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Physiology

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RIGHT VENTRICULAR FREE WALL EXCITATION IN THE GOAT WITH
EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

By
Phillip Nash Ogburn, D.V.M.

* * * * * *

The Ohio State University
1971

Approved by

[Signature]
Advisor
Department of Veterinary Physiology and Pharmacology
PLEASE NOTE:

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CHAPTER I

FUNCTIONAL AND MORPHOLOGIC CORRELATIONS OF EXPERIMENTAL
RIGHT VENTRICULAR HYPERTROPHY IN THE GOAT

Introduction

Right ventricular hypertrophy (RVH) is a condition resulting from an increase in the amount of work required of the right ventricle to maintain circulatory equilibrium. RVH may develop as a sequela to congenital or acquired lesions and frequently has been described in many domestic animals and in man. The recognition of RVH in various conditions, utilizing electrocardiographic (22,26,27,39,49,50,59,65,74), angiocardio­graphic (18,19,46,99), radiographic (39,45,48), and hemodynamic aids (22,65,73,105), primarily for domestic animals such as the dog and cat, has been described. Large domestic animals, such as the herbivores, have not lent themselves to common diagnostic techniques such as thoracic radiography due to their size. Intracardiac pressure measurements have been of value in diagnostic work. Although electrocardiograms of domestic animals have been reported beginning with the initial studies by Kahn (62), the development of diagnostic abilities in domestic animals, especially the large herbivores, has been exceedingly slow. The electrocardiographic recognition of hypertrophy, either right or left, has not been attempted in the ruminant even though congenital lesions and acquired lesions exist (40).
Of particular interest has been the observation that in many cattle maintained at elevations exceeding 7500 feet a syndrome occurs that includes RVH and congestive heart failure (5,9). Diagnostic methods have indicated that the condition is due to increased pulmonary vascular resistance from chronically lowered oxygen tension and results in the production of pronounced pulmonary hypertension (5). Although various hemodynamic measurements have been accomplished, no attempt has been made to describe any electrocardiographic alteration regarding the excitation process. Electrocardiographic criteria for diagnosing RVH in the ruminant remain unknown.

Models of RVH have been devised in several species to facilitate the study of pathological alterations associated with the condition. Banding of the pulmonary artery which results in the development of RVH has been accomplished by many investigators (4,8,25,28,77). Other methods of RVH production in dogs have included: inducement of pulmonary hypertension through pulmonary vein ligation, aortic to right atrial shunts, and experimental silicosis (101). Progressive pulmonary artery constriction either by repeated surgical intervention (4) or by devices which allow remote pulmonary artery constriction (8,25) have resulted in RVH and congestive heart failure.

Ideally, a model for the study of RVH in goats should provide a condition closely mimicing that of a naturally occurring disease, with a minimum of surgically induced physical alteration. The model also should provide precise control of the development of RVH.
Materials and Methods

Experimental Animals

Healthy goats, ranging in age distribution from weanlings to adult animals were accepted for the study by random selection. No criteria concerning sex was stipulated although only 3 of the 18 goats obtained were females. Their weights ranged from 15.9 to 47.7 kg. Six adult goats who developed RVH on the basis of cine-angiocardiograms, thoracic radiographs, and postmortem evidence are included in this report.

Surgical Procedure

The animals were prepared for surgery after a fasting period of 24 hours. Atropine\(^1\) (0.5 - 0.1 mg/kg) was used preoperatively to depress rumen motility and salivation.

Anesthesia was induced by IV sodium thiamylal\(^2\) and maintained by methoxyflurane\(^3\) and oxygen administered by positive pressure respiration.

The thorax was entered aseptically at the left fourth intercostal space. The pericardium was incised approximately 1 cm below and parallel to the course of the phrenic nerve. The dorsal flap of the pericardium was sutured to the skin incision to enable visualization of the base of the main pulmonary artery. After careful dissection, a 2 cm size siliconized\(^4\) Jacobson cuff\(^5\) (Fig.1) was placed around the

\(^1\) Atofate, W. A. Butler Co., Columbus, Ohio.
\(^2\) Surital, Parke-Davis & Co., Detroit, Michigan.
\(^3\) Methane, Pitman-Moore, Indianapolis, Indiana.
\(^4\) Silastic Medical Adhesive Type A, Dow Chemical.
\(^5\) Davol Rubber Co., Providence, Rhode Island.
Figure 1

Rubber Jacobson cuff in distended and undistended state. A thick rubber diaphragm in the bulb allows injection of radiopaque material through a fine gauge needle without leakage.

(Photograph reproduced through permission granted by Dr. Sanford P. Bishop, Assistant Professor, Pathology.)

Figure 2

Photograph of preserved heart with RVH with distended Jacobson cuff in position around the main pulmonary artery.
main pulmonary artery (Fig. 2), the tabs sutured together, and the
pericardium closed over it. The injection bulb was brought out through
the pericardial incision, through the fifth or sixth intercostal space
and secured subcutaneously on the lower left thorax. The thoracic
incision was then closed and the goat was allowed to recover.

Production and Evaluation of RVH

Two weeks following surgery and at varying intervals subse­
quently, the cuff was progressively distended by injection of a
radiopaque material, sodium diatrozoate 35% and meglumine diatrozoate,
into the subcutaneously placed injection bulb.

Electrocardiograms, phonocardiograms, right ventricular pressure,
right atrial pressure, lateral radiographs, and selective cineangio­
cardiograms of the right ventricle were recorded prior to placement of
the cuff, immediately prior to each succeeding inflation of the cuff,
and immediately prior to an epicardial and intramural electrode study
of the right ventricle. All electrocardiograms, phonocardiograms, and
pressure recordings were made on a Brush Mark 200 direct-writing
8-channel oscillograph. Electrocardiograms, phonocardiograms, and
pressures were recorded at 20, 50, 100, and 200 mm/sec paper speed.

Pressure. Pressure recordings were obtained using an 18-inch,
15-gauge polyethylene catheter inserted through a 14-gauge thin-walled
needle which was introduced into the left jugular vein percutaneously
and connected to a Statham P23a pressure transducer maintained at
right atrial level.

6Renovist 70%, E. R. Squibb & Sons, New Brunswick, New Jersey.
7Brush Instrument Co., Div. Clevite Corp., Cleveland, Ohio.
8CVP Infusor, Sorenson Research Corp., Salt Lake City, Utah.
The progressive inflation of the cuff was accomplished on awake non-premedicated animals in either a standing or right lateral recumbent position. The position was largely determined by the cooperation of the animal. Many would stand quietly with minimal restraint while certain animals became calm only while lying down under light restraint.

The degree of pulmonary artery constriction was assessed by monitoring the right ventricular pressure. Each subsequent constriction of the pulmonary artery lumen by inflation of the cuff was performed until ventricular premature beats, or a continuing decline in right ventricular pressure, occurred. The observation of ventricular premature beats or right ventricular pressure decline indicated too severe constriction of the pulmonary artery, and a small amount of inflation fluid was removed until stabilization occurred.

Phonocardiograms. Phonocardiograms were recorded at 100 cycles/sec frequency cutoff filter at the left apex and base utilizing a Sanborn\textsuperscript{9} phono-preamplifier, impedance box and crystal microphone with bell attachment.

Electrocardiograms and Vectorcardiograms. Two different lead systems were utilized to obtain electrocardiograms from the animals. The standard Wilson lead system was utilized which uses 6 limb leads (I, II, III, aV\textsubscript{R}, aV\textsubscript{L}, aV\textsubscript{F}) and V\textsubscript{10} (exploring unipolar electrode placed over the seventh thoracic dorsal spinous process). The McFee-Parungao

\textsuperscript{9}Sanborn Co., Waltham, Massachusetts
corrected orthogonal lead system (70) developed for dogs also was utilized to provide a better orthogonal representation of body surface information and less variability in the recordings by minimizing alterations seen in other systems with forelimb position, body shape or electrode position (58). The electrocardiograms were recorded with the animal in right lateral recumbency and with the limbs extended perpendicularly and parallel to one another when anesthetized. When awake and standing, a V_{10} lead was recorded. McFee X, Y, Z leads were taken and projections were made of constructed vector loops in the frontal, left sagittal, and horizontal planes. The maximum QRS vector magnitude in millivolts and its orientation angle were measured by the method of Vasquez (102) as well, noting the direction of loop inscription (counterclockwise versus clockwise). The maximum QRS vector was measured from the origin of the inscribed axis to the farthest point in the periphery of the loop (Fig. 3). All magnitudes were measured in millimeters and then converted into millivolts (10 mm = 1 mV). The orientation of the vectors was determined by utilizing a protractor.

**Cineangiocardiology and Radiography.** Right lateral projection angiocardiographic exposures were selected for measurement. The procedure was recorded on a 35 mm camera^{10} which was coupled to a Siemen's cineangiocardiographic unit^{11} with a 7-inch image intensifier. The exposures were made at 24 frames per second using an exposure time of 1 msec/frame. Approximately 8 to 10 cc's of contrast

^{10}Arriflex Co., West Germany.
^{11}Siemens Medical of America, Chicago, Illinois.
Figure 3

Diagrammatic representation of a vectorcardiographic loop indicating direction of inscription, amplitude, and axis. The maximum QRS vector is determined for amplitude (millivolts, mV.) and for axis (degrees°). The arrows located around the loop indicate the direction of loop inscription (clockwise or counter-clockwise).
medium were injected manually as rapidly as possible through the
catheter into the right ventricle. The cineangiocardiogram was
repeated if premature beats were recorded during injection to
insure a full dimensional representation of chamber and myocardial
wall dimensions during both systole and diastole. The left ventricle
was demonstrated after passage of the contrast medium through the
pulmonary circulation. Opacification of both ventricles was satis-
factory throughout the series. The film was calibrated by utilizing
a standard dimension marker (1 cm) and measurements of the right and
left ventricular chambers and walls were adjusted to this calibration.
The right ventricular free wall thickness (RW) was measured perpendi-
cular to a line tangent to a point on the epicardium which was
estimated to be at a level near the base of the pulmonary outflow
tract. The left ventricular free wall thickness was difficult to
measure accurately due to the anterior protrusion of the reticulum
making separation of the epicardial border of the left ventricle from
the wall of the reticulum and diaphragm impossible. The area of the
right ventricle (RVA) and area of the left ventricle (LVA) were
obtained by planimetering the perimeter of the outlined ventricular
chambers, and correcting them for magnification.

