a).

B. The isometric or pre-ejection waves

In recordings made during this study the pre-ejection waves were designated as the H', H" and H''' waves. Considerable evidence during catecholamine administration, during ectopic beats and from Q-time relationships indicating that these waves are inscribed during the isometric phase was accumulated (Fig. 25 Chapter 8). In the study of Pretorius et al. (1966), the administration of catecholamine and pitressin, hypothermia and ectopic beats led to the same conclusions. The H' wave was inscribed during the first part of the first heart sound (Chapters 6, 7 and 8). It preceded the carotid pressure pulse and is probably due

to heart and blood vibration during isometric contraction. This is in accordance with the views held by Hamilton et al. (1945), Honig and Tenney (1956^a), Noordergraaf and Heynekamp (1958), Noordergraaf and Horeman (1958), Noordergraaf (1961), Pretorius (1962^b) and Pretorius et al. (1966).

West and Corbascio (1959) are of the opinion that the H wave is mainly due to atrial activity. Moreira (1960) reported the abolishment of the H wave during atrial fibrillation.

In reporting the experiments on the UF Bcg (a) of man, Corbascio et al. (1966) noted that the H wave followed 0.07 seconds after the onset of isometric contraction and 0.035 seconds after the onset of ventricular ejection.

Although the first study (West and Corbascio 1959) was based on experiments with dogs and the latter (Corbascio et al. 1966) on man, some controversy seems to exist, which might be due to a difference in lettering the waves. Care should be taken, however, to compare the results found in rats to that of other species because three H waves can usually be identified in the UF Bcg (a) of rats.

The genesis of the H' and H''' wave in the UF Bcg (a) of rats is not yet clearly established. During normal conditions three H waves (H', H'' and H''') could usually be identified. The H' wave is largely due to events during

isometric contraction. It could be identified during ectopic beats (Fig. 39) but was then of smaller amplitude. By evaluating the contribution of the atrial wave towards the H' wave it was concluded that about 75% of the H' wave is due to isometric events and 25% of the H' wave might be of atrial origin.

Experiments described in Chapters 7 and 8 indicated that the H'' wave might be due to oscillations in left and right ventricles prior to aortic and pulmonic valve opening. The exact genesis of the H''' wave is not known and demands a further study. Experiments during this study, however, suggested that the H''' wave might contain components originating in forces associated with right ventricular activity. The exact position of the H''' wave in recordings varied considerably and this was conveniently termed the 'shift' of the H''' wave. During normal conditions, the H''' wave was usually a conspicuous positive (headward) wave immediately preceding the I wave. After sympathetic stimulation the H''' wave disappeared in most instances (Chapters 7 and 8). This usually coincided with a decrease in the duration of isometric contraction. The duration of the first heart sound was also decreased in most cases (Chapter 8). The commencement of ejection (pressure pulse and its time derivative) followed sooner than normally after the Q wave during sympathetic stimulation. These findings indicate that ejection followed sooner after the

beginning of electrical systole and that the pre-ejection period was shortened. This is in accordance with views held by Von Euler (1956), Rushmer (1961) and according to the Bcg findings of Pretorius (1962^b). The absence or partial abolishment of the H'' wave during a decreased isovolumetric time could thus indicate that it is of isometric origin.

Sympathetic stimulation might, however, also improve the synchronization of the heart. If it is assumed that the H'' wave represents, for instance, the 'J' wave of right ventricular ejection, an improvement of synchronization between the ejection of left and right ventricle might superimpose this 'J' wave of right ventricular ejection on the real J wave (left ventricular ejection) and result in a less complicated HIJ segment. Pretorius (1962^b) also noted the disappearance of a second 'I' wave in the UF Bcg (a) of dogs after sympathetic stimulation, and that an increased Q-ejection time interval resulted in a more complicated I wave. In the present study two 'I' waves were noted when ejection was delayed. Pretorius (1962^b) suggested that the first 'I' wave might be due to events during isovolumetric contraction while the second I wave remained in relation to the pressure pulse (Q-ejection). If the negative peak following the H'' wave in recordings

of rats is lettered the first 'I' wave as in the study of Pretorius (1962^b), the findings reported in this study dealing with rats would confirm his results.

It might therefore be concluded that the H''' wave in the UF Bcg (a) of rats is probably caused by isometric left ventricular contraction as well as some contribution from right ventricular ejection.

C. Ejection wave complex

(i) The HI wave: In general the genesis of the HI wave is fairly well established. When systole was simulated at necropsy, Starr et al. (1953) found I and J waves very similar in amplitude to normal recordings. Noordergraaf (1961) accounted quantitatively for the I wave in normal man by calculations of the forces of ejection. Animal experiments support the view that the I wave is caused by initial ventricular ejection (Honig and Tenney 1956^a, Moreira 1960, Corbascio and West 1961, Pretorius et al. 1966). Some animal experiments, however, indicated that the HI wave might contain isometric components (Pretorius 1962^b and Knoop 1962). Starr and Noordergraaf (1967) suggested that right ventricular ejection might also affect the HI wave in recordings of dogs. Experimental results in the present study indicated that both isometric and right ventricular components might affect

the amplitude and contour of the HI wave (see H^{'''} wave). In reporting on the time relationships between the UF Bcg (a) and intra-cardiac pressure of man, Corbascio and associates (1966) suggested that failure to demonstrate a close relationship between systolic Bcg waves and cardiac events in dogs could be due to the use of intravenous barbiturates as anaesthetic agents. Pretorius (1962^{a,b}) and Knoop (1962), however, demonstrated a reasonably close relationship in time and amplitude of the HI wave and ventricular ejection in experiments on dogs during barbiturate anaesthesia. Pretorius (1962^b) showed that the HI amplitude in dogs was maximal when the recording axis was parallel to the axis of the ascending aorta. In the present study the amplitude of the H^{'''}I wave in the UF Bcg (a) of rats was also greater when the axis of the ascending aorta was parallel to the recording axis. Although the experimental animals were anaesthetized by barbiturates in both cases, a clear relationship between forces evoked by ejection into the proximal ascending aorta and the HI segment of the UF Bcg (a) was demonstrated. After vena caval occlusion in dogs (Pretorius 1962^b), rats (Pretorius et al 1966) and rabbits (Green 1967) a reduction in HI amplitude was demonstrated. Inferior vena caval occlusion in dogs (Corbascio and West 1961) also resulted in a decreased slope of the HI segment. In experiments described in the present study (see Chapter 6) a decrease

in HI amplitude and slope followed inferior vena caval occlusion. The results of these experiments seem to indicate that the HI wave is mainly caused by blood flow at the beginning of ventricular ejection.