Radiographs were taken on all animals in right lateral
recumbency at a point during maximal inspiration using Siemens'
radiographic unit and a stationary grid of 50 lines per inch.
The cardiac silhouette was planimetered and total cardiac area was
recorded for each animal serially throughout the experimental period.
Post Mortem. Following euthanasia, the heart was removed, the chambers and coronary vessels were flushed with normal physiological saline solution. The heart was then perfused with 10% phosphate buffered formalin and was stored in that solution.

The heart was divided according to the method of Fulton et al. (42), except that the coronary vessels and fat were not removed. The atria were separated from the ventricles at the atroventricular ring and the right ventricular free wall was separated from the septum at its point of juncture. Total heart weight, atrial weight, ventricular weight, right ventricular free wall weight and left ventricular and septal combined weight were recorded for the fixed tissue.

Statistical Analysis of Data

The data were tabulated and analyzed utilizing a t test to determine statistically significant alterations from the control values. Values of P greater than 0.1 were regarded as not being statistically significant. Values of P between 0.05 and 0.1 were included as significant because it was felt that they indicated trends in information that otherwise might be overlooked on more rigorous evaluation. Values of P less than 0.05 were felt to be significant statistically.

Results

Six adult goats developed RVH following 2 to 4 progressive constrictions of the pulmonary artery and are included in this report. Two goats died of congestive heart failure of an extremely rapid onset. Four goats died post-surgically, 2 due to infection and 2 due to
inadequate ventilation caused by pneumothorax. The initial records of the 6 goats which developed RVH served as the control.

**Pressure.** Approximately two weeks after surgery, the pulmonary artery cuff was injected to facilitate an increase in right ventricular pressure. The first inflation of the cuff was intended to raise right ventricular pressure to approximately 60 mm Hg. This was done in most of the animals to avoid rapid decompensation of the right ventricle and allow time for compensatory responses of the myocardium to develop. No discernible changes in respiratory rate or heart rate were observed in the goats during or immediately following the first inflation. Subsequent pulmonary artery constriction was determined by the health and physical appearance of the animal as well as tolerance to increased constriction. The two goats which died of rapidly fulminating heart failure were inflated to approximately 80 mm Hg on their second inflation and both died one to two days later. Therefore, succeeding constrictions were carefully accomplished with final stabilization at peak right ventricular pressures ranging from 55 to 110 mm Hg. These levels were significantly above the pressures of the control group whose right ventricular pressure ranged from 15-30 mm Hg (p < .01) (Table 1). The end diastolic right ventricular pressures rose from a normal range of 0.7 mm Hg to a range of 5-20 mm Hg in the RVH group (Fig. 4). This increase was significant statistically (p < .01). Right atrial mean pressure was increased concomitantly with the increase of right ventricular end diastolic pressure. A mean value of 3.4 mm Hg for the control group increasing
### TABLE 1

**INTRACARDIAC PRESSURES BEFORE AND AFTER PRODUCTION OF EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY IN 6 GOATS**

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<tr>
<th></th>
<th>Right Ventricle</th>
<th>Right Atrial</th>
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<tr>
<td></td>
<td>Systolic (mm Hg)</td>
<td>Diastolic (mm Hg)</td>
</tr>
<tr>
<td><strong>CONTROL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>23.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>6.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Maximum</td>
<td>30.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Minimum</td>
<td>15.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>EXPERIMENTAL RVH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>89.2</td>
<td>13.9</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>22.4</td>
<td>6.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>110.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Minimum</td>
<td>55.0</td>
<td>5.0</td>
</tr>
<tr>
<td>P</td>
<td>&lt; .01</td>
<td>&lt; .01</td>
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Figure 4

Right ventricular pressure recordings and electrocardiograms during the development of experimental RVH in Goat 10. The presurgical control record indicates that the right ventricular pressure is 25/5 mm Hg. The right ventricular pressure 13 days after surgery and prior to the first inflation indicates the right ventricular peak systolic pressure has risen only slightly to 30 mm Hg, while the right ventricular end diastolic pressure has stayed approximately the same. On day 173 after two intervening inflations (not shown), the right ventricular pressure is 80/7 mm Hg. On day 210, prior to terminal studies, the right ventricular pressure is 95/15 mm Hg, indicating a relatively high right ventricular peak systolic and diastolic pressure when compared to the initial pressures.
GOAT 10

RIGHT VENTRICULAR PRESSURE

PRE-SURGICAL

DAY 13

DAY 173

DAY 210

20 mm. Hg

0 mm. Hg

ECG
to 8.8 mm Hg for the RVH group was shown to be significant statistically (p < .01). During subsequent inflations in the conscious goat, many of the animals would show signs of distress or pain coinciding exactly with the time of cuff inflation. This response was transitory, lasting only for a few seconds. The appearance of premature atrial, AV junctional, or ventricular beats was consistently associated with a gradual decline of right ventricular systolic pressure and an elevation of right ventricular end diastolic pressure.

**Auscultation and Phonocardiograms.** Short systolic murmurs (Grade I to II/VI) were auscultated after surgical recovery of all pulmonary artery cuffed goats. The murmurs were well localized over the base of the heart at approximately the left third intercostal space one third of the ventrodorsal distance between the sternum and the dorsal spinous processes.

With succeeding pulmonary artery constriction, the murmur increased in intensity in all animals (Fig. 5). The greatest amplitude was a Grade IV out of a possible VI in Goat 11. This murmur was accompanied by a palpable thrill located over the point of maximal intensity for that murmur. Splitting of the second sound also was noted in certain goats as was the occasional appearance of a third heart sound in goats with very high right ventricular pressure. Goat 13 had a loud fourth heart sound present presurgically and after RVH had been experimentally induced.

**Electrocardiograms and Vectorcardiograms.** Electrocardiograms were recorded prior to surgery and at periods throughout the duration
Figure 5

Right ventricular pressures, phonocardiograms and electrocardiograms in a goat before and after production of experimental RVH. Notice absence of systolic murmur (SM) at apex and base in the presurgical record. The murmur produced with constriction of the pulmonary artery by a cuff placed supravalvularly around the main pulmonary artery is holosystolic. The murmur begins with the first heart sound ($S_1$) and appears to build in intensity to the second heart sound ($S_2$). Recordings were made at 100 mm/sec paper speed using a 100 cps frequency cutoff filter.
GOAT 14
PRE-SURGICAL

LEFT APEX

R.V. Press.

PCG

LEFT BASE

TERMINAL

PCG

ECG

LEFT BASE

R. V. Press.

PCG

ECG
of the experimental study (Fig. 6). Although individual variations were present regarding amplitude, duration and axis, initially all were within normal limits (Tables 2 and 3). Serial electrocardiograms utilizing the McFee lead system were recorded on anesthetized animals in right lateral recumbency. Figure 6 illustrates the simultaneously recorded ECG of Goat 1 on day 63, approximately 2 months after surgery and 6 weeks after the first inflation. There are slight changes in waveform and amplitude, but none that indicate major alterations. A slightly broader S wave in the McFee Y lead and a slight increase in amplitude of the R wave in Z are noted.

In the Wilson system--with X representing lead I, Y representing aVF, and Z representing V10--the only noticeable variation is in the amplitude of the R wave in Y. When the initial record is compared with the terminal record on day 302, certain slight differences exist. In the McFee records, the X lead configuration changed slightly from a qs pattern to Qr. Y remained essentially the same although the amplitude of R and S waves increased. The amplitude of the R wave in the Z lead doubled. In the Wilson recordings X remained essentially the same. Y waveform changed from a Qr form to a qRS form with a slight increase in amplitude. The Z component did not show marked change. The appearance of small waveform changes as well as slight amplitude increases in this series of records indicates slight alterations of the maximum QRS vector in axis and amplitude. Also note, however, that at other recording periods there were slight changes in amplitude and waveform as well.
Figure 6

Simultaneous McFee and Wilson lead system electrocardiographic recordings of Goat 1 at representative periods throughout the production of experimental RVH.
<table>
<thead>
<tr>
<th></th>
<th>Frontal</th>
<th>Left Sagittal</th>
<th>Horizontal</th>
<th>Frontal</th>
<th>Left Sagittal</th>
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<td>.28</td>
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<td>.47</td>
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<td></td>
</tr>
<tr>
<td>Mean</td>
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<td>-96.8</td>
<td>.46</td>
<td>1.02</td>
<td>1.04</td>
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<td>Standard Deviation</td>
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<td>.25</td>
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<td>-103.0</td>
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n.s. = not significant
TABLE 3
ELECTROCARDIOGRAPHIC VALUES BEFORE AND AFTER PRODUCTION OF EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY IN 6 GOATS

<table>
<thead>
<tr>
<th></th>
<th>P - R (sec)</th>
<th>QRS (sec)</th>
<th>QT (sec)</th>
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<tr>
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<td>0.039</td>
<td>0.334</td>
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<td>0.004</td>
<td>0.004</td>
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</tr>
<tr>
<td>Maximum</td>
<td>0.105</td>
<td>0.042</td>
<td>0.370</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.090</td>
<td>0.035</td>
<td>0.290</td>
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<tr>
<td><strong>EXPERIMENTAL RVH</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
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<td>0.041</td>
<td>0.292</td>
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<tr>
<td>Standard Deviation</td>
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<td>0.004</td>
<td>0.037</td>
</tr>
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<td>0.048</td>
<td>0.340</td>
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<tr>
<td>Minimum</td>
<td>0.085</td>
<td>0.036</td>
<td>0.240</td>
</tr>
<tr>
<td>P n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

n.s. = not significant
Vectorcardiograms recorded from goats before and after the development of RVH were compared. Figure 7 illustrates, in three planes, the distribution of the vector forces for one goat. The vector loop in the frontal plane is complex with early activity oriented rightward and terminal activity directed cranial. The left sagittal vectorcardiogram shows forces generated in a counterclockwise manner with early forces directed ventrad and late activity oriented cranial and dorsad. A clockwise inscription of the loop is noted in the horizontal plane with forces directed: early--rightward and ventrad; late--dorsad. After development of RVH, the vectorcardiogram of Goat 1 is reexamined in Figure 8. Only slight differences are noted in the maximum QRS vector orientation, but the amplitude of the vector loop is dramatically altered. The change in amplitude, although marked in this animal, was not generally observed.

The maximum QRS vector orientation and amplitude was determined in the frontal, left sagittal and horizontal planes for both groups. The axis orientation and amplitudes for the control group were 161.8°, .49mV (frontal); 116°, .77mV (left sagittal); and 143°, .83mV (horizontal). The orientation and amplitudes for the experimental RVH group were 142.2°, .46mV; 105.0°, 1.02mV; and 96.8°, 1.04mV for the respective planes (Table 2).

In the frontal plane the mean change in orientation and amplitude was not shown to be significant statistically (Table 2). Mean maximum QRS vector reorientation in the left sagittal plane of 11 degrees, from -116° to -105° was significant statistically (p < .05). The maximum QRS vector reoriented in a dorsad and caudad direction.
Presurgical vectorcardiograms of Goat 1 in frontal, left sagittal, and horizontal planes. In the frontal plane the loop is somewhat complex with the major forces directed craniad and rightward. The left sagittal vectorcardiogram shows a generally counterclockwise inscription of the loop which is directed craniad and dorsad. The horizontal vectorcardiogram indicates a loop directed in a clockwise manner and oriented rightward and dorsad.
FRONTAL
CRANIAL

RIGHT
LEFT
CAUDAL

HORIZONTAL
DORSAL
CRANIAL
CAUDAL
VENTRAL

LEFT SAGITTAL
DORSAL
CRANIAL
CAUDAL
VENTRAL

0.1 mv.

RIGHT
LEFT

VENTRAL

GOAT 1
PRE-SURGICAL
Figure 8

Vectorcardiograms of Goat 1 after production of RVH. The loops are inscribed in the same direction as they were in the control record. Extremely slight differences exist in the maximum QRS vector axis between the initial and terminal record. The maximum QRS vector amplitude (mV) is changed dramatically in this goat. This is not consistent with what was found for the entire group of RVH goats when compared to the controls.
In the horizontal plane, the mean maximum QRS vector moved leftward and dorsad approximately 46 degrees from $-143^\circ$ to $96.8^\circ$. This re-orientation of vector forces was significant statistically ($p < .1$). Distribution of the maximum QRS vector orientation and amplitudes are compared in the frontal, left sagittal and horizontal planes in Figure 9. The mean amplitude of the respective maximum QRS vectors was compared for all planes with no significant statistical variation (Table 2).

In assessing the changes attendant to RVH in the goat, various electrocardiographic intervals were compared. No significant changes were noted for either the P-R or the QRS intervals which ranged from .090 to .105 sec and .035 to .042 sec respectively in the control records to .085 to .125 sec and .036 to .048 sec in the RVH group. The Q-T interval did change significantly ($p < .05$) from a mean of 0.334 sec in the control group to a mean of 0.292 in the RVH group (Table 3).

**Cineangiocardiology and Radiography.** The major cardiac dimension alterations derived by cinemangiocardiological measurement included: increased mean thickness of the right ventricular free wall in systole (4.6 mm to 10.0 mm - $p < .01$) and in diastole (3.4 mm to 8.2 mm - $p < .02$), and increased diastolic right ventricular area ($70.8 \text{ cm}^2$ to $84.5 \text{ cm}^2$ - $p < .1$). The increase in these parameters paralleled the development of RVH and is consistent with it. No significant alterations were evident in either of the left ventricular measurements, nor were significant alterations detected in right ventricular area measurements during systole (Table 4).
Figure 9

The orientation (degrees) and amplitude (mV) of the maximum QRS vector in 6 goats with RVH as compared to control data. For the control goats, in the frontal plane there is a wide range of maximum vector orientation from $-90^\circ$ to $+114^\circ$. After development of RVH the range becomes $-74^\circ$ to $+90^\circ$. In the left sagittal plane variation was markedly less for both groups and their distribution appears different. The RVH group has shifted caudad and dorsad. In the horizontal plane the vector distribution for the control goats is scattered widely. After developing RVH the vectors reorient in a dorsad and leftward direction, while the distribution becomes narrow.
### TABLE 4

**RADIOPHISTIC AND CINEANGIOCARDIOPHPHY VALUES BEFORE AND AFTER PRODUCTION OF RIGHT VENTRICULAR HYPERTROPHY IN 6 GOATS**

<table>
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<tr>
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<th>RW</th>
<th>RVA</th>
<th>LVA</th>
<th>TA</th>
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<td>Diastolic</td>
<td>Systolic</td>
<td>Diastolic</td>
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<td>34.0</td>
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<td><strong>EXPERIMENTAL RVH</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
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<td>8.2</td>
<td>60.0</td>
<td>84.5</td>
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<tr>
<td>Standard Deviation</td>
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<td>11.7</td>
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**RW** = Right Wall Thickness (mm)

**RVA** = Right Ventricular Area (cm²)

**LVA** = Left Ventricular Area (cm²)

**TA** = Total Heart Area (cm²)

n.s. = not significant
Qualitative assessments of the cineangiocardiograms indicated a tendency for the outflow tract to distend markedly during systole and for more dye to remain in the right ventricle during succeeding cardiac cycles than without pulmonary artery constriction.

Lateral thoracic radiographs demonstrated remarkable increases in size of the cardiac silhouette in some animals (Figs. 10, 11 and 12) as the hypertrophy developed. However, in others no apparent size changes in the cardiac silhouette resulted. Statistically there was no significant alteration in area when the RVH group was compared to the control (p < .1) in the means of the two groups (Table 4).

**Post Mortem.** Mean total heart weight to body weight ratio for the RVH group was 7.92 g/kg which is significantly greater than the mean of 6.32 g/kg for the normal group (p < .1) which consisted of 4 goats. The normal group's heart weight to body weight ratio mean was 6.32 g/kg which reflects approximately 1.5 g/kg difference in the two means (Table 5). The mean right ventricular free wall weight to body weight was 2.34 g/kg, reflecting a significant increase of right ventricular mass of approximately 0.80 g/kg in comparison to the control (p < .05). Mean right ventricular free wall weight to heart weight in the RVH group was 29.89% representing a statistically significant increase in RV mass of 5.5% over the percentage for normal goats. The right ventricular to ventricular weight ratio was statistically significant (p < .01) in that an increase in percentage to 38.28% for the RVH goats was observed versus 26.91% for the control goats. Left ventricular weight to body weight ratios did not alter significantly. However, the left ventricular weight was compared to heart weight and
Figure 10
Lateral thoracic radiograph of Goat 11 prior to surgery.

Figure 11
Lateral thoracic radiograph of Goat 11 on day 87 after production of experimental RVH. The cuff is in place around the pulmonary artery and is filled with a radiopaque medium.

Figure 12
Lateral thoracic radiograph of Goat 11 on day 190 after production of experimental RVH. The total cardiac silhouette is increased in area. The retrosternal space is diminished due to a marked enlargement of the right ventricle, and the tracheal angle is reduced.
<table>
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<th>RV/BW (g/kg)</th>
<th>RV/HW (%)</th>
<th>RV/VW (%)</th>
<th>LV/BW (g/kg)</th>
<th>LV/HW (%)</th>
<th>LV/VW (%)</th>
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<tr>
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<td>&lt; .01</td>
</tr>
</tbody>
</table>

HW = Total Heart Weight  
BW = Total Body Weight  
VW = Total Ventricular Weight  
RV = Right Ventricular Free Wall  
LV = Left Ventricle and Septum  
n.s. = not significant
ventricular weight indicated the mass of the ventricle was reduced significantly \((p < .01)\). Finally, the percentage of right ventricular to left ventricular weight was significantly increased from a level of 37.86% for the control mean to a value of 62.67% for the RVH group \((p < .01)\).

**Discussion**

The production of RVH in animals and the scrutiny of its development is not unique to this study. This study has followed closely the method instituted by Bishop (8)—to cause RVH and congestive heart failure in dogs. The utilization of this procedure has been modified only slightly to enable its use in goats.

As Bishop stated in his thesis, it is desirable to have an experimental model which is uncomplicated by secondary reactions when studying a certain diseased state. The model of RVH described in this paper while not eliminating these problems does reduce them to a minimum.

There is no attempt to interrelate this data except to indicate that progressive constriction of the main pulmonary artery produces a statistically measurable amount of RVH which can be utilized in subsequent activation studies. Certain interesting features of the data have been presented to confirm this observation.

**Pressure.** Peak right ventricular systolic pressure changes from a range of 15 to 30 mm Hg to a range of 55 to 110 mm Hg have been demonstrated to occur concomitantly with increased right ventricular end diastolic pressure, increased mean atrial pressure,
increased right ventricular free wall thickness and with increases in right ventricular diastolic chamber area subsequent to constriction of the main pulmonary artery by an inflatable rubber cuff. Controlled progressive constriction of the pulmonary artery was first accomplished by Davis et al. (25) to provide a model of right ventricular hypertrophy and congestive heart failure in the dog. Bishop (8) subsequently utilized an inflatable cuff sutured around the main pulmonary artery to produce RVH and congestive heart failure in dogs without reentering the thoracic cavity, and he had few complications after the cuff was siliconized. The results of pressure recordings in the right ventricle and right atrium of goats closely parallel these studies performed on dogs (8,25,28). In addition, Alexander (5) and Blake (9) have reported similar right-sided pressures in cattle with acquired pulmonary hypertension and right-sided congestive heart failure when exposed to high altitudes.

Auscultation and Phonocardiograms. Auscultation and phonocardiographic recordings of normal goats revealed the presence of two sounds which could always be heard. The first heart sound was uniformly single and of moderate intensity. The location of maximal intensity for the first heart sound was on the left thoracic wall just behind the olecranon. The second sound was generally single although respiratory splitting during inspiration was recorded in some animals. The second heart sound was best heard well forward at approximately the left third intercostal space one-third of the ventrodorsal distance from the sternum. With progressive development of RVH and with increasingly severe degrees of induced pulmonary artery stenosis, a
murmur mimicking pulmonic stenosis was produced. The amplitude and harshness of the murmur was subjectively determined to be comparable to murmurs heard in naturally-occurring pulmonic stenosis in dogs with but a few exceptions. The harshness of the murmur was less noticeable in the goats, indicating less noise production in the goat with experimental pulmonic stenosis than when the naturally-occurring pulmonic stenosis is present. Occasional systolic clicks were noted as well. The murmur produced frequently extended through the aortic component of the second heart sound when severe constriction was produced. This may be due to prolonged ejection of the right ventricle and is occasionally noted in severe pulmonic stenosis.