Pretorius (1962^b) noted a small increase in HI amplitude in recordings of dogs after small doses (1 gamma/kg) levarterenol were administered. In rats (Pretorius et al. 1966) and rabbits (Green 1967) an increase in the HI segment of the UF Bcg (a) resulted when arterenol was administered. The onset of ventricular ejection (Q-ejection time) followed sooner after the Q wave in dogs (Pretorius 1962^b) and rats (see Chapter 8) after catecholamine injection and coincided with a decreased Q-I time.

During hypothermia in rats (Pretorius et al. 1966) an increase in Q-ejection time resulted in an increase in Q-I time. These findings further support the view that the HI segment is mainly caused by forces resulting from initial ventricular ejection.

During sympathetic stimulation (e.g. arterenol) the HI amplitude did not increase to the same extent as the IJ wave amplitude. The inotropic effect of arterenol therefore affected the HI amplitude to a lesser extent than the IJ amplitude (Chapter 7). It was concluded that

this indicates a difference in the genesis of HI and IJ waves. As the HI wave was affected to a lesser extent by a mild reduction in blood volume (Chapter 8) than the IJ wave, and the isometric waves were the least affected, the probability that the HI wave in the UF Bcg (a) of rats might contain an isometric component cannot be excluded.

Further support for this possibility was found during ectopic beats. During some ectopic beats following soon after normal S-A nodal beats, no ejection of blood was recorded by the pressure pulse and the Bcg. No I and J waves could be identified in the Bcg but the H wave complex persisted although the amplitude was sometimes decreased. During some ectopic beats, a slight increase in the H wave complex was noted.

The persistence of H waves during ectopic beats in rats confirms the results obtained in dogs by Pretorius (1962), who concluded that the HI segment results from a co-action between the forces evoked during the commencement of ejection and those evoked during the last part of the isometric contraction. The results described in the present study confirm, therefore, the genesis of the HI wave as suggested by Pretorius (1962^b).

(ii) J wave: Less dispute on the genesis of the J, K and L waves was found in the literature (see Chapter 3).

From their calculations based on the accelerating and decelerating forces in segments of the aorta, Starr and Rawson (1941) and Hamilton et al. (1945) concluded that the J wave is of complicated origin. The genesis of the J wave was attributed to decelerating forces in the heart, ascending aorta and pulmonary arteries, and to accelerating forces in the descending aorta.

Noordergraaf (1956), Noordergraaf and Heynekamp (1958) and Noordergraaf and Horeman (1958) approached the mathematical evaluation of the UF Bcg in a different way. They calculated the total mass displacement within the body during cardiac activity and predicted, on this basis, the expected movements of the centre of gravity and the resulting Bcg. In a later study Noordergraaf (1961) made allowances for accepted values of blood pressure, vessel distensibility, pressure pulse contour and other physiological properties of the circulation in calculating Bcg amplitude and time intervals. This quantitative evaluation of the Bcg revealed that the J wave might be notched during asynchrony of the left and right ventricles. Noordergraaf (1961) also concluded that part of the J wave is caused by deceleration of blood in the heart and proximal arteries.

In the present study the J wave was greatly reduced in amplitude after vena caval occlusion (Chapter 6). This

coincided with a reduction in pulse pressure and mean arterial pressure. It was therefore concluded that maximal ejection of blood during late systole is the major cause of the J wave. When the myocardium was stimulated by sympathomimetic drugs, an increase in J wave amplitude resulted. The Q-J time was also decreased by arterenol administration. As arterenol is known to exert an inotropic and chronotropic effect on the myocardium, it was concluded that the J wave in the UF Bcg (a) of rats displayed these effects accurately.

A splitting or notching of the J wave usually followed the administration of arterenol in rats (Fig. 20). A J wave (J') of a greatly increased amplitude and slope followed within 10 to 15 seconds after arterenol administration. Part of the J wave remained at its usual position as shown by Q-time measurement. This wave was lettered the J" wave. When the effect of arterenol passed off, the J' wave became reduced and formed part of the main J wave (J"). The result was that a 'normal' J wave, now slightly slurred, was formed. It seemed therefore as if only a certain part of the J wave was increased in amplitude soon after arterenol injection. Depression of the rat myocardium by hypothermia, pitressin administration and vena caval occlusion, caused a marked decrease in the amplitude of the J wave and a corresponding but

lesser decrease in the amplitude of the first derivative of the pressure pulse (Pretorius et al 1965). Stimulation of the myocardium by catecholamine and amyl nitrite increased the J wave amplitude. These experiments showed that the J wave in the UF Ecg (a) of rats is caused by different haemodynamic events. This is in accordance with Noordergraaf's theory (1958) and the results obtained by Pretorius (1962^b).

The recording of the two 'J' waves during myocardial stimulation in rats may be explained as follows: The pulmonary arterial pressure differs markedly from the mean systemic arterial pressure during normal conditions. The chronotropic effect of arterenol might result in a greater difference in time of the achievement of maximal acceleration of blood in the right and left ventricles due to the difference in pressure heads. The primary and secondary pressor effects of arterenol could also affect the pulmonary system differently from the systemic circulation, thus affecting the ratio of mean pressures in the two circulations.

As acceleration ballistocardiography actually measures the rate of change of blood ejection forces, small changes in the rate of change of haemodynamic events between left and right ventricle may cause a splitting of the J wave. This is in accordance with the results of Noordergraaf

and Heynekamp (1958), Noordergraaf (1961) and Smith and Corbascio (1963). The mean duration of left and right ventricular ejection seemed to be synchronized because the second heart sound was of short duration and not divided. Of importance is the possibility that the time of achievement of maximal acceleration of blood from the left and right ventricle might be different (asynchronous).