Electrocardiograms and Vectorcardiograms. Initial electrocardiograms recorded from goats prior to inducement of RVH produced values within the normal range (61,75,97) for P-R interval, QRS duration, Q-T interval and orientation and amplitude of major QRS vectors. When values for goats with experimentally induced RVH were compared to the control values, certain statistically significant changes had occurred. The Q-T interval for the RVH group decreased from a mean control value of 0.334 to a mean value of 0.292. Although the mean value for the RVH group was within the range of normals in the control group, the RVH range extended well down below the normal value. Reports of Q-T interval alteration have not been discovered by this investigator in animals as a result of experimentally induced RVH. The alteration in Q-T intervals may reflect changes in rate and have been described as being due to changes in electrolyte concentration such as hypercalcemia and hyperpotassemia (41). No reports concerning
Q-T interval alterations have been reported in the literature in ruminants with RVH.

That axis reorientation occurs in RVH in man and dogs has been well documented. The current electrocardiographic diagnosis of RVH in man has been largely based upon the criteria originally established by Wilson (104), Meyers (73), and Sokolow (94). These criteria depend primarily upon changes seen in precordial leads—namely, increase in the R/S ratio, delay in the onset of the intrinsicsicord deflection, and ST-segment and T-wave changes. A qR pattern and a rSR' pattern has been described in the precordial leads.

Milnor (72) proposed criteria differing from these to decrease the incidence of "false positives" and "false negatives." His criteria is based on the presence of an axis of +110° to ± 180°, or between -90° and ± 180°, or an R/S or R'/S ratio in V₁ greater than 1.0 with R or R' greater than 0.5 mV. Other investigators (66,72,73,78,89) have refined the accuracy of the diagnosis of RVH in man by depending on the absolute and relative magnitudes of R's and S's and relationships between R/S ratios of V₁ and V₅ or V₆.

Similar criteria have been proposed for the recognition of RVH in dogs by Detweiler (26,27), Hill (57) and Hamlin (47). Most diagnostic methods have attempted to statistically place the RVH group out of the range of normal on the basis of axis orientation. In dogs, the normal range is estimated at approximately +30° to + 100° in the frontal, sagittal and horizontal planes. Values between 100° and -90° have been attributed to RVH or right bundle branch block. Obviously, these criteria are not valid for the assessment of RVH in the goat because
normal axis range in goats (97) and other ruminants (100) have been reported to be outside the normal axis range in man and in dogs. Also, the ventricular activation process is different in the ruminant than in the dog and man (23,34,52,79). By determining the normal axis orientation for the normal group of animals and by comparing that with the RVH group, certain axis alterations are noted. In the left sagittal plane, the variance of axis distribution decreased (Table 2) while the orientation of the mean axis shifted dorsocaudad. The re-orientation of vectors did not place the range of the RVH group out of the range of normals however. In the horizontal plane, the standard deviation of the RVH group diminished from 55.94° to 5.98° and the mean axis shifted leftward from −143° to 96.83°. The range of the RVH group remained within the range of the control group. The results of this data indicate that although there is a redistribution in the mean vectors for the two groups in the left sagittal and horizontal planes, it would be exceedingly difficult to attach a connotation of abnormality to any one of the values because of its distribution within the normal range. The wide variability of axis orientation in goats has been noted by Szabuniewicz (97) in the frontal plane. The data derived from construction of frontal plane axis in both the RVH and control groups substantiate his observation of wide variation and give even wider values for range than his using a corrected lead system. The amplitude of the maximum QRS vector did not change appreciably for the right ventricular hypertrophy group indicating no major alteration in potential impinged upon body surface points.
No reliable diagnostic criteria could be established for the electrocardiographic detection of RVH in the goat.

**Cineangiocardiography and Radiography.** The major cardiac feature alterations of the cineangiocardiograms included: increased thickness of the right ventricular free wall (p > .01), increased right ventricular chamber area, and ballooning of the right ventricular outflow tract. The increase in right ventricular parameters paralleled the development of hypertrophy and is consistent with it.

The correlation of increased end diastolic pressure and increased diastolic right ventricular chamber area measured by selective right ventricular cineangiocardiography is consistent with observations made by Bishop (8) in dogs. Although volumes were not calculated due to the relative shape of the right ventricle (80), there was an actual increase in the area of the right ventricle in the lateral planar view. The measurement of the right ventricular wall thickness by cineangiocardiography indicated a pronounced increase in thickness of the right ventricular wall in both systole and in diastole. The planimetered areas of the left ventricle did not change significantly nor did the total area of the heart when examined from the radiographs.

**Post Mortem.** Observations on the total heart weight to body weight ratio in normal dogs have been made by other investigators with values ranging between 5.0 and 11.0 g/kg. No values for the goat are reported in the literature. However, the value of 6.32 obtained in goats is within the range established for dogs. The mean value for goats with RVH shows a small but significant increase in heart weight to body weight ratio. The use of this index has been
reported as unreliable (42). Other indicators of RVH which have been shown to be more sensitive are the right ventricular free wall weight to total heart weight, body weight, or total ventricular weight. The data presented in this study all indicate an increase in RV mass relative to the other parameters measured. Left ventricular weight relative to heart weight and ventricular weight was shown to diminish. Similar observations in dogs with acquired and congenital lesions have been reported by Knight (65) in assessing ventricular ratios in dogs with acquired or congenital lesions of the right ventricle.

Correlations of cardiac structural changes have been reported in ruminants with RVH other than the goat. Alexander (5) described cardiac chamber and mass alterations of the right ventricle in 20 cattle with pulmonary hypertension and RVH at high altitude. Blake (9) studied the ventricular effects of exposure to altitudes of 9,000-10,000 feet in cattle who subsequently developed brisket disease. Ratios of right ventricular free wall weight to other measured parameters in the goat with experimental RVH were greater than those described for RVH in the cattle with pronounced brisket disease and RVH.

Summary

A method of producing RVH in the goat by progressive pulmonary artery constriction was described after the method utilized by Bishop in dogs. This method produced a statistically significant degree of right ventricular hypertrophy in 6 goats. The presence of RVH was determined through observations of increased
right ventricular weight and thickness relative to a control group. Mean vector orientation shifted and variance diminished in the left sagittal and horizontal planes with right ventricular hypertrophy. No other pattern of electrocardiographic or vectorcardiographic alteration was observed during the development of RVH.
CHAPTER II

RIGHT VENTRICULAR FREE WALL EXCITATION IN THE GOAT WITH
EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY

Introduction

The process of ventricular excitation has long been a subject of experimental study. Before 1950, however, direct observations of ventricular excitation were made only through the use of epicardial, cavity and endocardial leads.

Sir Thomas Lewis (69) performed the first detailed studies of ventricular epicardial activation in 1915. As well as defining the general sequence of activation in the dog, he observed that the Purkinje system probably was responsible for distributing the wave of excitation at a high velocity to the myocardial cell. Subsequent studies by Lewis (68), Harris (56), Sodi-Pallares and Calder (93), Schaefer (82), Durrer (34), Redding (79), Hamlin (52), Kisch (64) and Crocker (23) have clarified the understanding of normal epicardial excitation in many of the large mammals. Barker (7) and Durrer (30, 31, 33) in studies of activity on normal human hearts reported findings similar to those reported in other mammals.

Beginning with studies in the late 1940's, several investigators employed intramurally-placed electrodes to record potentials from the ventricular myocardium in various mammalian species (49, 53),
and in man (103). Initial studies by Sodi-Pallares (91,92,93), Burchell (20), Kennämer (63), Scher (84,85,86,87,88) and Durrer (34,35,36,37) have provided the basis for understanding the time sequence of ventricular activation.

Ventricular excitation in ungulates is said to be different from that found in other animals due to extensive ramifications and full depth penetration of Purkinje tissue in the ventricular myocardium (54,55,79). Cardwell and Abramson (21), in 1928, were the first to show that histological differences between Purkinje fibers, in form and distribution, did exist when compared to dogs and man. Other investigators have confirmed these observations (2,43,71,79,81). That the penetration of Purkinje fibers has a functional significance concerning excitation has been well documented by Durrer and Van der Tweel (34), Redding (79), and Hamlin (52). The ventricular activation process in ungulates and dogs has been found to differ on the basis of electrocardiographic (6,52,61,90,97,96,100), vectorcardiographic (97,101), and on studies of directly recorded excitation processes within the heart (23,34,52,79). One main feature of differentiation from dogs and man is that epicardial potentials recorded from the lateral wall of the left ventricle have been of the qRs type indicating general endocardial to epicardial spread. In the goat varying types of complexes are found indicating activity which emanates from various sites within the myocardium. Bipolar plunge electrodes that indicate direction of wave form spread have substantiated these observations. In addition, vectorcardiographic comparison indicates that in the dog there are three major vectors, as contrasted to two in the ungulate.
Initial septal activation with activity predominantly ventrocephalic is seen in both dog and goat. The next vector in dogs is oriented leftward and ventrocaudal whereas in the ungulate the next and final front of activity is directed dorsad and cephalad. The terminal activity in the dog is toward the base of the heart in a dorso-cephalad direction.

Hamlin offers a possible explanation for the difference in the vectorcardiogram on the basis of ventricular activation studies in the goat (52). In both ungulates and dogs, initial vectors which represent activation of the apical third of the interventricular septum are oriented predominantly cranio-ventrad or ventrad. In dogs, middle vectors of ventricular excitation representing endocardial-epicardial activation of the dominant left ventricular free wall are oriented predominantly caudad. In ungulates, middle vectors of ventricular excitation are oriented dorsad and slightly cranial, because activation of both free walls occurs with a single burst and the apico-basilar activity of the middle third of the interventricular septum dominates. Finally, in both groups, terminal vectors are oriented dorsad and slightly cranial, and represent apico-basilar activation of the septum (in dogs and ungulates) and of the septum and free walls (in dogs).

The study of ventricular hypertrophy in the natural state as well as in experimentally induced states has provided much data concerning ventricular activation in dogs and man. The body surface electrocardiographic and vectorcardiographic alterations in various right and left ventricular manifestations of hypertrophy have been well
49

defined in man (10,32,38,66,72,73,78,89,94) and in dogs (15,16,22, 27,47,60,65), but not in ungulates. The sequence of excitation in hypertrophied myocardium is beginning to be explored in a systematic fashion; however, much conjecture still exists about the genesis of alterations in the QRS with ventricular hypertrophy.

The hypothesis that the electrocardiographic and vectorcardiographic alterations produced by RVH are determined by the ventricular activation sequence, the relationship between the cardiac generators, and body surface and boundary effects at tissue interfaces is widely accepted. The most important factor of these mentioned is the pattern of ventricular excitation which is related to variation in cardiac mass and in the distribution of Purkinje tissue and conduction pathways (11,44,83). Alfredson and Sykes (6) studied abnormalities in the bovine electrocardiogram after the production of bundle branch block and were the first to suggest that differences in the conduction system accounted for the differences in the peripheral electrocardiogram based on those changes seen in dogs. They observed that section of either of the main bundles produced two to three fold prolongation of the electrocardiogram in dogs, but that the QRS prolonged only slightly in the bovine with similar measures. Pruitt subsequently described findings in left and right bundle branch block to include alteration of the waveform paralleling closely those in canine hearts with bundle branch block and showed that the QRS lengthened 0.02 seconds in the bovine (76). In studies performed on goats with ischemia of the left ventricular free wall (51), Hamlin noted re-orientation of the major vectors caudad and dorsad as opposed to
their craniad and dorsad orientation in the control state. The peak magnitude of the QRS increased and the duration doubled. The epicardium in the ischemic zone depolarized tardily and unopposed whereas it was depolarized early in the control QRS.

That alterations in QRS during ischemia of the left ventricular free wall of goats could be attributed to uncancelled depolarization of the ischemic free wall may be analogous to the production of late and uncancelled activity of the left or right ventricular free wall in dogs with either bundle branch block or with hypertrophy.

Definite information about the developmental response of the Purkinje fiber in the hypertrophied myocardium is lacking in all animals. However, if ventricular hypertrophy is accompanied by equivalent penetration of Purkinje tissue to that observed in the normal myocardium, then any alterations in QRS produced in ungulates must stem from altered activation of the septum—since the free-wall activity would continue to be totally or near-totally cancelling. If Purkinje fibers fail to penetrate into the hypertrophied epicardium and subepicardium, then vectors should reorient in a direction as if penetrating the hypertrophied mass from endocardium to epicardium. Thus, with left ventricular hypertrophy in an ungulate, major vectors should reorient caudad and mimic those seen in normal carnivores. This has been demonstrated when left ventricular subepicardium becomes ischemic and activated tardily and unopposed (51). With RVH, orientation of vectors would shift slightly from the normal dorso-cephalic dextrad orientation to a ventrocephalic and dextrad direction due to the anatomic location of the hypertrophied RV free wall.
It is the intent of this study, by correlation of ventricular epicardial and intramural potentials with those of the peripheral electrocardiogram and vectorcardiogram, to delineate any alterations in the surface information caused by RVH. Further, it is the purpose of this study to gain insight regarding Purkinje tissue response in RVH.

Materials and Methods
Experimental Preparation

Six adult goats with experimentally induced RVH resulting from progressive constriction of the pulmonary artery and 4 healthy, normal goats ranging in size from 15.9 to 47.7 kg were pre-anesthetized with atropine sulfate (0.5 - 1.0 mg/kg) and were anesthetized with intravenous pentobarbital sodium dosed to maintain light surgical depth anesthesia. Positive pressure ventilation was provided by a to and fro cycling respirator\(^1\). The heart was exposed via a mid-sternal incision. The pericardium was incised and its free edges were sutured to the chest wall to cradle the heart. A bipolar surface electrode was sutured to the anterior wall of the left ventricle to serve as a fixed time reference. The reference electrode, being stationary on the surface of the left ventricle, was not influenced by positional changes of the heart within the thorax which occurred during the exploration of the right ventricular epicardial surface.

\(^1\)Harvard Apparatus Co., Inc., Dover, Massachusetts.
Electrocardiographic and Vectorcardiographic Methods

Corrected electrocardiograms were recorded and vectorcardiograms were constructed for all animals using the lead system developed for the dog by McFee and Parungao (70). With the experimental RVH group electrocardiograms were recorded and vectorcardiograms were constructed before surgery to enable utilization of data derived from the normal animals as a control record. Vectorcardiograms were compared statistically after termination of the experimental period. Complete details of methods are presented in Chapter I.

Recording Apparatus and Methods

Bipolar Epicardial Electrodes and Methods. The epicardial scanning electrode consisted of three bipolar surface electrodes attached to a strip of flexible polyethylene tubing\(^2\) (Fig. 13). These surface electrodes were placed at one centimeter intervals along the strip of tubing (Fig. 14). The electrode contacts were of silver and the intercontact distance was 1.5 mm. The assembly allowed scans of 2.5 cm width along the epicardial surface.

Recordings were obtained in the following manner. The surface electrode assembly was placed in position on the right ventricular epicardial surface. When baseline stabilization and potential fluctuations had ceased, the potentials were recorded on a 7-channel tape recorder\(^3\). The tape recording as well as the original record contained the following information: time reference, 3 epicardial bipolar points, and lead II electrocardiogram (Fig. 15).

\(^2\)Tygon tubing, Norton Plastics and Synthetics Div., Akron, Ohio.
\(^3\)Technical Measurement Corp., North Haven, Connecticut.
Figure 13

Epicardial bipolar electrode assembly for recording synchronous epicardial electrograms. Individual bipolar electrodes have been mounted on a segment of flexible polyethylene tubing.

Figure 14

Schematic representation of arrangement of bipolar electrode assembly and intercontact distances.
Epicardial Exploring Electrode
Record from an epicardial scanning site. Electrograms recorded from Goat 13 illustrating one time reference potential located on the surface of the left ventricle, three bipolar potentials (1, 2, 3) from the surface of the right ventricle at six different loci (sites 3, 4, 5, 6, 7, 8) and a lead II electrocardiogram. Note distribution of potentials with respect to the time reference and the lead II electrocardiogram. Most potentials were recorded during the initial portion of the electrocardiogram well before major vector forces were inscribed.
A map of the external surface of the heart was drawn. Exploration sites were recorded on the map as the recordings were completed over the entire surface of the right ventricular epicardium. The exploration sequence was designed to provide an orderly, reproducible coverage of the entire surface of the right ventricular epicardium. An effort was made to begin at the dorsal (caudal in man) interventricular sulcus and move toward the outflow tract of the right ventricle maintaining perpendicular planes to the base throughout. A second series of explorations were then recorded on the same plane but closer to the apex. The number of points obtained depended entirely on the size of the right ventricular epicardial surface. In some large hearts, 52 points were recorded; however, in the small hearts as few as 24 points were obtained. The entire right ventricular free wall was explored from apex to base and from the dorsal interventricular sulcus to the ventral (anterior in man) interventricular sulcus (Fig. 16).

Times of excitation were determined by the peak of the bipolar record related to the time reference record in msec. before (-) and after (+) the signal peak. The total epicardial activation process was then synthesized from the arrival times plotted on the original map. Instantaneous maps of the dipole layer distributions of the right ventricular epicardium were drawn for 3 msec intervals to relate to surface data. Total right ventricular epicardial activation time was calculated from the time of earliest and latest recorded activation, and instants of activation were superimposed on the lead II electrocardiogram.
Diagrammatic illustration of sequence of epicardial scan. An outline of the anterior surface of the heart was drawn. As the epicardial surface of the right ventricle was scanned, electrode sites were recorded (1 through 13). The arrangement of the bipolar electrodes are numbered 1, 2, 3 for the assembly.
R.V.

BIPOLAR POINTS ON POSTERIOR RIGHT VENTRICULAR EPICARDIUM
BIPOLAR POINTS ON ANTERIOR RIGHT VENTRICULAR EPICARDIUM
BIPOLAR TIME REFERENCE
**Multipolar Plunge Electrodes and Methods.** The multipolar plunge electrode\(^4\) (Fig. 17) used in this study is constructed of 18 insulated platinum conducting wires laminated around the core of conventional stainless steel hypodermic stock. The 1 mm x 0.07 mm electrical contacts, one for each wire were made at preselected points on the shaft by cutting through the insulation. Contacts are platinized, providing good sensitivity even at low frequencies. All conductor tips are insulated. Probe length was 2.5 cm with location of contacts on alternate wires enabling an intercontact distance of 0.6 mm (Fig. 18). A matching connector and cable (harness) with 36-inch #28 AWG insulated leads were connected to the recorder.

Plunge electrode specifications were as follows:

<table>
<thead>
<tr>
<th><strong>Electrical</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter-element impedance</td>
<td>10 megohms</td>
</tr>
<tr>
<td>Max. applied voltage</td>
<td>50 volt</td>
</tr>
<tr>
<td>Contact impedance</td>
<td>5 kilohms nominal</td>
</tr>
<tr>
<td>Contact capacitance</td>
<td>30 nanofarads nominal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mechanical</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact length</td>
<td>1 mm</td>
</tr>
<tr>
<td>Contact width</td>
<td>0.07 mm</td>
</tr>
<tr>
<td>Effective inter-contact distance</td>
<td></td>
</tr>
<tr>
<td>Connector</td>
<td>18 pin (IBM P/N 249-428)</td>
</tr>
<tr>
<td>Probe diameter</td>
<td>0.85 mm</td>
</tr>
<tr>
<td>Needle stock</td>
<td>#24 stainless steel</td>
</tr>
<tr>
<td>Conductor</td>
<td>#39 platinum-iridium (90-10%)</td>
</tr>
<tr>
<td>Conductor insulation</td>
<td>Formvar</td>
</tr>
</tbody>
</table>

The probe, connector and switching arrangement allowed only the recording of bipolar potentials between adjacent terminals. The polarity of the bipolar records was such that if the terminal closer

\(^4\) Multi-Contact Depth Probe, International Business Machines Corp., Rochester, Minn.
Figure 17

Multi-contact, plunge electrode showing connecting cable attached. The electrode consists of 18 insulated platinum wires laminated around a central core. The electrode contacts, one for each wire, were made at preselected points on the shaft. All conductor tips are insulated. Probe length on electrode shown was 2.5 cm with location of contacts on alternate wires. A matching connector cable (harness) with 36-inch #28AWG insulated leads was connected to the recorder.

Figure 18

Schematic representation of multi-contact plunge electrode with arrangement of contacts spiraling around central core shown and indicating intercontact distance.
Plunge Electrode
to the tip of the plunge electrode was electrically negative, a down­ward deflection was recorded when paired with the adjacent electrode. The deflections in a series of bipolar pairs, therefore, would indicate the direction of the spread of excitation. If, for example, the wave form was proceeding in an endocardial to epicardial manner with the tip of the probe in the endocardial layers, then a succession of downward deflections would be recorded.