Furthermore, the chronotropic effect of arterenol might affect the time ratio between accelerating forces in the descending aorta and the deceleration forces in the heart and proximal arteries. According to Noordergraaf (1961) and Corbascio and West (1961), the J wave also contain decelerating forces in the proximal arteries. Applied to the recordings of rats, the chronotropic effect of arterenol might alter the balance between accelerating and decelerating forces and result in two J waves being recorded. As arterenol also exerts an inotropic effect, the increased amplitude of the J wave (J') could be due to enhanced ejection and acceleration forces. The J'' wave might then represent the decelerating forces as it remained more or less of the same amplitude and showed the same Q-time interval after arterenol administration. As the J'' wave amplitude was smaller than the J' wave amplitude, it was concluded that the acceleration forces play a more

important role in the genesis of the normal J wave.

The close time and pattern relationship between the J wave and the pressure pulse derivative was described in Chapter 8. When the pressure curve was slurred or notched by uneven or incoordinate ejection of blood, the pressure pulse derivative and the J wave showed corresponding notches. This further supports the view that blood flow during left ventricular ejection dominates the genesis of the J wave.

It follows that the J wave in the UF Bcg (a) of rats might then be caused by the interaction of the following forces: (a) the forces associated with the development of maximal blood acceleration in the descending aorta (these forces are responsible for the genesis of the major part of the J wave) and (b) acceleration forces developed in the right ventricle and pulmonary arteries during systole, and (c) the forces associated with the deceleration of blood in the heart and proximal arteries.

(iii) The K wave: The UF Bcg (a) of rats, as described in the present study, lacked clearly defined K waves. In the earlier reported studies on the human Bcg, Starr and Rawson (1941) recorded K waves of reasonable amplitude. They noted, however, that the recorded K waves were more prominent than the K waves in their predicted Bcg. Later Starr and Hildreth (1952) noted that the K wave seemed to

become more conspicuous as age advanced. Brown et al. (1952) and Grob et al. (1953) noted deep K waves in the UF Bcg of patients with hypertension. It was later realized that the K wave in HF Bcg of the early era (Starr and Rawson 1941) was largely due to artifacts and resonance introduced by the HF system. Hamilton et al. (1945) suggested that the K wave might be caused by pulse wave impact and reflection from the periphery.

The computed UF Bcg (a) of Noordergraaf (1961) and the UF Bcg (a) recordings of most investigators show a small inconspicuous K wave. In the present study it was found that the K waves in the UF Bcg (a) of rats were not easy to identify and that they were usually inconspicuous.

(iv) The L wave: The L waves were inscribed 4 to 8 milliseconds after the commencement of the second heart sound (Chapter 8). The amplitude of the L wave showed some correlation with the intensity of the second heart sound (Chapters 7 and 8). The L wave showed a close time relationship with the dicrotic notch of the carotid pressure pulse and its time derivative. These observations led to the conclusion that the L wave in the UF Bcg (a) of rats is caused by the rate of change of acceleration forces associated with closure of the aortic valve. The low amplitude of the L wave found during reduced ejection, e.g. during reduction in blood volume (Chapter 8), added

further support to this view. This suggested genesis of the L wave is in accordance with Noordergraaf's theory and most of the important experiments on the UF Bcg (a) of animals (Honig and Tenney 1957^a, Pretorius 1962 and Winter et al. 1966).

D. Diastolic waves

The M, N and O waves of the UF Bcg (a) of the rat showed considerable variations. During induced hypertension (Chapters 7 and 8) gallop rhythm developed in rats. The recording of a third heart sound coincided with abnormal Bcg waves following the L wave. The origin of these waves was not clearly established. It was suggested that these early diastolic waves might be caused by abnormal ventricular filling (Chapter 8). Gallop rhythm was also encountered when myocardial failure developed in dilated, flabby hearts during "gousiekte" in sheep and goats (Pretorius et al. 1967). The gallop rhythm in rats disappeared as blood pressure returned to normal values. It might be possible that arterial resonance (Honig and Tenney 1957^a) was partly responsible for the genesis of these abnormal late systolic or early diastolic vibrations.

From the experiments described in the present study, it was concluded that the UF Bcg (a) pattern of rats is

similar to that of man in some respects only. Important exceptions were the more conspicuous atrial waves, the more complex isometric wave complex and the relatively deeper HI wave found in the recordings of rats. The conspicuous HI wave in rats was also noted in an earlier study (Pretorius et al. 1966). The difference in the UF Bcg (a) pattern found in different experimental animals might be partly due to the anatomical difference in the contour of the aorta (Chapter 6). This was also illustrated in a recent publication by Pretorius et al. (1968^b).

CHAPTER 10

GENERAL DISCUSSION AND CONCLUSIONS

I. COMPARISON BETWEEN SMALL ANIMAL AND OTHER UF BCG METHODS

Physical studies of the UF Bcg method by Burger et al. (1953, 1956, 1957), Von Wittern (1953), Talbot and Harrison (1955), Rappaport (1956^{a,b,c}) and Noordergraaf (1958, 1961) have shown the advantages of the UF Bcg system. Some of these advantages were discussed in detail in Chapters 2 and 8, and those applying to the system used in the present study will now be discussed.

A. Desirable mechano-physical properties of the UF Bcg system

(i) Natural frequency: The natural frequency of the UF Bcg system is low (0.5 Hz). This system is therefore also sensitive to the low frequencies encountered in ballistocardiography. Because of this low natural frequency the higher applied frequency (heart rate) is not likely to introduce resonance or distortion. The widely different frequencies further facilitate identification of waves caused by cardiac activity. For taking recordings of man a natural frequency of 0.1 to 0.3 Hz is recommended by Starr and Noordergraaf (1967). The natural frequency of the system used in the present study was 0.38 Hz. As the heart rate of rats is about 4 times higher than that of man, the ratio between natural and applied frequency,

obtained in the present study, was well within the recommended range. The exact frequency of the different wave components in the UF Bcg (a) of rats, however, is not yet known.