One channel of the recorded displayed a constant time reference potential from a bipolar electrode located on the left ventricular epicardial surface. Four additional channels displayed myocardial potentials.

Exploration of the right ventricular free wall was accomplished in succeeding stages. Plunge electrodes--the number inserted varying with the accessibility to the preparation--were placed in the right ventricular free wall in three to four planes parallel to the base and perpendicular to the epicardial surface. The entire right ventricular free wall was thus explored from endocardium to epicardium and from apex to base by up to 18 individual plunge electrode insertions recording up to 150 points. The location of all insertions as well as the angle and the depth of the insertion was recorded to facilitate correlation of data. The electrode paths were easily determined on immediate postmortem examination of the right ventricular free wall and after fixing with 10% buffered formalin at the end of the experiment.

In many instances electrode insertion was followed by a long period of local injury potential. If injury had not abated within
20 minutes, the points were recorded routinely and eliminated from consideration during analysis. Potentials were selected following the criteria of Durrer (34) with regard to duration, speed of intrinsic deflection, amplitude and waveform. Potentials which were extremely low in amplitude, long in duration, slow in initial deflection, or were unipolar in appearance were discarded or were used in determining electrode position.

The time of arrival of the local potential was determined from the peak or nadir on the rapid spike of the bipolar record, as is suggested by Durrer. This peak was related to the fixed time reference in milliseconds. The total time scheme was then referred to the lead II electrocardiogram.

The total right ventricular activation process then was synthesized for each animal.

Recording Apparatus and Instrumentation. Outputs from the bipolar epicardial electrode assembly and time reference electrode were fed directly through shielded cabling to Sanborn Model 350-3200 A DC preamplifiers. The signals were fed into a 6-channel Mark 200 Brush oscillograph and a 7-channel tape system simultaneously with the lead II electrocardiogram.

Input switching for the multipolar plunge electrode was constructed in the laboratory to meet the requirements of the project. It consisted of an 8-pole, 4 position per pole, stacked wafer type switch, wired such that selection of 4 different sets of bipolar points, 8 different points, for each of the 4 positions was possible. Output coupling to the recorders was the same as for the bipolar epicardial assembly.
The information initially was recorded at 30 in/sec on the tape and at 100 mm/sec on the oscillograph. Later the same information was played back from the tape at 3-3/4 in/sec and recorded on the oscillograph resulting in an effective sweep speed of 800 mm/sec. Time measurements were taken off these expanded records.

The 6-channel Mark 200 oscillograph is a pressurized ink direct recorder with paper speeds from 0.05 mm/sec to 200 mm/sec. The 7-channel 1/2-inch tape drive and head system was a Model 02-30970-01 by Ampex. Tape speeds were 1-7/8, 3-3/4, 15, and 30 in/sec. The convertor units constructed by Technical Measurement Company, MNEMOTRON, were Model LC FM Data Convertors (Fig. 19).

Correlation of Data

Methods have been reported previously for correlating data obtained from peripheral electrocardiograms, vectorcardiograms, intramural and epicardial maps of ventricular excitation (11,13,57,65). That epicardial surface maps may contain information about ventricular excitation not contained in routine electrocardiograms or vectorcardiograms has been determined by Taccardi (98), Boineau (11,14), and Spach (95).

The sequence of ventricular activation was related to the electrocardiogram and vectorcardiogram in the following manner: (1) the range of local activation times of epicardial and intramural sites were recorded with respect to the time reference potential. Range of activity was then related diagrammatically to the lead II electrocardiogram. (2) Isochronous time-distance periods were determined for the epicardial surface information
Figure 19

Schematic representation of preparation, recording apparatus, and switching design.
External ECG

Time Reference Electrode

Plunge Electrode

Switch Box

Sanborn Model 350-3200A Pre-Amps

Brush Mark 200 Recorder

Ampex 7 Channel Tape Drive

Mнемotron Model LC Converter Unit
and were related to associated time intervals in the vectorcardiogram as significant periods in electrogenesis. The isochronous maps were constructed to conform to certain chosen periods in the sequence of excitation, their order corresponding to the instantaneous distribution and geometric balance of dipole layers. The areas between the outer and inner boundaries represent the general direction of wavefront spread, its relative speed, as well as the relative mass of myocardium depolarized during a given interval.

**Results**

**Electrocardiograms and Vectorcardiograms**

Electrocardiograms were recorded and vectorcardiograms were constructed prior to surgery and at varying periods during production of RVH. Vectorcardiograms were statistically compared before and after development of RVH. Results observed previously in Chapter I are summarized; the mean maximum QRS vector in the left sagittal plane reoriented 11 degrees in a dorso-caudal direction. In the horizontal plane the mean maximum QRS vector shifted leftward and dorsad approximately 46 degrees from \(-143^\circ\) to \(96.8^\circ\). The change in mean frontal plane vector distribution was not significant statistically. The mean amplitude of the maximum QRS vectors for all vector planes was not significantly altered. No statistically significant changes were observed in the P-R interval or in QRS duration. The mean Q-T interval was shortened significantly from a mean value of 0.334 sec to 0.292 for the RVH group. No reliable electrocardiographic index for the separation of the RVH group from normal animals was established.
Ventricular Excitation

The Normal Goat - Epicardial. Figure 20 illustrates the epicardial sequence map, the lead II electrocardiogram, and left sagittal vectorcardiogram of a normal goat. The ventral aspect of the goat's heart is viewed in the figure with slight diagrammatic alteration present to represent the lateral dorsal aspect in one view. The ventral interventricular sulcus is indicated as the line separating the right ventricle from the left ventricle. The dorsal interventricular sulcus is indicated by the margin of the right ventricular diagram. The time for right ventricular epicardial excitation is indicated in the graph below. The time to earliest epicardial activity ranged from 1.37 to 7.50 msec when related to the onset of activity in the lead II electrocardiogram (Table 6). The time to epicardial breakthrough in this animal was 7.50 msec after the onset of the electrocardiogram and vectorcardiogram. The pattern of epicardial spread was essentially the same in all normal goats studied. The earliest site of epicardial activity was observed in the midright ventricle near the base of the right ventral papillary muscle and close to the ventral interventricular sulcus. The activity spread in essentially a radial manner toward the outflow tract of the right ventricle (conus) and the dorsal interventricular sulcus (3-12 msec). Occasionally spread appeared tangential with excitation of apicobasilar areas occurring simultaneously. Late activation (12-15 msec) of the right ventricle was associated with areas in the basilar portions of the dorsal interventricular sulcus and pulmonary conus regions. Total right ventricular activation time in the normal group varied.
Figure 20

Schematic representation of right ventricular epicardial activation in a normal goat (Goat 15) and time relation to electrocardiographic and vectorcardiographic events. The general sequence of right ventricular epicardial activation is indicated below and the associated activation periods of 3 msec each are indicated by the accompanying graph. The lead II ECG and the left sagittal vectorcardiogram are presented for time correlation with the epicardial data. Note that the VCG loop tends to lie in a dorsally oriented manner with initial forces directed slightly ventral and caudal and with resultant major forces directed dorsad and slightly cranial. Epicardial breakthrough, at 7.5 msec after onset of lead II electrocardiogram and left sagittal vectorcardiogram, occurred initially in the midright ventricular free wall overlying the base of the right ventral papillary muscle and free wall ramifications of the right bundle branch. In subsequent time intervals, 3-6 msec, 6-9 msec, and 9-12 msec, activation may be seen generally spreading in radial fashion although tangential components are evident in regards to apicobasilar spread. Late activation was confined to the basilar portions of the dorsal left ventricular sulcus and over the outflow tract of the right ventricle. Epicardial activity terminated at 22.5 msec after initial activity in the electrocardiogram and vectorcardiogram began.
### TABLE 6

EPICARDIAL ACTIVATION DURATION IN 4 NORMAL GOATS AND 6 GOATS WITH EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY

<table>
<thead>
<tr>
<th></th>
<th>QRS (msec)</th>
<th>Right Ventricular Free Wall (msec)</th>
<th>Initial Activity (msec)</th>
<th>Terminal Activity (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CONTROL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>41.52</td>
<td>15.00</td>
<td>5.00</td>
<td>20.00</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4.05</td>
<td>2.00</td>
<td>1.37</td>
<td>2.77</td>
</tr>
<tr>
<td>Maximum</td>
<td>48.50</td>
<td>16.88</td>
<td>7.50</td>
<td>23.75</td>
</tr>
<tr>
<td>Minimum</td>
<td>36.25</td>
<td>11.25</td>
<td>3.75</td>
<td>15.62</td>
</tr>
<tr>
<td><strong>EXPERIMENTAL RVH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>45.31</td>
<td>16.25</td>
<td>5.34</td>
<td>21.59</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>3.68</td>
<td>1.90</td>
<td>2.17</td>
<td>1.05</td>
</tr>
<tr>
<td>Maximum</td>
<td>50.00</td>
<td>18.25</td>
<td>7.63</td>
<td>22.50</td>
</tr>
<tr>
<td>Minimum</td>
<td>41.25</td>
<td>14.38</td>
<td>2.50</td>
<td>20.62</td>
</tr>
<tr>
<td>(P)</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

n.s. = not significant
only slightly from animal to animal, 11.25 - 16.88 msec. In this goat activity terminated 22.5 msec after initial electrocardiographic and vectorcardiographic activity began, indicating a total duration of 15 msec for completion of epicardial excitation. The relative time zones of epicardial activity are displayed on the constructed vectorcardiogram. The sequence of epicardial excitation was very similar in all normal goats surveyed. In addition, the duration of the QRS was within normal limits for all goats (36 to 48 msec) as was vector loop orientation and configuration.