(ii) Platform weight: Light weight platforms are commonly used in UF Bcg systems. It was shown (see Chapters 2 and 3) that a platform with a small mass in relation to the the body weight increased the fidelity of recording the movements of the centre of gravity of the body. This great advantage is mainly due to the improved coupling between subject and support in a UF Bcg system. Elimination of most of the parasitic oscillations caused by poor coupling is realized, and the system, therefore, shows an overall improved frequency response.

Julius et al. (1966) recommended that the platform weight should not exceed 10% of the weight of the subject. Klensch et al. (1961) suggested that the body to platform weight ratio should be within 10:1 to 60:1. In the present study a mean body to platform weight ratio of 65:1 was obtained. The complete platform, including the accelerometer, weighed 4.1 grams. Experiments described in Chapter 5, where the body to platform weight ratio was decreased to 3:1 by loading of the platform, illustrated that a heavy platform might act as a filter. These experiments showed that a heavy platform might result in

serious attenuation of the atrial and isometric wave amplitude. It was shown that a less favourable weight ratio between subject and platform introduces phase lag, and adversely affects the frequency response of the system. These findings are in accordance with the results described by Julius et al. (1966) and Nickerson et al. (1966).

(iii) 'Free' suspension of the subject: By virtue of its low natural frequency, the platform in a UF Bcg system is weakly coupled to its surroundings. The ideal of free suspension of the subject is therefore better approached in the UF Bcg system (Burger et al. 1953, Rappaport 1956^a). The UF Bcg system is, however, sensitive to low frequencies and is therefore affected by mass displacements resulting from respiratory movements. To prevent after vibrations, especially in velocity and displacement recordings, external damping of the platform is commonly applied. The degree of damping would again affect the restraint or binding of the platform to its surroundings and may introduce distortion as indicated by Burger (1953) and Rappaport (1956^a). Rappaport (1956^a) recommended that external damping should be minimal in order to prevent distortion. In the present study no external damping was applied. It was assumed that the possible introduction of distortion by platform damping at the high heart rates

found in rats might outweigh the beneficial aspects of damping. As acceleration was recorded directly, the necessity of external damping was further reduced. This advantage of measuring acceleration directly was also noted by Jonnart (1952) and Von Wittern (1953).

(iv) Coupling between subject and platform: The studies by Von Wittern (1953) and Burger et al. (1956) proved that the body to platform coupling is superior in the UF Bcg system. According to Talbot and Harrison (1955) Burger and Noordergraaf (1956), Burger et al. (1956), Talbot (1958), Baan (1964), Cunningham (1964) and Baan et al. (1966) hardly any devices, e.g. footplates and shoulder straps, are necessary to increase the coupling when longitudinal UF Bcgs are recorded by means of a light weight platform.

Lateral supports and a 'yoke' were, however, fitted to the platform used in the present study. Although determination of the degree of coupling was not attempted, it was assumed that these devices, in addition to the favourable body to platform ratio, resulted in an ideal coupling between rat and support. The results of the loading experiments (see Chapter 5) and the general nature of the recordings obtained lend further support to this view.

(v) General: As a result of its simple construction and

superior fidelity the UF Bcg system was used by most investigators working on animals. The fidelity with which displacement, velocity and acceleration is measured in modern UF Bcg systems, greatly facilitates comparison of results obtained by various investigators. In dealing with the experimental and theoretical evaluation of the ballistocardiographic method, Starr and Noordergraaf (1967) concluded: "..... that the ULF ballistocardiograph, provided with a support of small mass and with external damping somewhat under the critical level, is the preferable instrument for the study of head-foot Bcgs. For such a system the coupling between body frame and support introduces negligible distortion up to around 30 cps. it seems that the ULF displacement and the major part of the acceleration record truthfully reflect the corresponding aspect of the internal motion of the centre of gravity."

B. Instrumentation

The properties of the UF Bcg system and the frequency response of the transducer and recording equipment are of major importance in obtaining reliable recordings. Most of the pertinent aspects of the UF Bcg system were discussed under the previous heading.

(i) The accelerometer: The U-effect accelerometer as

described by Elliot et al. (1954). and Elliot and Krill (1966) was modified for small animal platforms by Pretorius et al. (1966). The construction and calibration of the accelerometer used in the present study was described in Chapter 3. Small variations in construction of the accelerometers did not markedly influence the sensitivity or frequency response, confirming the results of Pretorius (1962). As this type of accelerometer shows a linear response over a wide frequency band according to Elliot and Krill (1966), it was assumed that the calibration performed at 0.38 Hz and 1.3 Hz would be valid at higher frequencies also. The small mass of the modified accelerometer (see Chapter 3) makes it the most suitable sensing device for Bcg (a) experimentation with small animals.

(ii) Amplifiers and recording unit: The frequency response of the pre- and final-amplifiers in combination with the galvanometers was found to be practically linear up to 500 Hz. No measurable time lag existed between the ECG, phono and Bcg recordings. The pressure signal showed a negligible time lag of 0.85 msec when the Bcg, phono and pressure transducers were activated by a simultaneous impulse (catheter inclusive). In calculations of the Q time intervals, the direct measurements were therefore considered as true values. Accurate time measurements were further facilitated by making recordings at a paper

speed of 500 mm/sec.

It was concluded that the over-all instrumentation was able to record with high fidelity the different aspects of cardiovascular dynamics in the rat. The reproducibility of changes brought about in the UF Bcg (a) pattern of rats by means of the various experiments confirmed this.

C. The rat as experimental animal in ballisto-
cardiography

The rat is one of the most widely used laboratory animals. Relatively little is, however, known about the haemodynamic physiology of the rat. Ballistocardiographic experiments on rats, for example, are very limited. Experiments on the UF displacement Bcg of rats were done by Juznic and Klensch (1962). Rademeyer (1963) and Pretorius et al. (1966) investigated some aspects of the UF acceleration Bcg of rats.