The Normal Goat - Intramural. That the electrograms from intramural recordings from goats have characteristics different from those obtained in dogs have been reported by Durrer (34) and Hamlin (52). This investigation observed similar differences regarding the lower potential amplitude, longer potential duration, and prolonged current of injury seen in goats. The electrograms recorded from within the myocardium did, however, display more rapid potential changes from those recorded within the right ventricular cavity (Fig. 21) and were easily separated from them for purposes of identification. The bipolar points located beyond the surface of the myocardium were affected by moisture or approximation of tissue and did register slight potential variations during recording. These potential variations were easily distinguished from the potentials arising from within the myocardium (Fig. 22). Pronounced prolongation of the electrogram, lower potential amplitude, and absence of a rapid deflection were evidence of extramural location of points.
Figure 21

Intramural and cavity potentials recorded from a normal control goat (Goat 14). Electrograms from bipolar recordings are arranged in sequence as recorded with the time reference channel at the top. Cavity potentials are noted near the tip of the plunge electrode assembly occurring in recordings from bipolar pairs 1-2, 2-3, 3-4, 4-5, 5-6, 6-7, 7-8, 8-9, 9-10, and 10-11. Bipolar pairs 11-12, 12-13, 13-14 and 14-15 illustrate the registration of electrograms from the right ventricular myocardium.
GOAT 14
TRANSMURAL POTENTIALS
PLUNGE - 5
Intramural potentials recorded from a normal control goat (Goat 13). Bipolar electrode pairs 1-2, 2-3, 3-4, 4-5, 5-6 and 6-7 illustrate electrograms recorded from the right ventricular myocardium. Note the frequent reversal in polarity of the recordings. Electrode pairs 7-8 to 16-17 illustrate slight variations in potential noted when electrodes were extramural in location.
GOAT 13
TRANS MURAL POTENTIALS
PLUNGE - 5

TIME REFERENCE

BIPOLAR ELECTRODE PAIR
Figure 23 illustrates the transmural sequence of right ventricular excitation in a normal goat. The tracts of 12 insertions within the free wall are shown.

An attempt was made to construct the time order depolarization of the right ventricular free wall in normal goats and in those with experimentally induced RVH. Patterns of activity within the myocardium of the right ventricular free wall are complex. Frequent reversals in direction of approaching wavefronts were recorded on most individual insertions. Large variations existed in arrival times at subjacent bipolar pairs as well on individual insertions negating attempts to accurately calculate conduction velocity from endocardial to epicardial sites. Right ventricular free wall depolarization does not appear to be initiated in the endocardial or subendocardial layers in a consistent manner. In many plunges the earliest activated points were at or near the epicardial surface (see plunge 5). In fact, because of the wide variation in direction of wavefront spread and because of the time differences in sequential points, it appears as though the right ventricular free wall is excited from many different focal areas within the myocardium, as was proposed by Redding (79) and later corroborated by Hamlin (52).

Earliest electrical activity was noted in the middle portion of the right ventricular free wall near or at the base of the right anterior papillary muscle where the moderator band enters, as is indicated in Figure 23. Early activity was not confined to this area as certain sites near the septum occasionally were seen to be activated
Figure 23

Schematic representation of an intramural plunge scan of the right ventricular free wall of a normal goat (Goat 15). The values indicated along the shaft of the needle indicate the time of activation (in milliseconds) of that particular point either before (-) or after (+) the activation of the time reference site located on the surface of the left ventricle. The right ventricular free wall is viewed as though it had been removed from the rest of the heart and had been laid flat.
simultaneously with activity in the mid-ventricular regions or slightly after (plunges 8, 9).

At 1.9 msec there are several points showing activity, many of them near the epicardial surface. As the points of electrode insertion migrate from the mid-portions of the right ventricular free wall, later and later activity is shown. Note that the latest recorded points in some of these plunges correspond to areas located near the endocardium (plunges 7, 8, 11). In certain plunges activity seems to arrive at the endocardial and epicardial layers simultaneously (plunge 4) or nearly so (plunge 12). Latest recorded activity was recorded from plunges associated with the basilar region (plunge 7) of the dorsal interventricular sulcus (plunge 3) and from plunges in the myocardium of the pulmonary outflow tract (plunges 11, 12). Although certain plunges indicated wavefront spread from endocardium to epicardium (plunges 2, 3), other sites indicated activity first at epicardial points progressing in time to latest activity nearer the endocardium (plunges 5, 8, 11).

Mean intramural activation time of the right ventricular free wall for the control group was 20.31 msec, whereas mean initial activity began 4.06 msec., after the initial deflection of the peripheral electrocardiogram (Table 7).

The Goat with RVH - Epicardial. Figure 24 illustrates the map of epicardial excitation, the lead II electrocardiogram, and left sagittal vectorcardiogram of a goat with experimentally induced RVH. The epicardial view is the same as depicted in Figure 20. The earliest site of epicardial excitation was observed in the mid-right
# TABLE 7

## INTRAMURAL ACTIVATION DURATION IN 4 NORMAL GOATS AND 6 GOATS WITH EXPERIMENTAL RIGHT VENTRICULAR HYPERTROPHY

<table>
<thead>
<tr>
<th></th>
<th>QRS (msec)</th>
<th>Right Ventricular Free Wall (msec)</th>
<th>Initial Activity (msec)</th>
<th>Terminal Activity (msec)</th>
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</thead>
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<tr>
<td><strong>CONTROL</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>20.31</td>
<td>4.06</td>
<td>24.38</td>
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<tr>
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<td>3.29</td>
<td>4.81</td>
</tr>
<tr>
<td>Maximum</td>
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<td>8.75</td>
<td>29.38</td>
</tr>
<tr>
<td>Minimum</td>
<td>41.25</td>
<td>16.88</td>
<td>1.25</td>
<td>19.38</td>
</tr>
<tr>
<td><strong>EXPERIMENTAL RVH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>41.52</td>
<td>20.73</td>
<td>3.65</td>
<td>24.38</td>
</tr>
<tr>
<td>Standard Deviation</td>
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<td>5.44</td>
<td>3.94</td>
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<tr>
<td>Maximum</td>
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<td>29.38</td>
<td>11.25</td>
<td>31.25</td>
</tr>
<tr>
<td>Minimum</td>
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<td>13.13</td>
<td>0.63</td>
<td>17.50</td>
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<tr>
<td>P</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

n.s. = not significant
Figure 24

Schematic representation of right ventricular epicardial activation in a goat with RVH (Goat 13) and time relation to electrocardiographic and vectorcardiographic events. The sequence of epicardial depolarization is shown for several instants of activity covering the epicardial surface of the right ventricle. The earliest point of epicardial activity occurred in the mid-right ventricle at 4.5 msec after the beginning of the lead II electrocardiogram and left sagittal vectorcardiogram. Note the similarity of sequential spread across the surface of the right ventricle in Goat 13 to that observed in Goat 15. The time relationships and duration of activation of this goat which is representative of the RVH group is not unlike those observed in normal goats. Values shown are in milliseconds.
GOAT 13
ventricle in essentially the same area that early activity was noted in the normal goat. A slight difference exists in the extent of area involved during the first 3 msec of activity when compared to Goat 15. However, no qualitative differences existed in the two groups when data from all animals was compared. Early activity existed that extended to the ventral left ventricular sulcus in the RVH group as well as in the normal group. Small areas of early activity in the normal group were noted resembling the epicardial map of Goat 15 as well. One goat with RVH had two separate foci of early activity which were separated by a zone of relatively later activity (3-6 msec). This was the only observation of this phenomena in the RVH group which showed nearly identical sites of early activity. Subsequent activity spread in a manner not unlike that seen in the normal group covering essentially similar time intervals and general distribution. In Goat 13 with RVH, early epicardial breakthrough can be seen commencing within 4.5 msec of initial electrocardiographic and vectorcardiographic activity. Total activity lasted approximately 16.5 msec, with termination of activity occurring 21.0 msec after peripheral activity commenced. The occupation of time distribution of the epicardial surface data within the vectorcardiogram is more pronounced than in the normal goat (Fig. 20). This probably is due to the different configurations of the left sagittal vector loops in the two animals since it is observed that activity is over well before the major vector forces are inscribed. Terminal activity is relegated to two zones as seen in the normal animals: the basilar zone of the dorsal left ventricular sulcus and the pulmonary outflow tract. Total
time for right ventricular epicardial excitation was not significantly different than that observed in the normal group (Table 6). The QRS duration and times to initial and terminal activity were not significantly different on statistical comparison.

The Goat with RVH - Intramural. An illustration of the intramural activity seen in a goat with RVH is seen in Figure 25. This illustration represents the actual arrival times of activity at numerous points within the right ventricular free wall. In comparison with the number of points recorded of the control right ventricular free wall, many more recording sites along the shaft are observed. This is due to the increased thickness of the wall--50% in some animals. Activity was first recorded near the epicardium in plunge 2 at 8.8 msec, before the time reference peak. The location of this plunge is in the mid-right ventricle near the base of the ventral papillary muscle. At a point near the endocardial layers activity was registered at 8.1 msec, which indicates that both endocardial and epicardial layers were activated nearly simultaneously. Relative early activity is seen in plunges 6 and 11 in the epicardial layers (6-9 msec) in plunge 7 and 12 at the endocardial level, in plunges 3 and 4 near the epicardium.

Later activity is recorded from plunges distributed away from the mid-ventricular region. Note, however, the relatively late activity recorded by plunge 3 in the endocardial and subendocardial layers. Latest activity was recorded at the epicardially placed electrode in plunge 1 in the region of the pulmonary outflow tract. However, late activity also was seen in plunge 4 at the endocardial layers and in
Figure 25

Schematic representation of an intramural plunge scan of the right ventricular free wall of a goat with RVH (Goat 13). The times of activation (in milliseconds) along the shaft of the electrode are shown for each insertion. Arrival times shown are related before (-) or after (+) the activation of a left ventricular epicardial site selected as a fixed time reference. Note that early sites of activation are located in the mid-right ventricle and that relatively late arrival times are located near the base of the left aspect of the diagram, corresponding anatomically to the dorsal interventricular sulcus, and over the pulmonary outflow tract. The time relationships and duration of activation of this goat, which is representative of the RVH group, is not unlike those observed in the normal goats.
the epicardial layer as well. Plunge 10 indicates late activity occurring in the basilar region of the dorsal interventricular sulcus. Mean recorded right ventricular free wall activation time was 20.73 msec (Table 7). Initial activity began 3.65 msec after the initial deflection of the peripheral electrocardiogram. No statistically significant alterations were observed in time to initial activity nor in total activation time.