Rats show certain advantages and disadvantages as an animal for experimental Bcg research.

(i) Direct advantages:

(a) Ageing in rats: According to Wilens and Sproul (1938) the normal lifespan of rats is about 700 days. Rats would therefore be extremely suitable animals to use in studying the changes in cardiovascular dynamics which are

associated with age. The study of Wilens and Sproul (1938) on the Osborne-Mendell strain, demonstrated fibrosis of the myocardium in about 60% of the series in post mortems performed after the rats had died of natural causes. The incidence of sclerosis of the coronary arteries amounted to 57.7%. For both diseases the incidence was higher in males than in females. The incidence of cardiovascular disease in man is also higher in males and in this respect shows aspects of similarity to the disease pattern in rats.

From the experiments described in Chapter 5 it was evident that the systolic Bcg waves of old rats showed a decrease in slope and amplitude. It was concluded that the UF Bcg (a) can be used to measure changes in cardiovascular dynamics associated with age and that rats are suitable animals to use in studying this particular aspect.

(b) Atrial wave complex: Apart from the usual systolic and diastolic UF Bcg (a) complexes, a well defined atrial wave complex can be identified in the recordings of rats (see Chapter 5). Exceptionally clear atrial waves were also noted in an earlier study on rats described by Pretorius et al. (1966).

The results of experiments described in Chapters 5 and 9 show that the atria in rats might play a relatively more

important role in the normal haemodynamics of rats than in other species. The significance of the atrial wave complex in the UF Bcg (a) was discussed in detail in the previous chapter. These results indicated that the rat is a suitable experimental animal in ballistocardiographic studies particularly to investigate the genesis and significance of the atrial wave complex.

(c) Homogenous anatomy: Rats of the same strain are usually very similar in cardiovascular anatomy. Individual variations in the UF Bcg (a) pattern as a result of anatomical differences are therefore limited or largely eliminated in rats. That anatomical differences might result in variations in the UF Bcg (a) pattern was demonstrated in the experiments described in Chapter 6. This confirmed the results of Pretorius (1962^b) and Pretorius et al. (1966, 1968^b). This might explain the high reproducibility of the UF Bcg (a) pattern of rats found in this study.

(iii) Indirect advantages:

(a) Heart rate: Perhaps unexpectedly, the high heart rate encountered in rats (mean about 380 beats per minute) was considered as an asset in the present study. The most important advantage of high heart rates is possibly the demand of high quality apparatus to cope with the relatively high frequency of the measured signals. This usually

improves the fidelity of the recordings. Physiologically, high heart rates in rats could explain the greater magnitude of the atrial waves.

(b) Breeding: Rats can be raised gnotobiotically or bred to have some congenital deficiencies, e.g. hypertension, hyperthyroidism, etc. Rats could thus be bred to match specific demands for certain long term cardiovascular or metabolic studies.

(c) Availability: Large stocks of rats can be kept economically. As a result experiments on rats can be done on a more representative basis especially if different strains are, for instance, included in the studies.

(iii) Disadvantages:

(a) Small blood-vessels: In rats the blood-vessels are small. Techniques and equipment to cannulate, for instance, certain blood-vessels, are still in a developmental stage. Flow meters or strain gauges which are suitable for implantation in rats are not readily available. This is regarded as a serious handicap to haemodynamic studies in the rat.

(b) Small blood volume: The small blood volume of rats demands careful manipulation when intravascular injections are given (see Chapter 6). The blood volume of rats was given as 4 to 5.3 ml/100 grams and 6.7 ml/100 grams by Griffith and Campbell (1937), and Cartland and Koch

(1928), respectively. If 1 ml of fluid was withdrawn or added to the circulation, cardiovascular function was affected (see Chapter 6). Farris and Griffith (1949) recommended that the fluid injected should be warmed if its volume exceeds 1 ml. Secondary effects caused by altering the volume of circulating blood or the cooling effect of large volumes (about 1 ml) of injected fluid, make the use of rats disadvantageous in cardiovascular research.

(c) Anaesthesia: In order to make recordings possible, rats must be anaesthetized. Different anaesthetic agents might affect the cardiovascular system in various unmeasurable ways. This disadvantage is, however, encountered in most animal experiments and is discussed in more detail under the next heading.

II DISCUSSION OF THE RESULTS OBTAINED

(i) Anaesthesia: Corbascio and Smith (1966) are of the opinion that the intravenous administration of barbiturate to obtain anaesthesia in dogs might be largely responsible for individual variations found in the Bcg of dogs. When additional amounts of pentobarbitone were administered to rats (Pretorius et al. 1966) and goats (Pretorius and Terblanche 1967) a general decrease in UF Bcg (a) amplitude resulted. The normal amplitude

was again re-established in goats 4.5 minutes after the administration of the additional ($\pm$ 90 mg total) pentobarbitone. In rabbits, Green (1967) found a general increase in HI and IJ amplitude in the UF Bcg (a) after additional intravenous injection of pentobarbitone. The results described by Krayenbühl (1964), Pretorius et al. (1966) and Green (1967) also showed that a small increase in heart rate and a small decrease in blood pressure usually resulted from barbiturate administration. Drill (1958) concluded that barbiturates do not significantly affect blood pressure and heart rate. Scarborough (1957) concluded that morphine-barbiturate anaesthesia might reduce venous return in the dog. He suggested the application of an abdominal binder to reduce splanchnic pooling. Pretorius and Knoop (1961), however, failed to demonstrate any improvement in the UF Bcg (a) of dogs by applying abdominal binders. From these studies it seems evident that great variation of barbiturate tolerance exists in different species. This tolerance difference to pentobarbitone was also noted by Ling (1957). According to Winter et al. (1967) the Bcg of an unanaesthetized dog was very similar to those described by Pretorius (1962^b) for barbiturate anaesthetized dogs. It seems, therefore, that the discriminate use of anaesthetics might eliminate measurable side effects on the cardiovascular system.

To minimize the possible detrimental effects of anaesthetic agents, rats were not premedicated with atropine or morphine in the present study. Furthermore, the minimum effective dose of pentobarbitone (35 to 45 mg/kg) was administered intraperitoneally and not intravenously. It was, however, noticed that a small decrease in Bcg (a) amplitude developed about 25 to 30 minutes after intraperitoneal pentobarbitone (Sagatal) injection. Recordings were therefore made immediately after anaesthesia became effective (see Chapter 4). This procedure minimized the possible detrimental effects of anaesthesia on the UF Bcg (a).

(ii) Normal UF Bcg (a) of rats: The normal UF Bcg (a) pattern of young outgrown rats were discussed in detail in Chapter 4.

The more conspicuous atrial wave complex in the UF Bcg (a) of rats might be due to the favourable properties of the apparatus used in the present study, and the possible increased haemodynamic importance of atrial activity associated with the high heart rates found in rats (see Chapter 9).

The relatively deeper HI wave in the UF Bcg (a) of rats might be due to a closer directional relationship between the ascending aorta and the longitudinal body axis as suggested by Pretorius et al. (1966). In the experiments

described in Chapter 6 it was found that small changes in the relative position of the aorta to the recording axis were reflected in the UF Bcg (a). These findings confirmed the results of Pretorius (1962^b) and Pretorius et al. (1966, 1968^b). These experiments showed that anatomical differences in the aorta of different species, and even individual differences within the same specie, must be taken into account when the UF Bcg (a) is interpreted. When the recording axis was aligned approximately parallel to the ascending aorta in dogs, Pretorius (1962^b) noted an increase in the amplitude of the HI and IJ waves. When the ascending aorta in rats was aligned parallel to the recording axis, a comparable increase in HI wave amplitude resulted (see Chapter 6). From these results it was concluded that the anatomy of the aorta of different species should be considered in recording longitudinal Bcgs and that optimal alignment of the recording axis to parallel the ascending segment of the aorta is essential.

(iii) Changes in the UF Bcg (a) with age: The UF Bcg (a) pattern of aged and young rats was analysed on a comparative basis in Chapter 5.

The ratio between Q-J time and the duration of mechanical systole altered significantly with age (see 'Myocardial efficiency index' below).

The pattern of the UF Bcg (a) of old rats also showed differences which are not easily expressed in numerical terms, e.g. a greater scatter in amplitude and pattern during different respiratory phases (Chapter 5).

The decreased HI and IJ amplitudes were interpreted as a reduction in the force of contraction associated with age. Moss (1961) also found a decreased HI amplitude in man with increased age. In old rats the Q-H''' time was also increased which was interpreted as an increased duration of the isometric contraction phase. It seems, therefore, that co-ordination of the myocardium is affected by age. The loading experiments described in Chapter 5 have shown that the body to heart weight ratio cannot account for the alterations in the UF Bcg (a) pattern found in old rats. Certain physiological changes in cardiovascular dynamics therefore develop with age in rats.

The study of Wilens and Sproul (1939^{a,b}) reflected a high incidence of coronary sclerosis and myocardial fibrosis in old rats (see point C (i)). It was therefore assumed that the changes in cardiovascular function, as measured by the UF Bcg (a) in rats, might be due to myocardial disease and cardiac incoordination associated with age. As none of the other recorded aspects, e.g. ECG, phonocardiogram, pressure pulse and its first time derivative, showed consistent changes, it was concluded

that the ballistocardiogram could be most valuable in assessing myocardial age. This is in accordance with the results described by Starr and Wood (1961) and Starr (1966) in reporting on a long term follow up Bcg study in man. It was thus concluded that the rat is a suitable experimental animal to use in investigating changes in the higher dynamic functions of the myocardium with age.

(iii) 'Myocardial efficiency index': A simple formula, which seemed applicable to the UF Bcg (a) of rats, was developed to calculate the 'myocardial efficiency index'. The formula is largely based on the ratio between Q-J time and the duration of mechanical systole and makes no provision for other variables, for instance mean arterial pressure. This 'myocardial efficiency index' was calculated by the following formula:

$$\frac{\text{IJ amplitude}}{\text{Q-J time}} \times \frac{\text{Duration of mechanical systole}}{\text{Q-J time}} \times K$$

where amplitude is expressed in cm/sec^{-2} , time in msec and $K = 1500$ to express efficiency on a percentage basis.

The 'myocardial efficiency index' calculated from the mean values of 'normal' rats by using this formula, amounted to 99.5%. The mean values of old rats (Table IIA and IIB) yielded a 'myocardial efficiency index' of 75%. For young rats (± 200 grams) a 'myocardial

efficiency index' of 100.5% was obtained. When five gamma/kg arterenol was administered (Fig. 20) a 'myocardial efficiency index' of about 380% was calculated.

From these calculations the following conclusions were reached:

(a) That a more refined mathematical expression, including perhaps other variables like mean arterial pressure or pulse pressure, might be developed from the crude formula to detect small alterations in myocardial efficiency and to distinguish between purely myocardial and peripheral vascular influences.

(b) When the individual variations found in the Bcg of normal rats were calculated by using the crude formula, the 'cardiac efficiency index' varied from about 80% to 130%. A more refined formula might discriminate more accurately between normal and abnormal Bcgs.

(c) That the age, amongst other important possible variables, of experimental animals should be taken into account when Bcg recordings are interpreted.

(d) Measurements made from the UF Bcg (a) might aid the accurate evaluation of the higher dynamic functions of the myocardium.

(iv) Mechanical and drug induced changes in the UF Bcg (a) pattern of rats: Mechanical changes in the circulation

e.g. vena caval occlusion, changes in the course of the aorta, etc., were discussed in Chapter 6. Changes brought about by cardiac stimulants (arterenol and levarterenol) were discussed in Chapters 7 and 8.

The main object of these experiments was to evaluate the wave identification as described in the present study. Once the identification of the waves was confirmed, these experiments were of further importance in obtaining information about cardiac function and drug action as measured by the UF Bcg (a).

From the results of these experiments it was evident that posterior vena caval occlusion provoked a more conspicuous lowering of the HI and IJ waves than in dogs (Pretorius 1962^b), and in rabbits (Green 1967 and Pretorius et al. 1968^a).