Discussion

Limitations

In assessing the significance of data derived from recording potentials directly from and in the right ventricular free wall, much would have been gained from potentials recorded from the interventricular septum and the left ventricular myocardium and epicardium. This was impossible due to the inability to position electrodes of the size available to the investigator in the time available before deterioration of the preparation occurred. It must be realized that this deterioration was significant due to the intrinsic state of the right ventricular myocardium in the hypertrophied and severely stressed state. Rotation, elevation, or displacement of the heart from its normal relationship within the prepared cradle of a magnitude necessary to approach the left ventricle and septum met with either abnormal rhythms or decline in ventricular performance of a significant nature requiring immediate return of the heart to its normal position. It was necessary to synthesize the right ventricular activation process independent of the other ventricular tissue. Excellent coverage of the right ventricle was obtained.
Comparison of Normal Data with Data from Previous Investigations of Ruminant Ventricular Activation

Intramural activation of the right ventricle in this series of normal goats parallels closely the mode of ventricular activation in goats described by Durrer (34) and Hamlin (52). Redding (79), in sheep, and Crocker (23), in later studies of the bovine heart, found the general type of ventricular excitation in these species to be identical with that seen in the goat. All investigators agreed that the observation of Meyling and Ter Borg (71) concerning the full depth of myocardial wall penetration by the Purkinje was functionally significant by showing that the ventricular myocardial wall is activated from numerous Purkinje fiber terminations depolarizing myocardial tissue at numerous sites throughout the myocardium in a nearly simultaneous manner.

Normal Right Ventricle - Epicardial. Redding (79) in a detailed analysis of epicardial activation in ruminants made certain interesting observations on the time order of excitation. In relating epicardial activation of the left ventricle to the V10 electrocardiogram, he noted that the apex and free wall were excited synchronously with the nadir of the Q wave. The anterior wall was activated by 10 msec followed by the posterior wall in 15 msec. The base of the anterior and posterior walls were activated last on an average of 25 msec from time zero. The results obtained from activation of the right ventricular free wall in the goat agree qualitatively with these observations in sheep of the left ventricle. The observation that in the right ventricle of goats the earliest activated site is present in
the mid-right ventricle and that similar early activity occurs near the apically oriented septal areas is consistent with Redding's observation of initial early activity near the arborization of the left bundle branch in the wall of the left ventricle. In general, activity in the right ventricle of goats spreads laterally with mid-portions of the basilar epicardium being activated relatively early when compared to late activity near the basilar portions of the dorsal interventricular sulcus and regions overlying the pulmonary outflow tract. The early occurrence of excitation of the mid-portion of the right ventricular free wall may be attributed to the presence of numerous Purkinje fibers in that area which cross the ventricular cavity via the moderator band as the main right bundle branch.

Quantitative differences exist regarding the duration of activation of the epicardial surfaces of the left and right ventricles. The mean time to completion of epicardial activation of the right ventricle of the goat was 15 msec. Redding noted activity being completed at approximately 25 msec in the basilar areas of the left ventricle. Epicardial activation of the right ventricular base is not as late as indicated by Redding for the left ventricle of sheep with most terminal activity occurring within 5 msec after activation of the majority of the right ventricle. Hamlin (52), however, in an intramural analysis of activation, disagreed with Redding regarding late activity and stated that activity was finished 10 msec earlier than Redding described; thus concluding the ventricular base is excited before the major electrocardiographic deflections in the peripheral electrocardiogram occur. His results indicate that
termination of right ventricular and left ventricular basilar portions occur nearly simultaneously.

Figure 20 represents the relationship of epicardial activity to the electrocardiogram and left sagittal vectorcardiogram. It will be noted that right ventricular epicardial activity begins 7.5 msec after the initial deflection of the electrocardiogram and lasts 15 msec, terminating 22.5 msec after peripheral activity began. This occupies a relative time zone on the left sagittal electrocardiogram encompassing 15 msec and appears to be related to early vector forces. The major vector forces were inscribed much later at 35 msec. This 15 msec period of right ventricular epicardial activity represents a somewhat diphasic period in the lead II electrocardiogram, with early positivity manifesting itself as a caudally directed vector force with the negative phase related to activity receding from it and resulting in dorsally oriented vectors. The result that epicardial activity terminates before the inscription of major vector forces confirms the observation of others that the major portion of ventricular free wall activity is over before the inscription of the R wave of V10.

Normal Right Ventricle - Intramural. Durrer (34) and Hamlin (52) both found that the bipolar potentials recorded from the myocardium of goats were different than those seen in dogs. Reference was made to the longer duration of current of injury and longer duration and lower magnitude of potentials in goats when compared to dogs, and similar results in this study have confirmed these observations.
That the sequence of activation within the myocardial wall is complex is seen in Figures 23 and 25 in representations of the individual plunge data. There is a general sequence of ventricular activity with general time distributions being evident in various portions of the right ventricular free wall. Earliest points of activity are noted in the mid-right ventricle being representative of the right bundle branch arborizations in this region. Adjacent areas of myocardium are subsequently activated in an ill-defined manner with excitation times being widely varied and with polarity reversals common throughout the tract of an individual electrode plunge. In the basilar portion of the dorsal interventricular sulcus and in the myocardium of the pulmonary outflow tract tardy activation can be seen lasting for a variable period of time.

The observation that potentials in the basilar zones were not different in general sequence of activity or time distribution from the other plunge areas (Figs. 23 and 25) is contrasted to Redding's observation of a time differential of approximately 15 to 20 msec between the endocardium and epicardium in the basilar zones, with the endocardium being activated first. In over 150 plunges this investigator could not obtain such wide differences in arrival times of the right ventricular basilar regions or in any region of the right ventricular wall. Although there is reported a lack of conduction tissue in these regions (79), no consistent observation of spread in a sequential manner from endocardium to epicardium, as seen in dogs, was forthcoming in this series of goats. The apparent disparity in observations
may be due to differences in experimental methods, in interpretation of regions explored, or in species studied.

However, observations in this study of intramural recordings from the right ventricular free wall in goats confirms the conclusion of others that the entire mass of the free wall is activated from multiple foci located throughout the ventricular wall and that it occurs in such a manner that the potentials generated are self-cancelling resulting in no major vector manifestation (1).

**Hypertrophied Right Ventricle - Epicardial and Intramural.** In the 6 goats which developed pronounced RVH, epicardial and intramural activation times closely paralleled times recorded for the control group. As indicated by Figures 24 and 25, the sequence of excitation and relative rates of spread in both epicardial and intramural studies are indistinguishable from the control group. These observations are different in certain ways from observations on dogs and man with RVH. Hill (57,59) found in dogs that total right ventricular epicardial activation time was slightly prolonged (10 msec) in some dogs with hypertrophy but that prolongation was not related to the degree of hypertrophy. In dogs with RVH, epicardial excitation was shifted in time within the QRS complex so that 39% of the sites were activated during the last third of the QRS complex whereas in his control group only 1% of the sites were activated during this time. The QRS electrocardiographic changes noted in the dog were due both to prolongation of epicardial activation time and to a shift in timing of activation within the QRS. Boineau, in studies of RVH performed on dogs with surgically produced atrial septal defects (12) and
congenital lesions (10), has indicated prolonged epicardial and intramural activity due to increased right ventricular mass and has described terminal QRS alterations as a result of the tardy activity. Brusca (17) found that activation times of the right ventricle in humans with RVH were prolonged, as did Durrer. Durrer (31, 36) found delays of epicardial activation up to 25 msec in people with RVH. In addition, he noted that the sequence of activation was not changed appreciably in pulmonary hypertension resulting from a ventricular septal defect or in pulmonic stenosis. He felt that the delay in activation was due to an increase in thickness of the right ventricular wall because no delay in Purkinje excitation was found with intramural studies nor was conduction velocity of the excitation wave affected in the hypertrophied myocardium. It, therefore, would seem likely that alterations in the electrocardiogram and vectorcardiogram in dogs and man stems from prolongation of right ventricular activation time due to increased mass, and from shifts in timing of right ventricular activation within the QRS. It does not appear that conduction velocity in hypertrophied myocardium is appreciably affected in dogs or in man (31, 36), although there is a report to the contrary (67).

The results of right ventricular excitation studies in goats with RVH have shown a remarkable stability in arrival times and sequence. That initial activity and activity at succeeding time intervals closely approximate that in the control group and that terminal activity was not changed appreciably in relative sequence or location is contrasted to results obtained in dog and man. The shift in location of the right ventricular activation sequence relative
to the QRS seen in dogs was not observed in goats nor was prolonged activation of the basilar regions and pulmonary outflow tract observed.

It seems evident that not only is the general ventricular activation process different in goats but that the electrocardiographic response to RVH as manifest in man and dogs is dissimilar as well. In man and dogs the major portion of the Purkinje network is located in the subendocardial layers with little or no evident penetration to the epicardium (2,43). The subendocardial layers are activated initially and the activation of outer layers of the free walls are accomplished by myocardial fiber to myocardial fiber spread in an endocardial to epicardial direction. When an increased muscular mass is superimposed on the initial mass, the longer it takes the mass to depolarize because of the relatively slow myocardial conduction velocity (30 cm/sec) (3). Thus, the longer it takes peripheral epicardial and intramural sites to be activated relative to the normal duration. (The Purkinje system which penetrates to the epicardial surface in ruminants (2,21,24,43,71,81) may explain the observed differences in conduction with hypertrophy.) In goats it is assumed that conduction velocity of Purkinje fibers remains constant (2.0 m/sec) (29) with hypertrophy and that the Purkinje fiber to myocardial fiber distribution throughout the wall remains the same. With these factors remaining constant, no appreciable change in sequence of activation nor in arrival times at the epicardial surface is seen even though pronounced hypertrophy exists.

That there is statistically significant reorientation of major vector forces in the sagittal and horizontal planes resulting from the
production of RVH is noteworthy. As initially hypothesized, if major vector forces do reorient themselves in a manner similar to that seen in dogs and man, then it may be assumed that any vector changes result from altered activation of the free walls of the ventricles with altered septal depolarization. Because no alteration in the sequence of activation or in activation times were noted in the hypertrophied right ventricular free wall, it is probable from consolidation and reorientation of vector forces that changes in vector forces are due to altered septal activation.

**Summary**

Epicardial and intramural excitation patterns were studied in 6 normal goats and in 6 goats with experimentally induced RVH produced by progressive pulmonary artery constriction.

Basic differences exist regarding the electrocardiographic response to RVH in dogs and man when compared to goats with RVH. Instead of redistribution of ventricular potentials relative to the peripheral QRS and late activation of regions such as the ventricular base and pulmonary outflow tract, goats manifest no alteration of arrival time relative to the QRS nor any tardy activation in the basilar regions. Concomitantly no significant alterations were noted in the peripheral electrocardiogram although slight reorientation of sagittal and horizontal vector forces may be attributed to the generation of tardy septal forces not directly observed in this study.

That the Purkinje distribution in the goat with RVH maintains the same basic relationship seen in the normal animal is inferred
because no sequential or time related activation changes were observed in epicardial and intramural studies.
BIBLIOGRAPHY