The administration of small doses of arterenol resulted in a decrease of the Q-H, Q-I and Q-J times. Small doses of both drugs caused a general increase in the heart rate. The ballistocardiographic action of arterenol and levarterenol on the myocardium of rats seemed to agree with that of other species as described by Green (1967) and Pretorius et al (1968^{a,b}). When large doses of arterenol (10 gamma/kg body weight) were injected intra-arterially, the heart rate was reduced. The reflex vagal activity in intact rats might therefore counteract the

cardiac chronotropic effect of arterenol when the mean arterial pressure is sufficiently increased. Doses of 10 gamma/kg arterenol and eight gamma/kg levarterenol resulted in bradycardia, ectopic beats and alternating rhythm.

Small amounts of arterenol and levarterenol showed a comparable chronotropic effect on the myocardium of the intact rat. The effects of large doses of catecholamine might be partly obscured by secondary (sympathetic or parasympathetic) reflex actions.

Arterenol decreased and levarterenol increased total peripheral resistance (Drill 1958, 1965). The site of injection of these drugs has been found to affect their peripheral and cardiac action (Drill 1958). It is suggested that arterenol stimulates both the alpha and beta adrenergic receptors causing vasoconstriction and vasodilation respectively (Drill 1958 and Moreira and de Freitas 1966).

Levarterenol seems to exert a more marked vasoconstrictor effect. In the present study levarterenol (8 gamma/kg) resulted in a more marked increase in blood pressure than 10 gamma/kg arterenol (Chapter 7).

Within five to 10 seconds after the administration of these drugs a more conspicuous increase in the HI and IJ waves resulted from arterenol than from levarterenol administration. Although the amplitude of the systolic waves might be

reduced by high systemic pressures according to Starr et al. (1953), the relatively greater increase in amplitude of the HI and IJ waves resulting from arterenol administration in the present study was possibly due to a stronger inotropic action of arterenol. Beta-receptor blockade (Moreira and de Freitas 1966) abolished to a large extent the cardiac stimulatory effect but not the pressor effect of arterenol. It seems therefore as if the cardiac stimulatory effect of arterenol is mediated through the beta-receptors. As levarterenol mainly stimulates the alpha-adrenergic receptors (Drill 1958), the conclusion that arterenol exerts a greater inotropic effect (Chapter 7) on the myocardium, seems valid.

According to Pretorius (1962^b) and Pretorius et al. (1966, 1968^{a,b}), the administration of cardiac stimulants and cardiac inhibitors, including the effects of hypothermia, are of great value in establishing the genesis of different Bcg waves in animals.

From the Q-time and amplitude measurements described in Chapter 8, the effects of drug induced sympathetic stimulation described in Chapter 7 and the mechanical alterations described in Chapters 5 and 6, a reasonable understanding of the genesis of the waves in UF Bcg (a) of rats could be reached. The possible genesis of the wave complexes found in the UF Bcg (a) of rats has been described in Chapter 9.

The results obtained in the present study indicated that only the systolic atrial waves (O', O'', F and G) were clearly shown in normal recordings. The diastolic atrial wave ('a') could not be identified in normal recordings as it was fused with the late isometric or systolic (HI and IJ) waves.

As the diastolic atrial wave was of small amplitude and represented small forces, it was concluded that it does not contribute to the ventricular systolic events in the UF Bcg (a). This was further confirmed by the lack of appreciable alteration in the ventricular ballistic waves during complete A-V block and complete separation of the atrial wave complex (see Chapters 5, 8 and 9).

Some controversy about the genesis of the H wave in the UF Bcg (a) of dogs is indicated in the literature. According to Pretorius (1962^b) the H wave in the UF Bcg (a) of the dog is mainly due to myocardial and blood vibrations during isovolumetric contraction. Pretorius (1962^b) also noted that the atrial wave might contribute to the H wave. Starr and Noordergraaf (1967) suggest that Pretorius (1962^b) minimized this effect, as a slightly larger contribution of the atrial wave to the H wave is expected according to Noordergraaf's theory. West and Corbascio (1959) are, however, of the opinion that the H wave in the UF Bcg (a) of dogs is largely due to atrial activity.

Moreira (1960) showed abolishment of the H wave when the atrial effects were isolated in the UF Bcg (a) of dogs. The recordings of West and Corbascio (1959) as shown by Starr and Noordergraaf (1967) are, however, void of wave identification (lettering of the waves). The possibility that the waves might have been lettered differently by West and Corbascio (1959) can therefore not be excluded.

From experiments in the present study it was concluded that the H wave complex in the UF Bcg (a) is mainly due to isometric cardiac events. According to the calculations described in Chapter 9, the atrial wave might contribute 25% to the H' wave in the UF Bcg (a) of rats under normal conditions.

Although it is not desirable to apply the findings obtained from the recordings of rats to those pertaining to dogs, it seems that the results of this study confirm the view of Pretorius (1962^b) concerning the genesis of the H wave and the contribution of the atrial wave to it.

Intensive care was, however, demanded to avoid confusion as the UF Bcg (a) of rats showed three H waves in comparison to the one H wave commonly found in the recordings of other species. Even when the isometric contraction phase was severely reduced in time by arterenol administration, the

least two H waves could still be identified.

The genesis of the HI, IJ, L, M and N waves in the UF Bcg (a) seemed to agree with the current view held by most investigators (see Chapter 9). The IJ wave in the UF Bcg (a) of rats is to be used to evaluate cardiac function (see point (iii) above). The results of Pretorius et al. (1966) indicated that the HI wave could also be of prognostic value. The value of the IJ wave was, however, not investigated in the latter study.

The results of the present study indicated that the HI wave in the UF Bcg (a) might show greater scatter in amplitude than the IJ wave. Although the higher stability shown by the IJ wave facilitated comparison between, for instance, old and young rats, it might be less sensitive to initial myocardial contraction (cardiac impulse according to Starr and Noordergraaf 1967). This could partially explain the greater individual variations found in the HI amplitude and Q-time interval. The experiments described in Chapters 7 and 8 indicated that the HI segment also contains an isometric component. This confirms the results obtained from experiments on dogs by Pretorius (1962^b) and might further explain the greater scatter in HI wave amplitude in the recordings of rats.

In comparing the different haemodynamic methods used in

the present study, it is evident from the results of experiments described, that the UF Bcg (a) detected changes in cardiac function the most conspicuously. When mechanical alterations were brought about in the circulation, the UF Bcg (a) reflected the greatest changes (see Chapter 6). The administration of small amounts of arterenol resulted in a marked increase in UF Bcg (a) amplitude (Chapter 7). During some of the ectopic beats described in Chapters 8 and 9, the UF Bcg (a) showed more marked changes than the pulse pressure and its first time derivative.

The UF Bcg (a), therefore, provides an excellent method to measure the dynamic functions of the cardiovascular system. The other recorded phenomena, e.g. pressure, pressure derivative, ECG and phonocardiogram, provided circumstantial evidence most valuable in understanding the UF Bcg (a) but, however, prove their own shortcomings concerning the assessment of the higher dynamic functions of the heart.

CHAPTER 11

S U M M A R Y

The recent progress made in ballistocardiography emphasized the urgent need for a clinical and experimental method that may furnish information about the higher dynamic functions of the heart. Very little experimental work on small animals has been done to establish the genesis of the UF Bcg (a) or to investigate the applicability of the method to experimentation with small animals.

In the present study a UF Bcg (a) system suitable for experiments with small animals is described. The physical properties of the system compare favourably with the ideal recommended values. A parallel suspended pendulum type of ballistocardiograph with a natural platform frequency of 0.38 Hz was used. The platform with accelerometer attached weighed 4.1 grams and a mean body to platform weight ratio of 65:1 was obtained.

When the body to platform ratio was reduced to 3:1, the atrial and isometric wave complexes were seriously attenuated. It is concluded that the system is able to record with high fidelity the UF Bcg (a) of rats.

To investigate the normal UF Bcg (a) pattern of rats, the ECG, phonocardiogram, carotid pressure pulse and its first time derivative were simultaneously recorded in most rats.

Q time interval and over-all amplitude measurements of the different waves were carried out.

Rats were divided into three different age groups according to weight, viz. a young group (mean weight 198 grams), a young fully outgrown (normal) group (mean weight about 275 grams) and an old group (mean weight about 400 grams). The UF Bcg (a) of old rats showed a decrease in HI and IJ wave amplitude and slope. The Q-H''' and Q-J times were increased in the recordings of old rats. The decreased HI and IJ wave amplitudes indicate a reduced force of ejection in old rats. The increased Q-H''' time indicates a longer period of isovolumetric contraction and an increase in the latent or energizing period. It is concluded that cardiac incoordination also developed with age and that the UF Bcg (a) demonstrates these changes in the higher dynamic functioning of the myocardium.

When the 'myocardial efficiency index' of rats was calculated by the use of a crude formula based mainly on the IJ segment of the UF Bcg (a), the recordings for old rats revealed an efficiency index of about 75%. Young adult rats showed an 'index' of about 99.3%. The administration of arterenol to young rats resulted in a 'cardiac efficiency index' of about 350%. The lowered 'myocardial efficiency' of old rats might be due to the development of myocardial fibrosis and possibly coronary sclerosis. The UF Bcg (a) could therefore be

utilized to demonstrate the development of myocardial disease.

Various experiments e.g. vena caval occlusion, reduction of blood volume, changes in the course of the aorta, administration of arterenol and levarterenol, to evaluate wave identification and to obtain information about the genesis of the different waves in the UF Bcg (a) of rats have been described.

From the results of these experiments it is evident that the general UF Bcg (a) pattern of rats shows some aspects of similarity to that of man and rabbits. Anatomical and age differences should be considered in the recording and interpretation of animal Bcgs.

The UF Bcg (a) of rats showed a clearly defined atrial wave complex in the normal recordings not seen in the recordings obtained from other species. When atrial activity was completely isolated during A-V block or ectopic beats, a systolic and diastolic atrial wave complex could be identified. Only the systolic part of the atrial wave complex was visible in normal recordings. Calculations showed that the atrial wave might contribute about 25% towards the H (isometric) wave complex.

The isometric wave complex (H', H'' and H''') in the UF Bcg (a) of rats is more complex than in other species.

The H wave complex persisted in some ectopic beats where no ejection of blood could be measured. A close time relationship between the H wave complex and the first heart sound was demonstrated. This indicated that the H wave complex in the UF Bcg (a) of rats is mainly due to myocardial and blood vibrations before aortic and pulmonic valve opening during isovolumetric ventricular contraction. The H' wave, however, exhibits some contribution of atrial systolic origin.

Arterenol administration increased the IJ amplitude to a greater extent than the HI amplitude. The IJ wave amplitude was more markedly decreased during vena caval occlusion and reduction of the blood volume than the HI amplitude. A close time relationship between the HI wave and the initial segment of the pressure pulse and its time derivative was demonstrated. The HI and IJ segments in the UF Bcg (a) of rats are therefore caused by different haemodynamic events. It is suggested that the HI wave is mainly caused by events during initial ventricular ejection but that it might reflect some late isometric components and possibly a component of right ventricular ejection.

The J wave in the UF Bcg (a) of rats might be caused by the interaction of:

(i) the forces associated with the development of maximal acceleration of blood in the descending aorta,

(ii) to a lesser extent the acceleration forces developed in the right ventricle and pulmonary arteries during systole,

(iii) the forces associated with the deceleration of blood in the heart and proximal arteries.

No clearly defined K waves in the UF Bcg (a) of rats would be identified.

The L wave is possibly due to the rate of change of acceleration forces associated with the haemodynamic events during closure of the aortic valve.

The UF Bcg (a) provides a useful experimental and clinical method for the accurate measurement of some aspects of the higher dynamic functions of the myocardium not yet possible by means of other available methods. The rat shows promise as a laboratory animal in experimental ballistocardiographic experimentation.

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